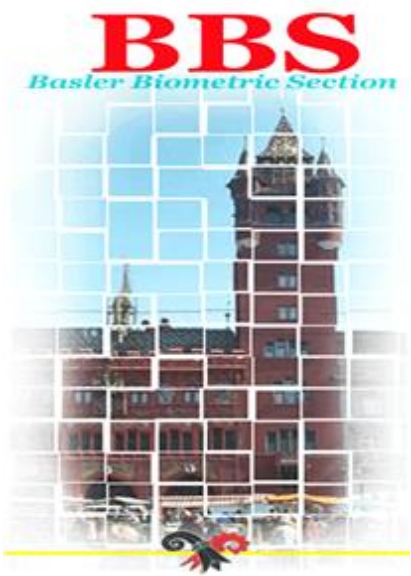


Overview on SARS-CoV2 & Challenges for COVID-19 Vaccine Development at Pandemic Speed

Jean Lang MD, PhD, FASTMH

SANOFI PASTEUR

R&D Head of Global Health, Partnerships & External Funding

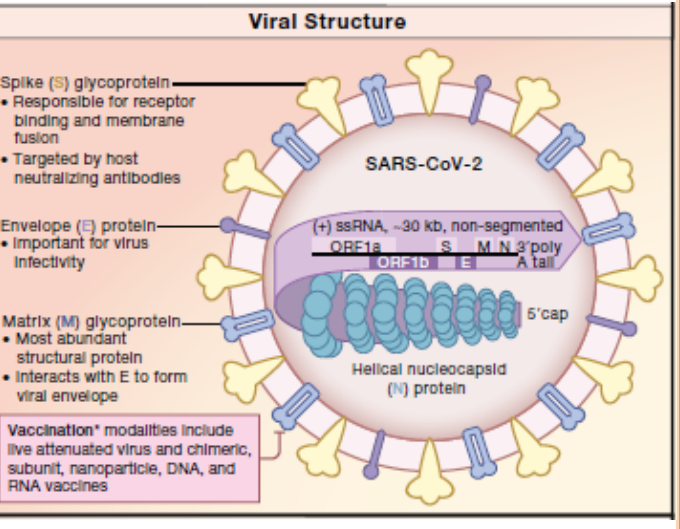
June 3d 2020

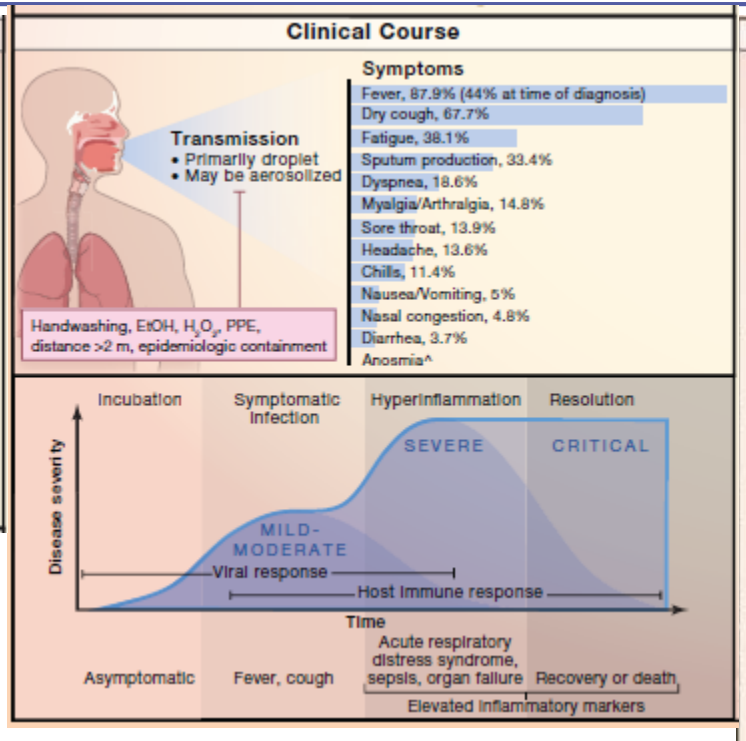
COVID-19 Cases

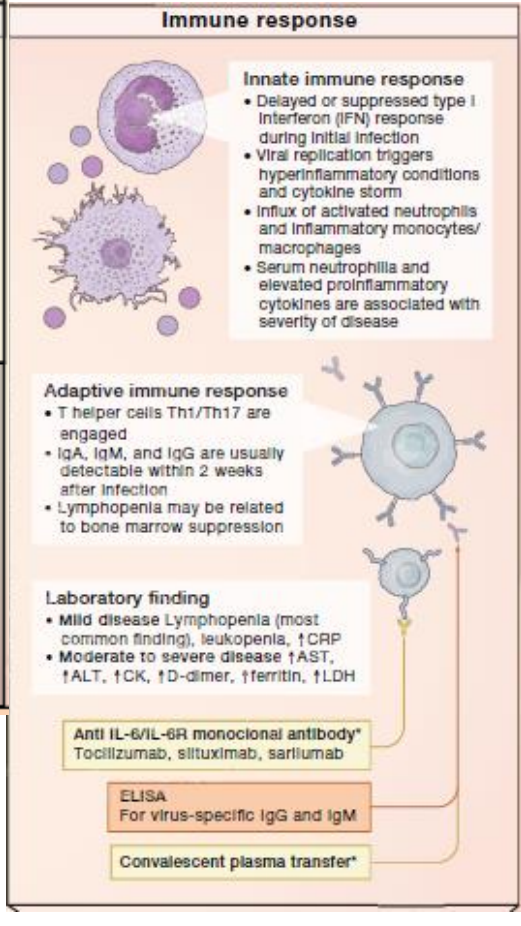
June 2d, 2020

#	Country, Other	Total Cases	New Cases	Total Deaths	New Deaths
	World	6,403,590	+40,394	378,119	+929
1	USA	1,860,613	+1,290	106,944	+19
2	Brazil	529,405		30,046	
3	Russia	423,741	+8,863	5,037	+182
4	Spain	286,718		27,127	
5	UK	276,332		39,045	
6	Italy	233,197		33,475	
7	India	199,785	+1,415	5,612	+4
8	France	189,220		28,833	

