# COVID-19 Second Wave Preparedness Part 2: Vaccines and Therapeutics

# COVID-19 Second Wave Preparedness

# Part 2: Vaccines and Therapeutics

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## I. Federal Efforts to Accelerate the Development of Vaccines and Therapeutics

### A. Overview of Federal Efforts

- The U.S. government is supporting several initiatives to help accelerate the development of vaccines for COVID-19. Some of these initiatives include, but are not limited to Operation Warp Speed and the Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) partnership.

- The Executive Branch should ensure coordination and communication among all of the efforts to accelerate the development, manufacturing, and distribution of COVID-19 vaccines, therapeutics, and diagnostics, and try to minimize any duplication or inefficiencies.

- The COVID-19 pandemic has brought an unprecedented level of collaboration and cooperation between the federal government and private sector. Congress, the Executive Branch, and the private sector should continue that collaboration to address other unmet medical needs once the COVID-19 public health emergency is over.

### B. Operation Warp Speed

- The Trump Administration established Operation Warp Speed to accelerate the development, manufacturing, and distribution of COVID-19 vaccines, therapeutics, and diagnostics.[1] This public-private partnership aims to facilitate, at an unprecedented pace, the development, manufacturing, and distribution of COVID-19 countermeasures, among: (1) components of the U.S. Department of Health and Human Services (HHS), including the Centers for Disease Control and Prevention (CDC), the U.S. Food and Drug Administration (FDA), the National Institutes of Health (NIH), and the Biomedical Advanced Research and Development Authority (BARDA); (2) the U.S. Department of Defense (DoD); (3) private firms; and (4) other federal agencies, including the U.S. Department of Agriculture, the U.S. Department of Energy (DOE), and the U.S. Department of Veterans Affairs. It will coordinate existing HHS-wide efforts, including the NIH's ACTIV partnership for vaccine and therapeutic development, NIH's Rapid Acceleration of Diagnostics (RADx) initiative for diagnostic development, and work by BARDA.[2]

    - The three main areas where the effort will accelerate the timeframe for countermeasures to reach the American public include development, manufacturing, and distribution.[3]

[1] U.S. Department of Health and Human Services, *Trump Administration Announces Framework and Leadership for 'Operation Warp Speed'* (May 15, 2020), *available at* https://www.hhs.gov/about/news/2020/05/15/trump-administration-announces-framework-and-leadership-for-operation-warp-speed.html.
[2] *Id.*
[3] *Id.*

- *Development*: Operation Warp Speed will select the most promising countermeasure candidates and provide coordinated government support throughout their development; align protocols for the demonstration of safety and efficacy, which will allow the trials to proceed more quickly; and protocols for the trials will be overseen and set by the federal government.[4]

- *Manufacturing*: The federal government is making investments in manufacturing and distribution at its own risk earlier than usual, giving companies confidence that they can invest in development; manufacturing capacity for selected candidates will be advanced while they are still in development; and manufacturing capacity developed will be used, to the extent practicable, for whatever vaccine is successful, regardless of which companies have developed the capacity.[5]

- *Distribution*: Before the countermeasures are approved or authorized, the program will build the necessary plans and infrastructure for distributing them; Operation Warp Speed will focus on expanding supplies of specialized materials and resources, such as cold-chain supplies, glass vials, and other materials, that can be necessary for distribution of countermeasures; and once a product is ready, the U.S. DoD's involvement will enable faster distribution and administration.[6]

- Among other things, the goal of Operation Warp Speed is to have a significant amount—300 million doses—of safe and effective vaccine for COVID-19 available to Americans by January 2021.[7]

- For the development of vaccines, Operation Warp Speed will select the most promising candidates and provide coordinated government support. As of May 15, 2020, Operation Warp Speed had chosen 14 promising vaccine candidates from the list of over 100 vaccine candidates currently in development. From there, 8 vaccine candidates will be selected from the list of 14 to go through additional testing in early stage small clinical trials. Then, large-scale randomized trials for the demonstration of safety and efficacy will proceed for 3 to 5 of the candidates. Finally, additional non-clinical testing will be performed at the same time when possible.[8]

    - Operation Warp Speed is working to align protocols for the demonstration of safety and efficacy to help clinical trials proceed more quickly. Clinical trial protocols will be overseen by the federal

[4] *Id.*
[5] *Id.*
[6] *Id.*
[7] *Id.*
[8] *Id.*

government rather than the more traditional model where pharmaceutical companies design their own protocols.[9]

- On May 21, 2020, Operation Warp Speed announced that the program was collaborating with the University of Oxford and AstraZeneca to make at least 300 million doses of their COVID-19 vaccine, AZD1222, available to Americans with the initial doses delivered as early as October 2020.[10] The $1.2 billion award from BARDA also includes a Phase 3 clinical trial with 30,000 participants in the U.S. beginning this summer.[11] HHS' funding of other vaccine candidate manufacturers such as Johnson & Johnson and Moderna also support Operation Warp Speed's efforts. This funding is discussed in more detail in Section II of this report.

- For manufacturing of a COVID-19 vaccine, the federal government will make investments in manufacturing and distribution of top vaccine candidates at its own risk—the manufacturing and distribution capacity of the top 3 to 5 leading vaccine candidates will be enhanced while the vaccine candidates are still in development.[12]

  - HHS' agreements with vaccine candidate manufacturers include investments in manufacturing capabilities. These agreements are discussed in more detail in Section II of this report.

  - On June 1, 2020, Emergent BioSolutions announced that they had expanded their 2012 Center for Innovation in Advanced Development and Manufacturing (CIADM) contract with BARDA "to deploy its contract development and manufacturing [organization] (CDMO) capacities, capabilities, and expertise to support the U.S. government's efforts to accelerate delivery of COVID-19 vaccines."[13] Emergent BioSolutions is part of BARDA's CIADM network.[14] The CIADM network is discussed further in Section IV. Under the $628 million

[9] U.S. Department of Health and Human Services, *Fact Sheet: Explaining Operation Warp Speed* (June 16, 2020), *available at* https://www.hhs.gov/about/news/2020/06/16/fact-sheet-explaining-operation-warp-speed.html.
[10] U.S. Department of Health and Human Services, *Trump Administration's Operation Warp Speed Accelerates AstraZeneca COVID-19 Vaccine to be Available Beginning in October* (May 21, 2020), *available at* https://www.hhs.gov/about/news/2020/05/21/trump-administration-accelerates-astrazeneca-covid-19-vaccine-to-be-available-beginning-in-october.html.
[11] *Id.*
[12] U.S. Department of Health and Human Services, *Trump Administration Announces Framework and Leadership for 'Operation Warp Speed'* (May 15, 2020), *available at* https://www.hhs.gov/about/news/2020/05/15/trump-administration-announces-framework-and-leadership-for-operation-warp-speed.html.
[13] Emergent BioSolutions, *Emergent BioSolutions Joins U.S. Government's Warp Speed Program in Landmark Public-Private CDMO Partnership for COVID-19 Vaccine Development and Manufacturing* (June 1, 2020), available at https://investors.emergentbiosolutions.com/node/19601/pdf.
[14] U.S. Department of Health and Human Services, Public Health Emergency, *BARDA leverages CIADM Partner for Development of Plasma-based Therapeutic Treatment for COVID-19, available at* https://www.medicalcountermeasures.gov/newsroom/2020/emergent-plasma/ (last visited on June 18, 2020).

task order, Emergent will use $85.5 million to expand Emergent's viral and non-viral CDMO drug product fill/finish capabilities in Camden and Rockville, and Emergent will use $542.7 million to offer molecule-to-market CDMO services and provide manufacturing capacity.[15]

- The task order creates a U.S.-based manufacturing supply chain for COVID-19 vaccine developers by expanding the original contract with BARDA establishing Emergent's Baltimore Bayview facility as a CIADM to include investments in Emergent's Rockville and Baltimore Camden facilities.[16]

- Currently, the Camden facility has two non-viral fill/finish lines and the Rockville facility has one viral fill/finish line. In 2021, Emergent will introduce a third fill/finish non-viral line at the Camden facility and a second high-speed fill/finish line for viral at the Rockville facility.

- Emergent's Bayview facility has capabilities across four independent suites to produce at clinical scale and can scale up to enable large-scale manufacturing to up to 4000L to prepare for production of commercial volumes.[17] The Bayview CIADM has the ability to produce tens to hundreds of millions of doses of vaccine depending on the platform technology being used.[18]

- For distribution of a COVID-19 vaccine, Operation Warp Speed is building the requisite plans and infrastructure to distribute a vaccine to hundreds of millions of Americans in a timely manner. Once a vaccine candidate is ready for distribution, the DoD will help distribute and administer the vaccine candidate.[19]

  - In May 2020, the DoD awarded ApiJect Systems of America a $138 million contract to expand U.S. production capability for domestically manufactured, medical-grade injection devices starting by October

[15] Emergent BioSolutions, *Emergent BioSolutions Joins U.S. Government's Warp Speed Program in Landmark Public-Private CDMO Partnership for COVID-19 Vaccine Development and Manufacturing* (June 1, 2020), available at https://investors.emergentbiosolutions.com/node/19601/pdf.
[16] *Id*.
[17] Emergent, *News Release: Emergent BioSolutions Signs Agreement to be U.S. Manufacturing Partner for Johnson & Johnson's Lead Vaccine Candidate for COVID-19* (Apr. 23, 2020), *available at* https://investors.emergentbiosolutions.com/news-releases/news-release-details/emergent-biosolutions-signs-agreement-be-us-manufacturing.
[18] *Id*.
[19] U.S. Department of Health and Human Services, *Trump Administration Announces Framework and Leadership for 'Operation Warp Speed'* (May 15, 2020), *available at* https://www.hhs.gov/about/news/2020/05/15/trump-administration-announces-framework-and-leadership-for-operation-warp-speed.html.

2020.[20] The agreement will support "Project Jumpstart"—an initiative designed to create a domestic supply chain for prefilled syringes with the use of a Blow-Fill-Seal (BFS) aseptic plastics manufacturing technology. The goal of Project Jumpstart is to enable the manufacture of more than 100 million prefilled syringes for distribution across the U.S. by the end of 2020, and more than 500 million in 2021.[21] The contract also enables RAPID USA, a consortium that was founded as a public-private partnership between the U.S. Assistant Secretary for Preparedness and Response (ASPR), the Strategic National Stockpile (SNS), and ApiJect Systems America, to build a network of 30 U.S.-based BFS manufacturing lines.[22]

- On June 8, 2020, SiO2 Materials Science announced that it received a $143 million contract from BARDA to help accelerate the scale-up of the company's primary packaging platform, which includes vials and syringes, for storing COVID-19 vaccines and therapeutics.[23] The patented material that SiO2 Materials Science uses "is a combination of a plastic container with a microscopic, thin, undetectable to the naked eye, pure glass coating for biological drugs and vaccines."[24]

- On June 9, 2020, Corning announced that it had received $204 million in funding to expand domestic manufacturing capacity of Corning Valor Glass vials to support the vaccination of billions of patients as part of Operation Warp Speed.[25]

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[20] U.S. Department of Defense, *DOD Awards $138 Million Contract, Enabling Prefilled Syringes for Future COVID-19 Vaccine* (May 12, 2020), available at https://www.defense.gov/Newsroom/Releases/Release/Article/2184808/dod-awards-138-million-contract-enabling-prefilled-syringes-for-future-covid-19/source/GovDelivery/.

[21] *Id*.

[22] ApiJect Systems Corp., *ApiJect Awarded HHS-DOD Title 3, Defense Production Act (DPA) Contract of $138 Million in Support of a Joint Federal Agency Accelerated Build-out of Domestic Surge Capacity for a High-Speed, Population-Scale Emergency Drug Injection Solution* (May 12, 2020), *available at* https://www.prnewswire.com/news-releases/apiject-awarded-hhs-dod-title-3-defense-production-act-dpa-contract-of-138-million-in-support-of-a-joint-federal-agency-accelerated-build-out-of-domestic-surge-capacity-for-a-high-speed-population-scale-emergency-drug-injecti-301058125.html; Rapid USA, *Bridging the Gap in Pandemic Response*, *available at* https://www.rapidusa.com/ (last visited Jun. 17, 2020).

[23] Ben Hargreaves, *U.S. government doubles down with $143m syringe investment*, BIOPHARMA REPORTER (June 9, 2020), *available at* https://www.biopharma-reporter.com/Article/2020/06/09/US-government-invests-in-SiO2-syringes.

[24] SiO2 Materials Science, *SiO2 Materials Science Receives $143 Million Contract from U.S. Government to Accelerate Capacity Scale-Up of Advanced Primary Packaging Platform for COVID-19 Vaccines and Therapeutics*, BUSINESS WIRE (June 8, 2020), *available at* https://www.businesswire.com/news/home/20200608005120/en/SiO2-Materials-Science-Receives-143-Million-Contract.

[25] Corning, *Corning Valor Glass Selected to Help Accelerate Delivery of COVID-19 Vaccines and Drugs* (June 9, 2020), *available at* https://www.corning.com/worldwide/en/about-us/news-events/news-releases/2020/06/us-departments-of-defense-health-human-services-select-corning-valor-glass-packaging-to-accelerate-delivery-of-covid-19-vaccines.html.

C. Efforts led by the National Institutes of Health (NIH)

- The NIH is engaged in several efforts to respond to the COVID-19 pandemic, including, but not limited to, accelerating the development and manufacturing of COVID-19 treatment options and vaccines.

- On April 17, 2020, the NIH announced the ACTIV public-private partnership to speed vaccine and treatment options. The ACTIV partnership is coordinated by the Foundation for the National Institutes of Health (FNIH) and brings together: (1) other divisions of HHS, including BARDA, CDC, and FDA; (2) other government agencies, including the DoD and the U.S. Department of Veterans Affairs; (3) the European Medicines Agency (EMA); and (4) representatives from academia, philanthropic organizations, and several biopharmaceutical companies.[26]

    - The ACTIV partnership will develop a collaborative framework for prioritizing vaccine and drug candidates, streamlining clinical trials, coordinating regulatory processes, and/or leveraging assets among all partners to rapidly respond to the COVID-19 pandemic.[27] ACTIV has four working groups, each with one co-chair from NIH and one from industry: (1) The Preclinical Working Group; (2) The Therapeutics Clinical Working Group; (3) The Clinical Trial Capacity Working Group; and (4) The Vaccines Working Group.[28]

        - *The Preclinical Working Group* is "charged to standardize and share preclinical evaluation resources and methods and accelerate testing of candidate therapies and vaccines to support entry into clinical trials."[29] The goals of this working group are to increase access to animal models and identify informative assays.[30]

        - *The Therapeutics Clinical Working Group* is "charged to prioritize and accelerate clinical evaluation of a long list of therapeutic candidates for COVID-19 with near-term potential."[31] The goals of this working group are to prioritize and test potential therapeutic agents and develop master protocol for clinical trials.[32]

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[26] National Institutes of Health, *Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV), available at* https://www.nih.gov/research-training/medical-research-initiatives/activ (last visited June 14, 2020).
[27] National Institutes of Health, *NIH to launch public-private partnership to speed COVID-19 vaccine and treatment options* (Apr. 17, 2020), *available at* https://www.nih.gov/news-events/news-releases/nih-launch-public-private-partnership-speed-covid-19-vaccine-treatment-options.
[28] Francis S. Collins, MD, PhD, Paul Stoffels, MD, *Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV), An Unprecedented Partnership for Unprecedented Times*, JAMA NETWORK (May 18, 2020), *available at* https://jamanetwork.com/journals/jama/fullarticle/2766371?guestAccessKey=5defc755-e585-47e5-b79a-fee2ec2dd42b&utm_source=For_The_Media&utm_medium=referral&utm_campaign=ftm_links&utm_content=tfl&utm_term=051820.
[29] *Id.*
[30] *Id.*
[31] *Id.*
[32] *Id.*

- *The Clinical Trial Capacity Working Group* is "charged with assembling and coordinating existing networks of clinical trials to increase efficiency and build capacity."[33] The goals of this working group are to develop survey instruments, develop inventory of clinical trial networks, and guide deployment of innovative solutions.[34]

- *The Vaccines Working Group* is "charged to accelerate evaluation of vaccine candidates to enable rapid authorization or approval."[35] The goals of this working group are to accelerate evaluation of vaccine candidates, identify biomarkers to speed approval, and provide evidence to address safety concerns.[36] Among other things, the ACTIV partnership's Vaccines Working Group is developing a harmonized master protocol for adaptive trails of multiple vaccine candidates, developing a trial network that potentially could enroll as many as 100,000 volunteers, and identify biomarkers to speed the authorization or approval of a vaccine candidate.[37]

- The National Institute of Allergy and Infectious Diseases (NIAID) of the NIH is engaged in numerous efforts to respond to the COVID-19 pandemic, including supporting clinical research to prevent, treat, and better understand COVID-19.[38]

- The National COVID Cohort Collaborative (N3C), funded by the NIH's National Center for Advancing Translational Sciences (NCATS), "aims to build a centralized national data resource—the NCATS N3C Data Enclave—that the research community can use to study COVID-19 and identify potential treatments as the pandemic continues to evolve. Specifically, the N3C will enable the rapid collection and analysis of clinical, laboratory and diagnostic data from hospitals and health care plans."[39]

    - The N3C uses NCATS-supported resources of Clinical and Translational Science Award Program hubs and the National Center for Data to Health to speed research and clinical care efforts at local, regional, and national levels.[40] The N3C will collect data from the electronic health records [EHR] of people who were tested for COVID-19 or who had related systems and the data will be harmonized and then managed in a way that maintains the data's validity while protecting patient privacy.[41]

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[33] *Id.*
[34] *Id.*
[35] *Id.*
[36] *Id.*
[37] *Id.*
[38] National Institute of Allergy and Infectious Diseases (NIAID), *NIAID COVID-19 Clinical Research, available at* https://www.niaid.nih.gov/diseases-conditions/covid-19-clinical-research (last visited June 14, 2020).
[39] National Institutes of Health, National Center for Advancing Translational Sciences, *About the National COVID Cohort Collaborative, available at* https://ncats.nih.gov/n3c/about (last visited on June 15, 2020).
[40] *Id.*
[41] *Id.*

- The goals of the N3C are to "1) to create a robust data pipeline to harmonize EHR data into a common data model; 2) to make it fast and easy for the clinical and research community to access a wealth of COVID-19 clinical data and use it to research COVID-19 and identify effective interventions as the pandemic continues to evolve; 3) to establish a resource for the next 5 years to understand long-term health impact of COVID-19; and 4) to create a state-of-the-art analytics platform to enable novel analyses that will serve to address COVID-19 as well as to demonstrate that this collaborative analytics approach could be invaluable for addressing other diseases in the future."[42]

D. Efforts led by the U.S. Food and Drug Administration (FDA)

- In April, FDA launched the Coronavirus Treatment Acceleration Program (CTAP), an emergency program for possible therapies, to use every available method to move new treatments to patients as soon as possible, while at the same time finding out whether they are helpful or harmful.[43]

  - As of April 16, 2020, FDA had received 950 inquiries and proposals for COVID-19 related drug development.[44] Examples of CTAP in action include:

    - "Immediately upon receipt, triaged requests from developers and scientists seeking to develop or evaluate new drug and biologic therapies, getting the right FDA staff in touch with them and the work to get studies going fast. With a first wave of requests behind us, FDA will generally respond within a day."

    - "Provided ultra-rapid, interactive input on most development plans. Interactions have generally been prioritized based on a product's scientific merits, stage of development, and identification as a possible priority product in consensus USG documents."

    - "Provided ultra-rapid protocol review – within 24 hours of submission, in some cases."

    - "Completed review of single patient expanded access requests around-the-clock – and generally within 3 hours."

[42] National Institutes of Health, National Center for Advancing Translational Sciences, *National COVID Cohort Collaborative Frequently Asked Questions, available at* https://ncats.nih.gov/n3c/about/program-faq.
[43] Stephen M. Hahn, M.D., Commissioner of Food and Drugs, Peter Marks, M.D., Ph.D., Director, Center for Biologics Evaluation and Research and Janet Woodcock, M.D., Director, Center for Drug Evaluation and Research, FDA, *The Path Forward: Coronavirus Treatment Acceleration Program* (Apr. 20, 2020), *available at* https://www.fda.gov/news-events/fda-voices-perspectives-fda-leadership-and-experts/path-forward-coronavirus-treatment-acceleration-program.
[44] U.S. Food and Drug Administration, *Coronavirus Treatment Acceleration Program (CTAP), available at* https://www.fda.gov/drugs/coronavirus-covid-19-drugs/coronavirus-treatment-acceleration-program-ctap (last visited on June 29, 2020).

        - "Worked closely with applicants and other regulatory agencies to expedite quality assessments for products to treat COVID-19 patients and to transfer manufacturing to alternative or new sites to avoid supply disruption."[45]

    - As of May 11, 2020, there are 144 active trials of therapeutic agents, and another 457 development programs for therapeutic agents in the planning stages.[46]

- As of June 19, 2020, FDA is working with at least 16 sponsors that are in the process of trying to develop a COVID-19 vaccine.[47]

- At a hearing before the Committee on Energy and Commerce on June 23, 2020, FDA Commissioner Dr. Stephen Hahn testified that FDA is "working with the sponsors across the board – private industry, Operation Warp Speed, et cetera – those who are developing vaccines, and [FDA is] providing technical assistance regarding clinical trial design, the number of participants in the clinical trials, as well as the endpoints that [FDA] want[s] to see to make an adjudication about safety and effectiveness."[48]

- The FDA provided new guidance in May with recommendations for innovators and researchers to help accelerate the development of prevention and treatment options for COVID-19.[49] The guidance aims "to make the process for submitting applications to initiate studies for new drugs and biological products more efficient and outline recommendations for ways to design clinical trials to evaluate safety and effectiveness of these medical products for COVID-19."[50]

    - The COVID-19 Public Health Emergency: General Considerations for Pre-IND Meeting Requests for COVID-19 Related Drugs and Biological Products guidance "outlines a more efficient process for developers to receive agency feedback on their supporting data with the goal of starting clinical trials as soon as possible."[51]

    - The COVID-19: Developing Drugs and Biological Products for Treatment or Prevention guidance "provides the FDA's current recommendations on later

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[45] *Id.*
[46] *Id.*
[47] U.S. Food and Drug Administration, *Answers to Questions Submitted by Members, Energy and Commerce Committee Briefing on April 21, 2020, FDA Commissioner Stephen Hahn, M.D.* (Jun. 19, 2020) (on file with Committee).
[48] *Oversight of the Trump Administration's Response to the COVID-19 Pandemic: Hearing Before the H. Comm. On Energy and Commerce*, 116th Cong., Preliminary Transcript at 58 (Jun. 23, 2020).
[49] U.S. Food and Drug Administration, *Coronavirus (COVID-19) Update: FDA Takes New Actions to Accelerate Development of Novel Prevention, Treatment Options for COVID-19* (May 11, 2020), *available at* https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-takes-new-actions-accelerate-development-novel-prevention-treatment.
[50] *Id.*
[51] *Id.*

stage clinical trials intended to establish safety and effectiveness for COVID-19 products. The guidance outlines critical sponsor considerations such as appropriate patient selection, including the evaluation of therapies in patients at high risk of complications from COVID-19 (e.g., the elderly). In addition, the guidance helps sponsors to understand how to design their trials, including considerations of study duration, assessment of efficacy and monitoring for safety."[52]

- The FDA's Center for Biologics Evaluation and Research (CBER) is addressing the COVID-19 pandemic in multiple ways, including, but not limited to, "[e]xpediting clinical trials for preventive vaccines and other therapeutic biological products," and "[s]upporting product development and scaling up of manufacturing capacity for high priority products for COVID-19."[53]

- On June 30, 2020, CBER issued guidance for industry with recommendations for entities developing COVID-19 vaccines with the goal of licensing the vaccine candidate.[54] The guidance describes the "agency's current recommendations regarding the data needed to facilitate the manufacturing, clinical development, and approval of a COVID-19 vaccine."[55] Among other things, the guidance outlines key considerations to satisfy regulatory requirements for: (1) chemistry, manufacturing, and controls (CMC) for COVID-19 vaccines; (2) nonclinical data through development and licensure of COVID-19 vaccines; (3) clinical data through development and licensure of COVID-19 vaccines; (4) post-licensure safety evaluation of COVID-19 vaccines; and (5) additional considerations for COVID-19 vaccine development and licensure.[56]

    - For clinical trials, the guidance provides key considerations regarding trial populations, trial design, efficacy considerations, statistical considerations, and safety considerations. The guidance notes that, because the current understanding of COVID-19 immunology is limited and evolving, "the goal of development programs should be to pursue traditional approval via direct evidence of vaccine efficacy in protecting humans from SARS-CoV-2 infection and/or disease."[57] Among other things, with respect to clinical trials, the guidance also states that:

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[52] *Id*.
[53] U.S. Food and Drug Administration, *Coronavirus (COVID-19): CBER-Regulated Biologics*, *available at* https://www.fda.gov/vaccines-blood-biologics/industry-biologics/coronavirus-covid-19-cber-regulated-biologics (last visited Jun. 19, 2020).
[54] U.S. Food and Drug Administration, *Guidance for Industry: Development and Licensure of Vaccines to Prevent COVID-19* (Jun. 2020), *available at* https://www.fda.gov/media/139638/download.
[55] Email from FDA Office of Legislation to Energy and Commerce Committee staff, *FDA Coronavirus (COVID-19) Update: FDA Takes Action to Help Facilitate Timely Development of Safe, Effective COVID-19 Vaccines* (Jun. 30, 2020) (on file with Committee).
[56] U.S. Food and Drug Administration, *Guidance for Industry: Development and Licensure of Vaccines to Prevent COVID-19*, at i (Jun. 2020), *available at* https://www.fda.gov/media/139638/download.
[57] *Id*. at 9.

