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Divyansh Sehgal
Legal Research Associate at Sanrachna SGT University, Daryaganj, Delhi, India

Corresponding Author:
Divyansh Sehgal
Legal Research Associate at SGT University, Daryaganj, Delhi, India

Analysis of vaccines to tackle Covid-19 with patent review

Divyansh Sehgal

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Abstract
As humans are spreading throughout the world, infectious diseases have been a constant companion such as Bubonic Plague (200 Million deaths), 17th Century Great Plague (3 Million deaths), Plague of Justinian (30-50 Million deaths), etc. Coronavirus Disease (COVID-19) which was published on 11th January 2020 showing the intensity of Global research and development activity to develop a drug/vaccine against the disease. COVID-19 is an infectious disease caused by a newly discovered coronavirus. Human to human transmission has created a pandemic situation across the world. Pharmaceutical companies play a crucial role in this scenario to provide Drugs/Vaccines/Therapies to treat and tackle the novel coronavirus disease of 2019. This paper consists of the Drugs and Vaccines which are developed, or in the process of development, their current stage of development (clinical trials) with their patent review.

Keywords: vaccines, Covid-19, patent

Introduction
Coronavirus was discovered in the early 1960s. The name of the virus comes from the crown-like spikes it has on its surface while the world "Corona" is derived from a Latin word "crown". Coronaviruses (CoV) are a large family of viruses that cause illness ranging from a common cold to more severe diseases. Novel coronavirus (nCoV) is a new strain that has not been previously ascertained in humans.
Coronavirus is one of the common viruses that can cause infection in your sinuses, nose, or upper throat. Most of the coronaviruses are not dangerous and are present with mild symptoms and are treated easily symptomatically, but it killed 858 people in MERS in 2015 and this was a result of a severe presentation causing respiratory failure [1]. To be more precise, Coronavirus comes under the family of Orthocoronavirinae and is surrounded by envelope like frame which gives a sense of the single-stranded RNA genome. This document aims at providing an analysis of Drugs/Vaccines/Therapies developed, developing, or under clinical trials to prevent the coronavirus disease 2019 outbreak.

Drugs/Vaccines
1. Chloroquine/Hydroxychloroquine
Description: Antimalarial Agent
Lead Developer: Sanofi
The antimalarials hydroxychloroquine and chloroquine have demonstrated antiviral activity against severe acute respiratory syndrome coronavirus 2 (SARS CoV2) in small, uncontrolled clinical trials. CQ and HCQ are well known to ophthalmologists because of retinal toxicity after long term usage for systemic lupus erythematosus (SLE) and other rheumatoid diseases. Hydroxychloroquine (HCQ) can effectively treat disease manifestations such as joint pain and rashes; reducing thrombotic events; prolong survival.

How is it working? What is the vaccine targeting?
It includes inhibition of viral enzymes or processes such as viral DNA and RNA polymerase, viral protein glycosylation, virus assembly, new virus particle transport, and release [2].
It also involves ACE2 cellular receptor inhibition, acidification at the surface of the cell membrane inhibiting fusion of virus, and immunomodulation of cytokine release [3].

Table 1: Clinical Trials Status

NCT04323527	Phase 2	NCT04321278	Phase 3
NCT04261517	Phase 3	NCT04318444	Phase 2 and 3
NCT04303507	Phase 4	NCT04322123	Phase 3
NCT04316377	Phase 4	NCT04328961	Phase 1
NCT04324463	Phase 3	NCT04307693	Phase 2
NCT04286503	Phase 4	NCT04315896	Phase 3
NCT04331600	Phase 4	NCT04328467	Phase 3
NCT04333732	Phase 2	NCT04308668	Phase 3
NCT04325893	Phase 3	NCT04318015	Phase 3
NCT04332991	Phase 3	NCT04332835	Phase 2 and 3
NCT04315948	Phase 3	NCT04321616	Phase 2 and 3
NCT04321993	Phase 2	NCT04330586	Phase 2

Table 2: Patent Review for the drug

EP0588430A1	Dated11.09.1993	WO2010027150A3	Dated 08.09.2008
CN104398514B	Dated28.10.2014	WO2019165337A1	Dated 16.02.2018
US5314894A	Dated 15.09.1992	CN102050781B	Dated 21.12.2010
US2546658A	Dated 23.07.1949	CN104230803B	Dated 28.08.2014
IN201821021981	Dated 11.06.2018		

2. NP-120 Ifenprodil

Description: Anti-Diabetic Nephropathy

Developer: Algernon Pharmaceuticals

Ifenprodil is an orally delivered small molecule that was originally developed by Sanofi to treat peripheral circulatory disorders. It is sold under the brand name of "Cerocal". Np-120 Ifenprodil is an N-Methyl-d-aspartate receptor glutamate receptor antagonist specifically targeting the NMDA-type subunit 2B. NP-120 was initially developed in the 1990s in French and Japanese markets for the treatment of circulatory disorders [4]. Algernon has also made the decisions to scale up cGMP manufacturing of Ifenprodil to support its quickly evolving clinical program for acute lung injury, its urgent clinical focus on COVID-19 coronavirus as well as its idiopathic pulmonary fibrosis (IPF) clinical program. Ifenprodil also exhibits agonist activity for the Sigma-1 receptor, a chaperone protein up-regulated during endoplasmic reticulum stress [5].

