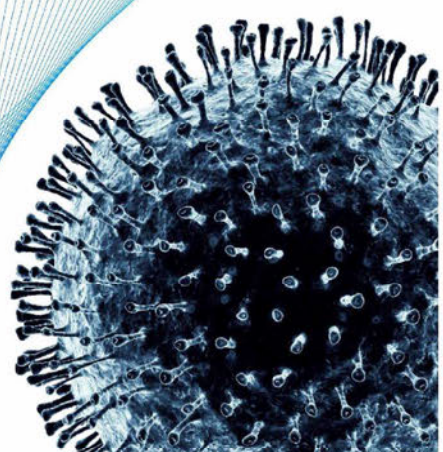
COVID-19 Therapeutics and Vaccines Landscape Overview

July 23, 2020

DOCUMENT INTENDED TO PROVIDE INSIGHT BASED PURELY ON CURRENT, PUBLICLY AVAILABLE INFORMATION FOR CONSIDERATION AND NOT SPECIFIC ADVICE



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- **COVID-19 is, first and foremost, a humanitarian challenge.** Thousands of health professionals are heroically battling the virus, putting their own lives at risk. Governments and industry are working together to understand and address the challenge, support victims and their families and communities, and search for treatments and a vaccine.

- **Solving the humanitarian challenge is the top priority.** Much remains to be done globally to prepare, respond, and recover, from protecting populations at risk, to supporting affected patients/ families/ communities and to developing a vaccine. To address this crisis, responses must be evidence-informed, and based on partnership among various stakeholders/sectors, including but not limited to: medical product industry, regulatory/ compliance agencies.

- **Separate materials are available that provide a richer view of the COVID-19 situation overall.** These include perspectives on how the COVID-19 situation may unfold and the implications for employees, customers, supply chains and financial results. For this broader view, please contact PMP (10)(2e) @mckinsey.com or read more on https://www.mckinsey.com/

CURRENT AS OF JULY 22, 2020

Document overview

To date, there is no **globally approved COVID-19 vaccine or treatment** available.

There are **over 250 vaccine candidates** and over **300 therapeutics candidates** in consideration.

This document and accompanying Excel trackers provide a **current snapshot of vaccine and therapeutic efforts for COVID-19.** They are based on **publicly available data** across candidate lists, clinical trial data and trial results.

Sources of insight:

- Multiple candidate lists (e.g. Milken Institute, BioCentury, WHO)
- Clinical trial registries (mainly CT.gov and ChiCTR)
- Press and literature searches

Vaccines and therapeutics can be targeted across a variety of use cases

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Patient journey	Therapeutic use case	Vaccine use case
Not exposed	**High risk[1] pre-exposure prophylaxis (PrEP)**	**Community level prophylaxis**
		High risk[1] prophylaxis
Exposed	**High risk[1] post-exposure prophylaxis (PEP)**	
Infected (tests positive)	**Prevent asymptomatic transmission**	
Disease (symptoms)	**Mild disease treatment disease treatment**	
Need oxygen / hospital	**Severe disease treatment disease treatment**	
Need ventilator / ICU	**Critical disease treatment disease treatment**	

1. Such as healthcare workers, emergency responders, immunocompromised individuals, immediate family of COVID-19 patients

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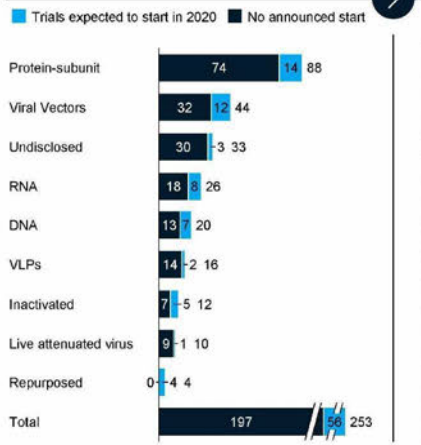
COVID-19 vaccines development effort overview

253 vaccines are currently in development; 12-18 month timeline expected

Pipeline overview



Weekly developments, as of July 22, 2020

Pfizer and BioNTech have reported positive early data from a German Phase I/II clinical trial demonstrating high neutralizing titers and strong T-cell responses[1]

US agrees to pay Pfizer and BioNTech ~$2B to produce & deliver 100M doses of their COVID-19 vaccine if it proves safe. They have also made a deal with the UK for 30M doses[2]

Oxford University and AztraZeneca have announced positive Phase I/II results, neutralizing antibodies were generated in more than 90% of participants across different assays. Responses were sustained up to 56 days of observation on an at-risk basis, as the vaccines are not yet approved[3]

CanSino released positive Phase II results including seroconversion occurred in more than 96% of participants, and neutralizing antibodies were generated in about 85%; more than 90% had T-cell responses[3]

Sinovac and Sinopharm began Phase III trials for their inactivated vaccines, in Brazil and UAE respectively and **Arcturus began their Phase I/II trial** in Singapore[4]

1. Clinical Trials Arena
2. Pfizer PR, Pfizer PR
3. Lancet
5. Sinopharm, Sinovac, Arcturus
6. [redacted]
7. HBR
7. SVB analyst on [redacted]
8. Moderna press release
9. FiercePharma
10. CNBC
11. Innovio press release

Source: Milken Institute, BioCentury, WHO, Nature, CT.gov, ChiCTR

Key takeaways

There are **253 vaccine candidates** and new players entering the space every week

- **56 vaccine candidates planning to enter into clinical trials in 2020**
- **33 vaccine candidates have already begun clinical trials**

Most experts estimate a 12-18 month timeline[5] to bring a vaccine to market (approved and available, not necessarily scaled-up), others believe an 18-24 month timeline or even longer is more realistic[6,7]

- The **earliest immunogenicity from Phase 2 will be available for 3-4 vaccine candidates this year** which could bring an EUA for high risk population into consideration depending on the data[8,9,10,11]

Multiple organizations across public and private sector are playing roles in the development of a COVID-19 vaccine

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1. Based on other vaccine development processes 2. UK government has pledged more than $17mn for manufacturing efforts (European Pharmaceutical Review) 3. Including biotech, MNCs, CMO and CMC partners 4. Including Médecins Sans Frontières / Doctors without Bordes rand UNICF

Source: WHO, GAVI, CEPI, NIH, MaF, CDC, UNICEF, USAID, The World Bank BMGF, GHIF, EU Commission

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There are 253 candidates in the pipeline for COVID-19 vaccines

	Description	Example companies / compounds	Number of candidates profiled[1]
RNA	**Nucleic acid RNA** packaged within a vector (e.g. lipid nanoparticles).	moderna, CUREVAC	26
DNA	**Plasmid containing the DNA sequence encoding the antigen(s)** against which an immune response is sought	inovio, SANOFI PASTEUR	20
Inactivated	Killed version of the germ that causes the disease, providing shorter-term protection and requiring boosts	sinovac, SINOPHARM	12
Viral vectors	**Chemically weakened** virus to transport pieces of the pathogen – **usually** antigen coding surface proteins	CanSinoBIO, MERCK, Johnson & Johnson	44
Attenuated virus	**Weakened virus** to stimulate immune response		10
VLPs	Virus-like-particles - **molecules that closely resemble viruses**, but are non-infectious because they contain no viral genetic material	medicago, VBI	16
Protein subunit	**Purified or recombinant proteinaceous antigens** from a pathogen to elicit immune response. Some assets employ a nanoparticles-delivery system for enhanced antigen presentation	NOVAVAX, Clover	88
Repurposed	Repurposed vaccines already on the market		4
Undisclosed[2]	Additional candidates with little public information	SaudiVax,	33

Not covered in this document

1. Compiled across multiple lists (Milken Institute, BioCentury, WHO, Nature) and supplemented with press
2. Not profiled moving forward. Vaccine type cannot be delineated due to lack of public information; typically in research setting or small biotech

Source: Milken Institute, BioCentury, WHO, Nature

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There are 56 COVID-19 vaccines planning to enter into clinical trials in 2020; 33 are already in trials (1/4)

Deep dive to follow

	Company/Group	Asset	Collaborators	Company country	Other gov't / funding	Development phase	Clinical trial start date[6]	Comment
RNA	Moderna	mRNA-1273	NIAID, Lonza	USA	CEPI, NIAID, BARDA	(10)(1c)	May-20	Stated EUA: Fall 2020[5]
	BioNTech	BNT162	Pfizer and Fosun Pharma	Germany	Industry		Apr-20	Stated EUA: Oct. 2020[6]
	Imperial college London	N/A	N/A	UK	Government/philanthropy/University Fund		Jun-20	
	CureVac		CEPI; European Commission; Gates Foundation; DARPA	Germany	European Commission, CEPI		Jun-20	
	Walvax Biotechnology		People's Liberation Army; Academy of Military Sciences	China			Jun-20	
	Arcturus Therapeutics	LUNAR-COV19	Duke University, Catalent	USA	Singapore government		Jul-20	
	Sanofi Pasteur	LNP-mRNA	Translate Bio	France	BARDA		Q4 2020[2]	
	Stemirna Therapeutics		Tongji University School of Medicine	China	N/A		Apr-20[3]	
DNA	Inovio	INO-4800	Beijing Advaccine Biotechnology, Ology Bioservices	USA	CEPI, Gates foundation		Jul-20	
	AnGes		Osaka University and Takara Bio	Japan	N/A		Jul-20	
	Aivita Biomedical, Inc.	AV-COVID-19		USA			Sep-20	
	Genexine	GX-19	Binex, GenNBio, Korea Advanced Institute of Sci. and Tech, Pohang University of Sci. and Tech.	South Korea	IVI		Jun-20	
	Zydus Cadila	nCov vaccine		India			Jul-20	
	Symvivo	bacTRL-Spike		Canada			Apr-20	No actual start date listed
	Applied DNA Sciences	Several candidates	Takis Biotech/Evvivax	USA	Industry		Fall 2020[4]	

2. Milken Institute
3. China Daily
4. Applied DNA Sciences release
5. Moderna press release
6. CNBC

Source: Milken Institute, BioCentury, WHO, Nature

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There are 56 COVID-19 vaccines planning to enter into clinical trials in 2020; 33 are already in trials (2/4)

Deep dive to follow

	Company / Group	Asset	Collaborators	Company country	Other gov't / funding	Development phase	Clinical trial start date[8]	Comment
Inactivated	Sinovac Biotech	PiCoVacc	Dynavax	China	Bank of Beijing	Phase III	Jul-20	
	Sinopharm		Beijing Institute of Biological Products	China		Phase III	Jul-20	
	Sinopharm		Wuhan Institute of Biological Products	China		Phase III	Jul-20	
	Chinese Academy of Medical Sciences		Institute of Medical Biology	China		Phase I/II	May-20	
	Bharat Biotech			India		Phase I/II	Jul-20	
Viral vectors	CanSino Biologics	Ad5-nCoV	Institute of Biotechnology at China's Academy of Military Medical Sciences	China	Chinese government	Phase II	Apr-20	
	University of Oxford (Jenner Institute)	AZD1222 / ChAdOx1 nCoV-19	AstraZeneca, Advent SRL, MilliporeSigma, Cobra Biologics	UK	UK government	Phase II/III	May-20	Stated EUA: Sep-20[7]
	Johnson & Johnson	Ad26 SARS-CoV-2	Beth Israel Deaconess Medical Center	US	BARDA	Phase I/II	Jul-20	
	Gamaleya Research Institute	Adeno-based		Russia		Phase I	Jun-20	
	Shenzhen University	COVID-aAPC	Shenzhen Third People's Hospital, Shenzhen Second People's Hospital	China	Chinese government	Phase I	Feb-20	Available in China Q42020 / Q12021[9]
	Vaxart		Emergent BioSolutions Inc.	USA	N/A	Preclinical	Jul-20[1]	
	IAVI / Merck		Merck, Batavia Biosciences	USA		Preclinical	Later in 2020[2]	
	Reithera		LEUKOCARE, Univercells	Italy		Preclinical	Q32020[3]	
	J&J	Ad26 SARS-CoV-2	Beth Israel, HHS	USA	BARDA	Preclinical	Jul-20[4]	
	Sumagen		IVI	Korea	Government of Canada	Preclinical - animal studies	Jul-20[5]	
	Themis / Merck		Institut Pasteur and University of Pittsburgh	USA	CEPI	Preclinical - animal studies	Later in 2020[6]	
	ImmunityBio		NantKwest	USA	CEPI	Preclinical	June 2020[10]	
	Novartis	AAVCOVID	Mass General Eye and Ear	USA		Preclinical	2H 2020[11]	

1. RAPS.org
2. Merck press release
3. Genengnews.com
4. J&J press release
5. Pulsenews.co.kr
6. University of Pittsburgh
7. Reuters
8. For clinical trials already started, dates come from clinicaltrials.gov
9. Reuters
10. Nantkwest press release
11. Masseyeandear.com

Source: Milken Institute, BioCentury, WHO, Nature

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There are 56 COVID-19 vaccines planning to enter into clinical trials in 2020; 33 are already in trials (3/4)

Deep dive to follow

Title	Company / Group	Asset	Collaborators	Company country	Other gov't / funding	Development phase	Clinical trial start date[11]	Comment
Live attenuated virus	Serum Institute of India	CDX-COV	Codagenix Bio Pharmaceuticals	India	VC	Preclinical - animal studies	June-20[1]	
VLPs	**Medicago**		**Laval University's Infectious Disease Research Centre**	**Canada**	**Government of Canada**	**Phase I**	**Jul-20**	
	VBI Vaccines, Inc.		National Research Council of Canada (NRC)	USA, Canada	N/A	Preclinical - animal studies	By end of 2020[3]	
Protein-subunit	**Anhui Zhifei Longcom Biopharmaceutical**		**Institute of Microbiology, Chinese Academy of Sciences**	**China**		**Phase II**	**Jul-20**	
	Clover Biopharmaceuticals	**SCB-2019**	**GSK, Dynavax**	**Australia, China**		**Phase I**	**Jun-20**	
	Vaxine Pty Ltd		**Flinders University, Oracle**	**Australia**		**Phase I**	**Jun-20**	
	Novavax	**NVX-CoV2373**	**Emergent BioSolutions, Praha Vaccines, Serum Institute of India**	**Australia**	**CEPI**	**Phase I**	**May-20**	
	University Queensland		**GSK, Dynavax, CSL (Parkville, Australia), Viroolinios Xplore**	**Australia**	**CEPI, Australian government**	**Phase I**	**Jul-20**	
	Kentucky Bioprocessing			**USA**		**Phase I/II**	**Jul-20**	
	University of Cambridge/DIOSynVax			UK		Preclinical	Jun-20[3]	
	Axon Neuroscience SE			Slovakia		Preclinical	Q32020[5]	
	MIGAL Galilee Research Institute	MigVax	N/A	Israel	N/A	Preclinical - animal studies	Jun-20[6]	
	Sorrento Therapeutics	STI-6991	SmartPharm	USA		Preclinical - animal studies	Mid-year 2020[7]	
	Sanofi Pasteur	Pre-clinical SARS vaccine candidate	GSK	France	BARDA	Preclinical - animal studies	September[5]	
	Immune System Regulation (ISR) Holding	Immunolid ISR50	TCER	Sweden		Preclinical - animal studies	Last quarter 2020[9]	
	IMV	DPX-COVID-19	Dalhousie University, Nova Scotia Health Authority, University of Laval	Canada	VC	Preclinical - animal studies	Summer 2020[10]	
	Walter Reed Army Institute of Research		USAMRIID	USA		Preclinical	Later in 2020[12]	

1. Thisweek in
2. Medicago press release
3. Milken
4. GAVI press release
5. Biospace.com
6. Israeli Post
7. Reuters
8. Reuters
9. Genengnews.com
10. IMV press release
11. For clinical trials already started, dates come from clinicaltrials.gov
12. US Army

Source: Milken Institute, BioCentury, WHO, Nature

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There are 56 COVID-19 vaccines planning to enter into clinical trials in 2020; 33 are already in trials (4/4)

Deep dive to follow

	Company/ group	Asset	Collaborators	Company country	Other funding/ gov't involvement	Development phase	Clinical trial dates (or targeted start)[1]	Timing to market and capacity
Repurposed		BCG vaccine	Multiple research institutions	Multiple		Clinical – Ph III (9 trials)[24]	Earliest end date: November 2020	
		Measles	Kast El Aini Hospital	Multiple		Clinical – Ph III	November 2020	
	Immunovative Therapies	AlloStim	Mirror Biologics	N/A		Clinical – Ph I	June, 2020	
	Canadian Cancer Trials Group	IMM-101	Immudolon Tx, BioCan Rx, CSSRI, AtGen, ARCC	Canada		Clinical – Ph III	July 2020	

1. For dates of clinical trials already started. End dates reflect full completion; actual read-outs may be sooner 24. One further study also evaluating if positive tuberculin test has an effect on the severity of symptoms if developed COVID-19

Source: Milken Institute, BioCentury, WHO, Nature

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RNA: Additional assets with undisclosed timelines

Company / group	Asset	Collaborators	Country	Other funding / gov't involvement	Development phase	Clinical trial starting date	Comment
BIOCAD			Russia		Preclinical		
CanSino Biologics		Precision Nanosystems	China		Preclinical		
Capricor Therapeutics	Exosome-SARS-CoV-2 mRNA	Johns Hopkins University	USA		Preclinical		
Centro Nacional Bio (CNB-CSIC)		IDIBAPS	Spain		Preclinical		
Chimeron Bio	Self amplifying RNA, delivery system	George Mason University's Center for Biodefense and Infectious Disease	USA		Preclinical		
Chula Vaccine Research Center	LNP-mRNA	University of Pennsylvania	Thailand		Preclinical		
Daiichi-Sankyo		University of Tokyo	Japan		Preclinical		
eTheRna		EpiVax, Nexelis, REPROCELL, and Centre for the Evaluation of Vaccination of the University of Antwerp	Belgium		Preclinical		
FBRI SRC VB VECTOR, Rospotrebnadzor			Russia		Preclinical		
Fudan University		RNACure Biopharma, Shanghai JiaoTong University	China		Preclinical		
Greenlight Biosciences			USA		Preclinical		
HDT Bio		PAI Life Sciences; University of Washington, InBios			Preclinical		
Helix Nanotechnologies			USA		Preclinical		
Houston Methodist		GeneOne Life Science	USA		Preclinical		
Max Planck Institute of Colloids and Interfaces			Germany		Preclinical		
RNAimmune, Inc.			USA		Preclinical		
Selcuk University			Turkey		Preclinical		
Ziphius Therapeutic	ZIP-1642	Ghent University	Belgium		Preclinical		

Source: Milken Institute, BioCentury, WHO, Nature, clinicaltrials.gov

DNA: Additional assets with undisclosed timelines

Company / group	Asset	Collaborators	Country	Other funding / gov't involvement	Development phase	Clinical trial starting date	Comment
BioNet Asia			Thailand		Preclinical		
Chula Vaccine Research Center	DNA with electroporation		Thailand		Preclinical		
Cobra Biologics	OPENCORONA	Karolinska Institutet, Karolinska University Hospital, the Public Health Agency of Sweden (FoHM), IGEA, Adlego, Giessen University	Sweden	Horizon 2020 - European Commission	Preclinical		
Ege University			Turkey		Preclinical		
Entos Pharmaceuticals	Several candidates	N/A	Canada	Seeking from government and industry	Preclinical		
Immunomic Therapeutics, Inc.		PharmaJet and EpiVax	USA		Preclinical - animal studies		
National Research Centre, Egypt			Egypt		Preclinical		
OncoSec	CORVax12	Providence Cancer Institute, part of Providence St. Joseph Health	USA		Preclinical - animal studies		
Pan Genome Systems		University of Wisconsin			Preclinical		
Scancell		University of Nottingham	UK		Preclinical		
Statens Research Institute			Denmark		Preclinical		
Takis	COVID-eVax	Rottapharm	Italy		Preclinical		
University of Waterloo			Canada		Preclinical		
Zydus Cadila			India		Preclinical		

Source: Milken Institute, BioCentury, WHO, Nature, clinicaltrials.gov

Inactivated: Additional assets with undisclosed timelines

Company / group	Asset	Collaborators	Country	Other funding / gov't involvement	Development phase	Clinical trial starting date	Comment
KM Biologics			Japan		Preclinical		
National Research Centre, Egypt			Egypt		Preclinical		
Osaka University		BIKEN and National Institutes of Biomedical Innovation	Japan		Preclinical		
Republic of Kazakhstan		Research Institute for Biological Safety Problems	Kazakhstan		Preclinical		
Selcuk University			Turkey		Preclinical		
Valneva	VLA2001	Dynavax	France		Preclinical		
Panacea Biotec		Refana	India		Preclinical		

Source: Milken Institute, BioCentury, WHO, Nature, clinicaltrials.gov

Viral vectors: Additional assets with undisclosed timelines (1/2)

