Evolution Briefing:
COVID 19 Vaccine Update

Introduction

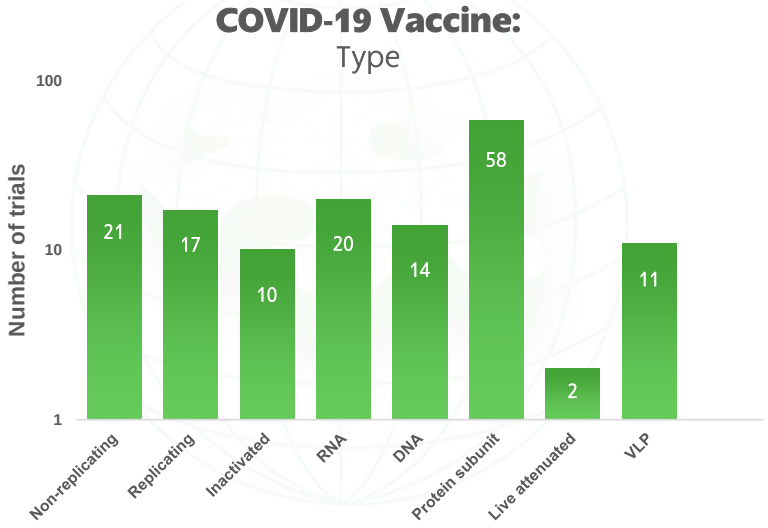
Researchers worldwide are working around the clock to find a vaccine against SARS-CoV-2. Experts estimate that a fast-tracked vaccine development process could speed a successful candidate to market in approximately 12-18 months, providing the process from conception to market availability runs smoothly.

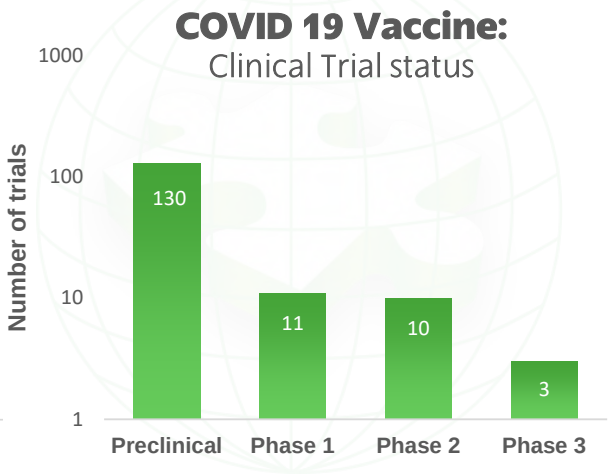
The pandemic has sparked many unprecedented partnerships between public and private companies in the pharmaceutical industry. An example lying in 'Operation Warp Speed' (OWS), a collaboration of several US federal government departments and its subagencies combining to tackle a single disease.

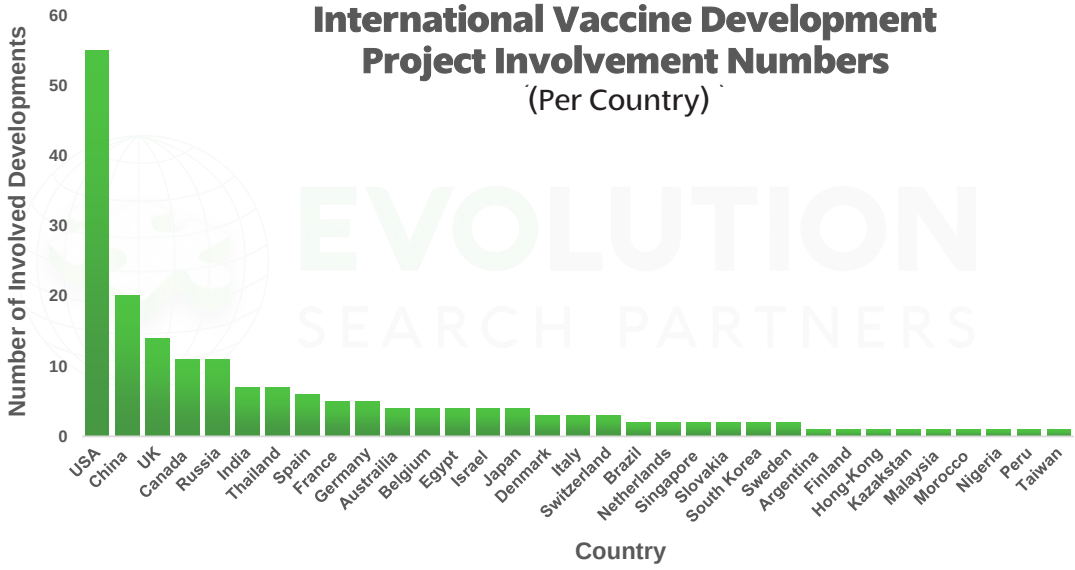
The US government plans to select 3 vaccine candidates to fund for Phase III trials under OWS:

- Moderna's mRNA-1273 (in July)
- The University of Oxford and AstraZeneca's AZD1222 (in August)
- Pfizer and BioNTech's BNT162 (in September)

Since the virus first emerged in January, around 170 vaccine candidates are now in development, with 15 already in human trials. This briefing aims to highlight selected COVID-19 vaccine candidates currently in Phase I-III trials, as well as major candidates in pre-clinical stages of development and research.







Source Data from WHO

Phase 3 – Vaccine Candidates

Chinese company 'Sinovac' is developing a vaccine based on inactivated Covid-19 particles. The vaccine has shown a promising safety profile in early stages of testing and is now moving into Phase III trials in Brazil, partnering with Brazilian vaccine manufacturer 'Instituto Butantan'. They plan to dose 9000 medical professionals working in close contact with coronavirus patients to check the safety and efficacy of the inactivated vaccine candidate 'CoronaVac', in an attempt to battle and subdue the novel coronavirus.

The University of Oxford's vaccine is delivered via a 'vaccine vector', a chimpanzee virus. The vector contains the genetic code of the protein spikes found on the coronavirus and triggers a strong immune response in the human body. The results of the Phase I/II trial, incorporating 1077 patients, illustrated that no early safety concerns were present and that strong immune responses in both parts of the immune system were induced. The vaccine provoked a 'T-cell response' within 14 days of vaccination. The vaccine is in a combined Phase II/III trial in the UK and has recently gone into Phase III trials in South Africa and Brazil. AstraZeneca is on track to begin rolling out up to 2 billion doses of their coronavirus vaccine in September, providing ongoing trials continue to be successful. The Oxford vaccine is one of the most advanced, described by the World Health Organisation's chief scientists as a "leading candidate." The UK has already ordered 100 million doses of the vaccine.

CanSino Biologics seems to be one of the front runners in the race to develop a vaccine for the novel coronavirus. The vaccine candidate has been approved for limited usage for the Chinese military, for a period of one year. Their vaccine candidate 'Ad5-nCoV' is developed using CanSino's adenovirus-based viral vector vaccine technology platform. The Phase II results showed that, as was seen in the Phase I data, the vaccine induced neutralizing antibody responses in most subjects. However, further study continues to show that this vaccine works better in certain groups of people. Among groups trialed, the vaccine was shown to have a reduced effect with those aged 55 and older, hindering a key target for Covid-19 vaccination.

The state-owned Chinese company became the first vaccine candidate to begin the last stage of clinical trials. Sinopharm has since entered Phase III clinical trials for a COVID-19 vaccine in the Emirates city of Abu Dhabi, incorporating around 15,000 volunteers.

As per Sinopharm's official statement, more than 1,000 employees of the Chinese pharmaceutical company have been dosed with vaccine candidate voluntarily. The results of the trial proved that the virus was safe and effective for human use. Sinopharm, which recieved approval for the trial in late June, is using an inactivated vaccine - a technology that is well known and has been used to make vaccines against diseases such as influenza and measles.

Phase 2 – Vaccine Candidates

Moderna is developing a vaccine candidate using mRNA to trick the body into producing viral proteins itself. No mRNA vaccine has ever been approved for an infectious disease, and Moderna has never brought a product to market. It could, however, be easier to mass produce than traditional vaccines. Moderna Inc's Phase III trials of its vaccine candidate 'mRNA-1273' has been put on hold due to changes in trial protocols.

