How Pharmaceutical Companies Utilize Platform Strategy: A Study of the COVID-19 mRNA Vaccine Development

by

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Abstract

This paper employs platform theory to investigate why Moderna and BioNTech were able to develop the COVID-19 vaccine so rapidly and provides new insights into platform theory.

The COVID-19 pandemic, which began in China in late 2019, spread globally within a month, causing immense damage. Vaccines were the most critical technology needed to fight the disease. Typically, vaccine developments take more than a decade; however, Moderna and BioNTech/Pfizer successfully developed an mRNA vaccine within approximately 300 days of the pandemic's onset.

In contrast, Daiichi Sankyo required around 1,000 days to develop a vaccine using the same mRNA technology. This paper utilizes platform theory as a framework to examine the factors contributing to this disparity. Various internal and external factors from the perspective of a pharmaceutical company can be considered behind the rapid development of vaccines. However, this study focuses mainly on internal factors, especially from the perspective of platform theory from management perspectives.

Platform theory has emerged as a crucial framework for understanding the dynamics of modern businesses and technologies. This theory distinguishes between three primary types of platforms: product-level platforms, industry-level platforms, and digital platforms.

In the pharmaceutical industry, mRNA technology can be considered a product- or technology-level platform. This is because by modifying the mRNA sequences, it will be a wide range of therapeutics targeting different diseases, not only infectious diseases but also cancers or other diseases. Although this study regarded mRNA technology as a product or technology-level

platform, we would like to discuss how it has led to the connection to the industry-level platform or digital platform through the COVID-19 vaccine development process.

In regard to the COVID-19 vaccine development story, the question that naturally arises is, 'Why could Moderna and BioNTech develop the vaccine so rapidly?' The answer must be they executed the necessary steps for vaccine development rapidly. These steps, namely 'Discovery' (development of vaccine candidate substances), 'Development' (conducting clinical trials and obtaining regulatory approval), and 'Manufacturing' (production of vaccines), were all carried out swiftly and in parallel.

These steps were executed so rapidly because, at the time of the pandemic, Moderna and BioNTech already had the financial and human resources, knowledge and patents, development experiences, digital infrastructures, efficient production facilities, influential partners, and a rational corporate culture for the project.

Then, the next question should be: why did Moderna and BioNTech have such organizational capabilities at the outbreak of the pandemic? In this paper, we examine in detail why and how such capabilities were nurtured after these companies were founded. Also, we examine the academic history even before the companies were founded and why and how Moderna and BioNTech were founded as mRNA platform companies.

In conclusion, this study demonstrates the importance of the pharmaceutical industry harnessing the "power of the platform" and provides concrete directions for leveraging its potential. The discussion should be expanded to explore how companies and policies can work together to address the health and healthcare challenges facing people around the world, utilizing the power of platforms to drive innovation, collaboration, and, ultimately, better health outcomes for all.

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My heartfelt thanks also go to my father, Kazuyoshi, whose wisdom and guidance have always inspired me, and to my mother, Midori, whose kindness, patience, and warmth have provided me with unwavering support throughout my life.

My family's belief in me has been a constant source of motivation and strength, propelling me forward even in the face of adversity.

Disclaimers

This thesis is intended for academic purposes. The views and opinions expressed are those of the author and do not represent any organization's opinions, intentions, or other information. The author is not responsible for using the information in this thesis.

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Executive Summary

Introduction

This paper employs platform theory to investigate why Moderna and BioNTech were able to develop the COVID-19 vaccine so rapidly, while also providing new insights into platform theory.

The COVID-19 pandemic, which began in China in late 2019, spread globally within a month, causing immense damage globally. Vaccines were the most critical technology needed to fight the disease. Typically, vaccine development takes more than a decade; however, Moderna and BioNTech/Pfizer successfully developed a mRNA vaccine within approximately 300 days of the pandemic's onset.

In contrast, Daiichi Sankyo required around 1,000 days to develop a vaccine using the same mRNA technology. This paper examines factors contributing to this disparity, utilizing platform theory as a framework.

Section 1.1 summarizes the significance of the COVID-19 vaccine development.

Section 1.2 delves into the specific research questions addressed in this study.

Scope of This Research

Various internal and external factors from the perspective of a pharmaceutical company can be considered behind the rapid development of the vaccine development. First, as for external factors, various types of government support have undoubtedly been a facilitating factor, as pointed out in previous studies.

Section 2.1 summarizes the previous studies. However, this study will focus mainly on internal factors, especially from the platform theory perspective.

Platform Theory Overview

Platform theory has emerged as a crucial framework for understanding the dynamics of modern

businesses and technologies. This theory distinguishes between three primary types of platforms: product-level platforms, industry-level platforms and digital platforms.

Product-level platforms, such as a car chassis, serve as a foundation for developing a series of related products. By standardizing the chassis, automotive companies can efficiently create new car models with reduced costs and shorter development cycles.
On the other hand, industry-level platforms, exemplified by the GAFAM (Google, Apple, Facebook, Amazon, and Microsoft) companies, have revolutionized entire sectors. These platforms facilitate interactions between multiple stakeholders, fostering innovation and exponential growth through network effects. Network effects occur when the value of a platform increases as more users and service providers participate, creating a virtuous cycle of adoption and engagement.

Furthermore, the concept of digital platforms has gained significant attention in recent years. Digital platforms leverage technology to digitize the interfaces of product platforms, enabling them to scale rapidly and create industry platforms.

In the context of the pharmaceutical industry, mRNA technology can be considered as a product or technology level platform. By modifying the mRNA sequences, companies can develop a wide range of therapeutics targeting different diseases, not only for infectious disease but also cancers or other diseases.

Section 2.2 explains overview of platform theory.

Rapid Vaccine Development Using Platform Strategy: Theoretical Hypotheses

In regard to the COVID-19 vaccine development story, the question that naturally arises is, "Why could Moderna and BioNTech succeed in developing the vaccine so rapidly?" The answer must be they executed the necessary steps for vaccine development rapidly. These steps, namely 'Discovery' (development of vaccine candidate substances), 'Development' (conducting clinical trials and obtaining regulatory approval), and 'Manufacturing' (production of vaccines), were all carried out swiftly and in parallel.

These steps were executed so rapidly because, at the time of the pandemic, Moderna and BioNTech already had the financial and human resources, knowledge and patents, development experiences, digital infrastructures, efficient production facilities, influential partners, and a rational corporate culture for the project.

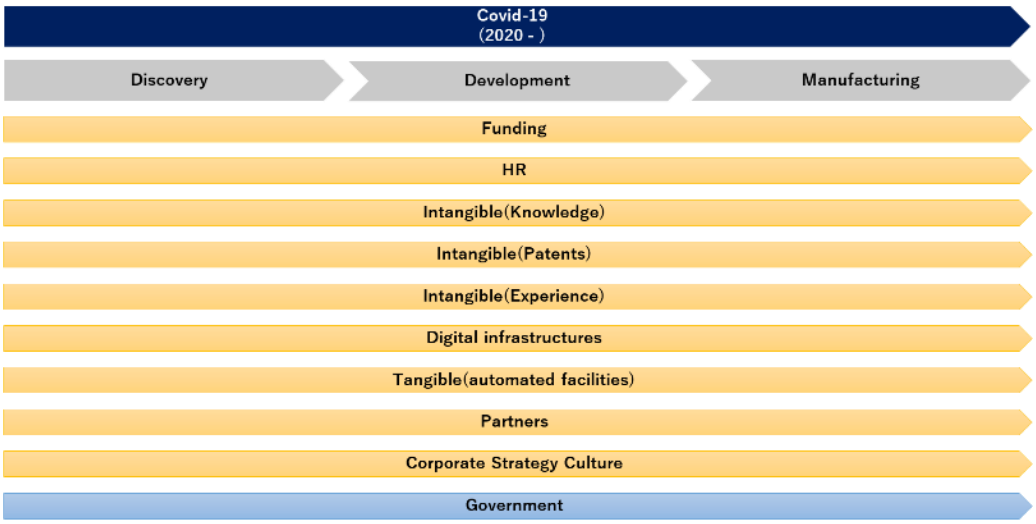


Figure 1 Moderna and BioNTech's Key Resources and Capabilities for Rapid COVID-19 Vaccine Development

(At the time of the pandemic, Moderna and BioNTech already had the financial and human resources, knowledge and patents, development experiences, digital infrastructures, efficient production facilities, influential partners, and a rational corporate culture for the project which enable to carry out the Discovery, Development and Manufacturing phase for the COVID-19 vaccine development.)

Then, the next question should be: why did Moderna and BioNTech have such organizational capabilities at the outbreak of the pandemic? In this paper, we examine in detail why and how such capabilities were nurtured after these companies were founded. Also, we examine the academic history even before the companies were founded and why and how Moderna and BioNTech were founded as mRNA platform companies.

Section 2.3 describes our theoretical hypotheses using platform theory about how Moderna and BioNTech implemented their platform strategies, amassed organizational competencies, and demonstrated these competencies after the pandemic. When establishing a company centered on drug platforms, it is hypothesized that the foundational scientific principles and leadership are

rooted for the foundation. Furthermore, in operating a company based on platform theory, several key mechanisms are expected to be at play for accumulate the capability for the rapid vaccine development in later stage. Firstly, the platform approach is presumed to foster a rational company culture that aligns with the scientific underpinnings of the drug platform. Secondly, the platform strategy is hypothesized to enable effective fundraising by attracting investors because of the four mechanisms which we describe in detail later. Thirdly, the platform-based approach is expected to facilitate the accumulation of knowledge, technology, and partnerships, as the platform serves as a focal point for R&D effort. Moreover, the construction of digital and automated facilities is presumed to further expand knowledge and partnerships by streamlining processes and enabling efficient data sharing. Lastly, in the context of the vaccine development during the pandemic, it is hypothesized that the platform-based approach allows for rapid response and resource mobilization, as the company can leverage its existing platform infrastructure and partnerships to quickly adapt to the crisis.

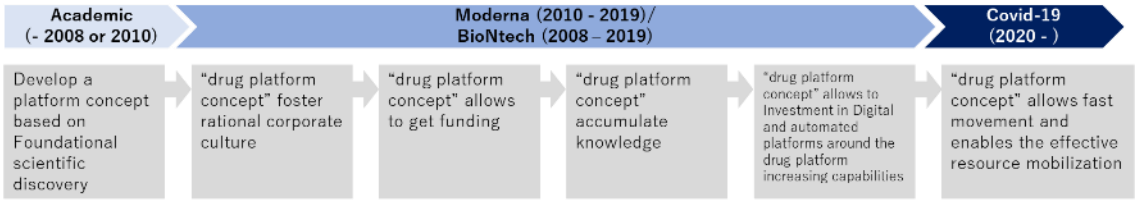


Figure 2 Theoretical Hypotheses about Why and How Moderna and BioNTech have Developed their Capabilities through the Platform Strategy

Rapid Vaccine Development Using Platform Strategy: Case Studies

Chapter 3 provides a comprehensive description of the factual information pertaining to the case study companies of Moderna, BioNTech, and Daiichi Sankyo. The chapter begins by examining the academic developments that laid the foundation for the establishment of these firms, highlighting the scientific advancements and research that preceded their inception. Subsequently, the background and leadership at the time of the companies' founding are explored, shedding light on the key individuals and their roles in shaping the organizations' direction and usage of platform strategy.

The chapter then delves into how these companies built their organizational capacity by the COVID-19 pandemic. This analysis is conducted through the lens of four critical aspects: corporate culture, funding, knowledge and experience accumulation, and digital and automated infrastructure.

Finally, the chapter explains how COVID-19 vaccine development projects were implemented by these companies after the pandemic, highlighting the platform strategy and the capabilities they had built before the pandemic.

Synthesis between Theory and Cases

Chapter 4 synthesizes the hypotheses developed in Section 2.3 and the facts presented in Chapter 3, providing an explanation of why and how Moderna and BioNTech were founded as platform companies, developed their capabilities, and then proceeded to develop vaccines after the pandemic.

Establishment of Drug Platforms

The chapter first addresses why companies with the concept of drug platforms arose. Establishing effective drug platforms requires a long history of natural science research, with mRNA and lipid nanoparticle (LNP) technologies being based on a vast body of scientific work spanning more than 50 years. Moderna established its drug platform concept through a pioneering approach called Flagship, while BioNTech was founded with a strategy centered around the mRNA platform, driven by Uğur Şahin's years of mRNA research and strong leadership.

Building Organizational Capacity for Rapid Vaccine Development

Four key elements explain why organizational capacity was built to enable rapid vaccine development.

First, both Moderna and BioNTech were founded on the concept of an established drug platform. Having the drug platform concept as one of their visions served as the North Star of the organization, bringing together its diverse constituencies. The drug platforms which are based on foundational natural science allowed the management team to make decisions based on deep

scientific understanding. In fact, Moderna has a company motto, "Moderna Mind," which calls for a scientific and rational culture. In contrast, Daiichi Sankyo has a narrative organizational vision and does not feel as scientific.

Second, the platform concept contributes to the establishment of effective financing because of its four characteristics.

(1) Unlike traditional drug development, drug platforms are not only once, which makes them more impressive to investors and easier to fund. Noubar Afeyan, the founder of Moderna, was clearly aware of this point.
(2) Moreover, drug platforms enable drug discovery in a variety of disease areas, making it possible to raise a diverse range of funds. For example, in the area of infectious diseases, it is possible to raise funds from public institutions, while in the area of oncology, it is possible to raise funds from private companies. In general, infectious diseases attract significant public investment because they impose a heavy burden on low- and middle-income countries (LMICs), while malignant tumors are diseases of developed countries and can be relatively easily financed in the private market. In fact, Moderna has received significant funding from DARPA, BioNTech from the Gates Foundation and others, and cancer research has received funding from several private pharmaceutical companies for both.
(3) On top of that, the rapid growth of industry platform companies in recent years has made investors more attracted to platform advocacy companies, an aspect that has made funding possible. This perception has been reinforced by the success of platform-centric companies such as GAFAM (Google, Apple, Facebook, Amazon, and Microsoft). Moderna employees have also noted this effect.
(4) Furthermore, solid drug platforms are being sought by other pharmaceutical companies for technical cooperation, which leads to new funding. Platforms naturally have the potential to generate a large number of drugs, enabling them to partner with pharmaceutical companies seeking new drugs. In fact, Moderna and BioNTech are undertaking development and further financing. This is also a way to gain knowledge and experience. Since the platform is not solely for specific disease, partnerships can be formed for each disease, and funding can be obtained from multiple partners.

Third, in addition, the concept of a drug platform allows for the accumulation of knowledge around it. Since research and development is conducted under the concept of a drug platform, knowledge in the field is accumulated. This knowledge can also lead to the acquisition of patents. In fact, mRNA patents were continuously obtained at Moderna and BioNTech. In particular, patents on LNPs and even combinations of LNPs and mRNAs were obtained at Moderna. It was also confirmed that mRNA and LNP have become the core of knowledge, according to the academic paper analysis of Moderna. Furthermore, the accumulated knowledge led to new partnerships, which in turn led to even more new knowledge, as illustrated by the story of BioNTech's partnership with Pfizer.

Finally, the drug platform enabled digital and capital investments to acquire additional human resources, knowledge, experience, and digital technology, highly automated equipment that could be leveraged for the vaccine development. By placing the drug platform at the center of management, a major investment axis can be defined, making investment decisions easier. It also enables the creation of digital or automated infrastructures based on scientific mechanisms at a deep level with the drug platform. By making many such investments, including digital investments, a digital platform centered on the drug platform was formed. This digital platform enabled the efficient incorporation of technical knowledge about drug platforms. These investments led to new patents and experiences. For example, the drug design studio at Moderna enabled researchers to be much more productive as mRNA optimization was performed and further inputs to the software were connected to the factory, which in turn delivered the mRNA to the lab, and researchers can research through the materials. This cycle increases the R&D productivity. Furthermore, the digital platform allows for efficient sharing of data and facilitates collaboration with stakeholders inside and outside the organization. Moreover, such progress as an organization requires a large number of human resources, and high-quality people were joining the company in rapid succession.

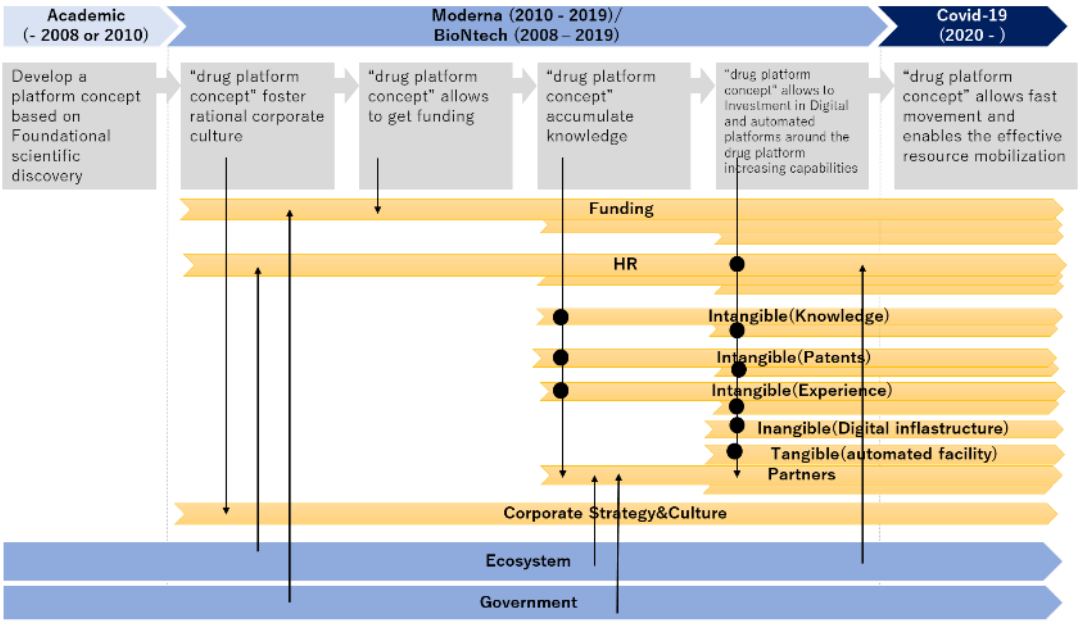


Figure 3 Why and How Moderna and BioNTech have Developed their Capabilities through the Platform Strategy

Rapid Vaccine Development After the Outbreak of the Pandemic

Given the facts discussed earlier, we can now answer the research question, "Why could Moderna or BioNTech develop the vaccine so rapidly?" In short, having a drug platform strategy increased the companies' sensitivity to the emergency response and enabled an early reaction. Furthermore, the platform-centered organizational structure allowed for rapid resource mobilization. Moreover, the "discovery," "development," and "manufacturing" processes proceeded efficiently and quickly in parallel due to the capabilities established prior to the pandemic, and the additional fund from the government during the pandemic.

The COVID-19 pandemic was an unprecedented global emergency, with the infection spreading worldwide. Under these circumstances, rapid decision-making based on scientific evidence was crucial for vaccine development companies. Moderna's CEO, Stéphane Bancel, personally decided to contact National Institute of Allergy and Infectious Diseases (NIAID) in early January 2020 to inquire about the status of the infectious disease and initiate vaccine development. Similarly, BioNTech's CEO, Uğur Şahin, decided to launch "Project Lightspeed" in late January. In contrast, Daiichi Sankyo did not start its vaccine development project until April 2020, following a bureaucratic process.

During the discovery phase, determining the most promising vaccine candidates was the goal. For the development of an mRNA vaccine against SARS-CoV-2, starting the process early using the viral information published on January 11 was essential. Researchers could infer the meaning of various sequences based on the structures of related viruses like SARS and MERS, and there was expert consensus on the validity of antigen design based on S proteins from existing studies. Integrating this information early on was vital to the development process. Moreover, the digital infrastructure that facilitated efficient and streamlined R&D activities was crucial. Moderna and BioNTech leveraged their accumulated knowledge, partnerships, and digital infrastructure to efficiently complete this phase. For Moderna, the accumulated knowledge, partnership with NIAID, simulation tools for mRNA sequence such as Drug Design Studio and LNP ratio optimization using high-throughput facilities were important. Importantly, the digital algorithms had prior experience stored within them, enabling rapid design during the pandemic. For BioNTech, in addition to the accumulated knowledge, Genevant's expertise in LNP technology was also significant.

In the development phase, demonstrating the efficacy and safety of the candidate substances identified in the discovery phase was necessary. This involved obtaining Investigational New Drug (IND) approval for First-in-Human Clinical Trials (FIH) and filing applications for drug approval through Phase I, II, and III clinical trials. Moderna was able to omit animal testing because the safety of the concept had already been confirmed, while BioNTech completed animal testing in a short period due to the urgency and sufficient safety data. The next steps included FIH trials, followed by Phase 1, 2, and 3 clinical trials, and finally, an application for Emergency Use Authorization (EUA). Large Phase 3 trials were necessary because the vaccine needed to be administered to a large number of healthy individuals. Digital tools and platforms facilitated the rapid design, conducting, and analysis of the clinical trials, enabling real-time data collection and analysis, streamlined trial document management, and efficient communication within the trial network. This digital infrastructure supported trial scale-up, adaptive trial design, and the management of complex logistics associated with large, multicenter trials, significantly reducing the typical vaccine development timeline. The use of AI for cleaning clinical trial data also improved productivity in large-scale trials. These factors, along with regulatory flexibility, allowed Moderna and the BioNTech group to complete the development phase more quickly.

During the manufacturing phase, there was an urgent need for rapid technology transfer and scale-up for early mass production of vaccines to address the global vaccine needs. Both companies already had highly digitized manufacturing facilities, and their established manufacturing know-how provided the basis for further production. Moderna and BioNTech completed technology transfers in just a few months, a process that normally takes several years. This allowed Lonza to scale up Moderna's manufacturing technology and Pfizer to effectively scale out BioNTech's manufacturing technology. The key factor behind this was that both companies had digitized facilities with complete access to manufacturing parameters, which were efficiently acquired and transferred through mechanisms like digital twins (virtual models that mirror physical manufacturing systems). Additionally, the fact that mRNA platform technology could be manufactured without biological processes and was relatively easy to produce contributed to its efficient manufacturing. Comparing mRNA vaccines to Novavax's recombinant protein vaccine, which took longer to develop due to the "cell culture" process involved in its production, highlights the influence of mRNA technology's inherent characteristics on the speed of vaccine development.

The utilization of these organizational capabilities allowed the "discovery," "development," and "manufacturing" phases of vaccine development to be accomplished in a remarkably short period. It is also important to note that these processes were developed in parallel, with ample government support and strong corporate leadership. The combination of these factors enabled the development of a vaccine within 300 days of the pandemic's outbreak.

Discussion and Conclusion

Chapter 5 presents a detailed summary of the analyses and discussions that emerged from our study.

Section 5.1 identifies three unique mechanisms that contribute to platform theory in the context of the pharmaceutical industry: (1) the platform strategy itself enables rapid platform development by attracting funding and collaborators more quickly than traditional product-level platforms; (2) the development of drug platforms is closely intertwined with the growth of the local ecosystem, creating a "chicken and egg" problem and providing insights into fostering thriving ecosystems;

and (3) the platform approach facilitates the digitization of manufacturing processes and more efficient technology transfer. These findings demonstrate the potential of platform strategies to foster innovation and efficiency in the pharmaceutical industry.

Section 5.2 discusses various strategies for leveraging drug platforms, including placing platforms at the core of management and organizational strategies, establishing autonomous divisions dedicated to exploiting the potential of platforms, and collaborating with companies dedicated to platform approach. It describes these strategies based on the relationship between Moderna, BioNTech, Pfizer, and Lonza in the development and manufacture of the COVID-19 vaccine.

Section 5.3 discusses the advantages of drug platforms as product-level platforms, highlighting the significant benefits to the pharmaceutical industry, such as building diverse product portfolios, increasing efficiency, reducing costs, simplifying complexity, reducing risk, improving economics, and enhancing patient access.

Section 5.4 analyzes the current case in terms of a project management portfolio, discussing how the cases of Moderna and BioNTech were platform projects, while Daiichi Sankyo's vaccine development is considered a breakthrough project, explaining the differences in development timelines.

Section 5.5 explores the potential of digital platforms in improving the performance of pharmaceutical platforms and inducing network effects, illustrating how the integration of digital and drug development platforms could create an industrial platform that leads to many innovations.

Section 5.6 discusses the potential for creating digital platforms in the manufacturing process to exert network effects in the manufacturing sector by enabling numerous partnerships and rapid manufacturing scale-up, with BioNTech's modularized manufacturing facility, BioNTainer, as an example.

Section 5.7 emphasizes the importance of regulatory flexibility and data sharing in accelerating development and approval during a crisis, as demonstrated during the COVID-19 pandemic, with initiatives like Accumulas and the FDA's precisionFDA showing the potential of collaborative platforms to streamline regulatory processes and foster innovation.

Section 5.8 discuses patent issues related to mRNA vaccine technology, noting that many underlying patents are in the public domain or nearing expiration, which may impact the patentability of future mRNA-based therapies.

Section 5.9 recognizes the unique circumstances of the COVID-19 pandemic as important factors that enabled rapid vaccine development, while questioning whether these conditions will be replicated in other settings.

Section 5.10 describes the limitations of the present study, including its focus on a limited number of case studies and reliance on qualitative data, and suggests directions for future research, such as investigating a broader range of drug platform technologies, conducting quantitative analyses, and examining the role of digital platforms in drug discovery.

Section 5.11 summarizes the study's valuable insights into the role of platform strategies in accelerating drug development and the importance of integrating these strategies into the core of pharmaceutical company operations.

In conclusion, this study demonstrates the importance of the pharmaceutical industry harnessing the "power of the platform" and provides concrete directions for leveraging its potential. The discussion should be expanded to explore how companies and policies can work together to address the health and healthcare challenges facing people around the world, utilizing the power of platforms to drive innovation, collaboration, and ultimately, better health outcomes for all.

Chapter 1: Introduction and Research Questions

1.1. Introduction

The COVID-19 pandemic, precipitated by the SARS-CoV-2 virus, has inflicted profound socioeconomic detriments, manifesting in extensive morbidity and leading to millions of fatalities across the globe[1]. As of 31 March 2024, over 774 million confirmed cases and more than seven million deaths have been reported globally[2].

The advent and dissemination of vaccines and antiviral therapies targeting SARS-CoV-2 have significantly mitigated the regional and international repercussions and burdens imposed by COVID-19[3]. Among these interventions, vaccines emerged as a pivotal innovation during the pandemic. Research conducted by Oliver et al. posits that the deployment of COVID-19 vaccines on a global scale is projected to have prevented approximately 19.8 million deaths within the initial year of its introduction (December 8, 2020-December 8, 2021) [4]. Furthermore, analyses by the Commonwealth Fund suggest that over a span of two years, from December 2020 to November 2022, vaccination efforts have averted an additional 18 million hospital admissions and 3 million mortalities, culminating in an estimated healthcare cost savings of $1.15 trillion within the United States [5].

The Moderna vaccine (Spikevax) and BioNTech/Pfizer vaccine (Comirnaty), were developed within 300 days of the COVID-19 pandemic's onset, whereas Daiichi Sankyo vaccine (DS-5670) took approximately 1000 days[6,7]. Despite the high priority placed on vaccine development during the COVID-19 pandemic by most nations and companies, Daiichi Sankyo, which also utilizes the mRNA technology as the vaccine, lagged even with substantial support from the Japanese government.

This study examines the development processes and outcomes of the Moderna vaccine (Spikevax), BioNTech/Pfizer vaccine (Comirnaty), and Daiichi Sankyo vaccine (DS-5670) in term of the development speed, through the lens of platform theory perspectives. Additionally, it explores the role of corporate strategies in contributing to these differences. The novelty of this research lies in its application of platform theory to the biopharmaceutical sector, a relatively unexplored area. Also, unlike previous studies that predominantly focused on external factors like national funding

or the history of mRNA technology, this research uniquely concentrates on the internal strategies involved in the development of COVID-19 vaccines.

1.2. Research Questions: Why Could Moderna or BioNTech Develop the Vaccine So Rapidly?

This study aims to discover the mechanisms behind the success of Moderna and BioNTech in developing effective vaccines earlier than their competitors. To address this primary question, we have established three sub-research questions and will conduct an in-depth analysis. The analysis will be informed by interviews with experts and stakeholders, grounded in publicly available information, and discussed based on this evidence.

1.2.1. Why Were the Concepts of mRNA, LNP Drug Platforms Established?

We will trace the historical development of each technology, which occurred before the establishment of each company, and also examine the foundation of the companies that utilize the technology as a drug platform. This will allow us to understand why and how their platforms became viable for drug development and why and how they led to the pharmaceutical business.

1.2.2. Why Were Organizations Based on Drug Platforms that Enable Rapid Vaccine Development Constructed?

Following the founding of Moderna and BioNTech, we examined how these companies constructed organizational capabilities that were conducive to rapid vaccine development. This analysis focused on the strategies employed by these companies to build their internal capabilities, foster a rational corporate culture, secure ample funding, acquire sufficient knowledge and intellectual property, develop digital or automated infrastructure, and establish collaborations with external partners. By understanding the development of these organizational structures, we were able to identify the critical mechanisms that positioned Moderna and BioNTech for success in the race to develop COVID-19 vaccines from the capability development aspect.

1.2.3. Why Could Moderna or BioNTech Develop the Vaccine so Rapidly?

Building upon the insights gained from the second sub-research question, we delved into the specific mechanisms that allowed Moderna and BioNTech to successfully develop their vaccines

in record time. This analysis considered various aspects, such as the companies' agility in adapting their platforms to target the COVID-19, their ability to leverage existing technologies and infrastructure, and their capacity to scale up manufacturing and distribution. By examining these mechanisms, we aimed to identify the key factors that differentiated Moderna and BioNTech from their competitors and enabled their rapid response to the global health crisis.

1.2.4. Methodology

To ensure a robust and comprehensive analysis, we gathered data from multiple sources, including:

1. Interviews with experts and stakeholders: We conducted interviews with individuals who have direct knowledge of or experience with Moderna and BioNTech's vaccine development processes or the pharmaceutical industry, such as company executives, scientists, collaborators, and experts in these fields. These interviews provided valuable first-hand insights into the challenges faced and the strategies employed by these companies.

2. Publicly available information: We collected and analyzed data from a wide range of publicly available sources, including scientific publications, company reports, press releases, and news articles. This information helped us construct a detailed timeline of events and identify key milestones in the vaccine development process.

3. Discussion and synthesis of evidence: We discuss and synthesize the collected evidence to identify patterns, trends, and critical factors that contributed to Moderna and BioNTech's success. This discussion was guided by our sub-research questions and aims to provide a comprehensive understanding of the mechanisms behind their rapid vaccine development.

1.2.5. Implications and Contribution to Platform Theory

By addressing these sub-research questions and conducting a thorough analysis of the available evidence, we aim to provide valuable insights into the mechanisms that enabled Moderna and BioNTech to develop effective COVID-19 vaccines more rapidly than their competitors. These insights may have important implications for future pandemic preparedness and the development

of novel vaccines and therapeutics. Additionally, we could extract valuable insights that contribute to platform theory itself.

Chapter 2: Prior Research and Hypothesis Development

2.1. Why Could Moderna or BioNTech Develop the Vaccine So Rapidly?

Several studies have been undertaken with the same approach as the current research question.

In the Kutar et al. study, the reasons for this are summarized as "All aspects of COVID-19 vaccine development, including vaccine formulation, clinical trials, manufacturing, and regulatory review, have been accelerated," and then a new vaccine technology, coronavirus knowledge, effective scale-up, international collaboration, funding, and regulatory investigations are comprehensively analyzed[8].

Also, Okumura 2022 et al. analyzed the factors that enabled the rapid development of the COVID-19 mRNA vaccine. They analyze factors such as regulatory harmonization, public-private partnership programs to stimulate investment, BioNTech's and Moderna's long-term R&D efforts, and Moderna's extensive experience in clinical trials. As a control, the study also analyzes Daiichi Sankyo, pointing out the pharmaceutical company's lack of experience in technology development and clinical trials[9].

In the article "Fast-forward: Will the speed of COVID-19 vaccine development reset industry norms?", McKinsey summarizes several key factors that contributed to the rapid development of COVID-19 vaccines:

1. Regulatory agencies streamlined processes and collaborated closely with vaccine developers, enabling faster review and approval of applications, overlapping clinical trial phases, and implementing rolling regulatory reviews.

2. The widespread availability of knowledge about related infectious diseases (e.g., SARS and MERS) and the swift publication of the SARS-CoV-2 genome sequence facilitated the rapid design and development of vaccines.

3. Extensively researched novel platform technologies, such as mRNA and viral vectors, allowed for fast development, adaptability, and scalability of vaccine candidates.

4. Companies and governments made significant investments at risk, making decisions based on limited information and funding manufacturing capacity in parallel with clinical trials to accelerate timelines.

5. Operational excellence and innovation, including round-the-clock lab operations, streamlined decision-making processes, and the strategic use of epidemiological models to open clinical trial sites in emerging hot spots, contributed to the speed of vaccine development.

The article concludes that these factors, along with unprecedented collaboration among pharmaceutical companies, biotech firms, health authorities, and public and private institutions, enabled the development of COVID-19 vaccines at an unparalleled pace[10].

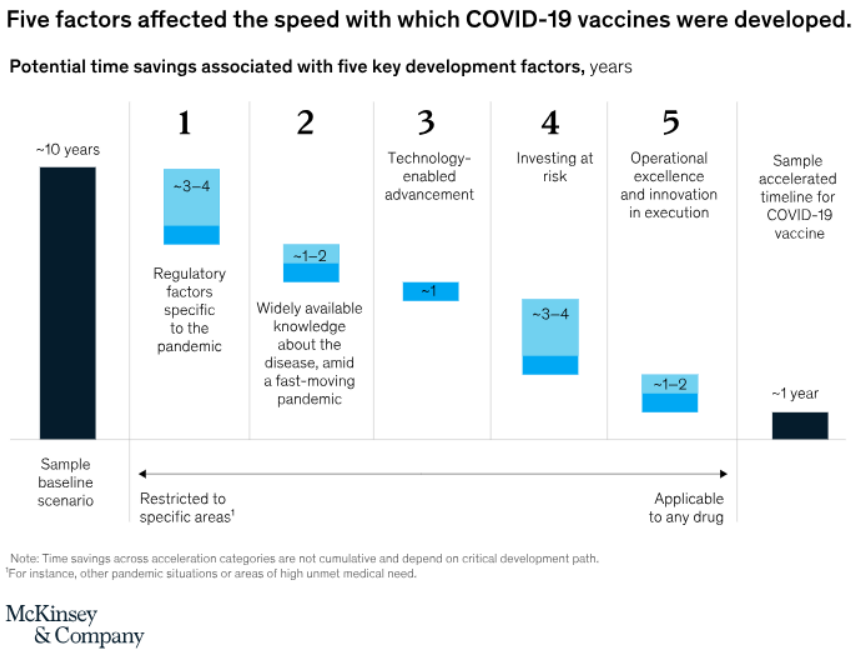


Figure 2.1 Five Factors Affected the Speed with Which COVID-19 Vaccines Were Developed[10]

The Harvard Business School case “Moderna (A)” is not a text compiled around the question of why vaccines were developed so rapidly, but it does provide a detailed summary of the company Moderna, including how it was founded and its digitization process[11].

However, in each case, there is no detailed analysis of how the drug platform was treated as a business strategy by the pharmaceutical companies and how this led to rapid development.

2.2. About Platform Theory:

Prior research suggests that there are three types of platforms: internal or firm-specific platforms and external, industry-wide platforms, or digital platforms. An internal (firm or product) platform is defined as a set of assets organized in a common structure that allows a firm to efficiently develop and produce a series of derivative products. External (industry) platforms are defined as products, services, or technologies that serve as the basis for external innovators organized as an innovative business ecosystem to develop their own complementary products, technologies, and services[12]. Digital platforms have revolutionized the way businesses operate, connecting multiple market actors and growing through network effects. The most valuable companies today, like Apple, Microsoft, Alphabet, Amazon, Facebook, Alibaba, and Tencent, are built on digital platforms, encompassing a market value of more than $6 trillion as of January 2020[13] and more than $11 trillion as of May 2024.

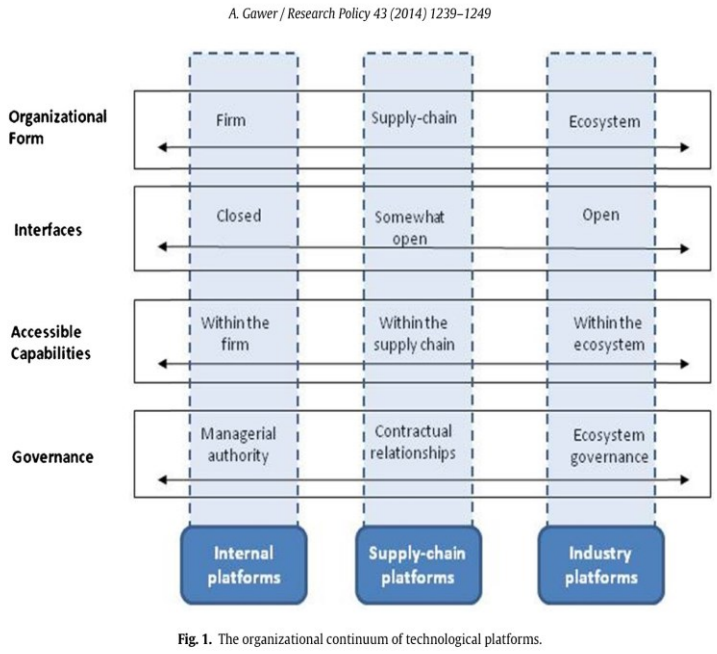


Figure 2.2 The Organizational Continuum of Technological Platforms[13]

2.2.1. The Product-Level Platform

Prior research has indicated that product platforms allow companies to offer distinctive products to the market while saving development and production resources.

Specific benefits include:

Product differentiation: companies can differentiate their products by developing a variety of models from a common platform that appeal to different customer segments.

Development and production efficiency: new products can be developed more quickly and at lower cost by using common parts and manufacturing processes; improved economic efficiency.

Reduced manufacturing costs: use of common machinery, equipment, and tooling reduces manufacturing investment.

Simplified system complexity: reduced number of parts and processes reduces logistics, inventory management, and other costs.

Reduced risk: each product developed from the platform can have its own unique components and manufacturing processes.

Reduced cost of ownership: use of common parts and manufacturing processes allows new products to be developed more quickly and at lower cost.

Improved service: sharing parts between products reduces inventory of manufacturing and service parts, which can improve service levels or reduce service costs. The benefits of sharing parts between products are noted following[14].

One of the benefits of product-level platforms is the benefit of commonality, which can be broken down into three categories: (1) revenue benefits, (2) cost savings, and (3) risk benefits[15]. According to the Crafting Platform Strategy Based on Anticipated Benefits and Costs, three benefits of commonality are (1) market benefits, (2) cost savings, and (3) risk benefits[15].

