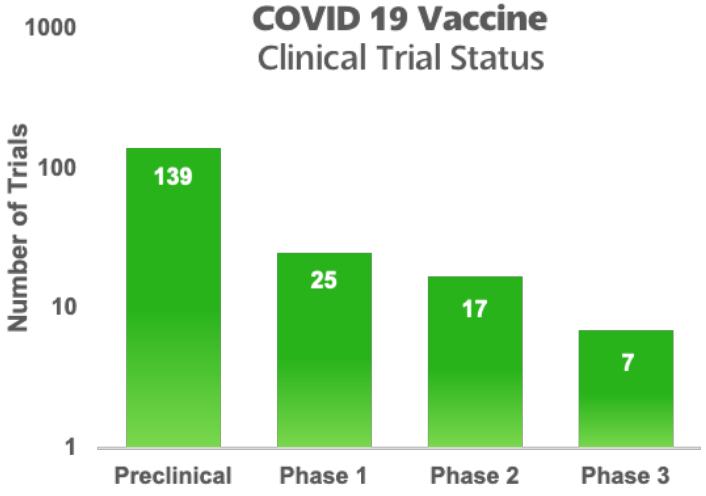
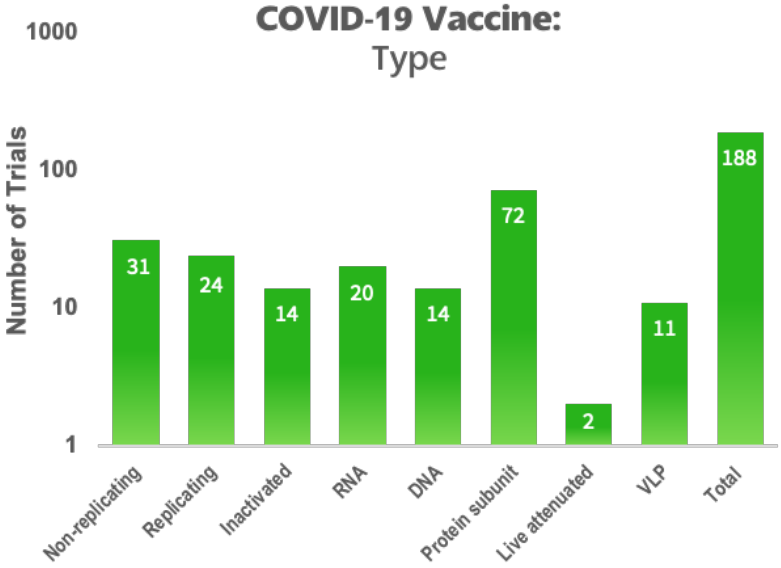
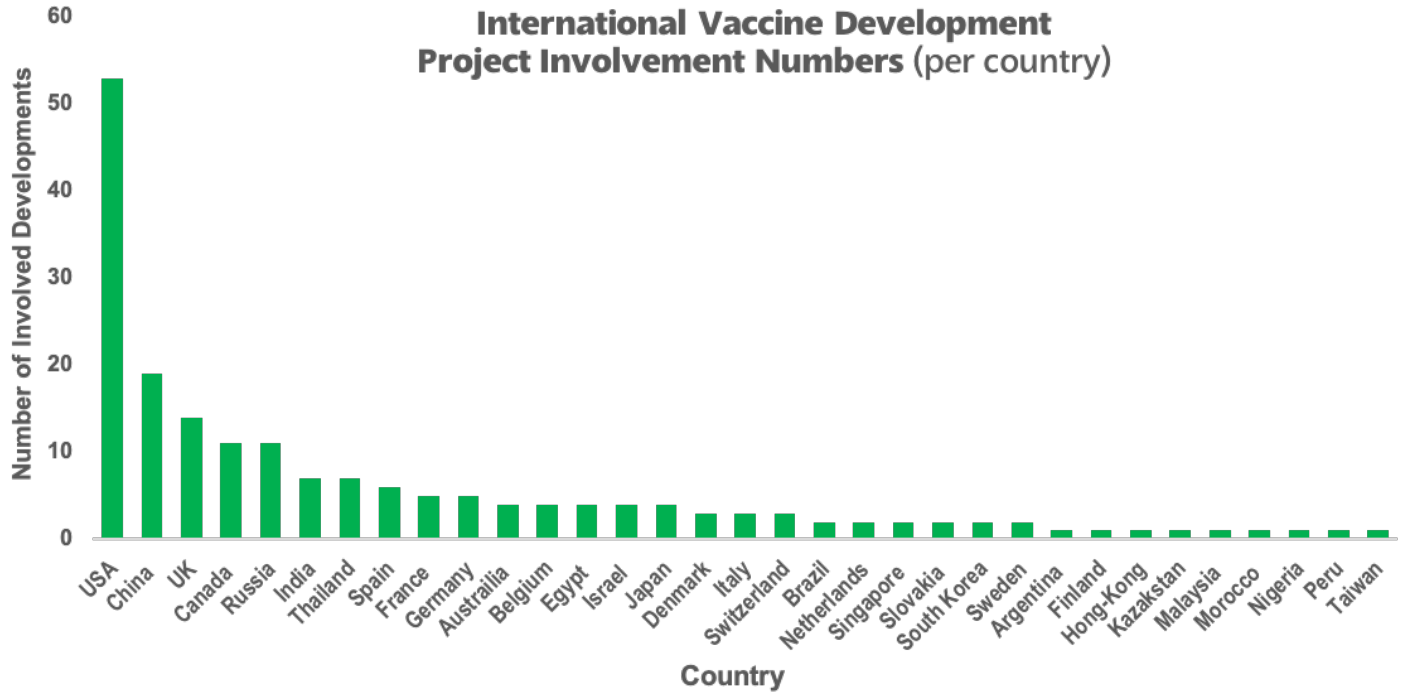
Evolution Briefing:
COVID-19 Vaccine Update

