Patent Landscape Report

COVID-19 vaccines and therapeutics

WIPO

Patent
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Report

COVID-19 vaccines and therapeutics

Insights into related patenting activity throughout the pandemic

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This publication was prepared with the stewardship of Marco Alemán (Assistant Director General, IP and Innovation Ecosystems Sector), under the direction of Alejandro Roca Campañá (Senior Director, IP for Innovators Department) and Andrew Czajkowski (Director, Technology and Innovation Support Division).

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Key findings

Since the start of the COVID-19 pandemic a remarkable research and innovation effort has gone into combating the SARS-CoV-2 virus and COVID-19 disease. This Patent Landscape Report provides observations on the field of COVID-19 vaccines and therapeutics, based on a comprehensive review of patenting activity and building on insights from the first WIPO COVID-19 Patent Landscape Report published in March 2022.

Pandemic-related filing activity has been extraordinarily active

The patent search undertaken for this report looked at related patent filings from January 2020 through September 2022. It found 7,758 patent filings on technologies related to COVID-19 in general, including 1,298 patent filings related to vaccine development and 4,787 to therapeutics. Patenting activity related to COVID-19 outpaced that of other recent viruses and illnesses, such as influenza and SARS, both in volume and speed of filing.

Patenting filing activity has been concentrated at four patent offices

Because COVID-19 vaccines and therapeutics have a global market, it should come as no surprise that related applications were filed and published by patent offices all over the world. Specifically, vaccine patents were published across 30 patent offices and therapeutic patents across 44 patent offices. The World Intellectual Property Organization (WIPO), administering the Patent Cooperation Treaty (PCT) system, received the most COVID-19-related vaccine and therapeutic patent applications, followed by the China National Intellectual Property Administration (CNIPA), the United States Patent and Trademark Office (USPTO) and the European Patent Office (EPO), all receiving a significant number of applications of either type. WIPO's current top ranking is a likely indication that patent applicants are leveraging the WIPO-administered PCT system in order to protect inventions across multiple jurisdictions.

Both business and the research community have contributed significantly to the patent landscape

Patent applicants are distributed almost equally between companies (52 percent of the vaccines and 49 percent of the therapeutics dataset) and universities and research organizations (42 percent of the vaccines and 38 percent of the therapeutics dataset), but with companies accounting for a larger proportion of the two datasets.

China is the leading origin of patent filings related to vaccines and therapeutics

A patent applicant's location can provide information about the profile and origin of the key players in terms of patenting activity. The top five patent applicant locations in the field of vaccines are China, the United States of America (US), Germany, the Republic of Korea and the Russian Federation. In the field of therapeutics, China, the United States, the Republic of Korea, India and Germany are the top applicant locations.

The relative frequency of discussions around mRNA and other types of vaccines for COVID-19 is at variance with patenting activity in the dataset

Although global discussion around vaccines was primarily focused on mRNA vaccines, a comparison of doses administered worldwide of the different categories of vaccine tells another story. Two apparent discrepancies are that COVID-19 mRNA vaccines accounted for the majority of vaccinations in the western world, but patents related to this type of vaccine accounted for just 11 percent of the dataset; but conversely, protein subunit vaccines accounted for less than 1 percent of vaccine doses administered in that same region, but represented the largest portion (47 percent) of the vaccine patent dataset. China has almost exclusively administered inactivated vaccines, whereas Africa has primarily administered viral vector vaccines.

Small molecule and biologic drugs are the two main types of therapeutics

Within the dataset, therapeutics for COVID-19 mostly fall into three main types: small molecules that include synthetic compounds but may also be natural products extracted and purified from plants; biologic drugs that include antibodies, non-antibody peptides/proteins, cell-based therapies and nucleic acid-based therapies; and traditional medicine. The largest proportion of COVID-19 therapeutics patent filings relates to small molecules and biologics (50 percent and 43 percent of the therapeutics patent dataset, respectively). However, traditional medicine also has a role to play in the fight against COVID-19. Within the therapeutics dataset, 10 percent of filings disclosed the use of traditional medicine in treating COVID-19.

Antibodies accounted for one-third of biologics, and in their newly developed virus-neutralizing form introduce a new class of antiviral

The fastest growing class of biologics, antibodies made up about one-third (34 percent) of the biologics disclosed in patent documents. COVID-19 therapeutic antibodies include newly developed neutralizing antibodies directed against the SARS-CoV-2 spike (S) protein, as well as previously developed antibodies that modulate the host's immune/inflammatory response to the virus. Virus-neutralizing antibodies represent a new class of antivirals. When given in combination, they are capable of binding to various regions of a crucial segment in the SARS-CoV-2 S protein and in so doing effectively block the viral S protein from interacting with its receptor on human cells. Other antibodies that target human host factors may be used to reduce inflammation and counter adverse effects from the cytokine storms seen in some severe cases of COVID-19.

The patent dataset discloses some innovative treatment approaches

The dataset includes information on other potential methods for COVID-19 treatment. Novel approaches include the use of CRISPR-Cas technology to target viral genes so as to disrupt the virus's ability to infect host cells; nucleic acid-based drugs (e.g., small interfering RNA, short hairpin RNA, microRNA, antisense oligonucleotides, aptamers) designed to attack SARS-CoV-2 at distinct stages of its lifecycle and/or to modulate host dependency factors; and, lastly, novel delivery vehicles, such as engineered exosomes (i.e., the membrane-bound extracellular vesicles of human cells). The advent of biotechnology related to exosomes enriched with the desired molecules, including drugs, has enabled the commercial production of novel delivery vehicles. Drug or cargo-loaded exosomes containing immune-modulating substances in combination with antiviral substances can provide rapid and targeted delivery for disease treatment. The potential application of these innovative strategies in the treatment of COVID-19 in clinical settings is yet to be determined.

Collaborations comprised pharmaceutical companies, biotech startups and universities

Cooperation between big pharmaceutical companies and relatively small biotech companies, and between universities and both these types of commercial organizations was evident across different regions of the world. For example, development of the oral antiviral therapeutic molnupiravir involved Emory University, Merck, and Ridgeback Biotherapeutics. Merck and the Medicines Patent Pool also had a licensing agreement to provide molnupiravir as a COVID-19 treatment to low- and middle-income countries. Developers of vaccines and therapeutics also collaborated with different manufacturers at the manufacturing stage (Global Healthcare Innovation Alliance Accelerator. (n.d.-a).

Patents related to booster vaccines are only a small part of the vaccine patent dataset

About 5 percent of vaccine patents in the dataset emphasized booster use. This is at variance with extensive media discussion, government recommendations and policy debates around the availability and use of boosters. Data on booster usage by country and income level show that high-income economies have higher levels of booster vaccination, whereas low-income regions have very low booster usage and middle-income countries range between the two.

Roughly a tenth of COVID-19 therapeutics patents related to traditional medicine

From January 2020 through September 2022, 523 patent applications related to traditional medicine were published. Most were filed by applicants located in Asia. Over 60 percent were filed at the China National International Property Administration (CNIPA). The intellectual property offices of India and Republic of Korea were the next biggest recipients of traditional medicine patents.

Patents related to long COVID made up less than 2 percent of the dataset

Therapeutics for the treatment of long COVID – defined by the World Health Organization as the continuation or development of new symptoms three months after an initial SARS-CoV-2 infection, with symptoms lasting for at least two months without another explanation – were disclosed in 22 patents (WHO, 2022b). The majority (13) disclosed small molecule therapeutics to treat long COVID. The remainder comprised biologics, traditional medicine and other types of therapeutics for long COVID treatment.

Corporate applicants filed the most patents related to pharmaceutical formulations for COVID-19 therapeutics

Over 90 percent of patent applications relating specifically to pharmaceutical formulations were submitted by corporate applicants, either alone or in combination with a university or research organization or an independent inventor. Within this subset of patents, the majority relate to formulations of small molecule therapeutics (64 percent), followed by biologics (34 percent).

Nearly one-quarter of patent applications were the result of collaboration between multiple applicants

Patent applications with more than one assignee made up 24 percent of the dataset. In the vaccine dataset, collaboration was between all applicant types, including companies, universities and research organizations. In the therapeutics dataset, the majority of collaborations were between universities and research organizations.

Introduction

In late 2019, a mysterious pneumonia-like illness emerged in China that caught the attention of the world's health experts and scientists. The illness quickly spread around the globe. Research into its cause revealed it to be the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). In January 2020, the World Health Organization (WHO) declared a global public health emergency and named the illness COVID-19, in February 2020 (WHO, 2020). Soon afterwards, in March 2020, the WHO officially declared COVID-19 a global pandemic. As of November 28, 2022, there had been more than 637 million cases confirmed worldwide, resulting in over 6.6 million deaths (WHO, n.d.-g), making it one of the deadliest pandemics in modern history, second only to the 1918 flu pandemic (Adam, 2022). Its severity and the complexity in battling COVID-19 pandemic has been compounded by the ongoing emergence of SARS-CoV-2 variants, with sublineages of the Omicron variant currently of most concern (WHO, n.d.-f).

In response to the pandemic, scientists around the world have made great strides in understanding the SARS-CoV-2 virus. This in turn has led to the development of preventive vaccines and therapeutic agents. By leveraging decades of vaccine technology research and development (R&D), scientists have been able to quickly first develop and then deploy a variety of COVID-19 vaccines. As of December, 2022, more than 13.04 billion vaccine doses had been administered globally (WHO, n.d.-c). In parallel, existing drugs have been repurposed and new therapeutics developed to combat the disease.

This report is a follow-up to WIPO's first *COVID-19-related Vaccines and Therapeutics* Patent Landscape Report published in early 2022 (WIPO, 2022). It presents an updated overview of global patenting activity related to COVID-19 vaccines and therapeutics from January 2020 through September 2022, based on information publicly available as of September 30, 2022. Because of the lag in time between patent filing and publication of the related application (on average 18 months), this report does not give a complete picture but rather a perspective on publicly available COVID-19-related patent information up until September 2022.

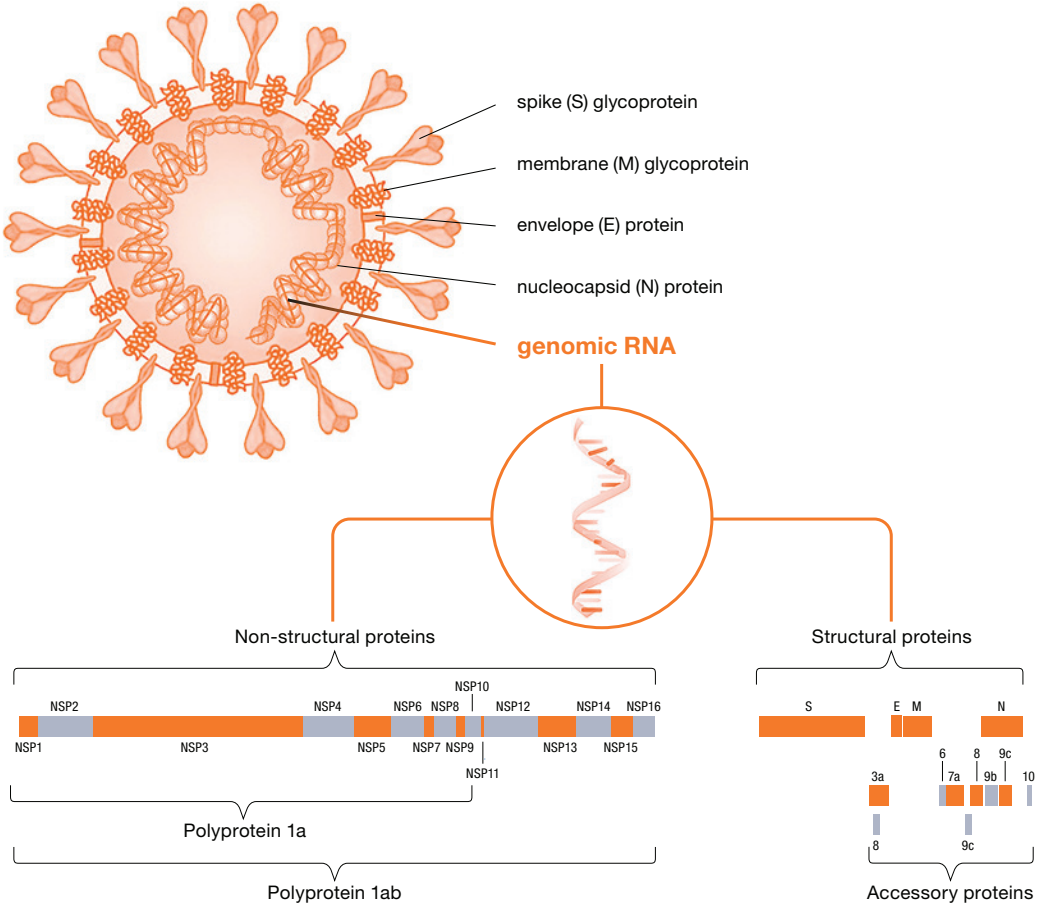
Since the pandemic began, various patent analytics and scientific publications have sought to shed light on patent activities and technologies related to COVID-19. A list of these publications can be found in the Further reading section.

Background – biology of COVID-19

The coronavirus that causes COVID-19 – SARS-CoV-2 – was unknown to the scientific community until discovered in late 2019. Since then, its structure and mechanism of action have been extensively studied. The full genetic sequence of the SARS-CoV-2 virus was first published on January 10, 2020, by Yong-Zhen Zhang at Fudan University, China (Zhang, 2020). Upon the sequence's release, it became possible to define the structure of the virus (shown in Figure 1). Since then, focus has been on identifying, understanding and tracking variants in order to predict whether existing vaccines and therapeutics are likely to prove effective in preventing and treating the associated disease.

Figure 1. The genomic landscape of SARS-CoV-2

The structure of the SARS-CoV-2 virus revealed the presence of the spike (S) glycoprotein that is key in causing infection.



Source: WIPO, based on Gordon *et al.*, 2020.

The SARS-CoV-2 virus's mechanism of action has been discussed in detail in the previous WIPO Patent Landscape Report on COVID-19 (WIPO, 2022). In short, the virus's outer lipid envelope is covered with spike glycoprotein (S protein). It is this S protein that interacts with human cells to cause infection. In the initial stage of infection, the coronavirus S protein binds to specific host cellular entry receptors. This opens the door for the virus to enter a cell. Once inside, the virus repurposes the host cell's system in order to replicate and invade further host cells. Vaccines and therapeutics are typically designed to disrupt this and associated subprocesses.

As viruses spread within a population, their genetic material mutates. Most mutations have little or no impact on the properties of a virus (Grubaugh *et al.*, 2020). Those mutations that do are typically called variants. Such variants can increase transmissibility or disease severity and decrease diagnostic effectiveness, as well as vaccine or therapeutic efficacy; all challenges impacting public health and the social measures needed to combat the virus (WHO, n.d.-f). Several variants of the original SARS-CoV-2 virus now exist, including the Alpha, Beta, Gamma, Delta and Omicron variants. Every one of these variants has subvariants or sublineages, commonly recognized by their Phylogenetic Assignment of Named Global Outbreak (Pango) identifier. Table 1 provides a high-level summary of SARS-CoV-2 variants. More information about variants can be obtained from the WHO's SARS-CoV-2 variant tracking website (WHO, n.d.-f).

Table 1. Summary of SARS-CoV-2 variants

Several SARS-CoV-2 variants have emerged since the pandemic began in early 2020. Omicron is the most recently sequenced variant of the SARS-CoV-2 virus. Unlike its predecessors, no one country of origin has been identified for this variant.

WHO label	Pango lineage	Date of 1st sequence documentation	Country of origin
Alpha	B.1.1.7	September 2020	UK
Beta	B.1.351	May 2020	South Africa
Gamma	P.1	November 2020	Brazil
Delta	B.1.617.2	October 2020	India
Omicron	B.1.1.529	November 2021	Multiple countries

Source: WIPO, based on data obtained from the World Health Organization, December 2022.

Omicron variant B.1.1.529 and its sublineages are currently of most concern. First classified as a *variant under monitoring* by the WHO on November 24, 2021, the Omicron variant was upgraded only two days later to a *variant of concern* on November 26, 2021 (WHO, 2021a). This variant has many sublineages, each of which has a variety of mutations that generally increase the risk of infection and reinfection through greater transmissibility and virulence (Fan *et al.*, 2022). The WHO has recommended that public health authorities monitor sublineages as distinct lineages, so as to track the virus's evolution and make informed public health decisions. A further concern is the ability of the Omicron variant and sublineages to evade not only natural but also vaccine-mediated immune responses. The only relief offered by this variant is its reduced pathogenicity, meaning less severe disease, fewer hospitalizations and not so many deaths (Fan *et al.*, 2022).

Substantial efforts have been made to develop safe and effective vaccines and therapeutics with which to combat COVID-19 and the many SARS-CoV-2 virus variants. Multiple vaccine platforms have been studied, including conventional (e.g., protein subunit and live attenuated and inactivated virus) and novel platforms (e.g., DNA and RNA-based). With the rise of SARS-CoV-2 variants, bivalent and multivalent vaccines to combat the virus more effectively are also being investigated. Additionally, the repurposing of many existing therapeutics to treat COVID-19 (e.g., remdesivir and fluvoxamine) has been considered and new therapeutics developed, including a diverse set of small molecule drugs and biologics.

Overview of patenting activity related to COVID-19

Patent filings during 2020–2022

Since 2020, 8,050 patent applications related to COVID-19 have been published across 49 patent offices, including on diagnostics, treatments, vaccines and otherwise relating either to the SARS-CoV-2 virus or COVID-19 disease. Among these, 1,298 patent applications related to COVID-19 vaccine development were first filed at 30 patent offices and 4,787 related to COVID-19 therapeutics at 44 offices (Table 2). These numbers have increased since WIPO published its first COVID-19 Patent Landscape Report leveraging data collected from January 2020 to September 2021. Also, since then, a greater number of offices are represented in both vaccine and therapeutic filings. In addition to the 8,050 patent applications published since the beginning of 2020, about 597,057 scientific literature articles, including in journals, books and meeting proceedings, had been published by the end of September 2022, based on CAS Content Collection (CAS, n.d.-a; CAS, n.d.-b).

Patent filings related to therapeutics continue to greatly outnumber those on vaccines, by a ratio of approximately 4:1. Advanced biomedical engineering research techniques and innovative tools have allowed scientists to better understand the SARS-CoV-2 infection pathway, as well as the key enzymes and proteins required for viral replication. Numerous patent offices have focused on technological innovation in the development of monoclonal antibodies, various drug delivery systems and nano-antibodies capable of binding to and neutralizing SARS-CoV-2 and its variants. Nanobodies present a more logistically advantageous alternative to intravenously delivered antibodies, since they can be nebulized and delivered directly into a COVID-19 patient's lungs through an inhaler (Sasisekharan, 2021). Most vaccine inventions have focused on polypeptides, such as SARS-CoV-2 antigens, that stimulate an efficient immune response, especially B cell production of neutralizing antibodies.

Table 2. **Patent applications related to COVID-19 in general, COVID-19 vaccines and COVID-19 therapeutics, first published and filed January 2020 through September 2022**
Over three-quarters of the overall COVID-19 patent dataset is related to COVID-19 vaccines or therapeutics. Patent filings related to COVID-19 therapeutics were almost four times higher than for COVID-19 vaccines and patent protection sought at most patent offices.

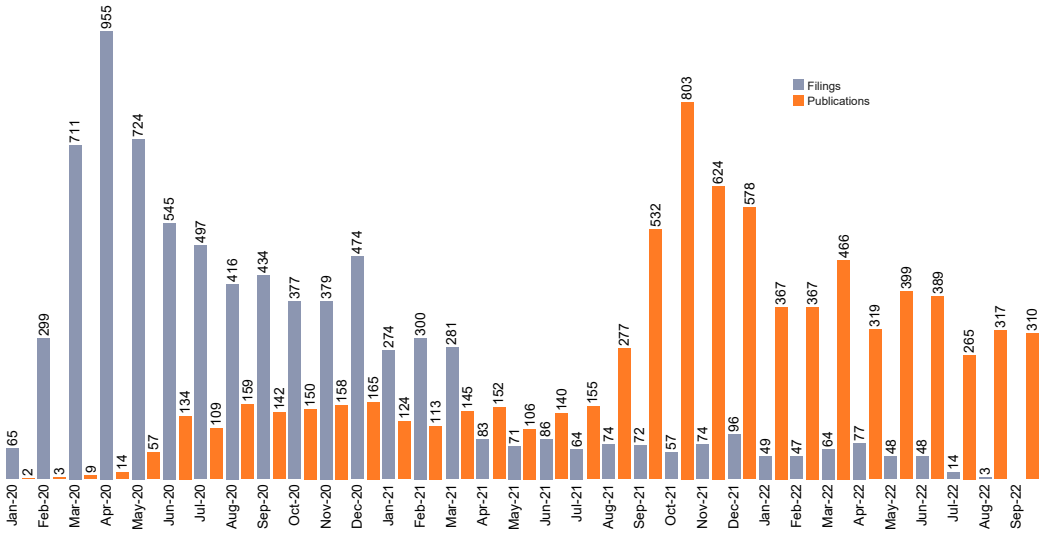
Patent dataset	Number of patent offices of filing	Number of patent applications published between 2020–2022	Number of patent applications first filed between 2020–2022
COVID-19 overall	49	8,050	7,758
COVID-19 vaccines	30	1,331	1,298
COVID-19 therapeutics	44	4,968	4,787

Source: WIPO, based on patent data from the CAS Content Collection, September 2022.

Filings and publication of COVID-19-related patent applications over time

Included in general patenting activity related to COVID-19 from January 2020 through the end of September 2022 are patent applications describing inventions of diagnostics, personal protective equipment, surface disinfectants, vaccines and therapeutics (Figure 2). Patent first-filings are shown in gray bars and patent publications are shown in orange bars. The dataset reflects the average 18-month lag between patent filing and patent publication. Over the 30-month period encompassed by the dataset, more first-filings are observed early in the period, followed by a similar pattern for publications later in the period. Figure 2 shows that a majority of filings occurred in 2020 and early 2021. This data trend describes a period when intense innovation drove early identification and the development of effective means of combating SARS-CoV-2.

Figure 2. **Patent applications related to COVID-19, first filed and published January 2020 through September 2022, by patent filing and publication month**
COVID-19-related patent application filing peaked in April 2020, followed by a corresponding peak in COVID-19-related publications in October 2021.

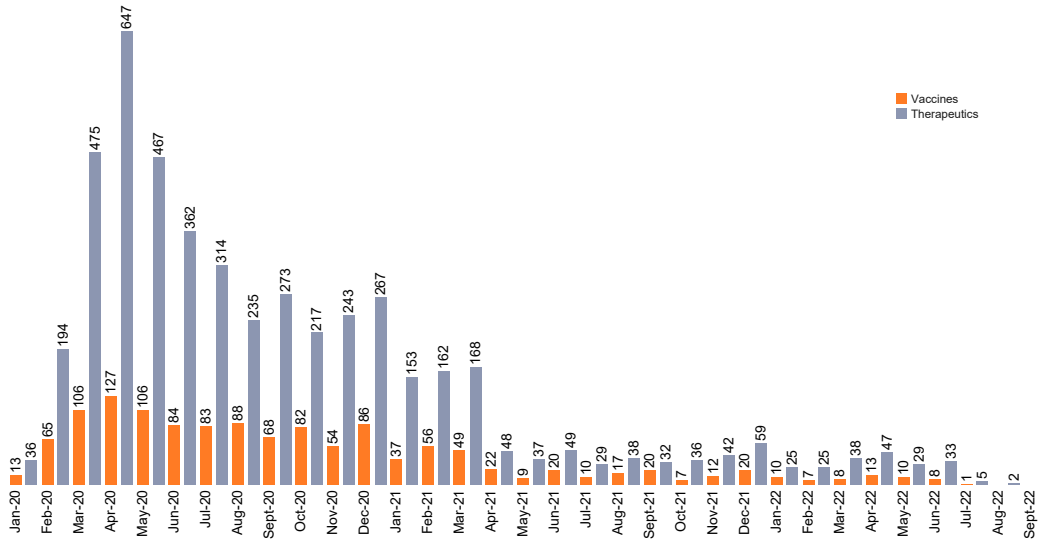


Source: WIPO, based on patent data from the CAS Content Collection, September 2022.

As Figure 3 shows, the patent filing trend for COVID-19 vaccines and therapeutics is similar to the overall COVID-19 patent filing trend, with patent filings peaking in April 2020, according to information publicly available as of the end of September 2022 (date of data collection). Throughout the period, therapeutic filings were consistently higher than vaccine filings. Because data collection for some of the period measured coincides with the average 18-month interval between a patent application and its publication, caution should be exercised when drawing conclusions about monthly trends, especially later on in the measured period.

Figure 3. **Patent applications related to COVID-19 vaccines and therapeutics, first filed January 2020 through September 2022**

Patent filings related to vaccines and therapeutics peaked in April 2020.

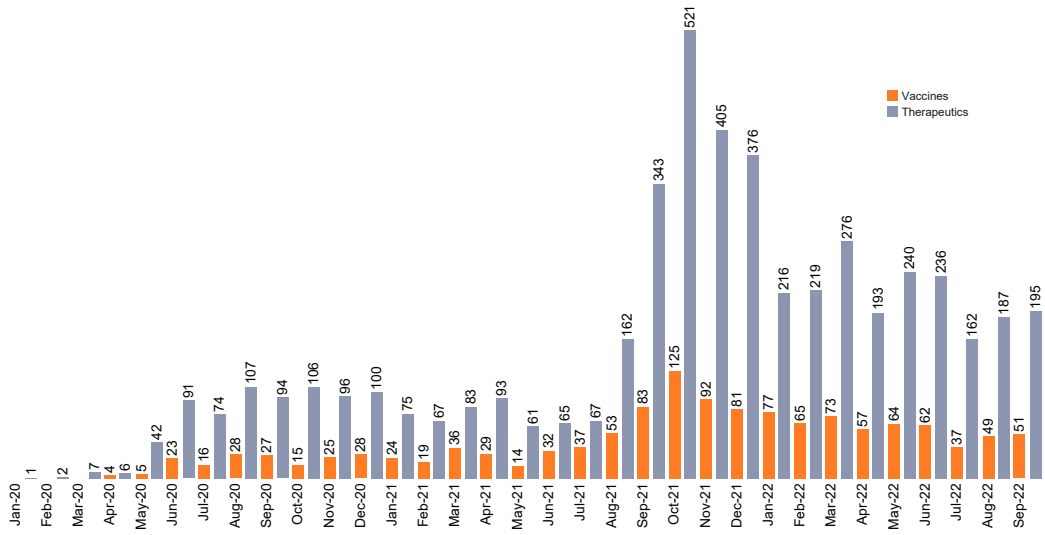


Source: WIPO, based on patent data from the CAS Content Collection, September 2022.

Patent publication trends of vaccines and therapeutics for the dataset are shown in Figure 4. The highest number of both vaccine and therapeutic patent applications were published in October 2021. The peaks in patent filings and in patent publications as observed in the dataset are separated by 18 months. This trend analysis is performed by analysis of peaks only and does not indicate a specific set of patents going from filing to publication during this period.

Figure 4. **Patent applications related to COVID-19 vaccines and therapeutics, first published January 2020 through September 2022**

Patent publications related to vaccines and therapeutics both peaked in October 2021.



Source: WIPO, based on patent data from the CAS Content Collection, September 2022.

COVID-19-related vaccine and therapeutic patent applicant profiles

Distribution of the dataset is similar in the vaccines and therapeutics areas, when considering applicant profiles (Table 3). Corporate applicants account for the largest percentage of filings in both categories (52 percent of vaccine filings and 49 percent of therapeutics). Universities and public research organizations make a similar contribution to both categories (42 percent of the vaccine dataset and 38 percent of the therapeutics), while independent inventors were more active in the field of therapeutics (12 percent) than in vaccines (6 percent).

Table 3. Contribution to COVID-19-related vaccine and therapeutic datasets, by patent applicant profile

Patenting activity related to COVID-19 vaccines and therapeutics is nearly equally distributed between companies and universities and research organizations, with companies making a slightly greater contribution.

	COVID-19 vaccines		COVID-19 therapeutics	
Patent applicant profile	**Number of patent families**	**Contribution to vaccine dataset**	**Number of patent families**	**Contribution to therapeutic dataset**
Companies	764	52%	2,624	49%
Universities and research organizations	611	42%	2,040	38%
Independent inventors	94	6%	652	12%

Source: WIPO, based on patent data from the CAS Content Collection, September 2022.

We investigated the overall rankings of top patent applicants (excluding individual inventors) to further describe the major players in the COVID-19-related vaccine and therapeutic patent landscape. Organization names were harmonized in order to perform this analysis. Within the vaccine patent dataset (Table 4), the top four applicants were universities and research organizations, while the number five spot was filled by a company, Liaoning Chengda Biotechnology Co., Ltd., followed by Sun Yat-Sen University, ModernaTX, Inc., Institut Pasteur, Tübingen Medical School, the Chinese Academy of Medical Sciences Institute of Medical Biology and additional companies, universities and research organizations.

Table 4. Applicants with the most COVID-19-related vaccine patent application filings

The top four vaccine patent applicants were universities and research organizations, with the first of the companies rounding out the top five applicants.

Top vaccine patent applicants	**Number of patent families**
Tsinghua University	24
Academy of Military Medical Sciences, PLA	22
The Gamaleya National Center of Epidemiology and Microbiology	21
Institute of Microbiology, Chinese Academy of Sciences	17
Liaoning Chengda Biotechnology Co., Ltd.	13
Sun Yat-Sen University	12
ModernaTX, Inc.	12
Institut Pasteur	12
Tübingen Medical School	12
Institute of Medical Biology, Chinese Academy of Medical Sciences	12
Sinovac	11
CanSino Biologics Inc.	10
State Research Center of Virology and Biotechnology VECTOR	10
Advaccine Biopharmaceuticals Suzhou Co. Ltd.	10
SK Bioscience Co., Ltd.	9
The Regents of the University of California	9

Source: WIPO, based on patent data from the CAS Content Collection, September 2022.

In the therapeutics dataset (Table 5), the top 15 applicants comprised exclusively of universities and research organizations.

Table 5. Applicants with the most COVID-19-related therapeutic patent application filings
The top 16 therapeutic patent applicants were all universities and research organizations.

Top therapeutic patent applicants	Number of patent families
Academy of Military Medical Sciences, PLA	60
The Regents of the University of California	40
Shanghai Institute of Materia Medica, Chinese Academy of Sciences	40
Centre National de la Recherche Scientifique (CNRS)	39
Institut National de la Santé et de la Recherche Médicale (INSERM)	36
Wuhan Institute of Virology, Chinese Academy of Sciences	31
Institute of Microbiology, Chinese Academy of Sciences	31
Fudan University	31
Shenzhen Institutes of Advanced Technology, Chinese Academy of Sciences	30
Shandong University	28
Sun Yat-Sen University	25
Korea Research Institute of Chemical Technology	22
Korea Institute of Oriental Medicine	20
Peking University	19
Institute of Medicinal Biotechnology, Chinese Academy of Medical Sciences	19
Dalian Institute of Chemical Physics, Chinese Academy of Sciences	19

Source: WIPO, based on patent data from the CAS Content Collection, September 2022.