- "FDA encourages the inclusion of diverse populations in all phases of vaccine clinical development … [to help] ensure that vaccines are safe and effective for everyone in the indicated populations."[58] The agency also "strongly encourages the enrollment of populations most affected by COVID-19, specifically racial and ethnic minorities."[59]

- "Later phase trials, including efficacy trials, should be randomized, double-blinded, and placebo controlled," and the guidance "discusses the importance of ensuring that the sizes of clinical trials are large enough to demonstrate the safety and effectiveness of a vaccine."[60]

- "To ensure that a widely deployed COVID-19 vaccine is effective, the primary efficacy endpoint point estimate for a placebo-controlled efficacy trial should be at least 50%," thereby conveying that "FDA would expect that a COVID-19 vaccine would prevent disease or decrease its severity in at least 50% of people who are vaccinated."[61]

  - The guidance notes that, once there is a better understanding of COVID-19 immunology, accelerated approval of a COVID-19 vaccine may be available via FDA's Accelerated Approval pathway for vaccine licensure.[62] The guidance also discusses the use of an Emergency Use Authorization (EUA) for a COVID-19 vaccine.[63]

- When the FDA issued guidance on June 30, 2020 on the development and licensure of vaccines to prevent COVID-19, both FDA Commissioner Dr. Stephen Hahn and Peter Marks, director of CBER, released statements highlighting the importance of expediting vaccine development without sacrificing the FDA's standards for quality, safety, and efficacy.[64]

  - For example, Commissioner Hahn stated: "We recognize the urgent need to develop a safe and effective vaccine to prevent COVID-19 and continue to work collaboratively with industry, researchers, as well as federal, domestic,

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[58] *Id*. at 11.
[59] *Id*.
[60] *Id*. at 12; Email from FDA Office of Legislation to Energy and Commerce Committee staff, *FDA Coronavirus (COVID-19) Update: FDA Takes Action to Help Facilitate Timely Development of Safe, Effective COVID-19 Vaccines* (Jun. 30, 2020) (on file with Committee).
[61] U.S. Food and Drug Administration, *Guidance for Industry: Development and Licensure of Vaccines to Prevent COVID-19*, at 14 (Jun. 2020), *available at* https://www.fda.gov/media/139638/download; Email from FDA Office of Legislation to Energy and Commerce Committee staff, *FDA Coronavirus (COVID-19) Update: FDA Takes Action to Help Facilitate Timely Development of Safe, Effective COVID-19 Vaccines* (Jun. 30, 2020) (on file with Committee).
[62] U.S. Food and Drug Administration, *Guidance for Industry: Development and Licensure of Vaccines to Prevent COVID-19*, at 18 (Jun. 2020), *available at* https://www.fda.gov/media/139638/download.
[63] *Id*. at 19.
[64] Email from FDA Office of Legislation to Energy and Commerce Committee staff, *FDA Coronavirus (COVID-19) Update: FDA Takes Action to Help Facilitate Timely Development of Safe, Effective COVID-19 Vaccines* (Jun. 30, 2020) (on file with Committee).

and international partners to accelerate these efforts. While the FDA is committed to expediting this work, we will not cut corners in our decisions and are making clear through this guidance what data should be submitted to meet our regulatory standards. This is particularly important, as we know that some people are skeptical of vaccine development efforts… We have not lost sight of our responsibility to the American people to maintain our regulatory independence and ensure our decisions related to all medical products, including COVID-19 vaccines, are based on science and the available data."[65]

- Similarly, Dr. Peter Marks stated: "In this particular crisis in which there is so much at stake, we need to help expedite vaccine development as much as we can without sacrificing our standards for quality, safety, and efficacy. We firmly believe that transparency regarding the FDA's current thinking about the scientific data needed to support approval of safe and effective COVID-19 vaccines will help build public confidence in the FDA's evaluation process, which will be critical in ensuring their use…. Right now, neither the FDA nor the scientific community can predict how quickly data will be generated from vaccine clinical trials. Once data are generated, the agency is committed to thoroughly and expeditiously evaluating it all. But make no mistake: the FDA will only approve or make available a COVID-19 vaccine if we determine that it meets the high standards that people have come to expect of the agency."[66]

- An initiative launched by the Reagan-Udall Foundation for the FDA, in collaboration with Friends of Cancer Research—The COVID-19 Evidence Accelerator—was created "to provide a unique venue for major data organizations, government and academic researchers, and health systems to gather and design quick-turn-around queries and share their results."[67] The COVID-19 Evidence Accelerator has two components: 1) The Diagnostics Evidence Accelerator; and 2) The Therapeutics Evidence Accelerator. There are two interactive workstreams within the Therapeutics Evidence Accelerator, the Therapeutics Evidence Accelerator Collaborative and the Therapeutics Evidence Accelerator Parallel Analysis Workgroup.[68]

    - Through the Therapeutics Evidence Accelerator Collaborative, "[i]nterested data partners share findings on critical questions during Therapeutics Evidence Accelerator Lab Meetings. Results are generated and analyzed in many different ways and using different methods and data sources. Lab meetings provide a venue for scientists across the country to discuss data generated from quick turnaround queries and share results with peers and experts from FDA, major data organizations, academic research institutions, professional societies, and health systems to help accelerate, and potentially

[65] *Id.*
[66] *Id.*
[67] COVID-19 Evidence Accelerator, Reagan-Udall Foundation for the Food and Drug Administration, Friends of Cancer Research, *available at* https://www.evidenceaccelerator.org/.
[68] Therapeutics Evidence Accelerator, Reagan-Udall Foundation for the Food and Drug Administration, Friends of Cancer Research, *available at* https://evidenceaccelerator.org/therapeutics-evidence-accelerator/about.

even confirm, findings from different data sources and leverage existing expertise."[69]

- The Therapeutics Evidence Accelerator Parallel Analysis Workgroup "worked closely with FDA to develop key research questions that multiple organizations and teams can address simultaneously. Initial activities of this work stream include (1) rapidly revising a list of core data elements; (2) identifying those critical to answering the primary question; and (3) establishing uniform collection parameters."[70]

E. Efforts led by the Biomedical Advanced Research and Development Authority (BARDA)

- BARDA, which is part of the ASPR, was established to help protect the country from chemical, biological, radiological, and nuclear threats, and also from pandemic influenza and emerging infectious diseases.[71] To respond to the COVID-19 pandemic, BARDA is rapidly developing new partnerships and building a robust COVID-19 Medical Countermeasure Portfolio, among other things.[72] These partnerships are focused on vaccines, diagnostics, therapeutics, rapidly deployable capabilities, and other items.[73]

  - As of June 29, 2020, BARDA's COVID-19 Medical Countermeasure Portfolio with respect to vaccines includes: (1) ModernaTX, Inc. for SARS-CoV-2 mRNA-1273 vaccine; (2) AstraZeneca for AZD1222; (3) Janssen Research & Development, LLC, a Johnson & Johnson company, for Viral Vector Vaccine for COVID-19; (4) Merck and IAVI for rVSVΔG-CoV2; and (5) Protein Sciences, a Sanofi company for Recombinant SARS-CoV-2 Protein Vaccine Candidate.[74] BARDA has provided more than $2.2 billion in funding for these efforts.

  - As of June 29, 2020, BARDA's COVID-19 Medical Countermeasure Portfolio with respect to therapeutics includes: (1) AstraZeneca for AstraZeneca SARS-CoV-2 monoclonal antibody combination; (2) Genentech USA, Inc. for MSTT1041A (anti-ST2) and UTTR1147A (IL-22Fc); (3) Grifols Shared Services North America, Inc. (Grifols) for convalescent plasma and hyperimmune globulin; (4) CIADM at Emergent BioSolutions for human immune Globulin for COVID-19 (COVID-19 HIG); (5) SAb Biotherapeutics, Inc. for SAB-185; (6) Genentech USA, Inc. for ACTEMRA (tocilizumab); (7)

[69] *Id.*
[70] *Id.*
[71] U.S. Department of Health and Human Services, *Biomedical Advanced Research and Development Authority*, *available at* https://www.phe.gov/about/barda/Pages/default.aspx (last visited June 13, 2020).
[72] U.S. Department of Health and Human Services, *BARDA's Rapidly Expanding COVID-19 Medical Countermeasure Portfolio*, *available at* https://www.medicalcountermeasures.gov/app/barda/coronavirus/COVID19.aspx (last visited June 29, 2020). This page is updated regularly but may not include all awards.
[73] *Id.*
[74] *Id.*

Regeneron Pharmaceuticals, Inc. for Sarilumab; (8) Janssen Research & Development, LLC for SARS-CoV-2 therapeutic drug screening efforts; and (9) Regeneron Pharmaceuticals, Inc. for REGN-COV2 (SARS-CoV-2 specific monoclonal antibodies).[75] BARDA has provided more than $495 million in funding for these efforts.[76]

- BARDA is also supporting other COVID-19 initiatives including, but not limited to, Operation Warp Speed and the ACTIV partnership.

F. Efforts led by the Centers for Medicare and Medicaid Services (CMS)

- In order to increase data to study treatment of COVID-19, on April 20, 2020, CMS announced that clinicians who participate in the Quality Payment Program (QPP) may now earn credit in the Merit-based Incentive Payment System, a performance-based track QPP that incentivizes quality and value, for participation in a clinical trial and reporting clinical information by attesting to the new *COVID-19 Clinical Trials* improvement activity.[77] This will help to gather actionable data to better understand the virus, improve patient care, and accelerate the development of new treatments.
    - The Executive Branch, Congress, and the private sector should further explore ways to incentivize providers to collect and report actionable data to better understand the virus, improve patient care, and accelerate the development of new treatments.

G. Efforts led by Congress

- Congress has provided funding to support COVID-19 medical countermeasure development broadly, including the development of vaccines, therapeutics, and diagnostics.
    - In the Coronavirus Preparedness and Response Supplemental Appropriations Act, enacted on March 6, 2020, Congress provided funding to multiple components within HHS for the development of COVID-19 vaccines, diagnostics, and therapeutics.[78] This includes, among other things, $3.1 billion in funding for the Public Health and Social Services Emergency Fund to prevent, prepare for, and respond to COVID-19, including the development of necessary countermeasures and vaccines, prioritizing platform-based technologies with U.S.-based manufacturing capabilities, and the purchase of

[75] *Id.*
[76] *Id.*
[77] CMS, *Trump Administration Champions Reporting of COVID-19 Clinical Trial Data through Quality Payment Program, Announces New Clinical Trials Improvement Activity* (Apr. 20, 2020), *available at* https://www.cms.gov/newsroom/press-releases/trump-administration-champions-reporting-covid-19-clinical-trial-data-through-quality-payment.
[78] Coronavirus Preparedness and Response Supplemental Appropriations Act, 2020 (P.L. 116-123), enacted on March 6, 2020.

vaccines, therapeutics, diagnostics, necessary medical supplies, medical surge capacity, and related administrative activities.[79]

- In the Coronavirus Aid, Relief, and Economic Security Act (CARES Act), enacted on March 27, 2020, Congress providing funding to multiple components within HHS for the development, manufacturing, and purchase of COVID-19 vaccines, diagnostics, and treatments.[80] This includes, among other things, $11 billion in funding for the Public Health and Social Services Emergency Fund to support the manufacturing, production, and purchase of vaccines, therapeutics, diagnostics, and other medical or preparedness needs. The CARES Act also expands coverage of COVID-19 diagnostics to include tests approved by state labs and developed by Clinical Laboratory Improvement Amendments (CLIA) labs before they get an emergency use authorization (EUA) from FDA, and mandates timely commercial insurance coverage of COVID-19 vaccines or preventive treatments in commercial plan. Coverage is provided for any future vaccine under Medicare Part B exempt from the deductible and at no cost in the Medicaid program. The law also provides a state option to provide vaccine coverage for the uninsured through the Medicaid program.

## II. Vaccines

A. What vaccines are under development? What platform is being used and what is the anticipated timeline for clinical trials and production?

- According to World Health Organization (WHO), there were 149 vaccine candidates in development and 17 vaccine candidates in clinical trials as of June 29, 2020.[81] According to the Biotechnology Innovation Organization's (BIO) COVID-19 Therapeutic Development Tracker, U.S. institutions are working on the highest number of COVID-19 vaccine candidates, accounting for 65 vaccine candidates on the list as of June 23, 2020.[82] Many other vaccines in development are expected to begin clinical trials in 2020.

    - The vaccine candidates in clinical trials are in various stages—currently ranging from Phase 1 to Phase 3 according to the WHO.[83] Recently, Dr. Anthony Fauci of NIAID said that the federal government plans to fund and conduct Phase 3 clinical trials later this summer for three vaccine candidates

[79] *Id*.
[80] Coronavirus Aid, Relief, and Economic Security Act (P.L. 116-136), enacted on March 27, 2020.
[81] World Health Organization, *DRAFT landscape of COVID-19 candidate vaccines* (June 29, 2020), *available at* https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines.
[82] Biotechnology Innovation Organization (BIO), *BIO COVID-19 Therapeutic Development Tracker*, *available at* https://www.bio.org/policy/human-health/vaccines-biodefense/coronavirus/pipeline-tracker (last visited June 29, 2020).
[83] World Health Organization, *DRAFT landscape of COVID-19 candidate vaccines* (June 29, 2020), *available at* https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines.

currently in development, including the vaccine candidates being developed by Moderna, AstraZeneca, and Johnson & Johnson.[84]

- Phase 3 clinical trials generally are used to confirm a product's safety and effectiveness across a wide range of populations. Phase 3 clinical trials are the "most time-consuming step in testing, because researchers have to wait for enough participants to be exposed to a virus naturally."[85]

- The COVID-vaccine candidates are being manufactured using a variety of different platforms, with some researchers and manufacturers using more traditional technologies while others are using more innovative, newer platforms such as DNA- and RNA- based platforms. According to BIO, as of June 23, 2020, there are 65 COVID-19 vaccine candidates that are protein-based vaccines, 19 that are viral-based vaccines, 18 that are rViral-based vaccines, 22 that are RNA-based vaccines, 16 that are DNA-based vaccines, 11 that are cell-based vaccines, and 4 that are nanoparticle vaccines.[86]

- Congress and the Executive Branch should continue to promote innovative manufacturing technologies for vaccine candidates, such as advanced manufacturing technologies, through enhanced funding and authorities, if needed.

- As previously mentioned in Section I of this report, Operation Warp Speed aims to have a vaccine ready for use by the general public by January 2021.[87]

  - Some experts have argued that this timeline is too optimistic and believe that the earliest possible date that a COVID-19 vaccine will be available to the general public is the spring of 2021.[88]

  - At a hearing held by the Committee on Energy and Commerce on June 23, 2020, Dr. Fauci testified he was "cautiously optimistic" that, if we are going to have a vaccine, a vaccine could be available by the very beginning of

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[84] Peter Loftus, *Coronavirus Vaccine Candidates' Pivotal U.S. Testing to Start This Summer*, THE WALL STREET JOURNAL (June 10, 2020), *available at* https://www.wsj.com/articles/coronavirus-vaccine-candidates-pivotal-u-s-testing-to-start-this-summer-11591781405?mod=hp_lead_pos1; Jim Sciutto, et al., *U.S. government to fund and conduct studies on three possible coronavirus vaccines, Fauci says*, CNN (Jun. 10, 2020), *available at* https://www.cnn.com/2020/06/10/politics/vaccine-trials-funding/index.html.

[85] Bob Holmes, *The Time of Trials: Waiting for a Coronavirus Vaccine*, DISCOVER MAGAZINE (May 27, 2020), *available at* https://www.discovermagazine.com/health/the-time-of-trials-waiting-for-a-coronavirus-vaccine.

[86] Biotechnology Innovation Organization, *BIO COVID-19 Therapeutic Development Tracker, available at* https://www.bio.org/policy/human-health/vaccines-biodefense/coronavirus/pipeline-tracker (last visited June 29, 2020).

[87] U.S. Department of Health and Human Services, *Trump Administration Announces Framework and Leadership for 'Operation Warp Speed'* (May 15, 2020), *available at* https://www.hhs.gov/about/news/2020/05/15/trump-administration-announces-framework-and-leadership-for-operation-warp-speed.html.

[88] Bob Holmes, *The Time of Trials: Waiting for a Coronavirus Vaccine*, DISCOVER MAGAZINE (May 27, 2020), *available at* https://www.discovermagazine.com/health/the-time-of-trials-waiting-for-a-coronavirus-vaccine.

2021.[89] Dr. Fauci said he was "cautiously optimistic" that "we will be successful in getting a vaccine" because "the early data that we are seeing regarding the immunogenicity and the induction of good responses makes [him] cautiously optimistic, always knowing that there is never a guarantee."[90]

- Some experts have raised concerns that reduced community infection rates may make Phase 3 clinical trials more challenging and potentially prolong the timeline.[91] The infection rates may, however, increase in certain parts of the world in the coming months. For example, the *Wall Street Journal* reported on June 23, 2020, that there were new daily records of infections in some states across the United States.[92]

- To help accelerate the development and manufacture of a vaccine for COVID-19, the U.S. government is supporting several different vaccine candidates. As noted in Section I.E of this report, the vaccine candidates that have received more than $2.2 billion in funding from BARDA as of June 29, 2020, include candidates being developed by: (1) ModernaTX, Inc.; (2) AstraZeneca; (3) Janssen Research & Development, LLC, a Johnson & Johnson company; (4) Merck and IAVI; and (5) Protein Sciences, a Sanofi company.[93]

  - **Moderna.** ModernaTX, Inc. is developing a COVID-19 vaccine candidate, mRNA-1273, in collaboration with NIAID.[94] The vaccine candidate is currently in Phase 2 clinical trials.

    - The Moderna/NIAID vaccine candidate "is an mRNA [messenger RNA] vaccine against the novel coronavirus encoding for a prefusion stabilized form of the Spike (S) protein, which was designed by Moderna in collaboration with NIAID."[95] According to Moderna, developing a vaccine with an innovative mRNA vaccine technology

[89] *Oversight of the Trump Administration's Response to the COVID-19 Pandemic: Hearing Before the H. Comm. On Energy and Commerce*, 116th Cong., Preliminary Transcript, at 69 (Jun. 23, 2020).
[90] *Id.*
[91] GlobalData Healthcare, *COVID-19 vaccines may only need to reach lowest bar for approval*, CLINICAL TRIALS ARENA (May 19, 2020), *available at* https://www.clinicaltrialsarena.com/comment/covid-19-vaccine-efficacy-approval/.
[92] Talal Ansari, *Coronavirus Cases Hit Daily Records in Some U.S. States*, THE WALL STREET JOURNAL (Jun. 23, 2020), *available at* https://www.wsj.com/articles/coronavirus-latest-news-06-23-2020-11592901807.
[93] U.S. Department of Health and Human Services, *BARDA's Rapidly Expanding COVId-19 Medical Countermeasure Portfolio*, *available at* https://www.medicalcountermeasures.gov/app/barda/coronavirus/COVID19.aspx (last visited June 14, 2020).
[94] Moderna, *Moderna Announced Positive Interim Phase 1 Data for its mRNA Vaccine (mRNA-1273) Against Novel Coronavirus* (May 18, 2020), *available at* https://investors.modernatx.com/news-releases/news-release-details/moderna-announces-positive-interim-phase-1-data-its-mrna-vaccine.
[95] National Institutes of Health (NIH), *NIH clinical trial of investigational vaccine for COVID-19* (Mar. 16, 2020), *available at* https://www.nih.gov/news-events/news-releases/nih-clinical-trial-investigational-vaccine-covid-19-begins; Moderna, *Moderna Ships mRNA Vaccine Against Novel Coronavirus (mRNA-1273) for Phase 1 Study* (Feb. 24, 2020), *available at* https://investors.modernatx.com/news-releases/news-release-details/moderna-ships-mrna-vaccine-against-novel-coronavirus-mrna-1273.

"offers potential advantages in efficacy, speed of development, and production scalability and reliability."[96]

- The first clinical batch of the vaccine candidate—which was funded by the Coalition for Epidemic Preparedness Innovations (CEPI)—was completed on February 7, 2020, and it was shipped to NIH on February 2, 2020, just 42 days from sequence selection.[97] NIAID and Moderna were able to develop the vaccine candidate so quickly because of prior research on related coronaviruses that cause severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS).[98]

- The Moderna/NIAID vaccine candidate was the first vaccine candidate in the U.S. to enter clinical trials. The Phase 1 clinical trial began on March 16, 2020, at Kaiser Permanente Washington Health Research Institute in Seattle, Washington.[99] On May 18, 2020, Moderna announced positive interim Phase 1 data for its vaccine candidate, and stated that it planned to begin the Phase 3 trial in July.[100] Moderna announced on May 29, 2020, that it had begun the Phase 2 trial and that the first participants in each age cohort had received a dose of the vaccine candidate.[101] On June 11, 2020, Moderna announced that it had finalized plans to begin the Phase 3 clinical trial in July.[102] The Phase 3 study will have 30,000 participants.[103] Moderna also noted that Phase 1 of the clinical trial was still ongoing as of June 11, 2020, and that NIH would be submitting the Phase 1 data to a peer-reviewed clinical publication.[104]

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[96] Moderna, *The Advantages of mRNA Vaccines*, *available at* https://www.modernatx.com/pipeline/therapeutic-areas/mrna-therapeutic-areas-infectious-diseases (last visited June 9, 2020).
[97] *Id*.; Moderna, *Moderna Receives FDA Fast Track Designation for mRNA Vaccine (mRNA-1273) Against Novel Coronavirus* (May 12, 2020), *available at* https://investors.modernatx.com/news-releases/news-release-details/moderna-receives-fda-fast-track-designation-mrna-vaccine-mrna.
[98] National Institutes of Health (NIH), *NIH clinical trial of investigational vaccine for COVID-19* (Mar. 16, 2020), *available at* https://www.nih.gov/news-events/news-releases/nih-clinical-trial-investigational-vaccine-covid-19-begins.
[99] *Id.*
[100] Moderna, *Moderna Announced Positive Interim Phase 1 Data for its mRNA Vaccine (mRNA-1273) Against Novel Coronavirus* (May 18, 2020), *available at* https://investors.modernatx.com/news-releases/news-release-details/moderna-announces-positive-interim-phase-1-data-its-mrna-vaccine.
[101] Moderna, *Moderna Announced First Participants in Each Age Cohort Dosed in Phase 2 Study of mRNA Vaccine (mRNA-1273) Against Novel Coronavirus* (May 29, 2020), *available at* https://investors.modernatx.com/news-releases/news-release-details/moderna-announces-first-participants-each-age-cohort-dosed-phase.
[102] Moderna, *Moderna Advances Late-Stage Development of its Vaccine (mRNA-1273) Against COVID-19* (June 11, 2020), *available at* https://investors.modernatx.com/news-releases/news-release-details/moderna-advances-late-stage-development-its-vaccine-mrna-1273.
[103] *Id*.
[104] *Id*.

- Moderna announced on May 12, 2020 that FDA granted Moderna's mRNA-1273 vaccine candidate Fast Track designation.[105]

- BARDA awarded Moderna $483 million on April 16, 2020, to fund the development of the mRNA-1273 vaccine candidate. The funding will also support manufacturing process scale up to enable large scale production in 2020.[106] To support the scale up, Moderna plans to hire up to 150 new team members in the U.S. this year.

- On May 1, 2020, Moderna announced a worldwide strategic collaboration with Lonza to manufacture Moderna's vaccine candidate.[107] The companies plan to manufacture the vaccine candidate at Lonza's facilities in the U.S. and Switzerland, with the first batch of the vaccine candidate being manufactured at Lonza U.S. in July 2020.[108] Some of the funding Moderna received from BARDA under their contract will help fund the establishment of manufacturing operations at Lonza U.S.[109]

- On June 11, 2020, Moderna announced that the company is on track to be able to deliver about 500 million doses per year, and potentially up to 1 billion doses per year, beginning in 2021 from Moderna's U.S. manufacturing site and the partnership with Lonza.[110]

- On June 25, 2020, Moderna and Catalent announced an agreement for Catalent to provide fill-finish capacity for Moderna's COVID-19 vaccine candidate, including providing vial filling and packaging capacity, "additional staffing required for 24x7 manufacturing operations at the site to support production of an initial 100 million doses of the vaccine candidate intended to supply the U.S. market starting in the third quarter of 2020," and providing "clinical supply services from its facilities in Philadelphia, Pennsylvania, including

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[105] Moderna, *Moderna Receives FDA Fast Track Designation for mRNA Vaccine (mRNA-1273) Against Novel Coronavirus* (May 12, 2020), *available at* https://investors.modernatx.com/news-releases/news-release-details/moderna-receives-fda-fast-track-designation-mrna-vaccine-mrna.

[106] Moderna, *Moderna Announces Award from U.S. Government Agency BARDA for up to $483 Million to Accelerate Development of mRNA Vaccine (mRNA-1273) Against Novel Coronavirus* (Apr. 16, 2020), *available at* https://investors.modernatx.com/news-releases/news-release-details/moderna-announces-award-us-government-agency-barda-483-million; U.S. Dep't of Health and Human Services, Public Health Emergency, *BARDA's Rapidly Expanding COVID-19 Medical Countermeasure Portfolio*, *available at* https://www.medicalcountermeasures.gov/app/barda/coronavirus/COVID19.aspx (last visited June 10, 2020).

[107] Moderna, *Moderna and Lonza Announce Worldwide Strategic Collaboration to Manufacture Moderna's Vaccine (mRNA-1273) Against Novel Coronavirus* (May 1, 2020), *available at* https://investors.modernatx.com/news-releases/news-release-details/moderna-and-lonza-announce-worldwide-strategic-collaboration.

[108] *Id*.

[109] *Id*.

[110] Moderna, *Moderna Advances Late-Stage Development of its Vaccine (mRNA-1273) Against COVID-19* (June 11, 2020), *available at* https://investors.modernatx.com/news-releases/news-release-details/moderna-advances-late-stage-development-its-vaccine-mrna-1273.

packaging and labeling, as well as storage and distribution to support Moderna's Phase 3 clinical study."[111] The companies are also still discussing Catalent providing fill-finish capacity for hundreds of millions of additional doses.[112]

- **AstraZeneca.** On April 30, 2020, AstraZeneca and the University of Oxford partnered together for the global development and distribution of the University of Oxford's potential COVID-19 vaccine candidate, AZD1222—formerly known as ChAdOx1 nCoV-19.[113] According to the WHO, the vaccine candidate is currently in Phase 3 clinical trials in some locations.[114]

  - The AstraZeneca/University of Oxford vaccine candidate "uses a replication-deficient chimpanzee viral vector based on a weakened version of a common cold (adenovirus) virus that causes infections in chimpanzees and contains the genetic material of SARS-CoV-2 spike protein."[115]

  - The University of Oxford began working on a COVID-19 vaccine on January 20, 2020.[116] On April 23, 2020, a Phase 1/2 clinical trial began for the vaccine candidate across multiple study sites in southern England.[117] On May 22, 2020, the University of Oxford announced that they had started recruiting to begin the Phase 2b/3 clinical trial at study sites across the U.K.[118]

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[111] Catalent, *Moderna and Catalent Announce Collaboration for Fill-Finish Manufacturing of Moderna's COVID-19 Vaccine Candidate* (Jun. 25, 2020), *available at* https://www.catalent.com/catalent-news/moderna-and-catalent-announce-collaboration-for-fill-finish-manufacturing-of-modernas-covid-19-vaccine-candidate/.
[112] *Id*.
[113] AstraZeneca, *AstraZeneca and Oxford University announce landmark agreement for COVID-19 vaccine* (Apr. 30, 2020), *available at* https://www.astrazeneca.com/content/astraz/media-centre/press-releases/2020/astrazeneca-and-oxford-university-announce-landmark-agreement-for-covid-19-vaccine.html#__prclt=8mfn5tcv.
[114] World Health Organization, *DRAFT landscape of COVID-19 candidate vaccines* (June 29, 2020), *available at* https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines.
[115] AstraZeneca, *AstraZeneca advances response to global COVID-19 challenge as it receives first commitments for Oxford's potential new vaccine* (May 21, 2020), *available at* https://www.astrazeneca.com/media-centre/press-releases/2020/astrazeneca-advances-response-to-global-covid-19-challenge-as-it-receives-first-commitments-for-oxfords-potential-new-vaccine.html.
[116] *COVID-19 Oxford Vaccine Trial*, *available at* https://covid19vaccinetrial.co.uk/ (last visited June 11, 2020).
[117] AstraZeneca, *AstraZeneca advances response to global COVID-19 challenge as it receives first commitments for Oxford's potential new vaccine* (May 21, 2020), *available at* https://www.astrazeneca.com/media-centre/press-releases/2020/astrazeneca-advances-response-to-global-covid-19-challenge-as-it-receives-first-commitments-for-oxfords-potential-new-vaccine.html; University of Oxford, *Oxford COVID-19 vaccine begins human trial* stage (Apr. 23, 2020), *available at* http://www.ox.ac.uk/news/2020-04-23-oxford-covid-19-vaccine-begins-human-trial-stage.
[118] COVID-19 Oxford Vaccine Trial, *The Oxford Vaccine Centre COVID-19 Phase II/III Clinical Trial Explained* (May 22, 2020), *available at* https://covid19vaccinetrial.co.uk/phase-iiiii-trial-explained.

- AstraZeneca is responsible for the development, manufacturing, and distribution of the vaccine candidate under the agreement.[119]

- On May 21, 2020, AstraZeneca announced that it had received $1.2 billion from BARDA for the development, production, and delivery of the vaccine candidate, including 300 million doses.[120] The development program includes a Phase 3 clinical trial with 30,000 participants and a pediatric trial.[121] Press reports indicate that U.S.-based Phase 3 clinical trials potentially will begin in August for the vaccine candidate.[122]

    - As discussed earlier in this report, this award was part of the Operation Warp Speed national program initiated by the Trump Administration.

- AstraZeneca plans to have clinical trial results available in August, and, depending on whether the clinical trial results show the vaccine is safe and effective, they potentially could begin delivering doses of the vaccine in the U.S. and U.K. in September and October of 2020.[123]

- AstraZeneca has entered into agreements with entities such as CEPI, Gavi the Vaccine Alliance, and the Serum Institute of India to support the manufacturing, procurement, and distribution of their COVID-19 vaccine candidate.[124] As of June 4, 2020, AstraZeneca had secured manufacturing capacity for two billion doses of the vaccine candidate.[125]

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[119] AstraZeneca, *AstraZeneca and Oxford University announce landmark agreement for COVID-19 vaccine* (Apr. 30, 2020), *available at* https://www.astrazeneca.com/content/astraz/media-centre/press-releases/2020/astrazeneca-and-oxford-university-announce-landmark-agreement-for-covid-19-vaccine.html#__prclt=8mfn5tcv.
[120] U.S. Department of Health and Human Services, Public Health Emergency, *BARDA's Rapidly Expanding COVID-19 Medical Countermeasure Portfolio*, *available at* https://www.medicalcountermeasures.gov/app/barda/coronavirus/COVID19.aspx; AstraZeneca, *AstraZeneca advances response to global COVID-19 challenge as it receives first commitments for Oxford's potential new vaccine* (May 21, 2020), *available at* https://www.astrazeneca.com/content/astraz/media-centre/press-releases/2020/astrazeneca-advances-response-to-global-covid-19-challenge-as-it-receives-first-commitments-for-oxfords-potential-new-vaccine.html (last visited June 10, 2020).
[121] *Id*.
[122] Peter Loftus, *Coronavirus Vaccine Candidates' Pivotal U.S. Testing to Start This Summer*, THE WALL STREET JOURNAL (Jun. 10, 2020), *available at* https://www.wsj.com/articles/coronavirus-vaccine-candidates-pivotal-u-s-testing-to-start-this-summer-11591781405.
[123] Peter Loftus and Joseph Walker, *AstraZeneca Signs More Coronavirus Vaccine Supply Deals*, THE WALL STREET JOURNAL (June 4, 2020), *available at* https://www.wsj.com/articles/astrazeneca-signs-more-coronavirus-vaccine-supplydeals-11591304979.
[124] AstraZeneca, *AstraZeneca takes next steps towards broad and equitable access to Oxford University's COVID-19 vaccine* (June 4, 2020), *available at* https://www.astrazeneca.com/content/astraz/media-centre/press-releases/2020/astrazeneca-takes-next-steps-towards-broad-and-equitable-access-to-oxford-universitys-covid-19-vaccine.html.
[125] *Id*.