Since the virus first emerged in January, around 170 vaccine candidates are now in development, with 29 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.

Preclinical = 139 | **Phase 1 = 25** | **Phase 2 =17** | **Phase 3 = 7** | **Approval = 1**







Phase 3 - Vaccine Candidates

PHASE 3 EFFICACY TRIALS:

Scientists give the vaccine to thousands of people and wait to see how many become infected, compared with volunteers who received a placebo. These trials can determine if the vaccine protects against the coronavirus. In June, the Food and Drug Administration (FDA) said that a coronavirus vaccine would have to protect at least 50% of vaccinated people to be considered effective.

PHASE 3

COVID 19 Developer	Vaccine Platform	Country
University of Oxford/ Astra Zeneca	NR-Viral Vector	UK
Sinovac	Inactivated	China
Sinopharm/Wuhan & Beijing Institute of Biological Products	Inactivated	China
Moderna/NIAID	RNA	USA
BioNtech/Fosun Pharma/Pfizer	RNA	Ger/USA

UNIVERSITY OF OXFORD AstraZeneca

Vaccine Name
ChAdOx1 nCoV-19

Vaccine Type
Non replicating viral vector

Stage
Phase 3 (Total patients on trial 15,732)

Clinical Trial
https://covid19vaccinetrial.co.uk/

Development Timeline

- **Phase 1 April 23rd** (1112 patients)
- **Phase 2 May 4th** (10620 patients)
- **Phase 3 July 11th** (2000 patients)

Distribution
Limited September 2020 (30 million doses); Mass Q4 2020 (100 million doses)

