



### RESEARCH ARTICLE

#### CATASTROPHE BY AN INVISIBLE GUEST- 2019 & ONGOING DRUG TRAILS ALONG WITH THE STATUS OF VACCINE PREPARATION

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#### Abstract

Within the first fifty days of the epidemic outbreak of novel corona virus in Wuhan, had killed more than eighteen hundred and infected over seventy thousand individuals. All the studies have reported that it is thought to be a member of the  $\beta$  group of corona viruses. The novel virus was named as Wuhan corona virus or 2019 novel corona virus (2019-nCoV) by the Chinese researchers because the epidemic began in Wuhan. The International Committee on Taxonomy of Viruses (ICTV) named the virus as SARS-CoV-2 and the disease as COVID-19. In the history, SARS-CoV (2003) infected 8098 individuals with a mortality rate of 9%, across 26 countries in the world; on the other hand, novel corona virus (2019) infected 120,000 individuals with mortality rate of 2.9%, across 109 countries, till date. It shows that the transmission rate of SARS-CoV-2 is higher than SARS-CoV and the reason could be genetic recombination event at S protein in the RBD region of SARS-CoV-2 may have enhanced its transmission ability. As a part of the study, we would like to highlight the comparison between SARS-CoV and SARS-CoV-2 along with their drug mechanism and their vaccine studies that came into existence till date.

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#### Introduction:-

Coronaviruses belongs to the family Coronaviridae and subfamily: Coronavirinae. These are the important pathogens of birds and mammals (1).

Coronaviruses are positive-sense RNA viruses and are currently classified into four genera:

1. Alpha Coronavirus.
2. Beta Coronavirus,
3. Gamma Coronavirus,
4. Delta Coronavirus.
  - i. Alpha Coronaviruses and beta coronaviruses are found in - mammals,
  - ii. Gamma coronaviruses and delta coronaviruses primarily infect- birds.

Interestingly, surveillance of coronaviruses in wild animals has led to the discovery of the greatest diversity of coronaviruses in bat and avian species, which suggests that these animals are the reservoirs. SARS (severe acute respiratory syndrome) is caused by the SARS corona virus, known as SARS CoV. Corona viruses commonly cause

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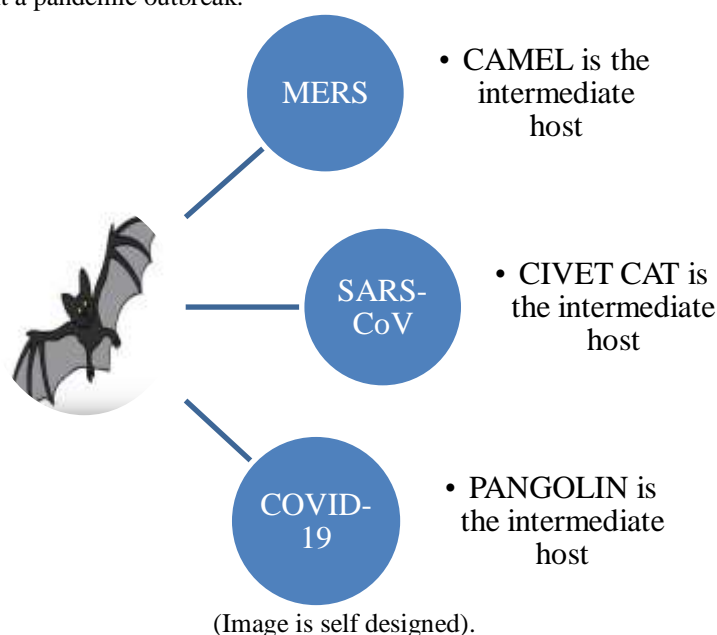
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infections in both humans and animals. There were 2 types of SARS outbreaks, which resulted in a highly contagious and potentially life-threatening form of pneumonia. These two outbreaks happened between 2002 & 2004 (2). An epidemic of SARS marked a huge decline by affecting nearly 26 countries and resulted in more than 800 cases and death of 774 took place in 2003 (3).

#### Origin OF SARS-COV & COVID-19:

The origin of the disease was observed by cataloging the genome from human cases, when viruses related to the SARS-CoV were identified in animals like Himalayan palm civets (*Paguma larvata*) and raccoon dogs (*Nyctereutes procyonoides*) in a live animal market in Shenzhen, China. They collected the nasal secretions from palm civets and observed the viral genomes from nasal swabs and found 99.8% homologous to the human SARS CoV, and represented a distinct phylogenetic group from the human isolates. They also found out that in the early epidemic, open reading frame 8 sequences from human isolates were identical to those from palm civets, this suggested animal to human transmission (zoonotic).

