

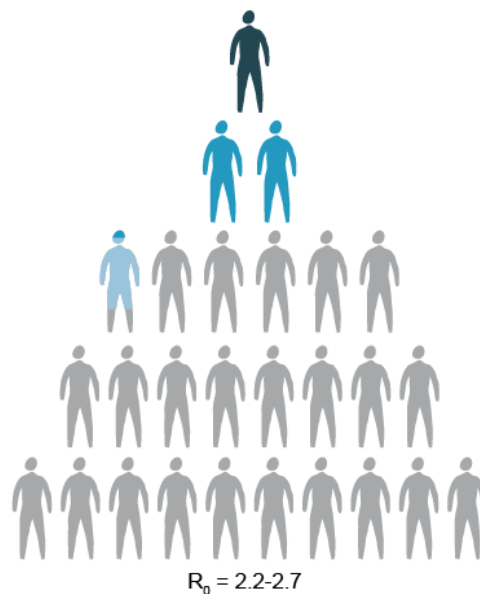
# COVID-19 Vaccine Development Report

## The COVID-19 Pandemic

Coronavirus disease 2019 (COVID-19) is an infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a novel pathogen identified in 2019 after clusters of idiopathic atypical pneumonia prompted extensive epidemiologic investigation. These early cases, reported in Wuhan, China, were linked to a wet animal wholesale market in the region. On March 11, 2020, the World Health Organization (WHO) declared the COVID-19 outbreak a pandemic (WHO, 2020). As of June 29, 2020, there are over 10 million confirmed cases of COVID-19 in 216 countries/territories, and nearly 500,000 deaths have been attributed to the disease (WHO, 2020).

## Rationale for Developing a Vaccine

When a single case is introduced into a totally susceptible population, the expected number of secondary cases is the basic case reproduction number ( $R_0$ , pronounced “R naught”). The  $R_0$  is a metric commonly used to quantify the contagiousness of an infectious agent (Delamater et al., 2019) or, in other words, the average number of people that an individual with the virus will infect. While our knowledge of SARS-CoV-2 is still evolving, the  $R_0$  of this virus has been estimated to range from 2.2 to 2.7, but this estimate is preliminary and may change over time (see Figure 1) (Sanche et al., 2020).



**Figure 1. Basic Reproductive Number ( $R_0$ ) of SARS-CoV-2**

It is widely understood that an  $R_0$  value  $> 1$  will sustain the transmission cycle of an infectious agent in a population and an outbreak will continue to spread. However, reducing the  $R_0$  to  $\leq 1$  will interrupt the transmission cycle and an outbreak will slow and eventually die out (Delamater et al., 2019). There are a variety of ways to slow the spread of an outbreak, including behavioral interventions (limiting physical contact between infectious and susceptible individuals), [testing](#), and contact tracing. Historically, however, widespread disease eradication has largely relied on a safe and effective vaccine (CDC, 2016).

## Four Main Types of Vaccines

Since the original vaccine, developed by Edward Jenner in the 1790s (Riedel, 2005), vaccines have progressed and can largely be divided into 4 different types, including live-attenuated; inactivated; subunit, recombinant, polysaccharide, or conjugate; and toxoid, all described in Table 1.

