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SUBMITTED ELECTRONICALLY VIA EDIS

Ms. Lisa Barton
Secretary
U.S. International Trade Commission
500 E Street, SW
Washington, D.C. 20436

Re: Pre-Hearing Brief, COVID-19 Diagnostics and Therapeutics: Supply, Demand, and TRIPS Agreement Flexibilities, Investigation No. 332-596

Dear Secretary Barton,

On behalf of the Pharmaceutical Research and Manufacturers of America (PhRMA), we hereby submit our pre-hearing brief in *COVID-19 Diagnostics and Therapeutics: Supply, Demand, and TRIPS Agreement Flexibilities*, Investigation No. 332-596, per the Federal Register notice issued on February 6, 2023.[1]

PhRMA member companies are devoted to inventing, manufacturing and distributing medicines that enable people to live longer, healthier and more productive lives. The U.S. biopharmaceutical industry is the world leader in new medicine research and innovation – producing more than half the world's new medicines in the last decade. This pioneering work by U.S. biopharmaceutical innovators contributes significantly to economic growth and supports good-paying, highly-skilled jobs in all 50 states and the District of Columbia. As a key component of America's high-tech economy, the research-based biopharmaceutical sector supports over 4.4 million jobs across the economy, including more than 900,000 direct jobs, and contributes more than $1.4 trillion in economic output on an annual basis when direct, indirect and induced effects are considered.[2] The U.S. biopharmaceutical industry is the largest exporter of goods among the most research and development (R&D)-intensive industries, with exports exceeding $80 billion in 2021.[3] The U.S. biopharmaceutical industry also is among the top five employers of U.S. manufacturing jobs, with more Americans directly employed in

[1] COVID-19 Diagnostics and Therapeutics: Supply, Demand, and TRIPS Agreement Flexibilities; Notice of Investigation and Scheduling of a Public Hearing," 88 Fed. Reg. 7757 (Feb. 6, 2023).

[2] TEConomy Partners for PhRMA, The Economic Impact of the U.S. Biopharmaceutical Industry: 2020 National and State Estimates, Mar. 2022.

[3] Analysis of National Science Foundation and Business Research and Development Survey (BRDIS) data by ndp | analytics; TradeStats Express™: National Trade Data for NAICS Code 3254 Pharmaceuticals and Medicines, http://tse.export.gov/TSE/TSEHome.aspx.

pharmaceutical manufacturing than in manufacturing in several other manufacturing industries, including each of the following: iron and steel products, aerospace products and parts, petroleum and coal products, and electric equipment and appliances.[4]

While the COVID-19 pandemic rattled health systems and economies globally, the innovative biopharmaceutical industry worked around the clock to research, develop and deploy vaccines and therapeutics to treat and prevent infections from the virus and associated conditions – all while maintaining the supply of existing treatments and vaccines and developing new medicines for other diseases. Indeed, in 2021 alone, PhRMA member companies invested more than $102 billion in R&D to facilitate new ways to tackle some of the most complex and difficult to treat diseases of our time.[5] The ability of the industry to meet this challenge was enabled, in large part, due to strong IP protection in a number of countries around the world. It is no coincidence that the first and most effective COVID-19 vaccines and therapeutics were developed in industrialized countries with a strong framework for the protection of IP. Most PhRMA members have active R&D programs for potential COVID-19 treatments and vaccines and all have provided donations of medicines, critical medical supplies or financial donations to support patients and first responders in addressing the pandemic. As a result of the unprecedented collaboration and hundreds of partnerships between the private sector, researchers, academia, governments and other organizations – which have been enabled and facilitated by robust IP frameworks – biopharmaceutical manufacturers have delivered numerous COVID-19 treatments and vaccines in record time.[6] PhRMA members have successfully worked closely with multilateral organizations such as COVAX, UNICEF and the Global Fund, as well the Medicines Patent Pool, to provide access pathways for these innovations to all countries, including the least developed, and are fully committed to providing global access to COVID-19 vaccines and treatments.[7] This commitment continues to result in vaccinations for patients all around the world.

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[4] U.S. Bureau of Labor Statistics, Current Population Survey (CPS) Labor Force Statistics, https://www.bls.gov/cps/home.htm.

[5] PhRMA 2022 Annual Membership Survey, https://phrma.org/-/media/Project/PhRMA/PhRMA-Org/PhRMA-Refresh/Report-PDFs/P-R/PhRMA_membership-survey_2022_final.pdf.

[6] PhRMA, The Dangers of Expanding the TRIPS Waiver (Sep. 19, 2022), https://catalyst.phrma.org/the-dangers-of-expanding-the-trips-waiver.

[7] For example, in addition to the hundreds of voluntary licensing agreements discussed further below in Section II.B, Pfizer is working through its initiative, Accord for a Healthier World, and with WHO, UNICEF, Global Fund and COVID GAP to improve access to PAXLOVID™ for vulnerable populations globally. See, e.g., Press Release, Pfizer, Pfizer to Supply Global Fund Up to 6 Million PAXLOVID™ Treatment Courses for Low-and-Middle-Income Countries (Sep. 22, 2022), https://www.pfizer.com/news/press-release/press-release-detail/pfizer-supply-global-fund-6-million-paxlovidtm-treatment. Merck & Co., Inc. (Merck), also signed an agreement with UNICEF to allocate up to 30 percent (three million courses) of its anti-viral supply to low and middle-income countries through the first half of 2022. These arrangements accelerated and diversified the production of molnupiravir and made it more accessible in 105 middle- and low-income countries. See Press Release, Merck, Merck and Ridgeback Announce Supply Agreement with UNICEF for Molnupiravir, an Investigational Oral Antiviral COVID-19 Medicine (Jan. 18, 2022), https://www.merck.com/news/merck-and-ridgeback-announce-supply-agreement-with-unicef-for-molnupiravir-an-investigational-oral-antiviral-covid-19-medicine/.

Despite this major accomplishment by American scientists, researchers and manufacturers, which was founded on IP protections, the Administration agreed to the waiver of commitments to protect IP under the TRIPS Agreement for COVID-19 vaccines – a harmful and unnecessary decision.[8] This "TRIPS waiver" decision will not address the real barriers to access for this pandemic and may have unintended consequences for future pandemics. The decision was made despite the fact that the TRIPS rules are essential to incentivize the development of vaccines, as well as the fact that a global surplus of vaccines existed at the time of the decision – and still does. This policy position constituted a reversal of longstanding U.S. policy under both Democratic and Republican Administrations concerning the protection of American IP rights from unfair use by foreign competitors.

Moreover, the Administration's support for the TRIPS waiver was offered absent any evidence that waiving international obligations would promote the development or manufacturing of additional COVID-19 vaccines. At the time of the waiver decision, more than 14 billion vaccine doses had been produced, with existing capacity to continue producing more than enough to vaccinate the world even in the event that new variants were to emerge.[9] Critically, nine months after its introduction, there has been no demonstrable evidence that the waiver has meaningfully impacted patient access to COVID-19 vaccines. This demonstrates IP rights were never a barrier to access but rather enabled the very collaborations among manufacturers and suppliers that were necessary to develop and produce COVID-19 vaccines on a global scale. Indeed, experience demonstrated that weak health systems, inadequate infrastructure and last-mile distribution and administration challenges unrelated to IP protection – such as cold storage, transportation and health workforce barriers – impeded the global response to the pandemic.[10] These challenges were exacerbated by export restrictions, regulatory delays and other trade-related barriers.[11] At odds with their stated intent to advance vaccines supply, many of the same countries that demanded the TRIPS waiver for vaccines had refused or destroyed millions of doses, due to an inability to distribute and administer excess supply. Reports indicated that countries destroyed vaccines because they were unable to distribute the vaccines within their shelf life or requested that manufacturers suspend delivery of vaccines because the countries had enough stock.[12]

Despite these facts, the Administration supported the TRIPS waiver efforts of foreign governments historically and consistently opposed to the TRIPS Agreement specifically and the global IP system more broadly. This decision undermined our global response to the pandemic –

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[8] WTO, Ministerial Decision on the TRIPS Agreement, WT/MIN(22)/30, WT/L/1141 (Jun. 17, 2022), https://docs.wto.org/dol2fe/Pages/SS/directdoc.aspx?filename=q:/WT/MIN22/30.pdf&Open=True.

[9] Source: Airfinity (https://science.airfinity.com); see Appendix 1: COVID-19 Vaccines: Production and Uptake.

[10] Adler, D., Stop Treating Vaccine Hesitancy Like an Afterthought, Foreign Policy (Dec. 2021), https://foreignpolicy.com/2021/12/09/covid-vaccine-hesitancy-issue-global-south-north-supplies-health/.

[11] World Trade Organization, *Indicative List of Trade-Related Bottlenecks and Trade-Facilitating Measures on Critical Products to Combat COVID-19* (Oct. 2021), https://www.wto.org/english/tratop_e/covid19_e/bottlenecks_update_oct21_e.pdf.

[12] Kew, J. and Cele, S., South Africa Asks J&J, Pfizer to Stop Sending Vaccines, Bloomberg (Nov. 2021), https://www.bloomberg.com/news/articles/2021-11-24/s-africa-wants-j-j-pfizer-vaccine-delivery-delay-news24-says; The Economist, Why are African countries destroying covid-19 vaccines? (Aug. 12, 2021), https://www.economist.com/the-economist-explains/2021/08/12/why-are-african-countries-destroying-covid-19-vaccines.

with tragic consequences for people in countries throughout the world – by distracting attention and resources from addressing actual barriers to global vaccination. Having produced more than enough doses to vaccinate the world, the innovative biopharmaceutical industry encouraged the Administration to demonstrate leadership at the World Trade Organization (WTO) by opposing any TRIPS waivers and refocusing global attention to resolving international challenges to distributing and administering that global vaccine surplus. Instead, the Administration prioritized the domestic political objective of attacking IP rights and joined foreign governments in championing the TRIPS waiver, to the detriment of American innovation and global public health.

As will be described in this submission, beyond the fact that the TRIPS waiver did nothing to address genuine barriers to access, it introduced several significant risks that taken together threaten to undermine an effective pandemic response going forward. These include risks to patient safety, supply chains, innovation and a higher risk of counterfeits.

In addition, the Administration's decision to effectively hand over American innovations to countries looking to undermine U.S. leadership in biomedical discovery runs counter to the Administration's stated objectives concerning the growth of American infrastructure, innovation and employment.[13] As noted, exports of vaccines and therapeutics have been an important contributor to supporting U.S. jobs and the U.S. innovation ecosystem. It also further alienated allied economies that support strong IP policies abroad and provided the political cover for other governments to advance legislation eroding national IP systems. Any effort to cede American IP to foreign countries is an effort to undercut American innovation and send American research and manufacturing jobs overseas.

As the United States and other WTO member states continue to consider whether to expand the TRIPS waiver to diagnostics and therapeutics, the innovative biopharmaceutical industry encourages the Administration and serious policymakers everywhere to reject any expansion of the TRIPS waiver and instead focus on solving evident challenges to distributing and administering the global surplus of COVID-19 vaccines and treatments; and fostering the R&D that will be needed to continue tackling the pandemic and prepare for public health crises to come. At a time when research and development have never been more important, our industry shares the goal to help ensure widespread availability of this surplus, a commitment to invest in research for unmet medical needs and hopes that all governments and stakeholders will refocus on these shared objectives.

I. America's World-Leading Biopharmaceutical Industry Innovated and Produced Safe and Effective Vaccines and Treatments in Record Time

America's biopharmaceutical companies came together to achieve one shared goal of fighting COVID-19. The decades-long investments made by the industry – founded on robust IP

[13] See, e.g., Exec. Order No. 14081, Advancing Biotechnology and Biomanufacturing Innovation for a Sustainable, Safe, and Secure American Bioeconomy (Sep. 12. 2022), https://www.whitehouse.gov/briefing-room/presidential-actions/2022/09/12/executive-order-on-advancing-biotechnology-and-biomanufacturing-innovation-for-a-sustainable-safe-and-secure-american-bioeconomy/.

protections[14] – enabled industry to swiftly respond in a manner never seen before. In an incredible display of modern technological capabilities, Pfizer and BioNTech together launched the world's first COVID-19 vaccine in December 2020.[15] Within a year of the WHO declaring a public health emergency, multiple COVID-19 vaccines were developed, produced and administered, including vaccines that use innovative mRNA and viral vector-based technologies. By the start of 2022, 20 companies were manufacturing enough doses to supply COVID-19 vaccines to the entire global population by the end of the year.[16] A larger and more diverse number of vaccines quickly emerged for COVID-19 than exist for any other virus, including for hepatitis B, which currently has four approved vaccines.[17] Furthermore, no single manufacturer dominated the global market, and R&D has fueled investment in 450 clinical trials to develop new COVID-19 vaccines that may address new variants or be more easily stored and delivered.[18] Although global demand waned for COVID-19 vaccines in 2022 due to vaccine hesitancy and last-mile delivery challenges, today more than 70 percent of the global population (5.6 billion people) have received at least one dose of a COVID-19 vaccine and more than 2.3 billion people have also received boosters, thanks to more than 15.5 billion vaccine doses being produced and delivered around the world.[19] It is estimated that 14.4-19.8 million lives have been saved[20] and over 80 million hospitalizations avoided thanks to COVID-19 vaccines.[21]

Similarly, decades-long investments made by industry enabled a swift response to developing effective COVID-19 treatments. Over 70 million courses of COVID-19 antivirals have been produced, an amount which far exceeded demand in 2022 (19 million) and has built up stockpiles (more than 30 million) large enough to exceed anticipated total global demand in

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[14] Highlighting "the remarkable research and innovation efforts to fight the SARS-COV-2 virus and the related disease", both the World Intellectual Property Office (WIPO) and the WTO have issued reports outlining the IP protections on COVID-19 vaccines and therapeutics. See WIPO, COVID-19-related vaccines and therapeutics: Preliminary insights on related patenting activity during the pandemic (2022), https://www.wipo.int/publications/en/details.jsp?id=4589; and WTO, Patent-related actions taken in WTO members in response to the COVID-19 pandemic (2020), https://www.wto.org/english/res_e/reser_e/ersd202012_e.htm.

[15] Press Release, Government of the United Kingdom, UK Marks One Year Since Deploying World's First COVID-19 Vaccine (Dec. 8, 2021), https://www.gov.uk/government/news/uk-marks-one-year-since-deploying-worlds-first-covid-19-vaccine.

[16] Airfinity (https://science.airfinity.com); see Appendix 1: COVID-19 Vaccines: Production and Uptake.

[17] See https://www.immunize.org/askexperts/experts_hepb.asp.

[18] Source: Airfinity (https://science.airfinity.com); see Appendix 2: Expanding the TRIPS Waiver Is Unnecessary and Harmful.

[19] Our World in Data (ourworldindata.org) Global Database of COVID-19 Vaccinations; Airfinity (https://science.airfinity.com); See Appendix 1: COVID-19 Vaccines: Production and Uptake.

[20] Watson, Oliver J, et al., Global Impact of the First Year of COVID-19 Vaccination: A Mathematical Modelling Study" The Lancet Infectious Diseases, vol. 22, no. 9 (June 2022), www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00320-6/fulltext, https://doi.org/10.1016/s1473-3099(22)00320-6.

[21] PhRMA analysis of Meagan C. Fitzpatrick et al., Two Years of U.S. COVID-19 Vaccines Have Prevented Millions of Hospitalizations and Deaths, Commonwealth Fund, (Dec. 13, 2022), https://doi.org/10.26099/whsf-fp90 (finding that the number of hospitalizations avoided was 5.7 times the number of deaths prevented in the United States).

2023.[22] In addition, over 5.5 million patients received antibody treatments approved or authorized for COVID-19 in 2022.[23]

Although several medicines, including antivirals and antibodies, have been approved or authorized by the FDA or EMA for the treatment of COVID-19, these treatments reflect just three percent of the pipeline of potential COVID-19 treatments.[24] Over 850 medicines have been tested for effectiveness against COVID-19 across almost 5,000 clinical trials.[25] Most (almost 60 percent) of these medicines are being developed, or were already being used, to treat other conditions, such as cancers and auto-immune diseases.[26] Similarly, medicines currently being developed to exclusively treat COVID-19 are highly likely to have applications beyond COVID-19, demonstrating (as discussed further in Section IV below) the infeasibility of defining a precise set of "COVID-19 therapeutics." Given the waning effectiveness of some of the approved antibody treatments against newer variants, the medicines still being tested and developed are of critical importance to patients, to health security and post-pandemic economic recovery. Patients with long-COVID are also in need of new and better medicines, which requires ongoing investment in medicines' development and testing.

Demand for COVID-19 treatments has been far less than expected, but the evidence does not suggest demand is lower due to affordability or lack of access. As a result of access agreements reached early on by major manufacturers of COVID-19 treatments, more than 130 countries (all low and middle-income countries in the world) are eligible to receive COVID-19 treatments through the Global Fund and UNICEF at no cost.[27] Yet, only a small number of countries have placed orders for these products through this body.[28] Further, only a small number of low and middle-income countries have approved or authorized existing new COVID-19 treatments for their own markets, including only five countries in Africa, even though several therapeutics are recommended by the World Health Organization (WHO).[29] Given this, many low and middle-income countries have refused donations of existing COVID-19 treatments from NGOs, manufacturers and governments despite them being offered at no cost.

Finally, even if every country in the world were to increase its demand for COVID-19 treatments to the same level as the United States (for which uptake is significantly higher than other high-

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[22] Airfinity (science.airfinity.com). See Appendix 2: Expanding the TRIPS Waiver is Unnecessary and Harmful.

[23] Airfinity (science.airfinity.com).

[24] Airfinity (science.airfinity.com). See Appendix 2: Expanding the TRIPS Waiver Is Unnecessary and Harmful.

[25] Informa (informa.com). See Appendix 2: Expanding the TRIPS Waiver is Unnecessary and Harmful.

[26] Id.

[27] See, e.g., Press Release, Pfizer, Pfizer to Supply Global Fund Up to 6 Million PAXLOVID™ Treatment Courses for Low-and-Middle-Income Countries (Sep. 22, 2022), https://www.pfizer.com/news/press-release/press-release-detail/pfizer-supply-global-fund-6-million-paxlovidtm-treatment; Press Release, Merck, Merck and Ridgeback Announce Supply Agreement with UNICEF for Molnupiravir, an Investigational Oral Antiviral COVID-19 Medicine (Jan. 18, 2022), https://www.merck.com/news/merck-and-ridgeback-announce-supply-agreement-with-unicef-for-molnupiravir-an-investigational-oral-antiviral-covid-19-medicine/.

[28] UNICEF, COVID-19 Market Dashboard, https://www.unicef.org/supply/covid-19-market-dashboard.

[29] Airfinity (science.airfinity.com). See Appendix 2: Expanding the TRIPS Waiver is Unnecessary and Harmful; WHO, Therapeutics and COVID-19: Living guideline (Jan. 13, 2023), https://www.who.int/publications/i/item/WHO-2019-nCoV-therapeutics-2023.1.

income countries) current production would be more than sufficient to satisfy demand and there would still be a global surplus of COVID-19 treatments at the end of 2023.[30]

A. Geographical Distribution of the Global Manufacturing Industries for COVID-19 Diagnostics and Therapeutics

USTR has requested that the Commission "catalog[] the reasons for market segmentation and barriers to a more diverse geographical distribution of the global manufacturing industries for COVID-19 diagnostics and therapeutics" in its report resulting from this investigation. As a threshold matter, PhRMA wishes to emphasize that global manufacturing for COVID-19 therapeutics is not as concentrated as USTR's directive to the Commission implies. COVID-19 medicines are manufactured in numerous countries, including developing countries. Indeed, as of late 2022, production sites for COVID-19 treatments [were] spread across more than 30 countries, including Brazil, India, Indonesia, Kenya, Singapore and South Africa.[31] Upstream producers of pharmaceutical ingredients also operate in a diverse array of countries. As discussed below in Section II, intellectual property ("IP") protections advance geographical diversification of high-quality therapeutics manufacturing.

B. Factors Affecting the Geographical Distribution of COVID-19 Diagnostics and Therapeutics Manufacturing

As a starting point, there is no evidence of global shortages for COVID-19 therapeutics. In fact, therapeutics manufacturers had significant unutilized production capacity in 2022.[32] The global surplus of COVID-19 therapeutics indicates that the existing geographical distribution of manufacturing facilities is more than adequate to ensure the provision of those products to a diverse range of markets. In other words, there is no evidence that IP rights on therapeutics have constrained supply of or access to these products. Further, surpluses for finished therapeutics indicate that sufficient global supplies of affordable ingredients and components for these products were also able to be sourced. Therefore, there is also no evidence that IP rights have limited access to inputs and ingredients for COVID-19 diagnostics and therapeutics manufacturing.

While as noted there is no shortage of manufacturing for therapeutics and such manufacturing is already geographically distributed, there are a host of policies that make a country more attractive as a site for manufacturing pharmaceuticals. These policies include: legal certainty and rule of law (including IP protections and enforcement as well as good regulatory practices); a clear, science-based, consultative regulatory framework harmonized with international standards; commitment to free trade and open markets (including refraining from unnecessary export restrictions, low or zero tariffs, streamlined customs protocols and measures to prevent illicit trade); open, transparent, predictable and value-based procurement systems in line with international standards; strong R&D investment, health care infrastructure and financing (including a highly skilled health workforce and digital infrastructure); and secure supply chains.

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[30] See Appendix 2: Expanding the TRIPS Waiver Is Unnecessary and Harmful.

[31] Id.

[32] Id.

For example, inefficient and antiquated customs procedures in many countries cause serious delays in the delivery of imported medical products. The Global Alliance for Trade Facilitation has documented such procedures – which include "manual, paper-based [import license] application and approval procedures," inadequate customs clearance training for border personnel and redundant documentation and inspection requirements – in various Central American, African and Asian countries.[33] As discussed in Section V.A below, tariffs and export restrictions on pharmaceutical ingredients and manufacturing equipment may further limit manufacturers' access to globally-sourced inputs and ingredients, particularly in developing countries.[34] Manufacturers in developing countries face difficulties recruiting qualified personnel and meeting national regulatory requirements for new pharmaceuticals. Even when manufacturers submit adequate product applications to regulatory authorities, those authorities may be under-resourced, product marketization requirements may be unnecessarily stringent and manufacturing standards may be too costly for manufacturers to meet. These regulatory barriers delay and may even prevent therapeutics manufacturing scale-ups in certain countries.

Finally, erratic – and potentially transient – demand for COVID-19 therapeutics discourages manufacturers in developing countries from entering these markets. As discussed above, demand for therapeutics was low in 2022. Without reasonable expectations that demand for COVID-19 therapeutics will remain robust for years to come, manufacturers that have not yet devoted resources towards COVID-19-related production have little incentive to divert resources away from other activities in order to scale up COVID-19-related production. This resource allocation problem affects manufacturers in developed and developing countries, but may be more acute for manufacturers in developing countries.

II. The Global IP System Enabled the U.S. Biopharmaceutical Industry's Successful Global Response to COVID-19

The rapid development, manufacture and deployment of the COVID-19 vaccines and therapeutics outlined in Section I would not have been possible without the global IP system. Before delving into the contribution of IP and the TRIPS Agreement to our ability to combat COVID-19, it is important to briefly recall the contribution that they make to pharmaceutical innovation more generally.

The simplest rationale for protecting IP is that without it, copying would be more rational than innovating.[35] Innovation takes resources, which rational actors would have no incentive to

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[33] Global Alliance for Trade Facilitation, Annual Report 2021, https://www.tradefacilitation.org/content/uploads/2022/04/global-alliance-for-trade-facilitation-annual-report-2021.pdf.

[34] Bauer, Matthias and Lamprecht, Philipp, How Tariffs Impact Access to Medicines, Geneva Network (Oct. 2021), https://geneva-network.com/research/how-tariffs-impact-access-to-medicines/. See also World Trade Organization and International Monetary Fund, WTO and IMF Joint Statement on Trade and the COVID-19 response (Apr. 2020), https://www.wto.org/english/news_e/news20_e/igo_15apr20_e.pdf.

[35] See generally, e.g., David M Gould & William C Gruben, The Role of Intellectual Property Rights in Economic Growth, in Dynamics of Globalization and Development 369-405 (Satya Dev Gupta & Nanda K. Choudhry, eds., Springer, 1997); see also Eric M. Solovy, The TRIPS Waiver for COVID-19 Vaccines, and Its Potential Expansion: Assessing the Impact on Global IP Protection and Public Health, Ctr. Intell. Prop. x Innovation Pol'y 3 (2022), https://cip2.gmu.edu/wp-content/uploads/sites/31/2022/12/GMU-C-IP2-Solovy-PolicyBrief-TRIPS.pdf.

invest, absent the prospect of returns.[36] IP protections, some of which are time-limited, e.g., patent protection, offer the innovator an opportunity to recover costs, and potentially make profits, before others are allowed to copy the innovation. With respect to patents, the requirement that the innovator disclose the invention in order to obtain patent protection incentivizes the dissemination of knowledge. As such, while the innovator benefits from these IP protections, it is ultimately society that gains from access to new knowledge and/or new products.[37]

In turn, there are numerous high-quality empirical studies that have set out to assess the effects of IP protection (patent protection in particular), on corporate research and development expenditures and, consequently, on firms' ability to innovate, grow, export and share innovative technologies internationally. While studies differ in the way they measure IP protection and in the outcome variables they examine, there is robust evidence that stronger and more harmonized IP protection increases corporate R&D intensity, drives innovation and ultimately achieves higher levels of economic growth and profitability of companies of any size and provenience. Appendix 3 to this submission provides a structured overview of key findings in the literature.

U.S. government laws, agencies, institutions, policies, reports and other programs are built on the foundational premise that IP drives innovation. The U.S. Patent and Trademark Office (USPTO), in fulfillment of the mandate of Article I, Section 8, Clause 8 to the Constitution of the United States, secures IP rights for innovators and creators. According to the USPTO, as a result of this system of protection, "[n]ew products have been invented, new uses for old ones discovered, and employment opportunities created for millions of Americans."[38] The Trade Act of 1974, as amended, authorizes the USTR to take action against any unreasonable act, policy or practice of a foreign government that "denies fair and equitable ... provision of adequate and effective protection of IP rights notwithstanding the fact that the foreign country may be in compliance with the specific obligations of the Agreement on Trade-Related Aspects of Intellectual Property Rights."[39] The USTR conducts a Congressionally-mandated annual review of the global state of IP rights protection and enforcement, "reflecting the Administration's resolve to encourage and maintain enabling environments for innovation, including effective IP protection and enforcement, in markets worldwide, which benefit not only U.S. exporters but the domestic IP-intensive industries in those markets as well."[40] Similarly, the USITC plays a key role in investigating claims of unfair competition and infringement of IP rights under Section 337 of the Tariff Act of 1930.[41]

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[36] Id.

[37] TRIPS Agreement, Article 7 ("The protection and enforcement of intellectual property rights should contribute to the promotion of technological innovation and to the transfer and dissemination of technology, to the mutual advantage of producers and users of technological knowledge and in a manner conducive to social and economic welfare, and to a balance of rights and obligations"); see also Eric M. Solovy, The Doha Declaration at Twenty: Interpretation, Implementation, and Lessons Learned on the Relationship Between the TRIPS Agreement and Global Health, 42 NW. J. Int'l L. & Bus. 253, 287-296 (2022).

[38] See https://www.uspto.gov/about-us.

[39] Public Law 93–618, as amended (Dec. 27, 2022), p. 127, https://www.govinfo.gov/content/pkg/COMPS-10384/pdf/COMPS-10384.pdf.

[40] See Office of the United States Trade Representative: Issue Areas – Intellectual Property – Special 301, https://ustr.gov/issue-areas/intellectual-property/special-301.

[41] U.S. International Trade Commission, Understanding Investigation of Intellectual Property Infringement and Other Unfair Practices in Import Trade (Section 337), https://www.usitc.gov/press_room/us337.htm.

The role of IP is particularly significant in the pharmaceutical industry, which relies on private investors making risky investments in research and development, where the ultimate success of the investment is uncertain. Biopharmaceutical companies invest enormous resources into R&D for new vaccines and therapeutics, and into the clinical testing needed to bring new medicines to market. While scientific breakthroughs can bring financial reward, the road to new medicine launches is paved with costly failures. Less than 12 percent of medicine candidates reaching clinical trials are ultimately approved.[42] To recall, while the Pfizer-BioNTech team, Moderna and Johnson and Johnson were successful in their efforts to develop COVID-19 vaccines, many others like Merck and CureVac undertook costly research into developing vaccines, which eventually proved unsuccessful.[43] Biopharmaceutical companies accept the risk of failure as inherent in new medicine development, but they can do so only based on the promise that IP rights will enable them to secure the rewards of their rare successes.[44] This promise applies both to successful inventions resulting in the launch of a new medicine and failed attempts which nevertheless produce technologies that may be useful down the line. Accounting for these failed attempts, it costs $2.6 billion, on average, to develop a new medicine,[45] and only 20 percent of approved medicines produce revenues sufficient to cover development costs.[46] As such, the necessity of IP rights to the viability of the biopharmaceutical sector cannot be overstated. Without the availability of IP rights, biopharmaceutical companies simply cannot secure the investments necessary to continue developing innovative technologies used in life-saving medicines around the globe. In short, strong IP rights are essential for ensuring access to medicine worldwide.

The TRIPS Agreement promotes access to medicine by establishing a baseline of critical IP rights protections that WTO Members must afford to one another. The TRIPS Agreement, thus, provides the legal framework needed to incentivize global investment in innovation which is essential for the development of new vaccines and therapeutics. In doing so, it explicitly recognizes the important goal of promoting the transfer of innovation for the improvement of global welfare. As set forth in Article 7 of the TRIPS Agreement, titled "Objectives," the TRIPS Agreement recognizes "[t]he protection and enforcement of IP rights should contribute to the promotion of technological innovation and to the transfer and dissemination of technology, to the mutual advantage of producers and users of technological knowledge and in a manner conducive to social and economic welfare, and to a balance of rights and obligations."[47] This articulation of

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[42] See Joseph A. DiMasi, Henry G. Grabowski & Ronald W. Hansen, Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs, Tufts Center for the Study of Drug Development 17 (Nov. 18, 2014), https://f.hubspotusercontent10.net/hubfs/9468915/TuftsCSDD_June2021/pdf/Microsoft+PowerPoint+-+Tufts+CSDD+briefing+on+R%26D+cost+study+-+Nov+18,+2014.pdf.

[43] Jennifer Brant & Mark F. Schultz, Unprecedented: The Rapid Innovation Response to COVID-19 and the Role of Intellectual Property 32-33 (Nov. 2021), https://www.unpackingip.org/.

[44] Id. at 15.

[45] See Joseph A. DiMasi, Henry G. Grabowski & Ronald W. Hansen, Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs, Tufts Center for the Study of Drug Development (Nov. 18, 2014), https://f.hubspotusercontent10.net/hubfs/9468915/TuftsCSDD_June2021/pdf/Microsoft+PowerPoint+-+Tufts+CSDD+briefing+on+R%26D+cost+study+-+Nov+18,+2014.pdf.

[46] See Joseph A. Vernon, Joseph H. Golec & Joseph A. DiMasi, Drug Development Costs When Financial Risk Is Measured Using the Fama-French Three-Factor Model, 19 J. Health Econ. 1002 (2010).

[47] TRIPS Agreement, Article 7 (emphasis added).

the TRIPS Agreement's objectives makes clear that the treaty was drafted with concerns regarding global access to medicines in mind (including the need to create incentives necessary for development of new medicines), and the substantive content of the TRIPS Agreement reflects this intention.[48] Indeed, as discussed below, many critical elements of the TRIPS Agreement directly serve the goals of encouraging innovation for the development of new medicines and facilitating global access to those medicines.

A. The Global IP System: Understanding the TRIPS Agreement

IP rights emerged and evolved as creatures of domestic law. As such, they evolved differently in different jurisdictions. Even among countries that recognized and protected IP rights, there were key differences as to the forms of IP protected, the conditions for such protection, the scope of the rights conferred on the holder of a particular form of IP and the duration of protection.[49] These differences raised significant obstacles to international commerce. When a product protected by IP in one country was exported to another country, it faced the risk of being copied by competitors in the destination country, if the differences in the IP systems left the product without IP protection or with inadequate protection in the destination.

The TRIPS Agreement, adopted within the framework of the WTO, seeks to remove this barrier to international trade. To be clear, the TRIPS Agreement does not replace domestic legislation on IP or aim at harmonization. Instead, it sets out certain minimum standards according to which WTO Members should protect IP through their domestic law.[50] Under the TRIPS Agreement, WTO Members have undertaken obligations to protect certain forms of IP, afford such protection when certain stipulated conditions are met, maintain those protections for certain minimum periods of time, include certain minimum rights in the scope of protection and abide by certain conditions when they interfere with the protection.[51] WTO Members are at liberty to offer IP protection beyond what TRIPS prescribes; the TRIPS rules are minimum standards.[52] Conversely and importantly, WTO Members have agreed to exempt least developed country Members from compliance with obligations under the Agreement by granting two extended transition periods for such Members. First, TRIPS Article 66.1 provides a general transition period during which such Members are exempted from compliance with the TRIPS Agreement (other than Articles 3, 4 and 5).[53] This general transition period has been routinely extended such that it currently is not set to expire until July 2034.[54] Additionally, in the Doha Declaration, least developed country Members were granted yet another extended transition period specific to

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[48] See Eric M. Solovy, The Doha Declaration at Twenty: Interpretation, Implementation, and Lessons Learned on the Relationship Between the TRIPS Agreement and Global Health, 42 NW. J. Int'l L. & Bus. 253, 262 (2022) ("[T]he very essence of the innovation-access debate is crystallized in the terms of Article 7 of the TRIPS Agreement, itself, with WTO Members urged to find 'balance.' That 'balance' is currently reflected in the TRIPS Agreement, with its combination of obligations and exceptions.").

[49] Id.

[50] TRIPS Agreement, Article 1.1.

[51] See TRIPS Agreement, Parts II and III.

[52] See TRIPS Agreement, Article 1.1.

[53] TRIPS Agreement, Article 66.1.

[54] Council for Trade-Related Aspects of Intellectual Property Rights, *Extension for the Transition Period Under Article 66.1 for Least Developed Country Members*, ¶ 1, WTO Doc. IP/C/88 (June 28, 2021).

pharmaceuticals – exempting them from enforcement of rights related to patents and undisclosed information in the pharmaceutical sector.[55] This transition period has similarly been extended over time and is currently not scheduled to expire until January 2033.[56]

The establishment of a common minimum set of standards concerning IP through the TRIPS Agreement has allowed innovators to manufacture and market their products internationally, with a substantially lower risk of copying. It has also allowed the society at large to access new and innovative products, even when they are created beyond that society's national borders. And as noted in Article 7 of the TRIPS Agreement, it "contribute[s] to the transfer and dissemination of technology …."

