

THE BIOPHARMACEUTICAL INDUSTRY LEADS THE WAY IN DEVELOPING NEW VACCINES AND THERAPEUTICS FOR COVID-19

America's biopharmaceutical companies have successfully researched, developed and distributed multiple vaccines and therapeutics to halt the spread of COVID-19. While the impact of these successes is immense, the industry continues to develop and build upon solutions to further diagnose, treat and prevent the virus and long-term complications. The biopharmaceutical industry carries on its long track record of developing solutions to combat a range of infectious diseases and brings deep scientific expertise from decades of working with similar viruses such as MERS, SARS and influenza.

Over the past several decades, PhRMA members have invested billions of dollars in the manufacturing infrastructure, research and development (R&D) infrastructure and critical technological advances which have allowed us to

advance vaccine development, identify and bring promising therapeutic options forward and quickly manufacture innovative solutions for patients.

As of July 7, 2021, there are over **3 billion vaccine doses administered globally**.ⁱ The United States continues to lead in vaccine development and production. Globally, vaccine manufacturers are estimated to produce more than 11 billion doses of COVID-19 vaccines by the end of 2021, enabled by the hundreds of partnerships and collaborations between manufacturers and stakeholders worldwide.ⁱⁱ In the United States, the U.S. Food and Drug Administration (FDA) has granted emergency use authorizations (EUAs) for three vaccines for COVID-19 and six therapeutics. The FDA has approved one antiviral therapeutic for the treatment of certain COVID-19 patients.

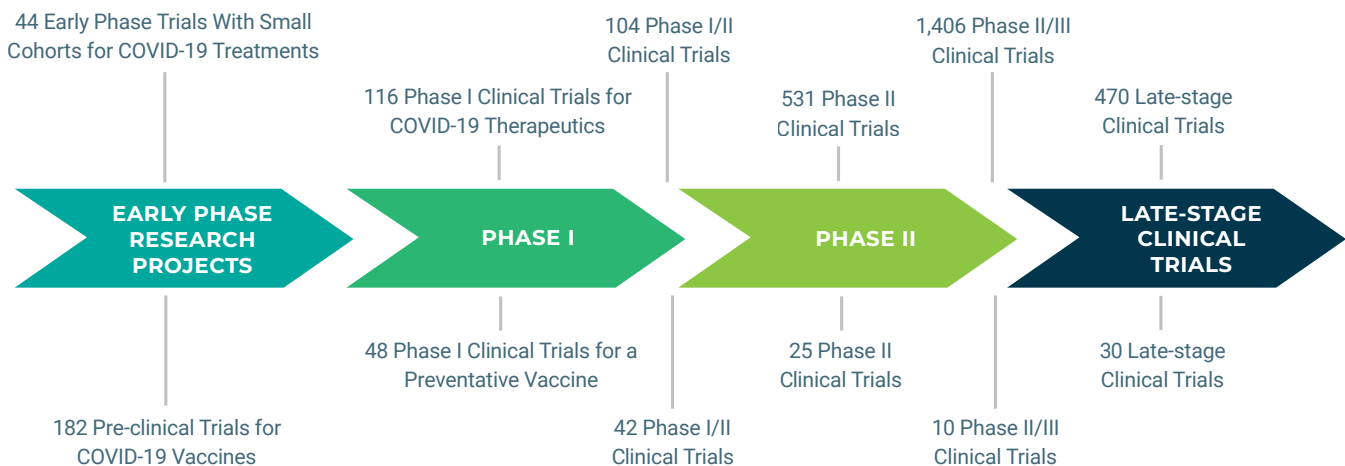
Still, biopharmaceutical companies work around the clock so additional patient populations can be eligible to receive COVID-19 vaccines. For instance, further safety and efficacy testing is ongoing for patient ages 5-11, 2-5 years of age and 6 months to 2 years of age. Beyond the vaccines currently authorized for use, biopharmaceutical research companies are continuing to develop different scientific approaches to vaccines, such as protein or DNA-based vaccines, which enables the body to learn, recognize and fight back against the virus. Several protein-based vaccines are in advanced clinical trials with one progressing to regulatory review. There are overall approximately **1,833 clinical trials that continue to test new, and iterate on existing, COVID-19 therapeutics and**

vaccines.ⁱⁱⁱ This innovation has been ongoing since the genetic sequence of COVID-19 was first released and today we are seeing:

- 1,604 clinical trials for COVID-19 therapeutics
- 229 clinical trials testing vaccines
- Over 400 of these clinical trials taking place in the U.S.

