The Future of Pharmaceutical Innovation
Tackling the R&D Productivity Gap
Performance indicators reveal the most significant challenge for pharmaceutical R&D is the productivity decline. The industry is developing fewer new molecular entities (NMEs), and the cost for each is increasing. Blockbuster drugs, once the industry’s historical success recipe, are more difficult to identify and face significant reimbursement challenges. Leading companies are more reliant on external molecules from smaller biotechs as sources of new products. The industry is exploring targeted therapies and patient sub-segmentation to support predictive efficacy, better attrition rates and potentially attractive pricing.

The lack of R&D productivity is not new. The industry has focused on closing the innovation gap for more than two decades through business and operating model shifts and restructuring initiatives. Companies have looked to silver bullet technologies such as the “omics,” process re-engineering, Six Sigma initiatives, adaptive trials and more. While these approaches have had a positive impact, spot measures, narrowly focused initiatives and incremental changes have not led to significant or sustained R&D productivity improvements.

No one solution can bridge the R&D productivity gap. The future of pharmaceutical innovation demands a holistic approach that addresses every R&D dimension—strategy, process and organization, and funding. High performers will be those companies that go against the grain and take comprehensive actions to improve pharmaceutical R&D returns, both immediately and over time, to gain the competitive edge in a challenging and changing market.

The Innovation Challenge

Pharmaceutical innovation is facing a troubled and uncertain future. Critical performance metrics highlight the extent of the challenge.¹

- **Blockbusters** - Blockbusters are increasingly rare, and most major pharmaceutical companies are facing substantial patent expirations.

- **New Molecular Entities (NMEs)** - The number of NMEs has been steadily declining over the past 15 years with no change in the downward trend expected.

- **Costs** - Industry data reveal that it cost approximately $800 million to develop a new NME in 1999. Estimates now range from $1.5 billion to $3 billion.

- **Drug Attrition** - Drug attrition has remained flat at approximately 85 percent across all phases, despite numerous initiatives and technologies designed to improve it.

- **Externalization** - Over the past decade, 60 percent of innovator small molecules and 82 percent of innovator biologics have their roots outside of big pharmaceutical companies.
Since pharmaceutical R&D productivity became a critical strategic challenge for the industry, many companies have implemented targeted improvement initiatives to accelerate change. For example, GlaxoSmithKline uses a model where biotech partners do an increasing share of research. Sanofi is aggressively externalizing R&D and making large acquisitions of biotech companies, e.g., Genzyme.

Most of these programs have been effective in isolation, but they have not had a sustained impact because they have not swiftly accommodated changing external influences. Reinventing pharmaceutical innovation means making significant changes in each area of a holistic framework that includes strategy and intellectual property (IP), process and organization, and funding sources (see figure 1).

This paper is not designed to solve all pharmaceutical R&D productivity challenges. The best brains in the industry are working on these issues on a daily basis. However, an exploration of the framework—both in terms of the current state and opportunities to improve the future state—lays the groundwork for developing the holistic solutions that could move the needle on the future of pharmaceutical innovation.
Strategy and Intellectual Property

Strategy and intellectual property include a company’s disease area focus, clinical targets, modalities and related IP. In terms of disease area focus, there are at least three major issues where the industry must rethink its current portfolio strategies.

The Current State

When comparing the pipelines of major pharmaceutical companies, it is evident that most are trying to cover all major disease areas, which can sometimes include as many as 40 to 50 distinctly different areas. While this approach may have worked five to 10 years ago, disease areas today are becoming increasingly competitive. Further, with biologically relevant targets requiring increasing expertise and hurdles for efficacy and safety, this strategy will not lead to first-in-class or best-in-class assets in targeted disease areas, which is essential for commercial success.

Another common problem is that many companies are pursuing the same disease areas, which is not sustainable in today’s payer climate. Consider the example of oncology, an area where almost every major biotech and pharmaceutical company is investing a double-digit proportion of its R&D budget. Oncology is clearly a rapidly growing disease area. Yet as cost containment pressures escalate and pipelines crowd, oncology will likely only be truly attractive to a few major pharmaceutical companies with established positions and existing advantages.

Beyond crowded disease areas, the pursuit of the blockbuster is increasingly challenging. With a few notable exceptions, such as anemia, cancer and rheumatoid arthritis, blockbusters have typically been developed in large primary care dominated disease areas, such as lipid control, hypertension, diabetes and gastroesophageal reflux disease.