How does it work? What is the vaccine targeting?

- Glutamate is the main excitatory neurotransmitter that acts on glutamate receptors in the **central nervous system** (CNS) but overactivation of these receptors can cause severe damage to neural cells including death [6].
- Glutamate agonist NDMA can trigger acute lung injury which is a direct and indirect injury to alveolar epithelial cells and capillary endothelial cell causing diffuse pulmonary interstitial and alveolar edema and acute hypoxic respiratory failure [7].

Clinical Trial: Data awaited Patent Review: Open Source

3. Favilavir/ Favipiravir

Description: Antiviral Agent

Developer: Fujifilm and Zhejiang Hisun Pharma

Favipiravir is a broad-spectrum antiviral agent designed to potently and selectively inhibit RNA viruses RNA-dependent RNA polymerase. The drug has been previously used to treat Ebola patients in Guinea and Japan had approved Avigan for the novel or re-emergent influenza [8].

How does it work? What is the vaccine targeting?

- It is an effective antiviral drug for fighting RNA infections by inhibiting the RNA dependent RNA polymerase, which is mainly used for treating influenza in Japan and China.

Table 3: Clinical Trials Status Patent Review for the drug

NCT04310228	**Phase 3**
NCT04310228	Phase (status awaited)
NCT04333589	Phase (status awaited)
NCT04319900	Phase 2 and 3
WO2016120301A1	Dated 28.01.2015
CN107226794A	Dated 17.07.2017
CN106478528A	Dated 26.08.2016

4. TJM2

Description: Neutralising Antibody

Developer: I-Mab Biopharma

TMJ2 is a neutralizing body against the human granulocyte-macrophage colony-stimulating factor (GM-CSF) discovered by I-Mab which is an important cytokine that plays a critical role in acute and chronic inflammation [9] The company has also

successfully cleared the phase 1 single ascending dose stud of TJM2 in the United States of America [10].

How does it work? What is the vaccine targeting?
TJM2 is a humanized immunoglobulin G1 neutralizing antibody targeting the **cytokine granulocyte-macrophage** colony-stimulating factor (GM-CSF) with the potential to treat patients with autoimmune and inflammatory diseases in which GM-CSF plays a crucial role [11].

Clinical Trials: Clinical trial data awaited
Patent Review: Open Source

5. TZLS-501
Description: Anti-Interleukin Receptor
Developer: Tiziana Life Sciences
Tiziana Life Sciences, is administering TZLS-501 using a proprietary formulation technology and the tests have already shown that the treatment rapidly depletes circulating levels of IL-6 (interleukin, which helps in preventing lung damage) in the good blood, as excessive production of IL-6 leads to chronic inflammation and is believed to be associated with severe lung damage observed with COVID-19 [12].

How does it work? What is the vaccine targeting?
- Tiziana's anti-**IL-6R (interleukin 6 receptor)** mAb binds to both the membrane-bound and soluble forms of IL-6R and rapidly depletes circulating levels of IL-6 in the blood.
- Excessive production of IL-6 is the driver of chronic inflammation and is believed to be associated with withs severe lung damage observed.

Clinical Trials: Clinical trial data awaited
Patent Review: Patent Application filed

6. APN01
Description: Recombinant Human Angiotensin
Developer: Aperion Biologics
The APN01 drug is built on a previous discovery that ACE2 protein is the key for the receptor of the SARS virus, as well as to protect the lung [13]. This discovery was made by the University of British Columbia life sciences institute in alliance with the University of Toronto and Peking Medical Union College. This drug will be assessed for its capability of improving the outcomes in COVID-19 patients with a serious infection.

How does it Work? What is the Vaccine Targeting?
APN01 has a unique dual mode of action:
- APN01 imitates the human enzyme ACE2, which is used by the virus to enter cells. The virus binds to soluble ACE2/APN01, instead of ACE2 on the cell surface, which means that the virus can no longer infect the cells [14].
- At the same time, APN01 reduces the harmful inflammatory reactions in the lungs and protects against acute lung injury (ALI/acute respiratory distress syndrome (ARDS) [15].

Table 4: Clinical Trials Status

NCT04335136	**Phase 2**
Patent Review for the drug	
US20110020315A1	Dated 18.12.2007
AT506258A1	Dated 18.12.2007

7. Remdesivir GS-5734
Description: Antiviral Compound
Developer: Gilead Sciences
Remdesivir is an investigational nucleoside analog with a broad-spectrum antiviral. It has demonstrated in vitro and in vivo activity in animal models against the viral pathogens MERS and SARS which also type of coronaviruses and are structurally similar to COVID-19.
Remdesivir is chemically known as 2-ethylbutyl (2S)-2-(((2R, 3S, 4R, 5R)-5-(4-aminopyrrolo -(2,1-f)(1,2,4)triazin-7-yl)-5-cyano-3,4-dihydroxytetrahydrofuran-2-yl)-methoxy)(phenoxy) phosphoryl) amino) propanoate, is a novel antiviral drug in the class of nucleotide analogs [16].

