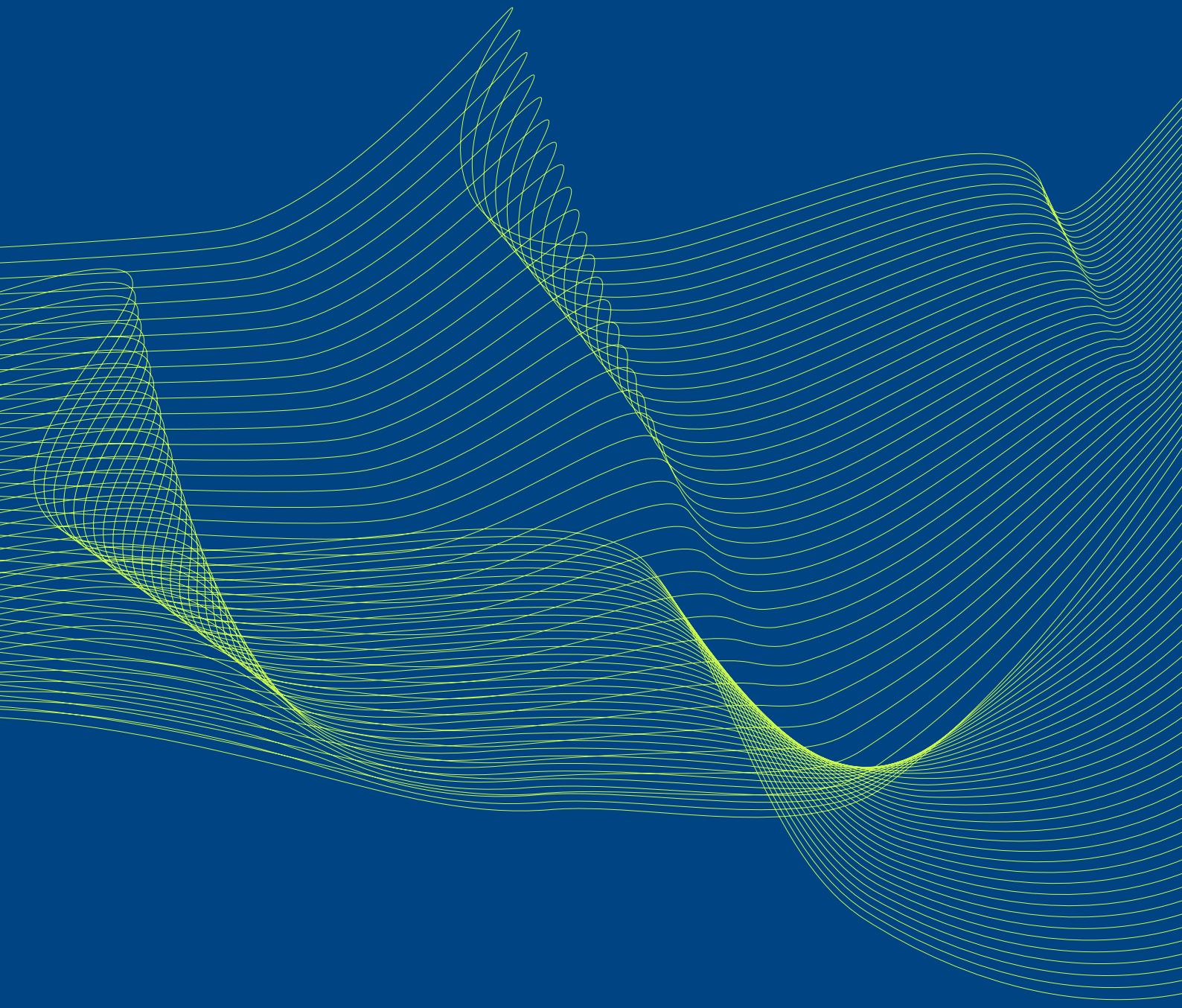

Unprecedented

The Rapid Innovation Response to COVID-19
and the Role of Intellectual Property

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I. Introduction

The COVID-19 pandemic has presented humanity with unprecedented challenges. In many ways, we have risen to meet those challenges; in other ways, we have fallen short. One of the triumphs has been the biopharmaceutical industry's development of COVID-19 vaccines and treatments in record time. While getting them to everybody, everywhere, remains a challenge, this singular achievement in innovation is remarkable and merits discussion and study.

COVID-19 vaccines and treatments are the product of great science, public-private partnerships, and many years of hard work and investments, supported by the intellectual property (IP) system. Without IP, the investment, cooperation, and innovation that led to the development and manufacturing of COVID-19 vaccines and treatments would not have happened as it did.

This report tells the story of how COVID-19 vaccines and treatments were rapidly developed and delivered to society, focusing on the enabling role of IP.

This report tells the story of how COVID-19 vaccines and treatments were delivered, focusing on the essential enabling role of IP. It is a story of innovation, investments, and cooperation, with IP serving as a foundation throughout. The report covers the period through August 1, 2021.

We are telling this story because, as much as people herald the development of vaccines and therapeutics in record time, the scope of the effort and the institutions that enabled it – including IP – are not fully appreciated. In fact, the discussion often suffers from hindsight bias, treating success as if it were inevitable. It was not. This innovation was built on a foundation of earlier investments, innovation, and collaboration. It required even further investments, cooperation, and risk-taking, and many of those risks did not work out. Both the foundational technology and the recent innovations were enabled by IP.

One unique contribution of this report is that it relates the views of IP counsel, manufacturing experts, and others in the biopharma industry who played a role in developing treatments. We interviewed more than a dozen executives from a wide variety of companies, some from companies that were responsible for vaccines and therapeutics that were approved for use, and others that contributed to their manufacturing. We also surveyed the publicly available information about the development of vaccines and therapeutics to provide a full account.

This report first sets the context by explaining the structure of the biopharma industry and the enabling role of IP for innovation within it. We then tell the story of innovation in response to the COVID-19 pandemic, focusing on the most important innovations. We conclude with lessons learned about IP and the COVID-19 response.

A. The Biopharma Industry and Intellectual Property

Innovative biopharmaceutical companies have delivered life-changing and life-saving improvements to our lives, including COVID-19 treatments. These innovations are the result of great science, extensive Research and Development (R&D) collaboration, and effective execution. These efforts draw on many different kinds of expertise, and tremendous investment at each step. The key enabler for all this work and investment is IP, which provides a foundation for many institutions and people to work together to take a new discovery from the research bench through the many steps to become a treatment that can be used by people.

To understand the role of IP in developing COVID-19 treatments, one must first understand its role in the biopharma industry generally. While it is a widely known fact that IP is important to the life sciences industry, its role is often less than fully understood. There is a simple account of how drug development works and how IP drives it. The simple story says that companies mainly innovate by researching new compounds, which are hard and expensive to develop, but easy and cheap to copy and manufacture. According to the simple but incomplete account, IP rights prevent copying for a limited time to allow innovators to recoup their costs and to incentivize yet more drug research.

The role of IP in biopharma innovation is evolving and is often less than fully understood.

The simple account of IP-driven drug development is far too simple, and it gets less accurate every year. Drug development and manufacturing was always more complex and challenging, and biologics have made it even more so. Every phase of drug development, from research to manufacturing to distribution, demands significant innovation and is challenging and expensive. Moreover, IP plays a much richer role in fostering innovation, investment, and, especially, collaboration than the simple account credits.

The next two subsections explain how this works, first relating information about innovation in the biopharma industry and then describing the enabling role of IP.

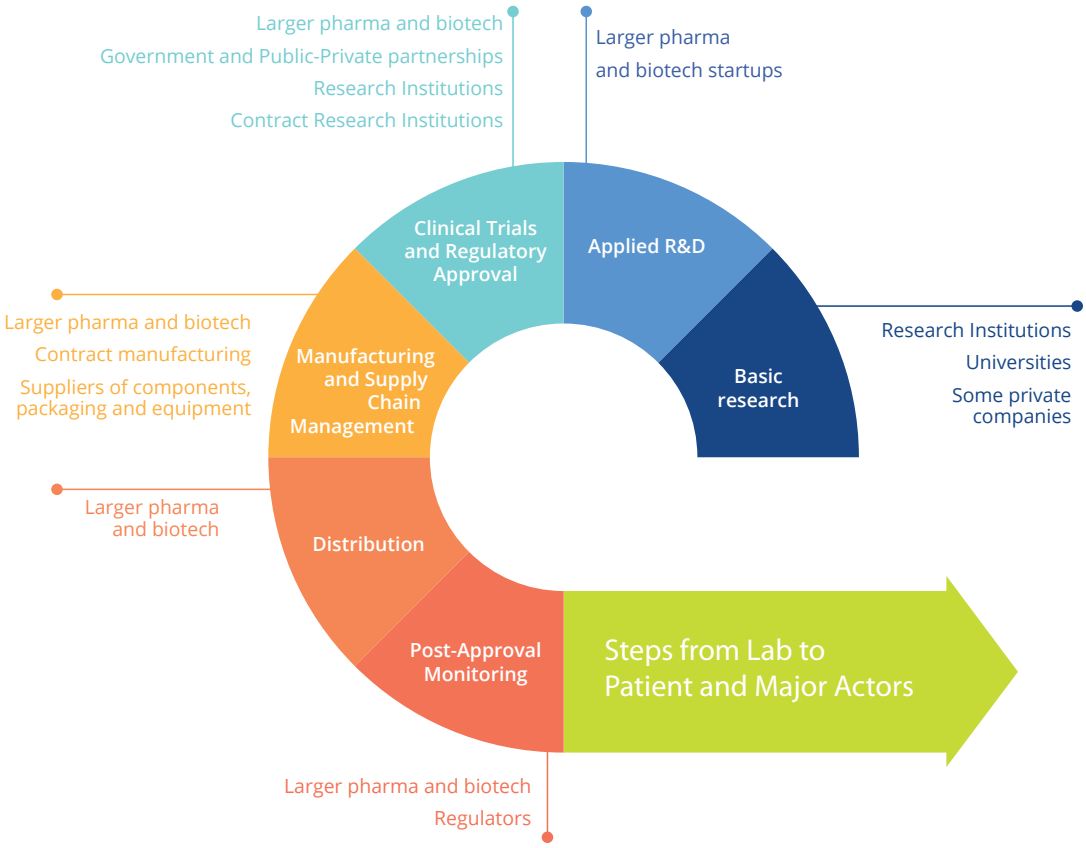
B. The Biopharma Industry

In the era of biotechnology, developing new treatments, bringing them to market and manufacturing them at scale is a far more challenging endeavour than simpler accounts of the industry credit. First, drug development and delivery require the expertise of many diverse actors. Second, developing drugs is costly and risky at every stage, from lab to market and beyond. Third, in the era of biotechnology, developing, manufacturing, and distributing treatments requires more complex business, manufacturing, and IP arrangements than ever before.

1. Understanding the Division of Labor in the Biopharma Industry

Bringing a treatment from lab to market requires many steps and between and within each step, the labor is divided among a diverse set of actors. Each step is significant, necessary, and draws on the unique expertise and capabilities of different individuals and institutions. Along the way, research institutions, universities, start-ups, large companies, contract manufacturers, and suppliers all play key roles. Each of them employs skilled scientists, doctors, manufacturing professionals, and others with unique expertise who each make essential contributions.

Figure 1: Steps from Lab to Patient and Major Actors



Author: Mark F. Schultz

Figure 1 illustrates these steps and the most significant institutions involved in each of the steps. Drugs and vaccines don't reach patients without going through all these steps, each of which requires significant investments. Without the ability to hand off responsibilities and share work from step to step, treatments would never reach patients. As we will discuss in the next section, IP is important for this process, securing investments at each of these steps and providing a foundation for the coordination and cooperation that happens within and between each step.

a. Basic Research

Many of the fundamental insights and new technologies that lead to treatments, as well as some treatments themselves, originate from universities and other research institutions.[1] This research, largely publicly funded, is essential to creating a pipeline for new vaccines and treatments. However, while publicly funded research is an essential complement to the work the private sector does, it is far removed from delivering a treatment to a patient.

Publicly funded research has historically focused on upstream, basic science, leaving the downstream research regarding clinical applications to the private sector.[2] Academics and research institutions focus on fundamental issues such as disease processes, biology, and identifying biomarkers that point to potential targets for treatment.[3] Meanwhile, industry actors also contribute a great deal of basic research, but, crucially, take the next step to carry out the applied R&D that focuses on discovering and manufacturing treatments for patients.[4]

The two activities – basic and applied research – represent a division of labor that is complementary. The large portion of basic research that is publicly funded generates a huge return on investment that is largely realized through, and only because of, the applied R&D done by the private sector.[5] For example, one study found that every one-time expenditure of $1.00 of public spending on basic research yielded a recurring annual benefit of $.43 a year indefinitely.[6] Another study estimated a total social benefit of 150 per cent from basic biomedical research funded by government.[7]

Developing research into a clinical application for patients requires engagement and investment from the private sector. Although research institutes develop some clinical applications, the number is a fraction of what the private sector develops.[8] Moreover, most of the other work that it takes to get a drug to patients – regulatory approval and distribution, among other things – is beyond the competence and outside of the interest of researchers. One of our interviewees described how, in the context of a public-private project to bring a new COVID-19 vaccine to market, his company stepped in to "work with regulatory agencies to understand the emergency use procedures and what the different pathways would look like. We liase with regulatory agencies all the time. We brought this expertise to the table. Launching trials with thousands of patients around the world then organizing and sharing with regulatory agencies is a heavy lift. Universities don't do this – they have less experience in this area."

Derrick Rossi, the academic founder of Moderna, explained the relationship of basic research and research institutions to the other steps in developing a drug in an interview shortly before the pandemic. He described it as an ecosystem that requires the contribution of many different parties, with each specializing in what they do well. "This industry of professionals is out there … The more people who are involved in the chain, post-academic discovery, the more you have pros involved – all the way from IP filings to VCs to due diligence to assembling a team," the more likely you are to develop a viable treatment.[9] Rossi summed up the division of labor: "Academics are good at academia and fundamental science. They are not good at developing drugs for patients."[10]

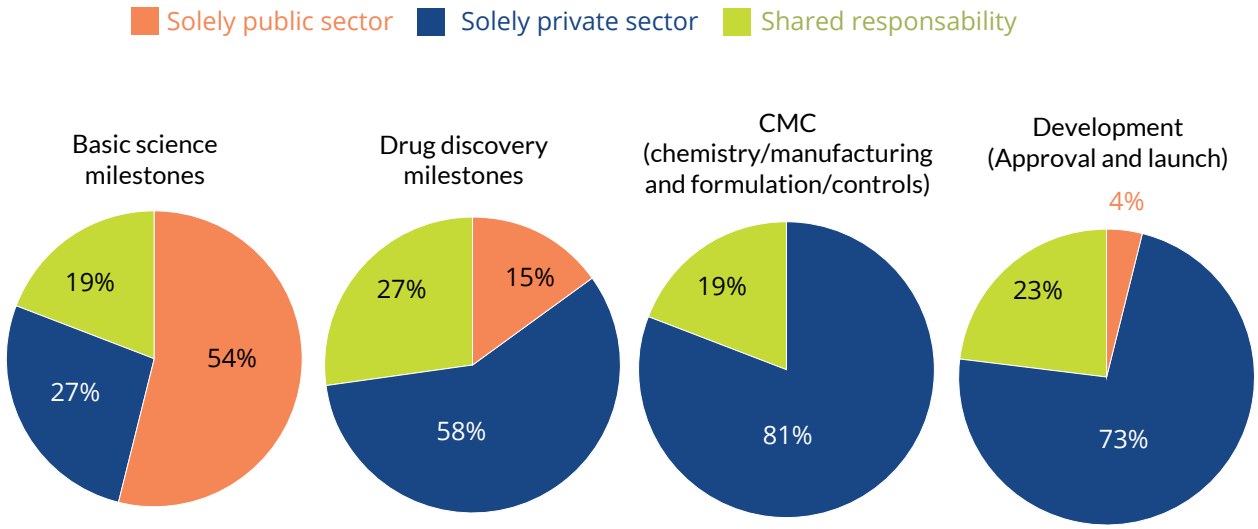
b. Applied R&D

This step, often described as the translational phase, is where most new drugs and vaccines get their start, as large biopharma companies and start-ups focus on developing treatments for patients. They spend vast amounts to do so; the biopharma industry reported global R&D spending estimated at $179 billon in 2018.[11]

Biopharma companies test thousands of compounds to find a single promising drug. Estimates indicate that it takes 5,000 – 10,000 candidates to find one drug approved for use. Of those initial candidates, about 250 make it to preclinical testing, five make it to clinical testing, and only one reaches the market.[12]

For innovations originating from basic research, there is typically a transfer of technology from research institutions to a commercial entity at this stage. Research institutions have technology transfer offices, which exist to identify basic research that may have practical applications, embody that research in IP, and find one or more licensees to develop the technology further for practical applications. Depending on technological and business considerations, the firm receiving the technology may be a start-up focused partly or solely on developing the technology, or a larger, established company, that adds the technology to its portfolio. The companies that commercialize technology pay royalties to the originating research institutions, which help support those institutions and their further research.

Figure 2: Public Sector vs. Private Sector Achievement of R&D Milestones for a Sample of Transformative Drugs



Source: Ranjana Chakravarthy et al., "Public- and Private-Sector Contributions to the Research and Development of the Most Transformational Drugs in the Past 25 Years: From Theory to Therapy," Therapeutic Innovation and Regulatory Science Vol. 50, 6 (July 2016), https://www.ncbi.nlm.nih.gov/pubmed/30231735.

