

The challenge in pharmaceutical R&D – How to increase productivity

Over the last few months, Otto & Company has talked to various clients about their efforts in establishing a productive R&D organization. Subsequently, Otto & Company analyzed the key pain points underlying the decline in R&D productivity and identified seven strategic levers to transform the R&D department in order to maintain historically successful R&D productivity.

BY MAXIMILIAN BLOME, PATRICK KANTERS AND HERBERT HENSLE

Most large-cap pharmaceutical companies such as Novartis, Pfizer or AstraZeneca have expanded their R&D departments over time along with top-line sales growth. Steadily increasing R&D budgets are a clear indication of that.¹ Currently, pharmaceutical companies spend on average about 20 % of their sales revenue on R&D. However, the returns those companies have seen on R&D investments have declined significantly over the last few years, from 10.1 % in 2010 to an all-time low of 1.9 % in 2018.²

national pharmaceutical companies by gross margins, 4 of the top 5 competitors are biotech companies with Celgene leading the way (93.1 %).³ It also takes underperforming companies as much as 1.5 times longer to develop a new compound while spending 1.9 times more money.⁴

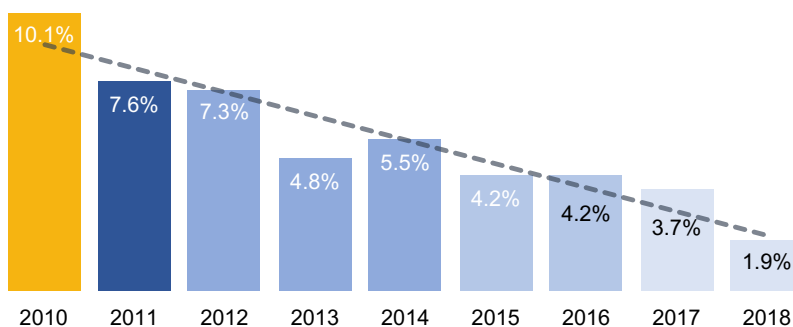
The latest development of ROI in pharmaceutical R&D should be understood as a wake-up call for companies to reconfigure their R&D organization. While industry profitability is still high, it might become more difficult to retain.

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time period (all numbers based on data available on 15th October 2019).⁶ This might be a sign that investors are less confident in the ability of pharmaceutical companies to maintain the historic profitability levels.

R&D returns for large pharmaceutical companies



Otto & Company based on EndPoints News; trend analysis based on EvaluatePharma data; Visualization of the IRR (Internal Rate of Return) based on public available information about R&D spend and in the future generated returns

But an efficient R&D organization and portfolio management are vital for pharmaceutical companies to keep up with their competitors. A look at biotech companies indicates that healthy R&D productivity is still possible, even though average productivity has declined. These companies are usually smaller, have a more concentrated research focus and manage smaller R&D budgets. Comparing major inter-

The S&P pharmaceutical index⁵ has lost on average 4.86 % over the last five years while the S&P 500 achieved returns of 9.58 % in the same time. Even though some industries such as IT (17.02 % returns over the last five years) might have factored into this development, also the more traditional companies of the Dow Jones Industrial Average have seen returns of 10.43 % over the same

Eroom's Law

In 2016, researchers coined Eroom's Law⁷, inspired by the famous "Moore's Law", to describe that pharmaceutical drug development, generally speaking, takes longer and becomes more expensive over time due to three underlying causes.

First, there are many well-proven drugs available that make it increasingly difficult to continue to develop groundbreaking innovation. Oncology is one major area companies are focusing on and expect positive returns from. Especially, since the turnover with oncology products is expected to succeed 200bn USD by 2024.⁸ It is this growth potential that excites large pharmaceutical companies. On the other hand, higher failure rates for investigational compounds

are the largest driver behind cost increases for launching new drugs.

Second, risk tolerance among regulators has declined over the years. This has led to high R&D costs, mainly because of complex processes. Also, regulators tend to have a lower risk tolerance toward experimental drugs dealing with diseases for which several treatment alternatives already exist. As a consequence, authorities' approval requires a solid number of patients per clinical trial but also different trial approaches to bolster the safety database.

Third, the industry itself has always had a comparably high level of available resources due to healthy profitability. This fact has led to the tendency "to throw money" at various projects, thereby increasing the attrition rates as projects with low probability of technical success have been pursued. Researchers have also lost strategic focus as many projects had few ties to the corporate and R&D strategy.

Even though there are companies that can better deal with Eroom's Law, the root causes still apply to the industry as a whole. Yet, they are especially relevant for large pharmaceutical companies as growing organizational complexity makes it difficult to tackle Eroom's Law's inherent causes.

Improvement potentials for the R&D department

Otto & Company identified seven major levers that can help large pharmaceutical companies improve their R&D productivity, namely strategy, organization, process, data, technology, people and culture.