COVID-19 is the infectious disease caused by the most recently discovered coronavirus. This new virus and disease were unknown before the outbreak began in Wuhan, China, in December 2019. COVID-19 is now a pandemic affecting many countries globally (4). In December 2019, many pneumonia cases appeared in Wuhan, China, caused by a newly identified  $\beta$ -coronavirus, occurred in. This coronavirus was initially named as the 2019-novel coronavirus (2019-nCoV) on 12 January 2020 by the World Health Organization (WHO). WHO officially named the infection as coronavirus disease 2019 (COVID-19) and Coronavirus Study Group (CSG) of the International Committee proposed the name of the new coronavirus as SARS-CoV-2, both issued on 11 February 2020. The Chinese scientists rapidly isolated a SARS-CoV-2 from a patient affected by COVID within a short time on 7 January 2020 and came out to genome sequencing of the SARS-CoV-2. As of 1 March 2020, a total of 79,968 cases of COVID-19 have been confirmed in mainland China including 2873 deaths. Studies estimated the basic reproduction number ( $R_0$ ) of SARS-CoV-2 to be around 2.2 or even more (range from 1.4 to 6.5), and familial clusters of pneumonia outbreaks add to evidence of the epidemic COVID-19 steadily growing by human-to-human transmission and making it a pandemic outbreak.



COMPARITIVE FEATURES OF SARS-CoV & COVID-19: The table is written on the basis of various reviews. Few of the features of these viruses are listed below in table-1 with references as stated (5-19).

**Table 1:-** Comparison between SARS & COVID-19.

FEATURES	SARS-CoV	SARS-CoV-2 (COVID-19)
Family	Coronaviridae	Coronaviridae
Subfamily	Coronavirinae	Coronavirinae

<b>Order</b>	Nidovirales	Nidovirales
<b>Genome</b>	+ve sense Single stranded RNA	+ve sense Single stranded RNA
<b>Size</b>	100 -130 nm – with envelop 50nm – without envelop	65-125 nm in diameter
<b>Length Of The Genome</b>	More than 30 kb	26-36 kb
<b>Morphology</b>	Spherical to pleomorphic	Crown like spikes present around
<b>Envelope</b>	Lipid bilayer	YES
<b>Transmission</b>	Airborne – Respiratory droplets	Airborne – droplet nuclei of saliva
<b>WHO Declaration Of Outbreak</b>	2004	January 30, 2020.
<b>Primary Host</b>	Bat	Bat
<b>Intermediate Host</b>	Civet cat	Pangolin
<b>Diagnosis</b>	ELISA, Immunofluorescence, PCR	RT-PCR
<b>Incubation Period</b>	2-10 days	14 days

#### Drugs on trail to treat covid-19 (sars-cov-2) till date:

The idea is that treating the symptoms will help prolong a patient's life and buy time for their own immune systems to kick in and remove the infection. While research into related coronaviruses over the last few decades has brought some promising looking drugs, only large clinical trials on patients with COVID-19 will be able to reveal precisely whether these interventions are safe and effective.

The World Health Organization (WHO) declared this disease as pandemic (20). Chinese Centre for Disease Control and Prevention showed an increased mortality in people with diabetes (2.3% vs. 7.3%; overall vs. in patients with diabetes respectively) from a report of 72,314 cases of COVID-19 (21). People with diabetes and COVID-19 may need special attention and clinical care (22). In the absence of any known efficient therapy and because of the situation of a “public health emergency”, many drugs have been tried recently in the treatment for COVID-19 that includes a low-cost antimalarial drug chloroquine and its derivative hydroxychloroquine (HCQ), along with several other antiviral drugs. Because HCQ has been approved in the treatment of type 2 diabetes in India since 2014 as a third- or fourth-line drug, it would be interesting to research its impact in patients with diabetes, infected with COVID-19.

While research into related coronaviruses over the last few decades has brought some promising looking drugs, only large clinical trials on patients with COVID-19 will be able to reveal precisely whether these interventions are safe and effective. Unfortunately, these kinds of large trials take time to carry out, but they are ongoing. The World Health Organization (WHO) announced it has helped to launch four "mega trials" on COVID-19 and there are countless smaller ones coordinated in countries worldwide.