Technology transferred from research institutions consistently requires significant work and investment from commercial actors to develop a viable treatment. Indeed, this work is what bridges the gap between basic and applied research. That's not to say that basic research is not essential; it is necessary but not sufficiently developed to result in a treatment for patients in most instances. As one study concluded, "Without the scientific advances yielded by private-sector research, most drugs would not be developed, and thus the economic returns to publicly funded research would be sharply reduced."[13]

This division of labor is illustrated by a study that examined the comparative contributions of the public and private sector to developing a sample of drugs from recent decades that a survey of physicians had designated as transformative. The study identified four categories of research and development milestones necessary to develop a new medicine, and the comparative contribution of each sector:

What this research indicates is that, as drug development leaves the initial phase of basic research and proceeds through the remaining steps, the private sector's role becomes dominant in the division of labor.

c. Clinical Trials and Regulatory Approval

Once preclinical testing identifies a potential candidate drug, the sponsor files an application to government regulators to proceed with human testing via clinical trials. If the regulator determines that it is safe to conduct trials, the sponsor then begins the first phase of clinical research.

Clinical trials are a significant undertaking. Prior to approval, the drug is tested in three phases, first on tens, then hundreds, then thousands of people to establish efficacy and safety sufficiently to secure regulatory approval. If the drug is approved and enters use, then the sponsor must continue to conduct a fourth phase of clinical trials to monitor the treatment's safety and effectiveness as it is deployed under real world conditions.

Clinical trials are an administrative and logistical challenge quite different from R&D. They require very different resources and know-how to handle the challenge of recruiting subjects, tracking results, and complying with regulatory requirements. Part or all of a clinical trial may be outsourced to a specialized Clinical Research Organization (CRO). One CRO identifies 19 categories of work in a clinical trial budget, including such tasks as regulatory affairs, securing and managing a site, managing drug and biological sample logistics, and statistics and data management.[14]

These demands require significant resources to meet. A 2014 study submitted to the U.S. Department of Health and Human Services estimated that the average total cost per study of conducting all four phases of clinical trials, broken down by therapeutic area, ranged from $54 million to $115 million.[15] The average costs for each phase, across all therapeutic areas, typically escalate between Phases 1 – 3, with Phase 1 trials costing $4 million on average, Phase 2 costing $13 million, Phase 3 costing $20 million, and Phase 4 costing $20 million but with high variability.[16]

If a sponsor is fortunate enough to achieve success in all phases of clinical trials, it can apply to the regulator (e.g., the FDA in the U.S.) for marketing approval. An application for marketing approval is a substantial undertaking. One study estimates the average cost of the work required to make the submission at $2 million.[17]

It is also important to note that regulatory requirements differ among countries, which creates additional work and requires broad expertise. While the phased approach to clinical trials is standard, the specifics of regulatory requirements and processes are different among many countries. A sponsor may need to conduct additional clinical trials specifically for a particular country.

This deployment of money and people typically requires the strengths and/or resources of a large biopharma company or a start-up that grows to add substantial capabilities. They are also often outsourced to CROs, which specialize in the many tasks involved in clinical trials. Public-private partnerships and research institutions also conduct clinical trials, although these may be more investigational in nature and/or focused on secondary uses and thus not directed at taking a treatment all the way through to secure new drug approval.

d. Manufacturing and Supply Chain Management

Once regulators authorize a drug for sale to patients, the next step is manufacturing. This is an entirely different challenge, from synthesizing a drug or vaccine and producing it in small batches for preclinical and clinical testing. Manufacturing processes are typically developed and optimized stepwise, as clinical trials progress and require larger quantities of the medicine. Making millions or even billions of doses is an industrial undertaking, which must be done efficiently and economically, with high precision and attention to safety. This step is typically handled by large pharmaceutical companies, which have the required resources at their disposal.

Regulatory and safety requirements for drug manufacturing are demanding. For example, the WHO's guidelines on good manufacturing processes for pharmaceuticals covers nearly 60 pages, with standards on a wide variety of points, from sanitation to equipment to quality control.[18]

Governments impose a variety of standards for manufacturers, not just on manufacturing done in their country, but for manufacturing done anywhere in the world of drugs sold in their country. Some conduct regular inspections of facilities around the world.

With the advent of biologics, manufacturing has become more challenging. Biologics typically are grown in living cells and then purified, in contrast to small molecule drugs, which are chemically synthesized. This methodology makes manufacturing far more challenging. As one study observed, "the manufacturing process for biologics is lengthy and complex, often involving many discrete unit operations and activities. Each step can have several input variables and, from start to finish, the manufacturing process involves simultaneously controlling dozens of input parameters while performing quality control checks throughout."[19] The authors of that study summed up the importance of manufacturing in biologics by stating throughout that "the process is the product."[20]

Fewer than 12 per cent of medicines that start Phase 1 trials are approved by the FDA.

The result of this complexity is that the manufacturing process presents significant logistical and management challenges. Each treatment today is likely produced in several steps and different locations and requires procurement of components from several dozen suppliers. For example, Pfizer's mRNA vaccine requires 86 different suppliers and 280 materials in total.[21]

e. Distribution

Distributing drugs and vaccines presents yet another set of challenges that call for investment and specialized expertise. Treatments are no ordinary product that can be put in a freight container on one end and simply placed onto a retail shelf for sale to a consumer at the other end. Rather, innovators must further invest and innovate to ensure products reach people safely and effectively.

Challenges abound with respect to the products themselves. For example, vaccines often have demanding "cold chain" requirements, meaning they can be kept continuously cold or frozen until use. Products must be labelled in particular ways to comply with regulations. To the extent that if products are controlled substances or impose other risks, they may require special restrictions in distribution.

Some drugs, particularly biologics, must be specially administered, which presents further logistical challenges. Unlike most small molecule drugs, most biologics cannot be administered as a pill but must be delivered through injection or intravenous infusion.[22] Infusion is a time-consuming process for the patient. These requirements mean that getting such a treatment to patients requires setting up specific sites where drugs can be administered.

f. Post-Approval Monitoring

The obligations of a biopharma manufacturer do not end upon approval of a drug. Even large clinical trials cannot capture all adverse events from use of a drug. Therefore, biopharma companies are required to continue clinical trials with an ongoing Phase 4 as the drug is distributed widely. Moreover, data regarding adverse events is collected and monitored by regulators.

2. Investment and Risk in Biopharma

Drug development is an enormously expensive and risky business. As the discussion above illustrates, every step in the process of bringing a medicine or vaccine from the research lab to the market and beyond is complex and costly. Each of those steps also carries some risk of failure. As the necessary investments at each step accumulate, the consequences of failure grow larger.

Drug development is expensive. Estimates vary,[23] with one putting the cost of drug development at $2.6 billion for an approved drug.[24]

That cost is not just a single expense. It is the product of a series of large and necessary investments as it proceeds through each of the steps of development described in the previous section. These investments are partly out-of-pocket costs devoted to a particular drug, but they also include investments in capabilities, such as setting up manufacturing facilities or training a skilled workforce.

Because of this need for investment at each step of drug development, proposals to reduce costs must contend with the unavoidable need to incur certain costs to bring a drug to consumers.[25] The question is who pays those necessary costs, not whether they must be paid.

These investments in developing a drug are risky. Fewer than 12 per cent of medicines that start Phase 1 trials are approved by the FDA.

Success is not guaranteed after approval either. There is competition in the drug market. Also, health care systems, doctors and payers need to accept that the treatment is worth prescribing. As a result, some drugs do not achieve a return on investment. A 2010 study found that 80 per cent of drugs do not recuperate capitalized R&D costs.[26]

3. The Changing Nature of Innovation in the Biopharma Sector

New treatments produced by the innovative biopharma industry are increasingly biologics rather than small molecule drugs. The transition to biologics has made both drug development and manufacturing more complex and the role of IP even more pervasive. However, much of the common understanding of drug development is based on an older paradigm, so it is worth explaining the differences.

Small-molecule drugs have the longest history of research and manufacture. Although they require significant research and development, these drugs rely on comparatively simple molecules to treat patients, which often makes them easier to manufacture than many other medicines.[27] Aspirin is a classic example of a small molecule drug.[28] Small molecule drugs are produced via artificial synthesis methods.[29] Once a drug is identified in laboratory test tubes for medical use, pharmaceutical companies hire synthetic chemists to develop a “recipe” to produce that drug more efficiently.[30] The result of this approach is that small-molecule drugs are relatively cheaper and more straightforward to manufacture, often allowing anyone who follows the recipe to easily reproduce the drug.

Biologic drugs are large and intricate molecules that are harvested from living microorganisms or produced from other biologic processes.[31] The nature of these drugs helps them treat complex ailments far more effectively than small molecule compounds.[32] While biologics have long existed – insulin is a classic example – they have become more common in recent years, with well-known examples including treatments for autoimmune diseases such as Humira (adalimumab) and Remicade.[33]

One of the most notable differences between small molecule drugs and biologics is in the manufacturing processes. Instead of relying on a manmade recipe to produce medicines, biologic researchers program microorganisms to produce the medicine.[34] While microorganisms are far more capable than humans at producing complex compounds, the setup of those microorganisms is complicated and expensive.[35] There is no standard "recipe" to program a microorganism, and researchers must rely on their accumulated know-how and expertise to develop a manufacturing process for a new drug.[36] Furthermore, the microorganisms used in drug production are carefully selected, cultivated, and guarded by the pharmaceutical companies that make biologic drugs.[37]

These differences in manufacturing between small molecule drugs and biologics are consequential and important. For small molecule drugs, the production process is standard across drugs and very well known, so when small-molecule drug patents expire, any company can easily follow the drug's "recipe" to make cheaper versions of the original therapeutic chemical.[38] Consider how common aspirin is, manufactured by many different producers.

For biologics, as one commentator put it, "the process defines the product."[39] The innovator must design a new manufacturing process with many steps and many inputs, some of which are likely to be entirely novel.

The complexity of developing and manufacturing biologics makes for a more complex and cooperative industry. An innovator may need to use other companies' proprietary techniques to make their treatments; for example, as we discuss later in this report, Pfizer and BioNTech licensed two of the most crucial pieces of technology that makes mRNA vaccines work from other companies. There is also greater specialization involved in complex processes and ingredients, and a drug manufacturer may need to turn to others for ingredients and production tasks. Again, later in the report, we describe the manufacturing processes and global supply chains required to develop a vaccine.

As a result of this complexity, the understanding of IP's role in the biopharma industry based on small molecule drugs is too limited. For small molecule drugs, an initially novel and patented compound is often made with a well-known, widely used process. In contrast, biologics are a novel product made using a novel process. For any given biologic, multiple patents or trade secrets may apply to various necessary ingredients and processes, some of which may be licensed from third parties. Thus, even after the initial patents expire on a biologic, there may be other related technologies that are still protected by the IP rights of the innovator or its partners. As a result, very few companies have the expertise or equipment needed to fully imitate name-brand biologic medicines, and in any event, they must pioneer their own manufacturing processes.[40]

II. The Fundamental Role of Intellectual Property in the Biopharma Industry

IP is essential to the biopharmaceutical industry, as it secures investments and enables cooperation, and thus supports and encourages the innovation that is essential to this industry. Below we describe the forms of IP that are most important to the biopharma industry.

Patents

Patents provide an owner the exclusive right to make, use, or sell an invention. Patents are granted by national governments, whose IP offices examine applications to determine whether they meet the requirements for patentability, which are:

- The invention must be new and not previously invented or discovered by others.
- The invention must be "non-obvious" (a U.S. term) or embody an "inventive step" (the term used elsewhere). What this means is that the invention must be a genuine contribution to the art that would not have occurred to others with ordinary skill in the same field.
- The invention must be capable of industrial application, that is, it must have a practical utility.
- The invention must be fully disclosed, meaning the disclosure proved by the inventor in the patent application must enable others to reproduce the invention.

Patents last twenty years from the filing of an application.

Examples of patented inventions in the biopharma industry include the composition of a particular drug. In addition, particularly for biologics, patented inventions may include various aspects of the process of making the drug.

Trade Secrets

A trade secret is information held by a business that is secret, which means not generally known, and which derives commercial value from being kept secret. Trade secrets are protected from unauthorized use or disclosure, whether by employees or former employees, or by third parties who use improper means to obtain the secret. Improper means include bad conduct such as computer hacking, breaking and entering, assault, or fraud, as well as economic espionage (e.g., electronic eavesdropping). A trade secret owner must use reasonable efforts to keep the information secret; a court will not do for an owner what they do not do themselves.

Trade secrets last for as long as information remains a secret and does not become generally known. Secrecy could theoretically last forever. In reality, secrets tend to be fragile as information leaks, or as others in an industry advance knowledge and progress makes what was once proprietary commonplace.

It is helpful to understand that a trade secret is different from what people typically call a "secret." While a secret would be something only very few people know, trade secrecy expands the circle of trust for confidential information, and many employees and even collaborating businesses might know and use a trade secret. The key is that the circle of protection must remain unbroken – there need to be safeguards such as contracts and security measures to keep the information from becoming generally known.

In this way, trade secret law supports relatively greater openness by facilitating sharing of information within companies and between partners. While trade secrecy does not allow for public disclosure as

patents do – quite the opposite – it does allow for limited sharing of information. Thus, two different companies or institutions might share data to advance the development of a treatment and not lose trade secret protection so long as they observe precautions. Similarly, a biopharma company might engage another company to manufacture a treatment. To do so, they may disclose or license trade secrets covering manufacturing techniques. So long as safeguards such as agreements exist, they remain trade secrets.

Examples of trade secrets in the biopharma industry include information regarding drugs that are still in development and manufacturing techniques and processes.

Regulatory Exclusivities

In the case of biopharmaceuticals, many governments grant certain exclusive rights to drug innovators that are similar to IP rights. These exclusivities vary, but essentially, they set conditions and limits on when a country's drug regulator can approve competitor's application to market drugs that compete against an innovator's product. This regulatory exclusivity period often overlaps with a patent term but differs both in duration and purpose. Governments use regulatory exclusivities to incentivize biopharma companies to accomplish various goals – for example, to market a drug in their country or to test the safety and efficacy of a drug for pediatric use.

In many ways, IP rights work like any other property right by giving the owner secure control of an asset and some freedom to determine how to use it. The owner gets to decide how to develop it, can invest in it with the security of knowing it belongs to them, and can choose whether and how to use it to cooperate with others. Understood in this way, IP rights in biopharma innovations are not simply a right to exclude others from making or selling a product. Rather, they are more like a parcel of commercial real estate, which, in a myriad of ways and with further investment, can be further developed, used, leased, shared, sold, and serves as the basis for collaboration with other businesses and individuals.

Throughout this paper, we highlight three broad roles that IP rights play in the biopharma industry and the development of treatments: (1) Encouraging innovation; (2) Fostering and securing investment; and (3) Enabling cooperation and coordination among private and public sector entities and individuals.

1. Encouraging Innovation

One of the primary purposes of IP is encouraging innovation, and there is a vast body of research on the relationship between the two. Here, we highlight a few key elements.

a. The Incentive to Invent

This is the most widely common, textbook understanding of the reason for the existence of IP rights, particularly patents and trade secrets. The opportunity to reap rewards for new inventions created by exclusive rights encourages people and businesses to work to invent new things.

b. Engaging in Continuous Research and Development

Just as the existence of copyright transforms the making of art, music, and literature from hobbies into careers and businesses, the existence of patents and trade secrets supports people and businesses who are skilled at and constantly engaged in innovation. While the most speculative, "blue sky" research is often done by the public sector, commercial research is not always as strictly goal driven as the incentive to invent story may imply.

For example, Gilead was doing research on coronaviruses years before the COVID-19 pandemic arose. Several years before the pandemic, Gilead "made a commitment … based on the unmet needs it saw in the field of emerging viruses and the belief that the company was in a unique position to make a difference due to Gilead's decades of expertise in antivirals."[41] In 2017, Gilead partnered with the University of North Carolina to establish a public-private partnership to confirm the effectiveness of remdesivir against coronaviruses.[42] As the UNC researcher presciently stated, the partners believed that "Emerging CoV represent a significant and ongoing global health threat."[43]

Because of IP, Gilead had resources to invest in long term Coronavirus research and the confidence that its investment would be protected if that research produced useful results. When a crisis eventually arose, its earlier work was available to deploy thanks to this investment.

Biopharma companies do not do research to create specific, new IP rights. Rather, they do research secure in the knowledge that they can get IP rights to protect useful results. According to one of the industry experts we interviewed, Corey Salsberg of Novartis, "The way drug development works – just like all science – is that we follow the science. There are discoveries all the time that are not expected. The patent system lends itself to filing when those new directions lead to promising inventions … if they meet the criteria for getting a patent. You file, then keep going, and yet you never know which direction is going to be successful and lead to a breakthrough."[44]

c. The Disclosure Function of Patents

Patents disclose how to make an invention and thus serve to bring knowledge to the public and other researchers.[45] Although the effectiveness of patents in achieving disclosure is often critiqued, even critics concede that disclosure works well in the biopharma industry.[46] One reason is that the patents relevant to a particular medicine can be easily identified through such mechanisms as the U.S. FDA's Orange Book.

Researchers and competitors interested in a particular area of treatment can review relevant patents to inform their own work. The availability of this knowledge can spur further innovation in the field.[47]

d. Innovation and Competition through Designing Around

The existence of IP-protected innovations encourages competitors to find their own, alternative solutions to problems. Through this "design around" function, IP encourages innovators to pursue unique technological approaches to address the same disease state. This competition ultimately results in new treatments and more choices for both patients and doctors. Competition also provides more opportunities to find the best solution.[48]

As a U.S. court explained, "Conduct such as … keeping track of a competitor's products and designing new and possibly better or cheaper functional equivalents is the stuff of which competition is made … One of the benefits of a patent system is its so called 'negative incentive' to 'design around' a competitor's products, even when they are patented, thus bringing a steady flow of innovations to the marketplace."[49]

One recent study of the biotech sector noted that trade secrets in the manufacturing of biologics spurred greater innovation and understanding. The study interviewed industry experts, several of whom "reported that trade secrets covering the original product helped to spur innovation and increase

scientific knowledge. Lacking information on the development of the originator biologic, biosimilar companies are often forced to develop their own processes, resulting in improved understanding of the biologic active substance's characteristics and function."[50]

2. Fostering and Securing Investment

As discussed in the previous section, developing new drugs is costly at every step, and the risk of failure is high whether through failure in clinical trials or failure to make a profit. All who invest in biopharma, from venture capitalists to public markets, to those who build a career in the industry, accept these costs and risks.

