Evolution Insights:
The Race for a COVID -19 Vaccine

The race is as much about reputation as it is about saving lives and earning revenue, but when can we expect the vaccine?

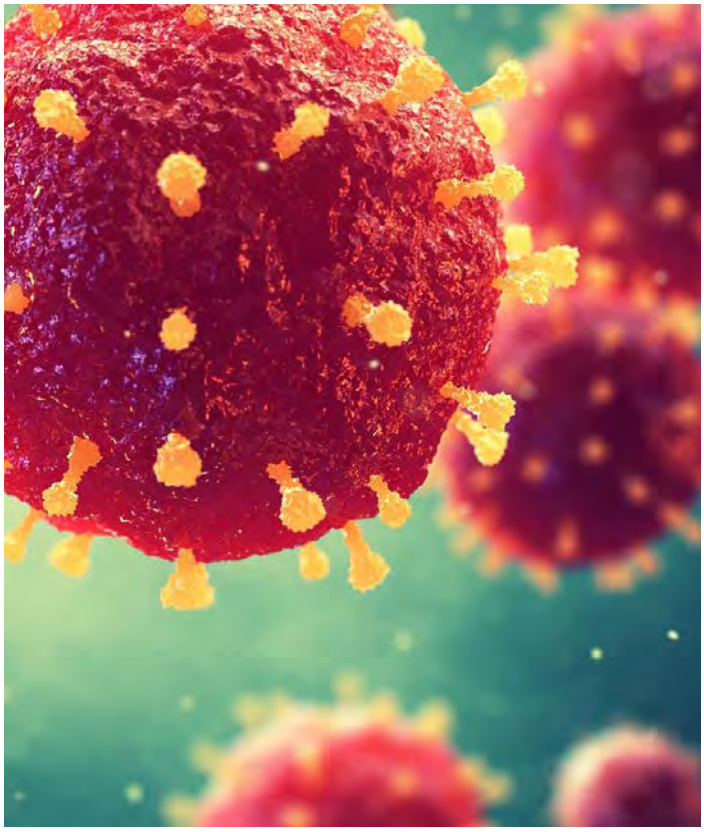
Rapid progress being made by several companies provides some encouragement that a vaccine will be coming soon.

While companies usually compete to create novel therapeutics and vaccines for a 'first-to-market' advantage, tackling COVID-19 is likely to require the contributions of multiple companies. There's going to be more than one winner in the vaccine field as billions of vaccine doses will be required globally.

The Chinese see themselves facing opposition in the form of a US effort, triggered by President Trump's call to develop a vaccine at 'warp speed.' To meet the target of a vaccine by October — in part motivated by the US elections in November — the US's Biomedical Advanced Research & Development Authority (BARDA) said they would provide $1.2 billion support to Oxford University's AstraZeneca project in order to deliver 300 doses of their potential vaccine by the end of September.

As of now, there are 224 candidate vaccines in development globally, according to the data collected by the Coalition for Epidemic Preparedness Innovations (CEPI). While North America has the largest number of projects — 49 per cent — China is the furthest along the track with five vaccines in phase II human trials, more than any other country.

Of the ten vaccines at the stage of human trialing, six are Chinese. As well as this, China is the only country with a vaccine which has advanced to phase II referring to the CanSino Biologics Beijing Institute of Biotechnology product using the 'non-replicating viral vector' design, similar to that of Oxford University's product. CanSino's phase I trial results were reported on May 22 by Lancet.



