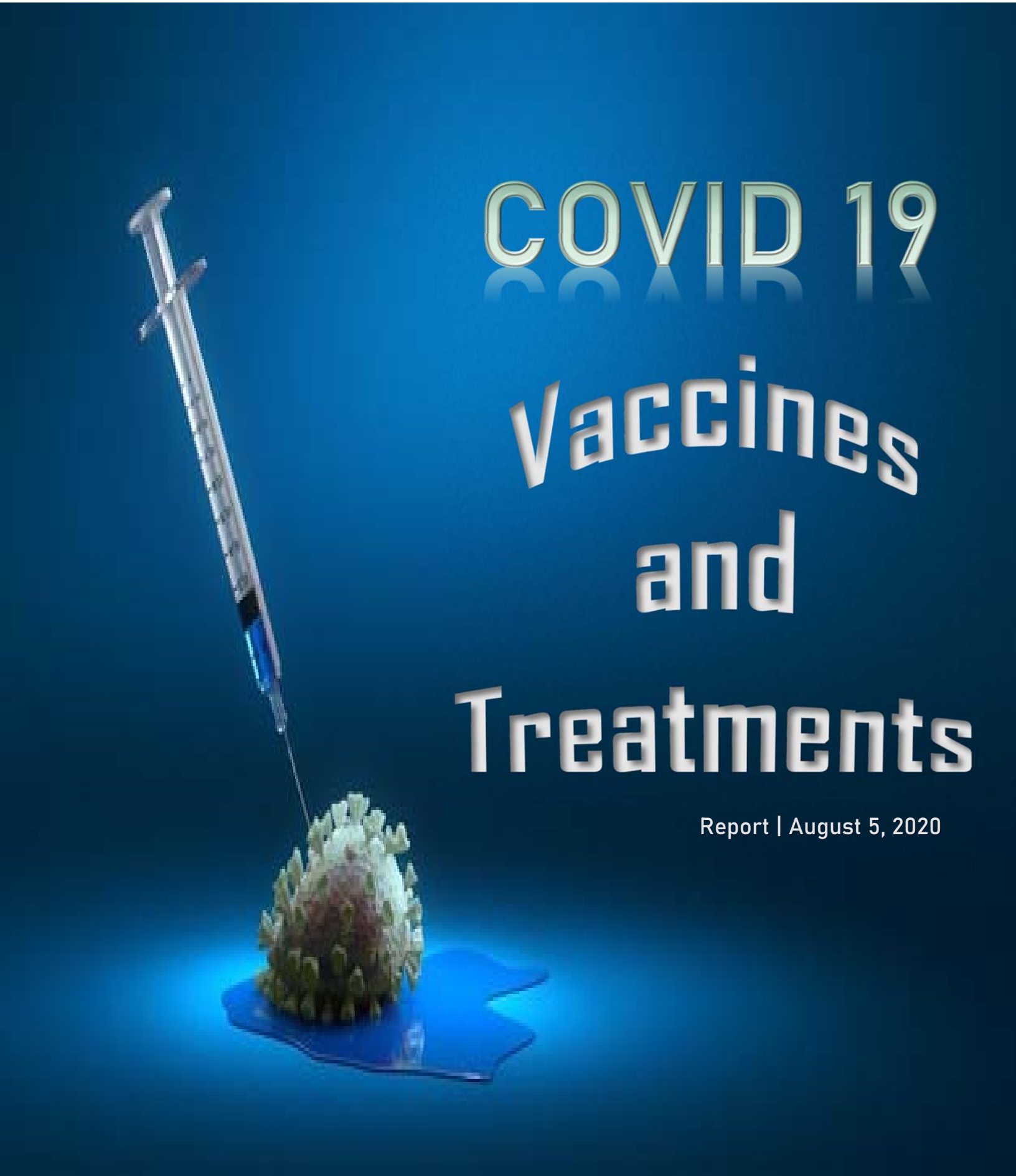
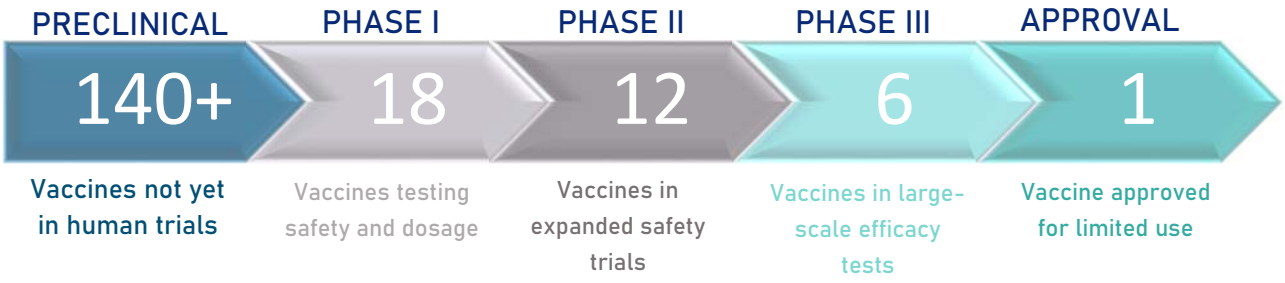