- On June 11, 2020, AstraZeneca announced a partnership valued at about $87 million with Emergent BioSolutions to provide development services, technology transfer, analytical testing, drug substance process and performance qualification and will reserve certain large-scale manufacturing capacity through 2020.[126]

- **Johnson & Johnson.** Johnson & Johnson is developing a COVID-19 vaccine candidate, Ad26.COV2-S, recombinant, through its Janssen Pharmaceutical Companies (Janssen), and the vaccine candidate is currently in the pre-clinical stages of development.

  - Johnson & Johnson began its efforts to develop a COVID-19 vaccine candidate as soon as the COVID-19 sequence became available in January 2020. After testing multiple vaccine candidates using Janssen's AdVac and PER.C6 technologies, Johnson & Johnson identified their lead COVID-19 vaccine, Ad26.COV2-S, recombinant, which uses a non-replicating viral vector platform.[127]

  - On March 30, 2020, Johnson & Johnson and BARDA announced a partnership to invest more than $1 billion together to co-fund research, development, and clinical testing of Johnson & Johnson's lead vaccine candidate.[128] BARDA has awarded Janssen, a subsidiary of Johnson & Johnson, $456 million to support development and licensure of the vaccine candidate.[129] Johnson & Johnson also has committed to expanding the company's global manufacturing capacity, including establishing new manufacturing capabilities in the U.S.[130]

  - On June 10, 2020, Johnson & Johnson announced that it expected to begin a Phase 1/2a clinical trial in the second half of July 2020.[131] Originally scheduled to begin in September, Johnson & Johnson

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[126] Emergent BioSolutions, *Emergent BioSolutions Signs Agreement to be U.S. Manufacturing Partner for AstraZeneca's COVID-19 Vaccine Candidate* (June 11, 2020), *available at* https://investors.emergentbiosolutions.com/news-releases/news-release-details/emergent-biosolutions-signs-agreement-be-us-manufacturing-0?field_nir_news_date_value[min]=.

[127] Johnson & Johnson, *Johnson & Johnson Announces a Lead Vaccine Candidate for COVID-19; Landmark New Partnership with U.S. Department of Health and Human Services; and Commitment to Supply One Billion Vaccines Worldwide for Emergency Pandemic* Use (Mar. 30, 2020), *available at* https://www.jnj.com/johnson-johnson-announces-a-lead-vaccine-candidate-for-covid-19-landmark-new-partnership-with-u-s-department-of-health-human-services-and-commitment-to-supply-one-billion-vaccines-worldwide-for-emergency-pandemic-use.

[128] *Id*.

[129] U.S. Department of Health and Human Services, Public Health Emergency, *BARDA's Rapidly Expanding COVID-19 Medical Countermeasure Portfolio*, *available at* https://www.medicalcountermeasures.gov/app/barda/coronavirus/COVID19.aspx (last visited June 10, 2020).

[130] *Id*.

[131] Johnson & Johnson, *Johnson & Johnson Announces Acceleration of its COVID-19 Vaccine Candidate; Phase 1/2a Clinical Trial to Begin in Second Half of July* (June 10, 2020), *available at* https://www.jnj.com/johnson-johnson-announces-acceleration-of-its-covid-19-vaccine-candidate-phase-1-2a-clinical-trial-to-begin-in-second-half-of-july.

explained that the clinical trial was accelerated, "[b]ased on the strength of the preclinical data [Johnson & Johnson has] seen so far and interactions with the regulatory authorities."[132] Johnson & Johnson is in discussions with NIAID to try to start the Phase 3 clinical trial earlier than originally scheduled, pending the outcome of the Phase 1 studies and the approval of regulators.[133]

- On April 23, 2020, Emergent BioSolutions announced that it signed an agreement with Johnson & Johnson to be a U.S. manufacturing partner for Johnson & Johnson's lead COVID-19 vaccine candidate.[134] Under the $135 million agreement, Emergent will provide Johnson & Johnson with drug substance manufacturing services and will reserve certain large-scale manufacturing capacity to manufacture up to 300 million doses of the vaccine candidate beginning in 2021.[135]

- On April 29, 2020, Catalent signed an agreement with Johnson & Johnson to help scale up manufacturing capacity for Johnson & Johnson's vaccine candidate. Catalent will hire about 300 additional employees at the program's site in Bloomington, Indiana starting in July 2020 to achieve operational readiness by January 2021.[136]

- In May 2020, Vibalogics—a global CDMO—announced that the company had entered into a partnership with Johnson & Johnson to manufacture additional clinical trial material for Johnson & Johnson's COVID-19 vaccine candidate.[137]

- **Merck and IAVI.** On May 26, 2020, Merck and IAVI announced they were collaborating to develop a COVID-19 vaccine candidate.[138] The vaccine candidate is currently in the pre-clinical stages of development.

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[132] *Id*.
[133] *Id*.
[134] Emergent BioSolutions, *Emergent BioSolutions Signs Agreement to be U.S. Manufacturing Partner for Johnson & Johnson's Lead Vaccine Candidate for COVID-19* (Apr. 23, 2020), *available at* https://investors.emergentbiosolutions.com/news-releases/news-release-details/emergent-biosolutions-signs-agreement-be-us-manufacturing?field_nir_news_date_value[min]=.
[135] *Id*.
[136] Catalent, *Catalent Signs Agreement with Johnson & Johnson to be U.S. Manufacturing Partner for Lead COVID-19 Vaccine Candidate* (Apr. 29, 2020), *available at* https://www.catalent.com/catalent-news/catalent-signs-agreement-with-johnson-johnson-for-lead-covid-19-vaccine-candidate/.
[137] HospiMedica International staff writers, *Johnson & Johnson Partners with Vibalogics on Development of Lead COVID-19 Vaccine Candidate*, HOSPIMEDICA (May 20, 2020), *available at* https://www.hospimedica.com/covid-19/articles/294782493/johnson--johnson-partners-with-vibalogics-on-development-of-lead-covid-19-vaccine-candidate.html.
[138] Merck, *IAVI and Merck Collaborate to Develop Vaccine Against SARS-CoV-2* (May 26, 2020), *available at* https://investors.merck.com/news/press-release-details/2020/IAVI-and-Merck-Collaborate-to-Develop-Vaccine-Against-SARS-CoV-2/default.aspx.

- The vaccine candidate is being developed using a recombinant vesicular stomatitis virus (rVSV) vaccine platform that uses an attenuated strain of vesicular stomatitis virus.[139] The rVsV vaccine platform is the same viral backbone that is used in Merck's Ebola vaccine that was approved by FDA in December 2019.[140]

- BARDA awarded Merck and IAVI about $38 million to assist with the development of the vaccine candidate.[141]

- IAVI started working on the vaccine at the end of January 2020. The companies plan to start clinical trials later this year.[142]

- **Sanofi and GSK.** In April 2020, Sanofi and GlaxoSmithKline (GSK) partnered to develop an adjuvanted vaccine for COVID-19. The vaccine candidate is currently in the pre-clinical stages of development.

  - The vaccine candidate is developed using a recombinant DNA technology that was developed with BARDA's support to make millions of vaccine doses quickly if needed during an influenza pandemic.[143] The platform is used for Sanofi's FDA-licensed seasonal influenza recombinant vaccine.[144]

    - On February 18, 2020, HHS announced that BARDA would work with Sanofi to develop a vaccine candidate using this egg-free, recombinant DNA platform.[145]

    - BARDA awarded about $30.8 million in funding to help with the development of this vaccine candidate.[146]

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[139] *Id*.
[140] IAVI, *Watch IAVI Experts Discuss Accelerating COVID-19 Vaccine Development with Merck* (June 3, 2020), *available at* https://www.iavi.org/newsroom/watch-iavi-experts-discuss-accelerating-covid-19-vaccine-development-with-merck.
[141] U.S. Department of Health and Human Services, Public Health Emergency, *BARDA's Rapidly Expanding COVID-19 Medical Countermeasure Portfolio, available at* https://www.medicalcountermeasures.gov/app/barda/coronavirus/COVID19.aspx (last visited June 29, 2020).
[142] IAVI, *Watch IAVI Experts Discuss Accelerating COVId-19 Vaccine Development with Merck* (June 3, 2020), *available at* https://www.iavi.org/newsroom/watch-iavi-experts-discuss-accelerating-covid-19-vaccine-development-with-merck.
[143] U.S. Department of Health and Human Services, *BARDA and Sanofi prepare for studies of COVID-19 vaccine, available at* https://www.medicalcountermeasures.gov/newsroom/2020/psc-sanofi-recombinant/ (last visited June 12, 2020).
[144] *Id*.
[145] U.S. Department of Health and Human Services, Public Health Emergency, *BARDA's Rapidly Expanding COVID-19 Medical Countermeasure Portfolio, available at* https://www.medicalcountermeasures.gov/app/barda/coronavirus/COVID19.aspx (last visited June 10, 2020).
[146] *Id*.

- Sanofi is contributing its S-protein COVID-19 antigen to the project, and GSK is contributing its pandemic adjuvant technology.[147] The adjuvant that GSK is contributing to the collaboration, AS03 adjuvant, has been used in GSK's H1N1 swine flu vaccine Pandemrix.[148] The addition of the adjuvant to the vaccine component potentially will reduce the amount of vaccine needed for each shot, therefore enabling manufacturers to make more doses.[149]

- Sanofi and GSK plan to begin Phase 1 clinical trials in the second half of 2020 and, if the Phase 1 trials are successful and subject to regulatory considerations, plan to complete the development required for the vaccine candidate to be available by the second half of 2021.[150]

- In addition to the previously mentioned vaccine candidates that have received funding awards from BARDA, there are over 100 additional vaccine candidates in development. The U.S. government is also supporting some, but not all, of these additional initiatives to help accelerate the development of a vaccine for COVID-19. Some of these initiatives include, but are not limited to:

  - Pfizer and BioNTech have partnered to develop a COVID-19 vaccine candidate—known as BNT162 vaccine program. The companies are currently conducting Phase 1/2 clinical trials.

    - There are four vaccine candidates being tested in the BNT162 vaccine program, each vaccine candidate is based on a different mRNA format and target antigen.[151]

    - On April 29, 2020, Pfizer and BioNTech announced the completion of dosing the first 12 study participants with the vaccine candidate in Germany for the Phase 1/2 clinical trial.[152] On May 5, 2020, Pfizer

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[147] GlaxoSmithKline, *Sanofi and GSK to join forces in unprecedented vaccine collaboration to fight COVID-19* (Apr. 14, 2020), *available at* https://www.gsk.com/en-gb/media/press-releases/sanofi-and-gsk-to-join-forces-in-unprecedented-vaccine-collaboration-to-fight-covid-19/.

[148] Angus Liu, *GlaxoSmithKline aims to make 1B doses of vaccine booster for multiple COVID-19 partners*, FIERCE PHARMA (May 28, 2020), *available at* https://www.fiercepharma.com/manufacturing/glaxosmithkline-aims-to-make-1b-doses-vaccine-booster-for-multiple-covid-19-partners.

[149] *Id*.

[150] GlaxoSmithKline, *Sanofi and GSK to join forces in unprecedented vaccine collaboration to fight COVID-19* (Apr. 14, 2020), *available at* https://www.gsk.com/en-gb/media/press-releases/sanofi-and-gsk-to-join-forces-in-unprecedented-vaccine-collaboration-to-fight-covid-19/.

[151] Pfizer, *Pfizer and BioNTech Dose First Participants in the U.S. as Part of Global COVID-19 mRNA Vaccine Development Program* (May 5, 2020), *available at* https://www.pfizer.com/news/press-release/press-release-detail/pfizer_and_biontech_dose_first_participants_in_the_u_s_as_part_of_global_covid_19_mrna_vaccine_development_program.

[152] Pfizer, *BioNTech and Pfizer Announce Completion of Dosing for First Cohort of Phase 1/2 Trial of COVID-19 Vaccine Candidates in Germany* (Apr. 29, 2020), *available at* https://investors.pfizer.com/investor-news/press-release-details/2020/BioNTech-and-Pfizer-announce-completion-of-dosing-for-first-cohort-of-Phase-1-2-trial-of-COVID-19-vaccine-candidates-in-Germany/default.aspx.

and BioNTech administered the first dose to participants in the U.S.[153] The Phase 1/2 study is designed to evaluate the safety, immunogenicity, and dose level of the four mRNA vaccine candidates.[154] The first clinical trial data is expected in June or July 2020.[155] Pfizer expects to start the Phase 3 clinical trial in July, and Pfizer expects to have safety and efficacy data from the Phase 3 clinical trials by the fall, potentially as early as September.[156] The clinical trials sites will be around the world, especially where there are increases of COVID-19 cases, including in Florida, Arizona, and Texas.[157] Pfizer's goal is to submit data to the FDA for the vaccine candidate for an EUA by October.[158]

- Pfizer and BioNTech are scaling-up manufacturing capacity at risk to increase global supply. Subject to the success of the development program and approval by the regulatory authorities, the companies are increasing production capacity to allow for the supply of hundreds of millions of vaccine doses by the end of 2020 and increasing to 1 billion by 2021.[159] Pfizer is investing $1 billion to develop and manufacture the vaccine candidate at risk.[160]

- INOVIO Pharmaceuticals is developing a vaccine candidate, INO-4800, that currently is in Phase 1 clinical trials.

  - INO-4800 is a COVID-19 vaccine candidate that is being developed using INOVIO's proprietary DNA medicine platform, and the vaccine

[153] Pfizer, *Pfizer and BioNTech Dose First Participants in the U.S. as Part of Global COVID-19 mRNA Vaccine Development Program* (May 5, 2020), *available at* https://www.pfizer.com/news/press-release/press-release-detail/pfizer_and_biontech_dose_first_participants_in_the_u_s_as_part_of_global_covid_19_mrna_vaccine_development_program.
[154] *Id*.
[155] Milken Institute, *COVID-19 Treatment and Vaccine Tracker*, *available at* https://milkeninstitute.org/covid-19-tracker (last visited June 13, 2020).
[156] Beth Wang, *Pfizer CEO: COVID-19 Vaccine May be Ready for October Approval*, INSIDEHEALTHPOLICY (Jun. 26, 2020), *available at* https://insidehealthpolicy.com/daily-news/pfizer-ceo-covid-19-vaccine-may-be-ready-october-approval.
[157] *Id*.
[158] Nathan Vardi, *The Race is On: Why Pfizer May be the Best Bet to Deliver a Vaccine by the Fall*, FORBES (May 20, 2020), *available at* https://www.forbes.com/sites/nathanvardi/2020/05/20/the-man-betting-1-billion-that-pfizer-can-deliver-a-vaccine-by-this-fall/#5389bf65382e.
[159] Pfizer, *Pfizer and BioNTech Dose First Participants in the U.S. as Part of Global COVID-19 mRNA Vaccine Development Program* (May 5, 2020), *available at* https://www.pfizer.com/news/press-release/press-release-detail/pfizer_and_biontech_dose_first_participants_in_the_u_s_as_part_of_global_covid_19_mrna_vaccine_development_program; Beth Wang, *Pfizer CEO: COVID-19 Vaccine May be Ready for October Approval*, INSIDEHEALTHPOLICY (Jun. 26, 2020), *available at* https://insidehealthpolicy.com/daily-news/pfizer-ceo-covid-19-vaccine-may-be-ready-october-approval.
[160] Nathan Vardi, *The Race is On: Why Pfizer May be the Best Bet to Deliver a Vaccine by the Fall*, FORBES (May 20, 2020), *available at* https://www.forbes.com/sites/nathanvardi/2020/05/20/the-man-betting-1-billion-that-pfizer-can-deliver-a-vaccine-by-this-fall/#5389bf65382e.

candidate was designed quickly after the genetic sequence of the coronavirus that causes COVID-19 was published.[161]

- On March 24, 2020, Ology Bioservices and INOVIO announced that they had partnered to manufacture the COVID-19 vaccine candidate, and that the DoD had awarded Ology Bioservices with an $11.9 million contract to work with INOVIO on DNA technology transfer to quickly manufacture the vaccine candidate, INO-4800, for the DoD for clinical trials.[162]

- On April 6, 2020, INOVIO announced that FDA had approved its Investigational New Drug Application (IND) for INO-4800 and it was initiating Phase 1 of its clinical trial in Philadelphia and Kansas City.[163] On April 16, 2020, International Vaccine Institute (IVI) announced that CEPI had granted $6.9 million in funding to INOVIO to work with Korea National Institute of Health on a Phase 1/2 clinical trial of the vaccine candidate—which is being conducted in parallel to the Phase 1 clinical trial in the U.S.[164] On May 20, 2020, preclinical data was published in the peer-reviewed journal *Nature Communications*, showing robust neutralizing antibody and T cell immune responses to COVID-19.[165] INOVIO expects that results from the Phase 1 trial in the U.S. will be released in June and the Phase 2/3 trial will begin in June or July 2020.[166]

- INOVIO plans to have 1 million doses of INO-4800 by the end of 2020.[167] On April 30, 2020, INOVIO announced that it had entered an agreement with a German contract manufacturer, Richter-Helm BioLogics GmbH & Co. KG to support large-scale manufacturing of

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[161] INOVIO, *INOVIO's COVID-19 DNA Vaccine INO-4800 Demonstrates Robust Neutralizing Antibody and T Cell Immune Responses in Preclinical Models* (May 20, 2020), *available at* http://ir.inovio.com/news-releases/news-releases-details/2020/INOVIOs-COVID-19-DNA-Vaccine-INO-4800-Demonstrates-Robust-Neutralizing-Antibody-and-T-Cell-Immune-Responses-in-Preclinical-Models/default.aspx.
[162] Ology Bioservices, *Ology Bioservices, Inovio Partner to Manufacture COVID-19 DNA Vaccine with $11.9 Million Department of Defense Grant* (Mar. 24, 2020), *available at* https://www.ologybio.com/ology-bioservices-inovio-partner-to-manufacture-covid-19-dna-vaccine-with-11-9-million-department-of-defense-grant/.
[163] INOVIO Pharmaceuticals, *INOVIO Initiates Phase 1 Clinical Trial of Its COVID-19 Vaccine and Plans First Dose Today* (Apr. 6, 2020), *available at* http://ir.inovio.com/news-releases/news-releases-details/2020/INOVIO-Initiates-Phase-1-Clinical-Trial-Of-Its-COVID-19-Vaccine-and-Plans-First-Dose-Today/default.aspx.
[164] INOVIO Pharmaceuticals, *IVI, INOVIO, and KNIH to Partner with CEPI in Phase 1/2 Clinical Trial of INOVIO's COVID-19 DNA Vaccine in South Korea* (Apr. 16, 2020), *available at* http://ir.inovio.com/news-releases/news-releases-details/2020/IVI-INOVIO-and-KNIH-to-Partner-with-CEPI-in-Phase-12-Clinical-Trial-of-INOVIOs-COVID-19-DNA-Vaccine-in-South-Korea/default.aspx.
[165] INOVIO, *INOVIO's COVID-19 DNA Vaccine INO-4800 Demonstrates Robust Neutralizing Antibody and T Cell Immune Responses in Preclinical Models* (May 20, 2020), *available at* http://ir.inovio.com/news-releases/news-releases-details/2020/INOVIOs-COVID-19-DNA-Vaccine-INO-4800-Demonstrates-Robust-Neutralizing-Antibody-and-T-Cell-Immune-Responses-in-Preclinical-Models/default.aspx.
[166] INOVIO, *INOVIO Urgently Focused on Developing COVID-19 Vaccine, available at* https://www.inovio.com/our-focus-serving-patients/covid-19/ (last visited June 12, 2020).
[167] *Id*.

the vaccine candidate, and that the agreement was partially funded with $1.3 million from CEPI.[168]

- Novavax is developing a COVID-19 vaccine candidate, NVX-CoV2373, and is currently conducting a Phase 1/2 clinical trial of the vaccine candidate.[169]
  - NVX-CoV2373 is a "stable, prefusion protein made using Novavax's proprietary nanoparticle technology."[170] Novavax is incorporating the company's proprietary Matrix-M adjuvant into the vaccine candidate to stimulate high levels of neutralizing antibodies and enhance immune responses.[171]
  - The DoD awarded Novavax a $60 million contract on June 4, 2020, for the manufacturing of its vaccine candidate.[172] The agreement includes a 2020 delivery by Novavax of 10 million doses of the vaccine candidate that DoD can use for Phase 2/3 clinical trials or, if approved by FDA, under an EUA.[173]
  - On May 25, 2020 Novavax initiated a Phase 1/2 clinical trial for its COVID-19 vaccine candidate.[174] For the Phase 1/2 clinical trial, Novavax enrolled about 130 healthy participants 18 to 59 years of age at two sites in Australia.[175]
  - In March 2020, Novavax entered into an agreement with Emergent BioSolutions for clinical production with the ability to leverage the capacity for large scale manufacturing of the vaccine candidate.[176]

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[168] INOVIO, *INOVIO Expands Manufacturing of COVID-19 DNA Vaccine INO-4800 With New Funding from CEPI* (Apr. 30, 2020), *available at* http://ir.inovio.com/news-releases/news-releases-details/2020/INOVIO-Expands-Manufacturing-of-COVID-19-DNA-Vaccine-INO-4800-With-New-Funding-from-CEPI/default.aspx.
[169] Novavax, *Novavax Initiates Phase 1/2 Clinical trial of COVID-19 Vaccine* (May 25, 2020), *available at* https://ir.novavax.com/news-releases/news-release-details/novavax-initiates-phase-12-clinical-trial-covid-19-vaccine.
[170] Novavax, *Novavax Identifies Coronavirus Vaccine Candidate; Accelerates Initiation of First-in-Human Trial to Mid-May* (Apr. 8, 2020), *available at* https://ir.novavax.com/news-releases/news-release-details/novavax-identifies-coronavirus-vaccine-candidate-accelerates.
[171] *Id*.
[172] Novavax, *Novavax Awarded Department of Defense Contract for COVID-19 Vaccine* (Jun. 4, 2020), *available at* https://ir.novavax.com/news-releases/news-release-details/novavax-awarded-department-defense-contract-covid-19-vaccine.
[173] *Id*.
[174] Novavax, *Novavax Initiates Phase 1/2 Clinical Trial of COVID-19 Vaccine* (May 25, 2020), *available at* https://ir.novavax.com/news-releases/news-release-details/novavax-initiates-phase-12-clinical-trial-covid-19-vaccine.
[175] *Id*.
[176] Novavax, *Novavax Identifies Coronavirus Vaccine Candidate; Accelerates Initiation of First-in-Human Trial to Mid-May* (Apr. 8, 2020), *available at* https://ir.novavax.com/news-releases/news-release-details/novavax-identifies-coronavirus-vaccine-candidate-accelerates.

- Massachusetts Eye and Ear and Massachusetts General Hospital are developing a gene-based COVID-19 vaccine candidate, AAVCOVID.[177]
    - The vaccine candidate "uses adeno-associated viral (AAV) vector, a clinically established gene transfer technology leveraging the properties of a harmless viral carrier."[178] The AAV technology has been used extensively for gene therapy.
    - On May 5, 2020, Massachusetts Eye and Ear and Massachusetts General Hospital said that the vaccine candidate was still in preclinical development with a plan to start clinical testing later this year.[179]
    - On May 28, 2020, AveXis, a Novartis company, entered into a manufacturing agreement with the AACOVID vaccine program run by Massachusetts Eye and Ear and Massachusetts General Hospital to manufacture the vaccine candidate.[180]

- In addition to the vaccine candidates discussed in this section, there are over 100 additional vaccine candidates in the pipeline. Numerous entities have developed trackers to follow the progress of these vaccine candidates through preclinical and clinical development.
    - For example, the World Health Organization (WHO), regularly updates a list of COVID-19 vaccine candidates and posts the list to its website. The list includes information about each vaccine candidate such as the platform, type of candidate vaccine, developer, current stage of clinical evaluation, coronavirus target, and whether the platform has been used for non-coronavirus candidates.[181]
    - Similarly, the Milken Institute has a COVID-19 Treatment and Vaccine tracker that is updated regularly. For vaccines, the tracker includes information about each vaccine candidate such as the type of platform, developer, funder, anticipated next steps, and clinical trial information.[182]

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[177] Massachusetts Eye and Ear, *Massachusetts Eye and Ear and Massachusetts General Hospital Advancing Novel Experimental Gene-based COVID-19 Vaccine, AAVCOVID* (May 5, 2020), *available at* https://masseyeandear.org/news/press-releases/2020/05/mee-and-mgh-advancing-aavcovid-vaccine.
[178] *Id*.
[179] *Id*.
[180] Massachusetts Eye and Ear, *AAVCOVID Vaccine Program from Mass. Eye and Ear and Mass General Enters Manufacturing Agreement with Gene Therapy Leader, AveXis, a Novartis Company* (May 28, 2020), *available at* https://masseyeandear.org/news/press-releases/2020/05/aavcovid-vaccine-program-enters-manufacturing-agreement-with-avexis.
[181] World Health Organization, *DRAFT landscape of COVID-19 candidate vaccines* (June 29, 2020), *available at* https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines.
[182] Milken Institute, *COVID-19 Treatment and Vaccine Tracker*, *available at* https://milkeninstitute.org/covid-19-tracker (last visited June 29, 2020).

- BIO maintains a COVID-19 Therapeutic Development Tracker that includes information about vaccines, antivirals, and treatments. For vaccines, the tracker includes information about certain vaccine candidates such as sponsor information, clinical trial status, and the target family. The tracker also has information about therapies in development by originating company headquarters, development start date, the top platform technologies used for vaccine candidates, among other things.[183]

- The Regulatory Affairs Professional Society has a COVID-19 vaccine tracker that lists COVID-19 vaccine candidates that are currently in Phase 1-3 clinical trials, and lists some of the major vaccine candidates in pre-clinical stages of development and research. For each vaccine candidate on the list, the tracker includes information such as the candidate name, sponsor, the trial phase, institution, and funding.[184]

B. Can an expedited approval process be created for COVID-19 vaccines, or infectious disease vaccines more broadly?

- The Food Drug and Cosmetic Act provides several options that allow a sponsor to bring a new vaccine to market faster. Generally these include: (1) FDA directing more of its resources to the product to accelerate the development and/or review processes (*e.g.*, fast track product designation, breakthrough therapy designation, and priority review); and (2) FDA modifying how it evaluates the risks and benefits of the vaccine before allowing its use, either by relying on different types of evidence (*e.g.*, the accelerated approval process) or lowering the evidentiary standard in emergency situations (*e.g.*, EUA).[185]

  - The Fast Track program at the FDA's Center for Drug Evaluation and Research is designed to facilitate the development and expedite the review of drugs to treat serious diseases and fill an unmet medical need. Filling an unmet medical need is further defined as providing a therapy where none exists or providing a therapy which may be potentially superior to existing therapy.[186]

    - This was to facilitate the discovery and marketing of drugs targeted for serious or rare diseases and to accelerate the approval of molecules

[183] Biotechnology Innovation Organization (BIO), *COVID-19 Therapeutic Development Tracker*, *available at* https://www.bio.org/policy/human-health/vaccines-biodefense/coronavirus/pipeline-tracker (last visited June 29, 2020).
[184] Regulatory Affairs Professional Society, *COVID-19 vaccine tracker* (June 11, 2020), *available at* https://www.raps.org/news-and-articles/news-articles/2020/3/covid-19-vaccine-tracker.
[185] Erin H. Ward, *COVID-19: Legal Considerations for Bringing a New Vaccine to Market*, Congressional Research Service (CRS) (Mar. 24, 2020), *available at* https://www.crs.gov/Reports/LSB10427?source=search&guid=2f455b40079e42a2b9c55ba73936430e&index=1.
[186] Krishnan Vengadaraga Chary, *Expedited drug review process: Fast, but flawed*, National Center for Biotechnology Information, U.S. National Library of Medicine, National Institutes of Health (2016 Apr.-June), *available at* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4936080/.

showing superior efficacy than the existing one. Fast-track approach was introduced in 1988.[187]

- A sponsor can apply for fast-track drug approval process along with an investigational new drug application. The FDA conveys the decision within sixty calendar days to the sponsor about fast-track consideration.[188]

- When a drug is provided a fast-track designation, it enables sponsors to work along with FDA to conduct the trial and to submit the relevant data on a rolling basis A Fast Track-designated drug candidate may be eligible for accelerated approval which allows the drug to be approved if it "has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments."[189]

- As previously noted earlier in this section, Moderna announced on May 12, 2020 that FDA granted Moderna's mRNA-1273 vaccine candidate Fast Track designation.[190]

- In 1992, the Prescription Drug User Fee Act (PDUFA) provided FDA with other drug review processes, namely, "Priority Review" by which a drug review process will be completed within six months rather than the 10 months of the standard review schedule. In 1992, the FDA instituted regulations for "Accelerated Approval" of a drug or biologic based on its efficacy shown by surrogate markers.[191] In 2012, Congress enacted the Food and Drug Administration Safety Innovation Act, which allowed "the FDA to base accelerated approval for drugs for serious conditions that fill an unmet medical need on whether the drug has an effect on a surrogate or an intermediate clinical endpoint.[192]

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[187] *Id*.
[188] *Id*.
[189] 21 U.S.C. §356(c)(1)(A).
[190] Moderna, *Moderna Receives FDA Fast Track Designation for mRNA Vaccine (mRNA-1273) Against Novel Coronavirus* (May 12, 2020), *available at* https://investors.modernatx.com/news-releases/news-release-details/moderna-receives-fda-fast-track-designation-mrna-vaccine-mrna.
[191] U.S. Food and Drug Administration, *Fast Track, Breakthrough Therapy, Accelerated Approval, Priority Review*, *available at* https://www.fda.gov/patients/learn-about-drug-and-device-approvals/fast-track-breakthrough-therapy-accelerated-approval-priority-review (last updated Feb. 23, 2018).
[192] U.S. Food and Drug Administration, *Accelerated Approval* (Jan. 4, 2018), *available at* https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/accelerated-approval#:~:text=Section%20901%20of%20FDASIA%20amends,or%20an%20intermediate%20clinical%20endpoint.