Patent office COVID-19 strategies and actions

Patent offices around the world have responded to the COVID-19 pandemic in a variety of ways and made significant efforts to provide continuous intellectual property processing throughout the COVID-19 pandemic. These include by teleworking, interacting with applicants virtually, permitting electronic signatures and supporting applicants through time limit options and fee relief (WIPO, n.d.). Some patent offices developed and implemented programs designed to expedite the review process for COVID-19-related patents meeting certain criteria (WIPO, n.d.).

As shown in Figure 5, eight countries created specific programs for expediting COVID-19-related patent applications (WIPO, n.d.). Such programs were identified by leveraging a combination of World Trade Organization and WIPO data. While there may have been additional programs around the world, these eight offices are highlighted in this report because of their presence in these two sources.

Figure 5. **Patent offices offering expedited COVID-19 application examination**
Eight countries represented in World Trade Organization and WIPO data collections giving the option for applicants, agents or federal agencies to request expedited examination of COVID-19-related patent applications.

Note: Any additional programs not present in the two data sources are not represented in this figure.
Source: Based on data from the World Trade Organization and WIPO, December 2022.

There were several commonalities between patent offices running programs to expedite COVID-19-related patent application examination. Canada, France and the United States required the subject of a patent application to have either entered, be already in, or have completed the submission process for marketing authorization for use in that country with the competent authority (CIPO, 2020; Institut National de la Propriété Industrielle, 2021; USPTO, n.d.). In the Republic of Korea, to qualify for the expedited program, patent applications could be treatments either supported by national R&D projects or from companies preparing for their production, clinical trial and approval (KIPO, 2020b). In early 2020, the Korean Intellectual Property Office (KIPO) developed a website designed to highlight patent technology information and provide a patent analysis and trend report and a research information portal, with the aim of stimulating research and patents to promote innovation. Much of the information available from the portal was posted in early 2020. The patent analysis and trend reports include historical information relating to vaccine technologies, therapeutics and coronaviruses, along with personal protective equipment, disease transmission prevention and diagnostics (KIPO, 2020a).

China's patent application acceleration program starting after the issuance of a policies/practices order by three government agencies in February 2020 was one of the earliest to commence (SAMR, 2020). Prioritization and accelerated procedures for COVID-19-related patent applications could be requested by applicants. In a July 2022 press conference, a CNIPA official stated that 2,572 COVID-19-related patent applications had been prioritized by the end of June 2022 (Information Office, Government of China, 2022).

Israel's program for expediting patent applications related to COVID-19 commenced in April 2020 and was enabled by the Patent Commissioner categorizing them as 'green technology'. Patent applications that qualified for the program focused on diagnostics, treatment, prevention and personal protective equipment related to SARS-CoV-2 (Pearl and Heiliczer, 2020).

Brazil's National Institute of Industrial Property's expedited review program included a provision allowing the Ministry of Health to request the fast-tracking of specific patents (Pessôa *et al.*, 2022). According to research undertaken by Pessôa *et al.*, the Brazilian Ministry of Health requested the expedited review of 63 patents. Patent applicants themselves requested expedited review of 51 patents, making a total of 114 patents processed in this manner. The National Institute of Industrial Property also created and published an information portal for COVID-19-related patents, featuring technologies and specific patent applications (Instituto Nacional da Propriedade Industrial, 2020).

In April 2020, the Russian Federation's Rospatent established a system to expedite COVID-19-related patent applications (FIPS, n.d.-a). In order to be considered, a patent application must be an antiviral drug or relate to diagnostic testing for viral disease, medical products, personal protective equipment or disinfecting materials. This system aims to issue the results of a first examination within two months. Additionally, Rospatent developed an information portal and launched it in May 2020. The portal features patent content fulfilling the same criteria that applies to the COVID-19 expedited examination program (FIPS, n.d.-b).

Throughout this period, the Japan Patent Office (JPO) has maintained an overarching focus on increasing the speed of review for all patent applications (JPO, n.d.). COVID-19 patent applications were not expedited through any special programs. Additionally, the JPO and the EPO issued a joint statement regarding their efforts on expediting examination through the Patent Prosecution Highway program (Japan Patent Office and European Patent Office, 2020).

Figure 6 highlights those countries whose patent offices offered time limit options to patent applicants at some point during the COVID-19 pandemic (WIPO, n.d.). Time limit provisions were not confined to COVID-19-related patent applications (WIPO, n.d.). Patent offices recognized the difficulties faced by many applicants, especially during periods when COVID-related restrictions were in operation. Those countries with more generalized time limit options are indicated in orange (Extended), those with case-by-case or request-basis time limit options indicated in gray (Potential for extension) and those with suspended or discontinued options indicated in blue (Suspended). Like Figure 5, this dataset has been collected from a combination of World Trade Organization data and WIPO data. There may be other countries with time limit options that were not disclosed in this manner.

Figure 6. **Patent offices that had time limit options available during the COVID-19 pandemic**
Many countries offered time limit options for patent applications during the COVID-19 pandemic to support patent applicants' intellectual property processes.

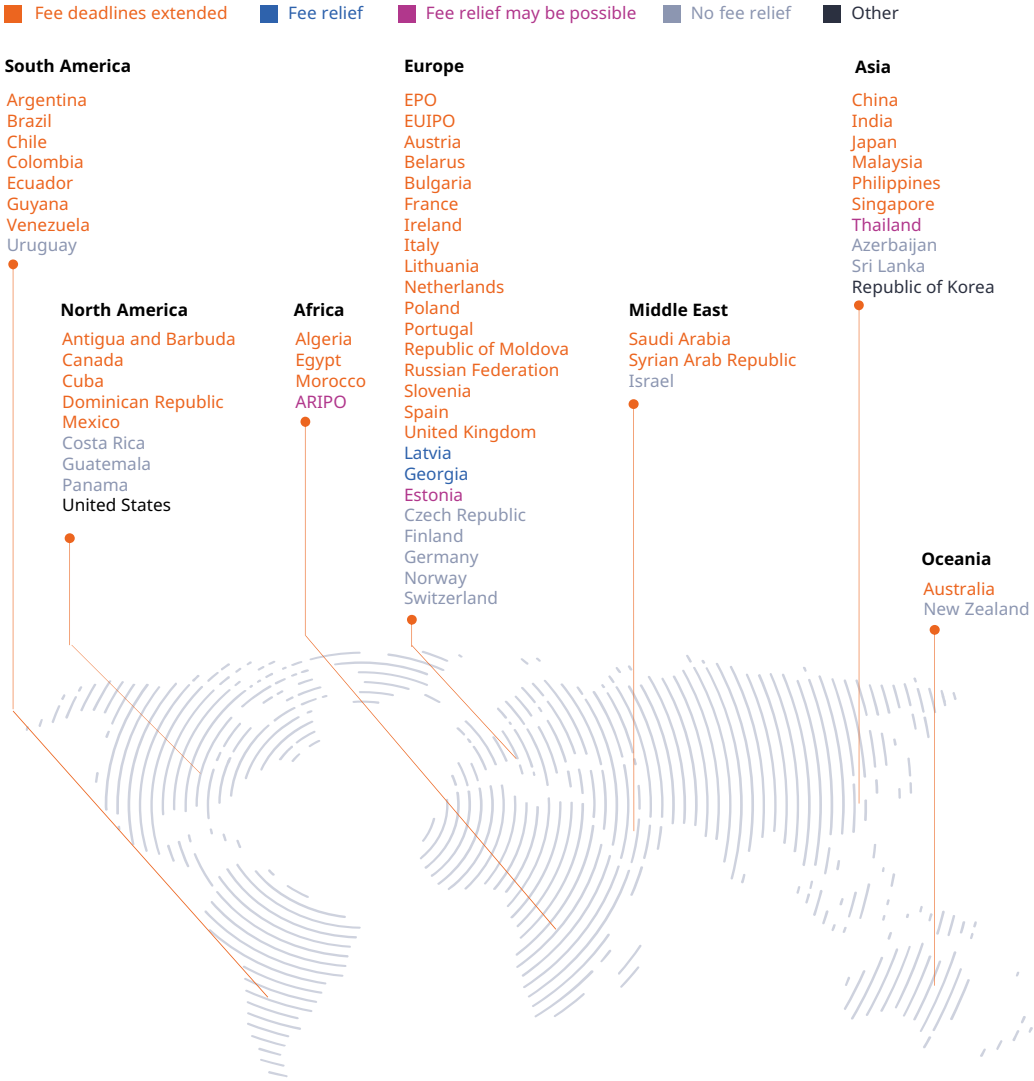
Note: ARIPO is the African Regional Intellectual Property Organization; BOIP is the Benelux Office for Intellectual Property (the Benelux countries are Belgium, Luxembourg and the Netherlands); EPO is the European Patent Office; EUIPO is the European Union Intellectual Property Office; OAPI is the African Intellectual Property Organization.

Source: Based on data from the World Trade Organization and the WIPO COVID-19 IP Policy Tracker, December 2022.

Figure 7 highlights those countries with fee relief options available for patent applicants at some point during the COVID-19 pandemic. Fee relief provisions were not confined to COVID-19-related patent applications. The patent offices recognized the financial difficulties and economic challenges applicants could encounter during this period. Fee relief provisions primarily included fee deadline extensions. Those countries with more generalized fee relief options are indicated in both orange (Fee deadline extensions) and blue (Fee relief). Countries with case-by-case or request-basis fee relief options are indicated in purple (Fee relief may be possible), and the countries reporting normal operations/no fee relief provisions indicated in gray (No fee relief). Like for Figures 5 and 6, this dataset is collected from a combination of World Trade Organization and WIPO data. There may be other countries with fee relief options that were not disclosed in this manner. Figure 7 excludes fee exemptions for expedited COVID-19-related patent applications.

Figure 7. Patent offices that had fee relief options available during the COVID-19 pandemic

Many countries offered fee relief options to patent applications during the COVID-19 pandemic in recognition of economic challenges while also supporting patent applicants' intellectual property processes.



Note: ARIPO is the African Regional Intellectual Property Organization; EPO is the European Patent Office; EUIPO is the European Union Intellectual Property Office

Source: Based on data from the World Trade Organization and the WIPO COVID-19 IP Policy Tracker, December 2022.

Licensing and other agreements related to COVID-19 vaccines and therapeutics

COVID-19's global impact was recognized by many governments, corporate entities, universities and research organizations, and non-governmental organizations. Many institutions came together during the pandemic to fund, develop, commercialize and supply diagnostics, protective equipment, vaccines and therapeutics.

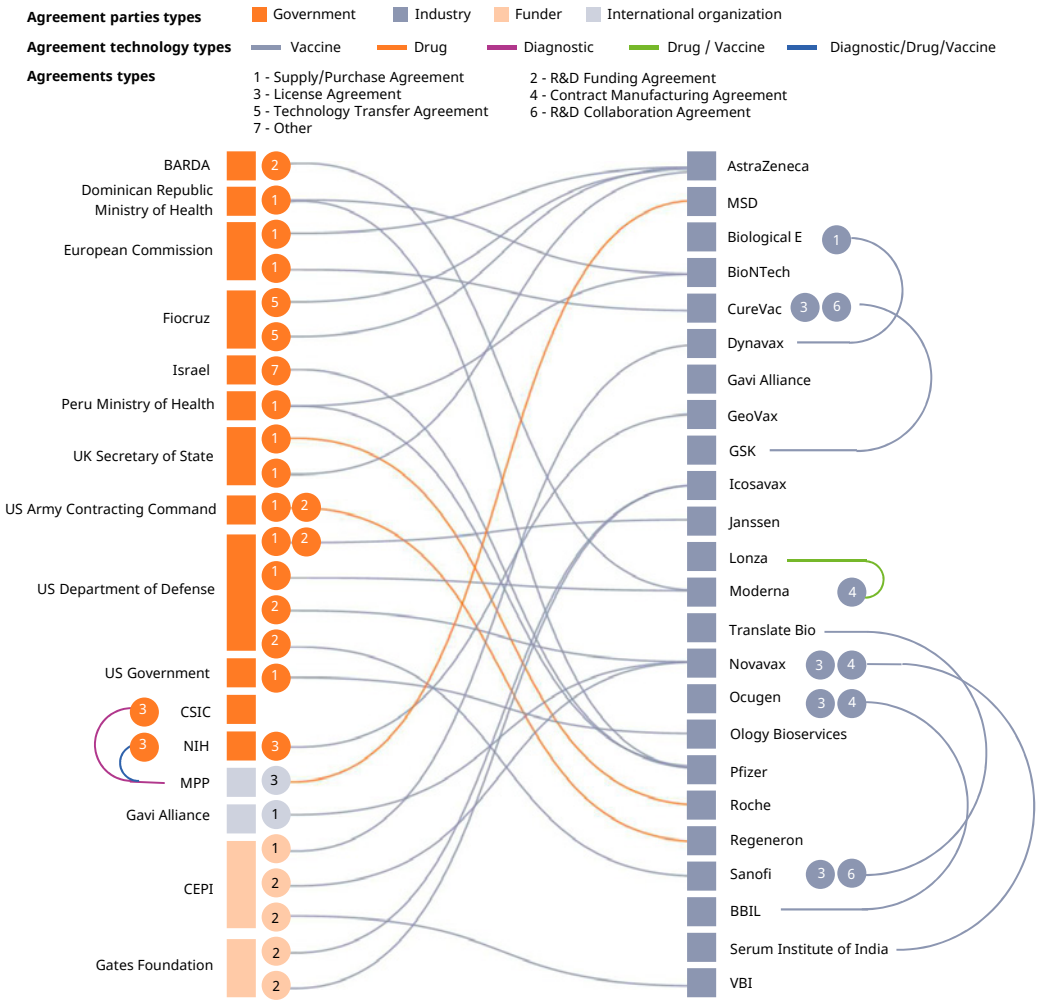
The Medicines Patent Pool (MPP), established in 2010 by Unitaid to increase access to and facilitate the development of life-saving medicines for low- and middle-income countries, expanded its mandate in early 2020 in response to SARS-CoV-2 and COVID-19 (MPP, n.d.). A detailed timeline of MPP activities and contributions from January 2020 through May 2022 can be found in Figure A1 in the Annex. Specific items from this timeline are discussed briefly hereafter.

In April 2020, MPP began working to leverage its expertise in licensing patented pharmaceuticals and technologies to support efforts to combat COVID-19 (MPP, n.d.). By October of 2020, MPP reported discussions were underway for the licensing of technologies and therapeutics (MPP, n.d.). In late 2021, MPP signed license agreements with two companies, Merck, Sharp & Dohme and Pfizer, for affordable access to COVID-19 therapeutics (MPP, n.d.). In early 2022, MPP signed agreements with generics manufacturers for the supply and production of COVID-19 therapeutics from originators Merck, Sharp & Dohme and Pfizer (MPP, n.d.).

The Global Healthcare Innovation Alliance Accelerator (GHIAA), a non-profit organization seeking to collect and provide global health agreements with a focus on agreements related to medical products access, has included COVID-19-related global health agreements in its Master Alliance Provisions Guide (MAPGuide) (GHIAA, n.d.-a). At the time of writing, GHIAA continues to seek the submission of agreements for its collection. In the COVID-19 section of the MAPGuide, a supply/purchase agreement is the most common type. This type of agreement is primarily between government and industry, ensuring the supply of vaccines. Data also include R&D funding agreements, license agreements, contract manufacturing agreements, technology transfer agreements and R&D collaboration agreements. Also to be found in the MAPGuide are funder–industry agreements, industry agreements and agreements with multilateral organizations (GHIAA, n.d.-b) (Figure 8).

Figure 8. Agreements for COVID-19-related technology

Funding, purchasing, licensing and R&D collaboration agreements for COVID-19-related vaccines, diagnostics and drugs among global government entities, industries and organizations.



Note: BARDA is the Biomedical Advanced Research and Development Authority; CEPI is the Coalition for Epidemic Preparedness Innovations; CSIC is the Consejo Superior de Investigaciones Científicas (Spanish National Research Council); NIH is the National Institutes of Health.

Source: WIPO, based on information from the GHIAA.

Discussions commenced at the 12th Ministerial Conference regarding proposals for extending the Decision's scope to cover the production and supply of COVID-19 diagnostics and therapeutics (WTO, 2022).

The WHO COVID-19 Technology Access Pool (WHO C-TAP) was launched in May 2020 (WHO, n.d.-i). The program's goal is to create affordable and faster access for all countries to COVID-19-related vaccines, therapeutics and other related health products. Governments and non-governmental organizations around the world have engaged in the program.

Disclosure of sequences within COVID-19 vaccine and therapeutics patents

Sequencing the SARS-CoV-2 genome in early 2020 was essential for the development of COVID-19 vaccines and identifying targets for therapeutics. Sequencing both the viral genes and the proteins that they encode was important in developing vaccines that stimulate the immune system effectively, treatments that inhibit the virus and diagnostic tests for detecting the virus.

Based on the CAS-related sequence indexing, approximately 29 percent of patent families in the overall COVID-19 dataset include biosequences that are claimed to be central to their novelty. Breaking this down by area, 76 percent of vaccine patent families and 16 percent of the therapeutics patent families include biological sequences. These include amino acid and nucleotide sequences related to vaccine development or the design of biologic drugs such as antibodies. Examples of patents in the dataset that disclose different types of biosequences are as follows.

- Patent applications CN113308493 and WO2021184987 (Guangzhou N Biomed Ltd.) disclose an S-protein-encoding nucleic acid sequence for use in adenovirus vector-based vaccines for SARS-CoV-2.
- Patent application KR2022014034 (Daegu Gyeongbuk Institute of Science and Technology) discloses a peptide that inhibits the ability of SARS-CoV-2 to interact with human angiotensin-converting enzyme 2 (ACE2) for use in diagnosing and treating coronavirus infection.
- Patent application WO2022117085 (Microbio (Shanghai) Co., Ltd, Oneness Biotech Co., Ltd.) discloses nucleic acid target sites for siRNA (small interfering RNA) in SARS-CoV-2 genes. The siRNAs are designed to treat COVID-19 infection.
- Patent application CN113234150 (Wuhan Frasergen Genomic Medicine Co., Ltd.) discloses a human immunoglobulin G1 single-chain antibody against SARS-CoV-2, for use in vaccine production and antibody drug development.
- Patent application WO2021245291 (Inotrem) discloses a peptide that inhibits TREM-1, which is involved in COVID inflammatory response. The peptide is for the treatment of severe SARS-CoV-2 infection with complications.
- Patent application WO2022203448 (Korea University Research and Business Foundation) discloses a siRNA designed to treat SARS-CoV-2 lung damage by targeting microRNA.
- Patent application WO2021252878 (Vir Biotechnology, Inc.) discloses anti-SARS-CoV-2 antibodies or antibody fragments, for treating SARS-CoV-2 infection.
- Patent application RU2730897 (Shemayakin-Ovchinnikov Institute of Bioorganic Chemistry *et al.*) discloses antigenic regions of SARS-CoV-2 Nucleoprotein (N) and S protein for use in assessing blood antibody levels and measuring immune response in infected patients.

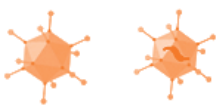
Some sequence listings disclosed by patent documents are fed into international collaborative platforms and repositories of sequence information, such as the International Nucleotide Sequence Database Collaboration (INSDC) and the EpiCoV platform of the Global Initiative on Sharing Avian Influenza Data (GISAID), by relevant patent offices or researchers (INSDC, n.d.; GISAID, 2022). Such international information sharing arrangements for the rapid exchange of sequences proved critical to the successful and swift global pandemic response and facilitated the development of vaccines and therapeutics (GISAID, 2022).

COVID-19 vaccines

Background – vaccine platforms

Like other coronaviruses, the SARS-CoV-2 virus mutates frequently. As variants emerge and are classified as variants of concern (VOCs), effective vaccination becomes vitally important. Since the COVID-19 pandemic began, various vaccine platforms have been explored for vaccine development. They range from conventional vaccine platforms, such as whole-virus vaccines (live attenuated and inactivated vaccines) and protein-based vaccines (virus-like particles and protein subunit vaccines), to novel platforms, such as viral vector-based vaccines, nucleic acid (DNA and RNA)-based vaccines and antigen-presenting cells, the last of which having little pre-existing data on safety and efficacy in humans (Li, Tenchov *et al.*, 2021). Table 6 summarizes the vaccine platforms. A more in-depth discussion of vaccine platforms can be found in the first WIPO COVID-19 Patent Landscape Report (WIPO, 2022). No new vaccine platforms have been identified in the dataset for this report.

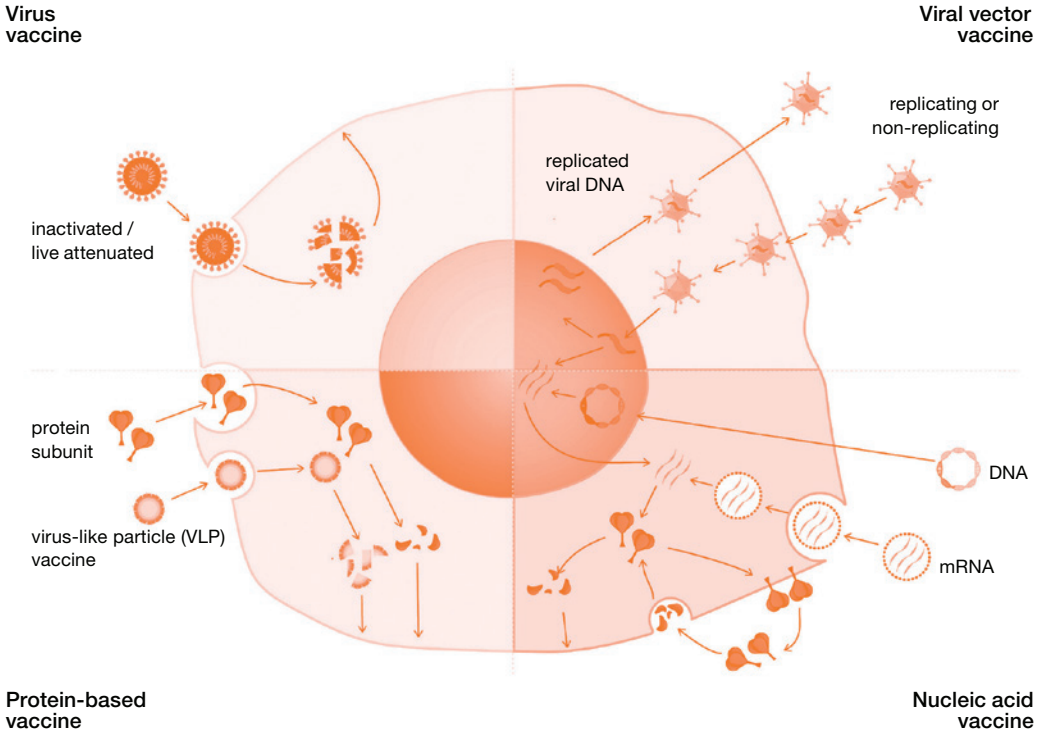
Table 6. Categories of COVID-19 vaccine platform

Conventional	
Protein-based 	Viral proteins or antigens used to stimulate an immune response Example: Novavax, Sanofi Pasteur/GSK, Dynavax, Vaxine Pty vaccines
Virus-like particle 	Protein structures that closely resemble viruses, but are non-infectious, because they contain no viral genetic material Example: Medicago Inc./GSK vaccine
Inactivated 	Vaccine consisting of pathogens (virus particles, bacteria) grown in culture and then killed, so as to destroy their disease-producing ability Examples: Sinovac, Sinopharm, Bharat Biotech vaccines
Live attenuated 	Vaccine comprising a pathogen with reduced virulence ("live"), so that it becomes harmless or less virulent, stimulating a strong, effective and long-lasting immune response Example: Codagenix (Serum Institute of India)
Novel	
Nucleic acid  DNA RNA	Pieces of DNA or mRNA that encode viral proteins or antigens and depend on the host's cells to produce the corresponding proteins to stimulate an immune response Examples: Moderna, Pfizer/BioNTech, Zydus Cadila Healthcare, Inovio Pharmaceuticals vaccines
Virus vector  Non-replicating Replicating	Like nucleic acid platforms, viral vectors encode proteins or antigens and depend on the host's cells to produce these proteins to stimulate an immune response. They are usually based on a modified and harmless version of a different virus, such as adenovirus Examples: AstraZeneca/Oxford University, Johnson & Johnson, CanSino Biologics, Gamaleya Research Institute vaccines
Antigen-presenting cell 	Immune cells that mediate the immune response by presenting antigens for recognition by the host's lymphocytes

Source: WIPO.

Each vaccine platform elicits a different immune response as shown in Figure 9. Inactivated vaccines provide a broad spectrum of protein antigens, whereas protein-based vaccines produce antigens specific to components of the virus. Protein antigens produced from both platforms stimulate a humoral (antibody-mediated) immune response. Interestingly, viral vector vaccines and nucleic acid-based vaccines deliver protein antigen-encoding genes to cells, which subsequently produce the desired antigens and potentially elicit both humoral and cellular (cell-mediated) immune responses (Li, Tenchov *et al.*, 2021).

Figure 9. Vaccine platforms and the ways in which they produce immunogens in cells



Source: Adapted, with permission, from Li, Tenchov *et al.*, 2021.

A detailed discussion of the patent landscape related to COVID-19 vaccines now follows. Information about COVID-19 vaccine clinical trials can be found in the Annex.

Speed of vaccine development

In the early stages of the pandemic, the scientific research community, world leaders and global patent offices responded with urgency, by accelerating vaccine development and associated patent activity. On average, vaccine development takes five to 10 years. However, after the emergence of COVID-19, vaccine development accelerated at an unprecedented rate. Within 11 months of the virus sequence being published, three vaccines were granted emergency use authorization (EUA) or some other form of advanced approval in the United States, Europe and the United Kingdom (UK) (Milken Institute, n.d.-b). There are currently an additional 11 vaccines with an emergency use listing with the WHO and dozens more in various stages of development and clinical trial (Milken Institute, n.d.-a). According to the WHO's vaccine tracker (WHO, n.d.-c), as of December 2022, 230 vaccines were in clinical development. Of those, 92 were in Phase 3 trials and 138 in either Phase 1 or 2 trials. A further 50 vaccines have been approved by various governing bodies around the globe.

There are several ways in which vaccine development for COVID-19 has been accelerated. Years of vaccine research into other respiratory viruses was leveraged to jump start the search for effective COVID-19 vaccines. Collaborative research was facilitated by tracking vaccine candidates globally and encouraging open discourse between researchers, vaccine developers and regulatory organizations. The WHO, among other organizations, coordinated clinical trials across the world to help accelerate regulatory action. The clinical trial process itself evolved to support faster delivery of effective vaccines. In many cases, Phase 1 trials were completed in

just two months, by allowing vaccine doses to be administered within a relatively short period, often no more than three to four weeks apart (Johns Hopkins University, n.d.). Furthermore, some COVID-19 clinical trials combined Phases 1 and 2, and others combined Phases 2 and 3 (Johns Hopkins University, n.d.). Owing to the high rates of COVID-19 infection during the pandemic, the number of people who could be monitored for disease risk was enormous, which made it easier to identify differences in disease risk between those who had received a vaccine and those who had received a placebo or comparative vaccine. This allowed vaccine efficacy to be determined at a relatively accelerated pace (Johns Hopkins University, n.d.). Lastly, several governments around the world accelerated investment into the manufacturing capacity needed to produce large quantities of vaccine doses before the full results of Phase 3 clinical trials were available (Johns Hopkins University, n.d.).

A global discussion on when COVID-19 is likely to become endemic has already begun and with it the pace of research, vaccine development and patent filing activity has slowed relative to the start of the pandemic (see Figure 3). While research continues, including new and ongoing clinical trials, the associated patent filing activity appears to be returning to how it was pre-pandemic.

Vaccine patent landscape

For this report, we have considered all patent filings related to COVID-19 vaccines. To compile Table 7, each patent office where patent protection was sought by every patent family was counted once (see Annex for an in-depth discussion of patent families). Analysis by patent office revealed that WIPO's PCT system received the most COVID-19-related vaccine patent applications, followed by the China National Intellectual Property Administration (CNIPA), the United States Patent and Trademark Office (USPTO) and the European Patent Office (EPO). This is in contrast with the first WIPO COVID-19 Patent Landscape Report which considered all COVID-19-related vaccine patent applications from January 2020 through September 2021. During that period, CNIPA received the most patent applications, followed by WIPO, USPTO, Rospatent (the Federal Service for Intellectual Property of the Russian Federation) and the EPO. WIPO's current top ranking is likely to be an indication that patent applicants are leveraging the WIPO/PCT system in order to protect their inventions across multiple jurisdictions.

Table 7. Distribution of COVID-19 vaccine patent applications across patent offices
Applications related to COVID-19 vaccines were filed at 30 patent offices. WIPO and CNIPA received the most applications, followed by the USPTO, the EPO and others.

Patent offices of filing for COVID-19 vaccines	Number of patent applications
WIPO	847
China	589
US	198
EPO	128
Republic of Korea	83
Canada	72
India	65
Australia	64
Russian Federation	49
Japan	31
UK	11
Germany	10
Argentina	10
France	6
Colombia	5
Spain	4

Source: WIPO, based on patent data from the CAS Content Collection, September 2022.

With regard to applicant location (Table 8), applicants from China accounted for the highest number of patent applications, followed by those from the United States, Germany, the Republic of Korea and the Russian Federation. The United Kingdom, Japan, India, France, Canada, Switzerland, Israel, Australia, Belgium and Italy rounded out the top 15 applicant origins.

Table 8. Distribution of COVID-19 vaccine patents across applicant location
Most patent applications were filed by patent applicants in China and the United States.

Patent applicant location	Number of patent families
China	573
US	356
Germany	57
Republic of Korea	56
Russian Federation	48
UK	35
Japan	30
India	25
France	24
Canada	20
Switzerland	13
Israel	12
Australia	10
Belgium	10
Italy	10
Austria	8

Source: WIPO, based on patent data from the CAS Content Collection, September 2022.

Applicants in different regions adopted different patent filing strategies during the course of the pandemic. From January 2020 through September 2021 – the period of the first report – patent applicants in China almost exclusively filed their patent applications at CNIPA, with a few exceptions also filing at the USPTO and the EPO (WIPO, 2022). However, during the period covered by this report, extending through September 2022, a much higher percentage of China-based applicants filed their patent applications at WIPO/PCT (Figure A2). Filings made from October 2021 through September 2022 indicate a greater interest more recently by Chinese applicants in seeking patent protection for their inventions across multiple jurisdictions. US-based applicants, on the other hand, continued to file mainly PCT and USPTO applications throughout the pandemic. Diverse filing strategies are seen for applicants based in other countries.

