Biotechnology Innovation Organization

The Latest on COVID-19: Vaccine and Therapeutic Research and Development

THBI Town Hall Meeting
August 6, 2020

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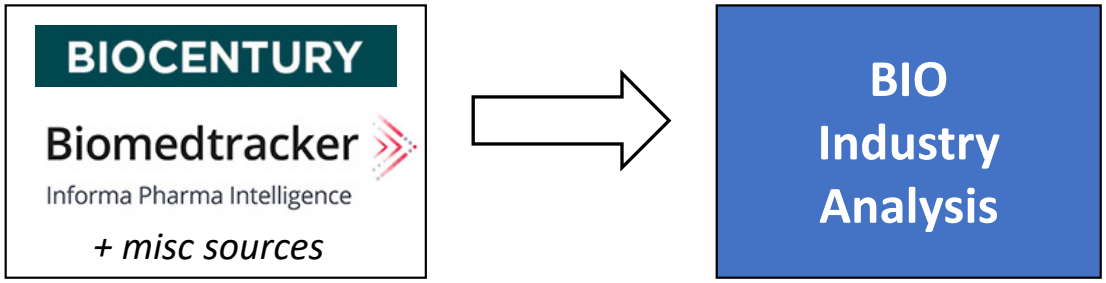
BIO's Approach to COVID-19 Pipeline Analytics



1. **Drug Name**
2. **Phase**
3. **Sponsoring Company**

bio.org/covidpipelinetracker

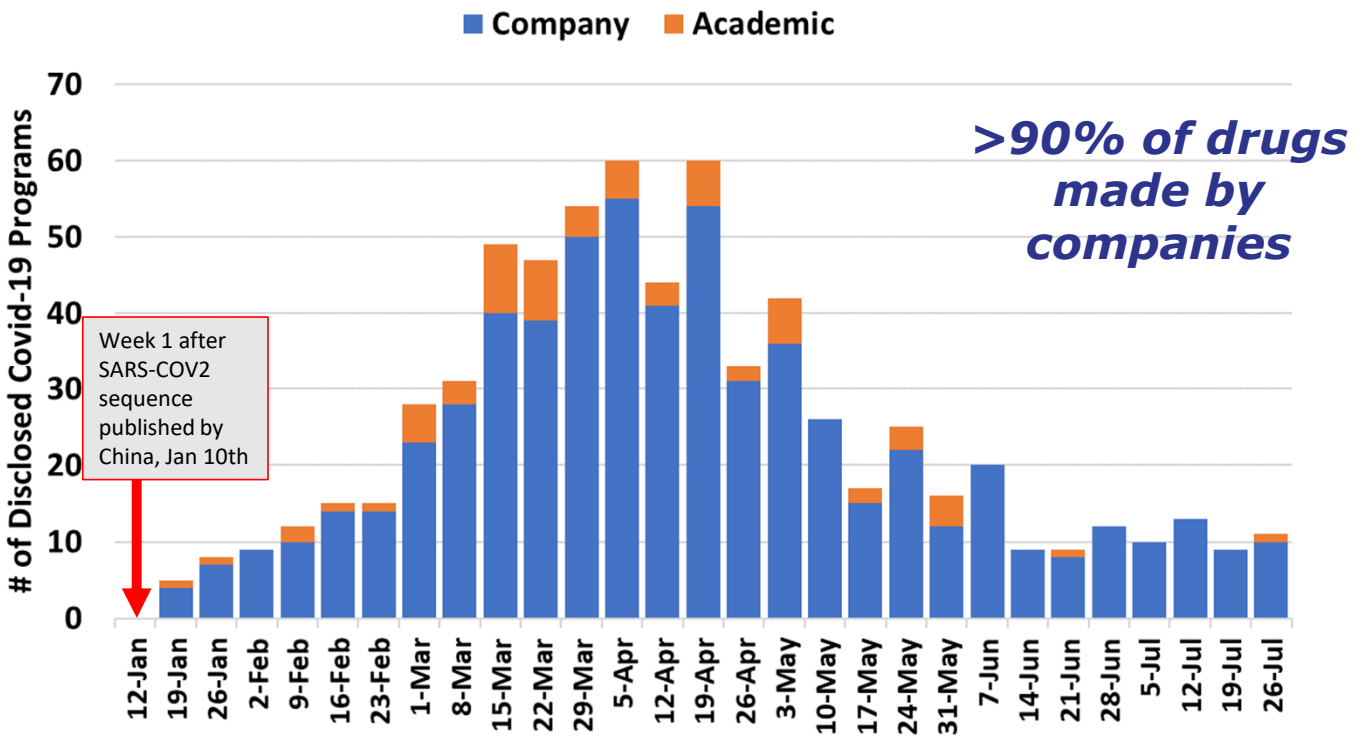
1. **<u>Originating</u> Company**
2. **Pipeline Category (Antiviral, etc.)**
3. **Drug Origin Type (Repurposed, etc.)**
4. **Modality**
5. **Strategy**
6. **Target Family**

Note: BIO **de-duplicates** multiple programs and trials for same drug

Timing of Response

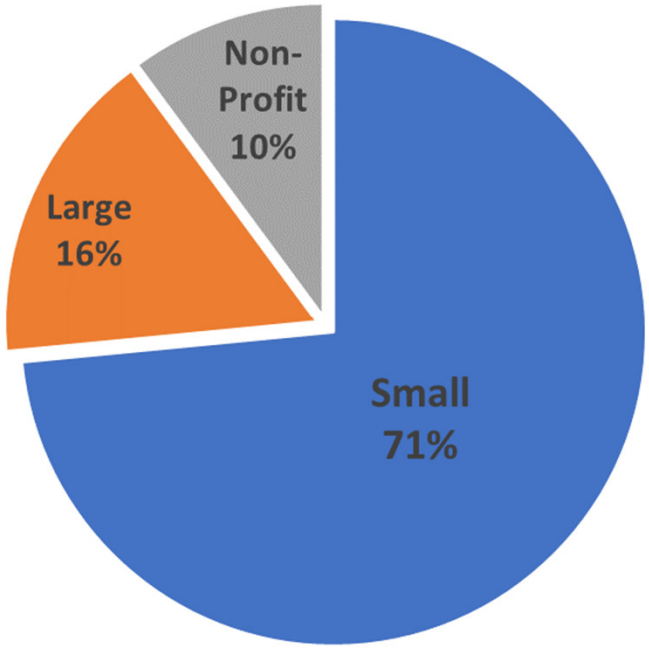
Week of first press release announcing program