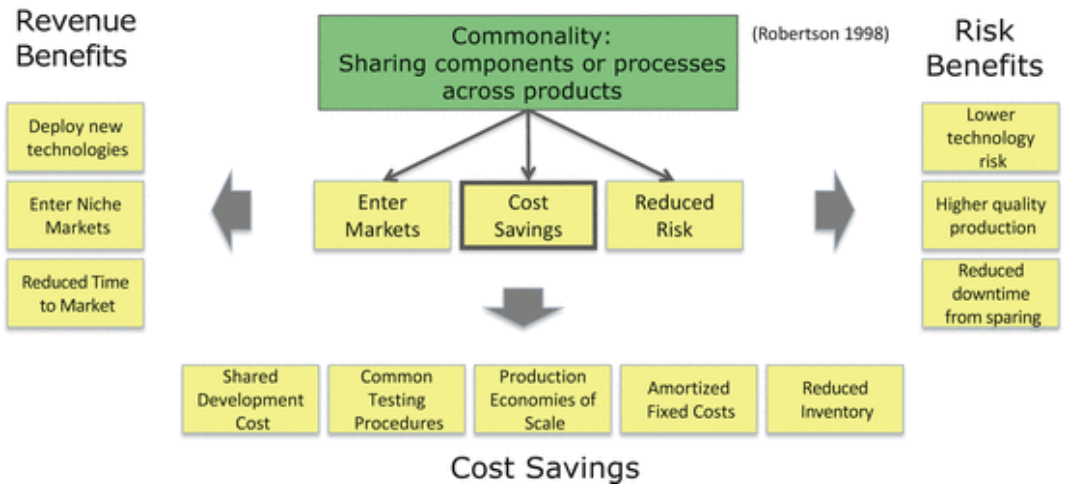


Figure 2.3 The Benefits of Product-Level Platforms Include the Benefit of Commonality[15]

2.2.1.1 Examples from the Automotive Industry

In many industries, platforms play an important role in improving development efficiency, but the way they are organized to take advantage of them is also important. For example, in the automotive industry, the platform, the chassis, facilitates the acceleration of the development process. More specifically, Toyota has created the Corolla and Prius based on the TNGA-C chassis platform. On the other hand, strategic organizational management is important to optimize the use of the platform. At Toyota, so-called heavyweight project managers lead vehicle product development, but such a project-oriented organization is not suitable for platform management. This is because heavyweight project managers have strong incentives to optimize their own products, and if the product development project team is strong, it will be difficult to efficiently utilize a platform for common use among multiple projects. Therefore, the platform manager is positioned above the multiple project managers[16].

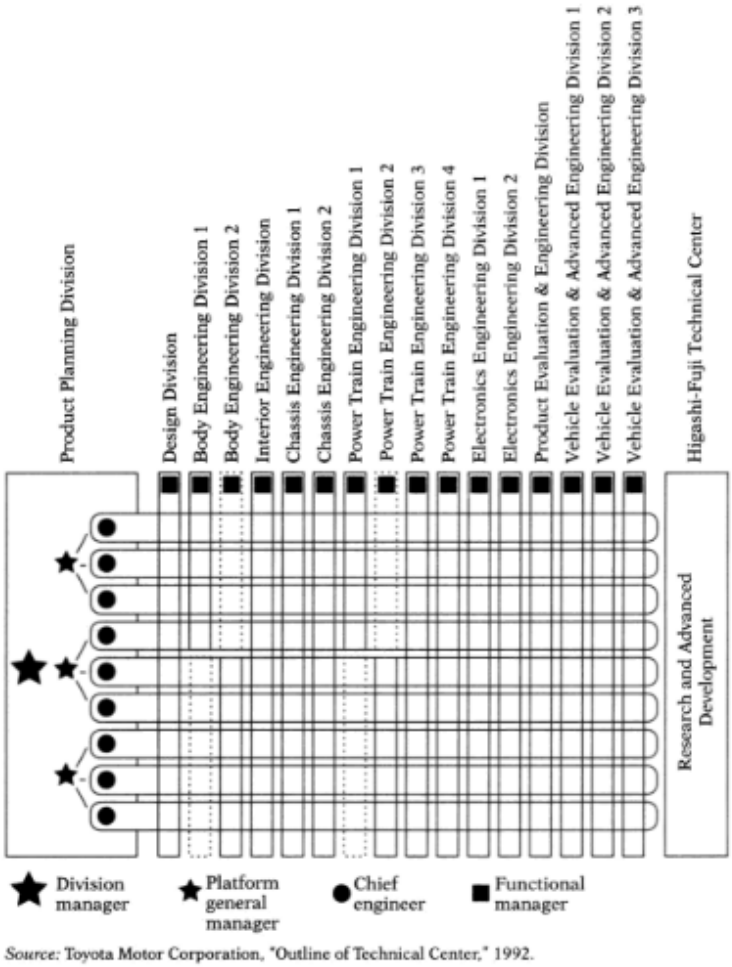


Figure 2.4 The Role of the Platform Mamager[16]

2.2.1.2 Definition of Drug Platform in This Thesis

In this thesis, we use the term "drug platform" to refer to a product-level platform or technology platform. This term is often called "modality" in the pharmaceutical industry.[17]

Meyer and Lehnerd (1997) offer a narrow definition of a product platform as a set of subsystems and interfaces that form a common structure from which a stream of derivative products can be efficiently developed and produced.[18] McGrath (1995) defines a product platform as a collection of common elements, particularly the underlying core technology, that is implemented across a range of products.[19] Robertson and Ulrich (1998) propose a broader definition, describing product platforms as a collection of assets (e.g., components, processes, knowledge, people, and relationships) that are shared by a set of products.[14,20]

In the context of the pharmaceutical industry, mRNA and LNP technologies can be considered as product-level platforms or technology level platforms. These technologies align with the definitions above, as mRNA technology has a set of common components such as "Cap," "Poly(A) tail," and "UTRs," while LNP technology includes components like "anion" and "cation."[21,22] These shared elements constitute the core of their respective platforms.

Furthermore, these technologies enable the development of various drugs by modifying the mRNA sequence or the components of the LNP. The common core technology allows these assets to be shared across a range of product families. For example, changing the mRNA sequence can adapt the platform to target different diseases or produce specific therapeutic proteins. Similarly, altering the LNP components or structure can optimize the delivery system for particular applications or tissue targets.

The modular nature of mRNA and LNP platforms, along with the ability to share assets and knowledge, is consistent with the key features of product platforms described in the literature. This approach allows pharmaceutical companies to develop and produce a stream of derivative products efficiently, each customized for specific therapeutic needs, while benefiting from economies of scale and scope provided by a shared platform.

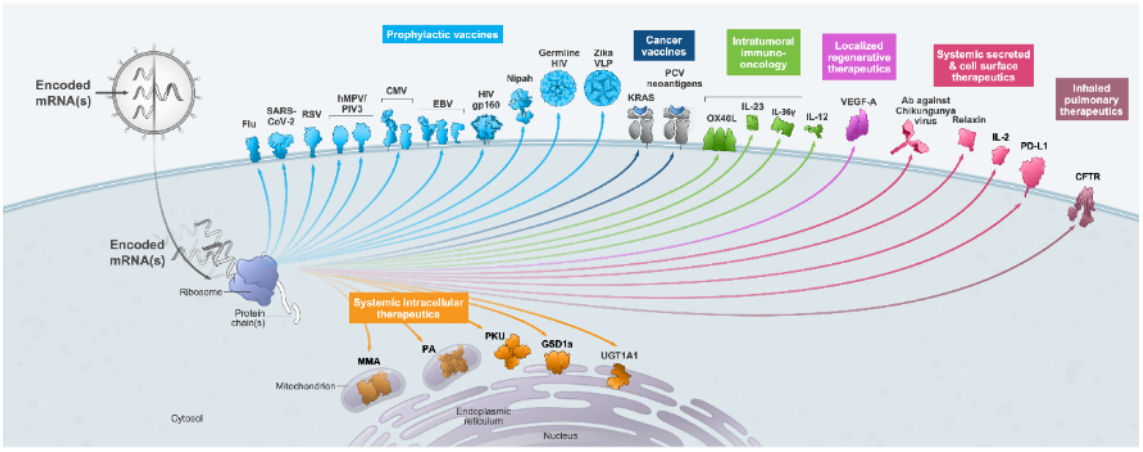


Figure 2.5 A mRNA Drug Platform Image (Moderna)[23]

2.2.2. The Industry-Level Platform

2.2.2.1. Definition and Categories

An industrial platform is a foundational framework developed by one or more firms upon which numerous firms build further complementary innovations, creating a network effect. Unlike internal platforms, which are proprietary and confined within a single organization, industry-level platforms are accessible to external firms, fostering broader ecosystem innovation [12].

The book "The Business of Platforms: Strategy in the Age of Digital Competition, Innovation, and Power" provides the following basic descriptions of innovation platforms, transaction platforms and hybrid enterprises[24].

Innovation Platforms

Innovation Platforms are platforms that serve as the foundation for products and services that other companies and developers can build upon. They provide the tools and resources to create new applications, services, or products. Examples include OS, Intel's CPU, and smartphones. Innovation platforms foster innovation throughout the ecosystem and are augmented by third-party products and services built on top of the platform.

Transaction Platforms

Transaction platforms are platforms that function as marketplaces connecting buyers and sellers. The main purpose of these platforms is to facilitate transactions between them and create a more efficient marketplace. Examples include eBay, Uber, and Airbnb. Transaction platforms increase market liquidity by creating value through the matchmaking process, reducing transaction costs, and providing a wider range of choices.

Hybrid Companies

Hybrid companies are those that have characteristics of both a transactional platform and an innovation platform. These companies not only provide a marketplace but also offer tools and services that other companies and developers can use. For example, Amazon serves both as an online retailer (transaction platform) and as a provider of cloud computing services to other

companies through AWS (innovation platform). Through these complementary functions, hybrid companies create a diversified business model and secure different revenue streams.

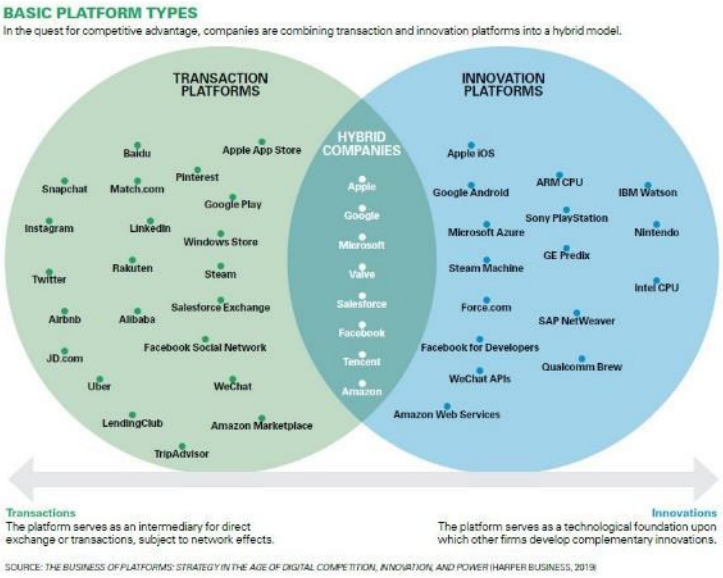


Figure 2.6 Basic Platform Types[24]

The Dominance of Digital Platforms: A Study of the World's Most Valuable Companies and Unicorns

Studies show that the world's most valuable publicly traded companies, as well as the world's first companies to grow to the $1 trillion level, are built on digital platforms that grow through network effects. The top companies by market capitalization are Apple, Microsoft, Alphabet, Amazon, Facebook, Alibaba, and Tencent; as of January 2020, the market capitalization of these seven companies exceeds $6.3 trillion, all of which are platform businesses. A study of the list of 959 unicorns (private companies valued at $1 billion or more) existing as of December 31, 2021, estimated that 42% were platform businesses, and of these 18% were innovation platforms and 82% were transaction platforms. The innovation platform premium in the sample was 34%[25].

2.2.2.2. Network Effect

One of the reasons behind the rapid development of these industrial platforms is the network effect. The network effect refers to the phenomenon whereby the value of a product or service increases with the number of people using it. In other words, the more users that participate in a

platform, the more valuable that platform becomes as a whole. This is especially true in the platform business model, where many digital platforms leverage this principle[24].

2.2.2.3. Example of an Innovation Platform: Intel

Intel's case is a well-known example of a successful innovation platform strategy. In the 1990s, Intel faced the challenge that improvements in the performance of its CPUs did not translate into improvements in PC performance. The reason was that the Peripheral Component Interconnect (PCI) architecture was outdated and was the bottleneck. Therefore, Intel decided to develop a new PCI architecture and release it to the public free of charge. As a result, the bottleneck in the PCI architecture was eliminated, and improvements in CPU performance directly led to improvements in PC performance. Subsequently, the CPU became the bottleneck, and the structure was such that higher CPU performance led to higher customer value.[26]

2.2.2.4. Example of a Digital Platform: Open AI

ChatGPT is an example of a digital platform that digitizes the product platform and interfaces that enable third parties to connect with the industry platform, including the provision of services. An article states that "It ‘productized’ and then ‘platformized’ generative AI technology" and also said that these APIs can connect third-party developers to the system of ChatGPT, integrating its functionalities into diverse applications and services. This aspect of ChatGPT is what truly "platformized" it, as it enables a vast network of developers and businesses to build upon and extend the core technology in innovative ways[27].

2.3. Why Does the Platform Strategy Enable Rapid Vaccine Development? Hypothesis Development

This section presents theoretical frameworks to explain how the pursuit of drug platform concepts can lead to rapid vaccine development. The discussion in this section serves as a foundation for the subsequent analysis in Chapter 3, which examines the factual information surrounding the actual development of COVID-19 vaccines, and Chapter 4, which synthesizes the ideas from Chapter 2 and 3 to provide a comprehensive explanation of the rapid vaccine development process.

2.3.1. Why Was the Concept of the mRNA and LNP Drug Platforms Established?

First and foremost, a product-level platform should be built upon foundational elements. In the case of generative AI technology, the underlying technology is machine learning, particularly neural network technology. However, to become an innovation platform, it should also have an operating system or API. Similarly, we can expect that a drug platform should be built on a strong scientific foundation and should have some interfaces.

Additionally, to transform the technology into a platform, a supportive corporate strategy should be in place. On top of that, the development of drug platforms requires huge investments over a long period of time. This is similar to the large investments required for platform development in industries such as automobiles and aircraft. For example, generative AI technology itself is just a technology and should not be considered a platform on its own. By providing an interface, it can become a platform, but this requires corporate power and leadership. In the case of OpenAI, it received $10 billion in funding from Microsoft, enabling it to create a platform. Likewise, in the case of drug platforms, there should be a significant intentional strategy to develop the drug platform concept beyond the mere technology[27].

2.3.2. Why Were Organizations Based on Drug platforms that Enable Rapid Vaccine Development Constructed through the Platform Strategy?

2.3.2.1. Why Does the Platform Strategy Enable the Creation of a Rational Corporate Culture?

The platform strategy enables the creation of a rational corporate culture by providing a clear, unifying objective for the entire organization. As stated in a McKinsey article, "To align R&D with its purpose and guide the design of the new operating model, an organization-wide aspiration or 'North Star' is needed."[28] By centering the company's efforts around a drug platform, employees have a shared understanding of the company's mission and values, fostering a sense of unity and purpose.

Moreover, because drug platforms are built upon a scientific foundation, corporate leaders must have a deep understanding of the underlying technology to make informed decisions. This focus

on scientific expertise at the leadership level promotes a culture of scientific-based decision-making and encourages employees to prioritize scientific evidence over other considerations.

2.3.2.2. Why Does the Platform Strategy Attract Funding?

The concept of the drug platform has enabled access to a diverse range of funding opportunities, significantly enhancing the potential for substantial funding. This concept contributes to the construction of effective funding mechanisms due to its intrinsic characteristics. There are four primary reasons why the platform concept is closely tied to funding.

Firstly, unlike traditional drug development projects, which are often isolated in nature, the platform approach appeals to investors as a product platform, offering a more continuous and potentially expansive investment opportunity. For instance, in the realm of mRNA-based drug discovery, the simple alteration of nucleotide sequences can theoretically enable the development of subsequent therapeutics, making it an attractive investment proposition.

Secondly, the inherent flexibility of the product platform allows for a broad targeting of diseases. In the case of mRNA therapeutics, altering sequences can potentially create vaccines for infectious diseases or treatments for cancer. Typically, vaccine development for infectious diseases might attract public funding, while cancer therapies could attract private investment, broadening the scope of potential funding sources. In general, drug development targeting vaccines and infectious diseases is difficult to fund. For example, drug development for infectious diseases is an area that is generally underfunded: the term "neglected tropical diseases" (NTDs) has been coined[29]. Development activities obviously require funding sources, but vaccine development is particularly risky: according to MIT Sloan finance professor Andrew Lo, "the economic model for vaccines is broken." Lo has analyzed data from hundreds of thousands of clinical trials of diseases and drugs to estimate the likelihood of success for each. Those researchers have found that despite the overwhelming 40% success rate of vaccines, there are fewer and fewer companies developing them. To find out why, ALPHA researchers ran a business simulation to determine the rate of return on investment in vaccine development. The results were extremely low: only a few million dollars. In fact, the lab estimates that the internal rate of return on a portfolio of vaccines using today's typical pricing model is negative 60%[30]. Hence, the

platform approach must be really important to attract funding for vaccine development in order to appeal investors.

Thirdly, the appeal to investors is also bolstered by the growth of the industry platform itself, as there are a lot of high growth platform companies and there is the premium which we have explained above. The industry platform evolves, and it becomes more attractive to investors, who see value in potential for exponential growth because of network effects.

Fourthly, since drug platforms are foundational scientific technology, the solid drug platforms are in demand for technological collaboration from other pharmaceutical companies, which leads to new funding. Moderna and BioNTech can then undertake the development and further funding. This is also a way to acquire knowledge and experience. Since platform is not related to the specific disease, partnerships can be formed for each disease, and funding can be obtained from multiple partners.

2.3.2.3. Why Does the Platform Strategy Enable the Integration of Knowledge?

The platform strategy must integrate a company's knowledge into the platform. First, since efforts would be centered around the platform, companies form their knowledge around it. Second, as their efforts would be invested while considering the platform, the company's knowledge would be connected through the platform's knowledge. Finally, since they focus on the platform, their efforts would be sequenced in the time horizon, and their knowledge would accumulate over time. Furthermore, since the company focuses on the drug platform, it has a strong incentive to invest in the platform. Consequently, the R&D expenses also contribute to the accumulation of knowledge.

2.3.2.4. Why Does the Platform Strategy Enable Investing in Automated Facilities or Digital Infrastructures that Enhance Corporate Capacity?

The drug platform enables investment in automated facilities or digital infrastructures. There are several reasons why the platform strategy enables the creation of a digital platform on top of the drug platform.

First, since drug platforms enable attracting funding, as previously explained, the funding can serve as a source of funds for investments. Another important aspect is that, as the platform consists of shared technical components, companies can easily understand what kind of infrastructure they should build. If the companies have numerous drug candidates with different mechanisms, they might not be able to identify the essential components of each drug candidate. In contrast, since the platform shares the same scientific mechanism, companies can invest in the core function of the drug platform, which would effectively enhance their productivity.

Moreover, if the digital platform has been built on top of the drug platform, it will accelerate collaboration both within the company and with external partners. The digital interface transforms the product platform into a digital platform. These digital platforms enhance the capabilities of companies through knowledge sharing among partners both inside and outside the organization, means enabling partnerships with external entities such as research institutions, suppliers, and other industry players.

2.3.3. Why could Moderna or BioNTech Develop the Vaccine so Rapidly Using the Platform Strategy?

2.3.3.1. Why Does the Platform Strategy Enable Efficient Project Launching?

First, drug platform companies will effectively start the project if the target falls within the drug platform concept. Since corporate leaders understand the technology, as previously explained, they can make decisions based on their deep understanding of the situation and their technological capabilities. Another key point is that, since the platform would want to collect similar funding for a new disease outbreak, as previously explained, companies would understand that they need to react and move quickly. Additionally, as drug platform strategy companies accumulate their knowledge within the drug platform, they can react with technological confidence without fear of legal issues that may arise if they do not have adequate patents. Furthermore, since they must have the infrastructure in terms of automation or digital technology, they also have the confidence to tackle the issue, and this infrastructure also urges the company to address the challenges.

2.3.3.2. Why Does the Platform Strategy Enable Effective Resource Mobilization?

The drug platform companies would also effectively mobilize their resources for a new disease. First, since the corporate leaders deeply understand the technology, they could have the leadership to deal with the issues. Also, since the employees also understand their platform, they comprehend their mission and how they can use their resources. Second, since the platform would have a lot of funding, they would have ample room to utilize the resources without taking on a lot of risks. Third, since their knowledge is connected to the drug platform concept, the entire company's knowledge could be utilized for the purpose if necessary. Lastly, since the infrastructure, such as automated facilities or digital technology, would be designed for the drug platform, they could utilize it without any changes, making the project truly efficient.

Chapter 3: Case Studies: Comparisons of Moderna, BioNTech, and Daiichi Sankyo

Chapter 3 presents a comprehensive description of the factual information pertaining to the case study companies Moderna, BioNTech, and Daiichi Sankyo. This chapter follows the hypotheses developed in Section 2.3 and connects to Chapter 4, which answers the research questions by synthesizing the theoretical aspects and factual information.

The chapter commences by examining the academic developments that laid the foundation for the establishment of these firms, highlighting the scientific advancements and research that preceded their inception. Subsequently, the background and leadership at the time of the companies' founding are explored, shedding light on the key individuals and their roles in shaping the organizations' direction and usage of platform strategies. The chapter then delves into how these companies built their organizational capacity from inception to the pandemic. This description is conducted through the lens of four critical aspects: corporate culture, funding, knowledge and experience accumulation, and digital and automated infrastructure. Finally, the chapter explains how COVID-19 vaccine development projects were implemented by these companies after the pandemic, highlighting the platform strategies and capabilities they had built before the pandemic.

Through the chapter, we could see why and how Moderna and BioNTech succeeded in developing vaccine rapidly and why and how Daiichi Sankyo fell behind.

Here is a brief overview of each company follows.

3.0.1 Moderna: Pioneering mRNA Technology in Vaccine Development

Moderna, Inc. has a rich history that begins with its formation in 2010 under the name ModeRNA Therapeutics. The company was established by a group of investors and scientists, including Noubar B. Afeyan, Robert S. Langer, Jr., Timothy A. Springer, Derrick J. Rossi, and Kenneth R Chien. Its founding was based on commercializing the groundbreaking research of Canadian stem

cell biologist Derrick Rossi, who had developed a novel method of using modified mRNA for cellular reprogramming[31].

The name "Moderna" is a fusion of "modified" and "RNA," emphasizing its focus on mRNA technologies. By 2011, the company was operational and had begun its journey into mRNA medicine research with Stéphane Bancel joining as the founding CEO. A significant milestone was achieved in 2014 when Moderna expanded its operations by opening new headquarters and labs in Cambridge, Massachusetts. The company's efforts in vaccine development were marked by its first-in-human dose of an mRNA vaccine candidate in 2015, specifically an H10N8 influenza vaccine[32].

Over the years, Moderna has entered into strategic collaborations, such as an exclusive agreement with AstraZeneca in 2013, focusing on the discovery, development, and commercialization of mRNA for treatments in various therapeutic areas[31]. The company's innovation continued to advance with the opening of a state-of-the-art clinical development site in Norwood, Massachusetts, in 2018, and the initiation of first-in-human dosing for a multivalent vaccine, mRNA-1653, in 2017[32].

A pivotal moment in Moderna's history came in 2020 with the development of the COVID-19 vaccine in collaboration with the United States National Institute of Allergy and Infectious Diseases (NIAID) and the Biomedical Advanced Research and Development Authority (BARDA). This achievement was a testament to Moderna's commitment to leveraging mRNA technology in addressing global health challenges. By 2022, the U.S. Food and Drug Administration fully approved Moderna's COVID-19 vaccine, SPIKEVAX, for individuals 18 years and older[33].

3.0.2. BioNTech: Harnessing mRNA Technology for Immunotherapy and COVID-19 Vaccine Development

BioNTech, co-founded by Prof. Uğur Şahin, Prof. Özlem Türeci, and Prof. Christoph Huber in 2008, has been at the forefront of mRNA technology development, aiming to utilize it for individualized cancer immunotherapy. Despite initial skepticism due to mRNA's instability and

low protein production efficiency, BioNTech's co-founders made pivotal scientific breakthroughs over three decades to harness mRNA's full potential. This included solving the low- and short-lived protein production issue and mitigating mRNA's immunogenicity through nucleotide modification, particularly through Katalin Karikó's work on uridine[34].

BioNTech's significant milestones include developing the first vaccines using non-nucleoside modified RNA for personalized cancer therapies and pioneering intravenous nanoparticle delivery of mRNA vaccines in humans. Their relentless innovation culminated in the development of the first authorized mRNA COVID-19 vaccine in 2020, marking a historic moment in medicine and vaccine development[34].

3.0.3. Daiichi Sankyo: Japanese Traditional Pharmaceutical Company

Daiichi Sankyo Company, Limited, with its headquarters in Chuo City, Tokyo, Japan, is a prominent player in the global pharmaceutical industry. The company came into existence on September 28, 2005, through the merger of two historical entities in the pharmaceutical field: Sankyo Co., Ltd., established in 1899, and Daiichi Pharmaceutical Co., Ltd., established in 1915. This merger blended the rich legacies of both companies, positioning Daiichi Sankyo as a significant force in the pharmaceutical sector[35].

As of March 31, 2023, Daiichi Sankyo reported substantial financial figures, with a capital of 50 billion yen and consolidated sales reaching 1.278 trillion yen for the fiscal year. The company's global workforce stands at 17,435 employees, showing its vast operational scale[36].

The company's commitment to innovation and patient care is encapsulated in its corporate slogan, "Passion for Innovation. Compassion for Patients.", which reflects its dedication to advancing pharmaceutical innovation while maintaining a patient-centric approach[36].

Daiichi Sankyo holds a prominent position in the Japanese pharmaceutical industry, ranking 4th in sales among its national peers as of 2023 and securing the 25th spot in the global pharmaceutical industry rankings in 2022. This status underscores its significant contributions to healthcare and medical research[36].

In response to the COVID-19 pandemic, Daiichi Sankyo has been at the forefront of vaccine research and development. Notably, the company has made significant strides with its DS-5670 vaccine, an mRNA-based vaccine targeting COVID-19. The development of this vaccine involved launching a national clinical trial in January 2022 to explore its booster effect and securing domestic manufacturing and marketing approval in Japan for its monovalent mRNA vaccine, "Daichirona® Intramuscular Injection", in August 2023. Further, in November 2023, the company obtained approval for a partial change in Japan for DS-5670 to target the Omicron strain XBB.1.5 lineage, showcasing its ongoing efforts to adapt to the evolving pandemic landscape[35].

3.1. Why Were the Concepts of mRNA and LNP Drug Platforms Established?

This section provides factual information on the academic developments that laid the foundation for the establishment of these firms, highlighting the scientific advances and research that preceded their founding. It then examines the background and leadership of each company at the time of its founding and describes the key individuals and organizations, as well as their roles in shaping the direction of the organization and its use of platform strategies.

The Convergence of Scientific Disciplines for the Development of mRNA Vaccines

First, the successful development of mRNA vaccines required contributions from scientists in many different fields. While all scientific progress is a complex interrelationship between different disciplines, at least four distinct lineages can be found in the development of mRNA vaccines from the fields of molecular biology, lipid chemistry, microbiology, and immunology, each of which made important contributions to their development [37].

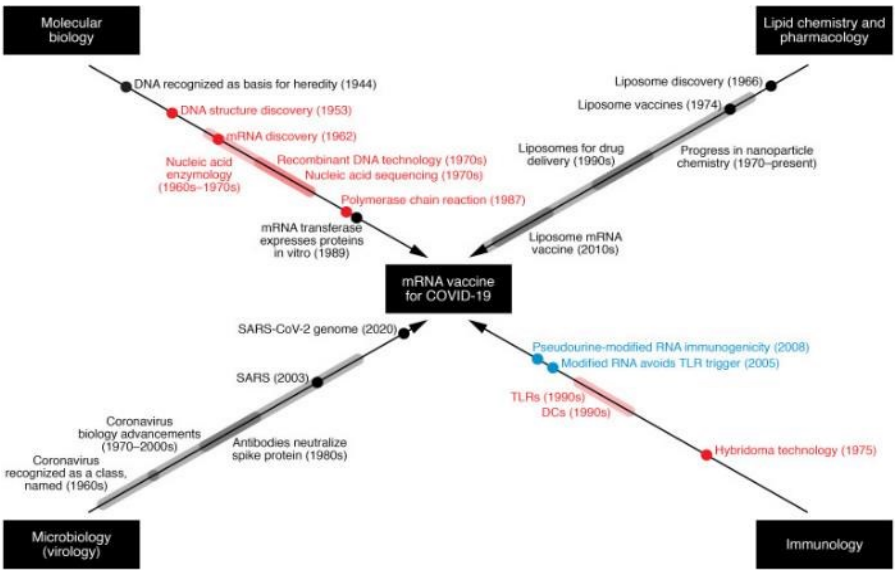


Figure 3.1 Four Major Lines of Research Converge to Produce mRNA Vaccines Against COVID-19[37]

Development of the mRNA Technology and Lipid Nanoparticle Technology

The establishment of the mRNA and LNP drug platform concepts can be attributed to the foundational accumulation of knowledge in the natural sciences, which provided essential insights necessary for the development of these platforms. This body of scientific discovery formed the underpinning for the conceptualization of platforms that harness the potential of mRNA and LNP technologies in drug development.

Both mRNA and liposomes were discovered in the 1960s. In 1978, scientists used fatty membrane structures called liposomes to transport mRNA into mouse and human cells to induce protein expression[38]. By the late 1980s, investigations of mRNA structure and function resulted in the development of in vitro-transcribed (IVT) mRNA. Since the first proof-of-concept animal study in 1990, numerous strategies have been explored to ameliorate the instability and immunogenicity of IVT mRNA. In 1993, the first mRNA vaccine was made of liposomes and mRNA encoding an influenza virus nucleoprotein[39]. In 2005, Katalin Karikó and Drew Weissman discovered that certain modifications of the building blocks of RNA prevented unwanted inflammatory reactions and increased the production of desired proteins, which discovery led to the Nobel Prize in Medicine in 2023[40].

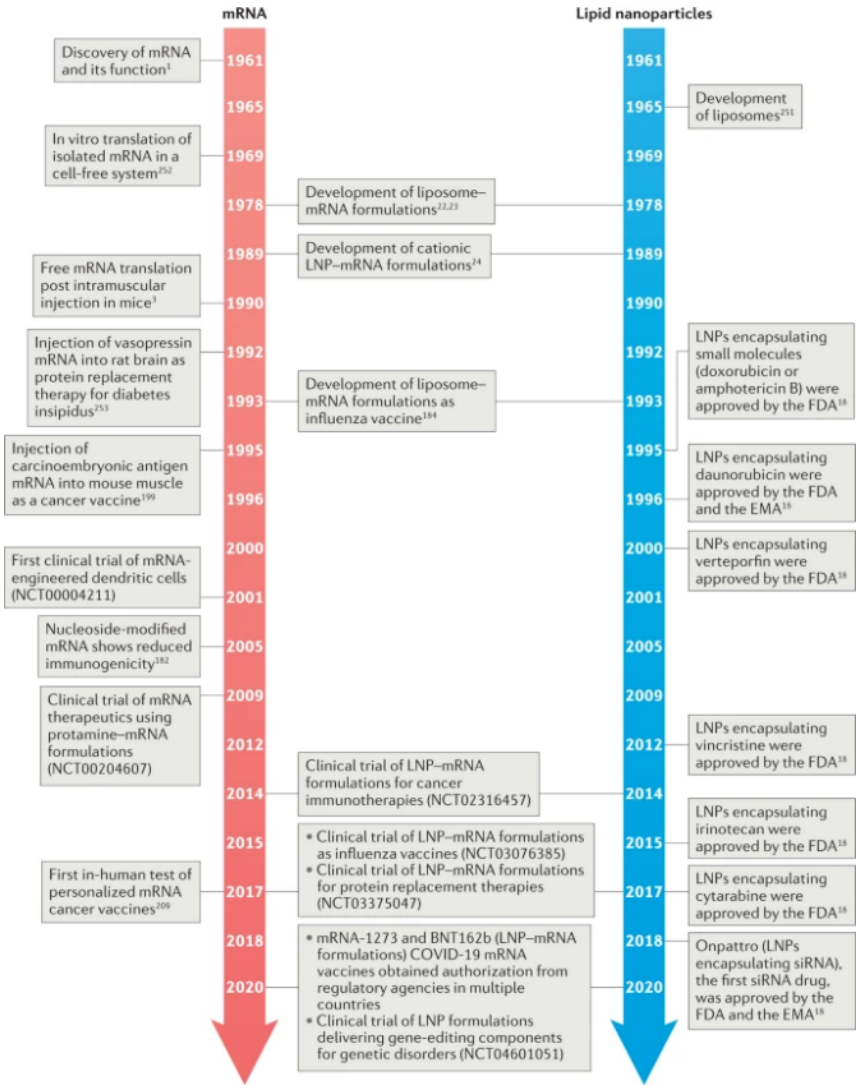


Figure 3.2 Timeline of Some Key Milestones for mRNA and Lipid Nanoparticle Development[39]

3.1.1. Moderna: Flagship's Structured Innovation Process and mRNA Platform Strategy

Flagship's Structured Innovation Process

Moderna started out as project LS18 in 2010 at Cambridge-based Flagship, at the time called Flagship Ventures. To understand the genesis of Moderna, one must understand Flagship," Noubar Afeyan, founder of the Flagship, explained. "Flagship follows a structured four-stage process to pioneer innovation through scientific discovery. The first stage is exploration. Hypotheses are formulated that are likely to yield breakthrough innovations; in Moderna's example, "What if mRNA could be a drug?" in Moderna's case. If these explorations prove promising, the second step is a prototype company (ProtoCos). If the science underlying the venture proves promising,

the third step would be NewCo, with the flagship investing a significant amount of capital. At this point, still, an in-house venture, the Flagship, and the venture team will hire a broader team to further develop the business. Fourth, NewCo spins out and becomes GrowthCo. At this stage, the company will begin building relationships with investors and partnering with outside parties[11,41].”

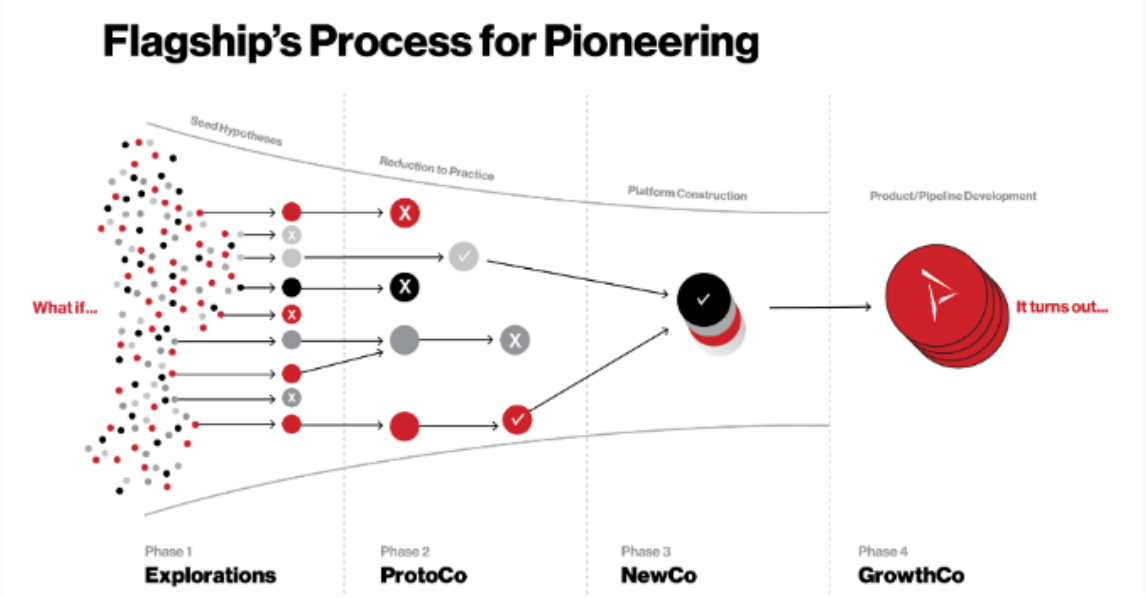


Figure 3.3 Flagship's Process for Pioneering[41]

Noubar Afeyan's Vision for Moderna

“This is not your typical unmet-need/breakthrough-solution approach to coming up with a business,” Afeyan explained. “We subscribe to a Darwinian process, covering creation, iteration, and selection of groundbreaking innovations for which no precedent exists. Asking ‘What if?’ questions propel you far into the future.”[11] As Noubar Afeyan met with Bob Langer and Derrick Rossi to review recent data on modified mRNA for reprogramming into induced pluripotent stem cells, Noubar came up with a different use for artificial mRNA as a new kind of medicine. The idea is that mRNA could be used to allow patients to produce their own biological agents. With that idea, he began a month-long exploration within the flagship VentureLab group, which eventually became Newco LS18, Inc[111]. Afeyan was interested in the logic of the platform, that if one drug works under certain conditions, many drugs will work, and if proven methods were introduced, the time to market for new drugs could be greatly reduced. He said, “We had long had a vision of creating new types of medicines for humans,” and also said “Developing drugs is the

most rewarding thing to do in the pharma industry. But at this point, big pharma only pursues incremental innovations, which leaves the riskier, less proven approaches unexploited".[11]

Moderna's Positioning of mRNA as a Product / Technological Platform

Following the history, Moderna has positioned mRNA as a product / technology platform for its corporate activities. For example, Moderna states about itself, "Messenger RNA is not new technology, but we are discovering new ways to use it to treat and prevent illnesses and diseases. Since our founding in 2010, we have worked to build the industry's leading mRNA technology platform.". It also says that "Moderna's name combines the words "modified" and "RNA", which happens to contain the word "modern."[32]. Thus, Moderna is a company that is aware of mRNA technology as a platform and built around it.

At Moderna, they have been clearly aware of the need to implement the utilization of the product platform feature for the efficient development of derivative products by utilizing a common infrastructure in mRNA-based pharmaceuticals. According to Melissa Moore, Chief Scientific Officer, "mRNA is the software, and LNPs are the hardware needed to make therapeutics work. In other words, we are not just an mRNA company; we are a delivery company. If Moderna can prove its approach works with one drug, it will work with all the others as well. mRNA is a platform, like the iPhone. Individual drugs - prophylactic vaccines and therapeutics - are like apps. Once the platform is functional, we can develop many apps on our platform." He said[8].

Moderna's Securities and Exchange Commission (SEC) document (10-K, 2019) also said that it will focus on mRNA because of the potential and foundational mechanism with the following diagram. Below, we can see that central dogma explains the most fundamental significance of the mRNA technology of Moderna.

