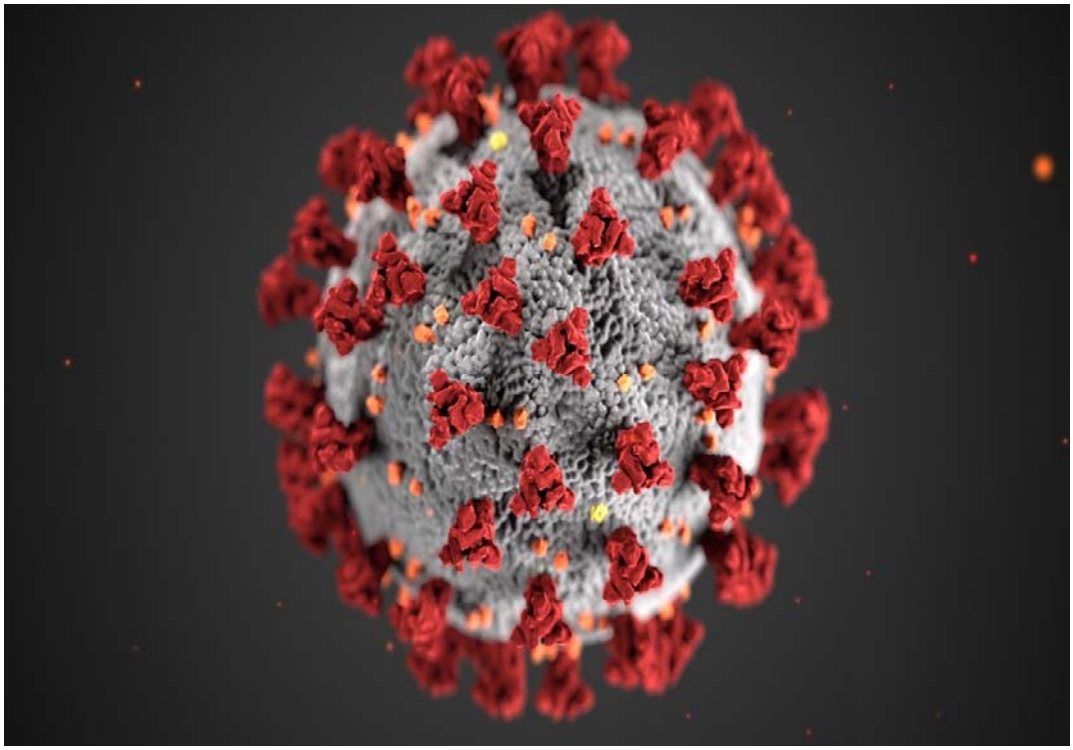

REPORT ON

TOP CONTENDERS FOR COVID-19 VACCINES & DRUGS

June 6, 2020

WHAT IS IN

THE TOP CONTENDERS FOR COVID-19 VACCINES AND DRUGS

Covid-19 vaccines in various trial phases

- Candidate vaccines in clinical evaluation
  - Oxford
  - Moderna
  - CanSino Bilogics
  - Sinopharm
  - Sinovac
  - Novavax
  - Pfizer and BioNtech
  - Inovio Pharma
- Candidate vaccines in pre-clinical evaluation
  - Johnson & Johnson
  - Sanofi and GlaxosmithKline
  - Merck

Covid-19 Treatments and Medications in the pipeline

- Remdesivir
- Avigan (Favipravir) and Other medication
  - Umifenovir(Arbidol)
  - Galidesivir
- Convalescent plasma
- Sun Pharma

THE TOP CONTENDERS FOR CORONAVIRUS VACCINES AND DRUGS

Even as countries toy with the idea of relaxing lockdown and restarting life in the COVID era, the novel coronavirus continues to claim more lives. According to John Hopkins experts' global health data, As of June 6, 2020 COVID-19 has infected more than 6.7 million people across the world and caused 394,786 fatalities. Vaccine makers are racing to develop COVID-19 vaccines, and have advanced 7 to 8 candidates into clinical trials. But challenges remain.

