






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# Immune-mediated approaches against COVID-19

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### SUPPLEMENTARY TABLES

**Supplementary Table 1. Innate and adaptive immune responses to viral infections.**

	COMPONENT	MAIN FUNCTION	TARGET	MAIN COMPONENT-TARGET RECOGNITION SITE	SIGNALLING PATHWAY TRANSDUCTION	IMMUNE EFFECT
INNATE IMMUNE RESPONSE	Toll-like receptors (TLR) <sup>1</sup>	<ul style="list-style-type: none"> <li>Recognition of pathogen-associated molecular patterns (PAMP)</li> </ul>	<ul style="list-style-type: none"> <li>Viral lipids, lipoproteins, proteins, &amp; nucleic acids</li> </ul>	<ul style="list-style-type: none"> <li>Cell membrane- TLR-2 and TLR-4</li> <li>Cytoplasm- TLR-3, TLR-7/8</li> <li>Endosome, lysosome, and endocytolysosome</li> </ul>	<ul style="list-style-type: none"> <li>Activation of adapter proteins Toll/Interleukin-1 receptor (TIR) - mainly activates NF-κB<sup>2</sup> and mitogen-activated protein kinases (MAPK) pathways to induce inflammatory factors expression.</li> <li>Activation of adapter proteins TRIF (Activation of adapter proteins)- activates the transcription factors interferon-regulatory factor (IRF)3 and NF-κB)- activates the transcription factors IRF3 and NF-κB</li> <li>Type I interferon (IFN) activates the downstream Janus kinase/signal transducers and activators of transcription (JAK-STAT) signal pathway, promotes the expression of IFN-stimulated genes.</li> </ul>	<ul style="list-style-type: none"> <li>Induction of the expression of type I IFN, immune-inflammatory factors and the TRIF-dependent pathway, which activates the type I IFN and inflammatory factors.</li> <li>Promotion of macrophage phagocytosis.</li> </ul>
	RIG-I-like receptors (RLR) <sup>3</sup>	<ul style="list-style-type: none"> <li>Recognition of viral RNA</li> </ul>	<ul style="list-style-type: none"> <li>Short double-stranded with a triphosphate</li> </ul>	<ul style="list-style-type: none"> <li>Cytoplasm</li> </ul>	<ul style="list-style-type: none"> <li>Activation of caspase initiates the downstream signalling, detected by the</li> </ul>	<ul style="list-style-type: none"> <li>Induction of type 1 IFN and inflammatory</li> </ul>

			structure and complementary ends and/or poly-U/UC-rich structure.		mitochondrial anti-viral signalling adaptor protein, present on the mitochondrial surface. Downstream signalling initiates the transcription of IFN $\alpha$ and $\beta$ . <ul style="list-style-type: none"> <li>• Activation of the transcription factors IRF3/7 and NF-kB<sup>4</sup></li> </ul>	cytokines to block viral replication.
	Nucleotide-binding and oligomerization Domain (NOD)-like receptors (NLR) <sup>5</sup>	<ul style="list-style-type: none"> <li>• Promotion of IRF3 translocation to the nuclei following endoplasmic reticulum (ER) stress caused by viral components.</li> </ul>	<ul style="list-style-type: none"> <li>• Mitochondrial antiviral - signalling protein (MAVS)</li> </ul>	<ul style="list-style-type: none"> <li>• Cytoplasm</li> </ul>	<ul style="list-style-type: none"> <li>• Activation of adapter proteins TIRF - activates the transcription factors IRF3</li> </ul>	<ul style="list-style-type: none"> <li>• IFN <math>\alpha/\beta</math> transcription</li> </ul>
	C-type lectin-like receptor (CLR) <sup>6</sup>	<ul style="list-style-type: none"> <li>• Expressed on macrophages and dendritic cells (DC)</li> <li>• Recognition and capture of pathogens.</li> </ul>	<ul style="list-style-type: none"> <li>• Pathogen ligands</li> </ul>	<ul style="list-style-type: none"> <li>• Transmembrane receptor- extra cellular and intra cellular</li> </ul>	<ul style="list-style-type: none"> <li>• Pathogen internalization following CLR binding, and further degradation in the lysosome.</li> <li>• Recruitment of acidified spleen tyrosine kinases, which promotes CARD9, B cell lymphoid tissue 10 (BcL10), and mucosa-associated lymphoid tissue lymphoma translocation protein (Malt)1 complex formation</li> <li>• Activation of NF-kB and MAPK pathways</li> <li>• Signalling pathways</li> <li>• B cell activation by Th2 and Tfh</li> </ul>	<ul style="list-style-type: none"> <li>• Cell phagocytosis</li> <li>• DC maturation</li> <li>• CD4<sup>+</sup> T helper cells and like Th1, Th2, follicular T helper cells (Tfh).</li> <li>• Cytotoxic CD8<sup>+</sup> T cells</li> <li>• Cytokine secretion from macrophages and DC, such as IFN<math>\alpha</math>, IL-6, IL10, IL-12p40, IL-27, CCL17, CCL22, TNF<math>\alpha</math>, IL-1<math>\beta</math>, Type 1 IFN<sup>7</sup>.</li> </ul>
	DC <sup>8</sup>	<ul style="list-style-type: none"> <li>• Antigen presenting cells (APC) – present the viral antigen.</li> </ul>	<ul style="list-style-type: none"> <li>• Pathogens, Pathogen ligands and RNA</li> </ul>	<ul style="list-style-type: none"> <li>• Cell membrane</li> </ul>	<ul style="list-style-type: none"> <li>• Stimulate the activation of T-lymphocytes (CD4<sup>+</sup> and CD8<sup>+</sup>) and B-lymphocytes.</li> <li>• Activation of NF-kB pathway</li> </ul>	<ul style="list-style-type: none"> <li>• Cytokine secretion, IFN <math>\alpha/\beta</math> release</li> </ul>
<b>ADAPTIVE IMMUNE RESPONSE</b>	T cells	<ul style="list-style-type: none"> <li>• CD4<sup>+</sup> T cells - B cells activation and regulation</li> </ul>	<ul style="list-style-type: none"> <li>• CD4<sup>+</sup> T cells - B cells activation</li> <li>• CD8<sup>+</sup> T cells- viral infected cells, virus structural proteins</li> </ul>	<ul style="list-style-type: none"> <li>• Cell membrane</li> </ul>	<ul style="list-style-type: none"> <li>• CD4<sup>+</sup> T cells - promote the production of virus-specific antibodies by activating T-dependent B cells. Produce</li> </ul>	<ul style="list-style-type: none"> <li>• IL-17- recruit monocytes and neutrophils to the inflammation site.</li> <li>• IL-1, IL-6, IL-8, IL-21, TNF-<math>\beta</math>, and MCP-1</li> </ul>