Company / group	Asset	Collaborators	Country	Other funding / gov't involvement	Development phase	Clinical trial starting date	Comment
Altimmune	AdCOVID	University of Alabama	USA	N/A	Preclinical - animal studies		
Ankara University			Turkey		Preclinical		
Bharat Biotech		Thomas Jefferson University	USA		Preclinical		
BIOCAD		IEM	Russia		Preclinical		
CaroGen	AVIDIO COVID-19 vaccine		USA		Preclinical		
Centro Nacional Biotecnologia (CNB-CSIC)		IDIBAPS	Spain		Preclinical		
DZIF - German Center for Infection Research			Germany		Preclinical		
DZIF - German Center for Infection Research		CanVirexAG	Germany		Preclinical		
FBRI SRC VB VECTOR, Rospotrebnadzor, Koltsovo			Russia		Preclinical		
FluGen	CoroFlu	UW Madison, Bharat Biotech	USA		Preclinical		
GeoVax		BravoVax	China	N/A	Preclinical - animal studies		
Greffrex		N/A	USA	NIAID	Preclinical - animal studies		
Gritstone		N/A	USA	N/A	Preclinical		
Hester Biosciences		IIT Guwahat	India		Preclinical		
ID Pharma			Japan		Preclinical		
Institute for Biological Research	VSV-S	Dyadic, Weizmann Institute	Israel	Defense Ministry Israel	Preclinical		
Intravacc		Wageningen Bioveterinary Research/Utrecht Univ.	Netherlands		Preclinical		
KU Leuven			Belgium		Preclinical		

Source: Milken Institute, BioCentury, WHO, Nature, clinicaltrials.gov

Viral vectors: Additional assets with undisclosed timelines (2/2)

Company / group	Asset	Collaborators	Country	Other funding / gov't involvement	Development phase	Clinical trial starting date	Comment
National Center for Genetic Engineering and Biotechnology (BIOTEC)	Inactivated Flu-based SARS-CoV2 vaccine + Adjuvant	Government Pharmaceutical Organization (GPO)	Thailand		Preclinical		
National Research Centre, Egypt			Egypt		Preclinical		
Oswaldo Cruz Foundation (Fiocruz)		Instituto Nacional de Ciência e Tecnologia em Vacinas (INCTV)	Brazil	Government of Brazil	Preclinical		
ReNeuron			UK		Preclinical		
Stabilitech Biopharma Ltd	OraPro-COVID-19		UK		Preclinical		
The Lancaster University			UK		Preclinical		
Thomas Jefferson University	CORAVAX		USA		Preclinical - animal studies		
Tonix Pharmaceuticals	TNX-1800	Southern Research	USA	N/A	Preclinical		
University of Georgia/ University of Iowa			USA		Preclinical		
University of Hong Kong		CEPI	Hong Kong	CEPI	Preclinical		
University of Manitoba			Canada		Preclinical		
University of Western Ontario			Canada		Preclinical		
Valo Therapeutics Ltd			UK		Preclinical		
Zydus Cadila		N/A	India	N/A	Preclinical		

Source: Milken Institute, BioCentury, WHO, Nature, clinicaltrials.gov

Live attenuated virus: Additional assets with undisclosed timelines

Company / group	Asset	Collaborators	Country	Other funding / gov't involvement	Development phase	Clinical trial starting date	Comment
DZIF - German Center for Infection Research			Germany		Preclinical		
Epitopoietic Research Corp.					Preclinical		
Indian Immunologicals		Griffith University, Australia	India		Preclinical		
Mehmet Ali Aydinlar University/ Acıbadem Labmed Health Services A.S.			Turkey		Preclinical		
Meissa Vaccines			USA		Preclinical		
Nascent Biotech		Manhattan BioSolutions	USA		Preclinical		
Tonix Pharmaceuticals	TNX-1810	University of Alberta	Canada		Preclinical		
Tonix Pharmaceuticals	TNX-1820	University of Alberta	Canada		Preclinical		
Tonix Pharmaceuticals	TNX-1830	University of Alberta	Canada		Preclinical		

Source: Milken Institute, BioCentury, WHO, Nature, clinicaltrials.gov

VLPs: Additional assets with undisclosed timelines

Company / group	Asset	Collaborators	Country	Other funding / gov't involvement	Development phase	Clinical trial starting date	Comment
ARTES Biotechnology			Germany		Preclinical		
Doherty Institute		GSK	Australia		Preclinical		
iBio	IBIO-200	Infectious Disease Research Institute	USA		Preclinical		
IrsiCaixa AIDS Research	S protein integrated in HIV VLPs	IRTA-CReSA/ Barcelona Supercomputing Centre/ Grifols	Spain		Preclinical		
Lomonosov Moscow State University	VLP + Adjuvant	Government Pharmaceutical Organization (GPO)	Russia		Preclinical		
Mahidol University		Siriraj Hospital	Thailand		Preclinical		
Middle East Technical University			Turkey		Preclinical		
Navarrabiomed	VLPs, lentivirus and baculovirus vehicles	Oncoimmunology group	Spain		Preclinical		
OSIVAX			France		Preclinical		
Saiba GmbH			Switzerland		Preclinical		
University of Bristol		Imophoron	UK		Preclinical		
University of Sao Paulo			Brazil		Preclinical		
University of Washington		Icosavax, Gates Foundation, GSK (?)	USA	Gates Foundation	Preclinical - animal studies		
Bezmialem Vakif University			Turkey		Preclinical		

Source: Milken Institute, BioCentury, WHO, Nature, clinicaltrials.gov

Protein subunit: Additional assets with undisclosed timelines (1/5)

Company / group	Asset	Collaborators	Country	Other funding / gov't involvement	Development phase	Clinical trial starting date	Comment
AJ Vaccines		N/A	Denmark	N/A	Preclinical		
Akers Biosciences		Premas Biotech	USA		Preclinical		
Akshaya	**Chimigan SARS-CoV-2**	Cytovance (Shenzhen Hepalink)	China		Preclinical		
AnyGo Technology			China		Preclinical		
Applied Biotechnology Institute, Inc			USA		Preclinical		
Baiya Phytopharm/ Chula Vaccine Research Center	Plant-based subunit (RBD-Fc + Adjuvant)		Thailand		Preclinical		
Baylor CoM; U of Texas MB and others		PATH	USA	N/A	Preclinical		
Biological E Ltd			India		Preclinical		
Biomay		Medical University of Vienna	Austria		Preclinical		
BiOMVis Srl		University of Trento	Italy		Preclinical		
Bogazici University			Turkey		Preclinical		
Capricor Therapeutics	**Exosome-SARS-CoV-2 Display vaccine**	Johns Hopkins University	USA		Preclinical		
Chongqing Zhifei Biological Products					Preclinical - animal studies		

Source: Milken Institute, BioCentury, WHO, Nature, clinicaltrials.gov

Protein subunit: Additional assets with undisclosed timelines (2/5)

Company / group	Asset	Collaborators	Country	Other funding / gov't involvement	Development phase	Clinical trial starting date	Comment
Chulalongkorn University	RBD protein fused with Fc of IgG + Adjuvant	Government Pharmaceutical Organization (GPO)	Thailand		Preclinical		
City of Hope					Preclinical		
Clover Pharmaceuticals	Covid-19 S-Trimer	GSK/Dynavax	China	Industry	Preclinical		
EpiVax	EPV-CoV-19		USA		Preclinical		
EpiVax; University of Georgia			USA		Preclinical		
Farmacore Biotecnologia	VF-COVID-19		Brazil		Preclinical		
FBRI SRC VB VECTOR, Rospotrebnadzor, Koltsovo			Russia		Preclinical		
Flinders University		Vaxine Pty Ltd and Oracle	Australia		Preclinical - animal studies		
Flow Pharma			USA		Preclinical - animal studies		
G+FLAS Life Sciences		N/A	Korea	VC	Preclinical		
Generex	Ii-Key peptide COVID-19	EpiVax	USA	Beijing Zhonghua Investment Fund Management Co.	Preclinical		
Genomics Research Hub of Helix Biogen Consult in Ogbomoso, Nigeria		Elizade University, Ondo State, Federal Medical Centre, Ido, Ekiti State/ Massasoit, Community College/ Ladoke Akintola University of Technology, Ogbomoso, Adeleke University, Ede	Nigeria		Preclinical		
Griffith University		Luina Bio	Australia		Preclinical		
Griffith University		Olymvax	Australia		Preclinical		

Source: Milken Institute, BioCentury, WHO, Nature, clinicaltrials.gov

Protein subunit: Additional assets with undisclosed timelines (3/5)

Company / group	Asset	Collaborators	Country	Other funding / gov't involvement	Development phase	Clinical trial starting date	Comment
Heat Biologics		University of Miami	USA	N/A	Preclinical		
iBio		Beijing CC-Pharma	USA	N/A	Preclinical		
ImmunoPrecise Antibodies; EVQLV			USA		Preclinical		
Indian Institute of Science		Mynvax	India		Preclinical		
InnoMedica					Preclinical		
Innovax		GSK, Xiamen University	China		Preclinical		
Intravacc		Epivax	Netherlands		Preclinical		
Izmir Biomedicine and Genome Center			Turkey		Preclinical		
LakePharma, Inc.			USA		Preclinical		
Ligandal		N/A	USA	N/A	Preclinical		
Lomonosov Moscow State University	Structurally modified spherical particles of the tobacco mosaic virus (TMV)		Russia		Preclinical		
Max-Planck Institute of Colloids and Interfaces			Germany		Preclinical		
Medigen Vaccine Biologics Corporation		NIAID and Dynavax	Taiwan		Preclinical		
National Institute of Infectious Disease			Japan		Preclinical		
National Research Centre, Egypt			Egypt		Preclinical		
Neovii		Tel Aviv University	Israel		Preclinical		
OncoGen			Romania		Preclinical		
OncoGen			Romania		Preclinical		

Source: Milken Institute, BioCentury, WHO, Nature, clinicaltrials.gov

Protein subunit: Additional assets with undisclosed timelines (4/5)

Company / group	Asset	Collaborators	Country	Other funding / gov't involvement	Development phase	Clinical trial starting date	Comment
Osaka University		BIKEN and National Institutes of Biomedical Innovation	Japan		Preclinical		
OSE Immunotherapeutics			France		Preclinical		
PDS Biotechnology	PDS0203		USA		Preclinical		
PDS Biotechnology	PDS0204		USA		Preclinical		
Phylex Biosciences		ATUM	USA		Preclinical		
Predictive Oncology			USA		Preclinical		
PREVENT-nCoV consortium	ExpreS2-CoV	(AdaptVac, Institute for Tropical Medicine at University of Tubingen, Leiden University Medical Center, University of Copenhagen, ExpreS2ion Biotechnologies, Wageningen University)	Denmark	European Commission	Preclinical		
Quadram Institute Biosciences			UK		Preclinical		
Sichuan University State Key Laboratory of Biotherapy		Zhejiang Teruisi Pharmaceutical; Chengdu National GLP Center; Sichuan Provincial People's Hospital; Chengdu Institute of Biological Products (Sinopharm)	China	N/A	Preclinical		
Soligenix	Heat-stabilization technology	University of Hawaii at Manoa and BTG Specialty Pharmaceuticals (a subsidiary of Boston Scientific)	USA	Expected US government	Preclinical - animal studies		
St. Petersburg Scientific Research Institute of Vaccines and Serums			Russia		Preclinical		
Treos Bio (PepTC Vaccines)	PolyPEPI-SCoV-2		UK		Preclinical		
UbiVac	UBI-VLP-201		USA		Preclinical		
UfoVax		Scripps Research	USA	N/A	Preclinical - animal studies		
UMN Pharma (Shionogi)		Japan Agency for Medical Research and Development*	Japan		Preclinical		
University of California, San Diego			USA	National Science Foundation (Rapid Response Research [RAPID] grant)	Preclinical		
University of Hyderabad			India		Preclinical		

Source: Milken Institute, BioCentury, WHO, Nature, clinicaltrials.gov

Protein subunit: Additional assets with undisclosed timelines (5/5)

Company / group	Asset	Collaborators	Country	Other funding / gov't involvement	Development phase	Clinical trial starting date	Comment
University of Pittsburgh School of Medicine	PittCoVacc		USA	NIAID, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Cancer Institute,	Preclinical - animal studies		
University of Saskatchewan		VIDO-InterVac, National Microbiology Laboratory in Winnipeg	Canada	N/A	Preclinical - animal studies		
University of Alberta			Canada		Preclinical		
Vabiotech		Bristol University	Vietnam		Preclinical		
Vaxil Bio		N/A	Israel	Debentures	Preclinical		
Vaxil Bio	VXL-301		Canada		Preclinical		
Vaxil Bio	VXL-302		Canada		Preclinical		
Vaxil Bio	VXL-303		Canada		Preclinical		
Verndari		University of California, Davis	USA		Preclinical		
Versatope		University of Massachusetts Lowell			Preclinical		
Versatope		University of Massachusetts Lowell			Preclinical		
Yisheng Biopharma			China		Preclinical		

Source: Milken Institute, BioCentury, WHO, Nature, clinicaltrials.gov

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Deep dive: 33 COVID-19 vaccine candidates are currently undergoing clinical trials (1/3)

Platform	Company / group	Asset	Collaborators	Country	Other funding / govt' involvement	Current dev. phase	Official start date	Cum. trial participants
RNA	Moderna	mRNA-1273	NIAID, Lonza, Catalent	USA	CEPI, NIAID, BARDA	Phase II	May-20	755
	BioNTech	BNT162	Pfizer and Fosun Pharma	Germany, US		Phase I/II/III	Apr-20	32,588
	Imperial College London			UK		Phase I	Jun-20	320
	CureVac		CEPI, European Commission; Gates Foundation; DARPA	Germany	German government	Phase I	Jun-20	168
	Walvax Biotechnology		People's Liberation Army, Academy of Military Sciences	China		Phase I	Jun-20	168
	Arcturus Therapeutics	LUNAR-COV19	Duke-NUS Medical School	USA	Singapore	Phase I/II	Jul-20	85
DNA	Genexine	GX-19	Binex, GenNBio, Korea Advanced Institute of Science and Technology, Pohang University of Science and Technology	South Korea	IVI	Phase I/II	Jun-20	190
	Aivita Biomedical, Inc.	AV-COVID-19		USA		Phase I/II	Jul-20	280
	Inovio	INO-4800	Beijing Advaccine Biotechnology, Ology Bioservices	USA, S. Korea	CEPI, BMGF	Phase I/II	Jun-20	200
	Zydus Cadila	nCov vaccine		India		Phase I/II	Jul-20	1048
	Anges	AG0301-COVID19	Osaka University and Takara Bio	Japan		Phase I/II	Jul-20	30
	Symvivo	bacTRL-Spike		Canada		Phase I	Jul-20	112
Inactivated	Sinovac Biotech	PiCoVacc	Dynavax	China, Brazil	Bank of Beijing	Phase III	Jul-20	10,036
	Sinopharm		Beijing Institute of Biological Products	UAE		Phase III	Jul-20	9,628
	Sinopharm		Wuhan Institute of Biological Products	UAE		Phase III	Jul-20	8,956
	Chinese Academy of Medical Sciences		Institute of Medical Biology,	China		Phase I/II	Jul-20	1,413
	Bharat Biotech	BBV152		India		Phase I/II	Jul-20	1,125

Source: clinicaltrials.gov, press search

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Deep dive: 33 COVID-19 vaccine candidates are currently undergoing clinical trials (2/3)

Platform	Company / group	Asset	Collaborators	Country	Other funding / govt' involvement	Current dev. phase	Official start date	Cum. trial participants
Viral vectors	University of Oxford (Jenner Institute)	AZD1222 / ChAdOx1 nCoV-19	AstraZeneca, Advent SRL manufacturer, MilliporeSigma, Cobra Biologics	UK, Brazil, South Africa[1]	UK government	Phase I/II	May-20	18,650
	CanSino Biologics	Ad5-nCoV	Institute of Biotechnology at China's Academy of Military Medical Sciences	China	Chinese government	Phase II[4]	Apr-20	1,304
	Gamaleya Research Institute	Adeno-based[2]		Russia[2]		Phase I/II	Jun-20	76
	Johnson & Johnson	Ad26 SARS-CoV-2	Beth Israel Deaconess Medical Center	USA, Belgium	BARDA	Phase I/II	Jul-20	1,045
	Shenzhen University	COVID-aAPC	Shenzhen Second and Third People's Hospitals	China	Chinese government	Phase I	Feb-20	100
VLPs	Medicago		Laval University's Infectious Disease Research Centre	Canada	Canadian gov't	Phase I	Jul-20	180
Protein-subunit	Anhui Zhifei Longcom Biopharmaceutical		Institute of Microbiology, Chinese Academy of Sciences	China		Phase II	Jul-20	950
	Kentucky Bioprocessing					Phase I/II	Jul-20	180
	Clover Biopharmaceuticals[3]	SCB-2019	GSK/Dynavax	Australia		Phase I	Jun-20	150
	Vaxine Pty Ltd		Flinders University, Oracle	Australia		Phase I	Jun-20	40
	Novavax	NVX-CoV2373	Emergent BioSolutions, Praha Vaccines, Serum Institute of India	Australia	CEPI	Phase I	May-20	131
	University of Queensland	NVX-CoV2373	GSK, Dynavax, CSL (Parkville, Australia), Viroclinics Xplore	Australia	CEPI, Queensland, Australian gov't, Paul Ramsay Foundation	Phase I	Jul-20	120

1. Reuters 2. Two formulations of the same asset in trials in two separate locations 3. Clover is testing three different versions of the vaccine, including two that use unique adjuvants, in this trial 4. Approved for Military use in China

Source: clinicaltrials.gov, press search

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Deep dive: 33 COVID-19 vaccine candidates are currently undergoing clinical trials (3/3)

	Company/ Asset	Trial sponsor	Location	Phase	Size	Clinical trial dates[1]	Trial ID
Repurposed	BCG vaccine	University of Campinas	Brazil	IV	1000	**Start:** June 2020 **End:** May 2022	NCT04369794
	BCG vaccine	Murdoch Children's Research Institute	Melbourne, Australia	III	4170	**Start:** March 2020 **End:** March 2022	NCT04327206
	BCG vaccine	UMC Utrecht and Radboud University	Various locations, Netherlands	III	1500	**Start:** March 2020 **End:** December 2020	NCT04328441
	BCG vaccine	Ain Shams University	Cairo, Egypt	III	900	**Start:** April 2020 **End:** December 2020	NCT04350931
	BCG vaccine	Baylor College of Medicine	Houston and Boston, USA	III	700	**Start:** April 2020 **End:** November 2021	NCT04328441
	BCG vaccine	University of Antioquia	Colombia	III	1000	**Start:** April 2020 **End:** November 2021	NCT04362124
	BCG vaccine	Bandim Health Project, University of Southern Denmark	Denmark	III	1500	**Start:** May 2020 **End:** January 2021	NCT04373291
	BCG vaccine	TASK Applied Science	South Africa	III	500	**Start:** May 2020 **End:** April 2021	NCT04379336
	BCG vaccine	Assistance Publique - HÁ´pitaux de Paris	Paris, France	III	1120	**Start:** May 2020 **End:** February 2021	NCT04384549
	Measles vaccine	Kasr El Aini Hospital	Cairo, Egypt	III	200	**Start:** May 2020 **End:** November 2020	NCT04357028
	Immunovative Therapies	Mirror Biologics	United states	I/II	40	**Start:** July 2020 **End:** December 2021	NCT04441047
	Canadian Cancer Trials Group	Immudolon Tx, BioCan Rx, CSSRI, AtGen, ARCC	Canada	III	1500	**Start:** July 1, 2020 **End:** March 2021	NCT04442048

Additional planned trials

	Company/ Asset	Trial sponsor	Location	Planned start date
Multiple	Solidarity: 4 arm platform trial[2]	WHO	Multiple	TBD

1. Start and study completion end date in CT.gov; actual read-outs may be sooner 2. WHO

Source: CT.gov as of July 15, 2020

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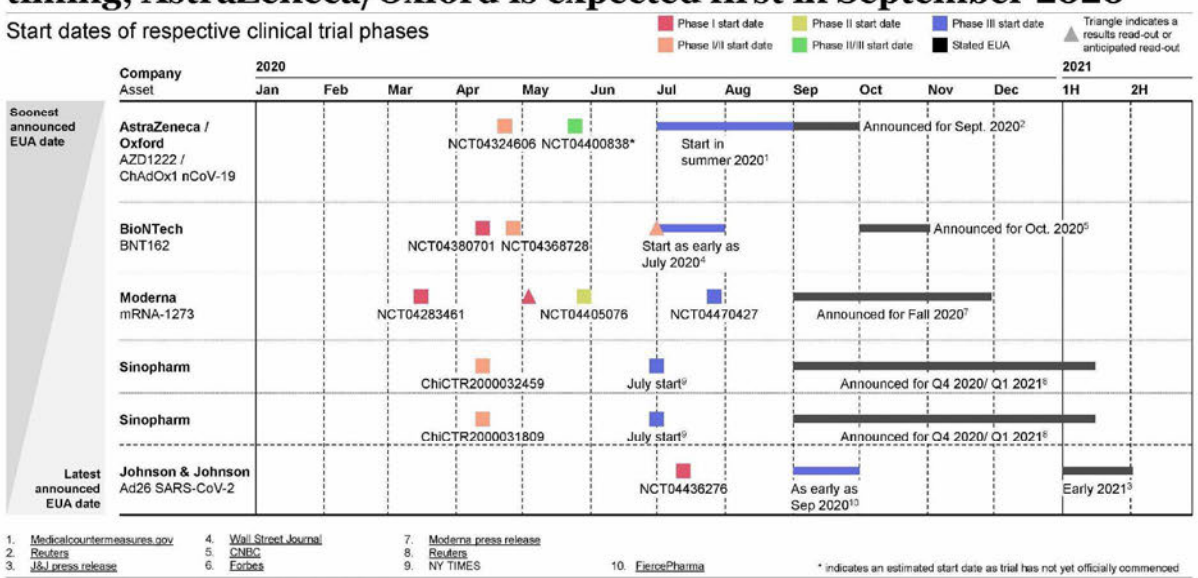
Six vaccine candidates have publicly announced potential EUA timing; AstraZeneca/Oxford is expected first in September 2020