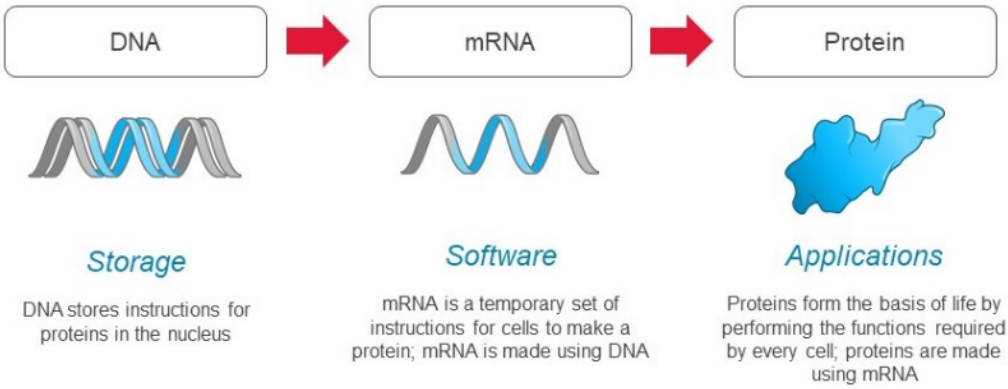


Figure 3.4 Moderna's Securities and Exchange Commission (SEC) Document (10-K, 2019)

The concept used in the Moderna letter below illustrates that various drugs would come out from the mRNA platform.[23]

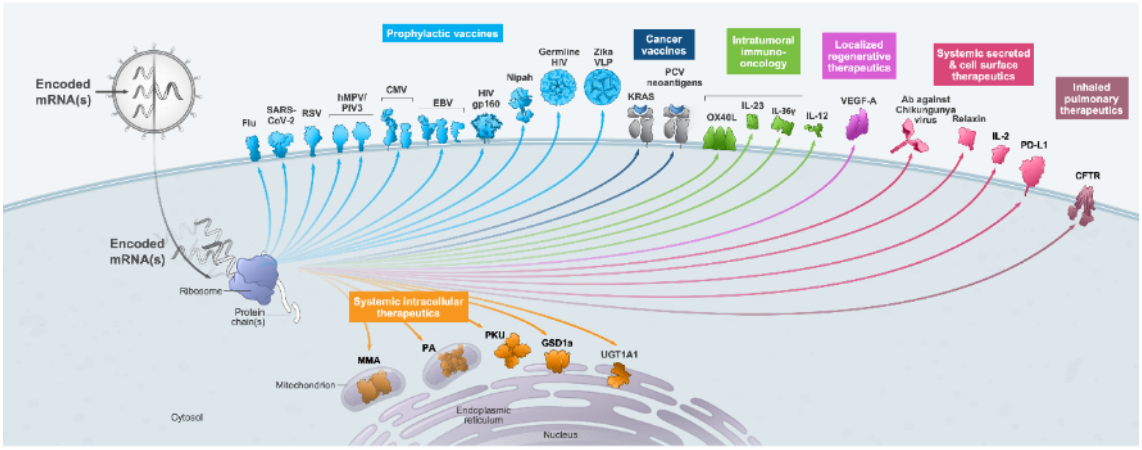


Figure 3.5 Moderna Drug Pipeline Images[23]

Need for Long-Term Investment to Build a Drug Platform

CEO Stéphane Bancel stated that although the company had raised $5.1 billion in funding over the course of ten years, including $750 million from several key strategic partners, it had yet to bring a drug or vaccine to market as of 2019 [11,30].

3.1.2. BioNTech: A Journey from Immunology Research to mRNA Platform Company

BioNTech is a mRNA platform company, although it does not make the same claims as Moderna regarding its technology.

Uğur Şahin, the co-founder and CEO of BioNTech, has been interested in the immune system since childhood. After becoming a physician, he worked as a hematologist in both clinical practice and research. In 2004, Sahin made a significant breakthrough when he successfully induced an immune response in T cells by ensuring that proteins made from mRNA information were properly taken up by dendritic cells. This achievement earned him a prize of 6 million euros, which was awarded on the condition that he establish a company within two years. This funding became the cornerstone of BioNTech. [42]

3.2. Why Were Organizations Based on Drug Platforms That Enable Rapid Vaccine Development Constructed?

This section presents the facts about how these companies developed their organizational capacity from inception to the pandemic while centering the mRNA platform as the corporate strategy. The analysis will be conducted along four key dimensions: corporate culture, financing, knowledge and experience accumulation, and digital and automated infrastructures.

3.2.1. Impact on Corporate Culture Resulting from the Establishment of the Drug Platform

In this section, we describe factual information of the corporate cultures at these companies, highlighting mRNA platform technologies are rooted in deep scientific discovery.

3.2.1.1. Moderna: Integrating the Drug Platform Concept Throughout the Organization

Moderna not only utilizes the drug platform concept, but also strives to streamline and integrate the platform concept throughout the entire organization. To achieve this, Moderna has identified and actively promotes 12 key mindsets across the company, called “Moderna's Mindsets”. The first mindset, "We act with urgency," clearly demonstrates the company's culture of rapid decision-making. As Moderna focuses on mRNA technology, it is crucial for the management team to have a deep understanding of the technology, enabling them to make swift and informed decisions. Moreover, the mindset "We prioritize the platform" suggests that Moderna seeks to utilize the platform concept in various aspects of its operations. For instance, although hypothetical, when employees propose experimental plans, they might be encouraged to consider whether the experiments could be designed in a way that allows others to build upon them, essentially serving as a platform for further research and development[43].

3.2.1.2. BioNTech: A Science-Oriented Company

First of all, BioNTech must be really science-oriented company because the corporate funded by the scientist of Uğur and the mission statement is “We are committed to improving the health of people worldwide with our fundamental research and development of immunotherapies.”, which is pretty scientific expressions. On top of that, BioNTech said that it focused on five innovation pillars, which is “Deep understanding of the immune system”, “Target discovery and characterization”, “Multi-platform innovation engine”, “Digital &AI/ML” and “Manufacturing and automation”[44].

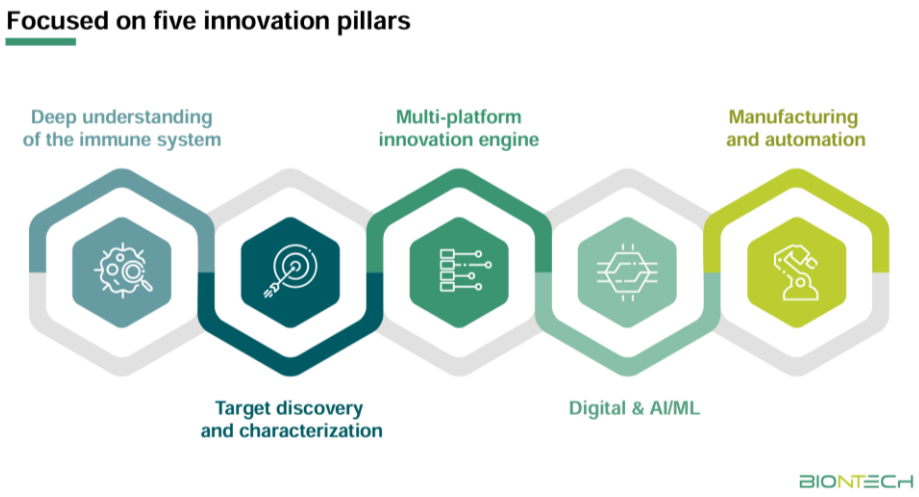


Figure 3.6 BioNTech’s Five Innovation Pillars[45]

Although the scientific orientation sense is not purely stemming from the platform vision, the platform concept might be key role to keep the company oriented to the scientific direction since the pharmaceutical product produce from them.

3.2.1.3. Daiichi Sankyo: Non-Scientific Focus

It says that its culture is “We know that our success is linked to the success of our employees. Each member of our organization contributes to our pursuit of our goals and our company vision. We hold ourselves to high standards in a competitive industry – but our culture sets us apart. Daiichi Sankyo is proud to foster an environment of collaboration and ideas.” It does not sound like a scientific goal in this sense[46].

3.2.2. Funding Enabled by Drug Platforms

This section describes how Moderna and BioNTech received substantial funding even before the pandemic, while Daiichi Sankyo relied on internal assets for its development.

3.2.2.1. Moderna: Leveraging the Platform Strategy for Successful Fundraising

Moderna precisely followed the hypothesized mechanism of successful fundraising, which was previously explained.

First, by highlighting the effectiveness of its product platform in the drug discovery field, it was able to show that its investment would not be limited to one drug but would lead to subsequent drug discoveries. Afeyan, founder of Moderna, said, "Pharmaceutical companies often focus on one product and invest enormous resources in it. Following the logic of the flagship platform, if one drug works under certain conditions, many drugs will work, and if proven methods are introduced, the time to market for a new drug can be significantly reduced," he explained, which was attractive to investors first[11].

Second, because the product platforms have diverse disease targets, they can appeal to different types of disease targets for funding. For example, mRNA drugs can be anti-cancer drugs, in which case they can obtain funding from investors who invest in cancer drug development, and by appealing to infectious disease and vaccine development, etc., funding can be obtained from public institutions. In fact, Moderna successfully raised $ 25 million from DARPA in 2013, assuming the development of vaccines during crisis management[47]. Also, Moderna got several funding from pharmaceutical companies shown in Table 3.1.

Third, the company's positioning itself as a "platform company" itself attracted investment. Platform companies are often very profitable companies that have achieved rapid growth due to network effects and other factors. For investors who were aware of this, Moderna's position as a "platform company" was attractive. Ravina Talukder, Head of Investor Relations at Moderna, said, "Our story to investors was different from that of established pharmaceutical companies. Therefore, we were also able to attract a different kind of investor than one might find in a large pharmaceutical company." These types of investors understand the value and learning curve of

digital platforms because they have seen those effects in high-tech companies," she said[11].In 2018, Moderna had been evaluated at a $7.5 billion valuation when it IPO and raised $500 million[48].

Fourth, as Table 3.1 suggests that Moderna got the funding not only for the pure investment, but it got funding for the “Strategic/Research Partners,” which is the funding as the R&D partnership. Because of this mechanism, Moderna had gotten not only the funding but also knowledge and experience in mRNA-related technology.

As you can see in Table 3.1, Moderna got funding of $2,821.85M even though it had not gotten any of the medical products into the market.

Table 3.1 Amount of the Funding of Moderna Before the Pandemic[49]

#	Deal Type	Date	Amount Raised	Raised to Date	Investor Type
1	Early-Stage VC (Series A)	4-Oct-10	$2.10M	$2.10M	Financial Investors
2	Early-Stage VC (Series B)	27-Dec-11	$9.20M	$11.30M	Financial Investors
3	Later Stage VC (Series C)	6-Dec-12	$27.60M	$38.90M	Financial Investors
4	Early-Stage VC	26-Mar-13	$240.00M	$278.90M	Strategic/Research Partners (AstraZeneca)
5	Grant	2-Oct-13	$24.60M	$303.50M	Strategic/Research Partners (DARPA)
6	Later Stage VC (Series D)	22-Jan-14	$135.00M	$438.50M	Financial Investors
7	Later Stage VC (Series E)	5-Jan-15	$450.00M	$888.50M	Financial Investors
8	Grant	7-Sep-16	$230.00M	$1,118.50M	Strategic/Research Partners (BARDA, Bill & Melinda Gates Foundation)
9	Later Stage VC (Series F)	7-Sep-16	$474.00M	$1,592.50M	Financial Investors
11	Later Stage VC (Series G)	1-Feb-18	$500.00M	$2,092.50M	Financial Investors
12	Later Stage VC (Series H)	4-May-18	$125.00M	$2,217.50M	Financial Investors
13	IPO	7-Dec-18	$604.35M	$2,821.85M	Financial Investors

3.2.2.2. BioNTech: Securing Funding and Strategic Partnerships through mRNA Technology

Table 3.2 suggests that BioNTech got the funding not only for the purely investment, but it got the funding as the “Strategic/Research Partners”, which is the funding as the R&D partnership. Because of this mechanism, BioNTech has gotten not only funding but also knowledge and experience in mRNA-related technology, same with Moderna.

As you can see in Table 3.2, BioNTech got funding of $1,440M even though it had not gotten any medical products into the market.

Table 3.2 Amount of the Funding of BioNTech Before the Pandemic[49]

#	Deal Type	Date	Amount	Raised to Date	Investor Type
2	Seed Round	1-Jan-08	$218.27 M	$218.27M	Financial Investors
5	Later Stage VC (Series A)	4-Jan-18	$270.00 M	$488.27M	Financial Investors
6	Later Stage VC	4-Jan-19	$425.00 M	$913.27M	Strategic/Research Partners (Pfizer Ventures, Sanofi)
7	Later Stage VC (Series B)	9-Jul-19	$325.00 M	$1.24B	Financial Investors
8	Later Stage VC	4-Sep-19	$55.00M	$1.29B	Strategic/Research Partners (Bill & Melinda Gates Foundation)
9	IPO	10-Oct-19	$150.00 M	$1.44B	Financial Investors

3.2.2.3. Daiichi Sankyo: Relying on Internal Assets for Research and Development

According to the pitchbook, Daiichi Sankyo has not gotten any funding after 2008, suggesting that they have done the research by using its asset[49].

The missed opportunity: Failure to raise funds for Japan's Mock-up mRNA Vaccine Project

According to Professor Takeshi Ishii from the Division of Vaccine Science at the Institute of Medical Science, University of Tokyo, a new project was initiated in 2016 to establish a rapid vaccine development. This platform was based on nucleic acid vaccine technologies (DNA, mRNA) and nucleic acid adjuvants (CpG ODN) as a measure against emergency infectious diseases. The initiative, known as the Mock-up Vaccine Project, aimed to create a mock vaccine and conduct clinical research from 2019 to 2021, with an estimated budget of around 400 million yen per year. However, the budget was not approved by AMED, resulting in a missed opportunity for development experience.
(https://www.kantei.go.jp/jp/singi/kenkouiryou/iyakuhin/dai4/siryou1-1.pdf).

3.2.3. Integration of Knowledge Enabled by Drug platforms

This section discusses how knowledge formation has been driven by the product/technology platform strategy of mRNA. To this end, we have objectively demonstrated the extent of knowledge, its structure, and intercompany collaboration based on an analysis of patents and academic literature. Furthermore, we have analyzed research expenditures, development experience, and partnerships centered around the mRNA platform within each company.

3.2.3.1. Horizontal Patent Analysis:

Summary:

As a pharmaceutical company, we analyzed patents, which are important in business. Through this analysis, it was found that Moderna holds patents on mRNA, patents on LNP, and patents related to both, suggesting that the company has obtained patents that cover the elements necessary for the development of the vaccine. On the other hand, BioNTech has a certain percentage of mRNA patents, but the percentage is not as high as that of Moderna. In addition, there are not many patents on LNP technology, suggesting that the acquisition of LNP technology through Genevant was important for vaccine development. Daiichi Sankyo did not have many patents on both mRNA and LNP, suggesting that the company was not as active as Moderna and BioNTech in developing these technologies. The time-series analysis shows that the number of patents filed by Moderna and BioNTech is increasing and that they are constantly filing applications for mRNA technology, suggesting that they are refining their platform technology. On the other hand, Daiichi Sankyo's mRNA technology applications were sporadic, suggesting that the company was not consistently developing its technology.

Method:

Using the Dimensions database, we extracted patents for Moderna, BioNTech, and Daiichi Sankyo. We extracted patents filed during the period 2010-2019 for Moderna, 2008-2019 for BioNTech, and 2008-2019 for Daiichi Sankyo.

For those patents, we estimated patents with keywords associated with mRNA technology, patents with keywords associated with LNP technology, and patents that are likely to contain both technologies.

Key Words Associated with mRNA: 'rna,"mrna,' 'messenger RNA,' 'ribonucleic,' 'messenger ribonucleic.'

LNP-associated keywords: "lipid nanoparticle," "lnp", "liposomal nanoparticle," "nano lipid carrier," "lipid-based nanoparticle," "nanoliposome," "liposome," "nanoemulsion," "nanocarrier," "lipid carrier", "lipid vesicle", "nanoparticulate lipid."

Results:

The results are shown in the following figure. In the following figure, the number of patents for Moderna was 542, while the number of patents for mRNA was 427, a fairly high percentage. 73 patents were for LNP, and 53 patents were for both mRNA and LNP.

For BioNTech, the total number of patents was 214, while the number of patents for mRNA was 67. Although the percentage is not as high as Moderna's, it is still a fair amount. 6 patents were for LNP, and 4 patents were for both mRNA and LNP.

For Daiichi Sankyo, the total number of patents was 983, but 35 patents were assumed to be mRNA technology, two patents were LNP-related, and 0 patents were assumed to be both technologies.

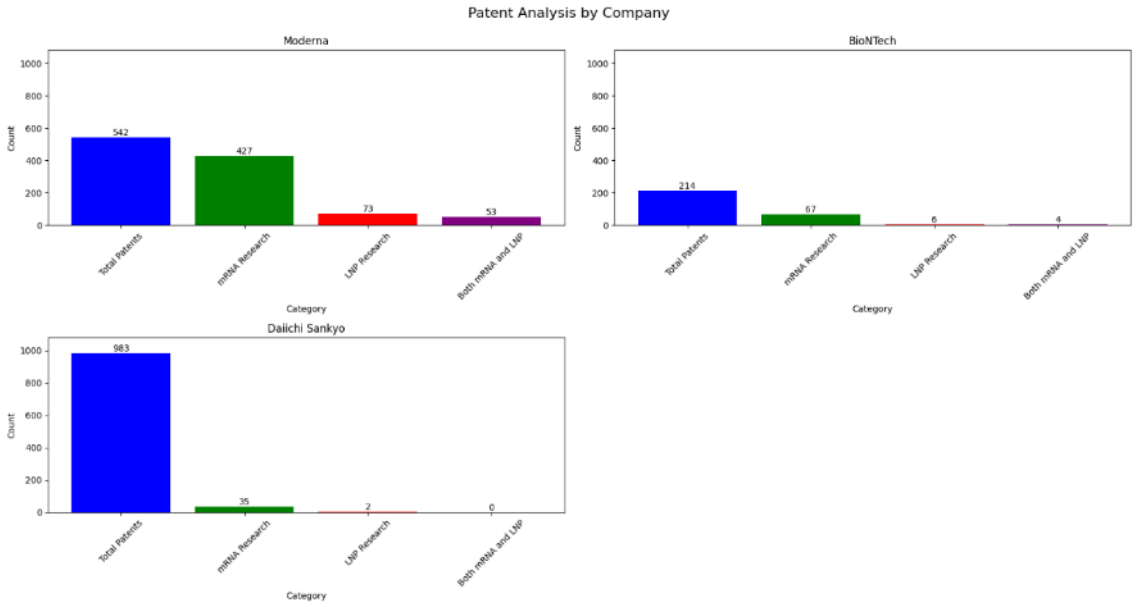


Figure 3.7 Patents of Moderna, BioNTech, and Daiichi Sankyo Related to mRNA or LNP Technologies

(The graph illustrates the number of patents held by three companies: Moderna (2010-2019), BioNTech (2008-2019), and Daiichi Sankyo (2008-2019). The blue bar represents the total number of patents held by each company during the specified period. The green bar indicates the number of patents that may be related to mRNA technology, while the red bar shows the number of patents potentially related to lipid nanoparticle (LNP) technology. Lastly, the purple bar represents the number of patents that are related to both mRNA and LNP technologies.)

Also shown are graphs and tables showing how each of the patents has changed over time.

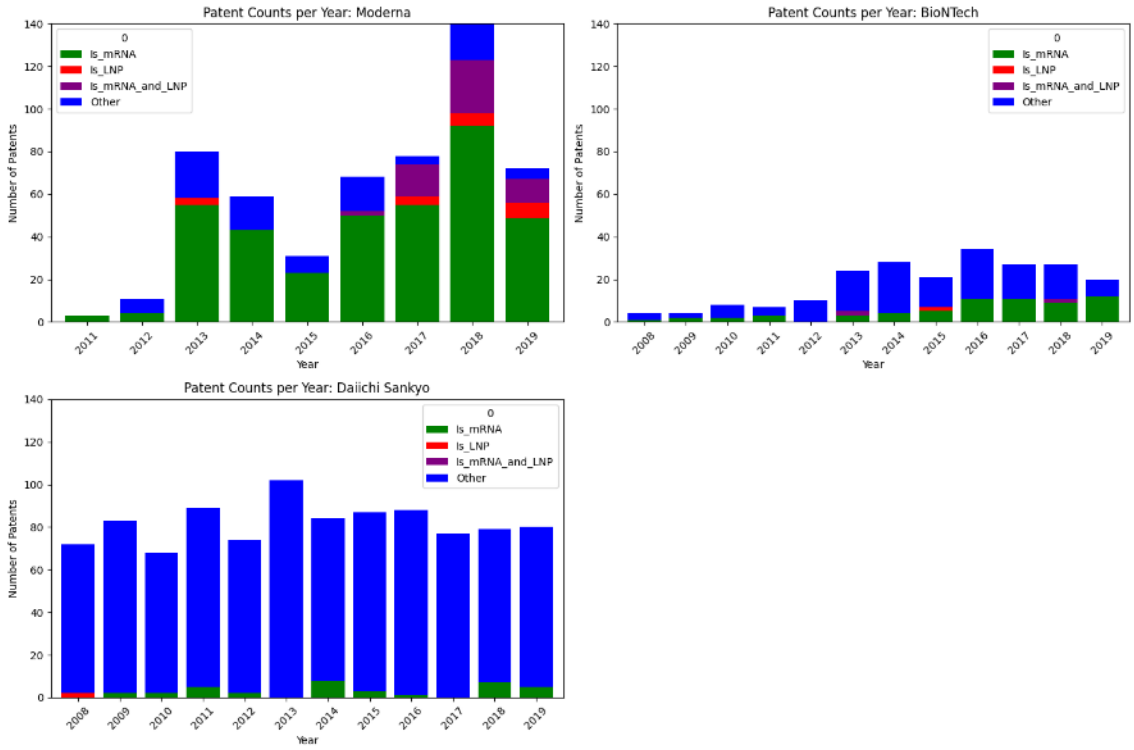


Figure 3. 8 Time Horizon of Patents Submitted by Moderna, BioNTech, and Daiichi Sankyo Related to mRNA and LNP Technologies

(The graph illustrates the number of patents held by three companies per year: Moderna (2010-2019), BioNTech (2008-2019), and Daiichi Sankyo (2008-2019). The blue bar represents the patents other than mRNA or LNP technologies held by each company in a given year. The green bar indicates the number of patents that may be related to mRNA technology, while the red bar shows the number of patents potentially related to lipid nanoparticle (LNP) technology. Lastly, the purple bar represents the number of patents that are related to both mRNA and LNP technologies.)

Discussion:

These results suggest that Moderna and BioNTech are continuously researching mRNA technology as platform technology and have applied for patents. On the other hand, Daiichi Sankyo's mRNA related patent applications were sporadic, suggesting that the company is not continuously developing mRNA technology as a platform technology.

In vaccine development, it is likely that each company will need to license a certain number of patents. The following figure shows a previous study of that patent network[50].

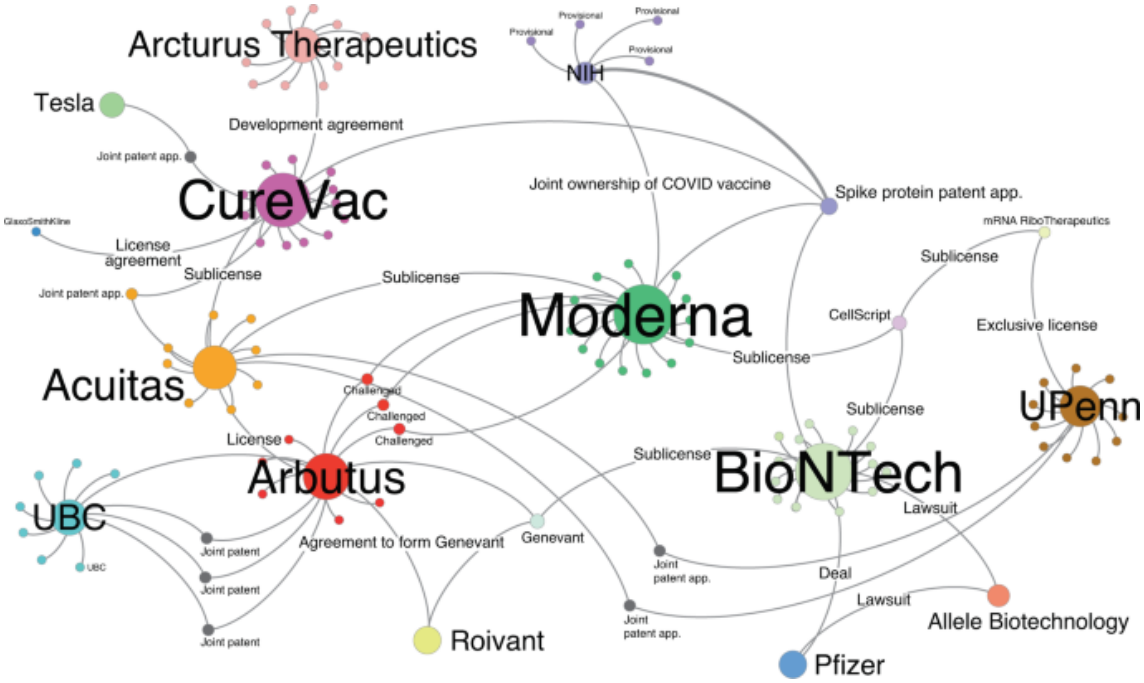


Figure 3.9 Patent Network Analysis of mRNA-Based Vaccine Candidates for COVID-19[50]

Although Moderna has patents on both mRNA and LNP technology, it used several important patents for vaccine development, including the use of mRNA modification technology invented by a group of researchers at the University of Pennsylvania. As this analysis clearly shows, the LNP technology was not sufficient for BioNTech, so the collaboration with Genevant, which appears in the figure above and is also mentioned below as a partner, was probably important[50].

Conclusion:

An analysis of the pharmaceutical company's patents reveals that Moderna holds a lot of patents related to mRNA and LNP (liposome-forming nanoparticle) technology and that it has continued to develop these essential technologies for vaccine development. Moderna holds a particularly high percentage of patents on mRNA technology. As for LNP, for BioNTech, the LNP technology obtained through Genevant was shown to be key for vaccine development. Daiichi Sankyo has a small number of patents on both mRNA and LNP, suggesting that it is not as active in technology development as Moderna and BioNTech. The time-series analysis shows that Moderna and BioNTech have increased their total number of patents and that patent applications are almost always filed with respect to mRNA technology, suggesting that these companies are strengthening their platform technologies. In the case of Daiichi Sankyo, however, patent applications related to mRNA technology are sporadic, and there is no consistent trend of technological development.

3.2.3.2. Horizontal Academic Paper Analysis:

Summary:

As a proxy variable for the level of knowledge of a pharmaceutical company, we analyzed academic papers. Through this analysis, we found that, as with patents, Moderna submitted papers on mRNA, papers on LNP, and papers related to both, indicating that the company is conducting research on the elements necessary for the development of this vaccine. On the other hand, as for BioNTech, a certain percentage of papers on mRNA, as well as patents, were submitted, but it was found that the percentage was not as high as that of Moderna. In addition, there were not many papers on LNP technology. As for Daiichi Sankyo, the population was larger in the first place compared to patents; Moderna and BioNTech had fewer academic papers than patents, but for Daiichi Sankyo, the number of academic papers was larger than the total number of patents, suggesting a corporate culture that emphasizes publication of academic papers.

In the time-series analysis, the total number of papers for Moderna and BioNTech increased, and moreover, mRNA technology applications were almost always filed, suggesting that they are also refining their platform technology in the same way. On the other hand, Daiichi Sankyo also showed a certain increase in the number of papers.

When we analyzed the relationship of co-occurrence of keywords to confirm the content of the research, we found that "messenger RNA" and "lipid nanoparticles" played an important role in connecting different concepts among academic papers, indicating that platform technology is also functioning as a platform for knowledge. On the other hand, for BioNTech, immunological terms such as "T cells" and "immune response" were used to connect concepts, suggesting that knowledge is rather structured around immunological concepts. On the other hand, for Daiichi Sankyo, realistic objects and experimental tools such as "patients," "Mice," and "Rats" were merely mentioned as co-occurrences, suggesting that there was no technology or scientific concepts core as a whole among academic papers. We further examined the co-occurrence relationship using "Vaccine" as a keyword, but again, targets and experimental tools such as "influenza" and "mice" were mentioned, and we could not find much of a core technological key word. Next to the keyword "T cells," specific names of cytokines and other information were recalled, which were considered to be purely research-related co-recollections. No words that could be assumed to be mRNA were mentioned here. In addition, "cell lines," "genes," and "tumor" were mentioned in the study of the keyword "mRNA," suggesting that mRNA is used in basic research or cancer research, and it did not appear that mRNA research was conducted with the infectious disease field in mind.

Method:

As with the patents, we used the Dimensions database to extract academic papers for Moderna, BioNTech, and Daiichi Sankyo. We extracted papers published during the period 2010-2019 for Moderna, 2008-2019 for BioNTech, and 2008-2019 for Daiichi Sankyo.

For those papers, as with patents, we estimated the number of papers with keywords associated with mRNA technology, the number of papers with keywords associated with LNP technology, and the number of papers that seemed to contain both technologies.

Results:

The results are shown in the figure below. In the following figure, while Moderna had a total of 97 publications, 62 were for mRNA, a much higher percentage for papers, 27 were for LNP, and another 27 were for both mRNA and LNP technologies; for BioNTech, while the total number of

publications was 137, the number of papers in which mRNA was assumed was 65, which is a larger number than for Moderna. 6 papers were related to LNP, and five papers assumed both LNP and mRNA technologies. Daiichi Sankyo had a total of 1,439 papers, with 233 papers that were assumed to be mRNA technology, three patents related to LNP, and one patent that was assumed to be both technologies. Thus, for Moderna and BioNTech, the number of publications was larger than the number of papers, while for Daiichi Sankyo, the number of papers was larger, indicating Daiichi Sankyo's culture of emphasizing academic paper publications.

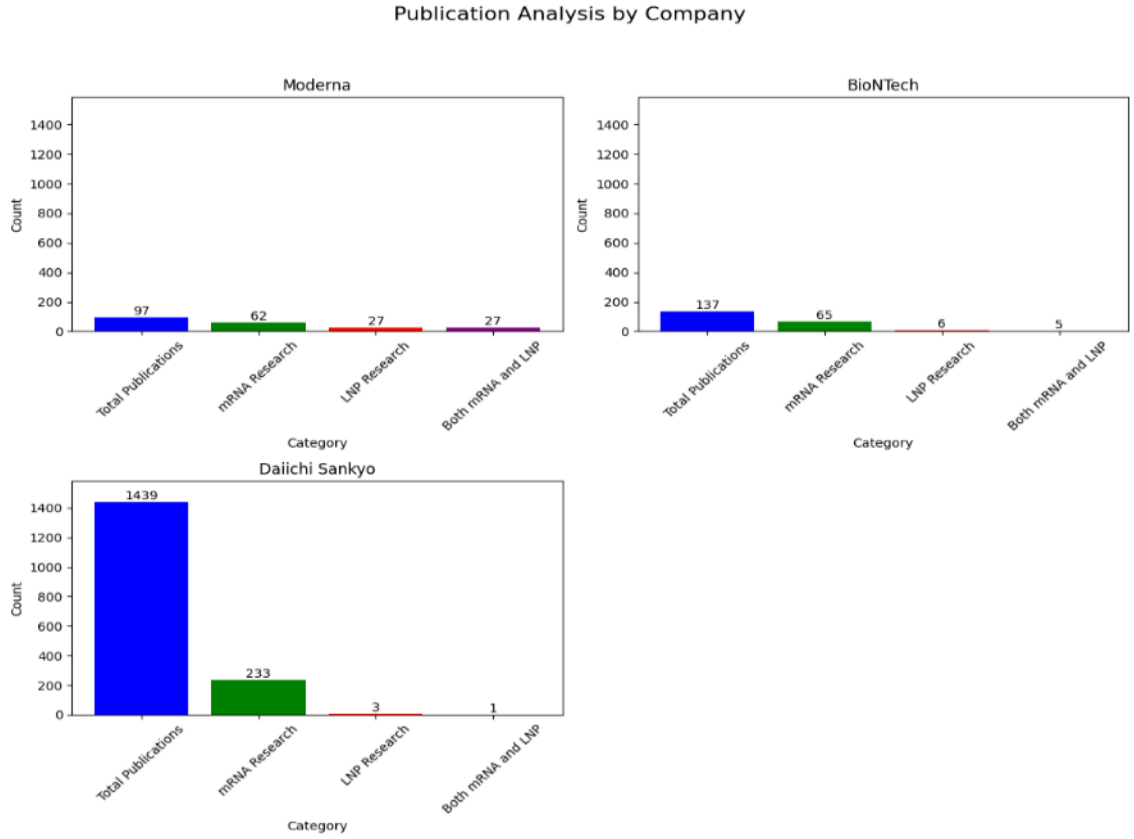


Figure 3.10 Academic Publications of Moderna, BioNTech, and Daiichi Sankyo Related to mRNA and LNP Technologies

(The graph illustrates the number of academic publications by three companies: Moderna (2010-2019), BioNTech (2008-2019), and Daiichi Sankyo (2008-2019). The blue bar represents the total number of academic publications by each company during the specified period. The green bar indicates the number of publications that may be related to mRNA technology, while the red bar shows the number of publications potentially related to lipid nanoparticle (LNP) technology. Lastly, the purple bar represents the number of publications that are related to both mRNA and LNP technologies.)

In addition, a time-series analysis shows that the total number of papers for Moderna and BioNTech is increasing and that they are almost constantly filing applications for mRNA technology, suggesting that they are also refining their platform technology in the same way. On the other hand, Daiichi Sankyo also showed a constant increase in the number of papers, suggesting that mRNA research is being conducted academically.

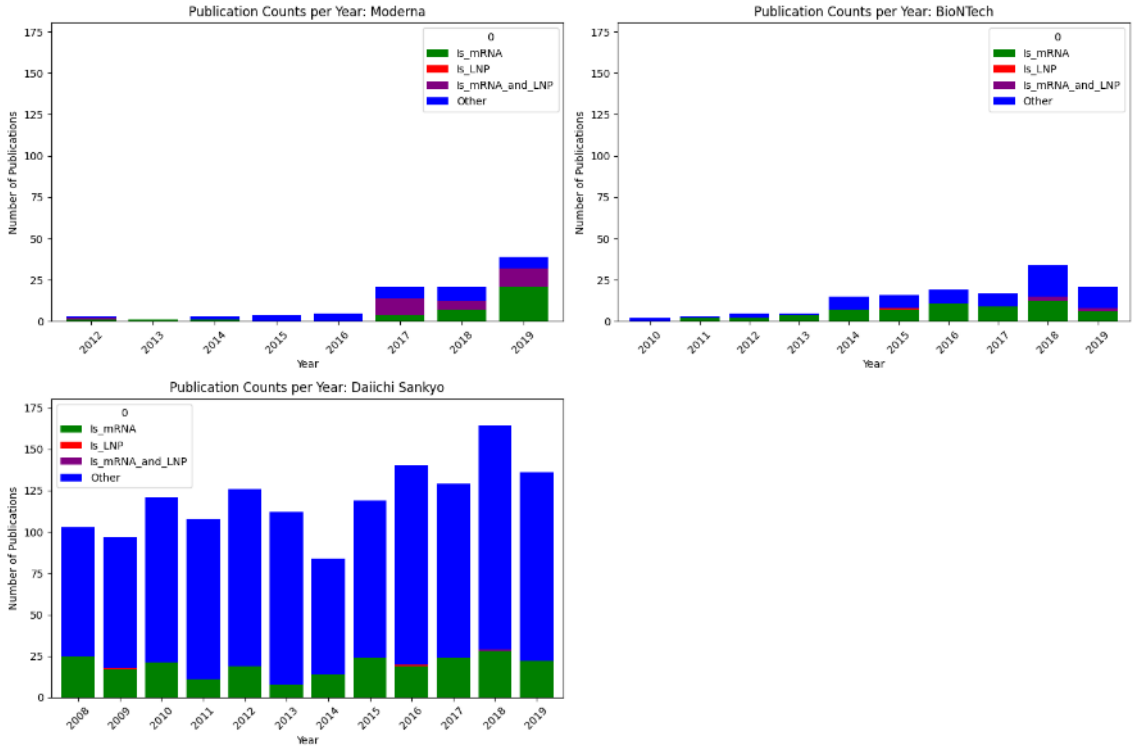


Figure 3.11 Time Horizon of Academic Publications by Moderna, BioNTech, and Daiichi Sankyo Related to mRNA and LNP Technologies

(The graph illustrates the number of academic publications by three companies per year: Moderna (2010-2019), BioNTech (2008-2019), and Daiichi Sankyo (2008-2019). The blue bar represents patents other than mRNA or LNP technologies of academic publications by each company in a given year. The green bar indicates the number of publications that may be related to mRNA technology, while the red bar shows the number of publications potentially related to lipid nanoparticle (LNP) technology. Lastly, the purple bar represents the number of publications that are related to both mRNA and LNP technologies.)

Discussion:

The graph below shows the analysis of the co-occurrence relationship of the keywords in Moderna's academic publications. The analysis of the co-occurrence relationship of the keywords

to confirm the content of the study showed that "messenger RNA" and "lipid nanoparticles" played an important role in connecting different concepts among academic papers and that the platform technology also functioned as a platform for knowledge in the company.

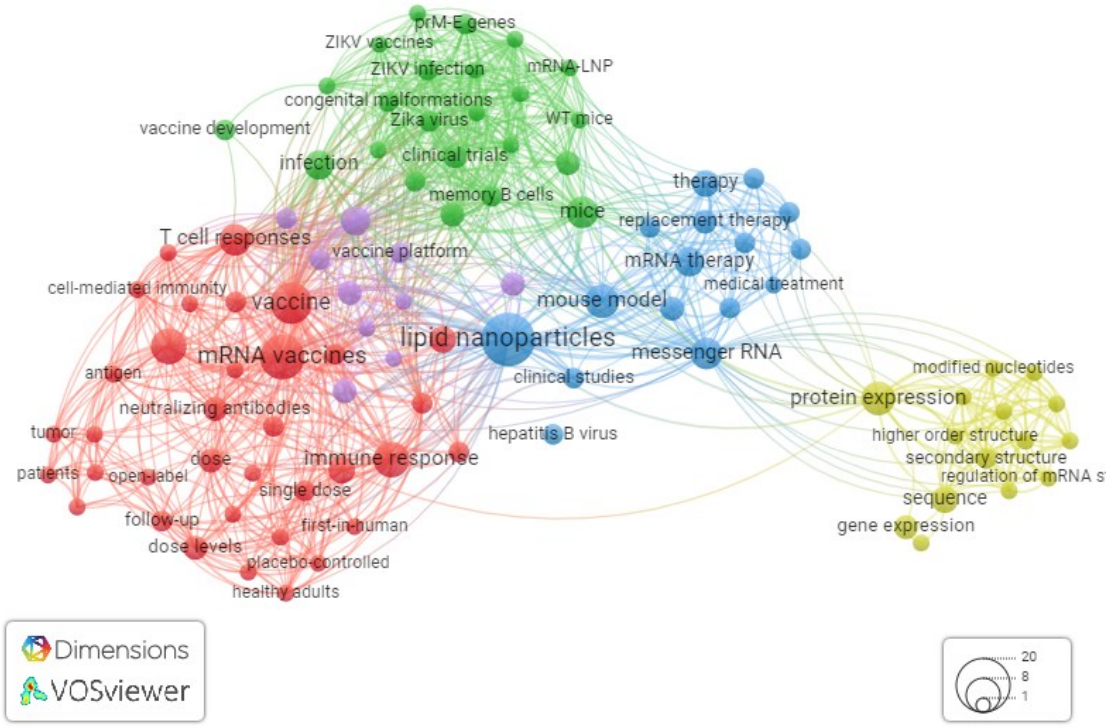


Figure 3.12 Co-occurrence Analysis of Keywords in Moderna's Academic Publications

(The image shows a co-occurrence analysis of keywords from Moderna's academic publications up to 2019, visualized using the VOSviewer and Dimensions tools. The analysis reveals the relationships and connections between various concepts based on their co-occurrence in the publications.)

On the other hand, for BioNTech, immunological terms such as "T cells" and "Immune response" were used to connect concepts, suggesting that knowledge was structured around immunology.