		<ul style="list-style-type: none"> <li>• CD8<sup>+</sup> T cells-elimination of the infected cells</li> </ul>			<p>pro-inflammatory cytokines via NF-kB pathway.</p> <ul style="list-style-type: none"> <li>• Cytotoxic CD8<sup>+</sup> T cells - infiltrate to the infected area and eliminate viral infected cells.</li> </ul>	<ul style="list-style-type: none"> <li>• Memory T cells</li> <li>• B cells activation- IgM and IgG production<sup>9</sup></li> </ul>
Humoral immune response		<ul style="list-style-type: none"> <li>• Activation of B cells by CD4<sup>+</sup> T cells - memory and antibodies secreting cells</li> </ul>	<ul style="list-style-type: none"> <li>• Viral proteins</li> </ul>	<ul style="list-style-type: none"> <li>• Cell membrane</li> </ul>	<ul style="list-style-type: none"> <li>• Increase in Type 1 IFN, result in B cell activation</li> <li>• Germinal centre reaction</li> </ul>	<ul style="list-style-type: none"> <li>• Memory B cells</li> <li>• Antibody secreting cells</li> <li>• IgM, IgG and IgA antibody production<sup>10,11</sup></li> </ul>

**Supplementary Table 2. Protein similarities (expressed as % identity) between SARS-CoV-2 and other Betacoronaviruses.**

<b>SARS-CoV-2</b>	<b>Orf1ab</b>	<b>S</b>	<b>ORF3a</b>	<b>E</b>	<b>M</b>	<b>ORF6</b>	<b>ORF7a</b>	<b>ORF8</b>	<b>N</b>	<b>ORF10</b>
<b>Bat-SL-CoV</b>	95%	80%	91%	100%	98%	93%	88%	94%	94%	-
<b>SARS-CoV</b>	86%	76%	72%	94%	90%	68%	85%	40%	90%	-
<b>MERS-CoV</b>	50%	35%	-	36%	42%	-	-	-	48%	-

*ORF - Open reading frame; S – Spike protein; E- Envelope protein; M – Membrane; N- Nucleocapsid proteins; SARS - Severe Acute Respiratory Syndrome; MERS - Middle East Respiratory Syndrome.*

**Supplementary Table 3. Sequences of SARS-CoV B and T cell epitopes that mapped to SARS-CoV-2.**

Protein	B cell Epitope SARS-CoV	B cell Epitope SARS-CoV-2	T cell Epitope SARS-CoV	T cell Epitope SARS-CoV-2	MHC Allele	Identity (%)	REF
N			ALNTPKDHI	ALNTPKDHI	HLA-A*02:01	100	12,13
			LALLLDRL	LALLLDRL		100	
			LLLDRLNQL	LLLDRLNQL		100	
			RLNQLESKV	RLNQLESKM		89	
			GETALALLLL	GDAALALLLL	HLA-B*40:01	80	
	KHIDAYKTFPPTPKKDK KKKTDEAQPLPQRQKKQ PTVTLLPAADMDD	NKHIDAYKTFPPTPKKDK KKKTDEAQPLPQRQKKQPT VTLLPAADM				100	
	NNAATVLQLPQGTTLPK GFYA	NNNAATVLQLPQGTTLPKGF				95	
S			FIAGLIAIV	FIAGLIAIV	HLA-A*02:01	100	12,13
			NLNESLIDL	NLNESLIDL		100	
			ALNTLVKQL	ALNTLVKQL		100	
			RLNEVAKNL	RLNEVAKNL		100	
VLNDILSRL	VLNDILSRL	100					
	KSFEIDKGIYQTSNFRVV QLIRAAEIRASA NLAATK	KSFTVEKGIYQTSNFRVQ QLIRAAEIRASA NLAATK			HLA-DRB1*04:01	78	
	DAVDCSQNPLAELKCSV KSFEIDKGIYQTSNF	DAVDCALDPLSETKCTLKSF TVEKGIYQTSN				100	
						69	12-15

*N – Nucleocapsid Protein; S – Spike Protein; Major Histocompatibility Complex (MHC); REF - References*

## Supplementary Tables 4

Supplementary Tables 4a. COVID-19 candidate vaccines currently undergoing preclinical development. Adapted and modified from<sup>16-22</sup>.

TECHNOLOGY	COMPANY	OTHER PLATFORM CANDIDATES
<b><i>DNA-based approaches</i></b>		
Linear DNA vaccine	TakisApplied DNA Sciences, Evvivax	
DNA vaccine	BioNet Asia	
DNA vaccine	University of Waterloo	
DNA vaccine	Entos Pharmaceuticals	
bacTRL-Spike	Symvivo	
DNA plasmid vaccine	Osaka University, AnGes, Takara Bio	
DNA plasmid vaccine	Zydus Cadila	
Plasmid DNA, Needle-Free Delivery	Immunomic Therapeutics, Inc./EpiVax, Inc./PharmaJet, Inc.	SARS
DNA with electroporation	Karolinska Institute, Cobra Biologics (OPENCORONA Project)	
<b><i>Live attenuated virus-based approaches</i></b>		
Codon deoptimized live attenuated vaccines	Indian Immunologicals Ltd, Griffith University	
Codon deoptimized live attenuated vaccines	Codagenix/Serum, Institute of India	HAV, influenza, Zika, FMD, SIV, RSV, DENV
<b><i>Inactivated virus-based approaches</i></b>		
Inactivated + CpG 1018	Sinovac, Dynavax	
Inactivated + CpG 1018	Valneva, Dynavax	
Inactivated	Institute of Medical Biology, Chinese Academy of Medical Sciences	
Inactivated	Osaka University, BIKEN NIBIOHN	
<b><i>RNA-delivery based approaches</i></b>		
LNP (encapsulated mRNA cocktail encoding VLP)	Fudan University, Shanghai JiaoTong University, RNACure Biopharma	
LNP-mRNA	Translate Bio, Sanofi Pasteur	
LNP (encapsulated mRNA encoding RBD)	Fudan University, Shanghai JiaoTong University, RNACure Biopharma	
LNP-encapsulated mRNA	University of Tokyo/Daiichi-Sankyo	MERS
mRNA candidates	RNAimmune, Inc.	
mRNA	FBRI SRC VB VECTOR, Rospotrebnadzor Koltsovo	
sRNA in an intranasal delivery system	eTheRNA	

mRNA	Greenlight Biosciences	
mRNA STARR® vaccine	Arcturus, Duke-NUS	Multiple candidates
Self-amplifying RNA	Imperial College London	Ebola, Lassa, MARV, influenza A subtype H7N9, RABV
mRNA	CureVac	RABV, Lassa, YFV, MERS, influenza A, Zika, DENV, HPV
Liposome-encapsulated mRNA	BIOCAD	
Replicating defective SARS-CoV-2 derived RNA	Centro Nacional Biotecnología (CNB-CSIC), Spain	
<b>VLP-based approaches</b>		
Plant-derived VLP	Medicago Inc.	Influenza, Rotavirus, NORV, West Nile virus, cancer
ADDomer™ multiepitope display	Imophoron Ltd and Bristol, University's Max Planck Centre	
Virus-like particle, based on RBD displayed on virus-like particles	Saiba GmbH	
VLP	OSIVAX	
ADDomer™ multiepitope display	Imophoron Ltd, Bristol University's Max Planck Centre	
eVLP	ARTED Biotechnology	Malaria