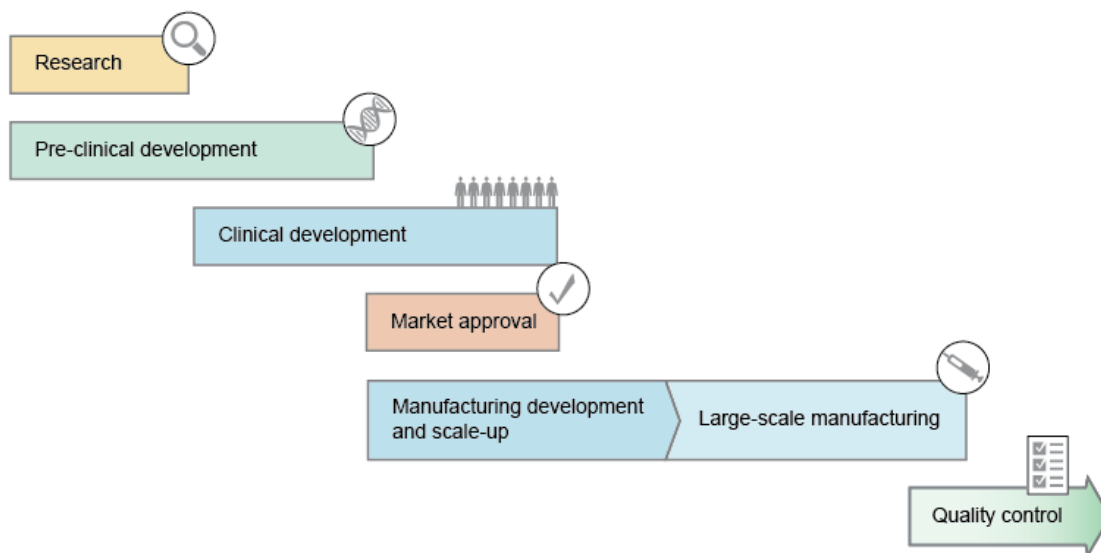
Table 1. Vaccine Types

Vaccine Type	Description	Dosing and Additional Information	Examples
Live-attenuated	Use a weakened (or attenuated) form of the infectious agent (bacteria, virus) that causes a disease.	These vaccines are similar to the natural infection that they help prevent. They provoke a robust and prolonged immune response. For most live vaccines, 1 or 2 doses provide lifelong protection.	Measles, mumps, rubella (MMR) Rotavirus Smallpox Chickenpox Yellow fever
Inactivated	Use the killed version of the infectious agent that causes a disease.	Inactivated vaccines usually do not provide the same high level of immunity as live vaccines. Several doses over time (booster shots) may be needed for ongoing immunity.	Hepatitis A Flu Polio Rabies
Subunit, recombinant, polysaccharide, or conjugate	Use specific parts of the infectious agent—such as a protein, sugar, or capsid (a casing around a virus).	These vaccines may be created through genetic engineering techniques. They use only specific pieces of the virus or bacteria and they provoke a very strong immune response targeted at key parts of the virus or bacteria. These vaccines can be used on nearly everyone who needs them, including those with weakened immune systems and long-term health problems. However, booster shots may be required for ongoing immunity.	Hib Hepatitis B HPV Whooping cough Pneumococcal disease Meningococcal disease Shingles
Toxoid	Use a toxin (harmful product) made by the infectious agent.	Toxoid vaccines create immunity to the parts of the infectious agent that cause a disease, rather than providing immunity to the germ itself. Booster	Diphtheria Tetanus

Vaccine Type	Description	Dosing and Additional Information	Examples
		shots may be required for ongoing immunity.	
Source: U.S. Department of Health & Human Services (HHS). Vaccine types. Updated March 2020. Available at: <a href="https://www.vaccines.gov/basics/types">https://www.vaccines.gov/basics/types</a> . Accessed May 18, 2020.			

## Phases of Vaccine Development

The human immune system can take weeks to produce antibodies following exposure to a vaccine, and some adverse events can take even longer to appear. As a result, a new vaccine must undergo the appropriate safety and efficacy trials that generally require multiple iterative phases, which can take anywhere from 12 to 18 months, at a minimum, to complete. The vaccine development process includes the preclinical phase, which consists of in vitro development and animal testing. It has been suggested that only 6% of candidate vaccines will make it past this preclinical phase and to the market (Pronker et al., 2013). Subsequently, the vaccine must undergo human clinical trials where the probability of success is 33.4% (Wong et al., 2019). Figure 2 illustrates the vaccine development process (CDC, 2014; MPH@GW, 2019). Even after a vaccine moves past the production stage, the safety and efficacy is continuously monitored.