Being part of the WTO's "single undertaking" (i.e., a basket of obligations that a Member undertakes while joining the WTO),[57] TRIPS obligations benefit from enforceability through the WTO's dispute settlement system. Where a Member fails to abide by TRIPS obligations, other Members can demand compliance, formally seek adjudication of the dispute and, as a last resort, impose trade sanctions.[58] The possibility of enforcement of TRIPS obligations has added to their effectiveness in protecting innovators in the course of international trade.

Finally, we reiterate that the TRIPS Agreement establishes a common baseline, not a ceiling for IP-protection.[59] Members are at liberty to protect IP to a greater extent than that required under the TRIPS Agreement.[60] In fact, certain Members, including the United States, have chosen to do so collectively and have entered into binding legal agreements with each other to provide more robust protections, thus raising the baseline applicable as between the parties to those agreements. An example is the United States-Mexico-Canada Agreement (USMCA), under which the United States, Canada and Mexico have assumed more extensive IP obligations than those stipulated in the TRIPS Agreement.[61]

The Administration's support for the TRIPS waiver on COVID-19 vaccines and willingness to consider supporting a TRIPS waiver on COVID-19 therapeutics and diagnostics is especially perplexing given that the United States historically has promoted, implemented and built on the global minimum standards of protection provided by the TRIPS Agreement. In the specific context of biopharmaceutical innovation, the United States has made clear that IP rights "are a

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[55] WTO Ministerial Conference, *Declaration on the TRIPS Agreement and Public Health*, ¶ 7, WTO Doc. WT/MIN(01)/DEC/2 (Nov. 20, 2001), https://www.wto.org/english/thewto_e/minist_e/min01_e/mindecl_trips_e.pdf (hereinafter, "Doha Declaration").

[56] Council for Trade-Related Aspects of Intellectual Property Rights, *Extension of the Transition Period Under Article 66.1 of the TRIPS Agreement for Least Developed Country Members for Certain Obligations With Respect to Pharmaceutical Products*, WTO Doc. IC/P/73 (Nov. 6, 2015).

[57] Appellate Body Report, *Brazil – Measures Affecting Desiccated Coconut*, p. 12, WTO Doc. WT/DS22/AB/R (adopted Mar. 20, 1997).

[58] See, e.g., Panel Report, *Saudi Arabia — Measures concerning the Protection of Intellectual Property Rights,* WTO Doc. WT/DS567/R (circulated June 16, 2020); see also Panel Report, *China — Measures Affecting the Protection and Enforcement of Intellectual Property Rights*, WTO Doc. WT/DS362/R (adopted Mar. 20, 2009).

[59] TRIPS Agreement, Article 1.1.

[60] Id.

[61] See Agreement between the United States of America, Mexico and Canada (USMCA), Chapter 20.

key component of countries that embrace the rule of law … and critical for any economy that wants to foster a culture of innovation."[62] The United States routinely promotes and celebrates the role of IP in facilitating collaborations and partnerships, as exemplified by the U.S. Patent and Trademark Office's (USPTO) recent launch of the "Patents 4 Partnerships" platform which connects patent owners who want to license their COVID-19 related IP rights to individuals and businesses "who can turn those rights into solutions for our health and wellbeing."[63] And just days after agreeing to the TRIPS waiver, the United States joined several other countries at the WTO in issuing a communication on the benefits of licensing IP.[64] Through a variety of trade and IP initiatives, including but not limited to bilateral and regional trade agreements, WTO accessions, eligibility criteria for trade preference programs and the U.S. Patent and Trademark Office's IP Attaché program, the United States systematically and consistently has sought to establish, enforce and strengthen IP protections globally.

B. The Global IP System Enabled Industry's Response to COVID-19 Pandemic

IP protections provided by the United States and other governments consistent with their TRIPS Agreement obligations have fueled COVID-19-related biopharmaceutical innovations and enhanced access to innovative COVID-19-related biopharmaceutical products. As amply evidenced during the COVID-19 pandemic, IP furthered, rather than hindered, access to COVID-19 vaccines and therapeutics all over the world.

Following the outbreak and global spread of the coronavirus in early 2020, mass testing and vaccination was critical to stopping the virus' spread and reducing the death toll worldwide. IP protections have facilitated 379 collaborations on COVID-19 vaccine manufacturing, enabling capacity to produce more than enough doses to vaccinate the world.[65] Similar collaborations were also enabled by robust IP systems for COVID-19 therapeutics – enabling partners to safely and confidently share technology and information across organizations and borders. According to Airfinity, more than 140 voluntary license (VL) and manufacturing agreements for COVID-19 treatments have been signed since the start of the pandemic.[66]

A widely-cited report, *Unprecedented: The Rapid Innovation Response to COVID-19 and the Role of Intellectual Property* authored by Jennifer Brant and Mark F. Schultz, highlights the essential – and yet "not fully appreciated" – role that IP rights played in the rapid response to the coronavirus pandemic.[67] In their report, Brant and Schultz explain that "[w]ithout IP, the

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[62] U.S. Embassy and Consulate in the Netherlands, Embassy Statement on Intellectual Property Rights (Jan. 30. 2020), https://nl.usembassy.gov/embassy-statement-on-intellectual-property-rights/.

[63] See USPTO launches platform to facilitate connections between patent holders and potential licensees in key technologies: Initial release focuses on COVID-19–related technologies (May 4, 2020), https://www.uspto.gov/about-us/news-updates/uspto-launches-platform-facilitate-connections-between-patent-holders-and.

[64] WTO, TRIPS Council: Intellectual Property and Innovation: IP Licensing Opportunities, IP/C/W/691 (Jun. 23, 2022), https://docs.wto.org/dol2fe/Pages/SS/directdoc.aspx?filename=q:/IP/C/W691.pdf&Open=True.

[65] Source: Airfinity (https://science.airfinity.com); see Appendix 1: COVID-19 Vaccines: Production and Uptake.

[66] Airfinity (science.airfinity.com). See Appendix 2: Expanding the TRIPS Waiver is Unnecessary and Harmful.

[67] Jennifer Brant & Mark F. Schultz, Unprecedented: The Rapid Innovation Response to COVID-19 and the Role of Intellectual Property 2 (Nov. 2021), https://www.unpackingip.org/.

investment, cooperation and innovation that led to the development and manufacturing of COVID-19 vaccines and treatments would not have happened as it did."[68] In particular, the report highlights the importance of IP in: (1) providing the certainty and predictability needed to secure critical investments to develop and create the background technology and know-how used in several of the COVID-19 vaccines and treatments; (2) enabling R&D partnerships to swiftly develop COVID-19 solutions in record time; and (3) facilitating hundreds of partnerships globally to manufacture COVID-19 vaccines and treatments at scale.[69]

The decades long development of the mRNA technology that underpinned both the Pfizer BioNTech and Moderna vaccines demonstrates the critical importance of IP for securing investment. Moderna went public with its mRNA technology in 2018 but before that point, the company had raised $2.6 billion in investments and partnership funding and $600 million in an IPO.[70] That is, market investors poured $3.2 billion into a company at a time when it had no successful product to market and its venture was extremely risky (indeed, for decades, the promise of mRNA innovation was plagued by technical challenges, including how mRNA could be delivered into the body without it degrading).[71] That investment was made possible only because the investors knew that there was upside potential if Moderna was successful – i.e., if Moderna successfully developed a marketable product, Moderna would have the opportunity to recoup its investments (without the risk of copying by its competitors during the term of protection) and would be able to repay its investors. Without that upside potential, enabled by IP protection, investments into Moderna would have been a fool's errand such that the company would have remained underfunded or unfunded and its vaccine would not have been on the market today.

The rapid development, manufacture and distribution of the Pfizer-BioNTech vaccine required BioNTech's Dr. Sahin and Dr. Tureci to share their work on mRNA technology with Pfizer – work they had dedicated their lives to for more than 25 years.[72] Knowing BioNTech would be unable to swiftly develop and produce sufficient quantities in the event their herculean efforts to develop the vaccine were ultimately successful, they licensed their mRNA technology to Pfizer.[73] The success of "pairing Pfizer's development, regulatory and commercial capabilities with BioNTech's mRNA vaccine technology and expertise as one of the industry leaders"[74] cannot be overstated. But, as Brant and Schultz argue, the promise of enforceable IP rights in facilitating this partnership has been underappreciated. BioNTech's Dr. Sahin noted that the

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[68] Id.

[69] Id.

[70] Moderna, Inc., U.S. Securities and Exchange Commission filing (Amendment No. 1 to Form S-1 Registration Statement), Nov. 28, 2018, at i, 1.

[71] Chris Beyrer, Johns Hopkins Bloomberg School of Public Health, The Long History of mRNA Vaccines, Oct. 6, 2021, https://publichealth.jhu.edu/2021/the-long-history-of-mrna-vaccines.

[72] Bojan Pancevski & Jared S. Hopkins, How Pfizer Partner BioNTech Became a Leader in Coronavirus Vaccine Race, Wall Street Journal (Oct. 22, 2020), https://www.wsj.com/articles/how-pfizer-partner-biontech-became-a-leader-in-coronavirus-vaccine-race-11603359015.

[73] Id.

[74] Press Release, Pfizer, Pfizer and BioNTech to Co-Develop Potential COVID-19 Vaccine (Mar. 17, 2020), https://investors.pfizer.com/investor-news/press-release-details/2020/Pfizer-and-BioNTech-to-Co-Develop-Potential-COVID-19-Vaccine/default.aspx.

partnership "was all based on trust,"[75] and, indeed, the two companies' collaboration took off even prior to finalizing a formal licensing agreement based on their prior relationship and security of trade secret protection.[76] Pfizer, too, acknowledged the "critical" role of IP protection, without which BioNTech would have been unlikely to share their "core technology and the result of all the investments they have made over several years."[77] Collaboration and licensing arrangements also facilitated the development of other hugely successful COVID-19 vaccines – such as between AstraZeneca and Oxford University. These achievements demonstrate that "voluntary collaboration, and the development of trust among the collaborators" was an "essential ingredient" in developing the vaccines that have transformed the global response to the coronavirus pandemic and enabled the resumption of social and commercial activity that had been halted around the world by the virus.[78]

In addition to bringing products into existence, IP protection enabled the rapid manufacture and distribution of COVID-19 vaccines and therapeutics. For a product to be manufactured rapidly and cost-effectively, many innovators entered into manufacturing contracts with partners in a number of different parts of the world.[79] These arrangements required manufacturers to share with those partners enough information to actually enable the manufacture of the product. Here, the innovator faces a significant risk – the possibility that its manufacturing partner takes the knowhow and then manufactures a product to compete with the innovator. Were this risk left unaddressed, the innovator would have to closely guard the relevant knowhow and rely on its own capabilities for manufacture. It is IP protection (specifically, patents and the protection of trade secrets) which protects the innovator against this risk. The fact that the TRIPS Agreement imposes a common baseline standard of IP protection for all WTO Members meant that the innovators could turn to manufacturers across the globe to accelerate the manufacturing process with significantly less risk of unfair competition from them.[80]

To take an example, UK-based AstraZeneca and the Serum Institute of India entered into a voluntary licensing agreement, pursuant to which they worked together to supply one billion doses of the COVID-19 vaccine first developed by Oxford University, in middle and low-income countries.[81] This would not have been possible absent AstraZeneca's trust, founded on the IP-

[75] Bojan Pancevski & Jared S. Hopkins, How Pfizer Partner BioNTech Became a Leader in Coronavirus Vaccine Race, Wall Street Journal (Oct. 22, 2020), https://www.wsj.com/articles/how-pfizer-partner-biontech-became-a-leader-in-coronavirus-vaccine-race-11603359015.

[76] Jennifer Brant & Mark F. Schultz, Unprecedented: The Rapid Innovation Response to COVID-19 and the Role of Intellectual Property 2 (Nov. 2021), https://www.unpackingip.org/.

[77] Id.

[78] See Eric M. Solovy, The Doha Declaration at Twenty: Interpretation, Implementation, and Lessons Learned on the Relationship Between the TRIPS Agreement and Global Health, 42 NW. J. Int'l L. & Bus. 253, 292 (2022).

[79] See Appendix 2: Expanding the TRIPS Waiver is Unnecessary and Harmful.

[80] See Moderna to build mRNA vaccine manufacturing facility in Kenya, Reuters (Mar. 8, 2022), https://www.reuters.com/business/healthcare-pharmaceuticals/moderna-build-mrna-vaccine-manufacturing-facility-kenya-2022-03-07/; see also Pfizer, Manufacturing and Distributing the COVID-19 Vaccine, https://www.pfizer.com/science/coronavirus/vaccine/manufacturing-and-distribution.

[81] See Press Release, AstraZeneca, AstraZeneca takes next steps towards broad and equitable access to Oxford University's potential COVID-19 vaccine (June 4, 2020), https://www.astrazeneca.com/media-centre/articles/2020/astrazeneca-takesnext-steps-towards-broad-and-equitable-access-to-oxford-universitys-potential-covid-19-vaccine.html.

framework, that Serum Institute would not simply steal its invention and compete with it. Other similar examples include AstraZeneca's use of CSL Behring's manufacturing facilities in Australia to supply vaccines in Australia and neighboring islands,[82] Johnson & Johnson's partnerships in India, South Africa and with Merck to expand manufacturing facilities for its vaccine,[83] the collaboration between Pfizer and BioNTech on the one hand and Novartis on the other,[84] and the partnership between Pfizer and BioNTech, and South Africa's Biovac to supply vaccines in the African Union.[85] In these examples, assurances offered by the IP-framework allowed even traditional competitors to collaborate with each other to make vaccines available rapidly, without the fear of copying.

Similar examples exist in the COVID-19 therapeutics space. Pfizer entered into a VL agreement with the Medicines Patent Pool (MPP) to share IP related to PAXLOVID® to help enable 38 generic manufacturers to manufacture and supply generic versions to 95 low- and middle-income countries, covering up to approximately 53 percent of the world's population. [86] Merck granted VLs to generic manufacturers and agreed, through the MPP, to make generic doses of an antiviral COVID-19 medicine, molnupiravir, available in over 100 low- and middle-income countries following regulatory approval or emergency authorization.[87] Gilead signed VLs with foreign generic manufacturers – including in Egypt, India and Pakistan – to expand access to remdesivir, an antiviral medication to treat COVID-19, in 127 countries, most of which are low-income or lower-middle-income and have populations with limited access to health care. Each of Gilead's licensees maintain contracts with Gilead that involve technology transfer and

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[82] See Press Release, CSL Behring, COVID-19 Update, CSL continues to provide medicines to patients around the world (Jun. 2, 2021), https://www.cslbehring.com/newsroom/2020/covid-19-update.

[83] See Press Release, Johnson & Johnson, Johnson & Johnson Announces Landmark Agreement to Enable its COVID-19 Vaccine to be Manufactured and Made Available by an African Company for People Living in Africa (Mar. 8, 2022), https://www.jnj.com/johnson-johnson-announces-landmark-agreement-to-enable-its-covid-19-vaccine-to-be-manufactured-and-made-available-by-an-african-company-for-people-living-in-africa; Press Release, Johnson & Johnson, Statement on Johnson & Johnson's Collaboration in India with Biological E to Expand Manufacturing Capabilities For its COVID-19 Vaccine Candidate (Aug. 30, 2020), https://www.jnj.in/about-jnj/company-statements/statement-on-johnson-johnsons-collaboration-in-india-with-biological-e-to-expand-manufacturing-capabilities-for-its-covid-19-vaccine-candidate; Press Release, Johnson & Johnson, Johnson & Johnson Statement on Collaboration with Merck (Mar. 2, 2021), https://www.jnj.com/johnson-johnson-statement-on-collaboration-with-merck.

[84] See Elizabeth Doherty, Novartis joins pharma-wide effort to meet global demand for COVID-19 vaccines, Novartis (Mar. 22, 2021), https://www.novartis.com/stories/novartis-joins-pharma-wideeffort-meet-global-demand-covid-19-vaccines.

[85] See Press Release, Pfizer, Pfizer and BioNTech announce collaboration with Biovac to manufacture and distribute COVID-19 vaccine doses within Africa (Jul. 21, 2021), https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontechannounce-collaboration-biovac.

[86] See Press Release, Pfizer, Pfizer and The Medicines Patent Pool (MPP) Sign Licensing Agreement for COVID-19 Oral Antiviral Treatment Candidate to Expand Access in Low- and Middle-Income Countries (Nov. 16, 2021), https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-medicines-patent-pool-mpp-sign-licensing.

[87] Press Release, Merck, The Medicines Patent Pool (MPP) and Merck Enter Into License Agreement for Molnupiravir, an Investigational Oral Antiviral COVID-19 Medicine, to Increase Broad Access in Low- and Middle-Income Countries (Oct. 27, 2021), https://www.merck.com/news/the-medicines-patent-pool-mpp-and-merck-enter-into-license-agreement-for-molnupiravir-an-investigational-oral-antiviral-covid-19-medicine-to-increase-broad-access-in-low-and-middle-income-countri/.

information sharing.[88] Together, these partnerships treated more than 13 million patients globally, including eight million in low and lower-middle income countries,[89] an accomplishment that was appropriately recognized by the USPTO in 2022 with a "Patents for Humanity" award.[90]

Absent a strong IP-framework, manufacturing an innovative product abroad, or even exporting it, puts an innovator at risk of unauthorized copying by competitors. It is IP protection, and the minimum standards in that respect imposed by the TRIPS Agreement, that safeguarded innovators against that risk and enabled COVID-19 vaccines and therapeutics to be manufactured and exported seamlessly around the world.

While it is certainly true that the unprecedented nature of the COVID-19 crisis accelerated voluntary collaborations, preexisting relationships and those developed over the past few years will surely outlast the pandemic and enable further important breakthroughs in medicine. Even as the urgency surrounding the coronavirus pandemic has subsided,[91] BioNTech and Pfizer recently announced their efforts to develop a next-generation COVID-19 vaccine as "part of the companies' long-term and multi-pronged scientific strategy to generate more robust, longer-lasting and broader immune responses against SARS-CoV-2 infections and associated COVID-19."[92] And, building on the success of their partnership in launching the COVID-19 vaccine, BioNTech and Pfizer have launched collaborative efforts to develop the first-ever mRNA vaccine for the shingles virus.[93] Merck and Orna Therapeutics have also announced efforts to pioneer a new class of vaccines and therapeutics with Orna's proprietary circular RNA (oRNA) technology for use against infectious diseases and cancer.[94] Other collaborations such as that between U.S.-based Vaxess Technologies, Inc. and Korea-based GC Biopharma Corp., in which the companies are developing a shelf-stable vaccine patch for seasonal influenza, can potentially revolutionize global medicine delivery systems that are increasingly challenged by factors such

[88] Gilead, Access Partnerships, https://www.gilead.com/purpose/medication-access/global-access/access-partnerships.

[89] Mike Boyd, Gilead's Path to Equitable Global COVID-19 Treatment Access (Oct. 4, 2022), https://stories.gilead.com/articles/gilead-path-to-equitable-global-covid-19-treatment-access.

[90] See USPTO, Patents for Humanity: COVID-19 category award recipients, https://www.uspto.gov/ip-policy/patent-policy/patents-humanity/patents-humanity-covid-19-category-award-recipients.

[91] U.S. Dep't Health & Hum. Serv., Fact Sheet: COVID-19 Public Health Emergency Transition Roadmap (Feb. 9, 2023), https://www.hhs.gov/about/news/2023/02/09/fact-sheet-covid-19-public-health-emergency-transition-roadmap.html (announcing the United States will soon "transition away from the emergency phase" of the pandemic where "daily COVID-19 reported cases are down 92%, [and] COVID-19 deaths have declined by over 80%").

[92] Press Release, Pfizer, Pfizer and BioNTech Advance Next-Generation COVID-19 Vaccine Strategy with Study Start of Candidate Aimed at Enhancing Breadth of T cell Responses and Duration of Protection (Nov. 16, 2022), https://www.pfizer.com/news/announcements/pfizer-and-biontech-advance-next-generation-covid-19-vaccine-strategy-study.

[93] Press Release, Pfizer, Pfizer and BioNTech Sign New Global Collaboration Agreement to Develop First mRNA-based Shingles Vaccine (Jan. 5, 2022), https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-sign-new-global-collaboration-agreement.

[94] Press Release, Merck, Merck and Orna Therapeutics Collaborate to Advance Orna's Next Generation of RNA Technology (Aug. 16, 2022), https://www.merck.com/news/merck-and-orna-therapeutics-collaborate-to-advance-ornas-next-generation-of-rna-technology/.

as climate change.[95] IP protections will likewise continue to facilitate these important partnerships.[96]

C. The Global IP System Inherently Balances Innovation and Access

A critically important means by which the existing rules of the TRIPS Agreement promote access to medicine is by setting a minimum standard for patent protection. Articles 27 and 28 of the TRIPS Agreement establish the scope of inventions eligible for patentability and the rights to be conferred under a patent. Article 33 establishes a 20-year minimum period for protection from the date of the patent application's filing and Article 62.2 preserves the effective period of patent protection from the time of the patent grant in recognition of significant patent backlogs that unreasonably erode patent protections in many countries.[97] Importantly, TRIPS Article 29.1 requires that patent applicants disclose their inventions to the public, enabling free use of new technologies following patent expiration. The disclosure function is one of the primary means by which patents promote investment in R&D and the dissemination of innovation.[98]

The rules on patent protection set forth in the TRIPS Agreement are among the most important factors in promoting the development and diffusion of new and innovative medicines.[99] A biopharmaceutical company's decision to invest in developing, marketing and distributing a new medicine is inextricably linked to the company's expectation of its ability to recoup its investment and generate the profits needed to invest in future medicine development.[100] Biopharmaceutical companies report that patents, specifically, are the most valuable IP rights tool for capturing the returns from their investments in R&D.[101] In fact, historical data shows

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[95] Press Release, Vaxess, Vaxess Announces Interim Results from Phase I Clinical Trial of MIMIX-Flu Vaccine Patch (Dec. 14, 2022), https://www.vaxess.com/vaxess-announces-interim-results-from-phase-i-clinical-trial-of-mimixflu-vaccine-patch; see also Rebecca Philipsborn et al., Climate Change and the Practice of Medicine: Essentials for Resident Education, 96 Academic Med. 355, 359 (2021) ("Extreme weather events threaten the availability of supplies and medications by not only disrupting the cold chain (i.e., the transport of items such as vaccines that require specific temperatures . . . .").

[96] Press Release, Merck, Merck and Orna Therapeutics Collaborate to Advance Orna's Next Generation of RNA Technology (Aug. 16, 2022), https://www.merck.com/news/merck-and-orna-therapeutics-collaborate-to-advance-ornas-next-generation-of-rna-technology/ (noting that under its agreement with Merck, "Orna will retain rights to its oRNA-LNP technology platform").

[97] Article 62.2 of the TRIPS Agreement states that WTO Members shall ensure that procedures for granting an IP right "permit the granting or registration of the right within a reasonable period of time so as to avoid unwarranted curtailment of the period of protection."

[98] See, e.g., Laura Magazzini et al., Patent Disclosure and R&D Competition in Pharmaceuticals, 18 Econ. Innovation & New Tech. 467 (2009).

[99] Many empirical studies have assessed to what extent patents matter for innovation in the health sector. Specifically, they analyze the relationship between strength of IP protection and pharmaceutical innovation. While studies may differ in the way they parametrize IP strength and in the outcome variables they examine, there is robust evidence that stronger and more harmonized patent protection facilitates innovation, mitigates the negative effect from economic policy uncertainty, increases corporate R&D spending and overall results in increased medicine development. Appendix 4 to this submission provides a structured overview of key findings in the literature.

[100] See Iain M. Cockburn, Jean O. Lanjuow & Mark Schankerman, Patents and the Global Diffusion of New Drugs, Nat'l Bureau of Econ. Rsch. (Working Paper No. 20492), at 2 (2014), https://www.nber.org/system/files/working_papers/w20492/w20492.pdf.

[101] Id. at 2.

that without patent protection, a majority of pharmaceutical products would not have been brought to market.[102]

Accordingly, patient access to medicines in a particular country can have a lot to do with the level of patent protection afforded by their government. But not only does patent protection influence the availability of new medicines in a given market, it also affects the speed at which new medicines become available and diffusion within the market. Empirical evidence shows that strong patent protection significantly speeds up new medicine diffusion – new medicines are more readily available at a quicker pace for patients in markets with stronger patent protections compared to patients in markets with weaker patent protections.[103] This is true for patients in countries of all levels of economic development.[104] It should also be pointed out that in many countries if there is no approved innovator product, it may not be possible for generic competitors to enter the market, again reducing patient access. These findings suggest that implementation and strict enforcement of the patent protection set forth in the TRIPS Agreement is critical for helping to facilitate the development of innovation ecosystems and drive faster access to new pharmaceuticals.[105]

Another rule set forth in the TRIPS Agreement that can be more effectively deployed to improve access to medicine is regulatory data protection (RDP). Under Article 39.3, the TRIPS Agreement provides that RDP must be accorded to test data submitted in order to obtain marketing approval for pharmaceutical with new chemical entities. The TRIPS Agreement recognizes that the development of this test data "involves a considerable effort," and thus WTO Members shall protect data against disclosure and unfair commercial use, except where necessary to protect the public, subject to safeguards.

RDP incentivizes investment in new medicine development by preventing third parties, within a certain timeframe, from relying on innovators' clinical test data generated with significant investments in time and resources. While patent protection, as discussed, provides the greatest incentives for developing and bringing to market a new product, patents alone are often not enough. For example, patents may not sufficiently protect revolutionary biologics – such as those developed to treat cancer, rheumatoid arthritis and asthma – where competition arises from biosimilars, as biosimilars are not exact replicas and may not be covered by the relevant

[102] Id. at 3-4.

[103] Id. at 3.

[104] Id. at 3-4 (noting that the effects observed are "large and robust to a variety of empirical specifications [such as] controlling for economic and demographic factors").

[105] Numerous high-quality empirical studies assess whether a correlation or causal relationship exists between changes in patent policy and indicators of access to medicines. Examples for patent policy changes include the introduction of a domestic patent regime; strengthening or weakening domestic patent regimes; patent expiration/loss of IP protection; and patent strengthening/harmonization via trade agreement. Indicators for access to medicine include likelihood of launch of new medicines in new markets; time to market ("launch delay") of new medicines; adoption of new medicines (i.e., sales); and prices of new medicines. Although the conceptual framing of the exact research questions may be different from study to study, there is ample evidence that stronger and more harmonized patent protection increases access to medicine to countries of all development levels, while weaker (and/or weakly enforced) patent protection decreases access to medicine. Appendix 5 to this submission provides a structured overview of key findings in the literature.

patents.[106] RDP protects biologics from premature competition because biosimilar manufacturers generally need to rely on biologics' regulatory test data to demonstrate comparable efficacy in order to obtain marketing approval.[107] Further, RDP protects against the disclosure of test data from costly clinical trials which are not ultimately successful in bringing a medicine to market, but may be instrumental in future development.[108] By assuring innovators protection against unfair competition, markets with reasonable periods of RDP attract more clinical trials – leading to the launch of new medicines.

The greatest achievement of RDP, however, is that it can provide these incentives for innovation while still serving the goal of promoting access to low-cost medicines. This is because RDP provides only a limited period of data exclusivity, allowing generic manufacturers to rely on originators' data after protection expires. In doing so, RDP, as provided under Article 39.3, reflects the intention of the drafters of the TRIPS Agreement to strike a "balance" between ensuring IP rights protection and promoting other policy objectives.[109]

As part of the inherent balance within the TRIPS Agreement between the rights of the IP owner and the interests of the wider society,[110] LDCs, as noted above, are exempt from implementing most of the commitments in TRIPS through July 2034 (with a separate exemption related to pharmaceuticals not scheduled to expire until January 2033). Separate from these broad exemptions, TRIPS also includes limited exceptions or mechanisms (which some refer to as "flexibilities") through which WTO Members may allow third parties to undertake an otherwise IP-infringing act, subject to certain conditions. With respect to patents, those mechanisms include compulsory licensing.

The TRIPS Agreement does not set out grounds for compulsory licensing and leaves the determination of grounds to domestic law. However, if a WTO Member chooses, based on grounds available in domestic law, to issue a compulsory license, it must abide by certain conditions listed in Article 31 of the TRIPS Agreement. These conditions include: (i) each

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[106] See Eric M. Solovy, Protection of Test Data Under Article 39.3 of the TRIPS Agreement: Advancements and Challenges After 25+ Years of Interpretation and Application, NW. J. Int'l L. & Bus. (forthcoming); see also How Biologics Have Changed the Rules for Pharma, Chemistry World (May 7, 2019), https://www.chemistryworld.com/molecule-to-market/how-biologics-have-changed-the-rules-for-pharma/3010301.article; Sanofi, Biological Medicines Target Disease Solutions, https://www.sanofi.com/en/about-us/biologic-medicines-target-disease-solutions ("Not only have new biologic therapies revolutionized cancer treatment, they are also becoming increasingly important as the most advanced therapies for other serious diseases, such as Crohn's disease, ulcerative colitis, rheumatoid arthritis (RA) and other autoimmune diseases.").

[107] Jack Ellis, Supporting Innovation in Next-Generation Medicines, WIPO Mag. (Jun. 2017), https://www.wipo.int/wipo_magazine/en/2017/03/article_0007.html.

[108] See Jennifer Brant & Mark F. Schultz, Unprecedented: The Rapid Innovation Response to COVID-19 and the Role of Intellectual Property 2 (Nov. 2021), https://www.unpackingip.org/ (noting "[b]iopharma companies do not do research to create specific, new IP rights. Rather, they do research secure in the knowledge that they can get IP rights to protect useful results.").

[109] Recall that Article 7 of the TRIPS Agreement states the objective that "[t]he protection and enforcement of intellectual property rights should contribute to the promotion of technological innovation and to the transfer and dissemination of technology, to the mutual advantage of producers and users of technological knowledge and in a manner conducive to social and economic welfare, and *to a balance of rights and obligations*." (Emphasis added.)

[110] See TRIPS Agreement, Articles 7, 8.

compulsory license be considered on its individual merits; (ii) a compulsory license be issued only after failure of attempts to obtain voluntary commercial licenses; (iii) the scope and duration of the license be limited to the purpose for which it is issued; (iv) non-exclusivity; (v) non-assignability; (vi) compulsory licenses be issued predominantly to supply the domestic market of the country issuing it; (vii) termination of the license when the circumstances warranting its grant cease to exist; (viii) payment of adequate remuneration to the patent owner; (ix) judicial or other independent review of validity; and (x) judicial or other independent review of remuneration.[111] As discussed below, some of these requirements were clarified through the Doha Declaration and the resulting TRIPS Amendment.

The Doha Declaration reiterates and further refines the balance in the TRIPS Agreement between protecting IP and addressing public health concerns by addressing a clearly defined concern that "WTO members with insufficient or no manufacturing capacities in the pharmaceutical sector could face difficulties in making effective use of compulsory licensing under the TRIPS Agreement." To address this concern, in August 2003, the WTO Members adopted a General Council Decision and the WTO General Council Chairman's Statement Accompanying the Decision, which was ultimately reflected in an amendment to the TRIPS Agreement, i.e., Article 31*bis* in the TRIPS Agreement. The Decision and subsequently Article 31*bis*, release Members from the obligation that compulsory licenses be issued predominantly to supply the domestic market of the country issuing them, to allow compulsory licensing for exports, so far as necessary for export to eligible importing Members. Eligible Members, for this purpose, were defined to be all least developed countries and other Members who made a requisite notification to the WTO of their intention to use the mechanism to import a pharmaceutical product or products for which it has insufficient or no manufacturing capacities. This relaxation of the requirement in Article 31(f) to allow compulsory licensing for the purpose of exportation was accompanied by certain and important notification requirements, which aimed to prevent products exported under this flexibility from being diverted away from the eligible destinations to more lucrative destinations.

D. The TRIPS Waiver for COVID-19 Vaccines Disrupts the Balance of the TRIPS Agreement in Multiple Critical Ways and Should Not be Extended to Diagnostics and Therapeutics

The 2022 TRIPS waiver decision[112] applies to patents claiming inventions necessary for production and supply of COVID-19 vaccines, as well as the ingredients and processes necessary for the manufacture of those vaccines.[113] Substantively, the waiver appears to undermine a number of the existing requirements related to compulsory licensing and blithely asserts "that Article 39.3 of the Agreement [related to the provision of RDP] does not prevent an eligible Member from enabling the rapid approval for use of a COVID-19 vaccine produced under this

[111] TRIPS Agreement, Article 31.

[112] WTO Ministerial Conference, *Ministerial Decision on the TRIPS Agreement Adopted 17 June 2022*, WTO Doc. WT/MIN(22)/30 (Jun. 22, 2022), https://docs.wto.org/dol2fe/Pages/SS/directdoc.aspx?filename=q:/WT/MIN22/30.pdf&Open=True (hereinafter, "TRIPS Waiver").

[113] TRIPS Waiver, ¶ 1 and footnote 2.

Decision."[114] The latter appears to disregard any regulatory data protection for that product, even though there is no such exception or mechanism in TRIPS (Article 31 applies solely to patents).

With regard to compulsory licensing, and with no explicit regard of the Article 31*bis* mechanism, the waiver appears to create yet another mechanism to allow for exceptions to the requirement in Article 31(f) that compulsory licenses be issued predominantly to supply the domestic market.[115] Article 31*bis*, as discussed above, includes a number of anti-diversion requirements to ensure that the exported products actually reach eligible destinations and are not diverted to more lucrative markets. The waiver appears to significantly dilute these anti-diversion requirements. Eligible Members acting under the waiver are only required to take "all reasonable efforts to prevent [] re-exportation," and all Members are required to "ensure the availability of effective legal means to prevent the importation into and sale in their territories of products manufactured" under the waiver that have been diverted to their markets.[116]

In addition, the waiver appears to dilute the requirement in Article 31(h) that the issuance of a compulsory license be accompanied by the payment of adequate remuneration to the patent owner, by stipulating that Members "may take account of the humanitarian and not-for-profit purpose of specific vaccine distribution programs."[117] The waiver also creates a significant risk of inadequate remuneration by referencing and endorsing as "good practice" the tiered royalty method advocated by the WHO and UNDP, which is inherently ill-suited for ensuring adequacy of remuneration.[118]

Critically, although it has been nine months since the adoption of the TRIPS waiver, no WTO Member has issued a compulsory license under the waiver. That is, while there are calls to expand the scope of the waiver, even the waiver as originally agreed remains fully unutilized.

Mexico and Switzerland submitted a communication to the TRIPS Council on November 1, 2022, concerning the proposed TRIPS waiver expansion and raising evidence issues regarding supply and demand, voluntary licensing, affordability and accessibility. The countries conclude that "we do not face a situation where we have an IP-induced lack of access to or a lack of manufacturing capacity of COVID-19 therapeutics and diagnostics. As a consequence, no adjustments to the IP system seem to be required. If the decision were extended nonetheless, it

[114] TRIPS Waiver, ¶ 5.