SARS-CoV2 : A snapshot







954 Cell 181, May 14, 2020 © 2020 Elsevier Inc. DOI
https://doi.org/10.1016/j.cell.2020.04.013

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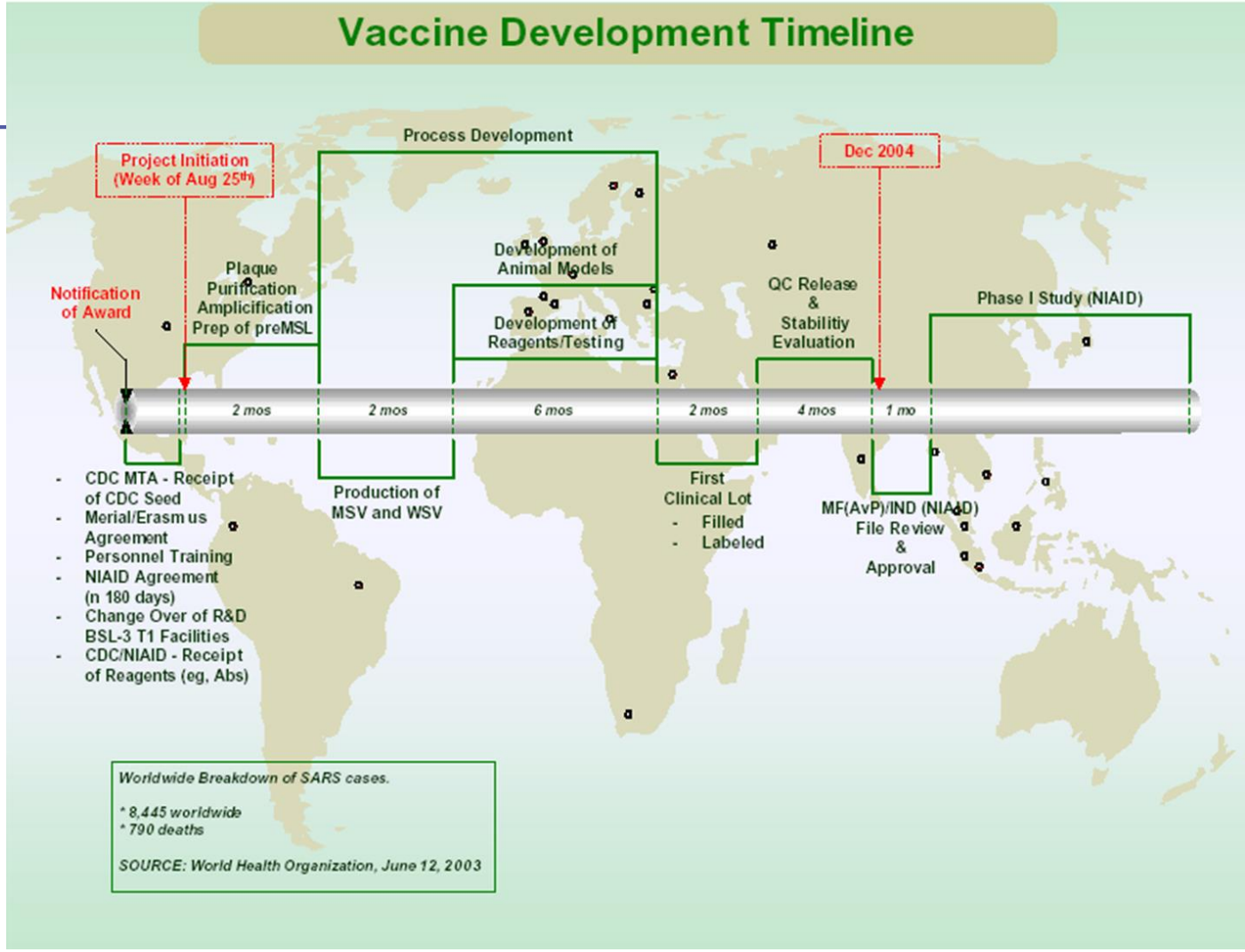
SARS 2003-2004
SP summary



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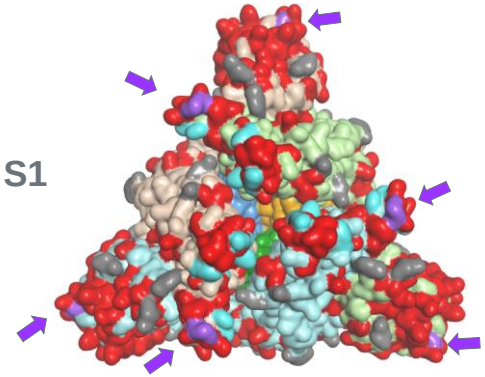
Antigenic differences with SARS CoV1

Low / no cross-reactivity of the neutralizing antibodies expected

Top view of S1

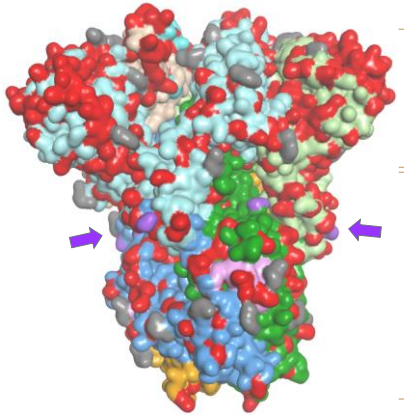


Legend

- Differences
- Additional loops

90°

Side view



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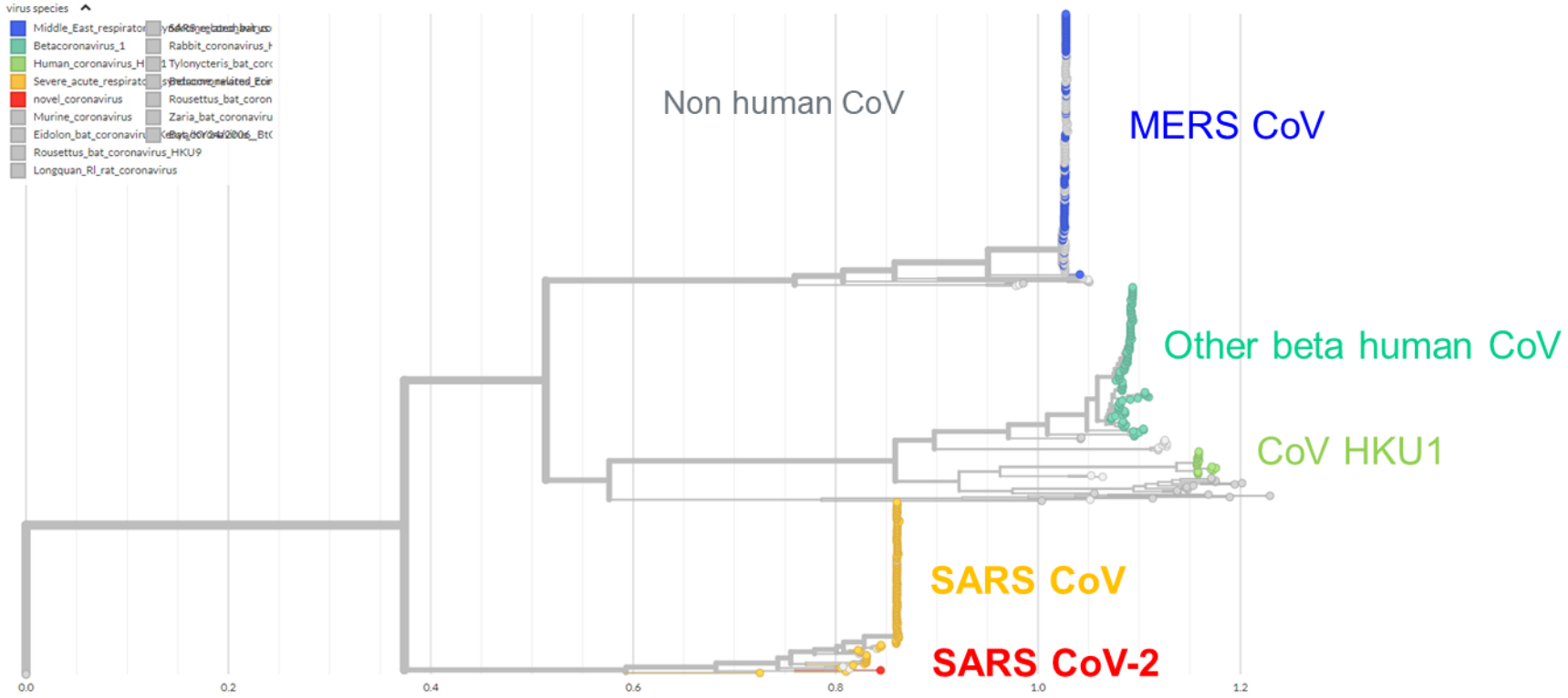
SARS Spike 3D structure from Li et al., 2005

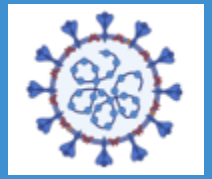
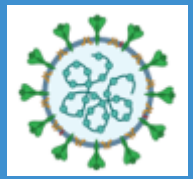
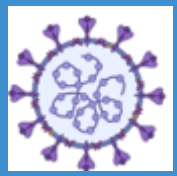
Beta-Coronaviruses family

SARS CoV-2 closest relative is SARS CoV1 (2003 pandemic)