The one risk that investors find intolerable, if unmitigated, is the risk that competitors might be able to appropriate the invention through copying without restraint. An inability to prevent copying (or removal of protection) deprives those who invest their money and time in developing a drug of their investment. Without IP rights, the threat of appropriation prevents necessary investment in drug development.

As Derrick Rossi, the academic founder of Moderna, observed, "you can be working on the coolest thing, but investors need to know that there is some protection for their investment, plain and simple." IP is "the future prospect that reassures investors."[51]

Paul Higgins, of Johnson & Johnson, put it similarly: "I sometimes explain this reality as follows: 'I have an investment opportunity for you, but it will cost 2.6 billion dollars, take 10-15 years to get off the ground, and has a 90% chance of failure … do you want in?' It is only with the hope that, if I am successful, I will have exclusivity on the back end to make a reasonable return that this becomes a viable investment opportunity."[52]

The necessity of IP to secure investment to develop treatments is demonstrated by the results of the Bayh-Dole Act in the United States. Passed in 1980, this law aimed to reap more public benefits from government funded research by allowing universities, small businesses, and non-profit research institutions, to secure intellectual property rights in government funded research.

Without IP rights, government funded research was failing to return a benefit to the public. Instead, the government asserted patent rights, but the inventions covered never received the investment they needed. Before Bayh-Dole, fewer than 5 per cent of government owned patents were commercialized.[53] In fact, one investigation in the late 1960s found that no drug had ever been developed after the U.S. Government asserted ownership of the relevant patent.[54]

The Bayh-Dole Act changed that underinvestment in the commercialization of government funded research. After Bayh-Dole, universities were able to obtain patents and license them for royalties. Technology transfer offices at universities multiplied and university patenting vastly increased. Most important, universities licensed these patents – 80,000 over the past 25 years.[55] Thousands of start-ups have been launched from universities,[56] and over 200 drugs and vaccines have been developed from university research.[57] Bayh-Dole is largely credited with launching the biotech industry in the United States.

3. Enabling Cooperation and Coordination

People are more willing to share resources and information with others when they have secure rights in what they contribute to the relationship. IP rights create trust, the trust that is necessary to work with strangers. IP also helps collaborators to define how they will work together, who will own the results, and how they will be used.

An IP owner can use IP in a variety of ways to work with others. She can license the right to use a patent or trade secret on an exclusive or non-exclusive basis. The right might be licensed in exchange for payment, or it might be a mutual arrangement where both parties share information. She also might simply sell her IP. Alternately, she may choose not to enforce her patent rights, either selectively or generally.

The transferability of IP also enables the division of labor in the biopharma industry, as an invention or proprietary information is placed into the hands of the entity or person who can next make the best use of it. Thus, patents based on academic research are licensed to a start-up, which then develops practical applications. The start-up might then sell or license the IP resulting from that applied research – e.g., a new patented drug – to a larger company that can afford to take it through clinical trials. Later, that larger company might license trade secrets and patents to enable a contract manufacturer to manufacture the drug. With each "hand off" the invention moves closer to becoming available for use in society.

Throughout the discussion that follows, there are numerous examples of IP facilitating trust and cooperation at every stage in developing COVID-19 treatments. Companies and researchers shared information to develop treatments. Pfizer, Moderna, and Astra Zeneca licensed key technology from academic labs. All the innovators discussed in this paper licensed their trade secrets and patents to manufacturers.

III. Responding to the Crisis in Record Time: An Industrial Drama in Three Acts

When the COVID-19 pandemic arose in 2020, the biopharma industry was able to rise to the occasion by building on previous innovations, innovating new treatments, and manufacturing them at scale, all in record time. This remarkable achievement displayed the strengths of an innovation ecosystem that is enabled by IP.

When the COVID-19 pandemic arose, the biopharma industry was able to rise to the occasion by building on previous innovations, developing new vaccines and treatments, and manufacturing them at scale, all in record time.

Here we tell this story. First, we describe the innovative landscape at the start of the pandemic, which served as the foundation for the biopharma industry's efforts to address the pandemic. Second, we describe how the industry cooperated and invested to develop the innovations that were used to combat COVID-19. Third, we describe how the industry has worked to meet the tremendous challenge of manufacturing new treatments at scale and getting them to patients, within a compressed timeframe never seen before. Our research covers developments before August 1, 2021.

We focus on a number of key technologies that are representative of the story as a whole. Many potential solutions have been tested and deployed, so one account cannot cover them all, but we do attempt broad coverage.

Throughout this story, we explain the essential role of IP in fostering innovation, securing investment, and supporting cooperation. While many other institutions and factors – government investment, great science, manufacturing expertise, and hard work – were essential, IP played a constant and essential role as a key enabler at every stage.

A. Building on Earlier Innovation: Pre-COVID-19 Technologies, Platforms, and Know-how

When the COVID-19 outbreak gained pandemic proportions in March 2020, the global community had no vaccines or treatments available to fight the new virus.[58] Based on historical precedents, medical and public health experts knew that they might expect the development of such complex products to take several years; the fastest vaccine development to date had been that of the MMR vaccine, which took four years.[59]

Fortunately, continuous innovation in the life sciences has built a foundation that allowed the researchers and industry to defeat historical expectations. Scientists and the biopharma industry were able to leverage a range of pre-existing technologies to develop COVID-19 vaccines and treatments in record time. Some of these technologies were older, such as inactivated virus vaccines. Some, such as monoclonal antibodies, are newer and familiar. Some of the most important, though, were less proven and still under development, including the mRNA and viral vector vaccine platforms.

The existence of these technologies was neither a mere lucky accident nor the result of the inevitable march of history. Rather, it was the product of a well-designed system of innovation in which basic research by both companies and publicly funded institutions is translated into life-saving clinical

applications by the private sector. These diverse platforms and other technologies, accompanied by substantial know-how, had been developed through R&D investments and other activities over many years.

The biopharma industry was able to address the urgent challenge thanks to decades of hard work, investment, and risk-taking, all of which was founded on and enabled by intellectual property laws. As explained by one of the interview subjects for this project Matthew Pugmire, Assistant General Counsel, Pfizer Inc., "The core technologies came together at the right time and were available for the COVID-19 response because we had a strong and robust IP system over the years. You could argue that those technologies would never have been developed without the protections afforded by the patent system we have."[60]

What follows is an overview of some of the tools available to the biopharma industry at the start of the pandemic.

1. Vaccine Technology at the Start of the Pandemic

Vaccines are one of the most important tools for fighting any viral outbreak or pandemic. The COVID-19 pandemic struck at a time when vaccine technologies include both long-established solutions and important emerging technology. To date, four types of vaccines have featured prominently in the fight against COVID-19: [61]

- mRNA vaccines;
- Viral vector vaccines;
- Subunit vaccines; and
- Inactivated virus vaccines.

We describe the state of each of these technologies at the start of the pandemic. While the purpose of each is the same, they are developed and manufactured in very different ways. These differences are important to consider when focusing on the applicability of skills, equipment, and infrastructure used for one solution to another.

a. mRNA Vaccines

mRNA-based vaccines were the first COVID-19 vaccines to go into clinical trials and the first in the world to be approved for use.[62] The existence of this technology before the pandemic thus helped to speed up the process of creating a functional COVID-19 vaccine.

Despite the speed with which mRNA vaccines were deployed, they were an overnight success that took decades to achieve. The use of mRNA in vaccines is a novel technology: before the COVID-19 pandemic, none had been fully developed or approved for use.

Previously, multiple companies – such as Pfizer, BioNtech, and Moderna – were attempting to harness the power of mRNA to cure or prevent other diseases, such as cancer and influenza.[63] By early 2020, Pfizer and BioNTech had already been working on an mRNA-based flu vaccine, and were about to initiate clinical trials before choosing, with the onset of the pandemic, to shift their focus to creating a COVID-19 vaccine.[64]

mRNA vaccines essentially harness the body to create proteins that trigger an immune response. Messenger ribonucleic acid, more commonly known as mRNA, is found within each cell in our body and is responsible for making proteins during protein synthesis.[65] mRNA vaccines introduce synthetic mRNA into cells. The synthetic mRNA works like sending instructions to a printer, causing the cell to make proteins that mimic a key subunit of the virus, thus triggering an immune response. The body then recognizes these proteins as foreign and mounts an immune response in which "helper T cells" and "B cells" generate antibodies, and "killer T cells" learn to seek out and destroy the virus' proteins, and thus the virus.[66]

There are several advantages to using mRNA technology in vaccines. One of these is the ease with which new mRNA vaccines can be developed; if one knows the specific protein that is needed to trigger the desired immune response, one can manipulate mRNA molecules to instruct the body to make that protein. In fact, it is theoretically possible to create a library of vaccines or drugs using this technique.[67] Other advantages of this approach include the fact that mRNA is easy to grow – making it less time consuming, simpler to mass produce, and potentially cheaper than other methods – and the fact that, since they can activate both B cells and killer T cells, mRNA vaccines produce a strong immune response.[68]

One disadvantage of using mRNA vaccines has been their novelty. Before the pandemic, they had never been produced at scale, so a new manufacturing process and supply chain needed to be created, which required further innovation. This work required the sophisticated capabilities and cooperation of many companies, several of which are normally competitors. We address this part of the story later in the paper.

Although the possibility of using mRNA in personalized medicine or vaccines was speculated about for decades, making the idea a reality required great persistence. mRNA was first discovered by two French scientists in 1961. The first reportedly successful use of in vitro transcribed (IVT) mRNA in animals was published in 1990. However, early efforts to develop mRNA technology were not followed by significant investment in its potential therapeutic uses.[69]

Adapting this technology to a clinical application posed two challenges.[70] First, mRNA is fragile and without protection would disintegrate before reaching its destination. Second, when the technique was first tried, the synthetic mRNA itself provoked a strong immune response, which prevented it from causing the body to produce the desired proteins.

Solving these problems required innovative basic science complemented by a large investment of funding and resources by start-ups and larger biopharma companies, in order to eventually deliver the mRNA vaccines. The development of this technology highlights how IP supports the investment, cooperation, and licensing needed to bring a new technology to market.

Researchers solved the problem of the fragility of mRNA by surrounding it with a lipid nanoparticle. One version of this technology is covered by patents owned by Arbutus Biopharmaceuticals, which are licensed to BioNTech (ultimately through a sublicensing arrangement).[71] Meanwhile, Moderna has its own version of lipid nanoparticles, which it treats as a trade secret.[72] (There is an ongoing dispute regarding this technology with Arbutus, which may need to be resolved later).[73] Merck KGaA, based in Darmstadt, Germany, was also engaged in developing a lipid nanoparticle at the start of the pandemic, an R&D project that was accelerated given the urgency of the situation.

The immune reaction problem was resolved in 2005 by scientist Katalin Karikó and her collaborator

Drew Weissman by creating a kind of "hybrid mRNA" that could evade the body's defences and stealthily enter its cells.[74] This breakthrough made feasible the delivery of mRNA-based instructions to cells and opened the door to clinical use of mRNA-based vaccines. Karikó and Weissman documented the breakthrough in scientific papers.[75]

These discoveries were an essential first step, but a long road lay ahead. Karikó even had trouble filing for a patent. While attempting to file for a patent at the University of Pennsylvania, she faced a tech transfer officer who was initially reluctant to grant a patent, and who reportedly only did so following a comment about potential uses of mRNA to grow hair.[76] This patent, which was filed by the University of Pennsylvania, has formed the basis for today's mRNA-based COVID-19 vaccines.[77] The University of Pennsylvania licensed that patent to a company known as mRNA RiboTherapeutics; this firm then sublicensed the patents to another company – Cell Script – which, in turn, sublicensed it to both Moderna and BioNTech. [78]

After academic researchers found ways to overcome the problems of mRNA fragility and immune reactions, it took many more years of applied research to develop clinical applications. There was no instant success, as evidenced by the fifteen years between their discovery and the development of the first mRNA vaccines (with the pandemic significantly speeding their development and adoption). It took further academic research, private investment, and the work of start-ups to develop clinical applications derived from the basic research.

One of the companies that built on the research of Karikó, Weissman, and others was Moderna. It started when Derrick Rossi, then a postdoctoral fellow at Stanford University, read Karikó and Weissman's 2005 paper and recognized the potential for mRNA-based therapies. As Rossi would later remark, "It's fun to think about how simply reading a cool paper on pluripotent stem cell science could lead to all of this."[79] His initial insight was that the technique might be used to create embryonic stem cells without using human embryos. When he became an assistant professor at Harvard with his own lab in 2007, he decided to pursue his insight. Rossi and his team worked to apply Karikó and Weissman's research. In 2009, they succeeded not only in creating stem cells, but in developing a technology that could program human cells to produce any protein.[80]

Moving Rossi's research from the lab and toward clinical applications required private investment. In 2010, Rossi presented his work to Robert Langer, a serial entrepreneur at MIT, and Noubar Afeyan, CEO of VC firm Flagship Pioneering. They immediately saw the potential of the work and supported the launch of Moderna that year. By the time it went public in 2018, it had raised over $2 billion in investments and partnership funding,[81] and another $600 million in a record-setting IPO. As impressive as these large numbers are, they represent only investment in and spending on the development of a technology, rather than a success story. By the time of the pandemic, Moderna had not yet launched a product or turned a profit.

BioNTech's story follows a similar trajectory. By early 2020, BioNTech had been working with mRNA for 25 years, in pursuit of immunology treatments for cancer and a new flu vaccine.[82] The German start-up had raised hundreds of millions and put in over a decade of work to develop its mRNA technology before the COVID-19 pandemic. But it too had yet to launch a product or turn a profit. The mRNA product that came closest to being

The Pfizer/BioNTech partnership to develop a COVID-19 vaccine was preceded by an earlier 2018 agreement to make an mRNA-based flu vaccine.

approved and available before the pandemic was the flu vaccine under development by Pfizer and BioNTech, and the companies' now-famous partnership on a COVID-19 vaccine was preceded[83] by an earlier 2018 agreement to make this mRNA-based flu vaccine.[84]

By the time the pandemic emerged, both Moderna and BioNTech had received billions in investment and done years of work to build the foundation of a technology that was essential to fighting COVID-19. Neither had quite yet delivered on the promise of mRNA vaccines, so the successful use of this innovative technology to create a COVID-19 vaccine was considered a breakthrough. With the technology now proven, it is expected to lead to more mRNA products becoming available in the future.[85]

b. Viral Vector Vaccines

Viral vector vaccines use a virus that is different from the pathogen – a "safe" virus, the vector – to deliver specific parts (proteins) of the target pathogen that can provoke an immune response from the body. Viral vector vaccines are a well-established technology, as scientists have been creating viral vectors since the 1970s.[86] One of the crucial discoveries that led to the use of viral vectors, specifically adenoviruses, was by Phillip Sharp and Richard Roberts, who found that rearranging RNA codes hinged on a single gene, making possible the chemical manipulation of adenovirus DNA.[87] This discovery won them the Nobel Prize in Physiology or Medicine in 1993. Prior to the COVID-19 pandemic, the only approved adenovirus vector vaccine was for Ebola, developed by Johnson & Johnson.

Viral vector technology works by inserting the genetic code for the target into the modified vector, or "safe" virus.[88] The viral vector provides a delivery system for the genetic code of the target virus. Most commonly in the COVID field, an adenovirus vector is used, after being modified so that it can enter the cells but is unable to replicate. Once the vaccine is injected into the arm, the viral vector (adenovirus) collides with the body's cells and attaches to the protein found on the cell's surface. The viral vector then enters the cell and travels to its nucleus, where mRNA can be generated based on the viral DNA. When the mRNA of the body's cell leaves to undergo protein synthesis, it contains the virus's protein sequence. In this way the viruses' proteins are created within the body, which recognises them as foreign and mounts[89] an immune response.[90]

There are several advantages to the viral vector technique. One is these vaccines' ability to be stored for long periods of time at around 2-8°C, thanks to the tough protein coat that surrounds the adenovirus.[91] This high thermostability makes them comparatively easy to transport and, thus, more accessible than many other vaccines. Other advantages include the possibility for easy application via the respiratory or systemic mucosal routes, and the possibility for adenoviruses to be grown at high titers, or high concentrations of antibodies in blood.[92]

One of many technologies that contributed to today's COVID-19 vaccines came from a patented technology that was initially unrelated to COVID-19 research. Adenovirus vaccines can be traced back to work on gene therapy methods in the 1990's. However, a more recent collaboration relating to viral fusion proteins furthered the development of the COVID-19 vaccines. In 2009, Jason McLellan, a structural virologist at the University of Texas, and Barney Graham, Deputy Director of the U.S. National Institute of Allergy and Infectious Diseases Vaccine Research Centre, formed a partnership which led to a publication in 2013 that described modifying the so-called "F-protein" in the RSV virus to prevent the protein from changing shape. Subsequently, McLellan and his post-doctoral fellow, Nianshuang Wang, found that, by adding prolines to the amino acid sequence of the spike protein in the MERS

coronavirus they could stabilize the spike protein. They then filed for a patent in 2017, calling their invention the "2P mutation." Their work was published and became part of the development story of the COVID-19 vaccine candidates.