[115] TRIPS Waiver, ¶ 3(b).

[116] TRIPS Waiver, ¶ 3(c).

[117] TRIPS Waiver, ¶ 3(d).

[118] See TRIPS Waiver, footnote 4. For a critique of the tiered royalty method, see Eric M. Solovy, The TRIPS Waiver for COVID-19 Vaccines, and Its Potential Expansion: Assessing the Impact on Global IP Protection and Public Health, Ctr. Intell. Prop. x Innovation Pol'y (2022), https://cip2.gmu.edu/wp-content/uploads/sites/31/2022/12/GMU-C-IP2-Solovy-PolicyBrief-TRIPS.pdf; see also generally Eric M. Solovy & Deepak Raju, The UNDP/WHO remuneration guidelines: a proposed formula for inadequate remuneration for compulsory licencing in violation of the TRIPS agreement, 16 J. IP Law & Practice 1192-1202 (2021).

would even have a detrimental effect and leave us ill-equipped to fight the COVID-19 pandemic and potential future pandemics effectively."[119]

And yet, proponents of the waiver continue to push for its extension to diagnostics and therapeutics asserting, as they long have, that the limited use of compulsory licenses and particularly Article 31*bis* demonstrates that the system requires reform and further flexibilities, rather than acknowledging that compulsory licensing is intended to be a limited exception and, even then, is unlikely to be the best mechanism to ensure patient access. To wit, they highlight that only one compulsory license for export has been granted under Article 31*bis*, specifically in 2007 to allow for export of certain pharmaceuticals from Canada to Rwanda.[120] What they do not tend to note is that the use of this mechanism by Canada and Rwanda was of "negligible benefit", because Rwanda was able to simultaneously purchase the same medicine from Indian companies for almost the same price.[121]

Similarly, although Bolivia and Antigua and Barbuda notified, in May 2021, that they intended to use the mechanism to import COVID-19 vaccines, no Member has yet notified the intention to issue compulsory licenses permitting the export of vaccines to these countries.[122] As the WTO secretariat notes, however, a notification "does not mean a commitment to procure medicines under this System" and a Member may choose to refrain from acting on a notification if it manages to procure the product through other channels.[123] Given the vaccination rates in these countries (over 60 percent in Bolivia and almost 70 percent in Antigua and Barbuda have received at least one dose)[124] and the significant surplus of COVID-19 vaccine doses, it is evident that both countries were able to fulfil their needs for the COVID-19 vaccine through voluntary arrangements.

Some WTO Members and commentators claim that the anti-diversion requirements that attach to compulsory licensing under Article 31*bis* are too onerous. However, the anti-diversion requirements exist precisely to ensure that medicines manufactured for an eligible Member which needs them actually arrive at the intended destination and are not diverted to more lucrative markets. The allegation that anti-diversion requirements are too cumbersome ignores the reality that tracking origin and destination of goods is a regular feature of international trade, even outside the context of compulsory licensing. In any event, it is telling that even after the

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[119] Council for Trade-Related Aspects of Intellectual Property Rights, *Communication from Mexico and Switzerland: TRIPS Council Discussion on COVID-19 Therapeutics and Diagnostics: Evidence and Questions on Intellectual Property Challenges Experienced by Members*, IP/C/W/693 (Nov. 1, 2023), https://docs.wto.org/dol2fe/Pages/SS/directdoc.aspx?filename=q:/IP/C/W693.pdf&Open=True.

[120] See *Canada is first to notify compulsory license to export generic drug*, WTO (Oct. 4, 2007), https://www.wto.org/english/news_e/news07_e/trips_health_notif_oct07_e.htm.

[121] See Reed F. Beall, Randall Kuhn & Amir Attaran, Compulsory Licensing Often Did Not Produce Lower Prices For Antiretrovirals Compared To International Procurement, 34 Health Affairs 493, 499 (2015).

[122] Eric M. Solovy, The Doha Declaration at Twenty: Interpretation, Implementation, and Lessons Learned on the Relationship Between the TRIPS Agreement and Global Health, 42 NW. J. Int'l L. & Bus. 253, 280-281 (2022).

[123] Council for Trade-Related Aspects of Intellectual Property Rights, *Annual Review of the Special Compulsory Licensing System, Report to the General Council*, Appendix I, ¶ 11, WTO Doc. IP/C/86 (Nov. 11, 2020), https://docs.wto.org/dol2fe/Pages/SS/directdoc.aspx?filename=q:/IP/C/86.pdf&Open=True.

[124] See Our World in Data: Coronavirus (COVID-19) Vaccinations, https://ourworldindata.org/covid-vaccinations.

2022 TRIPS waiver significantly diluted the anti-diversion requirements, the mechanism remains unused. The reality was aptly summarized by the Swiss Government, during an annual review of the implementation of paragraph 6 of the Doha Declaration:

> "compulsory licences are as such not an easy and quick-fix solution to address the broader problem of sustainable access to affordable medicines – whether in developing countries or any other WTO Member. Implementing a compulsory licence, and again I refer to normal or special compulsory licences even once granted, pose their own challenges. A generic manufacturer needs to be found who is ready, willing and available to produce the medicine needed and the quantities needed within a short time-period at an affordable and competitive price and at the required quality and safety standards. This demonstrates that a compulsory licence is never a quick-fix solution and this cannot be remedied by the Paragraph 6 System or by revising it for that matter.[125]

As Switzerland would similarly note in the context of Article 31*bis* not being used in 2018, "[n]o quick conclusions should be drawn from this fact with regard to the workability of the System."[126] In fact, limited use of compulsory licenses is an intended part of the system design.[127] Rather than "claim in the abstract that the System is not workable or should be amended," which is "not helpful,"[128] WTO Members confronting difficulty "when *actually* making use of the System" should look to the WTO to "examine these specific difficulties in its Annual Reviews [of the Special Compulsory Licensing System] and look into how they can be addressed best in a practical manner."[129] Even Canada, the only country to have actually made exports using the flexibility, recognized that the system "had never been intended to solve the issue of access to medicines on its own".[130] Similarly, the United States noted that the flexibility was "only one tool for addressing the larger issue."[131]

Complementing these general statements are the three specific explanations offered by the European Union in a 2011 intervention as to why the flexibilities remain underutilized: (1) the vast majority of essential medicines are already in the public domain (i.e., not protected by patents); (2) LDCs are still enjoying an extended transition period, such that they are not obligated to protect patents on pharmaceutical products; and (3) developing countries can acquire

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[125] Council for Trade-Related Aspects of Intellectual Property Rights, *Annual Review of the Decision on the Implementation of Paragraph 6 of the Doha Declaration on the TRIPS Agreement and Public Health, Report to the General Council*, Appendix 1, ¶ 64, WTO Doc. IP/C/76 (Nov. 23, 2016).

[126] Council for Trade-Related Aspects of Intellectual Property Rights, *Annual Review of the Special Compulsory Licensing System, Report to the General Council*, Appendix 1, ¶ 23, WTO Doc. IP/C/82 (Nov. 27, 2018).

[127] Id. (explaining that the system "has not been conceived for frequent use").

[128] Id. at ¶ 25.

[129] Council for Trade-Related Aspects of Intellectual Property Rights, *Annual Review of the Special Compulsory Licensing System, Report to the General Council*, Appendix 1, ¶ 75, WTO Doc. IP/C/86 (Nov. 11, 2020).

[130] Id. ¶¶ 14-15.

[131] Council for Trade-Related Aspects of Intellectual Property Rights, *Annual Review of the Decision on the Implementation of Paragraph 6 of the Doha Declaration on the TRIPS Agreement and Public Health, Report to the General Council*, ¶ 47, WTO Doc. IP/C/61 (Nov. 18, 2011), https://docs.wto.org/dol2fe/Pages/SS/directdoc.aspx?filename=Q:/IP/C/61.pdf&Open=True.

medicines through voluntary licenses or other means consistent with the TRIPS Agreement that do not require recourse to the system.[132] All of these points still hold true today.[133]

Studies also indicate that compulsory licensing is not always (or even usually) the most price-efficient way to procure medicines. According to a 2015 empirical study by Beall, Kuhn and Attaran, "[c]ompulsory license prices exceeded the median international procurement prices in nineteen of the thirty case studies, often with a price gap of more than 25 percent".[134] That is, for a country seeking access to low-priced medicines, international procurement through voluntary arrangements was a better option than compulsory licensing. While thus not delivering benefits in terms of access to cheaper medicines, compulsory licenses cost the issuing country the credibility of its IP-framework. Habitual issuance of compulsory licenses would signal that a country is not an IP-friendly jurisdiction, dissuading innovators from investing in that country or entering into collaborations with partners in that country, ultimately resulting in poorer (not better) access to innovative products and processes including medicines.

Blaming IP for inequities in access to medicine and calling for incremental addition of flexibilities to the point of the gradual dismembering of the whole IP-framework, distracts from the real problems and finding solutions to them. Solovy discusses several of these factors, including tariff and non-tariff barriers to trade in medicines.[135] Also noteworthy is a U.S. statement identifying the "tools" that can be deployed to solve these issues and improve access to medicines:

> (i) enhancing legal certainty for manufacturers of generic medicines; (ii) eliminating tariffs on medicines and medical devices, thereby decreasing costs for hospitals, clinics, aid organizations and consumers, among others; (iii) reducing customs obstacles to medicines by minimizing import barriers, such as discriminatory, burdensome, and unpredictable customs procedures, that impeded access to innovative and generic medicines; (iv) curbing trade in counterfeit medicines by making customs and criminal enforcement measures available to prevent medicines bearing counterfeit trademarks from entering national markets, and thus supporting efforts of countries to address the serious risks to patients posed by such counterfeits; (v) reducing internal barriers to distribution of medicines by guaranteeing importing, exporting, and distribution rights with respect to medicines and minimizing internal barriers that could stand in the way of efficiently distributing medicines to those in need; and (vi) minimizing unnecessary regulatory

[132] Council for Trade-Related Aspects of Intellectual Property Rights, *Annual Review of the Decision on the Implementation of Paragraph 6 of the Doha Declaration on the TRIPS Agreement and Public Health, Report to the General Council*, ¶ 64, WTO Doc. IP/C/61 (Nov. 18, 2011).

[133] Mark Schultz, McDole J., Essential Medicines and Patents: Recent Trends in the Latest Editions of the World Health Organization Essential Medicines List, (Nov. 2, 2020), https://geneva-network.com/research/essential-medicines-and-patents-recent-trends-in-the-latest-editions-of-the-world-health-organization-essential-medicines-list/ (noting that as of January 2020, only 47 of the 458 products (10.3 percent) included in the 21st edition of the WHO's Essential Medicines List are under patent somewhere in the world).

[134] Reed F. Beall, Randall Kuhn & Amir Attaran, Compulsory Licensing Often Did Not Produce Lower Prices For Antiretrovirals Compared To International Procurement, 34 Health Affairs 493, 493 (2015).

[135] See Eric M. Solovy, The Doha Declaration at Twenty: Interpretation, Implementation, and Lessons Learned on the Relationship Between the TRIPS Agreement and Global Health, 42 NW. J. Int'l L. & Bus. 253, 297-298 (2022).

> barriers by promoting transparent and nondiscriminatory regulatory structures to facilitate the availability of safe and efficacious medicines to the public…[136]

Further clarifications or waivers of the TRIPS Agreements are not needed to improve access to COVID-19 therapeutics. The U.S. Trade Representative, after supporting the TRIPS waiver for COVID-19 vaccines, in its December 17, 2022 summary of its consultations with stakeholders concerning potential TRIPS waiver expansion, noted that "[m]any proponents of extending the Ministerial Decision have longstanding critiques of the TRIPS Agreement" and conceded that "[c]reating further flexibilities in the TRIPS Agreement is, from this perspective, a matter of principle."[137]

Consistent with the Agreement's objective of balancing the protection of IP rights with policy objectives such as the promotion of global social and economic welfare, the TRIPS Agreement offers more than sufficient flexibility for low-income and least developed country Members of the WTO to facilitate greater access to medicine. It is unfortunate that – notwithstanding this flexibility, including the lengthy transition periods in which they are exempted from complying with the TRIPS Agreement – many factors unrelated to IP rights continue to restrict access in these countries, including those factors which created challenges for the distribution of COVID-19 therapeutics. These factors contribute to the view that existing flexibilities on IP standards are insufficient to enable or improve access for such Members to innovative new medicines. But, even if expansions of flexibilities within the TRIPS Agreement did not pose unacceptable risks to the security and predictability of the multilateral trading system and future medical innovation, the perceived need for further clarifications of TRIPS flexibilities is incorrect. In fact, the limited uses – with little success – of existing TRIPS flexibilities, such as compulsory licensing under Articles 31 and 31*bis* of the Agreement, demonstrate that challenges with access to medicine are multidimensional and thus require multifaceted solutions that cannot be provided under the legal framework of the TRIPS Agreement, or through the procurement or use of any particular instance of IP.

In addition to the limitations with compulsory licensing, the perceived need for a clarification of flexibilities under the TRIPS Agreement that would conceivably facilitate greater use of compulsory licensing have questionable bases. It is important to note that some countries calling for further expansion of flexibilities under the TRIPS Agreement have granted compulsory licenses under circumstances which are inconsistent with the rules set forth in Article 31. For example, in 2017, Malaysia employed a non-transparent process when granting a compulsory license for a hepatitis C treatment that suggested the government primarily sought to enhance the competitive posture of domestic producers of the patented product.[138] A number of countries

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[136] Council for Trade-Related Aspects of Intellectual Property Rights, *Annual Review of the Decision on the Implementation of Paragraph 6 of the Doha Declaration on the TRIPS Agreement and Public Health, Report to the General Council*, ¶ 48, WTO Doc. IP/C/61 (Nov. 18, 2011).

[137] USTR, Summary of Consultations (Dec. 6, 2022), https://ustr.gov/sites/default/files/2022-12/TRIPS%20Consultations%20Summary.pdf.

[138] Press Release, PhRMA, PhRMA Decries Damaging Foreign Practices in Special 301 Filing (Feb. 8, 2019), https://www.phrma.org/international/phrma-decries-damaging-foreign-practices-in-special-301-filing. It is also worth noting that when the compulsory license was imposed in Malaysia, just over 1,500 patients with hepatitis C

have enacted laws and regulations that permit government authorities to issue compulsory licenses when there is no local manufacture of patented products, suggesting that such licenses may be improperly used as a tool of industrial policy rather than public health solution. Such practices are at odds not only with the prohibition in the TRIPS Agreement of discriminating in the enjoyment of patent rights with respect to imported or locally produced products under Article 27.1, but also with the critical objectives of the 140-year old Paris Convention, which was incorporated into the TRIPS Agreement.[139] In Argentina, for example, 2019 legislation authorizes use of compulsory licenses as a tool for combatting medicine price increases[140] within a broader economic plan to restore the sustainability of public debt.[141]

The potential abuse by WTO Members of the compulsory licensing system suggests that expanding opportunities to utilize TRIPS flexibilities such as compulsory licenses could increasingly degrade incentives for investment in the development of new medicines in those countries (and beyond). This greatly disrupts the balance between protection of IP rights and facilitation of technology transfer intended under the TRIPS Agreement.[142] Indeed, the TRIPS waiver debate has emboldened, and provided political cover, to countries historically antagonistic towards the TRIPS Agreement to opportunistically weaken global IP protection, including through the increased use of compulsory licensing in ways not contemplated under the TRIPS Agreement. For example, after India and South Africa tabled the initial TRIPS waiver proposal in October of 2020, several countries considered or passed legislation expanding their compulsory licensing regimes beyond what is accepted under international norms, or leveraged compulsory licensing to brazenly encourage "medical tourism." Brazil considered mandating that right holders share necessary trade secrets, technical information and know-how as part of its compulsory licensing regime, a concept that the United States has opposed.[143] Malaysia, months after throwing its support behind the TRIPS waiver, announced that it would utilize the compulsory licensed hepatitis C treatment referenced above to boost medical tourism.[144] Indonesia even disregarded a voluntary licensing agreement already in place between the right

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received the licensed treatment over a 12-month period. The Star, "Malaysia to make drug to treat Hepatitis C," (Mar. 8, 2019), https://www.thestar.com.my/news/nation/2019/03/08/malaysia-to-make-drug-to-treat-hepatitis-c. In contrast, cooperative discussions and collaborative access policies like voluntary licensing treated over 15,000 patients over the same period in neighboring Vietnam. Observer Research Foundation, "Five Takeaways: Bridging access and innovation in healthcare policy," (Oct. 31, 2019), https://www.orfonline.org/research/five-takeaways-bridging-access-and-innovation-in-healthcare-policy-57163/.

[139] Paris Convention for the Protection of Industrial Property, Article 5.1 (Mar. 20, 1883) ("Importation by the patentee into the country where the patent has been granted of articles manufactured in any of the countries of the Union shall not entail forfeiture of the patent.").

[140] Republic of Argentina, Emergency Economic Law, Article 70 (Dec. 21, 2019), https://www.argentina.gob.ar/normativa/nacional/ley-27541-333564/texto.

[141] Press Release, Republic of Argentina (Apr. 22, 2020), https://www.argentina.gob.ar/sites/default/files/press_release.pdf.

[142] See Eric M. Solovy, The Doha Declaration at Twenty: Interpretation, Implementation, and Lessons Learned on the Relationship Between the TRIPS Agreement and Global Health, 42 NW. J. Int'l L. & Bus. 253, 253, 286-287 (2022).

[143] IAM, Brazil on the cusp of passing landmark compulsory technology transfer law (Aug. 19, 2021), https://www.iam-media.com/article/brazil-the-cusp-of-passing-landmark-compulsory-technology-transfer-law.

[144] Code Blue, Malaysia To Offer Hepatitis C Drug To Medical Tourists (Nov. 16, 2021), https://codeblue.galencentre.org/2021/11/16/malaysia-to-offer-hepatitis-c-drug-to-medical-tourists/.

holder and generic manufacturers to supply the Indonesian market with a COVID-19 therapeutic and issued a compulsory license for the same product.[145]

III. Expanding the TRIPS Waiver to COVID-19 Treatments would Undermine Development Across Many Therapeutical Areas, Compromising Global Public Health and Harming Patients – Especially Patients in Lower- and Middle-Income Countries

Extending the TRIPS waiver would negatively affect medical and technological innovation on multiple dimensions. As discussed above in Section II, the role of IP protections in facilitating medical innovation has long been recognized. The returns on investment generated by IP protection incentivize companies to devote the financial resources, human capital and time necessary to develop new medical products.[146] In addition, enforceable IP rights reassure innovators that they can share (i.e., voluntarily license) their product designs, manufacturing technologies and know-how with others – including potential competitors – without the risk of unpunished theft or misappropriation by those parties.[147] In this sense, IP rights engender trust among market participants and create space for innovative partnerships. By supporting investments in innovation, facilitating innovative partnerships and encouraging continuous refinement of existing medicines and technologies, IP rights are driving the expansion and improvement of COVID-19 therapeutics. Weakening IP protections for inventive COVID-19 diagnostics and therapeutics would not only threaten innovation in COVID-19-related solutions, but also threaten innovation aimed at treating other diseases.

There have been over 1,200 clinical trials for COVID-19 vaccines and treatments in the United States (more than 2,000 total around the world) since the start of the pandemic.[148] Of the more than $24 billion spent on COVID-19 clinical trials in the United States so far, almost 90 percent have been for COVID-19 treatments.[149] PhRMA member companies are currently testing 176 unique COVID-19 treatments in clinical trials.[150] Almost 60 percent of all COVID-19 treatments currently being tested in the pipeline also have other potential indications for which they are also being tested or used.[151]

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[145] Geneva Network, Why patents matter to Indonesia (Aug. 23, 2022), https://geneva-network.com/research/why-patents-matter-to-indonesia/.

[146] See Jennifer Brant & Mark F. Schultz, Unprecedented: The Rapid Innovation Response to COVID-19 and the Role of Intellectual Property 9 (Nov. 2021), https://www.unpackingip.org/ (highlighting that "[d]rug development is expensive. Estimates vary, with one putting the cost of drug development at $2.6 billion for an approved drug.") (internal citations omitted). Gilead Sciences, for example, has "has invested approximately $1.3 billion in R&D into remdesivir since 2000." See Jaci McDole & Stephen Ezell, Ten Ways IP Has Enabled Innovations That Have Helped Sustain the World Through the Pandemic, Information Technology & Innovation Foundation 9 (Apr. 2021), https://www2.itif.org/2021-ip-covid-case-studies.pdf (citing GAO, Information on Federal Contributions to Remdesivir 15 n. 35 (Mar. 2021)).

[147] See generally, Jennifer Brant & Mark F. Schultz, Unprecedented: The Rapid Innovation Response to COVID-19 and the Role of Intellectual Property (Nov. 2021), https://www.unpackingip.org/.

[148] Informa (informa.com). See Appendix 2: Expanding the TRIPS Waiver Is Unnecessary and Harmful.

[149] Id.

[150] Id.

[151] Informa (informa.com). See Appendix 2: Expanding the TRIPS Waiver Is Unnecessary and Harmful.

Extending the TRIPS waiver to cover COVID-19 therapeutics would damage the incentives underpinning this ongoing COVID-19 innovation. The waiver's relaxation of TRIPS Agreement rules on compulsory licensing of patents, including remuneration required for patent right holders subject to a compulsory license, creates uncertainty in the minds of patent owners, investors and commercial partners – including candidates for voluntary license agreements with owners of COVID-19-related patents.[152] This uncertainty diminishes the value of patents, which in turn reduces the investment returns associated with patents, discourages R&D and reduces the ability of inventors to secure rewarding voluntary license agreements.[153] In other words, an expanded TRIPS waiver would discourage companies from pursuing new and improved therapeutics for COVID-19, as well as investigating whether existing medicines could be effective therapeutics for COVID-19. In doing so, an expanded TRIPS waiver could delay an effective end to the pandemic.

A. The Broader Consequences of a TRIPS Waiver Extension for Medical and Technological Innovation

Extending the TRIPS waiver to cover COVID-19 therapeutics would jeopardize innovation in a variety of public health contexts. This is because many COVID-19 therapeutics use ingredients and biotechnological methods with applications far beyond COVID-19. For example, certain COVID-19 therapeutics authorized for emergency use in the United States can be used to treat HIV, hepatitis C and rheumatoid arthritis. Moreover, 57 percent of treatments in the COVID-19 pipeline are also being developed for other conditions, including cancer, autoimmune disorders, central nervous system disorders, cardiovascular disease, endocrine disorders and other infectious diseases. Cancer, the second leading cause of death in the United States, accounts for 42 percent of the 370 clinical trials being conducted for other conditions.[154] Similarly, medicines currently being developed to exclusively treat COVID-19 are highly likely to have applications beyond COVID-19.

Extending the TRIPS waiver could lead to relaxed rules for compulsory licensing of patents on multipurpose medicines and pharmaceutical ingredients.[155] It would be difficult, if not impossible, to guarantee that multipurpose medicines produced under a compulsory license are

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[152] Eric Solovy, The TRIPS Waiver for COVID-19 Vaccines, and Its Potential Expansion: Assessing the Impact on Global IP Protection and Public Health, Center for Intellectual Property x Innovation Policy 7 (Dec. 2022), https://cip2.gmu.edu/wp-content/uploads/sites/31/2022/12/GMU-C-IP2-Solovy-PolicyBrief-TRIPS.pdf.

[153] See id.

[154] Airfinity (science.airfinity.com). See Appendix 2: Expanding the TRIPS Waiver is Unnecessary and Harmful.

[155] The original TRIPS waiver applies to "the subject matter of a patent required for the production and supply of COVID-19 vaccines," which includes "ingredients and processes necessary for the manufacture of the COVID-19 vaccine." See WTO Ministerial Conference, *Ministerial Decision on the TRIPS Agreement, Adopted on 17 June 2022*, ¶ 1, n. 2, WTO Doc. WT/MIN(22)/30 (Jun. 22, 2022), https://docs.wto.org/dol2fe/Pages/SS/directdoc.aspx?filename=q:/WT/MIN22/30.pdf&Open=True; see also Eric Solovy, The TRIPS Waiver for COVID-19 Vaccines, and Its Potential Expansion: Assessing the Impact on Global IP Protection and Public Health, Center for Intellectual Property x Innovation Policy 4 (Dec. 2022), https://cip2.gmu.edu/wp-content/uploads/sites/31/2022/12/GMU-C-IP2-Solovy-PolicyBrief-TRIPS.pdf.

used only for COVID-19 treatment.[156] Not only do many COVID-19 antivirals and antibodies treat or potentially treat other indications, it is impossible to identify the many medicines being used to treat the broad range of symptoms suffered by patients with acute or long COVID-19. Therefore, there is a serious risk that multipurpose therapeutics would be developed under compulsory licenses permitted by the waiver extension and then used to harm patent owners' returns on investment in markets entirely unrelated to COVID-19 (a very real risk even within a voluntary licensing agreement). Faced with this uncertainty and possible damage to their investments, patent owners may limit their R&D into pharmaceutical innovation.

B. Waiving TRIPS Obligations Concerning COVID-19 Vaccines and Treatments Is Dangerous

Critically, stringent regulatory authorities, like the U.S. Food and Drug Administration, and innovators working in cooperation with partners under voluntary licensing agreements (including via the MPP), have ensured the quality, safety and efficacy of the resulting COVID-19 vaccines and therapeutics. While negotiating their own licensing terms, rights holders can scrutinize potential partners' manufacturing capabilities, supply chains and regulatory compliance programs to ensure that output is high-quality and produced in accordance with applicable laws. Companies are far better equipped to conduct this wide-ranging due diligence than government agencies, which may lack the resources to thoroughly examine all potential licensees in any given contract manufacturing arrangement. By contrast, waivers of patent rights on COVID-19 vaccines and/or treatments could invite copycat medicines from suppliers that lack the knowhow to manufacture them safely, which could expose patients to unsafe products.

Similarly, by eliminating the ability of original innovator companies to exercise oversight over production of COVID-19 vaccines and/or treatments, the TRIPS waiver could enable bad actors to supply adulterated, substandard or counterfeit versions of treatments and/or vaccines. These concerns are not hypothetical. For example, the failure to implement TRIPS-level IP protections in some countries has been correlated with wide availability of counterfeit medicines,[157] undermining efforts to improve access to medicine and threatening patients' health and safety. By forfeiting additional American IP to countries and other entities, expansion of the TRIPS waiver would hurt patients in low- and middle-income countries the most since those patients would be most likely to take any adulterated, substandard or counterfeit versions of treatments.

In addition to these safety, quality and efficacy concerns, waiving commitments to protect U.S. innovation through an expanded TRIPS waiver would allow and encourage global competitors to authorize domestic companies to produce the patented product for national industrial purposes. Nor can it be assumed that the TRIPS waiver will be limited to eligible countries or entities. Rather, untrustworthy governments or other bad actors could acquire American IP through

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[156] Eric Solovy, The TRIPS Waiver for COVID-19 Vaccines, and Its Potential Expansion: Assessing the Impact on Global IP Protection and Public Health, Center for Intellectual Property x Innovation Policy 12 (Dec. 2022), https://cip2.gmu.edu/wp-content/uploads/sites/31/2022/12/GMU-C-IP2-Solovy-PolicyBrief-TRIPS.pdf.

[157] Maria Nelson, Michelle Vizurraga & David Chang, Counterfeit Pharmaceuticals: A Worldwide Problem, 96 Trademark Rep. 1068 (2006), https://www.inta.org/wp-content/uploads/member-only/resources/the-trademark-reporter/vol96_no5_a6.pdf.

diplomatic, economic or other influence over countries – including developing countries – that utilize the waiver.

IV. Giving away American IP to foreign countries by expanding the TRIPS waiver to COVID-19 treatments will weaken American medical innovation and leadership, outsource American manufacturing jobs and jeopardize the United States' ability to respond to future pandemics.

A. The Economic Impact of the U.S. Innovative Biopharmaceutical Industry

The U.S. innovative biopharmaceutical industry contributes significantly to the U.S. economy and its workers. In turn, the United States leads the world in developing new medicines, with biopharmaceutical companies sponsoring more than 4,500 clinical trials in the United States alone, with trials in all 50 states, the District of Columbia and Puerto Rico. In 2017, these trials involved close to one million participants and accounted for nearly $43 billion in economic activity.[158]

The United States is the global leader in biopharmaceutical innovation and production and reaps an outsized share of the economic benefits of the global industry. For example: U.S. multinational biopharmaceutical companies locate 90 percent of their research and development (R&D) expenditures in the United States; nearly 80 percent of wages and salaries paid by U.S. multinational biopharmaceutical companies go to employees in the United States; and over 70 percent of the value added generated from all products manufactured globally by U.S. multinational biopharmaceutical companies occurs in the United States.[159] Unlike trade balance statistics, value added shows where multinationals develop and produce their products. Wages and salaries are the largest component of value added.

In short, the innovative biopharmaceutical sector generates high-quality American jobs, powers economic output and exports for the U.S. economy, and is the foundation of one of the nation's most dynamic innovation ecosystems. This large U.S. economic footprint, and the corresponding benefits that accrue to U.S. workers and their families, exist precisely *because* the sector is an active participant in the rules-based international trading system and a utilizer of longstanding, consistent and dependable U.S. trade policies that value innovation, protect IP rights and champion open trade.

The men and women of America's biopharmaceutical sector strive every day to discover, develop and deliver innovative medicines to patients across the country and around the world to ensure that they can benefit from the latest treatments and cures. The industry's varied occupational base and extensive research, manufacturing and distribution infrastructure generate and support high-wage jobs, significant tax revenues and growing economic output for local communities. The strength and ingenuity of the U.S. biopharmaceutical industry and innovation-

[158] TEConomy Partners; for PhRMA. Biopharmaceutical Industry-Sponsored Clinical Trials (Apr. 2019).

[159] U.S. Bureau of Economic Analysis, Activities of U.S. Multinational Enterprises, https://www.bea.gov/data/intl-trade-investment/activities-us-multinational-enterprises-mnes. Note: U.S. import data reflect the transaction value of goods at the port of entry (e.g., manufacturer price plus freight charges) even when most of the value added (e.g., wages and salaries) and R&D generated to create that transaction value occurred in the United States.

based policies have resulted in the United States being the global leader in biopharmaceutical innovation and production. The following economic metrics reflect this global and national leadership position.[160]

B. Sizeable, Stable and Diverse Employment

In 2020, the U.S. biopharmaceutical industry directly employed more than 903,000 U.S. workers and, with a substantial employment multiplier of 4.92, supported more than 3.5 million additional U.S. jobs, for a total U.S. employment impact of more than 4.4 million jobs. In 2020, 37 percent of U.S. biopharmaceutical industry employees were engaged in manufacturing at over 1,500 manufacturing plants across the country, nearly 35 percent were engaged in biopharmaceutical R&D, 25 percent were engaged in distribution and three percent were engaged in corporate administration.

The U.S. biopharmaceutical industry is among the top five employers of U.S. manufacturing jobs, with more Americans directly employed in pharmaceutical manufacturing than in manufacturing in several other manufacturing industries, including each of the following: iron and steel products, aerospace products and parts, petroleum and coal products, and electric equipment and appliances.[161]

The U.S. biopharmaceutical industry has outpaced U.S. manufacturing and the overall U.S. private sector in employment growth over the 2015-2020 period, demonstrating a combination of expansion, stability and economic resilience that makes the industry a key driver of the U.S. economy. Whereas direct employment in biopharmaceutical manufacturing increased 28.4 percent over this period, total manufacturing employment fell 5.1 percent and overall economy-wide employment decreased 0.7 percent over the same period.[162]

The U.S. biopharmaceutical manufacturing industry employs a diverse workforce.[163] For example, U.S. biopharmaceutical manufacturing is the second highest employer of women in the U.S. manufacturing sector and the fifth highest employer of minorities (Black, Asian, Latino). The industry created 55,000 U.S. manufacturing jobs for women over the past five years, the second highest among all manufacturing industries; women account for almost 60 percent of U.S. manufacturing jobs in the biopharmaceutical industry, but less than 30 percent of all U.S. manufacturing jobs. Similarly, the industry created 77,000 U.S. manufacturing jobs for minorities (Black, Asian, Latino) over the past five years, the second highest among all manufacturing industries; almost 80 percent of the U.S. manufacturing jobs created in the biopharmaceutical industry over the past five years went to minorities (Black, Asian, Latino).

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[160] Unless otherwise indicated, this data is available in a Report prepared by TEConomy Partners for PhRMA, The Economic Impact of the U.S. Biopharmaceutical Industry: 2020 National and State Estimates (Mar. 2022), https://phrma.org/resource-center/topics/economic-impact/industry-economic-impact.

[161] U.S. Bureau of Labor Statistics, Current Population Survey (CPS) Labor Force Statistics, https://www.bls.gov/cps/home.htm.

[162] Id.

[163] Id.

Innovative biopharmaceutical companies and their supply chains also play key roles in supporting local economies and a wide range of jobs in every state across the country. In fact, nearly every state is involved in the manufacturing of FDA-approved medicines.

C. High Skills, High Wage and High Productivity

The complexity of innovative biopharmaceutical production – driven by significant levels of research and development – requires a high proportion of STEM jobs and a significant share of employment in high-skill and advanced degree occupations. Yet, as a critical industry also requiring significant manufacturing and distribution infrastructure, the U.S. biopharmaceutical industry offers significant employment opportunities and careers for individuals with less than a bachelor's degree.

This unique employment mix benefits all workers, with average annual wages and benefits of more than $145,000 – nearly $60,000 more than the average U.S. manufacturing industry job and more than twice the U.S. average across all industries. From an overall productivity perspective, this high-wage and high-quality employment mix, combined with the R&D intensity of the U.S. biopharmaceutical industry, generates a productivity level of nearly $381,000 per employee – more than twice that of the U.S. average manufacturing worker and more than three and half times than that of the average U.S. worker.

D. Significant Economic Driver

The innovative biopharmaceutical industry is one of the most research-intensive in America, annually investing an estimated $122.2 billion in researching and developing new medicines.[164] In 2020, the U.S. biopharmaceutical industry's direct output exceeded $710 billion and supported output totaled an additional $700 billion, with the ripple effect of this production through suppliers and other sectors of the U.S. economy. This combined, total output impact constitutes 3.7 percent of total U.S. output. Through its research, production and overall operations, value added from the U.S. biopharmaceutical industry directly contributes 1.6 percent of U.S. GDP. This figure increases to 3.4 percent of U.S. GDP when indirect and induced effects, which support more than $720 billion in value added, are included.

Since 2015, over 50,000 jobs have been created in the U.S. biopharmaceutical industry by new foreign direct investment.[165] The biopharmaceutical industry attracts more new foreign direct investment into the United States than any other industry (over $143 billion over the past five years). In turn, the industry is by far the largest driver of new foreign direct investment in U.S. manufacturing, accounting for more than 20 percent over the past five years. The next-highest industry, computers and electronic products, accounted for only 7 percent over the same period.[166]

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[164] Research!America, U.S. Investments in Medical and Health Research and Development (Jan. 2022).