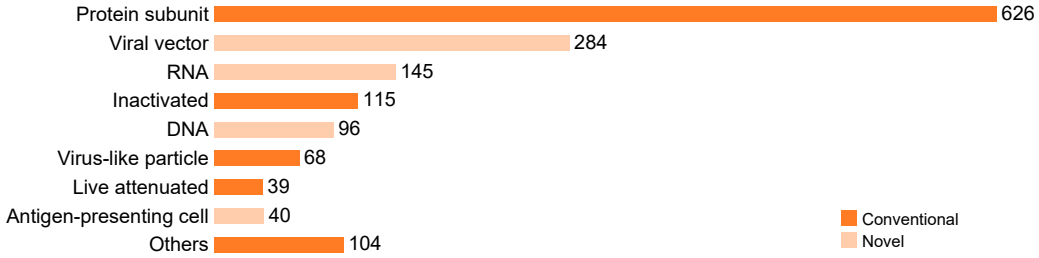
Similar trends are seen in the top applicant locations compared to the top offices of filing, but with major differences lower down the ranking. These differences are likely to be a result of different applicant filing strategies. Figure A2 further illustrates where applicants from different origins filed their applications.

Vaccine patent distribution by vaccine platform and published applicant location

A total of 1,331 patent documents related to COVID-19 vaccine development published up until September 30, 2022, were identified and analyzed. They included a wide variety of vaccine platforms, ranging from conventional platforms, such as protein subunit, inactivated virus, virus-like particle (VLP) and live attenuated virus platforms, to more innovative ones, such as viral vector-based, nucleic acid-based (DNA and RNA based vaccines) and antigen-presenting cell (APC)-based platforms (Figure 10).

Figure 10. Distribution of COVID-19-related patent applications across vaccine platforms, earliest published month between January 2022 and September 2022

Nearly half (47 percent) of the vaccine patent dataset related to protein subunit vaccines (conventional vaccine platform), followed by patent filings related to viral vector vaccines (novel vaccine platform), which accounted for almost one-quarter (21 percent) of the vaccine patent dataset.



Source: WIPO, based on patent data from the CAS Content Collection, September 2022.

Across platforms, protein subunit vaccine-related patent filings constituted the largest category (626, 47 percent), followed by viral vector (284, 21 percent), RNA (145, 11 percent), inactivated (115, 9 percent), DNA (96, 7 percent), VLP (68, 5 percent) and APC-based vaccine development (40, 3 percent).

In addition, 39 patent filings related to live attenuated vaccines and 104 patent filings classified as "other" included technologies related to nanoparticles, adjuvants, etc. It was observed that some patent applications claimed more than one type of platform and therefore counted in all the related platforms categories covered in Figure 3.

There was a substantial growth in interest around producing vaccines that incorporate novel technologies related to nanoparticles later on in the period covered by the dataset. Nanoparticle use in SARS-CoV-2 vaccines provides distinct advantages as they have proven to be suitable delivery vehicles and adjuvants (Huang *et al.*, 2022). Several of the nanovaccines disclosed in the vaccine dataset use coronavirus spike protein comprising ferritin nanoparticles, which has a higher stability and expression level compared to non-modified coronavirus spike protein. Ferritin, a unique iron-binding protein, can play an important role in COVID-19 vaccine delivery and elicit neutralizing antibody responses against SARS-CoV-2 (Powell *et al.*, 2021). Nearly 60 nanovaccine candidates were recently in various pre-clinical stages, and approximately 26 nanoparticle-based COVID-19 vaccines undergoing human clinical trials (Rauf *et al.*, 2022). Examples include:

- Patent application WO2022087255 (La Jolla Institute for Immunology) discloses a mutant coronavirus S protein, polymeric and ferritin-based nanoparticles that have a higher stability or a higher level of expression when compared to a non-modified coronavirus spike protein.
- Patent application WO2022027702 (Guangzhou Qianyang Bio-Technology Pharmaceutical Co., Ltd.) discloses a *Helicobacter pylori* ferritin-based novel coronavirus S protein subunit nanovaccine able to significantly improve a host's level of neutralizing antibody against the virus, thus preventing the virus from invading a target cell.
- Patent application WO2022177990 (Emergent Product Development Gaithersburg Inc.) discloses methods for engineering SARS-CoV-2 S protein and *Helicobacter pylori* ferritin fusion proteins for self-assembly into nanoparticle compositions for use in vaccines, as well as use of the antibodies created by such a vaccine in the prevention or treatment of SARS-CoV-2 infection.

Several other patent applications disclose a nucleic acid vaccine, comprising a sequence encoding a SARS-CoV-2 S protein and a lipid nanoparticle vaccine delivery method. Lipid nanoparticles offer a wide spectrum of advantages in comparison to other nanocarriers. They include greater stability, lower cost and the possibility of large-scale industrial manufacturing. Recent lipid nanoparticles usage in the development of the BNT162b2 (Pfizer-BioNTech) and mRNA-1273 (Moderna) vaccines, which have an unrivalled effectiveness in preventing COVID-19 disease, demonstrate a potential application for lipid nanoparticles in the delivery of nucleic acid-based vaccines (Wilson and Geetha, 2022). Examples include:

- Patent application WO2022155530 (ModernaTX, Inc.) discloses methods for engineering SARS-CoV-2 mRNA expressing strain-based S protein variants in lipid nanoparticle formulations and their use in mRNA vaccines.
- Patent application WO2022101469 (BioNTech SE) discloses technologies related to the stabilization of lipid nanoparticle mRNA compositions, including vaccines.
- Patent applications WO2022129918 (Imperial College Innovations Limited) and WO2022110099 (Guangzhou Argorna Biopharmaceuticals Co., Ltd.) disclose novel uses of and methods for thermally stabilizing RNA vaccine formulations, including self-amplifying RNA replicons and genetic constructs encoding such replicons.
- Patent application WO2022099003 (Sanofi) discloses lipid nanoparticles for delivering chemically-modified mRNA that encode hemagglutinin antigens and/or neuraminidase antigens.

Numerous patent applications published in 2022 focus on adjuvants for virus vaccines, where an adjuvant system might be composed of fungal polysaccharides, endogenous proteins or injectable micro-nanostructures that can act as immunomodulatory agents in the prevention of COVID-19 infection. Further discussion of vaccine adjuvant development can be found below.

Some of the vaccines described in the dataset are designed to target not only the SARS-CoV-2 virus, but also influenza viruses, cancer, allergies, bacterial infections and other infectious diseases. Among them are:

- Patent application WO2022011031 (Amyris, Inc.) discloses the synthesis and use of adjuvants in vaccines for diseases caused by viral or bacterial infection.
- Patent application EP4056579 (Institute of Organic Chemistry and Biochemistry AS CR, V.V.I.) discloses 3′3′ cyclic dinucleotides containing isonucleotidic units and their pharmaceutically acceptable salts for the treatment or prevention of diseases or conditions modifiable by STING protein modulation.
- Patent application WO2022013277 (Evaxion Biotech A/S) discloses methods and products for treating cancer and infections with microorganisms via the administration of specific fusion polypeptides or nucleic acids encoding such fusion polypeptides.

Patent applications related to VLP (virus-like particle) and APC (antigen-presenting cell) vaccine development overtook those of live attenuated vaccines in 2022. Companies designing COVID-19 vaccines are also shifting their focus to rapid, efficient and low-cost synthetic vaccinations. For example, cost-effective vaccine inventions are explored in two patent applications made in the United States (Patent application WO2022061264, University of Georgia Research Foundation, Inc.; Patent application WO2022155476, United States Dept. of Health and Human Services). Overall, APC and VLP vaccine inventions are being designed to protect against SARS-CoV-2 infection, prevent virus transmission and for prophylaxis and/or the inhibition of COVID-19 infection.

Applicant locations for SARS-CoV-2 vaccine patent filings have increased from 21 to 24 since the first COVID-19 Patent Landscape Report, with the addition of Argentina, Colombia and Iceland. However, China, the United States, Germany, the Republic of Korea, the Russian Federation and the United Kingdom remain the leading applicant locations for COVID-19 vaccine development, together accounting for over 80 percent of the vaccine patent dataset (Table 8). Applicants based in China filed 573 patents, those in the United States filed 356 applications, in Germany 57 applications, in the Republic of Korea 56 applications and in the Russian Federation 48 patent applications (Table 8). Vaccine patent application content analysis reveals that many patent filings included more than one vaccine platform. Table 9 shows the spread of patent applications across specific vaccine platforms. A total of 269 patent applications originating from China contained the protein subunit vaccine platform, significantly more than viral vector (134) and other types of platform. Patent applicants based in the United States, Germany, the Republic of Korea, and the United Kingdom demonstrated a similar pattern to those based in China, with the protein subunit vaccine platform found in 166, 26, 38 and 15 patent applications, respectively. However, patent applicants based in the Russian Federation demonstrated a different trend, with the viral vector vaccine platform contained most often in patent applications followed by protein subunit.

Table 9. Distribution of COVID-19 vaccine patent applications across vaccine platforms and patent applicant locations

While China and US-based applicants filed patent applications across different vaccine platforms, including adjuvants and technologies related to nanoparticles, applicants from Germany, the Republic of Korea, the United Kingdom, Japan and others focused on protein subunit, viral vector and RNA vaccine platforms. Russian Federation applicants filed mainly in the field of viral vector vaccines.

	Vaccine platforms								
Patent applicant location (country)	Protein subunit	Inactivated virus	Virus-like particles	Live attenuated virus	Viral vector	RNA-based	DNA-based	Antigen-presenting cell	Other
China	269	55	25	19	134	65	46	22	39
US	166	25	21	11	61	53	22	10	42
Germany	26	5	1	0	14	14	1	1	3
Republic of Korea	38	1	0	1	9	3	3	0	3
Russian Federation	15	2	2	1	25	1	4	0	0
UK	15	0	7	0	9	4	4	0	5
Japan	20	2	0	1	4	2	2	0	3
India	9	8	2	3	5	0	1	0	4
France	10	1	1	1	9	2	2	0	2
Canada	8	2	3	1	5	1	3	0	1
Switzerland	7	0	3	0	1	0	2	1	1
Israel	11	2	0	1	1	0	0	0	0
Australia	6	1	0	1	2	0	0	1	0
Belgium	4	0	1	0	1	4	1	0	2
Italy	6	0	0	0	0	1	2	0	3

Note: The data are not additional to the number of patent applications for each location but included within the total number of applications filed with overlaps between vaccine platforms.

Source: WIPO, based on patent data from the CAS Content Collection, September 2022.

On closer inspection, the distribution of vaccine patents by geographical region shows that almost 98 percent of patents originated from applicants in Asia, North America and Europe. Applicants from other regions of the world, namely, Africa, the Middle East, Oceania and South America, contributed less than 3 percent to the vaccine patent pool (Table 10).

Table 10. Regional distribution of COVID-19-related patent applications across vaccine platforms

Applicants based in Asia, North America and Europe together filed nearly 98 percent of vaccine patent applications across the different vaccine platforms.

	Vaccine platforms								
Patent applicant location (region)	Protein subunit	Inactivated virus	Virus-like particles	Live attenuated virus	Viral vector	RNA-based	DNA-based	Antigen-presenting cell	Other
Africa	3	0	0	0	1	0	1	0	0
Asia	349	73	28	26	156	71	52	22	52
Europe	106	16	20	4	62	27	18	7	24
Middle East	12	2	0	1	1	0	1	0	0
North America	179	27	25	12	66	55	25	10	44
Oceania	6	1	0	1	2	0	0	1	0
South America	2	1	0	3	2	0	0	0	0

Source: WIPO, based on patent data from the CAS Content Collection, September 2022.

Vaccine patent applicant collaborations

Patent collaborations come within the scope of this report. The WHO C-TAP program has been discussed briefly in the section on Licensing and other agreements related to COVID-19 vaccines and therapeutics. However, there are studies focusing on collaboration efforts that leverage methods beyond patent filings. For example, partnerships have been studied by evaluating the developers listed for vaccines registered with the WHO (Druedhal *et al.*, 2021). This section focuses more on patents identified in the vaccine dataset. From the vaccine dataset, nearly one-quarter (24 percent) of patents had more than one patent assignee. Moreover, the majority of collaborations on patent filings were a combination of universities and research institutes and corporate entities.

Those organizations that collaborated most frequently are presented in Table 11. For vaccine-related patents, there is no clear pattern of consistent collaboration between organizations. The two organizations that collaborated the most are Liaoning Chengde Biotechnology Co., Ltd. and Tsinghua University as shown in Figure 11.

Table 11. **Top patent applicant collaborators in COVID-19 vaccine patent applications**
Organizations with the most collaborations on patent filings in COVID-19 vaccine were a combination of universities and research institutions and corporate entities.

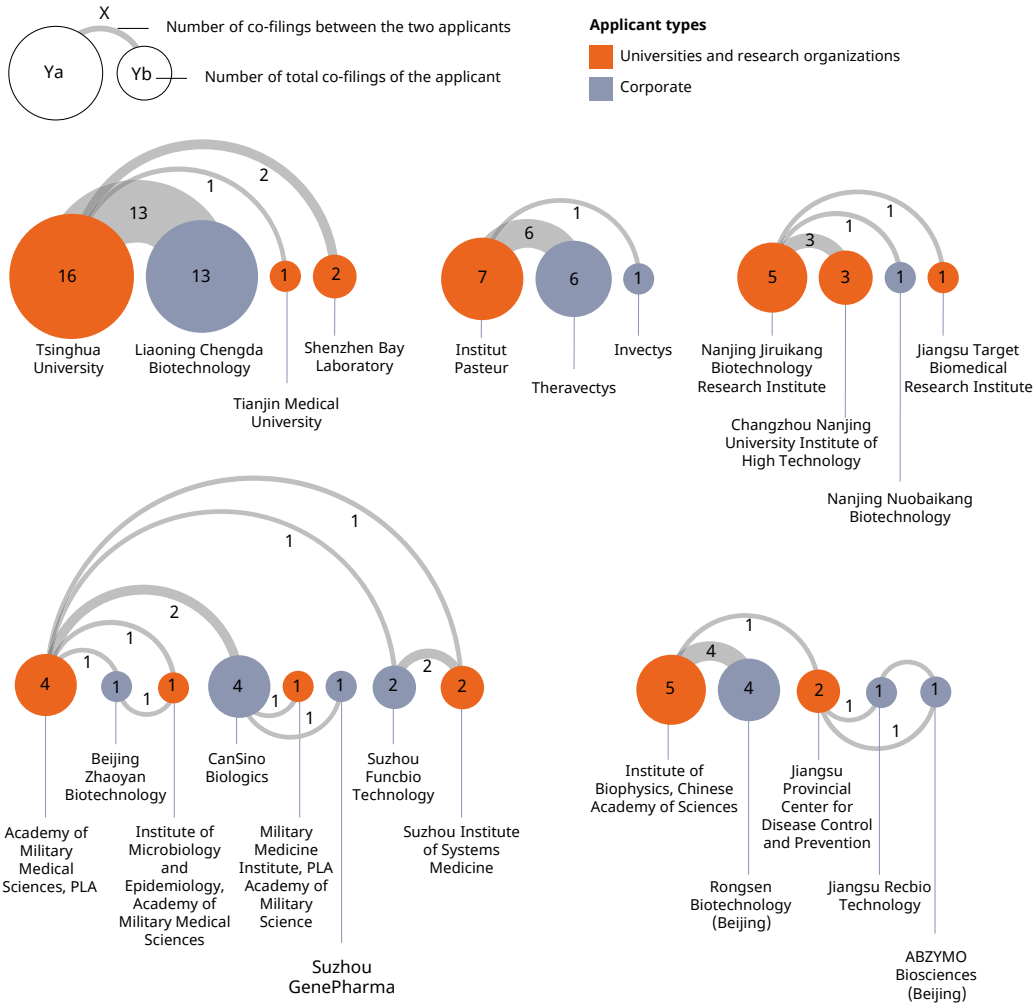
Patent applicant name	Total collaborations in vaccine (number of patent families)
Tsinghua University	16
Liaoning Chengda Biotechnology Co., Ltd.	13
Institut Pasteur	7
TheraVectys	6
Institute of Biophysics, Chinese Academy of Sciences	5
Nanjing Jiruikang Biotechnology Research Institute Co., Ltd.	5
Academy of Military Medical Sciences, PLA	4
CanSino Biologics Inc.	4
Rongsen Biotechnology (Beijing) Co., Ltd.	4

Note: The table lists top patent applicant names in the vaccine dataset having more than one entity as a patent applicant. They were identified using patent applicant names and number of times a pair was found together in the vaccine dataset. In this approach, a single patent in the dataset may be counted more than once, depending on the number of patent applicants.

Source: WIPO, based on patent data from the CAS Content Collection, September 2022.

Figure 11. **Network analysis of the top collaborating entities in COVID-19 vaccine patent applications**

Among COVID-19 vaccine patents, Chinese companies and research institutions show greatest cooperation, followed by French corporates and research institutions.



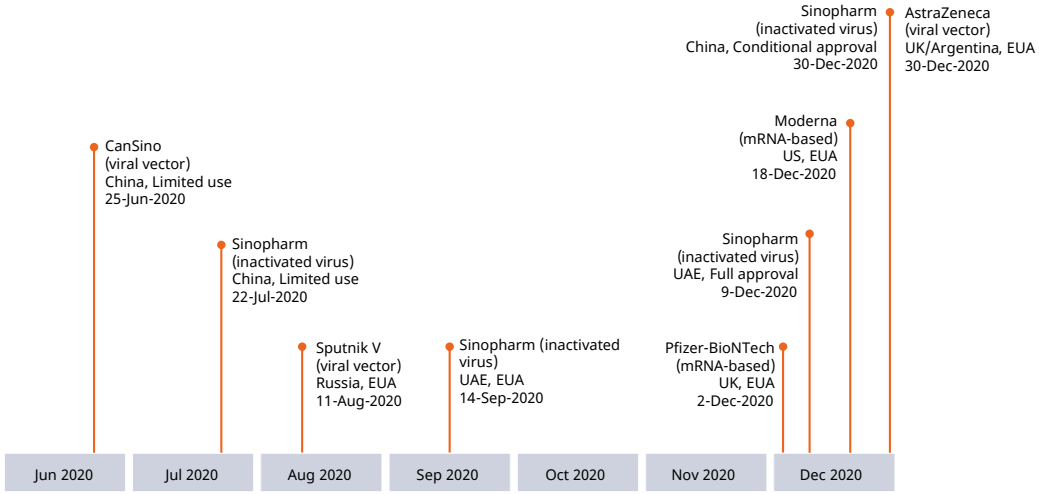
Note: The chart illustrates the relationships between collaborators and their frequency as shown by the size of the circles. In some cases the sum of co-filed patent applications marked on the lines connecting a particular applicant to other applicants may exceed the actual number of co-filed patent applications filed by that particular applicant. This is because some patent applications are filed jointly by three or more applicants.

Source: WIPO, based on patent data from the CAS Content Collection, September 2022.

Vaccine authorization and development of key technologies

Since the beginning of the COVID-19 pandemic, various vaccine platforms have been explored for vaccine development, with several vaccines having received authorization in some form by the end of 2020. Figure 12 shows the timeline for major milestones related to initial COVID-19 vaccine authorization and approval in 2020.

Figure 12. Authorization timeline for the first COVID-19 vaccines approved for use in humans



Note: EUA is emergency use authorization; UAE is the United Arab Emirates.
Source: WIPO, based on data from Zimmer *et al.*, 2022 and Pinghui, 2020

Decades of vaccine research into coronaviruses and other respiratory diseases facilitated the rapid development of vaccines for COVID-19. The first approved vaccine, CanSino, was a viral vector vaccine that came from China. It was approved on June 24, 2020, for limited use in the Chinese military and in high-risk occupations, for example, for frontline health workers, border officials and overseas workers (Pinghui, 2020). In July, China authorized another vaccine, an inactivated virus vaccine from Sinopharm, also for limited use in high-risk occupations. Throughout the next few months, the Sinopharm vaccine received additional EUA in other countries. Russia first granted emergency use approval for the adenovirus viral vector vaccine, Sputnik V, on August 11, 2020 (Kramer, 2020). It was not until December 2020 that mRNA vaccines received authorization. On December 2, 2020, the United Kingdom granted the Pfizer–BioNTech mRNA vaccine its first EUA. A fortnight later, the United States granted the Moderna mRNA vaccine its first EUA on December 18, 2020 (Thomas *et al.*, 2021; USFDA, 2020). The AstraZeneca vaccine was granted its first EUA in the United Kingdom and Argentina on December 30, 2020.

The first vaccine to receive full approval was the Sinopharm vaccine, which was granted on December 9, 2020, by the United Arab Emirates. By the end of 2020, many countries, as well as the European Union, had authorized or approved vaccines (European Commission, 2021). Additional authorizations and full approvals followed in 2021 and 2022 for these and other vaccines, such as Janssen (USFDA, 2022d), Novavax (USFDA, 2022e), Valneva (European Medicines Agency, 2022a), VidPrevtyn Beta (European Medicines Agency, 2022b). More information on vaccine authorizations can be found on the WHO website (WHO, 2023).

A broader discussion related to the timeline of the vaccine technology that enabled COVID-19 vaccine development can be found in the first WIPO COVID-19 Patent Landscape Report (WIPO, 2022). Some of the more recent noteworthy advancements in COVID-19 vaccine development are as follows.

The advancement of nucleic acid-based vaccine technologies has been essential to the COVID-19 vaccine landscape. The use of mRNA has several significant advantages over other vaccine technologies in terms of safety, efficacy and production, despite its need for storage at below-freezing temperature. Since mRNA is a non-infectious, non-cell platform there is no potential risk of insertional mutagenesis. Also, mRNA is degraded by normal cellular processes and its half-life in the human body can be regulated through various modifications. A variety of modifications make mRNA stable and highly translatable and thus highly efficient. Moreover, mRNA vaccines can be rapidly produced, and their manufacturing relatively easily scaled up. Several patents in the dataset outline advancements related to this technology. Among them are:

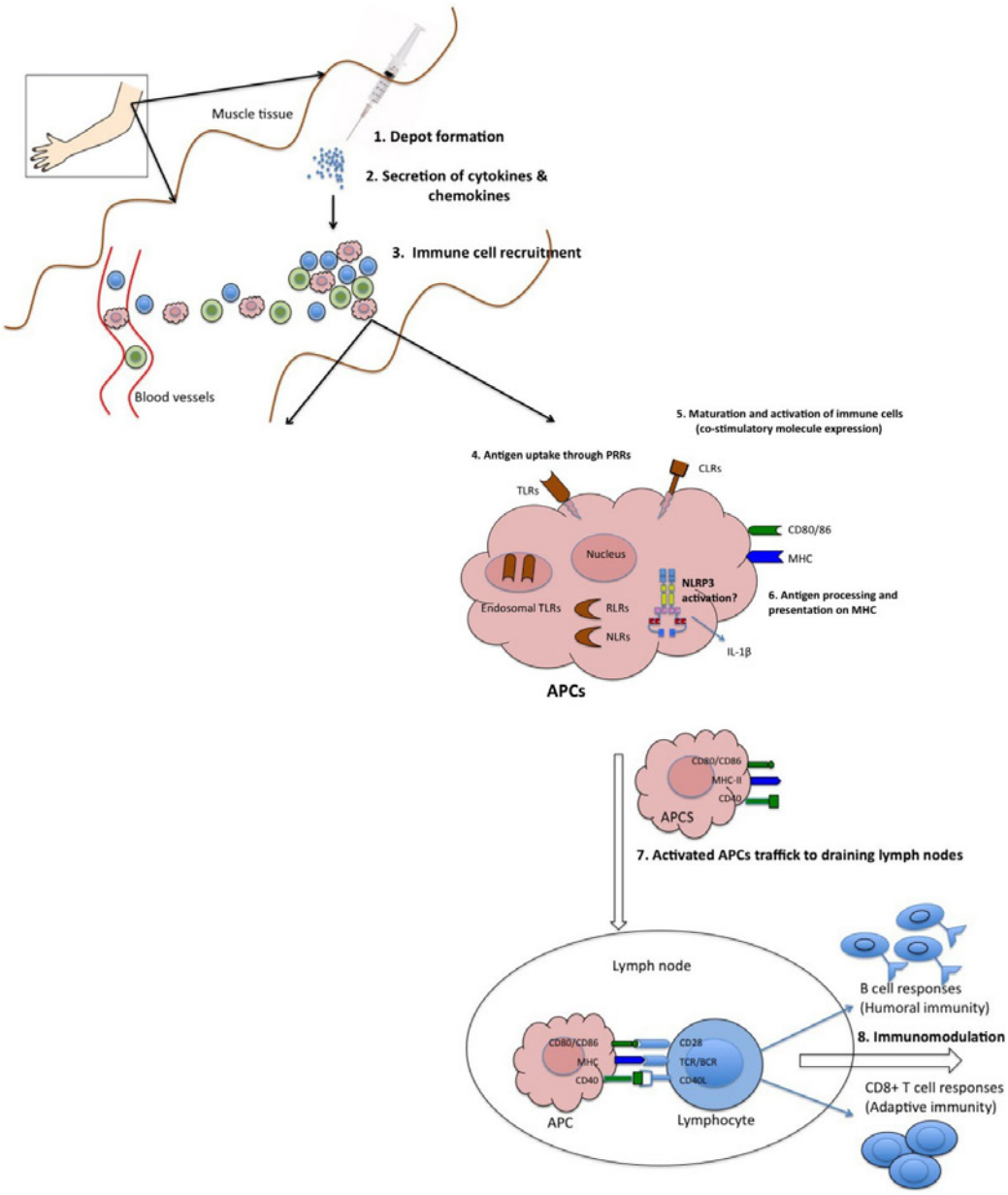
- Patent application WO2022067010 (ModernaTX, Inc.) discloses mRNAs encoding variants of highly immunogenic SARS-CoV-2 S protein antigens capable of producing powerful neutralizing antibody and immune cell responses against SARS-CoV-2.
- Patent application WO2022043551 (CureVac AG) discloses multivalent nucleic acid-based coronavirus vaccines comprising nucleic acid-encoding antigenic peptide or protein selected or derived from a coronavirus membrane protein (M), nucleocapsid protein (N), non-structural protein and/or accessory protein; the composition may additionally comprise nucleic acid encoding a coronavirus S protein. The compositions are in association with a polymeric carrier, a polycationic protein or peptide or a lipid nanoparticle.
- Patent applications WO2022155530 and WO2022155524 (ModernaTX, Inc.) disclose vaccines comprising a nucleic acid that encodes a SARS-CoV-2 S protein, or a 2P stabilized spike antigen of a second circulating SARS-CoV-2 virus, wherein the subject has previously been administered a first vaccine comprising a nucleic acid encoding a first SARS-CoV-2 2P stabilized spike antigen of a first circulating SARS-CoV-2 virus, and wherein each of the first and second 2P stabilized spike antigens are administered in an effective amount to induce an immune response specific for both antigens.
- Patent applications WO2022101469 and WO2022101470 (BioNTech SE) disclose highly stable lipid nanoparticle mRNA carrier compositions having an improved RNA integrity after a freeze-thaw cycle. The formulation includes cationically ionizable lipid, RNA and aqueous phases comprising a specific buffer system providing improved stability and a ready-to-use composition that can be stored at a temperature range compliant with regular technologies in pharmaceutical practice. Lipid nanoparticle (LNP)-formulated mRNA vaccines are currently considered the most promising and innovative COVID-19 vaccine approach.

Vaccine adjuvant development

Adjuvants contribute to the prophylactic and therapeutic efficacy of vaccines. These agents are structurally diverse and have been shown to enhance immune response to vaccines through several mechanisms, including through decreasing the amount of antigen required for eliciting immunity, leveraging cytokines and chemokines to recruit white blood cells, and activating helper T-cells (a special type of immune cell) to assist in antibody production (Figure 13).

Figure 13. Adjuvant impact on vaccine efficacy

The addition of an adjuvant enhances innate, T-cell, B-cell and memory cell immune responses to vaccines.



Source: Awate *et al.*, 2013.

A more detailed discussion of the general history of vaccine adjuvant development can be found in the first WIPO COVID-19 Patent Landscape Report (WIPO, 2022).

Most COVID-19 vaccines employ adjuvants that are exogenous materials and have existing clinical approval (i.e., aluminum salts, MP59, saponin mixtures and CpG oligonucleotides). However, newer research has shown that some adjuvants can be incorporated directly into vaccine formulations. The adjuvants in question include nucleic acids, lipids, lectins and pathogen-associated molecular patterns (PAMPs) and danger-associated molecular patterns (DAMPs). Interestingly, the functionality of some of these built-in adjuvants, such as PAMPs and DAMPs, is mediated by host receptors. In light of this, synthetic agents targeting those receptors are being developed so as to improve the adjuvanticity of these agents.

Examples of adjuvants used in publicly available COVID-19 vaccines include:

- Aluminum salt (alum) – used in BBIBP-CorV, CoronaVac vaccines (inactivated SARS-CoV-2 virus vaccines) (Xia *et al.*, 2021; Pulendran *et al.*, 2021).

- Matrix-M/IscoMatrix – comprising saponin – used in NVX-CoV2373 vaccine (Recombinant SARS-CoV-2 S protein) (Keech *et al.*, 2020).
- MF59 – comprising squalene oil-in-water emulsion – used in recombinant SARS-CoV-2 S protein as a soluble protein or on virus-like particles (Ko and Kang, 2018).
- AS03 – squalene oil-in-water emulsion plus α-tocopherol – used in recombinant SARS-CoV-2 S protein as a soluble protein or on virus-like particles (Pulendran *et al.*, 2021).
- CpG 1018 – comprising synthetic DNA alone or formulated with Alum – used in recombinant SARS-CoV-2 S protein on virus-like particles used in CoVaccine HT (Pulendran *et al.*, 2021; JeroenPollet, 2021; Haun *et al.*, 2020).
- Ligands adsorbed in alum – used in inactivated SARS-CoV-2 vaccines (Pulendran *et al.*, 2021).

In the initial stages of the pandemic corresponding to the early period of the patent dataset, patent filings focused heavily on vaccine development and their primary active ingredients. Later on in the dataset, while vaccine development remained the primary focus of patent filings, there was an increase in patents that focused on adjuvants for COVID-19 vaccines. Among recent patents that disclose advancements in adjuvant formulations are:

- Patent application CN113842455 (Beijing Health Guard Biotechnology Inc.) discloses an adjuvant for novel coronavirus vaccine and bivalent vaccine containing the novel coronavirus epidemic HuB strain and the South African mutant strain B.1.351 antigen. The adjuvant exhibits the advantages of a more stable sodium acetate buffer system for COVID-19 vaccine protein and a high level of neutralizing antibodies and cellular immunity.
- Patent application CN114504641 (The Hong Kong Polytechnic University Shenzhen Research Institute) discloses a vaccine adjuvant, which can prolong the retention time of vaccine antigen in the nasal cavity by using the calcium ion-binding protein S100A4 as an adjuvant, thereby providing sufficient time for antigen-presenting cells to take up and present the foreign antigen. Furthermore, because S100A4 is an endogenous protein widespread within the human body, the vaccine adjuvanted with S100A4 is able to avoid the body's immune response to the adjuvant, making this adjuvant suitable for repeated vaccination with different vaccine antigens.
- Patent application IN202041036825 (Bharat Biotech International Limited) discloses a novel TLR7/8 agonist, Algel-IMDG, chemisorbed onto the surface of aluminum hydroxide gel, that has been used as an adjuvant or an immunomodulator.
- Patent application WO2020244483 (LIANG, Pi-Hui) discloses novel compounds with a lipophilic moiety, such as a lipid, fatty acid, polyethylene glycol or terpene, covalently attached to a non-acylated or deacylated triterpene saponin via a carboxyl group present on the 3-O-glucuronic acid of the triterpene saponin, such as *Quillaja* desacylsaponin, lucyoside P or saponin from *Gypsophila*, *Saponaria* and *Acanthophyllum*. This enhances their adjuvant effects on humoral and cell mediated immunity.
- Patent application WO2021178306 (Dynavax Technologies Corporation) discloses a SARS-CoV-2 S protein-stable antigen vaccine adjuvanted with a TLR-9 agonist CpG oligonucleotide named MVC-COV1901 for protection against COVID-19 and suitable for stimulating an immune response against SARS-CoV-2.
- Patent applications WO2021185874 (Mead Johnson Nutrition Company *et al.*) and WO2021185876 (Mead Johnson Nutrition Company *et al.*) disclose use of lactoferrin as an immunological adjuvant for the prevention and treatment of COVID-19 before, during and/or after administration of a COVID-19 vaccine.