Start dates of respective clinical trial phases



1. Medicalcountermeasures.gov
2. Reuters
3. J&J press release
4. Wall Street Journal
5. CNBC
6. Forbes
7. Moderna press release
8. Reuters
9. NY TIMES
10. FiercePharma

* indicates an estimated start date as trial has not yet officially commenced

Source: Milken Institute COVID-19 Tracker, clinicaltrials.gov, BioCentury, press search

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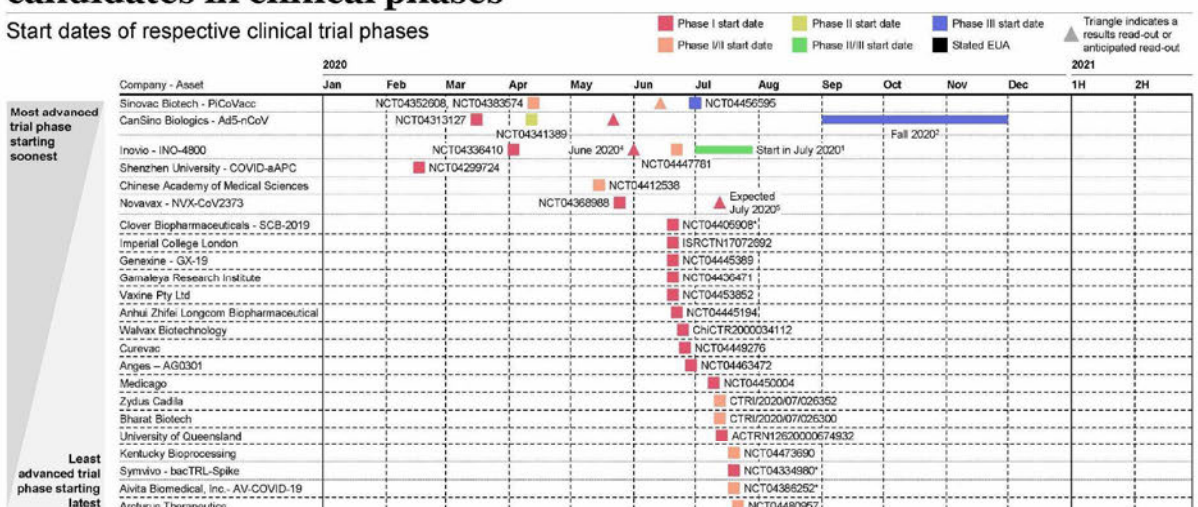
Publicly announced trial start dates for remaining candidates in clinical phases

Start dates of respective clinical trial phases



1. Inovio press release
2. Ipolitics.ca
4. Inovio press release
5. Novavax press release

* indicates an estimated start date as trial has not yet officially commenced

Source: Milken Institute COVID-19 Tracker, clinicaltrials.gov, BioCentury, press search

CURRENT AS OF JULY 15, 2020
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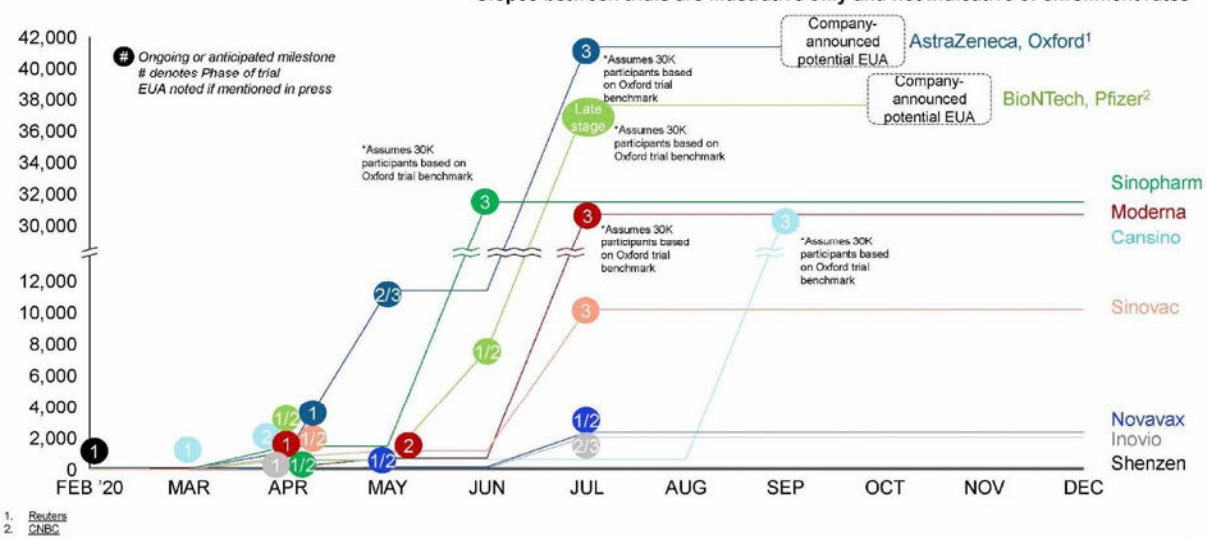
Timeline of participants in ongoing COVID-19 vaccine clinical trials based on publicly-available announcements

Outside-in view based on media coverage and published trial design if available; trials, timing, and EUA are estimates and subject to change

Slopes between trials are illustrative only and not indicative of enrollment rates



1. Reuters
2. CNBC

Source: clinicaltrials.gov, press search

Design elements for ongoing Phase 1, Phase 1/2 trials

Outside-in view based on media coverage and published trial design if available; trials, timing, and EUA are estimates and subject to change

	moderna[1]	BIONTECH Pfizer[2]	CanSinoBIO[3]	THE JENNER INSTITUTE OXFORD[4]	INOVIO[5] POWERING DNA MEDICINES	NOVAVAX[6]
Current phase	Phase I	Phase I/II	Phase I/II	Phase I/II	Phase I	Phase I of planned Phase I/II
End points	Safety, immuno.	Safety, immuno., potential efficacy	Safety, immuno.	Safety, immuno., efficacy	Safety, immuno.	Safety, immuno.
Dose schedule	2 doses	1 or 2 doses	1 or 2 doses	2 doses	2 doses	2 doses
Dose levels	3 dose levels	3 dose levels	2 dose levels	1 dose level for prime, 1 for boost	2 dose levels	2 dose level
Trial arms	9	21	28	9	2	5
Number of candidates	1 candidate	4 candidates	1 candidate	1 candidate	1 candidate	Up to 2 candidates, each with and without adjuvant
Trial size	105	560 in US & DE up to 7,800	696	1,090	40	131
Site geography	US	US, Germany	Canada	UK	US	Australia, USA (Ph II)
Special populations	Elderly	Elderly	None	None	Potential expansion into elderly, SARS-CoV-2 positive	None[7]

1. Clinicaltrials.gov
2. Clinicaltrials.gov
3. Clinicaltrials.gov
4. Clinicaltrials.gov
5. Clinicaltrials.gov
6. Clinicaltrials.gov
7. Novavax

Source: clinicaltrials.gov, press search

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Design elements for upcoming efficacy trials (e.g., Phase 2/3 or 3)

Outside-in view based on media coverage and published trial design if available; trials, timing, and EUA are estimates and subject to change

	moderna	moderna	BIONTECH Pfizer	THE JENNER INSTITUTE	AstraZeneca	sinovac	SINOPHARM
	Phase II	**Phase III**[10]	**Phase I/II/III**	**Phase II/III**	**Phase III**	**Phase III**	**Phase III**
Estimated start	May 25, 2020[1]	July 27, 2020	July[2]	May 2020[11]	Summer[12]	July[7]	July[14]
Dose schedule	2 dose for adults[1]	2 doses[15]	1 and 2 dose schedules being evaluated	1 dose for adults and ped., 1 or 2 doses for elderly[9]	Unknown	2 doses[7]	1 dose[14]
Dose levels	2 dose levels (50, 100 mcg)[1]	1 dose, 100 micrograms[15]	Unknown, current trial has 3 dose levels	1 dose level for adults and ped., 2 for elderly[9]	Unknown	Unknown	Unknown, current trial has 3 dose levels
Number of candidates	1 candidate[1]	1 candidate	1 – 3 candidates[2]	1 candidate[4]	1 candidate[12]	1 candidate[7]	Unknown
Trial size	600[1]	30,000[15]	Up to 32,000[2]	10,260[11]	30,000[5]	8,870[7]	15,000-30,000[14]
Site geography	USA[1]	USA[15]	USA	UK, Brazil, South Africa[13]	Unknown	Brazil[7]	UAE[14]
Special populations	None, trial includes adults 18+[1]	None, trials include adults 18+	Unknown, current trial includes elderly[3]	Elderly, pediatric (includes safety and immuno.)[6]	Pediatric	Adult + Elderly arms[7]	None, trials include adults 18+[14]

1. Clinicaltrials.gov
2. Clinicaltrials.gov
3. CNBC
4. CNBC
5. AstraZeneca press release
6. BBC
7. Clinicaltrials.gov
9. Clinicaltrials.gov
10. Clinicaltrials.gov
11. Reuters
9. World Vaccine Congress
10. Forbes
11. Clinicaltrials.gov
12. Reuters
13. Reuters
14. ChCTR
15. Clinicaltrials.gov

Source: clinicaltrials.gov, press search

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Compilation of published or pre-released trial results (1/5)

Sponsor / Asset	Platform type	Development phase	Results type	Results date	Results	Trial ID
Sinovac PiCoVacc	In-activated	Phase I/II	Nonclinical animal trials	May 6, 2020	• PiCoVacc induced SARS-CoV-2-specific neutralizing antibodies in mice, rats and non-human primates [1] • Antibodies neutralized 10 representative SARS-CoV-2 strains, suggesting a possible broader neutralizing ability against SARS-CoV-2 strains [2]	N/A
			Interim Phase II readout	June 14, 2020	• Induced neutralizing antibodies in "above 90%" of people who were tested 14 days after receiving two injections, two weeks apart[2] • No severe AEs reported[2]	NCT04383574
AstraZeneca/ Oxford AZ1222	Viral Vector	Phase II/III	Nonclinical animal trials	May 13, 2020	• Single vaccination induced a humoral and cellular immune response in six rhesus macaques[3] • Reduced viral load in vaccinated animals compared with control animals[3] • No evidence of immune-enhanced disease following viral challenge in vaccinated animals was observed[3]	N/A
		Phase II/III	Nonclinical animal trials	June 23, 2020	• "Pirbright Institute, working in collaboration with the University of Oxford, have successfully shown that two doses of the ChAdOx1 nCoV-19 (AZD1222) vaccine produce a greater antibody response than a single dose in pigs."[5] • No other statistics provided	N/A
			Interim Phase I/II readout	July 20, 2020	• "Neutralising antibodies were generated in more than 90% of participants across different assays. Responses were sustained up to 56 days of observation."[4] • "No serious adverse events occured."[4]	NCT04324606

1. Science Magazine
2. Statnews.com
3. BioRxiv paper
4. The Lancet
5. Pirbright Institute

Source: Press and literature as linked in footnotes

Compilation of published or pre-released trial results (2/5)

Sponsor / Asset	Platform type	Development phase	Results type	Results date	Results	Trial ID
Curevac	RNA	Preclinical	Nonclinical animal trials	May 14, 2020	• "Coronavirus lead vaccine candidate has generated high levels of virus neutralizing titers after two 2 microgram dose vaccinations in pre-clinical experiments" [1] • "Data showed a fast induction of a balanced immune response with high levels of virus neutralizing titers and T-cell responses" [1]	N/A
Moderna mRNA1273	RNA	Phase II	Interim Phase I readout	May 18, 2020	• 45 of 45 participants developed antibody levels at or above convalescent[2] • 8 of 8 participants developed neutralizing antibody titer levels, across the 25 and 100 microgram cohorts[2] • One grade 3 AE in 100 microgram cohort and no grade 4 AEs reported [2] • Titer levels were not disclosed in the preliminary results; FDA suggests levels of 160 and above [1]	NCT04283461
			Nonclinical animal trials	June 11, 2020	• "mRNA-1273 induces both potent neutralizing antibody and CD8 T cell responses and protects against SARS-CoV-2 infection in lungs and noses of mice without evidence of immunopathology" [3]	N/A
			Interim Phase I readout	July 14, 2020	• Neutralizing antibody titers were observed in 100% of evaluated participants [4] • "At Day 43, neutralizing activity against SARS-CoV-2 (PRNT80) was seen in all evaluated participants; . At the Phase 3 selected dose of 100 µg, the geometric mean titer levels were 4.1-fold above those seen in reference convalescent sera (n=3)." [4] • "Following second vaccination, mRNA-1273 elicited Th1-biased CD4 T-cell responses without significant elevation of Th2-biased CD4 T-cell responses." [4] • "mRNA-1273 was generally safe and well-tolerated" [4]	NCT04283461

1. CureVac press release
2. Moderna press release
3. biorxiv.org
4. Moderna press release

Source: Press and literature as linked in footnotes

Compilation of published or pre-released trial results (3/5)

Sponsor / Asset	Platform type	Development phase	Results type	Results date	Results	Trial ID
Harvard Research Group	DNA	Preclinical	Nonclinical animal trials	May 19, 2020	• Vaccinated animals developed humoral and cellular immune responses, including neutralizing antibody titers comparable to those found in convalescent humans and macaques infected with SARS-CoV-2.[1]	N/A
Inovio INO-4800	DNA	Phase I	Nonclinical animal trials	May 20, 2020	• Demonstrated neutralizing antibody and T cell immune responses against SARS-CoV-2 in mice and guinea pigs[2]	N/A
			Interim Phase I readout	June 30, 2020	• "94% of Phase 1 trial participants demonstrated overall immune responses at Week 6 after two doses of INO-4800 in trial with 40 healthy volunteers in preliminary analyses"[3] • No significant adverse events reported[3]	NCT04336410
CanSino Ad5-nCoV	Viral Vector	Phase II	Interim Phase I readout	May 22, 2020	• Reported mean neutralizing titers of 34 in its high-dose group, below FDA recommendations of 160[4] • Single dose elicited a four-fold increase in binding antibodies to RBD in 94–100% of participants, and a four-fold increase to live virus in 50–75% of participants[4]	NCT04313127
			Interim Phase II readout	July 20, 2020	• One injection of non-replicating adenovirus-vectored COVID-19 vaccine with two concentrations • "Seroconversion occurred in more than 96% of participants, and neutralising antibodies were generated in about 85%. More than 90% had T-cell responses."[5] • "No serious adverse events occured."[5]	NCT04398147

1. Science Magazine
2. Nature magazine
3. Inovio press release
4. BioCentury
5. The Lancet

Source: Press and literature as linked in footnotes

Compilation of published or pre-released trial results (4/5)

Sponsor / Asset	Platform type	Development phase	Results type	Results date	Results	Trial ID
USask	Protein subunit	Preclinical	Nonclinical animal trials	May 25, 2020	• "Vaccine induced a strong immune response, generated neutralizing antibodies, and decreased viral infection in the upper respiratory tract to almost undetectable levels" of ferrets[1]	N/A
Sinopharm BBIBP-CorV	In-activated	Phase I/II	Nonclinical animal trials	June 6, 2020	• Induced high-level neutralizing antibodies that can block the virus from infecting cells in monkeys, rats, guinea pigs and rabbits[2]	N/A
			Interim Phase I/II readout	June 16, 2020	• 100% of patients who received two doses over 28 days developed neutralizing antibodies[3] • Further data not included in release	ChiCTR-2000032459
			Interim Phase I/II readout	June 28, 2020	• "Relevant experts said that after vaccination showed good safety and immunogenicity, subjects in the vaccination group all produced high-titer antibodies"[4] • Further data not included in the release	ChiCTR-2000032459

1. University of Saskatchewan
2. Cell Medical Journal
4. CNBG.com
5. CNBG.com.cn

Source: Press and literature as linked in footnotes

Compilation of published or pre-released trial results (5/5)

Sponsor / Asset	Platform type	Development phase	Results type	Results date	Results	Trial ID
Pfizer / BioNTech BNT 162	RNA	Phase I/II	Interim US Phase I/II readout	July 1, 2020	• At day 28 (7 days after dose 2), all subjects who received 10 or 30 µg of BNT162b1 had significantly developed antibody levels 8 and 46.3 times that of convalescent patients [1] • Same patient group developed neutralizing antibodies 1.8 and 2.8 times the GMT of convalescent patients [1] • Results only reported for one of four vaccine candidates in the clinical trial	NCT04368728
			Interim Germany Phase I/II readout	July 20, 2020	• BNT162b1 elicited strong CD4+ and CD8+ T cell responses against SARS-CoV-2-receptor binding domain (RBD), compared to baseline[2] • The RBD-specific, interferon-γ+, IL-2+, CD8+ T cells elicited by BNT162b1 in immunized participants indicate a strong potential for cell mediated anti-viral activity[2] • T cell cytokine profile shows vaccine elicited T cells exhibit a Th1 phenotype, which is associated with antiviral propertie[2]	NCT04368728
Imperial College	RNA	Preclinical	Nonclinical animal trials	July 19, 2020	• According to preclinical data published in Nature Communications journal, two doses of the vaccine were able to generate highly specific antibodies that could neutralise the virus in mice.[3]	N/A

1. Pfizer press release
2. Pfizer press release
3. Nature

Source: Press and literature as linked in footnotes

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There are multiple COVID-19 therapeutics and vaccine partnership efforts underway: Government-led

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BARDA	Funding **screening, discovery, and some scale-up manufacturing / fill-finish** across **diagnostics, therapeutics and vaccines** Development is **contingent on new funds** from United States Congress
NIH **ACTIV**	**Public private partnership** to speed **vaccines and therapeutics** by identifying, prioritizing and facilitating the entry of some of the most promising candidates into clinical trials
World Health Organization	Serving as a **global convener and agenda setter** to support development of COVID-19 R&D for the most vulnerable **Fast-tracks availability** of effective tests, vaccines, and medicines
Operation Warp Speed	**Task force assembled by POTUS and HHS** aimed at accelerating the development, manufacturing, and distribution of vaccines, therapeutics, and diagnostics
ACT	**Initiative led by the EU commission (but with global focus),** structured around three workstreams: diagnostics, treatments, and vaccines **Established ACT partnership** between Bill & Melinda Gates Foundation, the Wellcome Trust and WHO, CEPI, and GAVI to purchase more than 15 billion doses of COVID-19 vaccines over six years
IVA	**Europe's Inclusive Vaccines Alliance** **Complementary deal between AstraZeneca and Italy, Germany, the Netherlands, and France** to procure 400M doses of their vaccine candidate on a pro rata basis for their population

Source: CEPI, IMI, HHS BARDA, Bill & Melinda Gates Foundation, NIH, BIO, EFPIA, and WHO websites. BioCentury article on R&D Leaders Forum. WeForum news for Bill & Melinda Gates Foundation vaccine manufacturing

There are multiple COVID-19 therapeutics and vaccine partnership efforts underway: NGO-led

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CEPI Gavi	Coordinating **vaccine development efforts** Funding **multiple candidates for COVID-19 vaccine development**, including partnerships with industry
IMI2-Call21	Announced a **EUR 45 million** call for proposals to support **development of therapeutics and diagnostics.** **Public-Private-Partnership** between the European Commission and the European Pharma Industry
Therapeutics Accelerator	Announced **$125M seed funding** to speed development and access to therapies for COVID-19 Includes on **repurposed and new drugs and biologics** end to end through to **scale-up**
Bill & Melinda Gates Foundation	Announced intent to fund construction of **factories** for **seven COVID-19 vaccine candidates**
COVID-19 R&D	Collaboration among **R&D heads** of 17 companies to accelerate new COVID-19 therapies and vaccines, with a focus on **trial acceleration** and **data sharing**
Industry associations	**Tracking research development** currently under way to help members **coordinate manufacturing** with one another and government authorities

Source: CEPI, IMI, HHS BARDA, Bill & Melinda Gates Foundation, NIH, BIO, EFPIA, and WHO websites. BioCentury article on R&D Leaders Forum. WeForum news for Bill & Melinda Gates Foundation vaccine manufacturing

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Public announcements indicate global vaccine manufacturing capacity of ~8 – 9 billion doses by end of 2021

Manufacturing type	Asset	Asset category	Company	Collaborators	YE 2020 (M)	YE 2021 (M)	In-source	Out-source	Partner	Comment
Specific-assets	mRNA-1273	RNA	Moderna	NIAID, Lonza		1,000[1]	✓	✓	Lonza, Catalent	
	BNT162	RNA	BioNTech	Pfizer and Fosun Pharma	100[2]	1,300[2]	✓	✓	Pfizer	
	INO-4800	DNA	Inovio	Beijing Advaccine Biotechnology, Ology Bioservices	1[4]		✓	✓	Richter-Helm	
		Viral vectors	Themis	Merck, Institut Pasteur and Uni. of Pittsburgh		1,000[5]	✓	✓		
	AAVCOVID	Viral vectors	Mass. Eye and Ear and Mass. General Hospital	Novartis	Millions[6]			✓	Novartis	
	Ad26 SARS-CoV-2	Viral vectors	J&J	Beth Israel, HHS		1,000[7]	✓	✓	Catalent, Emergent Biosolutions	
	AZD1222 / ChAdOx1 nCoV-19	Viral vectors	University of Oxford (Jenner Institute)	AstraZeneca, Advent SRL MilliporeSigma, Cobra Biologics	700[8]	2,000[9]		✓	SII, Oxford Biomedica, Emergent Biosolutions, Catalent, Scotland Symbiosis	
	AS03	Protein-subunit	Sanofi Pasteur	GSK		1,000[10]	✓			
	NVX-CoV2373	Protein-subunit	Novavax	Emergent BioSolutions, Praha Vaccines, Serum Inst. of India	100[15]	1,000[11]	✓		Praha Vaccines	
Other	PiCoVacc	Inactivated	Sinovac Biotech	Dynavax		100[12]			N/A	
		Inactivated	Sinopharm	Beijing Institute of Biological Products	100[13]				N/A	
		Inactivated	Sinopharm	Wuhan Institute of Biological Products	100[13]				N/A	
Government-funded	N/A	N/A	HSS / Operation Warp Speed	To be determined	N/A	N/A		✓	Emergent Biosolutions	$628M reservation[14]

1. Moderna press release
2. Pfizer press release
4. Inovio press release
5. FierceBiotech
6. Masseyeandear.com
7. J&J press release
8. AZ press release
9. AZ press release
10. FiercePharma
11. Novartis press release
12. BusinessWire
13. Chinadaily.com.cn
14. HHS press release
15. FiercePharma

Source: Milken Institute, BioCentury, WHO, Nature, clinicaltrials.gov, press searches as noted above

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US government's Operation Warp Speed

Accelerate development, manufacturing, and distribution of Vx, Tx, and Dx



Areas of focus

Expand COVID-19 countermeasures, including:

- Vaccines
- Therapeutics
- Diagnostics

Accelerate countermeasure development, specifically through:

- Development
- Manufacturing
- Distribution

Enablers

Commitment to affordability

Companies receiving support will provide a donated allocation of countermeasures developed

Financial resources, including:

$10B from CARES act

$6.5B from BARDA

$3B from NIH

Planned updates

Public will be kept abreast of latest updates with briefings

Leadership

Overall leads

Moncef Slaoui

General Gustave F. Perna

Countermeasure leads

Vaccines: Peter Marks, M.D., Ph.D.