[165] Financial Times Ltd, fDi Markets, https://www.fdimarkets.com/. Note: new foreign direct investment includes "greenfield projects" only and not acquisitions.

[166] U.S. Bureau of Economic Analysis, New Foreign Direct Investment in the United States, https://www.bea.gov/data/intl-trade-investment/new-foreign-direct-investment-united-states/supplemental-data.

The biopharmaceutical industry also is a major U.S. exporter. In 2021, U.S. biopharmaceutical goods exports exceeded $80 billion.[167] The biopharmaceutical sector was the largest exporter of goods among the most R&D-intensive industries in 2020 – which in addition to biopharmaceuticals included navigational equipment, semiconductors and other electronic components, medical equipment and supplies and communications equipment.[168]

In addition to its significant contributions to the U.S. economy and patients, the U.S. innovative biopharmaceutical industry seeks to serve patients around the world through local affiliates. Data demonstrates that U.S. multinationals that increase their investments abroad simultaneously increase the size and strength of their manufacturing activities in the United States.[169] For example, creation of jobs by U.S. multinationals abroad and the expansion of sales by U.S. multinational affiliates abroad both lead to more production and employment at home, especially in high value-added services such as R&D. On average, a 10 percent increase in U.S. multinational firms' overseas sales by their affiliates correlates with an 8.2 percent increase in U.S. domestic R&D spending; 2.6 percent increase in U.S. exports; and 2.2 percent increase in U.S. employment. Preponderance of net job loss in U.S. manufacturing comes from companies that do not invest abroad.

In short, the nation's biopharmaceutical industry is a major driver of innovation and economic growth both within the U.S. and globally. The ongoing COVID-19 pandemic has highlighted the critical need for the industry as well as the ability of the U.S. biopharmaceutical industry to respond effectively in times of national and global crisis, while also consistently providing jobs for significant numbers of highly skilled, highly productive and highly paid workers across the country.

E. The U.S. Economic Impact from R&D and Manufacturing of COVID-19 Vaccines and Treatments[170]

America's workers have been instrumental to the biopharmaceutical industry's response to the COVID-19 pandemic. A surge in COVID-19 related research in the United States, plus record high U.S. exports of biopharmaceutical products, has generated over 400,000 U.S. jobs that directly and indirectly support the development and manufacturing of COVID-19 vaccines and treatments. These supporting U.S. jobs span across several sectors; 60 percent are outside the biopharmaceutical industry. Roughly 110,00 jobs support COVID-19 related clinical trials in the United States and another 310,000 support the manufacturing of COVID-19 vaccines and treatments. This estimated economic impact understates the full extent of scientific research that also occurs outside the operation of clinical trials. More importantly, the vast majority of COVID-19 related scientific research in the United States is for treatments rather than vaccines.

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[167] TradeStats Express™: National Trade Data for NAICS Code 3254 Pharmaceuticals and Medicines, http://tse.export.gov/TSE/TSEHome.aspx.

[168] Analysis of National Science Foundation and Business Research and Development Survey (BRDIS) data by ndp | analytics.

[169] The Petersen Institute for International Economics, The U.S. Manufacturing Base: Four Signs of Strength (June 2014), https://www.piie.com/publications/policy-briefs/us-manufacturing-base-four-signs-strength.

[170] See Appendix 2: Expanding the TRIPS Waiver Is Unnecessary and Harmful.

One key role of the nation's biopharmaceutical industry in the COVID-19 pandemic response is scientific research, and one measurable aspect of scientific research is clinical trials. Over $24 billion has been spent in the United States on clinical trials for COVID-19 vaccines and treatments, with another $80 billion in spending expected over the next few years if clinical trials continue for COVID-19 products already in the pipeline. The vast majority (90 percent) of spending on COVID-19 related clinical trials in the United States are for treatments, just 10 percent are for vaccines.

The nation's biopharmaceutical industry has strengthened during the COVID-19 pandemic. In addition to producing vaccines and treatments for the domestic market, U.S. exports of biopharmaceutical products are now at all-time highs, After U.S. COVID-19 vaccine contracts were amended in mid-2021, U.S. exports of biopharmaceutical products surged 60 percent. It is estimated that more than half (55 percent) of the 310,000 jobs supporting COVID-19 related manufacturing are supporting exports. In addition, global new private investment in biopharmaceutical manufacturing and R&D facilities has further shifted to the United States. In 2021, new private investment in biopharmaceutical manufacturing and investment increased 70 percent in the United States, making it the destination for more than half of all global new investment in biopharmaceutical manufacturing and R&D.

V. Policymakers should Reject Expansion of the TRIPS Waiver and Focus on the Real Issues Impacting COVID-19 Medicine Access – Trade and Regulatory Barriers and In-Country Distribution and Administration Challenges

Having produced more than enough COVID-19 vaccine doses to vaccinate the world, the innovative biopharmaceutical industry encouraged the Administration to demonstrate international leadership at the WTO and elsewhere by opposing the TRIPS waiver and refocusing global attention to resolving global challenges to distributing and administering that global vaccine surplus. Instead, the Administration joined certain foreign governments in championing the TRIPS waiver, to the detriment of American innovation and global public health.

Governments should address the real constraints on access to these medicines instead of further undermining the IP protections that enabled, and continue to enable, the rapid development of COVID-19 vaccines and treatments. Trade and regulatory barriers and in-country distribution and administration obstacles are the most significant impediments to expanding access to COVID-19 treatments across the globe. None of these impediments result from IP protections. Addressing these barriers and avoiding a harmful expansion of the TRIPS waiver therefore is the most effective way to ensure that COVID-19 treatments continue to be developed, produced and delivered to patients in need.

A. Trade and Regulatory Barriers

The American innovative biopharmaceutical industry has long supported a strong international trading system rooted in the WTO's core principles regarding openness, fairness and predictability. These principles, as established by the WTO's key agreements, including the TRIPS Agreement, have played an essential role in helping to ensure that innovative COVID-19

vaccines and therapeutics can be developed, manufactured and distributed to health systems and patients around the world. Throughout the COVID-19 pandemic, our industry encouraged the United States and other WTO members to build on these principles by formalizing and pursuing a robust trade and health agenda that would enhance the open and rules-based international trading system and, in so doing, strengthen and accelerate global efforts to respond to COVID-19 and better prepare for future health crises.

In particular, our industry encouraged the United States and other WTO members to address and resolve multiple trade and regulatory barriers hindering successful and timely development, manufacturing and distribution of COVID-19 vaccines and therapeutics, including tariffs, export restrictions and unnecessary or inefficient regulatory procedures.[171] Despite the critical need to manufacture and distribute COVID-19 vaccines and treatments efficiently on a global basis, many countries have imposed unnecessary trade barriers that disrupt medical supply chains.

WTO Director-General Ngozi Okonjo-Iweala likewise has highlighted several of these issues throughout her tenure. For example, more than one year in advance of the WTO's decision to approve the TRIPS waiver on COVID-19 vaccines, Ngozi Okonjo-Iweala acknowledged the need for "[a]ction to further reduce export restrictions and supply chain barriers, and to facilitate logistics and customs procedures."[172] The WTO Secretariat also has raised these issues, including in the context of "trade-related bottlenecks and trade-facilitating measures on critical products to combat Covid-19."[173]

Multiple WTO members, including geographically diverse countries at various levels of economic development, similarly have advanced constructive proposals to eliminate these barriers and promote other trade-facilitating policies. For example:

- New Zealand and Singapore announced trade-facilitative measures (including tariff elimination and commitments not to impose export restrictions) in April 2020 to ensure supply chain continuity and the removal of impediments to trade in products essential for the response to COVID-19.[174]

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[171] ABPI, EFPIA, IFPMA, PhRMA, WTO Twelfth Ministerial Conference: A Critical Opportunity to Strengthen the Global Trade and Health Agenda, https://phrma.org/-/media/Project/PhRMA/PhRMA-Org/PhRMA-Org/PDF/V-Z/WTO-Twelfth-Ministerial-Conference---A-Critical-Opportunity-to-Strengthen-the-Global-Trade-and-Health-Agenda.pdf.

[172] Speech – DG Ngozi Okonjo-Iweala, *Chair Summary following "COVID-19 and Vaccine Equity: What Can the WTO Contribute?"* (Apr. 14, 2021), https://www.wto.org/english/news_e/spno_e/spno7_e.htm; see also Remarks by Director-General Ngozi Okonjo-Iweala, *Technical Symposium (WHO, WIPO, and WTO) on "COVID-19 Pandemic: Response, Preparedness, Resilience"*, (Dec. 16, 2022), https://www.wto.org/english/news_e/spno_e/spno37_e.htm (noting, in the context of COVID-19, that "[t]rade facilitation measures and export controls, regulatory requirements, government procurement practices, tariffs and other trade measures all had a direct bearing on the pace of vaccine production and the breadth of access").

[173] World Trade Organization, *Indicative List of Trade-Related Bottlenecks and Trade-Facilitating Measures on Critical Products to Combat COVID-19* (Oct. 2021), https://www.wto.org/english/tratop_e/covid19_e/bottlenecks_update_oct21_e.pdf.

[174] WTO, *Measures in Response to the COVID-19 Pandemic: Measures to Ensure the Free Flow of Trade in Essential Goods for Combatting the COVID-19 Pandemic, Communications from Singapore and New Zealand*, G/C/W/777 and 778 (Apr. 16, 2020).

- The "Ottawa Group" submitted a "Trade in Health" initiative to the WTO's General Council in November 2020.[175] This initiative proposes that WTO members limit export restrictions on essential medical goods, reduce tariffs, improve transparency, cooperate with other multilateral organizations and share information and implement best practices concerning trade facilitation measures, standards and technical regulations. This communication evolved into a Draft General Council Declaration that included the formal support of over 50 WTO members.[176]

- The European Union submitted a June 2021 communication to the WTO on "Urgent Trade Policy Responses to the COVID-19 Crisis" that outlined constructive proposals concerning trade facilitation, regulatory cooperation and disciplining export restrictions.[177]

Illustrative of the urgent need to address these trade and regulatory barriers, additional support for such initiatives was voiced in other important international fora well in advance of the WTO's TRIPS waiver decision. For example, the May 2021 G20 "Rome Declaration" acknowledged "the central role of the WTO, and the importance of open, resilient, diversified, secure, efficient and reliable global supply chains across the whole value chain related to health emergencies."[178] Similarly, the September 2021 "Declaration of the G20 Health Ministers" recognized the urgent need "to eliminate WTO-inconsistent barriers that jeopardize the effective operation of the supply chains for essential medical goods."[179] In addition, the June 2021 G7 "Carbis Bay Declaration" committed G7 members to pursue health objectives "based on the principles of open trade and transparency, including through terminating unnecessary trade restrictive measures and supporting open, diversified, secure and resilient supply chains."[180]

Even as the WTO approved the TRIPS waiver, the organization failed to take meaningful action to address these trade and regulatory barriers impeding the global COVID-19 response, settling instead for ministerial declarations that lack binding commitments.[181] The Administration likewise declined to address these pressing trade and regulatory barriers with any serious intent

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[175] General Council, *COVID-19 and Beyond: Trade and Health, Communication from Australia Brazil, Canada, Chile, the European Union, Japan, Kenya, Republic of Korea, Mexico, New Zealand, Norway, Singapore, and Switzerland*, WT/GC/223 (Nov. 24, 2020).

[176] Id.

[177] General Council, *Urgent Trade Policy Responses to the COVID-19 Crisis, Communication from the European Union*, WT/GC/231 (Jun. 4, 2021).

[178] Global Health Summit: The Rome Declaration (May 21, 2021), https://www.governo.it/sites/governo.it/files/documenti/documenti/Approfondimenti/GlobalHealthSummit/GlobalHealthSummit_RomeDeclaration.pdf.

[179] Declaration of the G20 Health Ministers (5-6 Sep. 2021), https://reliefweb.int/sites/reliefweb.int/files/resources/G20_Italia_2021_Health_Declaration_ f inal_05092021_OFFICIAL.pdf.

[180] Carbis Bay G7 Summit Communique: Our Shared Agenda for Global Action to Build Back Better (June 2021), https://www.g7uk.org/wp-content/uploads/2021/06/ Carbis-Bay-G7-Summit-Communique-PDF-430KB-25-pages-1-2.pdf.

[181] Ministerial Declaration on the WTO Response to the COVID-19 Pandemic and Preparedness for Future Pandemics, WT/MIN(22)/31 (Jun. 22, 2022).

(e.g., the Administration has not supported the United States becoming a signatory country to the Ottawa Group initiative).

As the primary global institution responsible for promoting and ensuring open and rules-based international trade, the WTO, rather than eliminating longstanding IP protections, should play a leading role in encouraging countries to eliminate trade barriers that impede the distribution of biopharmaceutical products, including COVID-19 vaccines and treatments, across borders.

Tariffs on medicines, inputs and equipment, for example, inhibit the ability of patients across the globe to access lifesaving medicines, including COVID-19 vaccines and treatments. Regarding tariffs, the WTO, in collaboration with the World Health Organization (WHO) and the World Intellectual Property Organization, have recognized that import tariffs applied to medicines and other health products "have a direct bearing on access" to these goods.[182] Tariffs impose direct costs on pharmaceutical products and the various inputs used to invent, manufacture and deploy those products, negatively impacting the ability of patients across the globe to access lifesaving medicines. Resources directed to tariff payments instead could be channeled into other elements of the health sector, including the research, development, clinical and manufacturing processes necessary to produce both new and existing treatments. The WHO has recommended that countries reduce or remove tariffs on medicines, but many countries continue to impose substantial tariffs on medicines and other health products.[183]

To date, only 34 countries have acceded to the WTO's 1994 Agreement on Trade in Pharmaceutical Products, which commits participants to eliminate import duties on a wide range of medicines and other health products on a most-favored-nation (MFN) basis.[184] Moreover, the volume of pharmaceutical trade occurring outside the Agreement has increased since its entry into force. According to recent estimates, pharmaceutical imports by jurisdictions and customs territories outside the Agreement increased from $39.7 billion in 2006 to US $65.73 billion in 2018, potentially subjecting a significant number of pharmaceutical imports to tariffs.[185]

According to an April 2020 WTO report, the average applied MFN tariff on COVID-19-relevant medical products (including medicines, medical supplies, medical equipment and personal protective products) for WTO Members was around 4.8 percent.[186] The average applied MFN

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[182] World Trade Organization, World Health Organization, and World Intellectual Property Organization, *Promoting Access to Medical Technologies and Innovation: Intersections between public health, intellectual property, and trade (Second edition)*, July 2020, https://www.wto.org/english/res_e/booksp_e/who-wipo-wto_2020_e.pdf.

[183] World Health Organization, How to develop and implement a national drug policy (Jan. 2023), http://apps.who.int/iris/bitstream/10665/67759/1/WHO_EDM_2003.pdf.

[184] Canada, the European Union, Japan, Macao (China), Norway, Switzerland, the United Kingdom and the United States currently participate in the Agreement.

[185] Stevens, Philip and Banik, Nilanjan. Abolishing Pharmaceutical and Vaccine Tariffs to Promote Access, Geneva Network, June 2020, https://geneva-network.com/research/2020-pharmaceutical-tariffs/.

[186] World Trade Organization Secretariat, *Trade in Medical Goods in the Context of Tackling COVID-19* (Apr. 2020), https://www.wto.org/english/news_e/news20_e/rese_03apr20_e.pdf. *See also*: World Trade Organization Secretariat, *Trade in Medical Goods in the Context of Tackling COVID-19: Developments in 2019-21* (July 2022), https://www.wto.org/english/tratop_e/covid19_e/med_goods_2019_21_e.pdf; and World Trade Organization and World Bank Group. *Trade Therapy: Deepening Cooperation to Strengthen Pandemic Defenses* (June 2022), https://www.wto.org/english/res_e/booksp_e/tradetherapy2022_e.pdf.

tariff on medicines was 2.1 percent, but many Members maintained higher tariffs on medicines, including Argentina (7.7 percent); Brazil (7.8 percent), Colombia (5.7 percent), Congo (5.0 percent), India (10.0 percent), Indonesia (3.8 percent), Korea (6.9 percent) and Thailand (7.6) percent.[187] Bound MFN tariff rates were significantly higher, averaging more than 20 percent for medicines and more than 25 percent for all COVD-19-relevant medical products.[188] The significant gap between bound and applied rates creates uncertainty concerning whether applied tariff rates will increase, potentially discouraging trade and investment.

Like tariffs, export restrictions impede patient access to pharmaceutical products, including immediate access to lifesaving medicines and vaccines. By imposing barriers on companies and other actors that are coordinating complex global pharmaceutical supply chains, such restrictions severely disrupt international collaborative efforts to invent, manufacture and deploy pharmaceutical products across borders. At the height of the first wave of the COVID-19 pandemic, governments around the world resorted to export restrictions intended to prevent shortages of critical goods. By April 2020, a total of 145 notified export restrictions had been imposed on medical goods. One year later, over 60 notified restrictions were still in place.[189] According to a June 2022 WTO report, nearly 80 percent of the export-restrictive measures imposed during the pandemic remained in place for more than one year, calling into question the temporary nature of these measures.[190]

Rather than secure domestic supply, these restrictions hindered the global response to the pandemic by imposing barriers on companies coordinating global medical supply chains. At a time when companies most needed to dedicate their time and resources to increasing global supply, these restrictions disrupted supply chains and distribution routes, produced delays and additional costs, and increased the risk of supply shortages during the pandemic. For example, India's decision to restrict exports of COVID-19 vaccines in 2021, significantly impeded vaccination efforts in many developing countries, particularly in Africa.[191]

B. In-country Distribution and Administration Challenges

Even before the COVID-19 pandemic, public health experts highlighted in-country delivery and administration barriers as among the most important obstacles to accessing medicines in developing countries.[192] Longstanding obstacles to the efficient delivery of health products in

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[187] Id.

[188] Id.

[189] WTO members' notifications on COVID-19, https://www.wto.org/english/tratop_e/covid19_e/notifications_e.htm.

190 World Trade Organization and World Bank Group. *Trade Therapy: Deepening Cooperation to Strengthen Pandemic Defenses* (June 2022), https://www.wto.org/english/res_e/booksp_e/tradetherapy2022_e.pdf.

191 Magomi, Mogomotsi. Africa's vaccine campaigns hurt by India's ban on exports, Associated Press (May 20, 2021), https://apnews.com/article/africa-health-coronavirus-pandemic-business-global-trade-dbbb7f559efc7e10d15036b80eddab8e.

[192] Kraiselburd, Santiago and Yadav, Prashant. Supply Chains and Global Health: An Imperative for Bringing Operations Management Scholarship into Action, *Production and Operations Management* 22 (2), 377-381 (Feb. 2012), https://asrames.org/wp-content/uploads/2012/04/Kraiselburd-and-Yadav-Supply-Chains-and-Global-Healt.pdf.

developing countries include challenges in warehousing (e.g., lack of adequate storage facilities, security issues and limited use of technology); distribution (e.g., limited availability of transportation, infrequent distribution to rural areas, last-mile delivery failures due to geographic and transportation constraints and coordination problems), and inventory and supply management (e.g., lack of systematic data collection to inform forecasting and inadequate methods of inventory control).[193] Indeed, WTO members have cited a long list of much-needed, non-IP improvements to health care systems.[194] Experts have also noted the unique challenges arising from the public-sector distribution model employed by many developing countries, in which government entities carry out key supply chain functions such as storage and distribution of medicines, and these responsibilities often are fragmented across multiple agencies and levels of government.[195]

These and other longstanding barriers have impeded efficient delivery of COVID-19 medicines to populations in need, undermining the global response to the pandemic. Last-mile distribution and administration challenges have resulted in the destruction of unused COVID-19 vaccines and countries around the world turning away vaccine donations – an obstacle that even the Administration has acknowledged.[196] Similar in-country delivery barriers have inhibited efforts to deploy rapidly COVID-19 therapeutics and diagnostics. As a result of these delivery bottlenecks, many populations face difficulty accessing COVID-19 vaccines and therapeutics despite ample production and supply of these products.

Efficient supply chains for the delivery of vaccines, therapeutics and other health products are a critical component of pandemic response and of effective health systems more broadly. Recognizing the scale of distribution and administration challenges in 2021, the G20 High Level

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[193] Steele, Pamela, Subramanian, Lakshmy and Tolani, Foyeke. Interventions to Improve Access to Medicine in Developing Countries: Mapping WHO's Building Blocks and Supply Chain Functions, ACTA Scientific Pharmaceutical Sciences, Vol. 3 Issue 7 (July 2019), https://dspace.lib.cranfield.ac.uk/bitstream/handle/1826/15713/Access_to_medicine_in_developing_countries-2019.pdf. See also: Yadav, Prashant. Health Product Supply Chains in Developing Countries: Diagnosis of the Root Causes of Underperformance and an Agenda for Reform, Health Systems & Reform, Vol. 1 Issue 2 (Apr. 2015), https://www.tandfonline.com/doi/full/10.4161/23288604.2014.968005; Matowe, Lloyd. Improving Pharmaceutical Supply Chain Management Systems in Resource-Limited Countries: Time to Change Approaches to Capacity Building, Journal of Pharmacy and Pharmaceutical Sciences, Vol. 4 Issue 2 (Sep. 2015), https://www.rroij.com/open-access/improving-pharmaceutical-supply-chain-management-systemsin-resourcelimited-countries-time-to-change-approaches-to-capacity-building.pdf.

[194] See Council for Trade-Related Aspects of Intellectual Property Rights, *Annual Review of the Decision on the Implementation of Paragraph 6 of the Doha Declaration on The TRIPS Agreement and Public Health*, Appendix 1, ¶ 72, WTO Doc. IP/C/76 (Nov. 23, 2016) (offering remarks from the United States on the agreement among WTO Members at the Trilateral Public Health Workshop about the need for various improvements to healthcare systems); *id.* at ¶ 50 (highlighting procurement and tariffs); Eric M. Solovy, The Doha Declaration at Twenty: Interpretation, Implementation, and Lessons Learned on the Relationship Between the TRIPS Agreement and Global Health, 42 NW. J. Int'l L. & Bus. 253, 296-297 (2022) (citing additional comments from the European Union and the United States).

[195] Yadav, Prashant. Health Product Supply Chains in Developing Countries: Diagnosis of the Root Causes of Underperformance and an Agenda for Reform, Health Systems & Reform, Vol. 1 Issue 2 (Apr. 2015), https://www.tandfonline.com/doi/full/10.4161/23288604.2014.968005.

[196] Relman, Eliza. Jen Psaki says South Africa turned down the US's offer of additional COVID-19 vaccine doses, Business Insider, Nov. 29, 2021, https://www.businessinsider.com/jen-psaki-says-south-africa-turned-down-us-offer-of-more-vaccine-doses-2021-11.

Independent Panel on pandemic preparedness and response has recommended that "[m]assive effort has to go into developing in-country systems for agile, last-mile delivery of essential supplies," including vaccines, therapeutics and other health supplies such as oxygen cylinders.[197]

Health workforce challenges also remain major concerns. In fact, governments surveyed by the WHO have cited health workforce challenges as the most common obstacle to scaling up access to COVID-19 therapeutics and diagnostics.[198] Health workforce challenges were the most-cited bottleneck for therapeutics in 61 of 95 countries (64 percent) surveyed by the WHO, and for diagnostics and testing in 53 of 95 countries (56 percent). Both at the height of the COVID-19 pandemic and currently, many developing countries face severe shortages of health workers, greatly limiting their capacity to administer COVID-19 therapeutics and other essential medicines and health services. For example, countries in the WHO African Region have a ratio of 1.55 health workers per 1,000 people, well below the WHO threshold density of 4.45 health workers per 1,000 people needed to deliver essential health services and achieve universal health coverage.[199] The WHO has projected a shortfall of approximately 10 million health care workers worldwide by 2030, concentrated primarily in low- and middle-income countries.[200]

Governments have acknowledged the urgent need to strengthen the health workforce in response to the COVID-19 pandemic. The 2021 "Rome Declaration" adopted by leaders of the G20 and other states recognized the need to "[i]nvest in the worldwide health and care workforce,"[201] and the 2021 "Declaration of G20 Health Ministers" called on member countries to "expand and transform the recruitment, development, education, training, distribution, retention and financing of the health and care workforce."[202] At an October 2022 meeting, G20 Health Ministers expressly acknowledged "the importance of training the workforce" from low- and middle-income countries "to bridge the gap in accessing" vaccines, therapeutics, and diagnostics.[203]

VI. Conclusion

The U.S. innovative biopharmaceutical industry rose to the challenge of researching, developing and deploying safe and effective vaccines and treatments to respond to the pandemic. That effort was underpinned by the global IP system. Disappointingly, it is that same global IP system that

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[197] Report of the G20 High Level Independent Panel on Financing the Global Commons for Pandemic Preparedness and Response (June 2021), https://pandemic-financing.org/wp-content/uploads/2021/07/G20-HLIP-Report.pdf.

[198] World Health Organization, Third round of the global pulse survey on continuity of essential health services during the COVID-19 pandemic (Feb. 7, 2022), https://www.who.int/news/item/07-02-2022-essential-health-services-face-continued-disruption-during-covid-19-pandemic.

[199] World Health Organization, Chronic staff shortfalls stifle Africa's health systems: WHO study (June 22, 2022), https://www.afro.who.int/news/chronic-staff-shortfalls-stifle-africas-health-systems-who-study.

[200] Rivlin, Adrienne and Lumley, Tara. Why is there a global medical recruitment and retention crisis? World Economic Forum (Jan. 9, 2023), https://www.weforum.org/agenda/2023/01/medical-recruitment-crisis-davos23/.

[201] Global Health Summit: Rome Declaration (May 21, 2021), https://global-health-summit.europa.eu/rome-declaration_en.

[202] Declaration of the G20 Health Ministers. G20 Italia, Sep. 5-6, 2021, https://www.salute.gov.it/imgs/C_17_pagineAree_5459_8_file.pdf.

[203] Chair's Summary: Health Ministers' of the G20 (Oct. 28, 2022), http://www.g20.utoronto.ca/2022/221028-health.html.

was undermined by the TRIPS waiver on COVID-19 vaccines. To ensure that further damage is not inflicted on the global IP system, public health and patients around the world, the waiver should not be extended to COVID-19 therapeutics and diagnostics. To do so would weaken American medical innovation and leadership, outsource American jobs and jeopardize the country's ability to respond to future pandemics and health crises. Instead, all policymakers should focus on the real issues impacting access to COVID-19 therapeutics, such as regulatory barriers and in-country distribution and administration challenges. We greatly appreciate this opportunity to provide input into this critical investigation and look forward to further engaging with the Commission.

Sincerely,

/s/ Kevin Haninger

Kevin Haninger
Vice President, International Policy

Appendices to PhRMA's Pre-Hearing Brief

COVID-19 Diagnostics and Therapeutics: Supply, Demand, and TRIPS Agreement Flexibilities, Investigation No. 332-596

Table of Appendices

Appendix 1

COVID-19 Vaccines: Production and Uptake

Using available data to model the supply and use of COVID-19 vaccines

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Industry Licensing Agreements Made Possible by Intellectual Property Are Meeting Demand for COVID-19 Vaccines

379 COVID-19 Vaccine Manufacturing Licensing Agreements Span 61 Markets

Source: Airfinity.

Estimating Production and Uptake of COVID-19 Vaccines

Production Capacity

Objective: The number of doses that could have been produced if peak production continued through 2022

Method: Extrapolate based on actual production during 2021:Q4 and manufacturer announcements

Source: airfinity HOME OF NEW SCIENCE

Production

Objective: The observed number of doses produced through 2022

Method: Actual number of doses produced through 2022

Source: airfinity HOME OF NEW SCIENCE

Doses Administered

Objective: The observed number of doses administered through 2022

Method: Actual number of doses administered through 2022

Source: Our World in Data

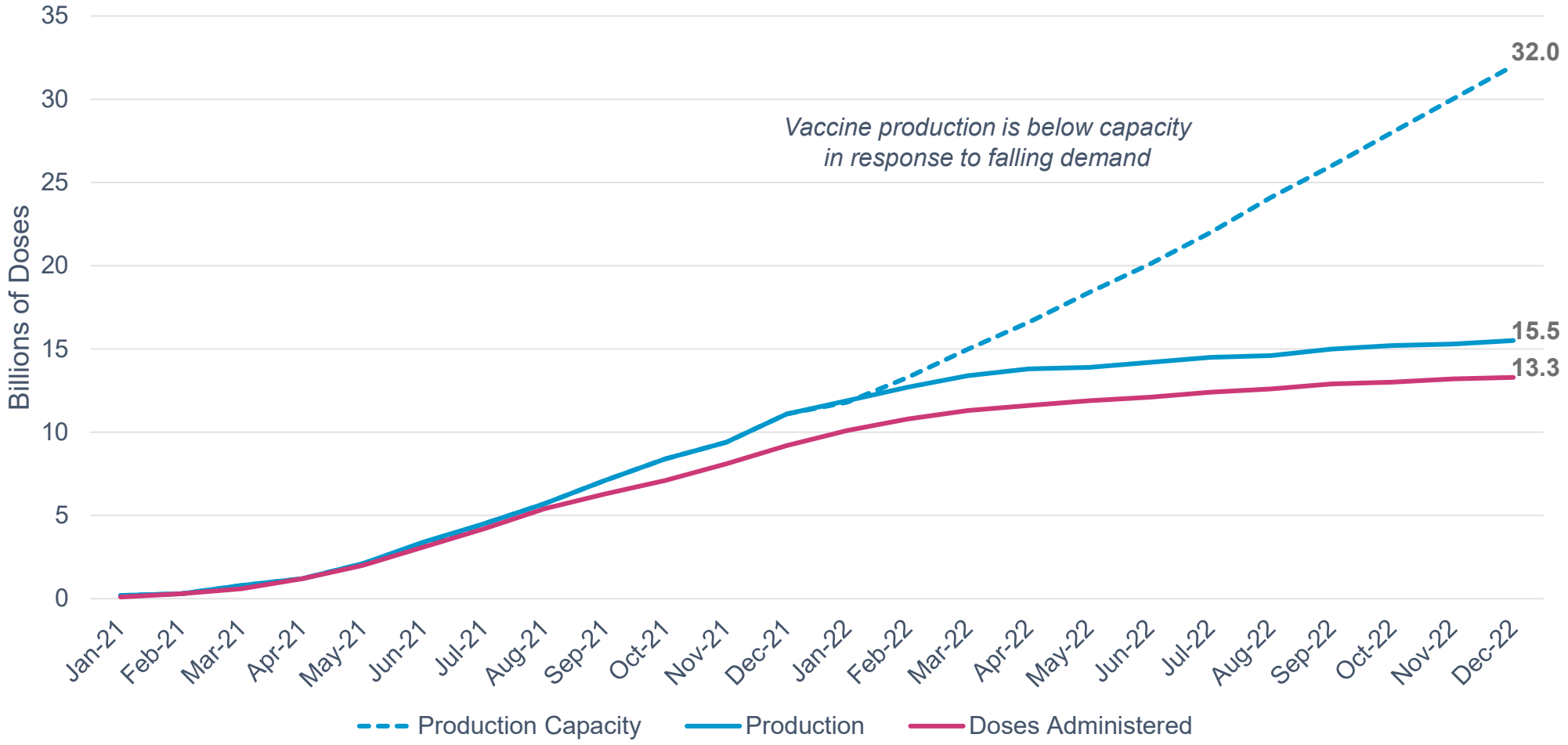
Doses Needed

Objective: The number of doses needed to achieve WHO target (plus boosters) in 2022

Method: Estimate number of doses needed based on current vaccination status in each country

Source: Our World in Data

Demand and Production Slowed in 2022, with Demand Falling Short of 70% WHO Target

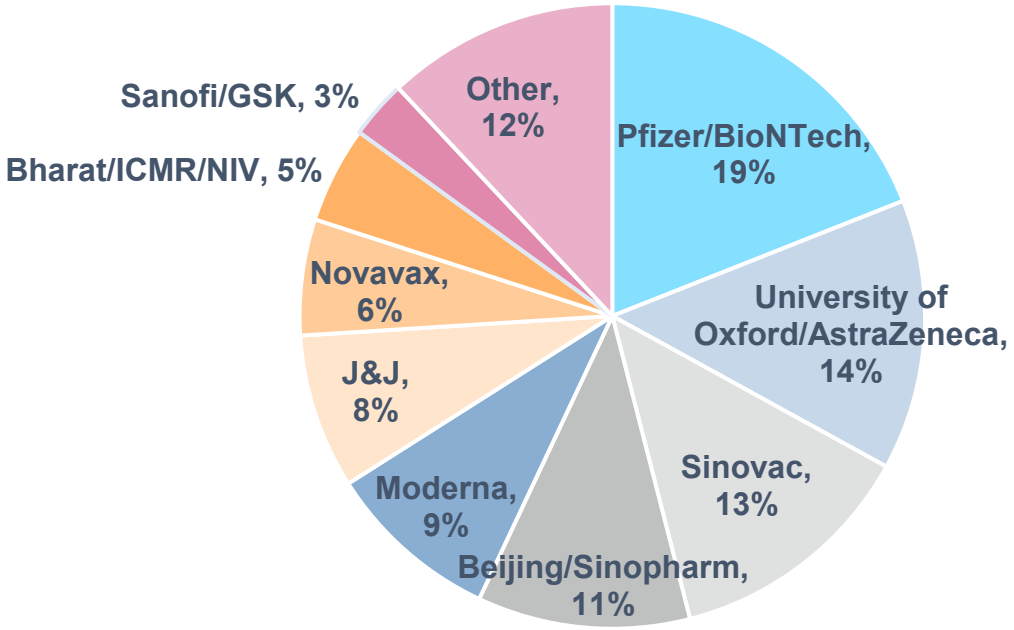


airfinity
HOME OF NEW SCIENCE

Our World in Data

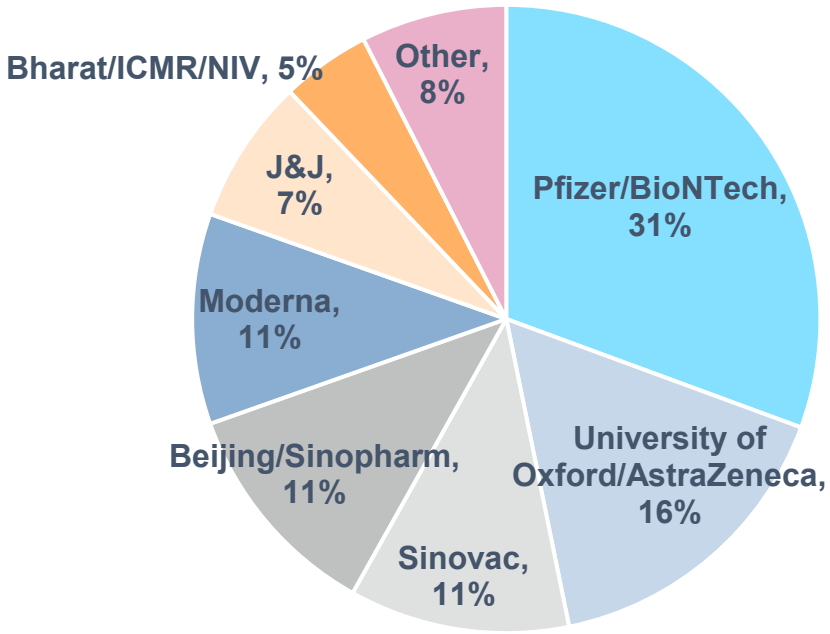
Source: Airfinity, URL: https://science.airfinity.com/; Our World in Data global database of COVID-19 vaccinations as of December 31, 2022. Note: *Production capacity* shows the number of doses that could have been produced through 2022 based on 2021:Q4 production volumes and company ramp-up projections at the start of 2022. *Production* shows the number of doses produced through 2022. *Doses administered* shows the number of doses administered through 2022.

