Twitter Thread by rubic3n

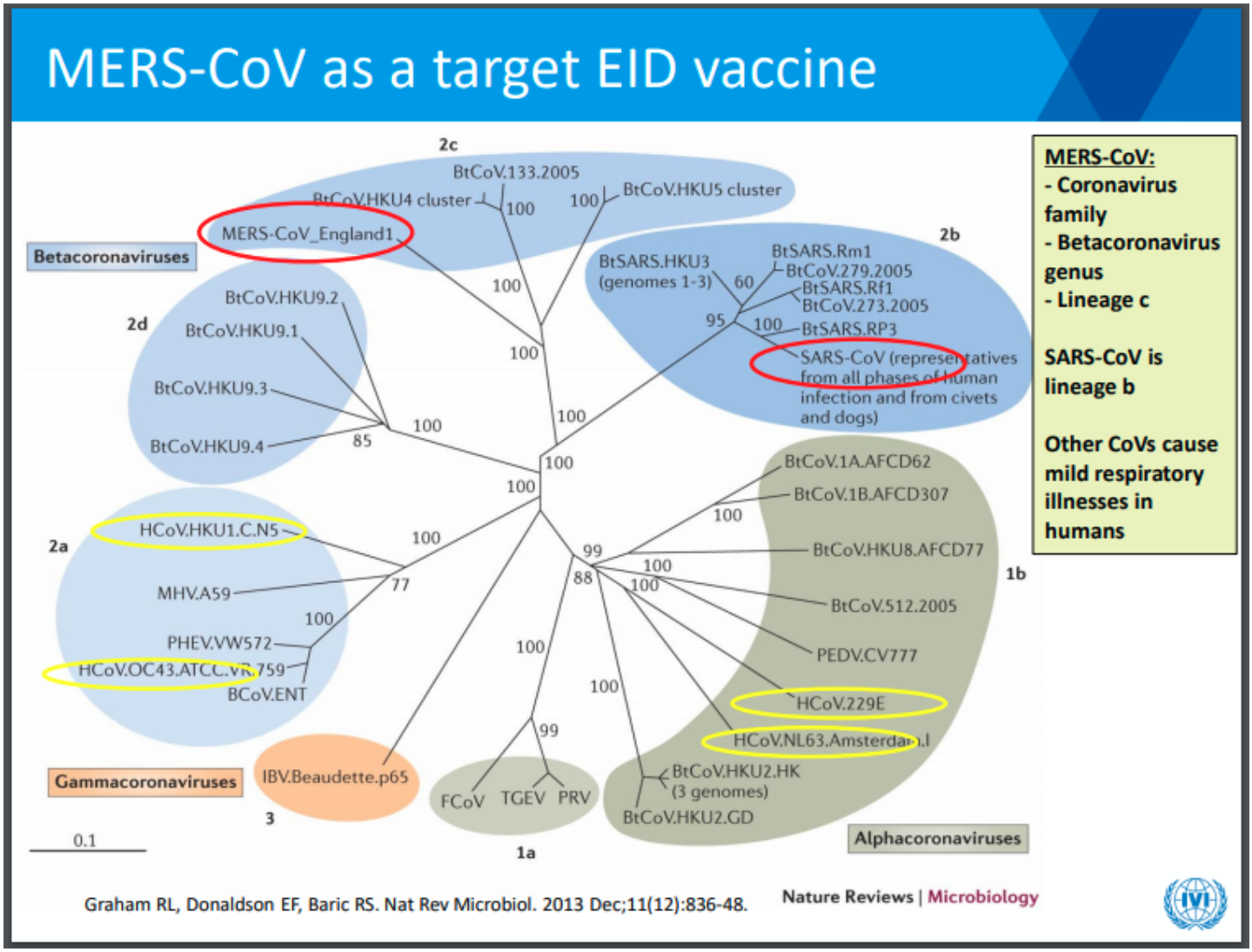


rubic3n
@rubic3n

Fondation Merieux
2017
Pushing the
CEPI Dialogue

Excellent presentation to see, how they, including Bancel, had layed out the narrative.
Quess, what they had specifically included in their list of targeted viruses?