Therapeutics: Janet Woodcock, M.D.

Diagnostics: Bruce Tromberg, Ph.D.

Various DoD officials

Select funding

- **Vaccines:**
  - $2B to Pfizer/BioNTech
  - $1.6B to Novavax
  - $1.2B to AstraZeneca / Oxford
  - $483M to Moderna
  - $456M to J&J
- **Manufacturing:**
  - $628M to Emergent Biosolutions
- **Distribution:**
  - $138M to ApiJet for prefilled syringes
  - $204M to Corning for glass vials
  - $143M to SiO2 Materials Science for glass-coated plastic containers

Source: HHS press release

DOCUMENT INTENDED TO PROVIDE INSIGHT BASED ON CURRENTLY AVAILABLE INFORMATION FOR CONSIDERATION AND NOT SPECIFIC ADVICE.
REFERENCES TO SPECIFIC ORGANIZATIONS ARE SOLELY FOR INFORMATIONAL PURPOSES AND DO NOT CONSTITUTE ANY ENDORSEMENT OR RECOMMENDATION

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Additional vaccine development efforts

The Human Vaccines Project and Harvard University launched the Human Immunomics Initiative, a joint effort to develop artificial intelligence–based models of immunity that can help accelerate the design and testing of vaccines and therapeutics for a range of diseases, including Covid-19[1]

Adding to a growing list of collaborative initiatives, sixteen major drugmakers will join a U.S. government- and European Medicines Agency-backed program to "focus and expedite" R&D on vaccines and therapeutics. Joining Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) are Bristol-Myers Squibb, Eli Lilly, GSK, J&J, Merck, Novartis, Pfizer, Sanofi, Takeda, Vir Biotechnology and six others[2]

Britain launched its Vaccine Taskforce, a government-backed effort to "expedite and coordinate" rapid development of a COVID-19 shot in the United Kingdom. Led by former GlaxoSmithKline R&D chief (10)(2e) (10)(2e) the team will include representatives from AstraZeneca and the Wellcome Trust[3]

CEPI launches new funding opportunity to accelerate COVID-19 vaccine development and production. It will be open until at least 30 June 2020 with applications reviewed on a rolling basis every two weeks. It will support the rapid development of vaccines which could be available for licensure in 12-18 months or less, and increase the availability of vaccines for wide-spread global deployment

1. The Human Vaccines Project 2. NIH press release 3. Gov.UK 4. CEPI

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Document overview

To date, there is no **globally approved COVID-19 vaccine or treatment** available.

There are **over 250 vaccine candidates** and over **300 therapeutics candidates** in consideration.

This document and accompanying Excel trackers provide a **current snapshot of vaccine and therapeutic efforts for COVID-19.** They are based on **publicly available data** across candidate lists, clinical trial data and trial results.

Sources of insight:

- Multiple candidate lists (e.g. Milken Institute, BioCentury, WHO)
- Clinical trial registries (mainly CT.gov and ChiCTR)
- Press and literature searches

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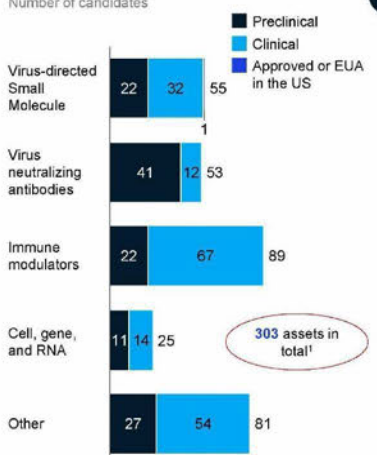
COVID-19 Therapeutics landscape update

Pipeline snapshot

Number of candidates



Key takeaways

Over 300 candidates are being considered across a range of modalities and use cases. **Remdesivir and Dexamethasone** are the two drugs with clinically proven benefits.

None have been approved globally for COVID-19, but some countries approved specific drugs: remdesivir received EUA by FDA[2] and is approved in EU, Japan, Taiwan, India, UAE and Singapore[3]; **Favipiravir** is approved in China, India, and Russia[4]; **Dexamethasone** is approved in Japan[9] and the UK[6]; Coronavir is approved in Russia[7]; Itolizumab is approved for emergency use in India[8]

- **Virus-directed small molecules:** Mostly repurposed drugs and many are in trials; Early results for many drugs are not yet robust, however.
- **Monoclonal & polyclonal antibodies (virus neutralizing):** Mostly in pre-clinical stage, but showing some early positive signals. Companies began entering clinical trials for mAbs treatments and expect to receive the first EUA as early as Sep 2020.[5]
- **Immune modulators:** Various immune modulators are being tried, mostly for severe/critical cases with acute respiratory distress syndrome and/or cytokine storm, but no drug with clear benefits yet.
- **Cell, gene, and RNA:** Multiple therapies in development, many in pre-clinical stage.

Weekly developments as of July 21

- **The New England Journal of Medicine published another promising study on the use of dexamethasone.** In a cohort of over 6,000 UK patients, those receiving dexamethasone exhibited lower mortality at 28d. This result was most pronounced in patients receiving invasive mechanical ventilation (29.3% mortality for dexamethasone patients vs. 41.4% for standard of care).[10]
- **On the heels of these promising results, Japan has approved dexamethasone for the treatment of COVID-19.** Along with remdesivir, dexamethasone becomes the second approved therapy for the disease in Japan.[9]
- **Glenmark Pharmaceuticals has announced positive topline data for FabiFlu (favipiravir).** In a Phase III trial in India, mild/moderate COVID-19 patients had greater achievement of "clinical cure" after 4 days when given FabiFlu vs. control (69.8% vs. 44.9%, respectively). FabiFlu patients also had 28.6% faster viral clearance. These results follow a busy week globally for favipiravir, with the announcement of mixed results (trials conducted in Japan and Bangladesh), approval for use in India, and public scrutiny towards Glenmark Pharma for FabiFlu pricing.[11]
- **Synairgen announced positive data for SNG001, an inhaled formulation of interferon beta.** In a study of UK COVID-19 patients, those receiving SNG001 had a 79% lowered chance of developing severe disease, in addition to reduced rates of breathlessness compared to placebo. However, there are critical question that remain, most notably the small sample size and lack of peer review.[12]

1. Includes 29 compounds not included on following page; clinical trial information may not have been captured if not registered at CT.gov or published otherwise
2. FDA 3. Gilead, Reuters, Reuters, Reuters, Press 4. RDIF, HosoMedica, PMlive 5. Reuters 6. Fiercepharma
7. CGTN 8. Indiatvnews 9. Reuters 10. NEJM 11. Glenmark Pharma, The Economic Times 12. GlobeNewswire, Fiercebiotech

Source: Milken Institute, BioCentury, WHO, Nature, CT.gov, ChiCTR, press as of July 14, 2020

There are over 300 candidates in the pipeline for COVID-19 therapeutics

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F| Not covered in this document

		Description	Candidates profiled[1]	Example candidates/companies
A| **Virus-directed small molecule**		**Largely repurposed** compounds, including **antivirals** (HIV, Influenza), **antimalarials**, **antiprotozoals**, and more	48	Remdesivir (GILEAD), Kaletra (abbvie), Chloroquine
B| **Antibodies** (to neutralize virus)	**Monoclonal antibodies** (mAbs)	**New development** using **survivor samples**, **genetically engineered** mice and **synthetic routes**; often a cocktail	32	VIR, REGENERON
	Polyclonal antibodies / plasma	**New development** using **survivor plasma** (convalescent plasma) or **genetically engineered** cows for hyper-immunized globulin. Also called plasma-derived therapy or IVIG.	15	CSL Behring, Takeda, SAb
C| **Immune modulators**		**IL inhibitors**, alpha or beta-**interferon** and other therapies often **repurposed**. Targets host immune response with severe and critical disease (e.g. cytokine release syndrome)	87	Actemra, Kevzara (REGENERON, Roche, SANOFI)
D| **Cell, gene and RNA therapies**		**Stem cells**, **T-cells**, cord blood cells and **RNA-based** therapies	24	remestemcel-L (mesoblast), siRNA (VIR, Alnylam)
E| **Other**		**Steroids**, **surfactants**, **oxygen carriers**, **immunotherapies**, and other modalities not included in the above	68	Losartan, Methylprednisolone, Bevacizumab (Roche, Takeda, AstraZeneca)
F| Traditional Chinese Medicine		Traditional herbal formulas and medicines	n/a	maxingshigan-yinqiaosan

1. Excludes 29 compounds with lack of public data; often in early stage research settings
2. Does not include compounds with lack of public data which are included on proceeding page

Source: Milken Institute, BioCentury, FiercePharma, FierceBiotech

A: COVID-19 virus-directed small molecule – selected candidates deep dive (1/5)

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Directionally positive result
Directionally negative result
FDA Emergency Use Authorization issued

Compound (Primary mode of action)	US Status (Licensed indication)	Use case	Registered trials on CT.gov[1]	Earliest trial end date[2]	Initial clinical evidence[3]	Efficacy in isolated use?	Additional information
Remdesivir (Antiviral) GILEAD	Under development (Ebola, SARS)	Treatment	16 *2 terminated due to low enrollment[8]*	May 2020	Positive Gilead and NIAID-sponsored results in moderate / severe patients, conflicting with the earlier Chinese trial	Improvement in compassionate use cases in US and other countries[4]	Approved approval in Japan, Taiwan, India, Singapore, and UAE[7] Planning a trial for paediatric use and inhalant version[9]
Chloroquine (Antimalarial)	Marketed (Malaria)	Prophylaxis, Treatment	26	Apr 2021 (prophy) Apr 2020 (treatment)	A large observational study showed increased mortality and cardiac arrhythmias, with or without macrolide		In-vitro SARS-CoV-2 efficacy data Used off-label for treatment and prophylaxis of Zika
Hydroxy-chloroquine (Antimalarial)	Marketed (Malaria)	Prophylaxis, Treatment	186	May 2020 (prophy) May 2020 (treatment)	Randomized trials in general have not found any benefit in treating hospitalized or non-hospitalized patients; no evidence of Prophylactic benefit However, mixed results from a couple of studies	Improvement in Japanese patient and patients in Australia[5,6]	FDA revoked EUA for COVID patients.[12] France also revoked its authorization of HCQ.[10] Italy also banned the drug's use outside of clinical trials and the UK has put limits on the use[11] WHO and NIH halted HCQ trials[8]
Azithromycin (Antibiotic)	Marketed (Bacterial infection)	Treatment	65	May 2020	Mixed results on viral clearance from small-mid size French studies and Brazilian study		Widely used for chest infections, pneumonia

1. Based on CT.gov registered trials related to COVID-19 as of July 13, 2020 2. From CT.gov trial end dates. Actual read-out may be sooner 3. See "Compilation of published results" for full set of references 4. CDC, Gilead
5. Pharma Japan 6. The Scientist, Tech Times 7. Gilead, Reuters, Reuters, Reuters, Press 8. Endpoint 9. STAT [redacted] 10. France24 11. Pharmafile 12. FDA

Source: Milken Institute, BioCentury, FiercePharma, FierceBiotech, CT.gov, CDC, Gilead, Pharma Japan, The Scientist, Tech Times, GenEng News

A: COVID-19 virus-directed small molecule – selected candidates deep dive (2/5)

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Directionally positive result
Directionally negative result

Compound (Primary mode of action)	US Status (Licensed indication)	Use case	Registered trials on CT.gov[1]	Earliest trial end date[2]	Initial clinical evidence[3]	Efficacy in isolated use?	Additional information
Kaletra lopinavir, ritonavir (Antiviral) abbvie	Marketed (HIV)	Treatment	38	Mar 2020	Two Chinese trials, the RECOVERY trial, the Solidarity trial all did not show any evidence of efficacy	Improvement in Thai patient and patients in Australia[4]	Both the RECOVERY and SOLIDARITY trials dropped Kaletra arms after concluding no benefits to severe / hospitalized patients[10]
Avigan favipiravir (Antiviral) FUJIFILM	Investigational (Influenza) *Approved in Japan and China	Treatment	25	Mar 2020	Positive results on viral load and clinical recovery in Chinese, Russian, and the 'Dhaka Trial'; but no evidence of efficacy in the Japanese trial	Test dosages effective in mild and asymptomatic cases[5]	China aproved for COVID[8] Russia temporarily approved Avifavir, for hospitalized cases[7] India approved for mild to moderate for restricted emergency use[9]
Prezcobix Darunavir (Antiviral) Johnson&Johnson	Marketed (HIV)	Prophylaxis, Treatment	2	Jun 2020 (prophy) Jun 2020 (treatment)	Study shows lack of antiviral activity[6]		Prior SARS efficacy data
Arbidol umifenovir (Antiviral) Pharmstandard	Investigational (Influenza) *Approved in Russia, China	Prophylaxis, Treatment	7	Aug 2020 (prophy) Apr 2020 (treatment)	Positive results on viral load and clinical outcomes in Chinese retrospective analysis		Marketed for influenza, respiratory viral infections in Russia and China; patented for use against atypical pneumonia
Norvir Ritonavir (Antiviral)	Marketed (HIV)	Treatment	6	Mar 2020			

1. Based on CT.gov registered trials related to COVID-19 as of July 13, 2020
2. From CT.gov trial end dates. Actual read-out may be sooner
3. See "Compilation of published results" for full set of references
4. The Scientist, Tech Times
5. GenEng News
6. MedRxiv
7. RDIF
8. HospiMedica
9. GlenmarkPharma
10. Recovery trial press release, WHO

Source: Milken Institute, BioCentury, FiercePharma, FierceBiotech, CT.gov, CDC, Gilead, Pharma Japan, The Scientist, Tech Times, GenEng News

A: COVID-19 virus-directed small molecule – selected candidates deep dive (3/5)

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Directionally positive result | Directionally negative result

Compound (Primary mode of action)	US Status (Licensed indication)	Use case	Registered trials on CT.gov[1]	Earliest trial end date[2]	Initial clinical evidence[3]	Efficacy in isolated use?	Additional information
Ganovo danoprevir (Antiviral)	**Investigational** (*Approved in China, Hepatitis C)	Treatment	2	**Mar 2020**	Clinical improvement in very small, non-controlled trial		
Galidesivir (Antiviral)	**Under development** (Yellow fever)	Prophylaxis, Treatment	1	**May 2021**			Shown broad-spectrum activity in vitro vs. >20 RNA viruses, including coronaviruses
Foipan Camostat mesylate (Antiviral)	**Investigational** (*Approved in Japan and South Korea, Pancreatitis)	Treatment	7	**May 2021**			Active against other corona-viruses, including SARS-CoV; blocks infection of cells with SARS-CoV-2-like particles and patient-derived SARS-CoV-2
Alinia Nitazoxanide (Antiprotozoal)	**Marketed** (Diahrrea)	Treatment	14	**Jun 2020**			In-vitro study showed efficacy against 2019-nCoV
Xpovio Selinexor (Antiviral)	**Marketed** (Multiple myeloma)	Treatment	2	**Aug 2020**			

1. Based on CT.gov registered trials related to COVID-19 as of July 13, 2020
2. From CT.gov trial end dates. Actual read-out may be sooner
3. See "Compilation of published results" for full set of references
4. The Scientist, Tech Times
5. GenEng News

Source: Milken Institute, BioCentury, FiercePharma, FierceBiotech, CT.gov, CDC, Gilead, Pharma Japan, The Scientist, Tech Times, GenEng News

A: COVID-19 virus-directed small molecule – selected candidates deep dive (4/5)

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Directionally positive result
Directionally negative result

Compound (Primary mode of action)	US Status (Licensed indication)	Use case	Registered trials on CT.gov[1]	Earliest trial end date[2]	Initial clinical evidence[3]	Efficacy in isolated use?	Additional information
EIDD-2801 (Antiviral) RIDGEBACKBIO MERCK	**Under development**	Prophylaxis, Treatment	3	June 2020			Promising in-vitro data from monkey kidney cells (IC50 of 0.3 μM) Blocked strain replication in human airway epithelial cells
AT-527 (Antiviral) ATEA	**Under development** (Hep C)	Treatment	1	Aug 2020			Internal *in-vitro* and *in-vivo* data shows efficacy against various single-stranded RNA viruses, including human flaviviruses and coronaviruses
Vicromax merimepodib (Antiviral) BioSig	**Under development** (Hep C, zika, foot and mouth virus)	Treatment	1	Aug 2020			In vitro testing shows strong activity against SARS-CoV-2 in cell cultures; reduction of over 90% of infectious viruses was observed
Ivermectin (Gx) (Antiparasitic)	**Marketed** (Onchocerciasis , lymphatic filariasis)	Treatment	29	Jun 2020	Small size retrospective / observational studies showed correlation with low mortalities	Small study at Univ. of Utah found the critically ill may benefit[4]	In-vitro Monash University study found it inhibited the activity of the virus in a petri dish
ATR-002 (MEK-inhibitor) Atriva	**Under development** (respiratory RNA viruses)	Treatment	0	-			Preclinical result shows reduced propagation of the virus and cytokine releases; Ph II to begin in July 2020[5]

1. Based on CT.gov registered trials related to COVID-19 as of July 13, 2020
2. From CT.gov trial end dates. Actual read-out may be sooner
3. See "Compilation of published results" for full set of references
4. LinksBridge
5. pharmaphorum

Source: Milken Institute, BioCentury, FiercePharma, FierceBiotech, CT.gov, CDC, Gilead, Pharma Japan, The Scientist, Tech Times, GenEng News

A: COVID-19 virus-directed small molecule – selected candidates deep dive (5/5)

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EXAMPLES FOR ILLUSTRATION PURPOSES ONLY

Directionally positive result | Directionally negative result

Compound (Primary mode of action)	US Status (Licensed indication)	Use case	Registered trials on CT.gov[1]	Earliest trial end date[2]	Initial clinical evidence[3]	Efficacy in isolated use?	Additional information
Coronavir (Antiviral)	**Under development**	Treatment	-	-	In a Russian study, the drug was associated with clinical improvement for of mild/moderate patients		The new antiviral drug is approved in Russia for COVID-19 treatment in July 2020[4]
Daclatasvir, Sofosbuvir (Antiviral)	**Marketed** (Hepatitis C)	Treatment	-	-	In a series of Iranian studies, patients treated with the drug showed faster recovery and reduced mortality		Several large-size, randomized trials are underway to confirm the finding[5]
Pyramax pyronaridine-artesunate (antimalarial) MMV	**Under development** (Malaria)	Treatment	1	**Feb 2021**	-		-

1. Based on CT.gov registered trials related to COVID-19 as of July 13, 2020
2. From CT.gov trial end dates. Actual read-out may be sooner
3. See "Compilation of published results" for full set of references
4. CGTN
5. Hepmag

Source: Milken Institute, BioCentury, FiercePharma, FierceBiotech, CT.gov, CDC, Gilead, Pharma Japan, The Scientist, Tech Times, GenEng News

B: COVID-19 virus-neutralizing monoclonal antibodies deep dive - select efforts with greater press (1/3)