Some of the trials are being conducted in multiple countries simultaneously with the most impactful biopharmaceutical company trials requiring significant investment. The rapid escalation of trials across the biomedical R&D ecosystem is a testament to robust collaboration, biopharmaceutical investment and the participation of thousands of clinical trial volunteers from all walks of life.

Clinical Trials for Treatments and Vaccines for COVID-19 (as of June 25, 2021)



RESEARCHING AND DEVELOPING VACCINES FOR COVID-19

Since identifying the COVID-19 associated virus in December 2019, biopharmaceutical research companies have made unprecedented progress developing vaccines of multiple different types. Two mRNA vaccines and one viral vector vaccine have been authorized by the FDA and are being administered globally along with others.

Vaccines train a person's immune system to recognize a pathogen such as the virus that causes COVID-19 and neutralize it before it can harm the body. Several PhRMA members are continuing to research vaccine candidates for prevention and evaluating how existing technologies can be leveraged to allow rapid upscale of production once additional successful vaccine candidates are identified.

COVID-19 vaccines undergo extensive clinical safety and efficacy testing and must complete successful clinical trials before receiving regulatory authorization or approval. Biopharmaceutical companies are using novel techniques to advance vaccine research at a more efficient pace than ever before.

As of June 25, 2021, there are currently 229 clinical trials underway to test **104 vaccine candidates**. The 229 trials in Phase I, Phase II and Phase III are collectively enrolling over 1.4 million patients. Additionally, there are 184 preclinical studies ongoing for vaccine candidates, with many looking to move into Phase I human clinical trials later this year. Biopharmaceutical researchers are working on more vaccine approaches to ensure adequate supply and fit different patient needs.

Continued progress has been made with the 104 vaccines in clinical trials.^{iv} Companies are also using ingredients that act as an "adjuvant" that can boost the body's immune system response to the vaccine while requiring a smaller dose. This can help companies more quickly scale up production of vaccines and optimize available raw materials by having potent vaccines with less drug product per vaccine once they are authorized or approved for use by the broader public.

RESEARCHING AND DEVELOPING POTENTIAL COVID-19 THERAPEUTICS

PhRMA member companies scrutinized inventories of existing research portfolio libraries of experimental medicines to identify potential therapeutics to treat COVID-19. In addition, biopharmaceutical research labs identified novel "purpose-built" molecules and therapeutics such as new monoclonal antibodies to provide additional treatment options. These therapeutics are directed at blocking or disabling the virus itself and for treating secondary clinical manifestations of COVID-19, including those potentially found with long COVID, defined by the CDC as a wide range of persistent symptoms that can last weeks or months after first being diagnosed with the infection and can happen to anyone who has had COVID-19 even if the illness was mild or asymptomatic.

Biopharmaceutical companies are also exploring with other research stakeholders therapies for long COVID conditions, defined by the CDC as a wide range of new, returning or ongoing health problems people can experience more than four weeks after first being infected with the virus that causes COVID-19.^v Long COVID is a type of post-COVID condition which refers to a collection of longer-term effects to multiple parts of the body that have been observed as a result of a

COVID-19 infection, treatment or hospitalization, which may be similar to effects after hospitalization for other respiratory infections. The best way to reduce the number of long COVID cases is to prevent COVID-19, a reminder that vaccines are our best defense against the virus.

As of June 25, 2021, there are **more than 585 unique therapeutics** being tested globally for COVID-19 and COVID-19 related complications.