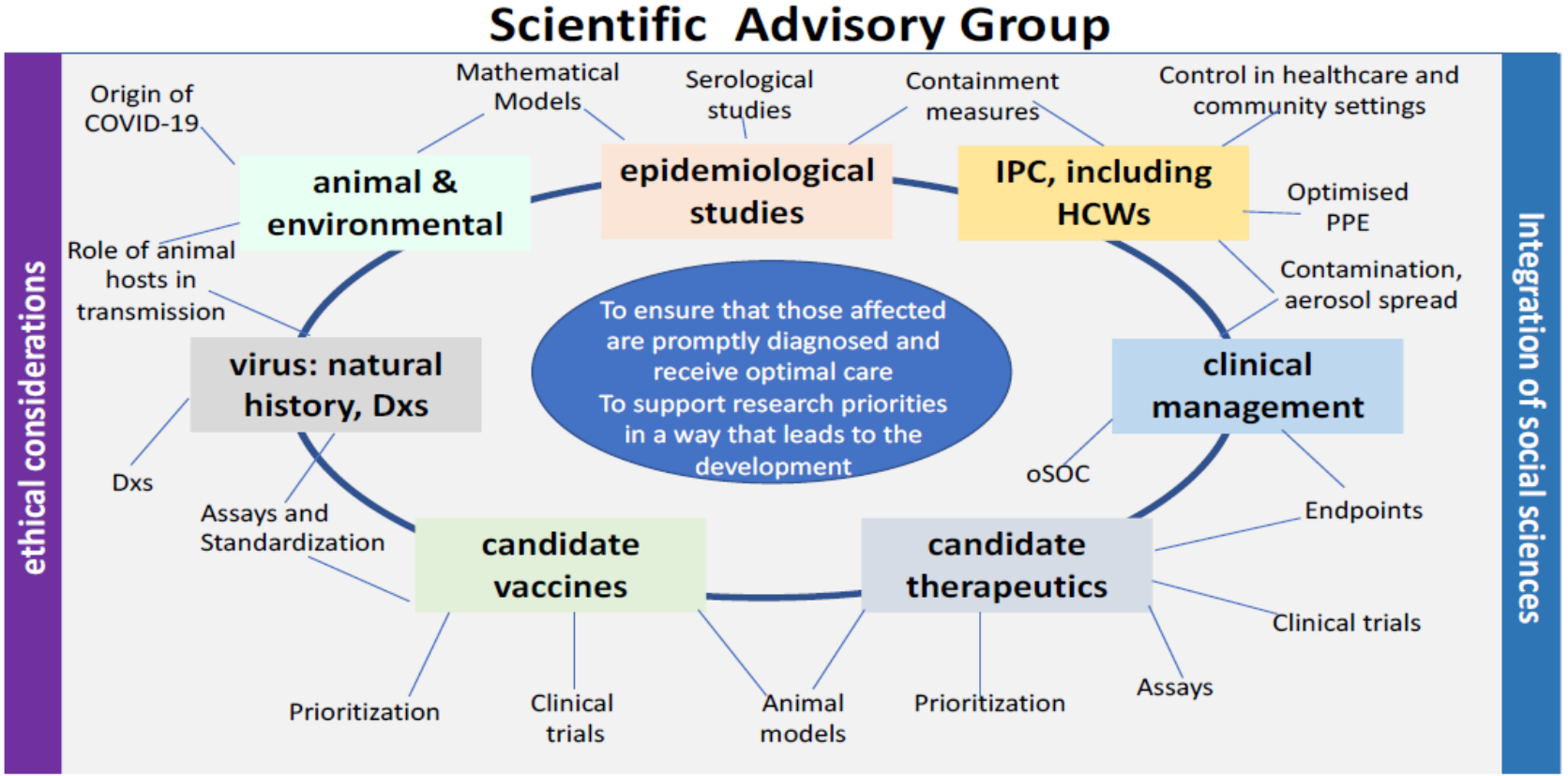


source: Nextstrain.org

Comparison between Flu, COVID19, SARS and MERS

	Flu	Covid19	SARS	MERS
				
R0	1.3	2.4 – 3.5	3	0.3 – 0.8
CFR	0.05 – 0.1%	3.4% (higher in older age group and people with comorbidities)	9.6 – 11%	34.4%
Incubation time	1 – 4 days	2 – 14 days	2 – 7 days	6 days
Hospitalization rate	2%	19 – 20%	Most cases	Most cases
Annual infected (global)	1 billion	N/A (ongoing)	8,098 in 2003	420 in 2014

WHO Target Research Priorities in Each R Thematic Areas - 2020 (WHO R&D Blueprint -2015)



https://www.glopid-r.org/about-us/members/

GLOPID-R

Global Research Collaboration for Infectious Disease Preparedness

- GLOPID-R an international network of research funding organizations

28 Members and 2 observers

"facilitate, accelerate and deepen collaboration among research funders on emerging diseases":

- to strengthen global research **preparedness** between crises.
- to **respond** rapidly and effectively to significant infectious disease outbreaks.

GLOPID-R

R&DBlueprint
Powering research to prevent epidemics

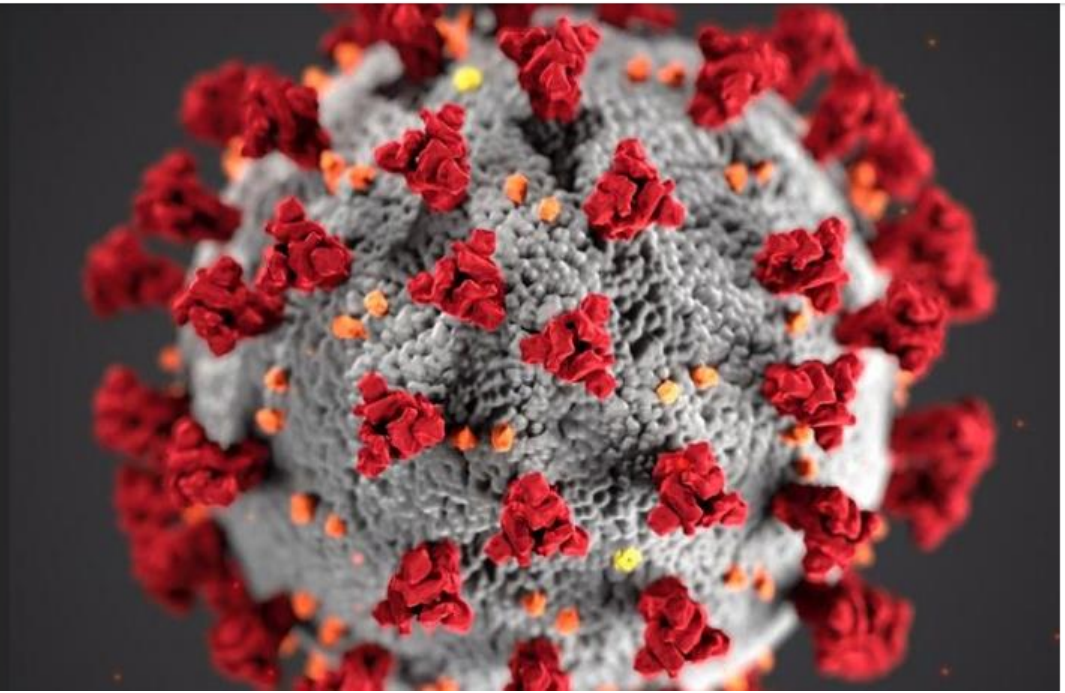
Pre-reads

REACTing

COVID-19 ABOUT US ACTIVITIES RESOURCES

REACTing is playing a key role in the coordination and information sharing regarding the COVID-19 outbreak in France.