The WHO-backed trials are focusing on drugs that are thought to directly block SARS-CoV-2 – the virus strain that causes COVID-19 – from replicating inside our lungs. Below are some of the main drugs these trials are looking at (23-26).

**Table 2:-** Drugs that are on trail to treat COVID-19.

<b>Drug name</b>	<b>Mechanism of the drug</b>	<b>Early used to treat</b>
Remdesivir	Targets key viral proteins involved in making new copies of the virus and prevents them from working, prevents viral replication	Ebola
Lopinavir/ ritonavir	Blocks the viral protein named “proteases”, prevents cellular entry of the virus	HIV
Chloroquine/ hydroxychloroquine	Blocks key element of virus infection machinery using a small size molecules, changes the ph of the endosomes, prevents post entry events to some extent	SARS-CoV
Japan flu drug / Avigan	Works by preventing certain viruses from replicating, seemed to shorten the duration of the virus as well as improve lung conditions	Influenza

Arthritis drug	It blocks a cell receptor that binds something called Interleukins (IL-6), that can trigger dangerous inflammatory cascades.	COVID-19 pneumonia
Losartan	Losartan works by blocking a receptor, or doorway into cells that the chemical called angiotensin II uses to enter the cells and raise blood pressure. SARS-cov-2 binds to the angiotensin-converting enzyme-2 (ACE2) receptor, and it's possible, the thinking goes, that because losartan might block those receptors, it may prevent the virus from infecting cells.	Hypertension
Ribavirin	Inhibits viral RNA synthesis and mrna capping	RSV infection, hepatitis C and some viral hemorrhagic fevers
Ribavirin + interferon	Inhibits viral replication	MERS- reported only few
Camostat mesilate	Blocks viral maturation and entry to the cells	Effectively blocked SARS-CoV-2 in lung cells in vitro
Darunavir/ cobicista	Blocks viral cellular entry	HIV
Favipiravir	Inhibits viral RNA-dependent polymerase	Influenza, bunya virus, filovirus
Umifenovir	Inhibits fusion between viral and cellular membrane	Antiviral agent against other corona viruses
SARS-CoV-2 specific protease drug	Blocks viral infectivity	Data not available
SARS-CoV-2 specific antibody	Binds to the virus and block infection, binds to infected cells and change the immune system	Trail on SARS-CoV-2
Oseltamivir	Inhibits viral replication	HIV
Baloxivir marboxil	Inhibits influenza viral replication	Approved for uncomplicated influenza through oral route
Interferon $\beta$ 1	Stimulates innate antiviral immunity	MERS-CoV- in animal studies.
Interferon $\beta$ + lopinavir	Inhibits viral replication	Ongoing study for SARS-CoV-2
Interferon $\alpha$ (aersolized)	Stimulates innate antiviral immunity	MERS

\*SARS- severe acute respiratory syndrome, MERS- Middle-East respiratory syndrome, HIV- Human Immunodeficiency syndrome, COVID-19- Corona virus disease 2019.

#### A detailed collection of vaccine study of covid-19:

Vaccines usually take years to develop. After research, it is tested on animals and then undergoes **human trials** — a controversial method of intentionally injecting the virus into people.

Each vaccine has to be tested for safety and efficacy in three phases — in **phase one**, small groups of people receive the trial vaccine; in **phase two**, it is administered to those who have characteristics similar to whom the new vaccine is intended; and in **phase three**, it is injected into several thousand people. Finally, Researchers worldwide are working around the clock to find a vaccine against SARS-CoV-2, the virus causing the COVID-19 pandemic. Experts estimate that a fast-tracked vaccine development process could speed a successful candidate to market in approximately 12-18 months, if the process goes smoothly from conception to market availability. This tracker lists COVID-19 vaccine candidates currently in Phase 1-3 trials, as well as major candidates in pre-

clinical stages of development and research. The below information is listed as per reviews from various articles as reference numbering was given (27-34).