*DENV - Dengue virus; FMD – Foot-and-mouth disease virus; HAV – Hepatitis A; HPV - Human papillomavirus; LNP – Lipid nanoparticles; MARV – Marburg virus; MERS - Middle East Respiratory Syndrome; NORV – Norovirus; RABV - Rabies lyssavirus; RSV - Respiratory syncytial virus; SARS - Severe acute respiratory syndrome; SIV - Simian immunodeficiency virus; YFV – Yellow fever*



**Supplementary Table 4b. COVID-19 protein-based vaccine candidates currently undergoing preclinical development.** Adapted and modified from<sup>16-22</sup>.

TECHNOLOGY	COMPANY	OTHER PLATFORM CANDIDATES
<b><i>Protein-based approaches</i></b>		
MVA encoded VLP	GeoVax/BravoVax	Lassa, Ebola, MARV, HIV
Recombinant vaccine based on Influenza A virus (intranasal)	FBRI SRC VB VECTOR, Rospotrebnadzor, Koltsovo	Influenza
VSV-S	University of Western Ontario	HIV, MERS
VSV vector	FBRI SRC VB VECTOR, Rospotrebnadzor, Koltsovo	
M2-deficient single replication (M2SR) influenza vector	UW–Madison, FluGen Bharat Biotech	Influenza
Replication defective Simian Adenovirus (GRAd) encoding SARS-CoV-2 S	ReiThera, LEUKOCARE Univercells	
Oral Ad5 S	Stabilitech Biopharma Ltd	Zika, VZV, HSV-2, NORV
Adenovirus-based + HLA-matched peptides	Valo Therapeutics Ltd	
Dendritic cell-based vaccine	University of Manitoba	
Parainfluenza virus 5 (PIV5)-based vaccine expressing the spike protein	University of Georgia, University of Iowa	MERS
Recombinant deactivated rabies virus containing S1	Bharat Biotech, Thomas Jefferson University	
Peptide	FBRI SRC VB VECTOR, Rospotrebnadzor Koltsovo	Ebola
Subunit	FBRI SRC VB VECTOR, Rospotrebnadzor Koltsovo	
Subunit protein, plant produced	iBio, CC-Pharming	
Nanoparticle vaccine	LakePharma, Inc.	
Recombinant spike protein with Advax™ adjuvant	Vaxine Pty Ltd	
Bacterial extracellular vesicle (BEV)-based mucosal vaccine	Quadram Institute Biosciences	Influenza A, plague
Spike (S)-based vaccine	University of Alberta	
Recombinant S1-Fc fusion protein	AnyGo Technology	
Recombinant protein	Yisheng Biopharma	
Recombinant S protein in IC-BEVS	Vabiotech	
Orally delivered, heat stable subunit	Applied Biotechnology Institute	
S-2P protein + CpG 1018	Medigen Vaccine Biologics Corporation, NIAID, Dynavax	
Ad26 (alone or with MHA-BN® boost)	Janssen Pharmaceutical Companies	Ebola, HIV, RSV

Oral vaccine based on recombinant chimeric proteins	MIGAL Research Institute	Avian coronavirus Infectious, Bronchitis Virus (IBV)
Ad5 S (GREVAX™ platform)	Greffex	MERS
Oral vaccine based on VAAST™ platform	Vaxart, Emergent BioSolutions	Influenza, CHIKV, Lassa, NORV, Ebola, RVF, HBV, VEE
Horsepox vector expressing S protein TNX-1800	Tonix Pharma, Southern Research	Smallpox, monkeypox
Live viral vectored vaccine based on attenuated influenza virus backbone (intranasal)	BiOCAD and IEM	
Influenza vector expressing RBD	University of Hong Kong	
VSV vector expressing S protein	IAVI, Batavia	Ebola, MARV, Lassa
MVA-S encoded	DZIF- German Center for Infection Research	Several
MVA expressing structural proteins	Centro Nacional Biotecnología (CNB-CSIC), Spain	HIV, HCV, chikungunya, Ebola, Zika, malaria, leishmania
Capsid-like Particle	AdaptVac (PREVENT-nCoV consortium)	
Drosophila S" insect cell expression system VLP	ExpreS2ion	
S protein	WRAIR/USAMRIID	
COVID-19 S-Trimer - Native like Trimeric subunit Spike Protein vaccine	Clover Biopharmaceuticals Inc., GalxoSmithKline (GSK), Dynavax	HIV, REV, influenza
Adenovirus-based NasoVax expressing SARS2-CoV spike protein	Altimmune	Influenza
Peptide antigens formulated in lipid nanoparticle formulation	IMV Inc	
Peptide	Vaxil Bio	
Peptide	Flow Pharma Inc	Ebola, Marburg, HIV, Zika, Influenza, HPV, therapeutic vaccine, BreastCA vaccine
S protein	AJ Vaccines	
Ii-Key peptide	Generex, EpiVax	Influenza, HIV, SARS-CoV
S protein + Adjuvant	National Institute of Infectious Disease, Japan	Influenza
VLP recombinant protein + Adjuvant	Osaka University, BIKEN, National Institutes of Biomedical Innovation, Japan	
S protein (baculovirus production)	Sanofi Pasteur	Influenza, SARS-CoV
Microneedle arrays S1 subunit	University of Pittsburgh	MERS
VLP (recombinant protein nanoparticle + Matrix M)	Novavax	RSV, CCHF, HPV, VZV, Ebola

gp-96 backbone	Heat Biologics, University of Miami	NSCLC, HIV, malaria, Zika
Molecular clamp stabilized Spike protein + AS03 Adjuvant System	University of Queensland, GSK, Dynavax	Nipah, influenza, Lassa
S1 or RBD protein	Baylor College of Medicine	SARS
Adjuvanted microsphere peptide	VIDO-InterVac, University of Saskatchewan	
Adjuvanted protein subunit (RBD)	Biological E Ltd	
Recombinant protein, nanoparticles (based on S protein and other epitopes)	Saint-Petersburg scientific research institute of vaccines and serums	
COVID-19 XWG-03 truncated S proteins	Innovax/Xiamen, Univ./GSK	HPV
Synthetic Long Peptide Vaccine candidate for S and M proteins	OncoGen	

