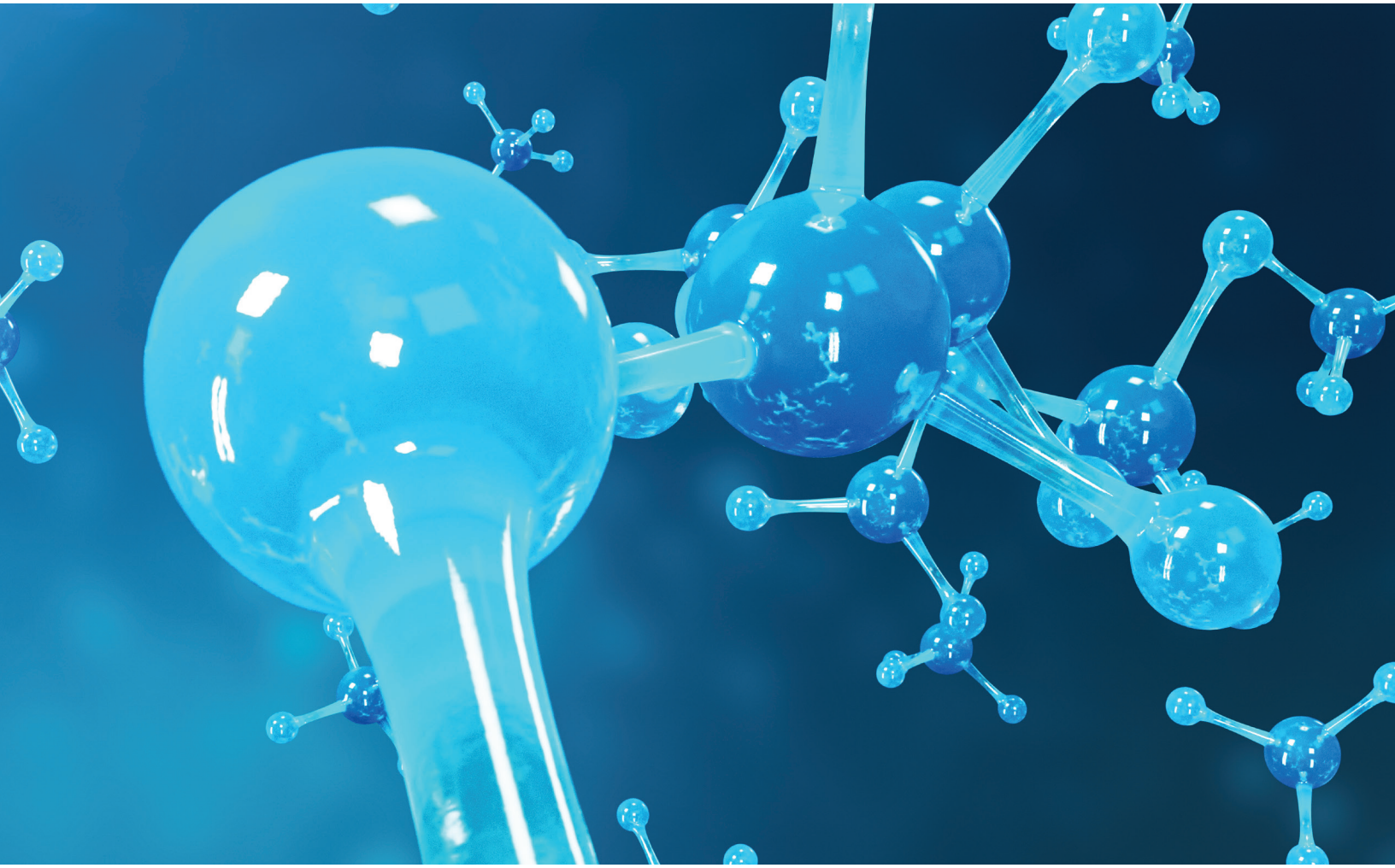
How new biomolecular platforms and digital technologies are changing R&D

Biotech pioneers are improving drug discovery and development—and transforming the pharmaceutical industry.

Olivier Leclerc and Jeff Smith



The use of digital technologies is transforming business as usual in industries ranging from aviation to retail to telecommunications. But other sectors—including the pharmaceutical industry—have been slower to embrace the potential of digital technology.