The chart on the following page shows the phases of development for current COVID-19 therapeutics.^{vi} When analyzing the 1,604 active clinical trials, a little more than half (58%) are targeting the virus directly, while the rest of the trials focus on related effects of COVID-19 such as pneumonia. Of the 1,604 active clinical trials, nearly 1,000 trials are testing medicines previously approved for another indication, such as antiviral combinations, and 260 trials are testing novel compounds.^{vii} There have been **six therapeutics, including three monoclonal antibodies**, and one antiviral, that have been authorized or approved by the FDA for COVID-19.^{viii}

COVID-19 Treatments in Development by Phase (as of June 25, 2021)

Early Clinical Research	Phase I	Phase I/II	Phase II	Phase II/III	Late-stage Clinical Trials	FDA EUA/Approval
31	76	69	271	88	196	6

MONOCLONAL ANTIBODIES TO FIGHT COVID-19

The immune system relies on antibodies to detect and destroy harmful substances. After discovering a potential invader—such as a virus, bacteria or fungus—the human body produces antibodies that attach to a part of the invader (usually a protein on its surface), which is called an antigen. Once an antibody binds to an antigen, it acts as a signal to other cells in the immune system to attack and destroy it.

In 2020 and 2021, the FDA issued an EUA for three monoclonal antibody therapeutics; two of these were specifically

developed to mimic the function of our immune system to help fight COVID-19 by blocking the ability of the coronavirus to attach and enter human cells. The virus must enter the cells to reproduce, as it cannot replicate on its own. By preventing it from doing so, these therapeutics—two of which are a combination of two different monoclonal antibodies—may help slow the spread of a person’s infection, potentially reducing the length and severity of symptoms.

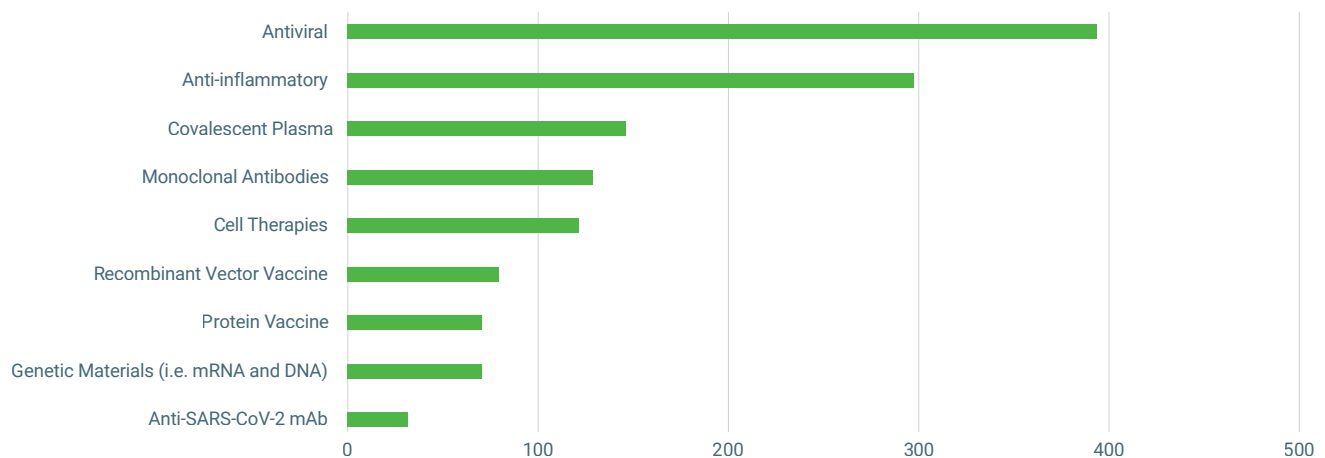
TRACKING EMERGING VARIANTS

Viruses are constantly changing, which can lead to genetic variations (commonly referred to as variants or mutations) that may have different characteristics, both positive and negative. Importantly, not all variants are created equal. Some variants may spread more easily or cause more severe

disease. Across the industry, companies are tracking variants using genomic surveillance to identify and decode changes in the virus, as well as further continuing clinical research to assess whether modifications or boosters are warranted to existing vaccines to address emerging variants.