The McLellan-Graham example highlights and important feature of the modern patent system: it encourages the disclosure of innovative research and development of potential clinical applications of basic research. Patent protection gives scientists the freedom to publish in academic journals without undermining the capacity of their institution to protect the IP. It also promotes the dissemination of research itself, since disclosing the details of an invention is a requirement for the filing of a patent. Patent filings contribute to information-sharing among those at the cutting edge of their fields.

c. Subunit Vaccines

Subunit vaccines function by inserting into the body only certain parts, either proteins or sugars, of the virus that can provoke an immune response.[93] Technologies for subunit vaccines – in particular, those using protein subunits – have provided a valuable foundation for the design of COVID-19 vaccines. Once the body has learned to associate the subunit in the vaccine with danger, it is able to attack and destroy a virus that features those subunits.[94]

This kind of vaccine technology, which is essentially a more streamlined version of the whole-virus approach, has been around since 1981. While working at that time for Merck Research Laboratories on the development of a vaccine for hepatitis B, Maurice R. Hilleman discovered that a vaccine that contained only protein subunits, rather than the whole virus particle, could "train" the body to fight an invading pathogen just as if the body had been exposed to the pathogen itself.[95]

This way of formulating a vaccine has a number of advantages. First, because such vaccines function merely by injecting pre-formulated protein subunits into the body, side effects are either few or totally absent.[96] This gives them an edge over a more recent technology, notably, mRNA vaccines, which have been known to cause mild to moderate adverse effects related to the process of compelling the body to create these antigens itself.[97] Furthermore, the stability of protein subunit antigens allows them to remain at mere refrigerator temperatures for extended periods of time without degrading, giving them an additional advantage over their mRNA competitors, which require extremely low temperatures in order to remain viable.[98]

d. Inactivated Virus Vaccines

Inactivated virus vaccines use a "deactivated" version of the target pathogen to provoke an immune response from the body without causing a full-blown infection. Inactivated virus vaccines are an established and well-tested technology. They have existed since the late eighteenth century, when Edward Jenner first used the method to create a vaccine that largely eradicated smallpox.[99]

The process of creating these inactivated viruses begins with growing them, a process that commonly uses Monkey Kidney cells known as "vero cells."[100] Once grown, the viruses are deactivated with the use of chemicals, heat, or radiation.[101] These deactivated viruses are then inserted into the body, where they are recognized as foreign thus prompting the immune system to generate the specific antibodies that are needed.[102]

In addition to their longstanding use and general reliability, inactivated virus vaccines have certain advantages. First, the fact that the whole virus is present in these vaccines, rather than just a section, means that the immune response initiated by these vaccines targets not only the spike proteins on the virus, but also the matrix, envelope, and nucleoprotein.[103] Furthermore, inactivated virus vaccines do not need to be frozen, which makes their transportation and storage easier and, thus, increases their accessibility in low to middle-income countries.[104] The virus being inactivated also renders these vaccines safe for use in individuals who suffer from immunosuppressive diseases, such as HIV.[105]

2. Therapeutic Technology at the Start of the Pandemic

In addition to vaccine science and technology, therapeutics technologies were quite advanced by the start of the pandemic. IP-driven investment in the biotech industry had established technologies in the areas of antiviral medication, monoclonal antibody treatments, and Janus Kinase Inhibitors, all of which have been used in the fight against COVID-19.

a. Anti-viral treatments

One type of therapeutic used during the pandemic is antiviral medications, in particular "broad-spectrum antivirals, such as Gilead Sciences' remdesivir.[106] Broad spectrum antivirals are meant to do for viruses what antibiotics do for bacteria: namely, to function effectively against a broad range of viruses.[107]

In the case of remdesivir, the antiviral functions by blocking the virus' ability to replicate, rather than attacking the virus directly in order to destroy it.[108] It thus slows down the virus' invasion of the body and gives both the immune system and other medications more time to fight the infection.[109]

Collaboration played a defining role in the history of remdesivir. Starting in 2014, Gilead Sciences worked with researchers from the CDC, NIH, and U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) to test remdesivir during the African Ebola pandemic, with the goal of creating an emergency treatment for potential global pandemic level viruses.[110] Although it was during this partnership that Gilead discovered the potential of remdesivir to act as a broad-spectrum antiviral, trials on Ebola patients by Gilead, the CDC, and USAMRIID on Ebola patients in West Africa ultimately revealed that it was not as effective as other Ebola treatments. This led Gilead to stop its remdesivir Ebola research in 2018.[111]

From 2014 to 2018, Gilead also worked with the University of North Carolina (UNC), Vanderbilt University, and a larger consortium of American universities – headed by the University of Alabama at Birmingham (UAB) – to test remdesivir's therapeutic effects against various viruses, including SARS and MERS.[112] This research, which was funded through grants from the National Institute of Health (NIH), yielded promising results and data for both SARS and MERS. However, due to the relative rarity of the viruses and qualified test subjects, remdesivir never advanced into full clinical trials for these viruses.[113]

b. Monoclonal Antibody Treatments

Monoclonal antibody treatments are another pre-existing technology that was harnessed to fight COVID-19. Monoclonal antibodies are synthetic molecules that are made to play the role of substitute antibodies in order to restore, reinforce, or imitate the immune system's own attack on invading

pathogens.[114] They can work in several ways, and there are COVID-relevant treatments that adopt the different approaches. Sotrovimab, for example is made to thwart a virus' attachment and entry into cells, thereby neutralizing the virus. The same is true of the two two-drug cocktails Bamlamivab+Etesevimab and Casirivimab+Imdevimab.[115] Regdanvimab, by contrast, is fashioned to reduce a virus' ability to enter cells in a different way, by attaching to the spike protein of the SARS-Co-V2 virus.[116]

c. Janus Kinase Inhibitors

Janus Kinase inhibitors (JAKs), which have traditionally been used to treat rheumatoid arthritis and psoriatic arthritis, are another example.[117] JAKs are intracellular enzymes that can influence the cellular process known as hematopoiesis, as well as immune cell function.[118] One JAK product, Olumiant, from Eli Lilly and Company, is approved in the United States as a treatment for rheumatoid arthritis. Based on recent scientific data, it has now been authorized for emergency use in combination with remdesivir to treat suspected or confirmed cases of COVID-19.[119]

d. Human Plasma

Human blood-plasma based treatments, which have existed in some form since the 1890s, have also been used to treat COVID-19.[120] So-called "plasma protein" therapies, which function by replacing missing or deficient proteins in blood plasma, are used to treat a number of well-defined medical conditions.[121] This established technology has been used in the form of COVID-19 convalescent plasma, which is blood plasma taken from individuals whose blood already contains antibodies against SARS-CoV-2.[122] Plasma was granted emergency use authorization in the United States[123] for the treatment of hospitalized COVID-19 patients who are still early in the course of the disease.[124]

3. Summary: Technologies available as of January 2020

The technologies underlying the therapies that eventually were developed to combat COVID-19 existed when the pandemic arose. Some were quite old, such as inactivated virus vaccines, which had been used against smallpox, polio, and many other diseases.[125] Viral vector vaccines were also already in limited use. Johnson & Johnson, which used this technique in its COVID-19 vaccine, had previously produced an Ebola vaccine, which was granted marketing approval by the European Medicines Agency on July 1, 2020.[126] In contrast, the mRNA technology used in the Pfizer/BioNTech and Moderna COVID-19 vaccines was not yet on the market but had been undergoing serious research and development for many years. The therapeutics discussed above similarly were based on existing technology, or in some cases had already been developed, but for other uses.

What happened next was that companies built on this legacy of innovation.

B. Accelerated Innovation: The Development of COVID-19 Treatments

The story of innovation for COVID-19 is one of widespread collaboration, big investments, and risk-taking.

While earlier innovation created a strong foundation to develop COVID-19 treatments, it was only a start. The biopharma industry faced a tremendous challenge to innovate quickly to meet the challenge of COVID-19. It met and continues to meet that challenge. The development of COVID-19 treatments is a story of great science,

execution, and hard work – but it is also a story of widespread collaboration, big investments, and risk-taking.

Much of the biopharma industry quickly shifted away from ordinary priorities, including promising work on other medical conditions, to focus on developing and delivering COVID-19 treatments. In doing so, they made large investments and took big risks. In this section, we describe the large investments, some of which succeeded famously but many of which ultimately did not.

As the first part of this paper explains, the biopharma industry embraces such risks and failures as they are intrinsic to developing new treatments. However, the one risk that would undermine everything is the risk of appropriation of otherwise successful work. While the biopharma industry responded to an urgent need, businesses needed the security of IP rights to be able to justify this use of resources to their stakeholders – their employees and the many individuals and institutions that invest in these companies.

One of our interview subjects described the unique use of resources and the need for the security provided by IP like this: "This was not business as usual. This was really an unprecedented situation requiring unusual efforts. Success was certainly dependent on our ability to protect the innovations that were put on the table."[127]

While investment mattered, cooperation was also key. As we observed earlier, as the biopharma industry has shifted more focus toward making biologics, both the development and manufacturing of treatments has become cooperative.

In this unprecedented effort, collaboration was essential as innovators quickly established new partnerships, pooling their knowledge and technology. IP protection made it possible for even competitors to work together by providing security for R&D investments and clarity as to each party's contributions. IP was often the precondition to people sitting down at the table to begin collaboration. As Dr. Kathrin Koerner, Head of Patents & Scientific Services at Merck KGaA, explained, "IP enabled the early discussions for COVID-19 collaborations and exchanges. Without it, things could not have been made available to other parties. Because we had already filed for the relevant patents, we were able to provide information to partners about things we had under development."[128]

The full IP story of the new vaccines, treatments, and diagnostics is not yet known. As Arno Hartmann, head of Patents, Pharmaceuticals, Merck KGaA, observed, "the earliest patent applications were filed in December 2019 in relation to COVID-19 solutions. You can easily do the math. It takes 18 months for publication to occur, and these 18 months – even if you count from February 2020 – will end in August. So none of us really knows for sure what others have filed. Of course, the pre-existing IP on mRNA or other pieces of the solution are known, but these elements alone do not enable anyone to come up with a COVID-19 vaccine program."[129]

Nevertheless, the innovators involved in the COVID-19 response said that patents and trade secrets protection for their background IP made it possible for them to share openly within innovation collaborations. They knew they could work with competitors, in the service of addressing the pandemic, while preserving their valuable business assets.

Here we tell the story of how the biopharma industry invested and cooperated to develop COVID-19

treatments in record time.

1. Developing COVID-19 Vaccines

The task of creating COVID-19 vaccines and treatments from these technologies was an urgent challenge of historic proportions. The technologies that existed before the outbreak of the COVID-19 pandemic were crucial in enabling pharmaceutical companies, universities, and governments to respond to the threat with the speed that they have.

The following stories about the creation of COVID-19 vaccines and treatments highlight the importance of collaboration and investments, secured by IP rights, in rapidly generating new bio-pharmaceutical technologies during a global health crisis.

a. The mRNA Vaccines: Pfizer/BioNTech and Moderna

After many years and billions of dollars of investment, mRNA vaccines were still only a promising technology that had not yet been fully tested and developed into a treatment. Moderna and the Pfizer/BioNTech partnership were able to take these technologies across the finish line when they were most needed.

The mRNA vaccines were the first two COVID-19 vaccines to be approved. The Pfizer/BioNTech vaccine was the first, approved for emergency use in the UK on December 2, 2020, and in the United States on December 11.[130] The Moderna vaccine was given authorization not long after: the FDA approved it for emergency use on December 18, 2020.[131] Importantly, both vaccines were produced in record-breaking time. Before these two COVID-19 vaccines, the fastest vaccine development had been that of the MMR vaccine, which took four years. [132]

BioNTech leveraged its existing relationship with Pfizer to help speed up development of its vaccine. Having worked together since 2018 on a potential mRNA-based influenza vaccine,[133] these two companies had a high level of trust. They started working together before they had a contract, relying on their earlier relationship and trade secret protection to secure their investments.[134] Under their March 17, 2020 agreement, BioNTech agreed to disclose all of its mRNA research to Pfizer.[135] In return, Pfizer contributed its manufacturing and regulatory expertise to get the vaccine approved and develop a manufacturing process capable of producing billions of doses.[136]

The BioNTech-Pfizer relationship was only possible with IP protection. As Pfizer's Pugmire observed of the relationship between the two companies, "IP protection was critical … I can't speak for BioNTech, but I cannot imagine they would be comfortable sharing their proprietary mRNA technology with a company like Pfizer without having IP protection. This is their core technology and the result of all the investments they have made over several years."[137]

Moreover, despite Pfizer being the party to seek U.S. regulatory approval, the agreement specifies that BioNTech owns the new IP developed in relation to their vaccine. Such IP rights will naturally enhance BioNTech's pre-existing work, as the company has been working on mRNA technology regarding cancer

vaccines.[138]

Moderna had been working on a vaccine for Middle Eastern Respiratory Syndrome (MERS) in conjunction with the National Institute of Health's (NIH) National Institute of Allergy and Infectious Diseases prior to the pandemic and, as a result, was able to quickly pivot this collaboration towards developing a COVID-19 vaccine. The speed at which these two partners worked was unprecedented. The National Institute of Health's scientists were able to design the spike protein molecule from SARS-CoV-2 in a single weekend in January 2020, and Moderna succeeded in producing a clinical batch of its vaccine – mRNA-1273 – within just 25 days. [139]

The company accepted support from the U.S. Government's Operation Warp Speed (OWS), receiving $1 billion for design and testing, and a further commitment of $1.5 billion in exchange for delivery of 100 million vaccine doses.[140]

Moderna has publicly committed that it would not enforce its COVID-19 related patents against those making vaccines during the pandemic and would also be willing to license its intellectual property during the post-pandemic period.[141] While the non-enforcement commitment surprised some, others speculated that it could help promote the greater use of mRNA vaccine technology for other purposes. Not enforcing its patents during the pandemic may contribute to accelerating the transition towards increased mRNA capacity over the long term and in new markets.[142] In any event, no entity appears to have taken advantage of Moderna's non-enforcement commitment to make a competing vaccine. This is likely owing to the fact that myriad factors are necessary to develop and commercialize a new vaccine including other third-party licenses to mRNA technology, trained scientists, appropriate facilities, access to inputs and equipment, and ongoing technology partnerships, financial investments – and time.

b. The Viral Vector Vaccines: Johnson & Johnson, Oxford/ AstraZeneca, Convidecia, and Sputnik V

Four innovators harnessed viral vector technology: Johnson & Johnson (with the Beth Israel Deaconess Medical Centre), AstraZeneca (in collaboration with Oxford University), CanSino Biologics, and the Gamaleya Research Institute of Epidemiology and Microbiology (the creators of Sputnik V). All their vaccines use different versions of the adenovirus. Johnson & Johnson uses the adenovirus 26 (Ad26) vector; for Sputnik V, Ad26 is used for the first dose and a different version of the virus (Ad5) is used for the second dose 21 days later; Convidecia is Ad5-based; and for AstraZeneca, a chimpanzee adenovirus known as ChAdOx1 is used.[143]

The technology used by Johnson & Johnson was based on the company's work in the adenoviral vector field during the past 15 years. To speed up the identification of COVID-19 vaccine candidates, a collaboration was built on a previous partnership that the company had with Dan Barouch, an immunologist and virologist from Beth Israel Deaconess Medical Centre (BIDMC).[144] Having already worked together with this same technology on other vaccines, such as HIV, Zika, and tuberculosis, the parties were able to quickly come to an agreement to create a COVID-19 vaccine; the agreement was signed on January 31, 2020.[145]

The collaboration between the Oxford University Jenner Institute and AstraZeneca is another example of technology transfer. The Jenner Institute had already been working with the chimpanzee adenovirus

vector in relation to other vaccines, and it was able to license this technology to AstraZeneca to enable the development of a COVID-19 vaccine.[146] As was the case with the Johnson & Johnson collaboration described above, IP rights made this hand-off work smoothly by defining and securing the rights each party brought to the relationship.