https://t.co/J5FDe6W986

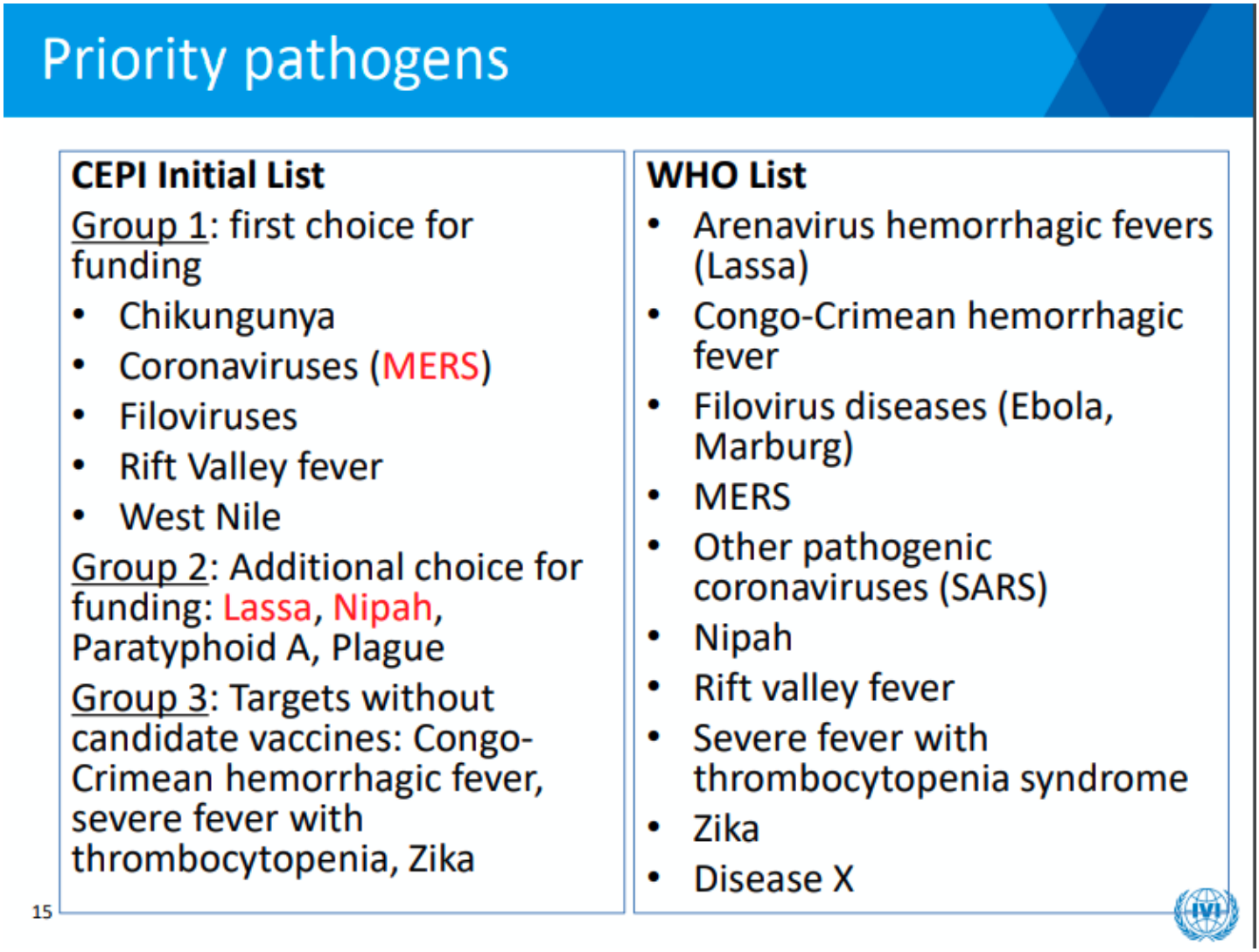


Fondation Merieux 2017

CEPI

Almost basking about their list being more inclusive, more emergent viruses based.

https://t.co/J5FDe6W986



Fondation Merieux 2017
Narrative: "Look, what ZIKA has done to your populace. Nasty ZIKA."

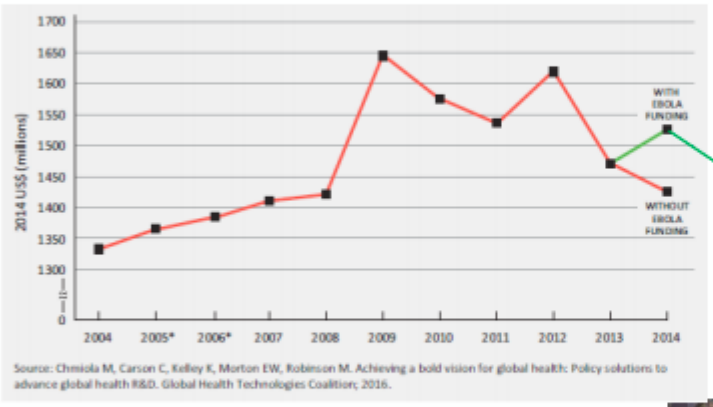
How much of that ZIKA damage was actually related to a virus? Was there a computer guy, who had invested in mosquitos as a vector?

https://t.co/J5FDe6W986

Incentivizing vaccines for EIDs

Millions in Ebola funding, a casualty of Zika virus, may not be replenished

By DYLAN SCOTT / JUNE 1, 2016



Source: Chmiola M, Carson C, Kelley K, Morton EW, Robinson M. Achieving a bold vision for global health: Policy solutions to advance global health R&D. Global Health Technologies Coalition; 2016.