**Figure 2. Vaccine Development Process**

## Operation Warp Speed

On May 15, 2020, a framework for a national program in the United States was introduced with the overall goal of accelerating the development process for a SARS-CoV-2 vaccine. With the overall goal of procuring a safe and effective SARS-CoV-2 vaccine by January 2021, the program, titled Operation Warp Speed (OWS), is intended to streamline efforts in the research phases (preclinical and clinical) and fast-track both manufacturing and distribution (HHS, 2020). To achieve this goal, OWS identified 5 promising vaccine candidates to receive focused resources and support (NYT, 2020). Additional details for each clinical trial can be found in Table 2.

**Table 2. Vaccine Candidates Selected for Operation Warp Speed**

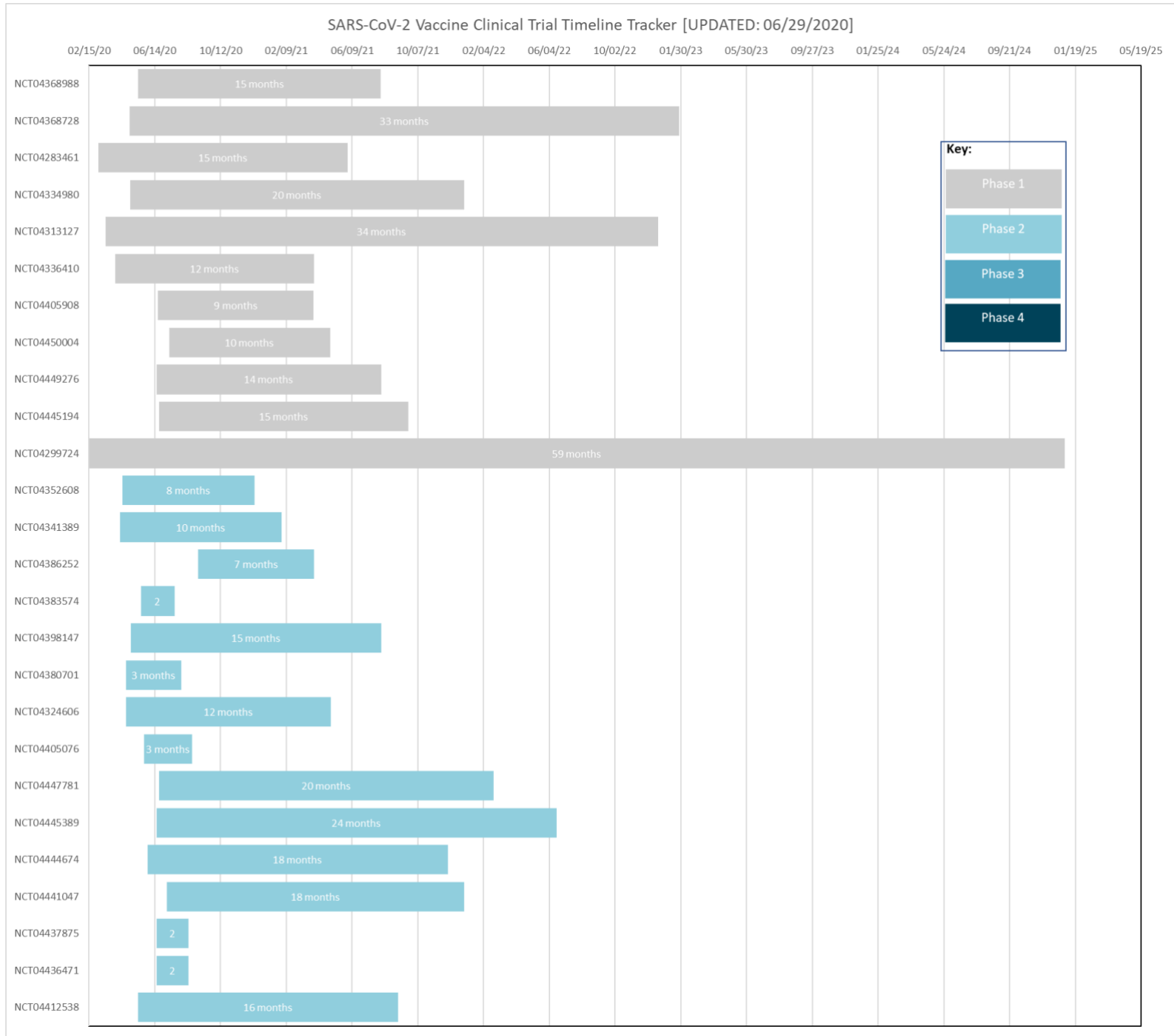
**Key:** BIDMC, Beth Israel Deaconess Medical Center; IAVI, International AIDS Vaccine Initiative; mRNA, messenger ribonucleic acid; NIAID, National Institute of Allergy and Infectious Diseases; rVSV, recombinant vesicular stomatitis virus