How does it work? What is the vaccine targeting?
- Remdesivir acts as an RdRp inhibitor, targeting the viral genome replication process. The RdRp is the protein complex CoVs use to replicate their RNA-based genomes [17].
- After the host metabolizes Remdesivir into active NTP, the metabolite competes with adenosine triphosphate (ATP; the natural nucleotide normally used in this process) for incorporation into the nascent RNA strand [18].

Table 5: Clinical Trials Status

NCT04292730	Phase 3	NCT04257656	Phase 3
NCT04252664	Phase 3	NCT04292899	Phase 3
NCT04302766	Status awaited	NCT04280705	Phase 3
NCT04321616	Phase 3 and 2	NCT04315948	Phase 3

Table 6: Patent Review for the Drug

US10065958B2	Dated 22.07.2010	JP5969471B2	Dated 22.07.2010
AU2011280910B2	Dated 22.07.2010	KR101821680B1	Dated 22.07.2010
CN103052631B	Dated 22.07.2010	MA34470B1	Dated 22.07.2010
CL2013000077	Dated 22.07.2010	ME01924B	Dated 22.07.2010
MX2013000744A	Dated 22.07.2010	MA34470B1	Dated 22.07.2010
CR20130073	Dated 22.07.2010	MX2013000744A	Dated 22.07.2010
CA2804840C	Dated 22.07.2010	NZ606156A	Dated 22.07.2010
CO6690740A2	Dated 22.07.2010	PE20130400A1	Dated 22.07.2010
EA025252B1	Dated 22.07.2010	PL2595980T3	Dated 22.07.2010
ECSP13012458A	Dated 22.07.2010	PT2595980E	Dated 22.07.2010
ES2524356T3	Dated 22.07.2010	SG186830A1	Dated 22.07.2010
HK1183487A1	Dated 22.07.2010	SI2595980T1	Dated 22.07.2010
IL224043A	Dated 22.07.2010	UA111163C2	Dated 22.07.2010

8. Tocilizumab

Description: Interleukin-6 (IL-6) receptor antagonist

Developer: Roche (as Actemra)

As of now, there is no robust well-controlled study showing the safety and efficacy of Actemra in the clinical treatment of COVID-19 pneumonia. Actemra has the potential to prevent cytokine storms or overreaction of the immune system which is considered as the main reason behind the organ failure leading to the death of the patient [19].

How does it work? What is the vaccine targeting?

- Tocilizumab is a recombinant humanized monoclonal antibody against human IL-6 receptor of immunoglobulin IgG1 subtype and has been approved for the treatment of rheumatoid arthritis and systemic juvenile idiopathic arthritis [20].

Table 7: Clinical Trials Status

NCT04317092	Phase 2	NCT04331795	Phase 2
NCT04332094	Phase 2	NCT04335071	Phase 2
NCT04320615	Phase 3	NCT04332913	Pre-Clinical
NCT04306705	Status Awaited	NCT04310228	Pre-Clinical
NCT04335305	Phase 2	NCT04333914	Phase 2
NCT04339712	Phase 2	NCT04315480	Phase 2
NCT04330638	Phase 3	NCT04322773	Phase 2
NCT04331808	Phase 2		

Table 8: Patent Review for the drug

EP2206775A1	Dated 26.09.2007	EP2787007A3	Dated 08.11.2010
US8580264B2	Dated 08.11.2010	US8562991B2	Dated 26.09.2008

9. Galidesivir (BCX4430)

Description: Broad-spectrum antiviral

Developer: BioCryst Pharmaceuticals

Galidesivir is an adenosine nucleoside analog that acts to block viral RNA polymerase. RNA polymerase plays a crucial role in the viral replication process, including transcription and replication of the virus genome [21]. Galidesivir (BCX4430) has shown broad-spectrum activity against a wide range of pathogens including coronavirus and it is a nucleoside RNA polymerase inhibitor that disrupts the process of viral replication [22].

It is currently in advanced development stage under the Animal Rule to combat multiple potential viral threats which include flaviviruses filoviruses, coronaviruses, paramyxoviruses, togaviruses, arenaviruses, and bunyaviruses [23].

How does it Work? What is the Vaccine Targeting?

- This nucleoside RNA polymerase inhibitor disrupts the viral replication process and has the potential to fight multiple viral threats.
- Nucleoside RNA polymerase inhibitors are metabolized to the active triphosphate (nucleotide) form by cellular kinases and also nucleotide binds to the viral enzyme active site and becomes incorporated into the growing viral RNA strand, leading to premature chain termination [24].

Clinical Trial: Clinical trial data awaited

Patent Review: Open Source

10. Kevzara (Sarilumab)
Description: interleukin-6 (IL-6) receptor antagonist
Developer: Regeneron & Sanofi
Kevzara is an interleukin-6 (IL6) receptor antagonist approved by the FDA in 2017 to treat adults with moderately to severely active rheumatoid arthritis who have had an inadequate response to disease-modifying antirheumatic drugs [25].