### **Phase 2/3:**

#### **Organizations:**

University of Melbourne and Murdoch Children's Research Institute (Australia); Radboud University Medical Center (The Netherlands); Faustman Lab at Massachusetts General Hospital (MGH) (United States)

Vaccine candidate: Bacillus Calmette-Guerin (BCG) live-attenuated vaccine for COVID-19

Original indication: Tuberculosis (TB) pediatric vaccine

Status: The randomized, controlled, Phase 3 BRACE trial in Australia is currently recruiting and aims to recruit 4,170 healthcare workers in hospitals in Australia. Researchers in The Netherlands launched the randomized, parallel-assignment, phase 3 BCG-CORONA trial on March 31 and plan to enroll 1,500 healthcare workers to receive the BCG vaccine or placebo. The Faustman Lab is currently evaluating the BCG vaccine's effectiveness in type 1 diabetes and is seeking funding to launch trial to assess whether the vaccine helps prevent COVID-19 in healthcare workers, according to independent reporting from the New York Times.

ClinicalTrials.gov Identifiers: NCT04327206, NCT04328441

### **Phase 2:**

#### **Company: Moderna:**

Vaccine candidate: mRNA-1273

Details: Moderna is the Massachusetts-based biotech company behind mRNA-1273, a vaccine candidate developed using prior studies of related coronaviruses, such as severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS).

Study Design: Phase 1, open-label, dose-ranging clinical trial of 105 healthy participants between 18-55 years old, including cohorts of adults aged 56-70 years and 71 years and older.

Institution: Kaiser Permanente Washington Health Research Institute

Status: FDA's successful review of Moderna's investigational new drug application (IND) allows the company to progress mRNA-1273 to Phase 2 testing. The company is finalizing the protocol for a Phase 3 trial, expected to start in early summer 2020, according to a statement.

ClinicalTrials.gov Identifier: NCT04283461

#### **Funding:**

NIAID, BARDA

#### **Organization:**

Beijing Institute of Biological Products/Wuhan Institute of Biological Products; the China National Pharmaceutical Group (Sinopharm)

Vaccine candidate: No name announced

Details: Researchers at Sinopharm and the Wuhan Institute of Virology under the Chinese Academy of Sciences are developing an inactivated COVID-19 vaccine candidate.

Study details: A randomized, double-blind, placebo parallel-controlled Phase 1/2 clinical trial of healthy individuals starting at 6 years old.

Status: On 30 April, Sinopharm told China Daily the vaccine had received approval from the National Medical Products Administration and had reached Phase 2 status.

Chinese Clinical Trials Registry Identifier: ChiCTR2000031809

### **Phase 1:**

#### **Company: CanSino Biologics**

Vaccine candidate: Ad5-nCoV

Details: China's CanSino Biologics has developed a recombinant novel coronavirus vaccine that incorporates the adenovirus type 5 vector (Ad5).

Study Design: A Phase 1 clinical trial of 108 participants between 18 and 60 years old who will receive low, medium, and high doses of Ad5-nCoV. A planned Phase 2 trial has identical inclusion criteria.

Institution: Tongji Hospital; Wuhan, China

Status: Preliminary safety data from the Phase 1 trial allowed the company to plan to initiate a Phase 2 trial, according to an announcement.

Chinese Clinical Trial Registry Identifier: (Phase 1: ChiCTR2000030906; Phase 2: ChiCTR2000031781)  
ClinicalTrials.gov Identifier: NCT04313127

**Organization:**

The University of Oxford

Vaccine candidate: ChAdOx1

Details: The Oxford Vaccine Group at the University of Oxford has identified a new vaccine candidate for COVID-19, a chimpanzee adenovirus vaccine vector called ChAdOx1. The team has previously developed a MERS vaccine.

Study Details: A Phase 1/2 single-blinded, multi-center study of 510 healthy adult volunteers aged 18-55 years randomized to receive an intramuscular vaccine (ChAdOx1) or MenACWY, a vaccine that protects against meningococcal bacteria A, C, W and Y.

Status: The Oxford COVID Vaccine Group announced on 21 April that they have received funding from the UK Secretary of State for Health. According to The New York Times, rhesus macaques given ChAdOx1 and then “exposed to heavy quantities of the virus” were considered healthy 28 days later. On 24 April, investigators said they had begun human testing in around 1,100 people.

ClinicalTrials.gov Identifier: NCT04324606

**Company: Inovio Pharmaceuticals**

Vaccine candidate: INO-4800

Details: Inovio is developing a DNA vaccine for SARS-CoV-2 that is in line with other DNA vaccines the company is developing, such as for the MERS coronavirus. The vaccine is injected intradermally through a device which Inovio plans to scale production of while they wait for results of INO-4800.