As of now, there are no new reports of when Phase III clinical trials will begin, as they were previously suggested to commence on July 9th. The highly anticipated last phase of Moderna's vaccine candidate will be conducted on 30,000 patients. Moderna is still hoping to start the trials in the month of July and push the vaccine out for public use by early 2021. Moderna is still at the forefront of the race to find a successful vaccine and was the first company to administer a COVID-19 vaccine candidate in human participants in March.

Moderna's highly anticipated COVID-19 vaccine candidate has shown promise in a key early trial, producing antibodies in all participants tested. Moderna Inc., will start its most important step around July 27: A 30,000-person study to prove if the shots really are strong enough to protect against the coronavirus.

BioNTech and Pfizer reported additional data from their experimental Covid-19 vaccine which showed it was safe and induced an immune response in patients. The companies said the data also demonstrated an induction of a high level of 'T-cell responses' against the novel coronavirus. Pfizer and BioNTech remain on track to begin an anticipated Phase II/III safety and efficacy trial later this month, to then seek regulatory review as early as October 2020 and manufacture up to 100 million doses globally by the end of 2020, and more than 1.3 billion doses by the end of 2021. 30 million doses are expected to be delivered in 2020 and 2021, subject to regulatory approval or authorization. Pfizer Inc. and BioNTech announced an agreement with the United Kingdom to supply 30 million doses of their 'BNT162 mRNA-based vaccine' candidate against SARS-CoV-2.

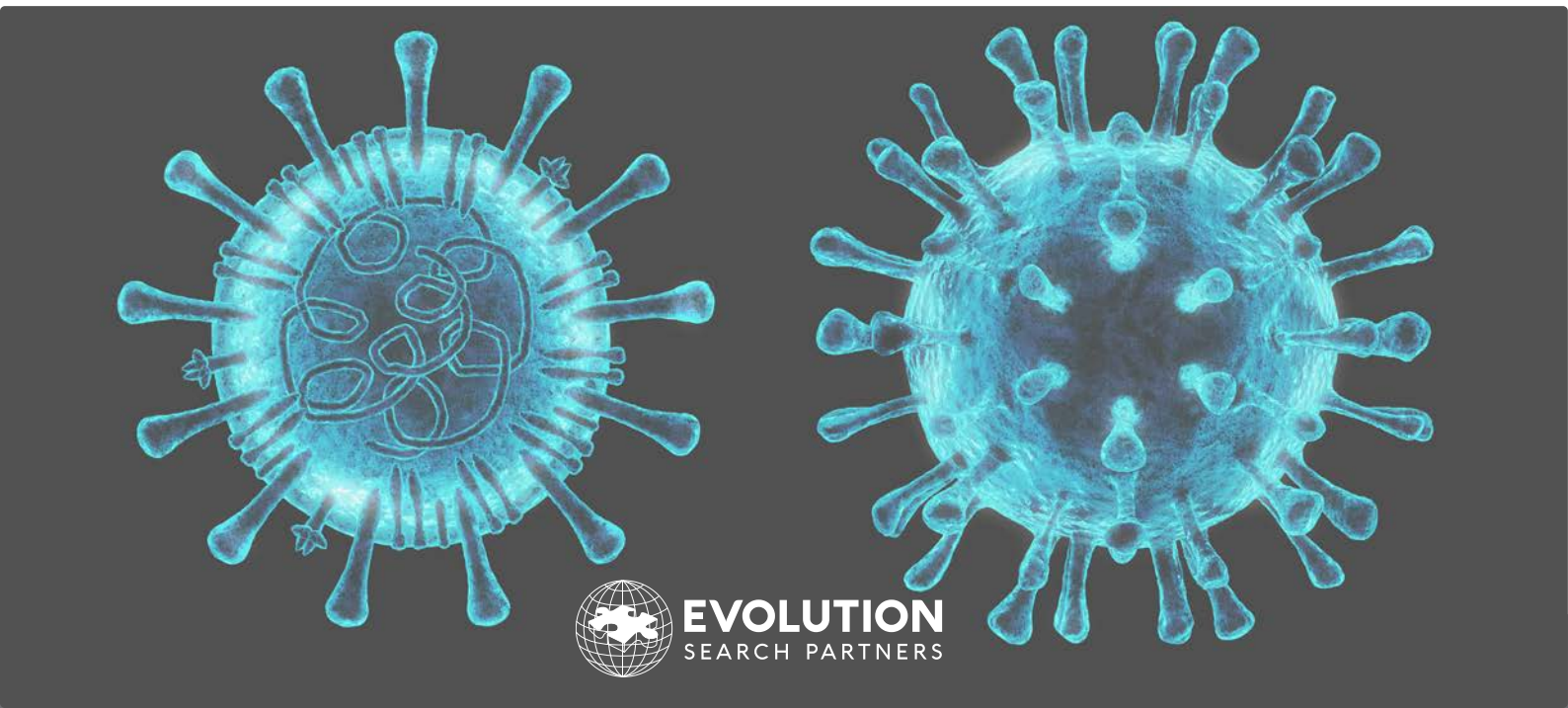
Valneva reached an agreement with the U.K. government to supply up to 100 million doses of its vaccine candidate, which will be produced in Scotland. An inactivated whole virus vaccine, the candidate uses the same platform as 'Ixiaro', Valneva's FDA-approved vaccine for protection against Japanese encephalitis. Valneva unveiled their COVID-19 vaccine program back in April however, they have not yet made as many headlines as other frontrunners in the race such as Moderna, Pfizer, AstraZeneca and Johnson & Johnson.