Timing of Response by Industry



Week of first press release announcing program

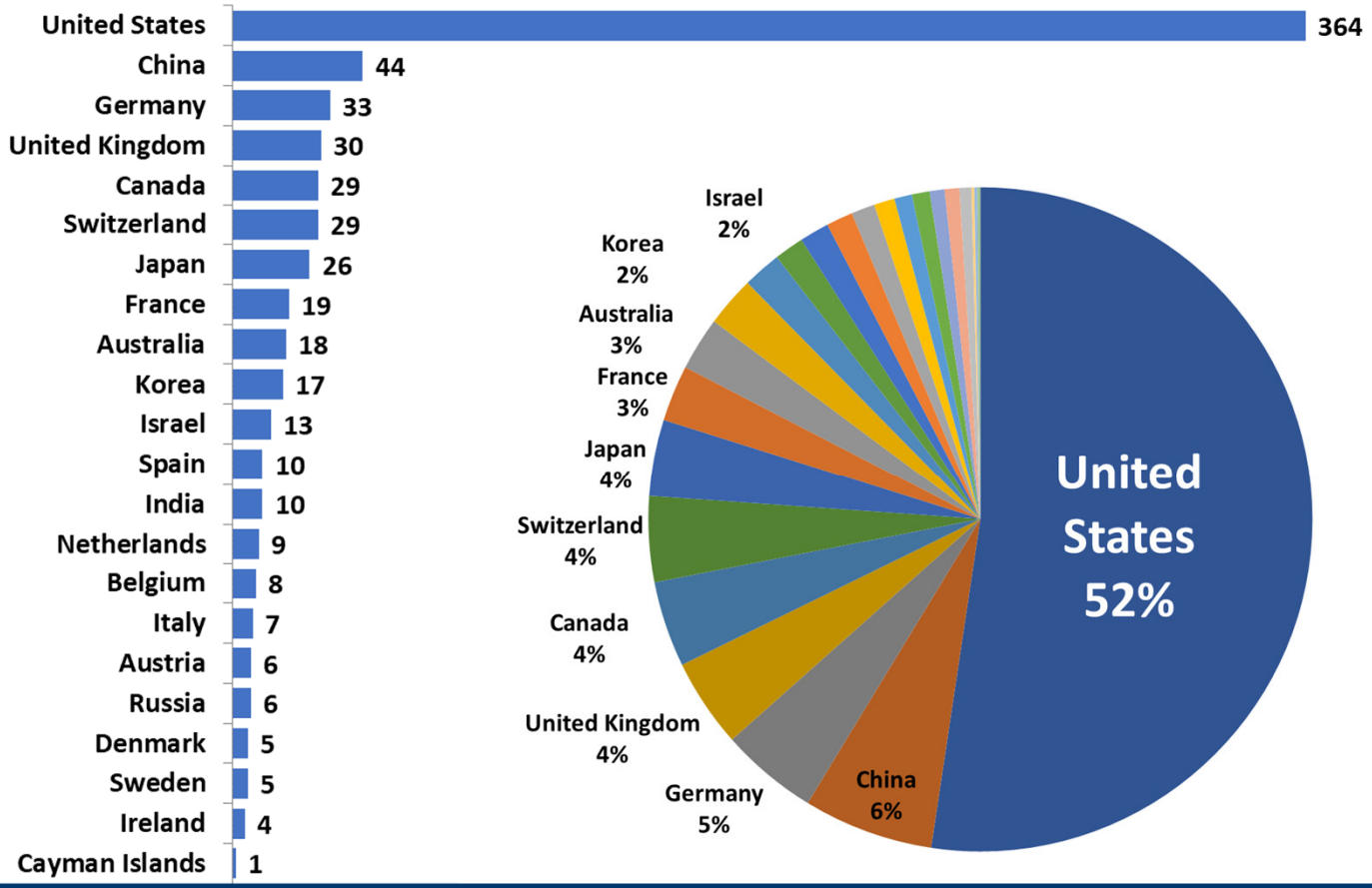
Small Companies Leading R&D Efforts



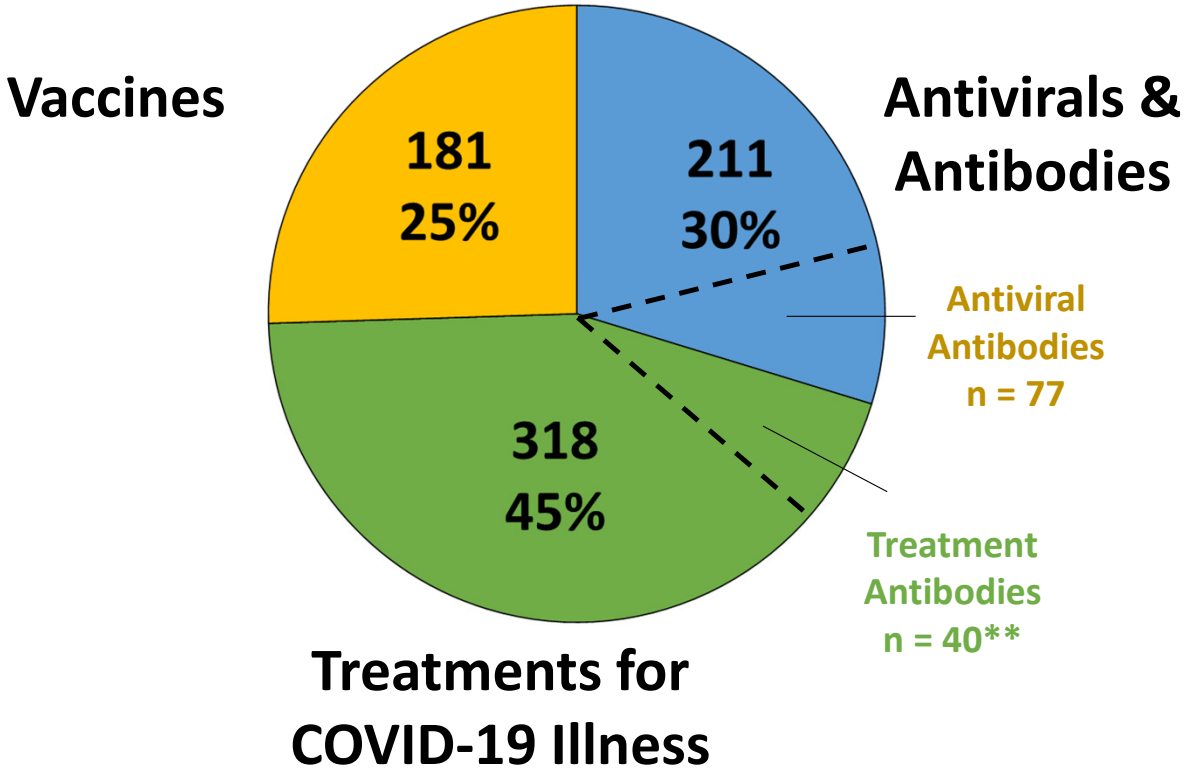
>70% of COVID-19 products originate from small companies