Study design: A non-randomized, open label Phase 1 trial of 40 healthy volunteers who will receive one or two intradermal injections (1.0 mg) of INO-4800 at baseline and at 4 weeks, followed by electroporation. There is also a Phase 1/2 parallel trial set to take place in South Korea concurrently with the U.S. trial.

Status: On 16 April, Inovio and The International Vaccine Institute (IVI) announced they are working with the Korea National Institute of Health (KNIH) to conduct a Phase 1/2 clinical trial in South Korea. Enrollment in the 40-person phase 1 trial was complete as of 28 April, and Inovio expects interim results in late June, according to a press release.

ClinicalTrials.gov Identifier: NCT04336410

**Companies: Pfizer and BioNTech**

Vaccine candidate: BNT162

Details: Pfizer and BioNTech have announced an agreement to collaborate on developing four COVID-19 vaccine candidates originally developed by BioNTech. Two candidates are nucleoside modified mRNA-based (modRNA), one is uridine containing mRNA-based (uRNA), and the fourth candidate is self-amplifying mRNA-based (saRNA). The companies had previously agreed to develop an mRNA-based influenza vaccine in 2018.

Study Design: In Germany, a Phase 1/2 trial is planned for 200 healthy participants between 18 and 55 years old, with a vaccine dose range of 1 µg to 100 µg. In the US, 360 healthy participants will be enrolled in cohorts of individuals aged 18-55 years, 65-85 years and 18-85 years.

Status: On 22 April, the Paul-Ehrlich-Institute in Germany approved BNT162 for a Phase 1/2 trial. Human trials in two US locations began on 5 May, Pfizer and BioNTech noted in an announcement.

EU Clinical Trials Register Identifier: 2020-001038-36

ClinicalTrials.gov Identifier: NCT04368728

**Company: Sinovac**

Vaccine candidate: Formalin-inactivated and alum-adjuvanted candidate vaccine for COVID-19

Details: Sinovac is working on a formalin-inactivated and alum-adjuvanted candidate vaccine for COVID-19.

Study Details: A randomized controlled Phase 1 trial of 144 healthy participants between 18 and 59 years old who will receive “two different dosages” of the vaccine or placebo.

Status: On 17 April, Sinovac released details of its Phase 1 randomized controlled trial and said initial enrollment was complete and participants had received their first vaccination doses.  
ClinicalTrials.gov Identifier: NCT04352608

**Pre-clinical:**

Organization: University of Pittsburgh's Center for Vaccine Research

Vaccine candidate: PittCoVacc

Details: Researchers at the University of Pittsburgh have received a \$4.9 million grant from CEPI to develop a COVID-19 vaccine candidate.

Status: On 2 April, University of Pittsburgh School of Medicine scientists announced they had developed a candidate COVID-19 vaccine that is effective in mice, delivered through a fingertip patch. According to a paper published in EBioMedicine, the vaccine creates antibodies in mice that the researchers believe is sufficient to neutralize the virus.

**Company: Novavax**

Vaccine candidate: NVX-CoV2373

Details: Biotech Company Novavax announced in March that it has produced several recombinant nanoparticle vaccine candidates for COVID-19 and is vetting them in animal testing.

Status: On 8 April, Novavax said they plan to start a Phase 1 trial in mid-May, according to a company announcement.

**Company: CureVac**

Vaccine candidate: No name announced

Details: CureVac announced they are developing an mRNA-based COVID-19 vaccine "within a few months," according to a press release.

Status: The Company plans to start clinical trials in the summer and have identified two study centers.

**Company: Genex Biotechnology**

Vaccine candidate: Ii-Key peptide COVID-19 vaccine

Details: Biotech Company Genex subsidiary NuGenex Immuno-Oncology is spearheading a vaccine project to create an Ii-Key peptide vaccine against COVID-19.

Status: In a company press release dated 27 February, Genex said they wanted to produce a vaccine candidate that could be tested in humans "within 90 days."

**Company: Vaxart**

Vaccine candidate: Oral recombinant COVID-19 vaccine

Details: Vaxart announced their agreement with Emergent Biosolutions to develop and manufacture their oral recombinant vaccine candidate for COVID-19.

Status: The Company plans to initiate a Phase 1 clinical study "early in the second half of 2020," according to a press release. On 21 April, the company said they had received "positive pre-clinical results" for its oral vaccine candidate.

