Epidemics of Infectious Diseases in Human History.  
Antiviral Drugs and Vaccines in the Development Stage to Protect 
Against Coronavirus SARS-CoV-2

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Abstract.

Infectious diseases have plagued humanity since the earliest days of civilizations. Civilizations and subsequent history have been altered profoundly by the outbreak of pathogenic infectious diseases that decimated societies and killed millions of people. The formation of agrarian communities facilitated and increased the spread of infectious diseases. Widespread trade created new opportunities for human and animal interactions that sped up such epidemics. Malaria, tuberculosis, leprosy, smallpox, influenza, smallpox, cholera, viruses and other infectious agents appeared during these early years. Urbanization, expansion of cities, globalization of trade and the explosion of mass international travelling increased contact with different populations of people, animals, and ecosystems. All these factors contributed to old and recent infectious disease pandemics. Vaccination is widely considered one of the greatest medical achievements of modern human civilization. Infectious diseases that were commonplace less than a generation ago are now increasingly rare because of vaccines and various antiviral drugs. The current outbreak of the pandemic of virus SARS-CoV-2 (2019-2020) caught developed and developing countries with widespread sickness and deaths. At the same time it initiated an urgent need by big pharmaceutical companies and research centers of medical institutions worldwide to search for new drugs and vaccines to combat the new virulent coronavirus. The virus has been proved to be very contagious and has already shown it has the potential to kill people like the elderly and people with underlying health conditions. This review covers all the recent developments all over the world for antiviral pharmaceutical agents and suitable vaccines. Also, the World Health Organization (WHO) announced in March 2020 a large global trial, called SOLIDARITY, to find out if can treat infections like COVID-19 coronavirus. It is an unprecedented effort—an all-out, coordinated push to collect robust scientific data rapidly during a pandemic. Also, the European community initiates the DISCOVERY project to include 3,200 European patients from Belgium, France, Germany Luxembourg, the Netherlands, Spain, Sweden, and the United Kingdom. In France, at least 800 hospitalized COVID-19 patients will be recruited.
Introduction: Infectious diseases and pandemics

Human history has been much affected by infectious diseases since the dawn of history and the formation of agrarian societies. In many ancient societies, people believed that spirits and gods inflicted disease and destruction upon those that deserved their wrath. This unscientific perception often led to disastrous responses. A typical example of epidemic was Justinian’s plague (A.D. 541-542, with ~25+ million deaths). The Byzantine historian Procopius of Caesarea traced the origins of the plague (the Yersinia pestis bacteria) to China and N.E. India, via land and sea trade routes to Egypt where it entered the Byzantine Empire through Mediterranean ports.

Epidemics of infectious diseases started the practice of quarantine in the 14th century, in an effort to protect coastal cities from plague epidemics. Venice port authorities required ships arriving in Venice from infected ports to sit at anchor for 40 days before landing (“quaranta giorni”).

Figure 1. There are lots of books on pandemics and history of infectious diseases and the effects on human civilization. The 2019-20 COVID-19 pandemic and the effects of spreading the infection worldwide will have dramatic changes on societal structure. The Wuhan coronavirus is no different from previous pandemics. History shows that humans and pathogens coexist in a unique ecological relationship spanning many centuries.
The cholera epidemic in London in the mid-19th century is another typical example of infectious disease spreading from infected drinking water. In 1854, Dr. John Snow came to the conclusion that cholera was spreading via tainted water and decided to display neighborhood mortality data directly on a map. This method revealed a cluster of cases around a specific pump from which people were drawing their water from.\textsuperscript{4,5}

Figure 2. The Broad Street cholera outbreak (or Golden Square outbreak, London) was a severe outbreak of cholera that occurred in 1854 near Broad Street (now Broadwick Street) in the Soho district of the City of Westminster, London and occurred during the 1846–1860 cholera pandemic happening worldwide.

Infectious diseases have plagued humanity since the earliest days of civilizations. Some historians believe that the history of mankind may be viewed and analyzed through the lens of occurrence of infectious disease and the changes in the political and societal structures. Infectious diseases have had a profound effect on migrating human populations and vice versa. World military conflicts and civil wars have been affected by infectious diseases from ancient times continuing to the present. Civilizations and subsequent history have been altered profoundly by infectious diseases. The plague of Athens changed the balance of power between Athens and Sparta, ending the golden age of Pericles and Athenian predominance in the ancient world. The formation of agrarian communities increased the spread of infectious diseases dramatically. Widespread trade created new opportunities for human and
animal interactions that sped up such epidemics. Malaria, tuberculosis, leprosy, influenza, smallpox, and others first appeared during these early years. Urbanization, expansion of cities, globalization of trade and the explosion of mass international travelling increased contact with different populations of people, animals, and ecosystems. So, all these factors made more likely pandemics to occur.\textsuperscript{5,6}