Update

- Interim results from the ongoing Phase I/II COV001 trial, led by Oxford University, showed AZD1222 was tolerated and generated robust immune responses against the SARS-CoV-2 virus in all evaluated participants. The potential vaccine has entered final trials with late-stage studies currently underway in the UK, Brazil and South Africa and are due to start in the US. Trials will determine how well the vaccine will protect from the COVID-19 disease and measure safety and immune responses in different age ranges and at various doses.
- AstraZeneca forged deals with multiple countries to produce more than two billion doses of the investigational Covid-19 vaccine and hopes to secure approval by the end of this year.
- The UK has agreed high-profile vaccine supply agreements in recent weeks, including 100 million doses of AstraZeneca and Oxford's vaccine candidate which has cost the UK £65.5 million ($79 million).
- India-based 'Wockhardt' has signed up to complete 'fill and finish' work on millions of COVID-19 vaccine doses for exclusive use in the UK, including AstraZeneca and the University of Oxford's frontrunner candidate.

Potential Vaccines

Vaccine Name
Inactivated + alum

Vaccine Type
Inactivated

Stage
Phase 3 (Total patients on trial 10,036 patients)

Clinical Trial
www.sinovac.com - www.butantan.gov.br

Distribution
Limited September 2020 (30 million doses); Mass Q4 2020 (100 million doses)

Development Timeline

- **Phase 1 April 13th** (744 patients)
- **Phase 2 May 20th** (422patients)
- **Phase 3 July 2nd** (8870 patients)

Update

The Chinese biopharmaceutical has developed an inactivated vaccine that uses a non-infectious version of the virus to provoke an immune response. Sinovac launched a Phase III trial of its vaccine in Brazil. Sinopharm will be testing their inactivated vaccines in the United Arab Emirates (UAE). 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.

Vaccine Name
Inactivated

Vaccine Type
Inactivated

Stage
Phase 3 (Total patients on trial 21448 patients)

Clinical Trial
www.tiantanbio.com/

Distribution
End of 2020 (100M doses)

Development Timeline

- **Phase 1 April 29th** (6448 patients)
- **Phase 2 June 16th** (600 patients)
- **Phase 3 July 18th** (15,000 patients)

Update

- Sinopharm and Parana State have agreed to launch the fourth major COVID-19 vaccine trial in Brazil and will seek regulatory approval in the next two weeks
- Sinopharm has partnered with the UAE's government and Group 42 Healthcare, a local artificial-intelligence company, for its phase III trial with 15,000 volunteers.
- Sinopharm may face difficulty as they try to push vaccines through Phase III trials, a crucial stage of testing that is needed to prove efficacy and secure approval from regulators. These trials usually require tens of thousands of participants and, with the outbreak in China largely under control, companies are having to test their vaccines elsewhere. However, researchers say they may still face struggle with the enrollment of such a large quantity of participants and the employment of a sufficient number of health-care professionals to collect data.

Potential Vaccines

Vaccine Name
mRNA-1273 LNP encapsulated mRNA
Vaccine Type
RNA
Stage
Phase 3 (Total patients on trial 30,755 patients)
Clinical Trial
https://clinicaltrials.gov/ct2/show/NCT04470427

Development Timeline

- **Phase 1 March 16th** (155 patients)
- **Phase 1 March 16th** (600 patients)
- **Phase 3 July 27th** (30,000 patients)

Update

- Moderna's vaccine candidate 'mRNA-1273' is one of the few to have begun Phase III safety trials (with plans to enrol 30,000 people) and results are expected as early as October.
- Moderna has received $1 Bn from the US government under a plan to accelerate vaccine development.
- Last month, results from early stage of trials showed that Moderna's experimental vaccines produced a robust immune response in all 45 individuals who participated.
- Moderna has been working to develop mRNA technology that could turn the body's cells into drug factories. In order for the approach to work, Moderna needs to safely deliver the mRNA to the body's cells without the payload breaking down in the bloodstream. As a result, any mRNA vaccine or therapeutic consists of two components, namely the actual sequence mRNA and the delivery mechanism. Moderna has clearly engineered the first component, however, questions remain regarding the latter. Last week, the US Patent Trial and Appeal Board rejected Moderna's challenge to a patent, owned by Arbutus Biopharma, related to the lipid nanoparticle (LNP) technology that is crucial to Moderna's mRNA medicines.
- Moderna will charge between $32- $37 per dose, under what it termed cheaper 'pandemic pricing'.