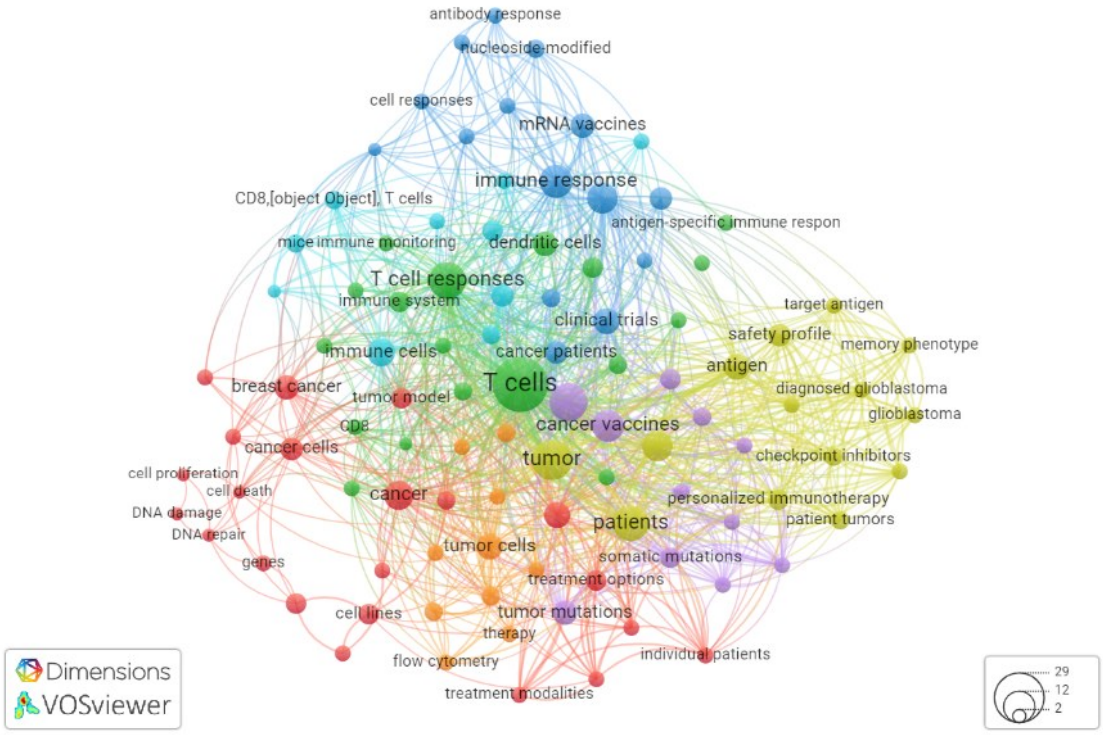


Figure 3.13 Co-occurrence Analysis of Keywords in BioNTech's Academic Publications

(The image shows a co-occurrence analysis of keywords from BioNTech's academic publications up to 2019, visualized using the VOS viewer and Dimensions tools. The analysis reveals the relationships and connections between various concepts based on their co-occurrence in the publications.)

Unlike Moderna, the knowledge of BioNTech has been connected by Uğur, who is the founder of the company. As he has strong scientific background which enables him to connect the knowledge of the company beyond the several disciplines. Another group we could see is Dr. Kariko, Katalin, who got the Novel prize in 2023, and her group must be researching mRNA. Still, Uğur also connects the group.

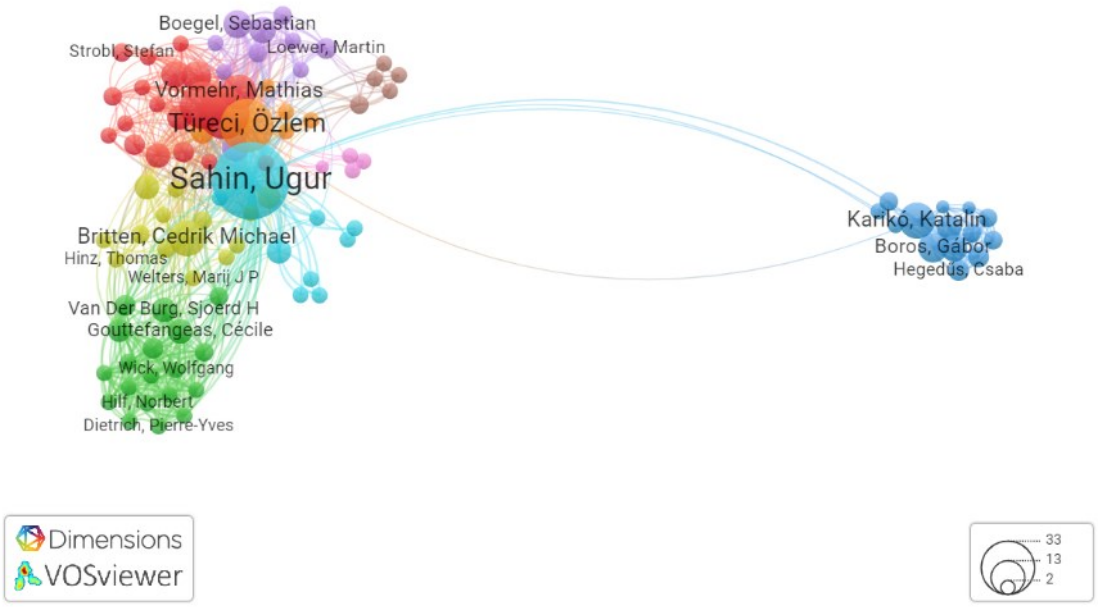


Figure 3.14 Co-Authorship Analysis of BioNTech's Academic Publications

(The figure shows co-authorship analysis of BioNTech's academic publications up to 2019, utilizing VOS viewer and Dimensions tools to visualize the relationships between authors based on their co-authored works.)

On the other hand, for Daiichi Sankyo, realistic objects and experimental tools such as "patients," "Mice," and "Rats" were merely mentioned as co-occurrences, and overall, there did not seem to be a core of technological concepts among papers.

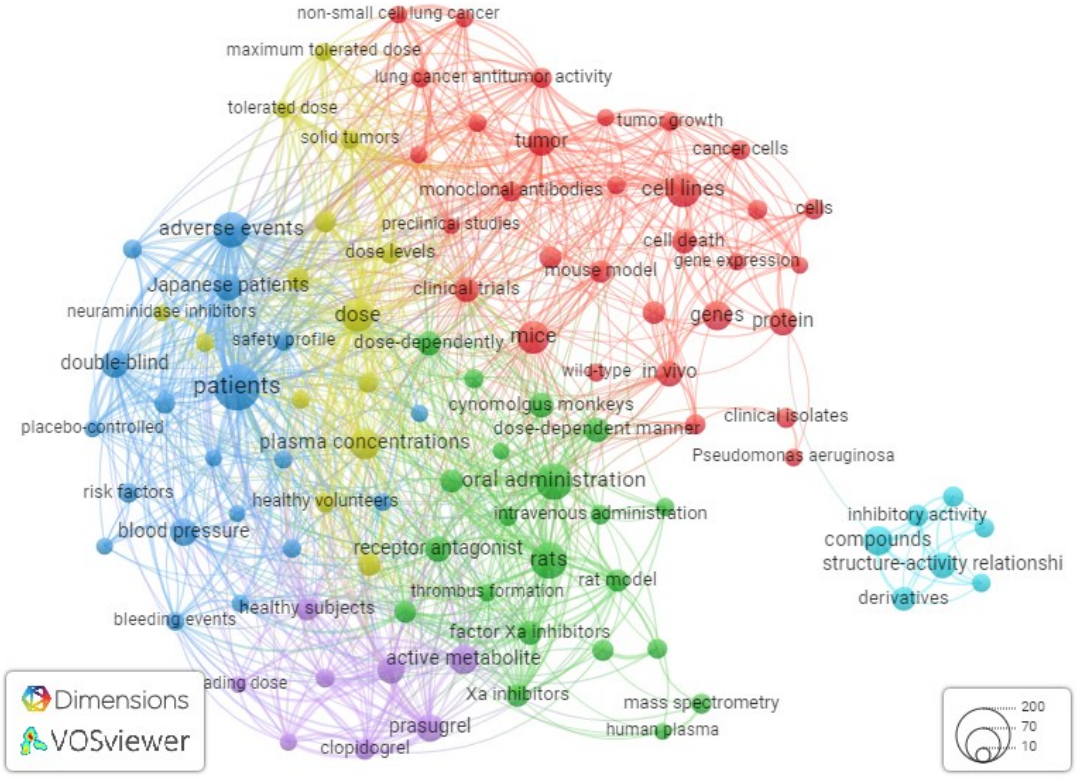


Figure 3.15 Co-occurrence Analysis of Keywords in Daiichi Sankyo's Academic Publications (ALL)

(The image shows a co-occurrence analysis of keywords from Daiichi Sankyo's academic publications from 2008 to 2019, visualized using the VOS viewer and Dimensions tools. The analysis reveals the relationships and connections between various concepts based on their co-occurrence in the publications.)

We further checked the co-occurrence relationship by using "Vaccine" as a keyword, but again, targets and experimental tools such as "influenza" and "mice" were mentioned, and we could not find much core technology. Next to the keyword "T cells," specific names of cytokines and other information were recalled, which were considered to be purely research-related co-recollections. No mRNA was assumed here.

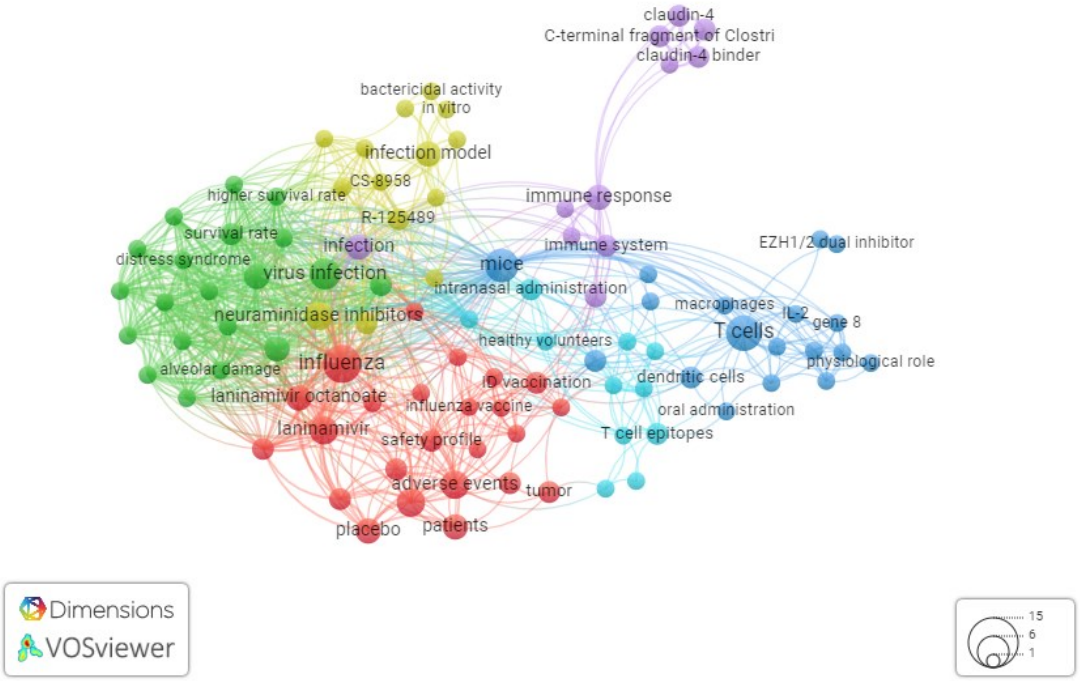


Figure 3.16 Co-occurrence Analysis of Keywords in Daiichi Sankyo's Academic Publications (Vaccine)

(The image shows a co-occurrence analysis of keywords from Daiichi Sankyo's academic publications from 2008 to 2019, having the keyword of “vaccine” for the academic papers, visualized using the VOS viewer and Dimensions tools. The analysis reveals the relationships and connections between various concepts based on their co-occurrence in the publications.)

In the study of the keyword "mRNA," "cell lines," "genes," and "tumor" were mentioned, suggesting that mRNA is used in basic research or cancer research, and it did not appear that mRNA research was conducted with the infectious disease field in mind.

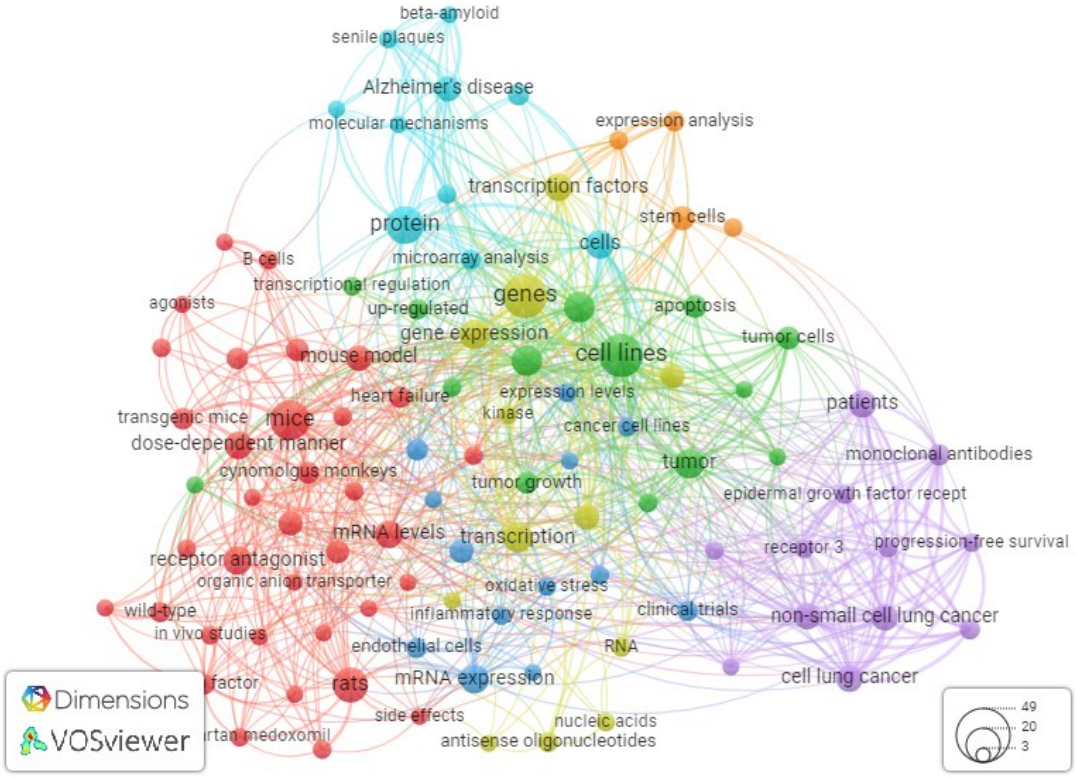


Figure 3.17 Co-occurrence Analysis of Keywords in Daiichi Sankyo's Academic Publications (mRNA)

(The image shows a co-occurrence analysis of keywords from Daiichi Sankyo's academic publications from 2008 to 2019, having the keyword of “mRNA” for the academic papers, visualized using the VOS viewer and Dimensions tools. The analysis reveals the relationships and connections between various concepts based on their co-occurrence in the publications.)

Conclusion:

In analyzing academic publications as an indicator of a pharmaceutical company's knowledge level, it was found that Moderna actively published papers on mRNA and LNP technologies, as well as those covering both areas, highlighting its research commitment to vaccine development essentials. BioNTech, while also contributing to mRNA research, had fewer publications on LNP technology. Daiichi Sankyo stood out for having more academic papers than patents, suggesting a corporate culture that values academic paper publications. Their research predominantly focused on mRNA, with fewer studies on LNP.

Over time, the publication counts for both Moderna and BioNTech increased, particularly in mRNA technology, indicating a continuous refinement of their platform technologies. Daiichi Sankyo also showed a rise in publications, but their research seemed less focused on core academic concepts, often mentioning practical objects and tools like "patients" and "mice" without a clear technological focus.

Co-occurrence keyword analysis revealed that "messenger RNA" and "lipid nanoparticles" were central to Moderna's research, linking various concepts and underscoring the role of their platform technology in the center of knowledge. BioNTech's research appeared to be more immunologically oriented, with terms like "T cells" and "immune response" connecting different ideas. In contrast, Daiichi Sankyo's publications lacked a unifying academic theme, with a scattered mention of subjects and tools.

When examining the keyword "vaccine," the focus again fell on targets and experimental tools, such as "influenza" and "mice," without a strong indication of core technology. The presence of cytokine names and other specific terms next to "T cells" suggested detailed research interests, but there was no direct mention of mRNA, implying a potential gap in infectious disease research within mRNA studies. References to "cell lines," "genes," and "tumors" in the context of mRNA research hinted at its application in basic or cancer research rather than infectious diseases.

3.2.3.3. Moderna: Leveraging mRNA Platform for Vaccine Development and Strategic Partnerships

Significant Investment in R&D

First of all, Because of the funding, Moderna expenses a lot of money for R&D, and below is the expense.

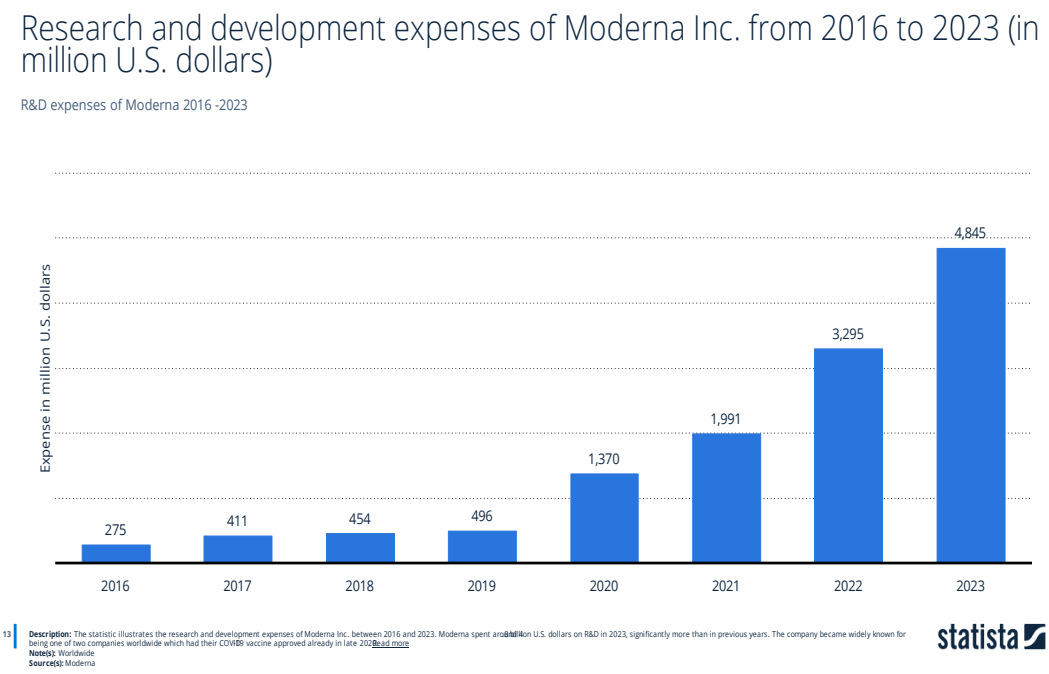


Figure 3.18 The R&D Expenses of Moderna

Extensive Experience in mRNA Vaccine Development

In May 2020, which is before the COVID-19 vaccine has been developed, Moderna had nine development candidates in its prophylactic vaccine's modality, including:

Vaccines against respiratory infections

· Respiratory syncytial virus (RSV) vaccine for older adults (mRNA-1777 and mRNA-1172 or V172 with Merck)

· RSV vaccine for young children (mRNA-1345)

· Human metapneumovirus (hMPV) and parainfluenza virus type 3 (PIV3) vaccine (mRNA-1653)

· Novel coronavirus (SARS-CoV-2) vaccine (mRNA-1273)

· Influenza H7N9 (mRNA-1851)

Vaccines against infections transmitted from mother to baby.

· Cytomegalovirus (CMV) vaccine (mRNA-1647)

· Zika vaccine (mRNA-1893 with BARDA)

Vaccines against highly prevalent viral infections

· Epstein-Barr virus (EBV) vaccine (mRNA-1189)

At that time, Moderna has demonstrated positive Phase 1 data readouts for seven prophylactic vaccines (H10N8, H7N9, RSV, chikungunya virus, hMPV/PIV3, CMV, and Zika). Moderna's CMV vaccine is currently in a Phase 2 dose-confirmation study. Moderna's investigational Zika vaccine (mRNA-1893), currently in a Phase 1 study, was granted FDA Fast Track designation in August 2019[51].

Strategic Partnerships Driven by mRNA Technology

The below is the partnership of Moderna[52]. As you can see, most of them are related to the mRNA or vaccine technology and we could see how the mRNA knowledge grow the partnership and how the Moderna could get experience from the partnership.

Table 3.3 Moderna Partnerships

Partner	Start Year	Purpose	Key Details
AstraZeneca	2013	Research, develop and commercialize mRNA medicines	Exclusive rights for cardiovascular disease and cancer therapies.
DARPA	2013	Research and develop mRNA medicines	Up to $25 million was awarded for vaccine and antibody programs against Chikungunya.
Karolinska Institute and Karolinska University Hospital	2014	Sponsor research grants for mRNA Therapeutics	Conduct preclinical research on novel mRNA therapies.
Institut Pasteur	2015	Sponsor preclinical and clinical research programs	Develop new approaches for viral and bacterial diseases using mRNA technology.
Merck	2015	Research, development, and commercialization of mRNA medicines	Focused on viral infections and cancer prevention and treatment.
Vertex	2016	Discovery and development of mRNA medicines	Treating cystic fibrosis, exploring pulmonary mRNA delivery potential.
BARDA	2016	Fund Zika vaccine program	Award of up to $125 million for the Zika vaccine development.
Bill & Melinda Gates Foundation	2016	Advanced mRNA-based development projects for infectious diseases	Global health project framework agreement for various infectious diseases.

3.2.3.4. BioNTech: Leveraging mRNA Platform for Infectious Diseases, Partnerships, and Talent Acquisition

Significant Investment in R&D

The below is the R&D expenses of the BioNTech[53].

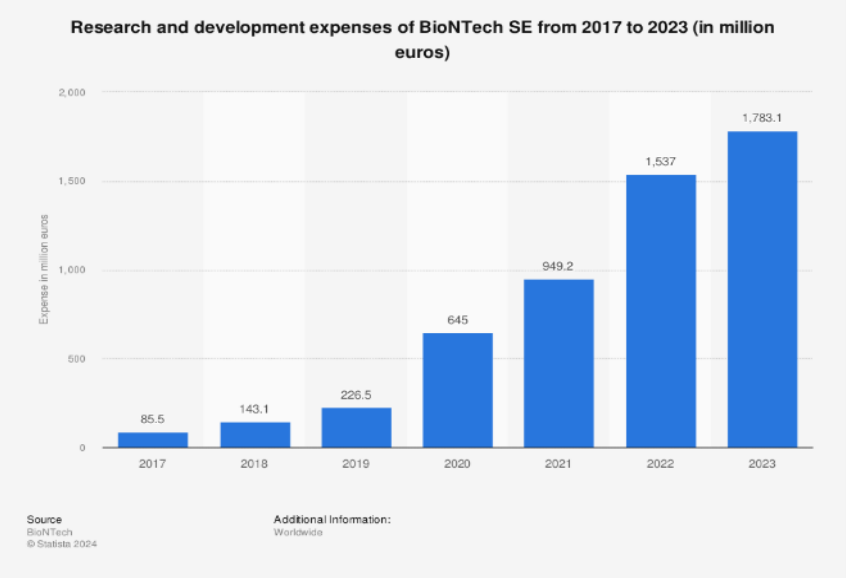


Figure 3.19 R&D Expenses of BioNTech from 2017 to 2023

BioNTech's Vision and Expansion into Infectious Diseases based on the mRNA Platform

In 2018, Uğur Şahin, the co-founder and CEO of BioNTech, was invited by the Gates Foundation to participate in the "Grand Challenges" General Assembly to discuss the company's mRNA technology. Although BioNTech's primary focus at the time was on cancer treatment, Sahin highlighted the potential of their technology to rapidly produce vaccines within weeks, which could be crucial in addressing rapidly spreading infectious diseases. During the panel discussion, Dr. Tedros Adhanom Ghebreyesus, who later became the Director-General of the World Health Organization (WHO), praised BioNTech's technology. In a subsequent conversation with Bill Gates, Sahin emphasized the potential of mRNA-based drugs in responding to a pandemic and advised the development of a system for immediate vaccine production. As a result, BioNTech expanded its infectious disease-related pipeline and established joint ventures with Pfizer Inc. and the University of Pennsylvania.[42]

The accumulation of mRNA platforms led to the formation of new partnerships and the acquisition of knowledge essential for vaccine development in the event of a pandemic. BioNTech recognized the concept that the accumulation of technology as a platform could be applied to various fields. While the company primarily conducted research on immunity with a focus on cancer, Özlem Türeci, BioNTech's Chief Medical Officer, commented on the potential of applying their research to infectious diseases: "It was a way to redirect the natural mechanisms of the immune system, which evolved to avoid viruses, to other areas. In just a few steps, we can utilize all of this knowledge and apply it to the original purpose of the immune system, which is to protect against viruses."[42]

BioNTech-Pfizer Collaboration and Partnerships Because of the Developed mRNA Platform

Also, the specialized mRNA technology knowledge accumulation at BioNTech enabled the partnership on the development of the 2018 influenza vaccine that led to the COVID-19 vaccine development.

Although Pfizer and BioNTech have been communicating since 2013, but no major partnership has been formed. February 2018 BioNTech's Uğur Şahin and Kathrin Jansen, Senior Vice President and Head of Vaccine R&D of Pfizer had a meeting. During their meeting, Kathrin pointed out a series of mRNA drug challenges, to which Uğur politely responded that made her a good impression of the BioNTech technology, and in August 2018, "BioNTech Signs Collaboration Agreement with Pfizer to Develop mRNA- based Vaccines for the Prevention of Influenza" in August 2018[42]. According to the agreement, "Under the terms of the agreement, BioNTech and Pfizer will jointly conduct research and development activities to help advance mRNA-based flu vaccines. Pfizer will assume sole responsibility for further clinical development and commercialization of mRNA-based flu vaccines, following BioNTech's completion of a first in human clinical study.

BioNTech will receive $120 million in upfront, equity, and near-term research payments and up to an additional $305 million in potential development, regulatory, and commercial milestone payments. In addition, BioNTech will receive up to double-digit tiered royalty payments associated with worldwide sales if the program reaches commercialization."[54,55]. And BioNTech

has gotten an important partnership with the funding. Kathrin explained why she chose the mRNA and partnership with the BioNTech like this “have experienced many different approaches to vaccine development, so I knew what would likely not work [against SARS-CoV-2] and what may work. I was not willing to forego getting a strong T-cell response, which steered us away from protein platforms. Then, having had the opportunity to work with BioNTech, it became clear to me that mRNA had to be the platform with the highest chance of success. I didn’t know whether it was possible at that time. All I knew was that, if anything works, it should be mRNA because it ticks all of the arms of the immune system — you get good T cell responses, antibodies and innate responses. T cell and innate responses, particularly for an older population, are where things usually fall down [with other platforms]. Another reason the mRNA platform came out as the front-runner was that we think you can boost as much and as long as you want and not get immune responses to the vector itself — the mRNA. If you use a viral vector, your immune response to the vector can tune down your response to the target — in this case, the SARS-CoV-2 spike protein.”[56]. It clearly depicts how important it is to give concrete evidence to make a partnership and make progress on the project.

Partnerships

Below is the partnership of the BioNTech. As you can see, most of the partners are related to mRNA technology, and we can see the importance of the platform in making the partnership through it.[57]

Table 3.4 BioNTech Partnerships

Partner	Purpose of Collaboration	Start Date	Key Details
Genmab	Develop mono- and bispecific cancer antibodies	5/1/2015	Utilizes Genmab's DuoBody® and HexaBody® platforms. Expanded collaboration in 2016 and 2022 for additional targets and technologies.
Siemens	Construct a digitalized commercial cGMP-production site	6/1/2015	Focused on manufacturing individualized vaccines. Expanded COVID-19 vaccine production capabilities.
Genentech (Roche Group)	Develop individualized mRNA-based cancer vaccines	9/1/2016	Targeting cancer neoantigens specific to individual patients. Includes iNeST development candidate autogene cevumeran (BNT122).
Genevant	Develop mRNA-based protein replacement therapies	7/1/2018	The collaboration includes exclusive licenses to Genevant's LNP technology for specified oncology targets.
Pfizer	Development of a mRNA-based influenza vaccine	8/1/2018	This partnership laid the foundation for the later collaboration on the COVID-19 vaccine, showcasing the potential of mRNA technology.
Bill & Melinda Gates Foundation	Develop HIV and tuberculosis vaccines	9/1/2019	Focus on mRNA vaccine technology aiming for affordable access in developing countries, representing the largest equity investment by the Foundation's Strategic Investment Fund at the time.

Smooth Collaboration Because of the Platform-Based Approach

BioNTech had another example of making partnership resulting from a platform-based approach. The company has accumulated expertise in lipid nanoparticles (LNPs) and drug delivery through its extensive research on cancer therapeutics. Prior to the pandemic, BioNTech conducted tests on several LNP formulations. Despite having its own LNP technology, BioNTech made the strategic decision to utilize Acuitas' LNP technology due to its superior quality[42]. This decision might be possible because BioNTech knew that its strength is mRNA, and it would like to use other resources which could enhance their mRNA platform. Hence, BioNTech could swiftly decide the collaboration.

mRNA Vaccine Development Experiences

BioNTech's extensive experience in administering mRNA-based drugs to human subjects has been a critical factor in the company's success for the COVID-19 vaccine project. Since 2012, BioNTech has administered its mRNA drug to more than 400 subjects, allowing the company to accumulate valuable data and insights for the COVID-19 vaccine development.[42]

Development of mRNA Platform Attracts Talents

Katalin Karikó, who would later win the Nobel Prize for her groundbreaking work on mRNA, first met Uğur Şahin in 1998. Their collaboration and shared passion for mRNA technology led to Karikó joining BioNTech as Vice President in 2013, further strengthening the company's expertise in this field.[42]

The case of Katalin Karikó joining BioNTech exemplifies how a strong emphasis on a technology platform can serve as a magnet for talented individuals in the field.

3.2.3.5. Daiichi Sankyo: Traditional Approach and Absence of mRNA-Based Partnerships

Below is the partnership of Daiichi Sankyo. However, unlike Moderna or BioNTech, none of the relationships are related to the mRNA or LNP technology, suggesting that the technology is not related to expanding the partnership and Daiichi Sankyo did not get the knowledge of mRNA or LNP technology through partnership[58].

Table 3.5 Daiichi Sankyo Partnerships

Partnering with ADC, including combination studies		
Partner	Press Release Date	Summary
AstraZeneca	Mar. 2019	Daiichi Sankyo and AstraZeneca Announce Global Development and Commercialization Collaboration for Daiichi Sankyo's HER2 Targeting Antibody Drug Conjugate [Fam-] Trastuzumab Deruxtecan (DS-8201)
Merck & Co., Inc.	Sep. 2018	Daiichi Sankyo Announces Clinical Research Collaboration to Evaluate DS-8201 in Combination with KEYTRUDA® (pembrolizumab) in HER2 Expressing Breast

		and HER2 Expressing or HER2 Mutant Lung Cancers.
Bristol-Myers Squibb	Aug. 2017	Bristol-Myers Squibb and Daiichi Sankyo Announce Research Collaboration to Evaluate Opdivo® (nivolumab) and DS-8201 in HER2-Expressing Breast and Bladder Cancers.
In-License Collaborations		
Partner	Press Release Date	Summary
Esperion	Jan. 2019	Daiichi Sankyo Europe Enters into European Licensing Agreement with Esperion for Bempedoic Acid and the Bempedoic Acid / Ezetimibe Combination Tablet
Kite Pharma (a subsidiary of Gilead Sciences)	Jan. 2017	Daiichi Sankyo Establishes Strategic Partnership for Cellular Therapy Pipeline with Kite Pharma
Out-license Collaborations		
Partner	Press Release Date	Summary
AnHeart Therapeutics	Dec. 2018	Daiichi Sankyo Out-Licenses ROS1/NTRK Inhibitor DS-6051 to AnHeart Therapeutics
Boston Pharmaceuticals	Aug. 2017	Daiichi Sankyo Enters Worldwide Licensing Agreement with Boston Pharmaceuticals for a Highly Selective RET Inhibitor for Solid Tumors
Oncology Research Collaboration		
Partner	Press Release Date	Summary
Sarah Cannon Research Institute	Dec. 2018	Daiichi Sankyo and Sarah Cannon Research Institute Launch Strategic Collaboration to Develop Novel Cancer Therapies
Zymeworks	May. 2018	Zymeworks and Daiichi Sankyo Expand Immuno-Oncology Collaboration Focused on Bispecific Antibodies
DarwinHealth	Apr. 2018	Daiichi Sankyo and DarwinHealth Enter Exclusive Research Collaboration for Novel Cancer Target Initiative

Puma Biotechnology	Dec. 2017	Daiichi Sankyo and Puma Biotechnology Announce Research Collaboration with Major Cancer Center in HER2-Mutated Cancer
MD Anderson Cancer Center	Sep. 2017	MD Anderson and Daiichi Sankyo Enter Research Collaboration to Accelerate Development of Acute Myeloid Leukemia Therapies
Max Planck Innovation and Lead Discovery Center	Jul. 2017	Daiichi Sankyo, Max Planck Innovation and Lead Discovery Center Announce Cancer Research Collaboration

Development Experience of a Nucleonic Acid Drug

Although Daiichi Sankyo did not have as much knowledge and experience with nucleic acid drugs as Moderna and BioNTech, its experience in developing DS-5141, a treatment for Duchenne muscular dystrophy, may have been useful in the production of mRNA vaccines[59].

3.2.4. The Platform Strategy Enables Investing in Automated Facilities or Digital Infrastructures that Enhance Corporate Capacity

This section summarizes the factual information regarding the digitization and automation enabled by the mRNA product/technology platform strategy, including the processes involved and their resulting effects.

3.2.4.1. Moderna: Leveraging Digital Platforms and Automation for Enhanced Drug Discovery and Development

Digital and Capital Investments for the Platform Strategy

According to the "Moderna(A)", Stéphane Bancel, serving as the CEO of Moderna, was driven by a compelling vision to transform the company into a leading digital entity within the pharmaceutical sector. His career began with a strong foundation of management role and digital experience in the life sciences industry, having held significant positions at Eli Lilly and Company and later as CEO of bioMérieux, a French diagnostics company. Bancel, a native of France with engineering and coding experience, recognized the challenges posed by unintegrated data systems and was determined to avoid these at Moderna. [11]

Bancel's commitment to digital innovation was evident from the early days of Moderna, a venture that began to take shape when one of its founders, Afeyan, approached him. With his background, Bancel was keenly aware of the advantages of starting digital, acknowledging that retrofitting digital processes into legacy systems would be more challenging. Bancel's perspective on the role of technology in Moderna's operations was clear from his assertive statement, “We’re a technology company that happens to do biology.” [11]

His resolve to digitize Moderna was rooted in his past experiences, where he witnessed firsthand the challenges posed by unintegrated data systems. He articulated his motivation and strategy, saying, "I've seen the disaster that unintegrated data and systems can cause. I have been in places where I know more about computers than the IT guys. From day one, I wanted to turn Modena into a digital company. To do that, we needed to build IT right, even if it meant investing heavily at a time when we had no revenue stream. It is much easier to go digital from the beginning than to go digital later with a legacy system." As you can see, to actualize this vision, Bancel made substantial investments in digital infrastructure, even at a stage when Moderna had not yet established a revenue stream. He also assembled a team of specialists, emphasizing the importance of having a skilled workforce to support the company's digital transformation. [11]

Digital Technology and Organizational Architecture for the Platform Strategy

According to the “Moderna(A)” case, in pursuit of this digital-first strategy, Bancel didn't just focus on incorporating technology into Moderna's workflow. He aimed to revolutionize the company's operations by streamlining them before integrating digital processes. This approach was not merely about adopting digital tools but about reimagining and restructuring operations to be more efficient and effective, thus laying a solid foundation for digital integration. [11]

Bancel's vision extended to the human resources aspect of digitization. He believed in a holistic approach to integrating digital processes throughout the organization's architecture. This was evident when Marcello was hired to oversee digital and operational excellence. Bancel's guidance to Marcello was pivotal, emphasizing the inseparability of digital and operational roles. He advised, "The key was to allow Marcello to design the process. Digitization only makes sense

when the process is complete. If you have crappy analog processes, you end up with crappy digital processes." [60]

Bancel's leadership and strategic foresight were pivotal in aligning Moderna's organizational architecture which the drug platform plays the central role with its digital platform, ensuring that both digital and operational excellence were interwoven into the fabric of the company's operations.

Formation of Digital Platforms Centered on the Drug Platform Based on the Scientific Mechanisms

The Moderna website said about the Business Strategy's Massively Parallel R&D Ecosystem Model, “Given the software-like nature of our technology and the repeatability enabled by our platform, our business strategy is to advance a broad array of mRNA medicines for many diseases simultaneously. To execute this strategy, we have created a unique ecosystem that enables parallel progress and shared learning. Across our ecosystem, scientists within Moderna, scientists at our pharma partners, and a bevy of academic collaborators are concurrently progressing dozens of mRNA R&D programs, all leveraging our platform. This model elicits a network effect on two levels: 1) within a modality and 2) between and among modalities. In both cases, scientists have access to real-time data readouts and information, and the resulting shared learnings are accelerating R&D efforts. Digitization is enabling seamless integration across the ecosystem, the ability to share and access data in real-time, the capability to scale, and the ability to meet ever-increasing demands for mRNA for both research purposes and clinical studies.”.[61]

Drug Design Studio Enables a Learning Cycle

One example of a digital platform-based learning cycle is Drug Design Studio. On this platform, scientists input mRNA sequence information they wish to study, protein sequence optimization and other processes are performed, and simulations are performed. This data is also connected to Northwood's automated factory, where researchers can obtain the materials needed for wet lab research, enabling more efficient research. This learning cycle has allowed Moderna to rapidly accumulate mRNA knowledge.

There is an article that comments on this, saying, “Johnson and his team put AI and automated robots to work making lots of different mRNAs for scientists to experiment with. Moderna quickly went from making about 30 per month to more than one thousand. They then created AI algorithms to optimize mRNA to maximize protein production in the body — more bang for the biological buck. For Johnson and his team’s next trick, they used AI to automate science itself. Once Moderna’s scientists have an mRNA to experiment with, they do pre-clinical tests in the lab. They then pore over reams of data to see which mRNAs could progress to the next stage: animal trials. This process is long, repetitive, and soul-sucking — ill-suited to a creative scientist but great for a mindless AI algorithm. With scientists’ input, models were made to automate this tedious process.”[62].

Moderna’s white paper says, “Our strategy at Moderna is focused on advancing mRNA medicines across many therapeutic areas and diseases simultaneously using mRNA as a medicine. Broadly exploring the potential of our mRNA technology to address many diseases simultaneously requires a digital model that deeply transforms how we design and manufacture medicines. This model elicits a cycle of continuous data generation, analysis, and learnings, which, in turn, inform and accelerate future R&D efforts.” [63]. As it is, Moderna accumulates knowledge through cycles in several forms.

High Throughput for the Lipid Nanoparticle Optimization

High-throughput methods have also efficiently increased the knowledge of Moderna. In LNPs, physical properties, particle size, and characteristics vary greatly depending on the proportion of anions, cations, and other chemical compounds. Therefore, it is necessary to obtain the optimal phospholipid composition for the application by conducting various experiments. It is also necessary to optimize the injection speed, injection sequence, etc., based on a myriad of combinations. In this case, the high-throughput method allows us to try those combinations exhaustively and to develop the manufacturing process information of LNPs with the required properties at an early stage.[64]

"mRNA Access" Initiative Which may Induce Network Effects

One notable example of a platform strategy is Moderna's "mRNA Access" initiative, launched in 2022. Through this program, researchers are granted access to Moderna's proprietary mRNA technology platform, enabling them to leverage the platform's capabilities for their own research on emerging and neglected infectious diseases. This open approach allows Moderna to expand its network of collaborators and partners. As the number of partners increases, it facilitates the accumulation of knowledge and expertise related to the mRNA platform. Consequently, as the platform becomes more robust and comprehensive, it attracts further partnerships, exemplifying the network effects inherent in platform business models[65,66].