Given that pharma companies depend on innovation, science, and research and development, it may seem counterintuitive that they lag behind the digital curve. In McKinsey's ongoing survey to measure companies' "Digital Quotient," the pharmaceutical industry ranks in the bottom third of industries measured. But consider the context: pharma is characterized by long, capital-intensive product-development cycles, and considerable technical and regulatory uncertainty. As a result, there is a degree of risk aversion.

A new breed of biotechnology firms, unencumbered by the accumulated practices and systems of large traditional ones, are pioneering impressive new digital capabilities. In the process, they are nudging the industry as a whole in this direction. This could significantly boost R&D productivity, benefiting both pharmaceutical companies and the patients they serve.

The emergence of biomolecular platforms

In recent years, a number of biotechnology companies have applied genetic-information-driven technologies to form "biomolecular platforms" (exhibit). These platforms intervene at different points in the information chain (often referred to as "the central dogma of biology") to modify biomolecular processes at the source of various diseases. In that respect, they have a software-like nature, that allows for the ready design of multiple new therapies by a single platform, that provides the instructions to modify the hardware of molecular biology, that in turn addresses disease.

Biomedical platforms have already yielded new treatments—spanning various DNA-, RNA- and cell-based therapies—with broad potential applications. Many of these new interventions offer a glimmer of hope for treating life-threatening diseases that have so far proved impervious to conventional approaches, such as small molecules or monoclonal antibodies.

Indeed, several such therapies have already received regulatory approval: of particular note are the US Food and Drug Administration's (FDA) recent green lights for Kymriah and Yescarta. These are chimeric-antigen-receptor therapies (CAR-T) for certain aggressive hematological malignancies. Similar CAR-T therapies are advancing rapidly. Luxturna, which treats a rare form of inherited vision loss, recently became the first FDA-approved DNA gene therapy. In addition, several antisense drugs have also been approved. These examples account for only a small number of the biomolecular-platform-derived therapies that are working their way through the pipeline and rapidly approaching the market.

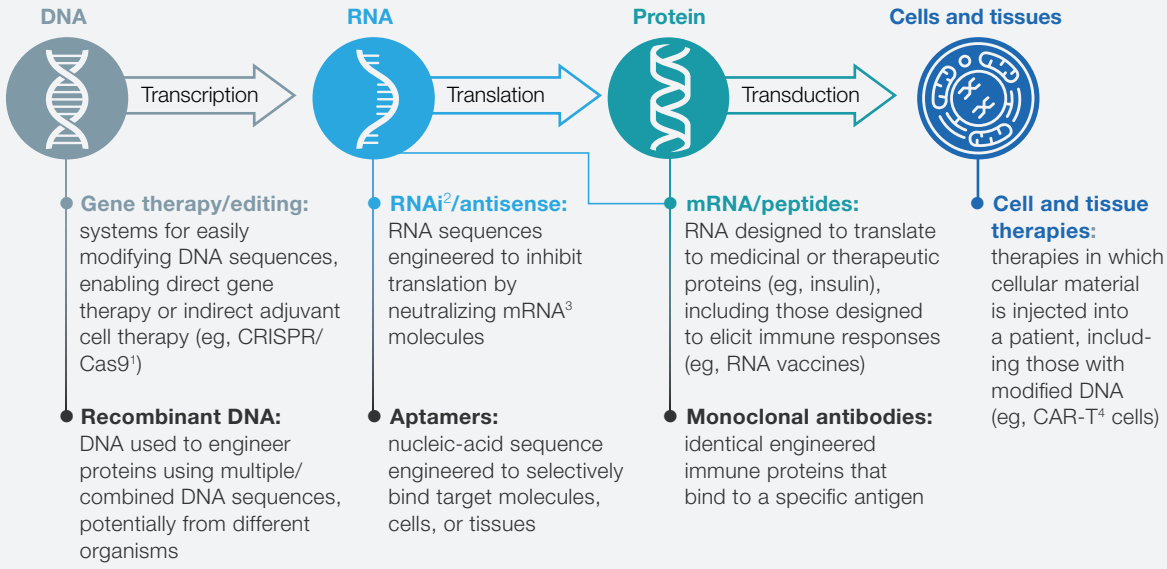
Biotech companies have raised significant amounts of capital to advance biomolecular platforms and their associated development programs. According to our analysis of data from *BioCentury*, a biotechnology review, at least five have each raised more than $1 billion in capital. Fundraising has accelerated rapidly over the past five years; all told, as of the end of 2017, 100 companies have raised at least $13 billion over the past several years to discover and develop biomolecular platforms.