How does it Work? What is the Vaccine Targeting?
- It is a recombinant humanized monoclonal antibody against the human IL-6 receptor of the immunoglobulin IgG1 subtype and has been approved for the treatment of rheumatoid arthritis and systemic juvenile idiopathic arthritis [26].
- The antibody specifically binds soluble-and membrane-bound IL-6 receptors (Sil-6R and Mil-6R) and inhibits Sil-6R-and Mil-6R-mediated signal transduction. It is effective in the treatment of severe CRS patients [27].

Table 9: Clinical Trials Status

NCT04315298	Phase 3	NCT04341870	Phase 2 and 3
NCT04327388	Phase 2 and 3	NCT04324073	Phase 2 and 3
NCT04322773	Phase 2	NCT04321993	Phase 2

Table 10: Patent Review of the Drug

US7582298B2	Dated 02.06.2006
WO2017079443A1	Dated 03.11.2015
WO2013053751A1	Dated 11.10.2011

11. SNG001
Description: Interferon beta (IFN-beta)
Developer: Synairgen Research
SNG001 is a formation of Interferon Beta for direct delivery to the lungs of the patients via nebulization to treat of tackle LRT illness caused by the respiratory virus. SNG001 which is an inhaled drug and is planned to be tested by the University of Southampton to treat asthma, chronic obstructive pulmonary disease and lower respiratory tract illness caused by a coronavirus. The trial will provide data on the efficacy of the inhaled interferon-beta treatment of ambulatory and hospitalized patients infected with the coronavirus [28]. Interferon Beta 1a is a naturally occurring protein that orchestrates the body's antiviral responses. Moreover, viruses like coronavirus have evolved mechanisms that suppress endogenous IDN-beta production, thereby helping the virus evade the innate immune system [29].

How does it Work? What is the Vaccine Targeting?
- SNG001, a formulation of IFN-beta-1a for direct delivery to the lungs via nebulization, is pH neutral and free of mannitol, arginine, and human serum albumin making it suitable for inhaled delivery direct to the site of action [30].

Table 11: Clinical Trials Status

Patent Review of the Drug	
NCT04315948	Phase 2
NCT01126177	Phase 2
US6962978B2	Dated 16.10.1998
US7527946B2	Dated 16.10.1998
CA2558212C	Dated 12.03.2004

12. Amnio Boost
Description: Amniotic fluid concentrate
Developer: Lattice Biologics
A drug Amnio Boost which was developed for chronic adult inflammatory conditions such as osteoarthritis. The company is exploring the efficacy of its amniotic fluid concentrate in treating the ARDS (acute respiratory distress syndrome) in coronavirus disease infected patients [31]. Although the drug has shown efficacy in reducing the inflammatory conditions caused by several diseases including COVID-19 patients.

How does it Work? What is the Vaccine Targeting?
- It acts via down-regulation of the production of the pro-inflammatory cytokines, increasing anti-inflammatory cytokines production, and facilitating the recruitment of natural anti-inflammatory cells [32].

Clinical Trial: Clinical trial data awaited
Patent Review: Open Source [33]

13. INO-4800
Description: DNA Vaccine
Developer: Inovio Pharmaceuticals
Inovio Pharmaceuticals has created a potential vaccine named INO-4800 to tackle the coronavirus disease. On January 30th the company announced the collaboration with the Beijing Advaccine Biotechnology to further advance in the development of INO-4800 [34].

How is it working? What is the vaccine targeting?
- The vaccine delivers optimized DNA into the cells where it is translated into proteins that activate an individual's immune system to generate a robust targeted T Cell and antibody response.
- Once it gets inside the cell, the plasmids begin replicating, thereby strengthening the body's own natural response mechanisms.

Table 12: Clinical Trials Status

NCT04336410	Phase 1
Patent Review	
WO2005081716A2	dated 24.11.2003
WO2015081155A1	dated 29.11.2013

14. mRNA-1273
Description: RNA
Developer: Moderna
The mRNA vaccine is targeted to the Spike (S) protein of the coronavirus. The vials of the drug made by Moderna are being manufactured by Moderna's Massachusetts manufacturing unit and are being shipped to NIAID for phase 1 human clinical trials [35].

How does it work? What is the Vaccine Targeting?
mRNA vaccine encodes for a prefusion stabilized form of the Spike (S) protein of the COVID-19 which was selected by the Vaccine Research Centre

Table 13: Clinical Trials for the Drug

NCT04283461	Phase 1
Patent Review	
WO2017070626	Dated 22.10.2015
WO2018115527	Dated 23.12.2016

15. AT-100
Description: Novel Recombinant Human Protein rhSP-D
Developer: Airway Therapeutics
AT-100 is a novel recombinant human protein rhSP-D which is an engineered version of an endogenous protein-that reduces inflammation and infection while modulating the immune response to break the cycle of injury and inflammation [36].
AT-100 is capable of serving as an innovative therapy for the novel coronavirus by targeting critical stages of the deadly virus by facilitating the clearance and binding the virus by lung immune cells, which will result in regulating the body's immune cells to reduce the overwhelming inflammation that is the primary mechanism of illness in several viral infections and also infectivity and replication for several types of bacteria and viruses which includes the novel coronavirus infection as well [37].