Vaccine Name
mRNA BNT162
Vaccine Type
RNA
Stage
Phase 3 (Total patients on trial 38,000 patients)
Clinical Trial
https://www.pfizer.com/health/coronaviru
Distribution
2021 (>100M doses)

Development Timeline

- **Phase 1 April 20th** (444 patients)
- **Phase 2 April 29th** (7600 patients)
- **Phase 3 July 27th** (30,000 patients)

Update

- Pfizer and BioNTech began late-stage human trial for coronavirus vaccine
- BioNTech and China's 'Shanghai Fosun Pharmaceutical' announced the start of another COVID-19 vaccine trial in China on Wednesday, with a total of 144 participants designed to support the regulatory approval process for the Chinese market. They intent to confirm that the safety and immunogenicity profile observed in participants from the German and US trials is comparable to that of Chinese participants
- Pfizer and BioNTech will provide 120 million doses of vaccine from their BNT162 development program, assuming regulatory approval is granted, to Japan in the first half of 2021. The companies have recently signed a deal with the US to supply 100 million doses of vaccine for $1.95 billion. The announcement referred only to BNT162, which collectively includes four vaccine candidates incorporating BNT162b2, the same vaccine that entered a global Phase IIb/III clinical trial last week.

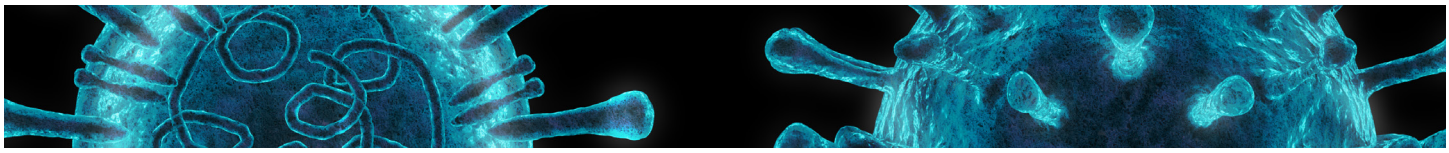
Phase 2 - Vaccine Candidates

PHASE 2 EXPANDED TRIALS:

Scientists give the vaccine to hundreds of people split into groups, such as children and the elderly, to see if the vaccine has alternative effects on different age groups. These trials further test the vaccine's safety and ability to stimulate the immune system.

PHASE 2

COVID 19 Developer	Vaccine Platform	Country
University of Oxford/ Astra Zeneca	NR-Viral Vector	UK
Moderna/NIAID	Inactivated	USA
CanSino Biological/Beijing Institute	NR-Viral Vector	China
Anhui Zhifei Longcom	Protein Subunit	China



康希诺生物股份公司
CanSino Biologics Inc.

Vaccine
Viral Vector Adenovirus Type 5 Vector

Vaccine Type
Non replicating viral vector

Stage
Phase 2 (Total patients on trial 608 patients)

Clinical Trial
http://www.cansinotech.com/

Distribution
Approved for military use.

Development Timeline

- **Phase 1 March 16th** (108 patients)
- **Phase 2 April 12th** (500 patients)

Update

- CanSino Biologics Inc.'s experimental coronavirus vaccine showed promising results in a mid-stage clinical study, paving the way for the next phase of tests as the Chinese company competes to deliver one of the first pandemic vaccines.
- CanSino's offering is made from a common-cold virus, tweaked to mimic the coronavirus and is ready to launch a Phase III trial. However, the Chinese government has already said that its vaccine can be used by the military, making CanSino the first company to have a vaccine for COVID-19 approved for limited use in people.
- CanSino emerged as one of the fastest movers on a vaccine in May, when it became the first firm to publish a full scientific study on its early human trials - a crucial step allowing researchers to assess a pharmaceutical product's potential.