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Compound/company		Description	Target /actual trial start date[1]
Monoclonal antibodies	VIR, Wuxi Biologics, Biogen, GSK	Isolated monoclonal antibodies from **SARS survivors** to develop **VIR-7831 and VIR-7832**	Targeting Phase II "**in 3-5 months**" as of early April[2]
	REGENERON	Cocktail of two different monoclonal antibodies (**REGN-COV2**) from COVID-19 survivors and genetically engineered mice. Preclinical data shows that no resistant mutants observed after using the antibody cocktail (v. single mAB).[7] Received $85M from BARDA, and $450M from Operation Warp Speed (through BARDA and DoD) for manufacturing scale up to produce 70K-300K treatment doses and 420K-1.3M preventive doses.[6]	**Began phase II/III treatment trials** (hospitalized & non-hospitalized) and phase III preventive trials in July; **aims to begin large-scale distribution as early as late summer of 2020**[6]
	Lilly, AbCellera	Testing **LY-CoV555**; Announced start of Ph 1 and large-scale manufacturing (6/1/2020) and plan to do a prevention trial later in 2020[3,5]	**June 2020 – aims to read out within a month[3]; expects EUA as early as Sep 2020[5]**
	CELLTRION	mAb candidate **CT-P59**; pre-clinical study showed x100 reduction in viral load and lung lesions improvement[4]	**July 2020[4]**
	sorrento, mabpharm	Proprietary fusion protein that binds to SARS-CoV-2	**June – September 2020**
	AstraZeneca	2 of 6 mAb candidates – targeting a specific sites on the virus' spike protein receptor binding domain – licensed from Vanderbilt for both prophylaxis & treatment. Working with BARDA and DARPA, which includes manufacturing support for Ph I[8]	**Aug 2020[8]**
	AMGEN, Adaptive	Leveraging of Adaptive's viral-neutralizing antibody platform	

1. Publicly stated targets or actual start date of human trials 2. BioCentury, Targeting 3 trials for different patient populations - prophylaxis, pre-respiratory distress and in respiratory distress 3. Eli Lilly 4. Celltrion
5. Reuters 6. Endpoint, Fierce pharma 7. Biocentury press release 8. Biocentury

Source: Milken Institute, BioCentury, CT.gov

B: COVID-19 virus-neutralizing monoclonal antibodies deep dive - select efforts with greater press (2/3)

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NONEXHAUSTIVE
EXAMPLES FOR ILLUSTRATION PURPOSES ONLY

Compound/company		Description	Target / actual trial start date[1]
Monoclonal antibodies	Brii Biosciences	Pool of 206 **antibodies** from 8 patients in China	**September - October 2020**
	ATREca, igm Biosciences, BeiGene	Atreca to identify, IGM to manufacture antibodies, BeiGene to lead clinical development	**Early 2021**
	sorrento THERAPEUTICS, Mount Sinai	**COVI-SHIELD** – 3-epitope antibody cocktail	**September - October 2020**
	sorrento THERAPEUTICS	**COVI-GUARD** – STI-1499 (which is also in COVI-SHEILD)	**August 2020**
	Lilly, TopAlliance	Antibody cocktail of **JS016** (incl. CB6) for both prophylaxis and treatment; the company announced they have secured capacity to serve 100,000 people by the end of 2020[4]; licensed Lonza's gene expression system GS Xceed[5]	**Began its China study in June; plan to begin its US study in 2Q of 2020**[2]
	abbvie	Abbvie partners to develop therapeutic using **47D11** discovered by with Harbour BioMed, Utrecht University and Erasmus Medical Center	-
	Lilly	Lilly's third monoclonal antibody candidate	"Could enter human clinical trials in the coming weeks" as of **early June**[3]
	INSTITUTE OF MICROBIOLOGY CHINESE ACADEMY OF SCIENCES	A fully human monoclonal antibody developed by a research team at the Institute of Microbiology of the Chinese Academy of Sciences (IMCAS). The research was supported by China's State Council and 4 other government agencies	**June 2020**[4]

1. Publicly stated targets or actual start date of human trials
2. Reuters 3. The Print 4. IMCAS 5. Reuters

Source: Milken Institute, BioCentury, CT.gov

B: COVID-19 virus-neutralizing monoclonal antibodies deep dive - select efforts with greater press (3/3)

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NONEXHAUSTIVE
EXAMPLES FOR ILLUSTRATION PURPOSES ONLY

Compound/company		Description	Target / actual trial start date[1]
Monoclonal antibodies	BIOBRILL	Multiple monoclonal antibody candidates identified from convalescent patients	Q3 2020
	YUMAB	Fully human mAB candidate – preclinical study showed full neutralization capacity	2H 2020
	VIRNA Therapeutics	Prioritized multiple monoclonal antibodies against spike proteins	Aug - Sep 2020
	Boehringer Ingelheim	28 prioritized antibodies showed potent in neutralizing the virus as well as low levels of mutation	By year end 2020[2]
	COLUMBIA | COLUMBIA UNIVERSITY IRVING MEDICAL CENTER	19 neutralizing mAb candidates from 5 COVID-19 patients hospitalized with severe disease[3]	N/A
	The Rockefeller University	Several promising mAb candidates identified from convalescent plasma are capable of neutralizing the virus at low concentrations[4]	N/A

1. Publicly stated targets or actual start date of human trials 2. [redacted] 3. Nature 4. Nature

Source: Milken Institute, BioCentury, CT.gov

B: COVID-19 virus-neutralizing polyclonal antibodies deep dive - select efforts with greater press (1/2)

CURRENT AS OF July 22, 2020
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EXAMPLES FOR ILLUSTRATION PURPOSES ONLY

Compound/company		Description	Target / actual trial start date[1]
Polyclonal antibodies / plasma	Takeda, CSL Behring, ADMA Biologics, bpl, LFB, GC Pharma, Biotest, octapharma, Sanquin, biopharma	A coalition of 10 companies, led by Takeda and CSL, to develop a hyperimmune globulin (H-IG) based COVID-19 treatment	**July 2020** –aims to complete the trial by Fall 2020, and obtain approval before YE 2020[3]
	KAMADA, KEDRION BIOPHARMA	H-IG from survivor plasma collaboration	
	CSL Behring	H-IG from survivor plasma	
	SAB BIOTHERAPEUTICS	H-IG from GE cows	
	GigaGen	Recombinant H-IG from survivor plasma	2021
	XBiotech, BioBridge GLOBAL	H-IG from survivor plasma	
	GRIFOLS	H-IG from survivor plasma[2]	
	emergent biosolutions	COVID-Human Immune Globulin (COVID-HIG) and COVID-Equine Immune Globulin (COVID-EIG). Received $14.5M from HHS for COVID-HIG and partnered with NIAID to test the treatment in severe and high-risk patients.[4] Received another $34.6M from the DoD to conduct clinical trials.[5]	Early summer of 2020 (read out in 45 days)[4]

1. Publicly stated targets or actual start date of human trials
2. Partnership with US Government, including FDA and BARDA
3. Business Insider
4. Biocentury
5. Biocentury

Source: Milken Institute, BioCentury, CT.gov

B: COVID-19 virus-neutralizing polyclonal antibodies deep dive - select efforts with greater press (2/2)

CURRENT AS OF July 22, 2020
NONEXHAUSTIVE
EXAMPLES FOR ILLUSTRATION PURPOSES ONLY

Compound/company		Description	Target / actual trial start date[1]
Polyclonal antibodies / plasma	xenothera	**XAV-19** – an animal origin, polyclonal antibody treatment	**July 2020**
	octapharma	Octagam (IVIG), a marketed drug for immunodeficiency syndromes, entered Ph III for COVID-19 treatment[6]	**June 2020**
	GC Pharma	COVID-19 survival plasma based therapy	**July 2020**[3]

1. Publicly stated targets
2. Octapharma
3. Korea Herald

Source: Milken Institute, BioCentury, CT.gov

C: COVID-19 immune modulators – selected candidates deep dive (1/8)

CURRENT AS OF July 22, 2020
NONEXHAUSTIVE
EXAMPLES FOR ILLUSTRATION PURPOSES ONLY

Directionally positive result Directionally negative result

Compound (Primary mode of action)	US Status (Licensed indication)	Use case[1]	Registered trials on CT.gov[2]	Earliest trial end date[3]	Initial clinical evidence[4]	Efficacy in isolated use?	Additional information
Actemra Tocilizumab (IL-6 inhibitor)	**Marketed** (RA)	Treatment - CRS	39	May 2020	Improved outcomes in France & China; mixed evidence in the Italy and retrospective studies	Improvement in patients in Italy[5]	Prior approval for CRS; EU struck a deal to secure Actemra supplies for its member countries[5]
Jakafi ruxolitinib (JAK inhibitor)	**Marketed** (Myelofibrosis)	Treatment - CRS	18	May 2020	-		Preclinical evidence and preliminary reports from independent studies support decision to pursue Phase III
Kevzara Sarilumab (IL-6 inhibitor)	**Marketed** (RA)	Treatment – CRS, ARDS	10	Jun 2020	Correlated with worse outcomes for severe patients; No meaningful benefit for critical patients	-	Efficacy supported by preliminary data from single-arm study in China using another IL-6 receptor antibody
Rebif (Interferon beta-1a)	**Marketed** (Multiple sclerosis)	Treatment - CRS	7	Apr 2020	- -		EU struck a deal to secure Rebif supplies for its member countries[6]
Kineret Anakinra (IL-1 inhibitor)	**Marketed** (RA)	Treatment - CRS	14	Jul 2020	Improved survival in high dose anakinra group in study in Italy		
Betaseron Interferon beta-1b (interferon)	**Marketed** (Multiple sclerosis)	Treatment - CRS	5	Apr 2020	- -		
Sylvant Siltuximab (IL-6 inhibitor)	**Marketed** (multi-centric Castle-man disease)	Treatment - CRS	3	May 2020	- -		
Olumiant baricitinib (JAK inhibitor)	**Marketed** (Rheumatoid Arthritis)	Treatment – COVID-19, CRS	11	Apr 2020	-	-	Lilly launched ph III to test baricitinib alone (NIH has tested it w/ remdesivir); readout expected in Sep 2020[7]

1. CRS - Cytokine Release Syndrome; ARDS - Acute Respiratory Distress Syndrome
2. Based on CT.gov registered trials related to COVID-19 as of July 13, 2020
3. Actual read-out may be sooner than CT.gov trial end date
4. See "Compilation of published results" for full set of references
5. Trieste All News
6. WKZO
7. Endpoint

Source: Milken Institute, BioCentury, FiercePharma, FierceBiotech, CT.gov

C: COVID-19 immune modulators – selected candidates deep dive (2/8)

CURRENT AS OF July 22, 2020
NONEXHAUSTIVE
EXAMPLES FOR ILLUSTRATION PURPOSES ONLY

Directionally positive result | Directionally negative result

Compound (Primary mode of action)	US Status (Licensed indication)	Use case[1]	Registered trials on CT.gov[2]	Earliest trial end date[3]	Initial clinical evidence[8]	Efficacy in isolated use?	Additional information
Soliris eculizumab (C5 inhibitor)	**Marketed** (PNH/atypical-HUS)	Treatment – COVID-19	3	**Aug 2020**	-	10-patient proof-of-concept trial showed improvement	"Preclinical scientific rationale" supporting the drug's use in patients with severe pneumonia or ARDS
Xpovio selinexor (XPO1 inhibitor)	**Marketed** (Cancers)	Treatment – COVID-19	2	**Aug 2020**	-	-	XPO1 Inhibitors demonstrated preclinical activity against respiratory viruses (incl. SARS-CoV) and associated inflammation
Calquence acalabrutinib (BTK inhibitor)	**Marketed** (Mantle cell lymphoma)	Treatment – CRS	2	**Sep 2020**	Case series of 19 hospitalized patients and severe hypoxia and/or inflammation showed clinical outcomes improvement[7]	Clinical benefit for small group of hospitalized patients with advanced lung disease[5]	
Xeljanz tofacitinib (JAK inhibitor)	**Marketed** (Rheumatoid arthritis)	Treatment – COVID-19	5	**Jul 2020**	-	-	
Farxiga dapagliflozin (SGL2 inhibitor)	**Under Development**	Treatment – COVID-19	2	**Dec 2020**	-	-	
Ultomiris ravulizumab (C5 inhibitor)	**Marketed** (PNH/atypical-HUS)	Treatment - ARDS	2	**Feb 2021**	-	Soliris showed benefits for ARDS lung damage (Ultomiris is long-acting form of Soliris)[6]	Animal studies show complement inhibition reduces lung inflammation and viral pneumonia pathology
Ilaris canakinumab (IL-1β inhibitor)	**Under Development**	Treatment – CRS	4	**Sep 2020**	-	-	

1. CRS - Cytokine Release Syndrome; ARDS - Acute Respiratory Distress Syndrome
2. Based on CT.gov registered trials related to COVID-19 as of July 13, 2020
3. Actual read-out may be sooner than CT.gov trial end date
4. FiercePharma
5. FiercePharma
6. BioCentury
7. AstraZeneca
8. See "Compilation of published results" for full set of references

Source: Milken Institute, BioCentury, FiercePharma, FierceBiotech, CT.gov

C: COVID-19 immune modulators – selected candidates deep dive (3/8)

CURRENT AS OF July 22, 2020
NONEXHAUSTIVE
EXAMPLES FOR ILLUSTRATION PURPOSES ONLY

Directionally positive result Directionally negative result

Compound (Primary mode of action)	US Status (Licensed indication)	Use case[1]	Registered trials on CT.gov[2]	Earliest trial end date[3]	Initial clinical evidence[5]	Efficacy in isolated use?	Additional information
PUL-042 PULMOTECT (Toll-like receptor ligands)	**Under Development**	Treatment - CRS	2	Oct 2020	-	-	
Thalidomide (TNF-alpha inhibitor)	**Marketed** (Hansen's disease, MM)	Treatment – COVID-19	2	May 2020	-	-	
Opdivo nivolumab (PD-1 blocker)	**Marketed** (cancers)	Treatment – COVID-19	4	Aug 2020	-	-	
TJ003234 TJM2 I-MAB (GM-CSF inhibitor)	**Under Development**	Treatment - CRS	1	Sep 2020	Trend of improved clinical outcome & reduced cytokine related diseases the ph1b/2	-	Shows promise as treatment for cytokine storm
Gilenya NOVARTIS Fingolimod (S1P receptor modulator)	**Marketed** (Multiple sclerosis)	Treatment - CRS	1	Jul 2020	-	-	
Leukine PTx Sargramostim (GM-CSF)	**Marketed** (Leukemia, infection)	Treatment – COVID-19	3	Dec 2020	-	-	In vivo studies showed efficacy in patients with viral pneumonia
PRO140 Leronlimab CytoDyn (CCR5 antagonist)	**Under development**	Treatment – COVID-19	2	Apr 2021	-	7 patients in New York; 4 improved[4]	
Gamifant Emapalumab SOBI (Interferon gamma)	**Marketed** (Primary HLH)	Treatment – COVID-19	1	Sep 2020	-	-	

1. CRS - Cytokine Release Syndrome; ARDS - Acute Respiratory Distress Syndrome 2. Based on CT.gov registered trials related to COVID-19 as of July 13, 2020 3. Actual read-out may be sooner than CT.gov trial end date
4. New York Post 5. See "Compilation of published results" for full set of references

Source: Milken Institute, BioCentury, FiercePharma, FierceBiotech, CT.gov

C: COVID-19 immune modulators – selected candidates deep dive (4/8)

CURRENT AS OF July 22, 2020
NONEXHAUSTIVE
EXAMPLES FOR ILLUSTRATION PURPOSES ONLY

Directionally positive result Directionally negative result

Compound (Primary mode of action)	US Status (Licensed indication)	Use case[1]	Registered trials on CT.gov[2]	Earliest trial end date[3]	Initial clinical evidence	Efficacy in isolated use?	Additional information
MORAb-022 Gimsilumab (GM-CSF inhibitor) ROIVANT	**Under development**	Treatment – COVID-19	1	**Oct 2020**	-	-	Favorable safety and tolerability profile to date in trials for other indications
OT-101 (TGF-beta 2 inhibitor) MATEON	**Under Development**	Treatment – COVID-19	0		-	-	
PegIntron, Sylatron (Peginterferon alfa-2b) MERCK	**Marketed** (Hepatitis C, cancers)	Treatment - CRS	0		-	-	
Novaferon, Nova (New interferon) Genova	**Investigational** (*approved in China, Hep B)	Treatment - CRS	0		-	-	
EDP1815 (Monoclonal microbial)	**Under Development**	Treatment - CRS	1	**May 2021**	-	-	Clinical trial in psoriasis shows efficacy in reducing production of inflammatory cytokines
SNG001 (Inhaled interferon beta-1a) synairgen	**Under Development**	Treatment - CRS	1	**August 2020**	Reduced risk of developing severe symptoms by 79%, including reduction in breathlessness		Previous trials for respiratory viral infections in asthma
Esbriet Pirfenidone (Antiviral) Roche	**Marketed** (Idiopathic pulmonary fibrosis)	Treatment	1	**Jun 2020**	-	-	

1. CRS - Cytokine Release Syndrome; ARDS - Acute Respiratory Distress Syndrome 2. Based on CT.gov registered trials related to COVID-19 as of July 13, 2020 3. Actual read-out may be sooner than CT.gov trial end date

Source: Milken Institute, BioCentury, FiercePharma, FierceBiotech, CT.gov

C: COVID-19 immune modulators – selected candidates deep dive (5/8)

CURRENT AS OF July 22, 2020
NONEXHAUSTIVE
EXAMPLES FOR ILLUSTRATION PURPOSES ONLY

Directionally positive result Directionally negative result

Compound (Primary mode of action)	US Status (Licensed indication)	Use case[1]	Registered trials on CT.gov[2]	Earliest trial end date[3]	Initial clinical evidence[4]	Efficacy in isolated use?	Additional information
ATYR1923 (Neuropilin-2 modulator) aTyr	**Under Development**	Treatment – COVID-19	1	Oct 2020	-	-	
IntronA Interferon alpha-2b (Interferon)	**Marketed** (Cancer, Hep B & Hep C)	Treatment – COVID-19	3	Jul 2020	China study showed clinical improvement including accelerated vital clearance	-	
Interferon lambda-1a (Interferon)	**Under Development**	Treatment – COVID-19	2	Nov 2020	-	-	
Clazakizumab (IL-6 inhibitor) ALDER Bristol Myers Squibb	**Under Development**	Treatment – COVID-19	4	Jul 2020	-	-	
Yeliva opaganib (SK2 inhibitor)	**Under Development**	Treatment - CRS	3	Dec 2020	-	-	
DSTAT dociparstat sodium (HMGB1 inhibitor) CHIMERIX	**Under Development**	Treatment - CRS	0		-	-	
Otilimab (GM-CSF inhibitor) gsk	**Under Development**	Treatment – COVID-19	1	Dec 2020	-	-	
Imatinib (TK inhibitor) NOVARTIS	**Under Development**	Treatment - COVID-19	5	Aug 2020	-	-	
T-COVID altimmune (Immune modulator)	**Under Development**	Treatment - COVID-19	0	4Q 2020	-	-	Altimmune received a $4.7 million from the U.S. military to fund Phase 1/2

1. CRS - Cytokine Release Syndrome; ARDS - Acute Respiratory Distress Syndrome
2. Based on CT.gov registered trials related to COVID-19 as of July 13, 2020
3. Actual read-out may be sooner than CT.gov trial end date
4. See "Compilation of published results" for full set of references

Source: Milken Institute, BioCentury, FiercePharma, FierceBiotech, CT.gov

C: COVID-19 immune modulators – selected candidates deep dive (6/8)

CURRENT AS OF July 22, 2020
NONEXHAUSTIVE
EXAMPLES FOR ILLUSTRATION PURPOSES ONLY

Directionally positive result Directionally negative result

Compound (Primary mode of action)	US Status (Licensed indication)	Use case[1]	Registered trials on CT.gov[2]	Earliest trial end date[3]	Initial clinical evidence[4]	Efficacy in isolated use?	Additional information
OP-101 dendrimer N-acetyl-cysteine (targeting reactive macrophages) Orpheris	**Under Development** (Adrenoleuco-dystrophy)	Treatment – CRS	1	Nov 2020	-	-	-
Auxora CM4620-IE (CRAC inhibitor) CalciMedica	**Under Development**	Treatment	1	Sep 2020	An open-labelled study showed reduced ventilator use and time to recovery		Demonstrated safety and potential efficacy in patients with hypoxemia secondary to systemic inflammatory response syndrome in acute pancreatitis
MSTT1041A (IL-33 inhibitor) Genentech	**Under Development**	Treatment - ARDS	1	Oct 2020	-		BARDA awarded $22.6M for ph2 of MSTT1041A and UTTR1147A[5]
UTTR1147A (Cytokine modulator) Genentech	**Under Development**	Treatment - ARDS	1	Oct 2020	-		BARDA awarded $22.6M for ph2 of MSTT1041A and UTTR1147A[5]
Bemcentinib (AXL kinase inhibitors) BerGenBio	**Under Development**	Treatment – COVID-19	0	Summer 2020	-		Ph II trials begun as part of the British government's ACCORD platform
Artlegia Olokizumab (IL-6 inhibitor)	**Under Development**	Treatment – CRS	2	Nov 2020	-		Russian's sovereign wealth fund and r-Pharm established a $57M JV to scale up Artlegia production for FOVID[6]
TZLS-501 Tiziana Life Sciences (IL-6 inhibitor)	**Under Development**	Treatment – CRS	0		-	-	The company is working on a proprietary inhalation technology