Funding for neglected "tropical" diseases with and without Ebola, GHTC 2016



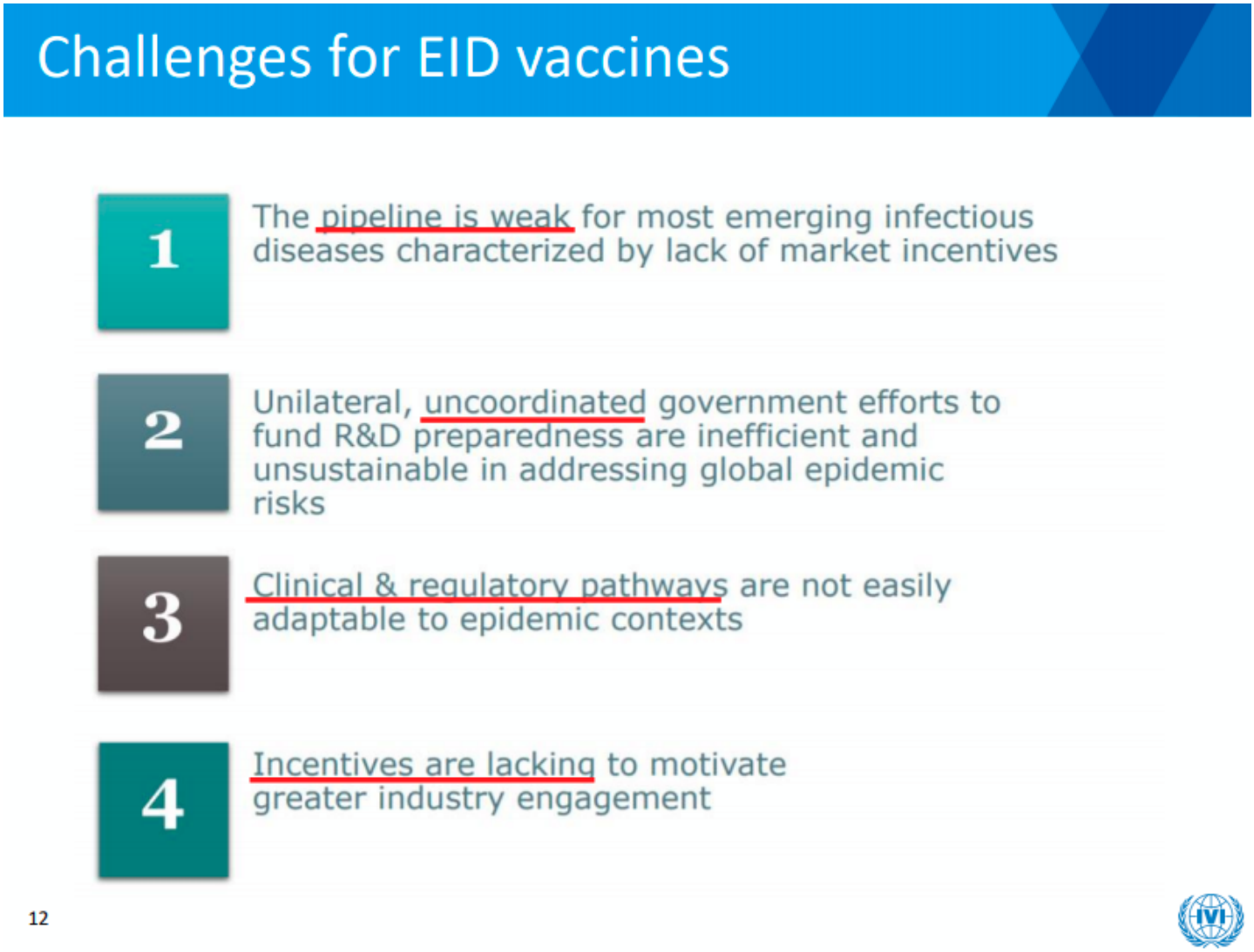
10

Fondation Merieux 2017
What is the advanges of a programme like CEPI.

And for who?

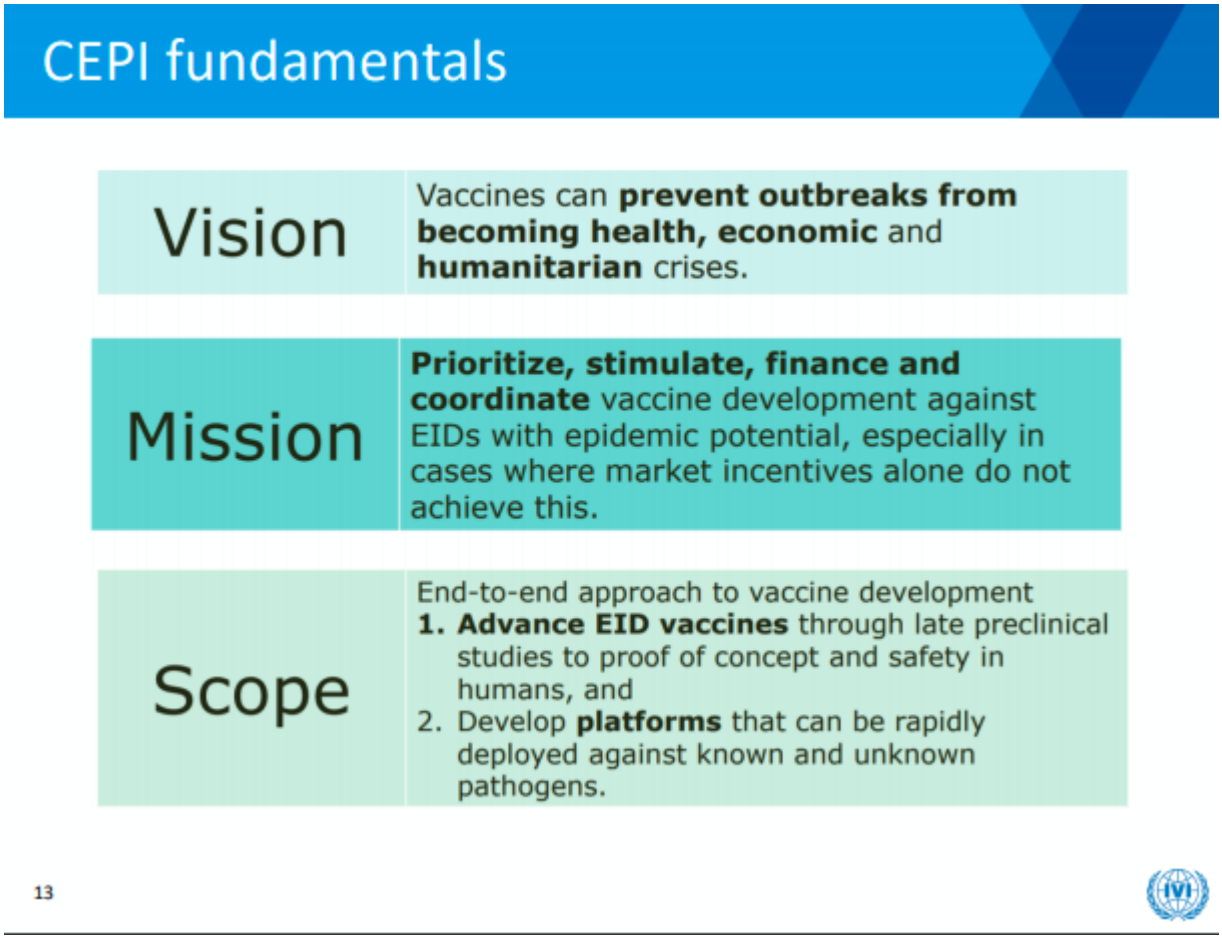
Let me translate: They want a coordinated vaccine production, with only one strong production pipeline, and solidly regulated pathsways.
Provide the incentives for big pharma.

They've made it.



Vision - look at nasty ZIKA, you surely do not want that
Mission - get the pipeline going of (only) the big ones
Scope - the anti-cancer platforms with their DNA, mRNA basis fit perfectly. They so far do not sell very well, but they could be recycled.

Correct me, if I am wrong.