Drug Type	Small	Large	Non-Profit
Antivirals	73%	16%	9%
Treatments	75%	21%	3%
Vaccine	63%	7%	23%

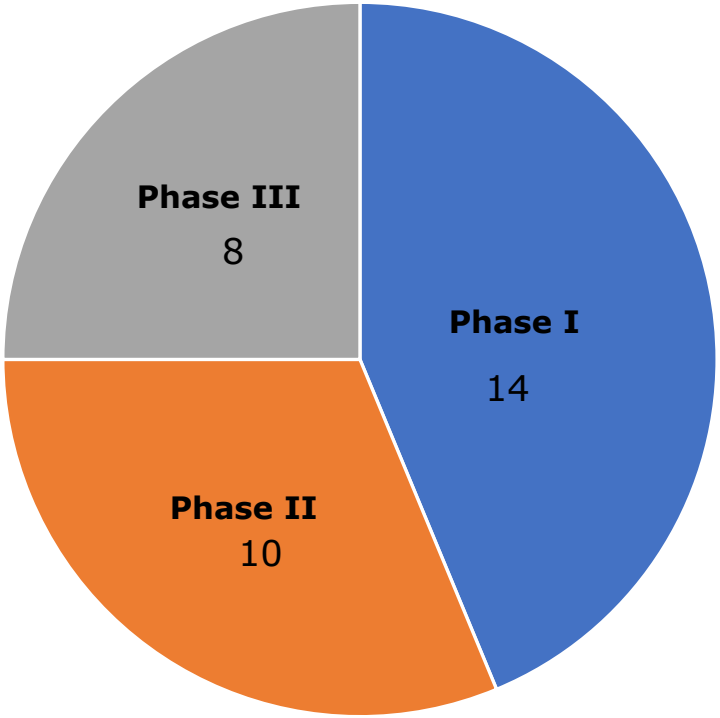
Country of Original Drug Discovery

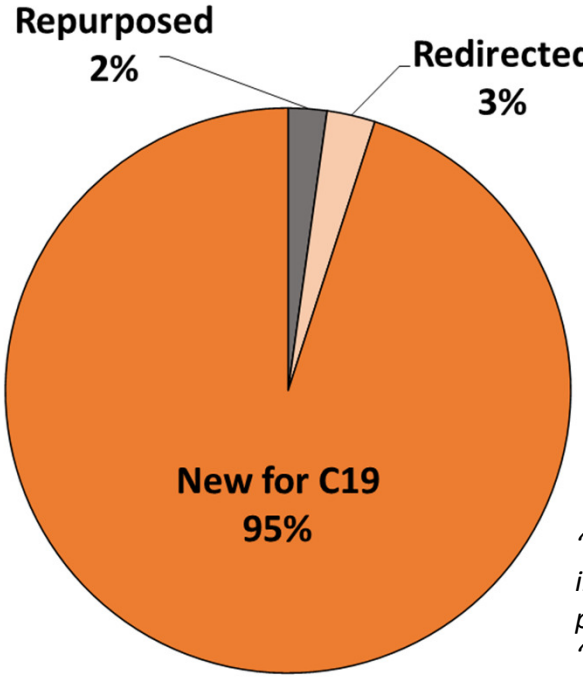


3 COVID-19 Pipelines



32 Clinical-Stage COVID-19 Vaccines





"Redirected" = drug placed into COVID pipeline from previously ongoing program
"Repurposed" = previously approved drug

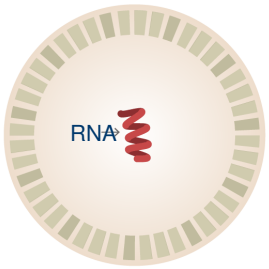
Biomedtracker, Biocentury, BIO Industry Analysis (Data as of 8/3/2020)

Vaccine Approaches to SARS-COV2

Recombinant Protein Vaccine

Yeast or other cells can be engineered to carry a virus's gene and spew out viral proteins, which are then harvested and put into a vaccine. A coronavirus vaccine of this design would contain whole spike proteins or small pieces of the protein.

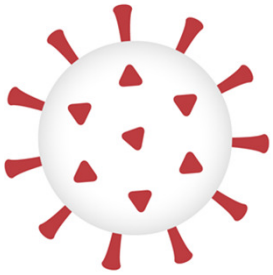
Genetic Vaccine (DNA or RNA)



DNA Vaccines: A circle of engineered DNA is delivered into cells. The cells read the viral gene, make a copy in a molecule called messenger RNA, and then use the mRNA to assemble viral proteins. The immune system detects the proteins and mounts defenses.

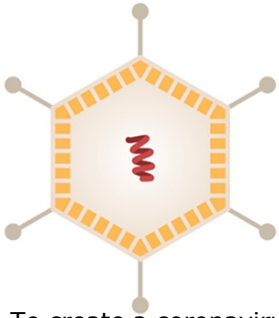
RNA Vaccines: Delivers messenger RNA into cells. The cells read the mRNA and make spike proteins that provoke an immune response.