*CCHF - Crimean-Congo haemorrhagic fever; CHIKV - Chikungunya virus; DENV - Dengue virus; FMD – Foot-and-mouth disease virus; HAV – Hepatitis A; HBV – Hepatitis B; HCV – Hepatitis C; HIV - Human Immunodeficiency Virus; HPV - Human papillomavirus; LNP – Lipid nanoparticles; MARV – Marburg virus; MVA - Modified vaccinia virus Ankara; MERS - Middle East Respiratory Syndrome; NORV – Norovirus; NSCLC - Non-small-cell lung carcinoma; RABV - Rabies lyssavirus; REV - Reticuloendotheliosis virus; RSV - Respiratory syncytial virus; RVF - Rift Valley fever; SARS - Severe acute respiratory syndrome; VEE - Venezuelan equine encephalitis virus; VLP – Virus-like particle; VSV - Vesicular stomatitis virus; VZV - Varicella zoster virus;*

## Supplementary Tables 5

**Supplementary Table 5a. Preclinical immune modulator approaches currently undergoing against SARS-CoV-2 virus.** Adapted and modified from<sup>16-22</sup>

Treatment name	Details/Status	Company
Rintatolimod (Ampligen)	Mismatched double stranded polymer of RNA (dsRNA) approved for chronic fatigue syndrome. Discovery for coronavirus (CoV) in February 2020	Aim Immunotech Inc., GP Pharma SA, Goethe University Frankfurt, National Institute of Infectious Diseases in Japan
AT-100	Recombinant human surfactant protein D (rhSP-D) that reduces inflammation and infection and modulates lung immune response across a range of respiratory diseases.	Airway Therapeutics Inc., National Institute of Allergy and Infectious Diseases (NIAID)
BPI-002	Small molecule as a potent T cell co-stimulator, alone or combined with a vaccine.	BeyondSpring
LEAPS	Peptide epitope delivery technology, T-cell modulation. Preclinical reduction of morbidity and mortality against H1N1.	CEL-SCI Corp.
Niagen (nicotinamide riboside)	Trigger innate immunity. Preclinical demonstration that COVID-19 causes nicotinamide adenine dinucleotide (NAD) reduction.	Chromadex Corp.
Allocetra	Following positive results of Enlivex's phase Ib trial in severe sepsis, it plans to start a clinical trial of Allocetra in COVID-19.	Enlivex Therapeutics Ltd., Israel Innovation Authority
GTB-3550	GT's first Trike therapy candidate and a tri-specific recombinant fusion protein conjugate (anti-CD16, anti-CD33, and a modified form of IL-15). Preclinical evaluation.	GT Biopharma Inc. Cytovance Biologics
7HP-349	Small-molecule integrin activator, as an oral adjuvant. Prophylactic vaccine responses to influenza, Chagas disease and tuberculosis in preclinical models. Clinical trials to start late this year.	Hillis Pharma
Brilacidin	Defensin mimetic candidate as a treatment for COVID-19.	Innovation Pharmaceuticals
Immune System Regulation(ISR)-500	In preclinical development for COVID-19.	ISR Immune System Regulation
Microbiome therapeutic	COVID-19 prevention or as stool-based diagnostic.	Persephone Biosciences Inc.
PRTX-007	Oral small molecules that specific activates toll-like receptor 7.	Primmune Therapeutics
RTB-101	Small-molecule inhibitor of target of rapamycin complex 1 (TORC-1). Clinical data expected by the first quarter of 2021.	Restorbio Inc. Adicet Bio Inc.
Nanofenretinide (ST-001)	PST-001-loaded phospholip-based nanoparticle. Preclinical <i>in vitro</i> antiviral activity against MERS, dengue, Zika, West Nile, HIV and HCV.	Scitech Development LLC

**Supplementary Table 5b. Preclinical antibody-based approaches currently undergoing against SARS-CoV-2 virus.** Adapted and modified from<sup>16-22</sup>

<b>Treatment name</b>	<b>Details/Status</b>	<b>Company</b>
IgM and IgA	Clinical trials planned for first half of next year.	Atreca Inc., Beigene Ltd., IGM Biosciences Inc.
ALT-100	Anti-inflammatory action to reduce acute respiratory distress syndrome mortality and ventilator-induced lung injury.	Aqualung Therapeutics Corp.
	C1 gene expression platform	Dyadic International Inc., The Israel Institute for Biological Research
	To block TLR4 and CXCL10	Edesa Biotech Inc. Light Chain Bioscience, unit of Novimmune SA
	Prevention of SARS-CoV-2 infection	Harbor Biomed, Mount Sinai Health System
Human neutralizing antibodies	Discovery of Advanced peripheral blood Hematopoietic Chimera	Hemogenyx Pharmaceuticals
	Screening of enriched B-cell libraries from convalescent COVID-19.	Immuncetye Life Sciences Inc.
	Polytope against COVID-19.	ImmunoPrecise Antibodies Ltd.
	Proprietary technology platform	Medicago Inc., Laval University
Pritumumab	Inhibition of virus' binding to target cells. Initiated tests against SARS-CoV-2.	Nascent Biotech Inc.
Variable new antigen receptor domain antibody fragments (VNAR) antibodies	Single-domain VNAR antibodies to the COVID-19 spike protein. Data on rodents and nonhuman primates.	Ossianix Inc.
	Preclinical and clinical-scale production. On track to begin human testing in June	Regeneron Pharmaceuticals
SAB-185	Human polyclonal antibody therapeutics, on track for clinical evaluations by early summer.	Sab Biotherapeutics, U.S. Department of Defense, CSL Behring LLC
TZLS-501	Fully human anti-IL-6 receptor monoclonal antibody.	Tiziana Life Sciences
VIR-7831 and VIR-7832	SARS-CoV-2 binding and neutralization. Phase II clinical trials planned.	Vir Biotechnology Inc., Wuxi Biologics, NIAID, Biogen Inc., Xencor Inc., Glaxosmithkline plc Samsung Biologics Co. Ltd.

**Supplementary Table 5c. Preclinical antiviral and anti-inflammatory approaches currently undergoing against SARS-CoV-2 virus.** Adapted and modified from<sup>16-22</sup>