Vaccine patenting activity compared to global discussion around COVID-19 vaccines

When COVID-19 emerged onto the global stage, little was known about the illness. Global discussion began by focusing on vaccines. Very quickly, mRNA vaccines became the primary focus of global discussion. First mention of an mRNA vaccine for COVID-19 was made in early 2020 and this category of vaccine has since had an ongoing and persistent presence in news articles, media reports, and social media posts. This can be largely attributed to the fact that the rapidity of development, application and effectiveness of mRNA vaccines was novel and there is the potential for their widespread use in combating other pathogens (Abbasi, 2020).

The relative frequency of discussion about and usage of mRNA vaccines for COVID-19 is at variance with the patenting activity seen in the dataset related to these vaccines. When comparing the number of doses given (Our World in Data, n.d.) of the different categories of vaccines to the number of patents in the dataset a large discrepancy emerges. In the United States, Canada and the European Union, mRNA vaccines account for the vast majority of vaccine doses administered (95 percent), whereas China has almost exclusively administered inactivated vaccines and Africa primarily viral vector vaccines (Our World in Data, n.d.; Statista, n.d.; WHO – Africa Region, n.d.). Although COVID-19 mRNA vaccines account for the majority of vaccinations in the western world, patents related to these vaccines account for only 11 percent of the dataset. Conversely, protein subunit vaccines account for less than 1 percent of vaccine doses administered in these same global regions (Our World in Data, n.d.; Statista, n.d.; WHO – Africa Region, n.d.), but make up the largest portion (47 percent) of the vaccine patent dataset. This volume of COVID-19 protein subunit vaccine patents is influenced by the very nature of other vaccine technologies. More traditional vaccine technologies that leverage the whole pathogen can struggle to provide needful protection without adverse reactions (Heidary *et al.*, 2022). Additional research and vaccine options are required in such cases. Protein subunit vaccines overcome this challenge by only including those antigenic components of the pathogen required to elicit an effective immune response (Heidary *et al.*, 2022) and are therefore an attractive alternative that still leverages a well-studied vaccine technology.

The frequent use of mRNA vaccines is largely owing to their consistent effectiveness in preventing serious COVID-19 illness (Klobucista, 2022), which further elevates discussion around these vaccines. The relatively limited patent activity related to COVID-19 mRNA vaccines can be attributed to the general costs associated with the research and intellectual property claims for key components. Indeed, Gaviria and Kilic (2021) argue that the complex web of patents, trade secrets and licensing activity related to mRNA vaccine technology could limit innovative product commercialization in this area. This does not, however, limit the interest in mRNA vaccines and it is likely they will continue to be a major focus of global discussion around COVID-19, scientific innovation and public health due to their rapid development and unique advantages brought to light by human clinical trials.

Patterns in global COVID-19 vaccine use

Achieving equality, equity and justice in global COVID-19 vaccine distribution and usage has been challenging. Over 30 countries have only vaccinated less than 10 percent of their population (Beaubien, 2022). According to the UN health agency, just over 3 percent of people in low-income countries have been vaccinated with at least one dose, compared to 60.2 percent in high-income countries (United Nations, 2022). Several factors, as described below, have impacted the campaign for global vaccine distribution and usage.

For 57 countries, income level tends to correlate with the vaccination rates for their population (Our World in Data, n.d.). Countries with the highest incomes have been vaccinating 10 times faster than those with the lowest (Bloomberg, n.d.). As of December 1, 2022, 68.5 percent of the world's population had received at least one dose of a COVID-19 vaccine. However, vaccination rates vary according to a country's wealth. Around 80 percent of people living in upper middle- and high-income countries had received at least one dose of vaccine, while 63.8 percent of people living in lower middle-income and only 24.6 percent of those living in low-income countries had been vaccinated (Our World in Data, n.d.). Low- and middle-income countries make up 85 percent of the world's population (Yarlagadda *et al.*, 2022).

The main obstacles to vaccine adoption in low-income countries are cost and access. The difficulty of cold transportation and storage in rural and high-altitude regions, lack of infrastructure, lack of manufacturing facilities and the instability caused by conflict and war hindered COVID-19 vaccine distribution. The costs of vaccine manufacture and delivery to these countries are enormous and represent a major barrier. Additionally, even in some wealthy nations, large portions of the population live in what is known as vaccine deserts, that is, where people have little or no convenient access to vaccination based on geographical location. In the United States, for example, there are 17 million people living in rural vaccine deserts and more than 50 million living in urban vaccine deserts across the country (Kansal *et al.*, n.d.).

Intellectual property rights, trade policies and manufacturing access have all been designated factors related to vaccine availability. Most pharmaceutical companies are based in high-income countries in the northern hemisphere, which could have also created difficulties for access and distribution to lower income southern countries. In June 2022, the World Trade Organization, at its 12th Ministerial Conference adopted the MC12 Decision on the TRIPS Agreement. The Decision includes a waiver of the requirement set out in Article (f) that authorized use be predominantly to supply its domestic market, therefore allowing the producing Member to export any quantity of COVID-19 vaccines. With regard to the obligation to protect regulatory test data required under Article 39.3 of the TRIPS Agreement, the Decision specifies that this does not prevent an eligible Member from taking steps for rapidly approving the use of a COVID-19 vaccine. The Decision also clarifies certain TRIPS flexibilities to enable Members to limit the exclusive effect of patent rights (WTO, 2022).

There are two global initiatives addressing the manufacturing and distribution deficit. The mRNA vaccine technology transfer hub seeks to enable low- and middle-income countries to build the capacity to manufacture mRNA-based vaccines locally through collaboration among universities, biotech and pharmaceutical companies based in 15 (mostly southern) countries (Maxmen, 2022; WHO, n.d.-e). The COVAX (COVID-19 vaccines global access) initiative coordinates the international distribution of donated vaccines and aims to accelerate the development and manufacture of COVID-19 vaccines in order to guarantee fair and equitable access for every country in the world (WHO, n.d.-b). Low- and middle-income countries depend heavily on COVAX to supply vaccines for their populations (Yarlagadda *et al.*, 2022).

In wealthier countries, attitude and opinion influenced vaccine adoption. Public concern over the safety of new vaccines, as well as misconceptions spread online and via social media, drove vaccine hesitancy in middle- and high-income countries (Yarlagadda *et al.*, 2022).

COVID-19 vaccine booster patenting activity

The purpose of a booster vaccine is to increase immune response and restore vaccine effectiveness (WHO, 2021b; Nealon, 2021). Over time, the degree of immune protection provided by primary vaccination wanes. Booster vaccines are administered during a specific period after primary vaccination, when immunity is known to begin to decline (WHO, 2022a). Boosters are generally considered safe and effective at increasing immune response and some studies have shown that COVID-19 vaccine boosters elevate SARS-CoV-2-specific neutralizing antibody levels (Burckhardt *et al.*, 2022).

Patents related to booster vaccines make up a small percentage of the overall vaccine patent dataset. Only around 5 percent of patents in this dataset emphasized booster use. Even fewer – under 1 percent – mention booster use in either the title or abstract. This contrasts with the extensive media discussion, government recommendations and policy debates surrounding the availability and use of boosters and is indicative of the secondary use of many vaccines, with little to no modification, as boosters.

Most public health officials agree that high-risk groups, such as health care workers, immunocompromised individuals and the elderly, should have priority access to booster vaccines (Meng *et al.*, 2022). According to the WHO and the Strategic Advisory Group of Experts on Immunization (SAGE) recommendations, "booster doses should be offered based on evidence that doing so would have substantial impact on reducing hospitalization, severe disease and death, and to protect health systems" (WHO, 2022a). Data show a short-term benefit for an additional booster dose of mRNA vaccine in health care workers, people aged over 60 and those with compromised immune systems (WHO, 2022a). However, booster doses may not be needed by all fully vaccinated individuals (Burckhardt *et al.*, 2022). Indeed, preliminary data suggest that in younger people the benefit is minimal (WHO, 2022a). Heterologous boosters (i.e., of a different vaccine platform than the primary vaccine) induce better immune responses and offer greater protection than do homologous boosters (i.e., of the same platform) (Meng *et al.*, 2022). Some believe that periodic boosters may be required over the next few years in order to sustain immunity (Nealon, 2021). More recently developed bivalent boosters show promise for improving immune response against variants (Chalkias *et al.*, 2022), but some studies show that most of the antibodies elicited by vaccines targeting newer variants continue to recognize only the

original virus, because of "immune imprinting," whereby the body repeats its immune response to the first variant encountered. Longer-term response and the ability to overcome immune imprinting are still under investigation (Mandavilli, 2022). Two research groups examined levels of neutralizing antibodies and differences in CD4+ or CD8+ T cell responses after receiving monovalent and bivalent COVID-19 booster vaccines to protect against omicron variants. Neither group found bivalent booster vaccines induced superior immune responses compared to monovalent vaccines (Collier *et al.*, 2022; Wang *et al.*, 2022). However, finetuning booster vaccine dosage might increase the efficacy against immune-escape COVID-19 variants (Offit, 2023).

COVID-19 vaccine boosters usage tends to correlate with the economic status of countries. Data on booster coverage by country and income level show that high-income economies have higher levels of booster vaccination (Hamadeh *et al.*, 2022), whereas low-income regions have very low booster usage, with middle-income countries ranging between the two (pandemic, n.d.). The use of boosters in more affluent countries may also limit the availability of primary vaccines in poorer countries. In 2021, the WHO Director General recommended a moratorium on booster vaccination through the end of the year for the sake of global equity in vaccine access (WHO, 2021c). That guidance has since been updated to recommend booster vaccination under certain criteria (WHO, 2022a).

COVID-19 therapeutics

Background – therapeutic categories

Like the development of therapeutics in other areas, two major categories of COVID-19 therapeutics have been explored: small molecule and biologic (also known as biopharmaceutical). Small molecule therapeutics are usually organic compounds, either synthetic or derived from a natural source, with a molecular weight of less than 1,000 Daltons (Da). Biologic therapeutics are relatively complex molecules, derived from a biological system, such as from living cells or blood, or produced using biotechnologies, such as recombinant DNA technology, with a molecular weight greater than 1,000 Da. Owing to the relative ease of development and production, small molecule therapeutics are typically more accessible and less costly than biologic therapeutics (Makurvet, 2021). Table 12 provides an overview of the primary therapeutic types encountered in the patent dataset. A more detailed discussion of biologic therapeutics can be found in the first WIPO COVID-19 Patent Landscape Report (WIPO, 2022).

Table 12. Categories of COVID-19 therapeutics

Small molecule	A broad category of organic chemical compounds with a molecule size smaller than 1,000 Da. These molecules can be synthesized chemically or extracted from natural sources (natural products)
Traditional medicine	Crude preparations of medicines produced according to the principles of traditional medicinal practice. These preparations usually are composed of a mixture of natural plant parts boiled in a liquid (decoction) or made into small balls or granules
Biologics	A broad category of large molecules produced from living systems or with the use of advanced biotechnologies such as recombinant DNA technology. Biologics are usually large molecules (>1,000 Da) complex in structure. Subclasses of biologics in the context of this report are listed below
Antibodies	Proteins that constitute part of the human immune system for identifying and neutralizing pathogens. Antibody biologics for COVID-19 treatment may be either obtained from patients who have recovered from COVID-19 or manufactured in large quantities using recombinant DNA technologies with the assistance of other biotechnologies
Cell therapy	Viable cells with or without modification, which can be placed into the human body to produce a beneficial effect
Nucleic acids	Biopolymers – essential to all forms of life – that store genetic information. They include DNA and RNA. Nucleic acid biologics in the context of this report include small interfering RNA, antisense nucleotides, and so on
Peptides and proteins	Large molecules (or biopolymers) made of chains of amino acids. They occur naturally in organisms but can also be produced synthetically (for some peptides) or with the use of recombinant DNA technology
Other biologics	CRISPR-related, probiotics, exosomes, and so on

Source: CAS, National Science Library, n.d.

Selection of drug targets is a critical step in drug design. All the enzymes and proteins involved in SARS-CoV-2 virus replication, as well as the host proteins mediating inflammation and tissue damage, are potential drug targets. To date, the R&D of COVID-19 therapeutics has focused primarily on two categories of biological targets:

1. therapeutics that target a viral protein/gene, such as the coronavirus S protein, 3cLpro protease, or RNA-dependent RNA polymerase; and
2. therapeutics that target a human protein involved in mediating viral entry into human cells (such as ACE2) or the exaggerated inflammatory process (cytokine storm) caused by the excess release of cytokine proteins triggered by virus infection, which may lead to tissue damage or dysfunction.

By acting on one of these targets, COVID-19 therapeutics may inhibit viral entry, block virus replication inside a host cell, enhance the immune system's ability to fight the virus, alleviate the cytokine storm or impact other physiological processes that may disarm or weaken the virus. A detailed discussion of the patent landscape related to COVID-19 therapeutics now follows. Information about clinical trials of COVID-19 therapeutics can be found in the Annex.

Therapeutics patent landscape

For this report, we considered all patent filings related to COVID-19 therapeutics from January 2020 through September 2022. For each patent family, every patent office where patent protection was sought was counted once (see Annex for an in-depth discussion of patent families). Analysis by patent office revealed that WIPO/PCT received the most COVID-19 therapeutics-related patent applications, followed by CNIPA, USPTO, EPO and KIPO (Table 13). This contrasts with the first COVID-19 Patent Landscape Report, which showed that during the January 2020 through September 2021 period, CNIPA received the most patent applications followed by WIPO, USPTO, the Indian Patent office and EPO. As already highlighted, WIPO's current top ranking is an indication that patent applicants are leveraging the PCT system to protect their inventions across multiple jurisdictions.

Table 13. **Distribution of COVID-19 therapeutic patent applications across patent offices**
WIPO, CNIPA and USPTO received the largest volume of patent applications related to COVID-19 therapeutics.

Patent offices of filing for COVID-19 therapeutics	Number of patent applications
WIPO	3,064
China	1,847
US	815
EPO	362
Republic of Korea	295
India	247
Australia	176
Canada	166
Japan	138
Russian Federation	85
Brazil	58
Germany	46
Argentina	27
France	22
Türkiye	19
Colombia	15
Israel	7

Source: WIPO, based on patent data from the CAS Content Collection, September 2022.

When considering applicant location, China, the United States, the Republic of Korea, India and Germany are the top five origins (Table 14). Patent applications filed by applicants based in these countries together accounted for about 78 percent of total patent filings in therapeutics.

Table 14. Distribution of COVID-19 therapeutic patents across applicant locations
The majority of patents related to COVID-19 therapeutics were filed by applicants located in China and the United States.

Patent applicant location	Number of patent families
China	1,850
US	1,447
Republic of Korea	229
India	195
Germany	184
Japan	135
France	110
UK	107
Switzerland	83
Russian Federation	78
Canada	71
Israel	62
Australia	48
Türkiye	36
Austria	29
Belgium	24

Source: WIPO, based on patent data from the CAS Content Collection, September 2022.

Patent filing strategies for COVID-19 therapeutic patents followed a similar pattern to that of COVID-19 vaccine patents. From January 2020 through September 2021, patent applicants in China almost exclusively filed therapeutics patent applications with CNIPA, with a few exceptions where filings were made at WIPO, the USPTO and a few other offices (WIPO, 2022). For the period covering January 2020 through September 2022, a higher percentage (27 percent) of China-based applicants filed applications at WIPO/PCT followed by a very small portion (2.5 percent) at USPTO. This difference is almost entirely accounted for by the filings made from October 2021 through September 2022, indicating Chinese applicants' more recent interest in seeking patent protection for their inventions more widely.

In contrast, throughout the entire period covered by this report, US-based applicants sought protection of their intellectual property at USPTO and WIPO, but also filed their patents in many more jurisdictions, including EPO, the Canadian Patent Office and the Australian Patent Office, albeit in relatively smaller numbers. This trend reflects the interest of US patent applicants in seeking patent protection for their inventions across multiple jurisdictions and markets. Applicants from Russia, India and the Republic of Korea filed patents in a similar fashion to applicants from China by mainly filing with WIPO and at their home country patent office. Applicants from both the United Kingdom and Germany filed patents mostly with WIPO and at the EPO. Figure A3 in the Annex further illustrates where applicants from different locations filed therapeutic patent applications.

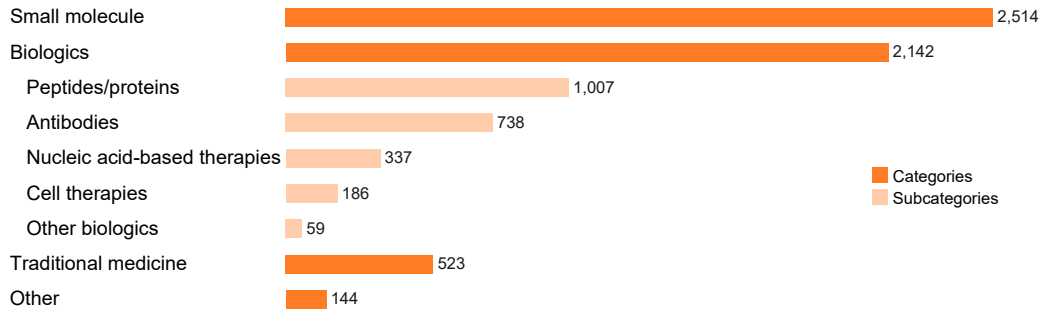
Therapeutic patent distribution by substance type and published applicant location

We identified and analyzed 4,968 patent documents related to the development of COVID-19 therapeutics published from January 2020 through September 2022. Patents were first categorized by type of therapeutics (see Table 12).

As shown in Figure 14, small molecule therapeutics constituted the biggest category (2,514, 50 percent). Patents related to biologics accounted for the next largest group (2,142, 43 percent). Within this category of therapeutics, peptides/proteins therapeutics made up the largest subset (1,007, 20 percent), followed by antibodies (738, 15 percent), nucleic acid-based (337, 7 percent), cell-based therapy (186, 4 percent) and other biologics (59, 1 percent), for example, exosomes, CRISPR and probiotics. In addition, 10 percent of patent documents (523) described the use of traditional medicine and a very limited number (144, 3 percent) described the use of

miscellaneous potential therapeutics, such as polymers and nanoparticles (classified as "others"). It is worth noting that some patent applications described the use of more than one category of therapeutics, and a few applications described the use of both vaccines and therapeutics. As a result, the total percentage value of all the categories together is more than 100 percent.

Figure 14. Distribution of COVID-19-related patent applications across therapeutic categories and subcategories, with earliest published month between January 2020 and September 2022
Patents related to small molecule therapeutics dominate the dataset, followed by patents related to biologic therapeutics.



Source: WIPO, based on patent data from the CAS Content Collection, September 2022.

While applicants in China and the United States filed about an equal number of small molecule and biologics-related patents, China-based applicants, unsurprisingly, filed many more patents disclosing the use of traditional medicine in treating patients with COVID-19 compared to the United States (Table 15). Also not unexpected, applicants in the Republic of Korea and India likewise filed more traditional medicine patents compared to applicants in the United States. When considering the wide range of biologics platforms, China-based applicants filed more antibody patents, fewer protein/peptide patents and fewer cell therapy patents compared to their US-based counterparts.

Table 15. Distribution of COVID-19 therapeutic patent applications across therapeutic categories and patent applicant locations
Distribution of COVID-19 therapeutics-related patent filings from January 2020 through September 2022 across different categories and subcategories of therapeutics.

	Therapeutic categories								
				Biologics subcategories					
Patent applicant location (country)	Small molecule	Traditional medicine	Biologics	Peptides/ proteins	Antibodies	Nucleic acid-based therapies	Cell therapies	Other biologics	Others
China	837	341	754	299	366	116	55	14	31
US	791	29	727	387	223	131	85	25	48
Russian Federation	52	1	27	16	6	5	0	3	4
UK	59	1	51	34	21	4	3	0	6
Germany	107	7	76	35	25	15	12	6	8
India	117	59	25	16	6	3	1	1	17
Republic of Korea	123	35	77	42	22	11	8	1	8
Japan	77	11	53	30	18	10	8	2	6
France	69	5	40	31	7	10	4	0	0
Switzerland	49	3	37	19	16	3	4	1	2
Canada	48	3	26	13	10	4	4	0	1
Israel	35	5	28	14	4	5	7	1	1
Australia	31	1	22	13	10	2	1	0	0
Türkiye	21	7	7	4	2	0	1	0	1
Austria	19	0	10	8	0	5	0	1	0
Belgium	16	0	10	5	3	1	2	0	0

Source: WIPO, based on patent data from the CAS Content Collection, September 2022.

The distribution of therapeutic patents by geographical region shows that almost 97 percent of patents came from applicants in Asia, North America and Europe. Applicants from the other regions of the world, Africa, the Middle East, Oceania and South America, contributed less than 4 percent to the therapeutic patent pool (Table 16).

Table 16. Regional distribution of COVID-19-related patent applications across therapeutic categories

Asia, North America and Europe-based applicants together filed nearly 97 percent of patent applications across the different therapeutic agents.

	Therapeutic categories								
				Biologics subcategories					
Patent applicant location (region)	Small molecule	Traditional medicine	Biologics	Peptides/ proteins	Antibodies	Nucleic acid-based therapies	Cell therapies	Other biologics	Others
Africa	12	3	5	2	1	2	0	0	0
Asia	1,215	464	942	406	423	145	74	18	67
Europe	513	25	366	205	105	67	41	18	35
Middle East	48	8	32	17	4	5	8	1	7
North America	848	34	761	407	232	138	89	26	49
Oceania	35	2	25	15	10	3	1	1	0
South America	7	0	10	6	5	0	0	0	0

Source: WIPO, based on patent data from the CAS Content Collection, September 2022.

Therapeutics patent applicant collaborations

Earlier the WHO C-TAP program was briefly described in the section on Licensing and other agreements related to COVID-19 vaccines and therapeutics. Although there are studies that use several other methods to understand collaboration, for the scope of this report, patent collaborations have been the subject of focus. For example, data sharing for clinical trial data, geospatial tracking of infection statistics, or information libraries to enable machine learning for drug discovery or drug re-purposing (Palm *et al.*, 2021). This section of the report focuses more on patents identified in the therapeutics dataset. From the therapeutics dataset, 24 percent of patents had more than one patent assignee. Within the dataset, organizations with the most collaborations on patent filings were universities and research institutes (Table 17).

Table 17. Top patent applicant collaborators in COVID-19 therapeutic patent applications
Organizations with the most collaborations on patent filings were universities and research institutes.

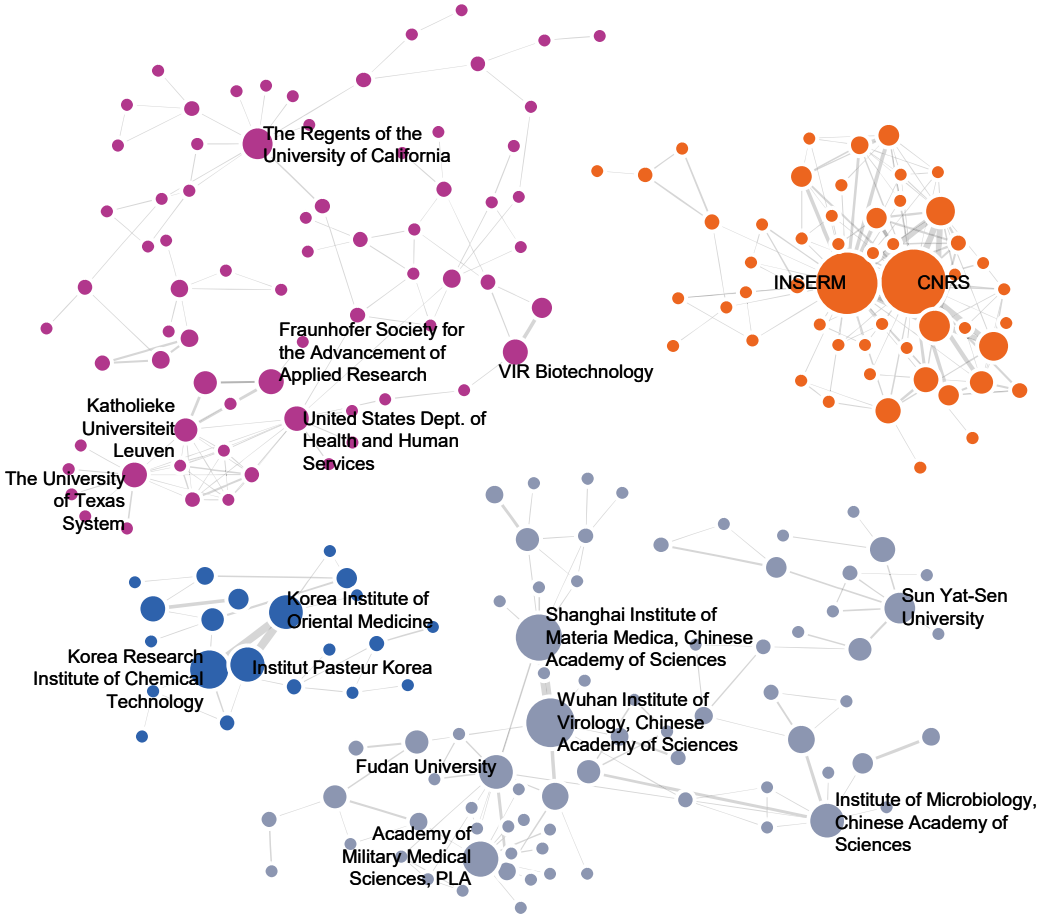
Patent applicant	Total collaborations in therapeutics (number of patent families)
Centre National de la Recherche Scientifique (CNRS)	39
Institut National de la Santé et de la Recherche Médicale (INSERM)	36
Wuhan Institute of Virology, Chinese Academy of Sciences	23
Shanghai Institute of Materia Medica, Chinese Academy of Sciences	21
Korea Research Institute of Chemical Technology	15
Academy of Military Medical Sciences, PLA	13
Korea Institute of Oriental Medicine	12
Institute of Microbiology, Chinese Academy of Sciences	12
Institut Pasteur Korea	12
Fudan University	12
The Regents of the University of California	10
Sun Yat-Sen University	10
École Normale Supérieure de Lyon	10
Université Claude Bernard Lyon 1	9
Université de Paris	9

Note: The table illustrates top patent applicants in the therapeutics dataset having more than one entity as a patent applicant.
Source: WIPO, based on patent data from the CAS Content Collection, September 2022.

In the therapeutics dataset, organizations that collaborated most frequently are presented in Figure 15. For therapeutic-related patents, there is a pattern of consistent collaboration between organizations, unlike in the vaccine dataset. The two organizations that collaborated most frequently were Centre National de la Recherche Scientifique (CNRS) and Institut National de la Santé et de la Recherche Médicale (INSERM).

Figure 15. **Network analysis of top collaborating entities in COVID-19 therapeutic patent applications**

Analysis shows four main collaborating communities: a community primarily composed of United States and European universities and research institutions (purple), a group centered around two French research institutions, CNRS and INSERM (orange), a group centered around research institutions from the Republic of Korea (blue) and a group primarily composed of Chinese corporate entities and research institutions (gray).



Note: The chart illustrates the relationship between collaborators and their frequency as shown by the size of the circles. CNRS, Centre National de la Recherche Scientifique; INSERM, Institut National de la Santé et de la Recherche Médicale. Organizations were identified using patent applicant names and the number of times a pair was found together in the therapeutics dataset. In this approach, a single patent in the dataset may be counted more than once, depending on the number of patent applicants.

Source: WIPO, based on patent data from the CAS Content Collection, September 2022.

Highlights of patent filings related to COVID-19 therapeutics development

Small molecule therapeutics

COVID-19 therapeutics act in a variety of ways. Some act directly on the virus to block its entry into human cells or else stop it from replicating once inside a human cell. Others either enhance the immune system's ability to fight the virus or attenuate the type of immune-system overreaction seen in the cytokine storms which affect many patients with severe COVID-19.

As of December 1, 2022, remdesivir (Veklury) was the only antiviral drug to be fully approved in the United States for the treatment of COVID-19. It has also been approved or authorized for emergency or temporary use by authorities in around 50 other countries worldwide, including Australia, the European Union, India, Israel, Japan, the Republic of Korea, Singapore, Taiwan province of China and the United Kingdom (RAPS, n.d-a). Veklury is a SARS-2-CoV-2 nucleotide analog RNA polymerase inhibitor indicated for the treatment of COVID-19 in adults and children aged 28 days or older and weighing at least 3 kg, who are either hospitalized or not, have mild-to-moderate COVID-19 and at a high risk of progressing to severe COVID-19 (Gilead, n.d.). Recent patents related to superior remdesivir formulations are:

- Patent application WO2022020940 (Apotex Inc.) discloses remdesivir salts, including napsylate, tosylate, hydrochloride, phosphate, maleate and oxalate, as well as pharmaceutical compositions including remdesivir salts and the crystalline forms thereof, and their use in the treatment of a viral infection, particularly one caused by SARS-CoV-2.
- Patent application WO2022091122 (Cipla Limited) discloses stable formulations of a nucleotide analog prodrug, in particular remdesivir, in the form of ready-to-use (RTU) and ready-to-dilute (RTD) formulations free of cyclodextrins.
- Patent application WO2022016073 (The University of Texas System Board of Regents; TFF Pharmaceuticals Inc.) discloses pharmaceutical compositions of remdesivir that may be inhaled directly into the lungs.
- Combination therapies:
    - Patent application WO2022029275 (Nuvamid SA) discloses a combination of remdesivir and nicotinamide mononucleotide derivatives.
    - Patent application WO2022015982 (The Regents of the University of California) discloses an RNA-dependent RNA polymerase inhibitor, such as remdesivir, and a second therapeutic agent for treating infection with an RNA virus.
    - Patent application WO2022076386 (Montelione, Gaetano T. *et al.*) discloses inhibitors of SARS-CoV-2 papain-like protease (pLpro), including hepatitis C virus (HCV) drugs grazoprevir, vaniprevir and paritaprevir, strongly synergistic with SARS-CoV-2 polymerases inhibitors, such as RNA-dependent RNA polymerase (RdRp) including remdesivir, as well as orally ingestible polymerase inhibitors, such as molnupiravir.
    - Patent application WO2022035911 (Tutela Pharmaceuticals) discloses a combination of an FKBP ligand, such as tacrolimus, everolimus or sirolimus, and an antiviral agent, such as the RNA polymerase inhibitors remdesivir and molnupiravir and/or the protease inhibitor M128533.