1. CRS - Cytokine Release Syndrome; ARDS - Acute Respiratory Distress Syndrome
2. Based on CT.gov registered trials related to COVID-19 as of July 13, 2020
3. Actual read-out may be sooner than CT.gov trial end date
4. See "Compilation of published results" for full set of references
5. HHS
6. RDIF

Source: Milken Institute, BioCentury, FiercePharma, FierceBiotech, CT.gov

C: COVID-19 immune modulators – selected candidates deep dive (7/8)

CURRENT AS OF July 22, 2020
NONEXHAUSTIVE
EXAMPLES FOR ILLUSTRATION PURPOSES ONLY

Directionally positive result Directionally negative result

Compound (Primary mode of action)	US Status (Licensed indication)	Use case[1]	Registered trials on CT.gov[2]	Earliest trial end date[3]	Initial clinical evidence[4]	Efficacy in isolated use?	Additional information
CT-P13 infliximab biosimilar (TNF blocker) CELLTRION	**Marketed** (Various inflammatory disorders)	Treatment – CRS	0		-	-	Will be tested as part of the CATALYST platform trials in the UK[5]
IZN101 IZANA namilumab (GM-CSF inhibitor)	**Under Development**	Treatment – CRS	0		-	-	-
TRV027 (AT1 receptor)	**Under Development**	Treatment – COVID-19	1	**Jan 2021**	-	-	-
IFX-1 (C5a complement inhibitor) InflaRx	**Under Development**	Treatment – ARDS	1	**Dec 2020**	Low mortality trend was observed in a Phase II trial	1 of the 2 patients who received anti-C5a mAb produced by IFX-1 cell line improved ARDS	-
Mavrilimumab (GM-CSF receptor inhibitor) KINIKSA	**Under Development**	Treatment – ARDS	5	**Jul 2020**	Better clinical result and mortality rate from a single-center pilot study	-	-
PTC299 (DHODH inhibitor) PTC	**Under Development**	Treatment – CRS	1	**Jan 2021**	-	-	-
EB05 (TLR4 inhibitor) Eiger BioPharm	**Under Development**	Treatment – CRS	1	**Oct 2020**	-	-	-
M5049 (TLR 7/8 antagonist) MERCK	**Under Development**	Treatment – CRS	1	**Nov 2020**	-	-	-

1. CRS - Cytokine Release Syndrome; ARDS - Acute Respiratory Distress Syndrome
2. Based on CT.gov registered trials related to COVID-19 as of July 13, 2020
3. Actual read-out may be sooner than CT.gov trial end date
4. See "Compilation of published results" for full set of references
5. Press

Source: Milken Institute, BioCentury, FiercePharma, FierceBiotech, CT.gov

C: COVID-19 immune modulators – selected candidates deep dive (8/8)

CURRENT AS OF July 22, 2020
NONEXHAUSTIVE
EXAMPLES FOR ILLUSTRATION PURPOSES ONLY

Directionally positive result | Directionally negative result

Compound (Primary mode of action)	US Status (Licensed indication)	Use case[1]	Registered trials on CT.gov[2]	Earliest trial end date[3]	Initial clinical evidence[4]	Efficacy in isolated use?	Additional information
ALZUMAb itolizumab; EQ001 (anti-CD6 IgG1 mAb) Biocon equillium	**Under Development** (plaque psoriasis)	Treatment – CRS; ARDS	1	**Jul 2020**	In a small size trial in India, treatment with the drug was associated with mortality reduction and clinical improvement	-	Approved in India for emergency use based on a small size randomized trial result – the first novel biologic therapy approved for treating COVID-19 complication[5]
Orencia abatacept (T cell costimulation modulator) Bristol-Myers Squibb	**Marketed** (rheumatoid arthritis)	Treatment	2	**Jan 2021**	-	-	In Ph 2 study, not yet recruiting
SAR443122 (RIPK1 inhibitor) SANOFI	**Under development** (early stage inflammatory indications)	Treatment	1	**Jan 2021**	-	-	In Ph 1 trial
Cinvanti aprepitant (substance P / neurokinin 1 receptor antagonist) HERON	**Marketed** (delay chemotherapy side effects)	Treatment	1	**Oct 2020**	-	-	Recruiting for Ph 2 trial

1. CRS - Cytokine Release Syndrome; ARDS - Acute Respiratory Distress Syndrome
2. Based on CT.gov registered trials related to COVID-19 as of July 13, 2020
3. Actual read-out may be sooner than CT.gov trial end date
4. See "Compilation of published results" for full set of references
5. Biocon

Source: Milken Institute, BioCentury, FiercePharma, FierceBiotech, CT.gov

D: COVID-19 Cell, Gene, RNA therapy – selected candidates deep dive (1/2)

CURRENT AS OF July 22, 2020
NONEXHAUSTIVE
EXAMPLES FOR ILLUSTRATION PURPOSES ONLY

Directionally positive result Directionally negative result

	Compound (Primary mode of action)	US Status (Licensed indication)	Use case[1]	Registered trials on CT.gov[2]	Earliest trial end date[3]	Initial clinical evidence[4]	Efficacy in isolated use?	Additional information
Cell therapy	Virus-specific T-cell therapies (Allogeneic T-cell therapies) allo Vir	Under Development	Treatment – COVID-19	0		-	3 patients in Israel[5]	Off-the-shelf; being studied for anti-inflammatory properties
	CYNK-001 (NK cells (placenta-derived)) sorrento celularity	Under Development	Prophylaxis, Treatment – COVID-19	1	**Nov 2021**	-	-	Investigated to treat liquid and solid tumors; shows potential against virally infected cells
	NK cells (various originators)	Under Development	Prophylaxis, Treatment – COVID-19	3	**Jun 2020**	-	-	
	LEAPS peptides (T-cell modulator) CELSCI	Under Development	Treatment – COVID-19	0		-	-	Technology can be used to construct immunotherapeutic peptides with antiviral and anti-inflammatory properties
RNA therapy	RNAi (RNAi (testing 150 RNAis)) sirnaomics	Under Development	Prophylaxis, Treatment – COVID-19	0		-	-	
	VIR-2703 VIR AlnylamTM	Under Development	Treatment – COVID-19	0		-	-	
	DeltaRex-g (RNA virus-based gene vector)	Under Development	Treatment – ARDS	1	**Mar 2021**	-	-	Nanoparticles can mimic SARS-CoV-2 and may serve as a decoy to prevent SARSCoV-2 cell entry

1. CRS - Cytokine Release Syndrome; ARDS - Acute Respiratory Distress Syndrome
2. Based on CT.gov registered trials related to COVID-19 as of July 13, 2020
3. Actual read-out may be sooner than CT.gov trial end date
4. See "Compilation of published results" for full set of references
5. Irish News

Source: Milken Institute, BioCentury, FiercePharma, FierceBiotech, CT.gov, Irish News, IEEE Spectrum

D: COVID-19 Cell, Gene, RNA therapy – selected candidates deep dive (2/2)

CURRENT AS OF July 22, 2020
NONEXHAUSTIVE
EXAMPLES FOR ILLUSTRATION PURPOSES ONLY

Directionally positive result Directionally negative result

	Compound (Primary mode of action)	US Status (Licensed indication)	Use case[1]	Registered trials on CT.gov[2]	Earliest trial end date[3]	Initial clinical evidence[4]	Efficacy in isolated use?	Additional information
Stem cells	Mesenchymal Stem Cells	Under Development	Treatment – COVID-19, ARDS	40	**June 2020**	Improved outcomes in severe patients	7 patients in China (all discharged)[5]	Efficacy shown in human COPD study (same biomarker as COVID-19)
	HB-adMSCs (MSC)	Under Development	Treatment – ARDS	3	**Oct 2020**	-	-	
	Ryoncil remestemcel-L (MSC)	Under Development	Treatment – ARDS	3	**April 2021**	Positive outcome in isolated use	-	
	AmnioBoost	Under Development	Treatment – ARDS	0		-	-	Efficacy in reducing inflammatory conditions caused by several diseases
	MultiStem HLCM051 (MAPCs)	Under Development	Treatment – ARDS	1	**Aug 2022**	-	Lower mortality for ARDS patients (not COVID-19)[6]	Starting Ph 3 trials for ARDS
	CAP-1002 (Allogeneic cardiosphere-derived stem cells)	Under Development	Treatment – ARDS	1	**N/A**	-	-	
	BM-Allo.MSC (mesenchymal stem cells)	Under Development	Treatment	1	**Jun 2020**	-	-	Proprietary "GMP-in-a-Box" for scalable manufacturing
	Autologous Adipose Tissue-Derived Mesenchymal Stem Cells (AdMSCs)	Under Development	Prophylaxis; Treatment	1	**Aug 2021**	-	-	-

1. CRS - Cytokine Release Syndrome; ARDS - Acute Respiratory Distress Syndrome
2. Based on CT.gov registered trials related to COVID-19 as of July 13, 2020
3. Actual read-out may be sooner than CT.gov trial end date
4. See "Compilation of published results" for full set of references
5. IEEE Spectrum
6. Athersys

Source: Milken Institute, BioCentury, FiercePharma, FierceBiotech, CT.gov, Irish News, IEEE Spectrum

CURRENT AS OF July 22, 2020
NONEXHAUSTIVE
EXAMPLES FOR ILLUSTRATION PURPOSES ONLY

E: COVID-19 other therapeutics – selected candidates deep dive (1/3)

Directionally positive result | Directionally negative result

Compound (Primary mode of action)	US Status (Licensed indication)	Use case	Registered trials on CT.gov[1]	Earliest trial end date	Initial clinical evidence[2]	Efficacy in isolated use?	Additional information
Cozaar (and Gx) MERCK losartan (Antihypertensive)	**Marketed** (hypertension)	Treatment	9	Oct 2020			
Methylprednisolone (Steroid)	**Marketed** (inflammation)	Treatment	14	May 2020			In Chinese study of n=200, seeming reduced risk of death for ARDS patients
Avastin Roche bevacizumab (Angiogenesis inhibitor)	**Marketed** (cancers)	Treatment	3	May 2020			
Activase Roche Alteplase (Tissue plasminogen activator)	**Marketed** (Stroke)	Treatment	2	Aug 2020			Preparing to launch compassionate use study in 12 people[3]
APN01 APEIRON (rhACE2)	**Under development**	Treatment	2	Feb 2020			In vivo data showed that ACE2 is essential receptor for COVID-19[4]
Nitric oxide (Vasodilator)	**Marketed** (PPHN, ARDS)	Treatment	16	Sep 2020			
Telmisartan (Angiotensin receptor blocker)	**Marketed** (High blood pressure)	Treatment	5	Aug 2020			
Famotidine (Histamine H2 receptor antagonist)	**Marketed** (Peptic ulcer disease)	Treatment	1	Apr 2021	Improved clinical outcomes in two retrospective studies		

1. Based on CT.gov registered trials related to COVID-19 as of July 13, 2020 2. See "Compilation of published results" for full set of references 3. [redacted] 4. Pipeline Review

Source: Milken Institute, BioCentury, FiercePharma, FierceBiotech, CT.gov

CURRENT AS OF July 22, 2020
NONEXHAUSTIVE
EXAMPLES FOR ILLUSTRATION PURPOSES ONLY

E: COVID-19 other therapeutics – selected candidates deep dive (2/3)

Directionally positive result | Directionally negative result

Compound (Primary mode of action)	US Status (Licensed indication)	Use case[1]	Registered trials on CT.gov[2]	Earliest trial end date	Initial clinical evidence[3]	Efficacy in isolated use?	Additional information
Sirolimus (Immunosuppressant)	**Marketed** (Peptic ulcer disease)	Treatment	4	**Sep 2020**			
Colcrys (colchicine (Anti-mitotic))	**Marketed** (gout)	Treatment	13	**May 2020**	A small trial showed effect on preventing progression of the disease		
Symbicort Rapihaler budesonide, formoterol (Steroid) AstraZeneca	**Marketed** (asthma, COPD)	Treatment	4	**May 2020**			
Dexamethasone (Steroid)	**Marketed** (inflammation, allergy)	Treatment	9	**Jun 2020**	A large RECOVERY platform trial in UK showed the drug's potential to reduce mortality rate of high-risk population		UK approved the drug after the favourable RECOVERY trial result[4]
DAS181 (Recombinant sialidase)	**Under Development**	Treatment	4	**Apr 2020**			Preliminary data from a Chinese trial is positive
Progesterone (Hormone)	**Marketed** (various)	Treatment	1	**Apr 2021**			
Aspirin (Anti-inflammatory)	**Marketed** (various)	Prophylaxis, Treatment	5	**Jun 2020**			Aspirin has 3 effects: inhibiting virus replication, anticoagulant and anti-inflammatory
LYT-100 (Multi-modal) PURETECH HEALTH	**Under Development** (Lung scarring)	Treatment - ARDS	0	**Mid 2021**			

1. CRS - Cytokine Release Syndrome; ARDS - Acute Respiratory Distress Syndrome
2. Based on CT.gov registered trials related to COVID-19 as of July 13, 2020
3. See "Compilation of published results" for full set of references
4. FiercePharma

Source: Milken Institute, BioCentury, FiercePharma, FierceBiotech, CT.gov

E: COVID-19 other therapeutics – selected candidates deep dive (3/3)

Directionally positive result Directionally negative result

Compound (Primary mode of action)	US Status (Licensed indication)	Use case[1]	Registered trials on CT.gov[2]	Earliest trial end date	Initial clinical evidence[3]	Efficacy in isolated use?	Additional information
Zocor Simvastatin (HMG-CoA reductase inhibitor)	**Marketed**	Treatment – ARDS	2	Aug 2021	-	-	-
COVIDTRAP STI-6991 (ACE2-Fc decoy protein) sorrento	**Under Development**	Treatment – COVID-19	0	-	-	-	Efficacy in neutralizing the virus and preventing infection in pre-clinical study
garadacimab (Factor XIIa inhibitor) CSL Behring	**Under Development**	Treatment – ARDS	0	-	-	-	Efficacy in neutralizing the virus and preventing infection in pre-clinical study

1. CRS - Cytokine Release Syndrome; ARDS - Acute Respiratory Distress Syndrome full set of references

2. Based on CT.gov registered trials related to COVID-19 as of July 13, 2020

3. See "Compilation of published results" for

Source: Milken Institute, BioCentury, FiercePharma, FierceBiotech, CT.gov

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EXAMPLES FOR ILLUSTRATION PURPOSES ONLY

The new, large scale observational study of HCQ and CQ

Directionally positive result Directionally negative result

A first large scale, observational study published on the Lancet on May 22, 2020 indicates that higher mortality rate and hear arrhythmias were associated with the use of chloroquine or hydroxychloroquine, either with or without with macrolide antibiotics, among hospital COVID-19 patients.[1]

Authors suggest the drugs not to be used outside of clinical trials until further confirmation of clinical benefits.[2]

Over 140 scientists raised concerns about the methodology and data integrity of the study – the authors has commissioned an independent audit of the data, but has not corrected the result of the study. The Lancet also issued an "express of concern" acknowledging such challenges.[3]

Location	Size (severity)	Arms: Dosing schedule	Results1
Global	**96032** (severe)	**Drug**: HCQ (mean dose 596 mg, 4.2 days) **Drug**: HCQ + macrolide (mean dose 597 mg, 4.3 days) **Drug**: CQ (mean dose 765mg, 6.6 days) **Drug:** CQ + macrolide (mean dose 790mg, 6.8 days) **Control**: Standard of care	**The mortality rate was higher in all four groups treated with HCQ or CQ.** ▪ The mortality rate in the control group was 9.3%, compared to 18.0% for HCQ, 23.8% for HCQ with macrolide, 16.4% for CQ, and 22.2% for CQ with macrolide.[1] ▪ After accounting for underlying factors such as age, race, BMI, and underlying health conditions, researchers still found that the use of HCQ and CQ were interpedently associated with the increased mortality rate.[2] **Cardiac arrhythmias were also higher in the groups treated with HCQ or CQ.** ▪ 0.3% in the control group developed ventricular arrhythmias, compared to 4.3% in the group treated with CQ, 6.5% in the group treated with CQ and macrolide, 6.1% in the group treated with HCQ, and 8% in the group treated with HCQ and macrolide.[1] ▪ After accounting for underlying factors, the risk of ventricular arrhythmias were 5x for treatment of HCQ and macrolide.[2] ***Observational, retrospective study***

RETRACTED FOR QUESTIONS ABOUT DATA INTEGRITY AND METHODOLOGY

1. Lancet Article
2. Science daily
3. Press
4. Lancet

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EXAMPLES FOR ILLUSTRATION PURPOSES ONLY

Compilation of published clinical trial results – Small Molecules (1/6)

Directionally positive result Directionally negative result

Compound	Location	Publish Date	Size (severity)	Arms: Dosing schedule	Results	Trial ID
Remdesivir GILEAD	Global	July 2020	**1130** (severe)	**Drug**: Remdesivir **Control**: standard care	Patients treated with the drug showed 62% reduction of mortality risk compared to the group received standard care (7.6% at Day 14 in the drug group v. 12.5%). Also, 74.4% of the patients treated with remdesivir improved their clinical status by Day 14 v. 59% of the standard care group[6] --- ***Comparative analysis of the Phase 3 SIMPLE-Severe trial and a RWD data of patients with severe COVID-19 who received standard care***	-
	Global	June 2020	**584** (moderate)	**Drug**: Remdesivir (5 days, 10 days) **Control**: standard of care	**The 5-day remdesivir treatment group were 65% more likely to have clinical improvement at Day 11** v. control group. At day 11, 76% of the 5-day group and 70% of the 10-day group showed at least 1-point ordinal score improvement v. 66% of the control group[5]	NCT04292730 (SIMPLE – moderate)
	US	May 2020	**1063** (severe)	**Drug**: Remdesivir (200mg D1, 100mg D2-10)	Remdesivir arm had **31% faster time to recovery than placebo** (11 days vs. 15 days); mortality rate in remdesivir arm was also lower (7.1% v. 11.9% for the placebo group) but not statistically significant. The benefit appeared much more limited in patients requiring mechanical ventilation. Overall, the probability of improvement in clinical status was 50% higher among remdesivir patients than in placebo patients[1]	NCT04280705
	US	April 2020	**397** (severe)	**Drug**: Remdesivir (200mg D1, 100mg D2-10)	**Similar clinical status improvement in patients** receiving a 5-day treatment course (10 days) vs. 10-day treatment course (11 days)[2]	NCT04292899 (SIMPLE – severe)
	Global	April 2020	**53** (severe, critical)	**Drug**: Remdesivir (200mg D1, 100mg D2-10)	**Improved oxygen-support class** in 68% of compassionate use patients, with 57% of patients on mechanical ventilation getting off the device. Almost 50% of patients were ultimately discharged[3]	
	China	April 2020	**237** (severe)	**Drug**: Remdesivir **Control**: placebo	**Rate of death** was similar for Remdesivir (13.9%) and the control arm (12.8%)[4]	NCT04257656

1. NEJM
2. Gilead Press release
3. NEJM
4. Press Release
5. Gilead
6. Gilead

Source: Press and literature as linked in footnotes

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EXAMPLES FOR ILLUSTRATION PURPOSES ONLY

Compilation of published clinical trial results – Small Molecules (2/6)

Directionally positive result | Directionally negative result

Compound	Location	Publish Date	Size (severity)	Arms: Dosing schedule	Results	Trial ID
Hydroxy-chloroquine	US, Canada	July 2020	491 (mile / moderate)	**Drug:** hydroxychloroquine **Control:** placebo	No substantial difference in change in symptom severity over 14 days. At 14 days, 24% of the drug arm had ongoing symptoms v. 30% placebo arm. Also, higher AE occurred in HCQ arm (43% v. 22% in placebo arm). [3]	-
	Spain	July 2020	293 (mild / moderate)	**Drug:** hydroxychloroquine **Control:** no antiviral treatment	No significant differences in mean viral load reduction at day 3 (-1.41 in the drug arm v. 1.41 Log_{10} copies/mL) and at day 7 (-3.37 v. -3.44), in risk of hospitalization (7.1% v. 5.9%), and symptom duration (12 days v. 10 days).[7]	-
	UK	July 2020	-	**Drug:** hydroxychloroquine	WHO Solidarity trial interim results show that hydroxychloroquine produce little or no reduction in the mortality of hospitalized COVID-19 patients.[4]	-
	US	July 2020	**2541** (severe / critical)	**Drug:** hydroxychloroquine **Drug:** hydroxychloroquine + azithromycin **Drug:** azithromycin	**Mortality rates reduced** in the patients who received HCQ (13.5%), HCQ and azithromycin (20.1%), and azithromycin (22.4%) compared to the control group (26.4%). Hazard ratio reduced by 66% in the HCQ only group and 71% in the HCQ + azithromycin group compared to the control group.[5] ***Observational, retrospective cohort study***	-
	UK	June 2020	**4674** (severe)	**Drug:** HCQ **Control:** standard of care	**In the UK Recovery trial, the data showed no evidence of benefit.** After about 28 days, 25.7% of the patients who received hydroxychloroquine had died compared with 23.5% of patients who received usual care alone, but statistically not significant[6]	NCT04381936
	US	June 2020	**821** (post-exposure prophylaxis)	**Drug**: HCQ (800mg upfront, followed in 6 to 8 hours by 600 mg, then 600mg QD D2-5) **Control:** placebo (vitamin folate or zinc)	**No statistical difference the drug's prophylaxis effect** – 11.8% of the HCQ arm developed Covid-19, compared to 14.3% in the control group. **~40% on HCQ showed side effects** (mild reactions most commonly nausea, diarrhea, or vomiting) compared to 17% on placebo. However, there was no significant increase in disturbances of heart rhythms or death.[1] — ***Conducted over the internet w/o patients seeing doctors; the COVID-19 counts include those with symptoms due to testing unavailability*	
	US	May 2020	**1438** (severe)	**Drug**: HCQ **Drug**: Azithromycin **Drug**: HCQ + Azithromycin	Among hospitalized patients, treatment with HCQ, azithromycin, or both was **not associated with significantly lower in-hospital mortality**[2] — ***Observational study, involved retrospective data analysis***	