COVID 19
Vaccines
and
Treatments
Report | August 5, 2020

COVID-19 VACCINES IN DIFFERENT PHASES



COVID-19 | GLOBAL CASE REPORT

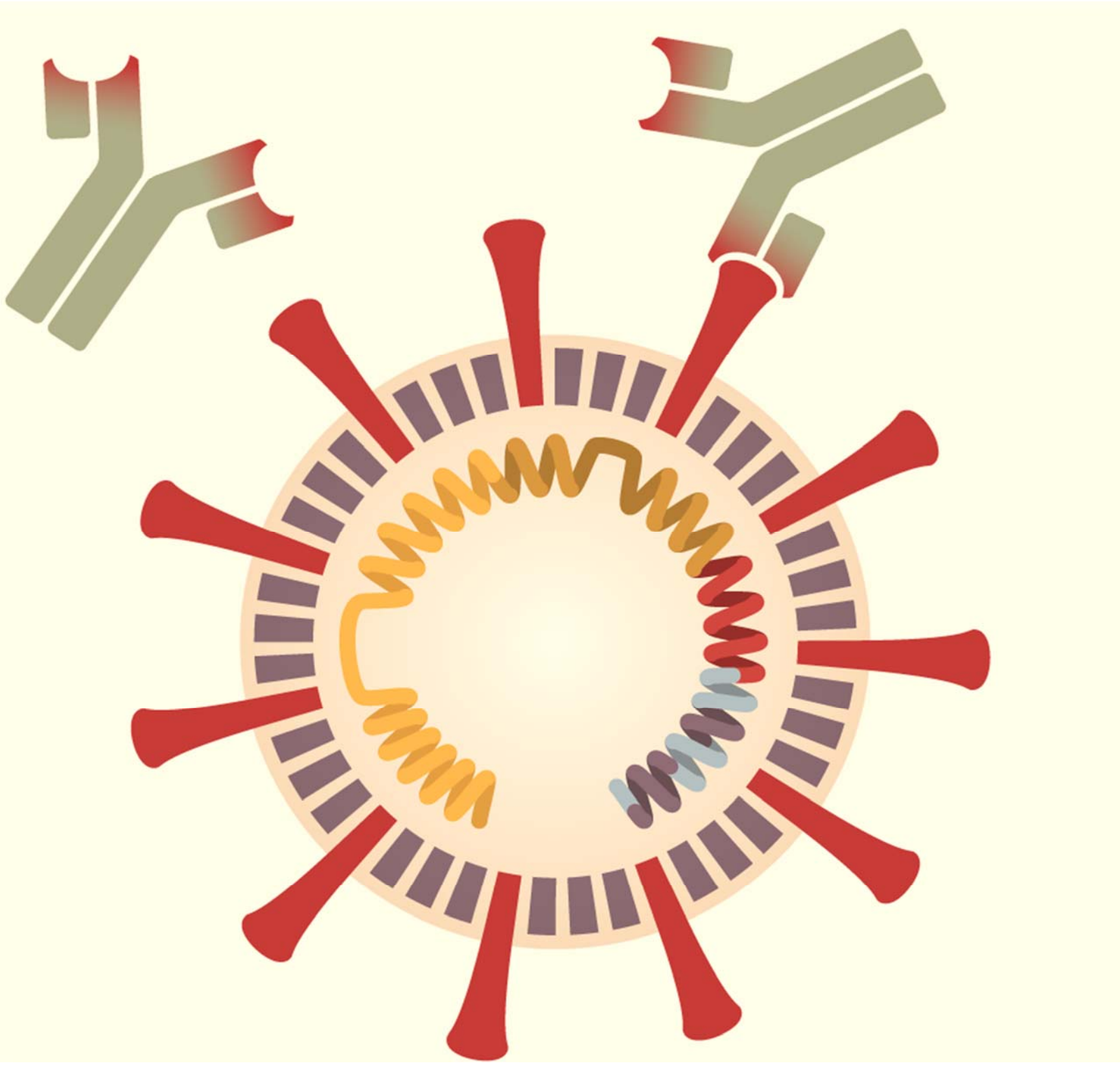
Total Confirmed	Global Deaths
18,317,520	694,713