- On February 4, 2020, HHS Secretary, Alex. M. Azar II, "determined that there is a public health emergency that has a significant potential to affect national security or the health and security of United States citizens living abroad, and that involves the virus that causes COVID-19. On the basis of this determination, the Secretary then declared that circumstances exist justifying the authorization of emergency use of drugs and biological products during the COVID-19 pandemic, pursuant to section 564 of the FD&C Act, effective March 27, 2020."[193]

- FDA can approve a vaccine candidate under an EUA if the Secretary concludes: (1) that EUA-product is to treat a serious or life-threating condition; (2) the totality of the evidence available to FDA shows that it is reasonable to believe (a) the vaccine may be effective in preventing COVID-19 and (b) that those benefits outweigh any known or potential risks from the vaccine; (3) there is no adequate, approved available alternative to the candidate product.[194]

    - Clinical trials conducted for a vaccine candidate will provide FDA with safety information about the vaccine candidate.

- The FDA recently told Members of the Committee on Energy and Commerce that: "FDA intends to use regulatory flexibility to help ensure the most efficient and timely development of safe and effective vaccines to prevent COVID-19" and that the FDA "will ensure that any licensed vaccine meets FDA standards for safety and efficacy." The FDA noted that "[b]ecause there is so much at stake, we need to try to move things through very quickly to get there—not cutting corners, but working to expedite development as much as possible."[195]

- Similarly, at a hearing held by the Committee on Energy and Commerce on June 23, 2020, both Dr. Fauci and Dr. Hahn emphasized that, while the Administration was accelerating the development of a vaccine by taking a financial risk around the development process, "[t]he acceleration is not cutting corners with respect to the assessment of safety and effectiveness."[196]

    - For example, Dr. Hahn testified: "I can tell you from the regulatory perspective of FDA we have world-leading experts in the assessment of

[193] U.S. Food and Drug Administration, *Emergency Use Authorization, Emergency Use Authorization (EUA) information, and list of all current EUAs, available at* https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization?utm_campaign=051120_PR_Coronavirus%20(COVID-19)%20Update:%20Daily%20Roundup%20May%2011,%202020&utm_medium=email&utm_source=Eloqua#coviddrugs (last visited on June 9, 2020).
[194] 21 U.S.C. § 360bbb-3(c)(2).
[195] U.S. Food and Drug Administration, *Answers to Questions Submitted by Members, Energy and Commerce Committee Briefing on April 21, 2020, FDA Commissioner Stephen Hahn, M.D.* (Jun. 19, 2020).
[196] *Oversight of the Trump Administration's Response to the COVID-19 Pandemic: Hearing Before the H. Comm. On Energy and Commerce*, 116th Cong., Preliminary Transcript, at 58-59 (Jun. 23, 2020).

vaccine safety and efficacy. The world looks to FDA. The world looks to the U.S. to actually make those assessments. What I can promise the American people, we will work with companies. We will work with Operation Warp Speed to provide the assistance so the right studies are done with the right information. But we will independently look at those data and we will make a decision in the best interest of the American people with respect to safety and efficacy. We will use science and data to do that."[197]

- Dr. Hahn also noted; "Let me be clear that data and science will dictate when we will have safe and effective treatments and vaccines for COVID-19, as Dr. Fauci just mentioned. Toward that end, FDA is using every available authority and applying every appropriate regulatory flexibility to facilitate the development and testing."[198]

- Likewise, Dr. Fauci testified: "I think there were some good intentions about using the word "Warp Speed," but I, myself, flinched a little because I know that people might think it is reckless because it is warp speed. It isn't. There are risks, but the risks are all financial risks that is what people need to understand. They are not compromising the safety at all nor is there compromise of scientific integrity. When you do a vaccine under non-emergent conditions there are various steps. And because companies make investments in this, what they do is they don't make an investment in this step until they are pretty sure this step works, and then they go to the next step. And one of the most important steps is when you start, you know, gearing up to make many, many doses. You are not going to make an investment of a half a billion or more dollars to produce doses unless you know it works. So what this particular program says, we are going to assume it is going to work so we are going to put investment in preparing the sites for Phase 3 even before we knew that the Phase 1 was successful. We are going to be making doses even before we know it is effective. So what you are doing is you are cutting down on time but you are not cutting down on the process of safety and science, so if you lose, the only thing you lose is a lot of money. Now nobody likes to lose a lot of money, but we feel we would rather lose a lot of money and gain 4, 5, 6, 7 months than have a result and have to wait 4, 5, 6, 7 months to get the vaccine."[199]

- The 21st Century Cures Act and reauthorizations of PDUFA have helped accelerate the discovery, development, and delivery of new cures and treatments by, among other things, modernizing clinical trials.[200] For example, PDUFA VI promotes

[197] *Id*. at 167.
[198] *Id*. at 38.
[199] *Id*. at 168.
[200] Energy and Commerce Committee Republicans, *21st Century Cures*, *available at* https://republicans-energycommerce.house.gov/cures/ (last visited June 18, 2020); Pharmaceutical Research and Manufacturers of America, *PDUFA: The Prescription Drug User Fee Act VI: Promoting the timely availability of safe and effective medicines to patients*, *available at* https://www.phrma.org/en/Advocacy/Research-Development/PDUFA (last visited June 18, 2020).

innovative clinical trial design and the use of real-world evidence to enhance clinical trials.[201]

- Congress and the Executive Branch should evaluate if there are ways to expedite the clinical trial process while still ensuring the safety and efficacy of products by modernizing the clinical trial process and/or using decentralized clinical trials.

- The Executive Branch should provide guidance on the use of decentralized clinical trials, including how to use digital health technologies.[202]

- FDA should consider the quickest pathways by which vaccines can be made available. Throughout the development process, and despite any expedited processes, it is critical that the safety and efficacy of vaccine candidates be thoroughly studied. As highlighted above, both NIAID Director Dr. Anthony Fauci and FDA Commissioner Stephen Hahn emphasized this point at the June 23, 2020 House Energy and Commerce Full Committee Hearing.

- FDA should also consider if there is a way to harmonize labeling requirements for COVID-19 vaccines in the U.S. with labeling requirements in other countries to help accelerate the distribution of a potential vaccine.

C. Routine Pediatric Immunizations and the Seasonal Influenza Vaccination

- Congress and the Executive Branch should examine ways to encourage continued routine immunizations during the pandemic, especially pediatric immunizations and the seasonal influenza vaccine in the fall, including enhanced vaccine education and vaccine surveillance.

- On March 24, 2020, CDC posted guidance to its website highlighting the importance of routine well child visits and pediatric immunization.[203] Many studies have shown, unfortunately, that there has been a decline in pediatric vaccination during the COVID-19 pandemic.

    - For example, a May 15, 2020 Morbidity and Mortality Weekly Report issued by the CDC identified "declines in routine pediatric vaccine ordering and doses" and noted that children and their communities might be at increased risks for vaccine-preventable diseases.[204] The report found that there were

[201] *Id*.
[202] Rep. Fred Upton and Rep. Diana DeGette, *21st Century Cures 2.0 Concept Paper*, *available at* https://upton.house.gov/uploadedfiles/cures_2.0_concept_paper_final.pdf (last visited June 19, 2020).
[203] Jeanne M. Santoli, MD, et al., Centers for Disease Control and Prevention, *Effects of the COVID-19 Pandemic on Routine Pediatric Vaccine Ordering and Administration—United States, 2020* (May 15, 2020), *available at* https://www.cdc.gov/mmwr/volumes/69/wr/mm6919e2.htm.
[204] *Id*.

increases in vaccine administration to children aged 24 months and younger beginning in late March 2020.[205]

- The American Academy of Pediatrics responded to the report by encouraging pediatric vaccination and raised concerns about the fact that the rate of pediatric immunization had dropped so significantly across the U.S. in such a short period of time.[206]

- A May 18, 2020 Morbidity and Mortality Weekly Report issued by the CDC found that there was a decline in child vaccination coverage during the COVID-19 pandemic according to data in the Michigan Care Improvement Registry.[207] The report raised concerns that the decline in immunization rates may leave children and communities susceptible to vaccine-preventable diseases such as measles.[208]

- A second wave of COVID-19 cases could occur at the same time as influenza season in the fall, and further complicate the COVID-19 pandemic response effort. To the extent the response to seasonal influenza can be strengthened, this will lessen the potential added burden of influenza on the healthcare system while responding to COVID-19. Public health experts have stressed the importance of high influenza vaccination rates in the upcoming influenza season. Additional resources may be necessary to help public service messaging and promotion to increase influenza vaccination rates, which nationally are only about 45 percent.

  - Persons 65 years or older are a particularly vulnerable population to both seasonal influenza and COVID-19. On average, persons 65 years or older represent about 90 percent of deaths in a severe seasonal influenza season in the U.S. Special measures should be taken by the CDC and public health departments to promote and highlight vaccines indicated for seniors that boost the immune response. There is an FDA-approved high-dose influenza vaccine and an FDA-approved adjuvanted influenza vaccine for seniors that have been on the market for several years and have substantial evidence of superior efficacy over standard dose influenza vaccines.

  - Because seasonal influenza preparedness is intertwined with the fall response to COVID-19, steps should be taken to strengthen the supply chain of the U.S. influenza vaccine supply. Only about 53 percent of the U.S. seasonal influenza vaccines are produced in the U.S, with 47 percent of vaccines imported. The supply chain for influenza vaccines is globalized. Policies

[205] *Id*.
[206] American Academy of Pediatrics, *AAP urges vaccination as rates drop due to COVID-19* (May 8, 2020), *available at* https://www.aappublications.org/news/2020/05/08/covid19vaccinations050820.
[207] Cristi A. Bramer, MPH, et al., Centers for Disease Control and Prevention, *Decline in Child Vaccination Coverage During the COVID-19 Pandemic, Michigan Care Improvement Registry, May 2016-May 2020* (May 18, 2020), *available at* https://www.cdc.gov/mmwr/volumes/69/wr/pdfs/mm6920e1-H.pdf.
[208] *Id*.

should be examined to encourage more U.S.-based production and supply for U.S. influenza vaccines.

- Vaccine manufacturers are making millions of extra doses of influenza vaccines this year in preparation for a possible second wave of COVID-19 during the annual influenza season.[209] The CDC usually purchases about 500,000 doses of the influenza vaccine to distribute to states; so far this year, CDC has spent $100 million to buy 7 million doses and has given $140 million to immunization programs across the U.S. to boost adult influenza vaccination.[210] Vaccine manufacturers are planning to boost production by about 10 percent to make 189 million doses this year, up from 170 million last year.[211] Public health experts are expecting an "unprecedented" number of people to get an influenza shot this year.[212]

## III. Therapeutics

A. What types of therapeutics are under development, either by testing current drugs or doing targeted development of new ones?

- There are no FDA-approved drugs specifically for the treatment of patients with COVID-19. At present, clinical management includes infection prevention and control measures and supportive care, including supplementary oxygen and mechanical ventilatory support when indicated.

- Researchers believe that there will be viable therapeutics or very promising candidates by the fall, which will help mitigate any resurgence of COVID-19.

- As previously mentioned, FDA launched the CTAP to move new treatments to patients as soon as possible, while at the same time finding out whether they are helpful or harmful.[213]

    - According to FDA, as of May 11, 2020, there are 144 active trials of therapeutic agents and another 457 development programs for therapeutic agents in the planning stages.[214]

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[209] Lena Sun, *CDC and drugmakers boost flu vaccine doses amid fears of an unprecedented respiratory illness season*, THE WASHINGTON POST (June 24, 2020), *available at* https://www.washingtonpost.com/health/2020/06/24/cdc-drugmakers-boost-flu-vaccine-doses-amid-fears-an-unprecedented-respiratory-illness-season/.
[210] *Id*.
[211] *Id*.
[212] *Id*.
[213] Stephen M. Hahn, M.D., Commissioner of Food and Drugs, Peter Marks, M.D., Ph.D., Director, Center for Biologics Evaluation and Research and Janet Woodcock, M.D., Director, Center for Drug Evaluation and Research, FDA, *The Path Forward: Coronavirus Treatment Acceleration Program* (Apr. 20, 2020), *available at* https://www.fda.gov/news-events/fda-voices-perspectives-fda-leadership-and-experts/path-forward-coronavirus-treatment-acceleration-program.
[214] U.S. Food and Drug Administration, *Coronavirus Treatment Acceleration Program (CTAP), available at* https://www.fda.gov/drugs/coronavirus-covid-19-drugs/coronavirus-treatment-acceleration-program-ctap (last visited on June 11, 2020).

- Hundreds of treatments for COVID-19 are in development around the world.

    - According to the Milken Institute COVID-19 Treatment and Vaccine Tracker, as of June 26, 2020, there are over 257 treatments for COVID-19 in consideration.[215] This tracker provides detailed information on each treatment including the developer/researcher, product category, stage of development, anticipated next steps, product description, clinical trials for COVID-19, funder, and published results.[216]

    - According to BIO's COVID-19 Therapeutic Development Tracker, as of June 29, 2020, there are 593 unique compounds in development, 256 of which are treatments and 182 of which are antivirals.[217] Of the 256 unique compounds in development for treatment, 128 are clinical compounds and 128 are preclinical compounds.[218] Of the 182 unique compounds in development for antivirals, 43 are clinical compounds and 139 are preclinical compounds.[219]

        - The tracker provides a breakdown of what compounds are new, redirected, or repurposed by therapy type. Of the treatments 8 percent are new for COVID-19, 63 percent are redirected, and 29 percent are repurposed.[220] Of the antivirals 54 percent are new for COVID-19, 29 percent are redirected, and 17 percent are repurposed.[221]

        - The tracker also provides a breakdown of the therapies in development by the location of the originating company headquarters. Of the treatments in development, the originating company headquarters are located in the U.S. for 127 therapies, which is more than any other country.[222] Of the antivirals in development, the originating company headquarters are located in the U.S. for 107 antivirals, which is also more than any other country.[223]

- The types of therapies in development for COVID-19 include:

    - **Antibodies:** An antibody is a blood protein produced in response to and counteracting a specific antigen. Antibodies combine chemically with substances that the body recognizes as foreign, such as bacteria and viruses. To treat and prevent disease, scientists can use antibodies from the blood of

[215] *FASTERCURES, COVID-19 Treatment and Vaccine Tracker*, Milken Institute, *available at* https://milkeninstitute.org/covid-19-tracker (last visited on June 29, 2020).
[216] *Id*.
[217] BIO, *Bio COVID-19 Therapeutic Development Tracker, available at* https://www.bio.org/policy/human-health/vaccines-biodefense/coronavirus/pipeline-tracker (last visited on June 29, 2020).
[218] *Id*.
[219] *Id*.
[220] *Id*.
[221] *Id*.
[222] *Id*.
[223] *Id*.

people who have recovered from COVID-19, also known as convalescent plasma, or use antibodies made in a laboratory that will attach to and neutralize the virus. In addition, antibodies that are created to attach to different molecules in the body can also be used to treat the disease.[224] For example, antibodies can be used to stop the immune system from overreacting and causing damage to the body, which is known as a cytokine storm.

- **Antivirals:** An antiviral is an agent that kills a virus or that suppresses its ability to replicate and inhibits its capability to multiply and reproduce.

- **Cell-based therapies:** Cell-based therapies involve transferring live cells into patients to treat a specific disease. To make these therapies, researchers take cells from patients or from a donor and transfer the cells unchanged or change the cells in specific way to treat a specific disease. For COVID-19, "potential cell-based therapies work, in general, by helping the patient's immune system work better (and not overreact) by releasing signals to other cells in the body to coordinate a proper reaction the infection."[225]

- **RNA-based treatments:** Modified RNA molecules, as disease treatments, are given to patients to make helpful proteins or block harmful proteins from being made.[226]

- Other categories of potential treatments being considered include but are not limited to steroids, malarial drugs, medications for high blood pressure, cancer drugs, drugs that treat the overreaction of the immune system, drugs that treat autoimmune diseases, and drugs that prevent blood clots.[227] Some of the other existing drugs or therapies that may be effective against COVID-19 are discussed further in Section III.B of this report.

- An array of drugs approved for other indications as well as several investigational drugs are being studied in several hundred clinical trials that are underway across the globe.

    - Several of the drugs under investigation are more widely known, including remdesivir, an investigational antiviral candidate, and dexamethasone, which is already approved by FDA and is being studied for effectiveness against COVID-19.

[224] *COVID-19 Treatment and Vaccine Tracker*, Milken Institute, *available at* https://milken-institute-covid-19-tracker.webflow.io/#treatment_antibodies (last visited on June 11, 2020).
[225] *Id.*
[226] *Id.*
[227] *Id.*

- NIH has established *Treatment Guidelines* to inform clinicians about how to care for patients with COVID-19.[228] The *Treatment Guidelines* are updated regularly as scientific and medical evidence evolves.

- Providers can access and prescribe investigational drugs or agents approved or licensed for other indications through an EUA, Emergency Investigational New Drug applications, compassionate use or expanded access programs with drug manufacturers, and/or off-label use.

    - However, the NIH *Treatment Guidelines* recommend that promising, unapproved, or unlicensed treatments for COVID-19 be studied in well-designed controlled clinical trials, which includes drugs that have been approved or licensed for other indications.[229]

    - With respect to hydroxychloroquine or chloroquine, FDA issued a Drug Safety Communication cautioning against the use of these drugs to treat COVID-19 outside of the hospital setting in certain hospitalized patients under the EUA or a clinical trial due to the risk of heart rhythm problems.[230] However, FDA has since withdrawn the EUA for chloroquine and hydroxychloroquine and some clinical trials have been suspended.[231] This is discussed in further detail below.

- While allowing the utilization of these drugs or agents for COVID-19 where appropriate, Congress, the Executive Branch, and the private sector should ensure continued supply and access of the drugs or agents for their intended purpose, where applicable.

    - For example, patients who are prescribed dexamethasone to treat inflammation, arthritis, or other disorders should not face shortages or access issues for dexamethasone due to the increase of utilization to treat patients with COVID-19.

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[228] National Institutes of Health, *COVID-19 Treatment Guidelines, Coronavirus Disease 2019 (COVID-19) Treatment Guidelines, available at* https://www.covid19treatmentguidelines.nih.gov/.
[229] National Institutes of Health, *COVID-19 Treatment Guidelines*, *available at* https://covid19treatmentguidelines.nih.gov/introduction/ (last updated Apr. 21, 2020).
[230] U.S. Food and Drug Administration, *FDA cautions against use of hydroxychloroquine or chloroquine for COVID-19 outside of the hospital setting or a clinical trial due to risk of heart rhythm problems* (Apr. 24, 2020), *available at* https://www.fda.gov/drugs/drug-safety-and-availability/fda-cautions-against-use-hydroxychloroquine-or-chloroquine-covid-19-outside-hospital-setting-or.
[231] U.S. Food and Drug Administration, *Emergency Use Authorization, Emergency Use Authorization (EUA) information, and list of all current EUAs, available at* https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization?utm_campaign=051120_PR_Coronavirus%20(COVID-19)%20Update:%20Daily%20Roundup%20May%2011,%202020&utm_medium=email&utm_source=Eloqua#coviddrugs (last visited on June 15, 2020).

B. What is the status of development and clinical trials for therapeutics to treat COVID-19?

- As previously noted in Section II.B of this report, on February 4, 2020, HHS Secretary, Alex. M. Azar II, "determined that there is a public health emergency that has a significant potential to affect national security or the health and security of United States citizens living abroad" and, on the basis of that determination, Secretary Azar then "declared that circumstances exist justifying the authorization of emergency use of drugs and biological products during the COVID-19 pandemic."[232]

    - As of May 8, 2020, FDA had issued four EUAs for drug products for the treatment of patients with COVID-19.[233] As of June 15, 2020, FDA revoked one of the EUAs, which is discussed further below. In addition to EUAs for drug products, the FDA has granted EUAs for in vitro diagnostic products, high complexity molecular-based laboratory developed tests, SARS-CoV-2 antibody tests, personal protective equipment and related medical devices, and ventilators and other medical devices. The EUAs listed below are only the EUAs listed in the drug products category.

        - An EUA for *Chloroquine Phosphate and Hydroxychloroquine Sulfate for Treatment of COVID-19* was issued on March 28, 2020, to only treat adults and adolescents who weigh 50 kg or more and are hospitalized with COVID-19 for whom a clinical trial is not available, or participation is not feasible.[234]

            - However, based on FDA's continued review of the scientific evidence available for chloroquine phosphate and hydroxychloroquine sulfate, on June 15, 2020, FDA determined that the statutory criteria for an EUA was no longer met and withdrew the EUA for chloroquine (CQ) and hydroxychloroquine (HCQ).[235] Specifically, FDA determined that these two drugs "are unlikely to be effective in treating COVID-19 for the authorized uses in the EUA. Additionally, in light of ongoing serious cardiac adverse events and other serious side effects, the known and potential benefits of CQ

[232] *Id*.
[233] The virus that causes COVID-19 has led to an increased number of patients requiring critical care, such as with severe respiratory illness. As a result, there is a shortage of adequate, FDA-approved drugs used for their treatment, such as propofol for sedation of mechanically ventilated patients. The EUA's granted by FDA for drug products during the COVID-19 pandemic include such products.
[234] U.S. Food and Drug Administration, *Emergency Use Authorization, Emergency Use Authorization (EUA) information, and list of all current EUAs, available at* https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization?utm_campaign=051120_PR_Coronavirus%20(COVID-19)%20Update:%20Daily%20Roundup%20May%2011,%202020&utm_medium=email&utm_source=Eloqua#coviddrugs (last visited on June 9, 2020).
[235] *Id*.

and HCQ no longer outweigh the known and potential risks for the authorized use."[236]

- An EUA for *Fresenius Medical, miltiFiltrate PRO System and multiBic/multiPlus Solutions* was issued on April 30, 2020, to provide continuous renal replacement therapy to treat patients in an acute care environment during the COVID-19 pandemic.[237]

- An EUA for *Remdesivir for Certain Hospitalized COVID-19 Patients* was issued on May 1, 2020, to only treat adults and children with suspected or laboratory confirmed COVID-19 and severe disease defined as Sp02 ≤ 94 percent on room air, requiring supplemental oxygen, mechanical ventilation, or extracorporeal membrane oxygenation (ECMO).[238]

- An EUA for *Fresenius Kabi Propoven 2%* was issued on May 8, 2020, to maintain sedation via continuous infusion in patients older than 16 with suspected or confirmed COVID-19 who require mechanical ventilation in an Intensive Care Unit (ICU) setting.[239]

- Numerous clinical trials for COVID-19 therapeutics are ongoing in the U.S. and around the world, some of which have already started to yield results.

  - BIO's COVID-19 Therapeutic Development Tracker provides a breakdown of the COVID-19 clinical pipeline by phase and strategy.

    - Of the 128 treatment clinical compounds listed on BIO's Tracker, 16 are in Phase 1; 62 are in Phase 2; 33 are in Phase 3; and 17 are in Phase 4.[240]

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[236] *Id*.

[237] *Id*.; According to FDA, the multiBic/multiPlus Solutions include multiBic dialysate and replacement fluid and multiPlus dialysate. The multiBic replacement fluid is regulated as a drug by CDER. The multiFiltrate PRO System, multiBic dialysate and the multiPlus dialysate solutions are regulated as devices by CDRH.

[238] U.S. Food and Drug Administration, Letter from RADM Denise M. Hinton, Chief Scientist, Food and Drug Administration, to Ashley Rhoades, MBS, RAC, Senior Association, Regulatory Affairs, Gilead Sciences, Inc. (May 1, 2020), *available at* https://www.fda.gov/media/137564/download.

[239] U.S. Food and Drug Administration, *Emergency Use Authorization, Emergency Use Authorization (EUA) information, and list of all current EUAs, available at* https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization?utm_campaign=051120_PR_Coronavirus%20(COVID-19)%20Update:%20Daily%20Roundup%20May%2011,%202020&utm_medium=email&utm_source=Eloqua#coviddrugs (last visited on June 9, 2020); According to FDA, in the circumstances of this public health emergency, it would not be feasible to require healthcare providers to seek to limit Fresenius Propoven 2% Emulsion only to be used for patients with suspected or confirmed COVID-19; therefore, this authorization does not limit use to such patients.

[240] BIO, *Bio COVID-19 Therapeutic Development Tracker, available at* https://www.bio.org/policy/human-health/vaccines-biodefense/coronavirus/pipeline-tracker (last visited on June 29, 2020).

  - Of the 43 antiviral clinical compounds listed on BIO's Tracker, 8 are in Phase 1; 19 are in Phase 2; 10 are in Phase 3; and 6 are in Phase 4.[241]

- In addition to candidates being developed and tested for treatment, some drugs are being studied as a prophylactic to prevent people from being infected with COVID-19.[242]

    - For example, there are ongoing studies that aim to assess hydroxychloroquine as a prophylaxis against COVID-19 infection.[243] In addition, there are studies assessing other drugs as a prophylaxis, such as providone-iodine.[244]

- The WHO launched a multi-arm, multi-country clinical trial, referred to as The Solidarity Trial, to test four drugs or drug combinations including: (1) remdesivir; (2) lopinavir/ritonavir; (3) lopinavir/ritonavir plus interferon beta-1a; and (4) hydroxychloroquine.[245] As of June 3, 2020, more than 3,500 patients have been recruited in 35 countries, with over 400 hospitals actively recruiting patients. According to the WHO, over 100 countries have joined or expressed an interest in joining the trial.[246]

    - *Remdesivir* was previously tested as an Ebola treatment and generated promising results in animal studies for MERS and SARS;

    - *Lopinavir/Ritonavir* is a licensed treatment for human immunodeficiency virus (HIV);

    - *Interferon beta-1a* is used to treat multiple sclerosis; and

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[241] *Id*.
[242] ClinicalTrials.gov, *available at* https://clinicaltrials.gov/ct2/results?cond=COVID&term=prophylaxis&cntry=US&state=&city=&dist=&Search=Search (last visited on June 15, 2020).
[243] *Hydroxychloroquine as Post-Exposure Prophylaxis Against COVID-19 Infection*, ClinicalTrials.gov, *available at* https://clinicaltrials.gov/ct2/show/NCT04372017?term=prophylaxis&cond=COVID&cntry=US&draw=2&rank=1 (last visited on June 15, 2020); ClinicalTrials.gov, *available at* https://clinicaltrials.gov/ct2/results?cond=COVID-19+prevention&term=hydroxychloroquine&cntry=&state=&city=&dist= (last visited June 22, 2020).
[244] *COVID-19: Povidone-Iodine Intranasal Prophylaxis in Front-line Healthcare Personnel and Inpatients (PIIPPI)*, ClinicalTrials.gov, *available at* https://clinicaltrials.gov/ct2/show/NCT04364802?term=prophylaxis&cond=COVID&cntry=US&draw=2&rank=2 (last visited on June 15, 2020).
[245] *"Solidarity" clinical trial for COVID-19 treatments*, World Health Organization, *available at* https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-clinical-trial-for-covid-19-treatments (last visited on June 8, 2020); In the initial trial protocol, chloroquine and hydroxychloroquine had both been selected as potential drugs to be tested within the Solidarity Trial, however the trial was only ever pursued with hydroxychloroquine, so chloroquine was removed as a listed treatment option under study.
[246] *"Solidarity" clinical trial for COVID-19 treatments*, World Health Organization, *available at* https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-clinical-trial-for-covid-19-treatments (last visited on June 8, 2020).

- *Hydroxychloroquine* is used to treat rheumatology conditions and can also be used to prevent malaria.[247]

  - On June 17, 2020, the WHO announced that the hydroxychloroquine arm of the Solidarity Trial was being stopped.[248] Data showed that hydroxychloroquine does not result in the reduction of mortality of hospitalized COVID-19 patients, when compared with standard of care.[249]

- **Remdesivir**, developed by Gilead Sciences Inc., is an investigational nucleotide analog with broad-spectrum antiviral activity and is being studied in clinical trials and has been granted an EUA by FDA for certain hospitalized COVID-19 patients.

  - At the start of the pandemic, remdesivir was not approved anywhere globally for any use but demonstrated in vitro and in vivo activity in animal models against MERS and SARS, which are structurally similar to COVID-19.[250] In addition to the EUA granted by the FDA in the U.S., remdesivir is now approved, or conditionally approved for emergency use, to treat SARS-CoV-2 in at least four other countries.[251] Outside of these countries, remdesivir is still an investigational and unapproved drug.