Clinical Trial: Pre-Clinical
Patent Review: Data awaited
16. Leronlimab
Description: HIV protease inhibitor
Developer: CytoDyn
The treatment with Leronlimab is targeted as a therapy for patients who experience respiratory complications as a result of contracting SARS-CoV-2 causing the COVID-19 [38]. Leronlimab provides therapeutic relief by enhancing the immune response while mitigating the cytokine storm that leads to morbidity and mortality in these patients. Leronlimab (PRO 140) inhibits the migration of Tregs into areas of inflammation, which can inhibit the innate immune response against pathogens and, most importantly, the migration of macrophages and release of pro-inflammatory cytokines in lungs. Leronlimab can potentially mitigate the cytokine storm [39].

Patent Review: Data awaited

Table 14: Clinical Trials Status

NCT04343651	Phase 2	NCT04347239	Phase 2

17. BPI-002
Description: Molecule Agent
Developer: Beyond Spring
Beyond spring has developed BPI-002 which is a novel orally administered small molecule agent that is a potent T-cell co simulator.

How does it work? What is the Vaccine Targeting?
- The molecule agent can potentially activate the adaptive immune system which is the body's strongest line of defence to directly attack and kill the virally infected cells which also includes RNA virus such as those causing COVID-19.
- Moreover, if it is combined with a COVID-19 vaccine the molecule agent can potentially function as an adjuvant to provide improved long-term humoral (B-cell dependent) protection against future viral infection [40].

Clinical Trial: Pre-Clinical
Patent Review: Data awaited

Drugs/Vaccines/Therapies Currently at Developing Stage

18. Enanta Pharmaceuticals
Description: Antiviral Drug
Developer: Enanta Pharmaceuticals
Enanta Pharmaceuticals has announced its efforts to discover a treatment for the Novel Coronavirus disease 2019. It also affirmed that it will launch a Phase II dose-ranging study in paediatric respiratory syncytial virus (RSV) patients and a Phase II study in adult transplant patients with RSV, in addition to its ongoing Phase IIb RSVP study in adult outpatients with community-acquired RSV [41].

Clinical Trial: Data awaited
Patent Review: Data awaited

19. OYA1
Description: Anti-Viral
Developer: OyaGen
A United States of America based biotechnology company OyaGen has declared positive findings from collaborative research of a drug candidate, OYA1 for treating coronavirus 2019.. OYA1 has antiviral activity against filoviruses such as Ebola virus, it is said to process broad-spectrum antiviral in lab assays against coronaviruses SARS-Cov-2 MERS-CoV [42].

Clinical Trial: Data awaited
Patent Review: Data awaited

20. Brilacidin (PMX-30063)
Description: Anti-viral & anti-inflammatory
Developer: Innovation Pharmaceuticals
Brilacidin which is a defensin mimetic drug that has a potential treatment capability for coronavirus. The drug has shown antibacterial, anti-inflammatory, and immunomodulatory properties in several clinical trials [43].

How does it work? What is the vaccine targeting?
Brilacidin inhibits PDE4B2 and PDE3A in vitro, in a dose-dependent manner. Brilacidin demonstrated similar IC50 values against both PDE4 (biochemical) and cytokine release in cell-based assays, suggesting Brilacidin has good cell membrane permeability [44].

Patent Review

Table 15: Clinical Trial: Data awaited

US10206894B2	Dated 16.05.2011

21. Linear DNA Vaccine
Description: Linear DNA
Developer: Applied DNA Sciences and Takis Biotech
Applied DNA Sciences subsidiary LineaRX and Takis Biotech formed a joint venture in February 2020 to create a linear DNA vaccine as a treatment for coronavirus while using Polymerase Chain Reaction (PCR) based DNA manufacturing technology to create the vaccine [45]. The PCR technology will offer several advantages including high purity, increased production speed, and absence of antibiotics and bacterial contaminants. The design of the vaccine is based on the entire spike gene of coronavirus and the rest of it is designed based on antigenic portions of the protein.

Clinical Trial: Pre-Clinical [46]

Patent Review: Application filed dated February 2020

22. Predictive Oncology
Description: To be determined
Developer: Predictive Oncology
Predictive Oncology, a US-based company that has launched an Artificial Intelligence (AI) platform for the discovery and development of vaccines against coronavirus. It has also signed an agreement with a company Inventa Biot Tech to acquire Soluble Therapeutics which will provide access to HSC Technology.

Drug Candidate: To be determined
Patent Review & Clinical Trial: Data awaited

23. Integral Molecular
Description: Reporter Virus Particles (RPVs)
Developer: Integral molecular
Integral Molecular, a company based in the USA has launched a vaccine program using two tech platforms including Shotgun Mutagenesis Epitope Mapping and Membrane Proteome Array to understand the human immune response to the virus and identify cellular receptors that will tell how the virus has been able to spread too quickly [47]. Integral molecular offers high quality controlled SARS CoV2 reporter virus particles that enable safe (BSL-2), easy and high throughout viral infectivity and neutralization assays using standard detection instrumentation. RVPs are designed to be antigenically identical to wild-type viruses but with a modified genome that expresses a convenient optical reporter gene (GFP or luciferase) upon cellular infection [48].