Researchers around the world are developing more than 165 vaccines against the coronavirus, and 27 vaccines are in human trials. Vaccines typically require years of research and testing before reaching the clinic, but scientists are racing to produce a safe and effective vaccine by next year.

Work began in January with the deciphering of the SARS-CoV-2 genome. The first vaccine safety trials in humans started in March, but the road ahead remains uncertain. Some trials will fail, and others may end without a clear result. But a few may succeed in stimulating the immune system to produce effective antibodies against the virus.

Here is the status of all the vaccines that have reached trials in humans, along with a selection of promising vaccines still being tested in cells or animals

- Moderna and the N.I.H. enter Phase III. July 27
- Pfizer begins Phase II/III trials. July 27
- Arcturus and Duke-NUS Medical School enter Phase I/II. July 21



LEADING CANDIDATES

FARTHEST ALONG*	CLINICAL PHASE
Univ. of Oxford/AstraZeneca	III
Wuhan Inst./Sinopharm	III
Beijing Inst./Sinopharm	III
Sinovac/Instituto Butantan	III
Moderna	III
BioNtech/Fosun/Pfizer	II/ III
Inst. of Medical Biology	II
Cansino Biologics	II
Imperial College London	I / II
Novavax	I / II

*Ranked by entry into latest phase of development. Clinical phases move when it is publicly reported that the product has been dosed in a trial.

PHASE III

A vaccine in development by the British-Swedish company AstraZeneca and the University of Oxford is based on a chimpanzee adenovirus called ChAdOx1. A study on monkeys found that the vaccine provided them protection. In May, the United States awarded the project $1.2 billion in support. Their Phase I/II trial reported that the vaccine was safe, causing no severe side effects. It raised antibodies against the coronavirus as well as other immune defenses. The vaccine is now in a Phase II/III trial in England, as well as Phase III trials in Brazil and South Africa. The project may deliver emergency vaccines by October. AstraZeneca has said their total manufacturing capacity for the vaccine, if approved, stands at two billion doses.

PHASE III

After finding that an inactivated virus vaccine was safe and provoked an immune response, the state-owned Chinese company Sinopharm launched Phase III trials in July in the United Arab Emirates. Abu Dhabi's health minister was the first volunteer to be injected, and 15,000 people were scheduled to participate in total. In July, the chairman of Sinopharm told Chinese state media that the vaccine could be ready for public use by the end of the year.

PHASE III

The private Chinese company Sinovac Biotech is testing an inactivated vaccine called CoronaVac. In June the company announced that Phase I/II trials on 743 volunteers found no severe adverse effects and produced an immune response. Sinovac then launched a Phase III trial in Brazil in July. The company is also building a facility to manufacture up to 100 million doses annually.

PHASE III

Moderna develops vaccines based on messenger RNA (mRNA) to produce viral proteins in the body. They have yet to bring one to the market. In partnership with National Institutes of Health, they found that the vaccine protects monkeys from the coronavirus. In March, the company put the first Covid-19 vaccine into human trials, which yielded promising results, After carrying out a Phase II study they launched a Phase III trial on July 27. The final trial will enrol 30,000 healthy people at about 89 sites around the United States. The government has bankrolled Moderna's efforts with nearly $1 billion in support.