Potential Vaccines

Vaccine
Adjuvanted recombinant protein

Vaccine Type
Protein Subunit

Stage
Phase 2 (Total patients on trial 950 patients)

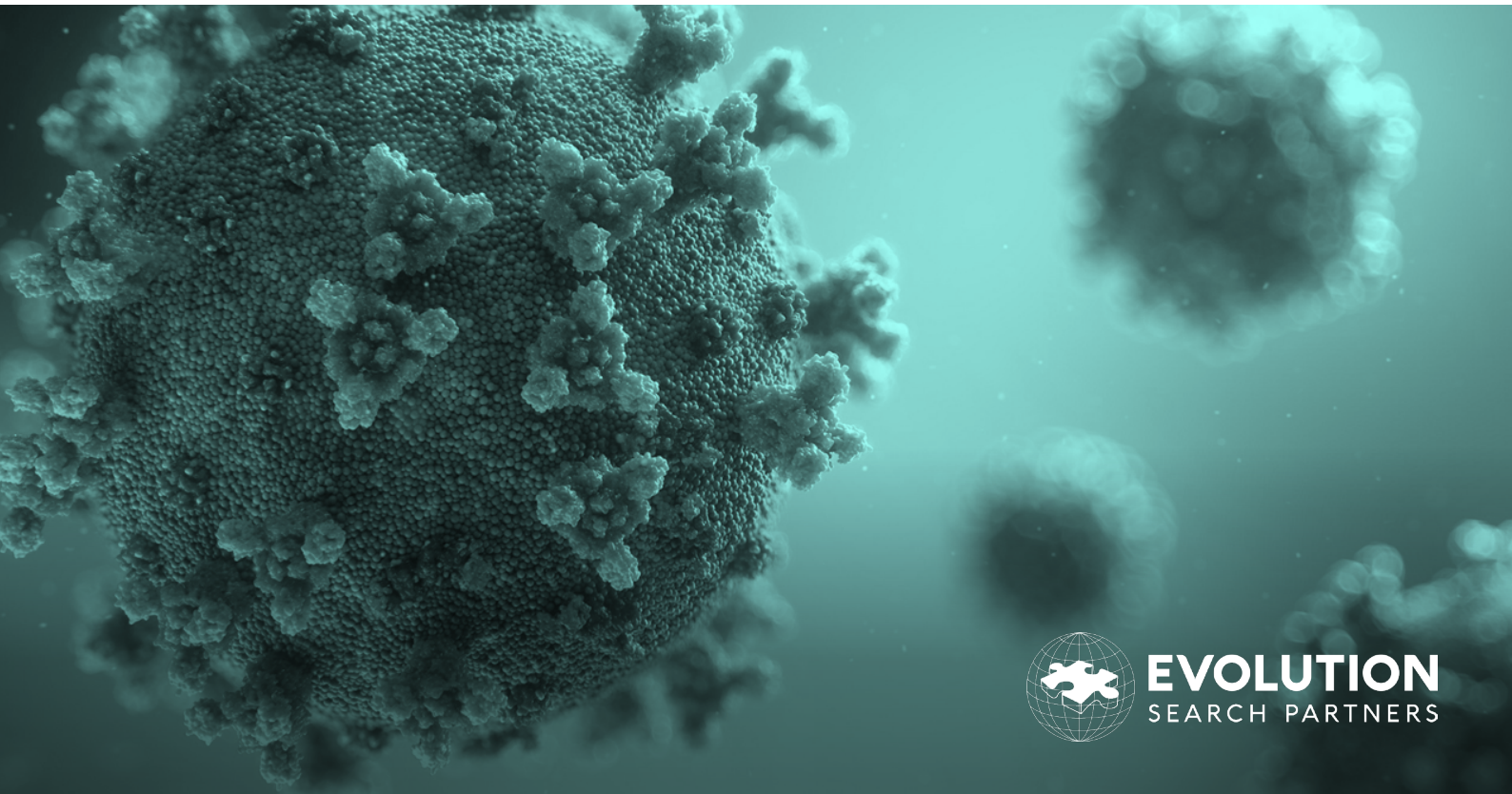
Clinical Trial
http://en.zhifeishengwu.com/about/zfgk/