\textbf{Table 1.} Some of the major pandemics that have occurred on Earth

<table>
<thead>
<tr>
<th>Pandemic, name</th>
<th>Time period</th>
<th>Type of infectious agents</th>
<th>Death toll (estimated)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antonine Plague Roman empire, during the reign of Marcus Aurelius</td>
<td>AD 165-180</td>
<td>Believed to be smallpox or measles</td>
<td>5 million</td>
</tr>
<tr>
<td>Plague of Justinian</td>
<td>AD 541-542</td>
<td>Yersinia pestis bacteria / Rats, fleas</td>
<td>30-50 million</td>
</tr>
<tr>
<td>Black death</td>
<td>AD 1347-1351</td>
<td>Yersinia pestis bacteria / Rats, fleas</td>
<td>200 million</td>
</tr>
<tr>
<td>New World Smallpox outbreak</td>
<td>1520-onwards</td>
<td>Variola major virus</td>
<td>56 million</td>
</tr>
<tr>
<td>Great Plague of London lasting from 1665 to 1666, was the last major epidemic of the bubonic plague to occur in England</td>
<td>1665-1666</td>
<td>Yersinia pestis bacteria / Rats, fleas</td>
<td>100,000</td>
</tr>
<tr>
<td>Italian Plague</td>
<td>1629-1631</td>
<td>Yersinia pestis bacteria / Rats, fleas</td>
<td>1 million</td>
</tr>
<tr>
<td>Cholera pandemic the first Asiatic cholera pandemic or Asiatic cholera, began in the city of Calcutta and spread throughout Southeast Asia to the Middle East, eastern Africa and Mediterranean coast</td>
<td>1817-1923</td>
<td>V. cholerae bacteria</td>
<td>1 million +</td>
</tr>
<tr>
<td>Third Plague major bubonic plague pandemic began in Yunnan, China, in 1855 during the fifth year of the Xianfeng Emperor, Qing dynasty</td>
<td>1885</td>
<td>Yersinia pestis bacteria / Rats, fleas</td>
<td>12 million (China &amp; India)</td>
</tr>
<tr>
<td><strong>Yellow Fever</strong></td>
<td><strong>Late 1800s</strong></td>
<td>Virus / Mosquitoes</td>
<td>100,000-150,000 (U.S.)</td>
</tr>
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<tr>
<td>acute viral haemorrhagic disease transmitted by infected mosquitoes.</td>
<td></td>
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<tr>
<td><strong>Russian Flu</strong></td>
<td>1889-1890</td>
<td>Believed to be H2N2 virus (avian origin)</td>
<td>1 million</td>
</tr>
<tr>
<td>November 1889, influenza-like illness appeared in St. Petersburg, Russia, and spread to Europe</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Spanish Flu</strong></td>
<td>1918-1919</td>
<td>H1N1 virus/ Pigs</td>
<td>40-50 million</td>
</tr>
<tr>
<td>deadly influenza pandemic, it infected 500 million people—about 25% of the world's population.</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>Asian Flu</strong></td>
<td>1957-1958</td>
<td>H2N2 virus</td>
<td>1.1 million</td>
</tr>
<tr>
<td>spread worldwide during which influenza vaccine was developed, lasted until 1958</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>HIV/AIDS, HIV</strong></td>
<td>1981-present</td>
<td>Virus/Chimpanzees</td>
<td>25-35 million</td>
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<tr>
<td>the virus that causes AIDS (acquired immunodeficiency syndrome). 37.9 million people are living with HIV</td>
<td></td>
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<tr>
<td><strong>Swine Flu</strong></td>
<td>2009-2010</td>
<td>H1N1 virus/Pigs</td>
<td>200,000</td>
</tr>
<tr>
<td>The swine flu was initially seen in the US in April 2009.</td>
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<td></td>
<td></td>
</tr>
<tr>
<td><strong>SARS Severe acute respiratory syndrome (SARS)</strong></td>
<td>2002-2003</td>
<td>Coronavirus/Bats, Civets</td>
<td>770</td>
</tr>
<tr>
<td>viral respiratory disease of zoonotic origin caused by the SARS coronavirus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Ebola</strong></td>
<td>2014-2016</td>
<td>Ebolavirus/wild animals</td>
<td>11,000</td>
</tr>
<tr>
<td>Ebola Virus Disease (EVD), rare &amp; deadly disease. The viruses that cause EVD are located mainly in sub-Saharan Africa.</td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>MERS Middle East Respiratory Syndrome (MERS)</strong></td>
<td>2015-present</td>
<td>Coronavirus/Wild bats, camels</td>
<td>912</td>
</tr>
<tr>
<td>viral respiratory illness that is new to humans. It was first reported in Saudi Arabia in 2012 and has since spread</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Wuhan, China</td>
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</tbody>
</table>

** Plague **, infectious disease caused by Yersinia pestis. This bacterium is found in mammals (prairie dogs, rats, squirrels, rabbits, cats) and their fleas in many areas around the world. Occasionally this organism infects humans. Usually fleas from the infected rodents carry the disease to humans. The WHO World reports 1,000 to 3,000 cases of plague worldwide every year. About 14% of all cases of plague are fatal.
Scientists have all learned about the importance of infectious diseases throughout history. The 1918 influenza pandemic was a typical example of global nightmare emerging as an infectious disease event with millions of victims. The 1918 influenza killed more people than the First World War. It was one of the most severe pandemic in recent history, caused by an H1N1 virus. Scientists estimated that about 500 million people or 1/3 of the world's population became infected with this virus. The effect of influenza epidemic was so severe that the average life span in the US was depressed by 10 years. The mortality rate was at 2.5% compared to less than 0.1% of previous influenza virus. After many epidemiological and historical studies the “official” mortality estimates kept rising and the pandemic is thought to have accounted for about 30-50 million or more deaths.\(^7\)\(^8\)

**Figure 3.** The Spanish influenza started in the Northern Hemisphere in 1918. The virus spread rapidly and reached all parts of the world: (pandemic). Estimates of 50 million deaths were published by Johnson and Mueller, it implies that the Spanish flu killed 2.7% of the world population [Johnson N.P., Mueller J. Updating the accounts: global mortality of the 1918-1920 “Spanish” influenza pandemic. *Bulletin of the History of Medicine, 76*(1):105-115, 2002]. Other scientists estimated that the Spanish Influenza contributed to 17-20 million deaths, but many think that is an underestimation.
Existing antiviral drugs that could be repurposed against the virus SARS-CoV-2

The current outbreak of the pandemic of virus SARS-CoV-2 initiated an urgent need by big pharmaceutical companies and research centers of medical institutions worldwide to search for new drugs and vaccines to combat the new virulent coronavirus. The virus has been proved to be very contagious and has already shown it has the potential to kill people like the elderly and people with underlying health conditions. What are the most important: People aged 65 years and older who live in a nursing home, with chronic lung disease or moderate to severe asthma, who have serious heart conditions, who are immunocompromised including cancer treatment. People of any age with severe obesity (body mass index [BMI] >40) or certain underlying medical conditions, such as those with diabetes, renal failure, or liver disease might also be at risk. [CDC Centers of Disease Control and Prevention, 2020, https://www.cdc.gov/coronavirus/2019-ncov/specific-groups/people-at-higher-risk.html].

The World Health Organization (WHO) declared SARS-Covid-19 a global public health emergency (pandemic). Medical advances in the last decades, from other similar cases of infectious diseases, in the field of new pharmaceuticals means that anti-coronavirus drugs or a vaccine can be found very quickly in the near future. The world is in better shape to come up with a medical solution than it’s ever been. Within a couple of weeks of discovering the outbreak, Chinese scientists sequenced the virus’s genome and shared it with the world. Pharmaceutical companies and research centers then began mobilizing and developing new ways to prevent and treat SARS-Covid-19. (SARS = Severe Acute Respiratory Syndrome).⁹

Statistical evidence (Johns Hopkins University Coronavirus Resource Center). Total confirmed cases 452,157 (China 81,496, Italy 74,383, USA 60,653, Spain 47,610), Deaths 15,375 (Italy 7,503, Spain 3,637, China 3,281), Total recovered 113,494 (25/3/2020). [https://coronavirus.jhu.edu/map.html].