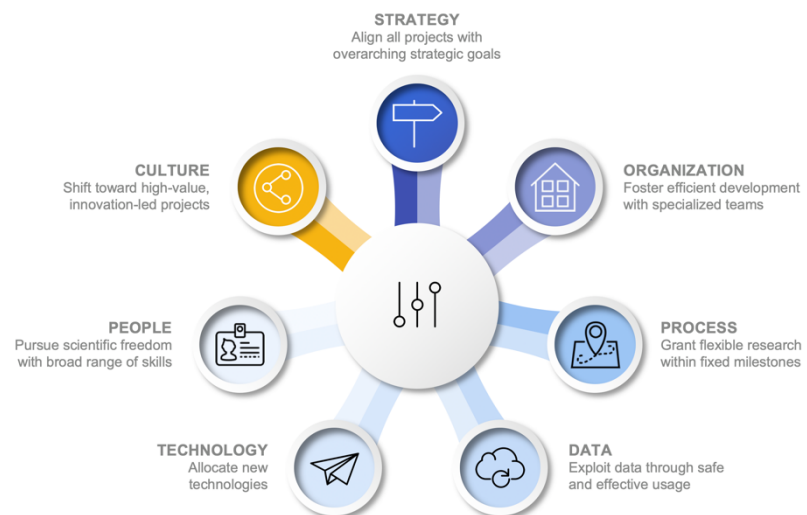
Strategy

First, researchers as well as executives should internalize the importance of their R&D strategy. This strategy provides the framework necessary to make good decisions consistently and sets the course for projects worth pursuing.

Large pharmaceutical companies need a mechanism to structure and integrate decisions that are made around the globe. Factors like blockbuster vs. precision medicine, pricing and valuations, research partnerships and more need to be considered. Also, the R&D strategy channels research projects to fit the overall business strategy and the corporate goals. How the company defines and articulates the R&D strategy is ultimately a decision based on the current state, size and intents of the company. Nonetheless, it is important for pharmaceutical companies to align their R&D and business strategies, because with ever increasing R&D budgets there is a threat that a portion of that budget is invested sideways.

that operate primarily independently, while R&D executives can monitor these teams ensuring the project's strategic fit.⁹

Pharmaceutical R&D departments face a major challenge, as they have to balance a large number of stakeholders and projects, whilst ensuring flexibility and efficiency of teams. Functional structures are commonly used in pharmaceutical R&D. Each function is responsible for a certain area, e.g. a different therapeutic area. Network or even helix organizations have a stronger emphasis on the team's independence. Network-centric structures allow for much smaller, more specialized teams that organize and direct themselves. They must be driven by company-specific goals



Otto & Company's strategic levers to improve pharmaceutical R&D departments

Organization

Second, pharmaceutical companies should rethink their current organizational set-ups, as R&D organizations have increased in size, resulting in large project teams as well as many stakeholders and interfaces being involved. This development has made it hard to move quickly in terms of R&D projects and has extended cycle times. Any company will struggle with a transformation of its R&D department if the organization does not allow for smaller teams, faster processes and easier communication. A modern R&D organization trusts in specialized teams

and guidelines, yet, operate almost completely independently.

Process

Third, companies should review the R&D department's processes. Within large organizations, people tend to diversify pre-defined processes. As a consequence, duplicate roles, structures and process steps consume valuable resources. However, these issues are often neglected as profitability margins are still satisfactory.

Pharmaceutical companies must find a way to develop a two-sided approach. In early development,

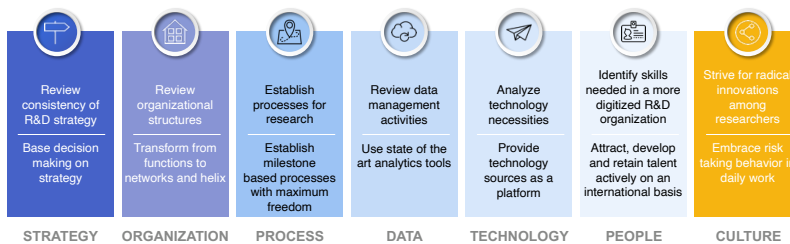
researchers should have a great degree of freedom in regard to how they go about their research activities, but there should be a standardized process for the organization and its projects. This means that researchers will be restricted to budgets and milestone-based goals. They should, however, be able to decide by themselves how they achieve these goals, e.g. by allocating the budget accordingly, to support the scientific space they need to foster innovation and creativity. In development, a more rigid process can be implemented. This approach offers unique advantages to the organization as it allows for a top-line strategic review of all relevant projects, while researchers can follow their approach. It allows teams to work productively, while the process remains transparent for executives.

panies with access to more powerful analysis tools (e.g. Machine Learning or Predictive Analytics) combined with more availability and quality of data will increase their productivity. Therefore, they need to enhance and align their data analysis capabilities in order to fully leverage the emergence of different data sources. For this purpose, pharmaceutical companies must be able to ensure proper handling of (privileged) data and stop collecting data only to put them into a “junk drawer”, where data is often not readily organized, collated or analyzed.