  - On April 29, 2020, NIAID reported that its Adaptive COVID-19 Treatment Trial (ACTT) showed that remdesivir accelerates recovery from advanced COVID-19. According to NIAID, preliminary results showed that "[h]ospitalized patients with advanced COVID-19 and lung involvement who

[247] *Id.*; Centers for Disease Control and Prevention, Center for Global Health, Division of Parasitic Diseases and Malaria, *Medicines for the Prevention of Malaria While Traveling Hydroxychloroquine (Plaquenil), available at* https://www.cdc.gov/malaria/resources/pdf/fsp/drugs/Hydroxychloroquine.pdf (last visited June 9, 2020). As discussed later in this report, on May 23, 2020, the Executive Group of the trial decided to pause the hydroxychloroquine arm of the trial due to published concerns in the medical journal *The Lancet* about the safety of the drug, which reported that patients given hydroxychloroquine were dying at higher rates than other patients. However, due to concerns raised about the data behind the study on June 3, 2020, the editors of *The Lancet* issued a statement acknowledging the criticism of the study and that same day, the WHO's Director-General announced that on the basis of the available mortality data, the members of the committee recommended that there are no reasons to modify the trial protocol and the Executive Group subsequently endorsed the continuation of all arms of the trial, including hydroxychloroquine.

[248] *Id.*

[249] *Id.*

[250] Gilead, *About Remdesivir, available at* https://www.gilead.com/purpose/advancing-global-health/covid-19/about-remdesivir (last visited on June 8, 2020).

[251] Gilead, *Gilead Announces Results from Phase 3 Trial of Remdesivir in Patients With Moderate COVID-19* (June 1, 2020), *available at* https://www.gilead.com/news-and-press/press-room/press-releases/2020/6/gilead-announces-results-from-phase-3-trial-of-remdesivir-in-patients-with-moderate-covid-19; Anuron Kumar Mitra and Manas Mishra, *India approves emergency use of remdesivir to treat COVID-19 patients,* REUTERS (June 2, 2020), *available at* https://www.reuters.com/article/health-coronavirus-india-gilead-sciences/india-approves-emergency-use-of-remdesivir-to-treat-covid-19-patients-idUSL4N2DF1SR; Ben Blanchard, *Taiwan approves Gilead's remdesivir to treat COVID-19,* REUTERS (May 30, 2020), *available at* https://www.reuters.com/article/us-health-coronavirus-taiwan/taiwan-approves-gileads-remdesivir-to-treat-covid-19-idUSKBN23609Q; *Singapore approves Gilead's remdesivir to treat Covid-19,* PHARMACEUTICAL TECHNOLOGY (June 11, 2020), *available at* https://www.pharmaceutical-technology.com/news/singapore-remdesivir-approval/.

received remdesivir recovered faster than similar patients who received placebo."[252] Full data was published in *The New England Journal of Medicine* on May 22, 2020.[253] The preliminary results indicated that those who received remdesivir had a median recovery time of 11 days as compared to 15 days in those who received placebo.[254] In addition, the Kaplan-Meier estimates of mortality by 14 days were 7.1 percent with remdesivir and 11.9 percent with placebo.[255] In conclusion, "[r]emdesivir was superior to placebo in shortening the time to recovery in adults hospitalized with COVID-19 and evidence of lower respiratory tract infection."[256]

- In response to these results, Dr. Anthony Fauci, Director of NIAID, noted that: "the data shows that remdesivir has a clear-cut, significant, positive effect in diminishing the time to recovery" and "what it has proven is that a drug can block this virus."[257] While the data still needed to be submitted to a peer reviewed journal and peer reviewed, Dr. Fauci noted that the reason for the announcement was because "whenever you have clear cut evidence that a drug works you have an ethical obligation to immediately let the people who are in the placebo group know so that they can have access and all of the other trials that are taking place now have a new standard of care."[258]

- NIAID is conducting a second trial with remdesivir, which was initiated in May, to evaluate the safety and efficacy of remdesivir in combination with the anti-inflammatory drug baricitinib compared to remdesivir alone.[259] This trial is the next iteration of NIAID's ACTT.[260]

- Gilead released topline results for Gilead's Phase 3 SIMPLE trial for remdesivir for severe disease on April 29, 2020.[261] This trial evaluated 5-day

[252] National Institutes of Health, National Institute of Allergy and Infectious Diseases, *NIH Clinical Trial Shows Remdesivir Accelerates Recovery from Advanced COVID-19* (Apr. 29, 2020), *available at* https://www.niaid.nih.gov/news-events/nih-clinical-trial-shows-remdesivir-accelerates-recovery-advanced-covid-19.
[253] John H. Beigel, M.D., Kay M. Tomashek, M.D., M.P.H., et al., *Remdesivir for the Treatment of Covid-19 – Preliminary Report* (May 22, 2020), *available at* https://www.nejm.org/doi/full/10.1056/NEJMoa2007764.
[254] *Id*.
[255] *Id*.
[256] *Id*.
[257] Erika Edwards, *Remdesivir shows promising results for coronavirus, Fauci says,* NBC NEWS (Apr. 29, 2020), *available at* https://www.nbcnews.com/health/health-news/coronavirus-drug-remdesivir-shows-promise-large-trial-n1195171.
[258] *Id*.
[259] Gilead, *Remdesivir Clinical Trials, available at* https://www.gilead.com/purpose/advancing-global-health/covid-19/remdesivir-clinical-trials (last visited on June 8, 2020).
[260] National Institutes of Health, *NIH clinical trial testing antiviral remdesivir plus anti-inflammatory drug baricitinib for COVID-19 begins* (May 8, 2020), *available at* https://www.nih.gov/news-events/news-releases/nih-clinical-trial-testing-antiviral-remdesivir-plus-anti-inflammatory-drug-baricitinib-covid-19-begins.
[261] Gilead, *Gilead Announces Results from Phase 3 Trial of Investigational Antiviral Remdesivir in Patients With Severe COVID-19* (Apr. 29, 2020), *available at* https://www.gilead.com/news-and-press/press-room/press-

and 10-day dosing durations in hospitalized patients with severe disease, and the study demonstrated similar efficacy between the two dosing durations.[262] Full results from the initial phase were published in *The New England Journal of Medicine* on May 27, 2020.[263] According to Gilead, "[d]ata from the expansion phase of the study are expected in the near future."[264]

- Gilead released topline results for Gilead's Phase 3 SIMPLE trial results for remdesivir for moderate disease on June 1, 2020.[265] The study evaluated 5-day and 10-day courses of remdesivir plus standard of care, versus standard of care alone and demonstrated that patients in the 5-day remdesivir treatment group were 65 percent more likely to have clinical improvement at day 11 compared with those in the standard of care group.[266] In addition, the odds of improvement in clinical status with the 10-day remdesivir treatment group were also favorable, trending toward but not reaching statistical significance.[267] Gilead plans to submit full data for publication in a peer-reviewed journal in the coming weeks.

- Gilead is also working with Roche to evaluate the safety and efficacy of remdesivir in combination with tocilizumab, an anti-inflammatory drug, compared to remdesivir plus placebo in patients with severe COVID-19 pneumonia.[268] The Phase 3 trial began enrollment in June with a goal of about 450 participants globally.[269]

- In addition, the aforementioned WHO Solidarity Trial includes remdesivir.

- Results from a study recently published in *Nature* showed that remdesivir prevented lung disease in macaque monkeys infected with the new

releases/2020/4/gilead-announces-results-from-phase-3-trial-of-investigational-antiviral-remdesivir-in-patients-with-severe-covid-19.

[262] *Id*.

[263] Jason D. Goldman, M.D., M.P.H., David C.B. Lye, M.B., B.S., et. al., *Remdesivir for 5 or 10 Days in Patients with Severe Covid-19,* THE NEW ENGLAND JOURNAL OF MEDICINE (May 27, 2020), *available at* https://www.nejm.org/doi/full/10.1056/NEJMoa2015301?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed.

[264] Gilead, *Remdesivir Clinical Trials, available at* https://www.gilead.com/purpose/advancing-global-health/covid-19/remdesivir-clinical-trials (last visited on June 8, 2020).

[265] Gilead, *Gilead Announces Results from Phase 3 Trial of Remdesivir in Patients With Moderate COVID-19* (June 1, 2020), *available at* https://www.gilead.com/news-and-press/press-room/press-releases/2020/6/gilead-announces-results-from-phase-3-trial-of-remdesivir-in-patients-with-moderate-covid-19.

[266] *Id*.

[267] Gilead, *Gilead Announces Results from Phase 3 Trial of Remdesivir in Patients With Moderate COVID-19* (June 1, 2020), *available at* https://www.gilead.com/news-and-press/press-room/press-releases/2020/6/gilead-announces-results-from-phase-3-trial-of-remdesivir-in-patients-with-moderate-covid-19.

[268] Gilead, *Remdesivir Clinical Trials, available at* https://www.gilead.com/purpose/advancing-global-health/covid-19/remdesivir-clinical-trials (last visited on June 8, 2020).

[269] *Id*.

coronavirus.[270] In the study, 12 monkeys were infected with COVID-19 and half of them were given early treatment with remdesivir.[271] The monkeys that received the drug did not show signs of respiratory disease and had reduced damage to the lungs.[272] In addition, the viral load in the lungs of the monkeys treated with remdesivir was lower.[273]

- As previously mentioned, the FDA granted an EUA for remdesivir on May 1, 2020, to treat hospitalized adult and pediatric patients with suspected or laboratory confirmed SARS-CoV-2 infection and severe COVID-19. While remdesivir is not approved by the FDA and the safety and efficacy for treatment of COVID-19 are not yet established, the EUA will enable appropriate patients more ready access to remdesivir.[274]

- Gilead announced that it will provide the entirety of its existing supply through June—1.5 million doses—at no cost, to treat patients with the most severe symptoms of COVID-19 and address the urgent medical needs around the world.[275] According to Gilead, "[a]ssuming a 10-day treatment course, Gilead's donation of 1.5 million individual doses of remdesivir equates to more than 140,000 treatment courses that will be provided at no cost to treat patients following potential emergency authorizations and regulatory approvals, including this EUA."[276] This is based on a conversion factor of approximately 11 vials equating to one course of treatment. Given the results from the SIMPLE trial to evaluate a 5-day treatment course and 10-day treatment course in COVID-19 patients with severe disease, which demonstrated similar efficacy with 5-day and 10-day dosing durations in patients with severe disease, this donation could potentially result in additional treatment courses.[277]

    - In addition to its donations of remdesivir, in anticipation of potential future needs, Gilead has accelerated manufacturing timelines to

[270] Manas Mishra and Deena Beasly, *Gilead's remdesivir prevents lung damage in COVID-19 study on monkeys,* REUTERS (June 9, 2020), *available at* https://www.reuters.com/article/us-health-coronavirus-gilead-sciences-re/gileads-remdesivir-shows-promise-in-covid-19-study-on-monkeys-idUSKBN23G1CW.
[271] *Id*.
[272] *Id*.
[273] *Id*.
[274] Gilead, *COVID-19, Gilead Sciences Update On The Company's Ongoing Response to COVID-19, available at* https://www.gilead.com/purpose/advancing-global-health/covid-19 (last visited on June 11, 2020).
[275] Daniel O'Day, *An Update on COVID-19 from our Chairman & CEO,* Gilead (Apr. 4, 2020), *available at* https://www.gilead.com/stories/articles/an-update-on-covid-19-from-our-chairman-and-ceo.
[276] Gilead, *Gilead's Investigational Antiviral Remdesivir Receives U.S. Food and Drug Administration Emergency Use Authorization for the Treatment of COVID-19* (May 1, 2020), *available at* https://www.gilead.com/news-and-press/press-room/press-releases/2020/5/gileads-investigational-antiviral-remdesivir-receives-us-food-and-drug-administration-emergency-use-authorization-for-the-treatment-of-covid19.
[277] The original conversion factor for a treatment course of remdesivir was that approximately 11 vials equaled one treatment. After the results from Gilead's trial for severe disease, the conversion rate went down to 7.89 vials per treatment. The most recent SIMPLE Trial results resulted in the conversion rate being further reduced. According to HHS, a treatment course of remdesivir is, on average, 6.25 vials.

increase its available supply as rapidly as possible.[278] Gilead "set a goal of producing at least 500,000 treatment courses by October, 1 million treatment courses by December 2020 and millions more in 2021, if required. These goals were based on a 10-day treatment course. Gilead now anticipates being able to cover significantly more patients based on the SIMPLE study results."[279]

- In addition, Gilead is developing easier-to-administer versions of remdesivir for COVID-19 that could be used outside of hospitals, including ones that can be inhaled.[280]

- On May 9, 2020, ASPR announced the allocation plan for remdesivir.[281] The allocation was from a donation by Gilead to the U.S. on May 3, 2020, in which Gilead committed to supplying 606,840 vials over six weeks to treat an estimated 78,000 hospitalized patients under the EUA granted on May 1, 2020.[282] The 78,000 estimate is based on the 7.8 vials per one course of therapy conversion rate. With the updated conversion rate of 6.25 vials equating one course of therapy, the 606,840 vials can treat closer to an estimated 97,000 hospitalized patients.[283] The donated doses will be used to treat hospitalized COVID-19 patients in areas of the country hardest hit by the pandemic.

  - On May 18, 2020, Gilead confirmed that it would donate an additional 333,160 vials of remdesivir to the U.S. with an expected delivery date in early June, bringing the total U.S. donation to 940,000 vials.[284] According to HHS, the 940,000 vials would be enough to treat

[278] Gilead, *Development of Remdesivir, available at* https://www.gilead.com/-/media/gilead-corporate/files/pdfs/covid-19/gilead_rdv-development-fact-sheet-2020.pdf (last visited on June 12, 2020).
[279] Gilead, *Gilead's Investigational Antiviral Remdesivir Receives U.S. Food and Drug Administration Emergency Use Authorization for the Treatment of COVID-19* (May 1, 2020), *available at* https://www.gilead.com/news-and-press/press-room/press-releases/2020/5/gileads-investigational-antiviral-remdesivir-receives-us-food-and-drug-administration-emergency-use-authorization-for-the-treatment-of-covid19.
[280] Deena Beasley, *Gilead's next step on coronavirus: inhaled remdesivir, other easier-to-use versions*, REUTERS (June 2, 2020), *available at* https://www.reuters.com/article/us-health-coronavirus-gilead-sciences/gileads-next-step-on-coronavirus-inhaled-remdesivir-other-easier-to-use-versions-idUSKBN2391FP.
[281] U.S. Department of Health and Human Services, *HHS announces shipment of donated remdesivir for hospitalized patients with COVID-19* (May 9, 2020), *available at* https://www.hhs.gov/about/news/2020/05/09/hhs-ships-first-doses-of-donated-remdesivir-for-hospitalized-patients-with-covid-19.html#:~:text=committed%20to%20supplying%20approximately%20607%2C000,the%20company%20is%20donating%20worldwide.
[282] *Id*.; U.S. Department of Health and Human Services, Public Health Emergency, *Remdesivir, ASPR's Portfolio of COVID-19 Medical Countermeasures under Investigation, available at* https://www.phe.gov/emergency/events/COVID19/investigation-MCM/Pages/remdesivir.aspx.
[283] This is an estimate since not all patients would be treated under the 6.25 vial to course of therapy ratio.
[284] U.S. Department of Health and Human Services, Public Health Emergency, *Remdesivir, ASPR's Portfolio of COVID-19 Medical Countermeasures under Investigation, available at* https://www.phe.gov/emergency/events/COVID19/investigation-MCM/Pages/remdesivir.aspx (last visited June 18, 2020).

120,512 hospitalized COVID-19 patients.[285] With the increased donation and using the updated conversion ratio of 6.25 vials per course of therapy, approximately 150,000 patients can be treated with Gilead's donation to the U.S.[286]

- According to HHS, this product is not being distributed all at once. Rather, cases—which contain 40 vials of product each—are being sent to states and territories over the course of approximately nine weeks.[287] A table providing the allocations of remdesivir by U.S. jurisdiction per week, is available on ASPR's website.[288] In addition to the U.S. jurisdictions, cases are being delivered to the Veterans Health Administration and the Indian Health Service for distribution within those health systems.[289]

- According to HHS, hospitals provide data via a data tracking technology on the number of patients with confirmed or suspected cases of COVID-19 in the ICU and not in the ICU.[290] In addition, the National Healthcare Safety Network and data submitted by the state health departments are used to understand the number of confirmed or suspected COVID-19 cases within each state.[291] Together, this data is used to determine the state-by-state percentage of suspected and confirmed COVID-19 patients in U.S. hospitals, and that percentage is applied to the amount of remdesivir to be shipped that week, and determines the amount to be shipped to each state, jurisdiction, and territory.[292]

- According to HHS, "State health departments will distribute the doses to appropriate hospitals in their states because state and local health departments have the greatest insight into community-level needs in

[285] *Id*. This calculation is based on the 7.8 vials to course of therapy ratio.
[286] This is an estimate since not all patients would be treated under the 6.25 vial to course of therapy ratio.
[287] U.S. Department of Health and Human Services, Public Health Emergency, *Remdesivir, ASPR's Portfolio of COVID-19 Medical Countermeasures under Investigation, available at* https://www.phe.gov/emergency/events/COVID19/investigation-MCM/Pages/remdesivir.aspx (last visited June 18, 2020).
[288] *Id*.
[289] U.S. Department of Health and Human Services, *HHS announces shipment of donated remdesivir for hospitalized patients with COVID-19* (May 9, 2020), *available at* https://www.hhs.gov/about/news/2020/05/09/hhs-ships-first-doses-of-donated-remdesivir-for-hospitalized-patients-with-covid-19.html.
[290] U.S. Department of Health and Human Services, Public Health Emergency, *Remdesivir, ASPR's Portfolio of COVID-19 Medical Countermeasures under Investigation, available at* https://www.phe.gov/emergency/events/COVID19/investigation-MCM/Pages/remdesivir.aspx.
[291] *Id*.
[292] *Id*.

the COVID-19 response, including appropriate distribution of a treatment in limited supply."[293]

- Gilead signed non-exclusive voluntary licensing agreements with nine generic pharmaceutical manufacturing companies based in Egypt, India, and Pakistan to further expand the supply of remdesivir by manufacturing remdesivir for distribution in 127 countries.[294] These companies include Cipla Ltd.; Dr. Reddy's Laboratories Ltd.; Eva Pharma; Ferozsons Laboratories; Hetero Labs Ltd.; Jubilant Lifesciences; Mylan; Syngene, a Biocon company; and Zydus Cadila Healthcare Ltd.[295] "Under the licensing agreements, the companies have a right to receive a technology transfer of the Gilead manufacturing process for remdesivir to enable them to scale up production more quickly. The licensees also set their own prices for the generic product they produce. The licenses are royalty-free until the World Health Organization declares the end of the Public Health Emergency of International Concern regarding COVID-19, or until a pharmaceutical product other than remdesivir or a vaccine is approved to treat or prevent COVID-19, whichever is earlier."[296]

- On June 29, 2020, HHS announced an agreement to secure more than 500,000 treatment courses of remdesivir from Gilead for the U.S. through September, allowing U.S. hospitals to purchase remdesivir in amounts that are allocated by HHS and state health departments.[297] According to HHS' announcement, this supply "represents 100 percent of Gilead's projected production for July (94,200 treatment courses), 90 percent of production in August (174,900 treatment courses), and 90 percent of production in September (232,800 treatment courses), in addition to an allocation for clinical trials. A treatment course of remdesivir is, on average, 6.25 vials."[298] After September, and once supplies are less constrained, HHS will no longer manage the allocation of remdesivir.[299]

    - Gilead announced that "[t]o ensure broad and equitable access at a time of urgent global need, we have set a price for governments of developed countries of $390 per vial. Based on current treatment

[293] U.S. Department of Health and Human Services, *HHS announces shipment of donated remdesivir for hospitalized patients with COVID-19* (May 9, 2020), *available at* https://www.hhs.gov/about/news/2020/05/09/hhs-ships-first-doses-of-donated-remdesivir-for-hospitalized-patients-with-covid-19.html.
[294] Gilead, *Voluntary Licensing Agreements for Remdesivir, available at* https://www.gilead.com/purpose/advancing-global-health/covid-19/voluntary-licensing-agreements-for-remdesivir (last visited June 25, 2020).
[295] *Id.*
[296] *Id.*
[297] U.S. Department of Health and Human Services, Public Health Emergency, *Remdesivir, available at* https://www.phe.gov/emergency/events/COVID19/investigation-MCM/Pages/remdesivir.aspx (last visited June 29, 2020).
[298] *Id.*
[299] Gilead, *An Open Letter from Daniel O'Day, Chairman & CEO, Gilead Sciences* (June 29, 2020), *available at* https://www.gilead.com/news-and-press/press-room/press-releases/2020/6/an-open-letter-from-daniel-oday-chairman--ceo-gilead-sciences.

patterns, the vast majority of patients are expected to receive a 5-day treatment course using 6 vials of remdesivir, which equates to $2,340 per patient."[300] "Because of the way the U.S. system is set up and the discounts that government healthcare programs expect, the price for U.S. private insurance companies, will be $520 per vial."[301] According to Gilead, at the level it has priced remdesivir and with government programs in place, along with additional assistance from Gilead as needed, Gilead believes all patients will have access to remdesivir.[302]

- According to HHS, hospitals will pay no more than Gilead's Wholesale Acquisition Price—approximately $3,200 per treatment course.[303] According to HHS, patients generally "do not pay directly for hospital-administered drugs like remdesivir; rather, for Medicare and most private insurers, the drug's cost is incorporated into payments made by the insurer, such as Medicare paying for the drug through a diagnostic-related group."[304]

- **Chloroquine** is an antimalarial medicine and **hydroxychloroquine** is an antiviral medication to prevent malaria and treat rheumatoid conditions such as arthritis. Clinical trials of chloroquine and hydroxychloroquine are underway in the U.S. and around the world. However, multiple trials were recently suspended, including the hydroxychloroquine arm of the WHO's Solidarity Trial, and an NIH clinical trial. A few examples are included below:

  - A multi-site clinical trial led by the University of Washington Department of Global Health/International Clinical Research Center and New York University's Grossman School of Medicine is trying to determine whether hydroxychloroquine can prevent transmission of COVID-19.[305] Results from the trial are expected in the summer.[306]

  - The NIH started a clinical trial in May, sponsored by NIAID, to evaluate whether hydroxychloroquine, given together with azithromycin, can prevent

[300] *Id.*
[301] *Id.*
[302] *Id.*
[303] U.S. Department of Health and Human Services, Public Health Emergency, *Remdesivir, available at* https://www.phe.gov/emergency/events/COVID19/investigation-MCM/Pages/remdesivir.aspx (last visited June 29, 2020).
[304] *Id.*
[305] University of Washington Department of Global Health, *Does Antimalarial Drug Prevent COVID-19? New DGH Study Seeks Answers (Ruanne Barnabas, ICRC)* (Apr. 1, 2020), *available at* https://globalhealth.washington.edu/news/2020/03/30/does-antimalarial-drug-prevent-covid-19-new-dgh-study-seeks-answers.
[306] *Id.*

hospitalization and death from COVID-19.[307] The estimated completion date of this study was in March 2021.[308]

- On June 20, 2020, NIAID stopped enrollment because NIAID, the study leadership, and the independent data and safety monitoring board overseeing the trial determined that the rate of participant enrollment has been inadequate for the trial to meet its objectives in a timely manner.[309]

- Researchers at the University of Washington Schools of Public Health and Medicine are conducting a multi-site randomized controlled trial to determine the effectiveness of hydroxychloroquine with and without azithromycin for patients with COVID-19.[310] Results of this trial are expected by July and the "findings will determine whether a treatment looks promising enough for larger clinical trials and whether the drugs are safe.[311]

- On April 9, 2020, NIH announced that a clinical trial to evaluate the safety and effectiveness of hydroxychloroquine in the treatment of adults hospitalized with COVID-19 had begun, with the first participants enrolled in Tennessee.[312] This trial was conducted by the Prevention and Early Treatment of Acute Lung Injury (PETAL) Clinical Trials Network of the National Heart, Lung, and Blood Institute (NHLBI). This blinded, placebo-controlled randomized clinical trial aimed to enroll more than 500 adults who were hospitalized with COVID-19 or in an emergency department with anticipated hospitalization. The estimated completion date for this study was July 2021.[313]

    - On June 20, 2020, NIH announced that it was halting this clinical trial, after data revised by a drug safety and monitoring board determine

[307] National Institutes of Health, *NIH begins clinical trial of hydroxychloroquine and azithromycin to treat COVID-19* (May 14, 2020), *available at* https://www.nih.gov/news-events/news-releases/nih-begins-clinical-trial-hydroxychloroquine-azithromycin-treat-covid-19.
[308] *Evaluating the Efficacy of Hydroxychloroquine and Azithromycin to Prevent Hospitalization or Death in Persons With COVID-19,* ClinicalTrials.gov, *available at* https://clinicaltrials.gov/ct2/show/NCT04358068.
[309] National Institute of Allergy and Infectious Diseases, *BULLETIN – NIH Clinical Trial Evaluating Hydroxychloroquine and Azithromycin for COVID-19 Closes Early* (June 20, 2020), *available at* https://www.niaid.nih.gov/news-events/bulletin-nih-clinical-trial-evaluating-hydroxychloroquine-and-azithromycin-covid-19.
[310] University of Washington School of Public Health, *New COVID-19 treatment trial to look at hydroxychloroquine-based regimens* (May 5, 2020), *available at* https://sph.washington.edu/news-events/news/new-covid-19-treatment-trial-look-hydroxychloroquine-based-regimens.
[311] *Id*.
[312] National Institutes of Health, *NIH clinical trial for hydroxychloroquine, a potential therapy for COVID-19, begins* (Apr. 9, 2020), *available at* https://www.nih.gov/news-events/news-releases/nih-clinical-trial-hydroxychloroquine-potential-therapy-covid-19-begins.
[313] National Institutes of Health, U.S. Clinical Library of Medicine, *Outcomes Related to COVID-19 Treated With Hydroxychloroquine Among In-patients With Symptomatic Disease (ORCHID), available at* https://clinicaltrials.gov/ct2/show/NCT04332991 (last visited on June 11, 2020).

that, while there was no harm, the drug was unlikely to be beneficial to hospitalized patients with COVID-19.[314]

- On April 20, 2020, Novartis announced that it reached an agreement with FDA to proceed with a Phase 3 clinical trial to evaluate the use of hydroxychloroquine for the treatment of hospitalized patients with COVID-19. This trial was to be conducted at more than a dozen sites in the U.S.[315]

    - On June 19, 2020, Novartis announced it discontinued its sponsored clinical hydroxychloroquine clinical trial for COVID-19 due to enrollment challenges that made the trial's completion infeasible.[316]

- In addition, the aforementioned WHO Solidarity trial included hydroxychloroquine.

    - On May 23, 2020, the Executive Group of the trial decided to pause the hydroxychloroquine arm of the trial due to published concerns in the medical journal *The Lancet* about the safety of the drug, which reported that patients given hydroxychloroquine were dying at higher rates than other patients.[317] According to the WHO, this decision was taken as a precaution while the safety data was reviewed by the Data Safety and Monitoring Committee of the Solidarity Trial.[318] Further, on May 27, 2020, European governments, including France, Italy, and Belgium, suspended the use of hydroxychloroquine in a second global trial, and the United Kingdom said that a separate trial was being put on hold, less than a week after it started.[319]

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[314] National Institutes of Health, *NIH halts clinical trial of hydroxychloroquine*, *available at* https://www.nih.gov/news-events/news-releases/nih-halts-clinical-trial-hydroxychloroquine (June 20, 2020).
[315] Novartis, *Novartis to sponsor large clinical trial of hydroxychloroquine in hospitalized COVID-19 patients,* (Apr. 20, 2020), *available at* https://www.novartis.com/news/media-releases/novartis-sponsor-large-clinical-trial-hydroxychloroquine-hospitalized-covid-19-patients.
[316] Novartis, *Novartis discontinues hydroxychloroquine clinical trial based on slow enrollment, remains committed to pandemic research efforts* (Jun. 19, 2020), *available at* https://www.novartis.com/news/media-releases/novartis-discontinues-hydroxychloroquine-clinical-trial-based-slow-enrollment-remains-committed-pandemic-research-efforts.
[317] *"Solidarity" clinical trial for COVID-19 treatments,* World Health Organization, *available at* https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-clinical-trial-for-covid-19-treatments (last visited on June 8, 2020); Jason Beaubien, *WHO Halts Hydroxychloroquine Trial Over Safety Concerns,* NPR (May 25, 2020), *available at* https://www.npr.org/sections/coronavirus-live-updates/2020/05/25/861913688/who-halts-hydroxychloroquine-trial-over-safety-concerns.
[318] *"Solidarity" clinical trial for COVID-19 treatments,* World Health Organization, *available at* https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-clinical-trial-for-covid-19-treatments (last visited on June 8, 2020).
[319] Matthias Blamont, Alistair Smout, and Emilio Parodi, *EU governments ban malaria drug for COVID-19, trial paused as safety fears grow*, REUTERS (May 27, 2020), *available at* https://www.reuters.com/article/health-coronavirus-hydroxychloroquine-fr/eu-governments-ban-malaria-drug-for-covid-19-trial-paused-as-safety-fears-grow-idUSKBN2340A6.

