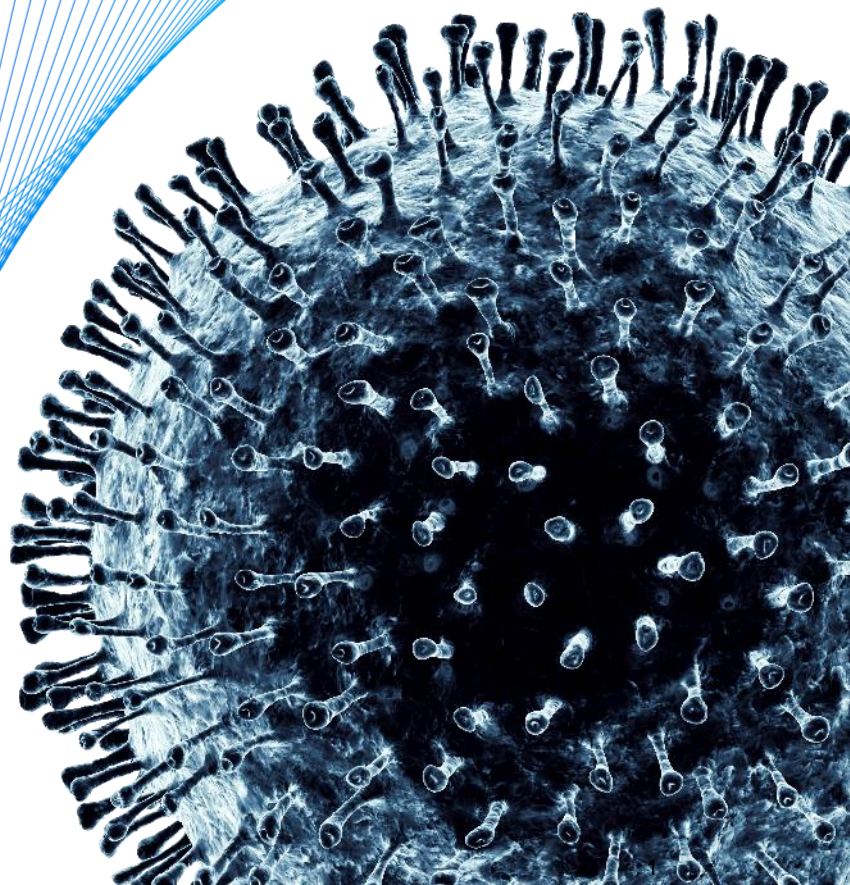
COVID-19 Therapeutics and Vaccines Landscape Overview