While most of the data that is provided by public institutions has usually already been de-identified, it is important that pharmaceutical companies ensure that all data cannot be tracked back to

technologies are as broadly applicable as possible within the whole organization. When researchers are given the freedom to pursue their projects with technologies that they consider beneficial, the probability of success will increase. However, these technologies often represent a huge investment for the R&D department.

Therefore, companies should conduct a top-down analysis of the technologies necessary for successful drug development. Subsequently, they should develop a technology platform that all research teams could employ and could therefore justify the initial investment into e.g. 3D bioprinting, CRISPR, Mass-spectrometry imaging (MSI) or Patient-derived xenograft (PDX) models. Furthermore, R&D departments need to choose to either develop a customized or use an industry-proven technology platform. Given the trend of stronger standardization, R&D companies tend to implement the latter. A platform management team should support the project teams, ensuring that the components are used as productively as possible.



Summary of solutions and attached example measures below for each strategic lever

Data

Fourth, pharmaceutical companies nowadays have a broader access to a variety of different data sources. Much of the data that has been gathered over the past was merely from clinical trials. Increasingly, pharmaceutical companies gain access to more extensive data, e.g. from public or private institutions (e.g. insurance companies or public health departments). Various countries are establishing or have already established electronic health records¹⁰ (EHR) that collect patients’ medical data. Pharmaceutical companies’ access to these platforms could be beneficial. Data not generated from a controlled environment such as clinical trials present a promising opportunity to examine how medicines perform in a real-world environment. Pharmaceutical com-

panies with access to more powerful analysis tools (e.g. Machine Learning or Predictive Analytics) combined with more availability and quality of data will increase their productivity. Therefore, they need to enhance and align their data analysis capabilities in order to fully leverage the emergence of different data sources. For this purpose, pharmaceutical companies must be able to ensure proper handling of (privileged) data and stop collecting data only to put them into a “junk drawer”, where data is often not readily organized, collated or analyzed.

While most of the data that is provided by public institutions has usually already been de-identified, it is important that pharmaceutical companies ensure that all data cannot be tracked back to individual patients. Further, they must ensure that data can be properly analyzed and therefore consistently harmonized, integrated and stored. Access within the companies should be carefully monitored by data stewards and only granted to staff on a need-to-know basis.

Technology

Fifth, R&D executives must find a balance between letting researchers choose the technologies that they prefer and ensuring that these

People

Sixth, the organization needs to attract and retain the right people with the right skills. Researchers, nowadays, are required to cover a broad skill set that exceeds traditional scientific knowledge. They must be able to apply core digital skills such as data analysis and at the same time be capable of communicating, presenting findings and working in teams effectively. If the organization allows teams to work autonomously on projects, these leadership skills are vital to guarantee efficient collaboration.

Furthermore, most R&D departments are focused on the company’s headquarter or at least a regional headquarter. What is often missing is broad, international collaboration. As a consequence, it is vital for employees to acquire new

leadership skills. This includes being able to lead virtual teams with different backgrounds, managing a large number of cultures in center of competencies and adapting leadership style to the respective cultural environment.

Culture

Seventh, R&D departments need to address their culture. As stated before, many large pharmaceutical companies try to minimize the risk attached to their portfolio, often by expanding the size of it. Once companies achieve a certain size, the risk-taking and innovation-seeking culture gets abandoned for a more risk-averse approach, emphasizing only incremental innovation. Therefore, with the cultural tendency to pursue a large number of projects and to involve many stakeholders, researchers can potentially lose the sense and the drive for radical innovation. It is quite difficult for large cap pharmaceutical companies to embrace risk-

taking behavior universally within the organization.

But how can pharmaceutical companies transform their behavior and culture? In order to improve R&D productivity, companies should shift their focus from high-volume to quality research and decrease the number of projects. Companies need to stimulate risk-taking attitude and behavior while clearly ensuring adherence to quality standards. Once all stakeholders have internalized a more innovation-led and risk-prone culture, specialization is possible. Combined with an objective decision-making process, researchers will also be able to evaluate projects more thoroughly.

Additionally, incentive schemes need to be reviewed. Many pharmaceutical companies' incentives value quantity over quality of projects.¹¹ This lets researchers shift their focus from potentially high value, but risky projects toward a high number of projects

with potentially low risk of failure. If incentives are aligned to support risk-taking behavior, they can be a powerful tool in successfully transforming a company's culture.

Summary

Pharmaceutical companies should acknowledge the severity of the current situation. In a period of only nine years, R&D productivity fell from 10.1 % to 1.9 %.¹² Should this trend continue, it will get harder to maintain the traditional business model. Decreasing returns on R&D, fewer breakthrough drugs and rising costs pose a threat to the existing business model. Ultimately, the levers identified by Otto & Company can be a powerful approach to transform and thereby ensure the R&D department's future competitiveness, even though this process will require considerable effort. ■

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