Development was also helped along by government funding, which took some of the risk out of development. The Biomedical Advanced Research and Development Authority (BARDA) – which is part of the Office of the Assistant Secretary for Preparedness and Response (ASPR) at the U.S. Department of Health and Human Services – had a cost share agreement with Johnson & Johnson in which each party contributed funds towards the research and development of a vaccine.[147] Like many of its peers, the company took on additional risk by upgrading manufacturing facilities and starting to produce its vaccine candidate at its own cost, before clinical trials were completed or approval had been granted. If the clinical testing data demonstrated that its vaccine candidate was safe and effective, Johnson & Johnson offered the U.S. Government a not-for-profit price that would not exceed $10 per dose during the pandemic for a certain quantity of its domestic output..[148] AstraZeneca also received an investment from BARDA to support development of its vaccine, and it agreed a purchase commitment, but the company also took a risk in beginning production before proof of efficacy and FDA authorization.[149]

c. The Subunit Vaccine: Novavax

When the pandemic struck, the company Novavax had been working on vaccines for years but had never successfully brought one to market.[150] In January 2021, Novavax announced that it had created a COVID-19 vaccine called NVX-CoV2373.[151] This vaccine relies on subunit protein technology, that is, it uses the spike protein found on SARS-CoV-2 as an antigen, tricking the body's immune system into believing that the whole virus is present and triggering an immune response.[152]

Partnerships, IP licenses, and technology transfer have played an important role in making the Novavax vaccine a reality. On August 7, 2020, Novavax formed a development partnership with the Japanese pharmaceutical firm Takeda for the development, production, and distribution of its vaccine in Japan. As part of this partnership, Novavax has agreed to license its IP and transfer technology related to COVID-19 to Takeda.[153] Novavax has similarly partnered with the Serum Institute of India. The parties entered into an agreement on July 30, 2020, whereby Novavax agreed to provide know-how and to license patents, and the Serum Institute agreed to assist with development and regulatory approval, as well as to ramp up manufacturing.[154]

Although Novavax is still working to achieve regulatory approval, its vaccine candidate appears to be highly effective at 89.7 per cent efficacy.[155] Its vaccine also enjoys advantages related to the use of protein subunit technology, for instance the vaccine's ability to remain stable for months at standard refrigerator temperatures, and a relative lack of side effects.[156] This may make it easier and more cost-effective to distribute in remote locations than vaccines requiring lower temperatures.[157] At present, the Phase 3 clinical trials for the Novavax vaccine are coming to an end, and the company is preparing to scale up manufacturing and distribution capacity to deliver the vaccines to patients.[158]

Novavax and its partners have also received funding from governments and NGOs to develop the vaccine. In June 2020, the U.S. Department of Defense supported Novavax with a $70 million for the manufacture of its vaccine for clinical trials, and, in July 2020, Operation Warp Speed granted the company $1.6 billion for last-stage clinical trials. In addition, Novavax formed a partnership with the Coalition for Epidemic Preparedness (CEPI) in May 2020, under which CEPI gave Novavax $380 million

for the vaccine's clinical development.[159] And Takeda's development work was funded in part by the Japanese government.[160]
Novavax also had one partnership that was unsuccessful, highlighting the fact that collaboration can carry risk. Although Novavax partnered with Emergent BioSolutions to start vaccine testing, it pulled out when it became known that Emergent was having production problems with other vaccine manufacturers.[161]

d. The Inactivated Virus Vaccines: CoronaVac and Covaxin

The majority of the COVID-19 vaccines that used the most traditional technologies available – the "whole virus" methods – have exhibited comparatively modest success. CoronaVac and Covaxin, both inactivated virus vaccines, have shown lower efficacy than much of their competition, with Covaxin at 78 per cent and CoronaVac at 51 per cent.[162] Furthermore, both have been subject to controversy. Clinical trials of CoronaVac in Brazil were temporarily suspended following the death of one participant; they were resumed when the Brazilian health authorities declared that the death was unrelated to the vaccine.[163] Covaxin, meanwhile, was granted emergency approval from the Indian Central Drugs and Standard Control Organization while Phase 3 trials were still underway, causing Indian healthcare professionals to express significant concern.[164]

2. Prepositioned and New Therapeutics to Fight COVID-19

Researchers and the biopharma industry have also worked to identify and develop therapeutics to treat COVID-19 symptoms and combat the virus. As with other parts of the battle against COVID-19, investment and collaboration supported by IP was important to these efforts. Like vaccines, many were developed and delivered to patients through collaborative efforts, underpinned by IP management and sharing.

Initially, a great deal of testing of existing compounds occurred to determine if they might help COVID-19 patients. As Novartis's Salsberg explained, "With COVID-19 we got not only new treatments. Companies and universities around the world looked at what was already on the market, in the pipeline, and in various stages of development in their labs, that might work for COVID. We saw a lot of investments of time and money to get things moving and tested at record pace. IP had not only created the starting points for this research. It also supported efforts to share information, assets, and technology, to let people into your laboratories, share compound libraries, tools and trade secrets, and to collaborate to figure out how to manage the outcomes."[165]

As a result of these efforts, a number of therapeutics were given Emergency Use Authorization (EUA) during the COVID-19 pandemic, in particular by the U.S. FDA.[166] They have, however, displayed mixed results, and some have proven more effective than others, a fact which underscores the need for the diversity of approaches that the IP-supported, competition-driven market facilitates. Applying an existing product for use against a novel disease is not as simple as it might appear at first glance. Even if a drug has been tested and approved for other uses, redirecting it to COVID-19 treatment would require significant investments in additional testing and regulatory approval.

Meanwhile, other efforts have been underway to develop new treatments.

One of the therapeutics most widely used to treat COVID-19 has been remdesivir, which is made by Gilead Sciences. Remdesivir had gone through extensive development and testing for eight years

before the pandemic and had already shown promise against coronaviruses. Nevertheless, it required additional testing before it could be authorized for COVID-19 patients. It was granted Emergency Use Authorization to treat COVID-19 after a 1063-patient trial in February 2020 demonstrated that patients who received the drug recovered five days more quickly than those who did not.[167] After three more clinical trials, the FDA approved it in October 2020 to treat COVID-19 in patients 12 and over.

Sotrovimab, which has shown positive results throughout its trial process, achieving "a 79 per cent reduction in hospitalisation for more than 24 hours or death due to any cause by day 29 compared to placebo."[168] The data gathered on Sotrovimab has been positive enough for it to have been granted Emergency Use Authorization from the FDA.[169]

The combination monoclonal antibody treatment Bamlanivimab+Etesevimab, which was created by Eli Lilly and Company, has also shown positive results. A Phase 3 trial concluded that the use of this drug combination reduced the hospitalizations or deaths from COVID-19 by 87 per cent, and it was awarded Emergency Use Authorization during the pandemic.[170]

The combination monoclonal antibody therapy, Casirivima+Imdevimab, has been approved for use in hospitals for COVID-19, for intravenous infusion, or, if needed, subcutaneous injection.[171] The Phase 3 trials showed the combination resulted in a faster recovery from symptoms and reduction in patients' hospitalization or death.[172]

Reganvimab, another monoclonal antibody, has been approved for use against COVID-19 in the EU[173] after a study indicating that it lowers the rate of hospitalization.[174]

Baricitinib (Olumiant), also created by Eli Lilly and Company, is a Janus Kinase Inhibitor that is used in combination with remdesivir for hospitalized adults and paediatric patients with COVID-19.[175] The results from trials undertaken with this drug combination, while not conclusive, indicate that it could be effective for mild to moderate COVID-19 in adults and children older than two who need supplemental oxygen, invasive mechanical ventilation, or ECMO.[176]

Collaboration, IP licensing and technology transfer have aided these efforts. For example, the treatment Bamlanivimab+Etesevimab is the result of several collaborations among research institutions and biopharma companies.[177] Researchers at AbCellera Biologics and at the Vaccine Research Center of the National Institute of Allergy and Infectious Diseases initially discovered Bamlanivimab, and Eli Lilly developed it. Similarly, Eli Lilly collaborated with the Institute of Microbiology of the Chinese Academy of Sciences and Junshi Biosciences to develop Etesevimab.

AstraZeneca similarly partnered with the Vanderbilt University Medical Centre, which has been working to understand pathogenic viruses and how to prevent their spread. During the pandemic, Vanderbilt licensed six antibodies to AstraZeneca, which enabled them to advance into Phase 3 clinical trials with COVID-19 long-acting antibodies.[178] The agreement was concluded in just ten days, which reportedly set a new speed record for reaching a therapeutic license agreement.[179]

Plasma has been used for many years, and it was therefore tried as a potential treatment. Chinese researchers were the first to claim, on April 28, 2020, that the ten patients who had received the plasma treatment were nearly fully recovered within 3 days of receiving it.[180] This extremely positive and successful result led to testing and, subsequently to petitions filed with the FDA for approval of plasma for Emergency Use Authorization, which was granted on August 23, 2020.[181] However, when data was gathered from its use in other countries, it was found that plasma was not as successful at

treating COVID-19 as previously thought.[182] This led to further trials and tests being carried out on the use of plasma, and the National Institute of Health announced on March 2, 2021, that it made no "significant difference" to a patient's recovery.[183] This discovery led to the FDA reducing the scope of its Emergency Use Approval and limiting its use to early-stage infections or to patients in hospitals who struggle to generate a sufficient antibody response.[184]

3. Risk and Setbacks in Developing COVID-19 Vaccines and Therapeutics

Due to the uncertain and risky nature of innovation in the pharmaceutical industry, a substantial return on investment is crucial to ensure continued up-and-coming innovation. At every stage, the development and manufacturing of a vaccine or therapeutic involves both high risks and high investments. Most research efforts in the pharmaceutical industry, ultimately fail to yield a commercially viable product. IP gives the assurance that those few successful research endeavors will have some exclusivity, which may eventually be used to secure a return on investment.

A research program can take years before showing any promise of discovery, which explains why risks are more easily taken by the private sector than by governments. To develop any kind of promising research into a successful treatment, long and extensive clinical trials need to take place. However, there is still no certainty that the treatment will be effective or safe enough to ever be authorized.

Even if a treatment can get the necessary approval to be authorized on the market, manufacturing complex biological products requires a lot of expertise. This expertise is acquired though investments which can become ultimately profitable through the licensing of trade secrets and know-how.

The accounts in this section and throughout this paper describe several big, risky bets that paid off for both innovators and society. Biopharma companies diverted people and resources to new R&D projects. Successful vaccine makers spent vast sums to develop new manufacturing processes, upgrade facilities, and manufacture doses before testing and approval. Governments reduced risks with subsidies and with promises to purchase successfully developed vaccines.

It paid off in the end – but not for everyone.

Costly failure is common in vaccine development, and COVID-19 vaccine development has been no exception. For example, Merck & Co, the world's second-largest vaccine maker, and German biotech CureVac, both failed in creating a COVID-19 vaccine. Merck & Co's two potential vaccines, known as V590 and V591, were abandoned just after Phase 1 clinical trials when it was revealed that the protection given by the vaccine was weaker than the natural protection of contracting the virus. Merck took a charge against 2020 fourth quarter earnings for the failure.

CureVac used the same mRNA-based technology used by Moderna and Pfizer/BioNTech but without success. In a surprising final-stage trial, the vaccine only reported a 47 per cent effectiveness.[185] This fell under the 50 per cent limit set by the WHO.[186] Whether the problem was due to variants, a false mRNA sequence, or higher storage temperatures which could have broken down the mRNA in the vial, this confirms how much of a risk creating a vaccine can be, as it can go wrong in any of the different stages of its development, testing, and commercialization.

In addition to vaccines, several therapeutics – which were seen by many as a first line of defence in the pre-vaccine era – have ultimately proven ineffective against COVID-19. As with the vaccines, testing

these technologies for effectiveness against COVID-19 still required substantial investments of time and resources, some of which was diverted from other R&D projects.
As successful as the COVID-19 manufacturing and distribution chains have been, there have also been failures. For example, at Emergent BioSolutions, cases of cross-contaminations between two different vaccines led to the destruction of 75 million doses of vaccine.[187] Product quality has also been a constant challenge for manufacturers when trying to produce on a global scale.

C. Innovating, Investing, and Cooperating to Manufacture and Distribute COVID-19 Treatments

Developing vaccines and treatments for COVID-19 was only the first part of the challenge. Manufacturing them at scale and getting them to patients globally has been a vast and ongoing undertaking, requiring that companies erect new manufacturing networks to meet global demand at a scale never seen before. Just as with developing treatments, manufacturing and distribution presents novel scientific and innovative challenges, given the cutting-edge nature of many of the technologies. In addition, it presents tremendous logistical and management challenges.

Manufacturing and distributing COVID-19 vaccines treatments required the biopharma industry to further innovate, collaborate, and invest to develop the capability to deliver needed doses to patients. This effort is still ongoing and, while there is work still needed to serve the majority of the world currently awaiting vaccines, it has resulted in billions of doses of vaccines manufactured and delivered. IP has been essential to supporting these efforts by securing investments in new infrastructure and enabling cooperation. Governments played an important role too, with direct funding and commitments to purchase successfully developed vaccines.

Here, we provide an account of the work done to make and distribute COVID-19 treatments, IP's role in supporting this work, and the key role of particular government interventions.

1. Innovation in Manufacturing and Distribution

Making and delivering vaccines and treatments to patients presented two challenges that called for creating and investing in new ways of manufacturing and increased capacity. First, some of the treatments were so new they had never been manufactured at a large scale, so entirely new supply chains and processes needed to be created. Second, the vast scale of the need also called for doing things in new ways.

Most of all, manufacturing mRNA vaccines required a great deal of innovation. Since the Pfizer/BioNTech and Moderna vaccines were the first of their kind to be approved, their makers had not previously manufactured them at an industrial scale. They had to take a process that produced small batches for testing and experimental uses and turn it into an industrial process. One expert summed up the engineering challenges of scaling up mRNA vaccine production from the laboratory to factory by quipping "gee, that 2000-liter reactor with process control and computers hanging off it doesn't look much like a test tube."[188]

Pfizer and BioNTech thus needed to design a new production process. It took several months of working with partners to identify the optimal process for making this mRNA vaccine.[189] It continued to invest in improving the process, eventually halving the production time.[190] Elements of this process are technically challenging. For example, combining mRNA with lipid nanoparticles at industrial scale was difficult.[191] Also, the production process needs to be completed from start to finish inside a hermetically

sealed system.[192]

Another innovation challenge involved creating a new supply chain. The Pfizer/BioNTech vaccine includes 280 materials in total, and about 10-15 of them were novel and had to be created for the mRNA vaccine. In July 2021, Pfizer's Zielinski said that "At this point we have about 86 supplier sites in 19 countries and over 260 manufacturing deals."[193]

Since the Pfizer/BioNTech and Modern vaccines were the first of their kind to be approved, they had never previously been manufactured at an industrial scale.

The distribution of these novel vaccines required further innovation. Both mRNA vaccines need to be stored at extremely low temperatures: the Moderna vaccine needs to be stored at between -15 degrees and -25 degrees Celsius, and similar temperatures are required[194] for the Pfizer/BioNTech vaccine.[195] Pfizer and BioNTech collaborated with Softbox Thermal Packaging systems on a new ultra-cold shipping box technology that maintains cold longer.[196] The new and innovative boxes all contain temperature trackers that are built in and monitor the temperature of the vaccine vials throughout the distribution process.[197]

Since modern biopharma manufacturing is specialized and distributed, suppliers of key ingredients had to innovate to meet the manufacturing challenge. For example, plasmid DNA is used in both mRNA and adenovirus vector vaccines as well as many other biotech treatments. Plasmid DNA is made by several independent manufacturers. An August 2020 study identified plasmid DNA production as "the bottleneck of the genetic medicine revolution."[198] At that point in time, there was only enough production capacity in the world to make just 2 billion doses of COVID-19 vaccine.[199] Moreover, the study said that "it is becoming increasingly clear that it is the fundamentals of plasmid DNA manufacture that render it incapable of enabling the future of genetic medicine" as the biological process for making it was both too slow and vulnerable to failure.[200] To address this challenge, Touchlight Genetics Ltd developed a proprietary process for producing a synthetic DNA vector, referred to as "doggybone DNA" (dbDNA).[201] This patented technology cuts months off production time and greatly increases capacity.[202]

2. Investing in Increased Manufacturing and Distribution Capacity

Meeting the extraordinary demand for COVID-19 vaccines and treatments required exceptional investments of time and human resources, as well as unprecedented risk-taking. Companies set aside pre-pandemic priorities, diverted resources, and began large-scale production long before they knew they had successful treatments. Two things helped encourage these efforts and mitigate some of the risks they entailed. First, IP protection removed the risk of losing the return on investment from an otherwise successful development program to appropriation and copying. Second, government funding provided resources for scaling production, and purchase commitments reassured innovators that, in the event of success, they would have a market. Nevertheless, failure was still a risk and some biopharma companies have indeed incurred the cost of failure when their vaccines and treatments did not make it to market.

Companies first turned inward for resources to meet production demands imposed by pandemic needs. As we describe in detail later, Novartis was a key partner in vaccine production, and it shifted resources quickly towards COVID-19-related projects. Rene Luginbuehl, Novartis' Global Head of Large Molecules, recalled: "A hundred people had to be mobilized in under three months, and we could do that only by moving people away from other activities."[203] Novartis's Corey Salsberg affirmed that its quick response required "re-assigning highly skilled people from other important projects, diverting resources, and so on. This approach took resources away from other activities. This undoubtedly had a cost for other patients and health needs."[204] Incurring such opportunity costs to other R&D and manufacturing programs represents a significant investment.

Merck KGaA, one of Pfizer and BioNTech's partners in developing and optimizing mRNA vaccine manufacturing processes, has said that it was able to quickly pivot its operation to work with Pfizer and BioNTech thanks to existing technologies and IP frameworks. Merck KGaA makes lipid nanoparticles for the Pfizer/BioNTech vaccine.[205] Vivien Tannoch-Magin, Head of Patents at MilliporeSigma, explained that the company "had planned to make a synthetic cholesterol anyway. When COVID-19 hit, we accelerated that and were able to launch nine months in advance. The condensed timeline required us to move people off other projects and put them on this instead. We tapped into this manpower and historical knowledge, and we had to sacrifice other projects. We focused on this and made it a priority." According to Tannoch-Magin, "IP enabled this," by securing the investment that enabled Merck KGaA to develop this technology and to divert resources to accelerate its deployment.[206]

Probably the most important thing that companies did to expedite production and distribution was simply to take the risk of producing and stockpiling doses of their vaccine even before they received regulatory approval. Every major vaccine innovator did so.

Scaling up manufacturing while research was still underway was a very unusual step. The development and scaling of manufacturing capacity usually follow the steps in the clinical trial process. Basic, but not optimal, manufacturing processes are normally put in place to produce enough doses for Phase 1 trials, while improved, but still not fully scaled, ones are implemented for Phase 2 trials. Complete, scalable process are only in place by the time that Phase 3 trials are carried out.

Given the compressed timetable of the COVID-19 pandemic, however, this incremental process, which would normally take years, had to be condensed into a matter of months. Companies such as AstraZeneca and Pfizer front-loaded the scaling of manufacturing, building out production capacity and optimizing processes while clinical trials were still underway. According to one person close to these activities: "We were building the plane as we were flying it. We were making manufacturing steps as we went, making cell lines, cooling cell lines, doing it all to expedite things and get things to clinical trials."[207] Companies maintained open dialogue with regulatory agencies, to dialogue in real time about relying on new, expedited methods for production and testing without compromising on quality or patient safety.