Virus-like or Nanoparticle Vaccine



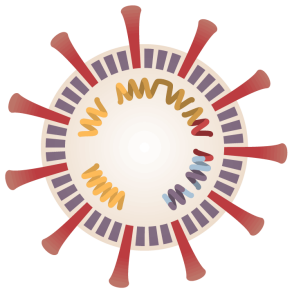
These vaccines are particles that contain pieces of viral proteins. They can't cause disease because they are not actual viruses, but they can still show the immune system what coronavirus proteins look like.

Viral Vector Vaccine



To create a coronavirus vaccine, several teams have added the spike protein gene to a virus called an adenovirus. The adenovirus slips into cells and unloads the gene. Because the adenovirus is missing one of its own genes, it cannot replicate and is therefore safe.

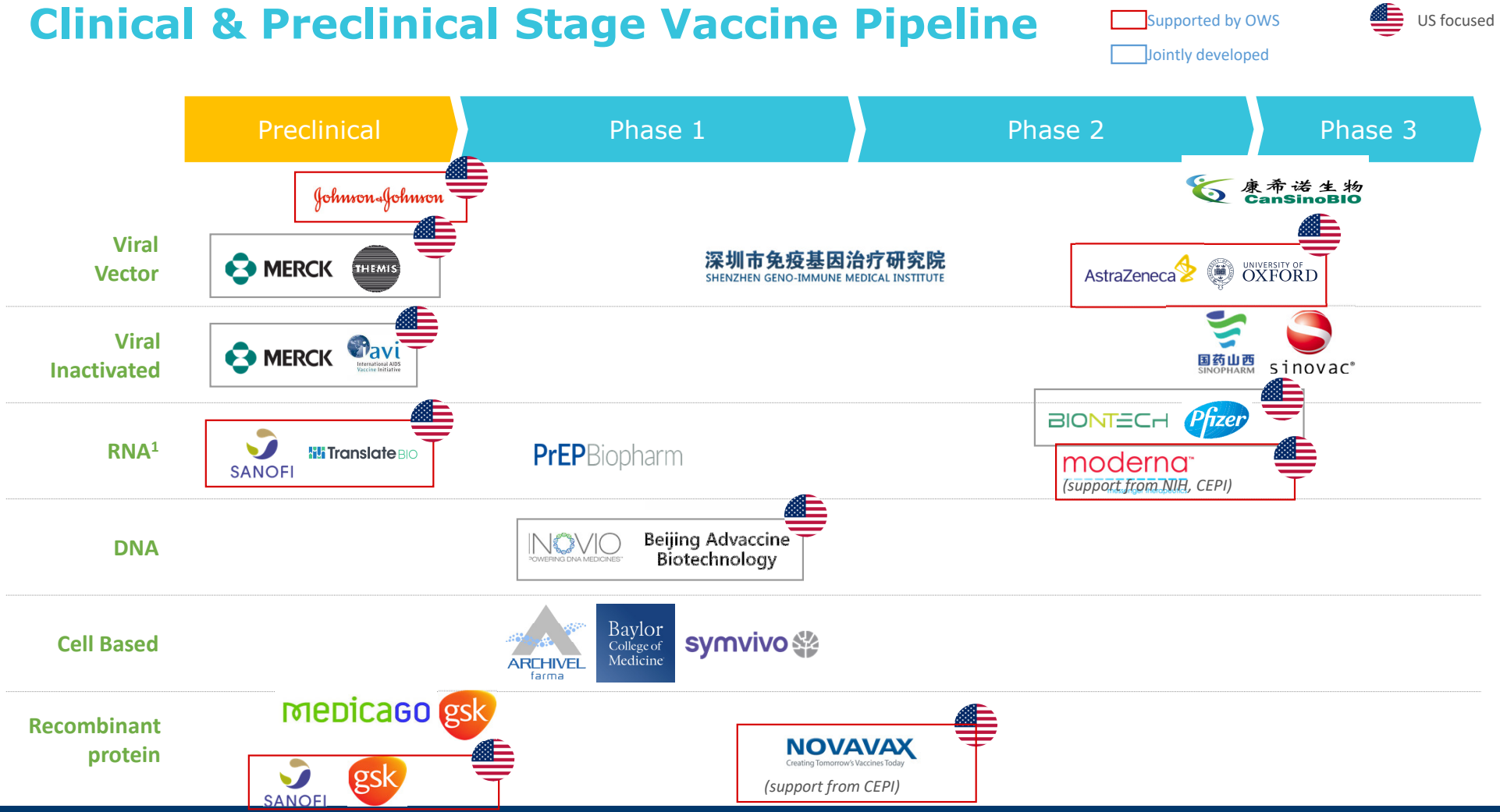
Whole-Virus Vaccine



Incorporates an inactivated or weakened form of a virus that is not able to cause disease. When immune cells encounter them, they make antibodies.

Source: https://www.nytimes.com/interactive/2020/05/20/science/coronavirus-vaccine-development.html