1. WashingtonPost
2. JAMA Article
3. ACPJournals
4. WHO
5. IJID
6. Press release
7. Oxford Academic

Source: Press and literature as linked in footnotes

CURRENT AS OF July 22, 2020
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EXAMPLES FOR ILLUSTRATION PURPOSES ONLY

Compilation of published clinical trial results – Small Molecules (3/6)

Directionally positive result Directionally negative result

Compound	Location	Publish Date	Size (severity)	Arms: Dosing schedule	Results	Trial ID
Hydroxy-chloroquine (Cont'd)	US	April 2020	**368** (severe)	**Drug**: HCQ (450mg BID D1-5) **Drug**: HCQ (600mg BID D1-10) **Drug**: HCQ + Azithromycin **Control**: standard of care	**Death rate in HCQ arm was higher** than control (28% vs. 11%) and no benefit of HCQ (+AZ) in reducing risk of mechanical ventilation[9] --- ***Study involved retrospective data analysis***	
	France	March 2020 April 2020	**36** (severe) initially, follow-up with **80** (severe), additional follow-up with **1061** (severe)	**Drug**: HCQ (600mg) **Drug**: HCQ as above + Azithromycin **Control**: placebo	**Initial results: HCQ only** – 57% negative viral load by day 6; **HCQ + azithromycin**: 100% negative viral load by day 6; 12.5% in **control** group[6] **Follow-up results: HCQ + azithromycin** (only) - negative viral load by day 7 for 83% of patients and 93% by day 8[7] **Additional follow-up results: HCQ + azithromycin** (only) - negative viral load by day 10 for 92% of patients[8] RETRACTED FOR POOR DESIGN	
	US	May 2020	**1446** (severe)	**Drug**: HCQ (600mg BID D1, 400mg QD for median of 5 days)	Hydroxychloroquine administration had **no association with increased or decreased risk** of intubation or death[1] --- ***Observational Study***	
	Brazil	April 2020	**636** (mild)	**Drug**: HCQ + Azithromycin **Control**: placebo	**HCQ + azithromycin group had 1.9% hospitalizations** vs. 5.4% in untreated control group[2] --- ***Study was suspended for ethical concerns***	NCT04348474
	France	April 2020	**181** (severe)	**Drug**: HCQ (600mg QD) **Control**: standard therapy	**No difference** in **ICU transfer** rate (20.2% HCQ, 22.1% control), **mortality rate** (2.8% HCQ, 4.6% control), or **ARDS within 7 days** (27.4% HCQ, 24.1% control)[3]	
	China	April 2020	**150** (severe)	**Drug**: HCQ (1200mg QD days1-3, 800mg QD days 4-21) + standard therapy **Control**: standard therapy	**No difference** in **28-day viral clearance** (85.4% HCQ, 81.3% control) or **symptom alleviation**[4]	ChiCTR2000029868
	China	April 2020	**62** (severe)	**Drug**: HCQ (100mg BID) **Drug**: HCQ (200mg BID) **Control**: placebo	**Improved pneumonia** in 81% of HCQ group compared to 55% in control. **Cough** and **fever** resolved faster, and the disease less likely to become severe in HCQ group[5]	ChiCTR2000029559

1. NEJM Article
2. Opinion Article
3. Preprint Publication
4. Preprint Publication
5. Preprint Publication
6. International Journal of Antimicrobial Agents
7. Mediterranee Infection
8. Preprint Abstract publication
9. Preprint Publication

Source: Press and literature as linked in footnotes

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EXAMPLES FOR ILLUSTRATION PURPOSES ONLY

Compilation of published clinical trial results – Small Molecules (4/6)

Directionally positive result Directionally negative result

Compound	Location	Publish Date	Size (severity)	Arms: Dosing schedule	Results	Trial ID
Hydroxy-chloroquine (Cont'd)	France	March 2020	**11** (severe)	**Drug**: HCQ (600mg) **Drug**: HCQ as above + Azithromycin	**Negative viral load** by day 5 to 6 for only 20% of patients[5]	
	China	March 2020	**30** (severe)	**Drug**: HCQ (400mg QD) + standard therapy **Control**: standard therapy	**Viral clearance rate** higher on placebo arm (93%) vs HCQ arm (87%) and temperature normalization was essentially the same[6]	NCT04261517
	US, Canada	June 2020	**423** (mild/moderate)	**Drug**: HCQ **Control**: placebo	**Drug did not reduce symptom severity or % of patients with symptoms.** However, HCQ patients recorded higher rates of medication adverse events.[8]	NCT04308668
Chloroquine	Brazil	April 2020	**81** (severe)	**Drug**: CQ (600mg BID) + Azithromycin + Ceftriaxone **Drug:** CQ (450mg BID D1), 450mg (QD D2-5) + Azithromycin + Ceftriaxone	High dose CQ arm presented a trend toward **higher lethality** (17%) compared to low dose arm. There was **no statistical benefit for mortality** compared to patients not on CQ[1] --- ***High dose arm recruitment halted***	NCT04323527
Kaletra (Lopinavir/ Ritonavir)	Global	July 2020		**Drug:** lopinavir-ritonavir **Control:** standard care	**WHO Solidarity trial interim results show that lopinavir/ritonavir produce little or no reduction in the mortality** of hospitalized COVID-19 patients compared to the patients in the control group[7]	-
abbvie	UK	June 2020	**4971** (severe / critical)	**Drug:** lopinavir-ritonavir **Control:** usual care	**Recovery trial - no significant difference for 28-day mortality** (22.1% in the lopinavir-ritonavir arm vs. 21.3% in the control arm). **Also no evidence of beneficial effects or reducing the risk of progression to mechanical ventilation or length of stay.** However, the result is not conclusive for the critical patients (i.e., requiring mechanical ventilation) as the study could not enroll many patients in this group due to the difficulty of the drug administration.[2]	NCT04252885
	China	March 2020	**44** (mild/moderate)	**Drug**: Kaletra (200mg/50mg BID) **Drug**: Arbidol (200mg TID)	**No significant differences** in negative viral load or clinical improvement (cough, chest CT) between Kaletra group vs. control[3]	NCT04252885
	China	March 2020	**199** (severe)	**Drug**: Kaletra (400mg/100mg BID) **Control**: standard therapy	**No benefit observed** with Kaletra treatment beyond standard care (e.g., supportive care – supplemental oxygen, ventilator support)[4]	ChiCTR2000029308

1. Preprint Article
2. Recovery trial press release
3. Preprint Publication
4. NEJM Article
5. Science Direct Article
6. Zhejiang University Hospital English Abstract
7. WHO
8. Annals of Internal Medicine

Source: Press and literature as linked in footnotes

CURRENT AS OF July 22, 2020
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Compilation of published clinical trial results – Small Molecules (5/6)

Directionally positive result Directionally negative result

Compound	Location	Publish Date	Size (severity)	Arms: Dosing schedule	Results	Trial ID
Avigan (Favipiravir) FUJIFILM	Japan	July 2020	88 (asymptomatic / mild)	**rug:** Favipiravir from day 1 **Control:** Favipiravir from day 6	**No statistically significant benefit was observed.** The virus disappeared by the morning of day 6 in 66.7% of the drug group and the same pattern was observed in the control group as well. Fever reduction began on average in 2.1 days for the drug group and 3.2 days for the control group, but not significantly meaningful	
	Bangla-desh	July 2020	50	**Drug: Favipira** **Control:** Placebo	**The 'Dhaka Trial' - Patients treated with favipiravir was associated with the faster recovery, lung function improvement, and viral clearance.** 48% of the drug arm patients were COVID-19 negative by 4th day and 96% by 10th day. The drug arm patients showed 3 times higher lung function improvement and 44% more viral clearance than those on the placebo, and no significant side effects[5]	
	China	March 2020	**80** (mild)	**Drug**: Favipiravir (1600mg twice then 600mg BID for 14 days) + IFN **Drug**: Kaletra (400mg/100mg BID for 14 days) + IFN	**Negative viral load** by day 4 and **91% lung improvement** on favipiravir vs. day 11 and 62% for control. 72% two-day fever reduction higher on favipiravir (72%) vs. control arm (26%)[2]	
	China	March 2020	**236** (various severity)	**Drug**: Favipiravir (600 mg twice then 600mg BID) **Drug**: Arbidol (200mg TID)	Better **7-day clinical recovery rate** with Favi (71%) vs. control (56%) for non-critical patients. O2 or vent support in 8% Favi patients vs. 17% control[3]	ChiCTR200030254
	Russia	May 2020	**40** (severe)	**Drug**: Favipiravir	**60% of patients tested negative after 5 days** of Favi treatment, 2x higher compared to those on a standard therapy[4]	

1. Trialsitenews
2. Engineering Journal
3. Pre-print publication
4. Press release
5. Trialsitenews

Source: Press and literature as linked in footnotes

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Compilation of published clinical trial results – Small Molecules (6/6)

Directionally positive result Directionally negative result

Compound	Location	Publish Date	Size (severity)	Arms: Dosing schedule	Results	Trial ID
Ganovo (Danoprevir) ascletis	China	March 2020	**11** (moderate/ severe)	**Drug**: Ganovo (100mg BID) + Ritonavir (100mg BID) + IFN spray inhalation (50µg BID)	**First negative RT-PCR** test at median of 2 days and absorption in CT scans at median 3 days[1]	NCT04291729
Arbidol (Umifenovir)	China	March 2020	**33**	**Drug**: Kaletra + Arbidol **Drug:** Kaletra	Day 7 viral negative rate was 75% for combination therapy vs. 35% for Kaletra alone; chest scans improved in 69% of combination patients vs. 29% with Kaletra alone[2] — ***Study involved retrospective data analysis***	
Ivermectin	US	June 2020	**280** (severe)	**Drug**: Ivermectin **Control:** Standard of care	**Ivermectin was associated with lower mortality** during treatment of COVID-19 (25.2% vs. 15.0%), especially in patients requiring higher inspired oxygen or ventilatory support (38.8% vs. 80.7%). There was so significant difference in successful extubation rates (36.1% vs. 15.4%).[3]	
	Global	April 2020	**52** (critical)	**Drug**: Ivermectin (150 mcg/kg one time)	**Better mortality rate (18.6%) vs control arm (7.7%),** improved length of stay (10.9 days vs. 15.7 days), and improved ICU length of stay (6.0 days vs. 8.2 days)[4] — ***Retrospective, cohort study*	
Coronavir	Russia	July 2020	**>110** - Mild / moderate (outpatients)	**Drug:** Coronavir **Control:** standard etiotropic therapy	"55% of the outpatient cased improved clinically on the 7th day in the drug group (v. 20% in the control group). Also, significant difference on 14th date. By the 5th day of treatment, the virus had been eliminated in 77.5% of the drug group.[5]	
Darvoni, Sovodak (Sofosbuvir, Daclatasvir)	Iran	July 2020	**66** (severe, critical)	**Drug:** Sofosbuvir, Daclatasvir **Control:** Standard care (lopinavir, ritonavir with or without hydroxychloroquine)	**88% of the patients in the drug arm had clinical recovery within 14 days,** compared with 67% of the patients in the control arm. In addition, **9% v. 21% required mechanical ventilation and 3 (9%) v. 5 (15%) patients died in respective groups. Time to discovery was significantly shorter** in the drug group 6 v. 11 days in the control group, but none was statistically significant.[6]	
	Iran	July 2020	**176**	**Drug:** Sofosbuvir, Daclatasvir	**The recovery rate was 94% for the patients in the drug arm v. 70%** for the control group. **The time to recovery was significantly faster** and mortality rate was significantly lower in the drug arm. (5% v. 20%)[6] — ***small sized metal analysis of 3 studies; one was not properly randomized*	

1. Press release
2. PubMed Article
3. Preprint Article
4. Department of Biomedical Engineering
5. CGTN
6. Hepmag

Source: Press and literature as linked in footnotes

Compilation of published clinical trial results – Monoclonal Antibodies

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Directionally positive result Directionally negative result

Compound	Location	Publish Date	Size (severity)	Arms: Dosing schedule	Results	Trial ID
S309 (for development of VIR-7831, VIR-7832) VIR		May 2020	N/A	N/A	**S309 showed neutralization potencies against SARS-CoV-2**. It is studied for prophylaxis in individuals at high risk of exposure or as post-exposure therapy to limit or treat severe disease[1] — **Preclinical study***	-
STI-1499 (for COVI-SHIELD and potentially for COVI-GUARD) sorrento THERAPEUTICS		May 2020	N/A	N/A	**The antibody completely blocked SARS-CoV-2 from infecting healthy cells**, and will likely be the first antibody in the COVI-SHIELD antibody cocktail[2] — **Preclinical study***	-
CB6, CA1 (for JS016) Lilly 君实生物 TopAlliance		May 2020	N/A	N/A	Both CB6 and CA1 antibodies demonstrated substantial neutralization activity in vitro against SARS-CoV-2, **CB6 exhibited superior neutralizing activities.** CB6 reduced virus levels by ~ 3 logs in rhesus monkeys when administered 1 day after infection. When given 1 day before viral challenge, CB6 was able to keep viral load at no more than 103 RNA copies/ml, demonstrating strong prophylactic protection[3] — **Preclinical study***	-
Celltrion mAB CELLTRION	Korea	June 2020	N/A	N/A	Reduced viral loads a hundredfold and showed improvement in lung lesions in animal models[4] — **Preclinical study***	-
REGN-COV2 REGENERON	US	June 2020			Resistance-conferring mutations could arise after treatment with single neutralizing mAbs or combinations of mAbs with overlapping epitopes. By contrast, no resistant mutants observed after treatment with REGN-COV2, a pair of mAbs that do not have overlapping binding sites.[5] — **Preclinical study***	-

1. Nature Article
2. Press release
3. Nature Article
4. Press release
5. Biocentury press release

Source: Press and literature as linked in footnotes

CURRENT AS OF July 22, 2020
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Compilation of published clinical trial results – Polyclonal Antibodies

Directionally positive result Directionally negative result

Compound	Location	Publish Date	Size (severity)	Arms: Dosing schedule	Results	Trial ID
Convalescent Plasma Therapy	China	June 2020	**103** (severe / critical)	**Drug:** Convalescent Plasma Transfusion	**91.3% had clinical improvement within 28 days** vs. 68.2% of the control group (p = 0.03). For those with life-threatening disease, however, convalescent plasma didn't seem to make a difference (20.7% vs. 24.1%)[1]	ChiCTR2000029757
	US	June 2020	**20,000** (severe)	**Drug:** Convalescent Plasma Transfusion	**Mortality rates declined to 8.6 percent compared to 12 percent** in a previous smaller safety study. Serious adverse events from getting the treatment hovered at 1 percent growth[2] — ***Follow up study to previous one with 5,000 patients*	NCT04338360
	US	May 2020	**5000** (severe)	**Drug:** Convalescent Plasma Transfusion	The incidence of all serious adverse events (SAEs) in the first four hours after transfusion was <1%. The 7-day mortality rate was 14.9%[3]	NCT04338360

1. JAMA Article
2. Mayo Clinic Press Release
3. Preprint publication

Source: Press and literature as linked in footnotes

Compilation of published clinical trial results – Immune Modulator (1/4)

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EXAMPLES FOR ILLUSTRATION PURPOSES ONLY

Directionally positive result | Directionally negative result

Compound	Location	Publish Date	Size (severity)	Arms: Dosing schedule	Results	Trial ID
Actemra (Tocilizumab) Roche	Italy	June 2020	**126** (Moderate)	**Drug**: Actemra **Control**: standard of care	**Similar % of respiratory symptom aggravations between** tocilizumab and control arms (28.3% vs. 27.0%). **No significant difference was observed in the total number of accesses to Intensive Care** (10.0% vs 7.9%) and in **30-day mortality** (3.3% vs. 3.2%) either.	-
	Italy	June 2020	**65** (severe)	**Drug**: Actemra (400 mg one-time, second dose given 24 hours later in case of respiratory worsening) **Control**: standard of care	During the 28-day follow-up, **69% of TCZ patients experienced a clinical improvement compared to 61% of standard treatment patients** (p = 0.61). **Mortality was also lower** – 15% in the tocilizumab group and 33% in standard treatment group (p = 0.15)[4] — ***Single center, retrospective, cohort study***	NCT04318366
	France	May 2020	**45** (severe/critical)	**Drug**: Actemra + standard treatment **Control**: standard treatment	**Death and/or ICU admission was higher in control group** than Actemra group (72% vs. 25%). Need for invasive mechanism ventilation was higher in the control as well (32% vs. 0%)[5]	
	France	April 2020	**129** (severe)	**Drug**: Actemra **Control**: control	A significantly lower proportion of **patients in the tocilizumab arm** required ventilation (mechanical or non-invasive) or had died by day 14[1]	NCT04331808
	China	April 2020	**15** (severe/ critical)	**Drug**: Actemra + methylprednisolone **Drug:** Actemra	**75% of the four critical patients** receiving a single dose of medication died[2] — ***Study involved retrospective data analysis***	
					100% of the severe patients returned to normal C-reactive protein levels within a week[2] — ***Study involved retrospective data analysis***	
	China	March 2020	**21** (severe)	**Drug**: Actemra	**Rapidly reduced fevers** and 75% of patients had a reduced need for supplemental oxygen[3]	
ALZUMAb itolizumab; EQ001 Biocon Equillium	India	July 2020	**30** (hospitalized patients with moderate to severe ARDS)	**Drug:** itolizumab + best supportive care **Control:** best supportive care	One month mortality rate was reduced in the drug arm - no deaths and all 20 patients have recovered in the drug arm v. 3 died in the control arm, and the other 7 recovered in the control arm. Also, statistically significant clinical improvement (oxygen saturation) and reductions in inflammatory cytokines (e.g., IL-6 and TNFα) in the drug arm compared to the control group.[6]	

1. Press release
2. Online publication
3. Press Release
4. EJIM Article
5. Science Direct Article
6. Biocon

Source: Press and literature as linked in footnotes

Compilation of published clinical trial results – Immune Modulator (2/4)

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Directionally positive result | Directionally negative result

Compound	Location	Publish Date	Size (severity)	Arms: Dosing schedule	Results	Trial ID
TJM2 (TJ003234) I-MAB	US	May 2020	**24** (severe/ critical)	**Drug:** TJM2 - low dose (3mg/kg) **Drug:** TJM2 - high dose (6mg/kg) **Control:** placebo	DMC confirmed that the antibody was tolerable and safe in patients, prompting I-Mab to proceed with Phase 2 testing[1] — ***Phase 1 study***	NCT04341116
Interferon-alpha-2b	China	May 2020	**77** (severe)	**Drug:** Nebulized IFN-α2b (5 mU BID) **Drug:** Arbidol (200mg TID) **Drug:** Nebulized IFN-α2b + Arbidol	Treatment with IFN-α2b with or without Arbidol **significantly reduced the duration of detectable virus in the upper respiratory tract** and in parallel **reduced duration of elevated blood levels** for the inflammatory markers IL-6 and CRP. Mean days to viral clearance from the onset of symptoms were 21.1 days for those treated with IFN-α2b alone and 20.3 days for those treated with IFN-α2b + Arbidol v. 27.9 days for Arbidol alone treated patients[2]	NCT04341116
Calquence (Acalabrutinib)	US	June 2020	**19** (severe / critical)	**Drug:** Calquence (100mg QD D1-10 or D1-14)	After 10-14 days of treatment, 8 of 11 (72.7%) patients in the supplemental oxygen cohort had been discharged on room air, and 4 of 8 (50%) patients in the mechanical ventilation cohort had been successfully extubated[3]	NCT04341116
Kineret (Anakinra) sobi	Italy	May 2020	**45** (moderate/ severe)	**Drug**: HCQ (200mg BID) + Kaletra (400/100mg BID) **Drug:** Anakinra (5mg/kg IV BID) [high dose] + HCQ (as above) + Kaletra (as above) **Drug:** Anakinra (100mg SC BID) [low dose] + HCQ (as above) + Kaletra (as above)	At 21 days, **survival was higher in high-dose anakinra group** (90%) vs. control (56%) *(p=0.009)*; **Mechanical ventilation-free survival** (72%) was better than control (50%) *(p=0.15)*[4] — ***Study involved retrospective data analysis***	NCT04318366
Interferon-lambda		June 2020			**Evidence that the risk of contracting life-threatening infections can increase when using** Interferon III due to "superinfections". The researchers warn that treating individuals in the advanced stages of the disease using interferon III can harm their lungs greatly.[5]	NCT04318366

1. Press release
2. Frontiers in Immunology Article
3. Science Immunology Article
4. Lancet Article
5. IB Times press release