Slowing Demand Discouraged Production from New Entrants and Some Established Producers



Production Capacity (2022)

(forecast based on 2021:Q4 production and company ramp-up projections)



Actual Production (2022)

(actual production during 2022)

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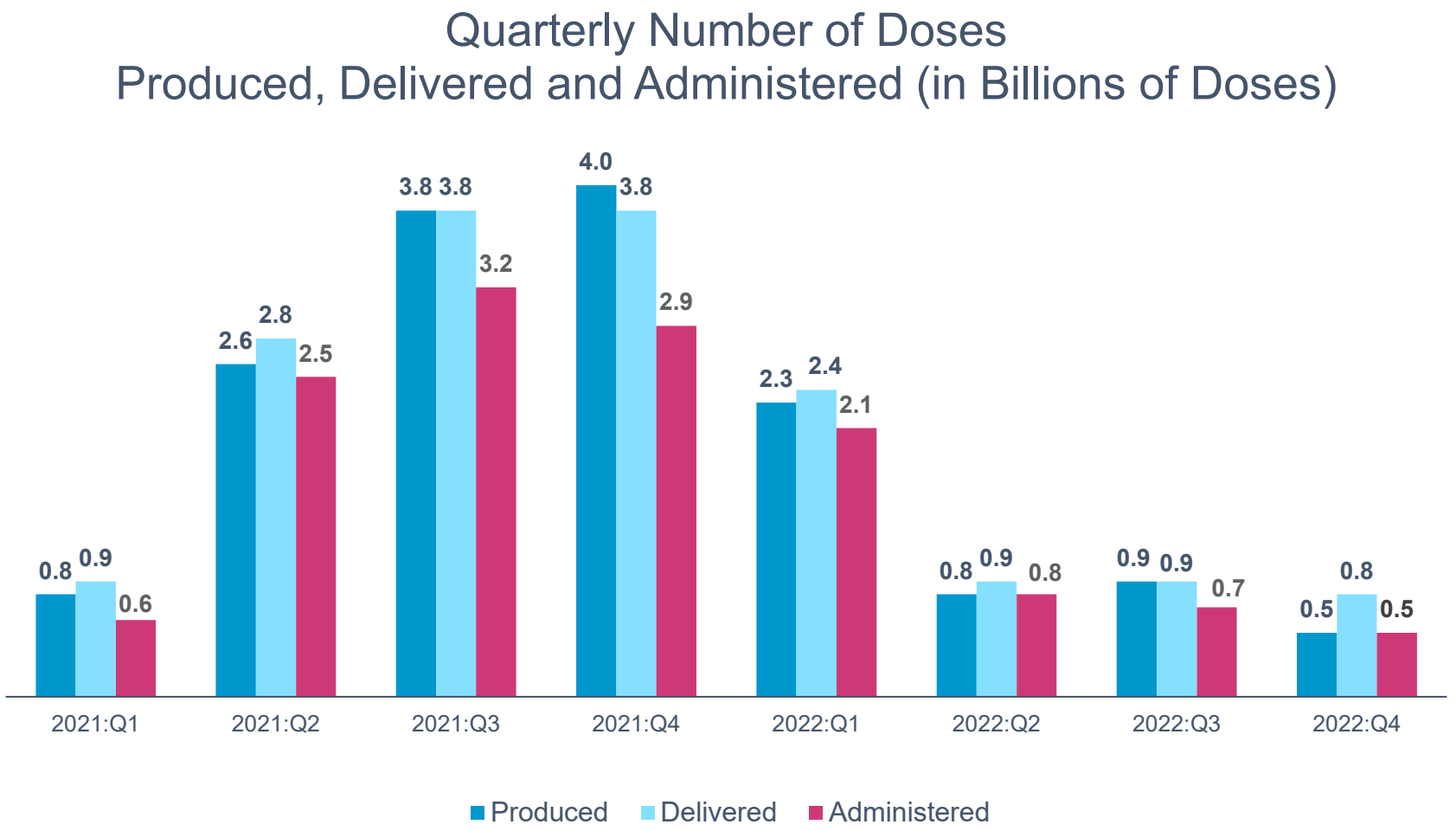
Source: Airfinity, URL: https://science.airfinity.com/. *Production capacity* shows the number of doses that could have been produced through 2022 based on 2021:Q4 production volumes and company ramp-up projections at the start of 2022. *Production* shows the number of doses produced through 2022. Other COVID-19 vaccines include: Anhui Zhifei, Clover/Dynavax, Covaxx/Vaxxinity, Shifa Pharmed, Gamaleya Research Institute, Inovio Pharma, Razi Vaccine and Serum Research Institute, Finlay Vaccine Institute, Center for Genetic Engineering and Biotechnology, Vector, Reitheral/LeukoCare/Univercells, Arcturus, Valneva/Dynavax, Medigen/Dynavax, Medicago/GSK, Shionogi, Zydus Cadila, Chumakov Federal Scientific Center, RI for Biological Safety Problems.

The Number of Doses Administered Began Slowing in 2021:Q4 Followed by Production Slowing in 2022:Q1



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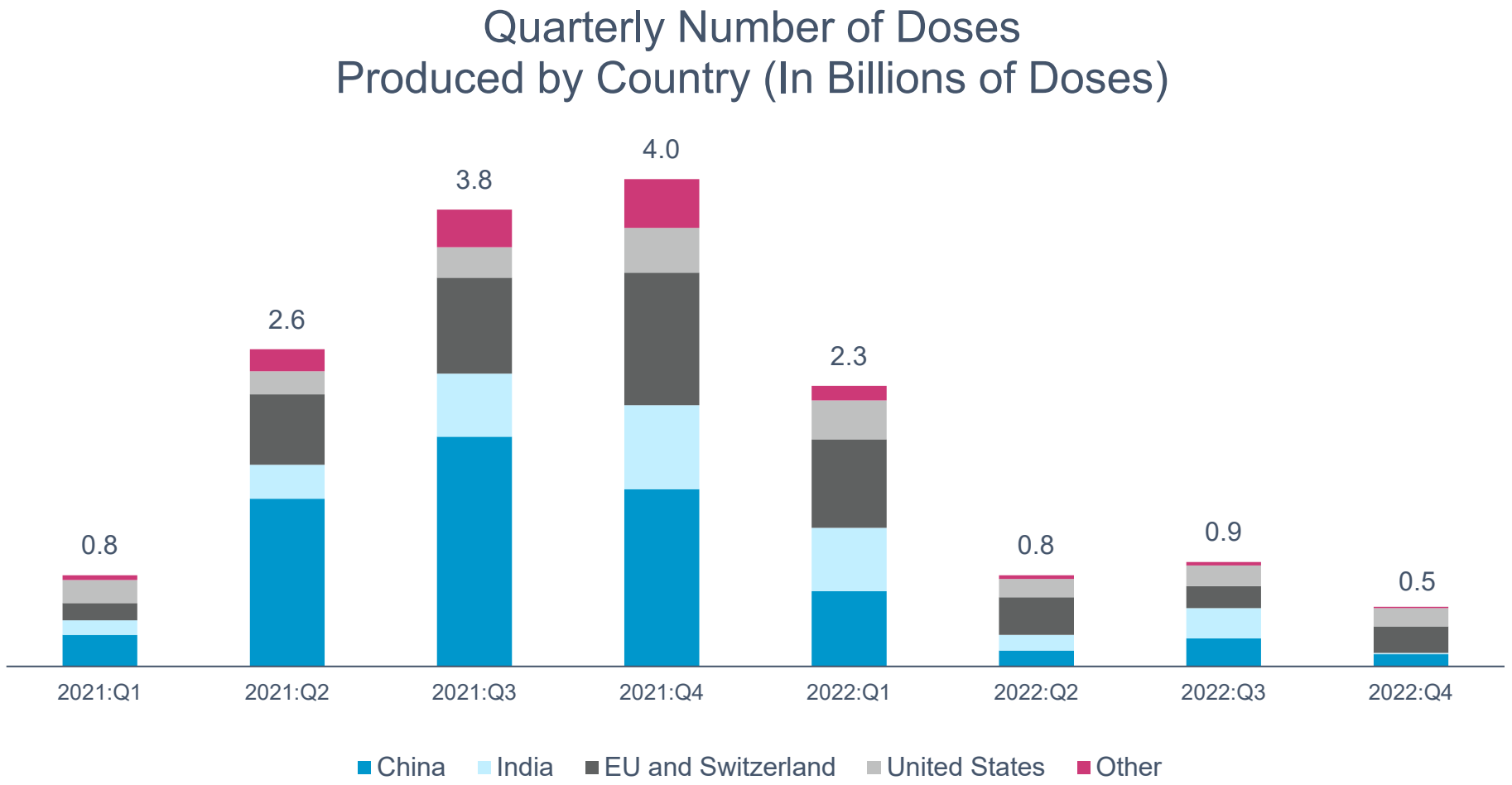
Our World in Data

Source : Airfinity, URL: https://science.airfinity.com/.

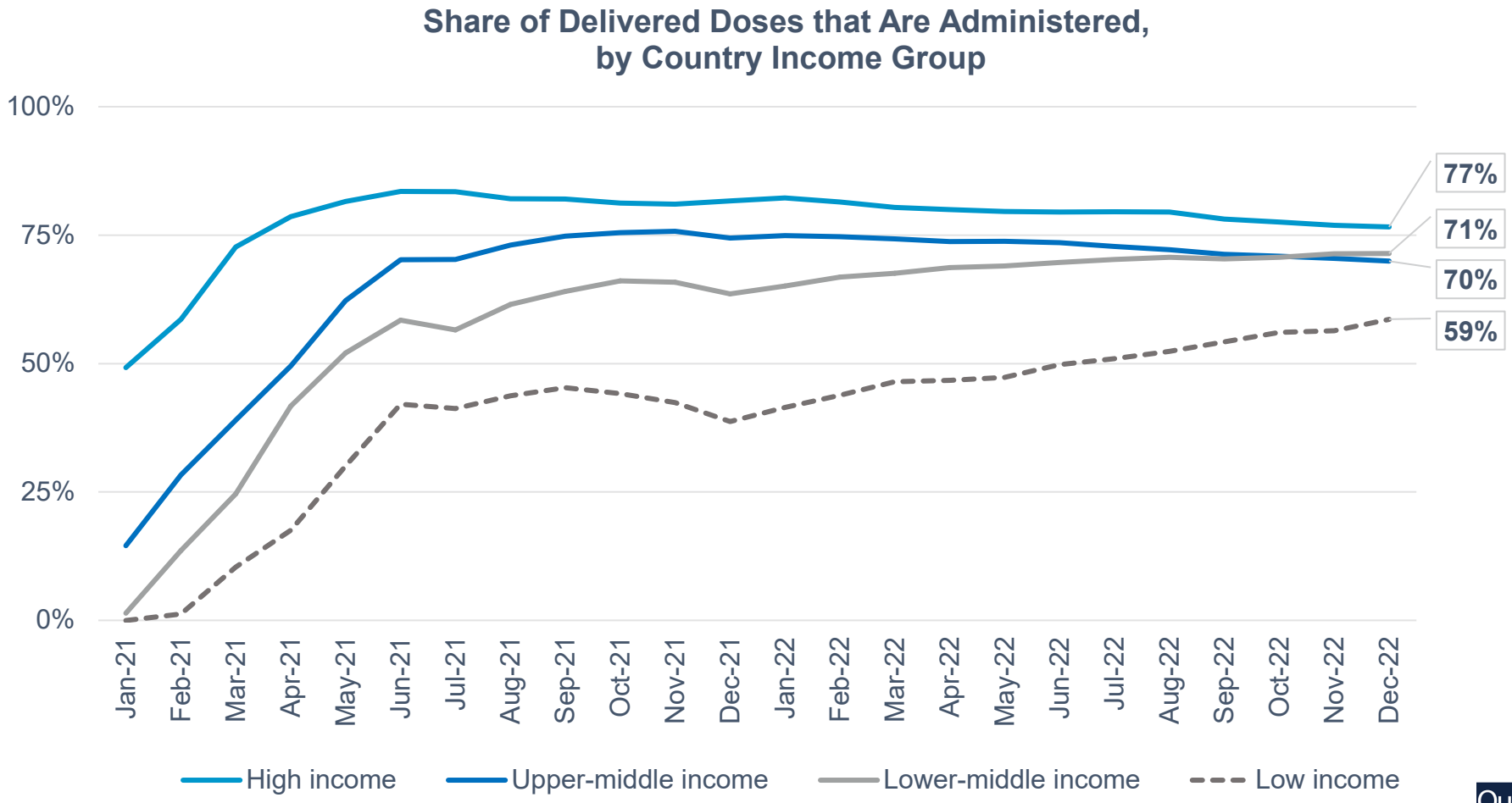
China and India Account for More than Half of the Overall Slowdown in Production After 2021:Q4



Source : Airfinity, URL: https://science.airfinity.com/.

Low Income Countries Struggled to Get More than 50% of Delivered Doses Into Arms

Impact: Last-mile challenges in getting shots in arms reduced vaccinations in low-income countries by more than 50 million*

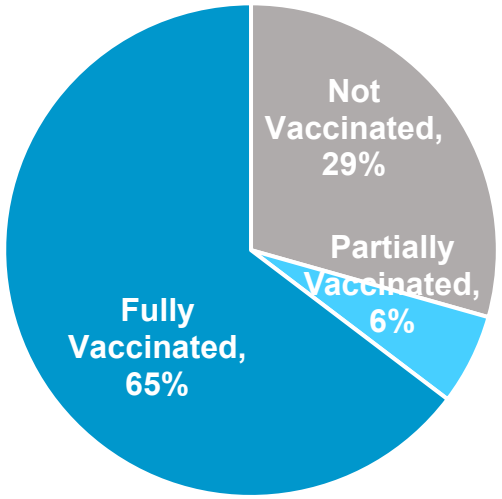


Our World in Data

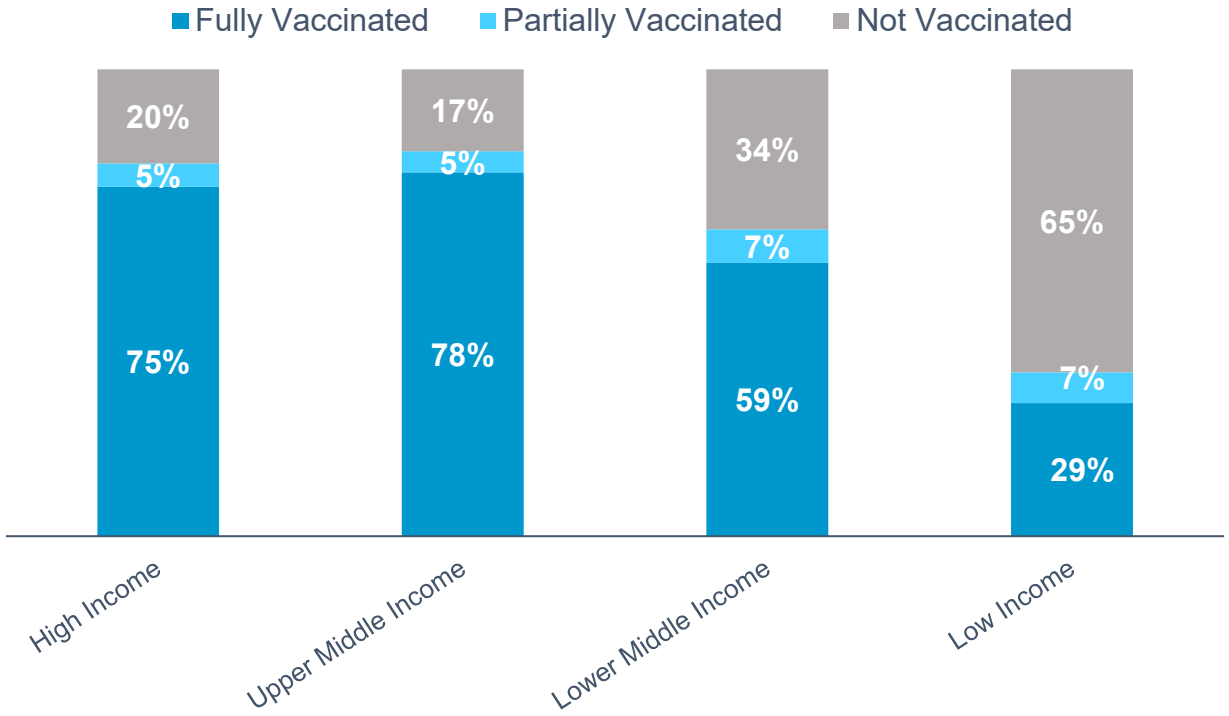
Source: Source: Our World in Data, URL: https://ourworldindata.org/. *The impact of low-income countries' distribution challenges is estimated by calculating the number of additional people in low-income countries that would have been vaccinated if low-income countries administered the same share of their delivered doses as did lower-middle-income countries between January 2021 and December 2022.

71% of World Population Received at Least One Dose of a COVID-19 Vaccine by End of 2022

All Countries



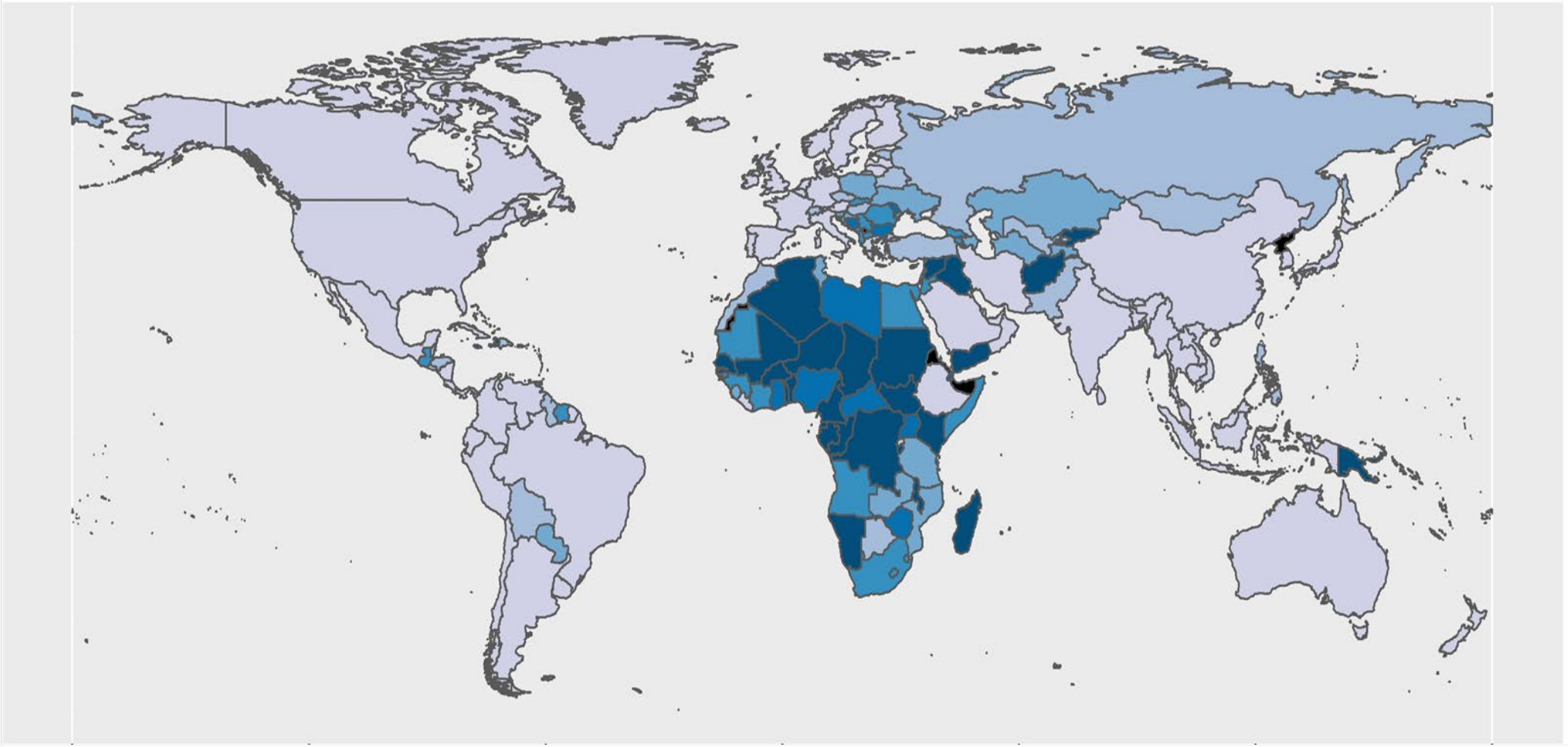
By Country Income Group



Our World in Data

Source: Our World in Data, URL: https://ourworldindata.org/. Note: COVID-19 vaccine status estimates are as of December 31, 2022. "Fully vaccinated" is defined as having received one complete regimen (e.g., 1-2 doses for most COVID-19 vaccines) with or without a booster. Not vaccinated" includes children under the age of 5, as well as any other populations deemed ineligible for COVID-19 vaccines in any country."Partially vaccinated" is defined as having received an incomplete regimen (e.g., 1 of 2 doses for most COVID-19 vaccines).

Countries with the Lowest Rates of COVID-19 Vaccinations Are Mostly in Africa



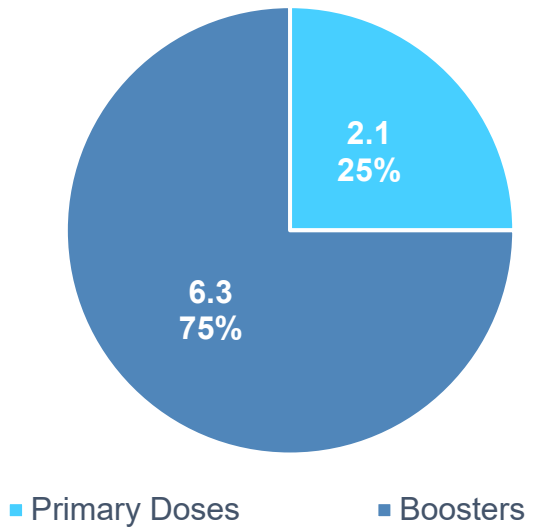
Our World in Data

Source: Our World in Data, URL: https://ourworldindata.org/. Note: COVID-19 vaccine status estimates are as of December 31, 2022.

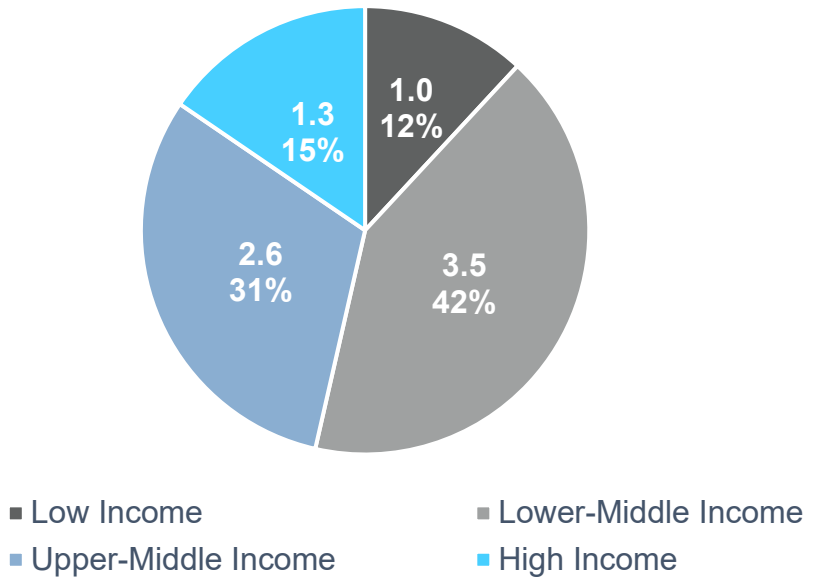
Doses Needed to Achieve 70% WHO Vaccination Target and Maintain Immunity in 2023

2.1 billion primary doses needed to achieve 70% WHO vaccination target in each country and **6.3** billion doses needed for boosters in 2023

Billions of Doses Needed: Primary Doses and Boosters



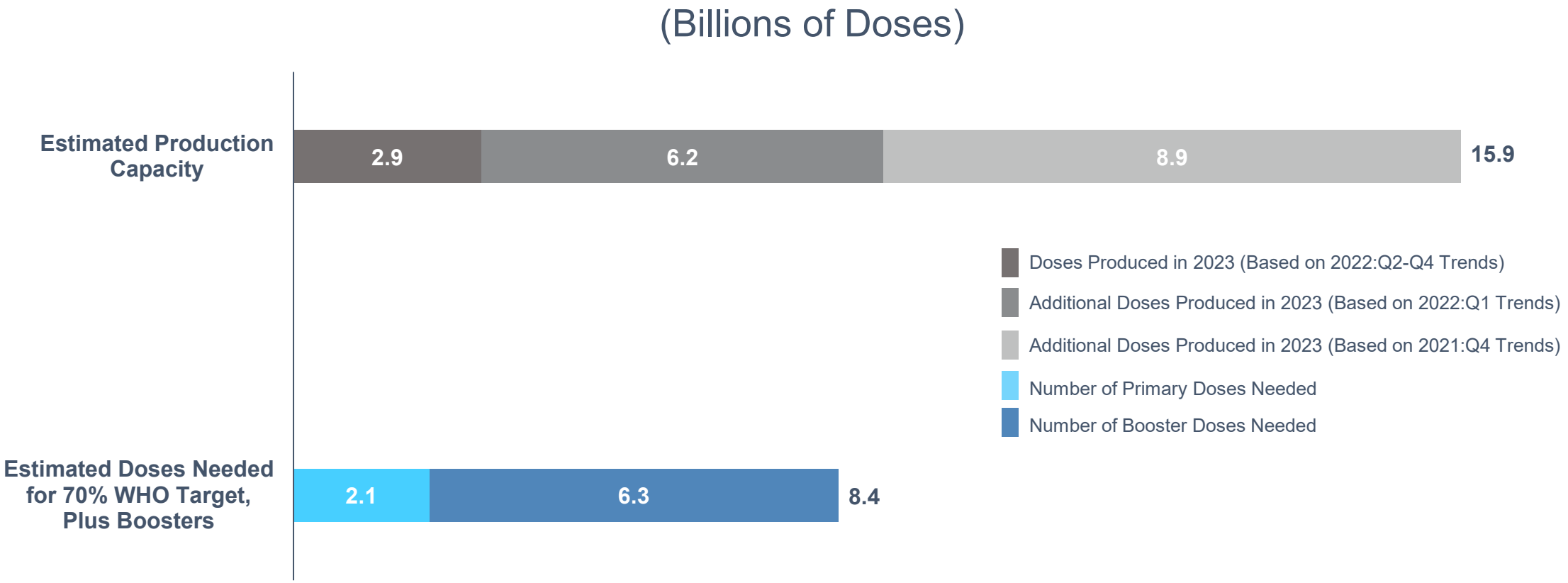
Billions of Doses Needed: By Country Income Group



Our World in Data

Source: Our World in Data global database of COVID-19 vaccinations as of December 31, 2022. Note: Estimates for the number of primary doses needed to achieve the 70 percent WHO target in every country, plus the number of boosters, is derived from data on vaccinations by country provided by the Our World in Data global database of COVID-19 vaccinations as of December 31, 2022. Estimates for the number of boosters needed in 2023 assumes that all persons that receive a final primary dose in 2023 will receive one booster in 2023, and all persons who received a booster in 2022 will receive another booster in 2023.

Estimating COVID-19 Vaccine Production Capacity and Needed Doses for 2023



Source: Airfinity, URL: https://science.airfinity.com/; *Production capacity* forecasts are the number of doses that could be produced in 2023 based on production volumes in 2022:Q2 -Q4, 2022:Q1, and 2021:Q4. Peak production volumes occurred in 2021:Q4 and production substantially slowed by 2022:Q2 . Estimates for the number of primary doses needed to achieve the 70 percent WHO target in every country, plus the number of boosters, is derived from data on vaccinations by country provided by the Our World in Data global database of COVID-19 vaccinations as of December 31, 2022. Estimates for the number of boosters needed in 2023 assumes that all persons that receive a final primary dose in 2023 will receive one booster in 2023, and all persons who received a booster in 2022 will receive another booster in 2023.

Appendix 2

Expanding the TRIPS Waiver Is Unnecessary and Harmful

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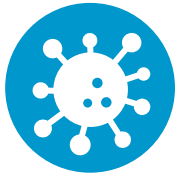
Key Takeaways

Biopharmaceutical manufacturers are already sharing their IP and remain committed to providing timely, equitable global access to safe and effective COVID-19 vaccines and treatments – Supply far exceeds demand

Giving away American IP on treatments to foreign countries will outsource U.S. manufacturing jobs and weaken U.S. biopharmaceutical leadership



Expanding the waiver to include COVID-19 treatments will undercut U.S. innovation and jeopardize our ability to fight COVID-19 and other conditions

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Global Partnerships Are Fueling Production and Patient Access to COVID-19 Treatments

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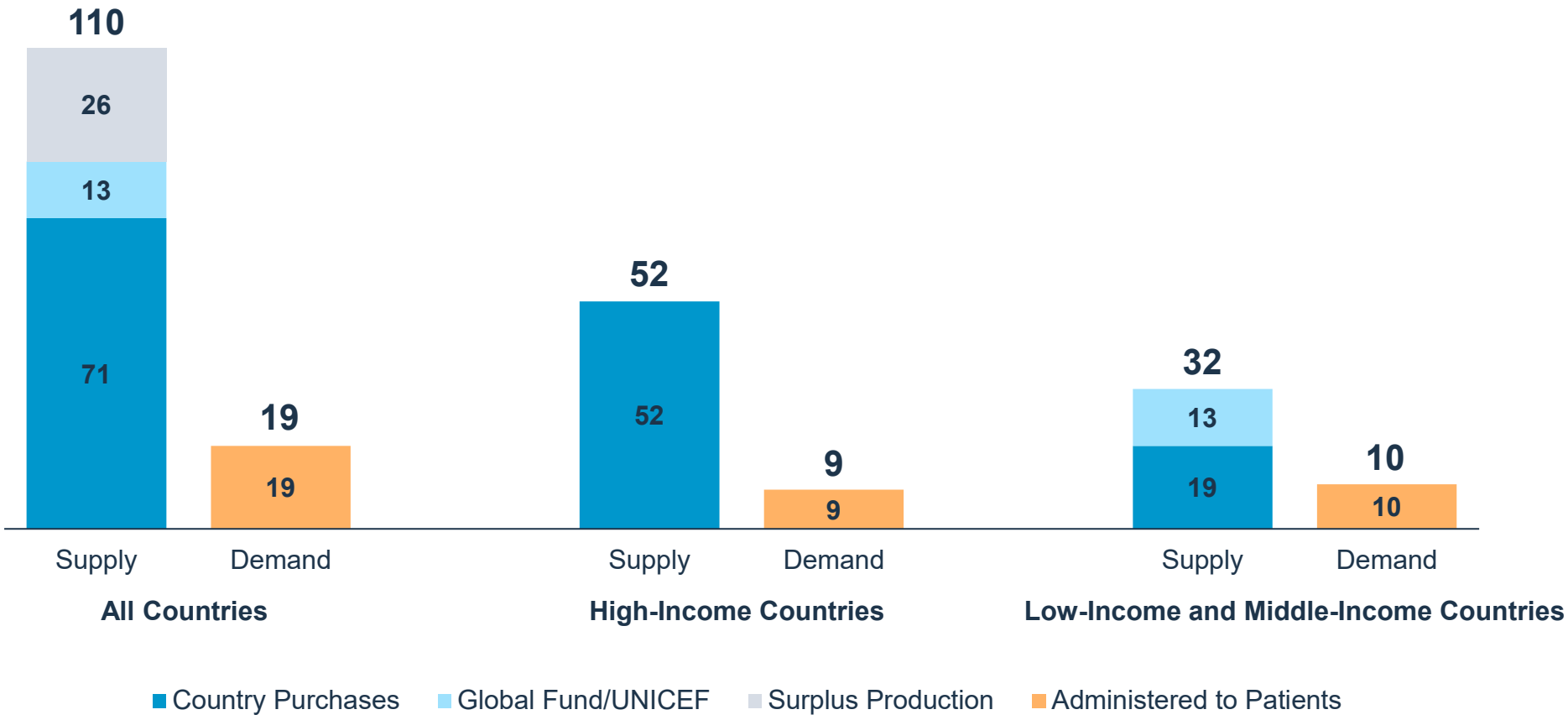
Supply of COVID-19 Treatments Has Far Exceeded Demand

Governments and NGOs Purchased 80 Million Courses of COVID-19 Treatments for 2022 But Administered Only 19 Million Courses



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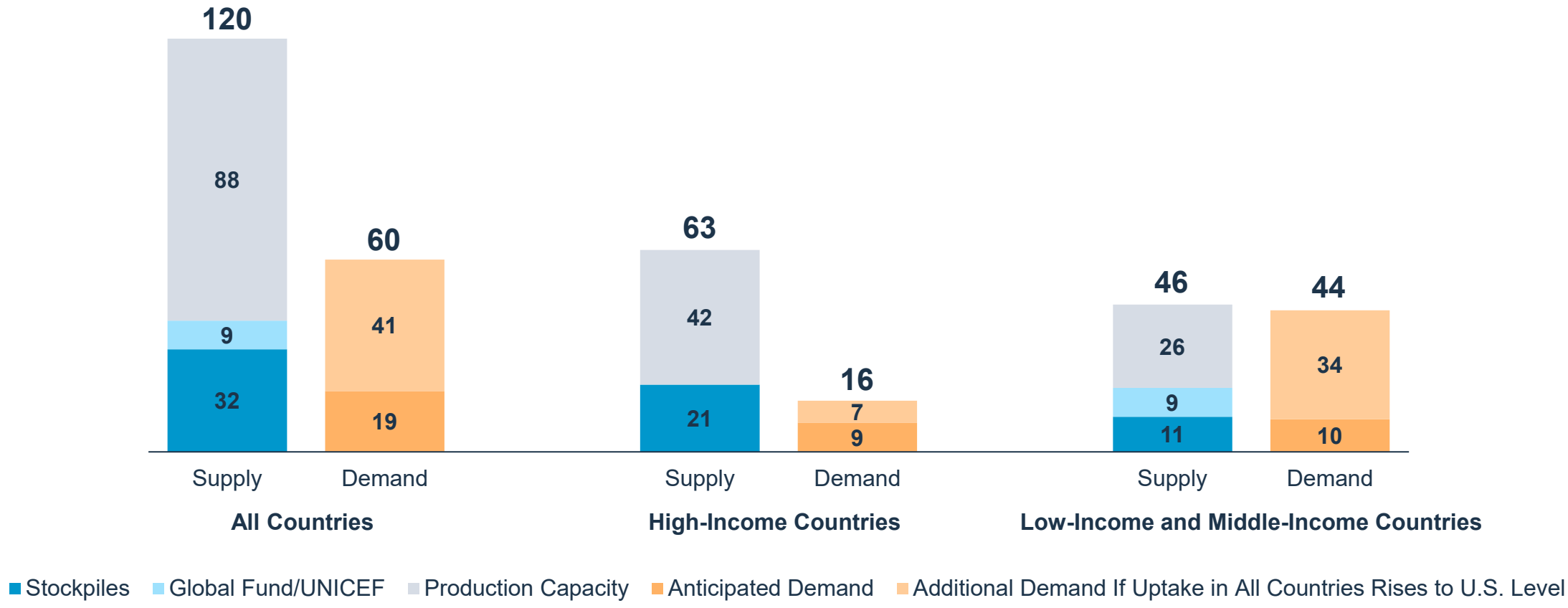
Sources: Estimates for purchases by governments and organizations (*e.g.*, Global Fund, UNICEF) and potential surplus production are provided by Airfinity. Estimates of treatments administered to patients are based on published uptake rates available for countries that have received COVID-19 treatments. Estimates are based on data for Paxlovid®, molnupiravir, Evusheld®, bebtelovimab, remdesivir, favipiravir and umifenovir.