Ritonavir-boosted nirmatrelvir (Paxlovid) is recommended by the WHO in the treatment of COVID-19, if specific criteria are met. Other health agencies and authorities in specific countries may have recommendations that differ from that of the WHO. The drug has received either EUA or conditional approval in many countries, including in the United States, the European Union, the United Kingdom and China (RAPS, n.d.-a).

Molnupiravir, an oral, broad-spectrum antiviral, has a similar mechanism of action to remdesivir and prevents virus replication. The WHO has conditionally recommended its use in treating patients with COVID-19 at high risk of developing severe disease (RAPS, n.d.-a). Molnupiravir is the first oral COVID-19 antiviral drug to receive EUA in the United States. Several other countries have also granted it a EUA or conditional approval, including the United Kingdom, Australia, India and South Africa (RAPS, n.d.-a). Several patents in the dataset refer to Molnupiravir, focusing primarily on the process used to prepare the drug, as exemplified by patent application WO2022200847 (Optimus Drugs Private Limited).

In November 2022, the U.S. Food and Drug Administration (USFDA) authorized the drug anakinra (Kineret) for emergency use. It had previously received authorization for use in treating certain hospitalized adults with pneumonia caused by COVID-19 (RAPS, n.d.-a). Two patent applications in the dataset, namely, WO2021185838 (Swedish Orphan Biovitrum AB) and WO2021113334 (Altavant Sciences GmbH), disclose effective methods for administering Kineret to COVID-19 patients to treat or alleviate respiratory distress.

Other COVID-19 therapeutics to have received EUA or conditional approval in some countries are Bebtelovimab and Olumiant (baricitinib) (RAPS, n.d.-a). Many more small molecule therapeutics for COVID-19 are currently undergoing clinical development.

Biologic therapeutics

This section addresses patenting activity within subclasses of biologics, namely:

- antibodies;
- non-antibody peptides/proteins;
- nucleic acid-based therapies;
- aptamer-mediated therapeutics;
- cell-based therapies;
- others, such as CRISPR and exosomes.

Antibody therapeutics

In general, antibody therapeutics has seen the fastest growth relative to other classes of biologics over the past two decades. Therapeutic antibodies for COVID-19 generally fall into either of two categories:

1. Virus-neutralizing antibodies directed against SARS-CoV-2 proteins (e.g., the S protein) that can be obtained from patients recovered after COVID-19 or manufactured using biotechnologies.
2. Antibodies that modulate the human immune system's response to the virus that are typically manufactured using biotechnologies.

While there have been several antibody therapeutics granted EUA to treat patients with COVID-19 (e.g., Bamlanivimab, Bebtelovimab, Etesevimab and Sotrovimab), several of these have recently been found to be no longer effective in some regions of the world (e.g., the United States), due the emergence of new SARS-CoV-2 variants (USFDA, 2022b; USFDA, 2022c). Thus, there is a need for new antibody therapeutics that are broad spectrum and/or multivalent and effective against new or predominant variants. Examples of some inventions beginning to address this need are:

- Patent application CN114573691 (The Eighth Affiliated Hospital of Guangzhou Medical University *et al.*) describes an anti-spike S1 protein neutralizing antibody active against several variants, including Omicron B.1.1.529.
- Patent application WO2022073138 (The Hospital for Sick Children) discloses a MULTi-specific, multi-Affinity antiBODY (Multabody) platform for making multivalent neutralizing antibodies using human apoferritin chains to help multimerize antibodies specific for SARS-CoV-2 glycoproteins (Rujas *et al.*, 2021).
- Patent application WO2022074628 (The Governing Council of the University of Toronto) discloses single-chain antibodies able to bind to more than one region of the SARS-CoV-2 proteins.

While monoclonal therapeutic antibodies have been generated for many years using hybridoma and phage display technologies, use of chimeric animals expressing human immunoglobulin

genes and/or cloning of single human B cells for production of desired antibodies has become more popular within the last decade (Lu *et al.*, 2020). The generation of fully human antibodies from transgenic animals (such as rats or mice) accounts for the increasing number of new therapeutics (Bruggemann *et al.*, 2015). Patent application WO2022046286 (SAb Biotherapeutics) discloses polyclonal antibody SAB-185, specific for the SARS-CoV-2 S protein, made using ungulates (bovine) genetically engineered to produce fully human immunoglobulins. As the virus continues to mutate, the use of polyclonal antibodies, such as SAB-185, has the potential to drive higher levels of effectiveness compared to monoclonal antibodies. SAB-185 was evaluated in clinical trials for use in treating patients with COVID-19, but owing to a decline in COVID-19 hospitalizations its Phase 3 ACTIV-2 trial was suspended (ClinicalTrials.gov, 2023; BioSpace, 2022).

Instead of designing antibodies that target viral proteins, some patents evaluated antibodies that target those host (human) proteins implicated in the infection process with a view to modulating the immune system response. Such a strategy may result in more effective therapeutics better able to address the continuously emerging SARS-CoV-2 variants, since it focuses on host proteins rather than the continually changing viral proteins. Examples of such patents are:

- Patent application WO2022204274 (Alector) discloses anti-TMEM106B antibodies that reduce viral cell entry and release of the virus from infected cells. These antibodies were shown to be as effective as Remdesivir at reducing cytopathic effects associated with SARS-CoV-2 infection in human lung cells.
- Patent application WO2022140697 (The Regents of the University of California) discloses anti-CD32b antibodies that could be used to block CD32b and restore interferon responses in patients with severe COVID-19 disease.
- Patent application WO2021243396 (Implicit Bioscience Limited) discloses anti-CD14 antibodies effective in tempering the immune system's harmful inflammatory response to SARS-CoV-2.

Over 10,000 published and/or patented antibodies and nanobodies that bind to coronaviruses, including SARS-CoV-2, are available in the Coronavirus-Binding Antibody Sequences & Structures database released by the Oxford Protein Informatics Group, Department of Statistics, University of Oxford (OPIG, 2022).

Non-antibody peptide and protein therapeutics

Peptide-mediated therapy

The primary strategy for using peptides to treat patients with COVID-19 centers on therapeutic peptides (usually with a chain length of under 20 amino acids) that inhibit the virus's ability to bind and/or enter host cells (Moroy and Tuffery, 2022). The dataset includes patents that explore this strategy and disclose peptides targeting the S protein-ACE or S-protein-Neuropilin-1 interactions. Examples of such patents are:

- Patent application WO2022040803 (Soricimed Biopharma) discloses C-terminal peptides of soricidin (a paralytic peptide found in the venomous saliva of *Blarina brevicauda*) that inhibit interaction between the SARS CoV-2 S protein and human ACE2. Soricidin peptides are also known to inhibit transient receptor potential vanilloid subfamily member 6 (TRPV6) and reduce cytoplasmic calcium influx.
- Patent application BR102020023728 (Universidade Federal do Ceará) discloses peptides derived from plant proteins (chitin-binding protein CBP^3, 2S albumin-like protein and chitinase) that inhibit the S protein.
- Patent application WO2021224803 (NONO) presents the use of viral peptides linked to an internalization peptide that helps facilitate entry into tissues or cells. The peptides bind to human host factors, such as neuropilin-1, and interfere with viral entrance.

An alternative approach uses peptides specific for host proteins rather than peptides that inhibit virus–host cell interaction. This strategy includes generating peptides from known mammalian proteins (e.g., carbohydrate-binding protein CLEC4G, tumor necrosis factor lectin-like domain (TIP) and β-defensin-4) for use in treating COVID-19 patients. Examples of such patents are:

- Patent application EP4039268 (IMBA-Institut für Molekulare Biotechnologie GmbH) presents a novel strategy for therapeutic intervention targeting virus-specific glycosylation. Because many N-glycosylation sites on the S protein are conserved, the use of CLEC4G peptides that interact with S proteins and block SARS-CoV-2 entry has potential as a pan-variant therapeutic strategy.

- Patent application WO2021185071 (The University of Hong Kong) discloses the use of peptide P9R derived from mouse β-defensin-4 in treating patients with coronavirus infections, including COVID-19. P9R binds to the virus and inhibits virus–host endosome acidification, which is a key stage in the life cycle of many pH-dependent viruses. This invention discloses that the antiviral activity of P9R can be enhanced by increasing its net positive charge.
- Patent application WO2021223894 (Apeptico Forschung und Entwicklung GmbH) discloses the use of Solnatide (a cyclic peptide derived from human TIP) in treating life-threatening lung failure in patients with acute respiratory distress syndrome (ARDS) and COVID-19. It has been tested in clinical trial on patients with COVID-19 and preliminary data support the use of solnatide in the treatment of patients with moderate-to-severe COVID-19 (Solnatide, n.d.).

Protein-mediated therapy

Larger non-antibody proteins (> approximately 50 amino acids), including fusion proteins, cytokines (soluble interferon α2b and pegylated α2b) and other proteins (recombinant human proteins ACE2, arginase 1 and CC10) are also being explored as potential COVID-19 therapeutics. Examples of patents featuring non-antibody proteins are:

- Patent application WO2021191436 (Apeiron Biologics AG *et al.*) discloses that recombinant soluble human ACE2, known as GSK2586881 (APN-01 or Alunacedase alfa), acts as a decoy molecule and is useful in treating or preventing COVID-19 (Apeiron Biologics, n.d.).
- Patent applications WO2021212220 (Altum Pharmaceuticals *et al.*) and WO2021245541 (Cadila HealthCare Limited) present the use of recombinant soluble human interferon α2b and pegylated α2b, respectively, in treating and/or preventing viral infections like those caused by SARS-CoV-2. The efficacy and safety of APN-01, recombinant α2b and pegylated α2b has been studied in patients with COVID-19 (U.S. National Library of Medicine, n.d.; Li, Luo *et al.*, 2021; Bhushan *et al.*, 2021).

The first WIPO COVID-19 Patent Landscape Report highlighted several patents using ACE2-Fc antibody fusion proteins as decoy proteins with a greater affinity for the S protein compared to human ACE2 (WIPO, 2022). By binding to the S protein, ACE2-Fc antibody fusion proteins prevent the S protein interacting with ACE2 on human host cells. Although they have shown therapeutic promise, there remains a need for novel approaches to achieve multivalent therapeutic outcomes using ACE2 to combat SARS-CoV-2 and its ever-changing VOCs (Obeng *et al.*, 2022). There are patents present in the dataset that begin to address this need by utilizing different approaches for first engineering variant ACE2 proteins and then using them to create immunoglobulin (Ig) Fc fusion proteins or non-immunoglobulin multimers for use in therapy. In most examples, the ACE2 undergoes modifications for enhanced binding to the S-protein and the addition of the Fc region of Ig helps to stabilize and increase its half-life. Examples of such patents are:

- Patent application WO2022184854 (Formycon AG) discloses that ACE2-IgG4 constructs v1261 and v1263, which were constructed using the IgG4 Fc fragment instead of IgG1 to avoid potential undesirable antibody-dependent disease enhancements, are effective in neutralizing SARS-CoV-2 VOCs (Svilenov *et al.*, 2020, 2021).
- Patent application WO2022075667 (IUCF-HYU, Industry-University Cooperation Foundation Hanyang University) presents the cloning of stabilized Ace2(N51C/V343C)-Fc protein, wherein the ACE2 is modified to enable disulfide bonding leading to a more stable therapeutic compound without affecting its function.
- Patent application WO2021183717 (NantCell) discloses ACE2(T27Y/H34A/H374N)-IgG1Fc, a triple mutant ACE2 decoy, displaying favorable biophysical characteristics compared to other triple ACE2 proteins and showing high S protein RBD affinity (Tanaka *et al.*, 2021).
- Patent application WO2022012688 (Shenzhen Bay Laboratory) discloses ACE2-Ig-v4.1, a hexavalent ACE2-Ig made up of four truncated ACE2-740-D30E and two truncated ACE2-615-D30E proteins, which shows at least a 10-fold higher anti-SARS-CoV-2 potency compared to bivalent forms.

Nucleic acid-based therapeutics

One of the most promising strategies to combat SARS-CoV-2 is nucleic acid-based therapeutics (NATs). These include antisense oligonucleotides, double-stranded RNAs (dsRNAs), microRNAs (miRNAs) and small interfering RNAs (siRNAs) (Liu *et al.*, 2020). NATs can be designed to inhibit replication or infection processes associated with SARS-CoV-2, as well as inhibit host factors, all of which may help quell the cytokine storm seen in some COVID-19 patients. Although NATs possess some advantages (e.g., high specificity, ease of design and lower production costs), more advances and testing are required to improve their safety, deliverability, scalability and effectiveness. This is especially true for miRNAs, owing to research having identified several miRNAs associated with COVID-19 infection with the greatest potential to break COVID-19 infection in general and suppress cytokine storms in particular (Abusalah *et al.*, 2022). Examples of patents disclosing the use of NATs in the treatment of patients exposed to SARS-CoV-2 are:

- Patent application WO2021186396 (Oncotelic, 2021) discloses the use of OT-101, a transforming growth factor beta (TGF-β) antisense oligonucleotide, for use in treating respiratory distress in patients with COVID-19. It has been tested in clinical trials, and in October 2022 Oncotelic received a U.S. Biomedical Advanced Research and Development Authority (BARDA) contract to develop OT-101 for treating patients after COVID-19 infection (Pharmaceutical Technology, 2022).
- Patent application WO2021248027 (Ionis Pharmaceuticals) discloses the design of numerous 3-10-3 gapmer antisense oligonucleotides specific for SARS-CoV-2 isolate Wuhan-Hu-1, and for host factors ACE2 and TMPRSS2. These gapmer oligonucleotides stimulate RNA degradation by recruiting RNase H and have been found to have some advantages compared to other antisense oligonucleotides, such as a high binding affinity to the target (Roberts *et al.*, 2020).
- Patent application WO2021252557 (Alnylam Pharmaceuticals) discloses the siRNAs AD-1184150 and AD-1184137 targeting COVID-19 and AD-1230934 targeting ACE2 and looks at their efficacy when delivered intranasally to hamsters. All three siRNAs were shown to prevent SARS-CoV-2 infection in hamsters, with an intranasal combination of AD-1184150 and AD-1184137 superior to subcutaneous administration.
- Patent application WO2022203448 (Korea University Research and Business Foundation) discloses siRNAs exhibiting anti-fibrotic miRNA activity with an inhibitory effect on SARS-CoV-2 for use in treating patients with COVID-19. The bioinformatics approach uses Argonaute-CLIP analysis to design potential siRNA drugs with increased accuracy that can silence SARS-CoV-2, as well as inhibit pulmonary fibrosis in patients.

Aptamer-mediated therapeutics

Oligonucleotide aptamers are single-stranded DNA or RNA molecules that bind to a specific target. Compared to antibodies, they can be chemically synthesized and modified to have high stability in a cost-effective manner. Aptamers are ideal for targeting ligands so as to impede viral entry and replication, or even further enhance anti-infection effects in infected host cells owing to their high specificity and affinity (Tan *et al.*, 2022). Several SARS-CoV-2-specific oligonucleotide aptamers have been designed to target the S and N proteins, including those binding to the RBD and N-terminal domain (NTD) of the S protein and those targeting trimeric S proteins (Zhang *et al.*, 2022). Examples of patents that disclose oligonucleotide aptamers for potential use in treating patients exposed to SARS-CoV-2 are:

- Patent application CN114410639 (Guangxi University) presents the use of BLI-SELEX technology to identify nucleic acid aptamer APT-S which binds to the S1 subunit of SARS-CoV-2 S protein and aptamer APT-A which binds to human ACE2. The APT-S aptamer is shown to successfully block interaction between the S protein and ACE2.
- Patent applications CN113151282 (University of Science and Technology of China) and CN111748558 (Anhui Angpu Tuomai Biotechnology) disclose nucleic acid aptamers that bind to the N protein of SARS-CoV-2 and their use in treating patients infected with SARS-CoV-2.

Cell-based therapeutics

As was explained in the first WIPO COVID-19 Patent Landscape Report (WIPO, 2022), cell-based therapies use immune cells (such as regulatory T-cells, chimeric antigen receptor (CAR) T cells, natural killer cells or dendritic cells) or stem cells (cells able to develop into other cell types) to induce, regulate and/or repair damaged parts of the body impacted by a viral infection. Use of mesenchymal stem cells (MSCs) derived from adipose, umbilical cord, bone marrow or dental pulp in treating patients with COVID-19 is the most common strategy being explored, with more than 100 clinical trials underway, as of the end of November 2022 (Zavvar *et al.*, 2022). While cell-based therapies hold potential promise for treating patients with COVID-19, the practicality of making these cells, alongside cost issues, continues to be an area of concern (Golchin, 2021). Examples of patents that disclose the use of cell-based therapies in treating patients with COVID-19 are:

- Patent application WO2022204523 (Cellenkos) presents several regulatory T cells derived from cryopreserved human umbilical cord blood that display immunosuppressive abilities. CK0802 cells, which display a $CD4^+CD25^+$ phenotype, are disclosed for use in treating ARDS, including in patients with COVID-19. CK0802 cells were tested in patients with lung damage due to COVID-19 (Cellenkos Inc., n.d.). Results showed CK0802 infusions were well-tolerated and improved patient outcomes (Gladstone *et al.*, 2021).
- Patent application WO2021155312 (Celularity) discloses natural killer (NK) cell CYNK-001s derived from human placental $CD34^+$ cells that contain CXCR3 transcripts known to direct NK cells to a viral infection site. The use of CYNK-001 in treating patients with COVID-19 is presented, and its safety and efficacy is to be tested as part of Clinical trial NCT04365101 (Celularity Incorporated, n.d.).
- Patent application WO2022077115 (Ottawa Hospital Research Institute) discloses MSCs genetically engineered to overexpress angiopoietin-1 (ANGPT1) and IFN-induced transmembrane (IFITM) proteins that decrease disease severity and increase survival rate in mouse ARDS models. Specifically, MSC candidates IFITM1-Angpt1 and IFITM3-Angpt1 increased survival rate in virus-induced ARDS.
- Patent application WO2021222389 (Factor Bioscience) discloses the use of mRNA-based reprogramming to create MSCs derived from induced pluripotent stem cells (iPSCs) for use in treating infections and ARDS caused by viruses, such as SARS-CoV-2. This invention relates that iPSCs contain an increased or decreased expression of those host factors either associated with enhanced antiviral activity or associated with the cytokine storm that occurs in some viral infections.

Other biologic-based therapeutics

CRISPR-Cas system

CRISPR is a gene-targeting system that uses a guide RNA and a nuclease enzyme (such as Cas9, Csm or Cas13d) to cut a gene at a specific location (WIPO, 2022). Its use in targeting highly conserved sequences of SARS-CoV-2, such as the RdRp or N genes, represents a potential new strategy for combating pan-coronaviruses. While this may seem promising, additional studies on potential toxic effects, as well as strategies for lowering overall high production costs, are needed before CRISPR-Cas can be fully utilized in a therapeutic setting (Abusalah *et al.*, 2022). Examples of patents that begin looking at this new approach are:

- Patent application WO2021183887 (The Board of Trustees of the Leland Stanford Junior University) presents a CRISPR-Cas13-based strategy, referred to as prophylactic antiviral CRISPR in human cells (PAC-MAN), that effectively degrades SARS-CoV-2 RNA and reduces influenza A virus load in human lung cells. Cas13d-PAC-MAN is effective at targeting and cleaving SARS-CoV-2 RNA, with six CRISPR-RNAs found that target more than 90 percent of all coronaviruses. In particular, crRNA PAC-MAN-T6 has been shown to target all known human coronaviruses with a broad coverage that includes other animal coronaviruses (Abbott *et al.*, 2020).
- Patent application WO2022132773 (New York Genome Center) discloses that creating chemically-modified CRISPR RNA (crRNA) can improve RNA targeting efficiency and half-life in human cells. This invention shows that Cas13d, along with the chemically modified crRNAs that target a conserved SARS-CoV-2 RNA, could suppress reporter protein expression. This invention also discloses the use of Cas13 ribonucleoprotein (RNP) complexes with crRNA for the delivery of Cas13 into human cells via a non-viral mechanism (Mendez-Mancilla *et al.*, 2022).

Exosome-mediated therapy

Exosomes are small extracellular vesicles (EVs) (30–200 nm in size) that have exceptional ability to target specific tissues or cells. They can therefore serve as good drug delivery vehicles. It has been shown that exosome therapy can overcome the difficulties associated with whole cell-based therapies and help with the regeneration of injured tissue, the suppression of inflammatory cytokines and/or the modulation of immune cells. Exosomes can carry specific therapeutic and/or modulating biomolecules, including bioactive molecules produced in genetically-modified MSCs (Rezabakhsh *et al.*, 2022). Examples of patents falling into these categories are:

- Patent application EP3895697 (Ichilov Tech) discloses the preparation of exosome Exo-CD24 which expresses CD24 and its use in reducing the cytokine storm seen in patients with moderate-to-severe COVID-19. Exo-CD24 was tested and shown to reduce cytokine levels in treated mice. Several clinical trials sponsored by the Tel-Aviv Sourasky Medical Center are evaluating the safety and efficacy of exosomes expressing CD24 in treating patients with moderate or severe COVID-19 (Sprecher, n.d.).
- Patent application WO2022144333 (Fundacion Para La Investigacion Del Hospital Universitario Y Politecnico) discloses EVs derived from MSCs genetically modified to overexpress hypoxia-inducible factor 1α (HIF-1α) and human telomerase (TERT), and their use in treating diseases associated with SARS-CoV-2 infection. The overexpression of HIF-1α increases the immunomodulatory capacity of secreted EVs.

Traditional medicine

The practice of traditional medicine in the maintenance of health, as well as in the prevention, diagnosis, improvement or treatment of physical and mental illness, is built upon centuries of theories, beliefs and experiences indigenous to different cultures (WHO, 2013). Therapies included under the term traditional medicine include those made from herbs, animals or other natural sources.

The global response to the pandemic included using medicinal plants and other traditional medicine to treat or prevent COVID-19. Some cultures rely heavily on traditional medicine and some governments actively promoted its use during the pandemic. The Governments of China, India and the Republic of Korea issued guidelines indicating traditional remedies for prevention and treatment of the disease (Ang *et al.*, 2020; Xiong *et al.*, 2021). China promoted traditional medicine in the treatment of COVID-19, particularly in areas where access to vaccines and treatments was limited (The Economist, 2022). In Asian cultures more generally, *Zingiber officinale* (ginger) and species of *Glycyrrhiza* were frequently used to treat COVID-19 infection (Liana and Phanumartwiwath, 2022). It has been documented that a number of Chinese traditional medicines have been used as a remedy for COVID-19 (Lyu *et al.*, 2021), with some evidence suggesting positive benefits (Li *et al.*, 2022; Xing and Liu, 2021). Sales of traditional Chinese medicines by pharmaceutical companies specializing in such products doubled or tripled during the pandemic. Companies selling traditional medicine even outperformed major Western COVID-19 vaccine producers (The Economist, 2022).

Asian communities were not alone in their use of traditional medicine. In Peru, medicinal plants were used to both prevent COVID-19 and treat the respiratory symptoms associated with SARS-CoV2-infection (Villena-Tejada *et al.*, 2021). A number of African medicinal plants show therapeutic potential for COVID-19 (Attah *et al.*, 2021). Emphasizing the importance of traditional medicine, the World Health Organization signed an agreement with the Government of India in March 2022 establishing a WHO Global Centre for Traditional Medicine (GCTM), which will focus on "evidence and learning; data and analytics; sustainability and equity; and innovation and technology to optimize the contribution of traditional medicine to global health and sustainable development" (WHO, 2022c).

Through September 2022, 523 patent applications related to traditional medicine were published (Figure 16). The vast majority (320) were first filed in 2020. Most were filed by applicants in Asia (86 percent). Only a handful of applicants were located in other regions of the world. Unsurprisingly, a large number of these patent applications (341) were filed with CNIPA in China, where traditional medicine is much more commonly prescribed than in other parts of the world.

Figure 16. Distribution of patent applications related to COVID-19 traditional medicine therapeutics across applicant locations

Over 60 percent of the COVID-19 patent dataset relating to traditional medicine therapeutics was filed by applicants in China.

Source: WIPO, based on patent data from the CAS Content Collection, September 2022.

Examples of traditional medicine disclosed in patent publications for the prevention or treatment of COVID-19 are:

- Patent applications CA3092398 (Alhassan Jamila) and CN111298034 (Leiyunshang Pharmaceutical Group) disclose anti-viral teas.
- Patent applications IN202021017835 (Khambe Sandeep Deepak), IN202021048992 (Waghchaure, Dnyaneshwar) and IN202041026972 (Jacob Zacharia) disclose ayurvedic compositions for either boosting immunity or as an antiviral against SARS-CoV-2.
- Patent application CN114504601 (Chongqing Chunzhi Biotechnology) discloses a fungal product for the treatment of novel coronavirus, based on *Ganoderma lucidum Karst*.
- Patent application WO2022191324 (Manda Fermentation) discloses fermented fruit and vegetable composition for use as cytokine storm inhibitor.
- Patent application KR10-2240432 (Kang Sung Cheon) discloses an herbal medicine containing pepper stem extract for treating COVID-19.
- Patent application US20220031792 (NutriScience Innovations) discloses a dietary supplement containing ashwagandha extract for treating lingering symptoms of COVID-19.
- Patent application WO2022131603 (Korea Institute of Oriental Medicine) discloses an antiviral *Geranium* extract for the treatment or prevention of COVID-19.
- Patent application TR2020005661 (Dericizade, Mecid *et al.*, Türkiye) discloses an herbal antiviral composition composed of several herbs, including *Glycyrrhiza glabra*, *Hypericum perforatum*, *Syzygium aomaticum*, *Vitis vinifera* and *Mentha arvensis*.
- Patent application MD1541 (Institutia Publica Institutul de Fiziologie si Sanocreatologie a MECC) discloses an herbal composition containing plant materials extracts, including from black wormwood, cornet, maral root, horseradish and ginseng for the treatment of COVID-19 in combination with other drugs.

Therapeutics for long COVID

Similar to what happens with other viral infections, some people who have been infected with the SARS-CoV-2 virus may experience long-term effects following infection. These long-term effects have generally come to be termed "long COVID," but are also known as post-COVID syndrome, acute post-COVID, long haul COVID and chronic COVID. The World Health Organization defines long COVID as "the continuation or development of new symptoms 3 months after the initial SARS-CoV-2 infection, with these symptoms lasting for at least 2 months with no other explanation" (WHO, 2022b). A recent study by Hao Zhang *et al.* (2022) identified four types of long COVID, each with a different set of symptoms requiring a different therapeutic treatment. Within the dataset, 22 patents were identified that discuss the treatment of long COVID. Table 18 shows the distribution of these patents by therapeutic type. The majority (13, 59 percent) describe the use of small molecule therapeutics to treat symptoms of long COVID. Biologic therapeutics make up the next biggest subset of patents (7, 32 percent), followed by traditional medicine and other types of therapeutics.

Table 18. Distribution of long COVID patent applications across therapeutic categories
Therapeutics for long COVID treatment were discussed in 22 patents. The majority of these (13, 59 percent) discuss small molecule therapeutics to treat long COVID.

Therapeutic category	Number of patent families
Small molecule	13
Traditional medicine	3
Biologic, others	3
Biologic, protein	2
Biologic, antibodies	1
Biologic, nucleic acid-based	1
Others	2

Source: WIPO, based on patent data from the CAS Content Collection, September 2022.

Examples of patents that disclose therapeutics for the treatment of long COVID are:

- Patent application WO2022006140 (Yale University) discloses the use of camostat or a pharmaceutically acceptable salt or solvate of camostat to prevent or reduce the occurrence and consequences of long COVID. Camostat blocks the TMPRSS2 protein. This prevents the virus from fusing with cells and replicating.
- Patent application US20220280547 (AIM ImmunoTech) discloses the use of Ampligen (Rintatolimid), a dsRNA that acts as a TLR3 agonist which stimulates interferon and necrosis factors, in treating patients with long COVID. In October 2022, Ampligen was given clearance by the USFDA to start a clinical trial treating long COVID (Solve M.E., 2022).
- Patent application WO2021198346 (Besitzgesellschaft, Nesselhut) discloses the use of human ezrin peptide 1 (HEP1) or an analog to treat COVID-19 and post-COVID-19 syndrome. HEP1 inhibits the expression of inflammatory cytokines, amplifies adaptive B cell and T cell immunity and enhances tissue repair.
- Patent application WO2021188334 (Noveome Biotherapeutics, Inc.) discloses the use of ST266, a novel cell-free platform biologic shown to improve cellular healing, to treat severe systemic inflammatory responses in patients experiencing post-acute COVID-19.

Formulations of COVID-19 therapeutics

Pharmaceutical formulation is a multistep process during which an active drug is mixed with other components that maximize the therapeutic potential, safety and stability of the final pharmaceutical product (Tovey, 2018). In addition to developing formulations for new drug candidates, researchers also investigated novel formulations of existing drugs, so as to make them easier to administer or enable enhanced pharmacokinetics and pharmacodynamics to efficiently manage and treat diseases, including COVID-19.

Through September 2022, 277 patent applications related specifically to pharmaceutical formulations were published. The vast majority (225, 81 percent) were first filed in 2020. Most were filed by corporate applicants (168, 61 percent), either alone or in collaboration with a university or research organization or an independent inventor (Table 19). This speaks to the high commercial interest in pharmaceutical formulations and the marketability of COVID-19 therapeutics (Afrin and Gupta, 2022).

Table 19. Distribution of pharmaceutical formulation patent applications across applicant profiles

Over 60 percent of patent applications relating specifically to pharmaceutical formulations were submitted by corporate applicants, either alone or in collaboration with a university or research organization or an independent inventor.

Type of applicant	Number of patent families
Corporate	152
Independent inventor	60
Universities and research organizations	49
Corporate, university and research organizations	14
Corporate, independent inventor	2

Source: WIPO, based on patent data from the CAS Content Collection, September 2022.

Within this subset of patents, a majority relate to formulations of small molecule therapeutics (179, 65 percent), followed by biologics (98, 35 percent) (Table 20). Traditional medicine therapeutics are represented, so too a small number of patents related to other, unclassified therapeutic types.

Table 20. Distribution of pharmaceutical formulation patent applications across therapeutic categories

Almost 65 percent of the patent applications relating to pharmaceutical formulations discussed small molecule therapeutics. Patents related to biologic therapeutics make up 35 percent of the dataset, the majority being protein biologics.

Therapeutic type	Number of patent families
Small molecule	179
Biologic, protein	57
Biologic, antibodies	19
Biologic, nucleic acid-based	14
Biologic, cell therapy	5
Biologic, others	3
Traditional medicine	33
Others	8

Source: WIPO, based on patent data from the CAS Content Collection, September 2022.

Examples of novel formulations for COVID-19 therapeutics disclosed in patent publications are:

- Patent applications WO2021207049 (Gilead Sciences, Inc.) and CN111956630 (Dalian University of Technology) disclose inhalable formulations of remdesivir for the treatment of COVID-19.
- Patent applications WO2021207599 (Akston Biosciences) and WO2022184854 (Formycon AG) disclose formulations of fusion proteins for the treatment of COVID-19.
- Patent applications IN202041015027 (CisGEN Biotech Discoveries Pvt Ltd.), WO2021188504 (Flow Pharma, Inc.), US20210403550 (Anovent Pharmaceuticals, LLC) and CN113274494 (Wuhan Institute of Biological Product Co., Ltd) disclose novel formulations of antibodies for the treatment of COVID-19.