Drug Candidate: To be determined
Patent Review & Clinical Trial: Data awaited

24. CEL-SCI
Description: Immunotherapy
Developer: CEL-SCI
CEL-SCI, a company pioneer in cancer immunotherapy, is developing immunotherapy against COVID-19 using its proprietary LEAPS peptide technology which utilizes conserved areas of the coronavirus proteins to generate T-cell responses and reduce viral load. Moreover, the peptides which are developed while using the technology can help in decreasing tissue damage from inflammation caused due to lung infection which is a major cause of mortality in older patients [49].

Drug Candidate: To be determined
Patent Review & Clinical Trial: Data awaited

25. AJ Vaccines
Description: Protein Subunit
Developer: AJ Vaccines
AJ Vaccines, a company located in Denmark, has launched the development of a vaccine to tackle the novel coronavirus-2019 and the company is using the latest technology antigens that can mimic the native structures of the virus. Moreover, it will have the potential of inducing a strong immune response in the body which will protect against the virus [50].

Drug Candidate: To be determined
Patent Review & Clinical Trial: Data awaited

27. Heat Biologics
Description: Protein Subunit
Developer: Heat Biologics
Heat Biologics vaccine platform focuses on engineering multiple protein regions of the virus into our gp96 platform and such design has the potential of generating long-term immune responses and may confer immunity to different coronaviruses [52]. The tech is capable of reprogramming live cells to produce antigens that can bind to the gp96 protein and generate an immune response against those antigens [53].

Drug Candidate: To be determined
Patent Review & Clinical Trial: Data awaited

28. OT-101
Description: Anti-Viral
Developer: Mateon Therapeutics
Artemisinin complements OT-101 which continues to demonstrate potent activity against SARS-CoV2 [54]. Like other potential COVID-19 therapeutic agents such as Hydroxychloroquine and Remdesivir, the efficacy of Artemisinin remains to be tested in well-controlled and sufficiently powered clinical trials. However, given the known safety profile and the widespread use of

Artemisinin the company anticipates that the clinical development of Artemisinin can be abridged to effectively deal with the current COVID-19 pandemic [55].

Patent Review: Data awaited
Clinical Trial: Data awaited

29. Influenza vector expressing RBD
Description: Replicating Viral Vector
Developer: Hong Kong University
The Hong Kong University of Science and Technology has ascertained several vaccines which can be created as a treatment for coronavirus. It has identified T-cell and B-cell epitopes which have the potential of generating an immune response against the SARS Virus and a similar response against the COVID-19 [56].

Drug Candidate: To be determined
Patent Review & Clinical Trial: Data awaited

30. Tulane University
Description: To be determined
Developer: Tulane University
Tulane University, established in New Orleans has launched a research program to identify a potential coronavirus medicine in the form of a vaccine.

Drug Candidate: To be determined

Patent Review & Clinical Trial: Data awaited

31. Synthetic Peptide vaccine
Description: Protein Subunit
Developer: Generex Biotechnology
Generex Biotechnology, a company based in Canada, is developing a vaccine to tackle the coronavirus-19 with its Li-Key immune system activation technology platform following an agreement from a Chinese consortium comprising of China Technology Exchange, Biology Institute of Shandong Academy of Sciences and Sinotek [57].

Drug Candidate: To be determined

Patent Review & Clinical Trial: Data awaited

32. Immuno Precise
Description: Anti-body
Developers: Immuno Precise
Immuno Precise Antibodies, a company based in the USA has launched a therapeutic and vaccine antibody program to develop the vaccine as well as the antibodies against coronavirus. It will use B Cell Select and Deep Display discovery platforms to develop the vaccine [58]. The company is also working on the generation of target antigens for the deadly virus as these antigens are intended to help identify prophylactic and therapeutic compounds using the discovery platforms of the company which also includes B Cell select and Deep Display [59].

Drug Candidate: To be determined

Patent Review & Clinical Trial: Data awaited

33. SWRI Vaccine
Description: To be determined
Developer: Southwest Research Institute
Southwest Research Institute is using rhodium which is a virtual screening to ascertain potential drug candidates for treating coronavirus from more than two million drug compounds. Rhodium speeds up the preliminary efficacy and safety evaluations. A 3D model of a coronavirus was used to evaluate potential drugs from a vast library of compounds and while using the 3D structure of the viral protein, Rhodium screens drug compounds and it predicts how protein structures in infectious disease will bind with compounds or a series of compounds known as ligands.