Treatment name	Details/Status	Company
<b>ANTIVIRAL</b>		
AB00-1	Cancer-targeting small molecule. Acts on ACE-2 to inhibit virus entry; acts on NSP15 to prevent virus replication. Clinical trials planned to start.	Agastiya Biotech LLC
Small molecules	Interfere with 3CL-protease and RNA polymerase. Selected 3 out of 2600 approved small molecule drugs; preclinical evaluation.	Aptorum Group Ltd., Covar Pharmaceuticals Inc. University of Hong Kong
ARMS-I	Formulation of Cetylpyridinium Chloride (CPC) that kills enveloped viruses, such as COVID-19. Clinical trial involving caregivers.	University Hospitals network in Cleveland
Anti-CB1 antagonist analogues	Theranostic platform for COVID-19 diagnosis, monitoring and treatment.	Vyripharm Biopharmaceuticals LLC
XRx-101	Xanthine oxidase inhibition by a formulation of oxypurinol, to treat acute kidney and lung injury.	Xortx Therapeutics Inc. Lonza Pharma & Biotech, a unit of Lonza Group AG
Thin film delivery of cannabigerol (CBG) and quercetin	Initiating an <i>in vitro</i> study.	Xphyto Therapeutics Corp. a subsidiary Vektor Pharma TF GmbH
2-DG	<i>In vitro</i> reduction of 2-deoxy-D-glucose (2-DG) replication of SARS-CoV-2.	CNS Pharmaceuticals Inc., University of Frankfurt WPD Pharmaceuticals Inc.
Broad-spectrum antiviral compounds	Protease inhibitors. Already licensed to treat Coronavirus (CoVs) and Norovirus.	Cocrystal Pharma Inc.
Zotatifin	Inhibitor of viral growth. Phase I trial in COVID-19 patients under preparation.	Effector Therapeutics Inc.
Drugs	Discovery of antiviral drug candidates against COVID-19.	Enanta Pharmaceuticals Inc.
Single-domain antibody	Single-domain antibody with high binding affinity to a unique, conserved conformational epitope present on the receptor-binding domain of SARS-CoV and SARS-CoV-2.	Flanders Institute for Biotechnology (VIB) Ghent University
IMU-838	Selective oral DHODH inhibitor of SARS-CoV-2 replication. Clinical development program ongoing.	Immunic Inc.
ACE-MAB fusion protein	Binds to the SARS-CoV-2 spike (S) protein. Clinical development and commercialization.	Mabpharm Ltd. Sorrento Therapeutics Inc.
Carragelose inhalation therapy	To target respiratory viral infections. Tolerance evaluation in healthy volunteers, and proof-of-concept on individuals with viral pneumonia.	Marinomed Biotech AG

	Tri-specific antiviral candidates that target three parts of the viral S protein. Preclinical testing to select a lead candidate.	Molecular Partners AG
Anti-SARS-CoV-2 program	Completed synthesis of nanoviricide candidates.	NanoViricides
Nitricil therapeutics	Potential topical oral or nasal candidate for COVID-19, based on NO's ability to inhibit viral replication.	Novan Inc.
2X-121	Small-molecule PARP inhibitor being tested against coronavirus.	Oncology Venture A/S; Pathogen and Microbiome Institute at Northern Arizona University
OYA1	Strong dose-dependent antiviral activity against SARS-CoV-2 <i>in vitro</i> .	OyaGen Inc.
Repositioned drugs	Identified 97 frequently prescribed drugs as potential candidates to be repositioned against COVID-19, that will be tested <i>in vitro</i> .	Pharnext SA
RT-001	Down-regulation of pro-inflammatory fatty acid oxidation against COVID-19-initiated lung damage.	Retrotope Inc.
S-protein/ACE2 targeted prophylactic polypeptide (inhalant)	Preclinical data in primates showed good biological activity & safety; planned clinical trials.	Sichuan Kelun Pharmaceutical Co. Ltd.
Interferon alpha	Nucleic acid test kits and COVID-19 treatment	Sinopharm Group
Cynarine or Prexasertib	Protease inhibitor. <i>In vitro</i> data against COVID-19.	Som Biotech SL
STI-4398	Neutralization and blocking activity in preventing SARS-CoV-2 virus from infecting ACE2-expressing cells. Starting preclinical studies.	Sorrento Therapeutics Inc.
Therapeutic nanobody	Nanobodies derived from llama and camels shown to neutralize SARS-CoV-2 infection. Possible development of bispecific or multifunctional antibodies.	Sysvax Inc.
<b>ANTI-INFLAMMATORY</b>		
Itanaprazed	Early intervention treatment of brain COVID-19 infection.	Cerespir Inc.
Fadraciclib (CYC-065) + Seliciclib (CYC-202 or Roscovitine)	Cyclin-dependent kinase-2/9 inhibitor.	Cyclacel Pharmaceuticals Inc
Lodonal and IRT-101	Previous data against HIV and H1N1 influenza.	Immune Therapeutics Inc. Cytocom Inc.
Lamellasome™	Synthetic lipidic mimetics of native human lamellar bodies found in lung tissue that inhibits fibroproliferative changes.	Lamellar Biomedical Ltd.
ST-266	To treat severe inflammatory cytokine storm response in COVID-19 patients.	Noveome Biotherapeutics Inc.

Veyonda (idronoxil)	Cytokine inhibition, including interleukin-6 (IL-6) involved in cytokine response syndrome	Noxopharm Co.
Apabetalone (RVX-208)	Inhibitor of bromodomain-containing proteins BRD2 and BRD4.	Resverlogix Corp.
Lonodelestat (POL-6014)	Inhibitor of human neutrophil elastase (hNE), as a therapeutic for COVID-19-related acute respiratory distress syndrome.	Santhera Pharmaceuticals Holding AG
PPP-003	Synthetic cannabinoid drug effective in preventing or treating inflammatory cytokine conditions. Completed preclinical testing against sepsis.	Tetra Bio-Pharma Inc.
Epaspire	Oral formulation of highly purified eicosapentaenoic acid free fatty acid. The companies have applied to FDA for a trial.	The KD Pharma Group SA and SLA Pharma AG
<b>ANTIVIRAL &amp; ANTI-INFLAMMATORY</b>		
Neumifil (mCBM40)	Carbohydrate binding molecule that reduced the number of SARS-CoV-2 plaques <i>in vitro</i> .	Pneumagen Ltd.
ADX-629 and reproxalap	Aldehyde inhibitors structurally related to chloroquine and hydroxychloroquine.	Aldeyra Therapeutics Inc.



**Supplementary Table 5d. Preclinical Advanced Therapy Medicinal Products (ATMP) and other approaches currently undergoing against SARS-CoV-2 virus.** Adapted and modified from<sup>16-22</sup>