Vaccine development is typically a long game. The US Food and Drug Administration only approved a first vaccine against Ebola virus last year, 43 years after the deadly virus was discovered. Vaccinologists have made little headway with HIV or respiratory syncytial virus, despite huge investments. On average, it takes 10 years to develop a vaccine. With the COVID-19 crisis looming, everyone is hoping that this time will be different.

It might be. Already, ten vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) are in clinical trials and researchers at the University of Oxford and AstraZeneca hope to have the first phase 3 data in hand this summer. **Although many infectious disease experts argue that even 18 months for a first vaccine is an incredibly aggressive schedule, a few optimists believe that hundreds of millions of doses of vaccine might be ready for roll-out by the end of 2020.**

COVID-19 VACCINES IN VARIOUS TRIAL PHASES

Candidate vaccines in clinical evaluation

1. OXFORD

Candidate Vaccine	Developer	Trial phase
ChAdOxl nCov-19	The University of Oxford/ AstraZeneca	Phase 2/3

One of the world's fastest-moving experimental Covid-19 vaccines, the University of Oxford researchers have begun recruiting for the next phase in human trials of a COVID-19 vaccine in human volunteers

More than 10,200 people — including children between the age of five and 12 and adults over 70 — are being enrolled for the second phase. The second phase of the study aims to assess the immune response to the vaccine in people of different age groups. The third phase will judge the effectiveness of the vaccine in a large number of people over the age of 18, researchers at the University of Oxford have said.

Earlier this week, AstraZeneca received a boost in its efforts after the US pledged as much as $1.2 billion towards development of the vaccine and said it would order 300 million doses. AstraZeneca has already signed an agreement to supply 100 million doses of the vaccine to the British government and it reiterated it hopes to start delivery in September 2020.

The proposed Covid-19 vaccine is made from a weakened version of a common cold virus that's genetically changed to make it unable to grow in humans. If the vaccine is proven to be safe and effective, the first doses to be produced under this agreement are anticipated to be available in early 2021. They will be released on a rolling basis as production is completed, and the full quota of 300 million doses is expected to be available by July next year.

2. MODERNA

mRNA-1273	Moderna and NIAD	Phase 2

US-based Modera Inc has already successfully finished its stage 1 of clinical trials and is among the leading candidates in the development of a possible vaccine for the novel coronavirus.

Started stage II trials for its vaccine candidate mRNA-1273, is looking to start the final phase of trials as early as July.

For Phase III trials, the final stage of vaccine development, about 30,000 people will be enrolled, mostly from the age group of 18-55 years, but also the elderly and people who are at risk of severe Covid-19. Dr Anthony Fauci, director of the National Institute of Allergy and Infectious Diseases, has told media the results of

the Phase-III trial would be available by November or December this year. He further said by that time, Moderna would have already produced about 100 million doses of the vaccine.

According to a current report filed by Moderna with the US Securities and Exchange Commission, a "…commercially-available vaccine is not likely to be available for at least 12-18 months, it is possible that under emergency use, a vaccine could be available to some people, possibly including healthcare professionals, in the fall of 2020".

Moderna, meanwhile, is working on its manufacturing capacity. "Moderna has already started to prepare for rapid acceleration of its manufacturing capabilities that could allow for the future manufacture of millions of doses should mRNA-1273 prove to be safe and of expected benefit. We are working around-the-clock to make sure a vaccine is available as quickly and as broadly as possible. We will continue to work together, with government, industry and other third parties to enable the best chance for success," Moderna says on its website

3. CANSINO BIOLOGICS

Ad5-nCoV	CanSino Biologics	Phase 2

The Chinese vaccine maker is being touted as one of the strongest contenders in developing a cure for novel coronavirus. CanSino is currently working on developing a vaccine namely Adenovirus Type 5 Vector by genetically modifying a common cold carrying virus which modifies the structure of the protein once it enters the human cells.
The Ad5-nCoV vaccine candidate has already moved into clinical trials in the month of April where 108 participants aged between 18-60 were injected with the vaccine candidate. According to the report published in the medical journal, Lancet showed that the vaccine being developed by CanSino Biologics Inc could help the body's immunity by producing T cells and was generally safe to use.

