Moderna's COVID-19 Vaccine – Phase III trial

Moderna's vaccine looks set to become the first vaccine to enter Phase III trials - the final phase before potential FDA approval.

The company announced that it would begin US trials in July and would conduct these trials alongside the National Institute of Allergy and Infectious Diseases (NIAID). It will include 30,000 participants, randomised and placebo controlled. Based on results from Phase I study, the 100 µg dose level was chosen as the optimal dosage, allowing for the maximum immune response whilst minimizing adverse reactions. Moderna says it can deliver approximately 500 million doses per year. Through a strategic collaboration with Lonza, Moderna will be able to manufacture up to 1 billion doses per year and they plan to start manufacturing even before the vaccine's efficacy is established, in an effort to get ahead of the competition.

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.

About mRNA-1273

mRNA-1273 is an mRNA vaccine against SARS-CoV-2 encoding for a stabilised form of the Spike (S) protein, which was selected by Moderna in collaboration with investigators from Vaccine Research Center (VRC) at the National Institute of Allergy and Infectious Diseases (NIAID), a part of the NIH.

The potential advantages of an mRNA approach to prophylactic vaccines include the ability to combine multiple mRNAs into a single vaccine, rapid discovery to respond to emerging pandemic threats and manufacturing agility derived from the platform nature of mRNA vaccine design and production.

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.

Challenges and Competition

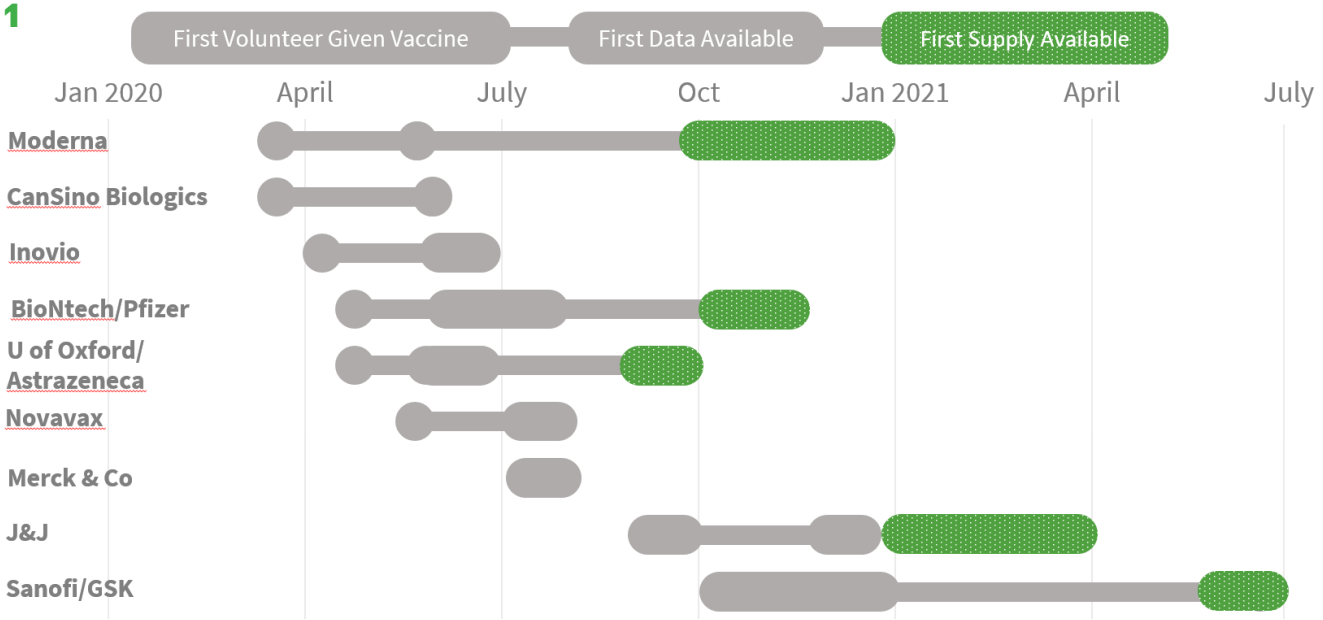
Challenges:-

- Vaccinating people who are actually at risk of getting infected/lack of circulating virus
- Hiring staff
- Manufacturing at risk (mass production at same time as clinical trials)
- Possible equipment shortages
- Vaccine distribution
- mRNA technology has yet to be approved in medicine and is unknown territory

Competition

The short-list in Trump's Operation Warp Speed includes vaccines from Moderna, Johnson & Johnson, Oxford University and AstraZeneca, Pfizer/BioNTech and Merck & Co.

Fig. 1



There are four-to-five vaccines that are getting close to Phase III trials, with the University of Oxford/ AstraZeneca project expected to enter Phase III shortly after that of the Moderna.

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.

About AZD1222

AZD1222:- ChAdOx1 nCoV-19, now known as **AZD1222**, was developed by Oxford University's Jenner Institute, working with the Oxford Vaccine Group. It uses a replication-deficient chimpanzee viral vector based on a weakened version of a common cold (adenovirus) virus that causes infections in chimpanzees and contains the genetic material of SARS-CoV-2 spike protein. After vaccination, the surface spike protein is produced, priming the immune system to attack COVID-19 if it later infects the body.

The recombinant adenovirus vector (ChAdOx1) was chosen to generate a strong immune response from a single dose and it is not replicating, so cannot cause an ongoing infection in the vaccinated individual.

AstraZeneca continues to build a number of supply chains in parallel across the world, including in Europe. The Company is seeking to expand manufacturing capacity further and is open to collaborating with other companies in order to meet its commitment to support access to the vaccine at no profit during the pandemic. AstraZeneca has reached an agreement with Europe's Inclusive Vaccines Alliance (IVA), spearheaded by Germany, France, Italy and the Netherlands, to supply up to 400 million doses of the University of Oxford's COVID-19 vaccine, with deliveries starting by the end of 2020. The IVA aims to accelerate the supply of the vaccine and to make it available to other European countries that wish to participate in the initiative. The IVA is committed to providing equitable access to all participating countries across Europe.

Earlier this month (June 2020), the company formed manufacturing agreements with several CMDOs/CMOs for its COVID-19 vaccine, including Emergent Biosolutions, Catalent, and Cobra Biologics. It also formed an agreement with Jacobs Engineering to retrofit a company facility in Ohio to manufacture the vaccine. AstraZeneca says it is seeking to expand manufacturing capacity further and is open to collaborating with other companies in order to meet its commitment to support access to the vaccine at no profit during the pandemic.

Coronavirus Front Runners

Other Vaccine News

Imperial College London

Another vaccine joined the list of those that have already advanced into clinical testing, after Imperial College London dosed the first healthy volunteer with its vaccine based on self-amplifying RNA (saRNA), known as LNP-nCoVsaRNA.

ZFSW The Biologics Company

Meanwhile, the authorities in China have just approved the first clinical trials of an adjuvanted recombinant protein coronavirus vaccine candidate developed by Chongqing Zhifei Biological Products.

SANOFI

Sanofi says it will start clinical testing of its experimental coronavirus in September, several months earlier than planned, and could have the vaccine ready for emergency use in January with planned capacity to make a billion doses of the vaccine each year. The phase 1/2 trial of the recombinant protein-based vaccine – which uses GlaxoSmithKline's AS03 adjuvant and is based on Sanofi's baculovirus expression system already used in its quadrivalent flu vaccine – could get "full approval by the first half of 2021", according to the company.

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