Biotech companies are typically formed around their unique insights into the underlying disease biology for a single disease or a related cluster of diseases. For these companies, the nature of drug discovery and development remains mostly unaltered from the recent past. Many have adapted by focusing on specialty-disease areas where few treatments exist; this allows them to make use of expedited development and regulatory pathways that could lead to reduced timelines and costs and increased probability of success.

Exhibit

In recent years, biotechnology companies have applied genetic-information-driven technologies.

Central dogma of biology and related biotechnologies



[1] CRISPR = clustered regularly interspaced short palindromic repeats. Cas9 = CRISPR associated protein 9.
[2] RNA interference.
[3] Messenger RNA.
[4] Chimeric-antigen-receptor therapies.

Biotech companies with a biomolecular platform are forging a different path, in which the platform itself is the source of value creation. They start by building the platform and designing a set of experiments to demonstrate the viability of the platform as a therapeutic modality. For instance, they may test whether the platform can be used to deliver vaccines. Then they identify a range of diseases across various therapeutic areas or clusters of related underlying biology that the modality could address, and prioritize drug discovery and development across those diseases (see sidebar, "Interview: How Moderna uses its digital capabilities to power its mRNA platform").

Biomolecular-platform companies therefore typically have a variety of different therapies in development. There is still correlated risk across drugs that are discovered and developed with the same genetic-information-driven platform. But the variety of modalities, and the ability to sequence development of drugs targeting different biological pathways, provides a more balanced risk-adjusted portfolio.

Companies that take this approach usually adopt a staged development process, which starts by selecting a disease for which the clinical end-point is established and straightforward to test. Once proof of concept has been validated, the platform then allows more-rapid and lower-risk development of therapies for other diseases. The careful selection of initial diseases can mitigate biology risks in certain related clusters of diseases with similar underlying etiology. This de-risking allows companies to stage

their investments, then scale them up to address a broad range of therapeutic areas. The approach is being applied across a range of biomolecular platforms, from DNA-based gene therapies to CAR-T therapies to emerging microbiome platforms.

The corollary of the versatility of these biomolecular platforms is the need to make significant investments and to scale up rapidly. This is difficult for three reasons. First, even before the specific disease targets are identified, significant up-front investment is required to establish the platform. Second, companies must take steps to protect their intellectual property and other proprietary investments. Third, running multiple clinical programs at the same time calls for efficient and scalable operational processes and a flexible operating model that allows for rapid resource allocation.

Digital as a source of value creation for biomolecular platforms

The combination of genetic-information-driven technologies and an innovative approach to R&D positions biomolecular-platform companies to transform their research enterprises by taking advantage of digital opportunities. It doesn't hurt that many of them have been formed in the past decade—and so lack the built-in brakes that can slow down bigger firms. These young companies are coming of age as "digital natives."

A number of characteristics make digital an integral part of the business model of biomolecular-platform companies. In fact, digital can help all along the value chain.

- Drug discovery:
  - Digital techniques can accelerate the progression from initial concept to drug candidate.
  - Optimizing drug design through the use of algorithms and advanced analytics may improve the chances of success.
  - Automation enhances repeatability and speed.
- Preclinical:
  - Digital technologies can be used to automate the production of clinical trial–grade material.
  - The ability to apply learning and data from other pipeline assets produced by the same platform may reduce the burden of data collection and obviate the need for certain steps in the development process, such as toxicology and preclinical safety.
- Clinical development:
  - Well-designed experiments in one or a small number of diseases can inform and reduce risks across a broad range of diseases. For example, experiments with microbiome-based therapies are being designed to guide entry into a broader range of diseases.
  - Many diseases have significant unmet needs, such as certain types of cancer or rare diseases, which enable the use of expedited development and regulatory paths and accelerates the approval process for new drugs.
- Manufacturing:
  - Digitization can help to reduce the number of ingredients and process steps.

Interview: How Moderna uses its digital capabilities to power its mRNA platform

Founded in 2011, Moderna Therapeutics has built a messenger RNA (mRNA) platform that is designed to accelerate the discovery and development of mRNA therapeutics that treat a range of diseases with high unmet needs. In this interview, CEO Stéphane Bancel discusses how Moderna uses digital technologies in its mRNA platform.