Development Timeline

- **Phase 1 June 22nd** (50 patients)
- **Phase 2 July 12th** (900 patients)

Update

- The recombinant novel coronavirus vaccine, jointly developed by Zhifei Longkema Co. Ltd (a wholly-owned subsidiary of Chongqing Zhifei Biological Products Co. Ltd) and Institute of Microbiology of the Chinese Academy of Sciences, started the Phase II clinical trial in Hunan's Xiangtan County Center for Disease Control and Prevention, to evaluate the safety and immunogenicity of the vaccine.
- Results from a Phase I study of an RBD-Dimer vaccine that began in June are expected in September. A subsequent Phase II clinical trial is actively recruiting and will enrol 900 subjects.
- The vaccine adopts recombinant DNA technology and takes the unique dimer of the receptor-binding domain (RBD) of the novel coronavirus' spike glycoprotein (S protein) as an antigen, which is supplemented with traditional adjuvant. It does not carry any form of exogenous tag and has unique conformation, high immunogenicity, and excellent safety.



Phase 1/2 -Vaccine Candidates

PHASE I SAFETY TRIALS

Scientists give the vaccine to a small number of people to test safety and dosage as well as to confirm that it stimulates the immune system.

PHASE 1/2

COVID 19 Developer	Vaccine Platform	Country
University of Oxford/ Astra Zeneca	NR-Viral Vector	UK
Sinovac	Inactivated	China
Sinopharm/Wuhan & Beijing Institute of Biological Products	Inactivated	China
BioNtech/Fosun Pharma/Pfizer	RNA	Ger/USA
Chinese Academy of Medical Sciences	Inactivated	China
Inovio Pharma	DNA	USA
Osaka University/Takara	DNA	Japan
Cadila Healthcare	DNA	India
Genexine Consortium	DNA	South Korea
Bharat Biotech	Inactivated	India
Janssen Pharma	NR-Viral Vector	Belgium
Novavax	Protein Subunit	USA
Kentucky Bioprocessing Inc	Protein Subunit	USA
Arcturus/Duke	RNA	USA

Phase 1/2 -Vaccine Candidates

Osaka University/Takara/Cytiva

- **Vaccine**: DNA Plasmid
- **Vaccine Type**: DNA
- **Stage:** Phase 1-2 (Total patients on trial 30 patients)
- **Timeline:** Phase 1-2 June 29th (30 patients);

Inovio Pharma

- **Vaccine:** INO-4800 DNA with electroporation
- **Vaccine Type:** DNA
- **Stage:** Phase 1-2 (Total patients on trial 280 patients)
- **Timeline:** Phase 1 April 3rd (120 patients); Phase 1-2 June 22nd (160 patients)
- **Distribution:** Q4 2020 1 million doses

Cadila Healthcare

- **Vaccine:** DNA Plasmid
- **Vaccine Type:** DNA
- **Stage:** Phase 1-2 (Total patients on trial 1048 patients)
- **Timeline:** Phase 1-2 July 13th (1048 patients)

Janssen Pharma

- **Vaccine:** Ad26 alone or with MVA boost
- **Vaccine Type:** Non replicating viral vector
- **Stage:** Phase 1-2 (Total patients on trial 1045 patients)
- **Timeline:** Phase 1-2 July 13th (1045 patients);
- **Distribution:** Limited: Q2 20212; mass distribution Q4 2021 (1 billion doses)

Genexine Consortium

- **Vaccine:-** GX-19 DNA
- **Vaccine Type:** DNA
- **Stage:** Phase 1-2 (Total patients on trial 190 patients)
- **Timeline:** Phase 1-2 June 17th (50 patients)