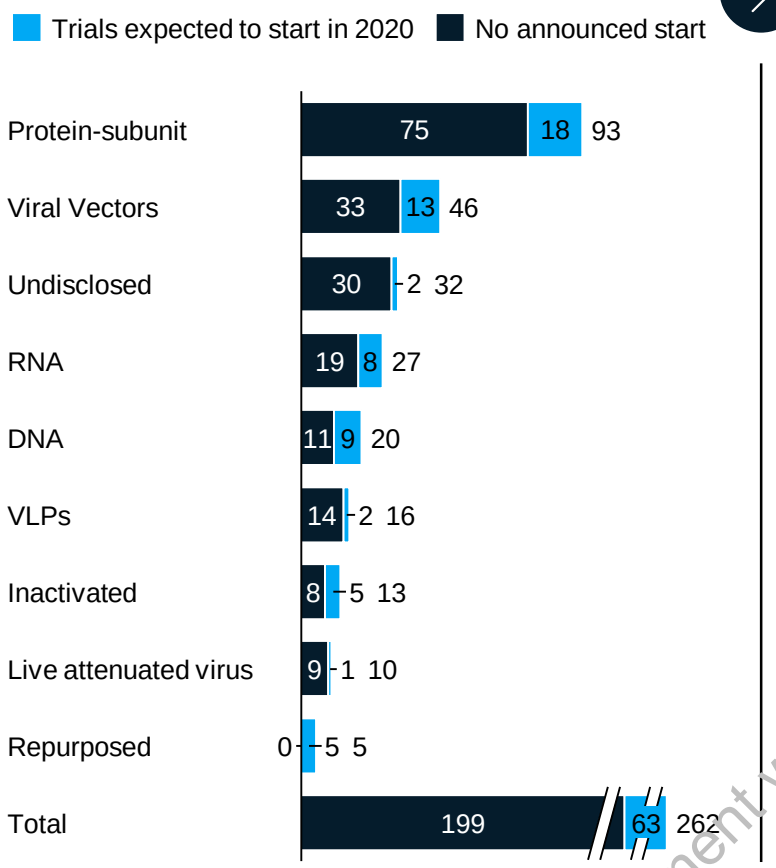
August 27, 2020

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

COVID-19 vaccines development effort overview

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

Pipeline overview



Weekly developments - August 27, 2020

Novavax expects to file for US approval in December, after kicking off Phase II this week, **Sanofi/GSK say the earliest approval for their candidate could be June 2021**[12]

CureVac begins Phase II and two vaccines started trials – Adimmune (Phase I in Taiwan) and **Finlay Vaccine Institute** (Phase I/II in Cuba)[1]

Pfizer/BioNTech publish interim Phase I/II results demonstrating neutralising GMTs in younger adults (18-55 years of age) that were 3.8 times the GMT of a panel of 38 convalescent patients, and 1.6 times in older adults (65-85 years of age)

Moderna publishes promising follow-up data on older adults, with the middle dose triggering the production of neutralising antibodies[13]

AstraZeneca/IVA supply deal expands to EU overall, including specific allocations to Spain, Slovakia; separately, AstraZeneca confirms a deal for 34 million doses with the Australian Government[3]

UK secures another 90M doses in deals with Novavax and J&J, and plans to partner with each company in Phase III trials[4]

Key takeaways

There are **260 vaccine candidates** and new players entering the space every week

- **63 vaccine candidates planning to enter into clinical trials in 2020**
- **37 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]

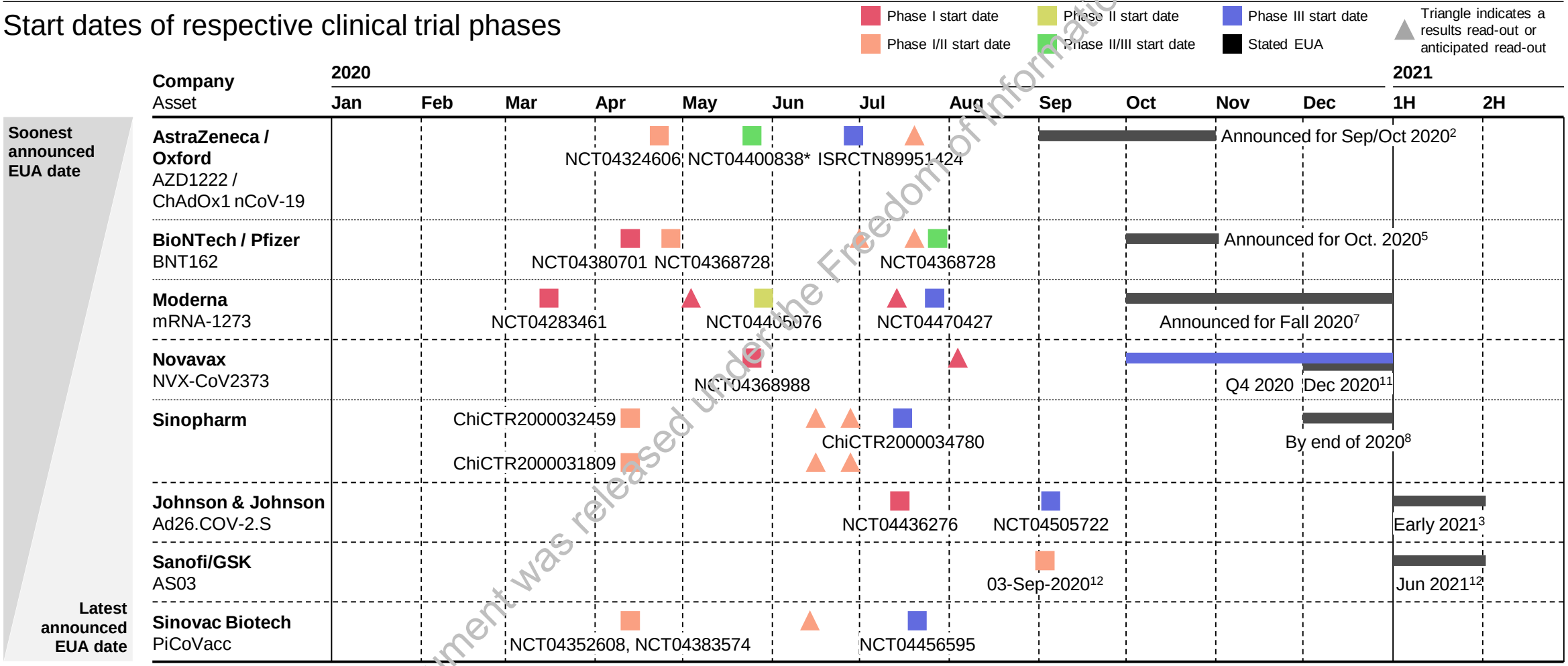
- The **earliest immunogenicity from Phase 2 will be available for 3-4 vaccine candidates this year** which could bring an EUA for high risk population into consideration depending on the data[8,9,10,11]