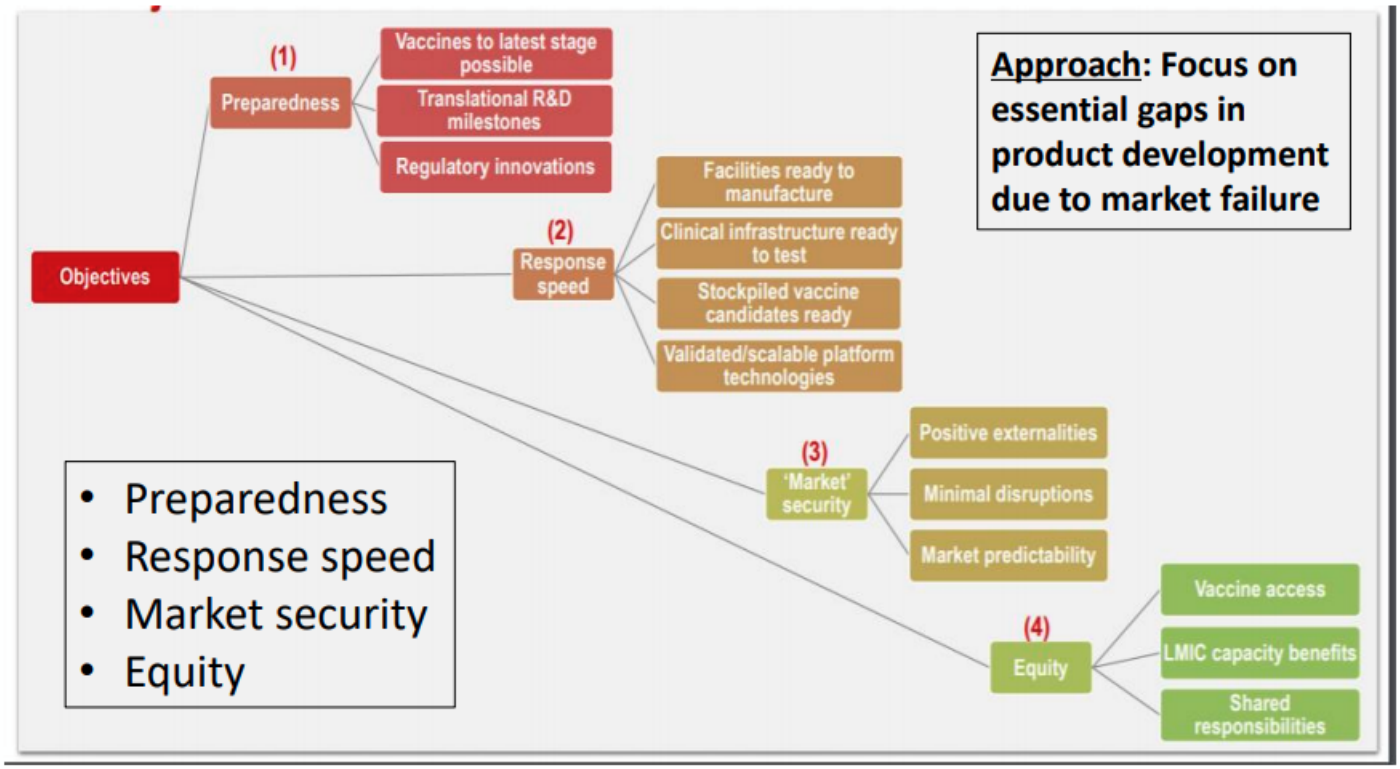
How to create your own market and exclude competitors right from the start.

Start even before the 'incident' - which will give you more advantage of your competitors.

'Booster' it. ZIKA, MERS?

Get people used to the forced vaccine narrative with measles?

Correct me,if I am wrong

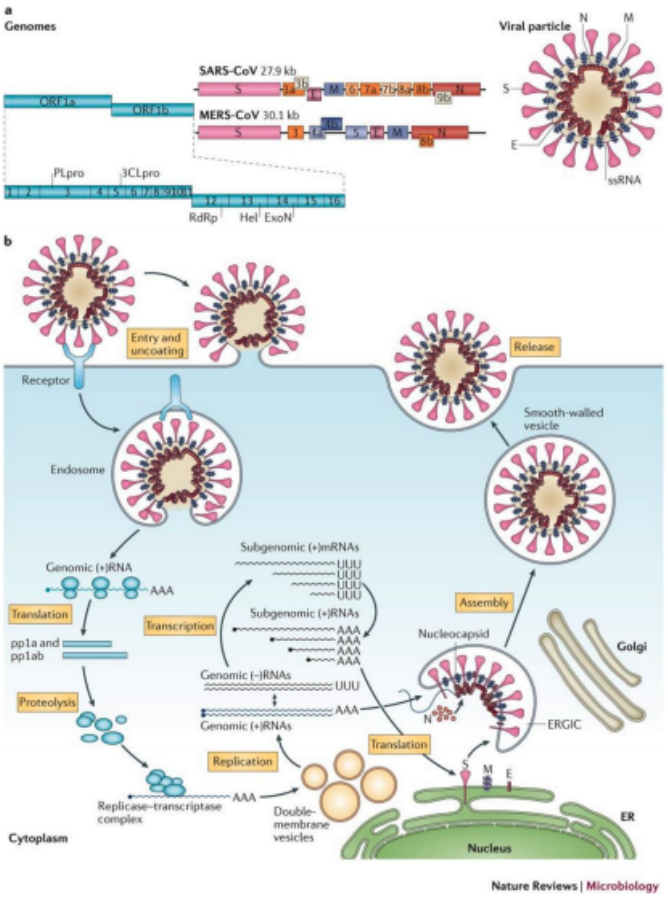


Fondation Merieux 2017
CEPI narrative presentation

They show a remarkable interest in MERS

A 'pipeline booster'?

MERS-CoV background



- 30 kb enveloped, single-stranded, positive-sense RNA virus
- 4 structural proteins: spike (S), envelope(E) matrix (M), nucleocapsid (N)
- S protein is primary target for neutralizing Abs during natural MERS-CoV infection
- S1 subunit contains **receptor-binding domain (RBD)**
- Host cell receptor for RBD is **dipeptidyl peptidase 4 (DPP4 or CD26)**

de Wit E et al. Nat Rev Microbiol. 2016 Aug;14(8):523-34.