MEDICINES AND VACCINES IN DEVELOPMENT FOR COVID-19

Number of Unique Clinical Trials for Therapies and Vaccines in Development for COVID-19 by Type (as of June 25, 2021)



“We always need a pharmaceutical partner. I can’t think of a vaccine, even one in which we’ve put substantial intellectual and resource input, that was brought to the goal line without a partnership with industry. So, this is a very natural process that we’re doing right now.... I have not seen in my experience situations in which we were involved in the development of a vaccine, particularly for low- and middle-income countries that really needed it, where the pharmaceutical companies priced it out of their reach.”

– NIAID Director Dr. Anthony Fauci (February 27, 2020)

MANUFACTURING AND DISTRIBUTION AND PARTNERSHIPS

Biopharmaceutical researchers are developing the critical, specific manufacturing methods to produce COVID-19 therapeutics and vaccines. Particularly for vaccines used in large populations, these methods then undergo massive scale up to ensure the ability to produce many millions of doses. This is an enormous undertaking, as the transition from laboratory to manufacturing facility is incredibly complex and the industry must ensure consistency in the vaccine composition throughout scale-up. As developing the manufacturing strategy is an ongoing process, biopharmaceutical companies are continuing to seek to expand their manufacturing capacity and enhance the formulation of products. Companies also initiated manufacturing capabilities at risk in parallel with clinical development, well before a COVID-19 vaccine received regulatory authorization or approval, to speed the delivery of approved/authorized products to the patients who need them.

Safely delivering a vaccine to patients around the world is an equally challenging undertaking, especially in less developed regions, as vaccines often require special handling, such as temperature control, during distribution. Biopharmaceutical companies are working closely with local governments and NGO partners to deliver the vaccines at global scale.

COVID-19 has demonstrated the importance of having global, innovative, cross-stakeholder partnerships. Armed with experience garnered from previous outbreaks and decades of knowledge about infectious diseases, America’s biopharmaceutical companies have joined forces to fight COVID-19. Companies are leading by collaborating with each

other and key health stakeholders on efforts to address the global health crisis through developing diagnostics, therapeutics and vaccines to help save lives and restore the rhythms of daily life for billions of people.

The biopharmaceutical industry continues to establish partnerships, facilitated in part by the U.S. IP policy framework, licensing agreements and the infrastructure the industry has developed over decades, aimed at boosting capacity to keep pace with global demand so that vaccines make it to those in need as quickly as possible. Globally, manufacturers are fully committed to providing worldwide access to COVID-19 vaccines.

The biopharmaceutical industry is committed to developing additional solutions to address this global public health emergency just as it has in the past. PhRMA member companies not only bring decades of expertise in infectious diseases, including other strains of coronavirus, but bring the infrastructure and technologies that allow us to quickly identify and advance potential vaccine and therapeutic candidates to clinical trials and have the manufacturing capabilities and expertise to allow for quick scale-up.

As of June 25, 2021, over 3 billion vaccines have been administered worldwide, a remarkable scientific and logistical achievement.^{ix} While this progress should be applauded, biopharmaceutical research companies are not done fighting COVID-19 and won’t stop until we beat the virus.

ⁱ https://ourworldindata.org/covid-vaccinations?country=OWID_WRL

ⁱⁱ https://www.ifpma.org/wp-content/uploads/2021/05/airfinity_production_19.05.2021.pdf

ⁱⁱⁱ Analysis of publicly available databases such as clinicaltrials.gov, AdisInsights and the World Health Organization’s International Clinical Trials Registry Platform (WHO ICTRP) as of June 25, 2021

^{iv} Clinical trial data as of June 25, 2021

^v <https://www.cdc.gov/coronavirus/2019-ncov/long-term-effects.html>

^{vi} Treatments in development by phase as of June 25, 2021. Note – some medicines may be in two different phases at the same time.

^{vii} <https://www.gilead.com/purpose/advancing-global-health/covid-19/about-remdesivir>

^{viii} <https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#coviddrugs>

^{ix} <https://www.nytimes.com/interactive/2021/world/covid-vaccinations-tracker.html>