In each of these areas, the development of a blockbuster is becoming increasingly complex. For one, it is difficult to develop a superior product in an area where a previous highly efficacious blockbuster went off patent. There is also increased payer pressure on frequently prescribed drugs and ever-increasing Food and Drug Administration safety hurdles for chronic drug therapies. In addition, the issue of the cost of the commercial infrastructure required to successfully commercialize these products comes into play.

Opportunities for Future Value

From blockbusters to very broad discovery and early development portfolios covering every disease area, the portfolio strategies that historically drove the pharmaceutical industry’s success can no longer drive growth and profitability. The future of pharmaceutical innovation requires more focused strategies, less emphasis on overly competitive areas, and flexible business models that drive outcomes in new ways. Leading companies should consider taking the following actions:

Focus the portfolio. Develop more focused portfolio strategies that target only those disease areas with the likelihood of successfully developing first-in-class or best-in-class assets or addressing unmet needs with meaningful health economic impact for payers. Examples include neurological disorders such as Alzheimer’s disease and Parkinson’s disease.

Lead with strengths. Conduct a realistic assessment of the core strengths of the organization. Assess clinical and scientific development, commercial call points, patient advocacy and brand reputation. Have the courage to go against the mainstream and exit highly competitive areas or areas pursued mainly for historical reasons.

Bury the blockbusters. Realize that blockbusters are becoming increasingly rare and costly to commercialize. Adapt the portfolio strategy to include a large proportion of commercially attractive specialty care assets with relevance in multiple disease areas and indications.

Pursue targeted therapies. Targeted therapies and ensuing patient sub-segmentation leads to potentially lower approachable patient numbers. However, they should be part of the portfolio because they present an opportunity to capture attractive pricing and efficacy prediction as a differentiator compared to therapeutic assets.
Process and Organization

Process and organization includes R&D processes, both internal and external, and the organizational structure and reporting that is in place to manage innovation.

The Current State

With one or two exceptions, the fully integrated pharmaceutical company (FIPCO) model is still prevalent across the industry today, and is a significant obstacle to improving pharmaceutical R&D productivity. Successful outsourcing deals like the one completed by Lilly and Sanofi with Covance reflect the industry’s realization of the difficulty keeping all R&D disciplines in house while remaining competitive in terms of cost, quality and speed to market.

However, as other maturing and R&D focused industries such as telecommunications, software and automotive demonstrate, fully integrated organizations not only lead to significant inefficiencies and lack of innovation, they are extremely complex to manage and lack the agility to respond to change. The FIPCO model also does not inherently foster innovation and entrepreneurship and tends to favor “wait and see” and incremental approaches to innovation.

The challenge of the FIPCO model suggests that the more complex and multidimensional today’s R&D organizations become, the more barriers they create to innovation. It is not uncommon for pharmaceutical R&D organizations to have three to four reporting dimensions, which include function, therapeutic area, project and modality.

Complexity becomes the enemy of progress. Multidimensional reporting structures invariably lead to a lack of accountability, focus and an inability to make rapid course corrections. A clinical research organization (CRO) focusing on select disciplines within research and development is more likely to gain scale advantages and, in the long run, outperform its customers in terms of relevant performance metrics.

Opportunities for Future Value

Based on our research and experience working with R&D productivity issues across the pharmaceutical industry, we see that the future of pharmaceutical innovation will be built on a smaller, less integrated and less complex R&D organization. It is a networked organization model that leverages externalization. In this model, the company manages the strategic direction and relies on skilled third parties such as CROs for execution. Leading companies should consider taking the following actions:

Establish a new vision. Explore an R&D model that focuses on the core parts of the value chain for a strategic advantage over the competition with know-how that allows for differentiation in select disease areas. Other parts of the value chain can be externalized or outsourced without giving up strategic control and without creating significant risk.

Leverage externalization. Externalization not only applies to CRO R&D activities, it is a strong option for an increasing share of the novel IP that can be in-licensed or acquired from early stage biotechs or potentially traded between major pharmaceutical companies.

Spin out assets. To create value for groups of assets in the portfolio—specific disease areas that are deemed nonstrategic for the future, but still have attractive commercial potential—consider spinning these assets out and creating biotech companies.

Be objective. Avoid the pitfalls of favoring in-house activities by keeping internal rate of return (IRR) for R&D superficially low. Objectively benchmark capabilities and IP of CROs and other third parties such as biotechs.

Reward innovation. Institutionalize a culture of innovation and entrepreneurship by rewarding leaders for informed risk taking and creative de-risking approaches through external funding and other mechanisms.