MERS in Korea

Why not try it out and create some interesting PR pictures at the same time?

https://t.co/hrCU2xVi3U

MERS in Korea





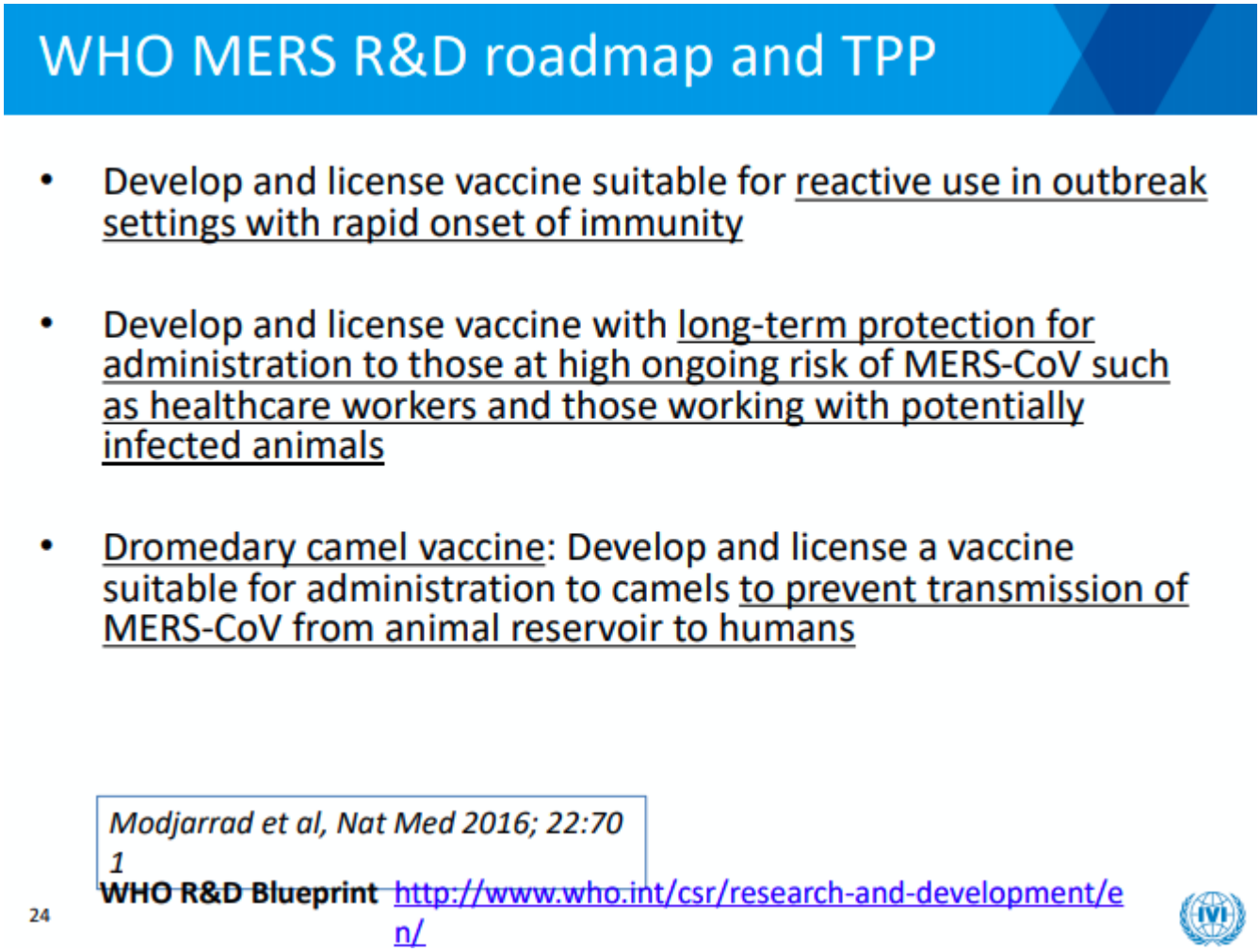


- About 17,000 people quarantined
- Massive disruption
- Huge economic impact

Fondation Merieux 2017
CEPI sales presentation

They were envisaging 3 different vaccines:
- quick response but not long lasting immunity
- long lasting immunity vaccines for specific groups of people
- vaccinating animals because of the animal reservoir.

ALL the markets



Nicola Bidoli, let us just pretend, you were still around here.

MERS Vx trial run?

Can you spot Baculovirus, production in mice, sf9, VLP, full length S trimers here.
We can already spot Novavax here, doing a trial run.

I am sure, you would spot more.

https://t.co/J5FDe6W986

MERS-CoV vaccine pipeline (1)

Vaccine type	Vaccine name	Design	Animal immunogenicity	Animal protection	Stage of development	Sponsor/ Developer
DNA	GLS-5300	Plasmid DNA encoding full-length S; with electroporation	C57BL/6 mice, rhesus, camels	Rhesus	Phase I ongoing in the US	GeneOne/Inovio
Protein subunit	MERS-S	Nanoparticles of full-length S trimers; with Matrix-M adjuvant	BALB/c mice	Transduced mice	Preclinical; SAB-301 polyclonal Abs from transgenic cows in Phase I	Novavax
	MERS-CoV VLP	VLP of S, E, M in baculovirus/Sf9; with alum	Rhesus	-	Preclinical	Jiangsu Center, China
	S-RBD-Fc	S1-RBD subunit fused with human Fc; with various adjuvants	BALB/c mice, rabbits	Transduced mice	Preclinical	New York Blood Center; Fudan Univ; Central South Univ
	MERS-CoV rRBD	Truncated S1-RBD subunit; with alum	BALB/c mice, rhesus	Rhesus	Preclinical	China CDC
Heterologous prime-boost	S-DNA/S1 Protein	Plasmid DNA encoding full-length S (prime) + S1	BALB/c mice, rhesus	Rhesus	Preclinical	US NIH/VRC

MERS Vx trial run

More good old known here
Nice sandbox toy area. Look who is all at play.
German PEI in it as well with a Measles Vector.
Drosten with a DZIF minimal vector approach.
And also some recombinant.

The REAL GERM GAMES
Sandbox. Give it a try.

MERS-CoV vaccine pipeline (2)

Vaccine type	Vaccine name	Design	Animal immunogenicity	Animal protection	Stage of development	Sponsor/ Developer
Vector	MVA-S	MVA vector with full-length S	BALB/c mice, camels	Transduced mice, camels	Preclinical; Phase I planned in Germany	DZIF consortium
	ChAdOx1-MERS-S	Chimp adenovirus 3 with full-length S	Mice	Mice	Preclinical; Phase I planned in UK	Jenner Institute, UK
	MERS-S/MERS-solS	Measles vector with full-length S/solS	IFNAR -/- mice	Transduced mice	Preclinical	Paul Ehrlich Insitut; German Cent for Inf Res
	Ad5-S & Ad41-S	Human adenovirus vector with full-length S	BALB/c mice	-	Preclinical	China CDC
	GreMERSfi	Human adenovirus 5 vector with full-length S	Mice	-	Preclinical	Greffex
Live recombinant	rMERS-CoV-ΔE	Recombinant without E	-	-	Preclinical	Universidad Autonoma de Madrid

Oh, and look

GeneOne Inovio is on board as well sailing the sandbox of a fading vx platform booster outbreak.