Formation of Digital Platforms Centered on the Drug Platform Create Partnerships

Prior to the COVID-19 pandemic, Moderna had already established strategic research collaborations with various partners, serving as precursors to a platform approach. A notable example is Moderna's extensive partnership with Merck, initiated in 2016. The depth and longevity of this relationship suggest that the companies shared access to Moderna's digital infrastructures, enabling more effective and integrated research collaboration[67].

Moderna's growing prominence as a digital pharma also led to the acquisition of outside partners. For example, Lonza, a well-established CDMO, is also strong in digital technology and was able to become a partner because Moderna was a pharmaceutical company that was proficient in digital technology.

Moderna invested very heavily in intangible assets such as digital platforms, tangible assets such as robots and automated factory equipment, the human resources to support them, and the creation of streamlined business processes.

Below is the Twitter of Moderna, saying that they have invested a lot in Digital technology, AI, process development, and manufacturing[68].

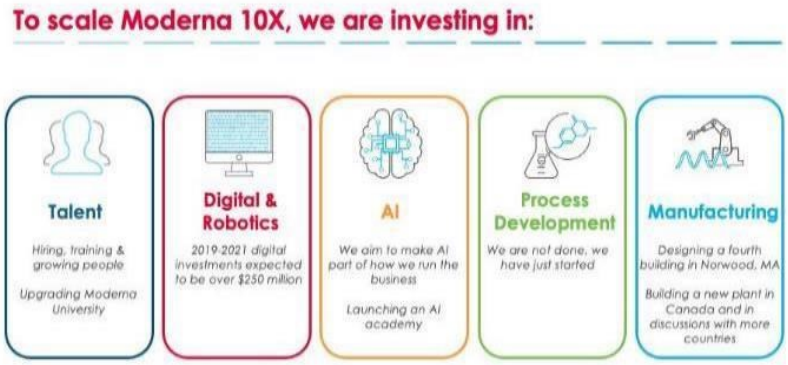


Figure 3.20 Moderna Investment Toward Digital or Automation Technologies[68]

Thus, it is clear that Moderna was aware of the model's strategy of digitizing around the drug platform and bringing about a network effect.

Digital Platform Enabling Efficient Incorporation of Technical Knowledge and Facilitating Collaboration with Stakeholders

The digital platform built by Moderna has dramatically improved the learning capacity of the organization. In particular, the combination of the digital platform, automated factory equipment, and talented scientists created a cycle of learning that synergistically increased the organization's knowledge of the technology platform. There are two important perspectives.

1. Digital, Automated Infrastructure Platforms Increase Research Productivity

Moderna's use of AWS's digital and automated infrastructure platform has significantly increased its research productivity. By utilizing AWS's highly scalable computer and storage infrastructure, Moderna can rapidly design and experiment with mRNA sequences for various protein targets. This allows the company to quickly shift between research priorities without the need to invest in new infrastructures. Moderna's Drug Design Studio, which runs on AWS, enables scientists to optimize mRNA sequences for production, ensuring that the automated manufacturing platform can successfully convert them into physical mRNA for testing. This streamlined process greatly reduces the time and resources required for experimentation, thereby increasing overall research productivity.[69]

2. Digital Infrastructure Platform Enables Knowledge Sharing and Collaboration

Moderna leverages Amazon Redshift, AWS's fully managed data warehousing service, to aggregate results from multiple experiments running in parallel. This centralized data repository allows Moderna's scientists and engineers to easily query and share insights, fostering a collaborative research environment. The ability to access and analyze data from various experiments simultaneously enables researchers to refine their design and production cycle quickly. This knowledge sharing and collaboration, facilitated by the digital infrastructure platform, accelerates the discovery process and promotes innovation within the organization.[69]

In order to evaluate the above points, below is the number of the co-authors of each research paper. It shows the number of the co-author is 12.31 in Moderna, 12.85 in BioNTech and 9.29 in Daiichi Sankyo. This result might suggest that the digital environments allow them to collaborate with large number of researchers.

However, it is important to note that research papers often involve collaborators from various disciplines, and the number of co-authors alone may not provide a complete picture of the extent and nature of collaboration within these organizations. The higher number of co-authors in Moderna and BioNTech's papers could be influenced by factors such as the complexity of the research, the number of institutions involved, and the overall research culture.

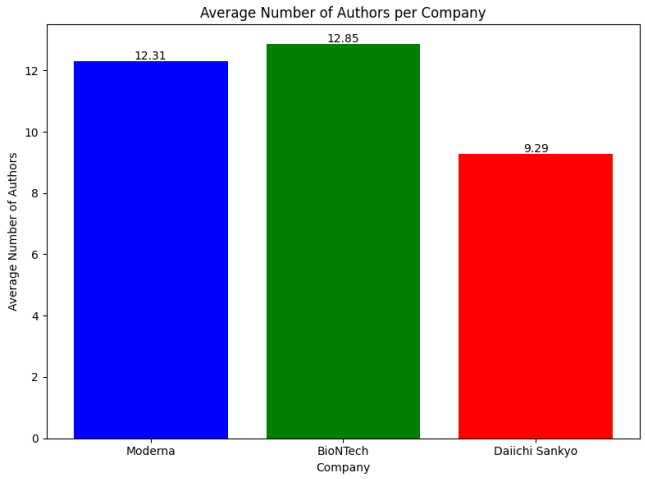


Figure 3.21 The Graph Shows the Number of Authors of the Academic Papers Published by Moderna (2010-2019), BioNTech (2008-2019), and Daiichi-Sankyo (2008-2019)

Platform Strategy Enhances Investment in Digital Manufacturing Facilities, Boosting Efficiency in Research, Development, and Collaboration

Moderna's digital factory concept allows for seamless switching between pharmaceutical products, underscoring the flexibility and efficiency of digital control technologies. This adaptability was crucial in facilitating a rapid pivot to COVID-19 vaccine production, underscoring the platform's ability to accommodate diverse manufacturing requirements from various partners.

In fact, in 2018, Moderna launched a fully digital manufacturing facility in Norwood, Massachusetts. The company announced plans to build the facility in September 2016. The plant's construction was completed in early 2018 and involved a $110m investment[70]. Moderna's facility won the International Society for Pharmaceutical Engineering's (ISPE) Facility of the Future award in 2019[70]. The ISPE web said that "The Norwood facility was designed to be highly flexible, adaptable and capable of manufacturing both for clinic and research. The digital production environment is designed to enable high throughput with a robust and diverse set of products. The enterprise and process control systems are integrated in a manner that enables flexibility and rapid new product introduction in a highly automated landscape. Digital technology is integrated throughout the site and includes integration of the enterprise resource planning system with electronic production records, process control systems, the data historian, and laboratory information management system. This digital platform streamlines product manufacturing, testing, and release. It also enables robust data management to support development activities and process characterization."[71]. It also noted below that the design of the new facility addresses Moderna's objectives of having a single, fully integrated Early Development Engine capable of manufacturing an expanding pipeline of drug candidates in a highly adaptable platform. Key design elements include:

- Designed for flexibility and rapid changeover between campaigns and for new development candidates, with manufacturing spaces that can be repurposed to address changes in product mix.
- Full digital integration in support of all operational aspects of the facility, process and quality systems delivering a fully integrated manufacturing and supply chain.
- Architectural design supports a highly collaborative flexible and energized work force. The design incorporates an open work plan, visibility from manufacturing spaces to the outside

by the generous use of glass partitions, free-access huddle rooms and soft-seating collaboration areas.

Moderna has built a highly automated and digital enterprise to seamlessly integrate and orchestrate cloud-based IT systems to manage and industrialize the complex planning and execution of its mRNA pipeline scale-up at every stage of development[71].

For the project, engineering and project management company DPS was awarded a contract to provide architectural, engineering and design services for Moderna's manufacturing facility. The contractual scope also included construction management, commissioning, qualification, and validation. Also, engineering and automation company Hallam-ICS provided instrumentation and control system infrastructure for the facility, while automation and control systems were produced by Siemens, an industrial manufacturing company based in Germany[70].

In the white paper of Moderna, it said, "Within our qualified digital systems, this design allows us to implement digital changes required to support a new product in only a few days."[63]. Bancel, the CEO of Moderna, mentioned that this technology enables the partnership to be built. He said, "Industry and government should consider a permanent public-private partnership to help companies take the sort of financial risks that lead to vaccine breakthroughs.

Such a partnership could build a large facility that companies could use to produce commercial vaccines for commercial use but would switch 100% of capacity to the public good during a pandemic to manufacture whatever vaccine was required. A process technology like Moderna's could make such a quick switch possible"[30].

Human Resource Strategy and Growth

Dave Johnson, who is the chief data and artificial intelligence officer at Moderna, said that "Moderna is the kind of company that likes to give people a lot of freedom — [a] highly motivated, smart, ambitious team working to do the best it can." We get people from biotechs, [from] five people to pharma of 100,000 people and everywhere in between, [from] inside the industry and outside the industry. I think for us, it's always about finding the right person for the job, regardless of where they come from and their background. I think the important thing for us is to make sure

that we set expectations appropriately as we bring them in and we say, “Look, this is a digital company. We’re really bold. We’re really ambitious. We have really high-quality standards.” And if we set those expectations really high, it does start to self-select a lot of the people who want to come through that process.”[72]. This suggests that digitalization is an important aspect of recruiting, and specific requirements set by the company's digitalization can attract increasingly talented individuals.

Table 3.6 Growth in Moderna's Employees Count Over Time[73]

Number of employees of Moderna	
Year	Number of employees
2013	80
2015	145
2016	460
2017	700
2018	760
2019	830

3.2.4.2. BioNTech: Investing in Digital Technologies and Strategic Partnerships

Digital and Capital Investments for the Platform Strategy

BioNTech also had been invested digital technology for a long time. For example, it said that “We at BioNTech invested early in developing ML-trained algorithms to improve the prediction of targets for our individualized #cancer immunotherapy approach, with initial results published in Nature in 2017.” In its LinkedIn page.

In 2019, when BioNTech was successfully funded, CEO Uğur Şahin said that “With our ongoing focus on bringing together transformative technologies, it is exciting to have the support from high-technology investors who see the accelerating convergence of biology with bioinformatics, robotics, and artificial intelligence as an opportunity to develop more precise, efficacious and cost-effective individualized immunotherapies.” Suggested that BioNTech heavily invested in digital technology, same with the Moderna[74].

Formation of Digital Platforms Centered on the Drug Platform Based on the Scientific Mechanisms

BioNTech has also been involved in manufacturing process innovation for some time. For example, the production of therapeutics associated with personalized therapies, which until 2016 required more than three months of needle-to-needle time due to manual production, was reduced to less than five weeks in 2017 due to semi-automation[44].

In the article of "Siemens and BioNTech cooperate on production of personalized cancer vaccines" in 2015 said that Siemens and BioNTech AG have entered into a strategic collaboration to develop and construct a fully automated and digitalized production site for the manufacturing of BioNTech's Individualized Vaccines against Cancer (IVAC®). The partnership aims to integrate all necessary process and production steps for manufacturing personalized cancer vaccines at a larger scale, leveraging Siemens' expertise in automation and digitalization technology and BioNTech's competence in individualized medicine. The collaboration seeks to optimize the manufacturing process for personalized medicines, enabling efficient, paperless production and accelerating the availability of personalized cancer treatments for patients worldwide with the below points[75].

- Strategic collaboration between Siemens and BioNTech AG to establish a fully automated and digitalized production site for personalized cancer vaccines.
- Integration of all necessary process and production steps for manufacturing BioNTech's IVAC® individualized vaccines at a larger scale.
- Combination of Siemens' expertise in engineering and optimizing automatic manufacturing processes with BioNTech's competence in individualized medicine.
- Implementation of Siemens' manufacturing operations management (MOM) software to handle the complexity of the innovative process technology.
- Siemens' paperless manufacturing solution enhances efficiency, product quality, and reduces costs by establishing fully integrated communication between the automation level and manufacturing IT.
- The collaboration aims to accelerate the design, execution, review, and release of pharmaceutical production processes and electronic batch records (EBRs).

Pfizer's Digitization Efforts

Pfizer has also been working on digitizing clinical trials for many years. Pfizer is expanding access through digital tools, new data collection methods, and diverse partnerships. It is also working to modernize, streamline, and simplify drug development through automation, artificial intelligence, and predictive analytics. By collecting and accurately analyzing vast amounts of data, we can reduce the risk of errors and speed up the drug development process. Other advances in remote data collection, including wearable devices and mobile apps, are also working to make it more convenient for people to participate in clinical trials[76].

Rapid Growth in Human Resources

The number of employees grows in time[73].

Table 3.7 Growth in BioNTech's Employees Count Over Time[73]

Number of employees of BioNTech	
Year	Number of employees
2013	352
2014	329
2016	400
2017	700
2018	750
2019	1310

3.2.4.3. Daiichi Sankyo: Limited Data on Pre-Pandemic Digitalization Efforts

There is a lack of useful information available regarding digitization efforts prior to the pandemic.

The number of employees in time[73].

Table 3.8 Growth in Daiichi Sankyo's Employees Count Over Time[73]

Number of employees of Daiichi-Sankyo	
Year	Number of employees
2008	15500
2009	29467
2010	29825
2011	30488
2012	31929
2013	32229
2014	32791
2015	16428
2016	15249
2017	14670
2018	14446
2019	14887

3.2.5. External Factors

The initiatives mentioned above, including the integration of drug discovery and digital platforms, are influenced not only by the management strategies within pharmaceutical companies but also by external factors such as government support, regulatory elements, and the broader ecosystem. These external factors can act as both accelerators and barriers to the development and implementation of such initiatives.

3.3. Why Could Moderna or BioNTech Develop the Vaccine So Rapidly?

This section provides a factual account of how these companies carried out the COVID-19 vaccine development project during the pandemic, leveraging the capabilities they had built beforehand.

3.3.1. Launch of the COVID-19 Vaccine Development Project

Below is the timeline, which is from December 2019 to January 2020, the COVID-19 pandemic, which is said to start at the end of 2019. As you can see, the situation is rapidly evolving, and each stakeholder has to decide to develop the vaccine based on the situation.

Early Days of the COVID-19 Pandemic: A Timeline from Outbreak to Global Emergency

On December 12, 2019, an unusual pneumonia emerged in Wuhan, Hubei, China. By December 31, WHO was alerted to this pneumonia of unknown cause. On January 1, 2020, Wuhan's Huanan Seafood Market closed, and WHO activated its Incident Management Support Team on January 2. Over 40 cases were reported by China on January 3. The CDC began an investigation on January 5, the same day the virus's genetic sequence was submitted by Yong-Zhen Zhang. By January 7, a novel coronavirus was identified as the cause. WHO named it "2019-nCoV" on January 10, the same day the CDC published outbreak information. The virus's genome was posted online by Edward C. Holmes on January 10. WHO received the genetic sequences on January 11, and the first death was reported in China. Thailand confirmed its first case on January 13, and WHO noted evidence of human-to-human transmission on January 14. The first U.S. case was reported by the CDC on January 20. On January 21, CDC artists created an identifiable image for the virus, and China confirmed human-to-human transmission. WHO decided not to declare a Public Health Emergency on January 22. Wuhan was locked down on January 23. By January 26, the U.S. had five confirmed cases. The FDA announced actions on January 27, and CDC issued a travel advisory on January 28. U.S. citizens were repatriated from Wuhan on January 29. The first U.S. person-to-person transmission was confirmed by the CDC on January 30, and on January 31, a federal quarantine was issued for repatriated citizens, WHO declared a Public Health Emergency, and the U.S. declared a public health emergency.[77]

3.3.1.1. Moderna: Swift Response to the Emerging Pandemic Threat(COVID-19)

In early January, Bancel learned about a new infectious agent causing a pneumonia-like disease and contacted Dr. Anthony Fauci's team at the NIH. Shortly after, it was determined that the agent was not the flu or bacteria, but a new type of coronavirus distinct from SARS or MERS. By the second week of January, Chinese scientists in Wuhan had isolated and sequenced the virus, leading to demands for the release of this information. The gene sequencing data was made

available on January 11 on Virological.org. Using this data, Moderna's team was able to finalize the design of a vaccine candidate against the new virus by January 13[11]. The story shows that Bancel was always up to date on the latest infectious disease situation and was in a position to smoothly exchange information with infectious disease experts in the public sector.

The Moderna (A) case illustrates how Moderna got into the vaccine project. It says “Moderna shifted into high gear when the first death was announced. Over the weekend of January 11 and 12, the Chinese authorities posted the genome sequence of the virus online for everybody to access. Given his deep experience in big pharma, Andres realized quickly what the situation meant. “This is pandemic response. If we decide to pursue this, it means we need to be all in. There’s no exit. You put one toe in the water, and you are all in.” The executive committee engaged in a lively discussion and decided that Moderna would try to develop a vaccine and be in the clinic before anyone else. “After January 13, all hands were on deck,” remembered Moore. “Though designing the actual mRNA sequence only took a few hours, manufacturing the vaccine and performing all the necessary testing was an around-the-clock effort. It really brought out the best in people. There was a clear goal and an urgent threat at the same time. We knew we had to act fast, and everyone was invested in this.” [11]

3.3.1.2. BioNTech: Leveraging Technological Readiness to Launch Project Lightspeed

On January 24, 2020, Uğur, the CEO of BioNTech, began to take an interest in infectious diseases, later called COVID-19, from an immunology standpoint. After surveying information on infectious diseases, he realized that this was the disease he had to tackle through vaccine development[42]. After careful thought and negotiation with a board member of BioNTech, it launched the COVID-19 vaccine development project named Project Lightspeed. The naming of the light speed is the project should be the fastest as possible as long as that is within the physical limit[42,45].

Having a sufficient reservoir of experience is crucial for starting vaccine development project. In their book "The Vaccine Race: Inside the Epic, Risky Race to Develop a COVID-19 Vaccine," emphasize the importance of BioNTech's technological readiness. They write, "If the novel coronavirus pandemic had occurred two years earlier, BioNTech's board would not have accepted

the vaccine development proposal. However, their technology platform had evolved significantly in recent years, and Uğur Şahin, the co-founder and CEO of BioNTech, was convinced that they possessed all the necessary tools to address a pandemic." This sentiment was echoed by Uğur, stated, "We should go all in on this."[42]

3.3.1.3. Daiichi Sankyo: Delayed Entry into the COVID-19 Vaccine Development

A press release of June 2020 said that “In April 2020, Daiichi Sankyo established a task force to promote company-wide R&D on vaccines and therapeutic agents for COVID-19; moreover, in our role as a pharmaceutical company, by leveraging our research properties, technologies and knowledge to the maximum extent, and through partnerships with other organizations, we are proactively involved in the establishment of medical systems in the fight against COVID-19, for which there is an urgent global social need.”[78]

Comments: While Daiichi Sankyo start the COVID-19 vaccine development project may be noble to embark, beginning in April is considered a slow start compared to Moderna and BioNTech, which launched their projects in January. The delay in starting could be attributed to two main factors.

Firstly, Daiichi Sankyo's vaccine project is just one of many divisions within the company, which is not primarily a platform company. This diversity might lead to speculation that Daiichi Sankyo's leadership did not promptly evaluate their assets or risks. To move the project forward, the leaders would need to consider bottom-up proposals from the vaccine division, which can be time-consuming.

Another significant concern might be the risk of patent issues. As analyzed earlier, Daiichi Sankyo's patents, particularly in mRNA or lipid nanoparticle (LNP) technologies, are not as robust as those of Moderna or BioNTech. Therefore, initiating an mRNA vaccine project could potentially expose Daiichi Sankyo to litigation risks. Given this, Daiichi Sankyo had to carefully consider whether to proceed with the project or not.

Hence, Daiichi Sankyo's slower start in April 2020 can be attributed to its diverse portfolio and the need to carefully assess potential patent litigation risks.

3.3.2. Discovery phase: Enabled by Accumulated Knowledge, Partnerships, and Digital Resources.

In the Discovery phase, the primary goal is to design vaccine-candidate substances. To achieve this, an integration of accumulated virological knowledge, information on the coronavirus, and the latest mRNA technology was necessary for the design of potential pharmaceutical compounds. Companies like Moderna and BioNTech had the requisite knowledge, partnerships, and digital infrastructure in place, enabling rapid execution of the Discovery process.

For the development of mRNA vaccines against SARS-CoV-2, it was crucial to start the development process early, using the viral information released on January 11. It was possible to infer the meanings of various sequences based on the structures of related viruses like SARS and MERS(Figure 3.22.)[79]. There was a consensus among experts on the efficacy of designing antigens based on the S protein derived from existing research. Thus, integrating this information early on was vital for advancing development. Furthermore, the availability of a digital infrastructure was essential for the specific development processes, facilitating efficient and streamlined research and development activities.

In the development of mRNA vaccines, sequence optimization is important for vaccine efficacy and safety, and the need for the use of AI algorithms has been identified[80].

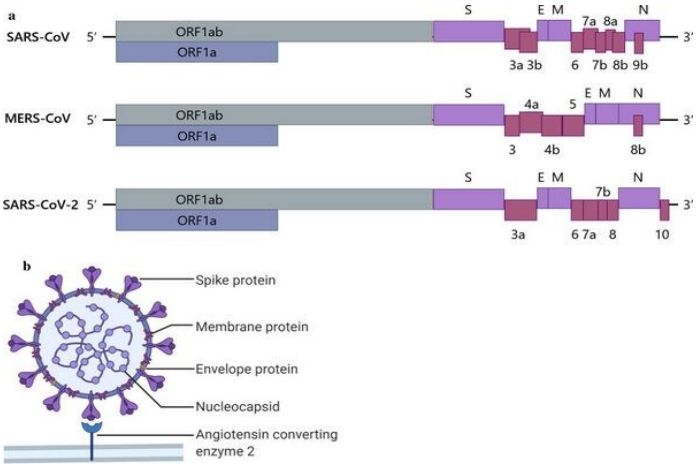


Figure 3.22 Comparison of the Genome Organizations and Virion Structures of SARS-CoV, MERS-CoV, and SARS-CoV-2[79]

3.3.2.1. Moderna (Discovery phase): Rapid Vaccine Design Leveraging Existing Knowledge, Partnerships and Digital Infrastructure

Regarding the Discovery phase: after the outbreak in Wuhan, China, at the end of 2019, on January 11, Chinese researchers published the sequence of the SARS-CoV-2 virus. Immediately, Moderna researchers and NIAID researchers analyzed the sequence and determined the design of mRNAs targeting the S protein based on SARS and MARS findings in a matter of days.[11]

In the discovery phase, Moderna leveraged its existing processes and digital platform model to generate the mRNA sequence for the COVID-19 vaccine. This was a routine endeavor for the company, as they had already built and tested these processes before. The vaccine was designed on the computer, taking advantage of Moderna's fully digital facility and platform model.[11]
Amazon's press release stated that "Moderna has selected AWS as its preferred cloud provider, as well as its standard for analytics and machine learning workloads. Leveraging its mRNA platform and manufacturing facility with the AWS-powered research engine, Moderna delivered the first clinical batch of its vaccine candidate (mRNA-1273) against COVID-19 to the NIH for the Phase 1 trial 42 days after the initial sequencing of the virus. By building and scaling its operations on the world's leading cloud, Moderna is able to quickly design research experiments and uncover new insights, automate its laboratory and manufacturing processes to enhance its drug discovery pipeline, and more easily comply with applicable laws and regulations during production and testing of vaccine and therapeutic candidates."[69]

Stéphane Bancel, Moderna's Chief Executive Officer said that "The science behind mRNA medicines is advancing at a rapid pace, and building Moderna's technology platform on AWS gives our scientists the insights, agility, and security they need to continue to lead in the industry," and also said "With AWS, our researchers have the ability to quickly design and execute research experiments and rapidly uncover new insights to get potentially life-saving treatments into production faster. AWS's breadth and depth of services are supporting our mission to create a new generation of medicines for patients and are instrumental in our quest to develop a vaccine for COVID-19 and other life-threatening diseases."[69]

For the rapid completion of the discovery phase, Melissa Moore, chief scientific officer of platform research at Moderna, said, “We had already invested years of fundamental research to find the best algorithms for designing mRNA. But we didn’t just do the basic science on mRNA; we are a delivery company, too. So, we had also done much research to find the best lipids to deliver mRNA once in the body. The final piece of the puzzle was knowing which viral protein to make. Our Infectious Disease group had also been working for years with colleagues at NIAID on coronavirus coat proteins, so they knew exactly what variant of the “spike” protein would produce a potent immune response. The combined know-how from mRNA science, research on LNPs to deliver mRNA, and knowing which protein we needed the body to make allowed us to act fast when the Chinese researchers published the sequence on January 11. We knew we could design the RNA that encoded the right viral protein and that we could do it fast.” [11]

3.3.2.2. BioNTech (Discovery phase): Collaborative Approach and Machine Learning in the Vaccine Development

Uğur Şahin, the co-founder and CEO of BioNTech, personally read the scientific literature and identified the S-protein as a potential target for the COVID-19 vaccine. To determine the specific target, Sahin consulted with infectious disease experts, focusing on whether to target the entire S-protein or the binding site. Also, BioNTech then conducted experiments with all combinations of the four types of RNAs (uRNA, modRNA, saRNA, and taRNA) to narrow down the candidate vaccines.[42]

Although BioNTech had developed its own lipid nanoparticle (LNP) technology, the company lacked experience in administering it to human subjects. Utilizing their own technology would have significantly prolonged the development period. Conversely, Acuitas Therapeutics' LNP technology was superior and had been previously administered to humans. Following the pandemic, BioNTech finally employed Acuitas' technology through Genevant Sciences. BioNTech had been in communication with Acuitas since 2018, which facilitated the smooth integration of the technology. At that time, the two companies had collaborated on drug development using mRNA technology, which later came to fruition.[42]

In the drug platform, even though the end use may differ, the underlying technology remains similar. As a result, partnerships formed during the development process can continue to thrive and adapt to various applications. The collaboration between BioNTech and Acuitas Therapeutics demonstrates how established partnerships can streamline the development process and contribute to the successful implementation of cutting-edge technologies in the face of a global health crisis. The article said that "The firm Instadeep began just before the pandemic a collaboration with BioNTech, to help find the optimal mRNA vaccine design by using machine learning. Machine learning speed up the process that would normally have been like 'looking for a needle in a haystack'"[81].

3.3.2.3. Daiichi Sankyo (Discovery Phase): Partnership with a University

The development of the vaccine was carried out in collaboration with the University of Tokyo under the guidance of the Japan Agency for Medical Research and Development (AMED), a national research and development organization, as stated in the press release. During the research and development process, the company participated in the "Basic Research for the Control of the COVID-19" project, led by Professor Yoshihiro Kawaoka from the Institute of Medical Science at the University of Tokyo. As part of this project, the company used a novel nucleic acid delivery technology, which involves the formation of lipid nanoparticle structures to stabilize active pharmaceutical ingredients and deliver nucleic acids into immune cells. The approach aims to induce more optimal immune responses compared to conventional vaccine technologies. Utilizing this newly discovered nucleic acid delivery technology, the company has been focusing on the development of an mRNA vaccine against COVID-19. [78]

3.3.3. Development Phase: Enabled by Digital Resources

In the Development phase, it is essential to demonstrate the efficacy and safety of the candidate substances identified during the Discovery phase, and have to get an FDA approval. This process, especially in the context of vaccine development, needed to be conducted swiftly on a large scale. The experience in conducting clinical studies with the technology in question, the capability to manage and execute such clinical trials, digital infrastructure, and organizational capacity were crucial components for success.

3.3.3.1. Moderna (Development Phase): Leveraging Digital Technologies and AI-Powered Clinical Trials

Generally speaking, drug candidates have to pass animal testing before going into the First-In-Human (FIH) trials. However, in the case of Moderna, as it had several experiences developing mRNA vaccines, as we have explained above, it could waive the animal experiments, which would typically take a few months, enabling it to speed up the development phase. [42]

During the development phase, according to Moderna (A), Moderna's paperless factory and digital manufacturing systems played a crucial role in streamlining the process. All machines were directly connected to these digital systems, enabling seamless integration and management of the entire manufacturing process. Integrated electronic batch records were utilized to save time and money across various aspects, such as equipment use, testing, and release. These records helped operators select, manage, and track raw materials through real-time integration with SAP. They also facilitated testing steps, including labeling, information-sharing, audit trails, and security controls, ensuring accuracy and speed. The digital system captured all batch record exceptions in real-time, enabling swift review and quality assurance, significantly reducing cycle time. By converting stacks of paper reports and manual updating into a fully digital system that was continually updated, Moderna was able to optimize the development phase of its COVID-19 vaccine.[11]

Moderna's integration of digital technology, particularly AI, has significantly accelerated and enhanced the quality of clinical trials in the development of COVID-19 vaccines. The clinical phase is pivotal in drug development, as it involves recruiting and retaining patients, making it crucial to minimize attrition for trial integrity and success. High dropout rates can compromise data reliability, but Moderna has leveraged AI to address this challenge. AI technology aids in diverse patient recruitment and retention while identifying potential attrition points in real-time, enabling timely interventions to prevent dropouts[82].

In the clinical trial, Dave Johnson’s Chief Data and AI Officer at Moderna said that “The nature of a massive 30,000-participant vaccine study vastly differs from a 200-person study on a rare disease. When conducting these studies, our platform significantly enhanced our ability to

efficiently process data and glean insights, which was especially crucial during the early pandemic days. We have established numerous systems for integration with our external collaborators and Contract Research Organizations (CROs), facilitating near-real-time study monitoring. A prime example of this system's effectiveness is our focus on diversity within our studies. It was imperative for our Phase 3 COVID-19 study to mirror the demographic makeup of the broader US population, ensuring the vaccine's efficacy across all groups. By leveraging real-time data on enrollment demographics and regional US census information, we could assess site performance accurately. This data was not only utilized internally but also shared with the study sites to foster collaboration and ensure appropriate enrollment and recruitment. In some instances, we deliberately slowed recruitment at certain sites to achieve the desired racial diversity within the study. We take great pride in the resultant diversity of this study, and the inclusion of diverse populations in our clinical trials is a priority for us.". He also mentioned, "Specifically, I often emphasize that our data scientists are not mere analysts; their role isn't to provide straightforward answers to isolated queries. For instance, determining locations for our clinical trial sites—a challenge we also faced during our COVID study—is not about pinpointing where to conduct a Phase 3 COVID trial in the U.S. on a case-by-case basis. Instead, our focus is on developing robust platforms that empower our scientists and operational teams to address their questions independently. Our goal is to create a system that facilitates the selection of clinical trial sites for any study and addresses racial and diversity metrics comprehensively, rather than providing solutions to individual problems." (https://www.youtube.com/watch?v=o0CKu_Gd-98&t=2s).

3.3.3.2. BioNTech (Development Phase): Accelerating Clinical Development through Digital Technologies

For BioNTech's limited experience with the combination of mRNA and lipid nanoparticles (LNP) made it challenging to completely exempt the animal study phase during the development of their COVID-19 vaccine. However, they could shorten the experiments considering the pandemic phase[42].

Pfizer said, "We harnessed Digital innovation to accelerate our COVID-19 vaccine efforts. Given the need to progress the vaccine clinical trial quickly, yet without compromising the safety and well-being of the researchers and clinical trial participants, we played a key role in accelerating

the clinical development of the vaccine: In just four months, we scaled our clinical trial to 46,000 participants at 150 sites in six countries, and real-time predictive models of COVID-19 county-level attack rates helped the clinical development team target clinical trial site selection and optimization. Using artificial intelligence and machine learning, our scientists were able to quickly quality-check and analyze the vast amounts of data associated with the trial. Remote site monitoring enabled clinical trial sites to share source documentation with site monitors, something that was previously done in person. Between March and December 2020, 75 percent of site monitoring visits for the vaccine study were conducted remotely, compliantly with applicable requirements."[83].

The protocol of the clinical trial suggests that they use the electronic diary to monitor the symptoms of the study participants[84]. Also, Pfizer utilizes AI technology in clinical trials. Pfizer says "Normally, when a clinical trial or trial phase ends, it can take more than 30 days for the patient data to be "cleaned up," so scientists can then analyze the results. This process involves data scientists manually inspecting the data sets to check for coding errors and other inconsistencies that naturally occur when collecting tens of millions of data points. However, thanks to process and technology optimizations, including a new machine learning tool known as Smart Data Query (SDQ), the COVID-19 vaccine clinical trial data was ready to be reviewed a mere 22 hours after meeting the primary efficacy case counts. The technology enabled the team to maintain an exceptional level of data quality throughout the trial, leaving minimal discrepancies to resolve during the final steps."[85]

The article of "Pfizer's vaccine proves the Power of Emerging Tech when the Burning Platform is Red Hot" points out "Their digital journey included adopting AI, smart analytics, and automation to both accelerate and improve the drug development process. A significant benefit of the digital journey was setting up remote clinical trials (including virtual engagement, candidate/patient data collection through wearables, etc.) that AI made more efficient. Remote trials helped retain patient engagement, which reduced attrition and accelerated the completion of trials and data collection. According to Fast Company, Pfizer's AI implementation helped rapidly identify signals within the noise of millions of data points across their 44,000-candidate COVID-19 clinical trial. They then applied a new machine learning tool from Saama Technologies, known

as Smart Data Query (SDQ), to review clinical trial data in less than 24 hours, instead of more than 30 days for the same type of reviews. This speed of access to data came with exceptional levels of data quality, making outcomes highly reliable. These steps led to the consolidation of a process from 10 years down to one year from molecule to market."[86]

3.3.3.3. Daiichi Sankyo (Development Phase): Balancing Promoting and Slowing Factors

The phase 1/2 clinical trial commenced in March 2021, followed by the phase 2 trial in November 2021, and the phase 1/2/3 trial in January 2022[87].

Comments: The timeline for these trials was not as rapid as those of Moderna or BioNTech. Various factors may have influenced the speed of the trials; however, due to the lack of information during the trial period, these remain speculative. There may have been factors that contributed to the faster progression of the trials, as well as factors that slowed them down.

One promoting factor is that since mRNA vaccines had already been approved prior to March 2021, regulatory organizations did not have to hesitate to conduct the trials. Conversely, there are several factors that may have slowed down the process.

Firstly, as mRNA vaccines were already available, there was less urgency to expedite the development of a new vaccine. Secondly, as the administration of mRNA vaccines had already begun, it may have been challenging to recruit patients who had not yet received a COVID-19 vaccine in the later phases of the trial. Thirdly, since the production of mRNA was a new process for Daiichi Sankyo, it might have taken additional time to prepare.

Considering these factors and the company's capabilities, the development speed of the vaccine was not fast. The interplay between the promoting and slowing factors, along with the company's resources and expertise, likely contributed to the observed timeline of the clinical trials.

3.3.4. Manufacturing Phase: Rapid Technology Transfer and Scale-up Enabled by Digital Platforms

During the Manufacturing phase, there was an urgent need for rapid technology transfer and scale-up to produce large quantities of vaccines early on, given the global pandemic context.

The McKinsey article of "Why tech transfer may be critical to beating COVID-19" in July 2020 discusses the importance of technology transfer in the context of ramping up COVID-19 vaccine production to meet the global demand. Technology transfer, which involves moving the knowledge and ability to produce a vaccine from development to manufacturing, is a complex process that requires a wide range of specialized skills and expertise. The article highlights that technology transfer is a time-consuming process, typically taking 18 to more than 30 months for sterile dosage forms like injectable vaccines. This process involves hundreds of separate activities and requires coordination among various functions across the donor and receiving sites. The complexity of the process is further compounded by the strict quality standards for vaccines, as they are administered to healthy individuals. Moreover, the article points out that technology transfer to an external organization takes, on average, 5.8 months longer than internal transfers. This additional time is due to the increased complexity of coordinating and communicating between different companies[88].

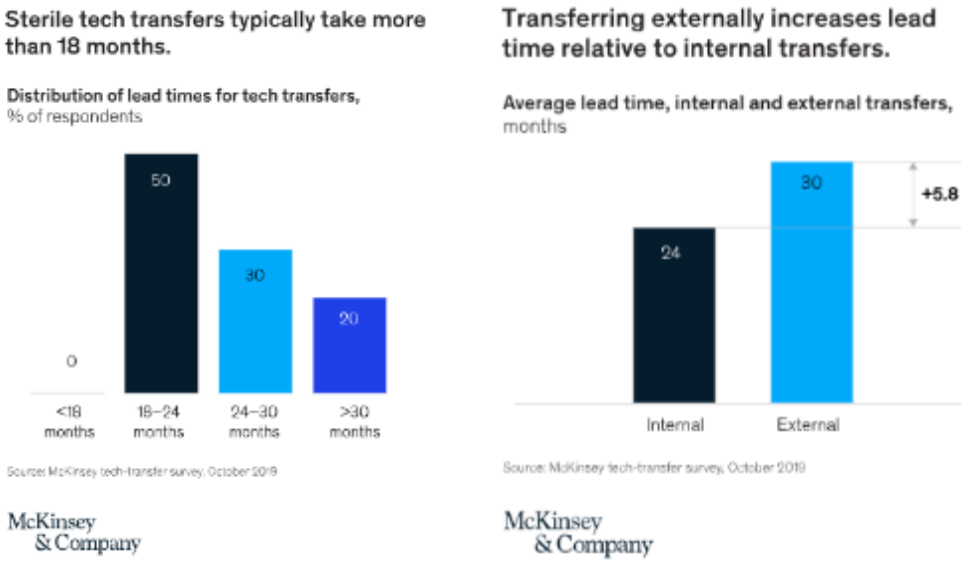


Figure 3.23 Time Required for Technology Transfer[88]

Moderna and BioNTech had the requisite manufacturing experience and digital infrastructure to achieve this.

Digital twins, virtual models that mirror physical production systems, allowing for the simulation and optimization of manufacturing processes in real time, reducing the need for physical trials and enabling quicker adjustments. MES provided the necessary control and documentation for efficient and compliant manufacturing operations. These digital tools streamlined the technology transfer process, significantly reducing the time required to scale up vaccine production in response to the urgent needs imposed by the pandemic.

In addition, the digital twin technology in the vaccine manufacturing process is also used at GSK, stating that "This digital 'factory' allows us to simulate, monitor closely, anticipate failures, and optimize quality and self-learning - ultimately allowing us to accelerate the vaccine manufacturing process and get vaccines to people much faster."[89].

The production of the mRNA is said to be relatively easy, and there is a production phase and purification phase[90]. For manufacturing or technology transfer, it is important to know the manufacturing parameters for these processes.