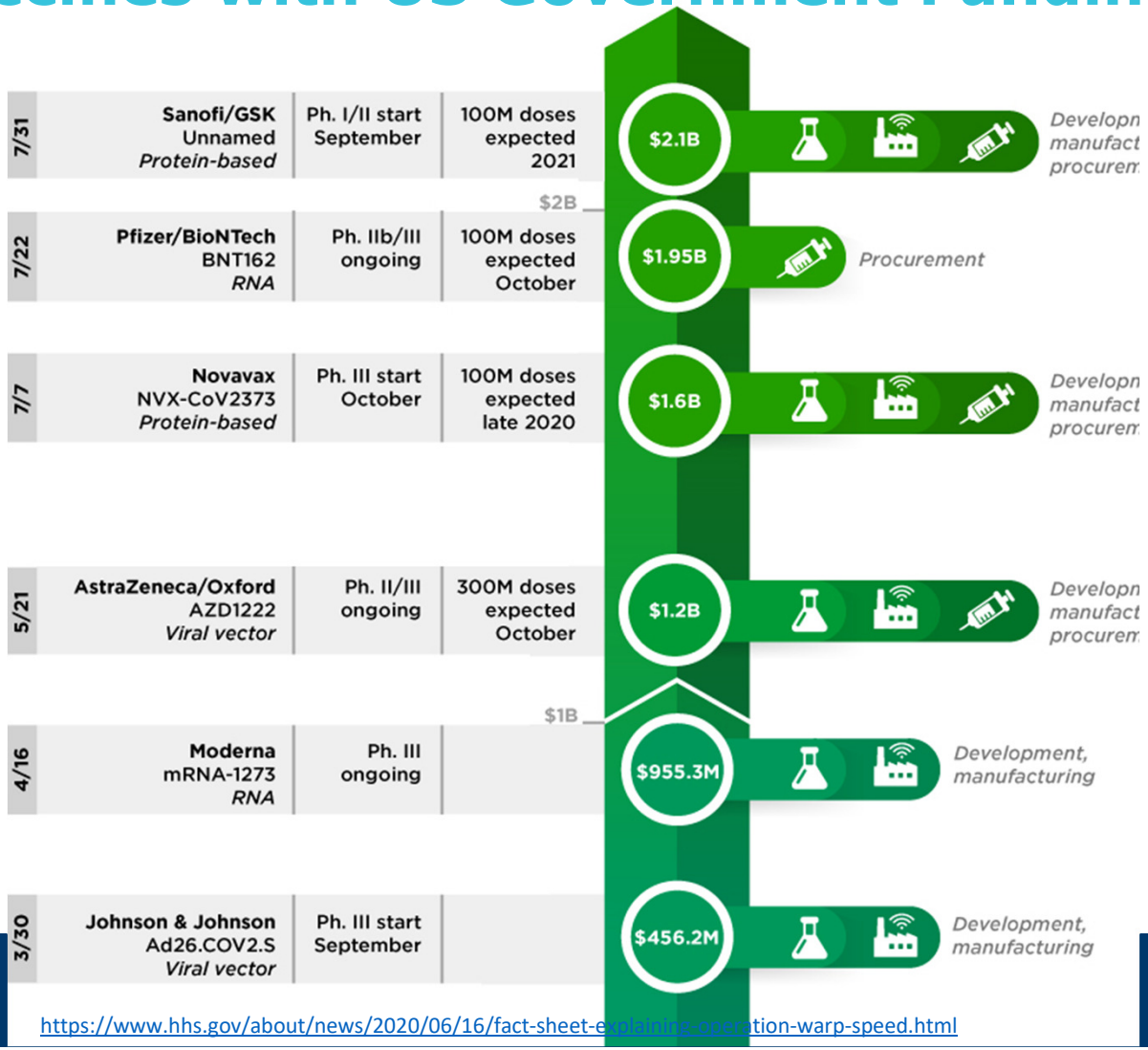
Clinical & Preclinical Stage Vaccine Pipeline



Source: Biomedtracker, Biocentury, BIO Industry Analysis
1. PrEP Biopharm vaccine dsRNA, all others mRNA
Oxford, Astrazeneca: ChAdOx1. Symvivo: bacTRL-Spike. Baylor College: BCG tuberculosis vaccine.
Sinopharm with two vaccines in phase 1 trials (one beginning Apr 12 the other Apr 27)

Info as of August 4, not exhaustive

Vaccines with US Government Funding (OWS)



https://www.hhs.gov/about/news/2020/06/16/fact-sheet-explaining-operation-warp-speed.html

Operation Warp Speed (OWS) aims to deliver 300 million doses of a safe, effective vaccine for COVID-19 by January 2021.

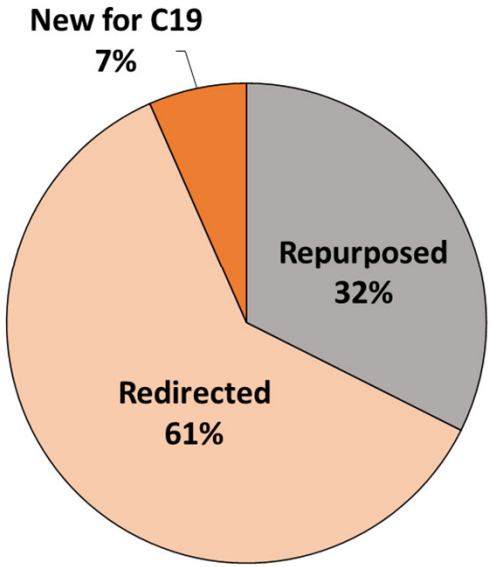
$483m + $472m (Jul26)
[goal 500m doses/year]

Source: Biocentury

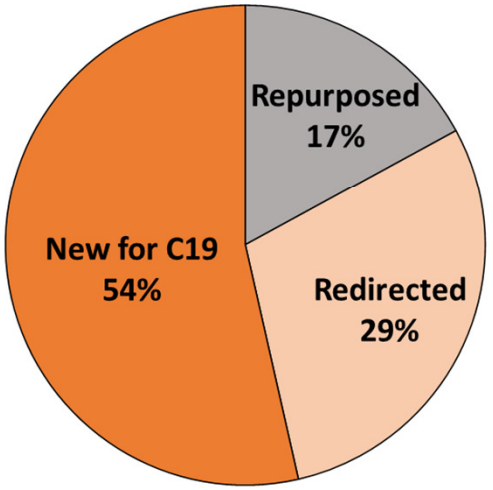
Repurposing & Redirecting Treatments

Novel projects ***7%*** ***54%***

Treatments for COVID-19 Illness



Antivirals & Antibodies



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Non-Antibody Antiviral Clinical Pipeline

N=43, but only 12 Late-stage (Phase III-IV)

Antiviral Type	Target Type for direct SARS-COV2 antivirals	Clinical Stage	
Anti-Cov2 cell therapy	NK cells	6	
Cell Entry	protease	9	*
Cell Entry	CD147	1	
Cell Entry	neuraminidase	2	
Cell Entry	surface glycans	2	
Trafficking	filament proteins	3	
Trafficking	exportin	1	
Trafficking	macrolide	2	
Replication	polymerase	9	**
Replication	oxidoreductase	1	
Replication	reverse transcriptase	3	
Replication	DHODH	5	
Replication	IMPDH	2	
Replication	translation	2	
Replication	farnesyl transferase	1	
Replication	adenosine pathway	1	
Replication	kinase inhibition	2	
Replication	demethylase	1	
Replication	ryanodine receptor	1	