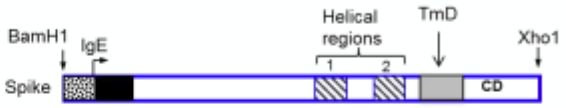
GeneOne/Inovio DNA vaccine

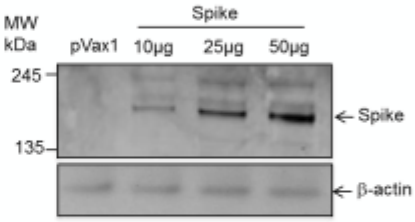
Most advanced candidate in development

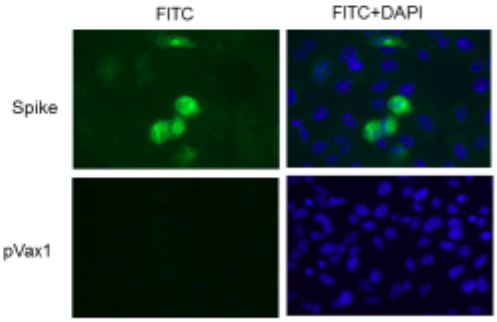
pVax1 plasmid DNA coding full-length S glycoprotein using consensus sequence

Given with electroporation









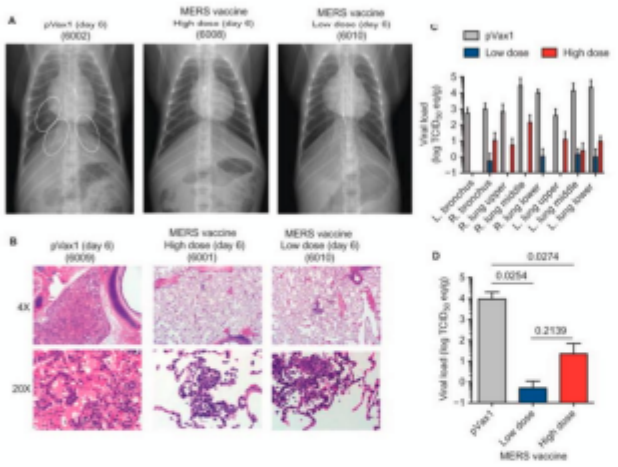
27

They knew what to look for - what makes a good immune response for a vaccine:
Antibodies and

Induction of strong T-cell immune responses
• Antigen specific CD4+ and CD8+
• Multiple epitopes recognized across length of S protein

Have they forgotten about cellular response now?

Rhesus immunogenicity and protection



- 12 rhesus macaques at control, low and high dose at 0, 3, 6 wks
- Challenged at 11 wks (4 wks after 3rd dose)
- Full protection by radiography

- Binding & neutralizing antibodies
  - *Seroconversion and induction of strong MERS-CoV Spike specific bAb responses after single immunization*
  - *bAb titers: 10^4 - 10^5*
  - *nAb titers: 1:80-240 post dose 3*
- Cellular immune responses
  - *Induction of strong T-cell immune responses*
  - *Antigen specific CD4+ and CD8+*
  - *Multiple epitopes recognized across length of S protein*

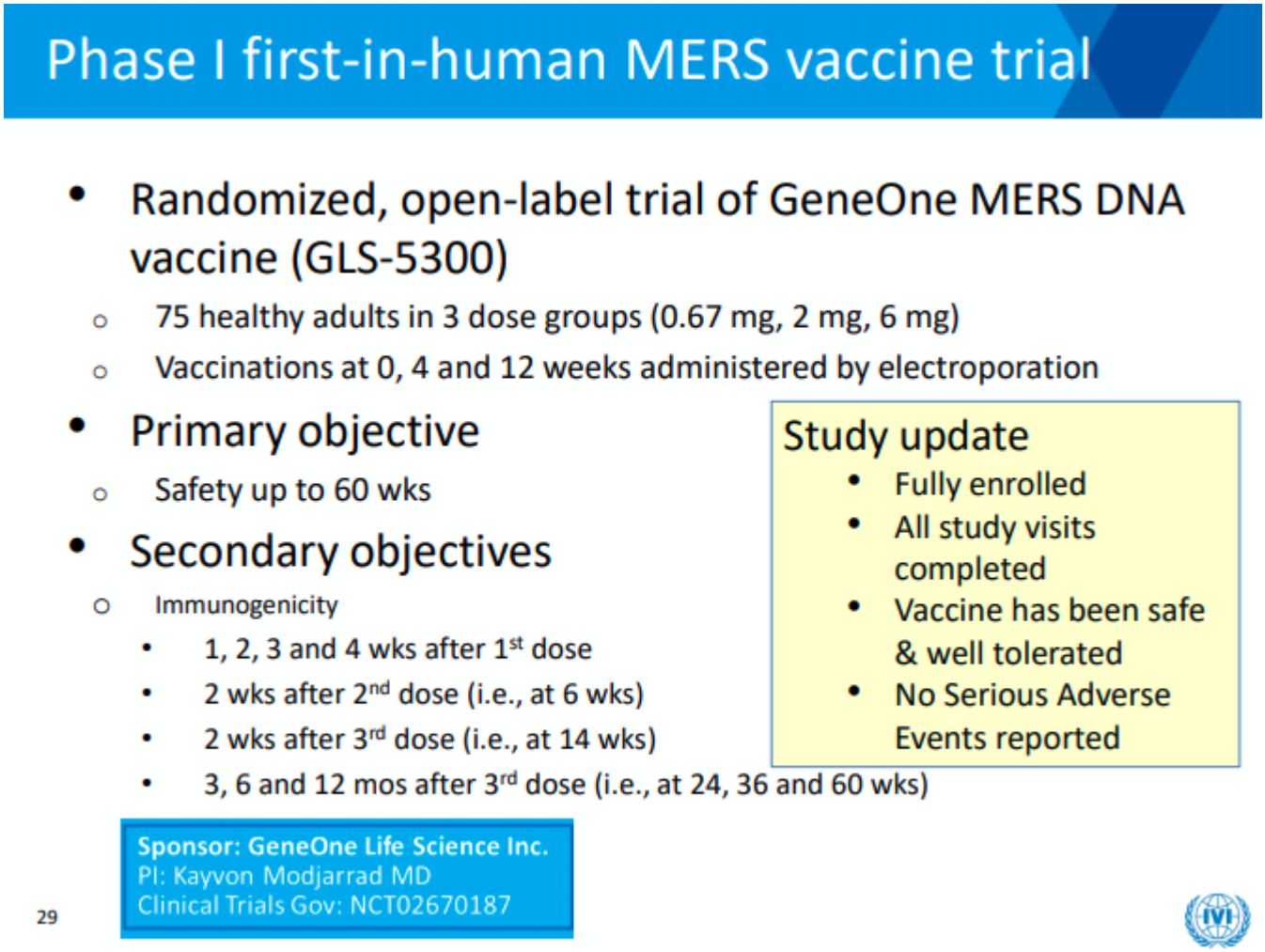
Muthumani K et al. Sci Transl Med. 2015 Aug 19;7(301):301ra132.