The Race for a COVID -19 Vaccine

Figure 1:- Vaccine Approaches

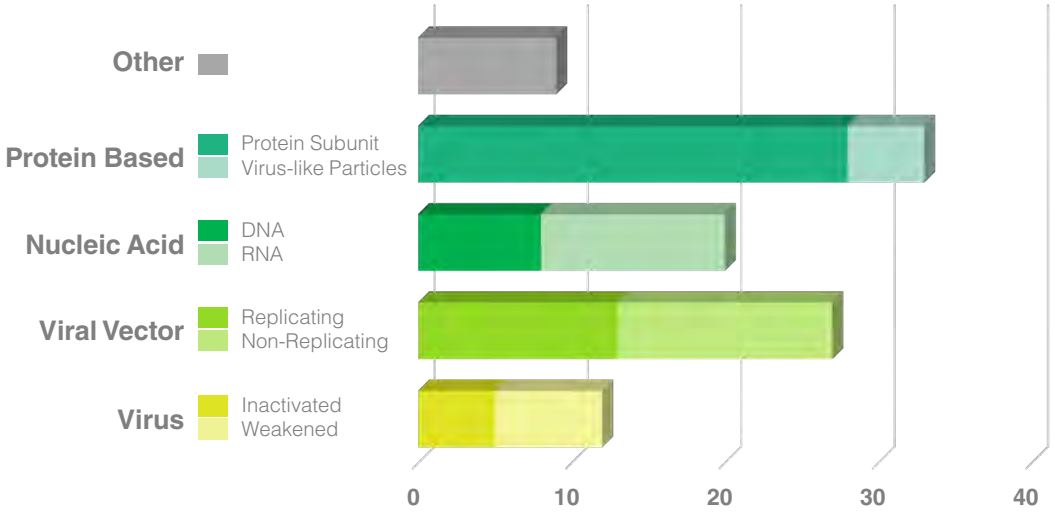
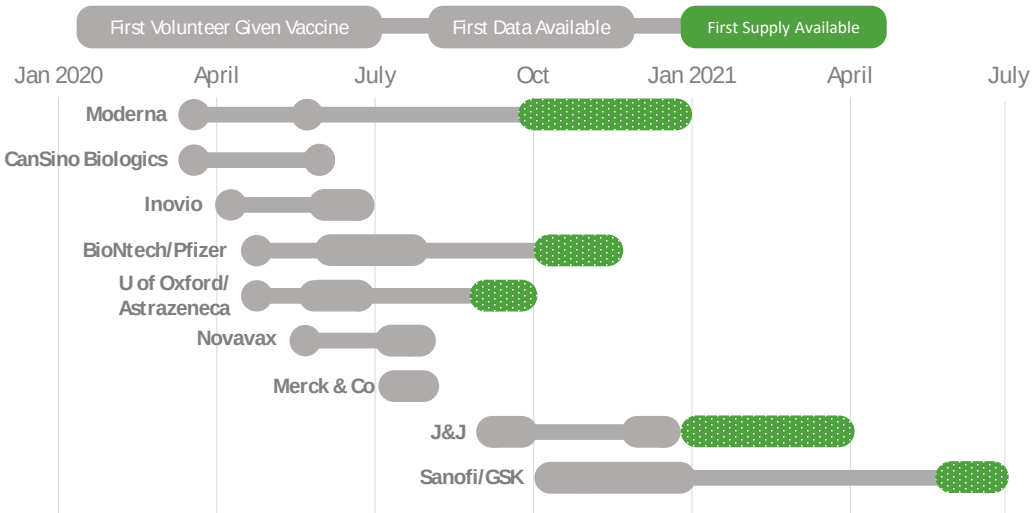


Table 1:- Vaccine Types

Vaccine Types	Target	Approx. No. of Vaccines in development	Examples
Viral Vector	Weakened Virus	25	Univ of Oxford/Astra Zeneca
Nucleic Acid	Spike Protein	20	Moderna
Protein based	Protein Sub Units	28	Novavax
Virus like	Empty Virus Shells	7	Sinovac Biotech

The objective is to have a vaccine ready for use by the end of the year, or sooner. No vaccine has ever been developed or manufactured within these timeframes

Figure 2:- Vaccine timelines



Potential Vaccines

Vaccine type
Messenger RNA: Genetic instructions for the coronavirus spike protein are encoded in mRNA, delivered via lipid nanoparticle.

Target supply
With Lonza, 1 billion doses per year.

External funding
Up to $483 million.

moderna

Development Timeline
- **1/13/20:** Vaccine Candidate Selected.
- **3/16/20:** First Volunteer Given Vaccine in Phase I.
- **5/18/20:** Phase I Data Disclosed.
- **5/29/20:** First Volunteer Given Vaccine in Phase II.
- **July 2020:** Phase III Study to Begin.
- **Autumn 2020:** First Supply Available.

Details
- Moderna's experimental coronavirus vaccine using messenger RNA technology, an unproven approach that instructs cells to produce specific proteins, can be used to make a vaccine much faster than traditional methods.
- The vaccine went from a computer design in January to human study in just three months. Since then, Moderna has kept up its record pace. Phase I data came in late May, as did the start of a mid-stage trial and a final study could begin in July, making the company's efforts one the best hopes for a vaccine potentially available within the aggressive timeframes of 'Operation Warp Speed.'
- No mRNA vaccine has been proven to prevent disease, nor manufactured and distributed at scale, let alone during a pandemic. Moderna still needs to show it can produce enough doses to vaccinate millions of people.

康希诺生物股份公司
CanSino Biologics Inc.

Vaccine type
Non-replicating viral vector:- DNA sequence for coronavirus spike protein delivered via adenovirus type 5 vector.