2023 Supply of COVID-19 Treatments Will Exceed Demand

Stockpiles of COVID-19 Treatments Exceed Anticipated Demand in 2023



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Sources: Estimates for stockpiles of COVID-19 treatments, remaining COVID-19 treatments available through the Global Fund and UNICEF, and anticipated demand are provided by Airfinity. Estimates for potential additional demand are based on the assumption that the uptake of COVID-19 treatments in all countries dramatically increases to the same uptake rate as the United States. Estimates of production capacity are based on the assumption that 2023 production is similar to 2022 production. Estimates are based on data for Paxlovid®, molnupiravir, remdesivir, favipiravir, umifenovir and ensitrelvir.

Industry Licensing Agreements Made Possible by Intellectual Property Are Meeting Demand for COVID-19 Treatments

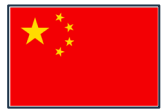
143 COVID-19 Treatment Licensing Agreements Span 31 Nations


Bangladesh


Belgium


Brazil


Canada


China


Dominican Republic


Egypt


Jordan


Korea


France


Germany


India


Indonesia


Ireland


Israel


Italy


Japan


Jordan


Kenya


Mexico


Pakistan


Paraguay


Portugal


Russia


Serbia


Singapore


South Africa


Switzerland


United Kingdom


United States


Vietnam

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Source: Airfinity.

U.S. Economic Impact of the Development and Manufacturing of COVID-19 Vaccines and Treatments

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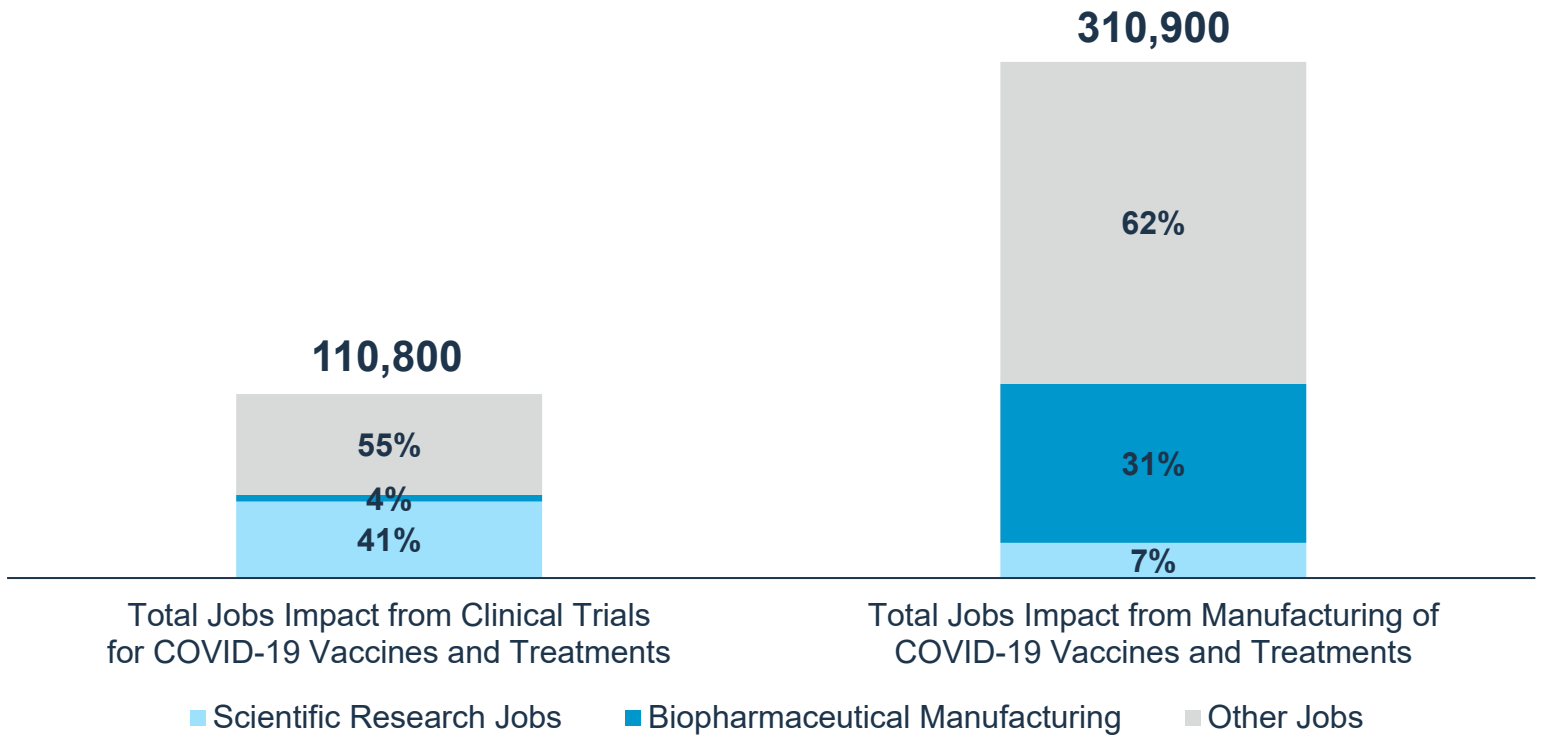
Over 400,000 U.S. Jobs Are Supported by the Development and Manufacturing of COVID-19 Vaccines and Treatments

Expanding the TRIPS Waiver Would Harm American Workers

Total Jobs Directly and Indirectly Supported by Development and Manufacturing



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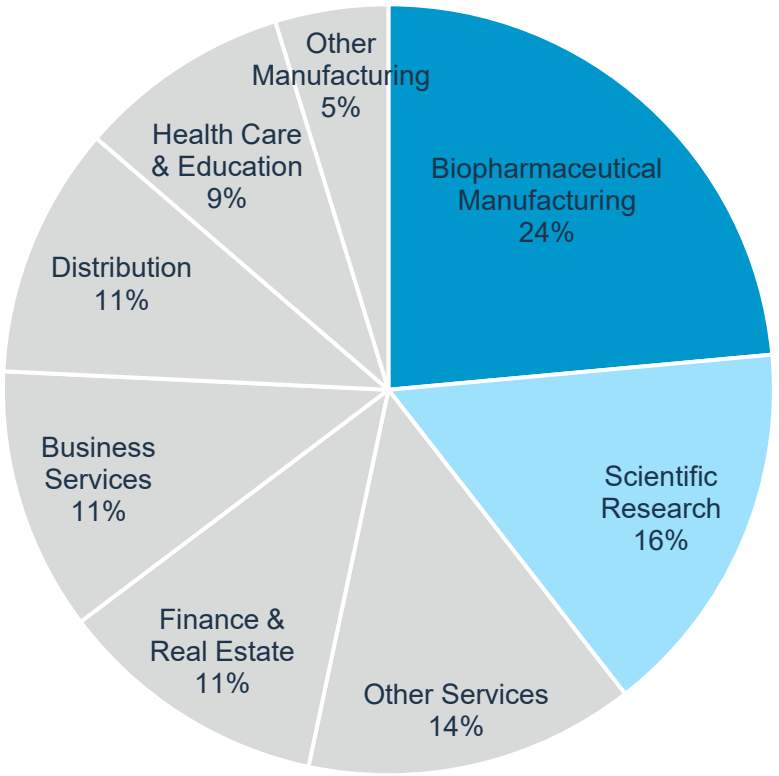
Sources: Informa data used to identify clinical trials for COVID-19 vaccines and treatments in the United States. Evaluate data used to estimate clinical trial costs. PhRMA analysis of U.S. Department of Commerce (BEA) data on U.S. exports, gross output of biopharmaceutical goods and RIMS II (Type II) multipliers used to estimate the total (direct and indirect) impact of clinical trial spending and biopharmaceutical manufacturing in the United States.

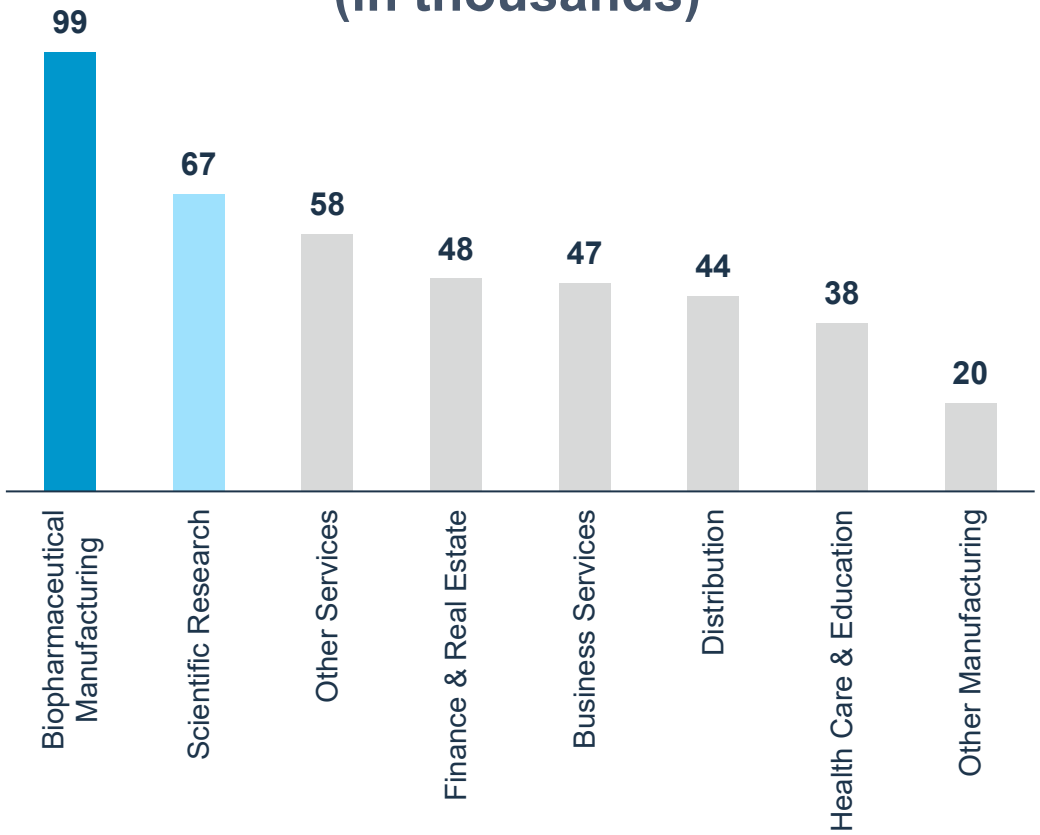
Total Economic Impact Occurs Across Several Sectors

60% of U.S. Jobs Supported by COVID-19 Vaccines and Treatments Are Outside the Biopharmaceutical Industry

Composition of Jobs by Sector



Number of Jobs by Sector (in thousands)



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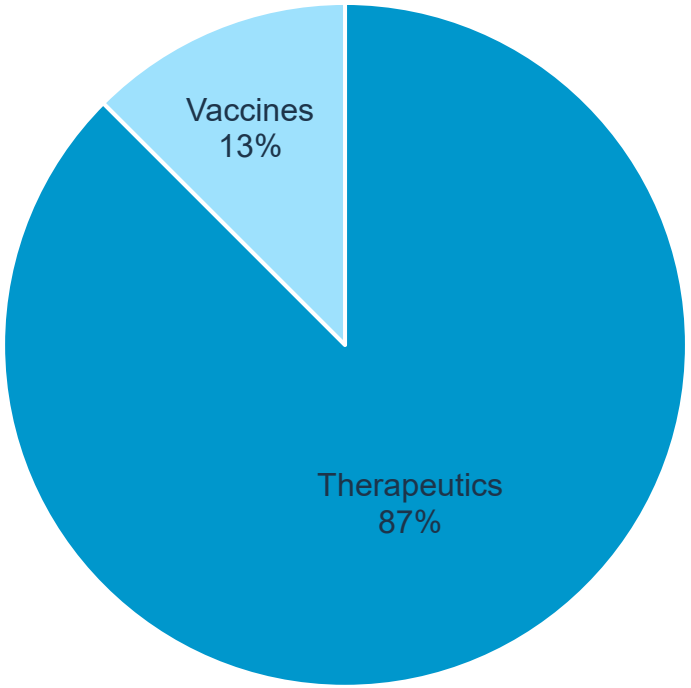
Almost 90% of COVID-19 Clinical Trial Costs in the United States Are for Treatments

There Have Been Over 1,200 U.S. Clinical Trials for COVID-19 Treatments

U.S. COVID-19 Clinical Trial Costs: $24 Billion to Date



- Over **$24 billion** has been spent on clinical trials for COVID-19 vaccines and treatments in the United States – supporting about **100,000 U.S. jobs**
- Another **$80 billion** will be spent in the United States over the next several years if vaccines and treatments in the pipeline continue through clinical trials to approval – supporting approximately **110,000 U.S. jobs** annually

PhRMA
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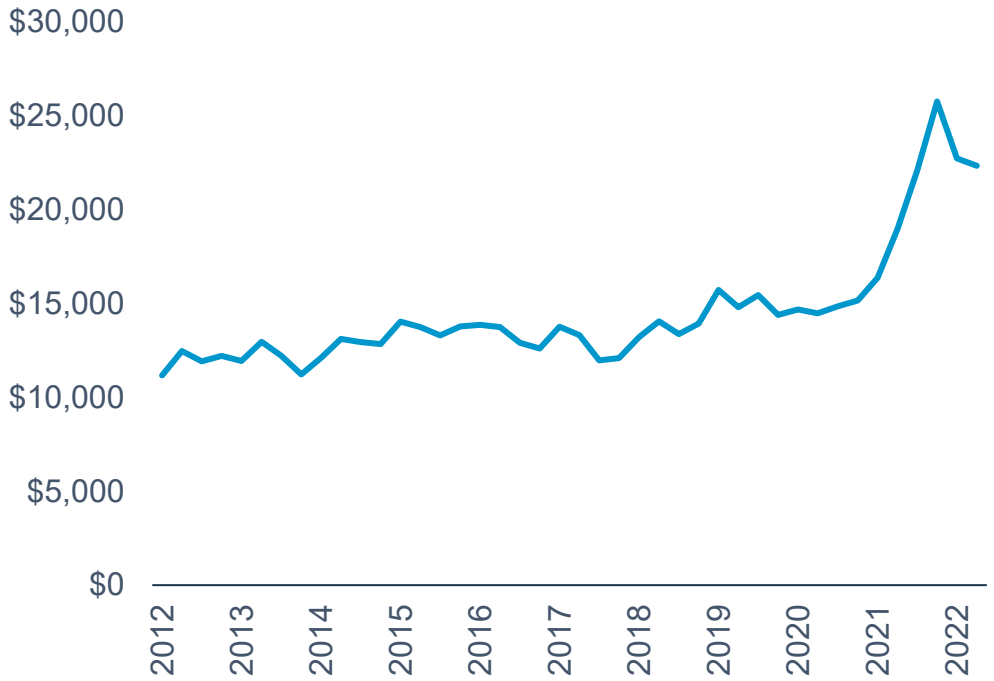
Sources: Informa data used to identify clinical trials for COVID-19 vaccines and treatments in the United States. Evaluate data used to estimate clinical trial costs. PhRMA analysis of U.S. Department of Commerce (BEA) RIMS II (Type II) multipliers used to estimate the total (direct and indirect impact) of clinical trial spending in the United States.

Exports Drive Over 55% of COVID-19 Product Manufacturing in the United States

U.S. Exports of Biopharmaceutical Products Have Surged to Highest Levels on Record

U.S. Biopharmaceutical Exports from 2012 to Q2 2022



- Over **300,000 U.S. jobs** are supported by the surge in U.S. biopharmaceutical manufacturing for COVID-19 vaccines and treatments
- **55%** of these jobs are supported by **U.S. exports** of biopharmaceutical products
- **U.S. exports** of biopharmaceutical products **increased over 60%** after the U.S. amended COVID-19 vaccine contracts in mid-2021

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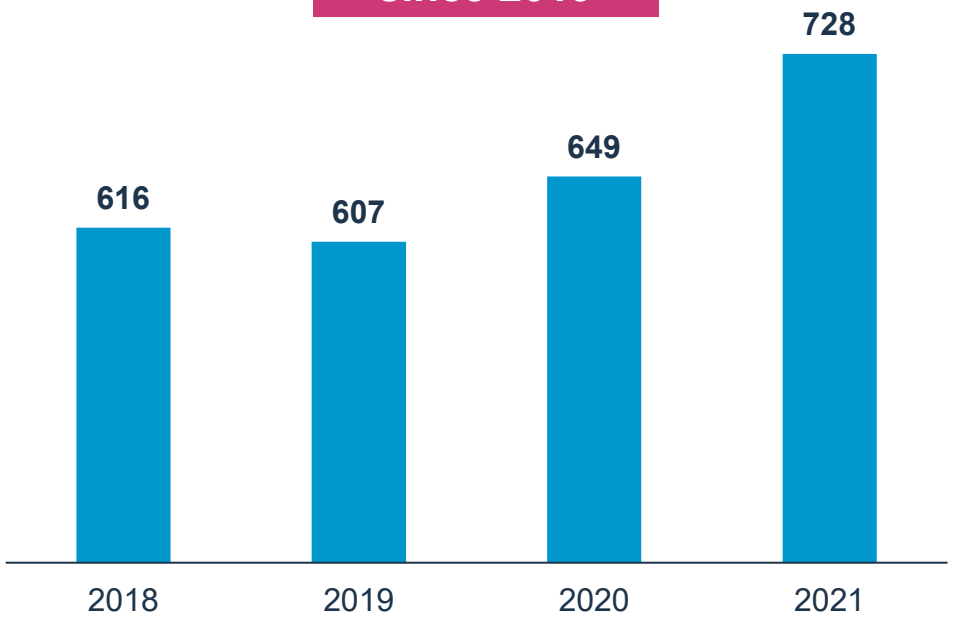
Sources: PhRMA analysis of U.S. Department of Commerce (BEA) data on U.S. exports as of July 29, 2022; gross output of biopharmaceutical goods and RIMS II (Type II) multipliers used to estimate the total (direct and indirect impact) of biopharmaceutical manufacturing in the United States.

U.S. Scientific Research and Manufacturing Jobs Have Increased by More than 180,000 Since 2019

Scientific Research Jobs for New Medicines Create Manufacturing Jobs

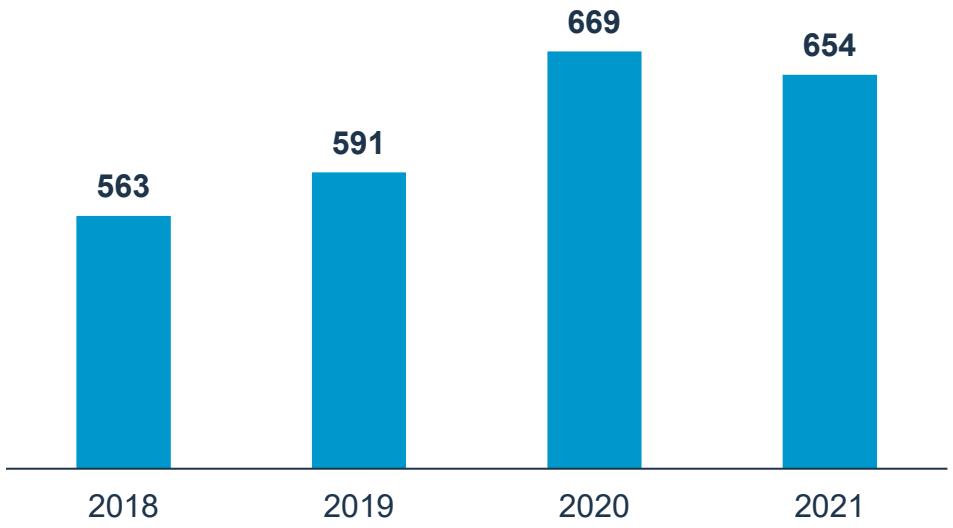
U.S. Scientific Research Jobs (in thousands)

+121,000 jobs since 2019



U.S. Biopharmaceutical Manufacturing Jobs (in thousands)

+63,000 jobs since 2019



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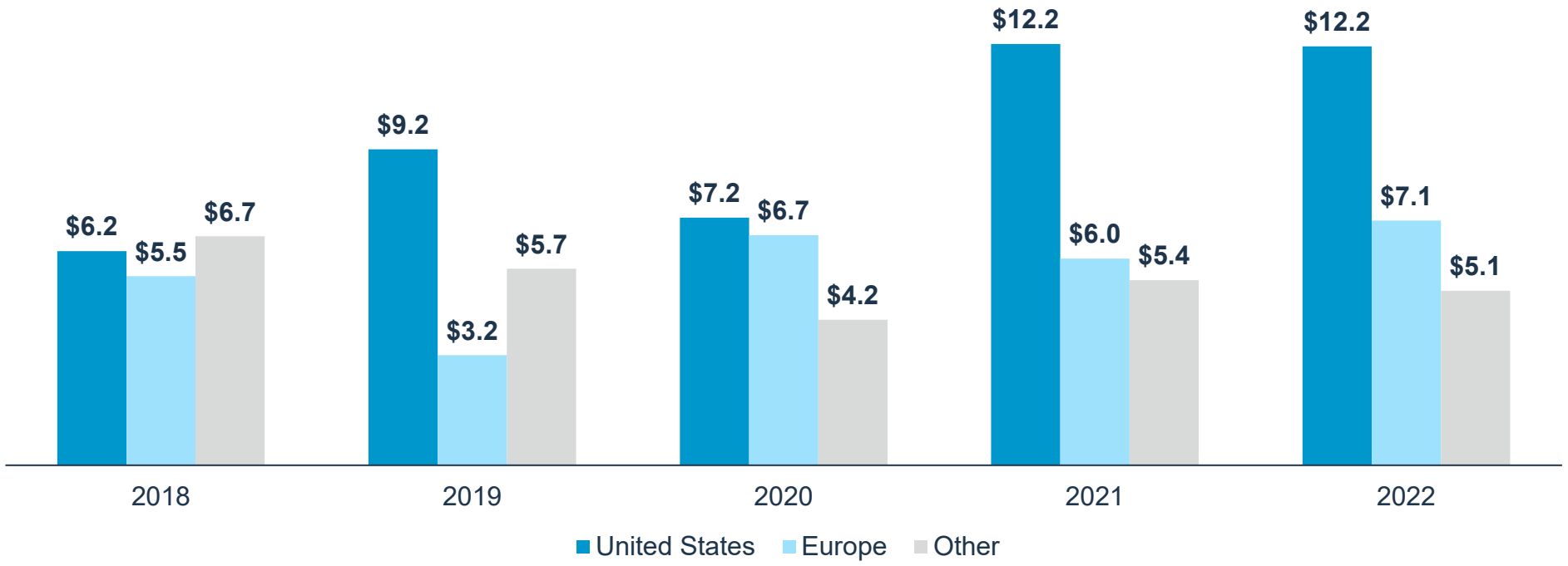
Source: U.S. Bureau of Labor Statistics, Current Employment Statistics for NAICS Industries 541700 (Scientific Research and Development) and 325400 (Pharmaceutical and Medicine Manufacturing) as of July 29, 2022.

New Biopharmaceutical Industry Investment in the United States Increased 70% in 2021 – Half of the Global Total

Expanding the TRIPS Waiver Would Put at Risk U.S. Biopharmaceutical Leadership

New Biopharmaceutical Industry R&D and Manufacturing Facility Investment by Destination County (in billions of U.S. dollars)



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Source: FDI Markets data on new biopharmaceutical investment in manufacturing and R&D facilities as of July 29, 2022. Estimates include green-field projects and expansions. Amounts for 2022 are annualized based on monthly data available through July 2022.

Expanding the TRIPS Waiver Would Undercut U.S. Medical Innovation and Our Ability to Fight Future Pandemics

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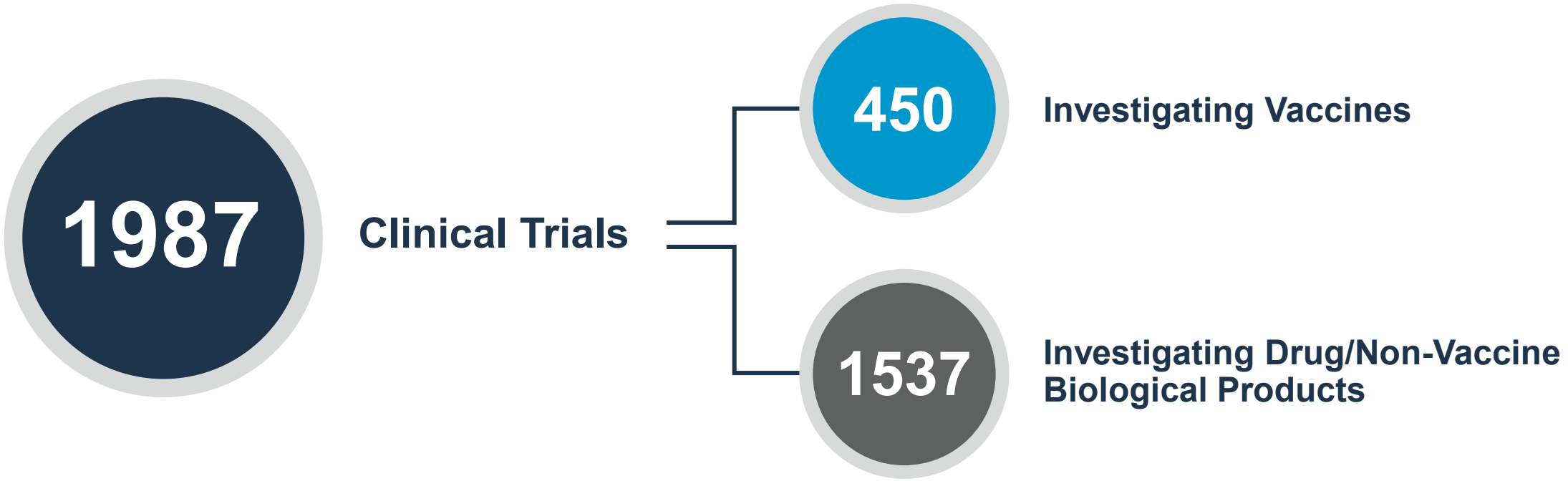
Nearly 2,000 Clinical Trials Underway Across the Globe to Fight COVID-19



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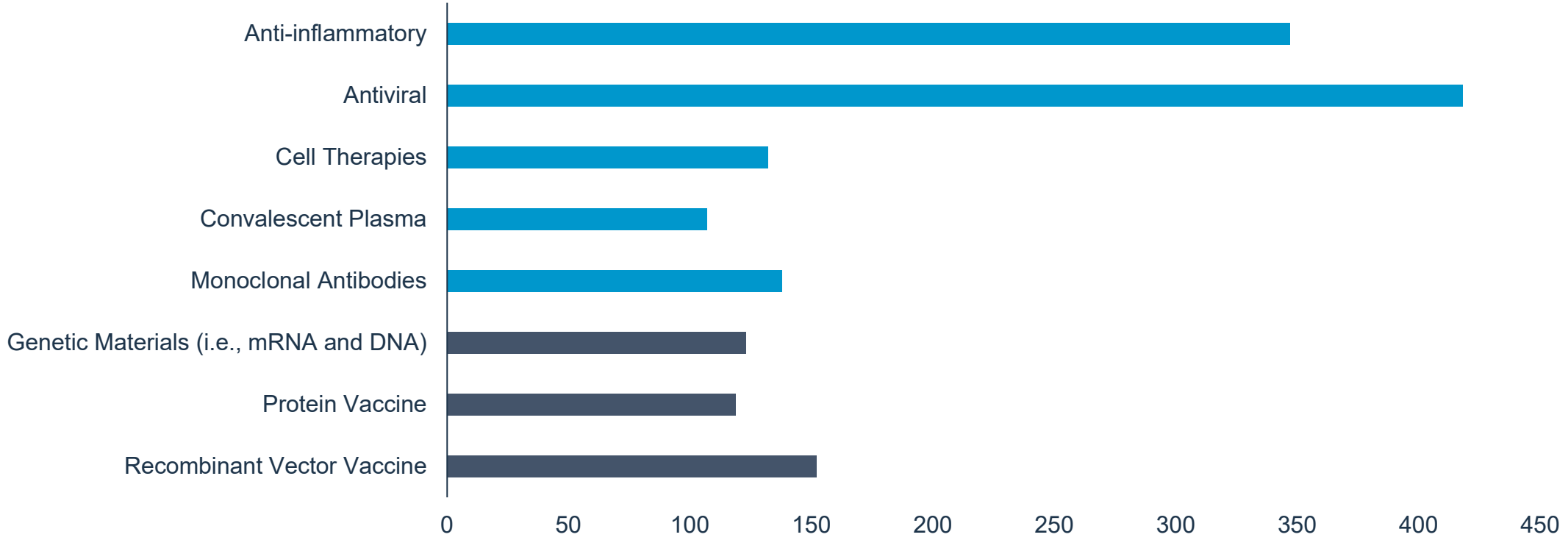
Source: World Health Organization International Clinical Trials Registry Platform data as of July 29, 2022.

Industry Has a Diverse Research and Development Pipeline

Ongoing Clinical Trials Represent Many Approaches for Preventing and Treating COVID-19

Number of Clinical Trials Testing Different Types of COVID-19 Vaccines and Treatments



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Source: World Health Organization International Clinical Trials Registry Platform data as of July 29, 2022.

Hundreds of Clinical Trials are Testing 176 Unique Investigational Treatments from PhRMA Member Companies

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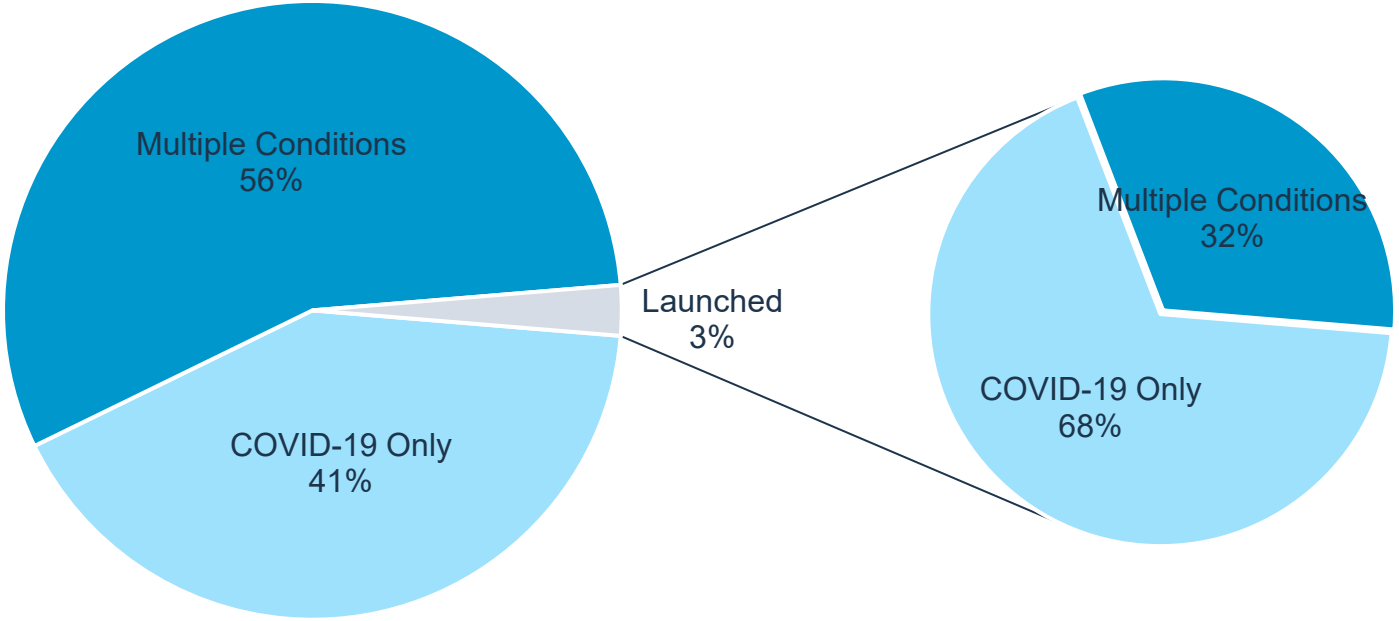
Source: World Health Organization International Clinical Trials Registry Platform data as of July 29, 2022.