Treatment name	Details/Status	Company
<b>ADVANCED THERAPY MEDICINAL PRODUCTS (ATMP)</b>		
T-cell therapies	Allogenic, off-the-shelf, virus specific T-cell therapies.	Allovir Inc., Baylor College of Medicine
Mesenchymal stem cells (MSC)	Safety and efficacy in autoimmune and vascular-related diseases, inflammatory lung conditions, pneumonia and chronic obstructive pulmonary disease.	Celltex Therapeutics Corp.
Natural Killer (NK) cells	The activation of NK cells through the NKp46 receptor aims to destroy the virus-infected cells while the other arm can either block the entry of the virus into epithelial cells or neutralize circulating viruses.	Cytovia Inc., Macromoltek Inc.
COVID-HIG and COVI-EIG	Manufactured from human and horse plasma.	Emergent BioSolutions Inc.
Cannabidiol-loaded exosomes	Administered by inhalation, the technology targets both central nervous system indications and COVID-19.	Innocan Pharma Corp., Ramot at Tel Aviv University
Immunoglobulin	Plasma-derived antibodies from donors recovered from virus.	Kamada Ltd., Biopharma Inc.
Antibody recruiting molecule (ARM)/NK therapy	ARM NK cell combination therapy for COVID-19. The NK cells are expected to move into the clinic for COVID-19 in the second half of this year.	Kleo Pharmaceuticals Inc., Green Cross Labcell
TAK-888 hyperimmune globulin	Anti-SARS-CoV-2 polyclonal hyperimmune globulin derived from convalescent COVID-19 patients.	Takeda Pharmaceutical, Behring LLC, Biotest AG, LFB SA, Octapharma AG
Allorx stem cells	Investigational New Drug (IND) application filed	Vitro Diagnostics Inc.
MesenCure	Activated mesenchymal cells (MSCs) isolated from the adipose tissue of healthy donors. Preliminary data show significantly increase of blood lymphocyte counts.	Wize Pharma Inc.; Bonus Biogroup Ltd.
<b>OTHER</b>		
Precision-driven treatment	Nanobody-based technology. Cytological experiments ongoing.	Beroni Group, Tianjin University
BXT-25	Galectin inhibitor to treat end-stage COVID-19 patients. Human trials to start shortly.	BioXyTran Inc.
VIR-2703 (ALN-COV)	RNAi therapies. Accelerated IND filing application at the end of 2020.	Alnylam Pharmaceuticals, Vir Biotechnology
SARS-CoV-2 targeting recombinant methioninase	Degrades the amino acid methionine in SARS-CoV-2 and infected cells. COVID-19 prevention or treatment.	Anticancer Inc.
Trans sodium crocetinate	FDA pre-IND submission	Diffusion Pharmaceuticals Inc. University of Virginia

LB-1148	Broad-spectrum serine protease inhibitor of digestive proteases. Developed to reduce recovery times and shorten hospital lengths of stay.	Leading Biosciences Inc.
INOmax®	Nitric oxide (iNO) as a supportive measure in treating of COVID-19.	Mallinckrodt
Prototype powders	Dry powder formulation using Technosphere® technology to treat acute respiratory distress syndrome. Development of prototype powders.	Mannkind Corp., Immix Biopharma Inc.
2-deoxy-D-glucose ester-type prodrug WP-1122	IND submitted.	Moleculin Biotech Inc. University of Texas Medical Branch at Galveston, Imquest Biosciences Inc.
KTH-222	KTH-222 regulates cell growth via inhibition of the mitogen-activated protein kinase (MAPK) pathway. To be used alone or in combination with antiviral drugs, in cancer patients infected with COVID-19 or in undiagnosed but symptomatic patients.	Oncology Pharma Inc., Kalos Therapeutics Inc.
Cenchaquine	Pre-registration for hypovolemic shock and hemodynamic stability, tissue oxygenation, as well as reduction of pulmonary edema, acute respiratory distress syndrome, multiple organ dysfunction score and decrease mortality in patients with COVID-19.	Pharmazz Inc.
Upamostat (RHB-107)	Protease inhibitor, alone or in combination with hydroxychloroquine. Preclinical ongoing.	RedHill Biopharma, Link Health Group
Lipocurc	Intravenous formulation of liposomal curcumin.	Signpath Pharma Inc.
RNAi therapeutics	RNAi-based prophylactics and therapeutics for COVID-19 severe acute respiratory infection.	Sirnaomics
Niclosamide	Optimized salt form of niclosamide as a treatment of COVID-19. <i>In vitro</i> studies showed that it is 25 times more potent than chloroquine and more than 40 times more potent remdesivir.	Union Therapeutics A/S, Institute Pasteur Korea
COVID-19 therapies	3D bioprinting technology to create human lung tissue to test potential COVID-19 therapies as a "clinical trial in a dish"	Viscient Biosciences Inc.
VBI-S	Phospholipid nanoparticles to redistribute NO. Improved blood pressure and oxygenation of septic shock patients.	Vivacelle Bio Inc.
KL4 surfactant	Positive effects in various models of severe lung injury and clinical effect in respiratory distress syndrome in premature infants	Windtree Therapeutics Inc.

## Supplementary Tables 6

**Supplementary Table 6a. Examples of immune-mediated approaches in clinical development against COVID-19.**

TREATMENT TYPE	TREATMENT	OBJECTIVE	MECHANISM OF ACTION	IDENTIFIER	STATUS	PHASE
Immune modulator	Baricitinib	COVID-19 Patients	Immune modulator Immunosuppressive JAK1\JAK2 inhibitor	NCT04320277 (Hospital of Prato)	Not yet recruiting	III
				NCT04362943 (Complejo Hospitalario Universitario de Albacete, Spain)	Recruiting	
				NCT04340232 (University of Colorado, Denver)	Not yet recruiting	II, III
	CD24Fc		Immune modulator Anti-inflammatory	NCT04317040 (OncoImmune, Inc.)	Recruiting	III
Vaccine	Modified antigen presenting cells (APC)	COVID-19 patients	LV-SMNP-DC vaccine and antigen-specific CTL	NCT04276896 (Shenzhen Geno-Immune Medical Institute)	Recruiting	I/II
			Pathogen-specific aAPC vaccine	NCT04299724 (Lung-Ji Chang, Shenzhen Geno-Immune Medical Institute)	Recruiting	I
	Non-replicating viral vector	Healthy volunteers	Ad5-nCov - Recombinant Novel Coronavirus Vaccine (Adenovirus Type 5 Vector)	NCT04313127 (CanSino Biologics Inc./ Beijing Institute of Biotechnology)	Active, not recruiting	I
				NCT04398147 (CanSino Biologics Inc./ Beijing Institute of Biotechnology))	Not yet recruiting	I/II
				NCT04341389 (Insitute of Biotechnology, Academy of Military Medical Sciences, PLA of China)	Active, not recruiting	II

		ChAdOx1 nCoV-19 vaccine	NCT04324606 (University of Oxford/AstraZeneca/Serum Institute of India)	Active, not recruiting	I/II
	Inactivated virus	Inactivated SARS-CoV-2 + aluminium	NCT04352608 (Sinovac Biotech Co., Ltd.)	Recruiting	I/II
		Inactivated SARS-CoV-2 + aluminium	NCT04383574 (Sinovac Biotech Co., Ltd.)	Not yet recruiting	I/II
		Inactivated SARS-CoV-2 (Vero cells)	ChiCTR2000031809 (Wuhan Institute of Biological Products Co., Ltd.)	Not yet recruiting	I/II
	RNA-based vaccine	BNT162a1	EudraCT 2020-001038-36 (BioNTech RNA Pharmaceuticals GmbH/Fosun Pharma/Pfizer)	Ongoing	I/II
		BNT162a1 BNT162b1 BNT162b2 BNT162c2	NCT04380701 NCT04368728 (BioNTech RNA Pharmaceuticals GmbH/Fosun Pharma/Pfizer)	Recruiting	I/II
		mRNA-1273	NCT04283461 (ModernaTX, Inc./National Institute of Allergy and Infectious Diseases (NIAID)) NCT04405076 (ModernaTX, Inc./Biomedical Advanced Research and Development Authority)	Recruiting	I  II
	DNA-based vaccine	INO-4800	NCT04336410 (Inovio Pharmaceuticals)	Recruiting	I
		bacTRL-Spike	NCT04334980 (Symvivo Corporation)	Not yet recruiting	I