** 2 protease inhibitors failed to show efficacy*

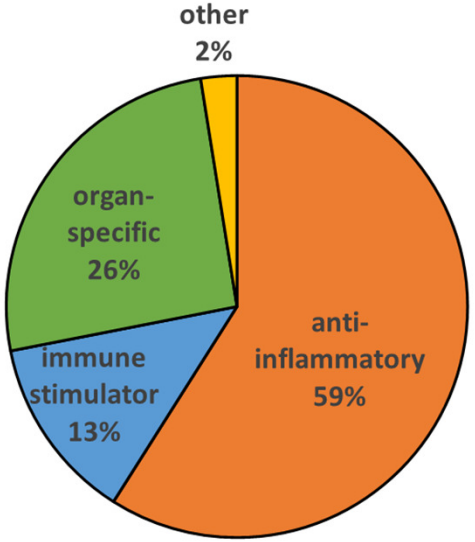
*** Remdesivir (polymerase inhibitor) is not counted here as it is now EUA in US and fully approved in Europe*

Anti-CoV-2 Antibodies Furthest Along

Mab Type	Company	Jul	Aug
anti-Spike Mabs	Regeneron [BARDA] (2 Mabs)		P3
anti-Spike Mab	AbCellera/Lilly		P3
anti-Spike Mab	Junshi/Lilly "JS06"		P1
anti-Spike Mab	Tychan (Singapore)		P1
anti-Spike Mab	Celltrion (Korea)		P1*
anti-Spike Mabs	Vir/GSK (2 Mabs)		PC
anti-Spike Mabs	Vanderbilt/AZ [NIAID] (2 Mabs)		PC
anti-Spike Mab	Sorrento 1499		IND*
Plasma-Derived	**Company**	**Jul**	**Aug**
conval. plasma	Multiple		P3*
human [HIG]	Emergent, BARDA "COVID-HIG"		P1*
human [HIG]	Octapharma "Octagam 10%"		P1*

	Preclinical
	Phase I
	Phase II
	Phase III
	EA/EUA

Treatment Clinical Pipeline by Strategy



(Treatments for COVID-19 illness, not antivirals)

Negative data:

Hydroxychloroquine/Chloroquine (multiple Phase III failures)
Anti-IL6 (multiple Phase III failures)

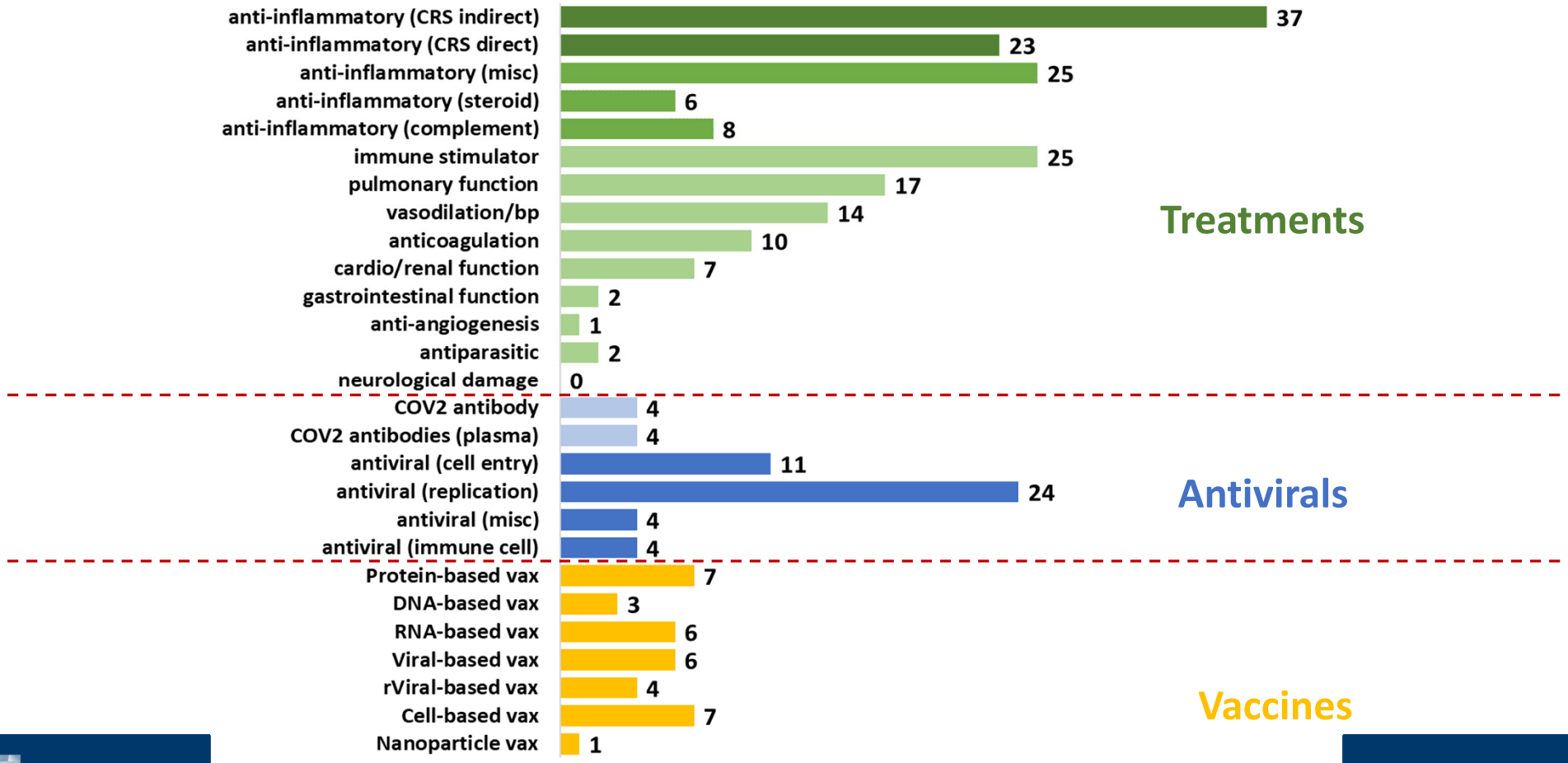
Positive data:

Dexamethasone (corticosteroid)
IFN-beta Phase II

Strategy	Phase I	Phase I/II	Phase II	Phase II/III	Phase III	Phase IV	EUA - US	EUA - Ex-US	EUA - US & Ex-US	Failed
anti-inflammatory	13	2	50	10	16	8		1		2
immune stimulator	3	3	12	2	3	2				
organ-specific	3	3	22	7	3	12		2		
other			1	1	1					2
total	19	8	85	20	23	22	0	3	0	4

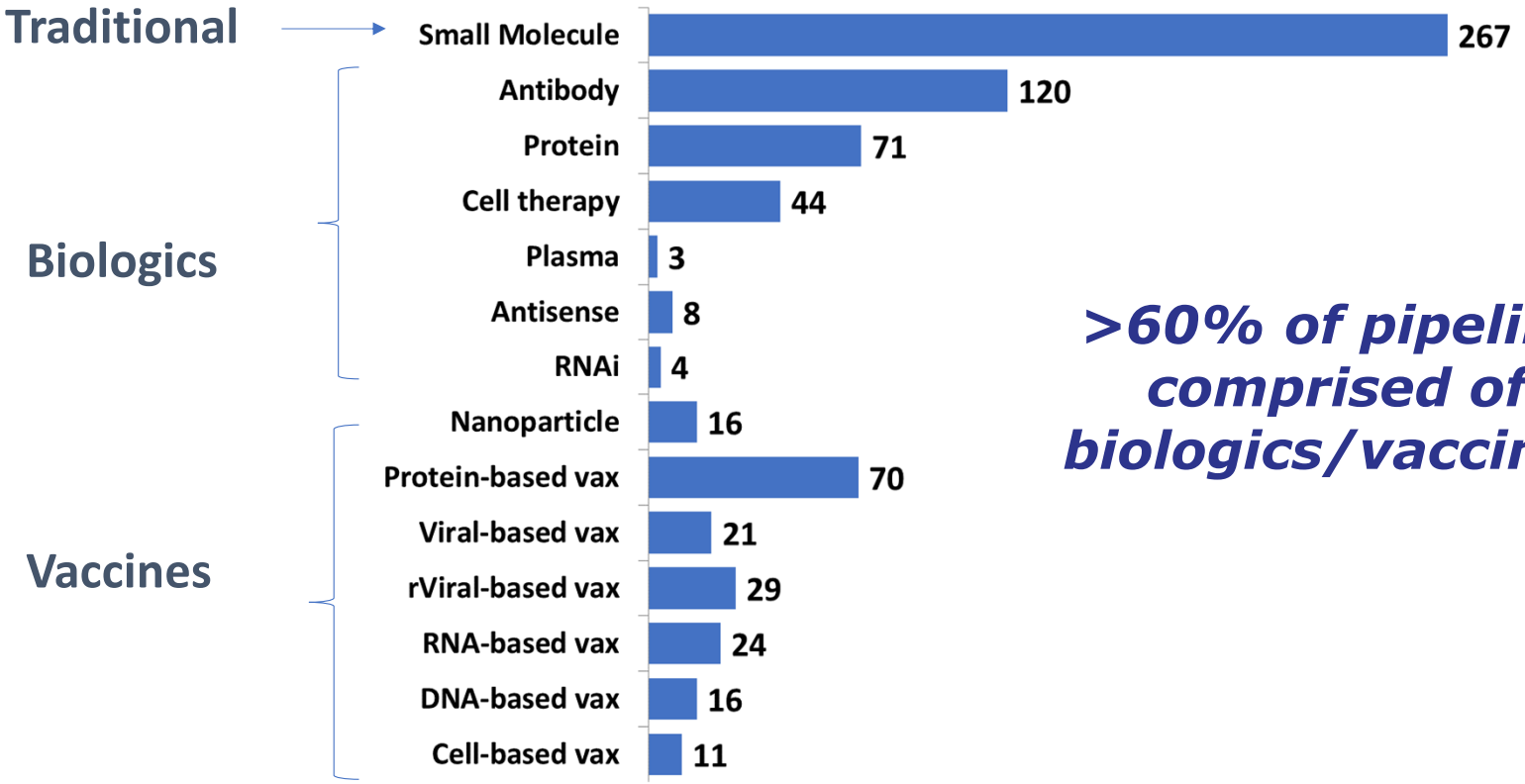
>60 late-stage

Strategies to Fight COVID-19 *(Phase I, II, III only)*



Biomedtracker, Biocentury, BIO Industry Analysis (Data as of 8/3/2020)

New Innovative Modalities to Fight COVID-19



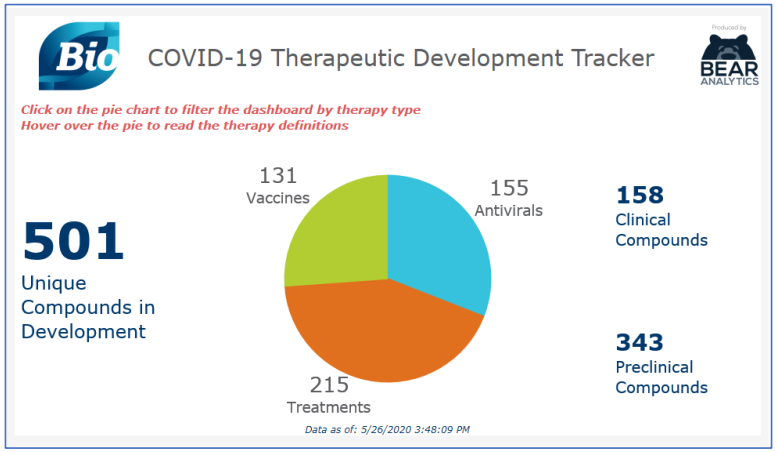
>60% of pipeline comprised of biologics/vaccines