Sponsor/Collaborators	Candidate Vaccine	NCT Number and Online Resources
<a href="#">Moderna</a> ; <a href="#">NIAID</a>	mRNA-1273	<a href="#">NCT04405076</a> <a href="#">NCT04283461</a> <a href="#">Moderna's work on a COVID-19 vaccine candidate</a> Moderna press releases: <a href="#">April 16, 2020</a> <a href="#">April 27, 2020</a> <a href="#">May 1, 2020</a> <a href="#">May 12, 2020</a> <a href="#">May 18, 2020</a> <a href="#">May 29, 2020</a> <a href="#">June 11, 2020</a> NIAID press releases: <a href="#">March 16, 2020</a> <a href="#">March 27, 2020</a> <a href="#">April 15, 2020</a> <a href="#">April 20, 2020</a>
<a href="#">AstraZeneca</a> ; <a href="#">University of Oxford</a>	AZD1222 (formerly ChAdOx1 nCov19)	<a href="#">NCT04324606</a> <a href="#">NCT04400838</a> AstraZeneca press releases: <a href="#">April 30, 2020</a> <a href="#">May 21, 2020</a> <a href="#">June 4, 2020</a> <a href="#">June 13, 2020</a> University of Oxford press releases: <a href="#">February 7, 2020</a> <a href="#">March 27, 2020</a> <a href="#">April 23, 2020</a> <a href="#">May 22, 2020</a> <a href="#">June 4, 2020</a>
<a href="#">Johnson &amp; Johnson</a> ; <a href="#">BIDMC</a>	Ad26.COV2-S	<a href="#">Johnson &amp; Johnson COVID-19 vaccine development efforts</a> Johnson & Johnson press releases: <a href="#">February 11, 2020</a> <a href="#">February 18, 2020</a> <a href="#">March 13, 2020</a> <a href="#">March 30, 2020</a> <a href="#">June 10, 2020</a> BIDMC press releases: <a href="#">May 20, 2020</a>
<a href="#">Merck</a> ; <a href="#">IAVI</a>	rVSV	Merck press releases: <a href="#">May 26, 2020</a> IAVI press releases: <a href="#">May 26, 2020</a>

## Vaccine Clinical Trial Tracker

Currently, there are more than 170 vaccines in development (Milken Institute, 2020); however, only a fraction of these have advanced to human clinical trials and are registered in the U.S. National Library of Medicine clinical trials database. A search of the [ClinicalTrials.gov](https://clinicaltrials.gov) database using the search terms ((COVID-19 OR coronavirus) AND vaccine), performed on June 29, 2020, identified 41 studies related to COVID-19 vaccinations. The following visualization provides a road map of the current clinical trials registered with the U.S. National Library of Medicine clinical trials database. Each clinical trial, identified by the NCT number, is represented by a bar on the graph. The color of the bar indicates the phase of vaccine development, while the length of the bar indicates the expected duration of the clinical trial as designated by the projected start and end dates recorded by the researchers in the database. The information in this road map will evolve over time. Additional details for each clinical trial can be found in Table 3.