Perspectives

This report provides an overview of patent documents published as of the end of September 2022 related to the development of vaccines and therapeutics for COVID-19. It builds upon and references the first WIPO COVID-19 Patent Landscape Report (WIPO, 2022), which had earlier reviewed patent documents published through until the end of September 2021. This report has covered a variety of new topics. For example, it has discussed patent office strategies adopted during the COVID-19 pandemic to facilitate patent filings. It has also explored the significant role played by traditional medicine in COVID-19 treatment and prevention, particularly in Asian countries, and the substantial number of COVID-19 therapeutics patents featuring traditional medicine. Other topics discussed are vaccine boosters and treatments for long COVID.

The abrupt outbreak and rapid spread of the COVID-19 pandemic had a devastating impact worldwide on public health and economies. Such was the impact that it catalyzed an unprecedented effort directed toward the development of vaccines and therapeutics. The development of a vaccine or a therapeutic is ordinarily a complex and slow process taking 10–15 years or longer. Yet, just three years after the pandemic's outbreak, COVID-19 vaccines of different types had either been conditionally or fully approved and deployed in a number of countries. Many things contributed to such remarkable progress, among which were persistent and innovative research over decades, scientific knowledge about the disease being made widely available, intensified collaboration across various organizations, and the policies and measures actioned by governments to facilitate cooperation and vaccine delivery.

It is likely that those innovative approaches taken in the development and testing of vaccines and therapeutics during the pandemic will shape how other global health issues are addressed in the future. For example, the method used to test COVID-19 vaccines could become the norm for other types of vaccines. Regulatory agencies may consider granting EUA more frequently for vaccines and treatments for other diseases or disorders. New vaccine development to address the everchanging virus genome itself could be enhanced and/or accelerated, because of what has been learnt during the COVID-19 pandemic. Philip Robinson *et al.* (2022) share some interesting thoughts about preparing therapeutics for the next pandemic in order to ensure that the effectiveness acquired during the COVID-19 pandemic is not lost. Some additional factors to consider are the quick dissemination of data, the continued accelerated distribution of viral genomic sequences, secure analysis of patient datasets and the development of a clinical trial system able to be deployed within a matter of days.

While the patents reviewed in this report disclose innovative approaches to making and/or repurposing of vaccines and therapeutics to combat COVID-19, translating this work into substantive clinical success will be a challenge. Most of these patents at the time of writing give little information on the effectiveness of the disclosed substances in humans, instead merely outlining potential clinical trials to be conducted in the future. To determine the effectiveness of these substances one must therefore look to outside organizations that track clinical trials and public data and/or review other scientific literature in order to find out whether the disclosed substance is being tested within a clinical setting and what is the effectiveness.

According to the Milken Institute's Vaccine Tracker and the Regulatory Affairs Professionals Society Vaccine Tracker, 290 COVID-19 vaccines are currently in clinical trials (including those for EUA or full approval). A total of 13.04 billion doses of COVID-19 vaccine have been administered globally, with 4.76 billion people (68.5 percent of the world's population) having received at least one dose (Our World in Data, n.d.). COVID-19 therapeutics are equally critical

in the effort to end this pandemic, even in the presence of vaccines. However, although there have been significantly more patents filed related to the development of COVID-19 therapeutics than to vaccines, to date, success in this area is not as substantial as it has been in vaccine development. Nevertheless, as of June end 2022, a few dozen unique drug candidates had entered Phase 3 (or Phase 2/3) clinical trials, according to analysis by the Milken Institute, the Regulatory Affairs Professionals Society (RAPS) COVID-19 tracker data, and the US Clinical trial data (Milken Institute, n.d.-a; RAPS, n.d.-b; U.S. National Library of Medicine, n.d.). About a dozen drugs, including both small molecule and antibody drugs, have been approved for use on an emergency basis (RAPS, n.d.-b; USFDA, 2022a).

Our earlier analysis of therapeutics in development in 2021 has shown that biologics (especially antibody drugs) and small molecule drug classes each accounted for roughly 50 percent of COVID-19 drugs. However, although virus-neutralizing antibody drugs have had notable clinical success, the emergence of new SARS-CoV-2 virus variants and subvariants has significantly reduced the effectiveness of those antibody drugs designed to target the viral S protein – the site at which mutations have largely occurred. There is therefore a need for new antibody therapeutics broad in spectrum and/or multivalent and effective against new or predominant variants. The declining clinical success of antibody drugs currently on the market due to viral mutation and resultant insensitivity (Bendix, 2022) has forced clinicians and patients alike to rely on a few small molecule antiviral drugs, such as nirmatrelvir by Pfizer and molnupiravir by Merck & Co, which target coronaviral proteins with fewer mutations than the S protein. Despite their ongoing success, these small molecule drugs have usage limitations, side effects and issues regarding worldwide access. Therefore, it remains a challenge to effectively translate the large volume of patent publications on COVID-19 into substantial clinical success. With the waning virulence of SARS-CoV-2 and a reduction in disease severity observed in the new and currently dominating variants and subvariants, it remains to be seen whether the incentive for drug developers to place large amounts of investment into developing new anti-COVID drugs will continue to be there, especially into those drugs able to cope with the continual mutations of SARS-CoV-2.

Technology breakthroughs, such as mRNA vaccine design and lipid nanoparticle technology for mRNA vaccine delivery, have not only profoundly benefited the fight against this pandemic, but may also have enormous potential in vaccine development for other infectious diseases. Furthermore, therapeutic strategies using RNA molecules may advance the treatment of diseases beyond COVID-19. But challenges remain. The rapid mutation of SARS-CoV-2 variants able to evade human immunity warrants expediting the development of new versions of COVID vaccines against newly mutated coronaviruses. The success of mRNA vaccines in this pandemic has offered the world hope that such a goal is indeed achievable. The development of pan SARS-CoV-2 vaccines offering simultaneous protection against multiple variants will enable us to fight this disease more effectively.

Despite extensive media discussion, government recommendations and policy debates centering on the availability and use of boosters, patents related to booster vaccines have been shown to comprise a fairly small percentage (5 percent) of the vaccine dataset. Two factors might be impacting this subcategory of patent. First, more patent applications might yet be filed related to vaccine boosters, but only at a future date, once further R&D has been conducted on this topic; a view supported by recent articles in *The New England Journal of Medicine* discussing the use of monovalent and divalent vaccines as boosters (Winokur *et al.*, 2023; Lin *et al.*, 2023). Second, it is possible that patents could have been filed as relating to a booster regimen rather than the booster itself. However, the answer to this question is outside the scope of the data search for this report and therefore not represented in the dataset.

In the area of therapeutics, both the incorporation of artificial intelligence and other enabling technologies to quickly identify molecules that might specifically bind to viral target proteins and the development of a mechanism to speed up clinical trials would be highly desirable. Although a number of virus-neutralizing antibodies have shown promising results, with some gaining conditional approval, the expensive and complex drug production process means such drugs are not yet available for every COVID-19 patient. The world is still awaiting further highly efficacious, less expensive and easily administered drugs to become widely available.

Confronted by these challenges, the high rate of patenting activity related to COVID-19 vaccines and therapeutics revealed in this report, along with an abundance of scientific literature reported in other resources and the unforeseen speed in COVID-19 vaccine and therapeutics development, offer hope that pandemics such as this and others can be effectively combated or even prevented in the future.

Annex

Data sources and methods

This report is focused on the analysis of patents related to vaccines and therapeutics for COVID-19 from January 2020 through September 2022. A project team was put together consisting of WIPO staff and scientific information specialists from CAS (a division of the American Chemical Society) in order to develop a patent search strategy. Patent information was extracted from the CAS Content Collection (CAS, n.d.-a, n.d.-b), which includes patents published by 97 patent offices around the world up to September 30, 2022.

A broad COVID-19 patent dataset was created by searching for patent documents related to COVID-19, SARS-CoV-2, its variants, other novel naming conventions and keyword variations thereof. Two search strategies were then developed for the creation of data subsets related to vaccines and therapeutics. A vaccine dataset was created based on search queries related to vaccine names and the CAS substance registry numbers of those vaccines associated with COVID-19 disease or virus. Moreover, the vaccine dataset incorporated a search for patent classification codes related to medical preparations and variations of prevention and prophylactics. This involved title-abstract and claims search queries using keywords (found in patent documents or assigned to documents by CAS), patent classification symbols, CAS indexing and concept approaches (based on full-text content) and role indicators, such as THU for therapeutic use, PAC for pharmacological activity and PKT for pharmacokinetics, to identify substances with potential as a therapeutic agent. Additionally, a therapeutics dataset identified anti-viral therapeutic records based on search queries of immune-related drug classes, variations of target compounds and therapeutic agent delivery systems. Irrelevant search results were removed by additional search refinements. The search results were further reviewed by both machine models and subject matter experts to remove noise, as well as to cluster patent documents across different vaccine and therapeutic categories. The patent search strategy and the patent datasets (broad COVID-19, vaccines and therapeutics dataset) are available on the WIPO website. Through this process, 8,132 patent families were identified related to COVID-19. Among them, 1,349 related to vaccine development and 5,013 to therapeutics. Various analyses were then performed on the datasets to reveal trends and gain insights.

In this report, all record counts and most of the analyses refer to patent families or inventions, unless stated otherwise. Patent families consist of the earliest patent application filed for patent protection, and the subsequent patent applications related to the same invention. Where patents for the same invention are filed in numerous jurisdictions, they are described as patent applications corresponding to the same invention or as members of the same patent family. The filings themselves may claim zero, one or multiple priorities. There are different definitions of patent families. For the purpose of this report, the CAS patent family approach was followed, based on grouping patent documents that share novel scientific content. CAS intellectually evaluates each patent family and will create additional connections (links) to include domestically-related applications, countries that have not ratified the Paris Convention or applications filed too late to claim priority.

A combination of technology and human intelligence is used to evaluate each patent family and verify similar content within families. For each patent document, CAS has identified other closely related patent family members that tend to have priority relationships with the representative patents, such as claiming the same priority applications (or same set of priority applications), as well as priorities claimed by this patent and other patent documents that claim priorities to this patent. Patent family members may not have exactly the same priority, but all family members are linked through at least one priority. Continuations-in-part are placed in separate families,

as are some divisions, depending on whether patent law in the jurisdiction allows new content for these types of filings. While most patent families consist of closely related patents, there are some cases where more than one patent within a patent family is curated separately. This may happen when related patents have somewhat different technical content or when family members have more complex relationships, such as multiple priorities from different countries or relationships resulting from division, continuation or continuation-in-part (CIP) patents.

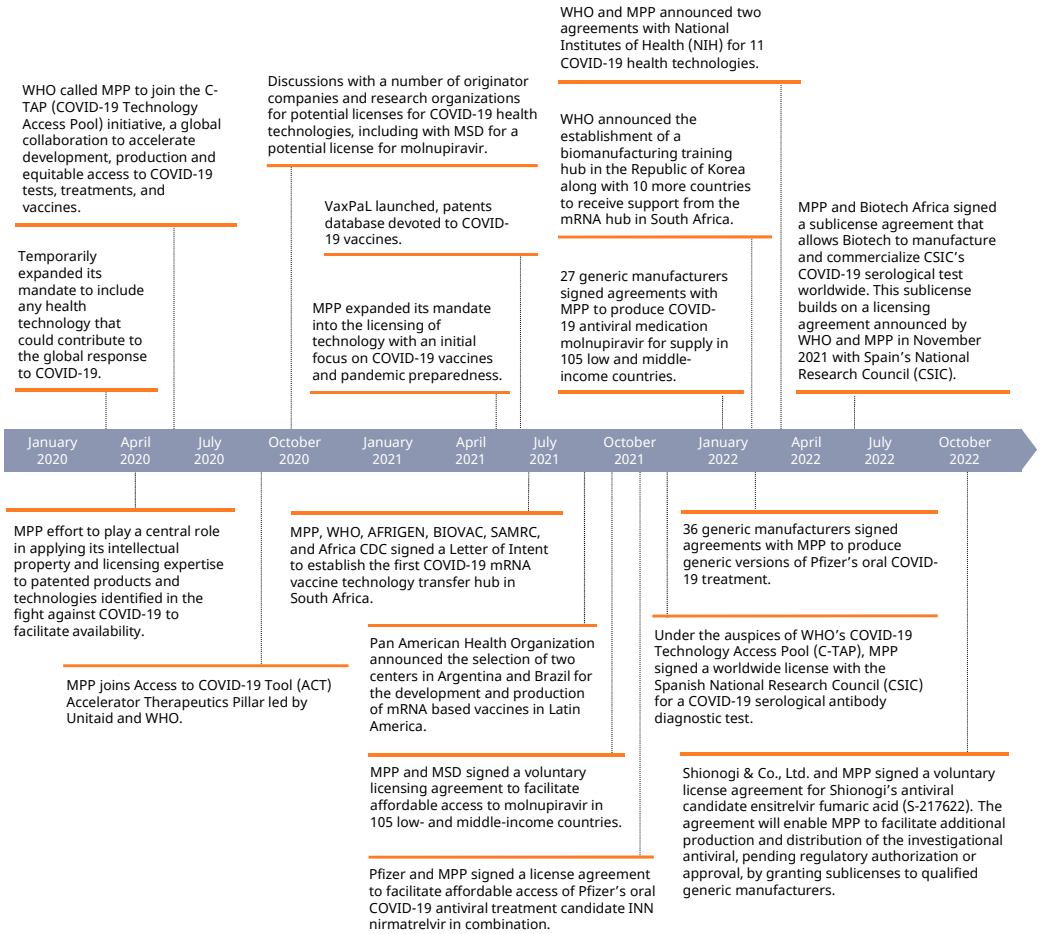
The analysis presented in this report refers to patent families, which in some cases may include a single patent family member. In most graphs and analysis, each patent family is represented by a single patent document. This ensures that even where there are several members of a patent family, it is only counted once – in this way we refer to invention numbers – giving a more accurate picture of actual innovative activity.

The analysis of collaborations was performed by normalization of patent applicant names using a combination of technology and human intelligence to obtain a count. Patent applicants, including corporate entities and academic institutions, may file patents with some variation in the institution name. For collaboration analysis, this report focused on corporate entities and universities and research institutes. Independent inventors were omitted from this analysis.

Licensing and other agreements related to COVID-19 vaccines and therapeutics: additional information

The Medicines Patent Pool (MPP) expanded its mandate in early 2020 in response to SARS-CoV-2 and COVID-19 (MPP, n.d.). Figure A1 details the timeline of MPP activities and contributions from January 2020 through May 2022.

Figure A1. **Medicines Patent Pool (MPP) activities and contributions, 2020–2022**
Timeline of MPP activities and contributions from January 2020 through May 2022.



Source: WIPO, based on data from the Medicines Patent Pool COVID-19 website.

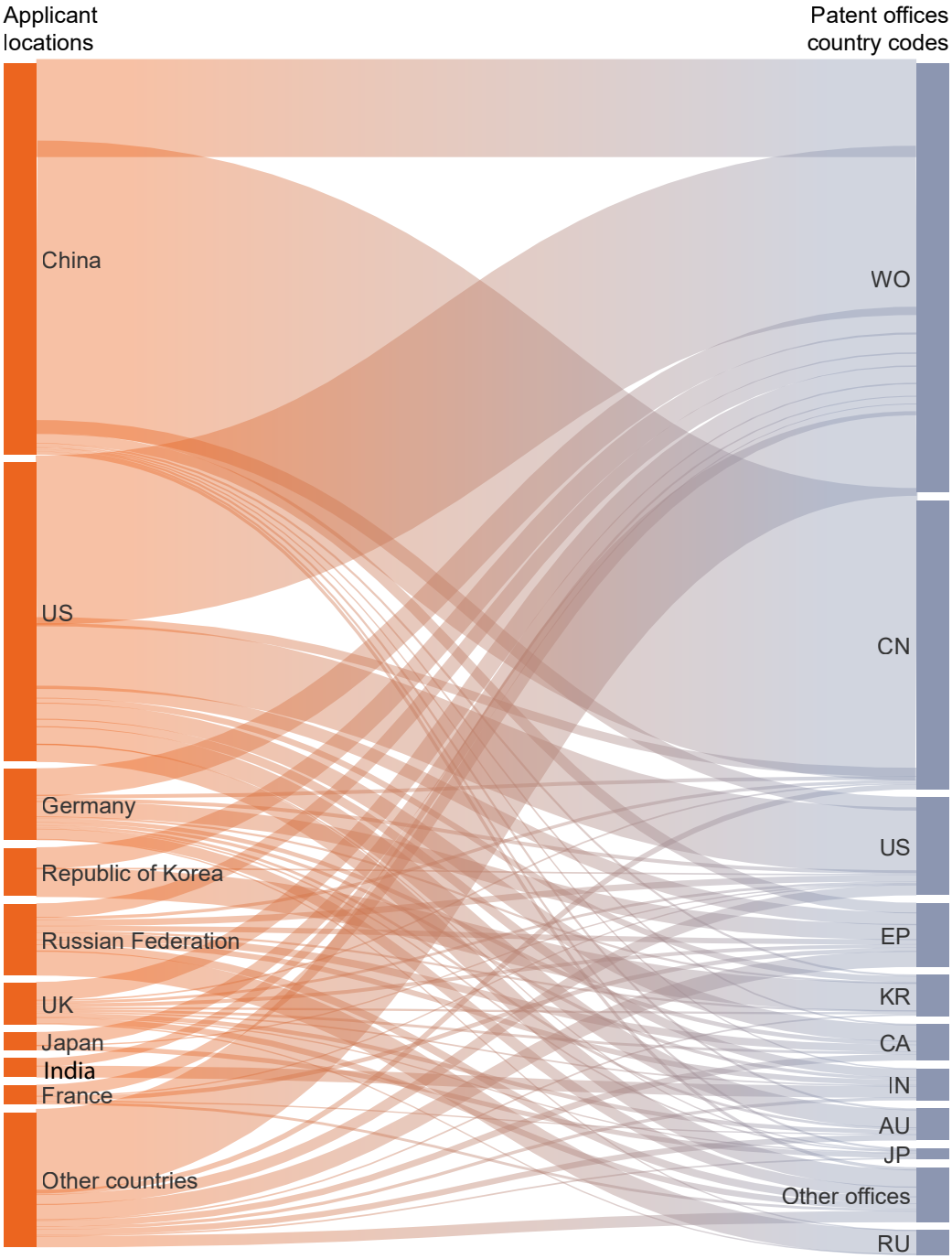
Flow of patent filings related to COVID-19 vaccines and therapeutics

Applicants in different regions used different patent filing strategies during the course of the pandemic.

Figures A2 and A3 further illustrate where applicants from different locations filed their applications related to COVID-19 vaccines and therapeutics, respectively.

Figure A2. Flow of patent filings related to COVID-19 vaccines

Patent filings related to COVID-19 vaccines from different application locations (left) are linked to the various patent offices of filing (right). Chinese applicants predominantly filed in China, with some also filing at WIPO/PCT, whereas US-based applicants followed a more diverse strategy.

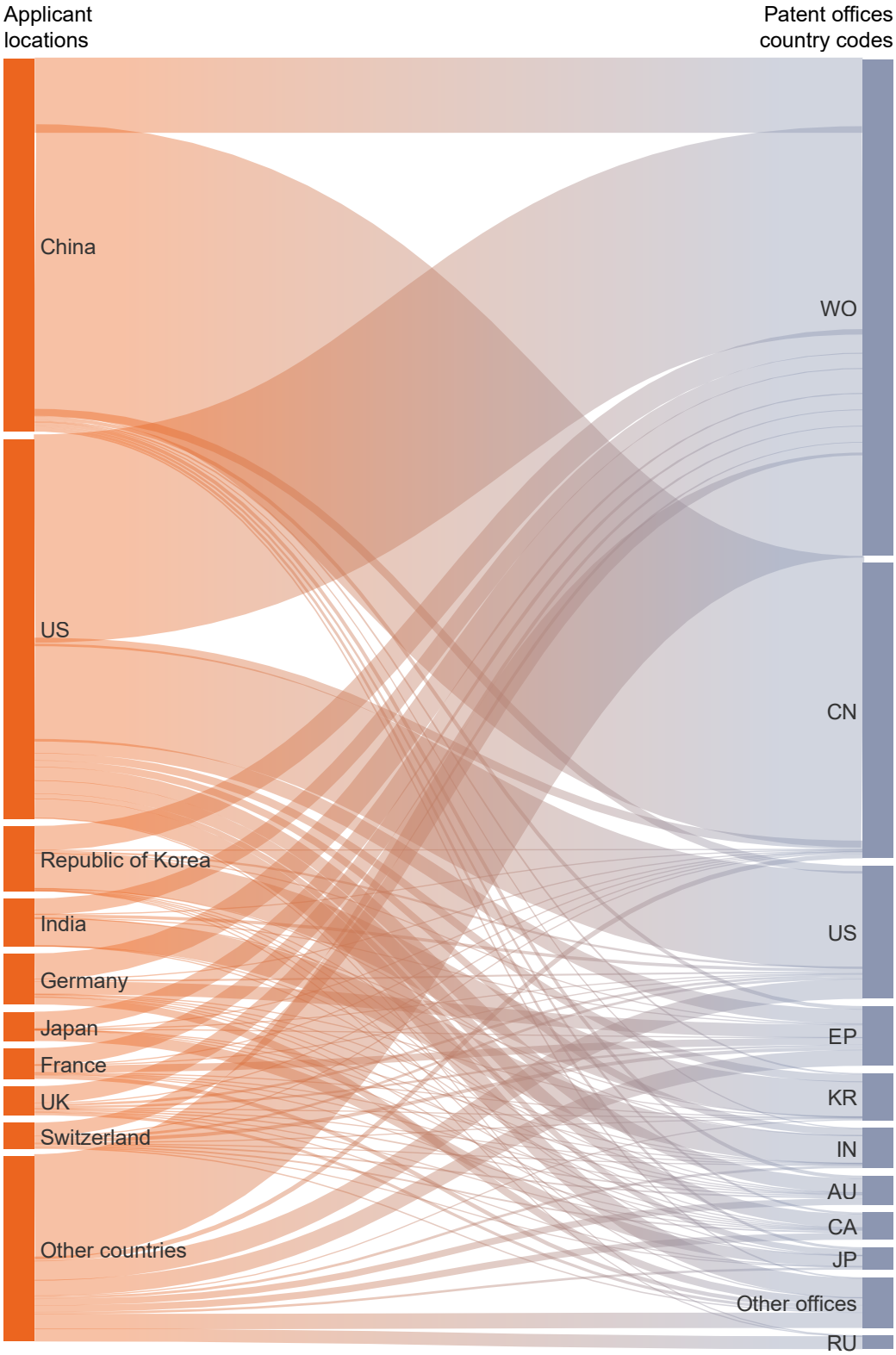


Note: The two-digit country codes used follow the WIPO Standard ST.3.

Source: WIPO, based on patent data from the CAS Content Collection, September 2022.

Figure A3. **Flow of patent filings related to COVID-19 therapeutics**

Flow of patent filings related to COVID-19 therapeutics from different applicant locations (left) to various patent offices of filing (right). Chinese applicants filed predominantly in China, whereas US-based applicants followed a more diverse strategy.



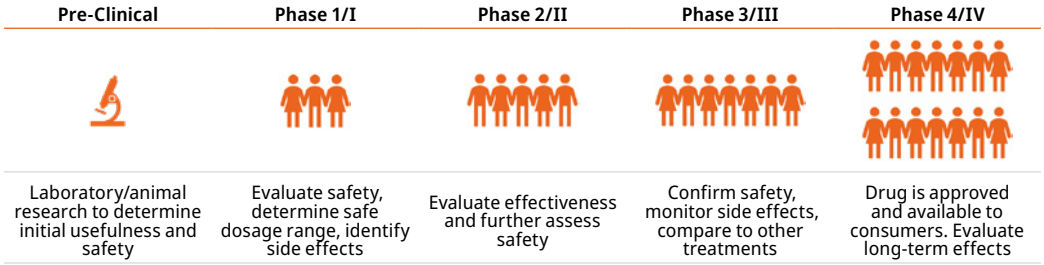
Note: The two-digit country codes used follow the WIPO Standard ST.3.

Source: WIPO, based on patent data from the CAS Content Collection, September 2022.

Clinical trials of COVID-19 vaccines and therapeutics

The COVID-19 pandemic fueled intense efforts to find and develop effective therapeutics and vaccines to prevent and treat the disease. Such efforts start in the research laboratory and typically include a series of clinical trials before the vaccines and therapeutics can be used by the general population. Clinical trials leverage volunteer participants to study new and existing medical interventions like vaccines and therapeutic treatments and evaluate their effects on human health outcomes. They are carefully designed and require the approval of government and public health institutions before they can begin. Clinical trials consist of several phases, each with its own purpose and value as summarized in Figure A4.

Figure A4. Clinical trial phases
Description of clinical trial phases, including participants and phase purpose or goal.



Source: WIPO, based on World Health Organization information on clinical trials (WHO, n.d.-a).

COVID-19 vaccines and therapeutics have undergone thousands of clinical trials around the globe, since the beginning of the pandemic in 2020. Several organizations track these clinical trials, including the WHO (n.d.-d, the Milken Institute (n.d.-a) and RAPS (n.d.-a, n.d.-b). Owing to the global impact of COVID-19 on human health, several broad clinical trials were instituted to gather large amounts of data from participants around the world, so as to identify those therapeutics most useful in combating COVID-19. A few such trials are now discussed in more detail below.

The WHO began sponsoring the Solidarity PLUS trial in March 2020. It is a "large, global randomized trial designed to provide robust results on whether a drug can save lives in those hospitalized with severe or critical COVID-19" (WHO, n.d.-h). This trial is to evaluate several existing drugs for the treatment of COVID-19, including the antimalaria drug artesunate, the monoclonal antibody inflizimab, the antivirals remdesivir, hydroxychloroquine, lopinavir and interferon beta-1a, and the cancer drug imatinib. Within six months of its start, the study provided conclusive evidence as to the effectiveness of these drugs when repurposed for treating COVID-19. Three of the drugs initially involved in the trial – artesunate, inflizimab and imatinib – showed promising results in the early phase of the study and have progressed for further study.

The University of Oxford began its RECOVERY trial in March 2020. "This international clinical trial aims to identify treatments that may be beneficial for people hospitalized with suspected or confirmed COVID-19" (University of Oxford, n.d.). This trial is likewise to evaluate several existing drugs for the treatment of COVID-19, including the antidiabetic drug empagliflozin, the monoclonal antibody sotrovimab, the glucocorticoid dexamethasone and the antivirals molnupiravir and Paxlovid. To date, this trial has involved over 47,000 participants across six countries. It has identified four effective COVID-19 treatments, namely, dexamethasone; corticosteroids with tocilizumab; baricitinib; and monoclonal antibodies. The trial is ongoing and continues to evaluate additional treatment options for COVID-19.

The National Institutes of Health (NIH) RECOVER initiative is developing multiple clinical trials to evaluate therapies for ameliorating symptoms associated with post-acute sequelae of SARS-CoV-2 infection (PASC) or long COVID. This clinical trial is utilizing a combination of nirmatrelvir and ritonavir antiviral oral medication. The trial is in the final stages of development and approval and expected to begin enrolling participants in early January 2023 (Zimmerman, 2022).

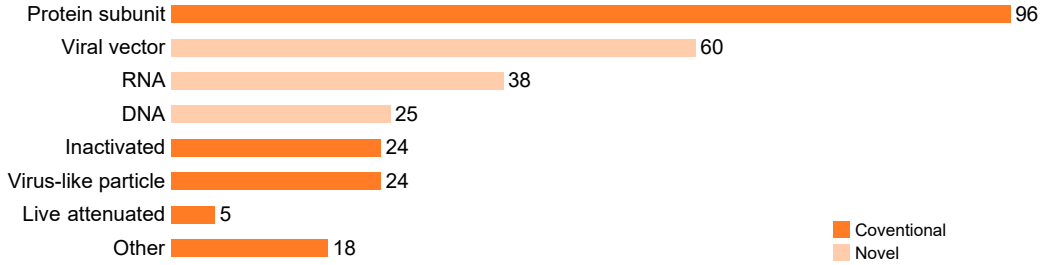
In this report, we have outlined patenting activity related to COVID-19 vaccines and therapeutics and discussed this in relation to specific types of vaccines and therapeutics. Clinical trial data has been analyzed in the same manner.

Analysis of COVID-19 vaccines in clinical trials

According to data contained in the Milken Institute's Vaccine Tracker (Milken Institute, n.d.-a) and the Regulatory Affairs Professionals Society (RAPS) Vaccine Tracker, there are 290 vaccines for COVID-19 in clinical trials (RAPS, n.d.-b). Figure A5 shows the distribution of these vaccines by vaccine type. A majority are protein subunit vaccines (96, 33 percent), followed by viral vector (60, 21 percent) and RNA-based vaccines (38, 13 percent), with other types represented in smaller numbers within the dataset.

Figure A5. COVID-19 vaccines in clinical trials

Distribution of 290 COVID-19 vaccines in clinical trials by vaccine type. The protein subunit type has the most vaccines in clinical trials.



Source: WIPO, based on clinical trial data from the Milken Institute and RAPS, December 2022.

Table A1 provides a sample listing of COVID-19 vaccines in clinical trials, by vaccine platform type, with the most advanced phase of active clinical trial being reported. The three most commonly used vaccines in the western hemisphere – Moderna's mRNA-1273, Pfizer's Comirnaty and AstraZeneca's AZD1222 – are all in either Phase 2/3 or Phase 3 clinical trials. CanSino's Ad5 nCoV vaccine, widely distributed among China's population, has entered a Phase 4 clinical trial. A more in-depth listing of these and the many other vaccines in various clinical trial phases can be found on Milken Institute's COVID-19 Vaccine Tracker and the RAPS COVID-19 Vaccine Tracker.

Table A1. Example COVID-19 vaccines undergoing clinical trials

Example COVID-19 vaccines in clinical trial, by vaccine type. The most advanced active clinical trial phase is reported.