This early preparation required making commitments to suppliers and distributors long before it would normally be done. For example, Johnson & Johnson and Pfizer each started to purchase their raw materials and take steps to set up their manufacturing and distribution chains before they received regulatory approval; usually this process doesn't begin until approval of use has been granted. Pfizer started preparing for global scale manufacturing and distribution as early as March 2020, and Johnson & Johnson started not long after, in April 2020. This advanced preparation contributed to the speed at which the vaccines were able to be produced and distributed once approved.[208]

Pfizer began forging distribution partnerships with logistics firms before being granted regulatory approval. As the company's Vice President in Charge of Supply Chains, Tanya Alcorn, explained at the time: "If we get the FDA approval, we will be able to ship the vaccines very shortly thereafter."[209]

Given the compressed innovation timetable required for the pandemic, the incremental process of developing and optimizing manufacturing processes, which normally takes years, had to be condensed into a matter of months.

Pfizer further invested in developing an innovative distribution system. Companies typically first ship to distributors that then ship the vaccine to the point of use, but Pfizer opted for what it calls a "flexible just-in-time system." This system delivers most doses straight from the company's sites in Kalamazoo, MI and Puurs, Belgium, to the point of use.[210] The vaccine is also contained in its multi-dose vials from the beginning to the end of distribution (from fill-and-finish until the point of use), in contrast to the common practice of shipping bulk quantities from production centres, which must then be divided up into smaller units closer to the point of use.[211] The company claims that, using its more direct approach, it can deliver vaccines within one or two days to points of use in the United States, and within three days around the world.[212]

Other companies opted to speed distribution by investing in localizing supply chains. AstraZeneca for example chose to focus on as much local manufacturing as possible, with the aim of reducing import and export costs and constraints. It was able to do this due to its global network of suppliers.[213]

Investing in manufacturing and distribution before approval was a risky strategy. IP rights eliminated one kind of risk – that an investment might be deprived of all or some value by competitors copying technology. Nevertheless, a treatment could fail clinical trials – most do. Health providers or government purchasers might deem it inferior or not worth the cost, or production difficulties and delays might render an investment less valuable.

By the time of the COVID-19 pandemic started, the pharmaceutical industry had experienced the risk of losing investments in vaccine development due to governments choosing not to purchase an otherwise effective vaccine. A 2018 article in STAT News related that vaccine developers felt "burned" by answering calls to governments to develop vaccines, in which governments then lost interest.[214] The article observed "Nearly all the major pharmaceutical companies that work on these vaccines have found themselves holding the bag after at least one of these outbreaks."[215] In the case of the H1N1 virus, companies lost significant sums when governments reneged on commitments to purchase vaccines after the pandemic subsided.[216]

Governments stepped up to mitigate some of these risks. They used a combination of strategies, including advance purchase agreements and direct funding to ramp up manufacturing. In the case of advance purchase agreements, companies still incurred risk, as the agreements only apply if the vaccine is successfully developed.

Operation Warp Speed, for example, is a project started by the U.S. Government to help aid vaccine development, production, and distribution. The majority of pharmaceutical companies involved in making the vaccines accepted the funding that was offered. Over 700,000,000 doses were purchased

by the U.S. Government under Operation Warp Speed from a variety of different companies, among them Moderna, Johnson & Johnson, AstraZeneca, and Novavax.[217]

Pfizer had the option to take funding from Operation Warp Speed to help with the vaccine development process, but it chose to decline. Some speculated that Pfizer wished to avoid government control of its vaccine, a point of view that was somewhat affirmed by Pfizer's Chairman and CEO, who said that Pfizer opted to fund the process itself to avoid third party interference that could slow down the distribution process.[218] Nevertheless, Pfizer's partner BioNTech did receive $445 million from the German Government to increase manufacturing capacity.[219]

Operation Warp Speed also provided funding to Corning Inc, which produces Valor glass vials, a novel, more advanced vial which provides advantages in manufacturing and distributing vaccines.[220] Operation Warp Speed signed a supply agreement with Corning Inc, to increase production.[221] The Biomedical Advanced Research and Development Authority (BARDA) was also involved in an agreement with Corning, as it signed a deal for $204 million to increase the production of Valor glass vials for use in the pandemic.[222]

The U.S. Government also supported a deal between the U.S.-based company Merck & Co[223] and Johnson & Johnson, companies that are competitors under normal circumstances. After Merck & Co was unsuccessful in producing its own vaccine, it contracted with Johnson & Johnson to support manufacturing of its vaccine. The government provided $268.8 million to support this arrangement, including $105.4 million to upgrade Merck & Co's manufacturing facilities.[224]

BARDA, which is part of the U.S. Department of Health and Human Services, has also provided support. It supported the collaboration between Johnson & Johnson and Grand River Aseptic Manufacturing (GRAM) to increase their fill and finish capacity.[225] BARDA has funded the partnership, with a new facility being built in Grand Rapids, Michigan, for this purpose.[226] Similarly, AstraZeneca received $1 billion of investment from BARDA, which doubled as an advance purchase agreement.[227]

Novavax also received $1.6 billion from Operation Warp Speed, which was granted as a combination of development investment and a 110 million-dose advance purchase agreement.[228]

The importance of government advance purchase agreements and direct support is, of course, not restricted to the United States. Investment by governments across the globe, both in the form of development funding and advance purchase agreements, has played an important role in manufacturing and distributing today's COVID-19 vaccines. For instance, the German Government provided financial support for BioNTech in relation to its COVID-19 vaccine development program.[229] Though it is not yet on the market, the Novavax vaccine has advance purchase agreements with the governments of Japan, South Korea, the United Kingdom, Australia, Canada, and Switzerland, and with Gavi, the Vaccine Alliance.[230] Novavax also has partnered with Takeda, the Japanese pharmaceutical company, to help with the production and distribution of the vaccine. The partnership is being funded from the Japanese

government, and the money will be used to upgrade Takeda's existing systems and facilities.[231]

3. Collaboration to Increase Manufacturing and Distribution Capacity

"No one party can do everything. No one entity has all the technology to bring to bear to solve a problem like COVID-19. It has taken a tremendous amount of collaboration. And IP has really facilitated collaboration. It allowed parties to share information freely, knowing there are frameworks to protect that information so it's properly used."
– Matthew Pugmire, Pfizer

One of the least-heralded but most essential aspects of the biopharma industry's response to COVID-19 has been collaboration among companies to manufacture vaccines and other treatments. This collaboration has included a great deal of technology transfer and knowledge sharing. While agreements have been reported individually, the total scope of manufacturing collaboration has largely gone unremarked.

One contribution of this report is to provide an overview of manufacturing collaboration and assess its implications. By August 1, 2021, when we concluded our research for this paper, collaboration and technology transfer in COVID-19 vaccine manufacturing was already widespread, and IP rights had facilitated that cooperation. Subsequently, global manufacturing networks continued to expand rapidly.

The existence of that collaboration and knowledge sharing, and especially the role of IP in supporting it, appears to have been widely overlooked and misunderstood. There is currently a proposal to suspend the IP treaty obligations of World Trade Organization members regarding COVID-19 treatments. It is often referred to as the "TRIPS waiver," since it would temporarily set aside WTO Members' obligations under the TRIPS Agreement. One motivation for that proposal is the contention that innovators are slowing vaccine manufacturing by refusing to grant manufacturing rights or share relevant know-how. One prominent critic asserts that "the knowledge that can help end the pandemic should not be a secret."[232]

The reality is that innovators have been widely sharing knowledge and technology with manufacturing partners, which in some cases include their competitors. The experts we interviewed emphasized that innovators have worked hard to increase global manufacturing capacity, searching widely and thoroughly for partners with the necessary equipment and skills to make effective use of technology transfer, then sharing the necessary information with those partners once found. Despite the claims of some, they have not found excess capacity, but rather challenges in finding up-to-date capacity, trained personnel, and raw materials. According to these experts, these challenges have been the barriers to producing more doses — not IP.[233]

This account was confirmed by a recent Wall Street Journal report reporting on Pfizer's efforts to find manufacturing partners for the mRNA vaccine and to transfer the necessary technology to them.[234] Pfizer has a small team of experts who are "among a relatively small number of professionals with the rare skill set to enable other companies to produce the shots."[235] They scout for companies with the capabilities to effectively receive and implement mRNA vaccine manufacture technology transfer.[236] The Wall Street Journal report further recounted that once Pfizer finds a potential partner, getting them ready to manufacture is a many months-long process of working hand-in-hand, which included sharing "more than 500 top-secret files – at least 5,000 pages of documents on making the vaccine – over secure computer servers."[237]

When an innovator engages in such voluntary technology transfer, it relies on trade secret law and contracts to protect valuable proprietary information from being misappropriated. Without the protection of trade secret law, it would indeed have to hide this information and avoid such sharing. More than one of our interviewees observed that biopharma companies would step up to help in a future health crisis such as the pandemic regardless, but that without IP protection, they would cooperate less widely to protect their proprietary information. This seeming contradiction – that trade secret laws encourage more sharing – is explained in detail earlier in this report. To sum it up, trade secret law allows innovators to rely on the legal system to expand their circle of trust so that they need not try to do everything in-house, substituting reasonable precautions and confidentiality agreements for absolute secrecy.

Innovators are collaborating widely. As of the time we did our research, we were able to identify numerous partnerships using public sources. As already noted, new partnerships have been added and disclosed frequently since. To summarize, among five leading vaccine innovators – AstraZeneca, Johnson & Johnson, Moderna, Novavax, and Pfizer/BioNTech – we found that as of August 1, 2021:

- over 40 manufacturing partnerships to produce the main components of the vaccine,
- 27 "fill and finish" partnerships, to place the vaccine in vials, label, and prepare for distribution, and
- six distribution partnerships to provide regional capabilities in over 25 countries.

Pfizer and BioNTech's primary partnership, which is assisted by a further network of partners, is an example of the collaboration needed to manufacture and distribute COVID-19 vaccines. The partnership began with urgency and a willingness to collaborate when Pfizer and BioNTech signed a Material Transfer and Collaboration Agreement on March 17, 2020. This allowed them to begin working together immediately and finalize the details of their partnership at a later date. BioNTech developed the vaccine, and the parties agreed that BioNTech would retain the IP rights to the vaccine and its earlier technology. Meanwhile, Pfizer contributed significant abilities in the areas of R&D, regulatory compliance, extensive capabilities in production and distribution. Pfizer has helped BioNTech to expand its manufacturing capacity substantially. The two companies now manufacture at sites[238] worldwide, which include both facilities owned by the two companies themselves and those of contract manufacturers.[239] Furthermore, according to Pfizer, many of its suppliers depend on the company for significant amounts of technical or financial assistance that Pfizer transfers backwards along the supply chain.[240]

Pfizer/BioNTech then partnered with many others to develop the necessary capabilities to deliver their vaccine. A notable partner was Novartis, a company that might otherwise be viewed as a competitor. Novartis was engaged to help develop the manufacturing process and carry out the fill-and-finish phase of production. Novartis was able to bring skilled personnel, quality-systems and regulatory expertise, and logistical competencies, as well as process optimization techniques, such as increased automation. The collaboration with Novartis necessitated significant – and swift – technology transfer. To begin this knowledge transfer as quickly as possible while still maintaining an environment of trust, the two companies put in place a confidential disclosure agreement in a period of just a few days. This allowed them to begin technology transfer while still negotiating the final terms of their arrangement, and, as a result, to mobilize a hundred Novartis employees for the project in a period of just three months and to have batches rolling off of Novartis' production line in four months. As Novartis' Global Head of Large Molecules, Rene Luginbuehl, recounted, this cooperative relationship among competitors simply made sense for all of the parties involved

since "We all had a common purpose which was to come together to address the pandemic."[241]

Pfizer's Zielinski observed that "IP facilitated these relationships. The same way that BioNTech was able to work with Pfizer due to IP protection, we were able to work with partners on manufacturing deals. Patents provided security, in addition to know-how and trade secret protections."[242]

The following is a list of Pfizer/BioNTech COVID-19 manufacturing facilities and partnerships, based on public sources as of August 2021:[243]

Company/Contractor	Location	Manufacturing Role
BioNTech	Germany	Main production
Siegfried	Germany	Main production
Pfizer	Belgium	Main production, fill-and-finish
Baxter	Germany	Main production, fill-and-finish
Biovac Institute Ltd.	South Africa	Fill-and-finish
Delpharm	France	Fill-and-finish
Dermapharm	Germany	Fill-and-finish
Eurofarma	Brazil	Fill-and-finish
Novartis[244]	Switzerland	Fill-and-finish
Sanofi	Germany	Fill-and-finish
Thermo Fisher	Italy	Fill-and-finish
Dura-Fibre	United States	Distribution
Rentschler Biopharma	Germany	Distribution

The other innovators discussed in this report also relied on partnerships and technology transfer to manufacture and distribute COVID-19 vaccines and treatments. Like Pfizer and BioNTech, other companies followed a strategy of establishing geographically distributed manufacturing and distributing networks. We detail these partnerships in the Annex and provide an example as follows:

By August 2021, AstraZeneca had established manufacturing agreements in Argentina, Australia, Belgium, Brazil, China, Germany, Italy, Malaysia, Mexico, the Netherlands, Japan, South Korea, Spain, the United Kingdom, and the United States. [245]

By this time, Moderna had also established a broad network of partnerships for manufacture and distribution, due to its small size.[246] The company's publicly disclosed partnerships spanned a network based in the United States, Switzerland, France, Israel, Japan, Saudi Arabia, Spain, and South Korea.

Johnson & Johnson had similarly established manufacturing and distribution partnerships abroad, including in the United States, Netherlands, France, South Africa, India, Italy, and other countries.

By August 2021, Novavax too had begun establishing partnerships. Although the company's vaccine was not yet on the market, Novavax had already begun partnering with Takeda for the clinical development, production, and distribution of its vaccine within Japan. The underlying agreement requires Novavax to share and transfer its COVID-19 technology and knowledge to Takeda and aims to produce more than 250 million doses per year.[247] Furthermore, Novavax produces the antigen component of its vaccine via several different partnerships. Outside of its own facility in Bohumil, Czech Republic, Novavax's antigen-production partners include Biofabri in Spain, UJIFILM Diosynth Biotechnologies (FDB) in the United States and the U.K., SIIPL in India, SK Bioscience in the Republic of Korea, and the Takeda Pharmaceutical Company Limited in Japan.[248] Novavax's adjuvant is also being produced by a Novavax facility in Uppsala, Sweden, at facilities of AGC Biologics in the United States and Denmark, and by the Polypeptide Group in the U.S. and Sweden.[249]

Gilead Sciences began in 2020 to produce its broad spectrum antiviral remdesivir via non-exclusive voluntary licensing agreements that it concluded with generic pharmaceutical manufacturers in Egypt, India, and Pakistan.[250] These licenses are aimed at increasing access to generic remdesivir in 127 lower income countries, with each manufacturer permitted to set its own prices in those countries. All nine companies to which Gilead licensed these manufacturing rights have contracts that involve technology transfer.[251]

Sinovac partnered with a range of companies to increase the speed at which its CoronaVac vaccine could be distributed—including in one collaboration with Indonesian PT Bio Farma to provide and produce CoronaVac, in which technology transfer from Sinovac was included in the agreement. It has been disclosed that Sinovac will provide technology to enable local production in Indonesia.[252]

The makers of Sputnik V pursued partnerships around the globe: countries in which companies or their governments have manufacturing facilities include Kazakhstan, India, South Korea, Brazil, Turkey, Venezuela, China, Italy, and Argentina, with the latter being the first Latin American country to produce the vaccine.[253] There are also negotiations to manufacture Sputnik V in Saudi Arabia, and Bahrain. [254]

The map below provides a visual depiction of the contract manufacturing partnerships that a variety of different pharmaceutical companies had entered into by August 1, 2021. The result was a vast, globally distributed manufacturing network for all COVID-19 treatments. Tables detailing the partnerships can be found in the Annex at the end of the paper.