1. CT.gov
2. BusinessWire
3. FiercePharma, UPI, information updated 7th September
4. Novavax, UK Government, J&J
5. Fierce Pharma
6. HBR
7. SVB analyst on Fierce Pharma
8. Moderna press release
9. FiercePharma
10. CNBC
11. Innovio press release
12. Reuters, SEC filing
13. Moderna press release

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

8 vaccine candidates are currently in Phase III or Phase II/III or have announced potential EUA timelines

Start dates of respective clinical trial phases



1. Oxford News
2. CNBC
3. FiercePharma
4. Wall Street Journal
5. Washington Post
6. Forbes
7. Moderna press release
8. Reuters
9. PBR
10. FiercePharma
11. Reuters
12. SEC filing, Sanofi Press Release, information updated 7th September

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

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

Overview of candidates with publicly announced target Emergency Use Authorisation dates (1/2)

Outside-in view based on media coverage and published research results if available

CURRENT AS OF AUGUST 27, 2020
NONEXHAUSTIVE
EXAMPLES FOR ILLUSTRATION PURPOSES ONLY
DOES NOT CONSTITUTE A MEDICAL OR SCIENTIFIC PERSPECTIVE

Vaccine	Developer and manufacturer	Current clinical trial phase	Dosing used in trial & pathway	Trial Countries	Most recent published or pre-released trial results	Total supply commitments (m doses)[2]	Announced EUA[3]
AZD1222 / ChAdOx1 nCoV-19	AstraZeneca; University of Oxford	Phase 2-3	1-2 doses Viral vector	UK, Brazil, South Africa, India, US	**Interim Phase I/II readout July 20th :** • Neutralising antibodies were generated in more than 90% of participants across different assays. Responses were sustained up to 56 days of observation."[1] • "No serious adverse events[1]	2020: 800 2021: 2,000	Sept-Oct 2020
BNT 162	BioNTech; Pfizer	Phase 2-3	2 doses RNA	Germany, USA and Argentina	**Interim Germany Phase I/II readout July 20th :** • BNT162b1 elicited strong CD4+ and CD8+ T cell responses against SARS-CoV-2-receptor binding domain (RBD), compared to baseline[4] • The RBD-specific, interferon-γ+, IL-2+, CD8+ T cells elicited by BNT162b1 in immunised participants indicate a strong potential for cell mediated anti-viral activity[4] • T cell cytokine profile shows vaccine elicited T cells exhibit a Th1 phenotype, which is associated with antiviral propertie[4] **Interim US Phase I/II readout August 20th :** • BNT162b2 elicited SARS-CoV-2–neutralising GMTs in younger adults (18-55 years of age) that were 3.8 times the GMT of a panel of 38 sera of SARS-CoV-2 convalescent patients, and in older adults (65-85 years of age) the vaccine candidate elicited a neutralising GMT 1.6 times[5] • Well tolerated with mild to moderate fever in fewer than 20% of participants[5]	2020: 100 2021: 1,300	Oct 2020
mRNA-1273	moderna	Phase 3	2 doses RNA	USA	**Interim Phase I readout August 26th :** • Follow-up results showed promising data for older adults – with the middle dose triggering the production of antibodies in patients over 56 (2-3x higher than patients recovered from COVID-19)[5] • Titer levels were not disclosed in the preliminary results; FDA suggests levels of 160 and above [6]	2020: 2021: 1,000	Sept-Nov 2020