Vaccine platform	Developer/manufacturer	Vaccine (CAS registry number)	Antigen	Phase
Inactivated virus	Sinovac Research and Development (China)	CoronaVac (2480309-93-9)	N/A	Phase 3
Inactivated virus	Sinopharm; China National Biotec Group Wuhan Institute of Biological Products (China)	WIBP-CorV (2699874-55-8)	N/A	Phase 3
Inactivated virus	Sinopharm; China National Biotec Group; Beijing Institute of Biological Products (China)	BBIBP-CorV (2503126-65-4)	N/A	Phase 3
Live attenuated virus	Codagenix/Serum Institute of India (India)	COVI-VAC (2695476-84-3)	N/A	Phase 1
Protein subunit	Novavax (US)	NVX-CoV2373 (2502099-58-1)	Spike protein nanoparticle (Sf9 cell)	Phase 3
Protein subunit	Vaxin (Australia)/Cinna Gen (Islamic Republic of Iran)	COVAX-19/Spikogen (2543231-22-5)	Spike (insect cell)	Phase 3
RNA-based	Moderna; National Institute of Allergy and Infectious Diseases (NIAID) (US)	mRNA-1273 (2457298-05-2)	Prefusion stabilized spike	Phase 3
RNA-based	Pfizer (US)/BioNTech; Fosun Pharma (China)	BNT162b2; Comirnaty (2417899-77-3)	Prefusion stabilized spike	Phase 2/3
Viral vector (non-replicating)	AstraZeneca; University of Oxford (UK)	AZD1222; ChAdOx1-S; ChAdOx1 nCoV-19; Covishield; Vaxzevria (2499737-08-3)	Spike	Phase 3
Viral vector (non-replicating)	CanSino Biological Inc./Beijing Institute of Biotechnology (China)	Ad5 nCoV (2540656-88-8)	Spike	Phase 4
Viral vector (non-replicating)	Janssen Pharmaceutical; Johnson & Johnson (US)	Ad26.COV2.S/ JNJ-78436735 (2541607-46-7)	Prefusion stabilized spike	Phase 3

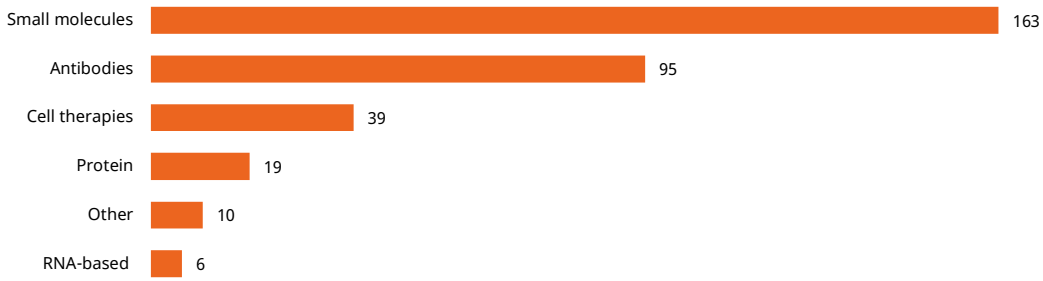
Source: WIPO, based on clinical trial data from the Milken Institute and RAPS, December 2022.

Analysis of COVID-19 therapeutics in clinical trials

According to data contained in the Milken Institute's COVID-19 Therapeutics Tracker and the Regulatory Affairs Professionals Society (RAPS) COVID-19 Therapeutics Tracker, there are 332 therapeutics for COVID-19 in clinical trials. Figure A6 shows the distribution of these therapeutics by therapeutic type. The majority are small molecule therapeutics (163, 49 percent), followed by antibody biologics (95, 29 percent) and cell-based therapies (39, 12 percent), with other types represented in smaller numbers within the dataset.

Figure A6. COVID-19 therapeutics in clinical trials

Distribution of 332 COVID-19 therapeutics in clinical trials, by therapeutic type. Small molecules make up the largest portion of therapeutics in clinical trials.



Source: WIPO, based on clinical trial data from the Milken Institute and RAPS, December 2022.

Table A2 provides a sample listing of COVID-19 therapeutics in clinical trials, by therapeutic type, with the most advanced phase of active clinical trial being reported. Most of the therapeutics in clinical trials for use against COVID-19 are repurposed drugs. Two widely discussed examples are molnupiravir and Paxlovid. Molnupiravir was originally developed to treat influenza infection and repurposed to treat COVID-19, because of its ability to inhibit virus replication. Paxlovid is a combination of two antivirals. The first, nirmatrelvir, was developed to specifically treat COVID-19, whereas the second, ritonavir, was initially developed to treat HIV/AIDS before being repurposed to treat COVID-19, owing to its ability to enhance the pharmacokinetic activity of other antiretroviral agents (Clinicalinfo.hiv.gov, n.d.). A more in-depth listing of these and the many other therapeutics in various clinical trial phases can be found on the Milken Institute's COVID-19 Therapeutics Tracker and the RAPS COVID-19 Therapeutics Tracker.

Table A2. Example COVID-19 therapeutics in clinical trials

Example COVID-19 therapeutics in clinical trial, by therapeutic type. The most advanced clinical trial phase is reported.

Therapeutic platform	Developer/manufacturer	Therapeutic (CAS registry number)	Phase
Biologic, antibodies	AstraZeneca; Vanderbuilt University Medical Center	Evusheld (tixagevimab and cilgavimab; AZD7442) (2603443-62-3)	Phase 3
Biologic, antibodies	Celltrion	Regkirona (regdanvimab, CT-P59) (2444308-95-4)	Phase 3
Biologic, antibodies	Janssen Pharmaceutical	Remicade (infliximab) (170277-31-3)	Phase 2/3
Biologic, antibodies	GSK, Vir Biotechnology	Sotrovimab (Xevudy) (2423014-07-5)	Phase 2/3
Small molecule	Pfizer	Paxlovid (nirmatrelvir) (2803933-60-8)	Phase 3
Small molecule	Ridgeback Biotherapeutics; Merck	Molnupiravir (Lagevrio) (2492423-29-5)	Phase 3
Small molecule	Lilly	Olumiant, Baricinix (baricitinib) (1187594-09-7)	Phase 3/4
Small molecule	Bristol Myers Squibb; National Center for Advancing Translation Science (NCATS); Biomedical Advanced Research and Development Authority (BARDA)	Orencia (abatacept) (332348-12-6)	Phase 3
Small molecule	Various	Dexamethasone (50-02-2)	Phase 2/3
Small molecule	Gilead Sciences	Veklury (remdesivir) (1809249-37-3)	Phase 2/3
Small molecule	Shionogi, Hokkaido University	Xocova (ensitrelvir, S-217622) (2647530-73-0)	Phase 3
Small molecule	NHLBI	Eliquis (Apixaban) (503612-47-3)	Phase 3/4
Small molecule	Bristol-Myers Squibb	Farxiga (dapagliflozin) (960404-48-2)	Phase 3

Source: WIPO, based on clinical trial data from the Milken Institute and RAPS, December 2022.

Acronyms

ARDS	acute respiratory distress syndrome
CIPO	Canadian Intellectual Property Office
CNIPA	China National Intellectual Property Administration
EPO	European Patent Office
EUA	emergency use authorization
FIPS	Federal Institute of Industrial Property
GHIAA	Global Healthcare Innovation Alliance Accelerator
GISAID	Global Initiative on Sharing Avian Influenza Data
INSDC	International Nucleotide Sequence Database Collaboration
JPO	Japan Patent Office
KIPO	Korean Intellectual Property Office
MPP	Medicines Patent Pool
PCT	Patent Cooperation Treaty
RAPS	Regulatory Affairs Professionals Society
SAMR	State Administration for Market Regulation, Government of China
USFDA	U.S. Food and Drug Administration
USPTO	United States Patent and Trademark Office
VOC	variant of concern
WHO	World Health Organization
WIPO	World Intellectual Property Organization
WTO	World Trade Organization

Glossary

Adenoviruses	A group of non-enveloped viruses that cause a wide range of diseases, such as cold and cold-like symptoms. They are named as such because they were first isolated from human adenoid tissue. These viruses have an icosahedral nucleocapsid containing a double stranded DNA genome. Modified adenoviruses have been used as viral vectors for delivery of targeted gene therapy and vaccines.
Adjuvant	Substance that enhances or modulates the immune response to an antigen.
ADME	Abbreviation in pharmacokinetics and pharmacology for absorption, distribution, metabolism and excretion. These four processes are considered the four steps of pharmacokinetics. ADME studies are designed to investigate how a chemical compound (e.g., a drug) is processed by a living organism. Characterization of ADME properties helps to explore and explain how pharmacokinetic processes happen, so as to provide safety considerations regarding a new drug on which risk-based assessments can be made.
Antibody	Protein that constitutes part of the human immune system for identifying and neutralizing pathogens. Antibody biologics for COVID-19 treatment may be either obtained from patients who have recovered from COVID-19 or manufactured in large quantities using recombinant DNA technologies with the assistance of other biotechnologies.
Antigen	Foreign substance inducing an immune response in the body, especially the production of antibodies.
Antigen-presenting cells	Immune cells such as dendritic cells, macrophages, Langerhans cells and B cells that mediate the cellular immune response by presenting antigens for recognition by lymphocytes such as T-cells.
Antisense oligonucleotide	A short, synthetic, single-stranded nucleic acid (RNA or DNA) molecule typically 19–23 base pairs in length that is complementary to a chosen target sequence. The complementary nature of the antisense oligonucleotide allows it to bind to a specific target thereby inhibiting gene expression or translation.
Biologic drugs (biologics)	Broad category of large molecules produced from living systems, containing components of living organisms or produced with the use of advanced biotechnologies, such as recombinant DNA technology. Biologics are usually large molecules (>1,000 Da) and complex in structure. Subclasses of biologics include, but are not limited to, antibodies, non-antibody proteins such as recombinant fusion proteins, gene/cell therapy products and nucleic acid-based therapy products in the context of this report.
Cell therapy	Placement of viable cells, with or without modification, into the human body to produce a beneficial effect.

Clinical trial	Clinical research designed to explore specific issues about biomedical interventions, including new treatments such as novel drugs, vaccines or medical procedures.
COVID-19	Viral infection caused by a coronavirus called SARS-CoV-2.
Cytokine	Small cell-signaling protein important in regulating host immune response to infection and inflammation. This protein influences the growth and activity of other immune system cells and blood cells.
DNA	Deoxyribonucleic acid, a molecule that carries genetic information and is formed from two chains of polynucleotides wound around each other, with backbones made of alternating sugar (deoxyribose) and phosphate groups.
DNA-based vaccine	Vaccine that transfects a specific antigen-coding DNA sequence into cells as a mechanism to induce immune response.
Enveloped virus	Virus exhibiting an outer wrapping/envelope made of lipids. This envelope originates from the host cell, where newly formed virus nucleic acid becomes wrapped in an outer coat made from the cell's plasma membrane and studded with viral proteins.
Exosome	Membrane-bound extracellular vesicles produced in the endosomal compartment of cells and released from cells into the extracellular environment. Exosomes may be engineered to serve as drug-containing vehicles for targeted drug delivery.
Fc fragment	Tail region of an antibody which interacts with cell surface receptors.
Fusion protein	Protein made up of parts from two or more other proteins joined together. Therapeutic fusion proteins are usually created artificially by recombinant DNA technology.
Inactivated vaccine	Vaccine consisting of whole pathogens (virus particles, bacteria) grown in culture and then killed to destroy their disease-producing ability.
Lipid nanoparticle	Nanoparticle composed of lipids used as a pharmaceutical drug and gene delivery system.
Live attenuated vaccine	Vaccine comprising a pathogen with reduced virulence ("live"), so that it becomes harmless or less virulent and yet can stimulate a strong and effective, long-lasting immune response.
MERS-CoV	Middle East respiratory syndrome coronavirus, or EMC/2012, a virus transferred to humans from infected dromedary camels.
MicroRNA	A single-stranded RNA molecule that is typically 21–25 base pairs in length and that binds to a specific mRNA. The microRNA is typically an endogenous molecule arising from larger precursors transcribed from non-protein-encoding genes, but can also be synthesized in the laboratory.
mRNA	Messenger ribonucleic acid, a single-stranded RNA that is complementary to one of the DNA strands of a gene; it is read by a ribosome throughout protein synthesis.
Natural product	Chemical compound or substance produced by a living organism such as a plant.

Neutralizing antibody	Antibody that protects a host cell from a virus. It is part of the normal human immune response, but can also be commercially produced using recombinant DNA technology.
Non-structural protein (NSP)	Protein encoded by a virus that is not part of the viral particle. Typically, nonstructural proteins include enzymes and transcription factors for virus replication, such as viral protease (3CL/nsp5, and so on), RNA replicate or other template-directed polymerases. The SARS-CoV-2 virus contains 16 non-structural proteins (NSP1–NSP16).
Pandemic	Epidemic of an infectious disease spread across multiple continents or worldwide, affecting a large number of individuals.
Patent	Legal title that gives inventors the right, for a limited period (usually 20 years), to prevent others from making, using or selling their invention without permission in those countries for which the patent has been granted.
Patent application/filing	Request for patent protection for an invention in a given jurisdiction filed with a patent office.
Patent Cooperation Treaty (PCT)	International treaty, administered by the World Intellectual Property Organization (WIPO), under which a single international patent application can be filed for patent protection in up to 154 countries.
Patent family	Set of interrelated patent applications filed in one or more countries to protect the same or a similar invention by a common inventor and linked by one or several common priority data. For this report's search and analysis, the Chemical Abstract Services (CAS) family approach was used, in which patent documents sharing similar content are grouped into a family following priority rules and manual review and validation.
Patent publication	Patent document published at different stages of the patent life cycle, including patent applications and granted patents. For the purposes of this report, "patent publication" is used interchangeably with "patent filing" or "patent application."
Protease	Enzyme that breaks apart proteins. The SARS-CoV-2 virus contains two proteases: NSP3 and NSP5, which are commonly called PLpro and 3CLpro.
RNA	Ribonucleic acid, a single-stranded chain of nucleotides, with a backbone made of alternating sugar (ribose) and phosphate groups. It plays a vital role in the essential biological processes of coding, decoding, regulation and expression of genes.
RNA-based vaccine	Vaccine using antigen-encoding messenger RNA (mRNA) to produce an immune response.
RNA interference	A biological process wherein small complementary RNA duplexes target and neutralize specific mRNA molecules resulting in the inhibition of gene expression or genetic translation. MicroRNAs and small interfering RNAs (siRNAs) generally 21–25 base pairs in length are often used in the RNA interference process.
SARS	Severe acute respiratory syndrome, a viral respiratory illness caused by a coronavirus SARS-CoV-1 or SARS-CoV-2.
SARS-CoV-1	Strain of coronavirus responsible for the 2002–2004 SARS outbreak.

SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2, the virus that caused COVID-19 (coronavirus disease 2019).
siRNA	A short, double-stranded RNA molecule typically 21–25 base pairs in length that interferes with the expression of specific genes by degrading mRNA after transcription thereby preventing translation. siRNAs are also known as short interfering RNA or silencing RNA.
Small molecule drug	Broad category of organic chemical compounds with a molecule size smaller than 1,000 Da. These molecules can be synthesized by chemical synthesis or extracted from natural sources (natural products).
Structural protein	Proteins playing an important role in shaping the skeletons and structures of cells, tissues and organisms. The amino acid sequences of structural proteins often show characteristic features notably different from those of functional proteins, such as enzymes and antibodies.
Subunit vaccine	Vaccine containing fragments of a pathogen (protein or polysaccharide) that are antigenic or required to induce an effective immune response.
Therapeutic drug	Substance used to treat or prevent disease.
Traditional medicine	Crude preparation of medication produced according to the principle of traditional medicinal practice. Preparations usually consist of a mixture of natural plant parts boiled in a liquid (decoction) or formed into balls or granules.
Vaccine	Substance intended to stimulate the production of antibodies and provide immunity against infectious diseases. A vaccine typically contains the agent causing the disease or a synthetic substitute that acts as an antigen without inducing the disease.
Viral vector	Modified virus used to deliver antigen-encoding genetic material into cells.
Virus	Infectious pathogenic agent that cannot reproduce by itself, but replicates inside the living cells of another organism (humans, animals, plants or bacteria).
Virus-like particle	Protein nanoparticle structure similar to wild-type virus, but has neither a viral genome nor infectious ability, producing safer vaccine candidates.
WHO	World Health Organization, a specialized agency of the United Nations responsible for international public health.
WIPO	World Intellectual Property Organization, a specialized agency of the United Nations dedicated to the promotion of innovation and creativity for the economic, social and cultural development of all countries through a balanced and effective international IP system.

References

Abbasi, J. (2020). COVID-19 and mRNA vaccines – First large test for a new approach. *Medical News & Perspectives*, 324(12), 1125–1127. doi:10.1001/jama.2020.16866

Abbott, T. R., Dhamdhere, G., Liu, Y., Lin, X., Goudy, L., Zeng, L., Chemparathy, A., Chmura, S., Heaton, N. S., Debs, R., Pande, T., Endy, D., La Russa, M. F., Lewis, D. B. and Qi, L. S. (2020). Development of CRISPR as an antiviral strategy to combat SARS-CoV-2 and influenza. *Cell*, 181(4), 865–876. doi:10.1016/j.cell.2020.04.020

Abusalah, M. A., Khalifa, M., Al-Hatamleh, M. A., Jarrar, M., Mohamud, R. and Chan, Y. Y. (2022). Nucleic acid-based COVID-19 therapy targeting cytokine storm: Strategies to quell the storm. *Journal of Personalized Medicine*, 12(3), 386. doi:10.3390/jpm12030386

Adam, D. (2022, January 18). The pandemic's true death toll: Millions more than official counts. *Nature*, 601, 312–315. doi:10.1038/d41586-022-00104-8

Afrin, S. and Gupta, V. (2022, June 23). *Pharmaceutical Formulation*. Retrieved December 2022, from StatPearls: www.ncbi.nlm.nih.gov/books/NBK562239.

Ang, L., Lee, H., Choi, J., Zhang, J. and Lee, M. (2020). Herbal medicine and pattern identification for treating COVID-19: A rapid review of guidelines. *Integrative Medicine Research*, 9(2), 100407. doi:https://doi.org/10.1016/j.imr.2020.100407

Apeiron Biologics (n.d.). *APN01 – Our work on a potential drug candidate for COVID-19 treatment*. Retrieved December 2022, from: www.apeiron-biologics.com/our-work-on-a-potential-drug-candidate-for-covid-19.

Attah, A. F., Fagbemi, A. A., Olubiyi, O., Dada-Adegbola, H., Oluwadotun, A., Elujoba, A. and Babalola, C. P. (2021). Therapeutic potentials of antiviral plants used in traditional African medicine with COVID-19 in focus: A Nigerian perspective. *Frontiers in Pharmacology*, 12. doi:10.3389/fphar.2021.596855

Awate, S., Babiuk, L. A. and Mutwiri, G. (2013). Mechanisms of action of adjuvants. *Frontiers in Immunology*, 4. doi:https://doi.org/10.3389/fimmu.2013.00114

Beaubien, J. (2022, January 14). For the 36 countries with the lowest vaccination rates, supply isn't the only issue. *Goats and Soda*. NPR. Retrieved from: www.npr.org/sections/goatsandsoda/2022/01/14/1072188527/for-the-36-countries-with-the-lowest-vaccination-rates-supply-isnt-the-only-issu.

Bendix, A. (2022, December 3). *New Coronavirus Variants Rendered the Last Remaining Monoclonal Antibody Treatment Useless*. Retrieved from NBC News: www.nbcnews.com/health/health-news/coronavirus-variants-monoclonal-antibody-drugs-ineffective-rcna59797.

Bhushan, B. L. S., Wanve, S., Koradia, P., Bhomia, V., Soni, P., Chakraborty, S., Khobragade, A., Joshi, S., Mendiratta, S. K., Kansagra, K. K., Parihar, A., Sharma, S. and Patel, J. (2021, October). Efficacy and safety of pegulated interferon-α2b in moderate COVID-19: A phase 3, randomized, comparator-controlled, open-label study. *International Journal of Infectious Disease*, 111, 281–287. doi:10.1016/j.ijid.2021.08.044

BioSpace (2022, Mar 2). *SAB Biotherapeutics Reports NIH is Discontinuing Phase 3 ACTIV-2 Trial Assessing SAB-185 for Treatment of COVID-19 Due to Declining COVID Hospitalizations*. Retrieved January 11, 2023, from: www.biospace.com/article/releases/sab-biotherapeutics-reports-nih-is-discontinuing-phase-3-activ-2-trial-assessing-sab-185-for-treatment-of-covid-19-due-to-declining-covid-hospitalizations.

Bloomberg (n.d.). More Than 12.7 *Billion Shots Given: Covid-19 Tracker*. Retrieved December 2022, from: www.bloomberg.com/graphics/covid-vaccine-tracker-global-distribution.

Bruggemann, M., Osborn, M. J., Ma, B., Hayre, J., Avis, S., Lundstrom, B. and Buelow, R. (2015). Human antibody production in transgenic animals. *Archivum Immunologiae et Therapiae Experimentalis*, 63(2), 101–108. doi:10.1007/s00005-014-0322-x

Burckhardt, R. M., Dennehy, J. J., Poon, L. L., Saif, L. J. and Enquist, L. W. (2022, February 9). Are COVID-19 vaccine boosters needed? The science behind boosters. *Journal of Virology*, 96(3). doi:10.1128/jvi.01973-21

Canadian Intellectual Property Office (CIPO) (2020). *Accelerate Examination for Canadian Patent Applications Related to COVID-19 Relief*. Retrieved December 15, 2022, from: https://ised-isde.canada.ca/site/canadian-intellectual-property-office/en/accelerate-examination-canadian-patent-applications-related-covid-19-relief.

CAS (n.d.-a). *CAplus*. Columbus, OH. Retrieved October 2022, from: www.cas.org/support/training/stnanavist/caplus-anavist.

CAS (n.d.-b). *STNext*. Columbus, OH. Retrieved October 2022, from: www.cas.org/solutions/stn-ip-protection-suite/stnext.

Cellenkos Inc. (n.d.). *Regulatory T Cell Infusion for Lung Injury Due to COVID-19 Pneumonia*. Retrieved December 2022, from U.S. National Library of Medicine – ClinicalTrials.gov: https://clinicaltrials.gov/ct2/show/NCT04468971.

Celularity Incorporated (n.d.). *Natural Killer Cell (CYNK-001) Infusions in Adults with COVID-19 (CYNKCOVID)*. Retrieved December 2022, from U.S. National Library of Medicine – ClinicalTrials.gov: https://clinicaltrials.gov/ct2/show/NCT04365101.

Chalkias, S., Eder, F., Essink, B., Khetan, S., Nestorova, B., Feng, J., Chen, X., Chang, Y., Zhou, H., Montefiori, D., Edwards, D. K., Girard, B., Pajon, R., Dutko, F. J., Leav, B., Walsh, S. R., Baden, L. R., Miller, J. M. and Das, R. (2022, October 6). Safety, immunogenicity and antibody persistence of a bivalent Beta-containing booster vaccine against COVID-19: A phase 2/3 trial. *Nature Medicine*, 28, 2388–2397. doi:https://www.nature.com/articles/s41591-022-02031-7

Clinicalinfo.hiv.gov (n.d.). *Drug Database: Ritonavir*. Retrieved December 2022, from: https://clinicalinfo.hiv.gov/en/drugs/ritonavir/patient.

ClinicalTrials.gov (2023). *ClinicalTrials.gov*. Retrieved January 11, 2023, from U.S. National Library of Medicine: https://clinicaltrials.gov/ct2/show/NCT04469179?cond=SAB-185&draw=2&rank=2.

Collier, A.-r. Y., Miller, J., Hachmann, N. P., McMahan, K., Liu, J., Bondzie, E. A., Gallup, L., Rowe, M., Schonberg, E., Thai, S., Barrett, J., Borducchi, E. N., Bouffard, E., Jacob-Dolan, C., Mazurek, C. R., Mutoni, A., Powers, O., Sciacca, M., Surve, N., VanWyk, H., Wu, C. and Barouch, D. H. (2022, October 25). Immunogenicity of the BA.5 Bivalent mRNA Vaccine Boosters. *bioRxiv*. doi:10.1101/2022.10.24.513619

Druedhal, L. C., Minssen, T. and Price, W. N. (2021). Collaboration in times of crisis: A study on COVID-19 vaccine R&D partnerships. *Vaccine*, 39(42), 6291–6295.

European Commission (2021, January 8). *Questions and Answers: COVID-19 Vaccination in the EU*. Retrieved January 12, 2023, from: https://ec.europa.eu/commission/presscorner/detail/en/qanda_20_2467.

European Medicines Agency (2022a, June 23). *COVID-19 Vaccine (Inactivated, Adjuvanted) Valneva (COVID-19 Vaccine (Inactivated, Adjuvanted, Adsorbed)): An Overview of COVID-19 Vaccine (Inactivated, Adjuvanted, Adsorbed) and Why it is Authorised in the EU*. Retrieved January 12, 2023, from: www.ema.europa.eu/en/documents/overview/covid-19-vaccine-inactivated-adjuvanted-valneva-epar-medicine-overview_en.pdf.

European Medicines Agency (2022b, November 30). *VidPrevtyn Beta*. Retrieved January 12, 2023, from: www.ema.europa.eu/en/medicines/human/EPAR/vidprevtyn-beta.

Fan, Y., Li, X., Zhang, L., Wan, S., Zhang, L. and Zhou, F. (2022). SARS-CoV-2 Omicron variant: Recent progress and future perspectives. *Signal Transduction and Targeted Therapy*, 7, 141. doi:10.1038/s41392-022-00997-x

Federal Institute of Industrial Property (FIPS) (n.d.-a). *Patent Documents on Coronavirus*. Retrieved December 10, 2022, from: www1.fips.ru/doc-virus.

FIPS (n.d.-b). *Rospatent COVID-19*. Retrieved December 5, 2022, from: www1.fips.ru/covid19.php.

Gaviria, M. and Kilic, B. (2021). A network analysis of COVID-19 mRNA vaccine patents. *Nature Biotechnology*, 39, 546–548. doi:10.1038/s41587-021-00912-9

Gilead (n.d.). *Medicines*. Retrieved December 20, 2022, from: www.gilead.com/science-and-medicine/medicines.

Gladstone, D. E., Howard, C., Lyu, M.-A., Mock, J., Adams, D., Gibbs, K., Li, L., Huang, M., Zeng, K., D'Alessio, F., Herlihy, J., Trevino, S., Hari, P., Sadeghi, T., Parmar, S., Slutsky, A. and Mukherjee, S. (2021). Randomized, multi-center, double-blinded, placebo controlled safety and early efficacy trial of cryopreserved cord blood derived T-regulatory cell infusions (CK0802) in the treatment of COVID-19 induced ARDS. *Blood*, 138(Supplement 1), 828. doi:10.1182/blood-2021-153616

Global Healthcare Innovation Alliance Accelerator (GHIAA) (n.d.-a). *Accelerating Global Health Partnerships*. Retrieved December 12, 2022, from: https://ghiaa.org/about-ghiaa.

GHIAA (n.d.-b). *Master Alliance Provisions Guide (MAPGuide) COVID-19*. Retrieved December 12, 2022, from: https://ghiaa.org/mapguide-home/search-results/?qs=covid+19.

Global Initiative on Sharing Avian Influenza Data (GISAID) (2022). *About Us: EpiCoV Data Curation Team*. Retrieved December 27, 2022, from: https://gisaid.org/about-us/acknowledgements/data-curation.

Golchin, A. (2021). Cell-based therapy for severe COVID-19 patients: Clinical trials and cost-utility. *Stem Cell Reviews and Reports*, 17, 56–62. doi:10.1007/s12015-020-10046-1

Gordon, D. E., Jang, G. M., Bouhaddou, M., Xu, J., Obernier, K., White, K. M. *et al.* (2020). A SARS-CoV-2 protein interaction map reveals targets for drug repurposing. *Nature*, 583, 459–468. https://doi.org/10.1038/s41586-020-2286-9.

Grubaugh, N. D., Petrone, M. E. and Holmes, E. C. (2020, February 18). We shouldn't worry when a virus mutates during disease outbreaks. *Nature Microbiology*, 529–530. doi:10.1038/s41564-020-0690-4

Hamadeh, N., Rompaey, C. V., Metreau, E. and Eapen, S. G. (2022, July 01). *New World Bank Country Classifications by Income Level: 2022–2023*. Retrieved from World Bank Blogs: https://blogs.worldbank.org/opendata/new-world-bank-country-classifications-income-level-2022-2023.

Haun, B. K., Lai, C.-Y., Williams, C. A., Wong, T. A., Lieberman, M. M., Pessaint, L., Andersen, H. and Lehrer, A. T. (2020). CoVaccine HT™ adjuvant potentiates robust immune responses to recombinant SARS-CoV-2 spike S1 immunization. *Frontiers in Immunology*, 11. doi:https://doi.org/10.3389/fimmu.2020.599587

Heidary, M., Kaviar, V. H., Shirani, M., Ghanavati, R., Motahar, M. and Sholeh, M. G. (2022). A comprehensive review of the protein subunit vaccines against COVID-19. *Frontiers in Microbiology*, 13, e927306. doi:10.3389/fmicb.2022.927306

Huang, J., Ding, Y., Yao, J., Zhang, M., Zhang, Y., Xie, Z. and Zuo, J. (2022). Nasal nanovaccines for SARS-CoV-2 to address COVID-19. *Vaccines*, 10(405), 1–15.

Information Office, Government of China (2022). *The State Council Information Office Held a Press Conference on the Statistical Data of Intellectual Property Related Work in the First Half of 2022*. Retrieved December 5, 2022, from: www.gov.cn/xinwen/2022-07/13/content_5700754.htm.

International Nucleotide Sequence Database Collaboration (INSDC) (n.d.). *International Nucleotide Sequence Database Collaboration*. Retrieved December 27, 2022, from: www.insdc.org.

Institut National de la Propriété Industrielle (2021). *Procédure de délivrance accélérée de brevets dans le cadre de la lutte contre la COVID-19*. Retrieved December 15, 2022, from: www.inpi.fr/nationales/procedure-de-delivrance-acceleree-de-brevets-dans-le-cadre-de-la-lutte-contre-la-covid-19.

Instituto Nacional da Propriedade Industrial (2020). *Observatório COVID-19*. Retrieved December 8, 2022, from: www.gov.br/inpi/pt-br/servicos/patentes/tecnologias-para-covid-19.

Japan Patent Office (JPO) (n.d.). *The JPO Quick Reads*. Retrieved December 12, 2022, from www.jpo.go.jp/e/news/quickreads/index.html.

Japan Patent Office and European Patent Office. (2020). *Joint message from the JPO and the EPO towards common solutions to global challenges*. Retrieved December 12, 2022, from: www.jpo.go.jp/news/kokusai/epo/20200716-jointmessage.html.

JeroenPollet, W.-H. U. (2021). Recombinant protein vaccines, a proven approach against coronavirus pandemics. *Advanced Drug Delivery Reviews*, 170, 71–82. doi:https://doi.org/10.1016/j.addr.2021.01.001

Johns Hopkins University (n.d.). *Coronavirus Resource Center*. Retrieved January 16, 2022, from Vaccine Research & Development: https://coronavirus.jhu.edu/vaccines/timeline#:~:text=A%20typical%20vaccine%20development%20timeline,vaccine%20doses%20for%20widespread%20distribution.

Kansal, M., Weintraub, R. and Brownstein, J. (n.d.). *Identifying COVID-19 vaccine deserts and implementing interventions*. Retrieved from: www.nlc.org/article/2021/08/11/identifying-covid-19-vaccine-deserts-and-implementing-interventions/#:~:text=COVID%2D19%20vaccination%20rates%20have,people%20have%20little%20or%20no.

Keech, C., Albert, G., Cho, I., Robertson, A., Reed, P., Neal, S., . . . Glenn, G. M. (2020). Phase 1–2 trial of a SARS-CoV-2 recombinant spike protein nanoparticle vaccine. *The New England Journal of Medicine*, 383(24), 2320–2332. doi:10.1056/NEJMoa2026920

Klobucista, C. (2022, December 5). *A Guide to Global COVID-19 Vaccine Efforts*. Retrieved from Council on Foreign Relations – Backgrounders: www.cfr.org/backgrounder/guide-global-covid-19-vaccine-efforts.