**Company: Imperial College London**

Vaccine candidate: Self-amplifying RNA vaccine

Details: Imperial College London researchers are developing a self-amplifying RNA vaccine for COVID-19. They developed a vaccine candidate within 14 days of receiving the sequence from China.

Status: Animal testing is underway. On 22 April, Imperial College London said they had secured funding from the Secretary of State for Health and planned to begin clinical trials in June 2020.

**Company: Medicago**

Vaccine candidate: Plant-based COVID-19 vaccine

Details: Medicago, which recently developed a seasonal recombinant quadrivalent virus-like particle (VLP) influenza vaccine, reported they created coronavirus VLP 20 days after working with the SARS-CoV-2s gene.

Status: The Company says their vaccine is in the pre-clinical testing stage, and they expect to begin human testing in July or August of 2020.

**Company: Takis Biotech**

Vaccine candidate: DNA-based vaccine for COVID-19

Details: The partnership between Takis Biotech and Applied DNA Sciences has resulted in four DNA vaccine candidates for COVID-19.

Status: Takis expects preclinical testing results in April 2020; their final vaccine candidate could begin human testing by fall, according to a company press release. On 10 April, Takis said their candidate exhibited a “strong antibody response” against COVID-19.

**Companies: Johnson & Johnson and BARDA**

Vaccine candidate: No name announced

Details: Johnson & Johnson has announced their intention to develop a COVID-19 vaccine, using their AdVac and PER.C6 systems, which were also used to develop the company’s Ebola vaccine.

Status: As of 30 March, the company had narrowed its focus to a lead vaccine candidate and two back-up candidates and aimed to start Phase 1 trials in September 2020, according to a statement.

**Company: Altimmune**

Vaccine candidate: Intranasal COVID-19 vaccine

Details: Altimmune has developed a COVID-19 vaccine candidate using the same technology they used build their influenza vaccine, NasoVAX. The COVID-19 vaccine would be delivered intranasal in a single dose.

Status: According to a company press release, animal testing is beginning, and clinical testing is slated for August 2020 or later.

**Early research:****Companies: GlaxoSmithKline, Sanofi, Clover Biopharmaceuticals and Xiamen Innovax**

Vaccine candidate: COVID-19 S-Trimer along with various vaccine adjuvant candidates

Details: GSK has entered into a collaboration agreement with Chinese company Clover Pharmaceuticals to use its adjuvant technology for Clover’s COVID-19 candidate S-Trimer. GSK also has partnered with Chinese company Xiamen Innovax Biotech and Sanofi, offering its vaccine adjuvant technology to the both companies.

Status: In a press release, GSK says its S-Trimer candidate is being “rapidly developed,” and pre-clinical studies are being planned. On 14 April, Sanofi and GSK announced their plan to collaborate on an adjuvanted vaccine and bring it to clinical trials by the second half of 2020.

**Companies: ReiThera; Leukocare; Univercells**

Vaccine candidate: Single-dose adenovirus-based COVID-19 vaccine

Details: Biotechnology companies ReiThera (Italy), Leukocare (Germany) and Univer cells (Belgium) are partnering to develop an adenovirus-based COVID-19 vaccine.

Status: ReiThera said the first human clinical trials are planned for summer of 2020 in Italy, according to a press release.

**Company: Heat Biologics**

Vaccine candidate: gp96-based vaccine

Details: The biotech company Heat Biologics announced it is pairing with the University of Miami to use the gp96 heat shock protein backbone to develop at least one COVID-19 vaccine.

Institution: University of Miami Miller School of Medicine

Status: On 29 April, Heat Biologics said it planned on developing a cell-based vaccine within the second quarter of 2020.

**Companies: CSL and The University of Queensland**

Vaccine candidate: Molecular clamp vaccine for COVID-19

Details: Researchers at the University of Queensland have achieved a proof-of-concept vaccine candidate for COVID-19.

Institution: The University of Queensland

Status: In a press release, the university said they will begin further development prior to pre-clinical testing.

**Company: Sanofi and Translate Bio**

Vaccine candidate: Repurposed SARS vaccine and mRNA vaccine candidate



Details: Sanofi announced in February that it was developing a COVID-19 vaccine candidate under its egg-free, recombinant DNA platform using work from a previous SARS vaccine and in partnership with the BARDA. Sanofi also announced in late March that they were partnering with Translate Bio to create an mRNA vaccine candidate for COVID-19.

Status: The Company hopes to have a vaccine candidate for lab testing within 6 months, according to original reporting from STAT.

