COVID-19 Conversations

Richard J. Hatchett

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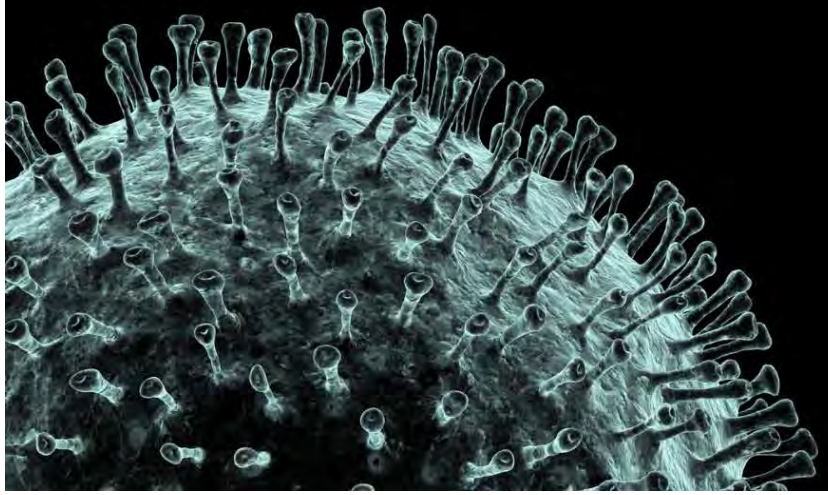

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#COVID19Conversations

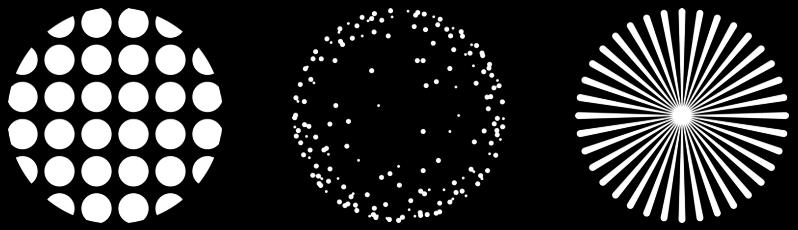
APHA
AMERICAN PUBLIC HEALTH ASSOCIATION
For science. For action. For health.

50 years NATIONAL ACADEMY of MEDICINE

The Road to Immunity During COVID-19: Developing & Distributing a Vaccine

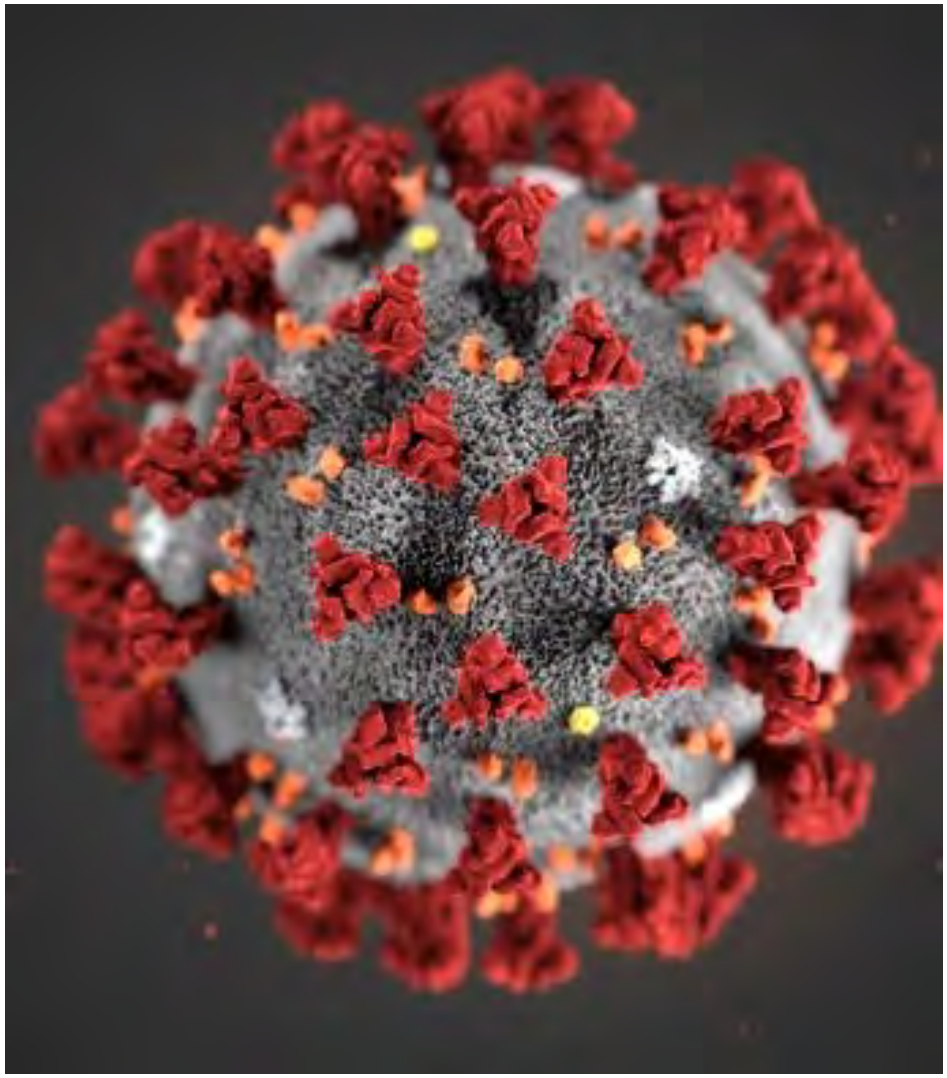
NAM-APHA COVID-19 Conversations Webinar
10 June 2020