Most Treatments in the COVID-19 Pipeline Are Also Being Developed for Other Conditions

Expanding the TRIPS Waiver Would Put at Risk the Pipeline for Many Conditions

COVID-19 Treatments in Development



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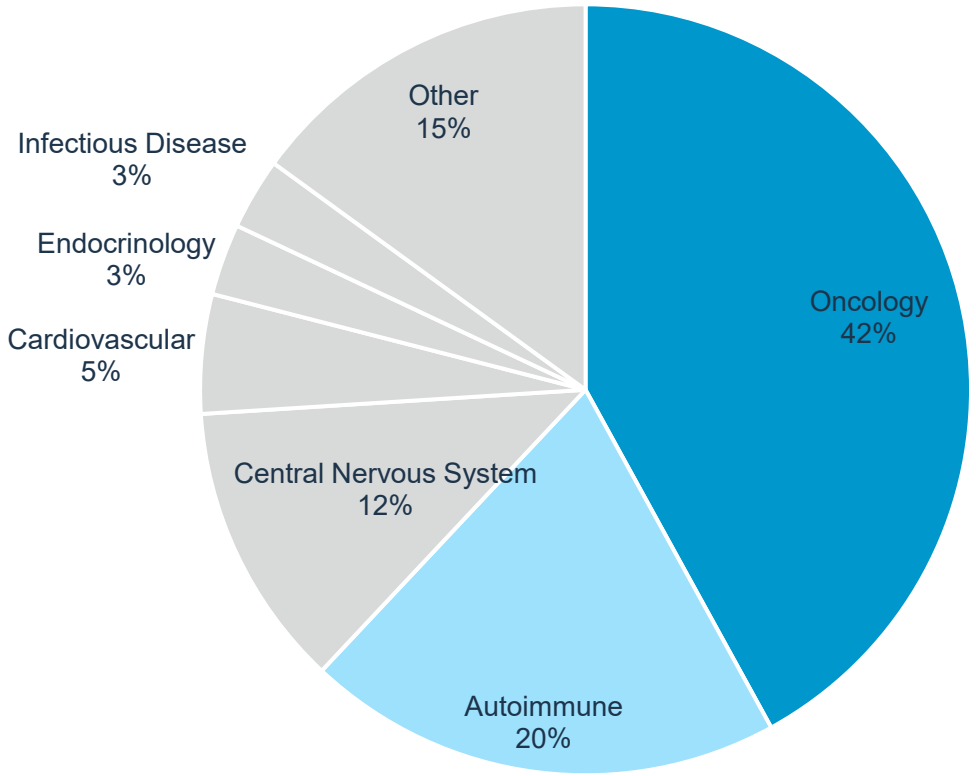
Sources: Informa data used to identify clinical trials for COVID-19 treatments as of July 29, 2022.

370 U.S. Clinical Trials Are Testing COVID-19 Treatments for Other Conditions

Oncology Accounts for 42% of these Clinical Trials



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Sources: Informa data used to identify clinical trials for COVID-19 treatments as of July 29, 2022.

Regulatory Approval of Innovative COVID-19 Treatments

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11 Innovative COVID-19 Treatments Are Currently Authorized for Use by at Least One Major Regulatory Authority

Products with Emergency Use Authorizations or Full Approvals

ACTEMRA®	Roche
EVUSHELD™	AstraZeneca
KINERET®	sobi
LAGEVRIO®	MSD
OLUMIANT®	Lilly
PAXLOVID™	Pfizer
REGKIRONA™	HEALTHCARE CELLTRION
RONAPREVE™	REGENERON
VEKLURY®	GILEAD
XEVUDY®	GSK VIR
XOCOVA®	SHIONOGI

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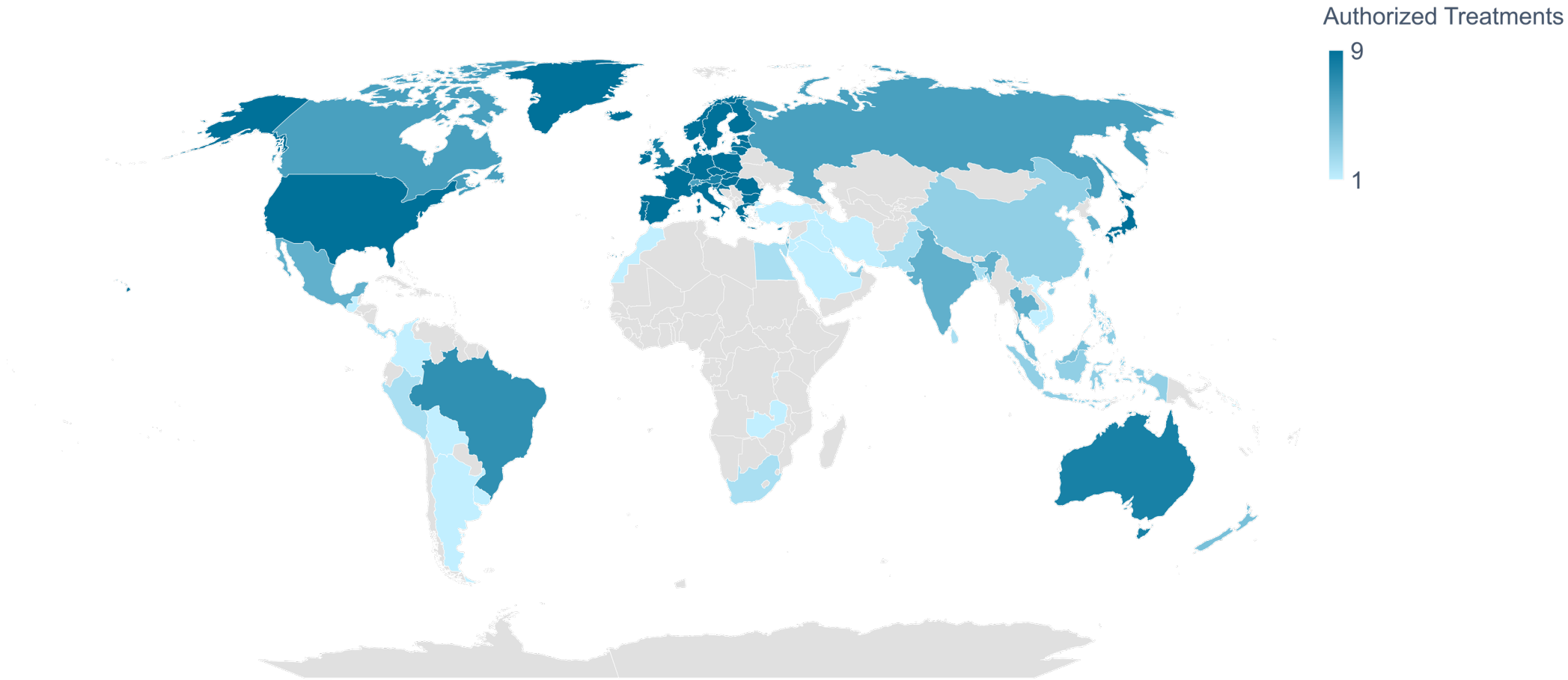
Source: Data on emergency use authorizations and full approvals for innovative COVID-19 treatments are provided by Airfinity.
Note: Innovative COVID-19 treatments include antivirals (LAGEVRIO®, PAXLOVID™, VEKLURY®, XOCOVA®), antibodies (ACTEMRA®, EVUSHELD™, REGKIRONA™, RONAPREVE™, XEVUDY®) and anti-inflammatories (KINERET®, OLUMIANT®).

Only Five Countries in Africa Have Authorized Innovative COVID-19 Treatments

The World Health Organization Has Prequalified 4 of 11 Innovative COVID-19 Treatments



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Source: Data on emergency use authorizations and full approvals for innovative COVID-19 treatments are provided by Airfinity and WHO as of March 2023.
Note: Innovative COVID-19 treatments include antivirals (LAGEVRIO®, PAXLOVID™, VEKLURY®, XOCOVA®), antibodies (ACTEMRA®, EVUSHELD™, REGKIRONA™, RONAPREVE™, XEVUDY®) and anti-inflammatories (KINERET®, OLUMIANT®).
The World Health Organization has prequalified ACTEMRA®, LAGEVRIO®, PAXLOVID™ and VEKLURY®).

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Appendix 3. The relationship between intellectual property protection and corporate R&D expenditures: Literature review

There are numerous high-quality empirical studies that have set out to assess the effects of intellectual property protection (patent protection in particular), on corporate research and development expenditures and, consequently, on firms' ability to innovate, grow, export, and share innovative technologies internationally. While studies differ in the way they measure IP protection and in the outcome variables they examine, there is robust evidence that stronger and more harmonized IPP increases corporate R&D intensity, drives innovation, and ultimately achieves higher levels of economic growth and profitability of companies of any size and provenance. Table 1, below, lists the studies reviewed and provides a basic overview of study population and sample data. Next, Table 2 reports the key findings of the studies reviewed.

Table 1: References and scope of studies

No.	Full Reference	Scope 1: Population – Which (pharmaceutical goods/industries covered?	Scope 2: Population – which countries covered	Scope 3: Sample data – data period covered and maximum number of observations ("N")
[1]	Wajsman, N., Yann Ménière, Michał Kazimierczak, and Ilja Rudyk. "High-growth Firms and Intellectual Property Rights: IPR Profile of High-potential SMEs in Europe." *European Patent Office and the European Union Intellectual Property Office* (2019).	Small and medium enterprises ("SMEs") in manufacturing industries (p. 4); results are also reported for high-technology industries that include, among others, pharmaceutical products	11 EU Member States and the UK (p. 28)	2000-2010 (pp. 27-28); N=208,084 (including 1,140 observations for pharmaceutical products) for 64,998 unique SMEs (pp. 28, 64)
[2]	Wajsman, N., Yann Ménière, Michał Kazimierczak, Muzio Grilli, Ilja Rudyk, and Carolina Arias Burgos. "Intellectual property rights and firm performance in the European Union: Firm-level analysis report." *European Patent Office and the European Union Intellectual Property Office* (2021).	All economic industries (Table 8); no separate results for pharma industry	27 EU Member States and the UK (p. 19)	2007-2019; N > 890,000 for 127,199 companies (p. 45)
[3]	Branstetter, Lee G., Raymond Fisman, and C. Fritz Foley. "Do stronger intellectual property rights increase international technology transfer? Empirical evidence from US firm-level panel data." *The Quarterly Journal of Economics* 121, no. 1 (2006): 321-349.	All economic industries; no separate results for pharma industry	Foreign affiliates of U.S. multinationals	1982-1999 (p. 321); N=31,739 (Table IV) for

Appendix 3. Relationship between IP protection and corporate R&D

No.	Full Reference	Scope 1: Population – Which (pharmaceutical goods/industries covered?	Scope 2: Population – which countries covered	Scope 3: Sample data – data period covered and maximum number of observations ("N")
			in 16 countries (p. 321)	12,961 affiliates from 2,156 parent companies (Table I)
[4]	Maskus, Keith E., Sahar Milani, and Rebecca Neumann. "The impact of patent protection and financial development on industrial R&D." *Research Policy* 48, no. 1 (2019): 355-370.	22 manufacturing industries (p. 359); results are also reported for more patent-intensive industries that include, among others, pharmaceuticals	20 OECD Countries (p. 359)	1990-2009 (p. 359); N=5,589 (Table 1B)
[5]	Konara, Palitha, Georgios Batsakis, and Vikrant Shirodkar. ""Distance" in intellectual property protection and MNEs' foreign subsidiary innovation performance." *Journal of Product Innovation Management* 39, no. 4 (2022): 534-558.	All manufacturing industries; no separate results for pharma industry (p. 542)	MNE subsidiary-level data, representing 47 home countries and 31 host countries (p. 542)	2005-2013 (p. 542); N=91,347 for 15,246 subsidiaries from 11,284 parent companies (p. 542)
[6]	Shapiro, Robert J., and Aparna Mathur. "The impact of intellectual property protections on research and development in India and on the growth and wages of key Indian industries." *SONECON Report* (2015). Available online at https://www.sonecon.com/wp-	Several manufacturing industries; results are also reported for "Pharmaceuticals and	26 OECD Countries (p. 10); India (p. 16)	1995-2009 for OECD countries (p. 10);

Appendix 3. Relationship between IP protection and corporate R&D

No.	Full Reference	Scope 1: Population – Which (pharmaceutical goods/industries covered?	Scope 2: Population – which countries covered	Scope 3: Sample data – data period covered and maximum number of observations ("N")
	content/uploads/2022/01/Report_on_Value_of_a_Strict_IP_Regime_for_Key_Indian_Industries-Shapiro-Mathur-November2015.pdf	Medical, Precision, and Optical Instruments" (pp. 3, 10, 11)		2000/2001-2009/2010 for India (p. 16)
[7]	Panda, Sidheswar, Ruchi Sharma, and Walter G. Park. "Patent protection, technological efforts, and exports: An empirical investigation." *The Journal of Developing Areas* 54, no. 2 (2020).	Whole economic sector, no separate results for pharma industry (pp. 145 and 150)	Panel data analysis on 67 countries (p. 150)	N=252 (Table 4) Panels of five-year averages during 1996-2014 (p. 150)
[8]	Ang, James S., Yingmei Cheng, and Chaopeng Wu. "Does enforcement of intellectual property rights matter in China? Evidence from financing and investment choices in the high-tech industry." *Review of Economics and Statistics* 96, no. 2 (2014): 332-348.	High-tech firms that include, among others, pharmaceuticals and medical industry firms (pp. 336-337)	China (p. 333)	2001-2005 (pp. 336-337); N=23,995 (firm-year observations; pp. 336-337)
[9]	Allred, Brent B., and Walter G. Park. "The influence of patent protection on firm innovation investment in manufacturing industries." *Journal of International Management* 13, no. 2 (2007): 91-109.	10 manufacturing industries that do not include pharmaceuticals (pp. 91 and 98)	29 countries (pp. 91 and 98)	1995 (p. 97); N=706 firms competing in ten manufacturing industries across 29 countries (Tables 2 and 3)

Appendix 3. Relationship between IP protection and corporate R&D

No.	Full Reference	Scope 1: Population – Which (pharmaceutical goods/industries covered?	Scope 2: Population – which countries covered	Scope 3: Sample data – data period covered and maximum number of observations ("N")
[10]	William, Mbanyele and Wang Fengrong. "Economic policy uncertainty and industry innovation: Cross country evidence." *The Quarterly Review of Economics and Finance*, Vol. 84 (2022): 208-228	89 industries of various innovation intensiveness (Table A2)	17 countries (p. 209)	1990-2015 N=11,115 (Table 4)
[11]	Pazderka, Bohumir. "Patent protection and pharmaceutical R&D spending in Canada." *Canadian Public Policy/Analyse de Politiques* (1999): 29-46.	Pharmaceutical industry (p. 30)	Canada (p. 30), OECD countries (p. 31)	1975-1997 (p. 34); N=23 (pp. 33-34)
[12]	Jagadeesh, Harishankar, and Subash Sasidharan. "Do stronger IPR regimes influence R&D efforts? Evidence from the Indian pharmaceutical industry." *Global Business Review* 15, no. 2 (2014): 189-204.	Pharmaceutical industry (p. 189)	India (p. 189)	1994-2010; N=3,866 for 424 firms in Indian pharmaceutical industry (pp. 199 and 201)
[13]	Kyle, Margaret K. and Anita M. McGahan. "Investments in Pharmaceuticals before and after TRIPS." *The Review of Economics and Statistics*, November 94.4 (2012): 1157–1172	Number of new clinical trials in pharmaceutical sector (p. 1157)	192 countries (Table 1)	1990-2006 N=1,428 (Table 2)

Appendix 3. Relationship between IP protection and corporate R&D

Table 2: Study findings

(Note: All reported results are statistically significant on at least a 10% level (i.e., confidence levels of 90% or more), unless otherwise reported.)

Theme(s): impact of intellectual property protection on firm activities	Study no. (see Table 1)	Findings
Strong patent protection increases corporate R&D expenditures	[4]	• Better patent protection, and enforcement of such protection, has a positive impact on R&D expenditure among high-patent industries, such as the pharmaceuticals industry (p. 362) • Key metrics (pp. 359 and 362) o R&D intensity (country-, industry-, and time-variant) is calculated as total industry R&D expenditures, relative to industry output o Patent Protection Index (country- and time-variant) is calculated as PR = GP * FI, where GP is the index of national patent laws developed by Ginarte and Park (1997) and Park (2008). FI is the Fraser Institute's index of the enforcement of property rights and contracts o Patent intensity (industry-variant) is calculated as the number of patents awarded to an industry relative to industry sales. • An **increase in Patent Protection Index** by one standard deviation contributes positively to **R&D intensity by up to 0.817 percentage points** (Table 4). Put in the context of the average R&D intensity (1.7 percentage points) across all countries, industries, and time, this impact is substantial in economic terms. • Moving an average R&D-intensity industry (e.g., machinery and equipment) **from a median-patent right country** (e.g., Italy) **to a high-patent right country** (e.g., Germany) results in an increase of about **41 percent points in R&D intensity**, or 0.7 percentage points (raising R&D intensity to from 1.7 percent to 2.4 percent; pp. 364-365; Table 4)
	[6]	• Improvements of IP rights in a given country significantly boosts the development of innovations measured by "R&D intensity" (p. 2) • Key metrics o R&D intensity of an industry is defined as the share of an industry's sales or output devoted to R&D, i.e., R&D investments (p. 2) o IP rights and enforcement as measured by the Ginarte-Park (G-P) Index (p. 2) o In order to obtain the relationship between the R&D intensity of several industries and a country's G-P Index score, the authors calculate the elasticity between changes in a country's IP protection regime and changes in the R&D intensity for each industry in the country in OECD countries (pp. 10-11) • Findings (pp. 10-11)* o R&D investments respond to **improvements** in IP protection **across countries** o The results also show variations **across industries** in the degree of responsiveness: industries including computers and peripherals, electrical machinery, and **medical, precision and optical instruments** show the **highest R&D intensity response** to improvements in IP protection. **Pharmaceuticals manufacturing**, telecommunications, aircraft and spacecraft, and motor vehicles show a slightly lower responsiveness

Appendix 3. Relationship between IP protection and corporate R&D

Theme(s): impact of intellectual property protection on firm activities	Study no. (see Table 1)	Findings
		○ The average elasticity in the **pharmaceuticals industry is 4.98%**, implying that a 1% improvement in IP rights index leads to 4.98% increase in R&D intensity in pharmaceuticals ○ The elasticity in the **medical, precision, and optical Instruments industry is 8.19%**, implying that a 1% improvement in IP rights index leads to 8.19% increase in R&D intensity in pharmaceuticals • Focusing specifically on **India**, the paper further examines the extent to which India's **most IP-sensitive industries would increase their R&D investments** (p. 3)* ○ If India were to upgrade its IP rights and enforcement regime to the level of China (the world's other very large nation at roughly the same stage of development as India), R&D intensity (i.e., the share of industry output devoted to R&D) would rise by 79.8 percent (from 4.9% to 8.8%) among Indian IT companies; by 21.4% (from 2.8% to 3.4%) in the scientific instruments industry; by 7.1% (from 1.4% to 1.5%) in the transportation sector; and by **9.4% (from 3.2% to 3.5%) across Indian drugs and pharmaceuticals companies** ○ If India were, however, to upgrade its IP rights and enforcement regime to the level of the United States, this would lead to substantially greater R&D commitments in four key Indian industries: R&D intensity would increase by 198% (from 4.9% to 14.6%) in the IT sector; by 46.4% (from 2.8% to 4.1%) in the scientific instruments sector; by 28.6% (from 1.4% to 1.8%) in transportation; and **by 12.5% (from 3.2% to 3.8%) in drugs and pharmaceuticals** * Results generated with descriptive statistics, however were very similar to the results (not reported here) obtained conducting regressions.
	[7]	• Using panel data analysis on 67 countries from 1996-2014, this paper finds that **patent rights influence the technological effort of a country** (pp. 145, 149, 150) ○ The study computes a technology effort index by principle component analysis. Five variables are included to construct the index: R&D expenditure as % of GDP; researchers in R&D per million population; number of patent application by non-residents; the number of the patent application by residents; and the number of published scientific and technical journal articles ○ The study further compiles a patent right ("PR") index based on Ginarte and Park (1997), Park (2008), and Property Rights Alliance (2016) to quantify the level of patent right protection by country ○ The result shows that the coefficient of the patent right index is positive and statistically significant for all country groups examined. This indicates that **strong property right protection stimulates domestic technological effort and does indeed spur innovative activities** in the source country (Table 4, p. 155)
	[9]	• There is a positive relationship between the **level** of a country's **patent rights** and a **firm's propensity to invest in innovation** (as measured by its R&D Intensity). After controlling for firm size, industry structure, and other national factors, a **country's patent rights are positively related to domestic firm innovation investment** (p. 101; Table 2) • There is a positive relationship between an ***increase*** **in the level of a country's patent rights** and a **firm's propensity to invest in innovation**. After controlling for firm size, industry structure, and other national factors, **changes in patent rights are positively related to domestic firm innovation investment** (p. 101; Table 2) • "This finding is especially important for managers who are considering expanding into new international markets. Countries with **strong and strengthening patent rights encourage innovation** through providing effective incentives

Appendix 3. Relationship between IP protection and corporate R&D

Theme(s): impact of intellectual property protection on firm activities	Study no. (see Table 1)	Findings
		and protections. However, the impact of patent rights on innovation varies by industry. Innovation in chemicals and instruments-based industries responds positively to patent rights, while those in other industries (such as food and household appliances) may not be as strongly influenced" (p. 106)
	[11]	• Patent **protection reforms in Canada significantly increased corporate R&D spending** in the pharmaceutical sector o After almost two decades of compulsory licensing of prescription drugs, Canada restored **full patent protection** in two legislative steps taken in 1987 and 1992. The study investigates the impact of this episode of strengthening of patent protection post-1987 on corporate R&D spending in the Canadian pharmaceutical industry (p. 29) o Interindustry comparisons of R&D spending trends within Canada, as well as OECD intercountry comparisons of R&D spending trends within the pharmaceutical industry suggest a **statistically significant increase in Canadian pharmaceutical R&D spending after 1987** (p. 29) o The empirically tested hypothesis was that that an upward change in the R&D spending trend occurred after 1987 (p. 33). The results of the *interindustry* regression show that the relevant coefficients are indeed positive both when the dependent variable is "pharmaceutical R&D as a percentage of R&D spending in all Canadian industries", as well as "pharmaceutical R&D as a percentage of Canadian *manufacturing* R&D spending". Both coefficients are statistically significant at the 99-percent level of confidence (pp. 33-34) o The results of an *intercountry regression* analysis performed both with OECD data are also consistent with the hypothesis of a structural change taking place in Canada pharmaceutical R&D spending after 1987 (p. 43)
	[12]	• **Stronger patent protection** pursuant to **India**'s TRIPS commitments **resulted in higher R&D spending** in the Indian pharmaceutical industry o India complied with the TRIPS agreement in a phased manner, and the Patent Act of 2005 completed the transition to product patents. This study empirically analyzes the technology behaviour (R&D) of the Indian pharmaceutical industry during the post-TRIPS regime (p. 189) o In the econometric model, R&D intensity (R&D expenditure as a percentage of total sales) was used as a dependent variable. As relates to the main variable of interest, the 2005 **TRIPS reform**, authors find a **positive and significant effect on R&D intensity** (p. 199) • The result confirms that the Indian pharmaceutical industry has made suitable changes to its R&D strategy after the transition to product patents in 2005 (p. 199)
	[13]	• Increased patent protection facilitates R&D expenditure in new clinical trials in pharmaceutical sector There is a statistically significant **link between patent protection strength and increased drug development efforts in the pharmaceutical sector** (expressed as the number of new clinical trials) o The authors assess the benefits of TRIPS compliance (i.e., increased IP rights) on the research and development of pharmaceutical treatments. Specifically, they assess "the dynamic benefits of IP protection by examining R&D efforts in the form of clinical trials on specific diseases over time" (p. 1157) o The authors find that "for both types of diseases [global and neglected diseases, such as HIV/AIDS], there is a **strong positive association between TRIPS compliance and R&D effort**, with **R&D more responsive to IP-protected**

Appendix 3. Relationship between IP protection and corporate R&D

Theme(s): impact of intellectual property protection on firm activities	Study no. (see Table 1)	Findings
		market size for global diseases than for neglected diseases. Thus we find that IP protection is associated with increased R&D effort for both types of disease" (p. 1167)
Stronger *enforcement* of IP rights improves firms' R&D investments, ability to innovate, and ability to sell more products	[8]	• Analyzing the impact of province-level enforcement of IP rights on firm-level financing of and investment in R&D in China, the study makes the following findings: o The econometric analysis shows that **IP rights enforcement** significantly increases the probability of a firm's having **access to new debt**. Moving from the lowest IPP1 province (IPP1 being a measure of Provincial IP rights enforcement, calculated as the fraction of intellectual property infringement cases won by the plaintiffs in each province) to the highest IPP1 province increases the **probability that a high-tech firm** (a category which includes firms in pharmaceutical and medical industry) will obtain new debt **by 7.9%,** holding all other independent variables at their mean values (pp. 333 and 339) o In provinces with better IP rights enforcement, high-tech companies **invest** a significantly higher proportion of newly acquired debt and new internal financing **in R&D**. When a firm moves from the lowest IPP1 province to the highest IPP1 province, **the percentage of new debt invested in R&D more than doubles**, from 3.1% to 8.5%, as does the percentage of **new internal financing invested in R&D**, which increases from 9.2% to 20.6% (p. 343) o **IP rights enforcement** also has a significant effect on **R&D output** ▪ The first measure of R&D output is *number of innovation patents*. Firms in provinces with more stringent IP rights enforcement receive greater protection from patent infringement, and therefore are more likely to seek patent generation, registration, and application. This is confirmed by a Poisson regression model that shows that **IP rights enforcement has a positive and significant impact on the number of innovation patents and total patents** (p. 343) ▪ The second measure of R&D output is the *ratio of new product sales to total sales*. Poor IP rights enforcement can adversely affect sales of novel products. The regression analysis result shows that the level of IP rights enforcement has a positive and highly significant effect on the new product sales ratio. **A one standard deviation increase in the level of IP rights enforcement improves new product sales ratio by 4.4 percentage points.** When controlling for provincial characteristics, the magnitude is even greater**: a one standard deviation increase in the IP rights enforcement is associated with an increase of 8.6 percentage points in the new product sales ratio** (pp. 343 and 347)
Difference in IP regime strength between home and host countries reduces firms' ability to innovate	[5]	• The "distance" in IP protection strength between multinational enterprises' home and host countries reduces the ability of MNEs to innovate at foreign subsidiary locations (measured by the number of patent applications). This logic applies in both directions, i.e., (1) "downwards", when MNEs originating from *stronger* IP protection regimes try to innovate in *weaker* IP protection regimes, and (2) "upwards", when MNEs originating from *weaker* IP protection regimes innovate in *stronger* IP protection regimes. However, the negative effect of IP protection distance will be stronger in the downward direction than in the upward direction (pp. 534 and 539) • In the econometric analysis, the key explanatory variable is IPR distance, measured as the differences in patent enforcement (p. 542). IPR distance spans from −7.6 to +8.1, hence, upward IPR distance measure varies from 0 to 7.6, and the downward IPR distance measure varies from 0 to 8.1 (pp. 542-544)

Appendix 3. Relationship between IP protection and corporate R&D

Theme(s): impact of intellectual property protection on firm activities	Study no. (see Table 1)	Findings
		○ Generally, a **one-unit *increase*** in absolute IPR distance results in **19% decrease** in subsidiary innovation performance (number of patents) ○ Specifically, **one-unit *increase*** in the IPR distance in the **downward** direction would result in a **24% decrease** in subsidiary innovation performance. This indicates that MNEs originating from stronger IP protection regimes also innovate less in weaker IP protection regimes ○ Similarly, a **single-unit *increase*** in the IPR distance in the **upward** direction would result in an **8% decrease** in subsidiary innovation performance. This indicates that MNEs originating from weaker IP protection regimes innovate less in countries with stronger IP protection regimes
Improvement in national IP regimes attracts international technology transfer and imports of high-tech products	[3]	• **IP reforms** in *host* countries **improves R&D expenditures** by local affiliates of multinational enterprises ("MNEs") ○ Specifically, econometric analysis shows that IPR reform in *host* country leads to a **23% increase in R&D spending** by affiliates of patent-intensive parents (p. 339)
	[7]	• **Patent rights influence the technological effort** of a country that further **stimulates its exports** and thus enables **technology transfer** abroad (pp. 145, 149, 150) ○ The study compiles a patent right index and a technology effort index consisting of five metrics: R&D expenditure as % of GDP; researchers in R&D per million population; number of patent application by non-residents; number of the patent application by residents; and the number of published scientific and technical journal articles ○ Looking at exports, empirical analysis shows that the technology effort index is highly significant for all countries, and high-income countries in particular (Table 5). This implies that technological efforts (which, in turn are affected by domestic patent rights) increase the likelihood that high-income countries will export high technology products. The destination countries' patent rights index is positively significant throughout, indicating that **patent rights help play a significant role in the economic development of economies by helping to attract high-technology products** (p. 156)
A strong IP protection system moderates the negative effect that economic policy uncertainty has on innovation	[10]	• Innovation output falls following high economic policy uncertainty episodes. However, the impact is significantly mitigated in countries with **higher intellectual property and patent rights protection** (p. 225) ○ The study shows that various empirical metrics of innovation (patent counts, patenting entities, patent citations, patent originality, and patent generality) fall following high economic policy uncertainty episodes via the risk-tolerance, financial, and information channels ○ However, the empirical analysis shows that a **strong legal system with well-enforced patent and property rights** moderates the relationship between economic policy uncertainty and innovation (p. 210; Table 15) ○ Specifically, the empirical results show that the impact of economic policy uncertainty on innovation is negative and statistically significant in economies with weaker patent rights protection. The same coefficients are not significant in all the models but one for countries with stronger patent rights protection (p. 224, Table 15)

Appendix 3. Relationship between IP protection and corporate R&D

Theme(s): impact of intellectual property protection on firm activities	Study no. (see Table 1)	Findings
Seeking IP protection increases firm growth and profitability through innovation	[1]	• Actively seeking **protection of intellectual property rights** ("IPR activities"), particularly patent protection, is an important **driver of growth for small and medium enterprises** ("SMEs") in Europe. SMEs with prior IPR activities are statistically more likely to grow than SMEs without prior IPR activities and are more likely to become a high-growth firm ("HGF" – firms with average annualised growth rate greater than 20% per annum over three consecutive years) o A European SME is about **1.1 times more likely** to experience a three-year **high growth period** when it has been applying for any **national or European IP rights** in the three-year window preceding growth (Figure 5.2) o The likelihood of experiencing a **positive turnover growth** over three years is likewise **1.21 times higher** when the SME has been a prior applicant of **any national or European IP rights** (Figure 5.2) o Similarly, an SME with a prior **European patent application** (only one category of IP) is **1.34 times more likely to become an HGF** and **1.25 times more likely to experience a positive growth** (Figure 5.5) o In high-technology industries that include manufacture of **pharmaceuticals**, an SME with any prior **national or European patent application** is **1.88 times more likely to become an HGF** and **1.35 times more likely to experience a positive growth** (Figure 5.6) o Similarly, in high-technology industry, an SME with a prior **European patent application** is **2.10 times more likely to become an HGF** and **1.45 times more likely to experience a positive growth** (Figure 5.7)
	[2]	• In the EU, companies actively seeking protection of intellectual property rights ("IPR owners") significantly outperform non-owners: o Overall, **revenue per employee is approximately 55% higher** for IPR owners than for firms that do not own IPRs. This relationship is particularly pronounced for small and medium enterprises ("SMEs"). **SMEs** that own IPRs have **68% higher revenue per employee** than SMEs that do not own any IPRs at all. In the case of **large firms**, revenue per employee is **18% higher** for IPR owners than for non-owners (p. 52) o **Patent-only** owners have **43% higher revenue** per employee for all firms, 50% higher revenues for SMEs and 18% higher revenues for large firms. (Figure 5) • IP protection is particularly important for companies in less innovative countries: IPR ownership premium generated by companies depends on how innovative the home Member State is according to the European Commission's annual European Innovation Scoreboard (p. 61): o Companies based in Member States that are classified "**modest" or "moderate"**, innovators generate significantly higher IPR ownership **premium of 70%**, compared with **55% for all companies**. Conversely, firms from Member States that are classified **"strong" or "leader"**, innovators generate an IPR ownership **premium of only 40% (**p. 63) o Corresponding premiums for **patent-only** owners are 43% for all companies, 51% in "modest" or "moderate" countries, and 32% in "strong" or "leader" countries (Figure A6)

Appendix 4. The relationship between patent protection and innovation in the health sector: Literature review

Many empirical studies have assessed to what extent patents matter for innovation in the health sector. Specifically, they analyze the relationship between strength of intellectual property protection and pharmaceutical innovation. While studies may differ in the way they parametrize IP strength and in the outcome variables they examine, there is robust evidence that stronger and more harmonized patent protection facilitates innovation, mitigates the negative effect that economic policy uncertainty, increases corporate R&D spending, and overall results in increased drug development. Table 1, below, lists the studies reviewed and provides a basic overview of study population and sample data. Table 2, next, reports the key findings of the studies reviewed.