The more immediate approach to an outbreak is to search for old drugs that exist in the medicine cabinet that could be repurposed against the new coronavirus and for which toxicological studies and clinical results are known.
The most advanced potential treatment is Gilead Sciences’ **Remdesivir**, an antiviral discovered during the 2014 Ebola epidemic. The compound is already being tested in four, Phase III trials—two in China and two in the US—against the respiratory disease COVID-19. Gilead expects the first dataset from those studies to come out in April.⁹

The drug, **Remdesivir**, is being studied in several large-scale clinical trials around the world, including a huge trial announced last week by the World Health Organization. But the results have not been reported yet, and it is still unclear whether the drug works against the coronavirus. It was studied to treat Ebola, but did not work well enough against that virus. [The New York Times, 23.3.2020, https://www.nytimes.com/2020/03/23/health/coronavirus-drugs-remdesivir.html].

Also, a Phase I study of an mRNA-based vaccine developed by Moderna has begun, and major pharmaceutical companies and small biotechnological laboratories are working on other types of vaccines. But even if they work, the most optimistic timelines put a vaccine a year to 18 months away.⁹

In China, 1,000 scientists are at work on a vaccine, and the issue has already been militarized: Researchers affiliated with the Academy of Military Medical Sciences have developed what is considered the nation’s front-runner candidate for success and is recruiting volunteers for clinical trials.¹⁰

**Antiviral Drugs that have been identified and tested until now by pharmaceutical companies**

Various old antiviral medications have been developed over the years.

**Baloxavir marboxil**

Baloxavir marboxil, sold under the brand name **Xofluza**, is an antiviral medication for treatment of influenza A and influenza B flu. It was approved for medical use in Japan and in the United States in 2018, and is taken as a single dose by mouth. Baloxavir marboxil was developed for the market by Shionogi Co., a Japanese pharmaceutical company, and Switzerland-based Roche AG.
Baricitinib

Baricitinib, sold under the brand name Olumiant among others, is a drug for the treatment of rheumatoid arthritis (RA) in adults whose disease was not well controlled using RA medications called Tumor Necrosis Factor (TNF) antagonists. It acts as an inhibitor of janus kinase (JAK), blocking the subtypes JAK1 and JAK2.

Chloroquine and hydroxychloroquine

Chloroquine is a drug used to prevent and to treat malaria. Certain types of malaria, resistant strains, and complicated cases typically require different or additional medication. Occasionally it is used for amebiasis that is occurring outside the intestines, rheumatoid arthritis, and lupus erythematosus. It is taken by mouth and is also being used experimentally in COVID-19 as of 2020. Common side effects include muscle problems, loss of appetite, diarrhea, and skin rash. It appears to be safe for use during pregnancy. Chloroquine was discovered in 1934 by Hans Andersag. It is on the World Health Organization's List of Essential Medicines, the safest and most effective medicines needed in a health system and available as a generic medication. It is a very cheap to develop drug and its price is very
low. Chloroquine can be prescribed to adults and children of all ages. It can also be safely taken by pregnant women and nursing mothers.\textsuperscript{11,12,13}

Also, the drug chloroquine has been investigated with nanoparticles (nanoparticle uptake in cells) for its efficacy recently for the fight against coronavirus COVID-19.\textsuperscript{14}

**Hydroxychloroquine**

Hydroxychloroquine is sold under the brand name Plaquenil among others, is a medication used for the prevention and treatment of certain types of malaria. It is used for chloroquine-sensitive malaria. Other uses include treatment of rheumatoid arthritis, lupus, and porphyria cutanea tarda.

The hydroxychloroquine shows antiviral activity in vitro against coronaviruses, and specifically, SARS-CoV-2. Pharmacological modelling based on observed drug concentrations and in vitro drug testing suggest that prophylaxis with hydroxychloroquine at approved doses could prevent SARS-CoV-2 infection and ameliorate viral shedding. Clinical trials of hydroxychloroquine treatment for COVID-19 pneumonia are underway in China (NCT04261517 and NCT04307693). The first study (NCT04261517)
Recent developments for hydroxychloroquine (19/3/2020)

Recently hydroxychloroquine was in the news. In March 2020 U.S. President Donald Trump announced that the Food and Drug Administration (FDA) has approved the common malarial drug hydroxychloroquine for the treatment of COVID-19. However, he was quickly contradicted by FDA officials who clarified that more research needs to be conducted before the drug is made available to patients. Hydroxychloroquine and chloroquine are among those touted by some experts as being the most promising. Trump told reporters at a press conference "....The nice part is, it's been around for a long time, so we know that if things don't go as planned it's not going to kill anybody. When you go with a brand new drug, you don't know that that's going to happen. It's shown very encouraging early results."

A highly referenced study, conducted in France, a small number of patients with COVID-19 received either hydroxychloroquine alone or hydroxychloroquine in combination with an antibiotic called azithromycin. The authors reported that detectable concentrations of SARS-CoV-2 fell significantly faster in the study participants than coronavirus patients at other French hospitals who did not receive either drug. In six patients also given azithromycin, this promising effect appeared to be amplified.

However, the CDC noted that the small, non-randomized study "did not assess clinical benefit[s]" associated with the treatment; in other words, the study did not probe whether the treated patients were more likely to recover and survive their illness. Additionally, the agency advised that doctors should be cautious when giving either drug to patients with chronic disease, such as kidney failure, and especially those "who are receiving medications that might interact to cause arrhythmias."  

Authorities in New York took the decision to begin trials, procuring 70,000 doses of hydroxychloroquine and 750,000 doses of chloroquine, Gov. Andrew Cuomo said. In addition, Bayer, the drug maker, has donated 3 million doses of Resochin, its brand name for chloroquine, to the federal government. Perhaps demonstrating why health officials are urging caution -- saying chloroquine requires further clinical study and might not be the panacea. [CNN, 23.3.2020, https://edition.cnn.com/2020/03/23/health/chloroquine-hydroxycholoroquine-drugs-explained/index.html].