Richard Hatchett
CEO, CEPI



Our mission

CEPI accelerates development of vaccines against emerging infectious diseases and enables equitable access to these vaccines for affected populations during outbreaks



Disease X: COVID–19

As of 9 June

7.1m **Confirmed cases**

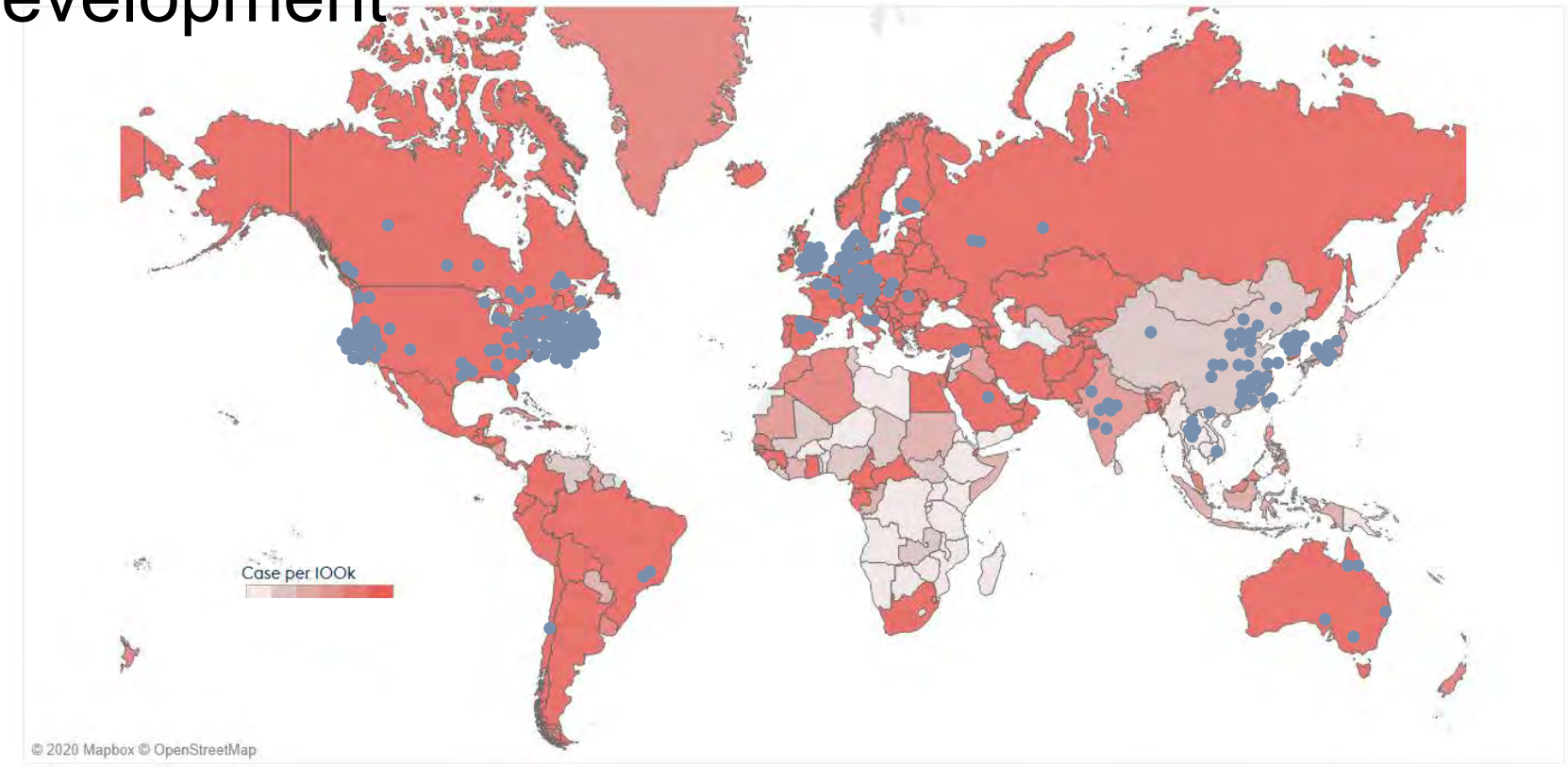
406,807 **Deaths**

188 **Countries**

The spread of COVID-19 has become a humanitarian and economic crisis, unprecedented in modern times.