McKinsey: *Moderna has brought drugs into the clinic across a range of diseases, specifically infectious disease, cancer, cardiology, and rare diseases. Tell us about Moderna's mRNA platform.*

Stéphane Bancel: We have spent considerable time thinking about, designing, and improving our platform. Simply put, our platform is a series of technologies that collectively allows us to deliver mRNA to patients to treat their disease. The promise of mRNA is very clear. In principle, it allows the translation of a protein whose absence (or insufficient quantity) results in disease. However, our immune systems are able to detect and remove foreign genetic material. Our scientists have discovered a number of technologies to address this challenge and thus harness the therapeutic potential of mRNA. For example, we have developed ways to stabilize the mRNA molecule to avoid detection and degradation, we have developed vehicles to deliver the drug to tissues of interest, and we have optimized manufacturing of mRNA therapeutics at high yields. These technologies and many others make our platform the foundation of everything that we do.

We have also given considerable thought to how we apply our platform across the broad range of diseases that we can reach with mRNA therapeutics. Our strategy is to pursue a range of mRNA modalities in parallel. For example, we are pursuing a number of mRNA vaccines, cancer therapies, and rare diseases, to name a few, at the same time. Our platform allows us to scale rapidly within and across these modalities and others as we validate the use of mRNA therapeutics through clinical studies with our lead assets.

McKinsey: *What role do digital technologies play in these efforts?*

Stéphane Bancel: We have been a digital company from the very beginning and in everything that we do. Our mission is to bring mRNA therapeutics to patients, and the digital nature of our platform enables us to do this more robustly and efficiently.

Due to the nature of mRNA therapeutics, we realized very early that we could significantly compress the time from when a researcher had an idea for a new mRNA therapeutic to the time when the drug enters the clinic. We did a few things to make this a reality. First, we created a digital drug-design studio that allows our researchers to design a protein, and then identify the mRNA sequence and appropriate vehicle to deliver the mRNA to the tissue of interest. Second, we use advanced analytics to identify the optimal sequence of mRNA—taking into account the impact that slight variations in sequence can have on 3-D structures and transcription rates. Third, we have automated most of the steps in producing a product that is ready to start laboratory testing. Taken together, these steps allow us to go from an idea to getting a drug ready for an investigational new drug application in a matter of months. For example, it took ten months to do discovery with our partner on mRNA MRK-1777.

McKinsey: *What has been the impact on Moderna's R&D productivity and timelines?*

Stéphane Bancel: The impact has been substantial. We have advanced more than ten assets into the clinic in the past two years and have an exciting pipeline of ten other development candidates following right behind. Our throughput is now running at five or more assets per year into the clinic, a pace that we are very proud of. On the cost side, we have made equally impressive gains. Our incremental cost to bring an additional asset into the clinic is well below the industry average. The speed and cost benefit is one of the reasons that our strategy is to scale rapidly within and across our modalities of interest. So it is the combination of the performance of our platform and our strategy to rapidly scale and discover and develop mRNA therapeutics for a range of diseases that holds enormous potential for patients and for Moderna.

— Optimizing product design and manufacturing may improve downstream yields as well as biological effects, such as sequence optimization for RNA products and transcription levels for DNA gene therapies.

That is the potential. In practice, there are few examples of companies using digital effectively all along the value chain. This may be a lost opportunity. We have found that areas where digital is not applied tend to become bottlenecks, delaying scale-up and depressing value creation. This also may be a factor in the recent burst of M&A activity. Larger companies sense a potential to add value by infusing expertise and capabilities to help accelerate the scale-up and apply their digital capabilities to the platform.

Digital technologies enable the fast, replicable, and systematic application of the underlying biomolecular-platform technology to a broad range of diseases. And the potential is growing, as more and more companies—including traditional biotech and pharmaceutical firms—are beginning to develop biomedical platforms. As the benefits of digital prove themselves, both biotech pioneers and larger pharma companies are increasingly positioning themselves to capture the potential of their biomolecular platforms. In so doing, we expect that this will be a major impetus to help the pharmaceutical industry close the digital gap relative to other industries. In the meantime, biomolecular-platform companies have demonstrated the value that digital can deliver. ■

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