Darunavir

Darunavir, sold under the brand name Prezista among others, is an antiretroviral medication used to treat and prevent HIV/AIDS. It is generally recommended for use with other antiretrovirals. It is often used with low doses of ritonavir or cobicistat to increase darunavir levels. Darunavir was approved for medical use in the US in 2006. It is on the WHO List of Essential Medicines, the safest and most effective medicines needed in a health system. The wholesale cost in the developing world is about US$66 per month. In the United States it costs more than $200 per month. Also, the combination darunavir/cobicistat is available as a single pill. Janssen R&D (Ireland) announced that the European Commission (EC) has approved a new PREZISTA® (darunavir) 800mg tablet allowing people living with HIV to take one darunavir tablet once a day. Darunavir is indicated in combination with other antiretrovirals for the treatment of human immunodeficiency virus (HIV-1) infection. Johnson & Johnson, which develops medical devices, pharmaceutical and consumer packaged goods, said in a statement on Monday 16 March 2020 that it had no evidence its HIV drug, Prezista, had any effect on patients suffering from the disease caused by coronavirus.
Favipiravir

Favipiravir, also known as T-705, Avigan, or favilavir is an antiviral drug being developed by Toyama Chemical (Fuji Film group) of Japan with activity against many RNA viruses. In experiments conducted in animals Favipiravir has shown activity against influenza viruses, West Nile virus, yellow fever virus, foot-and-mouth disease virus as well as other flaviviruses, arenaviruses, bunyaviruses and alphaviruses. Favipiravir has showed limited efficacy against Zika virus in animal studies, but was less effective than other antivirals. In February 2020, Favipiravir was being studied in China for experimental treatment of the emergent COVID-19 (novel coronavirus) disease. On March 17, Chinese officials suggested the drug had been effective in treating COVID in Wuhan and Shenzhen.

A team of researchers in China publicized potentially more promising results, stating that a trial of a generic version of Fujifilm Toyama Chemical’s influenza drug Avigan (favipiravir) was able to help patients recover more quickly than those who received placebo. News media reported that in a press conference, China National Center for Biotechnology Development Director Zhang Xinmin said treatment with Avigan resulted in patients recovering from fever in an average of 2.5 days and from cough in 4.6 days, compared with 4.2 and about six days for those in the control group.
Meanwhile, 8.2% of patients receiving the drug required breathing assistance, compared with 17.1% of those in the control. The results came from a trial of 200 patients in the Chinese cities of Wuhan, where the virus first emerged in December 2019, and Shenzhen.


**Lopinavir and Ritonavir**

**Lopinavir** is an antiretroviral of the protease inhibitor class. It is used against HIV infections as a fixed-dose combination with another protease inhibitor, ritonavir (lopinavir/ritonavir). It was patented in 1995 and approved for medical use in 2000.

**Ritonavir**, sold under the trade name **Norvir**, is an antiretroviral medication used along with other medications to treat HIV/AIDS. This combination treatment is known as highly active antiretroviral therapy

Treatment with **lopinavir–ritonavir** did not add value beyond standard care in severely ill patients hospitalized with novel coronavirus disease (COVID-19). Findings from the open-label, randomized trial appear in the *New England Journal of Medicine*. Roughly 200 adults in China hospitalized with COVID-19 and oxygen saturation of 94% or lower were assigned to lopinavir–ritonavir twice daily for 14 days plus standard care, or standard care alone. The primary outcome — time to clinical improvement — did not differ between the
groups (median, 16 days). Mortality at 28 days was numerically lower with lopinavir–ritonavir, but the between-groups difference did not reach statistical significance (19% with lopinavir–ritonavir, 25% with standard care alone).¹⁹

The antiviral drug kaletra, a combination of lopinavir and ritonavir, generated early excitement for antiviral treatment, but could not detect a benefit when patients took the drug. A total of 199 people with low oxygen levels were randomized to either receive kaletra or a placebo. While fewer people taking kaletra died, the difference was not statistically significant, meaning it could have been due to random chance. And both groups had similar levels of virus in their blood over time. However, other studies are still ongoing, and there's still a possibility this combination could show some benefit. As with other antivirals, this drug would likely work better if given earlier in the disease course. [LIVE SCIENCE, 23.3.2020, https://www.livescience.com/coronavirus-covid-19-treatments.html]

Remdesivir

Remdesivir is a novel antiviral drug in the class of nucleotide analogs. It was developed by Gilead Sciences and as a treatment for Ebola virus disease and Marburg virus infections, though it has subsequently also been found to show antiviral activity against other single stranded RNA viruses such as respiratory syncytial virus, Junin virus, Lassa fever virus, Nipah virus, Hendra virus, and the coronaviruses (including MERS and SARS viruses). It is being studied for SARS-CoV-2 and Nipah and Hendra virus infections. Based on success against other coronavirus infections, Gilead provided Remdesivir to physicians who treated an American patient in Snohomish County, Washington in 2020, infected with SARS-CoV-2 and is providing the compound to China to conduct a pair of trials in infected individuals with and without severe symptoms. Laboratory tests suggest
Remdesivir is effective against a wide range of viruses, including SARS-CoV and MERS-CoV. The medication was pushed to treat the West African Ebola virus epidemic of 2013–2016.


To qualify for an orphan designation, drug companies must show that their product will treat a population of fewer than 200,000 patients or that it would be unprofitable. With more than 52,000 confirmed U.S. cases of COVID-19 reported as of 22.3.2020 the illness is under the technical threshold for a rare disease. But cases are rising quickly and it seems inevitable that they will surpass 200,000. The FDA decision would provide lucrative incentives to the drug’s maker, Gilead Sciences, and could keep lower-priced generic versions of the medicine off the market for several years if Remdesivir is approved for use, public health advocates say. Remdesivir is an intravenous, antiviral medicine that is being studied in clinical trials around the world as a possible treatment for COVID-19. Clinical trials for Remdesivir as a COVID-19 treatment got started in China in early February 2020. Tests of the drug are now enrolling patients elsewhere, including the United States. Experts in the USA warn that the designation, reserved for treating “rare diseases,” could block supplies of the antiviral medication from generic drug manufacturers and provide a lucrative windfall for Gilead Sciences, which
maintains close ties with President Donald Trump’s task force for controlling the coronavirus crisis. Gilead Sciences’ Remdesivir was developed with at least $79 million in U.S. government funding. The origins of the drug came after the 2014 Ebola outbreak in western Africa, which spurred research into potential antiviral medications to control future potential pandemics. Early promising results from the U.S. Army Medical Research Institute of Infectious Disease revealed that Rhesus monkeys infected with Ebola survived after undergoing an antiviral treatment using GS-5734, the compound now known as Remdesivir.