# Clinical Trials Roadmap



# Clinical Trials Roadmap

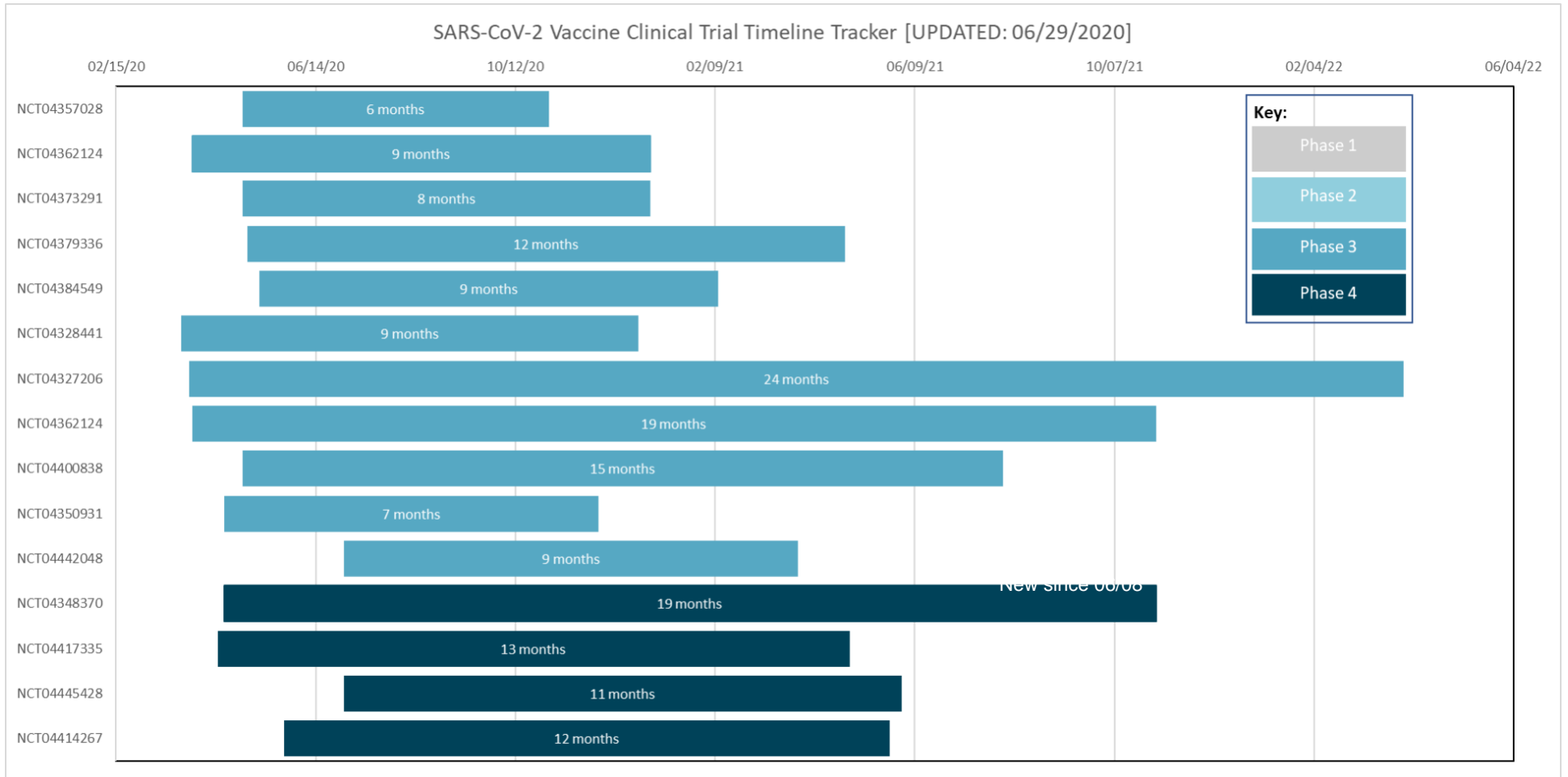


Table 3. Ongoing Clinical Studies Pertaining to COVID-19 Vaccines [UPDATED: 06/29/2020]