Visit our dedicated pages on :
- the role of REACTing
- our literature review on COVID-19
- funding opportunites on COVID-19



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Horizon 2020 Europe PPP : IMI2 EFPIA (Call published March 3d 2020)

The overall objectives of this topic are described in the following subtopics:
1.Accelerating the development of treatment agents (single products and their combinations) against coronaviruses:
1.1. Focusing on re-purposing of drugs
1.2. Identity novel chemical or biological antiviral treatment agents
2.Advancing the development of point of care diagnostics

- *This current programme will be launched in 2020 with a provisional total budget of about € 90 million (Half EFPIA Companies).*
- *Given the level of urgency and type of activity, the call will be set up as an emergency single stage procedure. The **indicative duration of the action is 72 months***
- ***Vaccines are not included in this call***
- http://bit.ly/2wkEuzQ

- **Another Research H2020 call was launched worth of € 47.5 million (2-3 MM / applicant) for Academic Consortia**
  https://ec.europa.eu/info/sites/info/files/research_and_innovation/research_by_area/documents/ec_rtd_coronavirus-factsheet.pdf

Bill & Melinda Gates Foundation COVID 19 Grants

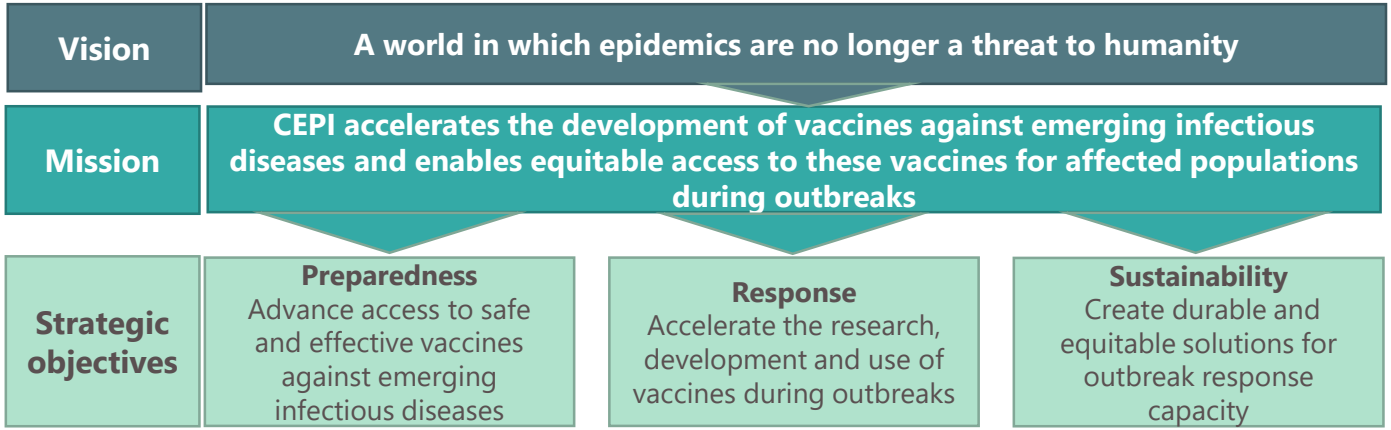
SEATTLE, February 5, 2020 – The Bill & Melinda Gates Foundation today announced that it will immediately commit up to $100 million for the global response to the 2019 novel coronavirus (2019-nCoV). The funding will help strengthen detection, isolation and treatment efforts; protect at-risk populations; and develop vaccines, treatments and diagnostics. The new funding is inclusive of $10 million the foundation committed to the outbreak in late January.

SEATTLE, March 10, 2020 – The Bill & Melinda Gates Foundation, Wellcome, and Mastercard today committed up to $125 million in seed funding to speed-up the response to the COVID-19 epidemic by identifying, assessing, developing, and scaling-up treatments. The partners are committed to equitable access, including making products available and affordable in low-resource settings. The COVID-19 Therapeutics Accelerator will play a catalytic role by accelerating and evaluating new and repurposed drugs and biologics to treat patients with COVID-19 in the immediate term, and other viral pathogens in the longer-term. Currently there are no broad-spectrum antivirals or immunotherapies available for the fight against emerging pathogens, and none approved for use on COVID-19.
The Gates Foundation and Wellcome are each contributing up to $50 million, and the Mastercard Impact Fund has committed up to $25 million to catalyze the initial work of the accelerator.

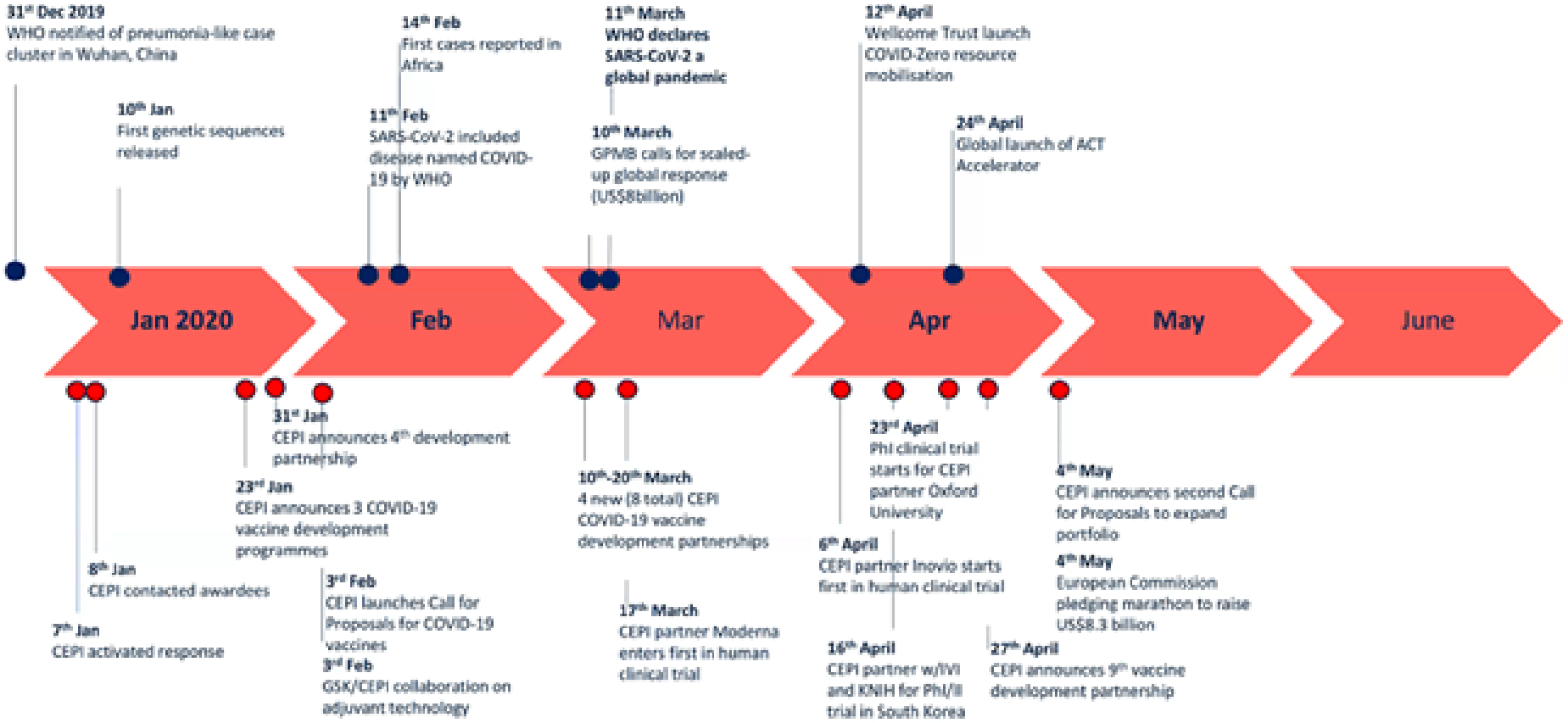
CEPI

Coalition for Epidemic Preparedness Innovations

Vision, mission, and strategic objectives



CEPI's vaccine development so far



Sanofi Pasteur: Two Approaches For A COVID-19 Vaccine

(February 18th, April 14th and March 27th 2020)