Human Trial MERS vax sandbox arena

They were even then working on a multi jab approach. Here they were looking at three jabs.

Dose 1: week 1
Dose 2: week 5
Dose 3: week 14

1 month, 3 months
75 people

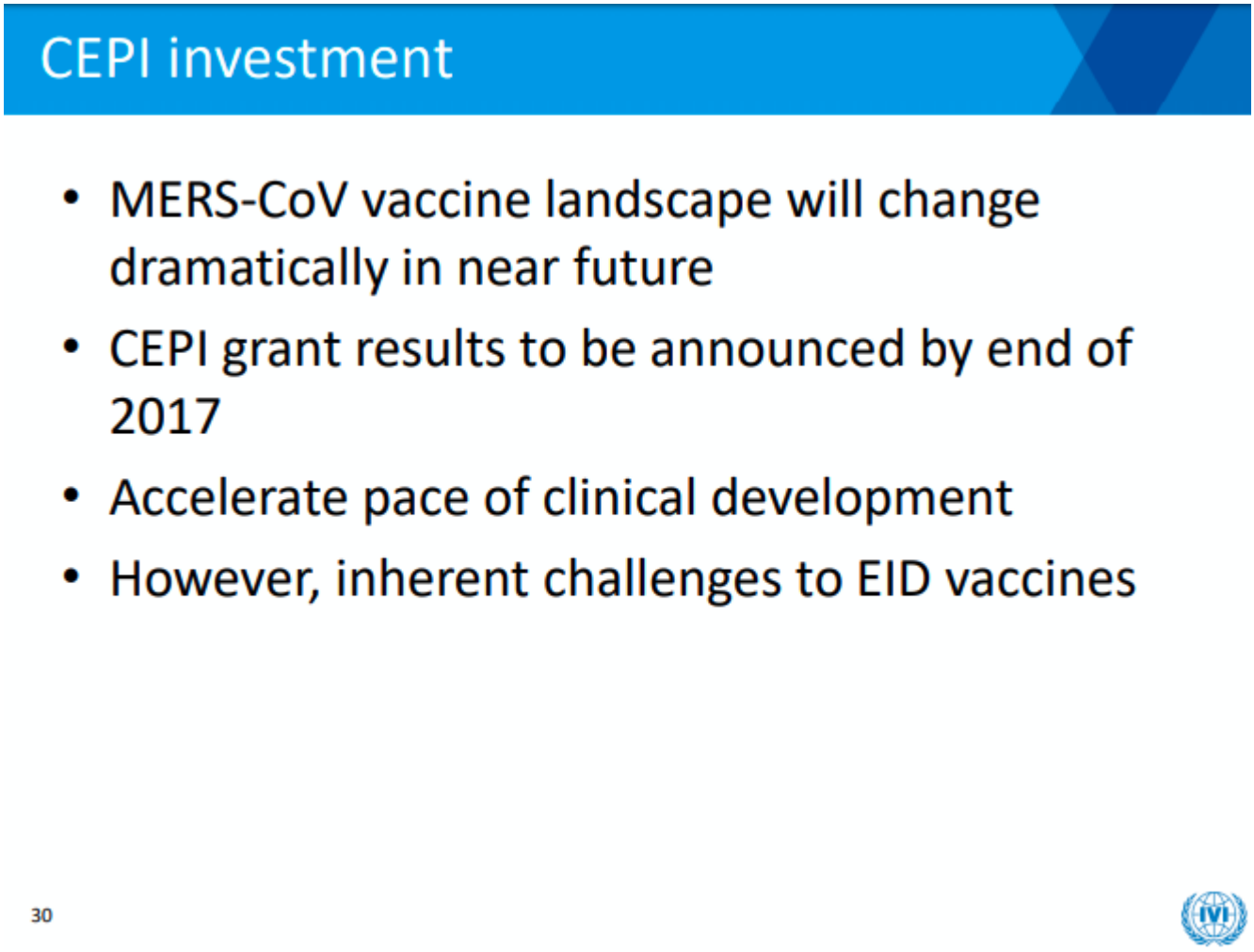


Fondation Merieux

"MERS-CoV vaccine landscape will change
dramatically in near future"

Yes, mRNA was in the pipeline. Still restricted by the toxicity of the LNP (Moderna first major pipeline). Bancel moved on to Moderna.

https://t.co/hsnNHePvRw



Up until very recently the LNP formulation had many problems, causing increasingly allergic reactions in test subjects with each dose. This was solved with their new PEG LNP formula, apparently.