Drug Candidate: To be determined

Patent Review & Clinical Trial: Data awaited

34. Sepsivac
Description: Immune Modulator
Developer: Zydus Cadila
Sepsivac is an immunotherapy treatment and it is the first in the word innovation in Sepsis management and also the drug has received a green light from the drug controller general if India for immunotherapy treatment in Sepsis or septic shock. It consists of mycobacterium, an immunomodulator which is a non-pathogenic mycobacterium, and consequent of the immunomodulatory effect, Sepsivac effectively saves more lives in sepsis. The drug has been shown to reduce the mortality of critically ill patients by more than half. It also leads to faster recovery of organ dysfunction seen in this condition [60].

Table 16: Clinical Trial

NCT04347174	Phase 2
Patent Review	
US8333978B2	Dated 23.11.2006

35. Vir Biotechnology
Description: Anti-bodies
Developer: Vir BioTechnology
The company has identified two monoclonal antibodies that can bind to the virus that causes COVID-19. The antibodies target the spike (S) protein of the virus by entering through the cellular receptor ACE2. Vir has also ascertained multiple potential targets against flu and other respiratory pathogens as well as the hepatitis B virus and is now focusing on SARS-CoV2 [61].

Drug Candidate: To be determined
Patent Review & Clinical Trial: Data awaited

36. Nano Viricdes
Description: Anti-Viral
Developer: Nano Viricd**es**
Nano Viricides, a clinical-stage company situated in the United States which is working on creating a treatment for nCoV-2019 using its Nano Viricides technology. The company's technology is used to develop ligands that can bind to the virus in the same way as a cognate receptor and attack various points of the various [62].

Drug Candidate: To be determined

Patent Review & Clinical Trial: Data awaited

37. Kaletra (Lopinavir-ritonavir)
Description: HIV protease inhibitor
Developer: Abbvie
Abbvie, a company based in Illinois, has announced its plan to evaluate HIV medicine as coronavirus disease 2019 treatment and has entered into a collaboration with health institutions and authorities around the globe to ascertain the drug's efficacy [63].

Patent Review: Open Source [64]

Table 17: Clinical Trials Status

NCT04307693	Phase 2	NCT04261907	Status Awaited
NCT04330690	Phase 2	NCT04295551	Status Awaited
NCT04328285	Phase 3	NCT04321993	Phase 2
NCT04328012	Phase 2 and 3	NCT04343768	Phase 4
NCT04286503	Phase 4	NCT04315948	Phase 3
NCT04255017	Phase 4	NCT04275388	Status Awaited
NCT04321174	Phase 3	NCT04251871	Status Awaited
NCT04331470	Phase 2 and 3	NCT04276688	Phase 2

38. Prezcobix (darunavir)
Description: HIV-1 protease inhibitor
Developer: Janssen Pharmaceutical Cos.
Prezcobix (darunavir and cobicistat) which is discovered and developed by Janssen Therapeutics is a fixed-dose antiretroviral combination tablet indicated for the treatment of human immunodeficiency virus (HIV-1) infection. Janssen has donated 300 boxes of Prezcobix to the shanghai Public Health Clinical0 Centre and Zhong Nan Hospital of Wuhan for use in research to support efforts in finding a solution against a deadly virus.

Table 18: Clinical Trials Status

NCT04303299	Phase 3
NCT04303299	Phase 3
NCT04252274	Phase 3
Patent Review	
DK2729130T3	dated 07.07.2011
EP2729128A1	dated 07.07.2011
WO2015145324A1	dated 25.03.2014
EP2729130A1	dated 07.07.2011
US20190175511A1	dated 08.08.2016

39. VLP (Virus-Like Particle)
Description: Virus-Like Particle
Developer: Medicago
Medicago has developed a Virus-Like Particle of the coronavirus from SARS-Cov-2 which is the virus causing the Covid-19 disease. Production of Virus-Like Particle is the first step in developing a vaccine to tackle the COVID-19 which is now moving towards preclinical testing for safety and efficacy [65]. Medicago's candidate plant-derived quadrivalent VLP influenza vaccine is expected to stimulate a balanced antibody and cellular immune response and efficacy against various influenza strains [66].

How does it work? What is the vaccine targeting?

- Virus-like particles are used to create plant-based vaccines that mimic viruses, enabling the body's immune system to recognize them and create an immune response. Moreover, they lack the core genetic material of a virus hence they are not infectious.

Patent Review

Table 19: Clinical Trial: Data awaited

EP2173886B1	Dated 12.07.2007
US9458470B2	Dated 27.11.2007
WO2015042373A1	Dated 19.09.2013
US10358652B2	Dated 28.03.2013

40. Modified Avian Vaccine
Description: Protein Subunit
Developer: Migal Research Institute

The MIGAL Research Institute based in Israel has developed an Infectious Bronchitis Virus (IBV) [67] vaccine to treat coronavirus, Moreover, it has been modified to treat COVID-19 and the vaccine has demonstrated efficacy in pre-clinical trials conducted by the Volcani Institute [68].

Drug Candidate: To be determined
Patent Review & Clinical Trial: Data awaited

41. TNX-1800
Description: Modified horsepox virus
Developer: Tonix Pharmaceuticals
The vaccine is a modified horsepox virus developed using Tonix's proprietary horsepox vaccine platform. The drug is designed to express protein derived from the virus that causes the coronavirus infection in humans [69]. The vaccines are based on Tonix's proprietary horsepox vaccine platform and are believed that horsepox has the potential to serve as a vector for vaccines to tackle against the infectious agents [70].