Source: Press and literature as linked in footnotes

Compilation of published clinical trial results – Immune Modulator (3/4)

CURRENT AS OF July 22, 2020
NONEXHAUSTIVE
EXAMPLES FOR ILLUSTRATION PURPOSES ONLY

Directionally positive result | Directionally negative result

Compound	Location	Publish Date	Size (severity)	Arms: Dosing schedule	Results	Trial ID
Mavrilimumab	Italy	May & June 2020	**39** (Severe)	**Drug:** Mavrilimumab, single IV dose **Other:** control, standard therapy	**Better clinical improvement rate** (85%) at day 14 (v. 42% in control group); **less mortality rate** (0% v. 27% in control group); **less on ventilator** (8% v. 35% in the control group)[1] — ***Single-center pilot*** **None of the 13 patients treated with mavrilimumab had died as of day 28; none of the patients had been mechanically ventilated**. By contrast, the mortality rate in 26 patients who received the standard of care (SOC) was 27% (p=0.086). Additionally, all patients had exhibited clinical improvement by day 28 vs. 65% of those given SOC (p=0.03)[2] — ***A follow up study to the previous entry of the May data***	-
IFX-1 InflaRx	-	June 2020	Severe	**Drug**: IFX-1 + supportive care **Control**: supportive care	**Trend toward lower mortality** in severe COVID-19 pneumonia patients treated with IFX-1 plus best supportive care vs. best supportive care alone in the Phase II portion of an adaptive Phase II/III trial	-
Lenzilumab Humanigen	US	June 2020	**12** (Severe)	**Drug:** Lenzilumab 600 mg IV for three doses	**Clinical improvement** (oxygenation, cytokine analysis) was observed in 11 out of 12 (92%), with a median time to discharge of 5 days ***A compassionate use study which informs the phase 3 registration study***	-
Kevzara (Sarilumab) SANOFI REGENERON		July 2020	Severe	**Drug:** Kevzara (400mg daily dose) **Control:** standard care	**Minor positive trends in favor of Kevzara were observed, but non was statistically significant.**[5] ***Critical arm recruitment, including a second cohort involving higher dose of 800mg, discontinued***	
	US	April 2020	**126** (severe) **276** (severe) **259** (critical)	**Drug**: Kevzara (low dose) **Drug**: Kevzara (400mg) **Control**: placebo	The drug appeared to correlate with worse outcomes, and showed little chance of having a positive effect in severe patients[4] — ***Severe arm recruitment and low dose arm discontinued*** 55% of critical patients died or were on a ventilator vs. 46% of low dose Kevzara and 32% of high dose Kevzara patients[4]	NCT04315298

1. Press release
2. Lancet Article
3. Press release
4. Press release
5. Pharma phorum

Source: Press and literature as linked in footnotes

Compilation of published clinical trial results – Immune Modulator (4/4)

CURRENT AS OF July 22, 2020
NONEXHAUSTIVE
EXAMPLES FOR ILLUSTRATION PURPOSES ONLY

Directionally positive result Directionally negative result

Compound	Location	Publish Date	Size (severity)	Arms: Dosing schedule	Results	Trial ID
Tocolizumab	US	July 2020	154 (Critical)	Drug: tocilizumab Other: standard of care	**Drug group saw lower mortality of critical patients (18%) compared to control (36%) at 28d**. However, those with tocilizumab exhibited greater rates of superinfection (54% vs. 26% for experimental and control, respectively)	-
SNG001 synairgen plc	UK	July 2020	101	Drug: SNG001 Control: placebo	**Experimental group had 79% lowered risk of developing severe symptoms compared to control.** Additionally, patients taking SNG001 had reduced rates of breathlessness.	-

1. Infectious Disease Society of America
2. GlobeNewswire

Source: Press and literature as linked in footnotes

CURRENT AS OF July 22, 2020
NONEXHAUSTIVE
EXAMPLES FOR ILLUSTRATION PURPOSES ONLY

Compilation of published clinical trial results – Cell / Gene / RNA

Directionally positive result Directionally negative result

Compound	Location	Publish Date	Size (severity)	Arms: Dosing schedule	Results	Trial ID
Ryoncil (Remestemcel-l) Mesoblast	US	April 2020	**12** receiving Ryoncil (critical)	**Drug**: Ryoncil **Control**: standard of care	Patients receiving cell therapy infusion had better outcomes for coming off ventilator (75% vs. 9% on standard of care) and better survival (83% vs. 12% for standard of care)[1] --- ***Study involved retrospective data analysis***	
Mesenchymal Stem Cells	China	May 2020	**7** (severe)	**Drug**: Mesenchymal Stem Cell Transplant	Allogeneic MSCs cured or significantly improved functional outcomes in all seven treated patients with severe COVID-19 pneumonia[2]	

1. Press release
2. Aging and Disease journal

Source: Press and literature as linked in footnotes

CURRENT AS OF July 22, 2020
NONEXHAUSTIVE
EXAMPLES FOR ILLUSTRATION PURPOSES ONLY

Compilation of published clinical trial results – Other

Directionally positive result Directionally negative result

Compound	Location	Publish Date	Size (severity)	Arms: Dosing schedule	Results	Trial ID
Methyl-prednisolone	China	March 2020	**201** (critical)	**Drug**: Methylprednisolone **Control**: placebo	**46% of ARDS patients receiving treatment died compared to** 62% of those not receiving methylprednisolone[1] — ***Study involved retrospective data analysis***	
Famotidine Johnson & Johnson MERCK	US	June 2020	**10** (mild)	**Drug:** Famotidine (80mg TID median of 11 days)	All patients reported marked improvements of disease related symptoms after starting famotidine. The combined symptom score improved significantly within 24 hours of starting famotidine[2] — ***Retrospective, case study***	NCT04389567
	US	May 2020	**1620** (severe)	**Drug**: Famotidine (median dose 136mg over 5.8 days)	Famotidine use was associated with a two-fold reduction in clinical deterioration leading to intubation or death[3] — ***Observational study, involved retrospective data analysis***	
Auxora (CM4620-IE) CalciMedica	US	June 2020	**26** (severe)	**Drug:** Auxora plus standard of care **Control**: standard of care	Greater than 50% reduction in both the proportion of patients requiring ventilators and in the length of hospital stay for people on the drug vs. the standard of care[4]	
Dexamethasone	UK	June 2020	**6,425** (moderate/ severe)	**Drug:** Dexamethasone (6mg QD, 10 days) **Control**: Standard of care	**Overall dexamethasone reduced the 28-day mortality rate by 17%** (p=0.0007) – by one-third (40% vs. 28%) in ventilated patients (p=0.0003) and by one fifth (25% vs. 20%) in other patients receiving oxygen only (p=0.0021), but no benefit among patients who did not require respiratory support (p=0.14). Based on these results, 1 death would be prevented by treatment of around 8 ventilated patients or around 20-25 patients requiring oxygen alone[5]	NCT04381936
Colchicine	Greece	June 2020	**105** (severe)	**Drug:** Colchicine (1.5-mg loading dose followed by 0.5 mg after 60 min; maintenance doses of 0.5 mg twice daily) + standard medical treatment **Control**: standard medical treatment	**Clinical condition deteriorated for only 1 of the 55 patients in the colchicine arm** (e.g., requiring mechanical ventilation) v. 7 of 50 patients in the control group.[6]	-

1. Preprint Release
2. BMJ Article
3. Preprint publication
4. Press release
5. BBC News Article
6. Jama Network

Source: Press and literature as linked in footnotes

CURRENT AS OF July 22, 2020
NONEXHAUSTIVE
EXAMPLES FOR ILLUSTRATION PURPOSES ONLY

Compilation of published clinical trial results – Multiple compounds

Directionally positive result Directionally negative result

Compound	Location	Publish Date	Size (severity)	Arms: Dosing schedule	Results	Trial ID
Multiple	Hong Kong	May 2020	**127** (mild/moderate)	**Drug**: Kaletra (400mg/100mg BID) + Ribavirin (400mg BID) + IFN beta-1b (3 doses 8M IU) D1-14 **Drug:** Kaletra (400mg/100mg BID) D1-14	Combination group showed better outcomes compared to control - shorter median **time to negative nasopharyngeal swabs** (7 days vs. 12 days), shorter median **time to symptom alleviation** (4 days vs. 8 days), shorter median **hospital stay** (9 days vs. 14.5 days)[1]	NCT04276688
	China	April 2020	**284** (severe)	**Drug**: Chloroquine **Drug**: Oseltamivir **Drug**: Arbidol **Drug**: Kaletra	**Viral RNA was cleared in 89% of the COVID-19 patients within 21 days after illness onset.** No antiviral drugs shortened viral RNA clearance, especially in non-serious cases[2] — ***Study involved retrospective data analysis***	
	Belgium	June 2020	**154** (mild/ moderate)	**Drug:** ARB, ACEi, and/or Statin	**Those who took a statin, such as Lipitor, were nearly three times more likely to be free of symptoms during their infection** than those who did not. There was also slight trend toward lower risks for lengthy hospital stays and death that was not statistically significant.[3] — ***Retrospective, multi-center cohort study***	
	US	June 2020	**2,773** (Severe)	**Drug:** Anticoagulation for a median of 3 days during a median hospitalization of 5 days	In-hospital mortality occurred in 22.5% in the anticoagulation arm vs. 22.8% control group. The median survival was 21 days for patients treated with anticoagulation and 14 days for those who did not receive anticoagulation. But **among patients requiring mechanical ventilation (n = 395), in hospital mortality was in 29.1% in the anticoagulation group v. 62.7% among the control group.** Patients treated with anticoagulation during hospitalization were more likely to need invasive mechanical ventilation vs. control group(29.8% vs. 8.1%; P < .001).[4]	

1. Lancet Article
2. Preprint Publication
3. Preprint Article
4. Press release

Source: Press and literature as linked in footnotes

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There are several platform trials underway that test multiple compounds at once (1/4)

CURRENT AS OF July 22, 2020
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EXAMPLES FOR ILLUSTRATION PURPOSES ONLY

Trial name (ID)	**Sponsor**	**Phase**	**Location**	**Patient population** (use case)	**Therapeutic Arms** (other than control arm)
Solidarity[1]	World Health Organization (**WHO**)	II/III	Global	**Hospitalized** patients (severe)	• Remdesivir • Kaletra (trial halted) • Kaletra + Interferon • HCQ / CQ (trial halted)
Discovery (NCT04315948)	Institut national de la santé et de la recherche médicale (**INSERM**)	III	Europe	**3100, hospitalized** patients (severe) and patients in **ICU** requiring ventilation (critical)	• Remdesivir • Kaletra • Kaletra + Interferon ß1a • Hydroxychloroquine
Recovery[4] (NCT04381936; Eudract 2020-001113-21; ISRCTN50189673)	**University of Oxford**	II/III	United Kingdom	**11,500, hospitalized** patients (severe / moderate)	• Kaletra (trial halted) • Dexamethasone (now only recruiting children)[3] • Hydroxychloroquine (trial halted)[3] • Azithromycin • Tocilizumab • Convalescent plasma
ACTT 2[5] (NCT04401579)	**NIAID**	III	Global	**1000, hospitalized** patients (severe)	• Remdesivir • Baricitinib
Principle[2] (2020-001209-22)	**University of Oxford**	III	United Kingdom	**3000, elderly outpatients** (mild)	• Hydroxychloroquine • Azithromycin (later)

1. WHO Solidarity 2. About the Principle Trial 3. RECOVERY trial; Recovery trial; RECOVERY stopped Kaletra and HCQ trials after the investigators concluded that the drugs has no benefits to hospitalized COVID-19 patients; Dexamethasone arm closed recruitment to adults 4. Recovery trial 5. Press release

Source: CT.gov, EudraCT, WHO website

There are several platform trials underway that test multiple compounds at once (2/4)

CURRENT AS OF July 22, 2020
NONEXHAUSTIVE
EXAMPLES FOR ILLUSTRATION PURPOSES ONLY

Trial name (ID)	**Sponsor**	**Phase**	**Location**	**Patient population** (use case)	**Therapeutic Arms** (other than control arm)
REMAP-CAP (NCT02735707)	**MJM** [redacted]	IV	Global	**6800, hospitalized** patients (severe) and patients in **ICU** (critical)	• Oseltamivir • Kaletra • Anakinra • Hydroxy-chloroquine • Interferon-β1a • Actemra
N/A	**University of Queensland**[1]	N/A	Australia	N/A	• Kaletra • Chloroquine
Early Intervention (NCT04354428)	**University of Washington, Gates Foundation**	II/III	United States	**630, high-risk outpatients** (mild)	• Hydroxychloroquine • Hydroxychloroquine + Azithromycin • Kaletra (later)
I-SPY COVID[2] (NCT01042379)	**Quantum Leap Healthcare Collaborative** (COVID-19 R&D Consortium)	N/A	United States	**Hospitalized patients with ARDS** (severe)	• Up to 4 therapies for ARDS
ASCOT	**Doherty Institute**	N/A	Australia, New Zealand[4]	**2500, hospitalized** patients (severe)	• Hydroxychloroquine • Kaletra
ACCORD	Department of Health and Social Care **(DHSC)** and UK Research and Innovation **(UKRI)**	N/A	United Kingdom	**120, hospitalized** patients (severe)	• Bemcintinib[3] • MEDI3506[5] • Zilucoplan[5] • Calquence[5] • heparin[5] • Additional treatments can be added in the future[5]

1. University of Queensland press 2. Press release 3. Accord press release 4. Biocentury 5. The Guardian

Source: CT.gov, EudraCT, WHO website

There are several platform trials underway that test multiple compounds at once (3/4)

CURRENT AS OF July 22, 2020
NONEXHAUSTIVE
EXAMPLES FOR ILLUSTRATION PURPOSES ONLY

Trial name (ID)	Sponsor	Phase	Location	Patient population (use case)	Therapeutic Arms (other than control arm)
REMDACTA[1]	**Roche, Gilead Sciences**	III		**450, hospitalized** patients (severe)	• Remdesivir • Actemra / RoActemra
CATALYST[2]	**University of Birmingham, UHB, NIHR BRC, and University of Oxford**		UK	**Hospitalized patients** (severe)	• Namilumab (IZN-101) • Infliximab (CT-P13)
ACTIV 1/4[3]	**NIH / ACTIV**	III, II/III	US	**ACTIV 1: 2,000, Hospitalized patients** (severe) **ACTIVE 4:** N/A	• ACTIV 1: 3 immune modulators against TNFα, CTLA-4 and CCR2/CCR5 • ACTIVE 4: 3 anticoagulants
ACTIV 2[3]	**NIH / ACTIV**	II/III	US, South America	**110** patients/agent - Phase II **900** patients/agent - Phase III **Outpatient use** (mild)	• COVID-19 mAbs
ACTIV 3[3]	**NIH / ACTIV**		US, South America	Stage 1 - 150 patients Stage 2 - 506 patients/agent **Hospitalized patients** (severe)	• COVID-19 mAbs
ACTIV 5[3]	**NIH / ACTIV**			Details of the ACTIV 5 to be worked out	• "Repurposed antivirals and those that have undergone extremely rapid preclinical development"[3]

1. Roche 2. Press release 3. Biocentury, Biocentury

Source: CT.gov

There are several platform trials underway that test multiple compounds at once (4/4)

CURRENT AS OF July 22, 2020
NONEXHAUSTIVE
EXAMPLES FOR ILLUSTRATION PURPOSES ONLY

Trial name (ID)	**Sponsor**	**Phase**	**Location**	**Patient population** (use case)	**Therapeutic Arms** (other than control arm)
NIH/ACTG	**NA**			**2000, Patients at home with COVID-19** (Mild)	• Hydroxychloroquine + Azithromycin • Hydroxychloroquine • Kaletra (later)
PEP (NCT04328961)[1]	**University of Washington, collaboration with Gates Foundation and NYU**		New York; Seattle	**2000, Prophylaxis - close contacts**	• Hydroxychloroquine
AGILE[2] (Eudract 2020-001860-27)	**University of Liverpool, the Liverpool School of Tropical Medicine, and the Southampton Clinical Trials Unit**	Ph I/II	UK	**~40 for each candidate-specific trial;** Adult patients (over 18 years) of both severe and mild/moderate conditions[3]	• EIDD-2801 • More early-stage drugs to be added

1. CT.gov 2 Pharma.phorum 3. NHS

Source: CT.gov

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CURRENT AS OF June 4, 2020
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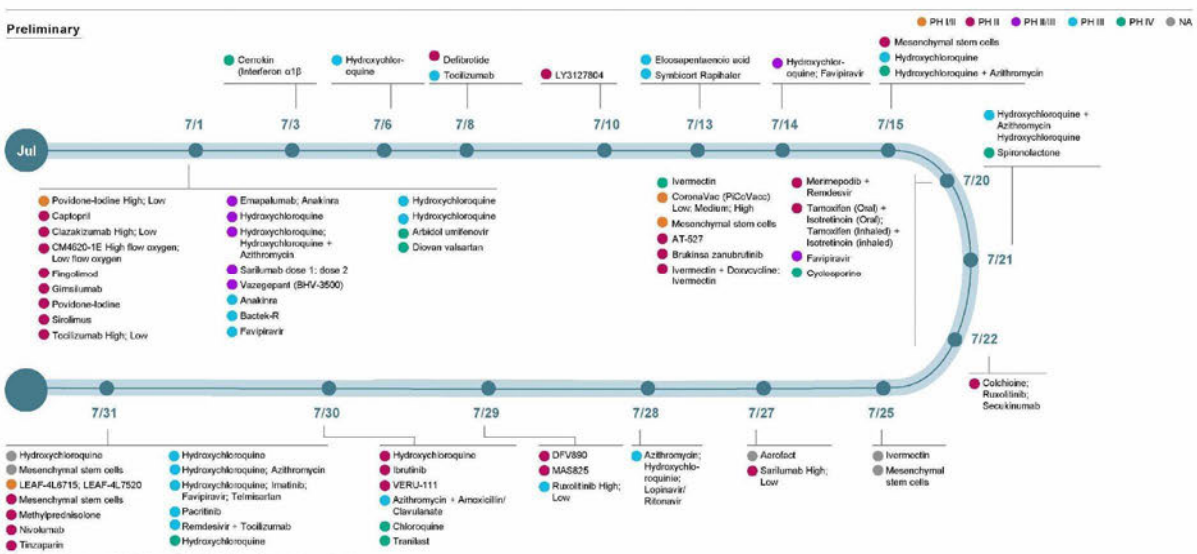
EXAMPLES FOR ILLUSTRATION PURPOSES ONLY

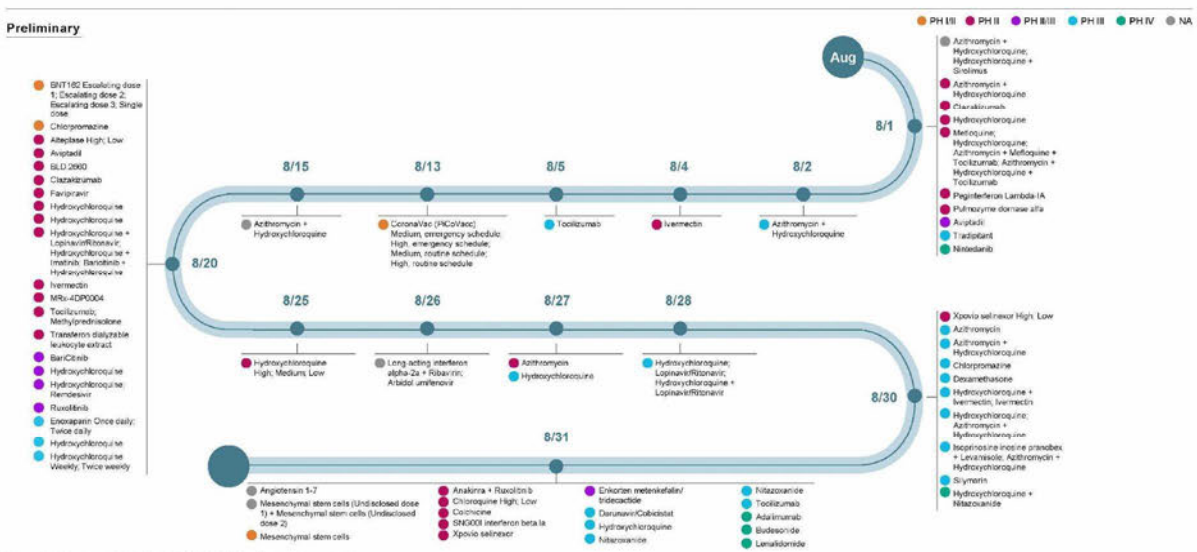
Trials with July milestones



Source: BioCentury - Daily Chart: COVID-19 trials with near-term milestones

CURRENT AS OF June 4, 2020
NONEXHAUSTIVE
EXAMPLES FOR ILLUSTRATION PURPOSES ONLY

Trials with August milestones



Source: BioCentury - Daily Chart: COVID-19 trials with near-term milestones

Appendix

CURRENT AS OF July 22, 2020
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EXAMPLES FOR ILLUSTRATION PURPOSES ONLY

Public resources for pipeline compounds and clinical trials

Live lists of vaccine and therapeutic candidates

- BioCentury
- Milken Institute
- Linksbridge (vaccine only)
- Biorender

Live clinical trial aggregators

- ReDo Project
- Anticovid by Inato
- COVID-Trials.org
- IDM visualization of trial dates