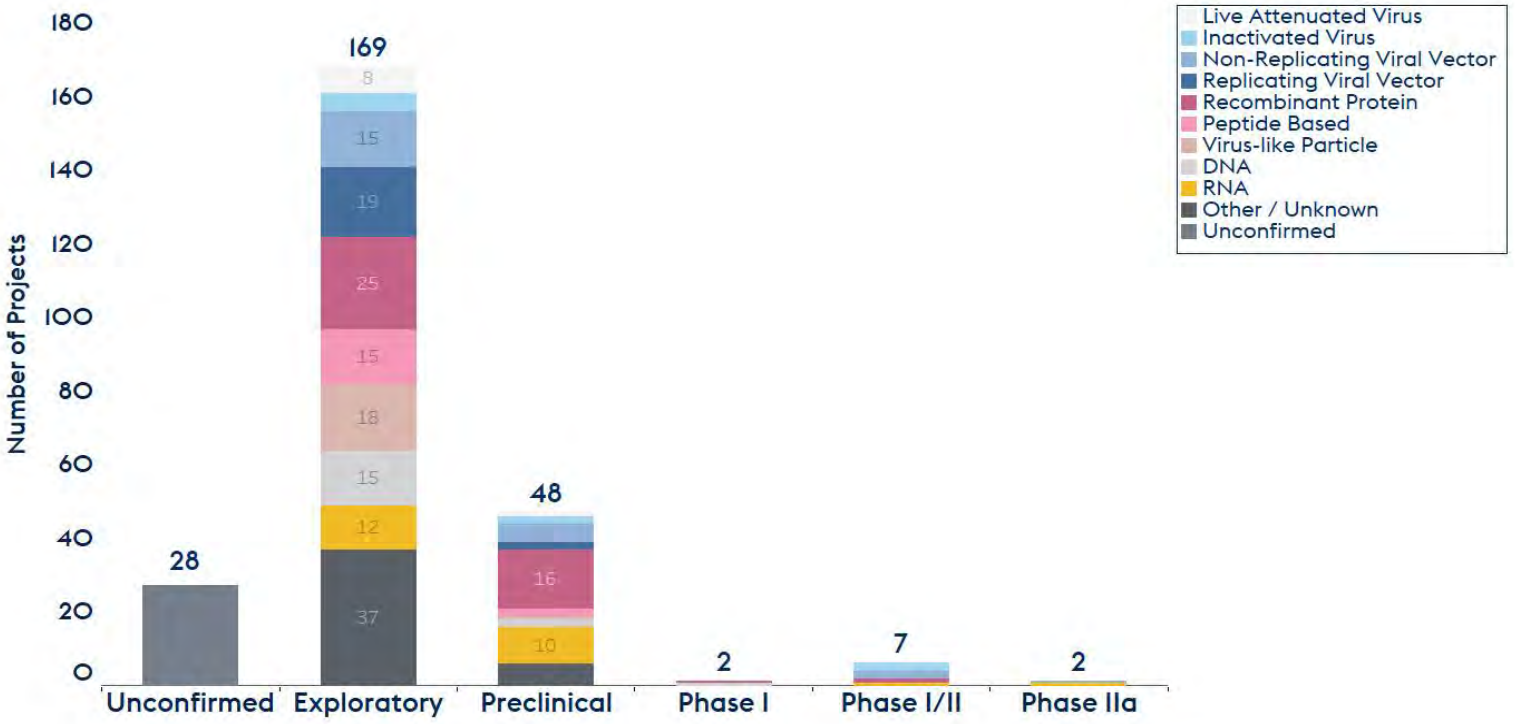
Date: 03 June 2020

Global Snapshot of COVID-19 Vaccine Development



Date: 03 June 2020

Covid-19 vaccine R&D landscape



- **Exploratory:** project has not started with in-vivo testing
- **Preclinical:** project started to test in-vivo / manufacture CTM but not yet started with testing on human
- **Phase I:** safety and immunogenicity; **Phase IIa:** Safety and efficacy and dose schedule; **Phase I/II:** combine of Phase I and IIa**. Start is defined as first subject dosed**
- **Unconfirmed:** the development status cannot be confirmed using available internal and publicly available information

Current CEPI COVID-19 vaccine portfolio consists of 9 projects

	Inovio	University of Queensland / CSL	CureVac	Moderna	Clover BioPharma	Merck / Themis	Novavax	University of Hong Kong	AZ / Univ. Oxford
Location	USA	Australia	Germany	USA	China	USA/Austria	USA	China	UK
Platform	DNA	Protein	RNA	mRNA	Protein	Viral Vector	Protein	Viral Vector	Viral Vector
Antigen / Adjuvant	Full-length S protein	Full-length S protein / MF59 or AS03 or CPG1018	Full-length S protein	Full-length S protein	Full-length S protein / AS03 or CPG1018	Full-length S protein	Full-length S protein / saponin-based Matrix-M	Receptor Binding Domain / AS03	Full-length S protein
Current phase	Phase 1	Preclinical	Preclinical	Phase I1a	Preclinical	Preclinical	Phase I	Preclinical	Phase I/II