4. SINOPHARM (WUHAN/ BEIJING)

No name announced yet	Beijing Institute of Biological Products/Wuhan Institute of Biological Products; China National Pharmaceutical Group (Sinopharm)	Phase 1/2

A Chinese vaccine, being jointly developed by the Beijing Institute of Biological Products and China National Biotec Group Co, has completed phase II testing and may be ready for the market at the end of this year or early next year, according to a report published by the State-owned Assets Supervision and Administration Commission.

The report, quoted by Reuters, said the production line for the vaccine would be fully disinfected would have a full manufacturing capacity of 100 million-120

million vaccines each year. The vaccine candidate employs a killed version of the novel coronavirus that can still trigger an immune response.

5. SINOVAC

PiCoVacc	Sinovac	Phase 1/2

Chinese biopharmaceutical company Sinovac Biotech has pinned hope on its inactivated vaccine, dubbed CoronaVac, and said it was 99 per cent sure of its efficacy. As per a Sky News report, Luo Baishan, a researcher at Sinovac, said, "It must be successful…99 per cent sure." The company has reached stage 2 of its vaccine trial, with more than 1000 volunteers participating. The company is in preliminary talks to hold stage 3 trials – the final part of the process in the UK.

6. NOVAVAX

NVX-CoV2373	Novavax	Phase 1/2

The vaccine candidate of the US-based drugmaker has already begun stage I/II trial of its Covid-19 vaccine candidate in Australia. The human trials will be conducted on 130 volunteers from Australia of Novavax's vaccine candidate NVX-CoV2373.

The potential vaccine candidate is being developed by genetic engineering. It used the genetic sequence of the SARS-COV-2 virus which showed a great promise on baboons and mice.

Moreover, the US-drugmaker has bought a manufacturing plant from the Pune-based Serum Institute of India, which is the world's largest manufacturer of vaccine by volume. Process development for scaled-up production to potentially allow manufacturing of up to 100 million vaccine doses by end of 2020. Access to large-scale manufacturing capacity in multiple countries with a goal of potentially producing over one billion doses during 2021.

7. PFIZER AND BIONTECH

BNT162	Pfizer and BioNTech	Phase ½

US pharmaceutical giant Pfizer has said a Covid-19 vaccine, which is being jointly developed with German firm Biontech, could be ready by the end of October 2020. "If things go well, and the stars are aligned, we will have enough evidence of safety and efficacy so that we can…have a vaccine around the end of October," Albert Bourla, the CEO of the firm, said at an event.

Pfizer is conducting clinical trials in the US and Europe for the BNT162 vaccine programme. The programme includes four vaccine candidates, each representing a different combination of mRNA format and target antigen. "The short, less than

four-month timeframe in which we've been able to move from pre-clinical studies to human testing is extraordinary," he further said.

8. INOVIO PHARMA

INO-4800	Inovio Pharmaceuticals	Phase 1

South Korea's first clinical trials of a vaccine for COVID-19 are slated to begin this month, a report in The Korea Herald said. The International Vaccine Institute and Seoul National University Hospital said Thursday they were partnering for phase 1 and 2 trials of pharmaceutical company Inovio's vaccine candidate INO-4800

The study will proceed in two stages. The first of which will include 40 healthy adults aged 19-50 years to assess the vaccine candidate's safety. An additional 120 people aged 19-64 will be enrolled in the next stage for examining its tolerability and immunogenicity, the report said. Preliminary data from the phase 1 trial is estimated to be available by early September.

Top candidate vaccines in pre-clinical evaluation

JOHNSON & JOHNSON - PRECLINICAL

Johnson & Johnson, which has in the past responded to outbreaks of the Ebola and Zika viruses, is using the same technology to develop a vaccine for the novel coronavirus. J&J's vaccine is made by grafting the coronavirus genes that confer immunity onto a harmless virus, injecting it triggering an immune response without causing infection. J&J expects to begin Phase 1 by September, with a vaccine available for emergency use as soon as early 2021

SANOFI AND GLAXOSMITHKLINE - PRECLINICAL

Sanofi is employing the same technology it employs for flu vaccines, which uses a genetically modified version of a virus to create proteins that train the immune system to react. The company is combining its approach with GlaxoSmithKline's proprietary adjuvant, an additive that makes vaccines more potent.