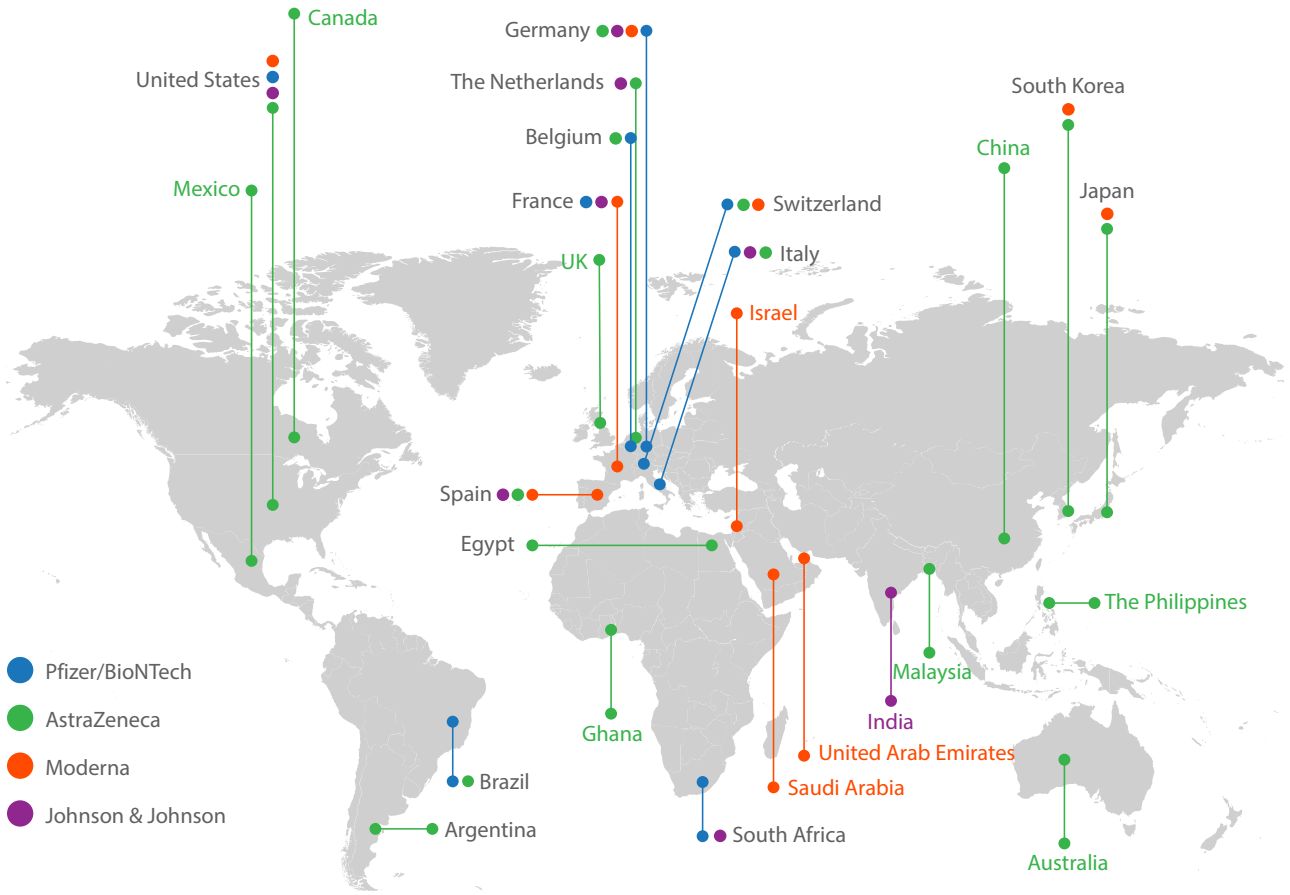


Figure 3: Global Manufacturing Networks for Four COVID-19 Vaccines

4. The Results So Far and the Road Ahead

UN Secretary-General Antonio Guterres has said that 11 billion doses would be needed to vaccinate 70 per cent of the world's population and end the pandemic.[255] Given the scope of the challenge, and the speed with which it had to be confronted, success in distributing medical products for COVID-19 – especially vaccines – has been striking. To date, a total of 3.25 billion vaccine doses have been administered globally. Malta has the highest proportion of their population, 81 per cent[256] fully vaccinated as of July 18, 2021.[257]

As of June 16, 2021, Moderna had successfully delivered 154,675,860 doses of its mRNA vaccine within the United States, and, as of May 6, it aimed to increase its supply to between 800 million and 1 billion doses by the end of 2021. To this end, the company is currently investing with a goal of increasing the global supply of its COVID-19 vaccines to up to 3 billion doses by 2022.[258] Similarly, BioNTech and Pfizer raised their previous target for 1.3 billion doses by the end of 2021 to 2.5 billion, and the companies said in separate statements that production could reach 3 billion doses in 2021[259] and 4 billion in 2022, the majority of this latter figure going to low-to-middle income countries.[260]

AstraZeneca said that it aims to "deliver up to 3 billion doses of COVID-19 vaccine across the globe by the end of 2021," and that it was able to set up more than 20 manufacturing sites across 15 countries.[261] Sinovac, too, added a new production line for the manufacturing of CoronaVac, increasing its manufacturing capacity to 2 billion doses as of April 2, 2021. The Russian Direct Investment Fund sold millions of doses of Sputnik V worldwide: 35 million to Uzbekistan, 32 million to Mexico, 25 million each to Nepal and Egypt, and 50 million to European countries.[262] In addition, Slovakia bought 2 million doses, though it had to sell most of the doses back to Russia after Slovakia's drug agency refused to give approval to the vaccine.[263] In addition, a long-term agreement was announced between the Russian Direct Investment Fund and UNICEF for the supply of Sputnik.[264]

Global cooperation has been the key to fulfilling the determined ambition to end the pandemic. Typical of that ambition and spirit of collaboration is the partnership between Johnson & Johnson and Merck & Co. to manufacture vaccines, which they characterized as a "wartime pact."[265] The COVAX partnership further typifies the importance and spirit of cooperation. At present, many countries have signed and agreed to be part of this effort to distribute the vaccines to the worlds low and middle income countries, with over 2 billion vaccine doses being administered in more than 190 countries as of June 2021, with the hopes for this number to increase.[266] Furthermore, at the G20 Summit in May 2021, the President of the European Commission, Ursula von der Leyen, stated some key principles that would be needed to help end the pandemic. These include "no export bans, keeping global supply chains open, and working to extend capacity everywhere."[267] This is the substance and spirit of cooperation that will be needed to reach the target goal of delivering 11 billion doses.

IV. Fulfilling the Unmet Need for COVID-19 Vaccines and Treatments

From one perspective, the development, manufacturing, and distribution of COVID-19 vaccines and treatments has been a triumph, but from other perspectives it has been disappointing. This report has largely recounted the innovation successes, as innovators used cutting-edge technologies to develop vaccines in an unprecedented timeframe, then partnered widely and urgently with contract manufacturers and competitors to ramp up production. Questions arise, however, as billions await vaccines while access has been inequitably distributed in favour of wealthy nations.

Concern as well as frustration is understandable. Some countries such as the U.K. have been able to vaccinate a large majority of their eligible populations as of this writing. However, other countries have barely had the opportunity to start vaccinating people. According to statistics from the Duke Global Health Innovation Centre, as of August 2021, the United States already has more than enough doses in hand for its needs while many countries (e.g., South Africa) have yet to establish *future* commitments to deliver all the doses they need.

The lack of equitable access for all has caused some to blame the market power possessed by innovators because of their IP rights.[268] They argue that manufacturing exists, but that innovators have refused to license the necessary IP or to share know-how.[269] This argument is part of what motivates the proposal for the TRIPS waiver, which, as noted earlier in this report, would allow countries to temporarily disregard WTO treaty obligations to respect and enforce IP rights with respect to COVID-19 solutions.

This report's accounting of the numerous, geographically distributed partnerships for manufacturing vaccines tends to contradict the premise of this argument.

The challenges in vaccine manufacturing appear to arise from roughly three causes. First, there is the nature of the challenge – a pandemic – which needed to be met with manufacturing at an unprecedented scale, relying largely on novel technology. Building requisite capacity in more places requires substantial investments – and time. Second, there are bottlenecks for key components and supplies, due to factors such as spike in demand. Third, "vaccine nationalism" has led several governments to claim a lion's share of vaccine production, beyond their needs, and to restrict the free flow of vaccines.

A. The Unprecedented Scope and Nature of the Vaccine Manufacturing Challenge

One could rightly wish for faster vaccine production, but the world is, in many respects, fortunate that innovators could produce effective vaccines at all and manufacture them as quickly as they have. While inequities in distribution should not be ignored, neither should the achievement in inventing and delivering the vaccine be dismissed. At the start of the pandemic, the world did not have the existing manufacturing capacity to deliver vaccine doses to all of humanity. One problem was that many of the technologies that worked best are new and demanded extremely sophisticated capabilities, new facilities, and new supply chains.

The most successful vaccines were the mRNA and adenovirus vector vaccines, which both relied on new or relatively new technology. Adenoviral vector vaccines – such as those produced by AstraZeneca and Johnson & Johnson – had been used experimentally for many years, but there had only one vaccine previously approved, an Ebola virus vaccine that was developed by Johnson & Johnson and approved by the European Medicines Agency in 2020.[270] By December 2020, the vector used in the Johnson & Johnson COVID-19 vaccine had been administered in a total of 193,831 doses for various investigational

vaccines, including the COVID-19 vaccine, as well as the Ebola vaccination program.[271] While Johnson & Johnson and its partners were already mass manufacturing and stockpiling doses at this date, the relatively small number of uses compared to the hundreds of millions of doses needed shows the ramp up that was needed from experimental to global production.

Meanwhile, the mRNA technology had never been produced at scale. The two leading companies pioneering this technology had to find more experienced partners to begin manufacturing. Even though BioNTech had been working with mRNA technology for 25 years, possessed considerable knowledge related to mRNA platforms, and had spent ten years developing a manufacturing process for mRNA vaccines, it needed to partner with Pfizer to begin producing at scale.[272] According to BioNTech, the validation of a single production site can still take up to a year.[273] Similarly, Moderna needed to partner with the Swiss firm Lonza to begin its production.

Previous experience and equipment in the general category of vaccine manufacturing was not necessarily sufficient preparation for making these newer kinds of vaccines as quickly as needed and in line with the controls demanded by regulatory authorities. Just as a factory manufacturing older internal combustion engine technology might not be ready to manufacture the newest electric engines, so was it with older facilities set up to manufacture inactivated virus vaccines.

Bryan Zielinski of Pfizer explained the challenge of finding partners that were ready to meet the need on a timely basis: "Just to get a plant operational takes a few years. A developing country building a plant specifically to make our mRNA vaccine would take a few years, for facility design, building, investments, and training people. The real limitation in terms of making more doses of our vaccine, or any vaccine, is raw materials and technical know-how, and the right buildings and machinery to make the materials. We've identified where manufacturing capacity exists, and we are not aware of any additional capacity in the world."[274]

Pfizer identified partners with sufficiently advanced technological capacity, but even they had to do work and investment to get ready. For example, Merck Life Science, part of Merck KGaA, had been working with customers to set up manufacturing of what turned out to be key mRNA vaccine components. But Merck's Arno Hartmann explained that additional work was required: "It is very hard to find facilities. You can't just take a building and make it into a vaccine manufacturing facility. In Germany, we have a manufacturing site, and they had vaccine manufacturing suites, but they were not up to date enough to deploy for COVID-19. You had to redesign and retrofit them to pass all regulations."[275]

Technology transfer has not been a one-way street, as the expertise of these partners was needed to develop a manufacturing process of these new vaccines. Experience setting up and managing supply chains is another form of valuable expertise that can be contributed to a collaborative effort. As Novartis' Rene Luginbuehl points out "ensuring the availability of primary packaging materials, raw materials, etc. is crucial. A company like Novartis has a well-established network with suppliers, and for many materials we have established more than one supplier, so that we really can make sure we get access to what is needed. Without glass vials you cannot fill the product – it's not just the capability to fill the product, but also things like well-managed and full stock."[276] Similarly, Luginbuehl recalled that when challenges arose at Novartis' fill-and-finish operations for the Pfizer/BioNTech vaccine, it was the knowledge of highly skilled Novartis employees that allowed the company to solve them.

As discussed earlier in this report, the Wall Street Journal recently reported on Pfizer's technology transfer process.[277] Pfizer identified Thermo Fisher as a potential manufacturing partner in May 2020.

The parties began exchanging information over the course of the year, using video conferencing. When it became apparent that Thermo Fisher had an Italian plant that could work, a 24-person team from Pfizer began transferring know-how in advance of a February 2021 agreement. After the agreement, Pfizer provided "at least 5,000 pages of documents on making the vaccine … over secure computer servers. And it trained Thermo Fisher workers on mRNA, which the plant had never used before."[278] Seven months later, in late August 2021, after various trial runs and testing, Pfizer and Thermo Fisher are gathering data and preparing to apply for regulatory approval for the plant to begun producing vaccine doses. According to the report, this represents a much faster ramp up than usual.

These accounts illustrate that at least some of the challenges arise from the novelty of the technology. The most effective vaccines proved to be those based on technology that was not yet widely in use. The necessary work to ramp up production has been done through technology transfer to partners, but it takes time.

Another problem was that creating the capacity to vaccinate the world had not, up until now, been practicable. As Corey Salsberg, Vice President and Global Head of IP Affairs, Novartis, explained "Most diseases don't affect everyone in the world at once. There is almost nothing in normal times that you need 7-14 billion doses for. You don't need to have manufacturing capacity to make things like that. It would be inefficient to maintain that for most circumstances, and also harmful to divert resources from things like cancer to focus on building out manufacturing capacity for an unknown problem that, outside of a true global pandemic, is unlikely anyway to affect large numbers of people all at once. There is always an opportunity cost when you divert resources."[279]

B. Bottlenecks for Vaccine Components and Supplies

The unprecedented demand to scale up vaccine production put stress on supply chains already challenged by the pandemic. Supply chains for biologics are highly complex and include many different participants – raw materials suppliers, equipment suppliers, contract manufacturers, and logistics companies.

All these moving parts must work together smoothly to keep doses rolling off the production line. For example, production of the Pfizer/BioNTech COVID-19 vaccine relies on over 280 physical inputs,[280] some of them unique and novel materials.[281] The Covaxin and Covishield vaccines, both manufactured in India, depend heavily on ingredients sourced from abroad:[282] both require an estimated 360 foreign inputs[283] and depend on supply relationships with international, particularly U.S.-based, partners.[284]

The physical inputs that are necessary are many, the value chains are geographically distributed, and it is difficult to respond effectively to spikes in demand. It can take years to scale up the production of bio-manufacturing inputs and in some cases the available raw materials are simply finite. Government policies that restrict the flow of inputs globally can further complicated prospects for COVID-19 R&D and manufacturing. Some have expressed concern that entry of new manufacturers during this time of crisis could divert critical inputs from the supply chains of established manufacturers towards unproven new entrants, potentially making it harder for established producers to secure what they need and thus potentially holding down the global supply of vaccines.[285]

As discussed earlier in this report, a key component of both mRNA vaccines and adenovirus vector vaccines is plasmid DNA, which was also a key bottleneck in production of vaccines. As of August 2020, only a fraction of the necessary production capacity existed to produce plasmid DNA for COVID-19 vaccines.[286] Since then, plasmid DNA suppliers have ramped up, but it remains a challenge.

Even some perhaps less-intuitive inputs have been in short supply, such as glass vials and filter systems. There are, for example, simply few companies that manufacture borosilicate glass vials, which have been the industry standard for over 100 years.[287] One of these companies, in fact – German firm Schott AG – claims that "three out of four COVID-19 vaccine projects rely on Schott vials."[288] Merck KGaA is in a similarly essential position, scrambling to fill orders for critical bio-manufacturing inputs like filters, which must be changed after each production run and for which demand has surged as a result of the COVID-19 pandemic. Whereas it previously took 4-6 weeks for delivery of essential filter systems, it can now take a reported 60 to 65 weeks to get them. This fact, exacerbated in some cases by counterproductive government policies that interrupted the flow of goods along global value chains, has made it harder to scale up manufacturing.

Another challenge has been securing the necessary equipment to maintain cold temperatures required for the Pfizer/BioNTech and Moderna vaccines. These temperatures can require the use of so-called "ultra-cold" freezers, which are not available in many countries and regions. For example, the country of Peru only has 30 ultra-cold freezers, significantly fewer than in just one of Pfizer's freezer facilities in the United States.[289] Pfizer's manufacturing partner, Thermo Fisher, had to build a new 5000 square foot facility with ultra-cold freezer to keep vaccines sufficiently cold.[290]

C. Vaccine Nationalism

The funding and purchase commitments that several governments have provided have proven to be a double-edged sword. On the one hand, they provided key assistance in developing vaccines and, particularly, manufacturing capacity. On the other hand, "high income countries have dominated global supply, and have overwhelmingly targeted those doses (understandably) at their domestic populations."[291] While the United States, the U.K., and Israel have vaccinated the majority of their populations, less than one per cent of people in low-income countries are fully vaccinated and only 8.4 per cent of the people in lower middle-income countries have been vaccinated.[292]

According to the Duke Global Health Innovation Centre, high income countries and jurisdictions – the U.S., Canada, and the EU, in particular – have claimed a total of the world's vaccine production equal to several multiples of their population. This "overbuying" seemed like a good thing, initially, as it was the result of making commitments to many different potential suppliers at an early date. This approach thus encouraged and supported a diversity of opportunities to succeed, helping to increase the chances for success despite the inevitable development and manufacturing failures which have occurred.

Even after high income countries had successfully vaccinated their most vulnerable populations, contractual commitments kept them first in line for vaccine supplies. As a result, the disparities in vaccine distribution among countries grew. These contractual priorities have produced some controversy, as in September when many criticised the fact that vaccine doses produced for Johnson & Johnson in South Africa were destined for the EU.[293] While some of the criticism was misdirected at Johnson & Johnson, it was the EU that had the prior, contractual claim on the doses. The doses were ultimately redirected to African countries when the EU consented.[294]

Another way in which wealthy countries' contractual priorities became problematic was that they began providing booster doses for their citizens while much of the world still waits for its first dose. Reports estimate that booster doses could divert 850 million to 2 billion doses in the next year from those who have yet to start receiving vaccines – a significant portion of the 11 billion doses needed.[295]

Nevertheless, government advance purchase commitments were essential to getting the vaccine developed and ramping up production. In prior recent pandemics, including the H1N1 pandemic, companies answered government calls to produce vaccines. When the pandemic subsided, governments declined to purchase the doses produced, and innovators lost their investments.[296] Without governments' firm contractual commitments to purchase COVID-19 vaccines, the H1N1 vaccine precedent may have made companies more cautious.

Moreover, the good news is that manufacturing is responding to the need. Andrea Taylor of Duke's Global Health Innovation Centre told the Atlantic that "Our best estimates are that the world is producing close to a billion doses a month now, and we think that will continue to increase … There is still a supply issue, but it is shrinking."[297] The bad news is that the supply is not yet sufficient to supply all, so vaccine production remains a zero-sum game where doses in wealthy countries represent a lost opportunity to vaccinate the most vulnerable in less wealthy countries.

Vaccine nationalism has led some scholars to propose that global procurement and manufacturing capabilities be set up to guarantee a global supply.[298] These proposals include an element of compulsory licensing of patents and, especially, trade secrets. Some acknowledge that building such a capacity would not occur in time for this pandemic,[299] whereas others consider this to be a remedy for the ongoing COVID-19 response.[300] None of the proposals seem to have contemplated the extent of voluntary licensing already occurring, which we have documented in this report.