1. The Lancet
2. Based on public announcements about manufacturing capacity
3. EUA date is an estimate and subject to change
4. Pfizer press release
5. Businesswire
6. Moderna press release

Overview of candidates with publicly announced target Emergency Use Authorisation dates (2/2)

Outside-in view based on media coverage and published research results if available

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Vaccine	Developer and manufacturer	Current clinical trial phase	Dosing used in trial & pathway	Trial Countries	Most recent published or pre-released trial results	Total supply commitments (m doses)[2]	Announced EUA[3]
NVX-CoV2373	NOVAVAX	Phase 1	2 doses Protein-subunit	Australia	**Interim Phase 1 readout August 4th :** • All subjects developed anti-spike IgG antibodies after a single dose of vaccine, many of them also developing wild-type virus neutralising antibody responses, and after Dose 2, 100% of participants developed wild-type virus neutralising antibody responses[1] **Nonclinical animal trials August 19th** • SARS-CoV-2 GMT antibody titers in immunised macaques were 7.9-10.1-fold higher than in convalescent sera[4] • Vaccine offered protection against SARS-CoV-2 replication in the nose and lungs; and the absence of pulmonary pathology in vaccinated macaques[4]	2020: 100 2021: "Billions"	Dec 2020
N/A[5]	SINOPHARM	Phase 3	2 doses Inactivated	UAE, Bahrain	**Interim Phase I/II readout August 14th :** • The trial linked the vaccine to increases in antibody titers. However, unlike other COVID-19 vaccine trials, the study lacked a comparison arm featuring serum samples from patients previously infected with the coronavirus, complicating the task of interpreting whether the response is likely to confer immunity[5]	2020: 100 2021:	End of 2020
Ad26 SARS-CoV-2	Johnson & Johnson	Phase 1-2	Viral vector	USA, Japan, Belgium	**Nonclinical animal trials July 30th :** • Demonstrated immunogenicity and protective efficacy of a single dose of adenovirus serotype 26 (Ad26) vector-based vaccines expressing the SARS-CoV-2 spike (S) protein in nonhuman primates[6]	2020: 2021: 1,000	Early 2021
As03	SA gsk	Phase 1-2	2 doses Recombinant protein	USA	**Pre-clinical results 3rd September:** • Preclinical data showed an acceptable reactogenicity profile and data based on two injections of the adjuvanted recombinant vaccine showed high levels of neutralizing antibodies that are comparable to levels in humans who recovered from the COVID-19 infection[7]	2020: 2021: 1,000	Jun 2021
PiCoVacc	sinovac	Phase 2-3	2 doses Inactivated	Brazil, Indonesia	**Interim Phase II readout August 10th :** • Reported that the vaccine candidate appeared to be safe and induced detectable antibody-based immune responses[8]	2020: 2021: 100	

1. Novavax press release
2. Based on public announcements about manufacturing capacity
3. EUA date is an estimate and subject to change
4. BioRxiv
5. Unclear which vaccine candidate the EUA date applies to so results for 'BBIBP-CorV' candidate have been used; FiercePharma
6. Nature
7. Sanofi Press Release, information updated 7th September
8. Reuters

Governments & organisations are creating supply contracts with rights to an allocation of doses (non-exhaustive)