NCT Number	Title	Phase	Allocation	Enrollment	Completion Date
<a href="#">NCT04362124</a>	Performance Evaluation of BCG Vaccination in Healthcare Personnel to Reduce the Severity of SARS-COV-2 Infection	Phase 3	Randomized	1000	11/01/21
<a href="#">NCT04357028</a>	Measles Vaccine in HCW	Phase 3	Randomized	200	11/01/20
<a href="#">NCT04352608</a>	Safety and Immunogenicity Study of Inactivated Vaccine for Prophylaxis of SARS CoV-2 Infection (COVID-19)	Phase 1 Phase 2	Randomized	744	12/13/20
<a href="#">NCT04350931</a>	Application of BCG Vaccine for Immune-prophylaxis Among Egyptian Healthcare Workers During the Pandemic of COVID-19	Phase 3	Randomized	900	12/01/20
<a href="#">NCT04348370</a>	BCG Vaccine for Health Care Workers as Defense Against COVID 19	Phase 4	Randomized	1800	11/01/21
<a href="#">NCT04341389</a>	A Phase II Clinical Trial to Evaluate the Recombinant Vaccine for COVID-19 (Adenovirus Vector)	Phase 2	Randomized	500	01/31/21
<a href="#">NCT04334980</a>	Evaluating the Safety, Tolerability and Immunogenicity of bacTRL-Spike Vaccine for Prevention of COVID-19	Phase 1	Randomized	84	12/31/21
<a href="#">NCT04328441</a>	Reducing Health Care Workers Absenteeism in Covid-19 Pandemic Through BCG Vaccine	Phase 3	Randomized	1500	12/25/20
<a href="#">NCT04327206</a>	BCG Vaccination to Protect Healthcare Workers Against COVID-19	Phase 3	Randomized	4170	03/30/22
<a href="#">NCT04324606</a>	A Study of a Candidate COVID-19 Vaccine (COV001)	Phase 1 Phase 2	Randomized	1112	05/01/21
<a href="#">NCT04313127</a>	Phase I Clinical Trial of a COVID-19 Vaccine in 18-60 Healthy Adults	Phase 1	Non-Randomized	108	12/20/22
<a href="#">NCT04299724</a>	Safety and Immunity of Covid-19 aAPC Vaccine	Phase 1	Single Group	100	12/31/24
<a href="#">NCT04283461</a>	Safety and Immunogenicity Study of 2019-nCoV Vaccine (mRNA-1273) for Prophylaxis SARS CoV-2 Infection (COVID-19)	Phase 1	Non-Randomized	45	06/01/21
<a href="#">NCT04336410</a>	Safety, Tolerability and Immunogenicity of INO-4800 for COVID-19 in Healthy Volunteers	Phase 1	Non-Randomized	40	04/01/21
<a href="#">NCT04373291</a>	Using BCG Vaccine to Protect Health Care Workers in the COVID-19 Pandemic	Phase 3	Randomized	1500	01/01/21
<a href="#">NCT04368988</a>	Evaluation of the Safety and Immunogenicity of a SARS-CoV-2 rS (COVID-19) Nanoparticle Vaccine With/Without Matrix-M Adjuvant	Phase 1	Randomized	131	07/31/21