“...There are no US Food and Drug Administration (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. 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. The purpose of this document is to provide information on two of the approved drugs (chloroquine and hydroxychloroquine), lopinavir-ritonavir and one of the investigational agents (Remdesivir) currently in use in the United States....’

References
Ribavirin

Ribavirin, also known as tribavirin, is an antiviral medication used to treat RSV infection, hepatitis C and some viral hemorrhagic fevers. For hepatitis C, it is used in combination with other medications such as simeprevir, sofosbuvir, peginterferon alfa-2b or peginterferon alfa-2a.

Umifenovir

Umifenovir is an antiviral treatment for influenza infection used in Russia and China. The drug is manufactured by Pharmstandard. Although some Russian studies have shown it to be effective, it is not approved for use in other countries. It is not approved by the US FDA for the treatment or prevention of influenza.

Nitazoxanide

Originally developed and commercialized as an antiprotozoal agent, Nitazoxanide was later identified as a first-in-class broad-spectrum antiviral drug and has been repurposed for the treatment of influenza. A Phase 2b/3 clinical trial recently published in The Lancet Infectious Diseases found that oral administration of nitazoxanide 600mg twice daily for five days reduced the duration of clinical symptoms and reduced viral shedding compared to placebo in persons with laboratory-confirmed influenza. The same study also suggested a potential benefit for subjects with influenza-like illness who did not have influenza or other documented respiratory viral infection.


Pimodicir

Pimodivir (VX-787, JNJ-63623872) is an antiviral drug which was developed as a treatment for influenza. It acts as an inhibitor of influenza virus polymerase basic protein 2, and has shown promising results in Phase II clinical trials.¹


Galidesivir

Galidesivir is an antiviral drug, an adenosine analog (a type of nucleoside analog). It is developed by BioCryst Pharmaceuticals with funding from NIAID, originally intended as a treatment for hepatitis C, but subsequently developed as a potential treatment for deadly filovirus infections such as Ebola virus disease and Marburg virus disease.

References


Science News. SOLIDARITY : WHO launches global megatrial of the four most promising coronavirus treatments.


The World Health Organization (WHO) announced in March 2020 a large global trial, called SOLIDARITY, to find out if any can treat infections with the new COVID-19 coronavirus for the dangerous respiratory disease. It’s an unprecedented effort—an all-out, coordinated push to collect robust scientific data rapidly during a pandemic. The study, which could include many thousands of patients in dozens of countries, has been designed to be as simple as possible so that even hospitals overwhelmed by an onslaught of COVID-19 patients can participate. The study of WHO is looking at unapproved drugs that have performed well in animal studies with the other
two deadly coronaviruses, which cause severe acute respiratory syndrome (SARS, 2002-2003) and Middle East respiratory syndrome (MERS, 2012).

Scientists have suggested dozens of existing compounds for testing but WHO is focusing on what it says are the four most promising therapies: an experimental antiviral compound called Remdesivir; the malaria medications Chloroquine and Hydroxychloroquine; a combination of two HIV drugs, Lopinavir and Ritonavir; and that same combination plus interferon-beta, an immune system messenger that can help cripple viruses. Some data on their use in COVID-19 patients has already emerged—the HIV combo failed in a small study in China—but WHO believes a large trial with a greater variety of patients is warranted. Enrolling subjects in SOLIDARITY will be easy. When a person with a confirmed case of COVID-19 is deemed eligible, the physician can enter the patient’s data into a WHO website, including any underlying condition that could change the course of the disease, such as diabetes or HIV infection. The participant signs an informed consent form that is scanned and sent to WHO electronically.

Remdesivir. The new coronavirus is giving this compound a second chance to shine. Originally developed by Gilead to combat Ebola and related viruses, remdesivir shuts down viral replication by inhibiting a key viral enzyme, the RNA-dependent RNA polymerase. Researchers tested remdesivir last year during the Ebola outbreak in the Democratic Republic of the Congo, along with three other treatments. It did not show any effect. (Two others did.) But the enzyme it targets is similar in other viruses, and in 2017 researchers at the University of North Carolina in Chapel Hill showed in test tube and animal studies that the drug can inhibit the coronaviruses that cause SARS and MERS.

Chloroquine and Hydroxychloroquine. The WHO scientific panel designing SOLIDARITY had originally decided to leave the duo out of the trial but had a change of heart at a meeting in Geneva on 13 March 2020, because the drugs significant attention” in many countries, according to the report of a WHO working group that looked into the drugs’ potential. The widespread interested prompted “the need to examine emerging evidence to inform a decision on its potential role.” The available data are thin. The drugs work by decreasing the acidity in endosomes, compartments inside cells that they use
to ingest outside material and that some viruses can coopt to enter a cell. But the main entryway for SARS-Cov-2 is a different one, using its so-called spike protein to attach to a receptor on the surface of human cells. Studies in cell culture have suggested chloroquines have some activity against SARS-CoV-2, but the doses needed are usually high—and could cause serious toxicities. Encouraging cell study results with chloroquines against two other viral diseases, dengue and chikungunya, didn’t pan out in people in randomized clinical trials.

**Hydroxychloroquine.** The drug has a variety of side effects and can in rare cases harm the heart. Since people with heart conditions are at higher risk of severe COVID-19, that is a concern, says David Smith, an infectious disease physician at the University of California, San Diego. “This is a warning signal, but we still need to do the trial,” he says. What's more, a rush to use the drug for COVID-19 might make it harder for the people who need it to treat their rheumatoid arthritis or malaria.

**Ritonavir/lopinavir.** This combination drug, sold under the brand name Kaletra, was approved in the US in 2000 to treat HIV infections. Abbott Laboratories developed lopinavir specifically to inhibit the protease of HIV, an important enzyme that cleaves a long protein chain into peptides during the assembly of new viruses. Because lopinavir is quickly broken down in the human body by our own proteases, it is given with low levels of ritonavir, another protease inhibitor, that lets lopinavir persist longer. The combination can inhibit the protease of other viruses as well, specifically coronaviruses. It has shown efficacy in marmosets infected with the MERS virus, and has also been tested in SARS and MERS patients, though results from those trials are ambiguous. The first trial with COVID-19 was not encouraging, however. Doctors in Wuhan, China, gave 199 patients two pills of lopinavir/ritonavir twice a day plus standard care, or standard care alone. But the authors caution that patients were very ill—more than a fifth of them died—and so the treatment may have been given too late to help.