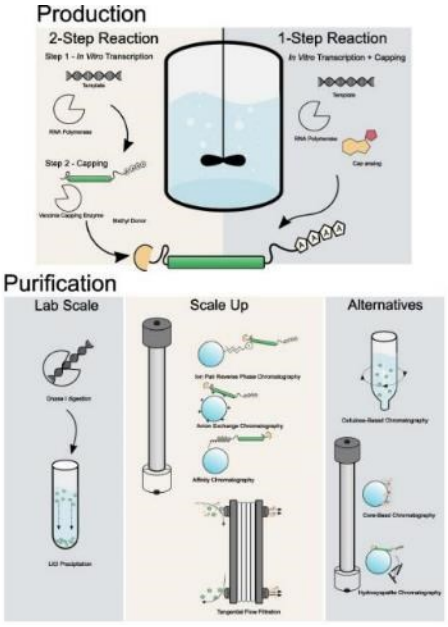


Figure 3.24 Schematic Representation of the Production and Purification Steps of mRNA Vaccine Manufacturing[90]

3.3.4.1. Moderna (Manufacturing Phase): Rapid Manufacturing Scale-up Through Strategic Collaboration with Lonza

Strategic Partnership with Lonza

Moderna had faced the challenge of scaling up production to meet global demand for the vaccine. To address this issue, Moderna formed a strategic partnership with Lonza, a renowned contract development and manufacturing organization (CDMO). The collaboration between Moderna and Lonza was facilitated by their shared expertise in digital technology, which proved to be a key factor in the success of their partnership. According to the "Moderna(A)", Lonza emerged as the ideal partner for Moderna due to several critical factors. Firstly, Lonza's U.S. plant, situated in close proximity to Moderna's Norwood facility, allowed for efficient collaboration between the two teams. Secondly, Lonza's production facility in Visp, Switzerland, provided a strategic supply base for the European market. Moreover, the pre-existing trust and shared values between the two companies, stemming from a prior working relationship between a Moderna executive and Lonza, further strengthened the foundation of their partnership. The collaboration between Moderna and Lonza aimed to expedite the technology transfer process, with the ambitious goal of completing it within three months, a significant reduction from the typical two to three-year timeline. This accelerated process was made possible by the partners' shared proficiency in digital technology and Lonza's ability to produce on a large scale. The partnership with Lonza, along with Moderna's overall progress in vaccine development, garnered significant media attention. This coverage enhanced Moderna's social status and communicate its story beyond the scope of the COVID-19 vaccine[11].

Scaling Vaccine Production and Expansion

In May 2020, Lonza and Moderna announced a ten-year strategic collaboration agreement to enable the manufacture of Moderna's COVID-19 vaccine and additional Moderna products in the future[51]. It said that "Collaboration goal to enable manufacturing of up to 1 billion doses per year", "Technology transfer expected to begin in June 2020", "First batches of mRNA-1273 expected to be manufactured at Lonza U.S. in July 2020," and "Collaboration leverages Lonza's worldwide expertise in technology transfer and manufacturing." Also, Bancel said that "This long-term strategic collaboration agreement will enable Moderna to accelerate, by 10-times, our manufacturing capacity for mRNA-1273 and additional products in Moderna's large clinical

portfolio. Lonza's global presence and expertise are critical as we scale at unprecedented speed. Our common goal is to potentially enable manufacturing of up to 1 billion doses of mRNA-1273." [51]. Following up, the partnership keeps expanding, and another press release in June 2021 said, "Once more, we are pleased to leverage our network as we expand our collaboration with Moderna further to extend our mRNA manufacturing to Lonza Geleen (NL). The extension reflects the continuing growth of our strategic collaboration with Moderna." And the announcement include "A new drug substance production line at Lonza's site in Geleen, Netherlands will complement the existing production network and support the manufacture of up to an additional 300 million doses per year" and "Operations are expected to begin by the end of 2021"[91]. According to this, the partnership could significantly expand the scale of Moderna production. On the other hand, the technology transfer must take place on a schedule that would begin in June 2020, with production starting in July 2020.

An article explains the technology transfer between Moderna and Lonza, saying, "The capability to perform technology transfer from Moderna to their contract manufacturing partner, Lonza, was enabled by the digital technologies deployed in their respective facilities," says Cody. "Both Moderna and Lonza utilize DeltaV as their process automation system and Syncade as their manufacturing execution system. NECI teams partnered with Moderna and Lonza teams to transfer equipment automation strategies and electronic batch records from company to company, accelerating the manufacturing capacity and establishing supply chain capability as the Moderna COVID-19 vaccine was completing clinical trials and FDA emergency use approval."[92]. Thus, the technology transfer from Moderna to Lonza, the contract manufacturing partner, was executed smoothly through the active use of digital technology. In this process, the two companies jointly employed the DeltaV process automation system and Syncade manufacturing execution system to enhance the automation and management of the manufacturing process. The implementation of these advanced digital systems is estimated to have increased the efficiency of the manufacturing process, enhanced quality control, and improved transparency. In addition, in cooperation with NECI, a company specializing in process automation and manufacturing execution systems, the automation strategy and electronic batch recording system were effectively transferred from Moderna to Lonza. This should enable the Lonza facility to achieve manufacturing processes comparable to those in Moderna and guarantee product quality and

consistency. The technology transfer between Moderna and Lonza was executed quickly and efficiently through the appropriate selection and implementation of digital technology and close collaboration with partners with expertise in the field. This enabled the rapid production and supply of COVID-19 vaccine, which contributed significantly to the response to the pandemic.

Impact and Results of the Partnership

The Bancel, CEO of Moderna explained that "In early 2021, we doubled our monthly deliveries of our COVID-19 vaccine to the U.S. government, and we were working to double them again by April to more than 40 million doses per month. As we worked to meet these goals, we were continually learning and working closely with our partners and the federal government to identify ways to address bottlenecks and accelerate production. By June, we made and delivered our 200 millionth dose of the Moderna COVID-19 Vaccine to the U.S. government. This was a heartening milestone, knowing that many tens of millions of people had been fully vaccinated or received their first dose in the U.S. It had taken us just two months to go from 100 million to 200 million doses. To put that into perspective, in 2019, we made fewer than 10,000 doses per month. By October, Moderna and our partners ramped up our capacity worldwide and supplied more than 500 million doses of our COVID-19 vaccine globally. There were several efforts in place to continue increasing capacity at a significant pace, including the expansion of our Moderna Technology Center in Norwood, MA, which I'll touch on shortly. "[23].

Because of that, Moderna's COVID-19 vaccine has been granted EUA or emergency use listing by the World Health Organization (WHO) and health agencies in more than 60 countries, to which we shipped approximately 800 million doses in 2021[23].

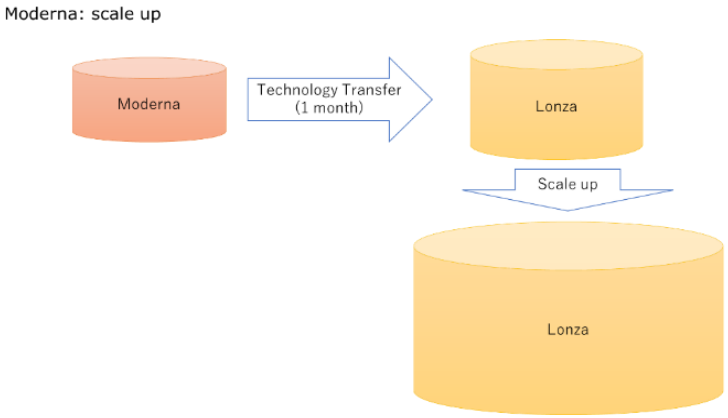


Figure 3.25 The Figure Illustrates the Conceptual Diagram of How Moderna Successfully Scaled Up mRNA Vaccine Production by Collaborating with Lonza

3.3.4.2. BioNTech (Manufacturing Phase): Efficient Production Expansion Leveraging Digital Technologies and Pfizer's Global Network

BioNTech's Manufacturing Sites

For mRNA production, BioNTech has two manufacturing sites, one in Mainz (Germany) and the other in Idar-Oberstein (Germany).

For the Idar-Oberstein one, at the time of the pandemic, BioNTech already owned the facility that enabled them to produce mRNA. The facility is owned by BioNTech Innovative Manufacturing Services (BioNTech IMFS), which became a subsidiary of BioNTech in 2009. The facility started producing mRNA in 2011. This manufacturing experience must have been important for manufacturing mRNA on a large scale[93].

Acquisition and Expansion of Marburg Manufacturing Hub

The manufacturing hub acquired from Novartis in Marburg (Germany) is expected to be fully operational in March 2021. The hub will complement the existing sites and, based on the latest projections, will be one of the largest mRNA plants in Europe, producing more than 1 billion doses per year[94].

Marburg's mRNA production has gone from 1 g in early 2020 to 350 g in late 2020 and 1.4 kg in 2022, which BioNTech attributes to digitalization and automation[44].

BioNTech effectively increased the production of the vaccine through utilizing digital and automated technology. In September 2020, BioNTech acquired a manufacturing facility formerly owned by Novartis in the German town of Marburg[95]. The facility had previously been producing influenza vaccines based on flu cell culture but was then converted to manufacture mRNA vaccines. The BioNTech and Siemens groups collaborated to convert the facility into an mRNA production facility within a few months. A project of this magnitude typically takes about a year, but in this case, the participants completed the conversion in just five months. The main components of the new manufacturing execution system (MES) were completed in only two and a half months. The conversion of the entire manufacturing plant took only five months. This facility is a totally paperless manufacturing facility, with batch production system recording done

electronically and testing performed automatically. Employees are guided through the 50,000 work steps required to produce the vaccine[96]. The first Marburg vaccines were shipped in April 2021. BioNTech stated that the Marburg manufacturing site is one of the largest mRNA vaccine manufacturing sites in Europe as well as worldwide, with an annual production capacity of up to one billion doses of their COVID-19 vaccine once fully operational. Due to optimized operational efficiencies initiated last year, BioNTech has been able to increase the expected annual manufacturing capacity by 250 million doses[97].

Pfizer's Manufacturing Sites and Technology Transfer

Pfizer was initially manufactured at four manufacturing sites: three in the United States (St. Louis, Andover, and Kalamazoo) and a plant in Pouf, Belgium[76].

Pfizer said, “To support the rapid manufacturing scale-up of the vaccine – over 3 billion doses of the Pfizer-BioNTech COVID vaccine in 2021 – we deployed our first-in-industry patent-pending Digital Operations Center, providing an end-to-end view of manufacturing, allowing us to predict issues and adjust operations in real-time to meet patient supply commitments. We also deployed augmented reality to diagnose and repair equipment remotely in our labs and manufacturing sites, keeping colleagues safe and reducing travel by technicians. And, within days of the Emergency Use Authorization, we deployed end-to-end cold chain capabilities, including Internet of Things (IoT) sensors, or devices that detect and respond to changes in the environment and GPS tracking. These tools ensured cold chain integrity with real-time monitoring of shipments and temperatures anywhere in the world with close to 100 percent accuracy.”[83]

Pfizer was able to complete a completely new set of formulations for the production of this vaccine in a short period of 100 days. In parallel, tests were conducted to scale up the LNP production process from lab scale to industrial scale. The company has been working on this project for over 20 years," said Pfizer[98].

Pfizer's technology transfer process includes establishing a scope, schedule, governance, and budget; purchasing equipment; conducting practical tests to train operators on the manufacturing process; conducting tests and conducting quality and safety audits to meet Pfizer's standards and

regulatory expectations; conducting regulatory inspections and approvals, among many other tasks. In the case of the COVID-19 vaccine, teams at outside facilities need to be trained in many aspects of this complex manufacturing process, from learning the intricacies of formulating lipid nanoparticles to encapsulate the mRNA, to sterilizing the product to make it safe for injection, to filling the vials, labeling the vials, packaging, and distributing the product around the world. While the typical technology transfer process can take up to three years from kick-off to submission, the vaccine has allowed the process to be shortened from five months to 18 months without sacrificing product quality or personnel safety in order to ensure expeditiousness. The company stated[99].

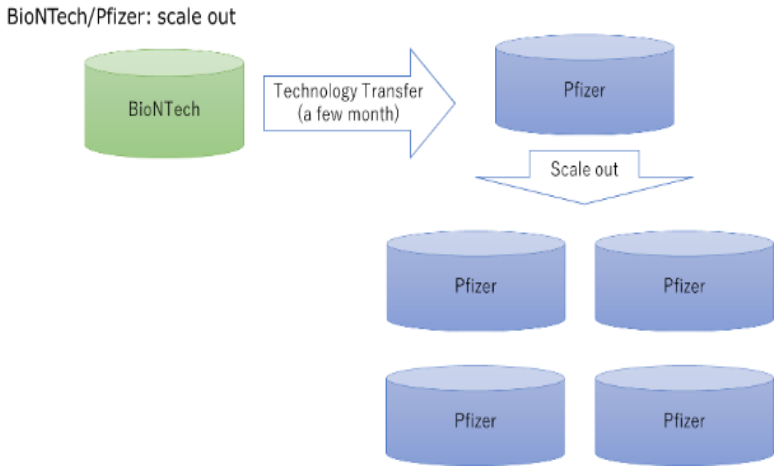


Figure 3.26 The Figure Depicts the Conceptual Diagram of BioNTech's Successful Scaling of mRNA Vaccine Production through their Collaboration with Pfizer

3.3.4.3. Daiichi Sankyo (Manufacturing Phase): Leveraging Nucleic Acid Drug Manufacturing Experience for mRNA Vaccine Production

Daiichi Sankyo's experience in nucleic acid drug production may have enabled the company to manufacture the mRNA vaccine[59].

Comments: Since the COVID-19 vaccine of the Daiichi Sankyo was approved in August 2023, the company likely did not need to produce a large quantity compared to Moderna or BioNTech/Pfizer. For instance, upon approval, Daiichi Sankyo entered into an agreement with the Japanese Ministry of Health, Labour and Welfare (MHLW) to supply 1.4 million doses in the 2023 fiscal year, with delivery commencing shortly thereafter as part of Japan's COVID-19

inoculation campaign[100]. This supply volume is at least three orders of magnitude lower than the production capacities of the aforementioned companies.

3.3.5. Rapid Vaccine Development Achieved through mRNA Platforms: Insights from Drug Platform Comparison

This section discusses how mRNA as a product / technology platform contributes to rapid vaccine development from a drug platform comparison viewpoint. The graph below (Figure 3.27.) compares the efficacy of COVID-19 vaccines worldwide in 2022, with the top two being mRNA vaccines (94-95% efficacy) and the third being Novavax (89% efficacy), a protein-based vaccine.[101] Figure 3.28. illustrates the nature of the Novavax vaccine and compares it to mRNA vaccines.[102]

When comparing the development speed of mRNA vaccines and Novavax, Figure 3.29. illustrates the time frame for each. The graph suggests that while mRNA vaccines were developed within 11 months, the Novavax vaccine took 16 months. The longer development time for the Novavax vaccine can be attributed to the difficulty in vaccine production. Specifically, while mRNA can be produced through a chemical process, the Novavax vaccine requires cell culture, a biological process that makes it challenging to scale up manufacturing. This biological process not only lengthens the development process but also the manufacturing process, especially when large-scale production is necessary[103,104]. Table 3.9 summarizes the differences between the two vaccine platforms.

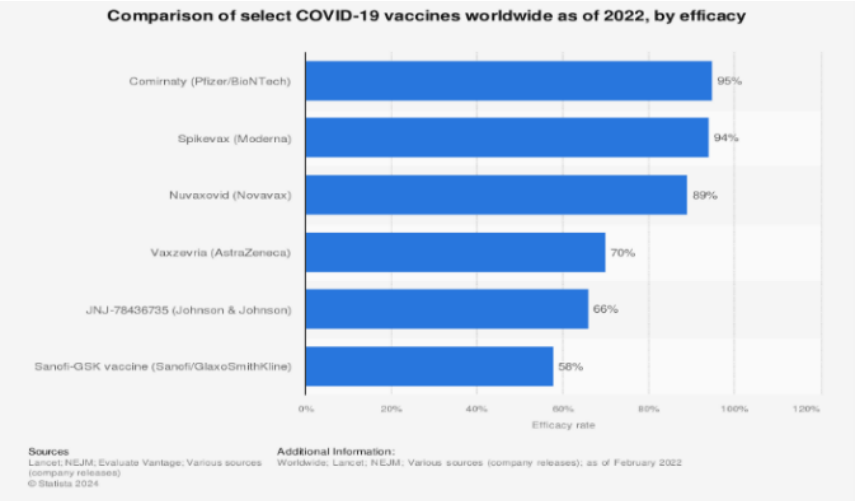


Figure 3.27 COVID-19 Vaccine Efficacy Comparison[101]

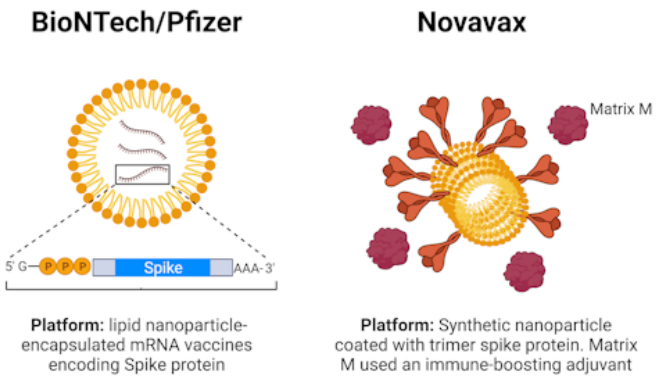


Figure 3.28 Novavax Vaccine vs. mRNA Vaccines[102]

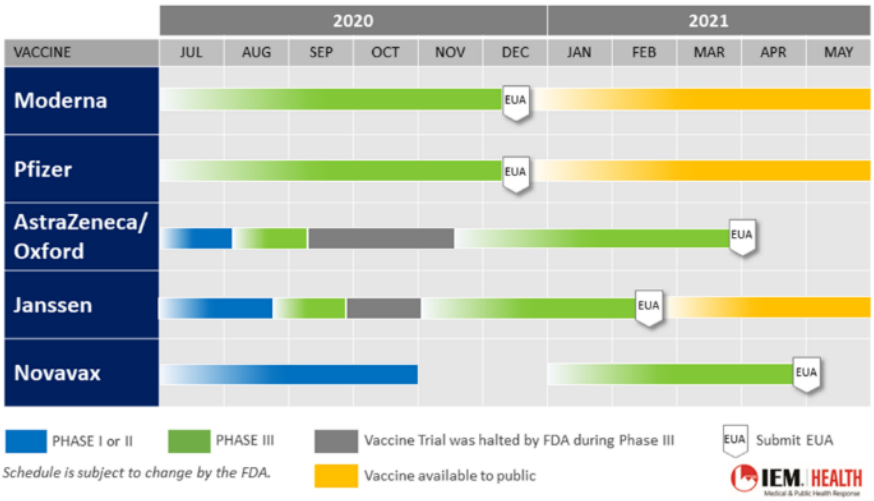


Figure 3.29 Development Timeline for mRNA and Novavax Vaccines[105]

Table 3.9 Comparison of mRNA and Novavax Vaccine Platforms

	Duration	Efficacy	Discovery	Clinical Trial	Manufacturing
mRNA	11 months	94-95%	Possible if the sequence and 3D structure of the pathogen is known.		Easy to scale up
Protain (Novavax)	16 months	89%	Possible if the sequence and 3D structure of the pathogen is known.	Manufacturing capacity could become a bottleneck	Requires live cells for production, difficult to scale up

The rapid development of mRNA vaccines can be attributed to several factors inherent to the mRNA platform. First, the chemical synthesis of mRNA allows for faster production compared to the biological processes required for protein-based vaccines like Novavax. Second, the modular nature of mRNA vaccines enables the rapid adaptation of the vaccine to target new variants or strains of the virus by simply altering the mRNA sequence. This flexibility is not as easily achievable with other vaccine platforms.

Furthermore, the scalability of mRNA vaccine production is another significant advantage. The chemical process used to produce mRNA vaccines is more easily scalable than the biological processes required for other vaccine types. This scalability enables the rapid manufacture of large quantities of vaccines, which is crucial during a pandemic when widespread vaccination is necessary to control the spread of the virus.

3.3.5. Accelerating Timelines with Parallel Processes Enabled by Abundant Funding While Mitigating Risks

The abundant funding facilitated the implementation of parallel processes across the Discovery, Development, and Manufacturing phases, as described in sections 3.3.1 to 3.3.3, leading to a significant acceleration of the vaccine development project. The concurrent execution of these phases, enabled by substantial financial resources, was instrumental in shortening the overall timeline for vaccine development.

This approach of running processes in parallel rather than sequentially represents a departure from traditional vaccine development pathways. It allowed for simultaneous progression in different stages of vaccine research, development, and production, effectively compressing the timeline without compromising the thoroughness of each phase. The ability to fast-track the project in such a manner was made possible by the immediate availability of funds to support the intense and simultaneous activities required across all phases of vaccine development. This strategic allocation of resources was crucial in responding to the urgent global demand for a COVID-19 vaccine.

By the way, the parallel implementation of various processes in vaccine development is not solely dependent on funding. BioNTech's "Project Lightspeed" serves as an example of how streamlining the development process can significantly reduce the time required to bring a vaccine to market. As described in "The Vaccine Race: Inside the Epic, Risky Race to Develop a COVID-19 Vaccine," Uğur, the CEO of BioNTech, focused on "eliminating time wastage" and directed her team to implement the processes of Discovery, Development, Manufacturing, and Product Supply in parallel as much as possible.[42]

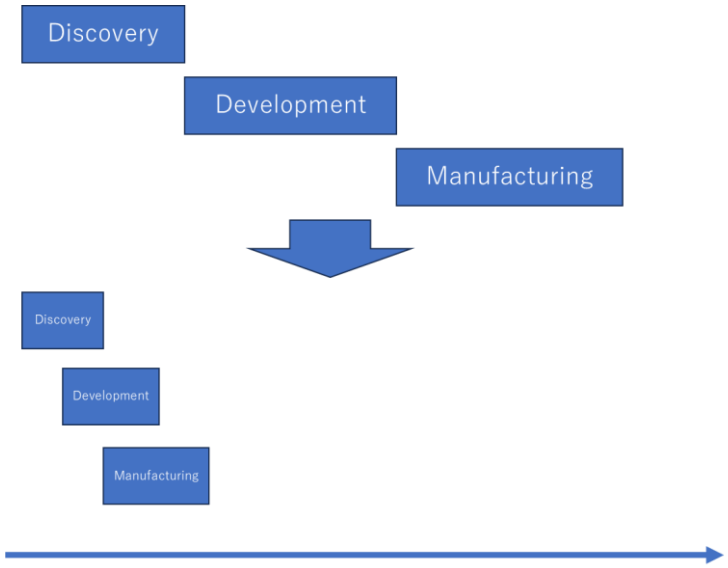


Figure 3.30 Accelerated COVID-19 Vaccine Development through Rapid and Simultaneous Discovery, Development, and Manufacturing Phases

(This figure illustrates the conceptual framework behind the unprecedented speed of COVID-19 vaccine development. Traditionally, vaccine development follows a linear, sequential process, with each phase building upon the completion of the previous one. However, in response to the urgent global need for COVID-19 vaccines, the development process was dramatically accelerated. As shown in the figure, the Discovery, Development, and Manufacturing phases were compressed and conducted simultaneously.)

3.3.6. Other External Factors

This thesis focuses on the management of companies involved in COVID-19 vaccine development. However, it is important to acknowledge that numerous factors contribute to the

success of vaccine development efforts. Among these factors, government support in terms of emergency funding and regulatory issues.

3.3.6.1. The Biotech Ecosystems Fostering Companies Development

The success of pharmaceutical companies like Moderna and BioNTech can be attributed not only to their internal factors but also to the broader ecosystem in which they operate. As Adner and Kapoor (2010) suggest, an ecosystem comprising multiple participants is crucial for coordinating knowledge flows and making necessary resources available to drive innovation.[106]

3.3.6.2. Emergency Funding for Vaccine Developments

Undoubtedly, substantial financial resources are required for vaccine development. Figure 3.31 illustrates the countries funding COVID-19 vaccine research and development (R&D). The United States, home to Moderna and Pfizer, spent $2.23 billion, while Germany, where BioNTech is based, invested $1.51 billion.[107]

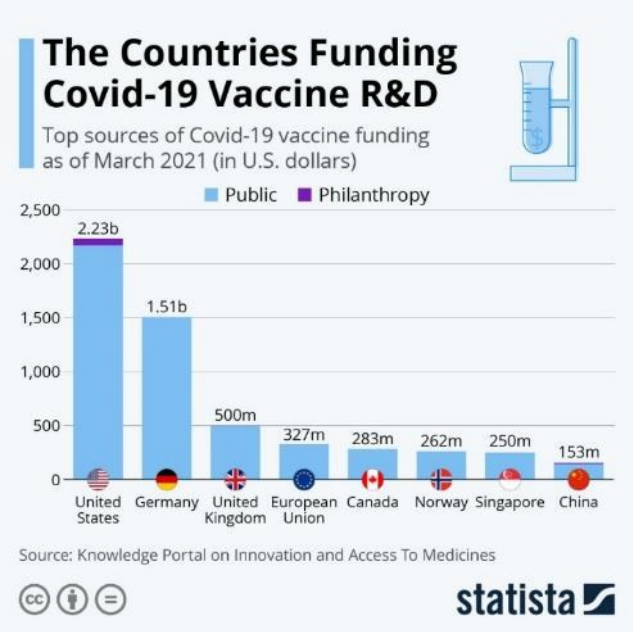


Figure 3.31 The Countries Funding for COVID-19 Vaccines

The Biomedical Advanced Research and Development Authority (BARDA), a U.S. Department of Health and Human Services (HHS) office, is responsible for the procurement and development

of medical countermeasures, including vaccines, drugs, therapies, and diagnostic tools, to combat public health emergencies such as pandemics, bioterrorism, and emerging diseases.[108]

As shown in Figure. 3.32., BARDA provided significant funding for both the BioNTech group ($5,973 million) and the Moderna group ($5,986 million).

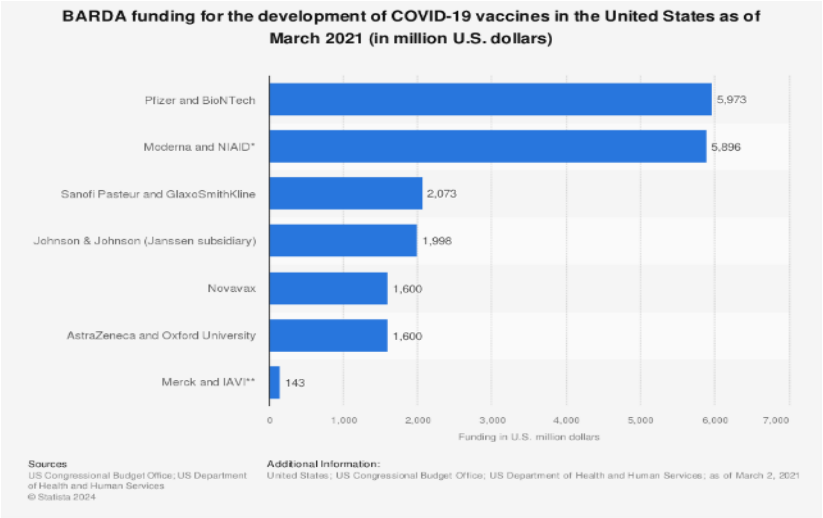


Figure 3.32 BRADA Funding for the Development of the COVID-19 Vaccines

In the United States, the Trump Administration's Operation Warp Speed (OWS) initiative has been instrumental in providing financial support to promising vaccine candidates. OWS has entered into six agreements with select manufacturers to support the development, manufacturing capacity, and/or purchase of vaccine doses (Table 3.10). These agreements vary in scope, with some supporting both development activities and manufacturing capacity, while others focus solely on manufacturing. All agreements include a commitment to provide a specified number of doses for distribution by the federal government.[109]

Table 3.10 Operation Warp Speed COVID-19 Vaccine Candidate Agreement[109]

Company/Vaccine Candidate	Phase of Development	Vaccine Platform	Federal Funding	Agreement
AstraZeneca/Oxford University (AZD1222)	Phase 3	Viral vector	$1,200,000,000	Supports advanced development and large-scale manufacturing. Involves collaboration to make at least 300 million doses available.
Novavax (dNVX-CoV-2372)	Phase 1	Adjuvanted protein subunit	$1,600,434,523	Supports large-scale manufacturing of 100 million doses.
Pfizer/BioNTech (BNT162)	Phase 2/3	mRNA	$1,9500,000,000	Purchase agreement of 100 million doses.
Sanofi/GlaxoSmithKline (Recombinant Protein Antigen and AS03 Adjuvant)	Phase 1/2	Adjuvanted protein subunit	$2,072,775,336.46 (Base Award, Option 1)	Supports advanced development and large-scale manufacturing of 100 million doses.
Moderna (mRNA-1273)	Phase 3	mRNA	$2,480,000,000 (Base Award, Option 1, Option 2, Option 3)	Supports advanced development and large-scale manufacturing of 100 million doses.
Janssen (AD26.COV2.S)	Phase 3	Viral vector	$1,457,887,081 (Base Award, Option 1)	Supports advanced development and large-scale manufacturing of 100 million doses.

Note: The Federal Government has also provided funding to Merck and IAVI to support accelerated development of its vaccine candidate (rVSVΔG-CoV2) which is currently in preclinical development with Phase 1 studies planned to start later this year.

3.3.6.3. Regulatory Assistance and Expedited Approval Processes

Regulatory considerations also play a vital role in the development of COVID-19 vaccines. To facilitate the rapid availability of vaccines without compromising the quality of regulatory review, countries worldwide have implemented emergency authorization mechanisms. These emergency use provisions allow for the use of unapproved products to prevent serious or life-threatening diseases or conditions when no adequate, approved, or available alternatives exist.[110]

The below chart illustrates the traditional and outbreak paradigms for vaccine development and regulatory approval. In the traditional paradigm, the development and approval process follow a linear sequence, with each phase building upon the previous one. This approach ensures a thorough evaluation of the vaccine's safety and efficacy but can be time-consuming. In contrast, the outbreak paradigm, employed during public health emergencies such as the COVID-19 pandemic, allows for a more compressed and overlapping process. This paradigm enables the parallel execution of various stages, such as preclinical studies, clinical trials, and manufacturing, to expedite the development and approval of vaccines.[110]

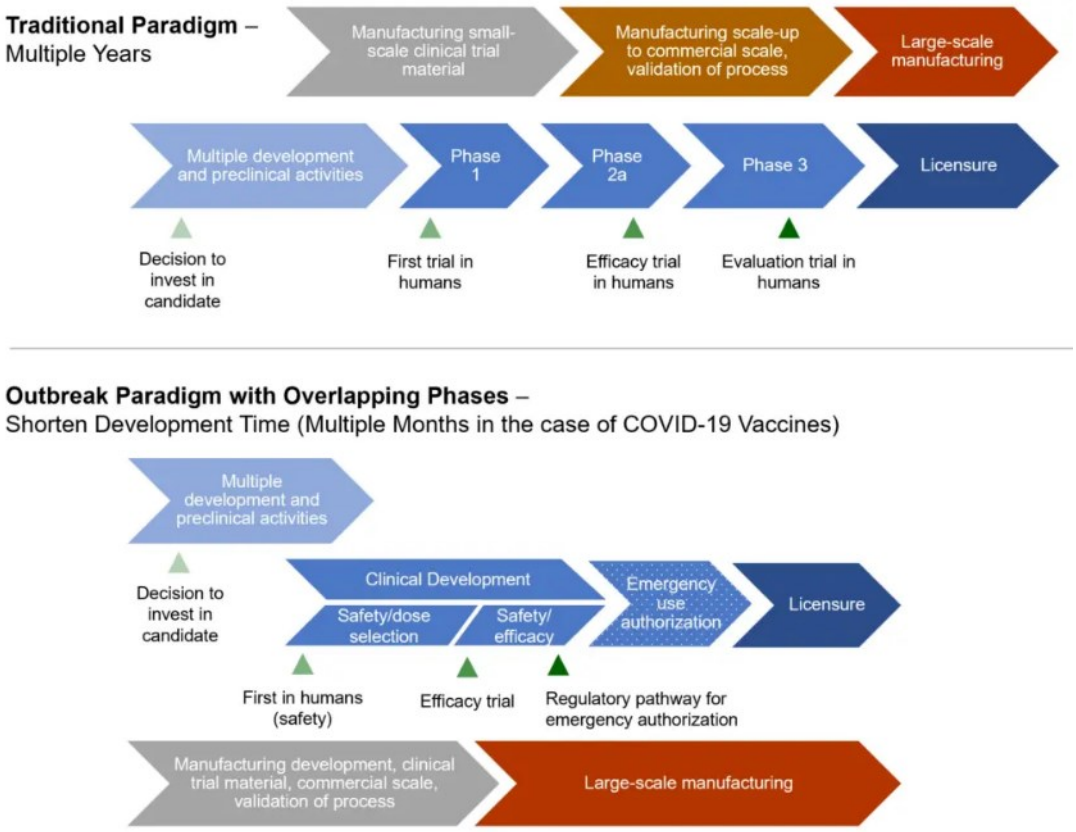


Figure 3.33 Traditional and Outbreak Paradigm for Vaccine Development [110]

3.3.6.4. Moderna: Leveraging the Cambridge Ecosystem, U.S. Government Funding, and FDA Support

Ecosystem: One of the key components of Moderna's ecosystem is its partnership with Flagship Pioneering, a venture capital firm that played a crucial role in the company's founding and rapid development. Flagship Pioneering's unique approach to venture creation, known as "Flagship Labs," involves identifying promising scientific concepts and assembling teams of experts to develop these ideas into viable companies. Moderna was born out of this process, with Flagship Pioneering providing the initial funding, strategic guidance, and access to cutting-edge technologies and resources necessary to establish the company and its mRNA platform.[41,111]

In addition to Flagship Pioneering's support, Moderna has benefited from collaborations with leading academic institutions and research organizations. For example, the company has a long-standing partnership with Harvard University, which has provided access to world-class researchers and scientific expertise. Moderna has also collaborated with the National Institutes of

Health (NIH) and the Defense Advanced Research Projects Agency (DARPA), which have provided funding and support for the development of mRNA-based vaccines and therapies.[47,112,113]

Emergency Funding: As previously discussed, Moderna received substantial funding from the U.S. government. On April 16, 2020, Moderna announced an award from the U.S. government agency BARDA for up to $483 million to accelerate the development of their mRNA vaccine (mRNA-1273) against COVID-19[114]. Subsequently, on July 26, 2020, Moderna announced an expansion of the BARDA agreement to support a larger Phase 3 program for the vaccine [115]. The U.S. government's Operation Warp Speed also supported the vaccine development. On August 11, 2020, under the leadership of President Trump, the U.S. Department of Health and Human Services (HHS) and Department of Defense (DoD) announced an agreement with Moderna, Inc. to manufacture and deliver 100 million doses of the company's COVID-19 vaccine candidate, with the federal government owning these vaccine doses [116,117].

In summary, the U.S. government invested nearly $1 billion in research funding for Moderna's COVID-19 vaccine development. Additionally, under Operation Warp Speed, Moderna received a supply order from the U.S. government that was worth up to $1.525 billion for 100 million doses of its vaccine, with options for more doses, bringing their total from U.S. government sources to about $2.48 billion. This extensive support was part of a broader strategy to accelerate vaccine availability and mitigate financial risks associated with vaccine development. [118,119]

Regarding the U.S. support, Stéphane Bancel, the CEO of Moderna, stated in an interview with McKinsey:[120] "It came down to the collaboration between the pharmaceutical industry and the US federal government. The US government picked three different technologies to invest in for a diversified risk profile and then chose two pharmaceutical companies per technology. In the end, they were betting on six different companies. It was a brilliant movie. The conditions of the contract included a base business of 100 million doses, with options to increase depending on the clinical data and the efficacy at the time of launch. This allowed us to take on a lot of business risk at a time when every single day mattered" [120]

Regulation: In terms of regulation, as Moderna had already passed the regulatory tests for mRNA vaccines, they could waive the animal testing in the development process[42]. Furthermore, the cooperative attitude of the FDA helped to accelerate vaccine development. Bancel stated: "The other key part of this equation is that the FDA worked relentlessly to authorize the Moderna COVID-19 vaccine, and others, with an emergency use authorization [EUA]. Usually, you submit a question to the FDA, and they have a defined timeline for responding and engaging with clinical-trial sponsors. But they adapted to the crisis situation. During the pandemic, we could reach out to them any time—including weekends"[120].

3.3.6.5. BioNTech: Benefiting from the Mainz Ecosystem, Government Funding, and Collaborative Regulation

Ecosystem: BioNTech's success can be partially attributed to the ecosystem in Mainz, Germany, which comprises several key research institutes and organizations, including the Translational Oncology at the University Medical Center of the Johannes Gutenberg University Mainz (TRON) and the Helmholtz Institute for Translational Oncology Mainz (HI-TRON).[1]

TRON, established in 2010, has been a crucial research partner for BioNTech in developing several of its cancer immunotherapy platforms and pipeline candidates. The long-standing collaboration between BioNTech and TRON has furthered their immunotherapy research.[121,122] Furthermore, HI-TRON, established in 2019, is a collaborative effort between the German Cancer Research Center (DKFZ) and TRON. The institute's focus on advancing translational oncology research aligns closely with BioNTech's mission to develop innovative cancer immunotherapies. The close connection between BioNTech and TRON, as BioNTech's founders, Uğur Şahin and Özlem Türeci, are also the founders of TRON, with Uğur Şahin serving as the Scientific Director of TRON. This relationship fosters a strong potential for ongoing research collaborations and knowledge exchange in the field of translational oncology and cancer immunotherapy.[123,124]
The close proximity of BioNTech, HI-TRON, and TRON in Mainz, Germany, facilitates close collaboration and knowledge exchange between these organizations.

Emergency Funding: The collaboration between Pfizer and BioNTech in developing a COVID-19 vaccine involved a distinctive financial arrangement that set it apart from other vaccine

projects, such as Moderna's. BioNTech, the German biotechnology company, received a sum of €375 million (approximately $445 million) from the German government to support the development of their mRNA-based COVID-19 vaccine[118]. In contrast to some other vaccine developers, Pfizer and BioNTech made the strategic decision not to accept funding from the U.S. government during the vaccine's development phase. Instead, they secured a pre-purchase agreement with the U.S. government, valued at $1.95 billion, for the delivery of 100 million doses of the vaccine. This agreement was made under the support of Operation Warp Speed, a U.S. government initiative aimed at accelerating the development, production, and distribution of COVID-19 vaccines, therapeutics, and diagnostics[125].

Regulation: The Paul Ehrlich Institute (PEI), a German federal agency, medical regulatory body, and research institution, has been at the forefront of vaccine and biomedicine development since its establishment.[126] In the late 2000s, PEI began focusing on mRNA technology, which has gained significant attention in recent years. This interest in mRNA technology can be attributed to the fact that two prominent German companies, BioNTech and CureVac, both of which are renowned for their work in this field, were founded in Germany. PEI has fostered a long-standing collaborative relationship with these companies to advance the development and ensure the safety of mRNA technology for human applications. This collaboration has resulted in joint publications between PEI researchers and BioNTech personnel, including Uğur Şahin, the CEO of BioNTech. Furthermore, BioNTech representatives have been invited to participate in research seminars organized by PEI, which focus on cutting-edge medical technologies. Despite Germany's stringent regulations regarding clinical trials, BioNTech has successfully conducted numerous trials within the country. This achievement can be largely attributed to the strong cooperative relationship that has been established between BioNTech and PEI over time[42].

On February 6, 2020, Uğur Şahin, CEO of BioNTech, met with representatives from the Paul Ehrlich Institute (PEI) to negotiate the regulatory approval plan for their mRNA-based COVID-19 vaccine. Sahin expressed strong confidence in the safety of the mRNA technology and proposed waiving animal testing based on scientific evidence. However, PEI initially rejected this viewpoint, citing two main reasons: first, the technology had not been sufficiently tested, and second, PEI did not consider COVID-19 to be a serious pandemic at that time. Undeterred,

BioNTech staff discovered an article titled "Guidelines for the Quality, Safety, and Efficacy of Ebola Vaccines" published by the World Health Organization (WHO). The guidelines contained a crucial recommendation stating that in the event of a public health emergency, regulators should allow pharmaceutical companies to proceed to Phase I trials once they have compiled interim reports of characterization studies. Armed with this information, BioNTech made a new proposal to PEI, which was ultimately accepted. The agreement allowed the Phase I trial to commence while the remaining toxicity studies were conducted in parallel with the clinical trial, provided that the rats were found to be healthy immediately after receiving the vaccine[42].