PHASE II / III

The German company BioNTech has entered into collaborations with Pfizer, based in New York, and the Chinese drug maker Fosun Pharma to develop their mRNA vaccine. In July, they posted preliminary results from their Phase I/II trials in the United States and Germany. They found that the volunteers produced antibodies against SARS-CoV-2, as well as immune cells called T cells that respond to the virus. Some volunteers experienced moderate side effects such as sleep disturbances and sore arms. On July 27, they announced the launch of a Phase II/III trial with 30,000 volunteers in the United States and other countries including Argentina, Brazil, and Germany.

The Trump administration awarded a $1.9 billion contract for 100 million doses to be delivered by December and the option to acquire 500 million more doses. Meanwhile, Japan made a deal for 120 million doses. If approved, Pfizer said they expect to manufacture over 1.3 billion doses of their vaccine worldwide by the end of 2021.

PHASE II

INSTITUTE OF MEDICAL BIOLOGY
CHINESE ACADEMY OF MEDICAL SCIENCES

Researchers at the Institute of Medical Biology at the Chinese Academy of Medical Sciences, which has invented vaccines for polio and hepatitis A, started a Phase II trial of an inactivated virus vaccine in June.

PHASE II

CanSinoBIO

The Chinese company CanSino Biologics developed a vaccine based on an adenovirus called Ad5, in partnership with the Institute of Biology at the country's Academy of Military Medical Sciences. In May, they published promising results from a Phase I safety trial, and in July they reported that their Phase II trials demonstrated the vaccine produced a strong immune response. In an unprecedented move, the Chinese military approved the vaccine on June 25 for a year as a "specially needed drug." CanSino would not say whether vaccination would be mandatory or optional for soldiers.

PHASE I / II

Imperial College London

MORNINGSIDE

Imperial College London researchers have developed a "self-amplifying" RNA vaccine, which boosts production of a viral protein to stimulate the immune system. They began Phase I/II trials on June 15 and have partnered with Morningside Ventures to manufacture and distribute the vaccine through a new company called VacEquity Global Health. The researchers expect to know if the vaccine is effective by the end of the year.

PHASE I / II

Maryland-based Novavax has developed a way to stick proteins onto microscopic particles. They've created vaccines for a number of different diseases using this platform; their flu vaccine finished Phase III trials in March. The company launched trials for a Covid-19 vaccine in May, and the Coalition for Epidemic Preparedness Innovations has invested $384 million in the vaccine. On July 6, Novavax announced a U.S. government award of $1.6 billion to support clinical trials and manufacturing. If the trials succeed, Novavax expects to deliver 100 million doses for use in the United States by the first quarter of 2021. Plants in Europe and Asia would be able to satisfy more of the world's demand.

RUSSIAN VACCINE

The superfast speed of development and approval has led to scepticism. Meanwhile, the Telegraph newspaper of London has reported that Britain was unlikely to use the Russian vaccine for its people.

The World Health Organisation has cautioned Russia against rushing through with its novel Coronavirus vaccine. Russia has announced plans to approve a vaccine candidate being developed by Moscow's Gamaleya Institute by the second week of this month. It has also said that the vaccine would be in market by next month, and mass vaccinations would begin by October.

The superfast speed of development and approval has led to scepticism.

"There are established practices and there are guidelines out… Any vaccine (or medicine) for this purpose should be, or course, going through all the various trials and tests before being licensed for roll-out," Christian Lindmeier, a spokesperson for WHO, was quoted by the AFP news agency.

"Sometimes individual researchers claim they have found something, which is, of course, as such, great news. But between finding or having a clue of maybe having a vaccine that works, and having gone through all the stages, is a big difference," the spokesperson said.

Russia's candidate vaccine was reported to have completed phase-I human trials in the second week of July. According to a news report in the Russia's TASS news agency at that time, the phase-II trials were started on July 13. It is not clear whether the phase-II trials have also declared to have been completed. Usually, each of these phases can take several months to be completed. But considering the prevailing emergency situation, vaccine trials are being fast-tracked across the world.

However, Russia has indicated that it planned to approve the vaccine without undertaking phase-III human trials, the final stage in which a candidate vaccine is tested for its effectiveness in real-life situations, outside laboratory conditions.

This rush to produce the vaccine is leading to a lot of discomfort. Over the weekend, while testifying before a panel of US lawmakers, Anthony Fauci, a top US public health expert and one of the most trusted voices on the Coronavirus epidemic, had expressed doubts over the vaccines being produced in China and Russia. A Chinese vaccine has already been approved for limited use, without going through phase-III trials. It is being administered only to army personnel right now.