**Ritonavir/lopinavir + interferon beta.** The SOLIDARITY study will also have an arm that combines the two antivirals with interferon-beta, a molecule involved in regulating inflammation in the body that also has shown an effect in marmosets infected with MERS. A combination of the three drugs is now
being tested in MERS patients in Saudi-Arabia in the first randomized controlled trial for that disease.

**DISCOVERY: European clinical trial to evaluate 4 experimental treatments for COVID-19 starts ar 22.3.2020 coordinated by INSERM.**


INSERM (Institut National de la Santé et de la Recherche Médicale) is the French National Institute of Health and Medical Research) will coordinate this trial and will include at least 800 French patients with severe forms of COVID-19. This is a European project, the French part of which is financed by the Ministries of Higher Education, Research and Innovation (MESRI) and Health and Solidarity (MSS). The European part is supported at least by COMBACTE, PREPARE and RECOVER. It is led by Florence Ader, infectiologist in the Infectious and Tropical Diseases Department of the Croix-Rousse Hospital of Lyon University Hospital and researcher at the CIRI International Research Centre in Infectiology (Inserm/CNRS / Claude Bernard University Lyon 1).

The objective is to evaluate the efficacy and safety of four experimental therapeutic strategies which, in light of latest scientific information, might be effective against COVID-19. DISCOVERY is planned to include 3,200 European patients from Belgium, France, Germany Luxembourg, the Netherlands, Spain, Sweden, and the United Kingdom. In France, at least 800 hospitalized COVID-19 patients will be recruited in conventional medicine departments or in intensive care. The DISCOVERY trial includes five treatment modalities: a. standard of care, b. standard of care plus remdesivir, c. standard of care plus lopinavir and ritonavir, d. standard of care plus lopinavir, ritonavir and interferon beta, e. standard of care plus hydroxychloroquine.
What is a virus and why is so infectious?

The origins of viruses in the evolutionary history of life are unclear. Viruses have their own, ancient evolutionary history, dating to the very origin of cellular life on Earth billion years ago. For example, some viral-repair enzymes—which excise and resynthesize damaged DNA, mend oxygen radical damage, and so on—are unique to certain viruses and have existed almost unchanged probably for billions of years.

Figure 4. Coronavirus virion structure shown with structural proteins. N: Nucleocapsid protein; S: Spike protein, M: Membrane protein, HE: Hemagglutinin-Esterase and E: Envelope protein.

There are various theories for the origins of viruses in the evolutionary history of life on Earth. Some scientists proposed that they have evolved from plasmids—pieces of DNA that can move between cells—while others may have evolved from bacteria. The evolutionary process on Earth took billion of years and viruses are thought to be an important means of horizontal gene transfer, which increases genetic diversity in a way analogous to sexual reproduction. Viruses are considered by some to be a life form, because they carry genetic material (DNA or RNA), reproduce, and evolve through natural selection, although they lack key characteristics (such as cell structure) that are generally considered necessary to count as life. Because they possess some but not all such qualities, viruses have been described as "organisms at the edge of life", and as replicators.
Viruses was seen in the beginning as poisons, then as life-forms, then biological chemicals, viruses today are thought of as being in a gray area between living and nonliving: they cannot replicate on their own but can do so in truly living cells and can also affect the behavior of their hosts profound.

In 1935 Prof. Wendell M. Stanley and colleagues (Rockefeller University in New York City) crystallized a virus—tobacco mosaic virus—for the first time. Microscopic pictures showed the virus consisted of a package of complex biochemicals (DNA, proteins). But viruses lacked essential systems necessary for live metabolic biochemical functions, like biological life. Stanley shared the 1946 Nobel Prize in Chemistry for this work. Further research established that a virus consists of nucleic acids (DNA or RNA) enclosed in a protein coat that may also shelter viral proteins involved in infection, but is not an organism. Viral infections start when virus enters a cell (called a host after infection), through mouth, lungs, nose and eyes. Upon entering the virus it sheds its coat, bares its genes and induces the cell’s own replication machinery. Viruses invade living organisms and attack their normal cells which are used to get new biological material (DNA, RNA, proteins) helping to multiply and produce other viruses like themselves. This can kill, damage, rise temperature, or change the cells and make animals or humans sick. Different viruses attack certain cells in the human body such as liver, respiratory system, or blood. When people get infected by a virus they do not get sick immediately, their immune system may be able to fight it off. For most viral infections, treatments can only help with symptoms while you wait for your immune system to fight off the virus. Antibiotics do not work for viral infections. There are antiviral medicines to treat some viral infections. Only Vaccines can help prevent humans from getting many viral diseases.
What is a vaccine and how is stimulating the immune system

A vaccine is a type of treatment aimed at stimulating the body's immune system to fight against infectious pathogens, like bacteria and viruses. The WHO claims that vaccines are "one of the most effective ways to prevent infectious diseases." The human body is particularly resilient to infectious disease, having evolved a natural defense system against infectious disease-causing microorganisms like bacteria and viruses. The human immune system is a very important defense system, composed of different types of white blood cells that can detect and destroy foreign invaders (bacteria, viruses, even cancer cells). Some of the immune system cells destroy bacteria, some others produce antibodies which can tell the body what to destroy and take out the germs, and other cells memorize what the invaders look like, so the body can respond quickly if they invade again (immunity). Immunity is the balanced state of multicellular organisms having adequate biological defenses to fight infections and diseases.

Figure 5. Vaccines are very safe and very effective. Vaccines routinely recommended worldwide today provide high levels of protection against targeted diseases. The benefits of vaccines greatly outweigh their risks. The safest decision for parents is to vaccinate their children according to the recommended schedule.

What vaccines contain?

Vaccines contain a handful of different ingredients depending on their type and how they aim to generate an immune response. However, there's some commonality between them all. The most important ingredient is the antigen. This is the part of the vaccine the body can recognize as foreign. Depending on the type of vaccine, an antigen could be molecules from viruses like a strand of DNA or a protein. It could instead be weakened
versions of live viruses. For instance, the measles vaccine contains a weakened version of the measles virus. When a patient receives the measles vaccine, their immune system recognizes a protein present on the measles virus and learns to fight it off. A second important ingredient is the adjuvant. An adjuvant works to amplify the immune response to an antigen. Whether a vaccine contains an adjuvant depends on the type of vaccine it is.