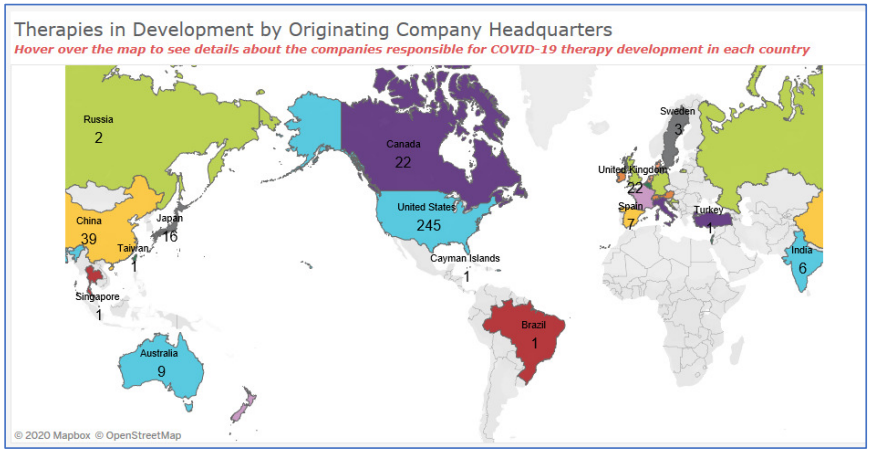
Biomedtracker, Biocentury, BIO Industry Analysis (Data as of 8/3/2020)

Challenges to COVID-19 Product R&D

- Scientific
  - Understanding of disease
  - Understanding of populations most at-risk
  - Clinical trial logistics
- Manufacturing
  - Record time scale-up
  - Fill/finish bottlenecks
  - Ancillary products
  - Not disadvantaging existing products
- Prioritization, distribution, and allocation
- Public confidence

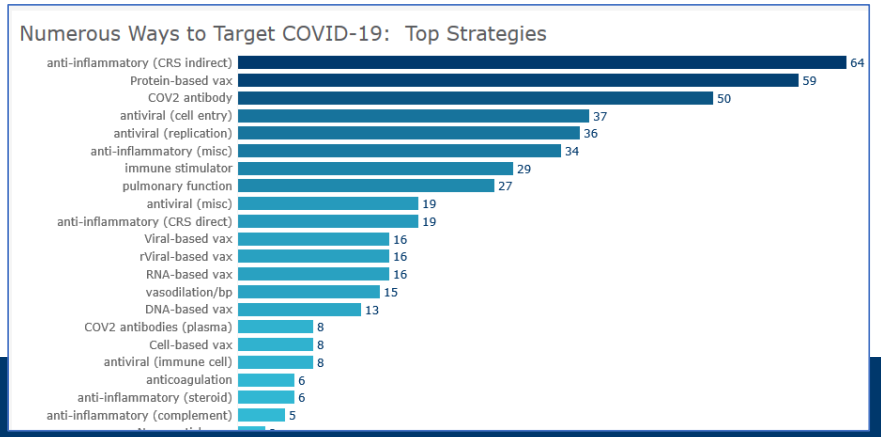
BIO COVID-19 Pipeline Tracker





Most Advanced COVID-19 Antiviral Candidates

Drug	Sponsors, Partners, [Funding]	Phase	Repurposed, Redirected, New	Target family
umifenovir (Arbidol)	Multiple, Ruijin Hospital	Phase IV	Repurposed	neuraminidase
danoprevir + ritonavir	Roche, Ascletis/Roche (Ganovo/Danoprevir), ..	Phase IV	Repurposed	protease
carrimycin	Shenyang Tonglian	Phase IV	Repurposed	macrolide
camostat (Foipan)	University of Aarhus, Heinrich-Heine University	Phase IV	Repurposed	protease
baloxavir marboxil (Xofluza)	The First Hospital Affiliated to Zhejiang Unive..	Phase IV	Repurposed	polymerase
azithromycin	Multiple	Phase IV	Repurposed	macrolide
oseltamivir (Tamiflu)	Multiple, Tongji Hospital, Rajavithi Hospital, U..	Phase III	Repurposed	neuraminidase
nitazoxanide (Alinia)	Romark Laboratories, Lupin, Materno-Perinat..	Phase III	Repurposed	oxidoreductase
favipiravir	.decimal, Inc., Zhejiang Hisun Pharma	Phase III	Repurposed	polymerase
ENU200	Ennaid Therapeutics	Phase III	Repurposed	ACE2/Spike
emtricitabine + tenofovir di..	Plan Nacional sobre el Sida (PNS)	Phase III	Repurposed	reverse transcriptase
ASC09 + ritonavir	J&J, Ascletis Pharma	Phase III	Redirected	protease
Leronlimab	CytoDyn, Inc., Vyera Pharmaceuticals	Phase II/III	Redirected	CCR Family
Hyperimmune plasma	Foundation IRCCS San Matteo Hospital	Phase II/III	New for C19	COV2 epitope
Convalescent Plasma	Multiple	Phase II/III	New for C19	COV2 epitope
Xpovio	Karyopharm Therapeutics	Phase II	Repurposed	exportin
selinexor	Karyopharm	Phase II	Repurposed	exportin
ribavirin (Virazole)	Bausch Health Companies Inc.	Phase II	Repurposed	IMPDH
PP-001	4SC Aq, Panoptes Pharma	Phase II	Redirected	DHODH
piclidenoson	Can-Fite BioPharma, Temple University	Phase II	Redirected	adenosine pathway
merimepodib (Vicromax)	BioSig	Phase II	Redirected	IMPDH
lonafarnib (Sarasar)	Eiger BioPharmaceuticals	Phase II	Redirected	Farnesyl transferase
IMU-838	Immunic, Inc., 4SC AG	Phase II	Redirected	DHODH
galidesivir	BioCryst, [NIH/NIAID]	Phase II	Redirected	polymerase
FW-1022 (niclosamide)	FirstWave	Phase II	Repurposed	NA
FP-025	ForeSee	Phase II	Redirected	protease
Fludase	Ansun BioPharma, Wuhan University	Phase II	Redirected	surface glycans
elsulfavirine (Elpida)	Viriom LLC, Roche, Chinese CDC, Ministry of ..	Phase II	Redirected	reverse transcriptase
bemcentinib	BerGenBio AS, [Department of Health and So..	Phase II	Redirected	kinase inhibition
azvudine	Zhengzhou Granlen PharmaTech	Phase II	Redirected	reverse transcriptase
Aplidin	PharmaMar, S.A., Centro Nacional de Biotecn..	Phase II	Repurposed	translation



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