1 – Baculovirus recombinant vaccine approach

Cell Culture

Protein Antigens

+

Adjuvants

AF03 SP/ASO3 GSK

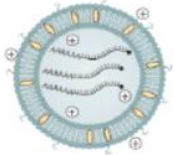
- Licensed platform
- Safety experience
- BARDA collaboration
- Existing large scale manufacturing capacity

2 – Translate Bio mRNA vaccine approach

In Vitro Transcription

mRNA

Delivery System



mRNA Formulation

- Different MoA
- Adds manufacturing capacity
- Building on current collaboration
- R&D synergies

Recombinant Influenza Vaccine

First recombinant hemagglutinin (rHA) containing influenza vaccine

- Baculovirus expression vector system used instead of eggs to produce rHA
- Developed by Protein Sciences *(acquired by Sanofi in 2017)*

- Baculovirus engineered with the gene of interest (e.g., hemagglutinin [HA] for influenza vaccine)
- Baculoviruses are highly specific to *Spodoptera frugiperda* [fall armyworm]-positive cells (SF+)
- SF+ cells infected with engineered virus
- Incubated for ~48 to 72 hours
- High yield of protein of interest generated (in this case, HA) – extracted and purified

The recombinant technology developed for influenza vaccines will also be used in efforts to combat COVID-19 disease

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Reference:
1. Cox MM, Hashimoto Y. *J Invertebr Pathol*. 2011;107(Suppl):S31-S41.

Benefits of Recombinant Vaccine Platform

Unique circumstances make this an attractive option for a vaccine

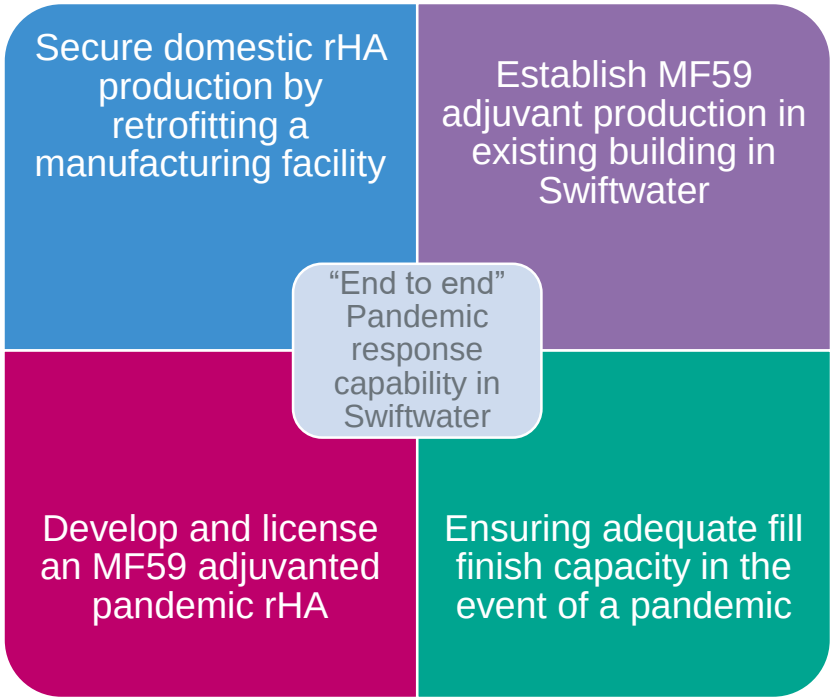
- **The experience with the SARS vaccine can be leveraged to expedite COVID-19 vaccine development**

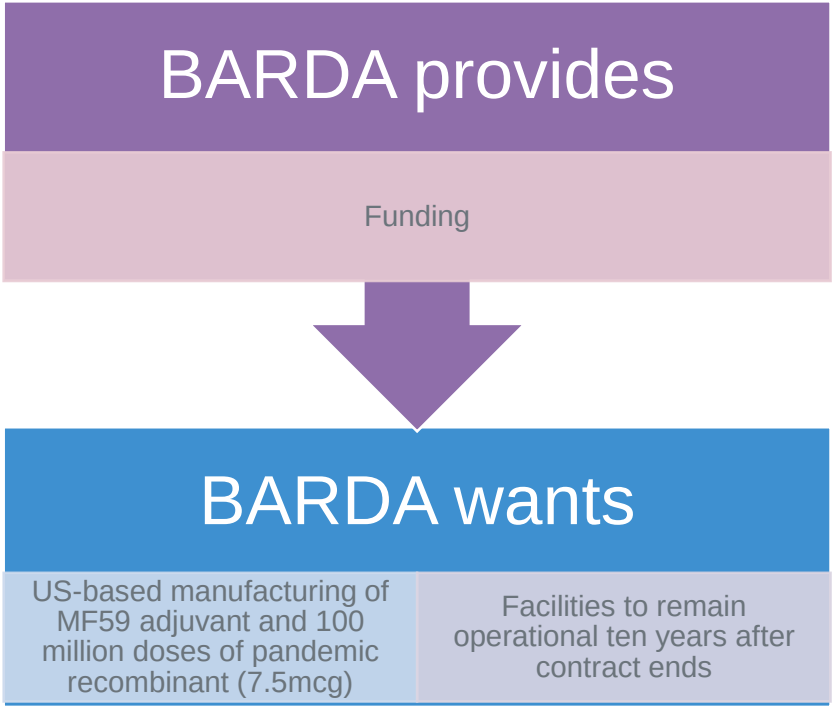
- **There is a US licensed recombinant influenza vaccine based on the platform**
  - **Research and Clinical material could be produced relatively quickly**
    - Assuming a similar purification process a vaccine candidate against the novel coronavirus could be produced with the expectation that the candidate would be immunogenic and have an acceptable safety profile
  - **The manufacturing platform is approved by the FDA and under consideration of other global regulatory authorities**
  - **Existing infrastructure to facilitate production of large quantities of vaccine**
    - Could be produced at our existing facilities (Pearl River, NY and Unigen, Akita, Japan)

- **The technology provides a rapid relatively low risk path to large scale supply**
  - **Assuming the SARS experience proves applicable to development of a vaccine candidate.**