**Initiation of vaccine tests and antiviral drugs worldwide for the coronavirus COVID-19 by pharmaceutical companies**

MARKET WATCH, 6/3/2020. [https://www.marketwatch.com/story/these-nine-companies-are-working-on-coronavirus-treatments-or-vaccines-heres-where-things-stand-2020-03-06](https://www.marketwatch.com/story/these-nine-companies-are-working-on-coronavirus-treatments-or-vaccines-heres-where-things-stand-2020-03-06)

Lee J. Pharma companies are working on coronavirus treatments or vaccines — here’s where things stand. Published: March 24, 2020

In the U.S., many of the companies that are initiating development of vaccines have received funding from two organizations: the Biomedical Advanced Research and Development Authority (BARDA), which is a division of the Department of Health and Human Services, and the National Institute of Allergy and Infectious Diseases (NIAID), a division of the National Institutes of Health. Some companies have also received funding from Coalition for Epidemic Preparedness Innovations (CEPI), a global organization based in Oslo. Other companies are funding trials by themselves or through partnerships with other life sciences companies.

1. **BioNTech SE and Pfizer Inc.**

On March 17, 2020, Pfizer announced that it would help develop and distribute BioNTech SE’s COVID-19 vaccine candidate, though the deal excludes China. BioNTech plans to put the vaccine candidate into clinical trials in late April, in Germany and the U.S. It is testing the vaccine in collaboration with Shanghai Fosun Pharmaceutical Group Co. Ltd. in China. Pfizer and BioNTech for several years have said they would partner to develop mRNA-based influenza vaccines.
2. **Gilead Sciences Inc. Name:** Remdesivir  
**Background:** Gilead is a longtime drugmaker. The company has experience developing and marketing HIV drugs, including Truvada for pre-exposure prophylaxis (PrEP), its preventive HIV medicine. Along with U.S. trials, Gilead is conducting a randomized, controlled clinical trial in Wuhan, testing remdesivir as a treatment for mild to moderate forms of pneumonia in people with the virus. The trial was given the go-ahead by China’s Food and Drug Administration in February 2020.  
**Clinical trials:**  
1. On Feb. 21, the National Institute of Allergy and Infectious Diseases started enrolling patients in a randomized, double-blind, placebo-controlled Phase 2 trial evaluating 394 hospitalized patients with COVID-19 at up to 50 sites worldwide, including at three sites in Singapore and South Korea. However, the majority of the study locations are in the U.S. The trial is expected to conclude April 1, 2023. Sites include the National Institutes of Health in Bethesda, Md., (not recruiting), the University of Nebraska Medical Center in Omaha (recruiting), the University of Texas Medical Branch in Galveston (not recruiting), and Providence Sacred Heart Medical Center in Spokane (recruiting).  
2. On March 3, Gilead said a randomized, open-label Phase 3 trial will evaluate remdesivir in 600 patients with moderate COVID-19. The trial start enrolling patients in March, with results to come in May. The clinical trial listing states the study is taking place in Hong Kong, Singapore, South Korea and the U.S.  
3. On March 3, Gilead said a randomized, open-label Phase 3 trial will evaluate remdesivir in 400 patients with severe COVID-19. The trial start enrolling patients in March, with results in May. The clinical trial listing states the study is taking place in Hong Kong, Singapore, South Korea and the U.S.

3. **GlaxoSmithKline**, **Type:** Pandemic adjuvant platform for vaccines  
**Name:** AS03 Adjuvant System  
**Background:** GSK is another leading vaccine maker, having brought to market vaccines for human papillomavirus (HPV) and the seasonal flu, among others. On Feb. 3, it said the CEPI-funded University of Queensland will have access to the British drugmaker’s vaccine adjuvant platform technology, which is believed to both strengthen the response of a vaccine and limit the amount of vaccine needed per dose. On Feb. 24, GSK said that Clover Biopharmaceuticals Inc., a Chinese biotechnology company, is also using its adjuvant technology in combination with its vaccine candidate, COVID-19 S-Trimer, in preclinical studies. Dr. Thomas Breuer, chief medical officer for GSK Vaccines, is leading work on vaccines and the adjuvant platform.

4. **Heat Biologics Inc. Type:** Vaccine, **Stage:** Preclinical  
**Background:** Heat Biologics has previously announced that it is developing a vaccine for the novel coronavirus with the University of Miami Miller School of Medicine. It disclosed March 17 in a financial filing that its COVID-19 vaccine candidate had been added to the World Health Organization’s “draft landscape” of 41 candidate vaccines. The company also recently joined the Alliance for Biosecurity, which may help it “secure government funding to
support its rapid development, production, and distribution” of its COVID-19 vaccine, according to Maxim Group analysts.

5. **Inovio Pharmaceuticals Inc.**  
   **Type:** DNA-based vaccine  
   **Stage:** Preclinical  
   **Name:** INO-4800  
   **Timeline:** Inovio develops immunotherapies and vaccines but hasn’t yet had a product approved for treatment. For INO-4800, preclinical testing was performed between Jan. 23 and Feb. 29. The company plans to begin clinical trials in the U.S. with 30 participants in April. It also plans to launch human trials in China and South Korea that same month, and says that it has a total of 3,000 doses prepared for the trials in the three countries. Inovio said it expects to have the first results from the trial in the fall and to have 1 million doses of the vaccine ready for additional clinical trials or emergency use by the end of the year. Inovio on March 12 announced a $5 million grant from the Bill & Melinda Gates Foundation to test a delivery device for its vaccine candidate. RBC analyst Gregory Renza recently downgraded the stock to sector perform from outperform on valuation grounds and said he believed in the technology.

6. **Johnson & Johnson**,  
   **Type:** Vaccine  
   **Background:** On Feb. 11, J&J said it is working with BARDA to test its vaccine candidate, with both organizations providing funding for research and development and the public-health organization funding the Phase 1 trials. Similar to GSK, J&J’s AdVac and PER. C6 technologies are used to improve the development process for a vaccine and were also used to develop J&J’s experimental Ebola vaccine. “We are also in discussions with other partners, that if we have a vaccine candidate with potential, we aim to make it accessible to China and other parts of the world,” On March 13, J&J said it started preclinical testing on multiple candidates in collaboration with Beth Israel Deaconess Medical Center in Boston, and it aims to have a vaccine candidate by the end of the month. J&J also said in February that it partnered with BARDA on a project that aims to screen existing antiviral medications, including experimental or approved therapies, that may be effective against COVID-19.  
   **Timeline:** The company aims to start a Phase 1 clinical trial by the end of 2020, “compared to the typical five to seven years it takes for this milestone in vaccine development,” Dr. Paul Stoffels, J&J’s chief scientific officer and leader of J&J’s global COVID-19 response, said March 2.