Moderna co founder in a 2016 paper: pic.twitter.com/IxcEZgKH2n

— realism fan \u73b0\u5b9e\u4e3b\u4e49\u7231\u597d\u8005 (@realism_fan) October 7, 2021

Giuseppe Ciaramella | Chief Scientific Officer
Valera - fully owned by Moderna
Has certainly brought the LNP development further

https://t.co/usCgynv5wU

Complete history of Giuseppe Ciaramella stock trades at Beam Therapeutics

Date	Company	Insider	Transaction	Shares	Price per share	Total value	Shares after	Source
29 Dec 2021	BEAM	Giuseppe Ciaramella President and CSO	Option	39,700	$0.67	$26,599	102,473	
22 Dec 2021	BEAM	Giuseppe Ciaramella President and CSO	Option	2,607	$7.22	$18,823	65,380	
20 Dec 2021	BEAM	Giuseppe Ciaramella President and CSO	Option	29,393	$7.22	$212,217	87,877	
17 Sep 2021	BEAM	Giuseppe Ciaramella President and CSO	Option	18,012	$0.67	$12,068	62,773	
28 Jun 2021	BEAM	Giuseppe Ciaramella President and CSO	Option	78,580	$17.00	$1,335,860	123,341	
5 Mar 2021	BEAM	Giuseppe Ciaramella President and CSO	Option	4,030	$0.67	$2,700	19,761	
30 Dec 2020	BEAM	Giuseppe Ciaramella President and CSO	Option	55,842	$0.95	$53,050	15,731	
30 Sep 2020	BEAM	Giuseppe Ciaramella President and CSO	Option	3,731	$0.67	$2,500	3,731	

A sight aside on
MODERNA LNP and the 'competitive landscape of mRNA vaccines'
Patents 069 435
#Patents #435 & #069

https://t.co/iAka69L1RO

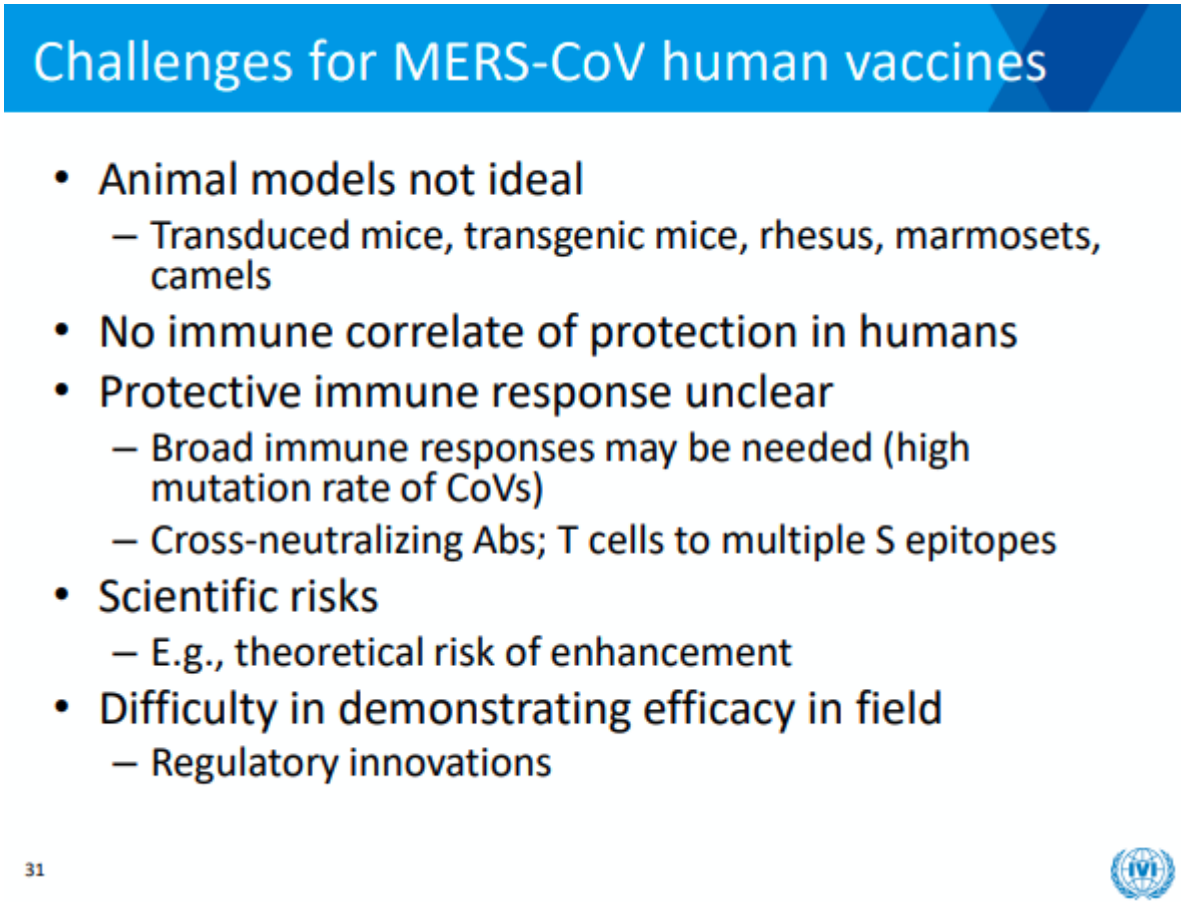
A sight aside on
MODERNA LNP and the 'competitive landscape of mRNA vaccines'
Part II
Patents 069 435
#Patents #435 & #069
https://t.co/68QlxcsbjH

Another just aside

MODERNA patents
Patents 069 435
#Patents #435 & #069
Lawyers
https://t.co/sLMtQwd0i8
https://t.co/8dCSyAKJgd
Property Dispute
https://t.co/saorrrZ8E1
Arbutus '19 article
https://t.co/d1B0IbdWBm
Arbutus '20 article
https://t.co/qbWjWBXY1l

Back to the sandbox MERS approach
They knew what they let themselves in for in 2017

Not so long ago. Has really that much changed since then - or, is there a lot of hot needle knitting involved?
https://t.co/J5FDe6W986



Merieux and the IVI vaccine institute

IVI is an International Organization dedicated to Global Health



Global Vaccine Research Institute

- **HQ and labs at Seoul National University**
- **Field programs in 29 countries: Asia, Africa, Latin America**
- **12 nationalities in workforce of ~130**

OECD-recognized International Organization (not for profit)

- **UNDP initiative**
- **First international organization in Korea (1997)**
- **35 countries and WHO as state parties**