Phase 1/2 -Vaccine Candidates

Kentucky Bioprocessing Inc

- **Vaccine:** RBD based
- **Vaccine Type:** Protein Subunit
- **Stage:** Phase 1-2 (Total patients on trial 180 patients)
- **Timeline:** Phase 1 July 22nd (180 patients)

Novavax/Emergent/Fujifilm

- **Vaccine:** NVX-CoV2373 Recombinant glycoprotein
- **Vaccine Type:** Protein Subunit
- **Stage:** Phase 1-2 (131 patients)
- **Timeline:** Phase 1-2 May 6th (Total patients on trial (131 patients)
- **Distribution:** 100M doses end of 2020; 1 billion doses 2021

Arcturus/Duke

- **Vaccine**: mRNA Lunar-Cov19
- **Vaccine Type**: RNA
- **Stage:** Phase 1-2 (85 patients)
- **Timeline:** Phase 1-2 July 22nd (Total patients on trial 85 patients)

Bharat Biotech

- **Vaccine:** Whole - Virion Inactivated (COVAXIN)
- **Vaccine Type:** Inactivated
- **Stage:** Phase 1-2 (Total patients on trial 1125 patients)
- **Timeline:** Phase 1-2 July 13th (1125 patients);

Distribution

Expected Distribution Dates

We do not yet have a vaccine that can be used to help protect people from contracting COVID-19. However, once a vaccine is proven to be both safe and effective it is evident that government, industry and healthcare providers will face the considerable task of figuring out how to distribute the vaccine fairly and efficiently.

Vaccines that have announced possible distribution dates if clinical trials are successful.

Vaccine	Researcher	Limited Distribution	Mass Distribution
ChAdOx1	**Jenner Institute (University of Oxford)**	Sep 2020 30M doses	Q4 2020 100M doses
NVX-CoV2373	**Novavax**	Q4 2020 100M doses	Q4 2021 1B doses
DNA INO-4800	**Inovio Pharma**	Q4 2020 1M doses	
Ad26	**Jannsen (Johnson & Johnson)**	Q2 2021	Q4 2021 1B doses
S protein	**Sanofi Pasteur + GSK**		H2 2021 600M doses

Commentary

The global race for covid-19 vaccines seems well underway to break all speed records. This said, the focus on rapid vaccine development fuelled by unprecedented political, financial, and populist pressures, births the dangerous prospect of missing the target of global access to effective vaccines that can curb the pandemic, while irreparably damaging public confidence for people desperate to return to their normal lives.

While the data from trials are encouraging, we have now seen promising data from multiple companies. It is not yet clear who is in the lead, as immunogenicity, B-cell and T-cell responses receive equal support for continued development, meaning current data fails to paint a clear picture of an obvious leader. Ultimately, awaited 'protection against disease' data remains the key piece to the puzzle to determine the true leaders of the vaccine race.

It is highly unlikely that a single vaccine will be equally effective and useful in all populations. Instead, we may need different types of vaccines inducing different kinds of immunity to effectively establish protection globally.

Of Interest

Chinese vaccine makers are among the front-runners. All three are already undertaking Phase III trials. This phase in the clinical trials involves thousands of volunteers to test the efficacy and safety of the candidate shots among a much wider age group and community. There are five Chinese vaccine projects among the frontrunners, if you include Fosun Pharma (working with Pfizer/BioNTec) whose mRNA vaccine candidate is also on Phase III trials, as well as Cansino/Beijing Institite of Biotechnology, now on Phase II.

The Russian government claims to have stolen a march on dozens of global rivals, including the US and UK, in the race to produce a viable coronavirus vaccine, stating the nation would start production of a vaccine next month and begin mass immunisation by October. While the Russian scientists made headlines last week 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 mid-July. According to recent reports, Russian scientists are hoping to launch the candidate for civil circulation in the next month.

Leading The Race:

University of Oxford AstraZeneca · BioNTech · Pfizer · moderna · NIH NIAID

Sources

World health Organisation
Fierce Biotech
GEN
Company websites/ press releases

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