"I do hope that the Chinese and the Russians are actually testing the vaccines before they are administering the vaccine to anyone," he had said.

Meanwhile, the Telegraph newspaper of London has reported that Britain was unlikely to use the Russian vaccine for its people.

The WHO spokesperson said the agency had not been informed by Russia about its plans to deploy the vaccine. "If there was anything official, then our colleagues in the European office would definitely look into this… In general terms, there are a set of guidances and regulations, rules, how to deal with safe development of a vaccine. These should be definitely followed in order to make sure that we know what the vaccine is working against, who it can help, and of course, also if it has any negative side effects," the spokesperson said.

Developers of other leading vaccine candidates have said they hope to be ready with the vaccine by early next year, if not by the end of this year itself.

COVID-19 DRUG AND TREATMENT

The Covid-19 pandemic is one of the greatest challenges modern medicine has ever faced. Doctors and scientists are scrambling to find treatments and drugs that can save the lives of infected people and perhaps even prevent infection.

Below is an updated list of 19 of the most-talked-about treatments for the coronavirus. While some are accumulating evidence that they're effective, most are still at early stages of research. We also included a warning about a few that are just bunk.

There is no cure yet for Covid-19. And even the most promising treatments to date only help certain groups of patients, and await validation from further trials. The F.D.A. has not fully licensed any treatment specifically for the coronavirus, but it has granted emergency use authorization to a few.

WHAT THE LABELS MEAN

WIDELY USED: These treatments have been used widely by doctors and nurses to treat patients hospitalized for diseases that affect the respiratory system, including Covid-19.

PROMISING EVIDENCE: Early evidence from studies on patients suggests effectiveness, but more research is needed. This category includes treatments

that have shown improvements in morbidity, mortality and recovery in at least one randomized controlled trial, in which some people get a treatment and others get a placebo.

TENTATIVE OR MIXED EVIDENCE: Some treatments show promising results in cells or animals, which need to be confirmed in people. Others have yielded encouraging results in retrospective studies in humans, which look at existing datasets rather than starting a new trial. Some treatments have produced different results in different experiments, raising the need for larger, more rigorously designed studies to clear up the confusion.

NOT PROMISING: Early evidence suggests that these treatments do not work.

PSEUDOSCIENCE OR FRAUD: These are not treatments that researchers have ever considered using for Covid-19. Experts have warned against trying them, because they do not help against the disease and can instead be dangerous. Some people have even been arrested for their false promises of a Covid-19 cure.

BLOCKING THE VIRUS

Antivirals can stop viruses such as H.I.V. and hepatitis C from hijacking our cells. Scientists are searching for antivirals that work against the new coronavirus.

PROMISING EVIDENCE EMERGENCY USE AUTHORIZATION

Remdesivir | Remdesivir, made by Gilead Sciences, was the first drug to get emergency authorization from the F.D.A. for use on Covid-19. It stops viruses from replicating by inserting itself into new viral genes. Remdesivir was originally tested as an antiviral against Ebola and Hepatitis C, only to deliver lackluster results. But preliminary data from trials that began this spring suggested the drug can reduce the recovery time of people hospitalized with Covid-19 from 15 to 11 days. (The study defined recovery as “either discharge from the hospital or hospitalization for infection-control purposes only.”) These early

results did not show any effect on mortality, though retrospective data released in July hints that the drug might reduce death rates among those who are very ill.

TENTATIVE OR MIXED EVIDENCE

Favipiravir | Originally designed to beat back influenza, favipiravir blocks a virus's ability to copy its genetic material. A small study in March indicated the drug might help purge the coronavirus from the airway, but results from larger, well-designed clinical trials are still pending.

EIDD-2801 | Another antiviral originally designed to fight the flu, EIDD-2801 has had promising results against the new coronavirus in studies in cells and on animals. It is still being tested in humans.

Recombinant ACE-2 | To enter cells, the coronavirus must first unlock them — a feat it accomplishes by latching onto a human protein called ACE-2. Scientists have created artificial ACE-2 proteins which might be able to act as decoys, luring the coronavirus away from vulnerable cells. Recombinant ACE-2 proteins have shown promising results in experiments on cells, but not yet in animals or people.