Adjuvants

gsk

DYNAVAX

Seqirus

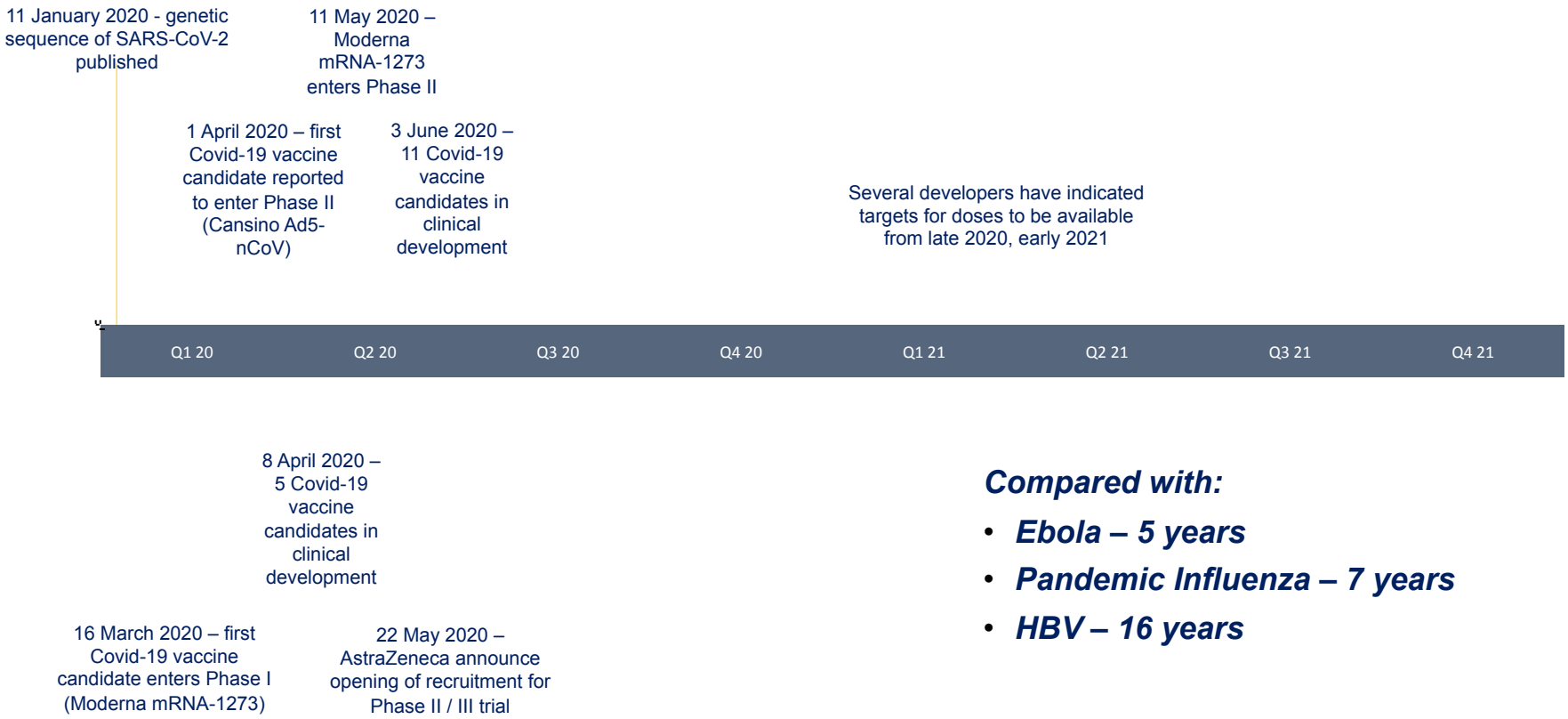
Speed **Scale** **Access**

Date: 03 June 2020

11 Covid-19 vaccine candidates in clinical trials

Candidate	Vaccine characteristics	Current stage	#Sites/Location	Lead Partner
Ad5-nCoV	Adenovirus type 5 vector that expresses S protein	Phase IIa (NCT04341389)	? sites / China	Cansino
SARS-CoV-2 inactivated	Inactivated Novel Coronavirus Pneumonia vaccine (Vero cells)	Phase I/II (ChiCTR2000031809)	? sites / China	Wuhan Institute of biological products
SARS-CoV-2 inactivated	Inactivated novel coronavirus (2019-CoV) vaccine (Vero cells)	Phase I/II (ChiCTR2000032459)	1 site / China	Beijing Institute of Biotechnology
Inactivated Virus	SARS-CoV-2 inactivated vaccine	Phase I/II (NCT04352608)	1 site / China	Sinovac Biotech
ChAdOx1 nCoV-19	ChAdOx1 vector that expresses S protein	Phase I/II (NCT04324606)	6 sites / UK	AZ / Oxford
LV-SMENP-DC	DCs modified with lentiviral vector expressing synthetic minigene based on domains of selected viral proteins; administered with antigen-specific CTLs	Phase I/II (NCT04276896)	3 sites / China	Shenzhen GIMI
mRNA-BNT162	mRNA NRM / SAM constructs with LNP	Phase I/II (NCT04368728)	1 site / Germany 7 sites / US	Pfizer; BioNTech
NVX-CoV2373	stable, prefusion protein, includes Matrix-M™ adjuvant	Phase I/II (NCT04368988)	2 sites / Australia	Novavax
Pathogen-specific aAPC	aAPCs modified with lentiviral vector expressing synthetic minigene based on domains of selected viral proteins	Phase I (NCT04299724)	1 site / China	Shenzhen GIMI
mRNA-1273	LNP-encapsulated mRNA vaccine encoding S protein	Phase IIa (NCT04283461)	10 sites / USA	Moderna Therapeutics
INO-4800	DNA plasmid encoding S protein delivered by electroporation	Phase I (NCT04336410)	2 sites / USA	Inovio Pharmaceuticals