NCT Number	Title	Phase	Allocation	Enrollment	Completion Date
<a href="#">NCT04368728</a>	Study to Describe the Safety, Tolerability, Immunogenicity, and Potential Efficacy of RNA Vaccine Candidates Against COVID-19 in Healthy Adults	Phase 1	Randomized	7600	01/27/23
<a href="#">NCT04379336</a>	BCG Vaccination for Healthcare Workers in COVID-19 Pandemic	Phase 3	Randomized	500	04/28/21
<a href="#">NCT04386252</a>	Phase Ib-II Trial of Dendritic Cell Vaccine to Prevent COVID-19 in Frontline Healthcare Workers and First Responders	Phase 1 Phase 2	Randomized	180	04/01/21
<a href="#">NCT04384549</a>	Efficacy of BCG Vaccination in the Prevention of COVID19 Via the Strengthening of Innate Immunity in Health Care Workers	Phase 3	Randomized	1120	02/11/21
<a href="#">NCT04383574</a>	Safety and Immunogenicity Study of Inactivated Vaccine for Prevention of SARS-CoV-2 Infection(COVID-19)	Phase 1 Phase 2	Randomized	422	07/20/20
<a href="#">NCT04380701</a>	A Trial Investigating the Safety and Effects of Four BNT162 Vaccines Against COVID-2019 in Healthy Adults	Phase 1 Phase 2	Non-Randomized	200	08/01/20
<a href="#">NCT04357028</a>	Measles Vaccine in HCW	Phase 3	Randomized	200	11/01/20
<a href="#">NCT04400838</a>	Investigating a Vaccine Against COVID-19	Phase 2 Phase 3	Randomized	10260	08/01/21
<a href="#">NCT04398147</a>	Phase I/II Clinical Trial of Recombinant Novel Coronavirus Vaccine (Adenovirus Type 5 Vector) (Ad5-nCoV) in Canada	Phase 1 Phase 2	Randomized	696	08/01/21
<a href="#">NCT04405908</a>	SCB-2019 as COVID-19 Vaccine	Phase 1	Randomized	150	03/30/21
<a href="#">NCT04405076</a>	Dose-Confirmation Study to Evaluate the Safety, Reactogenicity, and Immunogenicity of mRNA-1273 COVID-19 Vaccine in Adults Aged 18 Years and Older	Phase 2	Randomized	600	08/21/20
<a href="#">NCT04417335</a>	Reducing COVID-19 Related Hospital Admission in Elderly by BCG Vaccination	Phase 4	Randomized	2014	05/01/21
<a href="#">NCT04414267</a>	Bacillus Calmette-guérin Vaccination to Prevent COVID-19	Phase 4	Randomized	900	05/25/21
<a href="#">NCT04412538</a>	Safety and Immunogenicity Study of an Inactivated SARS-CoV-2 Vaccine for Preventing Against COVID-19	Phase 1 Phase 2	Randomized	942	09/01/21
<a href="#">NCT04450004</a>	Safety, Tolerability and Immunogenicity of a Coronavirus-Like Particle COVID-19 Vaccine in Adults Aged 18-55 Years.	Phase 1	Randomized	180	06/29/20
<a href="#">NCT04449276</a>	A Study to Evaluate the Safety, Reactogenicity and Immunogenicity of Vaccine CVnCoV in Healthy Adults	Phase 1	Randomized	168	06/26/20

NCT Number	Title	Phase	Allocation	Enrollment	Completion Date
<a href="#">NCT04447781</a>	Safety, Tolerability and Immunogenicity of INO-4800 Followed by Electroporation in Healthy Volunteers for COVID19	Phase 1 Phase 2	Randomized	160	06/25/20
<a href="#">NCT04445428</a>	OPV as Potential Protection Against COVID	Phase 4	Randomized	3400	06/24/20
<a href="#">NCT04445389</a>	Safety and Immunogenicity Study of GX-19, a COVID-19 Preventive DNA Vaccine in Healthy Adults	Phase 1 Phase 2	Randomized	190	06/24/20
<a href="#">NCT04445194</a>	Phase I Clinical Study of Recombinant Novel Coronavirus Vaccine	Phase 1	Randomized	50	06/24/20
<a href="#">NCT04444674</a>	COVID-19 Vaccine (ChAdOx1 nCoV-19) Trial in South African Adults With and Without HIV-infection	Phase 1 Phase 2	Randomized	2000	06/23/20
<a href="#">NCT04442048</a>	Immunization With IMM-101 vs Observation for Prevention of Respiratory and Severe COVID-19 Related Infections in Cancer Patients at Increased Risk of Exposure	Phase 3	Randomized	1500	06/22/20
<a href="#">NCT04441047</a>	Universal Anti-Viral Vaccine for Healthy Elderly Adults	Phase 1 Phase 2	Single Group	40	06/22/20
<a href="#">NCT04437875</a>	An Open Study of the Safety, Tolerability and Immunogenicity of "Gam-COVID-Vac Lyo" Vaccine Against COVID-19	Phase 1 Phase 2	Non-Randomized	38	06/18/20
<a href="#">NCT04436471</a>	An Open Study of the Safety, Tolerability and Immunogenicity of the Drug "Gam-COVID-Vac" Vaccine Against COVID-19	Phase 1 Phase 2	Non-Randomized	38	06/18/20

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