Clinical Trial: Pre-Clinical stage

Patent Review: Open Source

42. Recombinant subunit Vaccine
Description: Protein Subunit
Developer: Clover Biopharmaceuticals
The company is using patented Trimer-Tag technology to construct a recombinant of the 2019-nCOV S protein subunit-trimer vaccine (S-trimer) and will produce it via rapid mammalian cell culture-based expression system and which is responsible for binding with the host cell an causing the viral infection [71].

Drug Candidate: To be determined
Patent Review & Clinical Trial: Data awaited
43. Vaxart's coronavirus vaccine

Description: Non-Replicating Viral Vector
Developer: Vaxart
Vaxart has developed an oral recombinant vaccine in the form of a tablet using its proprietary oral vaccine platform which is VAAST. The company plans to develop vaccines based on the published genome of Coronavirus 2019 to be tested in pre-clinical models for mucosal and systemic immune responses [72].

Drug Candidate: To be determined

Patent Review & Clinical Trial: Data awaited

44. ChAdOx1 nCoV-19
Description: Live Attenuated Virus
Developer: Serum Institute of India & Codagenix
ChAdOx1 has been constructed with genetic material which is used to make proteins from SARS-CoV-2 coronavirus called Spike Glycoprotein (S) which is generally found on the surface of the SARS-CoV-2 virus.

Patent Review: Data awaited

Clinical Trial: Data awaited

45. GlaxoSmithKline (GSK)
Description: Protein Subunit
Developer: Glaxosmithkline
GSK has collaborated with Sanofi to develop an adjuvanted vaccine for COVID-19 using innovative technology from both companies to tackle the pandemic. While Sanofi will contribute its S-protein COVID antigen which is based on recombinant DNA technology it has produced an exact genetic match to proteins found on the surface of the virus, and the DNA sequence encoding this antigen has been combined into the DNA of the baculovirus expression platform, the basis of Sanofi's licensed recombinant influenza product in the US [73].

Drug Candidate: To be determined

Patent Review & Clinical Trial: Data awaited

46. Olumiant (Baricitinib)
Description: JAK inhibitor
Developer: Lilly
The vaccine is on a clinical trial stage which is a part of the National Institutes of Health to study Baricitinib as an arm in NIAID's adaptive COVID-19 treatment for hospitalized patients diagnosed with coronavirus [74]. Baricitinib which is an oral JAK1/JAK2 inhibitor marketed as OLUMIANT® is approved in more than 65 countries as a treatment for adults with moderately to severely active rheumatoid arthritis.

Patent Review

Table 20: Clinical Trial: Pre-Clinical

US8158616B2	Dated 11.03.2008
US8420629B2	Dated 11.03.2008

47. AdCOVID
Description: Non-Replicating Viral Vector
Developer: Altimmune
Altimmune, has developed, designed and synthesized a novel single-dose, intranasal vaccine to protect against COVID-19 which was made by its proprietary intranasal vaccine technology [75]. It is expected that Ad COVID has the potential to activate multiple arms of the immune system as shown in a recent Phase 2 clinical study with Naso VAX, an influenza vaccine candidate based on the same platform technology [76].

Patent Review

Table 21: Clinical Trial: Trial Data awaited

WO1988008718A1	dated 05.05.1987

48. Emergent BioSolutions
Description: DNA plasmid vaccine
Developer: Emergent BioSolutions
Emergent is developing two potential treatments, COVID-Hyper Immune Globulin (COVID-HIG), a human plasma-derived

therapy candidate for the treatment of COVID-19 in severe hospitalized and high-risk patients, and COVID-Equine Immune Globulin (COVID-EIG), an equine plasma-derived therapy candidate for the treatment of severe disease. Both candidates are anticipated to be in Phase 2 clinical studies over the summer [77].

Drug Candidate: To be determined

Patent Review & Clinical Trial: Data awaited

49. BNT162
Description: RNA
Developer: Pfizer & BioNTech
BNT162 is a vaccine candidate which is based on mRNA which is combined with a lipid nanoparticle (LNP) formulation. There are four vaccine candidates, two of them include a nucleoside modified RNA (modRNA), one includes a uridine containing mRNA(uRNA) and the fourth candidate utilizes self-amplifying mRNA (saRNA) [78].

Patent Review: Data awaited

Clinical Trial: Data awaited

50. BXT-25
Description: Novel Viral Inhibitor
Developer: BioXyTra**n**
BXT-25 is designed to be 5000 times smaller than a blood cell which can efficiently transport oxygen through the body for nine hours before processed by the liver and the drug can also help in supplying oxygen to the vital organs and which will allow the patient to recover and survive [79]. BXT-25 is an Anti-necrosis drug whose glycopolymers structure consists of hybrid molecules integrating the Haemoglobin molecule and a proprietary polymer chemical structure [80]. It is designed to carry oxygen to tissues when the flow of blood is blocked.

Clinical Trial: Pre-Clinical

Patent Review: Data awaited

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