The company, based in France, has partnered with Dynavax to explore BioNtech's adjuvant, in conjunction with its vaccine candidate. Valneva plans investments for their Scottish sitem as well as another factory in Sweden. Valneva plans to enter human testing by the end of this year and possibly score approvals in the second half of 2021. That timeline would put the company behind expectations for some of the speediest programs in the COVID-19 vaccine race.

Phase 2 – Vaccine Candidates

Company	Vaccine Type	Platform	Status
Novavax	Protein Subunit	Glycoprotein	Phase 1/2
Bharat Biotech	Virion inactivated	Inactivated	Phase 1/2
Inovio	DNA Plasmid	DNA	Phase 1/2
BioNTech/Pfizer	LNP mRNA	RNA	Phase 1/2
Cadila Healthcare	DNA Plasmid	DNA	Phase 1/2

Table1:- Candidate vaccines in Phase 2 clinical evaluation



Other Notable Vaccine Candidates

Researchers at **Imperial College London** have developed a candidate which, when injected, will deliver the genetic instructions to muscle cells to make the SARS-CoV-2 spike surface protein.

The first participants in London are now receiving the vaccine as part of the first phase of the trial, with a second booster dose to follow within four weeks. This will look at different doses of the vaccine, ensuring that safety to trial in larger numbers of volunteers, estimated at 6000 volunteers, across larger scale trials in October is feasible. Rather than giving people a weakened form of the illness, the Imperial vaccine instead uses synthetic strands of genetic code based on the virus' genetic material.

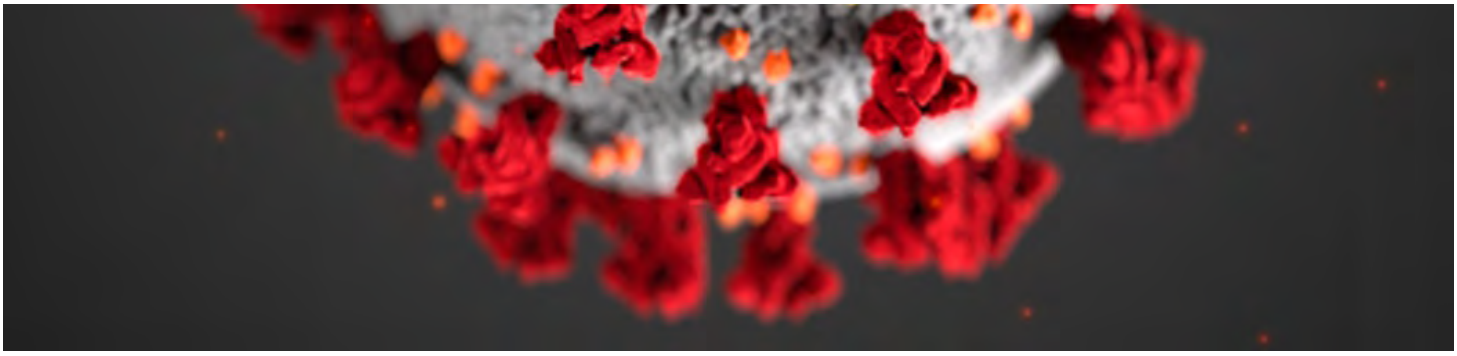
The research has been funded by £41 million from the UK Government, as well as £5 million from other donations.