NOT PROMISING

Lopinavir and ritonavir | Twenty years ago, the F.D.A. approved this combination of drugs to treat H.I.V. Recently, researchers tried them out on the new coronavirus and found that they stopped the virus from replicating. But clinical trials in patients proved disappointing. In early July, the World Health Organization suspended trials on patients hospitalized for Covid-19. But they didn't rule out studies to see if the drugs could help patients not sick enough to be hospitalized, or to prevent people exposed to the new coronavirus from falling ill. The drug could also still have a role to play in certain combination treatments.

Hydroxychloroquine and chloroquine | German chemists synthesized chloroquine in the 1930s as a drug against malaria. A less toxic version, called hydroxychloroquine, was invented in 1946, and later was approved for other diseases such as lupus and rheumatoid arthritis. At the start of the Covid-19 pandemic, researchers discovered that both drugs could stop the coronavirus from replicating in cells. Since then, they've had a tumultuous ride. A few small studies on patients offered some hope that hydroxychloroquine could treat Covid-19. The World Health Organization launched a randomized clinical trial in March to see if it was indeed safe and effective for Covid-19, as did Novartis and a number of universities.

Meanwhile, President Trump repeatedly promoted hydroxychloroquine at press conferences, touting it as a "game changer," and even took it himself. The F.D.A. temporarily granted hydroxychloroquine emergency authorization for use in Covid-19 patients — which a whistleblower later claimed was the result of political pressure. In the wake of the drug's newfound publicity, demand spiked, resulting in shortages for people who rely on hydroxychloroquine as a treatment for other diseases.

But more detailed studies proved disappointing. A study on monkeys found that hydroxychloroquine didn't prevent the animals from getting infected and didn't clear the virus once they got sick. Randomized clinical trials found that hydroxychloroquine didn't help people with Covid-19 get better or prevent healthy people from contracting the coronavirus. Another randomized clinical trial found that giving hydroxychloroquine to people right after being diagnosed with Covid-19 didn't reduce the severity of their disease. (One large-scale study that concluded the drug was harmful as well was later retracted.) The World Health Organization, the National Institutes of Health and Novartis have since halted trials investigating hydroxychloroquine as a treatment for Covid-19, and the F.D.A. revoked its emergency approval. The F.D.A. now warns that the drug can cause a host of serious side effects to the heart and other organs when used to treat Covid-19.

In July, researchers at Henry Ford hospital in Detroit published a study finding that hydroxychloroquine reduced mortality in Covid-19 patients. President Trump praised the study on Twitter, but experts raised doubts about it because it was

not a randomized controlled trial. Still, the White House has initiated a push for the F.D.A. to reauthorize hydroxychloroquine as an emergency Covid-19 treatment.

Despite negative results, a number of hydroxychloroquine trials have continued. A recent analysis by STAT and Applied XL found more than 180 ongoing clinical trials testing hydroxychloroquine or chloroquine, for treating or preventing Covid-19. Although it's clear the drugs are no panacea, it's possible they could work in combination with other treatments, or when given in early stages of the disease.

MIMICKING THE IMMUNE SYSTEM

Most people who get Covid-19 successfully fight off the virus with a strong immune response. Drugs might help people who can't mount an adequate defense.

TENTATIVE OR MIXED EVIDENCE

Convalescent plasma | A century ago, doctors filtered plasma from the blood of recovered flu patients. So-called convalescent plasma, rich with antibodies, helped people sick with flu fight their illness. Now researchers are trying out this strategy on Covid-19. Early trials with convalescent plasma have yielded promising, if preliminary, results, and the F.D.A. has authorized its use on very sick patients infected by the coronavirus.

Monoclonal antibodies | Convalescent plasma contains a mix of different antibodies, some of which can attack the coronavirus, and some of which can't. Researchers have been sifting through the slurry for the most potent antibodies against Covid-19. Synthetic copies of these molecules, known as monoclonal antibodies, can be manufactured in bulk and then injected into patients. Safety trials for this treatment have only just begun, with several more on the way.

Interferons | Interferons are molecules our cells naturally produce in response to viruses, rousing the immune system to attack. Injecting synthetic

interferons is now a standard treatment for a number of immune disorders. Rebif, for example, is prescribed for multiple sclerosis. Early studies, including experiments in mice and cells, hint that injecting interferons may help against Covid-19. An open-label study in China suggested that the molecules could help prevent healthy people from getting infected. On July 20, the British pharmaceutical company Synairgen announced that an inhaled form of interferon called SNG001 lowered the risk of severe Covid-19 in infected patients in a small clinical trial. The full data have not yet been released to the public, or published in a scientific journal.