7. **Moderna Inc.**,  
   **Type:** RNA-based vaccine,  
   **Stage:** Phase 1  
   **Name:** mRNA-1273  
   **Background:** Moderna received funding from CEPI in January to develop an mRNA vaccine against COVID-19. On Feb. 24, it said it had shipped the first batch of mRNA-1273 to the NIAID for a Phase 1 clinical trial in the U.S.  
   **Clinical trials:** The first patient in the Phase 1 trial received a dose of the vaccine candidate on March 16. The study is expected to enroll 45 healthy adult patients, between the ages of 18 and 55 years old, in an open-label Phase I clinical trial to test mRNA-1273 as a vaccine for COVID-19. It’s expected to conclude June 1, 2021. Participants will be followed for one year. The trial will be conducted at Kaiser Permanente Washington Health Research Institute in Seattle. CEPI funded the manufacturing of the
investigational vaccine for the first phase of the trial, which is evaluating different doses for safety and immune response.

8. **Novavax Inc.**  
**Type:** vaccines, **Phase:** preclinical  
**Background:** Novavax, a preclinical biotechnology company, announced Feb. 26 it had several vaccine candidates in preclinical animal studies, and that it plans to initiate a Phase I clinical study by June. In March the company it had received $4 million from CEPI to develop a COVID-19 vaccine.

9. **Regeneron Pharmaceuticals Inc.**  
**Type:** Treatment  
**Stage:** Preclinical, **Name:** No name yet  
**Background:** On Feb. 4, 2020, Regeneron announced it is working on developing monoclonal antibodies as treatments for COVID-19. The company’s VelocImmune platform uses genetically-engineered mice with humanized immune systems in preclinical testing. “We are aiming to have hundreds of thousands of prophylactic doses ready for human testing by end of August,” a spokesperson said.

10. **Regeneron Pharmaceuticals and Sanofi**  
**Type:** Treatment, **Stage:** clinical trial Phase 2/3, **Name:** Kevzara  
**Background:** The FDA previously approved Kevzara, a treatment developed by Regeneron and Sanofi, as a therapy for rheumatoid arthritis in 2017.  
**Clinical trials:** On March 16, the companies said they had trial started a Phase 2/3 testing Kevzara as a treatment for patients who have been hospitalized with severe COVID-19 infections. This randomized, double-blind, placebo-controlled trial is expected to enroll up to 400 patients and will take place at 16 sites in the U.S. New York’s Mount Sinai Hospital, the first site, has started enrolling patients, according to a company spokesperson. The aim is to evaluate if the drug lessens patient fevers and their need for supplemental oxygen. The Phase 3 trial will evaluate if Kevzara prevents deaths and reduces need for mechanical ventilation, supplemental oxygen, or hospitalization. Early results from a small 21-person trial in China that have not been peer-reviewed found that COVID-19 patients reported reductions in fever and 7% of them had a reduced need for supplemental oxygen within days of starting treatment.

11. **Roche Holding AG ROG,**  
**Type:** Treatment, **Stage:** Phase 3, **Name:** Actemra  
**Background:** Roche’s Actemra was first approved in 2010 as a rheumatoid arthritis drug. The Swiss drugmaker has initiated a Phase 3 clinical trial evaluating Actera as a treatment for patients with COVID-19 who have been hospitalized with severe pneumonia. Roche expects to begin enrolling around 330 patients in early April, in the U.S. and elsewhere in the world. The company plans to examine patient mortality and need for mechanical ventilation or an intensive care unit stay among other primary and secondary endpoints. The trial is in partnership with BARDA.
12. **Sanofi**, **Type:** Vaccine, **Stage:** Preclinical, **Name:** No name yet  
**Background:** Starting Feb. 18, Sanofi is working with BARDA to test a preclinical vaccine candidate for severe acute respiratory syndrome (SARS) for COVID-19 using its recombinant DNA platform. It has a long history of producing vaccines in its Sanofi Pasteur business and acquired this candidate through its 2017 acquisition of Protein Sciences for $750 million. The French drugmaker previously worked with the organization on flu vaccines. Scientists in Meriden, Ct., are working on the vaccine; David Loew, Sanofi Pasteur’s EVP, is leading the project. **Timeline:** A spokesperson said Sanofi aims to put a vaccine into a Phase 1 clinical trial between March 2021 and August 2021.

13. **Takeda Pharmaceutical Company Ltd.**  
**Type:** Treatment, **Stage:** Preclinical, **Name:** TAK-888  
**Background:** The Japanese drugmaker said March 4 it plans to test hyperimmune globulins for people who are at high risk for infection. As part of its research, which will be performed in Georgia, Takeda said it would need access to plasma from people who have recovered from COVID-19 or those who have received a vaccine if one is developed. Dr. Rajeev Venkayya, president of Takeda’s vaccine business, is the co-lead of the company’s COVID-19 response team. Like J&J, Takeda plans to examine whether other therapies, both experimental or with regulatory approval, may have treatment potential.

14. **Vaxart Inc.**  
**Type:** Vaccine, **Stage:** Preclinical  
**Background:** Vaxart was one of the first companies to announce plans to develop a vaccine when it did so Jan. 31. In March the clinical-stage company announced that Emergent BioSolutions will help develop and manufacture its oral vaccine candidate. “We believe an oral vaccine administered using a room temperature-stable tablet may offer enormous logistical advantages in the roll-out of a large vaccination campaign,” Vaxart CEO Wouter Latour said in a March 18 news release. The company plans to start a Phase 1 clinical trial in the U.S. in the second half of 2020.

15. **Vir Biotechnology Inc.** and **Biogen Inc.**  
**Type:** Treatment, **Stage:** Preclinical  
**Background:** Vir said Feb. 25 it is collaborating with Shanghai-based WuXi Biologics to test monoclonal antibodies as a treatment for COVID-19. If the treatment is approved, WuXi will commercialize it in China, while Vir will have marketing rights for the rest of the world. The preclinical company is run by George Scangos, the former CEO of Biogen. It later announced a partnership with Biogen to help develop and manufacture its monoclonal antibodies as a potential treatment for COVID-19. Biogen will handle clinical manufacturing of Vir’s antibodies.