The companies plan to initiate phase I clinical trials in the second half of 2020 and, if successful, subject to regulatory considerations, aim to complete the development required for availability by the second half of 2021.

MERCK - PRECLINICAL

Merck purchased a Vienna-based company called Themis, which is developing an experimental Covid-19 vaccine based on a measles vaccine. It also partnering with the nonprofit IAVI on the development of a coronavirus vaccine related to the company's existing Ebola vaccine.

Merck says the Themis vaccine will enter human trials in a matter of weeks while the second candidate could reach the clinic by the end of the year 2020.

COVID-19 TREATMENTS & MEDICATIONS IN THE PIPELINE

Key takeaways:

- There is currently no approved treatment or vaccine for COVID-19, but EU countries are already administering REMDESIVIR to patients under compassionate use rules.
- The drug that's furthest along in clinical trials for treating COVID-19 is REMDESIVIR, a new intravenous antiviral that the FDA has not yet approved, though they did grant an emergency use authorization for it to make it more accessible.
- Researchers are also testing older medications (that are typically used to treat other conditions) to see if they also effective in treating COVID-19.

Over 6.7 million people worldwide have tested positive for the novel coronavirus and that number is quickly growing. Our healthcare system is becoming increasingly strained and we are in desperate need of a safe and effective treatment for COVID-19. Scientists around the world are racing against time to find a cure.

Hospitals and research labs all over the world are testing many different therapies on coronavirus-positive patients in an effort to find a potential COVID-19 treatment. Below highlighted a few medications and treatments that have been making a buzz in the science community.

1) REMDESIVIR

Remdesivir is an antiviral that is given by intravenous (IV) infusion in the hospital. This is a brand-new drug that has not been approved by the FDA for use on the market yet, and is being tested in carefully controlled environments. It was previously shown to have some effect against SARS, MERS, and Ebola in cell and animal models. In a recent in vitro study (studies done in a petri dish or test tube rather than in animals or humans), Remdesivir prevented human cells from being infected with SARS-CoV-2 (virus that causes COVID-19).

Early results from a large study of 1,063 patients showed that hospitalized patients who got remdesivir recovered faster than those who got a placebo (11 days vs. 15 days, respectively). The death rate in the remdesivir group (7%) was also lower than that of the placebo group (12%). Patients who needed oxygen saw the most benefit with remdesivir. While these early findings support the use of remdesivir for hospitalized patients with COVID-19, the researchers concluded that treatment with remdesivir alone is likely not enough. This is because those who got the medication still experienced a high death rate.

Nonetheless, based on positive reports from the study above, Gilead's announcement of early results from a phase 3 trial in hospitalized patients with severe symptoms, and a small study in patients who received remdesivir through

a compassionate use program, the FDA issued an emergency use authorization (EUA) for remdesivir on May 1, 2020. The EUA does not mean that the FDA has approved remdesivir for the treatment of COVID-19. Rather, the intent of the EUA is to make it easier for doctors to get remdesivir for hospitalized patients with severe COVID-19 symptoms. These are patients who require mechanical ventilation or extra oxygen.

On June 1, 2020, Gilead announced more results from their phase 3 study — this time they looked at hospitalized patients with moderate symptoms of COVID-19. People who got remdesivir for 5 days were 65% more likely to improve on day 11 compared to those who did not get the treatment. Some people got remdesivir for 10 days, and they also seemed more likely to improve compared to those who didn't get any. The difference was not statistically significant, though (in other words, this might've happened by chance). Until more data is shared, it's unclear why remdesivir appears to work better when given for 5 days instead of 10 days.

Not all remdesivir studies have been positive. Take a study of 236 patients with COVID-19 in China, for example. (This was a randomized, double-blinded study, which is the gold standard for clinical trials.) In one specific analysis, a group of patients in the study who received remdesivir within 10 days of showing symptoms recovered slightly more quickly than those who received a placebo.

However, this difference was not statistically significant, meaning it could have been due to chance. When looking at all patients in the study (regardless of when they received remdesivir), there was no difference in time to improvement compared to placebo. The researchers state that larger studies are needed to confirm the results.