Putting Out Friendly Fire

The most severe symptoms of Covid-19 are the result of the immune system's overreaction to the virus. Scientists are testing drugs that can rein in its attack.

PROMISING EVIDENCE

Dexamethasone | This cheap and widely available steroid blunts many types of immune responses. Doctors have long used it to treat allergies, asthma and inflammation. In June, it became the first drug shown to reduce Covid-19 deaths. That study of more than 6,000 people, which in July was published in the New England Journal of Medicine, found that dexamethasone reduced deaths by one-third in patients on ventilators, and by one-fifth in patients on oxygen. It may be less likely to help — and may even harm — patients who are at an earlier stage of Covid-19 infections, however. In its Covid-19 treatment guidelines, the National Institutes of Health recommends only using dexamethasone in patients with COVID-19 who are on a ventilator or are receiving supplemental oxygen.

TENTATIVE OR MIXED EVIDENCE

Cytokine Inhibitors | The body produces signaling molecules called cytokines to fight off diseases. But manufactured in excess, cytokines can trigger the immune system to wildly overreact to infections, in a process sometimes called a cytokine storm. Researchers have created a number of drugs to halt

cytokine storms, and they have proven effective against arthritis and other inflammatory disorders. Some turn off the supply of molecules that launch the production of the cytokines themselves. Others block the receptors on immune cells to which cytokines would normally bind. A few block the cellular messages they send.

Against the coronavirus, several of these drugs, including tocilizumab, sarilumab and anakinra, have offered modest help in some trials, but faltered in others. The drug company Regeneron recently announced that a branded version of sarilumab, Kevzara, failed Phase 3 clinical trials.

TENTATIVE OR MIXED EVIDENCE EMERGENCY USE AUTHORIZATION

Cytosorb | Cytosorb is a cartridge that filters cytokines from the blood in an attempt to cool cytokine storms. The machine can purify a patient's entire blood supply about 70 times in a 24-hour period. It was granted emergency use authorization by the F.D.A. for Covid-19 based on a small study in March suggesting that it had helped dozens of severely ill Covid-19 patients in Europe and China. Further trials on patients with Covid-19 are now underway.

TENTATIVE OR MIXED EVIDENCE

Stem cells | Certain kinds of stem cells can secrete anti-inflammatory molecules. Over the years, researchers have tried to use them as a treatment for cytokine storms, and now dozens of clinical trials are under way to see if they can help patients with Covid-19. But these stem cell treatments haven't worked well in the past, and it's not clear yet if they'll work against the coronavirus.

Other Treatments

Doctors and nurses often administer other supportive treatments to help patients with Covid-19.

WIDELY USED

Prone positioning | The simple act of flipping Covid-19 patients onto their bellies opens up the lungs. The maneuver has become commonplace in hospitals around the world since the start of the pandemic. It might help some individuals avoid the need for ventilators entirely. The treatment's benefits continue to be tested in a range of clinical trials.

WIDELY USED EMERGENCY USE AUTHORIZATION

Ventilators and other respiratory support devices | Devices that help people breathe are an essential tool in the fight against deadly respiratory illnesses. Some patients do well if they get an extra supply of oxygen through the nose or via a mask connected to an oxygen machine. Patients in severe respiratory distress may need to have a ventilator breathe for them until their lungs heal. Doctors are divided about how long to treat patients with non-invasive oxygen before deciding whether or not they need a ventilator. Not all Covid-19 patients who go on ventilators survive, but the devices are thought to be lifesaving in many cases.

TENTATIVE OR MIXED EVIDENCE

Anticoagulants | The coronavirus can invade cells in the lining of blood vessels, leading to tiny clots that can cause strokes and other serious harm. Anticoagulants are commonly used for other conditions, such as heart disease, to slow the formation of clots, and doctors sometimes use them on patients with Covid-19 who have clots. Many clinical trials teasing out this relationship are now underway. Some of these trials are looking at whether giving anticoagulants before any sign of clotting is beneficial.

SOURCE AND REFERENCE

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