Table 1: References and scope of studies

No.	Full Reference	Scope 1: Population – Pharmaceuticals covered	Scope 2: Population – countries covered	Scope 3: Sample data – data period covered and maximum number of observations ("N")
[1]	Gamba, Simona. "The Effect of Intellectual Property Rights on Domestic Innovation in the Pharmaceutical Sector." *World Development* 99 (2017): 15–27.	Pharmaceutical sector (p. 15)	74 countries, 25 of which developing (p. 18)	1977-1998 N=1,408 (Table 3)
[2]	Deiss, Robert. "Intellectual property organizations and pharmaceutical patents in Africa." *Social Science & Medicine* 64 (2007): 287–291	HIV antiretroviral drugs (p. 287)	53 African countries (p. 288)	October 2000 – March 2001 N=49 (Table 1)
[3]	Kyle, Margaret K. and Anita M. McGahan. "Investments in Pharmaceuticals before and after TRIPS." *The Review of Economics and Statistics*, November 94.4 (2012): 1157–1172	Number of new clinical trials in pharmaceutical sector (p. 1157)	192 countries (Table 1)	1990-2006 N=1,428 (Table 2)
[4]	Cockburn, Iain and Genia Long. "The importance of patents to innovation: updated cross-industry comparisons with biopharmaceuticals." *Expert Opinion on Therapeutic Patents*, 25.7 (2015): 739-742	Cross-industry comparison with biopharmaceuticals (Table 1)	United States (p. 740)	2008-2010 (p. 740)

Appendix 4. The relationship between patent protection and innovation in the health sector

No.	Full Reference	Scope 1: Population – Pharmaceuticals covered	Scope 2: Population – countries covered	Scope 3: Sample data – data period covered and maximum number of observations ("N")
[5]	Pazderka, Bohumir. "Patent protection and pharmaceutical R&D spending in Canada." *Canadian Public Policy/Analyse de Politiques* (1999): 29-46.	Pharmaceutical industry (p. 30)	Canada (p. 30); OECD countries (p. 31)	1975-1997 (p. 34); N=23 (pp. 33-34)
[6]	Jagadeesh, Harishankar, and Subash Sasidharan. "Do stronger IPR regimes influence R&D efforts? Evidence from the Indian pharmaceutical industry." *Global Business Review* 15, no. 2 (2014): 189-204.	Pharmaceutical industry (p. 189)	India (p. 189)	1994-2010; N=3,866 for 424 firms in Indian pharmaceutical industry (pp. 199 and 201)
[7]	Maskus, Keith E., Sahar Milani, and Rebecca Neumann. "The impact of patent protection and financial development on industrial R&D." *Research Policy* 48, no. 1 (2019): 355-370.	22 manufacturing industries (p. 359); results are also reported for more patent-intensive industries that include, among others, pharmaceuticals	20 OECD Countries (p. 359)	1990-2009 (p. 359); N=5,589 (Table 1B)
[8]	Shapiro, Robert J., and Aparna Mathur. "The impact of intellectual property protections on research and development in India and on the growth and wages of key Indian industries." *SONECON Report* (2015). Available online at https://www.sonecon.com/wp-	Several manufacturing industries; results are also reported for	26 OECD Countries (p. 10); India (p. 16)	1995-2009 for OECD countries (p. 10);

Appendix 4. The relationship between patent protection and innovation in the health sector

No.	Full Reference	Scope 1: Population – Pharmaceuticals covered	Scope 2: Population – countries covered	Scope 3: Sample data – data period covered and maximum number of observations ("N")
	content/uploads/2022/01/Report_on_Value_of_a_Strict_IP_Regime_for_Key_Indian_Industries-Shapiro-Mathur-November2015.pdf	"Pharmaceuticals and Medical, Precision, and Optical Instruments" (pp. 3, 10, 11)		2000/2001-2009/2010 for India (p. 16)
[9]	Ang, James S., Yingmei Cheng, and Chaopeng Wu. "Does enforcement of intellectual property rights matter in China? Evidence from financing and investment choices in the high-tech industry" *Review of Economics and Statistics* 96, no. 2 (2014): 332-348.	High-tech firms that include, among others, pharmaceuticals and medical industry firms (pp. 336-337)	China (p. 333)	2001-2005 (pp. 336-337); N=23,995 (firm-year observations pp. 336-337)
[10]	Wajsman, N., Yann Ménière, Michał Kazimierczak, and Ilja Rudyk. "High-growth Firms and Intellectual Property Rights: IPR Profile of High-potential SMEs in Europe." *European Patent Office and the European Union Intellectual Property Office* (2019).	Small and medium enterprises ("SMEs") in manufacturing industries (p. 4); results are also reported for high-technology industries that include, among others, pharmaceutical products	11 EU Member States and the UK (p. 28)	2000-2010 (pp. 27-28); N=208,084 (including 1,140 observations for pharmaceutical products) for 64,998 unique SMEs (pp. 28, 64)

Appendix 4. The relationship between patent protection and innovation in the health sector

Table B.2: Study findings

(Note: All reported results are statistically significant on at least a 10% level (i.e., confidence levels of 90% or more), unless otherwise reported.)

Theme(s): impact of patent protection on health-sector innovation	Study no. (see Table 1)	Findings
Increased patent protection results in increased drug development and facilitates innovation	[1]	• **Patent protection** at the level of TRIPS commitments or stronger **stimulates pharmaceutical domestic innovation in developed and developing countries**. o The author compiles a dataset of domestic intellectual property rights ("IPR") reforms (treatment group) and statistically compares it to sample of similar countries and time periods without reforms (comparison group). She then applies a difference-in-difference approach to estimate the empirical impact of stronger IPR protection on innovation (measured as patent applications) in the pharmaceutical sector o The author finds that, in **developed countries**, TRIPS-compliant protection is responsible for a **58% increase in patent applications**, all things equal (p. 24) o The author further finds that, for **less-developed countries**, TRIPS-compliant protection is responsible for a **33% increase in patent applications**, all things equal (p. 24)
	[2]	• The study finds that the number of **patent applications** for HIV antiretroviral drugs is significantly **higher in countries that are member of an intellectual property organization** (IPO) (p. 290)
	[3]	• There is a statistically significant **link between patent protection strength and increased drug development efforts** (expressed as the number of clinical trials) o The authors assess the benefits of TRIPS compliance by examining the effects of increased global IP rights on the development of pharmaceutical treatments o Specifically, they assess "the dynamic benefits of IP protection by examining R&D efforts in the form of clinical trials on specific diseases over time" (p. 1157) o The authors find that "for both types of diseases [global and neglected diseases, such as HIV/AIDS], there is a **strong positive association between TRIPS compliance and R&D effort**, with R&D more responsive to IP-protected market size for global diseases than for neglected diseases. Thus we find that IP protection is associated with increased R&D effort for both types of disease" (p. 1167)
Stronger *enforcement* of IP rights improves firms' ability to innovate	[9]	• Analyzing the impact of province-level enforcement of IP rights on firm-level financing of and investment in R&D in China, the study makes the following findings: o The econometric analysis shows that **IP rights enforcement** has a significant effect on **innovation**, *inter alia* in the health sector**.** One measure of R&D output is *number of innovation patents*. Firms in provinces with more stringent IP rights enforcement receive **greater protection from patent infringement**, and therefore are more likely to seek **patent generation, registration, and application**. This is confirmed by a Poisson regression model that shows that **IP rights enforcement has a positive and significant impact on the number of innovation patents and total patents** (p. 343)
Patents and intellectual property rights protection help firms	[4]	• In the health sector **product patents are the most important tool to harness innovation** o The authors analysed the three annual Business R&D and Innovation Surveys ("BRDIS") conducted by the US Census Bureau during 2008-10, focusing on companies from sectors that were most likely to report that patents were "very" or "somewhat important" (p. 740)

Appendix 4. The relationship between patent protection and innovation in the health sector

Theme(s): impact of patent protection on health-sector innovation	Study no. (see Table 1)	Findings
harness the benefits of innovation		○ "**Pharmaceuticals** were the only industry in which **product patents** were rated by most [respondents] as **more effective than other methods of appropriating the benefits of innovation** (greater than secrecy, lead time, learning curve advantages, sales or service efforts)" (p. 740)* ○ "**Eighty-nine percent of respondents** in the healthcare (including biotechnology, pharmaceuticals and medical) industry characterized **patents as 'extremely important'** in 'creating a competitive advantage for your organization'" (p. 741)* ○ "Since the 1980s, US-focused researchers have found **patents to be relatively more important to R&D than other forms of IP protection** (trademarks, copyrights, confidential trade secrets, confidential or non-confidential know-how) and strategic complementary assets (such as lead time, sales and service, and manufacturing advantages) in biopharmaceuticals than in other industries. The most recent data from US government and annual US and Canada licensing professional surveys are consistent with these findings" (p. 741) ○ The authors conclude that this is most likely due to "high, increasing costs, and persistently high scientific risk, of bringing an FDA-approved drug to market, and the continuing importance of secure patents to attracting start-up investment capital, this difference is expected to persist" (p. 741) * Results generated with descriptive statistics
Stronger patent protection increases corporate R&D spending, and thus innovation	[5]	• Patent **protection reforms in Canada significantly increased corporate R&D spending** in the pharmaceutical sector ○ After almost two decades of compulsory licensing of prescription drugs, Canada restored **full patent protection** in two legislative steps taken in 1987 and 1992. The study investigates the impact of this episode of **strengthening of patent protection post-1987 on corporate R&D spending** in the Canadian pharmaceutical industry (p. 29) ○ Interindustry comparisons of R&D spending trends within Canada, as well as OECD intercountry comparisons of R&D spending trends within the pharmaceutical industry, suggest a **statistically significant increase in Canadian pharmaceutical R&D spending after 1987** (p. 29) ○ The empirically tested hypothesis was that that an upward change in the R&D spending trend occurred after 1987 (p. 33). The results of an *interindustry* regression show that the relevant coefficients are indeed **positive** both when the dependent variable is "**pharmaceutical R&D** as a percentage of R&D spending in all Canadian industries", as well as "pharmaceutical R&D as a percentage of Canadian *manufacturing* R&D spending". Both coefficients are statistically significant at the 99-percent level of confidence (pp. 33-34) ○ The results of an *intercountry* regression analysis performed with OECD data are also consistent with the hypothesis of a **structural change** taking place **in Canada pharmaceutical R&D spending after 1987** (p. 43)
	[6]	• **Stronger patent protection** pursuant to **India**'s TRIPS commitments **resulted in higher R&D spending** in the Indian pharmaceutical industry ○ India complied with the TRIPS agreement in a phased manner, and the Patent Act of 2005 completed the transition to product patents. The study empirically analyzes the R&D behaviour of the Indian pharmaceutical industry during the post-TRIPS regime (p. 189) ○ In the econometric model, R&D intensity (R&D expenditure as a percentage of total sales) was used as a dependent variable. As relates to the main variable of interest, the 2005 **TRIPS reform**, authors find a **positive and significant effect on R&D intensity** (p. 199)

Appendix 4. The relationship between patent protection and innovation in the health sector

Theme(s): impact of patent protection on health-sector innovation	Study no. (see Table 1)	Findings
		○ The result confirms that the **Indian pharmaceutical industry has made suitable changes to its R&D strategy** after the transition to product patents in 2005 (p. 199)
	[7]	• Better patent protection, and enforcement of such protection, has a positive impact on R&D expenditure among high-patent industries, such as **pharmaceuticals industry** (p. 362) • Key metrics (pp. 359 and 362) ○ R&D intensity (country-, industry-, and time-variant) is calculated as total industry R&D expenditures, relative to industry output ○ Patent Protection Index (country- and time-variant) is calculated as PR = GP * FI, where GP is the index of national patent laws developed by Ginarte and Park (1997) and Park (2008). FI is the Fraser Institute's index of the enforcement of property rights and contracts ○ Patent intensity (industry-variant) is calculated as the number of patents awarded to an industry relative to industry sales. • Findings ○ An **increase in Patent Protection Index** by one standard deviation contributes positively to **R&D intensity by up to 0.817 percentage points** (Table 4). Put in the context of the average R&D intensity (1.7 percentage points) across all countries, industries, and time, this impact is substantial in economic terms. ○ Moving an average R&D-intensity industry (e.g., machinery and equipment) from a median-patent right country (e.g., Italy) to a high-patent right country (e.g., Germany) results in an increase of about **41 percent**, or 0.7 percentage points, in **R&D intensity** (raising R&D intensity to from 1.7 percent to 2.4 percent; pp. 364-365; Table 4)
	[8]	• Improvements of IP rights in a given country significantly boosts the development of innovations measured by "R&D intensity" (p. 2) • Key metrics ○ R&D intensity of an industry is defined as the share of an industry's sales or output devoted to R&D, i.e., R&D investments (p. 2) ○ IP rights and enforcement is measured by the Ginarte-Park (G-P) Index (p. 2) ○ To obtain the relationship between industry R&D intensity and a country's G-P Index score, the authors calculate the elasticity between changes in a country's IP protection regime and changes in the R&D intensity for each industry in the country in OECD countries (pp. 10-11) • Findings (pp. 10-11) ○ R&D investments respond to **improvements** in IP protection **across countries** ○ The average elasticity in the **pharmaceuticals industry is 4.98%**, implying that a 1% improvement in IP rights index leads to 4.98% increase in R&D intensity in pharmaceuticals* ○ The elasticity in the **medical, precision, and optical Instruments industry is 8.19%**, implying that a 1% improvement in IP rights index leads to 8.19% increase in R&D intensity in pharmaceuticals* • Focusing specifically on **India**, the paper further examines the extent to which India's **most IP-sensitive industries (including pharmaceuticals) would increase their R&D investments**: (p. 3)*

Appendix 4. The relationship between patent protection and innovation in the health sector

Theme(s): impact of patent protection on health-sector innovation	Study no. (see Table 1)	Findings
		○ If India were to **upgrade its IP rights and enforcement regime to the level of China** (the world's other very large nation at roughly the same stage of development as India), R&D intensity (i.e., the share of industry output devoted to R&D) would rise by **9.4%** (from 3.2% to 3.5%) **across Indian drugs and pharmaceuticals companies** ○ If India were, however, to **upgrade its IP rights and enforcement regime to the level of the United States**, R&D intensity would increase **by 12.5%** (from 3.2% to 3.8%) **in drugs and pharmaceuticals** * Results generated with descriptive statistics, however were very similar to the results (not reported here) obtained conducting regressions.
Seeking IP protection increases firm growth through innovation	[10]	• Actively seeking protection of intellectual property rights ("IPR activities"), particularly **patent protection**, is an important driver of growth for small and medium enterprises ("SMEs") in Europe. SMEs with prior IPR activities are statistically more likely to grow than SMEs without prior IPR activities and are more likely to become a high-growth firm ("HGF" – firms with average annualised growth rate greater than 20% per annum over three consecutive years): ○ In high-technology industries that include manufacture of **pharmaceuticals**, a European SME is about **1.88 times more likely** to experience a three-year **high growth period** when it has been applying for any **national or European IP rights** in the three-year window preceding growth (Figure 5.6) ○ Similarly, in high-technology industries, the likelihood of experiencing a **positive turnover growth over three years** is likewise **1.35 times higher** when the SME has been a prior applicant of **any national or European IP rights** (Figure 5.6)

Appendix 5. The relationship between patent protection and access to medicine in LICs, LMICs, UMICs, and HICs: Literature review

Numerous high-quality empirical studies assess whether a correlation or causal relationship exists between changes in patent policy and indicators of access to medicines. Examples for patent policy changes include the introduction of a domestic patent regime; strengthening or weakening domestic patent regimes; patent expiration/loss of IP protection; and patent strengthening/harmonization via trade agreement. Indicators for access to medicine include likelihood of launch of new medicines in new markets; time to market ("launch delay") of new medicines; adoption of new medicines (i.e., sales); and prices of new medicines. Although the conceptual framing of the exact research questions may be different from study to study, there is ample evidence that stronger and more harmonized patent protection increases access to medicine to countries of all development levels, while weaker (and/or weakly enforced) patent protection decreases access to medicine. Table 1, below, lists the studies reviewed and provides a basic overview of study population and sample data. Table 2, next, reports the studies' key findings.

Table 1: References and scope of studies

No.	Full Reference	Scope 1: Population – Pharmaceuticals covered	Scope 2: Population –countries covered	Scope 3: Sample data – data period covered and maximum number of observations ("N")
[1]	Dai, Rong, and Jayashree Watal. "Product Patents and Access to Innovative Medicines." *Social Science & Medicine* (1982) 291 (2021): 114479–114479	578 patented drugs covering various disease categories	70 countries of varying degrees of development	2007-2017 186,647 observations (Table 5)
[2]	Trachtenberg, Danielle et al. "The Effects of Trade Agreements on Imports of Biologics: Evidence from Chile." *Journal of Globalization and Development* 10.2 (2020)	Biologics, as found in Chapter 30 of the Harmonized System	Chile	1997-2016 N= 7,067
[3]	Cockburn, Iain M., Jean O. Lanjouw, and Mark Schankerman. "Patents and the Global Diffusion of New Drugs." *The American Economic Review* 106.1 (2016): 136–164	634 new drugs	76 countries (low, middle, high-income)	1983-2002 N=298,605 (Table 3)
[4]	Bollyky, Thomas J., A Dose of TPP's Medicine: Why U.S. Trade Deals Have Not Exported U.S. Drug Prices (March 22, 2016). *Council on Foreign Relations Working Paper*, Available at SSRN: https://ssrn.com/abstract=2755754	All pharmaceuticals	15 countries with recent trade deals with the U.S. (Australia, Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua, Panama, Chile, Colombia, Dominican Republic, Jordan, South Korea, Morocco, Peru, Singapore)	2004-2014

Appendix 5. Relationship between patent protection and access to medicine

No.	Full Reference	Scope 1: Population – Pharmaceuticals covered	Scope 2: Population –countries covered	Scope 3: Sample data – data period covered and maximum number of observations ("N")
[5]	Berndt, Ernst R, and Iain M Cockburn. "The Hidden Cost Of Low Prices: Limited Access To New Drugs In India." *Health Affairs* 33.9 (2014): 1567–1575	184 new molecular entities approved by FDA	India, Germany, US	2000-2009
[6]	Qian, Yi, and Margaret Kyle. "Intellectual Property Rights and Access to Innovation: Evidence from TRIPS." *NBER Working Paper Series* (2014): 20799	716 patented drugs (Table 2)	60 countries of varying degrees of development (Table 1)	2000-2013 for prices and units sold and 1990-2013 for launch of new medicines N=1.1M (for launch) (Tables 7-18)
[7]	Borrell, Joan-Ramon. "Patents and the Faster Introduction of New Drugs in Developing Countries." A*pplied Economics Letters* 12.6 (2005): 379–382.	New HIV/AIDS ARV medicines launched in the US	34 countries (low and middle-income, and US)	1995-1999 N=1,273 (Table 3)
[8]	Lanjouw, Jenny. "Patents, Price Controls, and Access to New Drugs: How Policy Affects Global Market Entry." *NBER Working Paper Series* (2005): 11321	782 pharmaceutical drugs ("New Clinical Entities"; Table 1)	68 countries (all income levels; Table 3)	1982-2002 N=18,889 (Table 10)
[9]	Djolov, George G. "Patents, Price Controls, and Pharmaceuticals." *The Journal of World Intellectual Property* 6.4 (2003): 611–631	Pharmaceuticals	55 countries (developed and developing) (Table 1)	1999 N=18
[10]	Rozek, Richard P., and Ruth Berkowitz. "The Effects of Patent Protection on the Prices of Pharmaceutical Products." *The Journal of World Intellectual Property* 1.2 (1998): 179–243	6 therapeutic categories: antiulcerants, antidepressants, calcium antagonists, non-narcotic analgesics, broad-spectrum penicillins and ACE inhibitors	9 developing countries at the time of writing (South Korea, Mexico, Taiwan, Hungary, Brazil, Argentina, Egypt, Jordan, Turkey)	1985-1996 N=424

Appendix 5. Relationship between patent protection and access to medicine

No.	Full Reference	Scope 1: Population – Pharmaceuticals covered	Scope 2: Population –countries covered	Scope 3: Sample data – data period covered and maximum number of observations ("N")
[11]	Duggan, Mark, Craig Garthwaite, and Aparajita Goyal. "The Market Impacts of Pharmaceutical Product Patents in Developing Countries: Evidence from India." The American economic review 106.1 (2016): 99–135	All single-molecule medicines	India	2003-2012 N=5100

Appendix 5. Relationship between patent protection and access to medicine

Table 2: Study findings

(Note: All reported results are statistically significant on at least a 10% level (i.e., confidence levels of 90% and more), unless otherwise reported.)

Indicators of access to medicine	Study no. (see Table 1)	Findings
Availability; likelihood of launch	[1]	• **All countries**: o Introducing product patents in a given country is important for launch likelihood of new medicines:[1] "[P]ooling over all countries, **introducing pharmaceutical product patents increases the launch likelihood of innovative medicines by 14 percent**" (p. 2; see also Table 3) o For medicines against **non-communicable diseases**, introducing product patents facilitates launch of these drugs **by 7 percent** (Table 4) o For medicines treating **infectious diseases**, introducing product patents **significantly increases the launch likelihood** of *innovative* medicines (Table 4) o For medicines treating **HIV/AIDS, malaria, and tuberculosis**, introducing product patents **significantly increases the launch likelihood** of new medicines (Table 4) • **High-income countries**: o Product patentability facilitates drug diffusion: **Patentability increases the launch likelihood of new medicines by 22 percent** (p. 6; Table 3) • **Middle-income countries**: o **Product patentability facilitates drug diffusion:** Patentability increases the launch likelihood of new medicines in a statistically significant manner (p. 6; Table 3) o Estimates of launch likelihood are even higher for pharmaceutical product patents on *innovative* medicines (p. 6; Table 3) • **Low-income countries**: o Patentability increases the launch likelihood of new medicines, but that result is not statistically significant (Table 3)
	[6]	• **All countries**: o **Drugs are more likely to be marketed if they are protected by stronger post-TRIPS patents**: Drugs are more likely to be launched after patent harmonization (here: after the conclusion of the TRIPS Agreement), as compared to (1) drugs that have never been patented, (2) whose patent has expired, or (3) that were launched pre-TRIPS (p. 21; Figure 2). • **High-income countries:** o **Drugs are more likely to be launched after patent harmonization** (here: after the conclusion of the TRIPS Agreement), as compared to (1) drugs that have never been patented, (2) whose patent has expired, or (3) that were launched pre-TRIPS (p. 21; Figure 2). • **Middle-income countries:** o **Drugs are more likely to be launched after patent harmonization** (here: after the conclusion of the TRIPS Agreement), as compared to (1) drugs that have never been patented, (2) whose patent has expired, or (3) that were launched pre-TRIPS (p. 21; Figure 2).

[1] For the purposes of this literature review, the terms "drugs" and "medicines" can be used interchangeably.

Appendix 5. Relationship between patent protection and access to medicine

Indicators of access to medicine	Study no. (see Table 1)	Findings
		• **Lower-income countries:** o **Drugs are more likely to be launched after patent harmonization** (here: after the conclusion of the TRIPS Agreement), as compared to (1) drugs that have never been patented, (2) whose patent has expired, or (3) that were launched pre-TRIPS (p. 21; Figure 2).
	[7]	• **Low- and middle-income countries:** o "The main finding is that [the presence of a] **patent regime** [i.e., whether patent or other market exclusivity status was attainable] had a **positive effect on the introduction of new HIV/AIDS drugs** in the subset of countries […] with relatively equally distributed incomes" (p. 379)
	[8]	• **All countries:** o **Policy change**s from a weak IP protection regime towards a legal environment that is generally supportive of patent rights (i.e., longer process patents, product patents, limits on how patent rights can be curtailed) **significantlyy increase the probability that a new drug is launched** in a given country within either two years or ten years of the drug's first appearance in the global market (p. 41). • **High-income countries:** o "**[A]dding the protection of new products to an otherwise "short" patent regime** [i.e., policy change towards longer product patent regimes] gives **the greatest incremental boost to rapid market entry" within 2 years** (p. 36; see also Tables 10, 11) o Adding **longer process patents** and/or extending the **duration of product patent protection** gives the greatest incremental boost to **rapid market entry within 2 years** (p. 36; Tables 10, 11) o Policy change towards **a long process patent regime and/or extending the duration of product patent protection** gives the greatest incremental boost to **rapid market entry within 10 years** (p. 36; Tables 10, 11) • **Low- and middle-income countries:** o Policy change towards a **long process patent regime raises** the probability of **launch within 2 years by about 30 percent** (p. 30; Table 6; Table 7) o Further adding *product* patents and limits on how patent rights can be curtailed additionally increases the probability of launch within 2 years (p. 31; Table 7) o *Product* patents of less than 15 years protection increase the probability of **launch within 10 years by 25 percent** (p. 33; Table 8) o Policy change towards a long *process* patent regime also raises the probability of launch within 10 years (p. 33; Table 8) • **Low- and middle-income countries:** o Focusing on the subset of medicines most relevant to least developed countries, there is further evidence that ▪ Longer *process* patents increase the probability of launch within 2 years (p. 32; Table 7) ▪ Policy change towards long *process* patents, long *product* patents, and limits on how patent rights can be curtailed results further increases the probability of launch within 2 years (p. 32; Table 7) ▪ Drug patent extension (i.e., extension of the statutory term of patent protection to compensate for time taken in the marketing approvals process) shows the highest impact on the probability of launch within 2 years
	[9]	• **All countries:** o **Patent protection, or the strength thereof**, is of **major** (and statistically significant) **relevance** in accounting for the **level of access to essential drugs** (p. 620; Table 6):

Appendix 5. Relationship between patent protection and access to medicine

Indicators of access to medicine	Study no. (see Table 1)	Findings
		▪ **98.4 percent of the population** of countries with strong patent protection for pharmaceuticals have access to essential drugs; the corresponding figure for countries with weak patent protection is a **mere 76.0 percent** (p. 618; Table 4)* ▪ If countries with weak patent protection were to shift their protection to the levels of the countries with strong patent protection, 743 million additional people worldwide may be anticipated to gain access to essential drugs (p. 618)* ▪ "[T]he evidence indicates that the policies by any legislature most likely to benefit the consumer with regard to affordability and availability of medicines would be those that are not prescriptive or controlling but *safeguard intellectual property rights* and let competition at the supplier level do what it does best, namely keep prices down" (p. 629) • **High-income countries** o **99.53 percent of the population** of high-income countries with strong patent protection for pharmaceuticals have access to essential drugs (p. 619; Table 4)* • **Developing countries** o **91.3 percent of the population** of developing countries with strong patent protection for pharmaceuticals have access to essential drugs; the corresponding figure for developing countries with weak patent protection is a **mere 74.6 percent** (p. 619; Table 4)* * Results generated with descriptive statistics
Time to market	[1]	• **All countries**: o Introducing product patents in a given country is important for innovative medicines by speeding up their launch: "[P]ooling over all countries, **introducing pharmaceutical product patents increases the launch likelihood of innovative medicines by 14 percent**" (p. 2)
	[3]	• **All countries**: o Longer and stronger patent protection in a given country powerfully accelerates drug diffusion by promoting faster launches of new drugs: **Longer product patents reduce launch lags by 55 percent**, as compared to a regime of no product patents (p. 152) o **Medium-length process patents reduce launch lags by 32.4 percent** (fn. 21) o The strength of patent protection (as measured by the "Propatent Index", an index of the strength of protection that reflects the degree to which a country's patent law provisions protect patent holders) also matters: **one standard-deviation increase in the index reduces launch lags by 11.3 percent** (p. 152) • **Low-income countries**: o The **positive impact of longer and stronger patent protection** holds equally for low- and middle-income countries: Qualitative results, and most of the point estimates (in particular the coefficients on the patent policy regimes) are very similar to the baseline specifications where *all* countries are analyzed (p. 156) o "The important conclusion is that the impact of patent […] regulation policies is not confined to high-income countries" (p. 156)
	[5]	• **Low-income countries** (India): o Weak patent protection in a given country is associated with substantial launch delays: "[I]n practice, India's patent regime has offered very weak patent protection" in the period of examination (p. 7). **"[W]e found that the estimated median launch lag was 4.5-5.0 years in India, compared to about a year in Germany and less than two months in the United States [countries with high patent protection]"** (p. 5) o "We estimate that [in India] 50 percent of drugs had a launch lag of five years or more, and about 25 percent had a launch lag of nine years or more. (Note that the phrase or more encompasses never- some of these drugs may never be launched in India)" (p. 6). Indeed,

Appendix 5. Relationship between patent protection and access to medicine

Indicators of access to medicine	Study no. (see Table 1)	Findings
		many drugs took extremely long to become commercially available in India: Ten years after their first worldwide approval, almost one-quarter of the sample drugs were not yet available there (p. 5) o "Launch lags could be reduced by implementing policies that encourage innovator companies to bring new products to the Indian market. These policies include bringing India's patent law into closer conformity with laws in the United States and the European Union […] Such changes would promote faster access to a wider range of new drugs for residents of India without affecting the pricing of currently available drugs, and there is little evidence that they would result in substantially higher prices for new drugs than can be expected under the current regime" (p. 8)
	[6]	• **All countries**: o **Stronger patent protection** in a given country **accelerates drug diffusion** by promoting faster launches of new drugs: ▪ Products that currently benefit from patent protection are more likely to be launched faster than (1) products for which patents never existed or (2) products with expired patents (p. 20 and Tables 7-10). ▪ *Product* patents are particularly efficient in reducing launch lags (i.e., increasing time to market) (Table 7)
Adoption / consumption (i.e., sales)	[2]	• **Middle income countries** (Chile): o Free trade agreements (FTAs) concluded by Chile with **stronger IPR provisions** are associated with **larger volumes of imported biologics** relative to treaties with weaker IPR provisions, i.e. a market expansion effect for exporters to Chile where treaties containing strong intellectual property rights (IPR) provisions are present. While the mere *presence* of an FTA is *not* sufficient to increase the volume of biologic imports, - ▪ Adding only *one* patent-related provision to the IPR chapter of an FTA results in an approximately 19 percent increase in the imported volume of biologics, relative to an FTA with one fewer patent-related provision (p. 10, 11, Table 2) ▪ Adding an IPR provision with TRIPS-compliant language to an FTA results in an 11 percent increase in the imported volume of biologics, relative to an FTA with one fewer TRIPS compliant provision (p. 11, Table 2) ▪ Having any TRIPS-*plus* provisions in an FTA increases the imported volume of biologics by 114 percent, relative to an FTA with no TRIPS plus provisions (p. 11, Table 2) ▪ Adding a provision with TRIPS-*plus* language to an FTA results in a 22 percent increase in the imported volume of biologics, relative to an exporter to Chile with one fewer TRIPS-plus provision (p. 11, Table 2)
	[4]	• **Low- and middle income countries** (Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua, Panama, Chile, Colombia, Dominican Republic, Jordan, Morocco, Peru): o "[In all countries that strengthened and harmonized patent protection pursuant trade deals with the United States, **n]ational drug spending has remained flat** as a share of overall health expenditure in countries with recent U.S. trade agreements […] The growth in per capita pharmaceutical spending is in line with nations of similar income with no U.S. trade deals and no market exclusivity requirements, such as Brazil, Thailand, and South Africa […] The **consumption of pharmaceuticals has not declined** in the countries with recent U.S. trade deals" (pp. 4; see also Figures 1, 2)* o **Strengthening and harmonization of patent protection** pursuant trade deals with the United States did **not generate quantity shifts away from lower-cost generics**: "There has been no discernible trend toward on-patent or branded medicines and away from cheap generic drugs, either in the volume of medicines consumed or as a matter of spending" (p. 5; see also Figure 3)* * Results generated with descriptive statistics.

Appendix 5. Relationship between patent protection and access to medicine

Indicators of access to medicine	Study no. (see Table 1)	Findings
	[6]	• **All countries**: o **Stronger patent protection in a given target market increases sales quantities of new drugs**: Products that currently benefit from patent protection sell in higher quantities than (1) products for which patents never existed or (2) products with expired patents (p. 20 and Tables 7, 8, 9, 10). o *Product* patents are particularly efficient in increasing sales quantities of new drugs (Table 7) o Sales of drugs with *product* patents are increasing in country income (p. 21, Table 11) o Drugs are sold in **higher quantities after patent harmonization** (here: after the conclusion of the TRIPS Agreement), as compared to drugs that (1) have never been patented, (2) whose patent has expired, or (3) that were launched pre-TRIPS (p. 21, Figure 4). This suggests that originators invest in sales when IPRs protect them from generic competition • **High-income countries:** o **Drugs volumes are likely to be higher if drugs are protected by stronger post-TRIPS patents**: Drugs are sold in higher quantities after patent harmonization (here: after the conclusion of the TRIPS Agreement), as compared to drugs (1) that have never been patented, (2) whose patent has expired, or (3) that were launched pre-TRIPS (p. 21, Figure 4) • **Middle-income countries:** o **Drugs volumes are likely to be higher if drugs are protected by stronger post-TRIPS patents**: Drugs are sold in higher quantities after patent harmonization (here: after the conclusion of the TRIPS Agreement), as compared to drugs (1) that have never been patented, (2) whose patent has expired, or (3) that were launched pre-TRIPS (p. 21, Figure 4) • **Lower-income countries:** o Drugs volumes are likely to be higher if drugs are protected by stronger post-TRIPS patents: Drugs are sold in higher quantities after patent harmonization (here: after the conclusion of the TRIPS Agreement), as compared to drugs (1) that have never been patented, (2) whose patent has expired, or (3) that were launched pre-TRIPS (p. 21, Figure 4)
	[9]	• **All countries**: o **The strength of a patent protection regime affects national health expenditures**: "On average, countries with *strong* patent protection allocate 0.55 percent of their GDP on pharmaceuticals, relative to 0.70 percent for countries with *weak* patent protection. [This] means that a country awarding pharmaceuticals a weak patent protection spends a quarter more of its GDP on pharmaceuticals in relation to a country where pharmaceutical patent protection is strong" (p. 624)
	[11]	• **Lower-income countries** (India): o **No statistically significant declines in sales** of drugs sold grant resulting pursuant India's 2005 **TRIPS-based patent reform**. "[Estimated] coefficients show little change in the quantity sold in the quarters before or after a patent was granted" (p. 129; see also Table 4)
Prices	[4]	• **Low- and middle income countries** (Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua, Panama, Chile, Colombia, Dominican Republic, Jordan, Morocco, Peru): o **Strengthening and harmonization of patent protection** pursuant trade deals with the United States **did not result in drug price increases**: The average price of off-patent originator medicines after the conclusion of the trade deal has not increased (Figure 3)* * Result generated with descriptive statistics.

Appendix 5. Relationship between patent protection and access to medicine

Indicators of access to medicine	Study no. (see Table 1)	Findings
	[6]	• **All countries**: o Differential pricing across rich and poorer markets is not significantly different for patented drugs, as compared to non-patented drugs (p. 21; Tables 11, 12) • **Lower-income countries**: o The price premium associated with patented drugs in a given country is *negative* and statistically significant, as compared to drugs (1) that have never been patented or (2) whose patent has expired (p. 22/23, Table 18) o The price of drugs launched after patent harmonization (here: after the conclusion of the TRIPS Agreement) are *lower* on average, as compared to drugs (1) that have never been patented, (2) whose patent has expired, or (3) that were launched pre-TRIPS (p. 21, Table 16, Figure 3)
	[10]	• **Middle- and low-income countries:** o **No effect of increased patent protection on prices for pharmaceuticals**: "Our empirical analysis of pharmaceutical prices for products from six therapeutic categories in nine developing countries suggests that *improving IPP* [intellectual property protection] does not have a measurable impact on real or nominal prices of existing drugs (those marketed before the implementation of IPP). Moreover, in countries with price regulation, IPP [introduction or improvement] had little, if any, impact on price changes of all drugs, including those introduced after the change in patent protection. In cases where prices increased, other developments […] are likely causes. Therapeutic competition, regulation of pharmaceutical prices, monopsony buyers, and, most importantly, the actual provisions of the IP laws are four factors that keep prices for pharmaceutical products from increasing as a result of IPP [introduction or improvement]" (p. 215). o "Our cross-section analysis of prices […] showed that while prices for the same products in the same package size and dosage form differ across countries, the differences are *not* related to IPP. **Countries with IPP do not systematically have higher prices than countries without IPP**" (p. 213)
	[11]	• **Lower-income countries** (India): o **Smaller price increases for patented products than in developed countries**: "We find a statistically significant but economically *modest* price increase for molecules receiving a patent. Our estimate[s] suggest[] a price increase of only approximately 3 percent after a patent is granted [pursuant Indian patent reform intended to come into compliance with TRIPS] is granted and we can rule out average price increases […] of more than 5.3 percent. To provide some context for this magnitude, patented products are on average about *three times* more expensive than generic versions in the United States" (102; see also Table 4)