CureVac has lost some shine in the race for a COVID-19 vaccine opportunity after other mRNA-based hopefuls have captured regulators' attention. Even so, CureVac has reportedly snared a big partner to help build its game-changing RNA "printers" that could turn global interest back in their favor. **Tesla** and Curevac plan to make portable molecular RNA printers or 'RNA micro-factories' to help produce mass-doses of Curevac's vaccine. CureVac's printers are designed to rapidly create mRNA vaccine candidates against known pathogens and its mRNA vaccine candidates direct cells to make proteins or antigens against various diseases. The platform encapsulates mRNA in a shell of lipid nanoparticles to protect it for delivery. The RNA printer itself - essentially a vaccine production device - can make "more than a hundred thousand doses" in a couple of weeks. If successful, the printers could also be used for CureVac's COVID-19 shot candidate, 'CVnCoV', which received German and Belgian regulatory clearance to enter Phase I human testing. The European Investment Bank (EIB) will provide three 25 million instalments to support CureVac's vaccine development and expansion to mRNA production facilities.

GlaxoSmithKline has partnered with Medicago to develop a plant-based coronavirus vaccine candidate. GSK will manufacture the adjuvant system for the vaccine and combine it with 'CoVLP' (Coronavirus Virus-Like Particles) vaccine candidate of Medicago. In the preclinical trials, a single dose of Medicago's CoVLP had demonstrated the production of antibodies. It should be noted that GSK has already partnered with Sanofi for the development of a COVID-19 vaccine and is hoping to start clinical trials in September.

While the Russian scientists made headlines on Sunday with their claim of developing 'the world's first COVID-19 vaccine', the status of their vaccine candidate still suggests to be at Phase I of clinical trials (as per data from the World Health Organization (WHO)). The vaccine candidate developed by **Gamalei National Research Centre** for Epidemiology and Microbiology has cleared Phase I of clinical trials on 2 groups of volunteers and will commence the Phase II testing in the mid-July. According to recent reports, Russian scientists are hoping to launch the candidate for civil circulation in the next month.

Conclusion



As the pandemic accelerates, the world waits impatiently for the discovery of a vaccine. However, the true reality is that there is no guarantee one will be discovered or that it will be distributed fairly. A hurdle some clinical trials face lies in the fact that as infection rates fall in the community, the likelihood of vaccinated volunteers becoming exposed to coronavirus significantly lowers.

The AstraZeneca/Oxford vaccine 'AZD1222' is regarded as a front-runner as it is at the final stage of testing, is backed by US-funded OWS, and because manufacturing capacity is already in place. AstraZeneca has committed to supplying up to 400 million doses to European countries at no profit, with the first batches due for deployment as early as September.

The UK government has signed deals for 90 million doses of promising coronavirus vaccines in development.

The vaccines are being researched by an alliance between the pharmaceutical companies BioNtech and Pfizer as well as the firm Valneva. The new deals rest on top of the 100 million doses of the Oxford University vaccine being developed by AstraZeneca already agreed upon. However, uncertainty still exists over which of the experimental vaccines may work.

Using different styles of vaccine maximises the chance that one of them will work and, as such, the UK government has now secured access to vaccines that use three completely different approaches:

- **100m doses of the Oxford vaccine made from a genetically engineered virus.**
- **30m doses of the BioNtech/Pfizer vaccine, which injects part of the coronavirus' genetic code.**
- **60m doses of the Valneva, which uses an inactive version of the coronavirus.**

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