2) AVIGAN (FAVIPIRAVIR) AND OTHER ANTIVIRAL MEDICATIONS

Favipiravir (also known as Avigan) is an antiviral medication approved in Japan and China for the flu. In vitro studies have shown that high doses of favipiravir were able to prevent human cells from being infected with SARS-CoV-2.

Two studies in China looked at how favipiravir worked in comparison to other antivirals. In a study of 240 patients in China with mild COVID-19 symptoms, 71% of patients given favipiravir recovered after 7 days compared to 56% who were given umifenovir (Arbidol). Another small study in China looked at 80 patients with mild COVID-19 symptoms and saw that that favipiravir helped to clear the virus faster than Kaletra (4 days vs. 11 days, respectively). The patients who took favipiravir also showed greater improvements in their lungs based on chest images. The first U.S. clinical trials for favipiravir were recently approved to start in Boston.

Italy approved the drug for experimental use against COVID-19 and began conducting trials in the three regions most affected by the disease. Russia's health ministry has also approved an antiviral drug for the treatment of COVID-19.

Other antivirals being tested for COVID-19 include Umifenovir and Galidesivir:

- **Umifenovir (Arbidol)** is a flu medication that is used outside the U.S. As mentioned above, it was not as good as favipiravir in helping patients recover in a study from China. Another study of 81 patients looked at how long it took from when patients first had symptoms to when they tested negative for the coronavirus, and it found that there was no difference between people who got umifenovir and those who did not. However, it seems to be better than Kaletra at helping patients with COVID-19 clear the virus. In a small study of 50 people, the virus was not detected in any patients who had received umifenovir after 14 days. The virus was still present in almost half of the patients who got Kaletra.
- **Galidesivir** is a new drug that is currently being developed for a variety of viral infections; it has not yet been approved for human use. Clinical trials for galidesivir are starting in Brazil.

3) CONVALESCENT PLASMA

The FDA issued an Emergency Investigational New Drug (eIND) application for the use of convalescent plasma to treat people with COVID-19. Plasma is the liquid part of blood that carries blood cells. Convalescent plasma is collected from people who have recovered from COVID-19. It is then transfused into someone with an active coronavirus infection. It is thought that antibodies found in the convalescent plasma can help fight the coronavirus infection.

In China, 10 adults with severe COVID-19 symptoms were given convalescent plasma. The researchers reported that all symptoms (such as fever, cough, shortness of breath, and chest pain) had greatly improved within 3 days. Compared to a historic control group (a random group of patients who were previously hospitalized for COVID-19), the group who received convalescent plasma saw better improvements in their health.

The first convalescent plasma transfusion in the U.S. for COVID-19 was recently done in Texas. A physician can request convalescent plasma on an individual basis by contacting their local blood center, but it's not widely available since centers have just recently begun collecting it.

4) SUN PHARMA INITIATES PHASE-2 CLINICAL TRIALS FOR POTENTIAL COVID-19 TREATMENT DRUG

Drug major Sun Pharmaceutical Industries on 5th June 2020 said it has commenced phase-2 clinical trials on AQCH, a plant-derived drug, for potential treatment of COVID-19. The company received approval from the Drugs Controller General of India (DCGI) for conducting the trials of the phytopharmaceutical drug in April this year, Sun Pharma said in a statement.

"The clinical trials will be conducted across 12 centres in India on 210 patients. The treatment duration for patients will be 10 days. The results of the clinical trials are expected by October 2020," it added. Human safety study of AQCH has already been completed and the drug has been found safe at the recommended dose for phase-2 study. "This is the first phytopharmaceutical drug approved for clinical trials by the DCGI as a potential treatment for COVID-19. AQCH has shown anti-SARS-CoV-2 effects in in-vitro studies conducted in collaboration with ICGEB, Italy."

SOURCE & REFERENCES

- National Institute of Health (NIH)
- Reuters
- Oxford vaccine group official website
- Johnson and Johnson official website
- Raps.org (regulatory affairs professionals society)
- Merckvaccines.com
- Cansinotech.com
- Modernatx.com
- Pfizer.com
- Gilead Sciences
- The Lancet Journal
- CIMIT
- Johns Hopkins Reports
- Stats news
- timesnownews.com
- businessinsider.com
- businesstoday.com
- World Health Organization