**Company: ExpreS2ion Biotechnologies**

Vaccine candidate: No name announced

Details: Denmark-based ExpreS2ion won a European Union (EU) Horizon 2020 grant to fund a COVID-19 vaccine candidate.

Status: The Company decided to perform a Phase 1/2a clinical trial and aim to begin clinical testing within 12 months.

**Company: University of Saskatchewan Vaccine and Infectious Disease Organization-International Vaccine Centre**

Vaccine candidate: No name announced

Details: The University of Saskatchewan's Vaccine and Infectious Disease Organization-International Vaccine Centre (VIDO-InterVac) is developing a protein subunit vaccine for COVID-19, recently received \$1 million to accelerate COVID-19 vaccine candidate testing.

Status: Preclinical.

**Company: EpiVax; Entos Pharmaceuticals**

Vaccine candidate: Ii-Key peptide vaccine; DNA plasmid vaccine candidate

Details: EpiVax is developing two Ii-Key peptide vaccine candidates against COVID-19. The company is also developing a DNA plasmid vaccine candidate with Entos Pharmaceuticals.

Status: EpiVax's CEO said a vaccine could be ready within 5-6 months if the company receives the right level of funding. They have not currently released a timeline for the vaccine candidate being developed with Entos Pharmaceuticals.

**Company: Geovax and Bravovax**

Details: In January, Chinese biotech companies Geovax and Bravovax announced they would collaborate to create a modified vaccinia ankara virus like particles (MVA-VLP) vaccine candidate for COVID-19.

Status: Geovax said it's currently in the process of narrowing their vaccine candidates down from three to one, and from there will move to testing in humans.

**Company: Greffex**

Vaccine candidate: Adenovirus-based vector vaccine for COVID-19

Details: Genetic engineering Company, Greffex is developing an adenovirus-based vector vaccine for COVID-19.

Status: The company recently announced its vaccine candidate has entered the animal testing stage.

**Company: Walter Reed Army Institute of Research and United States Army Medical Research Institute of Infectious Diseases**

Vaccine candidate: No name announced

Details: Walter Reed, together with the U.S. Army Medical Research Institute of Infectious Diseases, is working on a COVID-19 vaccine. Researchers at Walter Reed had previously developed a MERS vaccine, and are using that work to help them create a vaccine candidate for COVID-19.

Status: Walter Reed has developed several vaccine candidates, and have begun testing in animals, but have not yet indicated when they would begin clinical testing in humans.

**Organization: MIGAL Galilee Research Institute**

Vaccine candidate: Modified avian coronavirus vaccine

Details: The institute said it plans to create a new COVID-19 vaccine candidate by adapting its research in developing a vaccine for the genetically-similar avian coronavirus Infectious Bronchitis Virus (IBV).

Status: On 27 February, the institute said it planned to create the vaccine within the next 8-10 weeks, will seek safety approval within 90 days, and is in discussion with partners for human trials.

**Organization: Baylor College of Medicine**

Vaccine candidate: Re-purposed SARS vaccine for COVID-19; S1 or RBD protein vaccine candidate

Details: Researchers at the Baylor College of Medicine say they have a shelved vaccine from the 2003 SARS outbreak that could be repurposed for use in the COVID-19 pandemic. They are also developing an S1 or RBD protein vaccine as a targeted vaccine candidate for COVID-19.

Status: The University has not released details on developing or testing at this time.

**Organization: Institute Pasteur**

Vaccine candidate: No name announced

Details: Institut Pasteur is partnering with the Coalition for Epidemic Preparedness Innovations (CEPI) to develop a COVID-19 vaccine candidate.

Status: No other details have been released at this time.

**Company: Tonix Pharmaceuticals and Southern Research**

Vaccine candidate: Horsepox vaccine with percutaneous administration

Details: Biopharmaceuticals company Tonix is partnering with Southern Research to develop a COVID-19 vaccine candidate based on the company's horsepox vaccine, TNX-1800, is working

Status: Tonix hasn't offered a timeline for further development or testing.

**Organizations: Fudan University, Shanghai JiaoTong University, and RNACure Biopharma**

Vaccine candidate: mRNA vaccine candidate for COVID-19

Details: Fudan University has entered into a partnership with Shanghai JiaoTang University, and RNACure to develop a COVID-19 mRNA vaccine candidate. They are using two methods to develop an mRNA-based vaccine: using mRNA to express the receptor-binding domain of the spike protein of COVID-19 to induce neutralizing-antibodies, and developing mRNAs that can instruct the host to produce virus-like particles similar to SARS-CoV-2.