- However, due to concerns raised about the data behind the study on June 3, 2020, the editors of *The Lancet* issued a statement acknowledging the criticism of the study.[320] That same day, the "WHO's Director-General announced that on the basis of the available mortality data, the members of the committee have recommended that there are no reasons to modify the trial protocol."[321] The Executive Group subsequently endorsed the continuation of all arms of the trial, including hydroxychloroquine.[322] On June 4, 2020, *The Lancet* retracted the study due to potential flaws in the research data because the authors were unable to confirm that the data set was accurate.[323]

- On June 17, 2020, the WHO announced that the hydroxychloroquine arm of the Solidarity Trial was being stopped. The decision was made based on evidence from the Solidarity trial, the UK Recovery trial, and a review of other evidence on hydroxychloroquine. Data showed that hydroxychloroquine does not result in the reduction of mortality of hospitalized patients when compared with the standard of care.[324]

- As previously mentioned, the FDA issued an EUA for chloroquine phosphate and hydroxychloroquine sulfate for treatment of COVID-19 on March 28, 2020. In making the decision, "officials said the drugs have shown activity in lab studies and anecdotal reports suggest they may offer some benefit to hospitalized COVID-19 patients."[325] However, as previously discussed, based on FDA's continued review of the scientific evidence available for chloroquine phosphate and hydroxychloroquine sulfate, on June 15, 2020, FDA determined that the statutory criteria for an EUA is no longer met and

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[320] The Lancet Editors, *Expression of concern: Hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19: a multinational registry analysis,* THE LANCET (June 3, 2020), *available at* https://www.thelancet.com/journals/lanpub/article/PIIS0140-6736(20)31290-3/fulltext?utm_campaign=tlpr&utm_medium=email&_hsmi=88871506&_hsenc=p2ANqtz--PMYW8s6iygCIHlYIlTZ1TbEnUPzCIB3vYhdEyzfSHm2LSQBRT6s0Q8IrF3D5b9XozG_KOD9K0qiyzWYhejdOd5yzA9A&utm_content=88871506&utm_source=hs_email; Chris Dall, *Controversy over data in hydroxychloroquine COVID-19 study grows,* Center for Infectious Disease Research and Policy, University of Minnesota (June 3, 2020), *available at* https://www.cidrap.umn.edu/news-perspective/2020/06/controversy-over-data-hydroxychloroquine-covid-19-study-grows.

[321] *"Solidarity" clinical trial for COVID-19 treatments,* World Health Organization, *available at* https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-clinical-trial-for-covid-19-treatments (last visited on June 8, 2020).

[322] *Id.*

[323] Erika Edwards, *The Lancet retracts large study on hydroxychloroquine,* NBC NEWS (June 4, 2020), *available at* https://www.nbcnews.com/health/health-news/lancet-retracts-large-study-hydroxychloroquine-n1225091.

[324] *"Solidarity" clinical trial for COVID-19 treatments,* World Health Organization, *available at* https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-clinical-trial-for-covid-19-treatments (last visited on June 21, 2020).

[325] Eric Sagonowsky, Unlike FDA, European regulators refuse to clear chloroquine for COVID-19 without data, FIERCEPHARMA (Apr. 2, 2020), *available at* https://www.fiercepharma.com/pharma/europe-locks-down-chloroquine-scripts-as-researchers-china-report-positive-controlled-covid.

withdrew the EUA for chloroquine and hydroxychloroquine.[326] Specifically, FDA determined that these two drugs "are unlikely to be effective in treating COVID-19 for the authorized uses in the EUA. Additionally, in light of ongoing serious cardiac adverse events and other serious side effects, the known and potential benefits of CQ and HCQ no longer outweigh the known and potential risks for the authorized use."[327]

- Earlier this year, several drug makers either pledged donations or scaled up manufacturing of chloroquine and hydroxychloroquine.
    - In March, Novartis committed to donating up to 130 million doses of hydroxychloroquine to support the global COVID-19 pandemic response, and the company announced that it is exploring further scaling of capacity to increase supply.[328]
    - Also in March, Bayer pledged to donate three million tablets of Resochin, chloroquine phosphate, to the U.S.[329]
    - On March 29, 2020, HHS announced that it accepted 30 million doses of hydroxychloroquine sulfate from Sandoz, Novartis' generic and biosimilar division, and one million doses of Resochin, medical grade chloroquine phosphate, from Bayer Pharmaceuticals for possible use in treating patients hospitalized with COVID-19 or for use in clinical trials.[330] According to HHS, the SNS, managed by ASPR, worked with the Federal Emergency Management Agency to ship donated doses to states while the EUA was in place.[331]
    - To date, Novartis has donated 88 million doses of hydroxychloroquine to HHS. With the change in FDA's EUA status for hydroxychloroquine, Novartis will not proceed with donating

[326] U.S. Food and Drug Administration, *Emergency Use Authorization, Emergency Use Authorization (EUA) information, and list of all current EUAs, available at* https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization?utm_campaign=051120_PR_Coronavirus%20(COVID-19)%20Update:%20Daily%20Roundup%20May%2011,%202020&utm_medium=email&utm_source=Eloqua#coviddrugs (last visited on June 15, 2020).
[327] *Id*.
[328] Novartis, *Novartis commits to donate up to 130 million doses of hydroxychloroquine to support the global COVID-19 pandemic response* (Mar. 20, 2020), *available at* https://www.novartis.com/news/media-releases/novartis-commits-donate-130-million-doses-hydroxychloroquine-support-global-covid-19-pandemic-response.
[329] *Bayer Partners With U.S. Government on Major Product Donation to Fight Coronavirus* (Mar. 19, 2020), *available at* https://eyewire.news/articles/bayer-partners-with-u-s-government-on-major-product-donation-to-fight-coronavirus/.
[330] U.S. Department of Health and Human Services, *HHS accepts donations of medicine to Strategic National Stockpile as possible treatments for COVID-19 patients* (Mar. 29, 2020), *available at* https://www.hhs.gov/about/news/2020/03/29/hhs-accepts-donations-of-medicine-to-strategic-national-stockpile-as-possible-treatments-for-covid-19-patients.html.
[331] *Id*.

additional doses of the drug, but it will continue to supply the normal commercial demand where the drug is approved for use and when there are requests for clinical trials worldwide.

- About 63 million tablets of hydroxychloroquine remain in the SNS and HHS has been in talks with drug makers about options for the remaining tablets.[332]

- On March 31, 2020, the FDA reported shortages of chloroquine phosphate tablets and hydroxychloroquine sulfate tablets.[333] The duration of shortage for the chloroquine phosphate tablets was from March 31, 2020 to May 8, 2020, and is now resolved.[334] However, the hydroxychloroquine sulfate tablets are still in shortage.[335]

- Some studies evaluating hydroxychloroquine have started to yield results.

  - For example, *The New England Journal of Medicine* published the results of an observational study of hydroxychloroquine in hospitalized patients with COVID-19 in May.[336] In this study involving patients with COVID-19 "who had been admitted to the hospital, hydroxychloroquine administration was not associated with either a greatly lowered or an increased risk of the composite end point of intubation or death."[337] The study further noted that randomized, controlled trials of hydroxychloroquine in patients with COVID-19 are needed.[338]

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[332] Anna Edney, *Trump's Drug Push Still Keeps Door Open for Banned Indian Firm,* Bloomberg (June 24, 2020), *available at* https://www.bloomberg.com/news/articles/2020-06-24/trump-s-drug-push-still-keeps-door-open-for-banned-indian-firm.

[333] U.S. Food and Drug Administration, *FDA Drug Shortages, Current and Resolved Drug Shortages and Discontinuations Reported to FDA, available at* https://www.accessdata.fda.gov/scripts/drugshortages/dsp_ActiveIngredientDetails.cfm?AI=Chloroquine%20Phosphate%20Tablets&st=r; U.S. Food and Drug Administration, *FDA Drug Shortages, Current and Resolved Drug Shortages and Discontinuations Reported to FDA, available at* https://www.accessdata.fda.gov/scripts/drugshortages/dsp_ActiveIngredientDetails.cfm?AI=Hydroxychloroquine%20Sulfate%20Tablets&st=c (last visited on June 11, 2020).

[334] U.S. Food and Drug Administration, *FDA Drug Shortages, Current and Resolved Drug Shortages and Discontinuations Reported to FDA, available at* https://www.accessdata.fda.gov/scripts/drugshortages/dsp_ActiveIngredientDetails.cfm?AI=Chloroquine%20Phosphate%20Tablets&st=r (last visited on June 11, 2020).

[335] U.S. Food and Drug Administration, *FDA Drug Shortages, Current and Resolved Drug Shortages and Discontinuations Reported to FDA, available at* https://www.accessdata.fda.gov/scripts/drugshortages/dsp_ActiveIngredientDetails.cfm?AI=Hydroxychloroquine%20Sulfate%20Tablets&st=c (last visited on June 11, 2020).

[336] Joshua Geleris, M.D., Yifei Sun, Ph.D., et al., *Observational Study of Hydroxychloroquine in Hospitalized Patients with Covid-19,* THE NEW ENGLAND JOURNAL OF MEDICINE (May 7, 2020), *available at* https://www.nejm.org/doi/full/10.1056/NEJMoa2012410.

[337] *Id*.

[338] *Id*.

- In addition, a cohort study of 1,438 patients with COVID-19 hospitalized in metropolitan New York evaluated whether there is an association between the use of hydroxychloroquine, with or without azithromycin, and in-hospital mortality.[339] The study found that treatment with hydroxychloroquine, azithromycin, or both was not associated with significantly lower in-hospital mortality.[340]

- As previously mentioned, hydroxychloroquine is one of the drugs being studies as a prophylaxis for COVID-19. *The New England Journal of Medicine* recently published the results of a randomized trial of hydroxychloroquine as postexposure prophylaxis for COVID-19.[341] The conclusion was that after high-risk or moderate-risk exposure to COVID-19, hydroxychloroquine did not prevent illness compatible with COVID-19 or confirmed infection when used as postexposure prophylaxis within four days after exposure.[342]

- **Dexamethasone** is a synthetic corticosteroid that was first approved by the FDA in 1958.[343] Dexamethasone is used to reduce inflammation in many conditions, allergic states that fail to respond to other treatments, dermatologic diseases, and more.[344]

  - The Randomised Evaluation of COVID-19 Therapy (RECOVERY) trial was established by the University of Oxford in March 2020, as a randomized clinical trial investigating whether treatment with either lopinavir-ritonavir, hydroxychloroquine, corticosteroids, azithromycin, convalescent plasma or tocilizumab prevents death in patients with COVID-19.[345] More than 11,500 individuals have been enrolled in the trial from over 175 National Health Service hospitals in the U.K.[346]

  - On June 8, 2020, recruitment to the dexamethasone arm was halted because the trial's Steering Committee believed that "sufficient patients had been

[339] Eli S. Rosenberg, PhD, Elizabeth M. Dufort, MD, et al., *Association of Treatment With Hydroxychloroquine or Azithromycin With In-Hospital Mortality in Patients With COVID-19 in New York State*, JAMA NETWORK (May 11, 2020), *available at* https://jamanetwork.com/journals/jama/fullarticle/2766117.
[340] *Id*.
[341] David R. Boulware, M.D., M.P.H., Matthew F. Pullen, M.D., et al., *A Randomized Trial of Hydroxychloroquine as Postexposure Prophylaxis for Covid-19*, THE NEW ENGLAND JOURNAL OF MEDICINE (June 3, 2020), *available at* https://www.nejm.org/doi/full/10.1056/NEJMoa2016638.
[342] *Id*.
[343] Omudhome Ogbru, PharmD, *dexamethasone (Decadron, DexPak)*, MEDICINENET, *available at* https://www.medicinenet.com/dexamethasone-decadron-dexpak/article.htm#what_is_dexamethasone_and_how_does_it_work_mechanism_of_action.
[344] *Id*.; DECADRON (DEXAMETHASONE TABLETS, USP), NDA 11-664/@-062, Center for Drug Evaluation and Research, *available at* https://www.accessdata.fda.gov/drugsatfda_docs/label/2004/11664slr062_decadron_lbl.pdf.
[345] *Randomised Evaluation of COVID-19 Therapy (RECOVERY)*, ClinicalTrials.gov, *available at* https://clinicaltrials.gov/ct2/show/NCT04381936.
[346] *Low-cost dexamethasone reduces death by up to one third in hospitalized patients with severe respiratory complications of COVID-19*, Oxford University (June 16, 2020), *available at* https://www.recoverytrial.net/files/recovery_dexamethasone_statement_160620_v2final.pdf?source=email.

enrolled to establish whether or not the drug had a meaningful benefit."[347] The results showed that there was no benefit among the patients who did not require respiratory support, however, dexamethasone reduced deaths by one-third in ventilated patients and by one fifth in other patients receiving oxygen only.[348] Researchers are working to publish the full details as soon as possible.[349]

- Dexamethasone is an inexpensive drug sold by a range of generic drug companies in the U.S.[350]

- **Convalescent plasma and plasma-based therapies:** This type of treatment has proven effective in other epidemics and involves giving patients who are sick blood plasma from those who have recovered. It can work because the plasma contains antibodies against the virus, weaponizing the immune system of the sick patient.

  - FDA has issued guidance to provide recommendations to health care providers and investigators on the administration and study of convalescent plasma.[351] The guidance includes pathways for use of investigational COVID-19 convalescent plasma; patient eligibility; collection of COVID-19 convalescent plasma, including donor eligibility and donor qualifications; labeling; and record keeping.[352]

    - Under the guidance for pathways for use of investigational COVID-19 convalescent plasma FDA lists several pathways that are available for administering or studying the use of COVID-19 plasma: (1) clinical trials; (2) expanded access; and (3) single patient emergency IND.[353]

    - As of June 29, 2020, the expanded access program for convalescent plasma has more than 40,660 patients enrolled with more than 27,504 patients infused.[354]

[347] *Id*.
[348] *Id*.
[349] *Id*.
[350] Sarah Owermohle, *Cheap steroid reduces Covid-19 deaths in large study*, POLITICO PRO HEALTH CARE (June 16, 2020), *available at* https://subscriber.politicopro.com/health-care/article/2020/06/cheap-steroid-reduces-covid-19-deaths-in-new-study-1952680.
[351] U.S. Food and Drug Administration, *Recommendations for Investigational COVID-19 Convalescent Plasma, available at* https://www.fda.gov/vaccines-blood-biologics/investigational-new-drug-ind-or-device-exemption-ide-process-cber/recommendations-investigational-covid-19-convalescent-plasma (last visited on June 12, 2020).
[352] *Id*.
[353] *Id*.
[354] COVID-19 expanded access program, *available at* https://www.uscovidplasma.org/ (last visited on June 29, 2020).

- One study from China reported that of ten patients given convalescent plasma, seven saw their viral loads become undetectable; the study also noted other improvements in their condition.[355]

- In May, Mayo Clinic and collaborators reported safety data on the first 5,000 hospitalized patients transfused with investigational convalescent plasma as part of FDA's Expanded Access Program for COVID-19.[356] "The early indicators suggest experimental convalescent plasma is safe in treating severely ill patients."[357] Mayo Clinic will continue to collect more safety data and continue studies to determine efficacy.[358]

- Twenty-five patients with severe and/or life threatening COVID-19 disease were enrolled in a study at the Houston Methodist hospital from March 28, 2020 to April 14, 2020, and were transfused with convalescent plasma from donors with confirmed SARS-CoV-2 infection who had recovered.[359] "The primary study outcome was safety, and the secondary outcome was clinical status at day 14 after transfusion. Clinical improvement was assessed on the basis of a modified World Health Organization six-point ordinal scale and laboratory parameters. "[360] The results showed that by day 14 after transfusion with convalescent plasma, 76 percent of patients had at least a one-point improvement in clinical status and no adverse events as a result of the plasma transfusion were observed.[361]

- Johns Hopkins School of Public Health was expected to begin two trials of convalescent plasma in May.[362] "The first trial is a prophylaxis clinical trial focused on healthcare workers and other high-risk populations that frequently

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[355] Kai Duan, Bende Liu, et. al., The feasibility of convalescent plasma therapy in severe COVID-19 patients: a pilot study, MEDRXIV, (Mar. 16, 2020), *available at* https://www.medrxiv.org/content/10.1101/2020.03.16.20036145v1.full.pdf+html.

[356] Robert Nellis, *Early indicators: Investigational convalescent plasma is safe for patients with COVID-19*, Mayo Clinic (May 14, 2020), *available at* https://newsnetwork.mayoclinic.org/discussion/early-indicators-investigational-convalescent-plasma-is-safe-for-patients-with-covid-19/.

[357] *Id*.

[358] *Id*.

[359] Eric Salazar, Katerine K. Pered, et al., *Treatment of Coronavirus Disease 2019 (COVID-19) Patients with Convalescent Plasma*, THE AMERICAN JOURNAL OF PATHOLOGY (May 26, 2020), *available at* https://ajp.amjpathol.org/article/S0002-9440(20)30257-1/fulltext.

[360] *Id*.

[361] *Id*.

[362] Chris Galford, *Johns Hopkins to begin convalescent plasma trials focused on high-risk and at-home COVID-19 infectees*, HOMELAND PREPAREDNESS NEWS (May 8, 2020), *available at* https://homelandprepnews.com/countermeasures/48791-johns-hopkins-to-begin-convalescent-plasma-trials-focused-on-high-risk-and-at-home-covid-19-infectees/; Eamon N. Dreisbach, *Johns Hopkins begins trials of blood plasma for COVID-19 treatment, prophylaxis*, Healio News (May 8, 2020), *available at* https://www.healio.com/news/infectious-disease/20200508/johns-hopkins-begins-trials-of-blood-plasma-for-covid19-treatment-prophylaxis.

face major exposure to the virus. The other will enroll those with mild COVID-19 symptoms that have taken to at-home isolation."[363]

- In addition to the use of convalescent plasma, multiple pharmaceutical companies are developing plasma-derived therapies.

  - In March, Emergent BioSolutions announced that it had initiated the development of two plasma-derived product candidates for the treatment and prevention of COVID-19—COVID-Hyper Immune Globulin (COVID-HIG) and COVID-Equine Immune Globulin (COVID-EIG).[364]

    - COVID-HIG is being developed as a human plasma-derived therapy candidate for treatment in severe hospitalized patients.[365] In addition, Emergent BioSolutions is conducting research to see if COVID-HIG may be able to provide protection for at-risk individuals.[366]

    - COVID-EIG is being developed as an equine plasma-derived therapy candidate for treatment of severe hospitalized patients.[367]

  - On April 2, 2020, Emergent BioSolutions announced it entered into a formal partnership with the U.S. government to expedite development of a plasma-derived therapy for patients with COVID-19.[368] Specifically, Emergent BioSolutions received $14.5 million from BARDA in support of its COVID-HIG program.[369] In addition, Emergent BioSolutions and NIAID "have agreed to incorporate the company's COVID-HIG product candidate into one of NIAID's clinical studies for assessment of treatments for COVID-19 once clinical material is available, and the study begins."[370] The

[363] Chris Galford, *Johns Hopkins to begin convalescent plasma trials focused on high-risk and at-home COVID-19 infectees*, HOMELAND PREPAREDNESS NEWS (May 8, 2020), *available at* https://homelandprepnews.com/countermeasures/48791-johns-hopkins-to-begin-convalescent-plasma-trials-focused-on-high-risk-and-at-home-covid-19-infectees/.
[364] Emergent BioSolutions, *Emergent BioSolutions Initiates Development of Plasma-Derived Product Candidates for the Treatment and Prevention of Coronavirus Disease* (Mar. 11, 2020), *available at* https://investors.emergentbiosolutions.com/news-releases/news-release-details/emergent-biosolutions-initiates-development-plasma-derived?field_nir_news_date_value[min]=.
[365] *Id*.
[366] *Id*
[367] *Id*.
[368] Emergent BioSolutions, *Emergent BioSolutions Partners with U.S. Government for Comprehensive Response to Expedite Development of Plasma-Derived Therapy for COVID-19* (Apr. 2, 2020), *available at* https://investors.emergentbiosolutions.com/news-releases/news-release-details/emergent-biosolutions-partners-us-government-comprehensive?field_nir_news_date_value%5bmin%5d=.
[369] *Id*.
[370] *Id*.

announcement also noted that Emergent BioSolutions "will seek a path forward with the FDA for the development of COVID-HIG and possible use under" EUA.[371]

- At least one hyperimmune globulin plasma-based treatment is also in development. Hyperimmune globulin is manufactured from plasma with specific antibodies.

  - A number of companies, including Biotest, BPL, CSL Behring, LFB, Octapharma, and Takeda announced an alliance—the CoVIg-19 Plasma Alliance—to develop one, unbranded anti-SARS-CoV-2 polyclonal hyperimmune immunoglobulin medicine with the potential to treat individuals with serious complications from COVID-19.[372] The companies will harness their collective capacity to manufacture the therapeutic. This partnership is unprecedented, bringing together multiple plasma companies including plasma collection, development, production, and distribution to work together rather than pursuing individual research.[373] The alliance also announced that it will work with NIAID "to test the safety, tolerability and efficacy of the hyperimmune therapy in adult patients with COVID-19. This global study is currently anticipated to start in the summer and will form the foundation for the potential regulatory approval of the hyperimmune therapy."[374]

  - The private sector should explore additional ways to collaborate in order to accelerate the development and manufacturing of therapeutics.

- While immediately available, and already in limited use, the supply of plasma from recovered patients may not be sufficient to meet all needs. In addition, studies of recovered patients are necessary to determine if all recovered patients produce a full immune response to the infection, including neutralizing antibodies at high enough levels to become donors.[375]

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[371] *Id*.
[372] Takeda, *Global Plasma Leaders Collaborate to Accelerate Development of Potential COVID-19 Hyperimmune Therapy* (Apr. 6, 2020), *available at* https://www.takeda.com/newsroom/newsreleases/2020/global-plasma-leaders-collaborate-to-accelerate-development-of-potential-covid-19-hyperimmune-therapy/; CoVIg-19 Plasma Alliance, *available at* https://www.covig-19plasmaalliance.org/en-us#recruitment (last visited on June 12, 2020).
[373] CoVIg-19 Plasma Alliance, *available at* https://www.covig-19plasmaalliance.org/en-us#recruitment (last visited June 12, 2020).
[374] Takeda, *CoVIg-19 Plasma Alliance Builds Strong Momentum Through Expanded Membership and Clinical Trial Collaboration* (May 7, 2020), *available at* https://www.takeda.com/newsroom/newsreleases/2020/covig-19-plasma-alliance-builds-strong-momentum-through-expanded-membership-and-clinical-trial-collaboration/.
[375] Christine Soares, *Reasons for hope: the drugs, tests and tactics that may conquer coronavirus*, REUTERS (Apr. 17, 2020), *available at* https://www.reuters.com/article/us-health-coronavirus-lifeline/reasons-for-hope-the-drugs-tests-and-tactics-that-may-conquer-coronavirus-idUSKBN21Z2HP.

- FDA is encouraging recovered patients to donate plasma for the development of blood-related therapies.[376]

- In addition, the Office for Civil Rights at HHS recently "issued guidance on how the Health Insurance Portability and Accountability Act of 1996 (HIPAA) Privacy Rule permits covered health care providers to contact their patients who have recovered from COVID-19 to inform them about how they can donate their blood and plasma containing antibodies to help other patients with COVID-19."[377]

- A coalition of more than 30 organizations created a national donor recruitment campaign, called "The Fight Is In Us," to connect COVID-19 survivors with licensed blood and plasma donor centers.[378] This effort will bring together several coalitions and organizations including academic medical institutions, plasma companies, national blood organizations, Anthem, Inc., LabCorp, community and non-profit leaders, and marketing and media support.[379] In addition, celebrities have joined the campaign, encouraging COVID-19 survivors to urgently donate their plasma.[380]

    - Congress, the Executive Branch, and the private sector should explore ways to further encourage the donation of plasma from those who have recovered from COVID-19.

    - In addition, the private sector should explore additional ways to collaborate in order to achieve their respective goals. For example, scientists who are still trying to learn more about antibodies, companies who are in need of plasma for therapeutic development, blood bank organizations who are seeking out additional donors, and companies that develop antibody tests who need additional samples may be able to develop a partnership to more efficiently achieve their respective goals.

- **Arthritis drugs:** Drugs against autoimmune diseases like rheumatoid arthritis work by tamping down the immune system. This could be useful against in COVID-19,

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[376] U.S. Food and Drug Administration, *Coronavirus (COVID-19) Update: FDA Encourages Recovered Patients to Donate Plasma for Development of Blood-Related Therapies* (Apr. 16, 2020), *available at* https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-encourages-recovered-patients-donate-plasma-development-blood.

[377] U.S. Department of Health and Human Services, *OCR Issues Guidance on How Health Care Providers Can Contact Former COVID-19 Patients About Blood and Plasma Donation Opportunities* (June 12, 2020), *available at* https://www.hhs.gov/about/news/2020/06/12/guidance-on-hipaa-and-contacting-former-covid-19-patients-about-blood-and-plasma-donation.html.

[378] The Fight Is In Us, *available at* https://thefightisinus.org/en-us#about (last visited on June 18, 2020).

[379] *Id*.

[380] Rebecca Klar, *The Rock, Samuel L. Jackson among celebs urging recovered coronavirus patients to give blood*, The Hill (June 18, 2020), *available at* https://thehill.com/blogs/in-the-know/in-the-know/503431-the-rock-samuel-l-jackson-other-celebrities-urge-recovered.

because the SARS-CoV-2 virus can make the body overreact, causing what's called a "cytokine storm," damaging the body. These drugs may treat the cytokine storm.

- Actemra, one such drug made by Roche, is approved for treating the cytokine storm when it is caused by cancer treatments. An unpublished 21-patient study in China showed Actemra reduced fevers and need for supplemental oxygen. Roche is also beginning clinical studies on Actemra in the U.S.[381]

- Two other companies, Regeneron and Sanofi, have launched studies of their similar drug, Kevzara, in COVID-19 patients.[382] Kevzara is a fully-human monoclonal antibody that inhibits the IL-6 pathway by binding and blocking the IL-6 receptor.[383] This drug is approved by FDA for the treatment of rheumatoid arthritis.[384]

    - Regeneron is leading the U.S. trials and Sanofi is leading the trials outside of the U.S.[385]

    - On March 21, 2020, HHS announced that BARDA will provide support for a U.S. Phase 2/3 clinical trial to evaluate Kevzara as a potential treatment for severely ill COVID-19 patients.[386] This partnership is among the first to be issued by BARDA using funding from the Coronavirus Preparedness and Response Supplemental Appropriations Act, 2020.[387]

    - On April 27, 2020, Regeneron and Sanofi announced the preliminary results from the Phase 2 portion of an ongoing Phase 2/3 trial evaluating Kevzara in hospitalized patients with "severe" or "critical" respiratory illnesses caused by COVID-19.[388] After reviewing the

[381] Matthew Herper, *When might experimental drugs to treat Covid-19 be ready? A forecast*, STAT (Mar. 24, 2020), *available at* https://www.statnews.com/2020/03/24/when-might-experimental-drugs-to-treat-covid-19-be-ready-a-forecast/.
[382] *Id*.; Sanofi, *Sanofi and Regeneron begin global Kevzara (sarilumab) clinical trial program in patients with severe COVID-19* (Mar. 16, 2020), *available at* http://www.news.sanofi.us/2020-03-16-Sanofi-and-Regeneron-begin-global-Kevzara-R-sarilumab-clinical-trial-program-in-patients-with-severe-COVID-19.
[383] Sanofi, *Our Response to COVID-19*, *available at* https://www.sanofi.us/en/about-us/our-stories/our-response-to-covid-19 (last visited on June 18, 2020).
[384] U.S. Department of Health and Human Services, *HHS Funds Phase 2/3 Clinical Trial for Potential Treatment for COVID-19* (Mar. 21, 2020), *available at* https://www.hhs.gov/about/news/2020/03/21/hhs-funds-phase-2-3-clinical-trial-for-potential-treatment-for-covid-19.html.
[385] Sanofi, *Sanofi: First patient outside U.S. treated in global Kevzara (sarilumab) clinical trial program for patients with severe COVID-19* (Mar. 30, 2020), *available at* https://www.sanofi.com/en/media-room/press-releases/2020/2020-03-30-07-00-00.
[386] U.S. Department of Health and Human Services, *HHS Funds Phase 2/3 Clinical Trial for Potential Treatment for COVID-19* (Mar. 21, 2020), *available at* https://www.hhs.gov/about/news/2020/03/21/hhs-funds-phase-2-3-clinical-trial-for-potential-treatment-for-covid-19.html.
[387] *Id*.
[388] Regeneron, *Regeneron and Sanofi Provide Update on U.S. Phase 2/3 Adaptive-Designed Trial of Kevzara (Sarilumab) in Hospitalized COVID-19 Patients* (Apr. 27, 2020), *available at* https://investor.regeneron.com/news-releases/news-release-details/regeneron-and-sanofi-provide-update-us-phase-23-adaptive.

Phase 2 and Phase 3 data, the Independent Data Monitoring Committee recommended continuing the ongoing Phase 3 trial only in the more advanced "critical" group with Kevzara higher-dose versus placebo, and discontinuing the less advanced "severe" group.[389] The companies expect to report results from the ongoing Phase 3 trial this summer.[390]

- The ex-U.S. trial dosed its first patient in late March and has since dosed patients in multiple countries including Italy, Spain, Germany, France, Canada, Russia, Israel, and Japan.[391] Sanofi expects initial results from its ex-U.S. trials in the third quarter of 2020.