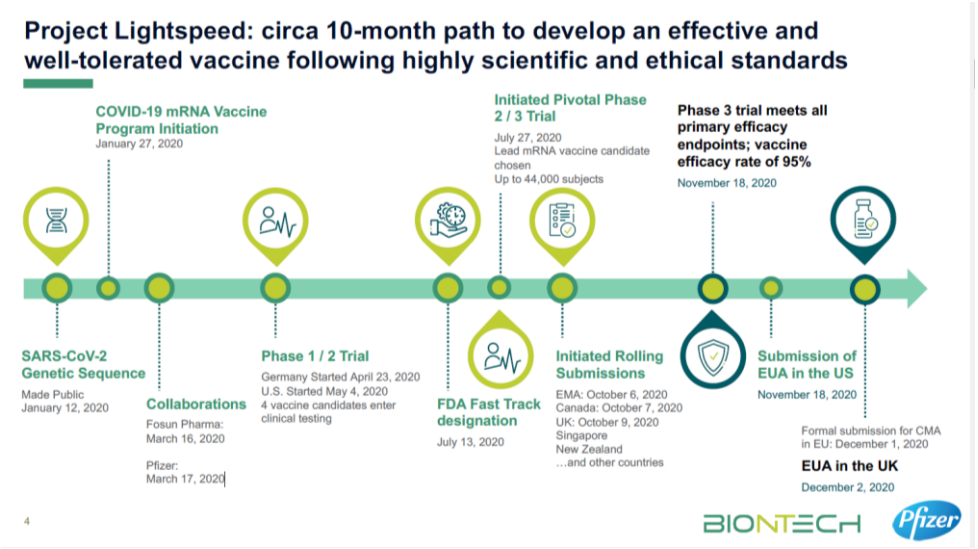


Figure 3.34 Project Light Speed[42]

3.3.6.6. Daiichi Sankyo: Limited Ecosystem Benefit, Though Certain Level of Japanese Government Funding, and PMDA's Regulatory Adaptations

Ecosystem: Daiichi Sankyo's ecosystem in Japan is not as well-documented as Moderna's ecosystem in Cambridge, US, or BioNTech's ecosystem in Mainz, Germany. However, based on the available information, it appears that Daiichi Sankyo has collaborated with academic institutions and government agencies to advance its research and development efforts, particularly in the context of its COVID-19 vaccine development.

One notable collaboration is with the University of Tokyo, specifically with Professor Yoshihiro Kawaoka from the Institute of Medical Science. For the prevention of COVID-19, Daiichi Sankyo participated in "Fundamental Research on the Control of a Novel Coronavirus (2019-nCoV)"*,

which is an initiative supported by the Japan Agency for Medical Research and Development (AMED). This project, led by Professor Kawaoka, involved utilizing a novel nucleic acid delivery technology developed by Daiichi Sankyo to initiate a basic research project on an mRNA vaccine titled "Development of a Genetic Vaccine for 2019-nCoV".[35]

However, compared to the extensive ecosystems and long-standing collaborations that Moderna has established in Cambridge, US, and BioNTech in Mainz, Germany, the available information suggests that Daiichi Sankyo's ecosystem in Japan is not as comprehensive or well-established. This difference in the strength and depth of the research ecosystems could be one of the factors contributing to the slower progress made by Daiichi Sankyo in developing its COVID-19 vaccine compared to Moderna and BioNTech.

Emergency Funding: In 2020, the Japanese government allocated approximately 150 billion yen to support research and development (R&D) initiatives focused on COVID-19 drug-related technologies. The government provided Daiichi Sankyo with a total of 60 billion yen in financial support, which was distributed over a period extending until August 2023.[127]

Regulation: In terms of the Japanese regulation, the article of "Emergency diagnostic and therapeutic measures and vaccine regulations at PMDA" provided discusses the role of the Pharmaceuticals and Medical Devices Agency (PMDA) in Japan during the COVID-19 pandemic. Here's a summary of the key points:[128]

1. PMDA actively reviewed various COVID-19-related products for diagnosis, treatment, and prophylaxis, and provided consultations to companies and academia in the early stages of development.
2. Despite the emergency conditions, PMDA adapted to various restrictions by implementing remote operations and other measures to avoid delays.
3. The therapeutic drug Remdesivir, which was distributed in the United States on May 1, 2020, under the Emergency Use Authorization (EUA), was approved in Japan on May 7, 2020, as a special exception.
4. PMDA reviewed ventilators in response to shortages and needs in the medical field and reviewed PCR test kits to enhance the testing system for COVID-19.

5. In collaboration with overseas regulatory authorities, PMDA published its approach to vaccine evaluation on September 2, 2020, and prepared for domestic applications, including domestic clinical trials for foreign-developed vaccines.

6. An application for the Pfizer vaccine, which was urgently approved in the U.S., was filed in Japan in December 2020 and received special exception approval on February 14, 2021. Two more vaccines were approved in May 2021.

7. PMDA has also responded to a large number of suspected adverse reaction reports received since the launch of the vaccines.

Chapter 4: Synthesis: Why Rapid Vaccine Development was Possible with an mRNA Platform

This section synthesizes the theoretical framework discussed in Chapter 2 and the factual information presented in Chapter 3 to address the research question of why Moderna and BioNTech were able to develop their COVID-19 vaccines so rapidly. By combining the insights from both sections, we can gain a comprehensive understanding of the key factors that contributed to the success of these companies in responding to the global health crisis while answering the research questions.

4.1. Why Were the Concepts of the mRNA and LNP Drug Platforms Established?

The rapid development of vaccines by Moderna and BioNTech can be attributed to the establishment of the mRNA and LNP drug platform, which was built upon a foundation of numerous significant scientific discoveries. However, transforming these technologies into a drug platform required more than just scientific advancements; it necessitated strong leadership and substantial investments.

The visionary leadership of individuals such as Noubar Afeyan and Stéphane Bancel at Moderna, and Uğur Şahin at BioNTech, played a crucial role in driving the development of the mRNA and LNP technologies into a fully-fledged drug platform. These leaders recognized the immense potential of the technologies and made strategic decisions to invest heavily in their development, despite the inherent risks and uncertainties associated with such a novel approach. Furthermore, the establishment of the mRNA and LNP drug platform required significant financial investments. In contrast, Daiichi Sankyo, despite working with similar technologies, did not develop them into a drug platform. Instead, the company utilized the mRNA and LNP technologies for a specific drug candidate, rather than investing in the creation of a platform that could support the development of multiple drugs across various therapeutic areas.

4.2. Why Were Organizations Based on Drug Platforms That Enable Rapid Vaccine Development Constructed?

The construction of organizations based on drug platforms that enable rapid vaccine development can be explained by four key mechanisms, as discussed in Chapter 2.

4.2.1. Development of a Rational Corporate Culture Driven by the Platform Strategy

The first mechanism is that the platform strategy enables the creation of a rational corporate culture. Utilizing a platform provides a clear goal for the company, helping employees share corporate values and fostering a rational corporate culture. A prominent example is Moderna, whose documents frequently state, "we are an mRNA technology platform company." This is embodied in their "Moderna's mindset," which prioritizes the platform concept in every aspect of the company. Furthermore, as drug platforms are based on foundational technology, incorporating this concept into the core of the corporation encourages scientific leadership and science-based company strategies. BioNTech, for instance, focuses on mRNA and immunology, developing strategies based on scientific evidence. In contrast, Daiichi Sankyo, which may find it challenging to focus on specific scientific areas, has a more narrative and ambiguous corporate vision.

4.2.2. Funding Enabled by the Drug Platform Strategy

The second mechanism is that the platform strategy attracts funding through four distinct mechanisms.

First, unlike traditional isolated drug development projects, the platform approach appeals to investors as a product platform, offering continuous and potentially expansive investment opportunities. For example, in mRNA-based drug discovery, altering nucleotide sequences can theoretically simplify the development of subsequent therapeutics, making it an attractive investment proposition. Moderna intentionally utilizes the platform concept for funding to address the problematic one-time issue in traditional drug developments.

Second, the inherent flexibility of the product platform allows for targeting a broad range of diseases. mRNA therapeutics can potentially create vaccines for infectious diseases or cancer treatments by altering sequences. Vaccine development for infectious diseases might attract public funding, while cancer therapies could attract private investment, broadening the scope of potential funding sources. Both Moderna and BioNTech received significant investments from various stakeholders, ranging from public fund organizations like DARPA or the Bill & Melinda Gates Foundation to pharmaceutical companies like Merck and Sanofi, as well as venture capitalists.

Third, the appeal to investors is bolstered by the growth of the industry platform itself. As there are many high-growth platform companies, and a premium exists for such companies, the industry platform's evolution makes it more attractive to investors who see value in the expanding network and potential for exponential growth within the platform ecosystem. A Moderna executive commented that this is one of the advantages of utilizing the platform strategy.

Fourth, solid drug platforms are in demand for technological collaboration with other pharmaceutical companies, leading to new funding. Platforms have the potential to generate a large number of drugs, enabling partnerships with pharmaceutical companies seeking new drugs. Moderna and BioNTech can undertake development and receive further funding from AstraZeneca, DARPA, BARDA, the Bill & Melinda Gates Foundation, Pfizer, Sanofi, and others, which also allows them to acquire knowledge and experience. As the platform can be applied to multiple disease areas, partnerships can be formed for each disease, and funding can be obtained from multiple partners.

Through these mechanisms, Moderna had been funded around $3 billion, and BioNTech around $1.5 billion, even though they did not have any commercial drugs at that time.

In the case of Daiichi Sankyo, a research collaborator, Professor Takeshi Ishii from the Division of Vaccine Science at the Institute of Medical Science, University of Tokyo, initiated a new project in 2016 to establish rapid vaccine development. The initiative, known as the Mock-up Vaccine Project, aimed to create a mock vaccine and conduct clinical research from 2019 to 2021, with an estimated budget of around 400 million yen per year. However, AMED did not approve the budget, resulting in a missed opportunity for development. While some may argue that AMED overlooked the potential of mRNA technology for pandemic countermeasures, which organizations like DARPA, BARDA, the Bill & Melinda Gates Foundation, and NIAID had recognized much earlier, the lack of a platform perspective in the project made the one-time rejection crucial. If the project or company had treated the technology as a drug platform, they could have secured alternative funding opportunities despite AMED's rejection, as the platform technology would be useful for vaccine development projects even if it were initially intended for cancer-related research, for example.

4.2.3. Knowledge Integration Enabled by the Drug Platform Strategy

The third mechanism is that the platform strategy enables the integration of knowledge. The platform strategy must integrate a company's knowledge into the platform. First, since efforts are centered around the platform, companies form their knowledge around it. Second, as efforts are invested while considering the platform, the company's knowledge is connected through the platform's knowledge. Third, as they focus on the platform, their efforts are sequenced in the time horizon, and their knowledge accumulates over time. Furthermore, since the company focuses on the drug platform, it has a strong incentive to invest in the platform, and consequently, the R&D expenses also contribute to the accumulation of knowledge. Moreover, the collaboration centered on the drug platform must also contribute to the knowledge accumulation.

Moderna's focus on mRNA and LNP technology has resulted in a patent structure that seems ideal for mRNA vaccine development, holding both mRNA and LNP technology, which must be a huge advantage in vaccine development. BioNTech's patents are more focused on mRNA and not as strong for LNP. However, BioNTech acquired LNP technology from Genevant to complement their technology. By utilizing the platform strategy, they can apply the modularity concept, meaning that if the technology is modular, it can be obtained from outside sources if necessary. Additionally, their constant development over time might be helpful for continuous technological development. In contrast, Daiichi Sankyo's patents are not as numerous as Moderna's or BioNTech's for both mRNA and LNP, and it was unfortunate not to have technological partners who could provide Daiichi Sankyo with the necessary technologies. The lack of patents must make it difficult to develop business in these areas and may also make them hesitant to engage in COVID-19 vaccine development projects due to legal risks. In terms of knowledge, Moderna's paper analysis suggests that its internal knowledge is connected through platform technology. Hence, the platform technology acts as a platform even within the company, helping to consolidate the company's knowledge. On the other hand, Daiichi Sankyo's keyword analysis suggests that it did not have a strong concept connecting the knowledge within the company. It is also important to note that Moderna and BioNTech had experience developing mRNA technology through partnerships. In contrast, since Daiichi Sankyo does not regard mRNA as a platform, it did not have partners related to mRNA technology other than the University of Tokyo.

4.2.4. The Platform Strategy Fosters Investment in Automated Facilities and Digital Infrastructures that Enhance Corporate Capacity

The fourth mechanism is that the platform strategy enables investing in automated facilities or digital infrastructures that enhance corporate capacity. Since the drug platform enables attracting funding, as previously explained, the funding can serve as a source of investment funds. Another important aspect is that, as the platform consists of shared components, companies can easily understand what kind of infrastructure they should build. If the companies have numerous drug candidates with different mechanisms, they might not be able to identify the essential components of each drug candidate. However, since the platform shares the same scientific mechanism, companies can invest in the core function of the platform, which would effectively enhance their productivity.

On top of that, as we discussed, the platform strategy enables the company to attract partners. Their partnerships sometimes provide them with funding and complementary technologies, such as automated technology from Siemens for both Moderna and BioNTech.

Moreover, if a digital platform has been built on top of the drug platform, it will accelerate collaboration both within the company and with external partners. The digital interface transforms the product platform into a digital platform. These digital platforms enhance the capabilities of companies through knowledge sharing among partners both inside and outside the organization.

In the case of Moderna, in addition to utilizing the platform strategy, CEO Stéphane Bancel demonstrated strong leadership in transforming Moderna into a digital company. With his extensive management and digital experience, Bancel brought in several digital experts to shape Moderna into a digital pharmaceutical company. He also aligned the business processes to fit the digital infrastructure. It is important to recognize that the drug platform concept allows a company to become digital, as it provides a focus for investments. These investments enabled Moderna to develop several digital and automated technologies, such as the drug design studio, Amazon data house, and automated facilities in Norwood. As the digital support environments facilitate experiments, they efficiently increase R&D productivity. Moreover, these digitalized

environments attract talented people. The digital environment also allows for data and knowledge sharing within the company, with the large number of co-authorships being one example of this.

It is crucial to note that both Moderna and BioNTech developed automated factories capable of producing mRNA technology. These facilities utilize manufacturing execution systems and are paperless, making the manufacturing process highly efficient. These facilities must have accelerated the research and development efforts of both companies. Furthermore, it is important to recognize that these manufacturing facilities were developed before the pandemic and had collected a significant amount of manufacturing data. This data serves as a valuable asset, providing algorithms and datasets for both companies, which were heavily utilized during the COVID-19 vaccine development phase.

The significant role played by digital technology in the rapid development of the COVID-19 vaccines, which is also suggested by Ashwani Sharma et al..[129] Moderna and BioNTech's investments in digital platforms, tools, and infrastructure prior to the pandemic proved to be invaluable assets during the vaccine development process. These digital technologies enabled efficient data management and analytics, contributing to the unprecedented speed of vaccine development.

4.3. Why Could Moderna or BioNTech Develop the Vaccine So Rapidly?

4.3.1. Efficient Project Launching

Drug platform companies are well-positioned to effectively initiate projects when the target aligns with their drug platform concept. As previously explained, corporate leaders deeply understand the technology, enabling them to make decisions based on their comprehensive knowledge of the situation and their technological capabilities.

Another crucial aspect is that, since the platform should attract similar funding for incidents such as infectious disease outbreaks, as previously discussed, companies would recognize the need to react and move swiftly. Moreover, as drug platform strategy companies accumulate their knowledge within the drug platform, they can respond with technological confidence without fear of legal issues that may arise if they lack adequate patents. Additionally, their infrastructure in

terms of automation or digital technology provides them with the confidence to tackle the issue, and this infrastructure also compels the company to address the challenges.

This is precisely the case for both Moderna and BioNTech, in contrast to Daiichi Sankyo. CEO Stéphane Bancel, with his deep understanding of technology and Moderna's mission, personally contacted the infectious disease expert at NIAID to assess the situation and decided to start the project under his leadership. Similarly, Uğur Şahin, CEO of BioNTech, researched the infectious disease situation himself and developed the "Project Lightspeed" with strong leadership. In contrast, Daiichi Sankyo's decision to launch the vaccine development project was based on a bureaucratic process, with a starting point in April 2020, three months behind Moderna and BioNTech. Furthermore, as Moderna and BioNTech had already developed their capabilities to address such issues, their leaders could make decisions rationally. On the other hand, as Daiichi Sankyo lacked the resources to tackle the issue, the decision to start the project must have been challenging, because the leader had to care about the legal risk or so on.

4.3.2. Effective Resource Mobilization

Drug platform companies would also effectively mobilize their resources for the infectious disease outbreak incident. First, as corporate leaders deeply understand the technology, they can provide the necessary leadership to deal with the issues. Additionally, since employees also understand their platform, they comprehend their mission and how they can utilize their resources. Second, as the platform would have substantial funding, they would have ample room to utilize resources without taking on significant risks. Third, since their knowledge is connected to the drug platform concept, the entire company's knowledge could be utilized for the purpose if necessary. Lastly, as the infrastructure, such as automated facilities or digital technology, would be designed for the drug platform, they could utilize it without any changes, making the project truly efficient.

4.3.3. Discovery Phase: Enabled by Accumulated Knowledge, Partnerships, and Digital Resources

For the discovery phase, the accumulated knowledge, partnerships, and digital resources as well as the mechanism above worked precisely for both Moderna and BioNTech for the COVID-19

vaccine development. In the discovery phase, a basic understanding of the virus is essential. In this case, Moderna's collaboration with NIAID made the process quite efficient, and Moderna successfully developed the drug candidate within a few days. This rapid development can be attributed to the digital infrastructure that allows for efficient candidate design, with algorithms trained before the pandemic and effectively designing the structures during the pandemic. The same story applies to both mRNA structures and LNP formulations.

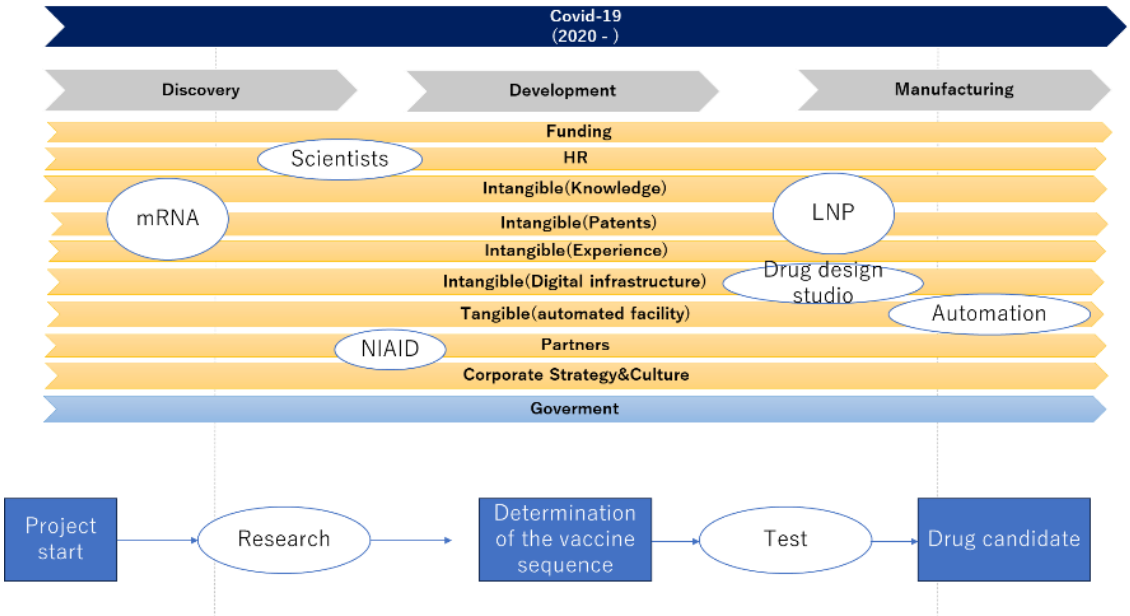


Figure 4.1 Discovery Phase: Through Leveraging Resources, Partnerships and Technologies

4.3.4. Development Phase: Enabled by Digital Resources

In the development phase, ensuring safety and efficacy is crucial. Even though the regulative agency is cooperative, the process involves a significant amount of documentation. In this case, the digitalized format greatly assisted them in organizing the tremendous amount of documentation. Moreover, they could effectively navigate the process by using their capabilities and experiences. The first important process was the animal test, which Moderna could waive because the company had previously developed vaccines with the same mechanism. Omitting this process was crucial for rapid development. Furthermore, as this was during a pandemic, they could conduct the clinical trials in parallel, saving time. The phase three clinical trial presented difficulties, as it required recruiting more than 30,000 people. Additionally, to complete the process quickly, they had to effectively identify hot spots where infectious disease patients would

appear frequently. For this process, collaboration with epidemiologists using the digital platform effectively designed the clinical trial. Moreover, to obtain patient agreements or symptom information, the digitalized system accelerated the process. After collecting data, AI technology effectively cleaned up the data, enabling faster submission to the regulatory agency. Again, the regulatory attitude of enabling timely acceptance of clinical trial documents, even during holidays, significantly helped speed up the process.

Development (Moderna)

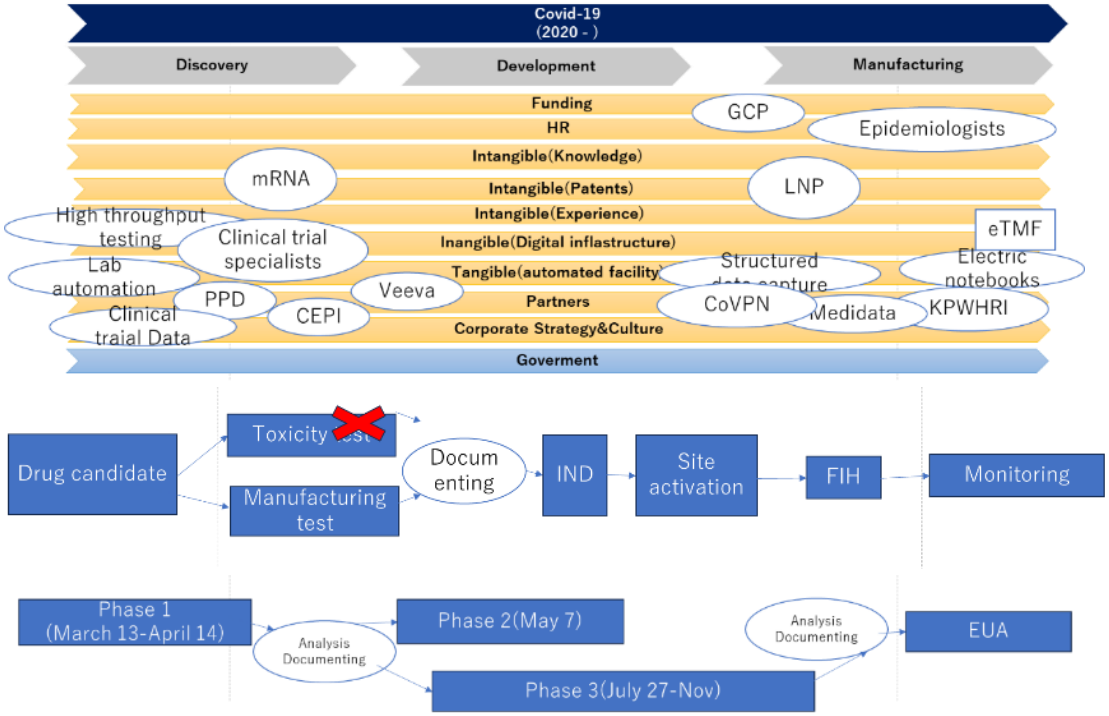


Figure 4.2 Development Phase: Through Leveraging Resources, Partnerships and Technologies

(The diagram illustrates how Moderna successfully completed the development phase by leveraging their resources and expertise. During this phase, Moderna conducted clinical trials, which were supported by various key resources and partnerships.)

4.3.5. Manufacturing Phase: Rapid Technology Transfer and Scale-up Enabled by Digital Platforms

In the manufacturing phase, having a good manufacturing partner and the company's own experience with automated systems was important, as digital technology enables the capture of manufacturing parameters essential for technology transfer. Because they knew their

manufacturing parameters well, they could successfully transfer technology to partner companies, enabling large-scale production. In this story, it is also important to note that this large-scale manufacturing was successful because of the mRNA platform. Since mRNA platform manufacturing is less complex and enables production without a biological process, unlike protein-based vaccines such as Novavax, it allowed for timely large-scale manufacturing.

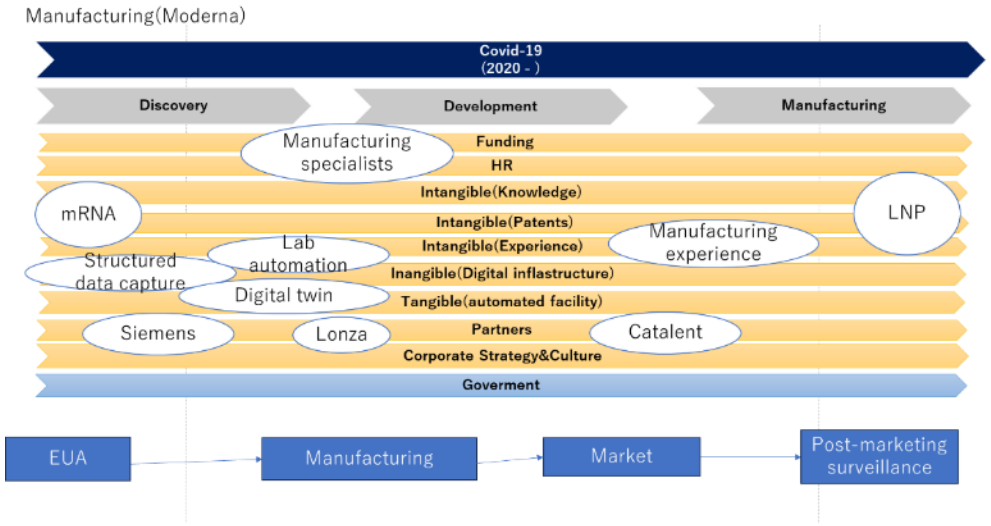


Figure 4.3 Manufacturing Phase: Through Leveraging Resources, Partnerships, and Technologies

(The diagram illustrates how Moderna successfully completed the manufacturing phase by leveraging their resources and expertise. During this phase, Moderna utilized their manufacturing experience, partnerships, and advanced technologies to produce the vaccine at scale.)

4.3.6. Accelerating Timelines with Parallel Processes Enabled by Abundant Funding While Mitigating Risks

These factors enabled the shortening of the discovery, development, and manufacturing phases. Moreover, the reason for the development in such a short time is that they had developed the processes in parallel. The ability to do the processes in parallel was due to the U.S. government's significant investment in vaccine development as part of Operation Warp Speed, allowing pharmaceutical companies to invest in the manufacturing phase even while the drug development phase was in the discovery stage.

4.3.7. Summarizing Factors Enabled Rapid the COVID-19 Vaccine Developments

The table below summarizes the key factors that influenced the vaccine development process. The orange cells highlight the facilitating factors that positively contributed to the development, while the blue cells indicate factors that may have hindered or negatively impacted the process. For Moderna and BioNTech/Pfizer, most of the cells are colored orange, suggesting that these companies had several facilitating factors working in their favor. These factors include the availability of a suitable drug platform, strong research capabilities, collaboration with external partners, the use of digital technologies, and support from regulatory authorities and governments. On the other hand, Daiichi Sankyo's table contains more blue cells, indicating the presence of factors that may have hindered their vaccine development efforts. These factors include a lack of a suitable drug platform, limited research capabilities in mRNA technology, and the absence of strong partnerships or collaborations. The table also highlights the importance of external factors, such as funding and support from governments and regulatory authorities. Moderna and BioNTech/Pfizer benefited from substantial funding and support, while Daiichi Sankyo's external support is limited.

Overall, the table provides a visual representation of the key differences between the three companies and the factors that contributed to the success, or challenges faced by each company in their vaccine development efforts.

Table 4.1 Facilitators and Negative Factors in COVID-19 Vaccine Development: Moderna, BioNTech/Pfizer, and Daiichi Sankyo

Company	Before/After	Phase	Internal Factors								External Factors		
			Quantifiable							Unquantifiable				
			Funding	HR	Tangible	Intangible				Corporate Stragtegy	Partners	Ecosystem	Government Support	Regulation
						Platform Scientific	Degital Platform	Intangible	Experience					
						R&D		Patent						
Moderna	Befor Pandemic	Discovery	around $3b	increasing	automated facility	Both mRNA and LNP	Drug design studio high-throughput method	patents for both mRNA and LNP	done	mRNA paltform strategy, Bancel(management)	NIAID	Boston-cambridge	DARPA NIAID	Experience
	Befor Pandemic	Development			automated facility		Automated documentation Digital aid for clinical trial		done	Digital pharma platform, rational business process	AstraZeneca, Merck			
	Befor Pandemic	Manufacturing			automated facility		Digital twin		done		Siemens			
	After Pandemic	Start the project	Starting from January 2020, under the leadership of CEO											
	After Pandemic	Discovery	around $2.5b		automated facility		Drug design studio high-throughput method			science-based quick dicision making	NIAID		Wrap operation	EUA collaborative
	After Pandemic	Development			automated facility		Automated documentation Digital aid for clinical trial							
	After Pandemic	Manufacturing			Lonza		Digital twin				Lonza			
BioNtech/Pfizer	Befor Pandemic	Discovery	around $1.5b	increasing	automated facility	mRNA	digital	patents for mRNA	done	Ugur(MD.PhD) immuno disease, multi platfrom staretegy, strong scientific leadership	instadeep	Frankfurt		collaborative
	Befor Pandemic	Development			automated facility				a little					
	Befor Pandemic	Manufacturing			automated facility		digital and automation		a little		Siemens			
	After Pandemic	Start the project	Starting from January 2020, under the leadership of CEO											
	After Pandemic	Discovery	around $2.5b		automated facility		digital			Strong leadership	Genevant, Acuitus	World	Wrap operation	EUA collaborative
	After Pandemic	Development			Pfizer		Pfizer			BioNtech and pfizer	Pfizer			
	After Pandemic	Manufacturing			Pfizer		Pfizer			CEO cared a lot	Pfizer			
Daichi Sankyo	Befor Pandemic	Discovery	-	stable	Traditional	Both mRNA and LNP(different scientist) but different from vaccine research	None	patents for mRNA(a little bit LPN)	done	Not scientific	The Univ of Tokyo	Tokyo		
	Befor Pandemic	Development			Traditional		None		none		None			
	Befor Pandemic	Manufacturing			Experience in nucleic acid		None		none		None			
	After Pandemic	Start the project	Starting from April 2020											
	After Pandemic	Discovery	around $0.4b		Traditional		None			Fragmented knowledge one of the project	None	Tokyo	Support through funding	Special Support
	After Pandemic	Development			Traditional		None				None			
	After Pandemic	Manufacturing			Traditional		None				None			

Facilitators
Negative factors

(The table presents a comparative analysis of three companies - Moderna, BioNTech/Pfizer, and Daiichi Sankyo - across various stages of vaccine development, including Discovery phase, Development phase and Manufacturing phase.)

In summary, the successful and rapid development of COVID-19 vaccines by Moderna and BioNTech can be attributed to a combination of factors, including their establishment of mRNA and LNP drug platforms, the construction of organizations that leveraged these platforms, and their ability to effectively mobilize resources and expertise across the vaccine development process. The platform strategy, coupled with strong leadership, diverse funding sources, and investments in digital technologies and automated facilities, enabled these companies to respond quickly and effectively to the global health crisis.

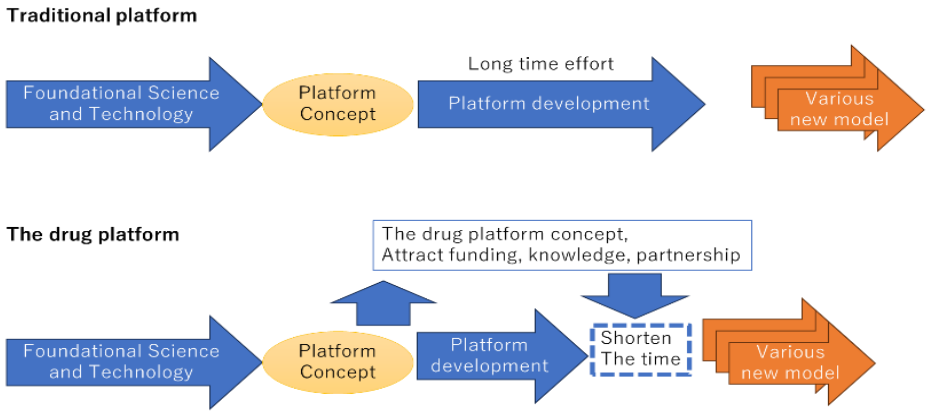
Chapter 5: Discussion and Conclusion

5.1. Distinct Mechanisms of Drug platforms: Implications for Platform Theory

Our analysis of the COVID-19 vaccine development by Moderna and BioNTech has revealed three unique mechanisms that extend our understanding of platform theory, particularly in the context of the pharmaceutical industry.

Firstly, we observed that the platform strategy itself enables the rapid development of the platform. Unlike traditional product-level platforms, which often require momentous time and resources to establish before yielding benefits in terms of shortened product development cycles, drug platforms can accumulate funding and attract collaborators more quickly by appealing to the inherent attractiveness of the platform concept. This self-reinforcing mechanism, wherein the platform strategy drives the swift development of the platform itself, represents a departure from the conventional understanding of platform dynamics.

The cases of Moderna and BioNTech demonstrate how their emphasis on mRNA technology as a platform, rather than a single project, allowed them to secure substantial funding from diverse sources and establish strategic partnerships with key stakeholders. This influx of resources and expertise accelerated the development of their mRNA platforms, enabling them to respond rapidly to the COVID-19 crisis. In contrast, Daiichi Sankyo, which treated mRNA technology as a standalone project, did not benefit from the same level of platform-driven support and consequently lagged in its vaccine development efforts.



The traditional platform requires a long duration for development, though it can effectively produce a new product after the platform is developed. The drug platform attracts various resources and shortens the development duration.

Figure 5.1 Resource Attraction on Shortening Development Time in Drug Platforms

Secondly, based on the point above, we could develop arguments about the relationship between the drug platform and the ecosystem. As discussed earlier, in order to develop a drug platform, it will absorb funding, knowledge, partnerships, and other resources from the ecosystem. If the drug platform is successfully developed, it will greatly contribute to the development of the regional ecosystem, as the company will raise profits, offer funding for further research, and continue to attract talented people. This growing ecosystem will, in turn, foster the next drug platform.
For example, the success of Moderna and BioNTech's mRNA platforms has likely spurred interest and investment in similar technologies, encouraging new participants to enter the ecosystem and fostering the growth of complementary products and services.

This dynamic between the drug platform and the ecosystem creates a "chicken or egg" problem. Although the ecosystem supports the development of the platform by providing necessary resources and expertise, and the growth and success of the platform contribute to the expansion and maturation of the ecosystem itself, it is unclear whether the drug platform or ecosystem should be established first. This discussion could lead to insights on how to cultivate the ecosystem in each region.

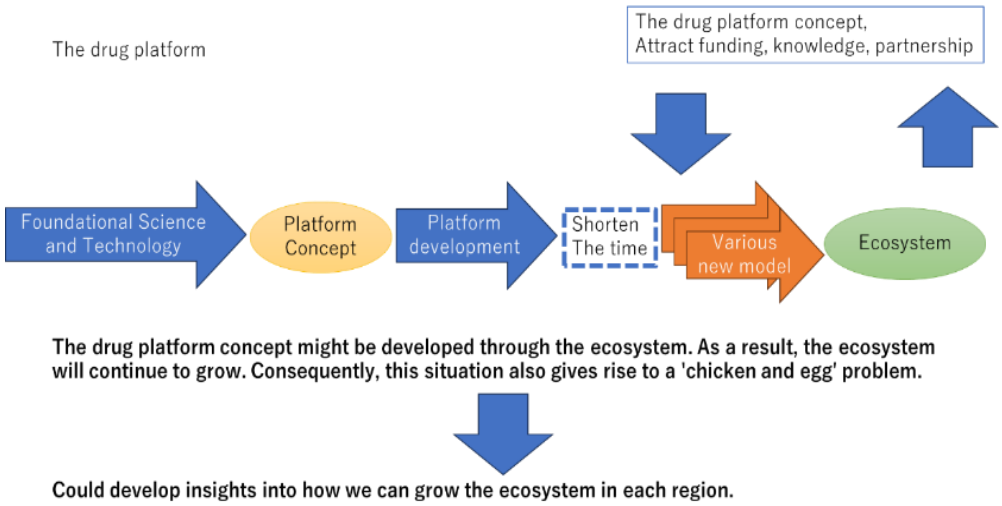


Figure 5.2 Dynamic Between the Drug Platform and the Ecosystem

Thirdly, our study highlights the role of platform strategies in shortening technology transfer durations. We found that the platform approach promotes the digitalization of manufacturing processes, such as the adoption of digital twins and other digital technologies, which in turn

facilitates more efficient technology transfer. This mechanism is particularly relevant in the context of the pharmaceutical industry, where the speed and effectiveness of technology transfer can significantly impact the scale-up and distribution of life-saving treatments.

Moderna and BioNTech's investments in digital infrastructure, integrated with their mRNA platforms, allowed them to streamline technology transfer to manufacturing partners, such as Lonza and Pfizer, respectively. The use of digital tools and real-time data sharing enabled these companies to rapidly adapt their production processes of their vaccines. This digitally enabled technology transfer mechanism, which is closely tied to the platform strategy, represents a novel finding that extends the current understanding of platform theory. This concept could address global health issues where equitable access to vaccines or pharmaceutical products is essential.

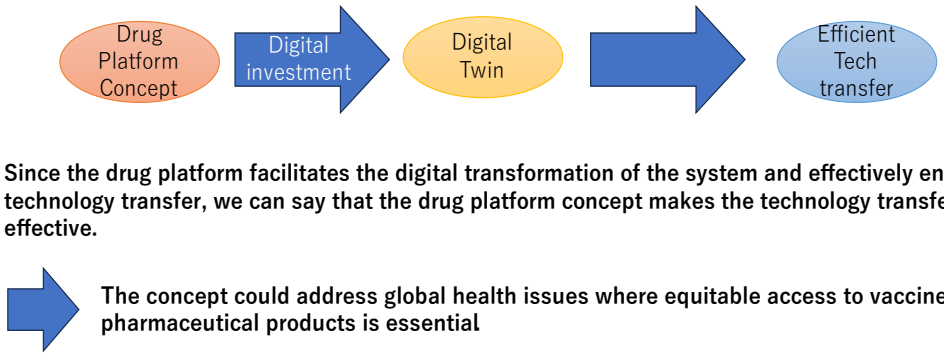


Figure 5.3 The Drug Platform Concept Leads to Efficient Technology Transfer

These three distinct mechanisms – the self-reinforcing development of the platform, the dynamic relationship between the platform and the ecosystem, and the digitally-enabled technology transfer – underscore the unique dynamics at play in the pharmaceutical industry's adoption of platform strategies. They suggest that drug platforms, when supported by a strong platform strategy, can yield benefits not only in terms of shortened product development timelines but also in terms of accelerated platform development, ecosystem growth, and more efficient technology transfer.

These findings have important implications for platform theory, as they highlight the need to consider industry-specific factors and the potential for platform strategies to drive innovation and efficiency in previously unexplored ways. By examining these mechanisms in the context of the

pharmaceutical industry, our study contributes to a more nuanced understanding of platform theory and its application across diverse sectors, while also providing insights into the development of thriving ecosystems that support drug platforms.