Keep it simple. Simplify overly complex matrix organizations by creating smaller, independent business units with decision and budget authority. Reduce the number of management layers and decision-making bodies. Link responsibility for strategic direction with budget responsibility and accountability.

Start small then scale. Start the change process with controlled experiments in which specific and emerging therapeutic franchises pave the way for the broader organization.
Funding

This section describes the mechanisms in place to fund R&D across different phases, both through internal funding as well as external funding sources.

The Current State

Large pharmaceutical companies used to be the safe haven for conservative, institutional investors, who were mindful of their customers’ retirement savings. Over the past decade, this picture has changed rapidly. These very same investors are now weary of the commercial and regulatory uncertainty facing the pharmaceutical industry related to late stage failures of potential blockbusters, single-digit growth rates and declining profitability.

In R&D, there is even more obvious misalignment between the risk/return profile of pharmaceutical innovation and the typical pharmaceutical investor. Investors in pharmaceutical companies may tolerate late stage R&D risk, but only venture investors are aligned with earlier stage risk profiles (see figure 2).

This issue is also reflected in the way the pharmaceutical industry is handling its cost of capital when making investment decisions. Overall cost of capital is typically kept low, around 10 percent, which is reflected in the IRR used for making investment decisions. Although a low IRR may be relevant for an investment in a commercial or late stage infrastructure, it does not reflect the inherent risk in earlier stage investments. By keeping the IRR for early stage investments low, companies artificially favor internal investments in R&D infrastructure. This provides an unfair advantage over external investments.

Figure 2. Expected returns and potential external funding sources across the R&D value chain

<table>
<thead>
<tr>
<th>Phase</th>
<th>Expected Returns</th>
<th>Potential External Funding Sources</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basic Research</td>
<td>&gt;35%</td>
<td>Government, Foundations</td>
</tr>
<tr>
<td>Discovery and Preclinical</td>
<td>~35%</td>
<td>Venture Capital</td>
</tr>
<tr>
<td>Early Stage Development (Phase I-IIa)</td>
<td>~30%</td>
<td>Venture Capital</td>
</tr>
<tr>
<td>Late Stage Development (Phase IIB-III, Regulatory)</td>
<td>~20%</td>
<td>Private Equity, Hedge Funds, Public Investors</td>
</tr>
<tr>
<td>Phase IV</td>
<td>~15%</td>
<td>Private Equity, Royalty Investors, Public Investors</td>
</tr>
</tbody>
</table>

Source: Accenture Research, 2011
Opportunities for Future Value

Historically, the availability of cash to fund R&D was never a significant challenge for the pharmaceutical industry. One successful blockbuster could pay for R&D and commercial failures. Today, the reality is very different. Resources to fund R&D are increasingly scarce, and late stage failures are impacting share prices.

In this climate of scarce resources and sensitivity to late stage clinical failures, the industry should more aggressively pursue partnerships, external funding and de-risking approaches. Leading companies should consider taking the following actions:

**Explore collaboration.** For accessing and developing early stage assets, a collaborative model between pharmaceutical companies, biotechs, venture capitalists and other risk tolerant sources of early funding—and CROs for execution—has strong potential. Variants of this model are currently being implemented by Quintiles and Lilly respectively.

**Approach risk differently.** For de-risking and co-funding of risky late stage and commercial investments, the model pioneered by Lilly in collaboration with Quintiles, and funded by TPG, is viable. In this model, the partially at risk CRO will develop the asset with funding from the investment partner. The pharmaceutical company will pay that partner a premium upon the successful outcome. This model can help overcome short-term cash constraints and minimize the profit and loss and subsequent share price impact of a late stage failure.

**Choose the right partners.** Identify partnerships with funding sources backed by content and execution expertise. This way, individual projects can be rapidly and expertly assessed and implemented.
Looking to the Future

Pharmaceutical R&D productivity has been on the decline for far too long. The need for change is too great—and the stakes are too high—to continue with the status quo. To close the productivity gap, the industry must act boldly to change the current R&D model across every dimension. This will require a significant evolution and a holistic perspective that accounts for strategy, process, people, organization and funding. It is time to begin the future of pharmaceutical innovation—a future much different than the past, but full of opportunity.
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Footnotes


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About Accenture

Accenture is a global management consulting, technology services and outsourcing company, with approximately 236,000 people serving clients in more than 120 countries. Combining unparalleled experience, comprehensive capabilities across all industries and business functions, and extensive research on the world’s most successful companies, Accenture collaborates with clients to help them become high-performance businesses and governments. The company generated net revenues of US$25.5 billion for the fiscal year ended Aug. 31, 2011.

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