Target supply
Undisclosed.

External funding
Not Disclosed.

Development Timeline
- **3/17/20:** First volunteer given vaccine.
- **4/12/20:** Phase II study begins.
- **5/15/20:** Study cleared to start in Canada.
- **5/22/20:** Phase I Data Published.

Details
- China's CanSino Biologics appears to have progressed the furthest among the many Chinese groups researching coronavirus vaccines.
- CanSino has moved equally quickly as they were first to enroll healthy adults into a Phase I study. Data suggested immune responses in the 108 participants treated, an encouraging first step. But it's not certain whether the vaccine's effects would actually be protective against infection and so, side effects forced researchers to scrap the highest dose.
- CanSino's choice of vaccine design may also limit the shot's potential. Pre-existing immunity to the adenovirus, or viral vector, that CanSino uses to deliver its vaccine appeared to compromise its effectiveness.
- The company has since advanced its vaccine into mid-stage tests in China and Canada.

Potential Vaccines

Vaccine type
DNA:- DNA plasmid encoding coronavirus spike protein delivered via electroporation.

Target supply
1 Million by Year-End.

External funding
$29 Million.

INOVIO
POWERING DNA MEDICINES

Development Timeline
- **1/10/20:** Vaccine Candidates Selected.
- **4/6/20:** First Volunteer Given Vaccine.
- **June 2020:** First Data Expected.
- **Summer 2020:** Phase II/III Study to Begin.

Details
Inovio looks to be an outsider in the race with the company lacking a 'big-pharma partner,' as well as only assembling about $29 million in external funding. This said, Inovio has moved swiftly, completing dosing in a 40-patient Phase I trial with early safety and immunogenicity data expected in late June. A Phase II/III efficacy trial is expected to begin this summer.

Its candidate uses DNA to coax cells to produce coronavirus proteins, thereby stimulating an immune response to protect against infection from the virus. To allow the DNA molecules to enter cells, Inovio uses a process called *electroporation*.

Questions remain specific to manufacturing. Partnering with Ology Bioservices and Richter-Helm BioLogics, Inovio has committed only to producing 1 million doses by the end of the year.

Additional problems facing Inovio include a lawsuit against VGXI and GeneOne Life Science.

BIONTECH

Pfizer

Vaccine type
Messenger RNA:- Genetic instructions for the coronavirus spike protein are encoded in mRNA, delivered via lipid nanoparticle.

Development Timeline
- **3/17/20:** Pfizer partners with BioNTech.
- **4/23/20:** First volunteer in Germany receives vaccine.
- **5/5/20:** First volunteer in U.S. receives vaccine.
- **Jul. 2020:** First data expected.
- **Oct. 2020:** First supply available.

Target supply
Millions of doses in 2020 - Hundreds of millions in 2021.

External funding
None.

Details
BioNTech is developing multiple mRNA vaccines for the coronavirus. The drugmaker had already been working with Pfizer on an influenza vaccine for over a year when COVID-19 emerged as a global threat. The two companies moved towards coronavirus research in mid-March.

Pfizer and BioNTech have since started clinical trials in Germany and the US. They are advancing four prototypes, each with slight differences.

The timeline fits well with 'Operation Warp Speed' in the US, hence, Pfizer and BioNTech's program is reportedly among the finalists. However, Pfizer won't rely on government funding, stating they can move faster on their own and so expect to spend more than $1 billion on a vaccine.

Potential Vaccines

Vaccine type
Non-replicating viral vector:- DNA sequence for coronavirus spike protein delivered via chimpanzee viral vector.

Target supply
With partners, 2 billion doses.

External funding
UK:- $80 billion; USA:-$1.7M.

UNIVERSITY OF OXFORD

AstraZeneca

Development Timeline
- **4/23/20:** First Volunteer Given Vaccine.
- **5/22/20:** Recruitment for Phase II trial begins.
- **Sept. 2020:** First supply available for U.K.
- **Oct. 2020:** First supply available for U.S.
- **Year end 2020:** First supply available for CEPI, GAVI.

Details
AstraZeneca became a front-runner in coronavirus drug development when they licensed work by the University of Oxford, who invented one of the first vaccines for SARS-CoV-2 to enter human testing.

Dubbed AZD1222, Oxford's vaccine takes an adenovirus and, much like gene therapies seeking to correct defective DNA, uses it to coax the body's cells to produce the coronavirus' characteristic "spike" protein. The adenovirus used causes infections in chimpanzees - but not in humans.