- Both Actemra and Kevzara are artificial antibodies that target a protein involved in the immune system called IL-6 and are given by injection.[392]

- In addition, GSK is looking at its own compounds as potential therapies for COVID-19 and identified an investigational rheumatoid arthritis drug, Otilimab, which could potentially ease the effect of COVID-19 on the lungs, but not suppress it directly.[393] GSK believes that the drug may be able to help block the effects of one of the types of cytokine, GM-CSF, and plans to study that in Phase 2.[394] The Investigating Otilimab in Patients With Severe Pulmonary COVID-19 Related Disease (OSCAR) study began in May and the estimated completion date is December 2020.[395]

- **Antibodies and artificial antibodies against the virus**

  - Monoclonal antibodies are laboratory-produced molecules engineered to serve as substitute antibodies. Once developed, they are then made into drugs that can be injected into patients. A manufactured antibody, or a mix of manufactured antibodies, could have a more consistent impact than blood plasma.

  - Several companies are currently pursuing monoclonal antibody treatments, some of which are highlighted below.

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[389] *Id*.
[390] *Id*.
[391] Kyle Blankenship, *After disappointing early numbers, Sanofi and Regeneron scale back Kevzara's COVID-19 test*, FIERCE PHARMA (Apr. 27, 2020), *available at* https://www.fiercepharma.com/pharma/sanofi-regeneron-scale-back-kevzara-study-after-disappointing-results-severe-covid-19.
[392] Matthew Herper, *When might experimental drugs to treat Covid-19 be ready? A forecast*, STAT (Mar. 24, 2020), *available at* https://www.statnews.com/2020/03/24/when-might-experimental-drugs-to-treat-covid-19-be-ready-a-forecast/.
[393] *GSK plans to assess rheumatoid arthritis drug otilimab for COVID-19*, CLINICAL TRIALS ARENA (May 8, 2020), *available at* https://www.clinicaltrialsarena.com/news/gsk-otilimab-covid-19-trial/.
[394] *Id*.
[395] Investigating Otilimab in Patients With Severe Pulmonary COVID-19 Related Disease (OSCAR), ClinicalTrials.gov, *available at* https://clinicaltrials.gov/ct2/show/NCT04376684 (last visited on June 18, 2020).

- Regeneron, which had success developing such a treatment for Ebola, announced on June 11, 2020, that it is entering clinical trials for its antibody cocktail REGN-COV2, which consists of two antibodies, for the treatment and prevention of COVID-19. Both of the antibodies are targeted at the receptor binding protein but bind distinctly and do not compete with each other so that they can bind to the spike protein at the same time. The "clinical program will consist of four separate study populations: hospitalized COVID-19 patients, non-hospitalized symptomatic COVID-19 patients, uninfected people in groups that are at high-risk of exposure (such as healthcare workers or first responders) and uninfected people with close exposure to a COVID-19 patient (such as the patient's housemate)."[396]

    - On June 15, 2020, BARDA announced its plans to fund two first-in-human studies for Regeneron's COVID-19 antibody cocktail.[397]

- Eli Lilly, working with AbCellera announced on June 1, 2020, that patients have been dosed in the world's first study of a potential antibody treatment, LY-CoV555, designed to fight COVID-19.[398] The announcement noted that they will review the results later this month and if Phase 1 results show the antibody can be safely administered, Eli Lilly expects to move into the next phase of testing, studying the treatment in non-hospitalized COVID-19 patients.[399]

    - While studying the safety and efficacy of the potential treatment, the company is starting large scale manufacturing of LY-CoV555 so it can be ready to deliver the treatment to patients as quickly as possible, with the goal of having several hundred thousand doses available by the end of the year.[400]

    - Eli Lilly also intends to test other neutralizing antibodies against SARS-CoV-2 over the next several months, including single antibody therapy and combinations of antibodies (antibody cocktails).[401]

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[396] Regeneron, *Regeneron Begins First Clinical Trials of Anti-viral Antibody Cocktail REGN-COV2 for the Treatment and Prevention of COVID-19* (June 11, 2020), *available at* https://investor.regeneron.com/news-releases/news-release-details/regeneron-begins-first-clinical-trials-anti-viral-antibody.
[397] U.S. Department of Health and Human Services, *BARDA funds two first-in-human studies for Regeneron's COVID-19 antibody cocktail* (June 15, 2020), *available at* https://www.medicalcountermeasures.gov/newsroom/2020/regeneron-study/.
[398] Eli Lilly, *Lilly Begins World's First Study of a Potential COVID-19 Antibody Treatment in Humans* (June 1, 2020), *available at* https://investor.lilly.com/news-releases/news-release-details/lilly-begins-worlds-first-study-potential-covid-19-antibody.
[399] *Id*.
[400] Eli Lilly, *Lilly Begins World's First Study of a Potential COVID-19 Antibody Treatment in Humans* (June 1, 2020), *available at* https://investor.lilly.com/news-releases/news-release-details/lilly-begins-worlds-first-study-potential-covid-19-antibody.
[401] *Id*.

- Vir Biotechnology has three product candidates in the pipeline for SARS-CoV-2, including two monoclonal antibody candidates that are in the pre-clinical stage and have demonstrated the ability to neutralize SARS-CoV-2 live virus.[402] In addition, Vir Biotechnology has one siRNA candidate that is also in the pre-clinical stage and has demonstrated the ability to significantly reduce SARS-CoV-2 live virus replication.[403]

    - Vir Biotechnology and Biogen announced that they are partnering to advance the development and clinical manufacturing of Vir Biotechnology's human monoclonal antibodies as potential treatments for COVID-19.[404]

    - In addition, GSK and Vir Biotechnology announced a collaboration to research and develop solutions for coronaviruses, including COVID-19.[405] "The collaboration will use Vir's proprietary monoclonal antibody platform technology to accelerate existing and identify new anti-viral antibodies that could be used as therapeutic or preventative options to help address the current COVID-19 pandemic and future outbreaks. The companies will leverage GSK's expertise in functional genomics and combine their capabilities in CRISPR screening and artificial intelligence to identify anti-coronavirus compounds that target cellular host genes."[406] The immediate focus will be a pair of monoclonal antibodies, VIR-7831 and VIR-7832, identified by Vir Biotechnology's monoclonal antibody technology that bind to the spike protein of SARS-CoV-2.[407]

- In April, Novartis announced plans to initiate a Phase 3 clinical trial—the CAN-COVID trial—to study canakinumab, a human anti-IL-1β monoclonal antibody, in patients with COVID-19 pneumonia.[408] Specifically, the trial will examine the efficacy of canakinumab in treating cytokine release

[402] Vir Biotechnology, Pipeline, *available at* https://www.vir.bio/pipeline/ (last visited on June 12, 2020).
[403] *Id*.
[404] *Biogen, Vir to Partner on Manufacturing Antibodies to Treat COVID-19*, Genetic Engineering & Biotechnology News (Mar. 12, 2020), *available at* https://www.genengnews.com/news/biogen-vir-to-partner-on-manufacturing-antibodies-to-treat-covid-19/.
[405] GSK, *GSK and Vir Biotechnology enter collaboration to find coronavirus solutions* (Apr. 6, 2020), *available at* https://www.gsk.com/en-gb/media/press-releases/gsk-and-vir-biotechnology-enter-collaboration-to-find-coronavirus-solutions/.
[406] *Id*.
[407] Amirah Al Idrus, *GSK becomes Vir's newest partner on COVID-19 treatments, vaccines* (Apr. 6, 2020), *available at* https://www.fiercebiotech.com/biotech/gsk-becomes-vir-s-newest-partner-covid-19-treatments-vaccines.
[408] Novartis, *Novartis announces plan to initiate clinical trial of canakinumab for patients with COVID-19 pneumonia* (Apr. 28, 2020), *available at* https://www.novartis.com/news/novartis-announces-plan-initiate-clinical-trial-canakinumab-patients-covid-19-pneumonia; Eugen Dhimolea, *Canakinumab*, NCBI, U.S. National Library of Medicine, National Institutes of Health (2010), *available at* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2828573/ (last visited on June 18, 2020).

syndrome in people with COVID-19.[409] Novartis aims to enroll 450 patients across multiple countries, including the U.S., and anticipates top-line results in late summer 2020.[410]

- AbbVie also recently announced that it would develop an antibody therapy to prevent and treat COVID-19 in partnership with the Netherlands' Utrecht University, Harbour BioMed, and Erasmus Medical Center.[411]

- On June 9, 2020, AstraZeneca announced that it has signed new agreements with academia and U.S. government agencies and confirmed plans to move forward with a combination approach consisting of a pair of monoclonal antibodies as a potential combination therapy for the prevention and treatment of COVID-19.[412] Specifically, AstraZeneca has licensed six candidate antibodies from Vanderbilt University and plans to advance two of the six monoclonal antibodies in Vanderbilt's portfolio "into clinical evaluation as a combination approach within the next two months."[413] In addition, AstraZeneca signed an interagency agreement with the Defense Advanced Research Projects Agency and BARDA to support its efforts to develop monoclonal antibody treatment against SARS-CoV-2.[414]

    - In addition to working on monoclonal antibodies, AstraZeneca is investigating potential treatments by exploring how its compounds might help in the treatment of COVID-19. For example, in April, AstraZeneca announced that it would initiate a randomized, global clinical trial to assess Calquence (acalabrutinib)—a Bruton's tyrosine kinase (BTK) inhibitor—for the treatment of the cytokine storm associated with COVID-19 infection in severely ill patients.[415] "Calquence is a next-generation, selective BTK inhibitor currently approved in the US for the treatment of certain haematological

[409] Novartis, *Novartis announces plan to initiate clinical trial of canakinumab for patients with COVID-19 pneumonia* (Apr. 28, 2020), *available at* https://www.novartis.com/news/novartis-announces-plan-initiate-clinical-trial-canakinumab-patients-covid-19-pneumonia.
[410] *Id*.
[411] Vishwadha Chander, *Abbvie strikes partnership to develop COVID-19 antibody therapy* (June 5, 2020), *available at* https://www.reuters.com/article/us-health-coronavirus-abbvie/abbvie-strikes-partnership-to-develop-covid-19-antibody-therapy-idUSKBN23C1I5.
[412] AstraZeneca, *Advancing our discovery of novel coronavirus-neutralising antibodies against COVID-19* (June 9, 2020), *available at* https://www.astrazeneca.com/media-centre/articles/2020/advancing-our-discovery-of-novel-coronavirus-neutralising-antibodies-against-covid-19.html.
[413] *Id*.
[414] *Id*.
[415] AstraZeneca, *AstraZeneca initiates CALAVI clinical trial with Calquence against COVID-19* (Apr. 14, 2020), *available at* https://www.astrazeneca.com/media-centre/press-releases/2020/astrazeneca-initiates-calavi-clinical-trial-with-calquence-against-covid-19.html; AstraZeneca, *Calquence showed promising clinical improvement in majority of 19 hospitalised COVID-19 patients* (June 5, 2020), *available at* https://www.astrazeneca.com/media-centre/press-releases/2020/calquence-showed-promising-clinical-improvement-in-majority-of-19-hospitalised-covid-19-patients.html.

malignancies."[416] Recently published results from a trial led by researchers at the National Cancer Institute, showed that Calquence (acalabrutinib) "reduced markers of inflammation and improved clinical outcomes of patients with severe COVID-19 disease."[417] This encouraging preliminary data has informed the initiation of global Phase 2 trials.[418]

- In addition, AstraZeneca and Saint Luke's Mid America Heart Institute have initiated a randomized, global Phase 3 trial, called DARE-19, to assess the potential of Farxiga (dapagliflozin)—a sodium-glucose cotransporter 2 (SGLT2) inhibitor—as a treatment in patients hospitalized with COVID-19 who are at risk of developing serious complications, such as organ failure.[419] "Farxiga is a first-in-class, oral, once-daily SGLT2 inhibitor indicated in adults for the treatment of insufficiently controlled T2D as both monotherapy and as part of combination therapy as an adjunct to diet and exercise to improve glycaemic control, with the additional benefits of weight loss and blood-pressure reduction."[420]

- SAb Biotherapeutics is rapidly advancing the development of an antibody therapeutic candidate, SAB-185, for COVID-19 which SAb believes is on track to have ready for clinical trials by early summer 2020.[421] This novel high-potency immunotherapy candidate is designed to treat COVID-19 by delivering "human polyclonal antibodies targeted specifically to the SARS-CoV-2 virus, that are generated, collected and purified using SAB's proprietary in vivo platform technology, without the need for human donors or serum from recovered coronavirus patients."[422]

  - This therapeutic "is moving forward in development through a partnership between BARDA, the Department of Defense Joint Program Executive Office for Chemical, Biological, Radiological, and

[416] AstraZeneca, *Calquence showed promising clinical improvement in majority of 19 hospitalised COVID-19 patients* (June 5, 2020), *available at* https://www.astrazeneca.com/media-centre/press-releases/2020/calquence-showed-promising-clinical-improvement-in-majority-of-19-hospitalised-covid-19-patients.html.
[417] *Id*.
[418] Id.
[419] AstraZeneca, *AstraZeneca and Saint Luke's Mid America Heart Institute initiate Phase III Dare-19 trial with Farxiga in COVID-19 patients* (Apr. 23, 2020), *available at* https://www.astrazeneca.com/media-centre/press-releases/2020/astrazeneca-and-saint-lukes-mid-america-heart-institute-initiate-phase-iii-dare-19-trial-with-farxiga-in-covid-19-patients.html.
[420] *Id*.
[421] SAb Biotherapeutics, COVID-19, *available at* https://sabbiotherapeutics.com/covid-19/ (last visited on June 17, 2020).
[422] U.S. Department of Health and Human Services, Public Health Emergency, *BARDA's Rapidly Expanding COVID-19 Medical Countermeasure Portfolio, available at* https://www.medicalcountermeasures.gov/app/barda/coronavirus/COVID19.aspx (last visited on June 17, 2020)

Nuclear Defense (JPEO - CBRND), and SAb Biotherapeutics, Inc."[423] Specifically, "BARDA transferred approximately $7.2 million in funding to (JPEO - CBRND) to support SAb to complete manufacturing and preclinical studies, with an option to conduct a Phase 1 clinical trial."[424] SAb began manufacturing product for initial clinical trials on May 25, 2020.[425]

- There are other drugs that do not fall into the aforementioned categories that are under development and being tested. Some, but not all, of these drugs are discussed below.
    - One of the most frequent causes of death following COVID-19 infection is acute respiratory distress syndrome, which can be induced by the virus.
        - Athersys is running a Pivotal Phase 2/3 clinical trial evaluating the safety and efficacy of a drug called MultiStem, which is an investigational cell therapy that has shown promise for the treatment of acute respiratory distress syndrome and has been granted Fast Track designation by the FDA.[426]
    - In April, Novartis announced its plans to initiate a Phase 3 clinical trial in collaboration with Incyte to evaluate the use of Jakavi (ruxolitinib)—an oral inhibitor of the JAK 1 and JAK 2 tyrosine kinases—for the treatment of the cytokine storm in patients with COVID-19.[427] Ruxolitinib is marketed in the U.S. as Jakafi "for patients with [polycythemia vera] PV who have had an inadequate response to or are intolerant of hydroxyurea, for patients with intermediate or high-risk [myelofibrosis] MF, and steroid-refractory acute GvHD in adult and pediatric patients 12 years and older."[428] Jakavi is approved in 101 countries for patients with MF and more than 75 countries for patients with PV.[429]

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[423] U.S. Department of Health and Human Services, Public Health Emergency, MedicalCountermeasures.gov, *BARDA Department of Defense, and SAb Biotherapeutics to Partner to Develop a Novel COVID-19 Therapeutic, available at* https://www.medicalcountermeasures.gov/newsroom/2020/sab-185/ (last visited on June 18, 2020).
[424] *Id*.
[425] SAb Biotherapeutics, COVID-19, *available at* https://sabbiotherapeutics.com/covid-19/ (last visited on June 17, 2020).
[426] Athersys, *Acute Respiratory Distress Syndrome (ARDS), available at* https://www.athersys.com/clinical-trials/ards/default.aspx (last visited June 12, 2020).
[427] Novartis, *Novartis announces plan to initiate clinical study of Jakavi® in severe COVID-19 patients and establish international compassionate use program* (Apr. 2, 2020), *available at* https://www.novartis.com/news/media-releases/novartis-announces-plan-initiate-clinical-study-jakavi-severe-covid-19-patients-and-establish-international-compassionate-use-program.
[428] Novartis, *Novartis announces plan to initiate clinical study of Jakavi® in severe COVID-19 patients and establish international compassionate use program* (Apr. 2, 2020), *available at* https://www.novartis.com/news/media-releases/novartis-announces-plan-initiate-clinical-study-jakavi-severe-covid-19-patients-and-establish-international-compassionate-use-program.
[429] *Id*.

        - In addition to initiating a Phase 3 clinical trial, "Novartis has also set up an international compassionate use program for eligible patients, subject to local regulations."[430]

- Clinical trials underway involve adults infected with COVID-19. Children infected with COVID-19 are also being prescribed various medicines off-label, given that there are no therapeutics authorized for emergency use or otherwise for children with COVID-19.

    - In order to determine the correct dosing for children, an NIH-funded study was recently launched to evaluate drugs prescribed to treat COVID-19 in infants, children, and adolescents. "The study leverages an existing clinical trial that examines drugs that are prescribed off-label to children for a variety of medical conditions."[431] The study is designed to gather information to refine dosing and improve safety for infants, children, and adolescents; it is not designed to determine which drug is best to treat COVID-19 in children.[432] As part of the study, researchers will investigate several drugs currently given to children with COVID-19.[433]

- Some clinical trials, including ones in the U.S., have been suspended or terminated due to a drop of incidents in COVID-19 cases, and as a result no eligible patients being able to be recruited.

    - As previously mentioned, the ACTIV partnership has a Clinical Trial Capacity Working Group, which is "charged with assembling and coordinating existing networks of clinical trials to increase efficiency and build capacity."[434]

        - Through ACTIV's Clinical Trial Capacity Working Group, and other efforts, the Executive Branch should leverage existing clinical trial networks and explore ways for clinical trials to be more efficient and mobile so that if the rate of disease incidence in a given location declines, clinical trials can continue and produce complete, reliable, and timely results.

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[430] *Id*.
[431] National Institutes of Health, *NIH-funded study to evaluate drugs prescribed to children with COVID-19* (June 10, 2020), *available at* https://www.nih.gov/news-events/news-releases/nih-funded-study-evaluate-drugs-prescribed-children-covid-19.
[432] *Id*.
[433] *Id*.
[434] Francis S. Collins, MD, PhD, Paul Stoffels, MD, *Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV), An Unprecedented Partnership for Unprecedented Times*, JAMA NETWORK (May 18, 2020), *available at* https://jamanetwork.com/journals/jama/fullarticle/2766371?guestAccessKey=5defc755-e585-47e5-b79a-fee2ec2dd42b&utm_source=For_The_Media&utm_medium=referral&utm_campaign=ftm_links&utm_content=tfl&utm_term=051820.

- When it comes to infectious disease treatments, data from BIO puts the success rate of new medicines just starting clinical testing at one in five.[435] Many therapeutics that appear promising are likely to fail.

C. What efforts are underway to discover additional drugs or therapies that may be effective against COVID-19?

- The specific examples of therapeutic candidates discussed above are just a few examples of the therapeutics being researched and in development for the treatment of COVID-19. The federal government, academia, and pharmaceutical companies are continuing to evaluate existing therapeutics for their effectiveness in COVID-19 and are working to develop new therapies.

    - For example, Amgen plans to investigate "Otezla (apremilast), an oral treatment approved in more than 50 countries for inflammatory diseases such as psoriasis and psoriatic arthritis" as a potential immunomodulatory treatment in adult patients with COVID-19 in upcoming trials.[436] Otezla, which inhibits the activity of phosphodiesterase 4, an enzyme found in inflammatory cells in the human body, is thought to modulate the production of inflammatory cytokines and other mediators.[437]

    - In addition, "Amgen has partnered with Adaptive Biotechnologies to discover and develop fully-human neutralizing antibodies to potentially prevent or treat COVID-19."[438]

    - Pfizer, through its antiviral compound screening, confirmed a lead compound and analogues are potent inhibitors of the SARS-CoV-2 3C-like (3CL) protease, and preliminary data suggests the lead protease inhibitor shows antiviral activity against the virus.[439] The company is looking to begin clinical trials in the next few months.

- **New antivirals:** If existing antivirals cannot control SARS-CoV-2, new medicines may be needed. Targeted drug development is underway but will take longer than testing already-existing therapeutics.

- In addition, efforts are underway to search chemical and compound libraries for medicines that could prove effective by researchers, pharmaceutical companies, the

[435] Clinical Development Success Rates 2006-2015, BIO, Biomedtracker, Amplion (June 2016), *available at* https://www.bio.org/sites/default/files/legacy/bioorg/docs/Clinical%20Development%20Success%20Rates%202006-2015%20-%20BIO,%20Biomedtracker,%20Amplion%202016.pdf.
[436] Amgen, *COVID-19 Information Center, available at* https://www.amgen.com/covid-19/ (last updated June 10, 2020).
[437] *Id*.
[438] *Id*.
[439] Pfizer, *Pfizer Advances Battle Against COVID-19 on Multiple Fronts* (Apr. 9, 2020), *available at https://www.pfizer.com/news/press-release/press-release-detail/pfizer-advances-battle-against-covid-19-multiple-fronts.*

DOE, the Bill and Melinda Gates Foundation and others. Medicines that have gone through some previous testing, as remdesivir has, could move more quickly into development and clinical trials. Further, "some researchers are using new technologies like artificial intelligence to try to use characteristics of the virus to find or design drugs that might successfully treat COVID-19."[440]

- The FDA and the NCATS have also created a database to compile clinical information on the use of existing drugs to treat COVID-19.
    - According to FDA, "CURE ID is an internet-based repository that lets the clinical community report novel uses of existing drugs for difficult-to-treat infectious diseases through a website, a smartphone or other mobile device. The platform enables the crowdsourcing of medical information from health care providers to facilitate the development of new treatments for neglected diseases."[441]
    - FDA and the NCATS recently made updates to CURE ID to be a more effective tool for COVID-19 to make it easier for health care providers to share their experiences treating COVID-19 patients who are unable to be enrolled in a clinical trial.[442]
- The FDA is partnering with the Critical Path Institute and the NCATS on the CURE Drug Repurposing Collaboratory (CDRC).[443] "CDRC is a forum for the exchange of clinical practice data to inform potential new uses of existing drugs for areas of high unmet medical need, advancing research in these areas. CDRC will focus on capturing relevant real-world clinical outcome data through the FDA-NCATS CURE ID platform. In a pilot project focused on COVID-19, CDRC will use data collected via the CURE ID platform to aggregate global clinician treatment experiences to identify existing drugs that demonstrate possible treatment approaches warranting further study."[444]
- In addition, the White House announced the launch of the COVID-19 High Performance Computing Consortium to provide COVID-19 researchers worldwide with access to the world's most powerful high-performance computing resources that

[440] COVID-19 Treatment and Vaccine Tracker, Milken Institute, *available at* https://milken-institute-covid-19-tracker.webflow.io/#treatment_antibodies (last visited on June 11, 2020).
[441] U.S. Food and Drug Administration, *CURE ID App Lets Clinicians Report Novel Uses of Existing Drugs, available at* https://www.fda.gov/drugs/science-and-research-drugs/cure-id-app-lets-clinicians-report-novel-uses-existing-drugs (last visited on June 11, 2020).
[442] *Id*.
[443] U.S. Food and Drug Administration, *Coronavirus (COVID-19) Update: Daily Roundup June 23, 2020* (June 23, 2020), *available at* https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-daily-roundup-june-23-2020.
[444] *Id.*

can significantly advance the pace of scientific discovery in the fight to stop the virus.[445]

  - The sophisticated computing systems available through this consortium can process massive numbers of calculations related to bioinformatics, epidemiology, and molecular modeling, helping scientists develop answers to complex scientific questions about COVID-19 in hours or days versus weeks or months.

- The DOE is also utilizing the supercomputing capabilities of the National Laboratories and received additional funding from Congress to expand this effort in five primary areas: high-performance computing, imaging, gene sequencing, advanced manufacturing, and clinical surveillance and testing.

  - The National Nuclear Security Administration (NNSA) has also announced it will contribute its supercomputing in the COVID-19 response.[446]

  - The CARES Act provided DOE with $99.5 million in funding for the Office of Science and the NNSA to support operations of the National Laboratory scientific user facilities for research and development efforts related to the coronavirus.[447]

- An example of how supercomputing can be harnessed to discover a treatment for COVID-19 was recently highlighted in an article in *The New England Journal of Medicine,* which notes that the SARS-CoV-2 genome encodes approximately 25 proteins that are needed by the virus to infect humans and replicate, including the spike (s) protein.[448] According to the article, "a preliminary report of a supercomputer-driven ensemble docking study of a repurposing compound database to the viral S protein was published on a preprint server in mid-February, with 8000 compounds ranked according to the calculated binding affinity to the receptor-binding domain of the S protein.[449] Top-ranked compounds from the original S-protein

[445] The White House, *White House Announces New Partnership to Unleash U.S. Supercomputing Resources to Fight COVID-19* (Mar. 23, 2020), *available at* https://www.whitehouse.gov/briefings-statements/white-house-announces-new-partnership-unleash-u-s-supercomputing-resources-fight-covid-19/.
[446] National Nuclear Security Administration, *NNSA contributes world-class supercomputers to COVID-19 fight* (Mar. 27, 2020), *available at* https://www.energy.gov/nnsa/articles/nnsa-contributes-world-class-supercomputers-covid-19-fight.
[447] U.S. Department of Energy, *Department of Energy Applauds Passage of The CARES Act* (Mar. 27, 2020), *available at* https://www.energy.gov/articles/department-energy-applauds-passage-cares-act.
[448] Jerry M. Parks, Ph.D. and Jeremy C. Smith, Ph.D., *How to Discover Antiviral Drugs Quickly*, THE NEW ENGLAND JOURNAL OF MEDICINE (June 4, 2020), *available at* https://www.nejm.org/doi/full/10.1056/NEJMcibr2007042?af=R&rss=currentIssue.
[449] Smith MD, Smith JC. *Repurposing therapeutics for COVID-19: supercomputer-based docking to the SARS-CoV-2 viral spike protein and viral spike protein-human ACE2 interface*, CHEMRXIV (Mar. 11, 2020), *available at* https://chemrxiv.org/articles/Repurposing_Therapeutics_for_the_Wuhan_Coronavirus_nCov-2019_Supercomputer-Based_Docking_to_the_Viral_S_Protein_and_Human_ACE2_Interface/11871402.

virtual screen are being tested for activity against the live virus. The results will inform future calculations in a speedy, iterative process."[450]

D. How can the timeline for therapeutic development be shortened?

- As discussed above in Section I, the Trump Administration has created initiatives and public-private partnerships to speed the development and manufacturing of therapeutics.
    - The ACTIV partnership brings together more than a dozen leading biopharmaceutical companies and government entities and will develop a collaborative framework for prioritizing vaccine and drug candidates, streamlining clinical trials, coordinating regulatory processes, and/or leveraging assets among all partners to rapidly respond to the COVID-19 pandemic.[451]
    - The Operation Warp Speed public-private partnership aims to facilitate, at an unprecedented pace, the development, manufacturing, and distribution of COVID-19 countermeasures, between government entities and private firms. It will coordinate existing HHS-wide efforts, including the NIH's ACTIV partnership for vaccine and therapeutic development, NIH's RADx initiative for diagnostic development, and work by BARDA.[452]
    - The CTAP program aims to use every available method to move new treatments to patients as soon as possible, while at the same time finding out whether they are helpful or harmful.
    - The federal government and the private sector have taken steps to accelerate the development, testing, and manufacturing of medical countermeasures during the COVID-19 pandemic. Congress, the Executive Branch, and the private sector should evaluate best practices from the U.S.' response to the COVID-19 pandemic and ensure those best practices continue once the public health emergency is over to help advance other areas of medicine and prepare for future pandemics.
- In addition, the FDA has the ability to use the Fast Track program, discussed in more detail in Section II.B of this report, which is designed to facilitate the development

[450] Jerry M. Parks, Ph.D. and Jeremy C. Smith, Ph.D., *How to Discover Antiviral Drugs Quickly*, THE NEW ENGLAND JOURNAL OF MEDICINE (June 4, 2020), *available at* https://www.nejm.org/doi/full/10.1056/NEJMcibr2007042?af=R&rss=currentIssue.
[451] National Institutes of Health, *NIH to launch public-private partnership to speed COVID-19 vaccine and treatment options* (Apr. 17, 2020), *available at* https://www.nih.gov/news-events/news-releases/nih-launch-public-private-partnership-speed-covid-19-vaccine-treatment-options.
[452] U.S. Department of Health and Human Services, *Trump Administration Announces Framework and Leadership for 'Operation Warp Speed'* (May 15, 2020), *available at* https://www.hhs.gov/about/news/2020/05/15/trump-administration-announces-framework-and-leadership-for-operation-warp-speed.html.

and expedite the review of drugs to treat serious diseases and fill unmet medical needs.[453]

- The FDA can use a drug review process such as priority review and the accelerated review process, both discussed in more detail in Section II.B of this report, to help a sponsor bring a new product to market faster.[454]

- These products undergo scrutiny by the Center for Drug Evaluation and Research or Center for Biologics Evaluation and Research before obtaining marketing authorization.
- The FDA should continue to study and consider additional, quicker pathways by which promising therapeutics can be made available, such as through an EUA.