BARDA Sanofi Pandemic Preparedness Partnership

US-based adjuvant and antigen manufacturing of pandemic flu vaccine

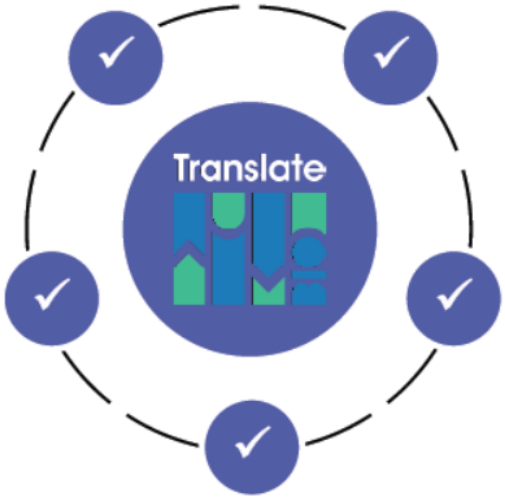




Sanofi's collaboration on mRNA vaccine platform

Existing agreement to develop mRNA vaccines for five infectious diseases

Rodent and non-human primate studies complete on other vaccine programs



Lead mRNA and LNP candidates tested across disease targets

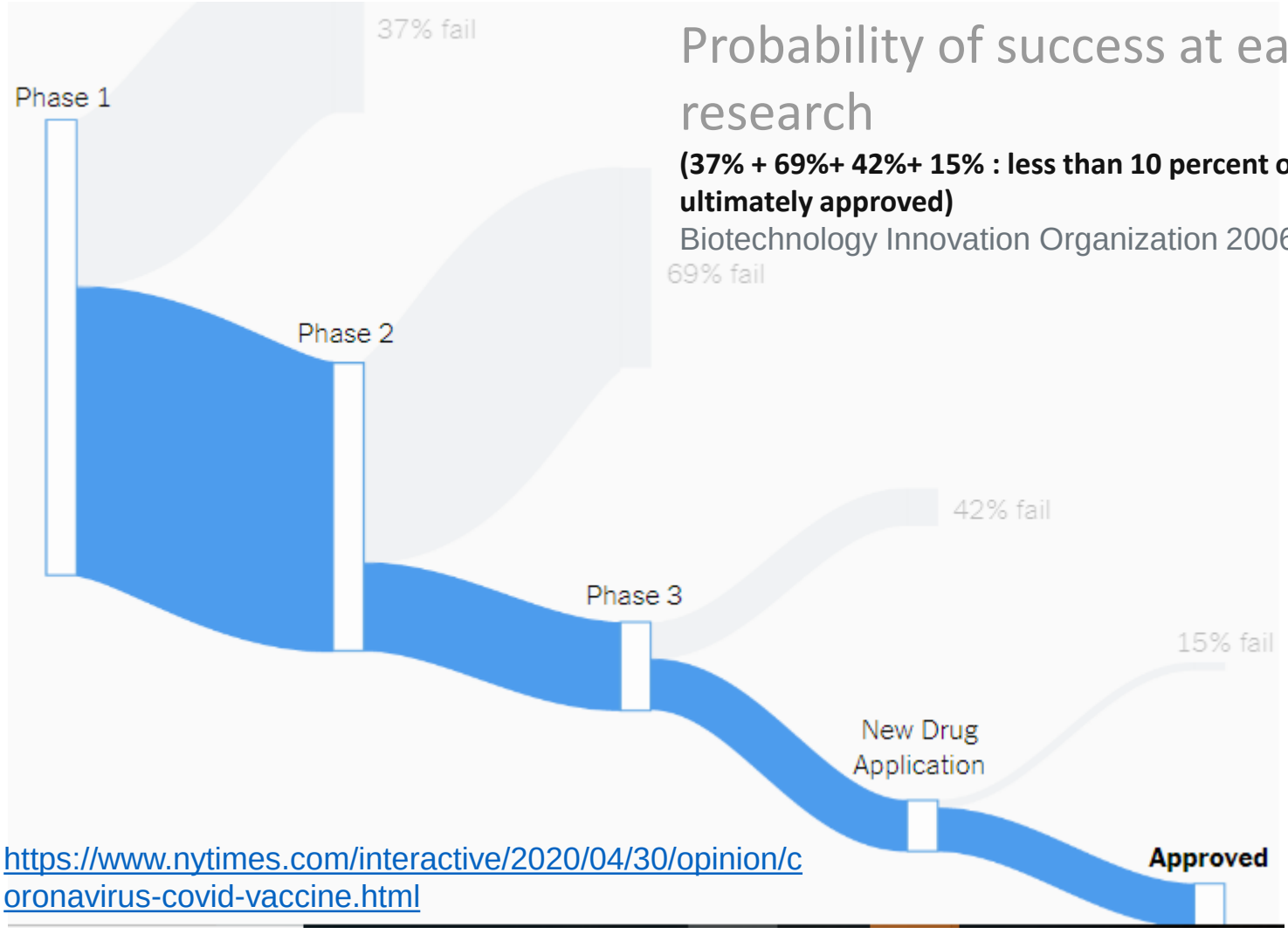
Large scale process development in progress for lead mRNA constructs

Opportunity to scale-up to commercial volumes

Probability of success at each phase of research

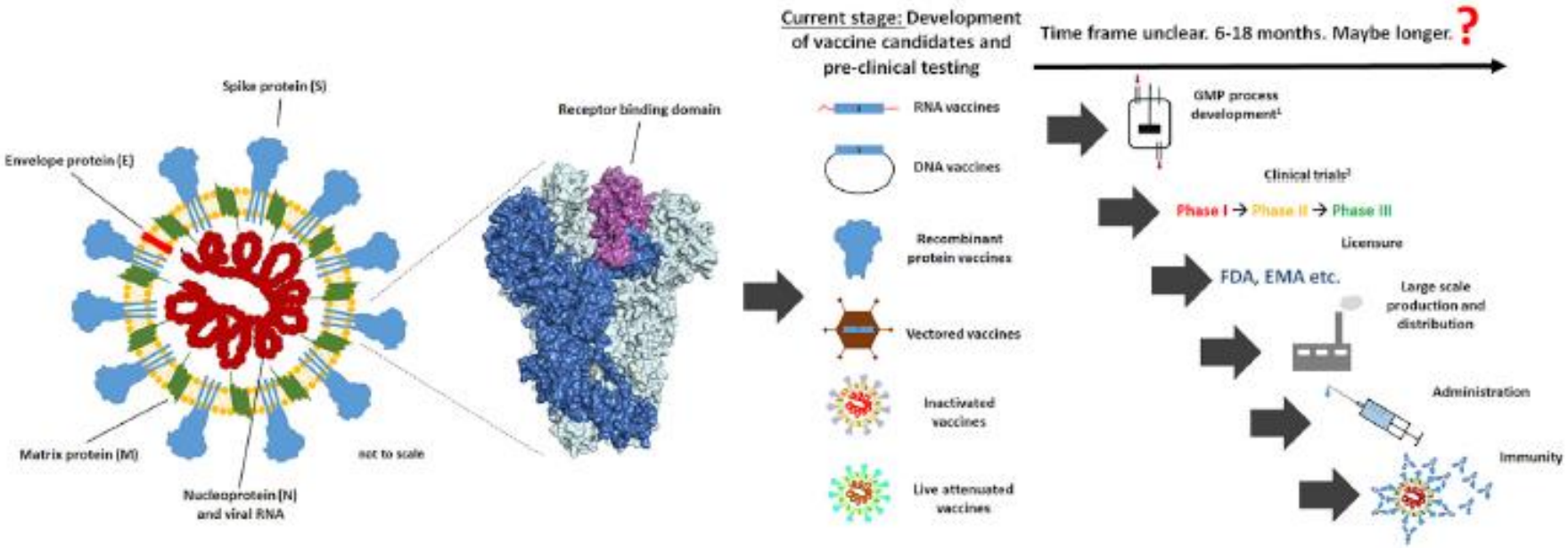
(37% + 69%+ 42%+ 15% : less than 10 percent of drug trials are ultimately approved)