A large Phase I study began in late April and should deliver results shortly. Oxford has already advanced the vaccine into mid-stage testing in more than 10,000 patients (UK), and could progress to late-stage trials by mid-year, with a 30,000-person Phase III study in the US.

AstraZeneca has stated that initial supply will go to the UK and, with the company receiving more than $1 billion in funding from the US government, the US will be next in line.

Deals struck by Astrazeneca with two health charities and India's Serum Institute will provide for supply elsewhere, particularly in low- and middle-income countries, however, first deliveries to CEPI and GAVI aren't expected until the end of the year.

NOVAVAX

Development Timeline
- **4/8/20:** Vaccine Candidates Selected.
- **5/25/20:** First Volunteer Given Vaccine.
- **July 2020:** First Data Expected.

Vaccine type
Protein-based:- Coronavirus-derived protein produced in insect cell lines, extracted and delivered alongside an adjuvant.

Target supply
1 billion doses beginning in 2021.

External funding
US:- £60 Billion; CEPI $388 million.

Details
Novavax was among the first companies to begin working on a COVID-19 vaccine, and one of the first to start a Phase I clinical trial. However, Novavax faces significant challenges to prove it's a real contender. Their nanoparticle-based vaccine technology, which uses recombinant proteins to trigger an immune response, has a mixed track record. Other experimental vaccines, among them projects for coronavirus cousins SARS and MERS, never made it to late-stage testing.

A deal with Emergent Bio and, more recently, an acquisition of Praha Vaccine, have given the company the manufacturing capability to produce over 1 billion doses of its vaccine by next year. But, unlike the larger companies involved with coronavirus vaccine development, making and distributing a product at that scale is something that Novavax has never done.

Potential Vaccines

Vaccine type
Replicating viral vector: DNA sequence for viral antigen delivered via measles (Themis) or vesicular stomatitis (IAVI) virus.

Target supply
Undisclosed.

External funding
$38 million (via IAVI).

MERCK

Development Timeline
- July 2020 First volunteer given Themis vaccine.

Details
Merck came late to the coronavirus vaccine race, having publicly announced its efforts near the end of May. But, given its track record developing drugs and vaccines for infectious diseases, its involvement shouldn't be underestimated.

Merck also has no interest in being first. The company is not trying to use new, less proven technologies to move quickly. Instead, Merck homed-in on approaches they know they can manufacture at a global scale, and believes will produce immunity quickly, with one shot.

Those preferences led Merck to license two vaccines that use viruses to deliver their payloads. Merck procured one by buying privately held Themis, and the other by teaming up with the nonprofit group IAVI. The Themis vaccine should start first human tests in July, while the other program will get there later this year.

The company, for their part, believes they will make up ground on their rivals later on, given newer technologies like mRNA and DNA vaccines have never been produced at scale, and may require booster shots to confer immunity.

Johnson & Johnson

Development Timeline
- **3/30/20:** Vaccine candidate selected.
- **July 2020:** First volunteer given vaccine.
- **Year-end 2020:** First data expected.
- **Early 2021:** First supply available.

Vaccine type
Non-replicating viral vector: - DNA sequence for coronavirus spike protein delivered via adenovirus type 26 vector.

Target supply
1 billion doses globally.

External funding
$456 million.

Details
J&J was one of the first to pursue a coronavirus vaccine, announcing in late January plans to develop one using the same technology that underpins several other of the pharma's experimental vaccines.

In early June, J&J sped up their plans and now targets the second half of July for the start of their first clinical trial - which will take place in the U.S. and Belgium - and plans to go from Phase I to Phase II and III very quickly. J&J expects to be able to supply 1 billion doses of its vaccine, beginning early next year.

J&J's scale makes it a natural partner for governments looking ahead to widespread inoculation drives. The U.S. government has pledged over $450 million to J&J's work and the company is one of a handful reportedly selected as a finalist for 'Operation Warp Speed.'

Potential Vaccines

Vaccine type
Inactivated viral vaccine.

Target supply
100 million doses (manufacture via new Sinopharm site.)

External funding
$17 Million.

sinovac®

Development Timeline
- **April:** Phase I (144 patients) = April.
- **May:** Phase II (1000 vol.)
- **July:** Phase III (sponsored by Instituto Butantan in Brazil.)

Details
Sinovac Biotech announced preliminary study results on Saturday showing its experimental Covid-19 vaccine generated immune responses in patients and was safe — early data that suggests it might protect people against infections with the novel coronavirus. The vaccine, called CoronaVac, induced neutralizing antibodies in "above 90%" of people who were tested 14 days after receiving two injections, two weeks apart.