5.2 Strategies for Utilizing Drug Platforms

For organizations with a high degree of flexibility and promising technologies, integrating a drug platform as a core aspect of the product platform within management and organizational strategies is crucial. This integration necessitates a different approach from traditional pharmaceutical development, highlighting the need for organizations to pivot from viewing drug discovery as a series of isolated projects to a foundational platform that can generate a diverse array of new drugs. Therefore, the drug platform should be central to the organization, with business processes designed around this core.

Traditional pharmaceutical companies like Daiichi Sankyo face several options regarding the utilization of drug platforms. One approach mirrors the aforementioned strategy, where a new organization or division is established with high autonomy and flexibility, focusing on leveraging the drug platform's potential. However, creating such an entity within a traditional framework can be challenging. An alternative model, exemplified by the relationship between Pfizer and BioNTech, involves collaborating with companies that possess specialized drug platforms, thereby engaging in drug discovery through clinical trials, manufacturing, and sales facilitated by this partnership. For instance, the collaboration between Pfizer and BioNTech was initiated by BioNTech's proactive outreach, leading to a successful partnership. The below figure suggests BioNTech's core capabilities and how Pfizer supplements them[76].

Figure 5.4 BioNTech's Core and Pfizer's Supplementing Capabilities[76]

The figure below illustrates the simplified relationships among Moderna, BioNTech, Pfizer, and Lonza in the context of COVID-19 vaccine development and manufacturing. Both Moderna and BioNTech possess internally developed drug platforms, which serve as the foundation for their vaccine development processes.

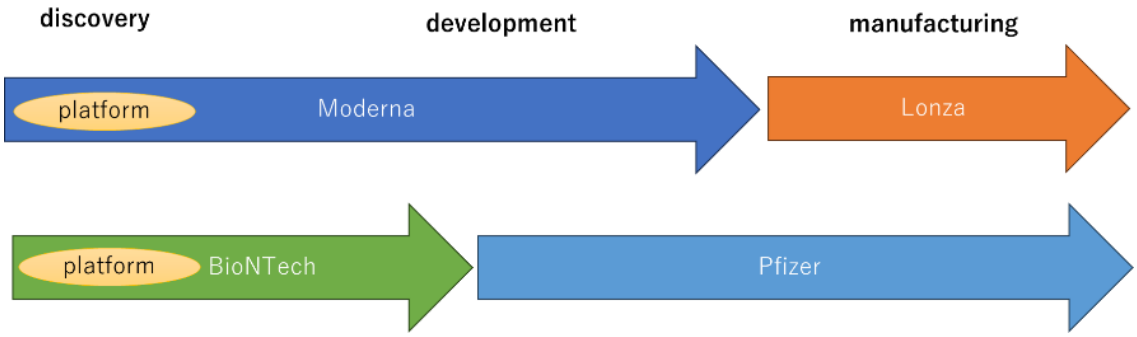


Figure 5.5 Relationships Between Moderna, BioNTech, Pfizer, and Lonza in COVID-19 Vaccine Development and Manufacturing

(The figure is a simple diagram illustrating the relationships between four companies involved in COVID-19 vaccine development and manufacturing: Moderna, BioNTech, Pfizer, and Lonza. The arrows represent the flow of the vaccine development process, starting from the drug platform and ending with manufacturing.)

In the case of Moderna, the company utilized its mRNA platform to develop the COVID-19 vaccine candidate. Upon completing the development phase, which includes preclinical studies

and early-stage clinical trials, Moderna partnered with Lonza, a contract development and manufacturing organization (CDMO). Lonza assumed responsibility for manufacturing the Moderna vaccine on a large scale, leveraging its expertise in pharmaceutical production to ensure an adequate supply of the vaccine for global distribution.

BioNTech, similarly, employed its proprietary mRNA platform to create a COVID-19 vaccine candidate. However, BioNTech's approach to clinical development and manufacturing differed from Moderna's. After successfully completing Phase 1 clinical trials, which primarily assess the safety and initial efficacy of the vaccine, BioNTech collaborated with Pfizer, a multinational pharmaceutical corporation. Pfizer took over the further development of BioNTech's vaccine candidate, including the execution of Phase 2 and Phase 3 clinical trials, as well as the large-scale manufacturing and distribution of the vaccine.

This strategic partnership between BioNTech and Pfizer allowed BioNTech to focus on its core competency of vaccine design and early-stage development while benefiting from Pfizer's experience in late-stage clinical development, regulatory affairs, and global manufacturing and distribution networks. By outsourcing these critical aspects of the vaccine development process to Pfizer, BioNTech was able to accelerate the timeline for bringing its vaccine to market and ensuring widespread availability.

The figure below illustrates four strategic options for pharmaceutical companies to utilize drug platforms, each represented by a different arrow configuration.

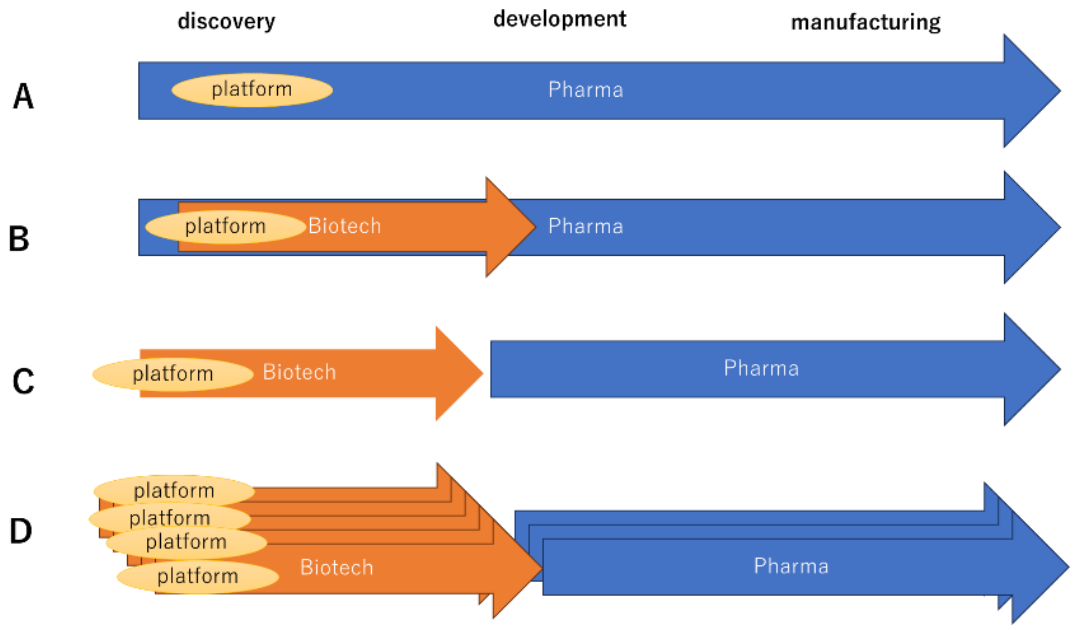


Figure 5.6 Four Strategic Options for Pharmaceutical Companies and Biotech Firms to Utilize Drug Platforms

(The figure is a diagram illustrating four strategic options for pharmaceutical companies and biotech firms to utilize drug platforms. Each option is represented by a different arrow configuration.)

Strategy A, exemplified by companies like Moderna or Eli Lilly, involves the pharmaceutical company owning the drug platform and completing the entire process from discovery to development and potentially manufacturing in-house.[130,131] In this model, the platform is fully integrated into the company's operations, allowing for a streamlined and vertically integrated approach to drug development.

Strategy B involves a pharmaceutical company acquiring a biotech company that possesses a drug platform. The example provided is the relationship between Otsuka Pharmaceutical and Visterra, where Visterra has an antibody platform.[132] This strategy allows the pharmaceutical company to gain direct access to the platform technology and expertise by bringing it under their corporate umbrella.

Strategy C involves a biotech company with a drug platform forming a partnership with a pharmaceutical company. The BioNTech/Pfizer could be in this category. Also, the partnerships

between Aventis (now Sanofi) and Regeneron Pharmaceuticals illustrate this approach. [133] In this model, the biotech company leverages its research capabilities and platform technology, while the pharmaceutical company contributes its expertise in development, manufacturing, and commercialization. This symbiotic relationship allows both companies to focus on their core strengths and share the risks and rewards of drug development.

Strategy D represents a model where a biotech company with a drug platform develops drug candidates independently and then licenses or sells them to interested pharmaceutical companies at a later stage.[134] This approach allows the biotech company to maintain control over the early stages of drug discovery and development, while ultimately partnering with pharmaceutical companies for further development and commercialization. A story of Regeneron and Sanofi is one of the example of the scheme. Regeneron Pharmaceuticals, a biotech company, used its VelocImmune platform to develop fully human therapeutic antibodies. In 2007, Regeneron collaborated with Sanofi to further develop and commercialize these antibodies. Sanofi provided an upfront payment, research funding, and equity investment in Regeneron.[133]Similarly, Xenon Pharmaceuticals used its ion channel drug platform to develop XEN901, a treatment for epilepsy. In 2019, Xenon licensed XEN901 to Neurocrine Biosciences, granting exclusive development and commercialization rights. Neurocrine provided an upfront payment, potential milestone payments, and royalties on future sales to Xenon.[135]

These examples show how biotech companies can successfully employ Strategy D by leveraging their drug platforms to independently develop drug candidates and then partner with pharmaceutical companies for later-stage development and commercialization.

These different models demonstrate the flexibility and adaptability of modern drug platforms, allowing companies to engage in platform-related R&D through various strategies. By leveraging external innovations and partnerships, traditional pharmaceutical companies can access and benefit from these platforms without necessarily conducting all the research and development internally. This strategic approach opens new pathways for pharmaceutical companies to participate in the evolving landscape of drug discovery and development, ultimately leading to the creation of innovative therapies for patients.

5.3 Benefits of Drug Platforms as a sorely on Product-Level Platforms

While this thesis primarily focuses on the effects of pharmaceutical companies aligning their product-level platforms with their organizational strategies and discussed the subsequent effects, it is essential to acknowledge the inherent benefits of drug platforms as product-level platforms. The adoption of drug platforms, such as mRNA and LNP technologies, offers several significant advantages in the pharmaceutical industry. These platforms enable companies to efficiently develop and produce a series of derivative products tailored to specific therapeutic needs while benefiting from the economies of scale and scope associated with a common platform.

Firstly, pharmaceutical platforms allow to produce a diverse portfolio of products. By leveraging a common platform, pharmaceutical companies can derivatively develop various drugs targeting different diseases, develop patient families and various therapeutic applications. This ability to create distinctive products from a shared platform enables companies to address diverse market segments and customer needs. For instance, mRNA technology has been used to develop therapeutics for a wide range of diseases, including cancer and infectious diseases, as discussed in this thesis.

Secondly, pharmaceutical platforms increase the efficiency of development and production. Utilizing common components, processes, and manufacturing technologies for multiple drugs, it will increase the efficiency. The nature of mRNA platforms allows companies to rapidly design and synthesize new mRNA sequences targeting different proteins or antigens without developing entirely new manufacturing processes. Similarly, LNP platforms can serve as a product level platform of drug delivery systems for various targets by modifying their composition, reducing the time and resources required for drug developments.

Thirdly, drug product platforms improve economic efficiency by reducing manufacturing costs. The use of common machinery, equipment, and tools for multiple drugs minimizes the need for additional capital investment. By sharing infrastructure, pharmaceutical companies can achieve economies of scale, spreading the fixed costs of production over a larger volume of output. The Moderna and BioNTech manufacturing facilities, as mentioned in this thesis, exemplify the potential for producing diverse products using same mRNA manufacturing facilities.

Fourthly, pharmaceutical platforms simplify system complexity. The use of standardized components and processes reduces the number of proprietary parts and materials required for pharmaceutical production. This simplification will lead to increased operational efficiency and cost savings. Although no specific factual references are provided in this thesis, the nature of product platforms suggests that this benefit is likely to be realized.

Fifthly, pharmaceutical platforms reduce the risk of new product development. While each drug derived from the platform may have unique characteristics and indications, the underlying core technology has been proven and validated. This reduces the technical and regulatory risks associated with developing entirely new drug modalities and delivery systems. Companies can leverage safety and efficacy data from previous platform-based products to support the development of new drugs and reduce the risk of failure. As discussed in this thesis, animal studies were waived for Moderna due to its prior mRNA drug development experiences.

Sixthly, drug platforms reduce the cost of ownership for pharmaceutical companies. As multiple drugs can be developed from a common platform, companies can amortize the initial investment in platform development over a larger portfolio of products. This cost-sharing approach makes it economically feasible to pursue drug development for a broader range of indications, including rare diseases and niche markets that were previously considered unprofitable under the traditional single product development model. The extensive pipelines of mRNA platforms from Moderna and BioNTech, as highlighted in this thesis, demonstrate the potential for expanding the range of targeted indications.

Finally, drug platforms can improve patient access. The efficiency gains and cost savings achieved through platform-based drug development can be passed on to patients in the form of lower drug prices and improved drug availability. The rapid deployment of mRNA-based COVID-19 vaccines, as discussed in this thesis, highlights the potential for drug platforms to address urgent public health needs.

In conclusion, the adoption of pharmaceutical platforms as product-level platforms offers numerous benefits to pharmaceutical companies. These benefits include the ability to build a

diverse portfolio of products, increase efficiency, reduce costs, simplify complexity, reduce risk, improve economic efficiency, and enhance patient access. Even when considering only the expected benefits from the product platform alone, the advantages of drug platforms are substantial and far-reaching.

5.4 Project Management Portfolio Perspective

The comparison between the case of the development of the COVID-19 mRNA vaccine by Moderna and BioNTech and the Daiichi Sankyo example can also be explained in terms of differences in project concepts. In other words, the emphasis on the concept of "product platform projects" when categorizing projects into categories such as breakthrough projects, product platform projects, and derivative product projects, facilitated rapid success in vaccine development. This can be explained as follows.

Derivative projects are incremental innovation projects that reduce production costs of existing products, add new features, or improve production processes. On the other hand, radical innovation projects (breakthrough projects) involve significant changes in both product features/attributes and production processes, and may require investments in new equipment and operating technologies, and the establishment of new supply chains. Platform projects are intended to create new product families with intermediate innovations that fall between the two previous categories[136].

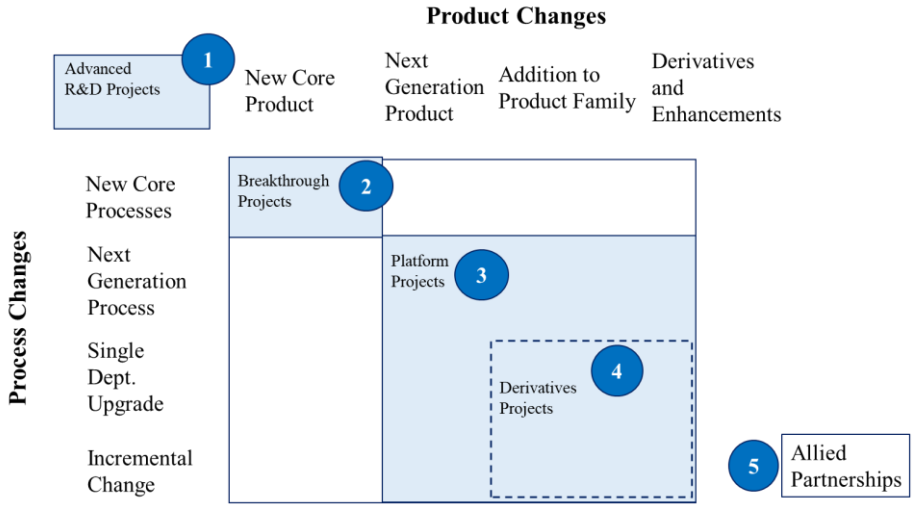


Figure 5.7 The Five Types of Development Projects[136]

In the cases of Moderna and BioNTech, the strategic focus on the development of mRNA technology as a product platform was critical. As resource-constrained startups, they chose to focus on a single platform while intending to create multiple derivative products in the future. This platform-centric approach allowed them to accumulate expertise and efficiently develop derivative products such as a Zika virus vaccine (Moderna) and a cancer vaccine (BioNTech). The two companies were well prepared to expedite the development of the vaccine and treated it as a derivative product project based on their established mRNA platforms. By leveraging both companies' platform technologies, they were able to significantly shorten the typical vaccine development timeline and bring solutions to market quickly.

Conversely, Daiichi Sankyo, a more traditional pharmaceutical company, did not adopt a platform strategy and approached mRNA vaccine development as an independent, "Breakthrough project". This explains Daiichi Sankyo's slower progress compared to Moderna and BioNTech and illustrates the advantages of having an established product platform.

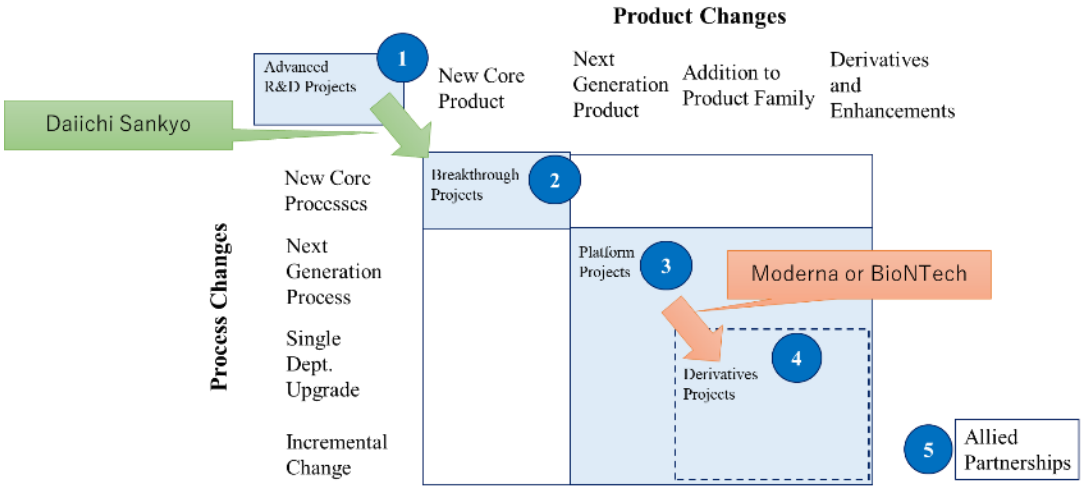


Figure 5.8 COVID-19 Vaccine Development Projects Image of Moderna, BioNTech and Daiichi Sankyo[136]

According to the story, we could say that by allocating the development of the platform, these companies can establish a solid foundation of platforms for future growth and innovation. This strategy allows them to compete effectively with larger, more established firms in areas.

However, this portfolio approach can also demonstrate another way of thinking. For example, it has been suggested that large pharmaceutical companies such as Daiichi Sankyo could benefit from implementing a multi-platform strategy. By managing multiple product platforms simultaneously, these companies can leverage their extensive resources and expertise to develop new drugs across a variety of therapeutic areas. BioNTech's current strategy to address a variety of immunological diseases using multiple drug platforms (mRNA, antibodies, CAR-T, and small molecule compounds) is one example of this approach.

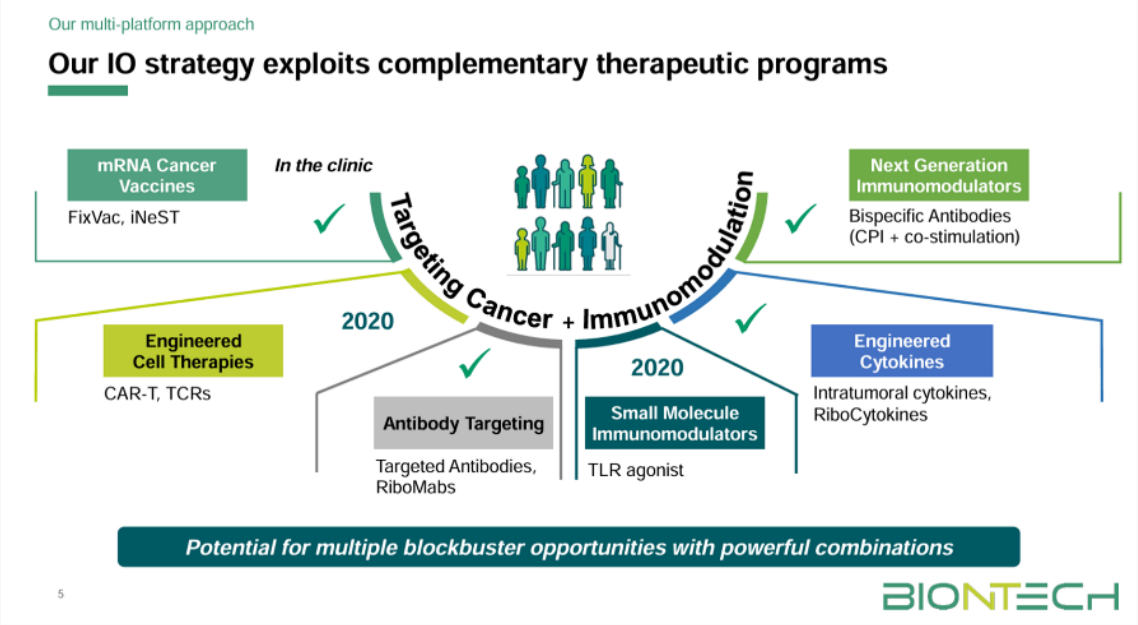


Figure 5.9 The Multi-Platform Strategy of BioNTech[45]

In conclusion, the analysis of this case by applying project management principles provides valuable insights for pharmaceutical companies seeking to optimize the drug development process. The rapid and successful development of the COVID-19 mRNA vaccine by Moderna and BioNTech demonstrates the effectiveness of a platform-centric approach, especially for startups and small entities. It also suggests that large companies with significant resources could adopt a multi-platform strategy to facilitate more efficient resource allocation and accelerate drug development across diverse therapeutic areas. By carefully evaluating the strategic importance of breakthroughs, platforms, and derived projects, pharmaceutical companies may be able to make

informed decisions about their resource investments and establish a strategic position for long-term success in a highly competitive industry.

5.5 The Potential of Digital Platforms in Enhancing Drug Platforms Performance and Inducing Network Effects

In the modern pharmaceutical industry, the integration of digital platforms with existing drug development platforms has the potential to revolutionize their business. As discussed in Chapter 2, when a product-level platform incorporates a digital interface, it can transform into a digital platform capable of inducing network effects, similar to industry-level platforms. Moderna's "mRNA Access" platform exemplifies this concept, showcasing how effective utilization of such a platform can lead to network effects and establish the company as an innovation leader in the field.

Another notable example of Moderna's digital platform integration is the JAMDAS platform, which enables real-time monitoring and visualization of infectious disease situations(https://moderna-epi-report.jp/). By leveraging this platform effectively, Moderna could potentially identify and focus on the most pressing vaccine demands, as well as make informed decisions regarding vaccine development based on the platform's ability to capture and evaluate the risk of infectious diseases.

In the current phase, digital platforms are closely tied to product-level platforms due to the numerous physical factors that must be considered during the drug development process. The relationship between digital and product-level platforms in the pharmaceutical industry bears similarities to that of the automotive industry, where digital platforms play a crucial role in manipulating and controlling various mechanical and control mechanisms within vehicles. As the automotive industry progresses, digital platforms are becoming increasingly important in connecting suppliers and inducing network effects, although this trend is still in its early stages[137].

In conclusion, the integration of digital platforms with drug development platforms has the potential to significantly enhance the performance and innovation capabilities of pharmaceutical companies. By harnessing the power of digital platforms to induce network effects and facilitate

data-driven decision-making, companies like Moderna can establish themselves as leaders in the industry and drive the development of effective medical solutions.

5.6. Creation of Industry Platforms of Manufacturing by Digital Platforms

This study suggests that building a digital platform for the manufacturing process will grow into an industry-level platform. This implication has significant implications for the business models of contract development and manufacturing organizations (CDMOs).

First, by integrating a manufacturing execution system (MES) with a digital twin, CDMOs can supply products to a large number of customers, as shown in Figure. 5.10 below. This is because of Moderna’s statement of by utilizing digital processes, we can switch manufacturing items quickly. This is also evident from Moderna's comment of by using digital processes, they can quickly switch production items and thus contract with more partners.

In addition, as shown in Figure. 5.10 below, the creation of a digital platform for the manufacturing process facilitates the scaling up of manufacturing. This is exemplified by the case of Moderna's outsourcing of manufacturing to Lonza and the technology transfer that was made possible in a short period of time due to the digital twin and MES.

Based on these factors, an industrial platform with network effects is constructed, as shown in Figure 5.10 below. In other words, it will be possible to construct a business model that meets the needs of many customers while scaling up as needed.

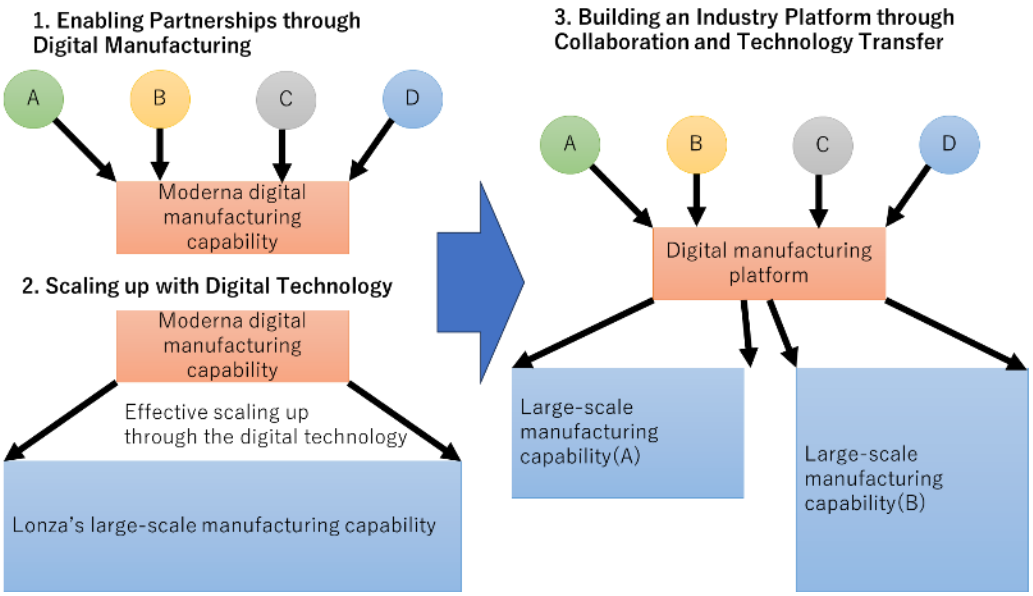


Figure 5.10 Building an Industry Platform of Manufacturing through Collaboration and Technology Transfer

BioNTech is doing another strategy. BioNTech's strategy of developing modular mRNA manufacturing facilities in African countries can be related to the concept of coring in platform strategy. [138]. Through that, it aims to build an mRNA manufacturing network to address infectious diseases in Africa and beyond[44].

Figure 5.11 BioNTainer[138]

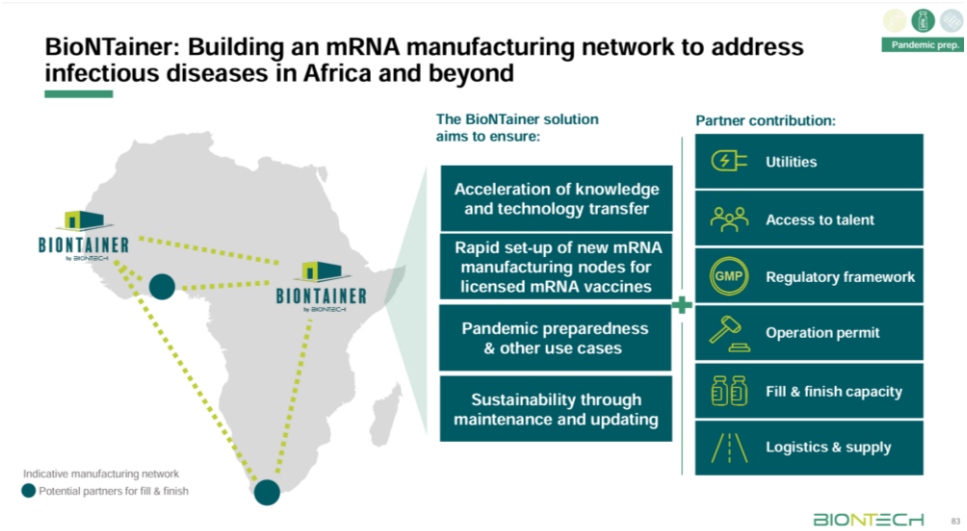


Figure 5.12 BioNTainer: Building and mRNA Manufacturing Network to Address Infectious Disease in Africa and Beyond[44]

It said that it "Enabling regional mRNA vaccine manufacturing and supply" and "The BioNTainers will be equipped to produce a range of mRNA-based vaccines, including the Pfizer-BioNTech COVID-19 vaccine and, if approved, BioNTech's Malaria and Tuberculosis vaccines, targeted towards the needs of the specific region.". [139] More specifically, it is "The manufacturing solution consists of one drug substance and one formulation module, each called a BioNTainer. Each module is built of six ISO-sized SIO-sized containers (2.6m x 2.4m x 12m). This allows for mRNA vaccine production in bulk (mRNA manufacturing and formulation) while fill-and-finish will be taken over by local partners. Each BioNTainer is a clean room that BioNTech equips with state-of-the-art manufacturing solutions. Together, two modules require 800 sqm of space and offer an estimated initial capacity of up to 50 million doses of the Pfizer-BioNTech COVID-19 vaccine each year. The BioNTainer will be equipped to manufacture a range of mRNA-based vaccines targeted to the needs of the African Union member states, for example, the Pfizer-BioNTech COVID-19 vaccine and BioNTech's investigational malaria and tuberculosis vaccines, if they are successfully developed, approved, or authorized by regulatory authorities.". And interestingly, "The capacity can be scaled up by adding further modules and sites to the manufacturing network on the African continent. One of the most critical parts of the manufacturing process is quality control, which includes all necessary tests for each finished vaccine batch. In partnership with local quality control testing labs, BioNTech will help to ensure

the identity, composition, strength, purity, absence of product- and process-related impurities, as well as the absence of microbiological contamination of each produced batch."[138].

Then, this could be similar to the strategy of the "coring" which the company sell the core product and make the market who produce the complement products[140].

5.7. Implications for Regulations

In the development of this vaccine, it is said that the regulatory response was quite flexible, with the review being conducted using data from time to time because of the pandemic situation[42,141]. For instance, Prisha and colleagues highlight that the implementation of rolling review and real-time data sharing for BNT162b2(The BioNTech/Pfizer vaccine) expedited the review process.[142] This approach of quickly sharing data with each other seems to be an important approach for fast pace confirming the efficacy and safety of drugs, but a mechanism for doing so is needed to implement it in a permanent manner, even if there were not pandemic era. Accumulas' initiative is useful as an effort to create such a mechanism. Accumulas is a "nonprofit organization developing a transformative data exchange platform that aims to enable enhanced collaboration and efficiency between life sciences organizations and global health authorities, while also affording users the ability to extract dynamic, data-driven insights."[143] Such an initiative will not only enable the rapid review of the efficacy and safety of medical technologies but also, the platform may serve as an innovation platform to create new medical innovations. One direction in this direction is the FDA's "precisionFDA" initiative to create innovation through data sharing, and future developments in innovation creation through collaboration between regulators and developers are expected[144].

5.8. Patent Issues Related to the mRNA Vaccine Technology

First of all, many of the patents, such as the foundational intellectual property, date back to claims made in 1989 by Felgner, Malone, and their colleagues at Vical (and in 1990 by Liljeström), have been in the public domain. Also, even the Karikó–Weissman patents, licensed to Cellscript and filed in 2006, will expire in the next five years. Hence, "Industry insiders say this means that it will soon become very hard to patent broad claims about delivering mRNAs in lipid nanoparticles, although companies can reasonably patent particular sequences of mRNA — a form of the spike

protein, say — or proprietary lipid formulations." And also said "We don't feel there's a lot that is patentable, and certainly not enforceable," says Eric Marcusson, chief scientific officer of Providence Therapeutics, an mRNA vaccines company in Calgary, Canada."[38].

5.9. The Unique Situation of the COVID-19

The unique circumstances presented by the COVID-19 pandemic provided several key insights and implications for the pharmaceutical industry. The "Coronavirus exception" refers to the extraordinary conditions under which the industry operated, highlighted by the urgent global demand for vaccines and treatments, unprecedented levels of funding, and the collaborative efforts that led to the rapid development of vaccines.

Highlighted Situation: The COVID-19 pandemic brought an unprecedented focus on the pharmaceutical industry, pushing it to the forefront of global attention. The urgent need for effective vaccines and treatments against the COVID-19 demanded swift action, innovation, and agility from all stakeholders involved.

Funding: The pandemic saw a significant influx of funding from various sources, including governments, private investors, and international organizations. This influx supported the accelerated research and development efforts. The scale and speed of this funding were unparalleled, reducing financial barriers and enabling a rapid response to the health crisis.

Development Enabled by the COVID-19: The very nature of the COVID-19 and its global impact necessitated and enabled the rapid development of vaccines. The global spread of the virus, its significant morbidity and mortality rates, and the societal and economic disruptions it caused created a unique scenario where traditional timelines and processes for vaccine development were dramatically shortened. This situation fostered an environment of global collaboration, sharing of scientific information, and regulatory flexibility that was instrumental in developing vaccines in record time.

In a the time of COVID-19, the "Competitors become partners" happened, and the Accumulus Synergy mentioned above was founded in July 2020 by ten biopharmaceutical companies (Pfizer, Amgen, Takeda, Bristol Myers Squibb, Astellas, Sanofi, GSK, Janssen, Roche, and Lilly) came

together, in order to “building a data-sharing platform that supports the real-time exchange of information with regulators, stored safely and securely in the cloud”.[145]

The COVID-19 pandemic creates a collaborative environment, and people work extremely hard to combat the disease. Kathrin Jansen, Senior Vice President and Head of Vaccines R&D at Pfizer, said, “It wasn’t about who publishes first, but a willingness to share scientific data for the sake of dealing with this beast of the pandemic.”. Also, for the question of “How replicable is that development speed?”, she said, “This was a model for special circumstances, where people were willing to do whatever, it takes. But we were working around the clock, and there was a lot of burnouts. It’s not a model for the future where you can aim to do everything that way. It’s not sustainable.”.[56] Also, it is important to note that although mRNA technology is really effective for the SARS-CoV-2 virus vaccine; we are not sure whether or the drug platform works for the next pandemic. Also, Kathrin answer answered the question, “Do you think mRNA vaccine platforms will now become more dominant?” she said, “For some viral diseases, the mRNA platform is super, and there’s a bunch of mRNA candidates now that are being worked on. [Target pathogens include influenza, rabies, and others]. She also mentioned “You can’t just take technology and throw it at every pathogen — it’s not going to work. I was always interested in finding the right technology.”.

However, the jury is still out on whether mRNA vaccines could play a role in the fight against some of the bacterial pathogens. For example, for the pneumococcal conjugate vaccines, you need a protein carrier and a polysaccharide that has been derived from the pathogen. That doesn’t lend itself to mRNA at all.”[56] Also, it is really important to note that the COVID-19 vaccine has been developed due to the experience of SARS and MERS. The nature article said, “Because of knowledge gained from the initial development of vaccines for SARS-CoV and MERS-CoV, the discovery phase was omitted.”. Hence, we could start to develop the vaccine from the standpoint that we have the knowledge of the vaccine. On the other hand, Kathrin said, “Understanding the pathogen is crucial.”[56]. Hence, if we would like to prepare for the next pandemic, it is obvious that we have to take care of the research, which would understand the pathogen, which is also important.

5.10. Limitations and Future Work

This study has explored the application of platform theory in the pharmaceutical industry, focusing on the cases of Moderna, BioNTech, and Daiichi Sankyo in the development of COVID-19 vaccines. While our analysis provides valuable insights into how drug platform concepts can be established and leveraged to accelerate vaccine development, there are several limitations to consider and opportunities for future research.

Firstly, our study is based on a limited number of case studies, specifically focusing on mRNA technology. To further validate the generalizability of our findings, it would be beneficial to examine a broader range of drug platform technologies, such as cell therapies, CAR-T, stem cell technology, and CRISPR.[17] By investigating how platform strategies are employed across different modalities, we can gain a more comprehensive understanding of the key management activities that transform foundational science into effective drug platforms.

Secondly, while we have argued that the drug platform concept attracts funding, our analysis did not quantitatively compare the funding levels of platform-based companies to those of traditional pharmaceutical companies. Future research could conduct a more thorough examination of the financial aspects, investigating the extent to which platform strategies influence funding attraction across various modalities. This could involve comparing funding levels, sources, and trends between platform-based and non-platform-based companies, as well as analyzing the impact of funding on the success and growth of drug platform companies.

Furthermore, our study primarily relied on qualitative data and narrative analysis. To strengthen the validity of our findings, future research could employ quantitative methods to assess the relationship between platform strategies and various performance indicators, such as R&D efficiency, clinical trial success rates, and time-to-market. By combining qualitative and quantitative approaches, researchers can develop a more robust understanding of the mechanisms through which platform strategies drive innovation and accelerate drug development.

Additionally, while we have touched upon the role of digital platforms in enhancing drug discovery and inducing network effects, this area warrants further exploration. Future studies

could delve deeper into the interplay between digital and physical platforms in the pharmaceutical industry, examining how digital technologies, such as artificial intelligence, machine learning, and big data analytics, can be integrated with drug platforms to enable more efficient and collaborative drug development processes. Investigating the potential of digital platforms to create innovation ecosystems and foster knowledge sharing among various stakeholders in the pharmaceutical industry could provide valuable insights for companies seeking to harness the power of platform strategies.

Lastly, our study focused on the specific context of the COVID-19 pandemic, which presented unique challenges and opportunities for vaccine development. While this crisis highlighted the potential of platform strategies to accelerate drug developments, it is essential to examine the applicability of these strategies in more conventional settings. Future research could explore how platform approaches can be employed to address other pressing health challenges, such as cancer, rare diseases, and chronic conditions, and assess the factors that influence the success of platform strategies in these contexts.

By addressing these limitations and pursuing the suggested research directions, scholars can contribute to a more comprehensive understanding of platform strategies in the pharmaceutical industry.

5.11. Final Thoughts

The COVID-19 pandemic was a devastating global health crisis, but the rapid development of vaccines undoubtedly saved countless lives. This paper argues that the unprecedented speed of vaccine development can be explained through the lens of platform theory and serves as a prime example of the "power of platforms" described in "The Business of Platforms"[24]. The contrasting cases of Moderna and BioNTech's rapid development of an mRNA-based COVID-19 vaccine and Daiichi Sankyo's slow progress highlight the critical role of integrating platform strategies into the core operations and management of pharmaceutical companies.

Furthermore, this study identifies new mechanisms for the self-enhancing development of pharmaceutical platforms and digital technology transfer, emphasizing the importance of platform strategies in the pharmaceutical industry. These findings contribute to the advancement of

platform theory and provide valuable insights for pharmaceutical companies aiming to leverage the potential of pharmaceutical platforms to drive innovation and improve patient health outcomes worldwide.

The integration of digital and pharmaceutical platforms opens new ways for dramatically improving performance, inducing network effects, and fostering collaborative ecosystems within the pharmaceutical industry. Drug discovery platforms are increasingly encouraged to build digital platforms, which can lead to significant advancements in the sector.

While the unique circumstances of the COVID-19 pandemic undoubtedly influenced the rapid development of vaccines, the lessons learned from this experience are invaluable for the pharmaceutical industry to prepare for and respond to future global health challenges.

In conclusion, this study demonstrates the importance of the pharmaceutical industry harnessing the "power of the platform" and provides concrete directions for leveraging its potential. The discussion should be expanded to explore how companies and policies can work together to address the health and healthcare challenges facing people around the world, utilizing the power of platforms to drive innovation, collaboration, and ultimately, better health outcomes for all.

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