Ko, E.-J. and Kang, S.-M. (2018). Immunology and efficacy of MF59-adjuvanted vaccines. *Human Vaccines & Immunotherapeutics*, 14(12), 3041–3045. doi:10.1080/21645515.2018.1495301

Korean Intellectual Property Office (KIPO) (2020a). *COVID-19 Patents Information Navigation*. Retrieved December 5, 2022, from: www.kipo.go.kr/ncov/index_e.html.

KIPO (2020b). *Official Notice of 2nd ex-officio Extension for Designated Periods Due to the Effects of the COVID-19*. Retrieved December 5, 2022, from: www.kipo.go.kr/en/BoardApp/UEngBodApp?c=1003&board_id=kiponews&catmenu=ek06_01_01&seq=1695.

Kramer, A. E. (2020, September 19). *Russia is Slow to Administer Virus Vaccine Despite Kremlin's Approval*. Retrieved January 12, 2023, from *The New York Times*: www.nytimes.com/2020/09/19/world/europe/russia-coronavirus-vaccine.html.

Li, C., Luo, F., Liu, C., Xiong, N., Xu, Z. and Zhang, W. (2021, February 23). Effect of a genetically engineered interferon-alpha versus traditional interferon-alpha in the treatment of moderate-to-severe COVID-19: A randomised clinical trial. *Annals of Medicine*, 53(1), 391–401. doi:https://doi.org/10.1080/07853890.2021.1890329

Li, M., Zhu, H., Liu, Y., Lu, Y., Sun, M., Zhang, Y., Shi, J., Shi, N., Li, L., Yang, K., Sun, X., Liu, J., Ge, L. and Huang, L. (2022). Role of traditional Chinese medicine in treating severe or critical COVID-19: A systematic review of randomized controlled trials and observational studies. *Frontiers in Pharmacology*, 13. doi:10.3389/fphar.2022.926189

Li, Y., Tenchov, R., Smoot, J., Liu, C., Watkins, S. and Zhou, Q. (2021). A comprehensive review of the global efforts on COVID-19 vaccine development. *ACS Central Science*, 7(4), 512–533.

Liana, D. and Phanumartwiwath, A. (2022). Leveraging knowledge of Asian herbal medicine and its active compounds as COVID-19 treatment and prevention. *Journal of Natural Medicines*, 76, 20–37. doi:https://doi.org/10.1007/s11418-021-01575-1

Lin, D.-Y., Xu, Y., Gu, Y., Zeng, D., Wheeler, B., Young, H., Sunny, S. K. and Moore, Z. (2023, January 25). Effectiveness of bivalent boosters against severe Omicron infection. *The New England Journal of Medicine*. doi:10.1056/NEJMc2215471

Liu, C., Zhou, Q., Li, Y., Garner, L. V., Watkins, S. P., Carter, L. J., Smoot, J., Gregg, A. C., Daniels, A. D., Jervey, S. and Albaiu, D. (2020, March 12). Research and development on therapeutic agents and vaccines for COVID-19 and related human coronavirus diseases. *ACS Central Science*, 6(3), 315–331. doi:10.1021/acscentsci.0c00272

Lu, R.-M., Hwang, Y.-C., Liu, I.-J., Lee, C.-C., Tsai, H.-Z., Li, H.-J. and Wu, H.-C. (2020). Development of therapeutic antibodies for the treatment of diseases. *Journal of Biomedical Science*, 27(1). doi:10.1186/s12929-019-0592-z

Lyu, M., Fan, G., Xiao, G., Wang, T., Xu, D., Gao, J., Ge, S., Li, Q., Ma, Y., Zhang, H., Wang, J., Cui, Y., Zhang, J., Zhu, Y. and Zhang, B. (2021). Traditional Chinese medicine in COVID-19. *Acta Pharmaceutica Sinica B*, 11(11), 3337–3363. doi:https://doi.org/10.1016/j.apsb.2021.09.008

Makurvet, D. (2021). Biologics vs. small molecules: Drug costs and patient access. *Medicine in Drug Discovery*, 9, e100075. doi:10.1016/j.medidd.2020.100075

Mandavilli, A. (2022, November 18). *Will Covid Boosters Prevent Another Wave? Scientists Aren't So Sure*. Retrieved January 4, 2023, from *The New York Times*: www.nytimes.com/2022/11/18/health/covid-boosters-surge.html.

Maxmen, A. (2022). Unseating big pharma: The radical plan for vaccine equity. *Nature*, 607, 226–233. Retrieved from: www.nature.com/immersive/d41586-022-01898-3/index.html?utm_source=Nature+Briefing&utm_campaign=0c37fb994f-briefing-dy-20220714&utm_medium=email&utm_term=0_c9dfd39373-0c37fb994f-44037757.

Medicines Patent Pool (MPP) (n.d.). *MPP's Contribution to the Global Response to COVID-19*. Retrieved December 12, 2022, from: https://medicinespatentpool.org/covid-19.

Mendez-Mancilla, A., Wessels, H.-H., Legut, M., Kadina, A., Mabuchi, M., Walker, J. and Sanjana, N. (2022). Chemically modified guide RNAs enhance CRISPR-Cas13 knockdown in human cells. *Cell Chemical Biology*, 29(2), 321–327. doi:10.1016/j.chembiol.2021.07.011

Meng, H., Mao, J. and Ye, Q. (2022, January 13). Booster vaccination strategy: Necessity, immunization objectives, immunization strategy, and safety. *Journal of Medical Virology*, 94(6), 2369–2375. doi:10.1002/jmv.27590

Milken Institute (n.d.-a). *COVID-19 Treatment and Vaccine Tracker*. Retrieved December 2022, from: https://covid-19tracker.milkeninstitute.org.

Milken Institute (n.d.-b). *Vaccines in Use*. Retrieved December 16, 2022, from: www.covid-19vaccinetracker.org/authorized-vaccines.

Moroy, G. and Tuffery, P. (2022, May 10). Peptide-based strategies against SARS-CoV-2 attack: An updated *in silico* perspective. *Frontiers in Drug Discovery*, 2. doi:10.3389/fddsv.2022.899477

Nealon, D. (2021, November 23). *Breaking Down Boosters*. Retrieved from The Harvard Gazette/Health & Medicine: https://news.harvard.edu/gazette/story/2021/11/understanding-the-science-behind-a-vaccine-booster.

Obeng, E. M., Fianu, I. and Danguah, M. K. (2022). Multivalent ACE2-engineering – A promising pathway for advanced coronavirus nanomedicine development. *Nano Today*, 46(46), 101580. doi:10.1016/j.nantod.2022.101580

Offit, P. A. (2023, January 11). Bivalent Covid-19 vaccines – A cautionary tale. *The New England Journal of Medicine*, 388, 481–483. doi:10.1056/NEJMp2215780

Oncotelic Therapeutics (2021, November 23). *Oncotelic Announces Positive Topline Data for OT-101 C001 COVID Study*. Retrieved from NewsDirect: https://newsdirect.com/news/oncotelic-announces-positive-topline-data-for-ot-101-c001-covid-study-488291465.

OPIG (Oxford Protein Informatics Group) (2022). *The Coronavirus Antibody Database*. Retrieved January 11, 2023, from University of Oxford Protein Informatics Group: http://opig.stats.ox.ac.uk/webapps/covabdab.

Our World in Data (n.d.). *Coronavirus (COVID-19) Vaccinations*. Retrieved December 15, 2022, from: https://ourworldindata.org/covid-vaccinations.

Palm, M. E., Lindsell, C. J. and Selker, H. P. (2021). Sharing data among clinical trials of therapeutics in COVID-19: Barriers and facilitators to collaborating in a crisis. *Journal of Clinical and Translational Science*, 6(1).

pandemic (n.d.). *Booster Coverage of Population by Country and Income*. Retrieved December 2022, from pandemic: https://pandem-ic.com/booster-coverage-of-population-by-country-and-income.

Pearl, Z. and Heiliczer, E. (2020, April 26). The Israeli Patent Commissioner has authorized accelerated examination of patent applications relevant to the fight against the coronavirus. *Globes*. Retrieved from: https://en.globes.co.il/en/article-israel-fast-tracks-examinations-for-coronavirus-related-patent-applications-1001326674.

Pessôa, R. F., Corrêa, É. G. and Vasconcellos, A. G. (2022). Concessão rápida de patentes para enfrentamento da COVID-19 no Brasil. *Rev Panam Salud Publica (Pan American Journal of Public Health)*, 46. doi:https://doi.org/10.26633/RPSP.2022.149

Pharmaceutical Technology (2022, October 13). *Oncotelic Receives BARDA Contract for lLong COVID-19 Therapy Development*. Retrieved from Pharmaceutical Technology: www.pharmaceutical-technology.com/news/oncotelic-barda-long-covid-19.

Pinghui, Z. (2020, September 25). *Coronavirus: WHO Backed China's Emergency Use of Experimental Vaccines, Health Official Says*. Retrieved January 12, 2023, from *South China Morning Post*: www.scmp.com/news/china/society/article/3103121/coronavirus-who-backed-chinas-emergency-use-experimental.

Powell, A., Zhang, K., Sanyal, M., Tang, S., Weidenbacher, P., Li, S., Pham, T. D., Pak, J. E., Chiu, W. and Kim, P. (2021). A single immunization with spike-functionalized ferritin vaccines elicits neutralizing antibody responses against SARS-CoV-2 in mice. *ACS Central Science*, 7(1), 183–199.

Pulendran, B., Arunachalam, P. S. and O'Hagan, D. T. (2021). Emerging concepts in the science of vaccine adjuvants. *Nature Reviews. Drug Discovery*, 20(6), 454–475. doi:10.1038/s41573-021-00163-y

Rauf, A., Abu-Izneid, T., Khalil, A. A., Hafeez, N., Olatunde, A., Rahman, M., Semwal, P., Al-Awthan, Y. S., Bahattab, O. S., Khan, I. N., Khan, M. A. and Sharma, R. (2022). Nanoparticles in clinical trials of COVID-19: An update. *International Journal of Surgery*, 104(106818), 1–11.

Regulatory Affairs Professionals Society (RAPS) (n.d.-a). *COVID-19 Therapeutics Tracker*. Retrieved December 2022, from: www.raps.org/news-and-articles/news-articles/2020/3/covid-19-therapeutics-tracker.

RAPS (n.d.-b). *COVID-19 Vaccine Tracker*. Retrieved December 2022, from: www.raps.org/news-and-articles/news-articles/2020/3/covid-19-vaccine-tracker.

Rezabakhsh, A., Mahdipour, M., Nourazarian, A., Habibollah, P., Sokullu, E., Avci, C. B. and Rahbarghazi, R. (2022). Application of exosomes for the alleviation of COVID-19-related pathologies. *Cell Biochemistry & Function*, 40(5), 430–438. doi:10.1002/cbf.3720

Roberts, T. C., Langer, R. and Wood, M. J. (2020). Advances in oligonucleotide drug delivery. *Nature Reviews Drug Discovery*, 19, 673–694. doi:10.1038/s41573-020-0075-7

Robinson, P. C., Liew, D. F., Tanner, H. L., Grainger, J. R., Dwek, R. A., Reisler, R. B., Steinman, L., Feldmann, M., Ho, L.-P., Hussell, T., Moss, P., Richards, D. and Zitzmann, N. (2022, April 6). COVID-19 therapeutics: Challenges and directions for the future. *PNAS*, 119(15). doi:doi.org/10.1073/pnas.211989311

Rujas, E., Kucharska, I., Tan, Y. Z., Benlekbir, S., Cui, H., Zhao, T., . . . Julien, J.-P. (2021). Multivalency transforms SARS-CoV-2 antibodies into ultrapotent neutralizers. *Nature Communications*, 12(1). doi:10.1038/s41467-021-23825-2

Sasisekharan, R. (2021, April 22). Preparing for the Future – Nanobodies for Covid-19? *New England Journal of Medicine*, 384, 1568–1571. doi:10.1056/NEJMcibr2101205

Solnatide (n.d.). *Exploration of Safety, Tolerability and Clinical Efficacy of Solnatide IMP in Patients Infected with 2019 New Coronavirus*. Retrieved December 2022, from: www.solnatide.eu.

Solve M.E. (2022, October 12). *Breaking News: FDA Clears Ampligen to Start a Clinical Trial in Long Covid*. Retrieved from Solve M.E.: https://solvecfs.org/breaking-news-fda-clears-ampligen-to-start-a-clinical-trial-in-long-covid.

Sprecher, E. (n.d.). *A Phase II Randomized, Double-blind, Placebo-controlled Study to Evaluate the Safety and Efficacy of Exosomes Overexpressing CD24 to Prevent Clinical Deterioration in Patients with Moderate or Severe COVID-19 Infection*. Retrieved December 2022, from ClinicalTrials.gov: https://clinicaltrials.gov/ct2/show/NCT04969172?term=Exo-CD24&cond=COVID-19&draw=2&rank=3.

State Administration for Market Regulation, Government of China (SAMR). (2020). *State Administration for Market Regulation State Food and Drug Administration State Intellectual Property Office*. Retrieved December 5, 2022, from: https://gkml.samr.gov.cn/nsjg/zhghs/202002/t20200215_311667.html.

Statista (n.d.). 'COVID-19 vaccination' search. Retrieved December 15, 2022, from: www.statista.com/search/?q=COVID-+19+vaccination&Search=&qKat=search&newSearch=true&p=1.

Svilenov, H. L., Sacherl, J., Reiter, A., Wolff, L., Chen, C.-C., Stern, M., Wachs, F.-P., Simonavicius, N., Pippig, S., Wolschin, F., Buchner, J., Brockmeyer, C. and Protzer, U. (2020, December 11). Efficient inhibition of SARS-CoV-2 strains by a novel ACE2-IgG4-Fc fusion protein with a stabilized hinge region. *bioRxiv*. doi:10.1101/2020.12.06.413443

Svilenov, H. L., Sacherl, J., Reiter, A., Wolff, L. C.-C., Stern, M., Grass, V., Feuerherd, M., Wachs, F.-P., Simonavicius, N., Pippig, S., Wolschin, F., Keppler, O. T., Buchner, J., Brockmeyer, C. and Protzer, U. (2021). Picomolar inhibition of SARS-CoV-2 variants of concern by an engineered ACE2-IgG4-Fc fusion protein. *Antiviral Research*, 196, 105197. doi:10.1016/j.antiviral.2021.105197

Tan, K. X., Jeevanandam, J., Rodrigues, J. and Danquah, M. K. (2022). Apatmer-mediated antiviral approaches for SARS-CoV-2. *Frontiers in Bioscience-Landmark*, 27(11), 306. doi:10.31083/j.fbl2711306

Tanaka, S., Nelson, G., Olson, C. A., Buzko, O., Higashide, W., Shin, A., Gonzalez, M., Taft, J., Patel, R., Buta, S., Richardson, A., Bogunovic, D., Spilman, P., Niazi, K., Rabizadeh, S. and Soon-Shiong, P. (2021, June). An ACE2 Triple Decoy that neutralizes SARS-CoV-2 shows enhanced affinity for virus variants. *Scientific Reports*, 11, 12740. doi:10.1038/s41598-021-91809-9

The Economist (2022, June 30). *The Pandemic is Boosting Sellers of Traditional Medicine: Whether or Not They Work, Herbal Remedies are a Healthy Business*. Retrieved December 22, 2022, from The Economist: www.economist.com/business/2022/06/30/the-pandemic-is-boosting-sellers-of-traditional-medicine.

Thomas, K., LaFraniere, S., Weiland, N., Goodnough, A. and Haberman, M. (2021, September 17). *F.D.A. Clears Pfizer Vaccine, and Millions of Doses Will Be Shipped Right Away*. Retrieved January 12, 2023, from The New York Times: www.nytimes.com/2020/12/11/health/pfizer-vaccine-authorized.html.

Tovey, G. (Ed.). (2018). *Pharmaceutical Formulation: The Science and Technology of Dosage Forms*. Royal Society of Chemistry. doi:10.1039/9781782620402

U.S. National Library of Medicine (n.d.). *Study to Assess the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of Inhaled APN01 Developed as Treatment for COVID-19*. Retrieved December 2022, from: https://clinicaltrials.gov/ct2/show/NCT05065645.

United Nations (2022, March 28). *UN Analysis Shows Link Between Lack of Vaccine Equity and Widening Poverty Gap*. Retrieved from UN News: https://news.un.org/en/story/2022/03/1114762.

United States Patent and Trademark Office (USPTO) (n.d.). *COVID-19 Prioritized Examination Pilot Program*. Retrieved December 10, 2022, from: www.uspto.gov/initiatives/covid-19-prioritized-examination-pilot.

University of Oxford (n.d.). *Recovery: Randomized Evaluation of COVID-19 Therapy*. Retrieved December 2022, from: www.recoverytrial.net.

U.S. Food and Drug Administration (USFDA) (2020, December 18). *FDA Takes Additional Action in Fight Against COVID-19 by Issuing Emergency Use Authorization for Second COVID-19 Vaccine*. Retrieved January 12, 2023, from: www.fda.gov/news-events/press-announcements/fda-takes-additional-action-fight-against-covid-19-issuing-emergency-use-authorization-second-covid.

USFDA (2022a, July 6). *Coronavirus (COVID-19) Update: FDA Authorizes Pharmacists to Prescribe Paxlovid with Certain Limitations*. Retrieved December 2022, from United States Food and Drug Administration/Press Announcements: www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-pharmacists-prescribe-paxlovid-certain-limitations#:~:text=Paxlovid%20is%20authorized%20for%20the,to%20severe%20COVID%2D19%2C%20including.

USFDA (2022b). *Emergency Use Authorization*. Retrieved December 20, 2022, from: www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#coviddrugs.

USFDA (2022c, November 30). *FDA Announces Bebtelovimab is Not Currently Authorized in Any US Region*. Retrieved December 20, 2022, from: www.fda.gov/drugs/drug-safety-and-availability/fda-announces-bebtelovimab-not-currently-authorized-any-us-region.

USFDA (2022d, May 11). *Janssen COVID-19 Vaccine*. Retrieved January 12, 2023, from: www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/janssen-covid-19-vaccine.

USFDA (2022e, October 31). *Novavax COVID-19 Vaccine, Adjuvanted*. Retrieved January 12, 2023, from: www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/novavax-covid-19-vaccine-adjuvanted.

Villena-Tejada, M., Vera-Ferchau, I., Cardona-Rivero, A., Zamalloa-Cornejo, R., Quispe-Florez, M., Frisancho-Triveno, Z. and Yanez, J. (2021, September 22). Use of medicinal plants for COVID-19 prevention and respiratory symptom treatment during the pandemic in Cusco, Peru: A cross-sectional survey. *PLoS ONE*, 16(9), e0257165. doi:https://doi.org/10.1371/journal.pone.0257165

Wang, Q., Bowen, A., Valdez, R., Gherasim, C., Gordon, A., Liu, L. and Ho, D. D. (2022, October 24). Antibody responses to Omicron BA.4/BA.5 bivalent mRNA vaccine booster shot. *bioRxiv*. doi:10.1101/2022.10.22.513349

Wilson, B. and Geetha, K. M. (2022). Lipid nanoparticles in the development of mRNA vaccines for COVID-19. *Journal of Drug Delivery Science and Technology*, 74(103553), 1–6.

Winokur, P., Gayed, J., Fitz-Patrick, D., Thomas, S. J., Diya, O., Lockhart, S. and Kitchin, N. (2023, January 19). Bivalent omicron BA.1-adapted BNT162b2 booster in adults older than 55 years. *The New England Journal of Medicine*, 338, 214–227. doi:10.1056/NEJMoa2213082

WHO (2013). WHO Traditional Medicine Strategy: 2014–2023. Retrieved from World Health Organization: https://www.who.int/publications/i/item/9789241506096.

WHO (2020). *Novel Coronavirus(2019-nCoV): Situation Report – 22*. World Health Organization. Retrieved from: www.who.int/docs/default-source/coronaviruse/situation-reports/20200211-sitrep-22-ncov.pdf.

WHO (2021a, November 26). *Classification of Omicron (B.1.1.529): SARS-CoV-2 Variant of Concern*. Retrieved December 2022, from: www.who.int/news/item/26-11-2021-classification-of-omicron-(b.1.1.529)-sars-cov-2-variant-of-concern.

WHO (2021b, December 22). *Interim Statement on Booster Doses for COVID-19 Vaccination*. Retrieved from World Health Organization/News: www.who.int/news/item/22-12-2021-interim-statement-on-booster-doses-for-covid-19-vaccination---update-22-december-2021.

WHO (2021c, September 8). *WHO Director-General's Opening Remarks at the Media Briefing on COVID-19 – 8 September 2021*. Retrieved from: www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---8-september-2021.

WHO (2022a, May 17). *Interim Statement on the Use of Additional Booster Doses of Emergency Use Listed mRNA Vaccines Against COVID-19*. Retrieved from World Health Organization/News: www.who.int/news/item/17-05-2022-interim-statement-on-the-use-of-additional-booster-doses-of-emergency-use-listed-mrna-vaccines-against-covid-19.

WHO (2022b, December 7). *Post COVID-19 Condition (Long COVID)*. Retrieved from: www.who.int/europe/news-room/fact-sheets/item/post-covid-19-condition#:~:text=Definition,months%20with%20no%20other%20explanation.

WHO (2022c, March 25). *WHO Establishes the Global Centre for Traditional Medicine in India*. Retrieved December 22, 2022, from: www.who.int/news/item/25-03-2022-who-establishes-the-global-centre-for-traditional-medicine-in-india.

WHO (2023). *COVID-19 Vaccines with WHO Emergency Use Listing*. Retrieved January 12, 2023, from: https://extranet.who.int/pqweb/vaccines/vaccinescovid-19-vaccine-eul-issued.

WHO (n.d.-a). *Clinical Trials*. Retrieved December 2022, from: www.who.int/health-topics/clinical-trials#tab=tab_1.

WHO (n.d.-b). *COVAX: Working for Global Equitable Access to COVID-19 Vaccines*. Retrieved from: www.who.int/initiatives/act-accelerator/covax.

WHO (n.d.-c). *COVID19 Vaccine Tracker*. Retrieved January 3, 2022, from: https://covid19.trackvaccines.org.

WHO (n.d.-d). *International Clinical Trials Registry Platform*. Retrieved December 2022, from: www.who.int/clinical-trials-registry-platform.

WHO (n.d.-e). *The mRNA Vaccine Technology Transfer Hub*. Retrieved from: www.who.int/initiatives/the-mrna-vaccine-technology-transfer-hub.

WHO (n.d.-f). *Tracking SARS-CoV-2 Variants*. Retrieved December 2022, from: www.who.int/activities/tracking-SARS-CoV-2-variants.

WHO (n.d.-g). *WHO Coronavirus (COVID-19) Dashboard*. Retrieved November 28, 2022, from: https://covid19.who.int.

WHO (n.d.-h). *WHO COVID-19 Solidarity Therapeutics Trial*. Retrieved December 2022, from: www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-clinical-trial-for-covid-19-treatments.

WHO (n.d.-i). *WHO COVID-19 Technology Access Pool*. Retrieved December 2022, from: www.who.int/initiatives/covid-19-technology-access-pool.

WHO – Africa Region (n.d.). *COVID-19 Vaccines*. Retrieved December 15, 2022, from: www.afro.who.int/health-topics/coronavirus-covid-19/vaccines.

World Intellectual Property Organization (WIPO) (2022). *COVID-19-related Vaccines and Therapeutics: Preliminary Insights on Related Patenting Activity during the Pandemic*. Geneva: World Intellectual Property Organization.

WIPO (n.d.). *COVID-19 IP Policy Tracker*. Retrieved December 15, 2022, from: www.wipo.int/covid19-policy-tracker/#/covid19-policy-tracker/ipo-operations.

World Trade Organization (WTO) (2022, June 22). *Ministerial Decision on the TRIPS Agreement*. Retrieved from: https://docs.wto.org/dol2fe/Pages/SS/directdoc.aspx?filename=q:/WT/MIN22/30.pdf&Open=True.

Xia, S., Zhang, Y., Wang, Y., Wang, H., Yang, Y., Gao, G., . . . Yang, X. (2021). Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBIBP-CorV: A randomised, double-blind, placebo-controlled, phase 1/2 trial. *Lancet Infect. Dis*., 21(1), 39–51. doi:10.1016/S1473-3099(20)30831-8

Xing, D. and Liu, Z. (2021). Effectiveness and safety of traditional Chinese medicine in treating COVID-19: Clinical evidence from China. *Aging and Disease*, 12(8), 1850–1856. doi:10.14336/AD.2021.0906

Xiong, Y., Gao, M., van Duijn, B., Choi, H., van Horssen, F. and Wang, M. (2021). International policies and challenges on the legalization of traditional medicine/herbal medicines in the fight against COVID-19. *Pharmacological Research*, 166, 105472. doi:https://doi.org/10.1016/j.phrs.2021.105472

Yarlagadda, H., Pate, M. A., Gupta, V., Bansal, T., Upadhyay, S., Shaheen, N. and Jain, R. (2022). COVID-19 vaccine challenges in developing and developed countries. *Cureus*, 14(4), e23951. doi:10.7759/cureus.23951

Zavvar, M., Yahyapoor, A., Baghdadi, H., Zargaran, S., Assadiasl, S., Abdolmohammadi, K., Abooei, A. H., Sattarian, M. R., JalaliFarahani, M., Zarei, N., Farahvash, A., Fatahi, Y., Deniz, G., Zarebavani, M. and Nicknam, M. (2022). COVID-19 immunotherapy: Treatment based on the immune cell-mediated approaches. *International Immunopharmacology*, 107, 108655. doi:10.1016/j.intimp.2022.108655

Zhang, H., Zang, C., Xu, Z., Zhang, Y., Xu, J., Bian, J., Morozyuk, M., Khullar, D., Zhang, Y., Nordvig, A. S., Schenck, E. J., Shenkman, E. A., Rothman, R. L., Block, J. P., Lyman, K., Weiner, M. G., Carton, T. W., Wang, F. and Kaushal, R. (2022, December 1). Data-driven identification of post-acute SARS-CoV-2 infection subphenotypes. *Nature Medicine*. doi:10.1038/s41591-022-02116-3

Zhang, Y., Juhas, M. and Kwok, C. K. (2022, August 1). Aptamers targeting SARS-CoV-2: a promising tool to fight against COVID-19. *Trends in Biotechnology*. doi:10.1016/j.tibtech.2022.07.012

Zhang, Y.-Z. (2020, January 10). *Novel 2019 Coronavirus Genome*. Retrieved from Virological.org: https://virological.org/t/novel-2019-coronavirus-genome/319.

Zimmer, C., Corum, J., Wee, S.-L. and Kristoffersen, M. (2022, August 31). *Coronavirus Vaccine Tracker*. Retrieved January 12, 2023, from *The New York Times*: www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html.

Zimmerman, K. O. (2022). *clinicaltrials.gov*. Retrieved January 11, 2023, from: https://clinicaltrials.gov/ct2/show/study/NCT05595369.

Further reading

Alshrari, A. S., Hudu, S. A., Imran, M., Asdaq, S. M. B., Ali, A. M. and Rabbani, S. I. (2022). Innovations and development of Covid-19 vaccines: A patent review. *Journal of Infection and Public Health*, 15(1), 121–131. https://doi.org/10.1016/j.jiph.2021.10.021

Berinato, S. (2022). Moderna v. Pfizer: What the Patent Infringement Suit Means for Biotech. *Harvard Business Review*, 16 September 2022. Available at: https://hbr.org/2022/09/moderna-v-pfizer-what-the-patent-infringement-suit-means-for-biotech.

Brittain, B. (2022). Pfizer, BioNTech countersue Moderna over COVID-19 vaccine patents. *Reuters*, 6 December 2022. Available at: www.reuters.com/legal/pfizer-biontech-countersue-moderna-over-covid-19-vaccine-patents-2022-12-05.

Chiang, T. W. and Wu, X. (2022). Innovation and Patenting Activities of COVID-19 Vaccines in WTO Members. *WTO Working Papers*, February 10, 2022. https://doi.org/10.30875/25189808-2022-1

Fang, L. (2022). Moderna among firms quietly granted powers to seize patent rights during early days of COVID pandemic. *The Intercept*, 23 August 2022. Available at: https://theintercept.com/2022/08/23/covid-vaccine-patents-moderna-big-pharma-section-1498.

Gaviria, M. and Kilic, B. (2021). A network analysis of COVID-19 mRNA vaccine patents. *Nature Biotechnology*, 39, 546–548. https://doi.org/10.1038/s41587-021-00912-9

Italia, M., Rossa, F. D. and Decole, F. (2022). A mathematical analysis of the socio-economic impacts of a patent waiver on COVID-19 vaccines. *2022 IEEE Workshop on Complexity in Engineering*, 2022, 1–6. https://doi.org/10.1109/COMPENG50184.2022.9905430

LENS.org (n.d.). Searchable COVID-19-related datasets of patent documents, scholarly research works metadata, and biological sequences from patents. Available at: https://about.lens.org/covid-19.

Li, M., Ren, J., Si, X., Sun, Z., Wang, P., Zhang, X., Liu, K. and Wei, B. (2022). The global mRNA vaccine patent landscape. *Human Vaccines & Immunotherapeutics*, 18, 6. https://doi.org/10.1080/21645515.2022.2095837.

Liu, K., Zhang, X., Hu, Y., Chen, W., Kong, X., Yao, P., Cong, J., Zuo, H., Wang, J., Li, X. and Wei, B. (2022). What, where, when and how of COVID-19 patents landscape: A bibliometrics review. *Frontiers in Medicine*, 9, 925369. https://doi.org/10.3389/fmed.2022.925369

Medicines Patent Pool (n.d.). *VaxPal: COVID-19 Vaccines Patent Dataset*. Available at: www.vaxpal.org/?page=1.

Medicines Patent Pool (n.d.) *mRNA Technology Transfer Hub Programme*. Available at: https://medicinespatentpool.org/covid-19/mrna-technology-transfer-hub-programme.

Morales-Nunez, J. J., Muñoz-Valle, J. F., Torres-Hernández, P. C., and Hernández-Bello, J. (2021). Overview of neutralizing antibodies and their potential in COVID-19. *Vaccines*, 9(12). https://doi.org/10.3390/vaccines9121376.

Storz, U. (2022). The COVID-19 vaccine patent race. *Nature Biotechnology*, 40, 1001–1004. https://doi.org/10.1038/s41587-022-01376-1.

Trotta, D. (2022). Moderna sues Pfizer/BioNTech for patent infringement over COVID vaccine. *Reuters*, 26 August 2022. Available at: www.reuters.com/legal/moderna-sues-pfizerbiontech-patent-infringement-over-covid-vaccine-2022-08-26.

United States Patent and Trademark Office (USPTO) (n.d.). *Licensing Information for Applicants*. Available at: https://developer.uspto.gov/ipmarketplace/search/platform.

United States Patent and Trademark Office (USPTO) (n.d.). *Licensing Options for Inventions*. Available at: https://developer.uspto.gov/ipmarketplace/search/patents.

World Trade Organization (n.d.). *COVID-19: Measures Regarding Trade-related Intellectual Property Rights*. Available at: www.wto.org/english/tratop_e/covid19_e/trade_related_ip_measure_e.htm.

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