Biotechnology Innovation Organization 2006 – 2015



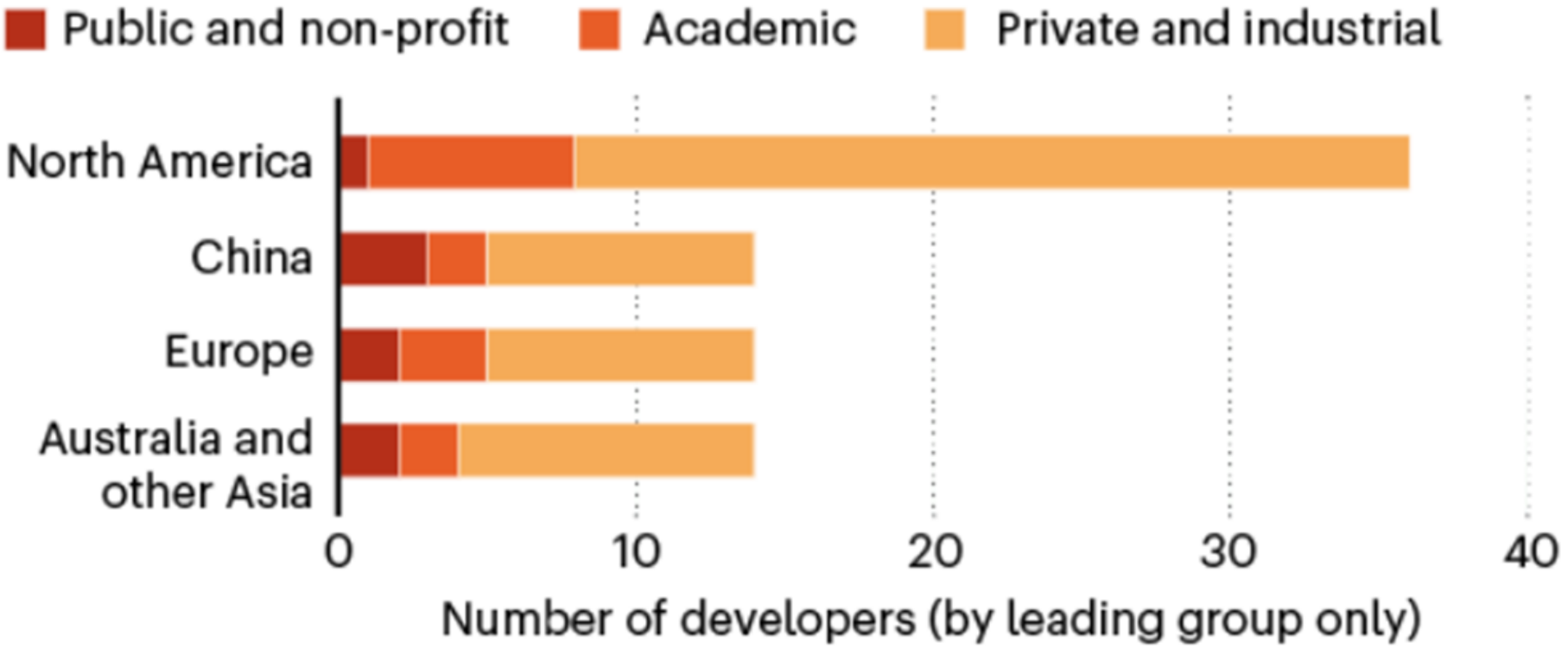
https://www.nytimes.com/interactive/2020/04/30/opinion/coronavirus-covid-vaccine.html

Overview of Potential SARS-CoV2 Vaccine Platforms



Immunity 52, April 14, 2020
Perspective SARS-CoV-2 Vaccines: Status Report
https://doi.org/10.1016/j.immuni.2020.03.007

PUBLIC AND PRIVATE DEVELOPMENT LANDSCAPE



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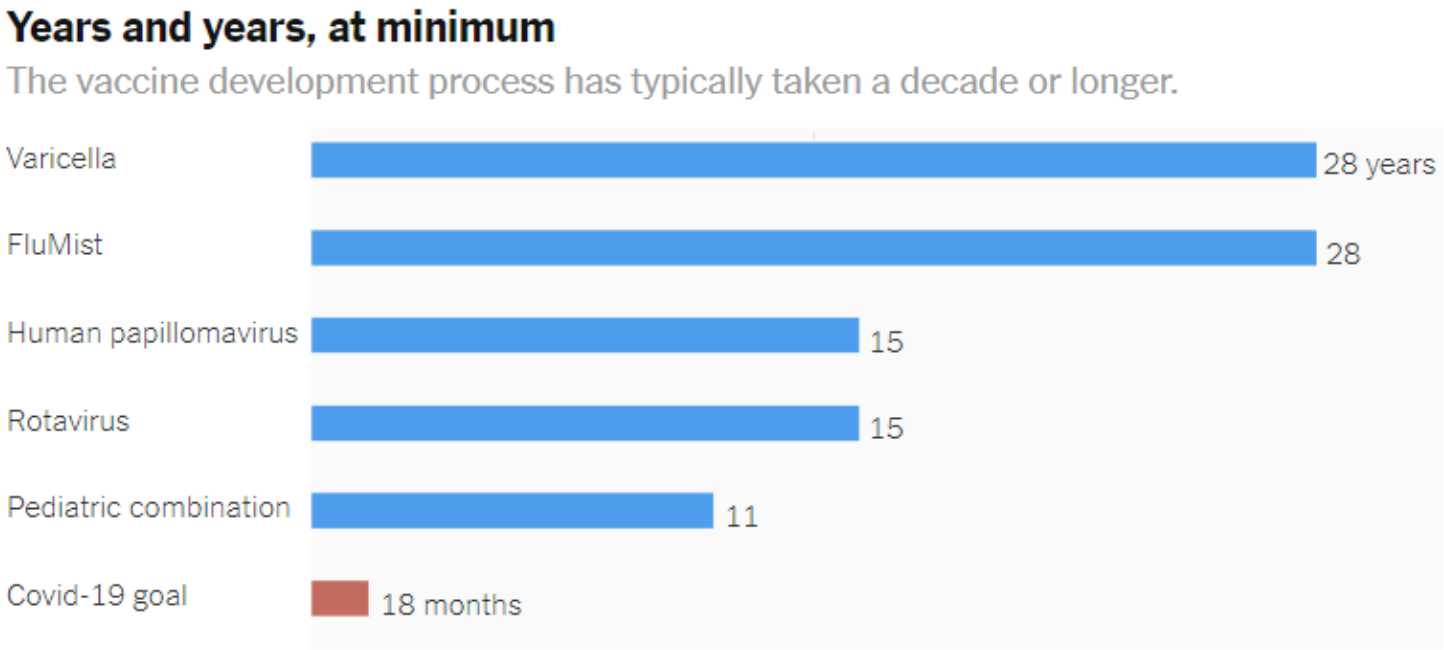
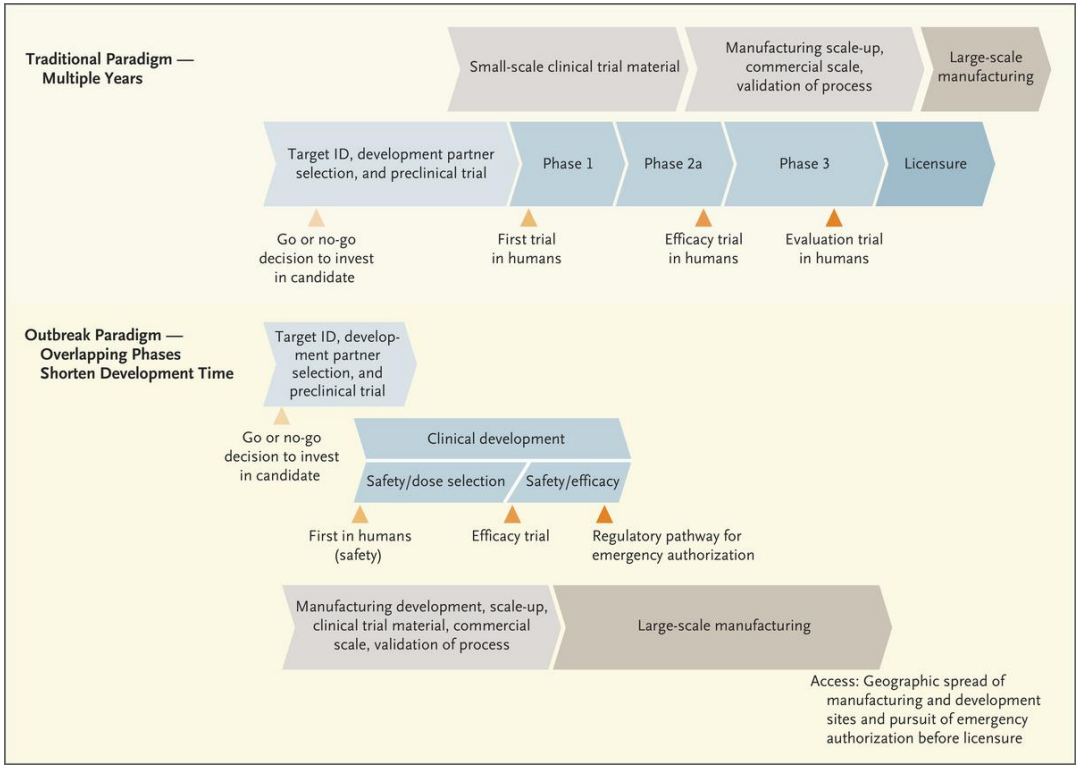
Nature **580**, 576-577 (2020)
doi: 10.1038/d41586-020-01221-y

Vaccine Time to licensure benchmarks



https://www.nytimes.com/interactive/2020/04/30/opinion/coronavirus-covid-vaccine.html

Difference between Traditional Vaccine Development and Development Using a Pandemic Paradigm



N Lurie et al. N Engl J Med 2020. DOI: 10.1056/NEJMp2005630

How to move to pandemic paradigm ?