	Protein subunit nanoparticle vaccine		SARS-CoV-2 rS	NCT04368988 (Novavax)	Recruiting	I/II
	Recombinant SARS-CoV-2 Trimeric S protein subunit vaccine		SCB-2019	NCT04405908 (Clover Biopharmaceuticals AUS Pty Ltd)	Not yet recruiting	I
	Dendritic cell (DC) vaccine	Healthcare providers and first responders	AV-COVID-19	NCT04386252 (Aivita Biomedical, Inc.)	Not yet recruiting	I/II
Immune suppressant	Thalidomide	Moderate New Coronavirus (COVID-19) Pneumonia	Immune modulator Anti-inflammatory Anti-fibrosis	NCT04273529 (First Affiliated Hospital of Wenzhou Medical University)	Not yet recruiting	II
	Thalidomide + Low-dose Hormones			NCT04273581 (First Affiliated Hospital of Wenzhou Medical University)	Not yet recruiting	II
	Fingolimod		Anti-inflammatory Sequesters lymphocytes in lymph nodes. Down regulator of sphingosine 1-phosphate (S1P) receptor.	NCT04280588 (First Affiliated Hospital of Fujian Medical University)	Recruiting	II

**Supplementary Table 6b. Examples of antimalaria and antiviral repurposed drugs in clinical development against COVID-19.**

TREATMENT TYPE/ ACTION	TREATMENT	OBJECTIVE	IDENTIFIER	STATUS	PHASE
<b>Antimalaria/</b> Anti-inflammatory	Hydroxychloroquine sulfate	COVID-19 patients	NCT04315896 (Sanofi)	Recruiting	III
			NCT04353271 (William Richards, University of South Alabama)	Active, not recruiting	II/III
		Treating healthcare personnel exposed to COVID-19 patients.	NCT04315896 (National Institute of Respiratory Diseases)	Recruiting	III
			NCT04333225 (Baylor Research Institute)	Active, not recruiting	II
<b>Antiviral/</b> RNA-polymerase inhibitor	Remdesivir	COVID-19 patients with mild-to-moderate, or severe disease	NCT04292899 (Gilead Sciences Inc.) NCT04292730 (Gilead Sciences Inc.)	Recruiting	III
			NCT04252664 (Capital Medical University)	Suspended	
			NCT04257656 (China-Japan Friendship Hospital)	Terminated	
			NCT04280705 (National Institute of Allergy and Infectious Diseases (NIAID))	Recruiting	II, III
			NCT04323761 (Gilead Sciences Inc.)	Available	Treatment IND/Protocol
			NCT04302766 (U.S. Army Medical Research and Development Command)	Available	Treatment IND/Protocol
<b>Antiviral/</b> RNA-polymerase inhibitor + guanosine (ribonucleic) analogue to prevent RNA synthesis + immune modulator	Lopinavir/ritonavir + Ribavirin + IFN- $\beta$ 1B	COVID-19 patients with mild-to-moderate, or severe disease	NCT04276688 (The University of Hong Kong)	Completed	II
<b>Non-specific antiviral/</b> Immune modulator	IFN- $\alpha$ 2 $\beta$		NCT04293887 (Tongji Hospital)	Not yet recruiting	I
<b>Antiviral + Antimalaria/</b> Anti-inflammatory + RNA-polymerase inhibitor	Remdesivir + Hydroxychloroquine sulfate	COVID-19 patients with mild-to-moderate, or severe disease	NCT04321616 (Oslo University Hospital)	Recruiting	Norwegian Solidarity II/III

<b>Antiviral/ Anti-inflammatory + RNA- polymerase inhibitor + protease inhibitor</b>	Remdesivir+ Hydroxychloroquine sulfate+ Lopinavir/ritonavir	COVID-19 patients with mild-to- moderate, or severe disease	NCT04330690 (AbbVie Apotex Inc.)	Recruiting	II
	Remdesivir+ Hydroxychloroquine sulfate+ Lopinavir/ritonavir + IFN-β1A	COVID-19 patients with mild-to- moderate, or severe disease	NCT04315948 (Institut National de la Santé Et de la Recherche Médicale, France)	Recruiting	III
<b>Antiviral + Antimalaria + Immune modulator/ Anti-inflammatory + protease inhibitor + tyrosine kinase inhibitor or janus kinase inhibitor</b>	Hydroxychloroquine + Lopinavir/ritonavir or Imatinib or baricitinib	COVID-19 patients with pneumonia	NCT04346147 (Hospital Universitario de Fuenlabrada)	Recruiting	II
<b>Antiviral+ Monoclonal antibodies/ Anti-inflammatory + immune modulator</b>	Favipiravir + Tocilizumab	Treating COVID-19 positive patients.	NCT04310228 (Peking University First Hospital)	Recruiting	N/A
<b>Non-specific anti- inflammatory</b>	Corticosteroids		NCT04273321 (Beijing Chao Yang Hospital)	Completed	N/A
			NCT04344288 (Hospices Civils de Lyon)	Recruiting	II
			NCT04355247 (Hospital Auxilio Mutuo Cancer Center San Juan, Puerto Rico)	Recruiting	II
			NCT04355637 (Groupe Hospitalier Pitie Salpetriere, Paris, France)	Recruiting	IV
			NCT04344730 (Assistance Publique - Hôpitaux de Paris)	Recruiting	NA
			NCT04348305 (Aarhus University Hospital - Dept of Intensive care Aarhus, Denmark)	Recruiting	III