One challenge for such proposals is the fact that they would require investing in creating a large amount of excess capacity that would (one hopes) sit idle for a long time. However, both the state of the art and regulatory requirements evolve constantly. Employees need know-how to address challenges, which they need to gain through learning by doing. Novartis's Salsberg related to us, "people don't usually set out to develop know-how. Rather, it is often the natural product of doing scientific and technical work. It's hard to distill and put in a manual. Real know-how cannot just be written on a paper. You have to share know-how through doing and through collaboration."[301]

Novartis's manufacturing expert, Rene Luginbuehl, expressed concern that facilities that were under-utilized or dormant could not effectively respond to a crisis. "Having idle capacity that is ready for the moment it is needed would require that you have well-trained personnel prepared to handle challenging products on short notice. You would not have the quality system or logistics systems fully established. Capacity alone is not the guarantee that you can actually produce demanding products like vaccines. You really need to have operations ongoing in full and adapt them to new and challenging needs as required."[302]

Nevertheless, it appears that some sort of collective action to avoid vaccine nationalism and put some measure of preparedness might be in order. However, given the level of private investment, innovation, and voluntary cooperation this report documents, it would be wise to avoid disrupting the functioning of the private market. Many of the experts we interviewed expressed the belief that in the event of a crisis, the biopharma industry would step up regardless.

The challenge of proposals to increase vaccine manufacturing that would take away IP is that they might undermine cooperation and investment. Interviewees expressed the concern that companies would hold information closer, avoiding partners in locations that did not respect IP and generally hesitating to put information in a form that could be easily transferred. They would be more likely to carry out R&D, manufacturing, and other activities in-house. Moreover, investors might direct money toward less risky ventures, particularly those who are investing the start-up space. None of these things would happen out of spite, but rather as natural reactions to increasing risk.

V. Conclusions and Lessons Learned

The effort to develop and distribute COVID-19 vaccines and treatments is likely to be seen by history as one of the most remarkable achievements of the IP-enabled biopharma industry. Since the need is so urgent and vast, there is still much work to be done and many improvements to make. Nevertheless, we can already begin to draw lessons from the successes and challenges about the biopharma industry, about IP, and about public health policy.

A. Takeaways from the COVID-19 pandemic about IP and Biopharma Innovation

IP played an essential enabling role in the development and delivery of solutions to address the COVID-19 pandemic. Although investment in applied research and the work and cooperation of many were responsible for solutions, IP helped to make all of these efforts possible.

Below we identify a few takeaways, based on our research and interviews.

1. IP-Enabled Innovation Created the Necessary Background Technology and Knowledge to Develop Vaccines and Treatments on an Accelerated Timeline.

When the pandemic started, the global research community and the biopharma industry were able to draw on a diverse set of technologies and know-how that had already been developed. Many of these technologies owed their existence to an IP system that had incentivized investments in R&D. Among the benefits of the IP-driven biopharma R&D system are the following.

- IP has enabled the existence of companies that engage in continuous innovation. Innovators and their manufacturing partners were able to draw on a wealth of pre-existing know-how, processes, and equipment in order to develop and optimize the production of COVID-19 solutions, some of which had never been produced at commercial scale.
- Patents and trade secrets have long promoted "design around" and competitive innovation, encouraging innovators to compete by pursuing different avenues to solving health problems. This results in "more shots at the target."
- The biopharma industry's continuous IP-driven innovation also contributed to the existence of a large number of potential solutions. Companies hope and search for blockbuster drugs, but the uncertain nature of drug discovery causes them to research in many directions. Scientists mined the results of earlier R&D efforts to identify promising compounds and platforms that they could apply to fighting COVID-19, including vaccine, monoclonal antibody, and anti-viral programs, as well as those for totally different health issues.[303]

2. IP Secured Big Investments at Every Step of Developing and Delivering Treatments to Society.

During the pandemic, innovators invested in developing new technologies, establishing and upgrading facilities and networks for manufacturing, identifying new approaches to securing regulatory approval, testing existing compounds for relevance to the pandemic, and setting up new global distribution networks. They worked with partners and carried out significant technology transfer to rapidly move COVID-19 treatments from the lab to patients. In relation to the above, IP reduced one kind of risk: that an investment might be deprived of all or some value by a competitor copying the technology or know-how without agreement.

The full extent of COVID-19 innovations is not yet in public view. To our knowledge, no patents have issued to date on novel COVID-19 products. Moreover, the first patent applications arising from

COVID-19 were filed in early 2020. It takes 18 months before patent applications are published; thus, at the time of writing, it is still unclear what new IP has been developed as a result of the pandemic. What is clear, however, is that innovative platforms and solutions have been developed, along with new manufacturing processes and substantial know-how with diverse future applications.

3. IP Enabled Collaboration to Develop COVID-19 Treatments.

Every COVID-19 solution required partnerships along the pathways of R&D, commercialization, and distribution. Even solutions developed in-house, such as the Moderna vaccine, required contract manufacturing to achieve commercial scale. Technology transfer was a crucial part of these relationships.

Innovators would not have been willing to share their knowledge regarding platform technologies such as mRNA vaccines without the security of IP. IP rights removed some of the risk for innovators that collaborating on COVID-19 treatments would give away other valuable opportunities. IP rights also ensured a potential return on investment in COVID-19-related R&D.

IP also helped foster trust, which allowed companies to divide their labor effectively. They were even able to work with competitors thanks to the security provided by IP laws. These collaborations among rivals were important to COVID-19 innovation, as traditional competitors often had the most knowledge and overall capacity to take on the challenge.

Sound IP rights allowed partnerships to come together rapidly by enabling the up-front sharing of technologies and know-how, in some cases before the details of working relationships had even been worked out. As a result, companies were able to complete technology transfer and have medicines rolling off production lines with speed that had not been previously seen.

4. IP Enabled Collaboration with Contract Manufacturers across Supply Chains.

Contract manufacturing organizations (CMOs) were critical to the COVID-19 response, as no one party had the necessary manufacturing capacity to meet global needs in house. IP contributed to this disaggregated manufacturing, as it took much of the risk out of the huge amounts of technology transfer – through the licensing of patents and trade secrets – that were necessary in contract manufacturing relationships. In addition, IP allowed innovators and contract manufacturers to safely transfer know-how and technology, and this IP exchange often became a two-way street, with partners learning from each other as the COVID-19 response evolved. Both contract manufacturing and supply relationships were made possible by sound IP rights.

Furthermore, ensuring sustainable, predictable access to necessary equipment and raw materials also involved the significant transfer of know-how and trade secrets, and the trust engendered by proper IP protections allowed for companies to more safely and quickly source the hundreds of inputs that went into their vaccines and treatments.

B. Lessons Regarding Factors Complementary to IP

IP-driven commercial innovation has been one necessary factor among many in responding effectively to the pandemic. For example, government policies not directly related to IP contributed to success. Public funding and coordination programs, such as the U.S.'s Operation Warp Speed, both increased the pace and lowered the risk of developing, producing, and distributing vaccines and treatments. Public research institutes, too, acted as important actors in the innovation ecosystem. As was the case

with the AstraZeneca and Moderna vaccines, frameworks that enabled public research outcomes to be protected and licensed for further development enabled private sector actors to turn research outcomes into real-world products, a task which government labs and departments were unable to do on their own.

Unfortunately, there remain many challenges to developing and commercializing new products for COVID-19. These challenges include the inherent complexity of designing, manufacturing, and distributing the relevant products, access to raw materials and other inputs, and the many steps needed to ensure quality and safety. In some cases, governments created challenges with export restrictions and tariffs. Notably, expanding production capacity – even in non-emergency situations – takes significant time and expertise, and industry experts have stressed that capacity cannot be created in order to sit idle and be activated only in time of need.

C. Removing Protection for COVID-19 Innovations

Without IP, the range of background technologies and know-how would probably not have been available to apply to the pandemic response. Moreover, while some innovators might have pitched in regardless, IP rights gave them the security needed to assure investors and other stakeholders.

Without IP rights, innovators may still have come forward to help, but they would opt to work differently in the absence of reliable IP protection. They would undoubtedly share less, slowing the development of new solutions. Innovators would work with fewer partners – or with no partners at all, keeping everything in house. Working with competitors would become particularly treacherous, so trade secrets would need to be kept strictly under wraps. Perhaps fewer patents would be filed, so as to not disclose early on the discoveries that could ultimately become the new solutions. In relation to COVID-19, this type of approach would have stalled the response significantly. For instance, it would have made it impossible to rapidly manufacture the number of vaccines needed for the global population.

It is worth noting that the financial decision-making as to whether to step in and address a pandemic is already fraught. Losing control over important background IP, developed as part of longstanding R&D programs and intended to be integrated into normal business operations, could tip the scales against participating fully in such efforts.

Setting aside IP protection cannot necessarily expedite pandemic response because, even with the most experienced actors sharing all their technology and knowledge with peers, it can take many months to solve manufacturing challenges and get things right. Anything that would slow this could be counterproductive.

We note that, in light of the gravity and urgency of the current situation, most innovators are not asserting any of their COVID-relevant patents, and no patents have been issued yet on new COVID-19 solutions. One said: “The patents are out there and available to assert – but most companies have explicitly stated they have no intention to sue anyone. All the existing knowledge is out there and can be applied without assertion or lawsuits.”

D. Insights for Policymakers

Innovation during the COVID-19 pandemic was accelerated by certain enabling policies and actions. By applying lessons learned, policymakers can support the ongoing COVID-19 response and enhance future pandemic preparedness.

IP was an important enabler of the pandemic response. Alongside patent protection, trade secrets protection has been crucial. Systems for IP protection support efforts by innovators to develop and move new vaccines and drugs to society – especially during a crisis.

Innovators had a range of pre-existing innovative tools and technologies to apply to the COVID-19 response when the pandemic started. IP had supported their development in the past. IP systems stimulate the development of a variety of possible solutions to the same challenges, given the need to design around others' IP.

Collaboration and knowledge-sharing provided a foundation for rapid innovation in response to the crisis. IP enabled the sharing of valuable technology and know-how without innovators losing their competitive edge.

At every stage of development of COVID-19 vaccines and other solutions, significant investments were required. IP protection helped to enable investments, whether in relation to product innovation, regulatory approval, scaling production, or distribution.

Some IP assets relevant to the COVID-19 response were licensed by the public sector research institutes to the private sector, which further invested to transform them into products. One example is the mRNA platform. This underlines the need for policy frameworks for public-private collaboration.

Some have called for removing IP protection for COVID-19 solutions. This would have made it impossible in the case of COVID-19 to innovate so quickly, by making knowledge and technology sharing unduly risky. It would also have made it more difficult to establish distributed manufacturing networks, which require tech transfer. Without IP, innovators would be less likely to work with partners, setting back innovation to address health crises.

Other types of policies also affected the COVID-19 response. Government support, whether financial support or cooperation with innovators to expedite regulatory approval without compromising safety and quality, accelerated the response. In contrast, some policies, such as export restrictions and other counterproductive trade policies, interfered with the operation of efficient value chains.

The COVID-19 response can be considered to have been the IP system's finest moment, allowing different types of innovators to immediately share knowledge, technology, and resources in order to develop and manufacture new life-saving solutions at unprecedented speed. Their efforts resulted in a competitive marketplace of vaccines and treatments that includes technologies that had never before made it to market. The role of IP in supporting investments to develop new health technologies is well known. What the COVID-19 experience underscores, in addition, is the crucial role of IP in enabling the collaboration and knowledge transfer necessary to solve global health challenges.

VI. Annex: Collaboration and Technology Transfer for Vaccine Production and Distribution

Collaboration and Technology Transfer for Vaccine Production and Distribution

ASTRAZENECA

AstraZeneca formed manufacturing agreements in different regions for main production and fill-and-finish.

Company/Contractor	Location	Role
BioKangtai[304]	China[305]	Main production
CSL Behring[306,307]	Australia	Main production
Emergent BioSolutions[308]	United States	Main production
Halix B.V[309]	Netherlands	Main production
Novasep which has now been acquired by Thermo Fisher[310]	Belgium	Main production
Oxford Biomedica[311]	United Kingdom	Main production
SK Bioscience[312]	South Korea[313]	Main production
mAbxience[314]	Argentina	Main production
IDT Biologika[315]	Germany	Main production and fill-and-finish[316]
Albany Molecular Research Inc.	United States	Fill-and-finish
Catalent[317]	Italy	Fill-and-finish
CP Pharmaceuticals[318]	United Kingdom	Fill-and-finish
Daiichi Sankyo Co.[319]	Japan	Fill-and-finish
Fiocruz	Brazil	Fill-and-finish
Insud Pharma	Spain	Fill-and-finish
KM Biologics	Japan	Fill-and-finish
Liomont[320]	Mexico	Fill-and-finish
Nipro Corp	Japan	Fill-and-finish
Oswaldo Cruz Foundation[321]	Brazil	Fill-and-finish
Seqirus	Australia	Fill-and-finish
Wockhardt Limited	United Kingdom	Fill-and-finish
Pharmaniaga	Malaysia	Vaccine distribution

JOHNSON & JOHNSON

Johnson & Johnson also created a variety of different partnerships to increase their global manufacturing capacity. These include both main production and fill-and-finish.

Company/Contractor	Location	Role
Biological E[322]	India	Main production
Emergent BioSolutions[323]	United States	Main production
Merck & Co.[324]	United States	Main production
Aspen Pharmaceuticals[325]	South Africa	Main production and fill-and-finish
Catalent Biologics[326]	United States	Main production and fill-and-finish
Sanofi[327]	France	Main production and fill-and-finish
Catalent Biologics[328]	Italy	Fill-and-finish
Grand River Aseptic Manufacturing[329]	United States	Fill-and-finish
IDT Biologika[330]	Germany	Fill-and-finish
Merck & Co.[331]	United States	Fill-and-finish
Reig Jofre Group	Spain	Fill-and-finish
McKesson[332]	United States	Distribution

NOVAVAX

Novavax formed manufacturing agreements around the world for main production and fill-and-finish.

Company/Contractor	Location	Role
AGC Biologics	Sweden	Main production
Biofabri	Spain	Main production
Praha Vaccines	Czech Republic	Main production
Polypeptide Group	Sweden	Main production
Polypeptide Group	United States	Main production
Serum Institute of India (SIIPL)	India	Main production
Diosynth Biotech (FDB)	United States	Main production, fill-and-finish
Diosynth Biotech (FDB)	United Kingdom	Main production, fill-and-finish
SK Biosceince	South Korea	Main production, fill-and-finish
Takeda	Japan	Main production, fill-and-finish
Endo International	United States	Fill-and-finish
GlaxoSmithKilne (GSK)	United Kingdom	Fill-and-finish
Jubliant Life Sciences Limited	United States	Fill-and-finish
Biocelect	Australia	Distribution

MODERNA

Moderna has manufacturing agreements with partners around the world, for activities including DNA production, DNA/RNA production, lipid production, lipid nanoparticle assembly, and fill-and-finish.

Company/Contractor	Location	Role
Aldevron[333]	United States	DNA production
Lonza[334]	Switzerland	DNA/RNA production
Lonza[335]	United States	DNA/RNA production
CordenPharma[336]	United States	Lipids production
CordenPharma[337]	Switzerland	Lipids production
CordenPharma[338]	France	Lipids production
Lonza[339]	Switzerland	Lipid nanoparticle (LNP) assembly
Lonza[340]	United States	Lipid nanoparticle (LNP) assembly
Catalent[341]	United States	Fill-and-finish
Baxter International[342]	United States	Fill-and-finish
Laboratorios Farmacéuticos Rovi	Spain	Fill-and-finish
Recipharm[343]	France	Fill-and-finish
Sanofi[344]	United States	Fill-and-finish
Thermo Fisher Scientific[345]	United States	Fill-and-finish
Samsung Biologic[346]	South Korea	Fill-and-finish
McKesson Corp[347]	United States	Vaccine distribution
Takeda[348]	Japan	Vaccine distribution
Magenta[349]	United Arab Emirates	Vaccine distribution
Medison Pharma[350]	Central Eastern Europe & Israel	Vaccine distribution
Tabuk Pharmaceuticals[351]	Saudi Arabia	Vaccine distribution
GC Pharma	South Korea	Vaccine distribution
Kuehna + Nagel International AG	Germany	Vaccine distribution

PFIZER/BIONTECH

Pfizer and BioNTech relied on their own manufacturing facilities, in addition to forming global partnerships to increase their capacity in the areas of main production and fill-and-finish.

Company/Contractor	Location	Manufacturing Role
BioNTech	Germany	Main production
Siegfried	Germany	Main production
Pfizer	Belgium	Main production, fill-and-finish
Baxter	Germany	Main production, fill-and-finish
Biovac Institute Ltd.	South Africa	Fill-and-finish
Delpharm	France	Fill-and-finish
Dermapharm	Germany	Fill-and-finish
Eurofarma	Brazil	Fill-and-finish
Novartis[352]	Switzerland	Fill-and-finish
Sanofi	Germany	Fill-and-finish
Thermo Fisher	Italy	Fill-and-finish
Dura-Fibre	United States	Distribution
Rentschler Biopharma	Germany	Distribution

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Our analysis benefitted from interviews with senior executives from the biopharma industry whose companies were directly involved in developing and commercializing new COVID-19 vaccines and treatments. We interviewed:

Syed Ahmed and Susmita Mukherjee, Techinvention Lifecare Pvt. Ltd, June 16, 2021

Bryan Zielinski and Matt Pugmire, Pfizer Inc., June 25, 2021

Gavin Lawson and Hemal Shah, Gilead Sciences, Inc., June 25, 2021

Kathrin Körner, Arno Hartmann, and Vivien Tannoch-Magin, Merck KGaA, June 28, 2021

Rene Luginbuehl and Corey Salsberg, Novartis, June 30 and July 1, 2021

William Krovatin, Merck & Co., Inc., July 8, 2021

Jacob Oyloe, AstraZeneca plc., July 9, 2021

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Endnotes

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