Clinical development is proceeding at unprecedented speed

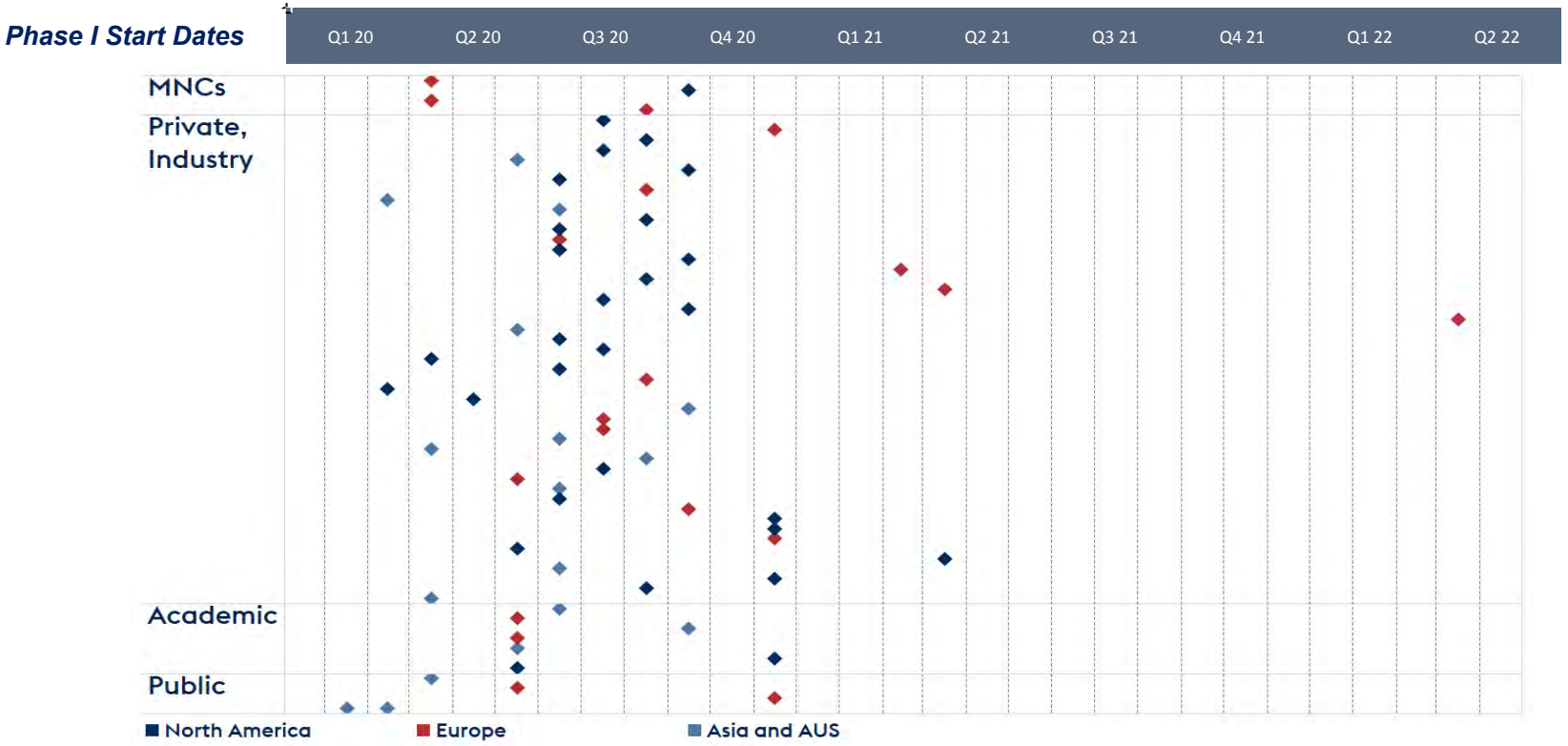


Compared with:

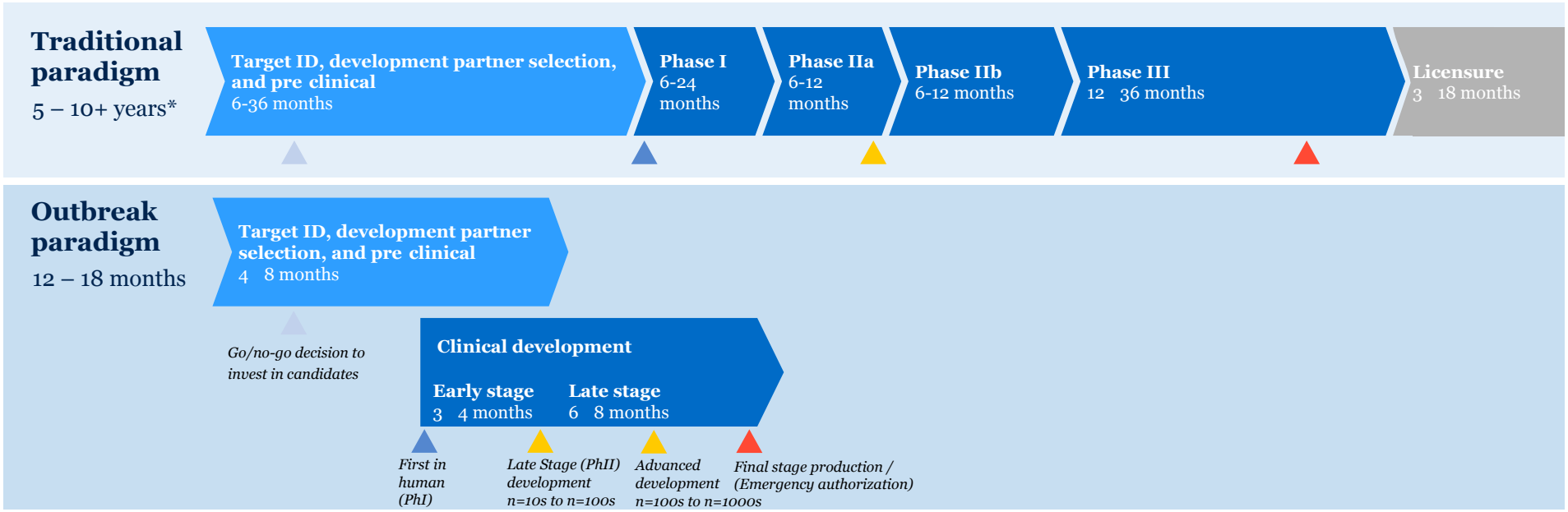
- ***Ebola – 5 years***
- ***Pandemic Influenza – 7 years***
- ***HBV – 16 years***

Date: 03 June 2020

>60 vaccines will enter clinical development by the end of 2020



Speed requires a paradigm shift



*Source: Pronker ES, Weenen TC, Commandeur H, Claassen EHJHM, Osterhaus ADME (2013) Risk in Vaccine Research and Development Quantified. PLOS ONE 8(3): e57755. https://doi.org/10.1371/journal.pone.0057755
https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0057755

COVID-19 vaccines are being developed on many platforms

Technology platform	Advantages	Disadvantages
Attenuated / inactivated	Relative ease of development; if replicating, may lead to longer lasting response	If non-replicating, requires more frequent boost than live vaccine; generally requires BSL3 / BSL4 manufacturing capability
Viral vector	High antibody and T-cell response; ability to select optimal antigen; possible for single-dose protection; replicating virus can use a lower dose; higher productivity in manufacturing; reproducible for different pathogens	Relatively long development time to make master virus/release production starting materials; may not be appropriate for immune-compromised patients; may elicit immune response against vector rather than antigen; stability may require low temperature storage or lyophilization
Recombinant protein / subunit	Ability to select optimal antigen; existing manufacturing capacity / productive platforms / many licensed products with the technology; allows for relatively easy dose optimization	Generally require adjuvant; often process development needed for new targets (platforms that don't change are being developed)
Virus-like particles	Safe; ability to select optimal antigen; can display antigens from multiple strains; more immunogenic than soluble protein	Likely to require adjuvant
DNA	Scalable manufacturing process for bulk drug; fast response time to new disease target; flexible for a variety of disease targets (bacterial, viral)	Requires a device that is currently limited in supply and high in cost for LMIC
RNA	Potential fast response to new disease target; flexible for a variety of disease targets (bacterial, viral);	Delivery requires specialist delivery systems (e.g. LNPs); new technology, so capacity needs to be created (limited existing production capabilities); stability may require low temperature storage or lyophilisation

Concluding thoughts and open questions

- There is no scenario in which vaccines will not be in short supply in 2021
    - The careful management of COVID-19 vaccines as a scarce resource will be essential if we are to end the acute phase of the pandemic and achieve equitable access.
- Many of the Covid-19 vaccine development approaches are high-risk
- Many questions are likely to remain and require longer term follow up, e.g.:
    - Long-term effectiveness / durability of response
    - Long-term safety follow-up
    - Potential for differential responses due to population heterogeneity
    - Breadth of protection against virus mutation or genetic drift / shift
- The first vaccines to market may not be optimal and it will be important to maintain a comprehensive strategic approach for the long term – built on an evolving understanding of disease epidemiology and vaccine effectiveness