CURRENT AS OF AUGUST 27, 2020
NONEXHAUSTIVE
EXAMPLES FOR ILLUSTRATION PURPOSES ONLY

Value ($) / **Doses** Unk for unknown	AstraZeneca	NOVAVAX	BIONTECH	valneva	SANOFI	ARCTURUS	moderna	J&J	**Total**
USA	$1.2B / 300M	$1.6B / 100M	$1.95B / 100M (+500M)		~$1B / 100M[1]		$1.525B / 100M (+$6.6B /400M)	$1B+ / 100M (+200M)	$8.3B+ / 800M+
UK	Unk / 100M	Unk / 60M	Unk / 30M	Unk / 60M[9]	Unk / 60M			Unk / 30M	Unk / 340M
EU	$843M / 300M (+100M)								$843 / 400M
Brazil	$356M / 100M								$356M / 100M
Israel						Unk / Unk	$66M / Unk		$66M / Unk
Japan	Unk / 120M	Unk / 250M (via Takeda)	Unk / 120M						Unk / 490M
Canada			Unk / Unk				Unk / Unk		Unk / Unk
China	Unk/ 100M+200M YoY[15]								Unk / 100M
Argentina & Mexico (LatAm)	Unk / 150M-250M								Unk/150M
Switzerland							Unk / 4.5M		Unk / 4.5M
Australia	Unk / 34M								Unk/ 34M
CEPI, Gavi (LMIC)	$750M / 300M								$750M / 300M
Serum Inst. of India (LMIC)	Unk / 1B	Unk / 1B							Unk / 2B
Total	$3.1B+ / 2.8B+	$1.6B / 1.4B	$1.95B+ / 250M+	Unk / 60M	$1B / 160M	Unk / Unk	$1.6B+ / 105M+	$1B+ / 130M+	**$10.3B+ / 4.9B+**

1. Sanofi press release – "over half of $2.1B for dev., other for doses"

Source: Economist, Reuters, FiercePharma, BBC, The Marker, Pharmaceutical Technology, GlobalNews, Bloomberg, FOPH Switzerland, UPI, Company press releases

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, ROVI	
	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 Univ. of Pittsburgh		1,000[5]	✓	✓		
	AAVCOVID	Viral vectors	Mass. Eye and Ear and Mass. General Hospital	Novartis	Millions[6]			✓	Novartis	
	Ad26.COV-2.S	Viral vectors	J&J	Beth Israel, HHS		1,000[7]	✓	✓	Catalent, Emergent Biosolutions, Biological E	
	AZD1222 / ChAdOx1 nCoV-19	Viral vectors	University of Oxford (Jenner Institute)	AstraZeneca, Advent SRL MilliporeSigma, Cobra Biologics	800[8,3]	2,000[9]		✓	SII, Oxford Biomedica, Emergent Biosolutions, Catalent, Scotland Symbiosis, Wockhardt, BioKangtai	
	AS03	Protein-subunit	Sanofi Pasteur	GSK		1,000[10]	✓			
	NVX-CoV2373	Protein-subunit	Novavax	Emergent BioSolutions, Praha Vaccines, Serum Inst. of India	100[15]	""Billions"[11]	✓		Praha Vaccines, Takeda (250M doses), Fujifilm	
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]