- Throughout the development process, and despite any expedited schedules, it is critical that safety and efficacy be thoroughly studied.

## IV. Manufacturing and Supply Chain Issues Related to COVID-19 Vaccines and Therapeutics

A. What is the HHS Centers for Innovation in Advanced Development and Manufacturing (CIADM) program and how can the CIADM centers be used to respond to manufacturing and supply chain issues for the COVID-19 pandemic?

- The HHS Centers for Innovation in Advanced Development and Manufacturing (CIADM) program is a public-private partnership created to "provide a significant domestic infrastructure in the United States capable of producing medical countermeasures to protect Americans from the health impacts of bioterrorism as well as pandemic influenza and other disease in response to public health emergencies."[455] There are currently two centers "to develop and manufacture medical countermeasures, such as vaccines and therapeutics used to protect health in emergencies, which can transition quickly and cost effectively between products."[456]

[453] Krishnan Vengadaraga Chary, *Expedited drug review process: Fast, but flawed*, National Center for Biotechnology Information, U.S. National Library of Medicine, National Institutes of Health (2016 Apr.-June), *available at* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4936080/.
[454] U.S. Food and Drug Administration, *Accelerated Approval* (Jan. 4, 2018), *available at* https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/accelerated-approval#:~:text=Section%20901%20of%20FDASIA%20amends,or%20an%20intermediate%20clinical%20endpoint.
[455] U.S. Department of Health and Human Services, Public Health Emergency, *Department of Health and Human Services Centers for Innovation in Advanced Development and Manufacturing, available at* https://www.medicalcountermeasures.gov/barda/core-services/ciadm/ (last visited on June 18, 2020).
[456] *Id*.

- Emergent Manufacturing Operations Baltimore LLC leads one center, with facilities in Baltimore and Gaithersburg, Maryland.[457] "This contract is for approximately $163 million over the first eight years."[458]

  - Emergent BioSolutions' CIADM has been awarded four task orders by BARDA to develop Ebola and Marburg therapeutics and a Zika vaccine.[459]

- Texas A&M University System leads a second center and "[t]his contract is valued at approximately $176 million over the first five years."[460]

- The CIADMs can be used to help accelerate the delivery of COVID-19 vaccines and therapeutics. As discussed throughout this report, some of the capabilities of these centers have already been engaged by the federal government and private entities to help scale up manufacturing capacity for vaccines and therapeutics.

- Congress and the Executive Branch should continue to examine if there are additional ways to use CIADMs to scale up manufacturing capacity for the delivery of vaccines and therapeutics.

B. Does the U.S. have sufficient domestic manufacturing capacity and capabilities to produce enough vaccines for clinical trials and, if approved, mass production to administer to the broader population?

- At a Senate hearing on March 3, 2020, Dr. Kadlec, the Assistant Secretary for Preparedness and Response, testified that the U.S. lacks the capacity for manufacturing COVID-19 vaccines the federal government is currently pursuing.[461] Congress and the Executive Branch should continue to study and implement what can be done in the short term to scale-up manufacturing for a COVID-19 vaccine, and also consider long term needs for domestic manufacturing capacity and capabilities in this area.

  - Congress and the Executive Branch should examine whether there are ways to ensure manufacturing capacity for different platform technologies for COVID-19 vaccine candidates can be shifted as the vaccine pipeline advances and certain candidates are approved or authorized for use and other vaccine candidates fail.

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[457] *Id*.
[458] *Id*
[459] *Id*.
[460] *Id*.
[461] Hearing Before the S. Committee on Health, Education, Labor and Pensions titled "An Emerging Disease Threat: How the U.S. is Responding to COVID-19, the Novel Coronavirus" (Mar. 3, 2020), *available at* https://www.help.senate.gov/hearings/an-emerging-disease-threat-how-the-us-is-responding-to-covid-19-the-novel-coronavirus.

- The Executive Branch should ensure there is a comprehensive national vaccine plan and efforts to accelerate the development and delivery of a vaccine are coordinated. On May 22, 2020, bipartisan leaders of the Energy and Commerce Committee sent a letter to White House Coronavirus Task Force Coordinator, Dr. Deborah Birx, urging the Trump Administration to develop a national COVID-19 vaccine plan that includes plans for the development, manufacturing, distribution, provider training, public education, and broad vaccine access.[462]

- In response to the COVID-19 pandemic, and the lack of requisite manufacturing capacity to produce enough vaccines for clinical trials and mass production, the federal government and the private sector have been working to ramp up manufacturing capacity.

    - Several private partnerships and public-private partnerships have already been established to scale up manufacturing capacity in parallel to the development of a vaccine candidate. Given that fewer than ten percent of vaccine candidates generally make it through clinical trials successfully, these efforts are done at risk.[463]

        - Recently, Dr. Fauci said that COVID-19 vaccine candidates will start being manufactured before they are approved or authorized for use in the U.S., thereby saving a significant amount of time that it would otherwise take to manufacture the vaccines after FDA approval or authorization. Dr. Fauci noted: "Something that people need to understand is that we proceed at risk [with manufacturing the vaccine]. And at risk, doesn't mean at risk for the patient regarding safety and integrity of the science. The risk is to the financial investment."[464] Dr. Fauci further explained that manufacturing vaccines at-risk is "very risky from a financial situation," but it will potentially reduce the timeline to potentially have a COVID-19 vaccine available to the public by months.[465]

    - At a June 9, 2020, panel discussion at a BIO convention, the Chief Executive Officer at Moderna said that scaling up manufacturing capacity is "going to be bumpy" and that the company's primary concern right now is finding enough

[462] Energy and Commerce Committee, *Bipartisan Energy and Commerce Leaders Urge Trump Administration to Develop a National COVID-19 Vaccine Plan* (May 22, 2020), *available at* https://energycommerce.house.gov/newsroom/press-releases/bipartisan-energy-and-commerce-leaders-urge-trump-administration-to-develop.
[463] Bob Holmes, *The Time of Trials: Waiting for a Coronavirus Vaccine*, DISCOVER MAGAZINE (May 27, 2020), *available at* https://www.discovermagazine.com/health/the-time-of-trials-waiting-for-a-coronavirus-vaccine.
[464] Soo Kim, *Dr. Fauci Says Coronavirus Vaccine Doses Will be Manufactured 'Before We Even Know That the Vaccine Works*, NEWSWEEK (June 4, 2020), *available at* https://www.newsweek.com/dr-fauci-coronavirus-vaccine-manufactured-before-we-know-it-works-1508642.
[465] *Id*.

raw materials.[466] As previously discussed in Section II.A of this report, Moderna already has made significant commitments to scale up its manufacturing capacity including a collaboration with Lonza and a $483 award from BARDA to, among other things, scale up the manufacturing process.[467]

- Many of the partnerships established to scale up manufacturing capacity for vaccine candidates are discussed in more detail in Sections I.B and II.A of this report, including funding by BARDA to several manufacturers of lead COVID-19 vaccine candidates.

- Some of the COVID-19 vaccine candidates are utilizing vaccine adjuvant technology. In addition to several other benefits, one potential benefit of utilizing an adjuvant is that, by adding adjuvant to a traditional vaccine, the amount of vaccine that is needed may be significantly decreased.

    - For example, the Infectious Disease Research Institute is working with Houston's Baylor College of Medicine to study whether adjuvants can be added to a certain stockpiled vaccine candidate to enhance the vaccine candidate's immunizing effect and reduce the amount of vaccine needed per dose.[468]

    - On May 28, 2020, GSK announced that it planned to produce 1 billion doses of its pandemic vaccine adjuvant in 2021 to support multiple COVID-19 vaccine collaborations, and that the adjuvant was beneficial because, among other things, the pandemic adjuvant can reduce the amount of vaccine protein required per dose.[469] GSK has collaborations with multiple scientific groups working on developing a COVID-19 vaccine candidate to provide their

[466] Donna Young, *Lack of raw materials, capacity may delay coronavirus vaccines – experts*, S&P GLOBAL MARKET INTELLIGENCE (June 9, 2020), *available at* https://www.spglobal.com/marketintelligence/en/news-insights/latest-news-headlines/lack-of-raw-materials-capacity-may-delay-coronavirus-vaccines-8211-experts-58980598.
[467] Moderna, *Moderna Announces Award from U.S. Government Agency BARDA for up to $483 Million to Accelerate Development of mRNA Vaccine (mRNA-1273) Against Novel Coronavirus* (Apr. 16, 2020), *available at* https://investors.modernatx.com/news-releases/news-release-details/moderna-announces-award-us-government-agency-barda-483-million; U.S. Dep't of Health and Human Services, Public Health Emergency, *BARDA's Rapidly Expanding COVID-19 Medical Countermeasure Portfolio* (last visited June 10, 2020), *available at* https://www.medicalcountermeasures.gov/app/barda/coronavirus/COVID19.aspx; Moderna, *Moderna and Lonza Announce Worldwide Strategic Collaboration to Manufacture Moderna's Vaccine (mRNA-1273) Against Novel Coronavirus* (May 1, 2020), *available at* https://investors.modernatx.com/news-releases/news-release-details/moderna-and-lonza-announce-worldwide-strategic-collaboration.
[468] Alan Boyle, *Infectious Disease Research Institute is working on a multiplier effect for coronavirus vaccine* (June 2, 2020), *available at* https://www.geekwire.com/2020/infectious-disease-research-institute-works-multiplier-effect-covid-19-vaccine/.
[469] GlaxoSmithKline, *GSK announces intention to produce 1 billion doses of pandemic vaccine adjuvant in 2021 to support multiple COVID-19 vaccine candidates* (May 28, 2020), *available at* https://www.gsk.com/en-gb/media/press-releases/gsk-announces-intention-to-produce-1-billion-doses-of-pandemic-vaccine-adjuvant/.

adjuvant, including Sanofi, the University of Queensland, Clover Biopharmaceuticals, Xiamen Innovax Biotech Co., Ltd., and others.[470]

- GSK will manufacture, fill, and finish adjuvant for use in COVID-19 vaccines and has started to manufacture the adjuvant at risk; the company is also working on increasing manufacturing capacity and developing partnerships with third parties.[471]

- To scale up manufacturing capacity, many vaccine manufacturers and their partners will need to hire additional employees. For example, Johnson & Johnson entered into an agreement with Catalent to scale up manufacturing capacity, and as previously mentioned, Catalent will hire about 300 additional employees at the program's site in Bloomington, Indiana starting in July 2020 to achieve operational readiness by January 2021.[472] Similarly, Moderna announced in April 2020 that it would hire up to 150 new team members to support its efforts to scale up its manufacturing capacity.[473]

    - Delays in hiring and training of new employees may impact how quickly entities are able to scale up manufacturing capacity.

- In the CARES Act, Congress provided funding that may be used to produce vaccines at commercial scale ahead of approval, including to purchase vaccines pre-approval and to provide funding for commercial manufacturing.

    - Congress and the Executive Branch, working with the private sector, should consider what additional funds or authorities, if any, may be needed so that manufacturers can begin producing vaccines at a commercial scale ahead of approval.

- The Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices (ACIP) is a group of medical and public health experts who are responsible for developing recommendations on the use of vaccines for Americans, including how a vaccine should be distributed, to whom, and when after

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[470] GlaxoSmithKline, *GSK actions to support the global response to COVID-19* (last visited June 16, 2020), *available at* https://www.gsk.com/en-gb/media/resource-centre/our-contribution-to-the-fight-against-2019-ncov/.
[471] GlaxoSmithKline, *GSK announces intention to produce 1 billion doses of pandemic vaccine adjuvant in 2021 to support multiple COVID-19 vaccine collaborations* (May 28, 2020), *available at* https://www.gsk.com/en-gb/media/press-releases/gsk-announces-intention-to-produce-1-billion-doses-of-pandemic-vaccine-adjuvant/; RTTNews, *GSK Plans Significant Expansion in Manufacturing Capacity for Vaccine Adjuvant*, BUSINESS INSIDER (May 28, 2020), *available at* https://markets.businessinsider.com/news/stocks/gsk-plans-significant-expansion-in-manufacturing-capacity-for-vaccine-adjuvant-1029240476.
[472] Catalent, *Catalent Signs Agreement with Johnson & Johnson to be U.S. Manufacturing Partner for Lead COVID-19 Vaccine Candidate* (Apr. 29, 2020), *available at* https://www.catalent.com/catalent-news/catalent-signs-agreement-with-johnson-johnson-for-lead-covid-19-vaccine-candidate/.
[473] Moderna, *Moderna Announces Award from U.S. Government Agency BARDA for up to $483 Million to Accelerate Development of mRNA Vaccine (mRNA-1273) Against Novel Coronavirus* (Apr. 16, 2020), *available at* https://investors.modernatx.com/news-releases/news-release-details/moderna-announces-award-us-government-agency-barda-483-million.

FDA approval.[474] Given that it is likely when a vaccine is approved for COVID-19 there will not be a sufficient amount of vaccine available to immediately immunize all Americans, ACIP is already developing a plan on how to distribute available COVID-19 vaccine once one is approved or authorized for use by the FDA.[475] ACIP's most recent public meeting on vaccine recommendations was June 24, 2020.[476] The agenda included discussing "COVID-19 vaccine prioritization considerations," among other things.[477]

- Congress and the Executive Branch should continue to consider how to deploy limited amounts of vaccines as they become available.

- At a hearing held by the Committee on Energy and Commerce on June 23, 2020, Dr. Redfield, the Director of the Centers for Disease Control and Prevention, was asked about how a vaccine would be distributed to Americans if approved.[478] Dr. Redfield testified that "[i]t is a critical issue that is currently under discussion within the team to look at what the appropriate prioritization for distribution is" and that the decision "may be very dependent on what the product is" since "[e]ach of these vaccine products that are currently being developed may in fact have differential utilization for different populations."[479]

C. Does the U.S. have sufficient domestic supply chain capacity and capabilities to administer a vaccine, including sufficient production of vials, needles, syringes, and alcohol pads?

- Similar to the manufacturing capacity needed for a vaccine, Congress and the Executive Branch should study and implement what can be done in the short-term to scale up domestic supply chain capacity and capabilities to administer a vaccine, and also consider long-term needs for domestic manufacturing capacity and capabilities in this area.

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[474] Centers for Disease Control and Prevention, *Advisory Committee on Immunization Practices (ACIP): General Committee – Related Information* (last updated Oct. 23, 2018), *available at* https://www.cdc.gov/vaccines/acip/committee/index.html; Elizabeth Weise, *When a coronavirus vaccine is developed, who will be first in line to get it? A CDC panel usually decides*, USA TODAY (May 18, 2020), *available at* https://www.usatoday.com/story/news/health/2020/05/18/coronavirus-vaccine-who-get-first-cdc-panel-usually-decides/5202932002/.

[475] Elizabeth Weise, *When a coronavirus vaccine is developed, who will be first in line to get it? A CDC panel usually decides*, USA TODAY (May 18, 2020), *available at* https://www.usatoday.com/story/news/health/2020/05/18/coronavirus-vaccine-who-get-first-cdc-panel-usually-decides/5202932002/.

[476] Centers for Disease Control and Prevention, *ACIP meeting information*, *available at* https://www.cdc.gov/vaccines/acip/meetings/index.html (last visited Jun. 22, 2020).

[477] *Id*.

[478] *Oversight of the Trump Administration's Response to the COVID-19 Pandemic: Hearing Before the H. Comm. On Energy and Commerce*, 116th Cong., Preliminary Transcript, at 64 (Jun. 23, 2020).

[479] *Id*.

- In the HHS Public Health Emergency Medical Countermeasures Enterprise Multiyear Budget Fiscal Year (FY) 2017-2021, BARDA identified needles and syringes as significant gaps in pandemic preparedness.[480]

- Many private entities have raised concerns about a potential shortage of medical glass bottles oftentimes used to bottle vaccines. One of the biggest global medical glassmakers, Schott AG, indicated that the requests it has received for a billion vials are twice as much as the company can produce this year.[481] Vaccine manufacturers have requested about 1 billion glass vials from Schott, but Schott can only produce about 500 million vials for COVID-19 vaccines by the end of 2020.[482] CEPI recently said that there is a global glass shortage.[483]

    - Some vaccine manufacturers are considering alternative forms of packaging to help reduce demand for medical glass vials, including multi-dose vials, multi-dose plastic bags, plastic vials, and plastic pre-filled syringes.[484]

- The Committee is aware of initiatives underway within the Executive Branch to develop medical countermeasures to more easily administer a vaccine. The Executive Branch should evaluate the current initiatives to see if the timetable can potentially be shortened and if there are additional efforts to expand and strengthen the aims of these initiatives.

    - As previously discussed in Section I.B of this report, there are several initiatives supporting Operation Warp Speed to help accelerate the delivery of COVID-19 vaccines and drugs, including an agreement with Corning to expand its domestic manufacturing capacity of Corning Valor glass vials for vaccines, an agreement with SiO2 Materials Science to scale-up the production of its primary packaging for COVID-19 vaccines and therapeutics, which includes vials and syringes, and an agreement with ApiJect to deliver prefilled syringes and increase manufacturing capacity.[485]

    - On March 18, 2020, HHS announced a new public-private partnership to develop a U.S.-based, high-speed, high-volume emergency drug packaging

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[480] U.S. Department of Health and Human Services, *Public Health Emergency Medical Countermeasures Enterprise: Multiyear Budget* (Fiscal Years 2017-2021), *available at* https://www.phe.gov/Preparedness/mcm/phemce/Documents/phemce-myb-2017-21.pdf.
[481] Jared S. Hopkins and Drew Hinshaw, *Coronavirus Vaccine Makers Are Hunting for Vital Equipment: Glass Vials*, THE WALL STREET JOURNAL (June 16, 2020), *available at* https://www.wsj.com/articles/coronavirus-vaccine-makers-are-hunting-for-vital-equipment-glass-vials-11592317525.
[482] *Id*.
[483] *Id*.
[484] *Id*.; Alicia Wallace, *Finding a coronavirus vaccine is hard. Getting it to people is a whole other problem*, CNN (June 12, 2020), *available at* https://www.cnn.com/2020/06/11/business/vaccine-glass-vials-coronavirus/index.html.
[485] Corning, *Corning Valor Glass Selected to Help Accelerate Delivery of COVID-19 Vaccines and Drugs* (June 9, 2020), *available at* https://www.corning.com/worldwide/en/about-us/news-events/news-releases/2020/06/us-departments-of-defense-health-human-services-select-corning-valor-glass-packaging-to-accelerate-delivery-of-covid-19-vaccines.html.

solution using low-cost prefilled syringes.[486] HHS launched the new consortium for Rapid Aseptic Packaging of Injectable Drugs, or RAPID, to develop a surge capacity network of up to eight domestic facilities that can manufacture prefilled syringes using a process called Blow-Fill-Seal (BFS) aseptic plastics manufacturing technology.[487] HHS awarded the company leading RAPID, ApiJect Systems America, up to $456 million for this initiative.[488]

D. Is there sufficient manufacturing capacity and capabilities to produce enough of a therapeutic if large numbers of patients need access to the therapeutic?

- Any therapeutic that shows success could have shortages if large numbers of people need it. While Congress and the Executive Branch are already working with the private sector to reduce any such shortages as much as possible, all parties should continue to examine innovative approaches to prevent shortages.
    - Further, many biologics involve complex processes to manufacture. Similar to vaccines, it is critical for the Executive Branch and private sector to take steps now to ensure that a treatment can be widely available once studies shown it is safe and effective.
    - Congress, the Executive Branch, and the private sector should determine what already-existing resources can be used to increase production of therapeutics, such as the CIADMs at BARDA, to avoid shortages or limited supplies of therapeutics. If additional resources are needed, Congress, the Executive Branch, and private sector should work to address those needs.
    - To the extent that the private sector needs to shift its manufacturing of other products to other facilities, including international facilities, to accommodate for at risk manufacturing of COVID-19 vaccines and therapeutics, Congress and the Executive Branch should examine ways to reduce the regulatory hurdles to expedite the pharmaceutical industry's ability to do that safely and efficiently.
    - Congress, the Executive Branch, and the private sector should explore if there are ways to shorten the manufacturing process for therapeutics while maintaining product integrity to improve the U.S.' ability to rapidly produce large quantities of drug supply in an emergency situation.

[486] U.S. Department of Health and Human Services, *HHS Announces New Public-Private Partnership to Develop U.S.-Based, High-Speed Emergency Drug Packaging Solutions* (Mar. 18, 2020), *available at* https://www.hhs.gov/about/news/2020/03/18/hhs-announces-new-public-private-partnership-to-develop-us-based-high-speed-emergency-drug-packaging-solutions.html.
[487] *Id*.
[488] *Id*.

- In addition to evaluating the resources for increased production of the therapeutic itself, Congress, the Executive Branch, and the private sector should evaluate a potential increased need for supplies needed to administer the therapeutic. For example, if the therapy is not in pill form (and accordingly needs needles and syringes or other supplies to administer), demand on those supplies could already be increased in order to administer the influenza vaccine, routine vaccines on CDC's recommended immunization schedule, and a potential COVID-19 vaccine.

- Early doses of successful therapeutics will need to be prioritized for administration to patients. For example, and as discussed above in Section III.B, Gilead made a large donation of remdesivir to the U.S., which HHS, through ASPR, is distributing to the states.

    - Congress and the Executive Branch should also consider how to prioritize and deploy limited amounts of therapeutics as they become available, including through EUAs.

## V. Recommendations

### A. Federal Efforts to Accelerate the Development of Vaccines and Therapeutics

- The Executive Branch should ensure coordination and communication among all of the efforts to accelerate the development, manufacturing, and distribution of COVID-19 vaccines, therapeutics, and diagnostics, and try to minimize any duplication or inefficiencies.

- The COVID-19 pandemic has brought an unprecedented level of collaboration and cooperation between the federal government and private sector. Congress, the Executive Branch, and the private sector should continue that collaboration to address other unmet medical needs once the COVID-19 public health emergency is over.

- The Executive Branch, Congress, and the private sector should further explore ways to incentivize providers to collect and report actionable data to better understand the virus, improve patient care, and accelerate the development of new treatments.

### B. Vaccines

- Congress and the Executive Branch should continue to promote innovative manufacturing technologies for vaccine candidates, such as advanced manufacturing technologies, through enhanced funding and authorities, if needed.

- Congress and the Executive Branch should evaluate if there are ways to expedite the clinical trial process while still ensuring the safety and efficacy of products by modernizing the clinical trial process and/or using decentralized clinical trials.

- The Executive Branch should provide guidance on the use of decentralized clinical trials, including how to use digital health technologies.

- FDA should consider the quickest pathways by which vaccines can be made available. Throughout the development process, and despite any expedited processes, it is critical that the safety and efficacy of vaccine candidates be thoroughly studied.

- FDA should also consider if there is a way to harmonize labeling requirements for COVID-19 vaccines in the U.S. with labeling requirements in other countries to help accelerate the distribution of a potential vaccine.

- Congress and the Executive Branch should examine ways to encourage continued routine immunizations during the pandemic, especially pediatric immunizations and the seasonal influenza vaccine in the fall, including enhanced vaccine education and vaccine surveillance.

- Because seasonal influenza preparedness is intertwined with the fall response to COVID-19, steps should be taken to strengthen the supply chain of the U.S. influenza vaccine supply. Only about 53 percent of the U.S. seasonal influenza vaccines are produced in the U.S, with 47 percent of vaccines imported. The supply chain for influenza vaccines is globalized. Policies should be examined to encourage more U.S.-based production and supply for U.S. influenza vaccines.

C. Therapeutics

- While allowing the utilization of these drugs or agents for COVID-19 where appropriate, Congress, the Executive Branch, and the private sector should ensure continued supply and access of the drugs or agents for their intended purpose, where applicable.

    - For example, patients who are prescribed dexamethasone to treat inflammation, arthritis, or other disorders should not face shortages or access issues for dexamethasone due to the increase of utilization to treat patients with COVID-19.

- The private sector should explore additional ways to collaborate in order to accelerate the development and manufacturing of therapeutics.

- Congress, the Executive Branch, and the private sector should explore ways to further encourage the donation of plasma from those who have recovered from COVID-19.

- In addition, the private sector should explore additional ways to collaborate in order to achieve their respective goals. For example, scientists who are still trying to learn more about antibodies, companies who are in need of plasma for therapeutic development, blood bank organizations who are seeking out additional donors, and

companies that develop antibody tests who need additional samples may be able to develop a partnership to more efficiently achieve their respective goals.

- Through ACTIV's Clinical Trial Capacity Working Group, and other efforts, the Executive Branch should leverage existing clinical trial networks and explore ways for clinical trials to be more efficient and mobile so that if the rate of disease incidence in a given location declines, clinical trials can continue and produce complete, reliable, and timely results.

- The federal government and the private sector have taken steps to accelerate the development, testing, and manufacturing of medical countermeasures during the COVID-19 pandemic. Congress, the Executive Branch, and the private sector should evaluate best practices from the U.S.' response to the COVID-19 pandemic and ensure those best practices continue once the public health emergency is over to help advance other areas of medicine and prepare for future pandemics.

- The FDA should continue to study and consider additional, quicker pathways by which promising therapeutics can be made available, such as through an EUA.

D. Manufacturing and Supply Chain Issues Related to COVID-19 Vaccines and Therapeutics

- Congress and the Executive Branch should continue to examine if there are additional ways to use CIADMs to scale up manufacturing capacity for the delivery of vaccines and therapeutics.

- Congress and the Executive Branch should continue to study and implement what can be done in the short term to scale-up manufacturing for a COVID-19 vaccine, and also consider long term needs for domestic manufacturing capacity and capabilities in this area.

- Congress and the Executive Branch should examine whether there are ways to ensure manufacturing capacity for different platform technologies for COVID-19 vaccine candidates can be shifted as the vaccine pipeline advances and certain candidates are approved or authorized for use and other vaccine candidates fail.

- The Executive Branch should ensure there is a comprehensive national vaccine plan and efforts to accelerate the development and delivery of a vaccine are coordinated. On May 22, 2020, bipartisan leaders of the Energy and Commerce Committee sent a letter to White House Coronavirus Task Force Coordinator, Dr. Debra Birx, urging the Trump Administration to develop a national COVID-19 vaccine plan that includes plans for the development, manufacturing, distribution, provider training, public education, and broad vaccine access.

- Congress and the Executive Branch, working with the private sector, should consider what additional funds or authorities may be needed so that manufacturers can begin producing vaccines at a commercial scale ahead of approval.

- Congress and the Executive Branch should continue to consider how to deploy limited amounts of vaccines as they become available.

- Similar to the manufacturing capacity needed for a vaccine, Congress and the Executive Branch should study and implement what can be done in the short-term to scale up domestic supply chain capacity and capabilities to administer a vaccine, and also consider long-term needs for domestic manufacturing capacity and capabilities in this area.

- The Committee is aware of initiatives underway within the Executive Branch to develop medical countermeasures to more easily administer a vaccine. The Executive Branch should evaluate the current initiatives to see if the timetable can potentially be shortened and if there are additional efforts to expand and strengthen the aims of these initiates.

- Any therapeutic that shows success could have shortages if large numbers of people need it. While Congress and the Executive Branch are already working with the private sector to reduce any such shortages as much as possible, all parties should continue to examine innovative approaches to prevent shortages.

- Further, many biologics involve complex processes to manufacture. Similar to vaccines, it is critical for the Executive Branch and private sector to take steps now to ensure that a treatment can be widely available once studies shown it is safe and effective.

- Congress, the Executive Branch, and the private sector should determine what already-existing resources can be used to increase production of therapeutics, such as the CIADMs at BARDA, to avoid shortages or limited supplies of therapeutics. If additional resources are needed, Congress, the Executive Branch, and private sector should work to address those needs.

- To the extent that the private sector needs to shift its manufacturing of other products to other facilities, including international facilities, to accommodate for at risk manufacturing of COVID-19 vaccines and therapeutics, Congress and the Executive Branch should examine ways to reduce the regulatory hurdles to expedite the pharmaceutical industry's ability to do that safely and efficiently.

- Congress, the Executive Branch, and the private sector should explore if there are ways to shorten the manufacturing process for therapeutics while maintaining product integrity to improve the U.S.' ability to rapidly produce large quantities of drug supply in an emergency situation.

- In addition to evaluating the resources for increased production of the therapeutic itself, Congress, the Executive Branch, and the private sector should evaluate a potential increased need for supplies needed to administer the therapeutic. For example, if the therapy is not in pill form (and accordingly needs needles and syringes or other supplies to administer), demand on those supplies could already be increased in order to administer the influenza vaccine, routine vaccines on CDC's recommended immunization schedule, and a potential COVID-19 vaccine.

- Congress and the Executive Branch should also consider how to prioritize and deploy limited amounts of therapeutics as they become available, including through EUAs.