**Supplementary Table 6c. Examples of monoclonal antibody-based approaches in clinical development against COVID-19.**

TREATMENT	OBJECTIVE	MECHANISM OF ACTION	IDENTIFIER	STATUS	PHASE			
Tocilizumab	Severe COVID-19 pneumonia	Anti-inflammatory Anti-IL-6 antibody Anti-IL-1 antibody	NCT04317092 (National Cancer Institute, Naples)	Recruiting	II			
			NCT04306705 (Tongji Hospital)	Recruiting	Retrospective			
			NCT04320615 (Actemra by Hoffmann-La Roche)	Recruiting	III			
			NCT04330638 (University Hospital Ghent)	Recruiting	IV			
			NCT04322773 (Frederiksberg University Hospital)	Recruiting	II			
			NCT04315480 (Università Politecnica delle Marche)	Active, not recruiting	II			
			NCT04345445 (University of Malaya)	Not yet recruiting	III			
			NCT04331795 (University of Chicago)	Recruiting	II			
			NCT04377750 (Hadassah Medical Organization)	Recruiting	IV			
			NCT04335071 (University Hospital Inselspital, Berne)	Recruiting	II			
			NCT04370834 (National Cancer Institute (NCI))	Not yet recruiting	II			
			PD-1 blocking antibody+ standard treatment		Immune modulators Induces T cell response	NCT04268537 (Southeast University, China)	Not yet recruiting	II
			Bevacizumab		Anti- angiogenic Anti-VEGF antibody Reducing pulmonary oedema	NCT04305106 (Qilu Hospital of Shandong University)	Recruiting	N/A
NCT04275414 (Qilu Hospital of Shandong University)	Recruiting	II, III						
NCT04344782 (Assistance Publique - Hôpitaux de Paris)	Not yet recruiting	II						
Eculizumab	Reducing immune response related damage in	Anti-inflammatory, inhibiting complement activation.	NCT04288713 (Hudson Medical)	Available	N/A			
			NCT04355494	Available	NA			



	COVID-19 infected patients	Anti-Complement protein C5	(Alexion Pharmaceuticals) NCT04346797 (Assistance Publique - Hôpitaux de Paris)	Recruiting	II
Sarilumab	Severe COVID-19 infection	Anti-inflammatory Anti-IL-6 antibody	NCT04315298 (Kevzara by Regeneron Pharmaceuticals & Sanofi)	Recruiting	II, III
			NCT04359901 (Boston Healthcare System United States)	Suspended	I, II
			NCT04357808 (Hospital Universitario de la Princesa Madrid, Spain)	Recruiting	II
			NCT04357860 (Maimónides Biomedical Research Institute of Córdoba)	Not yet recruiting	II
			NCT04327388 (Sanofi)	Recruiting	II/II
			NCT04324073 (Assistance Publique - Hôpitaux de Paris)	Active, not recruiting	II/III
Meplazumab	Add-on therapy for COVID-19 infected patients Blocking host cell invasion	Anti-CD147 Prevents SARS-CoV-2 spike protein from binding to CD147	NCT04275245 (Tang-Du Hospital)	Recruiting	I, II
Leronlimab	COVID-19 patients with mild-to-moderate respiratory complications	Anti-CCR5 IgG4 mAb	NCT04343651 (CytoDyn, Inc.)	Recruiting	II
	COVID-19 patients with severe or critical disease		NCT04347239 (CytoDyn, Inc.)	Recruiting	II
LY-CoV555	Hospitalised COVID-19 patients	SARS-CoV-2 spike protein-targeted preventive antibody LY3819253 for prevention and treatment	NCT04411628 (Eli Lilly and Company/ AbCellera Biologics Inc.)	Recruiting	I

**Supplementary Table 6d. Examples of Advanced Therapy Medicinal Products (ATMP) in clinical development against COVID-19.**

TREATMENT	OBJECTIVE	MECHANISM OF ACTION	IDENTIFIER	STATUS	PHASE
NestCell® Mesenchymal Stem Cell	Severe COVID-19 pneumonia	Anti-inflammatory Immune modulation Tissue regeneration Cell-therapy	NCT04315987 (Azidus Brasil)	Not yet recruiting	I
Dental Pulp Mesenchymal Stem Cells			NCT04302519 (CAR-T (Shanghai) Biotechnology Co., Ltd.)	Not yet recruiting	I
Human Umbilical Cord Derived Mesenchymal stem cells	Severe COVID-19		NCT04273646 (Wuhan Union Hospital, China)	Not yet recruiting	N/A
			NCT03042143 (Belfast Health and Social Care Trust, United Kingdom)	Recruiting	I, II
			NCT04333368 (Hôpital Pitié-Salpêtrière - APHP Hôpital Européen Georges Pompidou - APHP Paris, France)	Recruiting	I, II
			NCT04355728 (Union Hospital, Wuhan, China)	Recruiting	I, II
	Severe COVID-19 pneumonia		NCT04269525 (Tuohua Biological Technology Co. Ltd.)	Recruiting	I
Mesenchymal Stem Cell	Severe COVID-19 pneumonia Severe COVID-19		NCT04252118 (Beijing 302 Hospital)	Recruiting	I
			NCT04288102 (Beijing 302 Hospital)	Recruiting	II, III
	COVID-19 patients		NCT04366271 (Hospital Infantil Universitario Niño Jesús, Madrid, Spain)	Recruiting	II
	Severe COVID-19		NCT04377334 (University Hospital Tuebingen)	Not yet recruiting	II
			NCT04366323	Not yet recruiting	I, II

			(Andalusian Network for Design and Translation of Advanced Therapies)		
			NCT04371393 (Annetine Gelijns, Icahn School of Medicine at Mount Sinai)	Recruiting	III
			NCT04366063 (Royan Institute)	Recruiting	II/III
			NCT04361942 (Red de Terapia Celular)	Recruiting	II
			NCT04348461 (Instituto de Investigación Sanitaria de la Fundación Jiménez Díaz)	Not yet recruiting	II
			NCT04336254 (Renmin Hospital of Wuhan University)	Recruiting	I
Wharton's Jelly-Mesenchymal Stem Cells	COVID-19 patients		NCT04313322 (Stem Cells Arabia)	Recruiting	I
Stem Cell Educator Therapy	Severe COVID-19 pneumonia		NCT04299152 (Tianhe Stem Cell Biotechnologies, Inc.)	Not yet recruiting	II
Inhalation of Mesenchymal Stem Cells Exosomes	Severe COVID-19 pneumonia	Anti-inflammatory Tissue repair	NCT04276987 (Ruijin Hospital)	Not yet recruiting	I
NK Cell Treatment	Severe COVID-19 pneumonia	NK immune response against SARS-CoV-2 virus	NCT04280224 (Xinxiang medical university)	Recruiting	I
	COVID-19 patients		NCT04324996 (Chongqing Sidemu Biotechnology Technology Co., Ltd.)	Recruiting	I, II
			NCT04344548 (Fundacion Salud De Los Andes, Bogotá, Colombia)	Not yet recruiting	I, II
			NCT04365101 (Lung Biotechnology PBC)	Recruiting	I, II
Immunoglobulin from Cured Patients	Severe COVID-19 Pneumonia		NCT04264858 (Wuhan Union Hospital)	Not yet recruiting	N/A

		Induce specific immune-response against COVID-19 virus	NCT04345523 (Puerta de Hierro University Hospital)	Recruiting	II
			NCT04358783 (Hospital Universitario Dr. Jose E. Gonzalez)	Recruiting	II
			NCT04261426 (Peking Union Medical College Hospital)	Not yet recruiting	II/II
V-SARS	Healthy individuals	Tableted heat-inactivated plasma from donors with COVID-19	NCT04380532 (Immunitor LLC)	Recruiting	I/II

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