The preliminary results were from a 600-patient, placebo-controlled Phase II study. Sinovac is also conducting a 143-patient, placebo-controlled Phase I study. Using a killed version of the coronavirus, Sinovac's vaccine is among five Chinese experimental shots that have reached the crucial final stage of human testing before they can be approved for public use. The company announced a partnership this month with Instituto Butantan to conduct its phase III trial in Brazil, where the novel pathogen has caused the second-largest outbreak in a global pandemic that so far infected more than 7.7 million people and killed over 428,000.

gsk SANOFI

Development Timeline
- **2/18/20:** Partnered with BARDA.
- **4/14/20:** Partnered with GSK.
- **Q4 2020:** First volunteer given vaccine.
- **Mid- to second half of 2021:** First supply available.

Vaccine type
Protein-based:- Coronavirus-derived protein produced in insect cell lines, extracted and delivered alongside an adjuvant.

Target supply
1 billion doses by mid-2021.

External funding
$30 million.

Details
In April, Sanofi and GlaxoSmithKline, two of the biggest vaccine manufacturers, agreed to join forces with the former contributing their protein-based vaccine technology and the latter its immune-boosting adjuvants, both of which have previously been use against influenza.

They probably won't be the first to market, however, the timeline the two companies have laid out is months behind that of Moderna, Pfizer and even Novavax, which is using a similar approach.

What Sanofi and GSK might be able to bring, though, is a more potent vaccine. Adjuvants are added to vaccines to enhance the immune response, in theory resulting in stronger inoculation against an invading virus. With herd immunity the goal of any mass vaccination program, public health leaders will want a vaccine capable of preventing infections in at least 70% to 80% of the people who get it.

Sanofi and GSK hope to begin human study of their vaccine later this year.

Evolution Prediction

Top 4 Ranked

1: Sinovac

Sinovac may be the safest bet as it uses the long-proven route of an inactivated virus vaccine. For this reason, this Chinese company is the one to watch.

2: Moderna

Moderna is leading the race with its mRNA platform and, with Phase III trials and 30,000 volunteers due to begin in July, this is the first vaccine candidate to pass this milestone. However, this said, this is an unproven approach that has never been manufactured at scale.

3: University of Oxford

University of Oxford's adenovirus candidate has the backing of pharma giant AstraZeneca — and is also rushing to Phase III trials in the UK, US and Brazil. Italy, Germany, France and the Netherlands have signed a contract with AstraZeneca to supply Europe with a vaccine for coronavirus, with the aim of beginning the first deliveries before the end of 2020.

4: BioNTech/Pfizer

A strong contender due to: BioNTech's expertise in mRNA vaccines, Pfizer's manufacturing experience and support from 'Operation Warp Speed,' in the US.

Other Promising Vaccines

Novavax was among the first companies to begin working on a COVID-19 vaccine, however, making and distributing a product at that scale is something that Novavax has never done.

J&J's scale makes it a natural partner for governments looking ahead to widespread inoculation drives. Credibility makes it a leading contender mid/long-term.

Merck came late to the coronavirus vaccine race, however, given its track record developing vaccines, a credible long term option.

Sanofi/GSK:- Probably won't be the first to market, however, credibility of the two Pharma giants, and robust protein-based vaccine technology and immune-boosting adjuvants make it the choice mid/long-term.

CanSino adenovirus vaccine also looks promising, however, choice of vaccine design may limit potential.

Inovio was initially the first mover when the COVID viral sequence was published. However, major issues with manufacturing.

Conclusion

Coronaviruses present unique challenges that make vaccine development problematic. They are among one of the diverse groups of viruses affecting a variety of animals and mutated strains are emerging unpredictably.

Human Coronavirus Types

Scientists have divided coronaviruses into four sub-groupings, called: alpha, beta, gamma, and delta. Seven of these viruses can infect people. The four common ones are;

- 229E (alpha.)
- NL63 (alpha.)
- OC43 (beta.)
- HKU1 (beta.)

The three less-common ones are:

- MERS-CoV, a beta virus that causes Middle East respiratory syndrome (MERS.)
- SARS-CoV, a beta virus that causes severe acute respiratory syndrome (SARS.)
- SARS-CoV-2, which causes COVID-19.

Existing drugs, like those developed to vaccinate against coronaviruses SARS and MERS, are not necessarily effective against new strains, however, the coronavirus mutates more slowly than the flu, which means a vaccine will likely be effective long-term.

There are a further 71 vaccine candidates that could soon follow;
https://www.who.int/blueprint/priority-diseases/key-action/novel-coronavirus-landscape-ncov.pdf

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