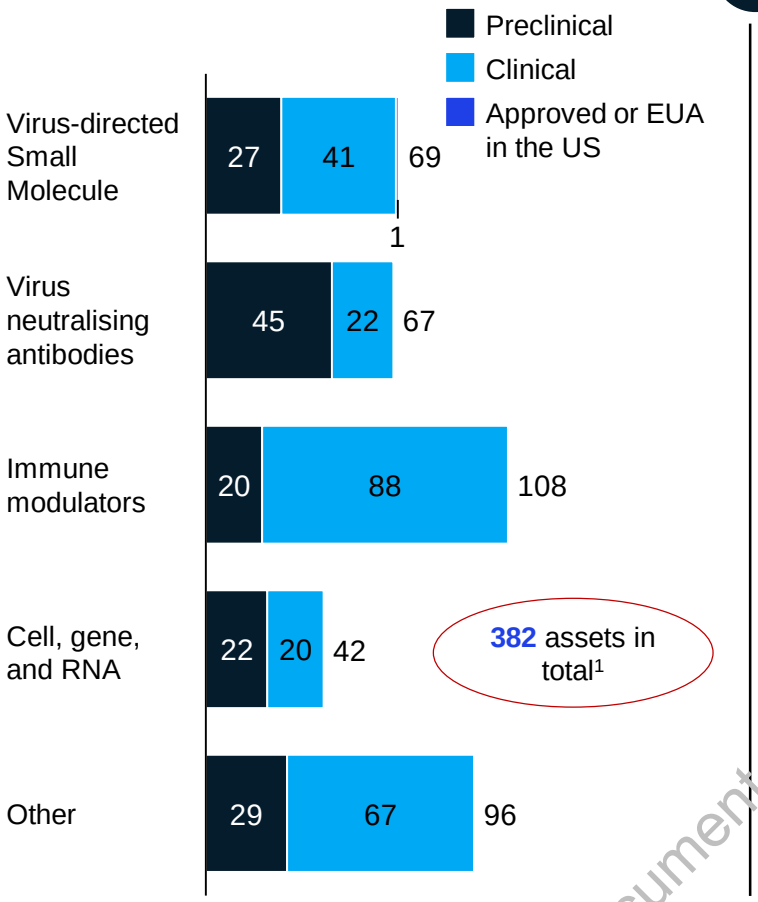
1. Moderna press release
2. Pfizer press release
3. FiercePharma
4. Inovio press release
5. FierceBiotech
6. Masseyeandeal.com
7. J&J press release
8. AZ press release
9. AZ press release
10. FiercePharma
11. FiercePharma
12. BusinessWire
13. Chinadaily.com.cn
14. HHS press release
15. FiercePharma

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

COVID-19 Therapeutics landscape update

Pipeline snapshot

Number of candidates



Key takeaways

Over 380 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 (not comprehensive): remdesivir received EUA by FDA[2] and is approved in EU, Japan, Taiwan, India, UAE, Australia, and Singapore, UK, and Canada[3]; **Favipiravir** is approved in China, India, and Russia[4]; **Dexamethasone** is approved in Japan and the UK and provisionally approved in Taiwan[6]; Coronavir is approved in Russia[7]; Itolizumab is approved for emergency use in India[8]; **convalescent plasma** from COVID-19 patients is approved under emergency use authorisation in the US[9]

- **Virus-directed small molecules:** Mostly repurposed drugs; early results for many drugs are not yet robust, however.
- **Monoclonal & polyclonal antibodies (virus neutralising):** Mostly in pre-clinical stage, but showing some early positive signals. Several companies have entered late-stage clinical trials and expect to receive first EUA as early as late 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 August 27

- **The US approved convalescent plasma for emergency use authorisation (EUA).** A recent study of 35,000 patients sponsored by Mayo Clinic and NIH demonstrated that patients receiving convalescent plasma at 3 vs. 4+ days post-diagnosis had reduced mortality at day 7 (8.7% vs. 11.9%, respectively) and day 30 (21.6% vs. 26.7%, respectively). However, this study is limited by the lack of a placebo group. During the press conference to announce the approval, FDA commissioner Stephen Hahn incorrectly remarked that the treatment is responsible for a “35% improvement in survival.” In subsequent statements, Hahn corrected the language, noting “What I should have said better is that the data show a relative risk reduction not an absolute risk reduction.”[10]
- **Roche signs deal to manufacture and distribute Regeneron’s COVID-19 antibody cocktail outside the US.** The deal triples the manufacturing capacity of the therapy, which is currently in Phase III trials.[11]
- **Takeda and Johnson & Johnson lead a new collaborative initiate aimed at addressing the current and potential future coronavirus pandemics.** The group, called CARE, will focus on repurposing existing drugs and developing novel antibodies and small molecules.[12]

1. 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, Department of Health , Reuters, gov.uk 4. RDIF, HospiMedica, PMlive 5. Reuters 6. Fiercepharma; Reuters
7. CGTN 8. Indiatvnews 9. FDA, STATNews 10. MedRxiv, Fiercepharma 11. Roche, Fiercepharma 12. Pharmaphorum, Fiercepharma

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