Assume We Already Understand the Coronavirus

Start trials early

Rely on work from studying SARS and MERS to shorten preparations before clinical trials

Don't wait for academic research

Skip to clinical phases using what we know about the coronavirus so far

Move at 'Pandemic Speed' Through Trials

Use 'pandemic speed' timeline

Start subsequent steps before previous phases are completed

Push to large-scale tests sooner

Move more swiftly to Phase 3 trials by combining phases

Use emergency provision

Vaccinate front-line and essential workers early

Start Preparing Factories Now

Make vaccines early

Build and manufacture early, anticipating that factories will be useful for a future vaccine and that the product will clear regulatory hurdles

Speed Up Regulatory Approvals

Take a bet on a successful Technology

The experimental may be faster to produce/leverage existing facility

Fast-track federal approvals

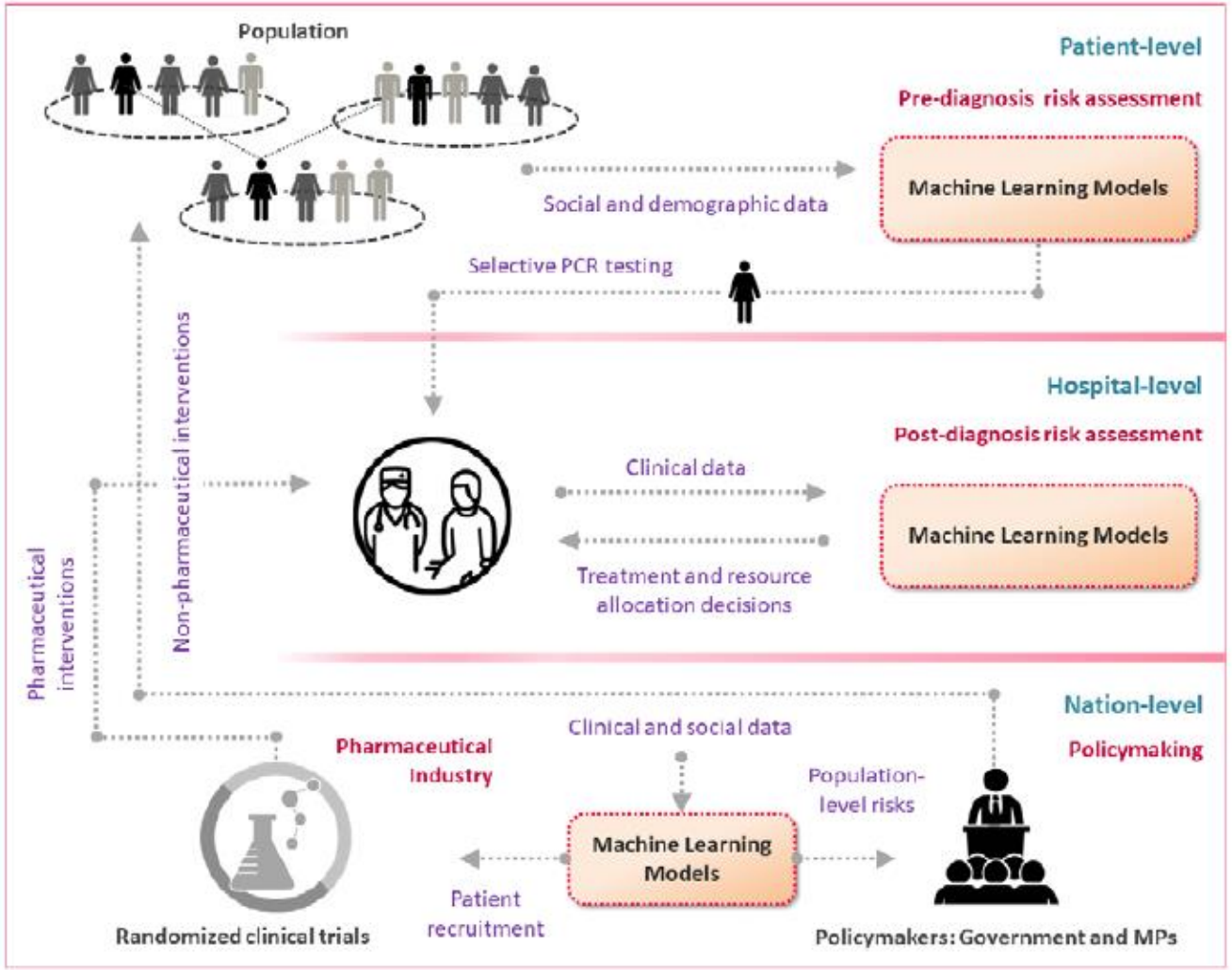
Shorten approval window from a year to six months

How artificial intelligence and machine learning can help healthcare systems respond to COVID-19

Mihaela van der Schaar, John Humphrey Plummer et al.

Cambridge Centre for AI in Medicine

March, 27th,2020



Summary I : COVID-19 : partnerships will be essential to success

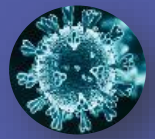
The United States Government

- ✓ FDA
- ✓ BARDA
- ✓ NIH
- ✓ Trump's "Operation warp speed"

European governing bodies

- ✓ EU Commission
- ✓ EMA
- ✓ ECDC
- ✓ EU countries' national governments (France, Germany…)

National scientific networks

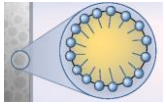
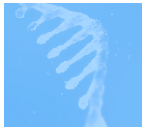
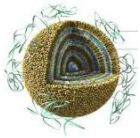


- ✓ French COREVAC
- ✓ REACTING
- ✓ INSERM

Act-Accelerator Global organizations targeting an end-to-end access solution

- ✓ Bill & Melinda Gates Foundation
- ✓ Wellcome Trust
- ✓ WHO
- ✓ CEPI
- ✓ GAVI

Summary II : Two complementary vaccine approaches with unparalleled pandemic capacity

	1 Baculovirus recombinant vaccine approach	2 mRNA vaccine approach (Translate BIO)
Platform	 Protein Antigen +  Adjuvant	 mRNA →  Lipid nanoparticle
Advantage	• Licensed recombinant platform(1) • Existing large scale capacity • BARDA collaboration • Collaboration with gsk for proven AS03 adjuvant	• Innovative approach(2) • Potential for accelerated development • Significant existing investment in mRNA capacity to be applied towards vaccine
Expected timelines	• FIH study start: Q4 2020 • Earliest approval: H2 2021	• FIH study start: Q4 2020 • Earliest approval: end of H2 2021
Capacity	• Existing capacity for 100-600 million doses • Goal to extend to >1 billion doses in 12 months(3)	• Capacity for 90-360 million doses by H1 2021 • Investigating to extend capacity significantly(3)

BARDA: Biomedical Advanced Research & Development Authority; gsk: GlaxoSmithKline; FIH: first in human

(1) Flublok® is manufactured with this platform and licensed in the U.S.

(2) In collaboration with Translate Bio

(3) Estimates pending clinical doses and industrial yields outcome

Thank You !

❖ **Interdependence : Trust based Sharing of Interests**