Status: No details on further development or testing are available at this time.

**Company: Arcturus Therapeutics and Duke-NUS Medical School**

Vaccine candidate: No name announced

Details: Arcturus and Duke are partnering to develop a COVID-19 vaccine candidate that uses Arcturus' self-replicating RNA and nanoparticle non-viral delivery system.

Status: The companies have not released further details about development or testing.

**Organization: Peter Doherty Institute for Infection and Immunity**

Vaccine candidate: No name announced

Details: The Doherty Institute has received \$3.2 million from the Jack Ma foundation to accelerate the creation of a COVID-19 vaccine with an active and passive platform.

Status: No other details have been released at this time.

**Organization: Tulane University**

Vaccine candidate: The Tulane National Primate Research Center has launched a COVID-19 research program to help develop a vaccine candidate.

Status: The organization has not established a timeline for testing, but has indicated it will use a primate model for animal testing.

**Company: Sorrento Therapeutics, Inc. and SmartPharm Therapeutics Inc.**

Vaccine candidate: Gene-encoded antibody vaccine candidate

Details: In late March, Sorrento Therapeutics announced a collaboration with SmartPharm Therapeutics to develop a next-generation, gene-encoded antibody vaccine for COVID-19.

Status: In a press release, SmartPharm Therapeutics said it hopes to have a candidate within several months.

**Organization: University of Bristol (Imophoron)**

Vaccine candidate: No name announced

Details: On 7 April, Imophoron, a spin-out company from the University of Bristol's BrisSynBio research center, has announced it is producing several vaccine candidates for COVID-19 using its ADDomer platform.

Status: Vaccine development is in a pre-clinical stage, according to a press release from the university.

**Company: IMV**

Vaccine candidate: DPX-COVID-19

Details: IMV, a biotech company based in Canada, announced its intent to create a vaccine candidate for COVID-19 based off DPX-Survivac, a T-cell activating immunotherapy antigen vaccine currently being tested in trials for effectiveness against recurrent ovarian cancer, advanced and recurrent solid tumors, and survivin-expressing diffuse large B-cell lymphoma DLBCL.

Status: The company is developing a phase 1 clinical study of 48 healthy subjects and plans to begin the trial in the summer of 2020, according to a press release.

**Organization: University of Waterloo**

Vaccine candidate: Intranasal DNA-based vaccine candidate

Details: Researchers at the University of Waterloo in Ontario, Canada, have announced they are developing a COVID-19 DNA-based vaccine that would be delivered through a nasal spray, stimulating an immune response in the nasal cavity.

Status: The delivery mechanism for the vaccine has been completed, but more designing and testing is needed to modify the system for COVID-19, according to a press release from the university.

**Organization: University of Georgia**

Vaccine candidate: Unnamed vaccine candidate

Details: Researchers at the University of Georgia have announced they are developing a COVID-19 vaccine candidate together with the university's College of Veterinary Medicine.

Status: No other details on testing or timing have been released at this time.

**Organization: Rochester Clinical Research**

Vaccine candidate: RNA vaccine candidate

Details: The Rochester Clinical Research team is developing an RNA vaccine candidate for COVID-19.

Study Details: A 2-year study of healthy participants between 18 years and 85 years of age who have not been diagnosed with COVID-19.

Status: The team is currently evaluating qualified participants, but no other details are available at this time.

**Organizations: Verndari and University of California, Davis**

Vaccine candidate: Single-dose patch delivery vaccine

Details: California-based biotech company Verndari is working with the University of California, Davis to develop a vaccine candidate for COVID-19 delivered through a single-dose patch.

Status: Testing in mice is expected to begin on 1 May, according to a Verndari company press release.

**Conclusion:-**

This review provides updated information about COVID-19. SARS-CoV-2 can affect patients of different age groups. COVID-19 can present as asymptomatic carriage, ARD, and pneumonia. To date, effective treatment for SARS-CoV-2 is lacking; however, few trials investigating the clinical efficacy of the drugs that stated in the review are underway in various countries all over the world. Currently, effective infection control intervention is the only way to prevent the spread of SARS-CoV-2.

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The author is not aware of any affiliations, memberships, funding, or financial holdings that might be perceived as affecting the objectivity of this review.

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