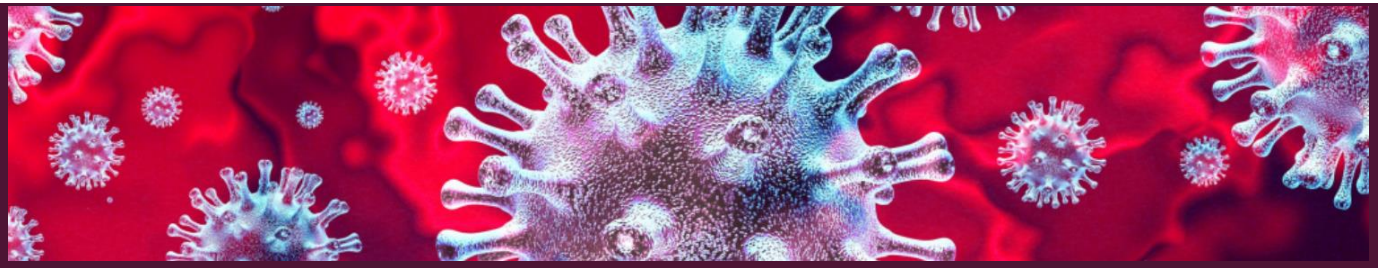
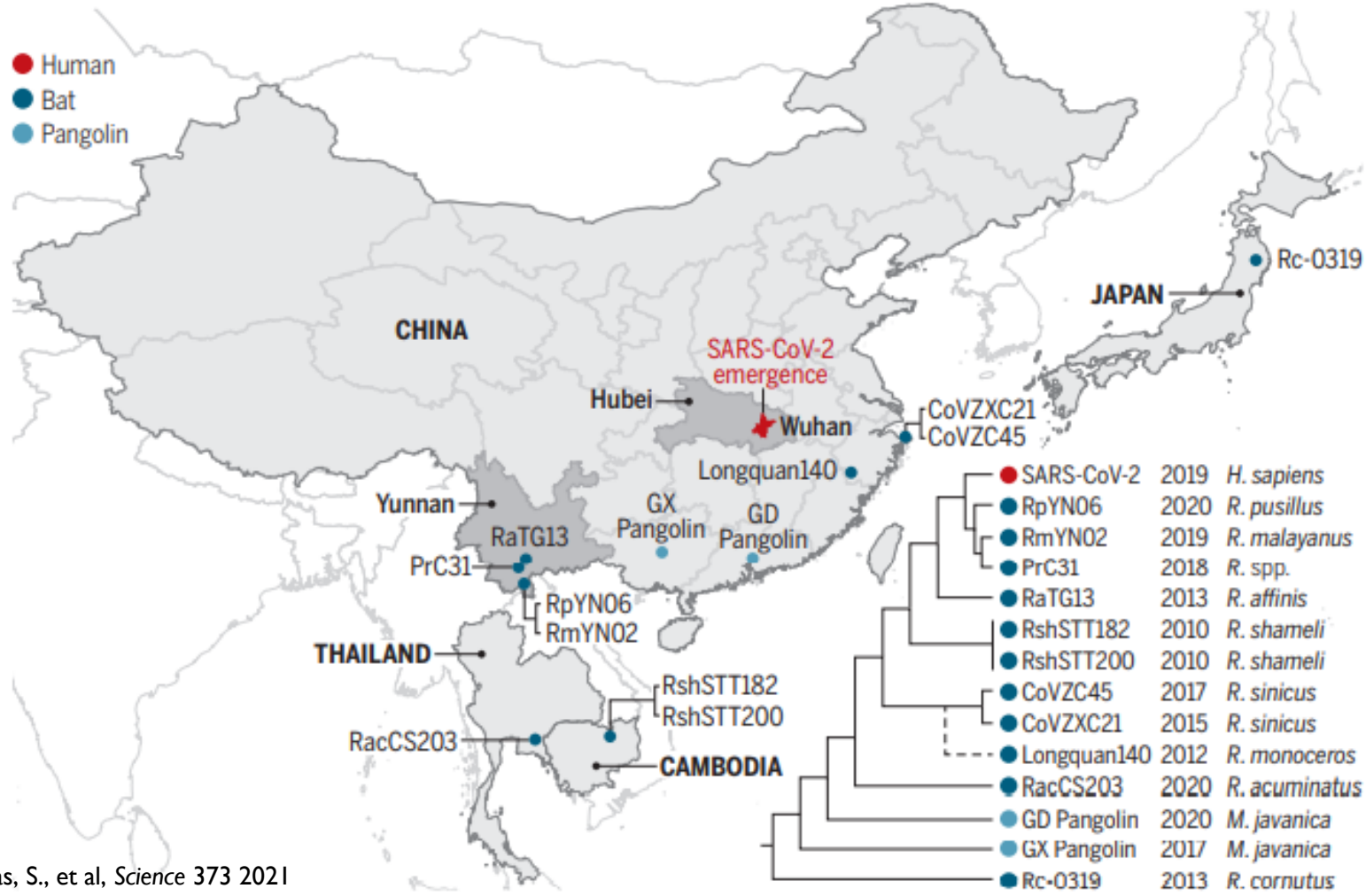


We Need a PAN-SARBECOVIRUS Vaccine

by Stanley A. Plotkin
University of Pennsylvania

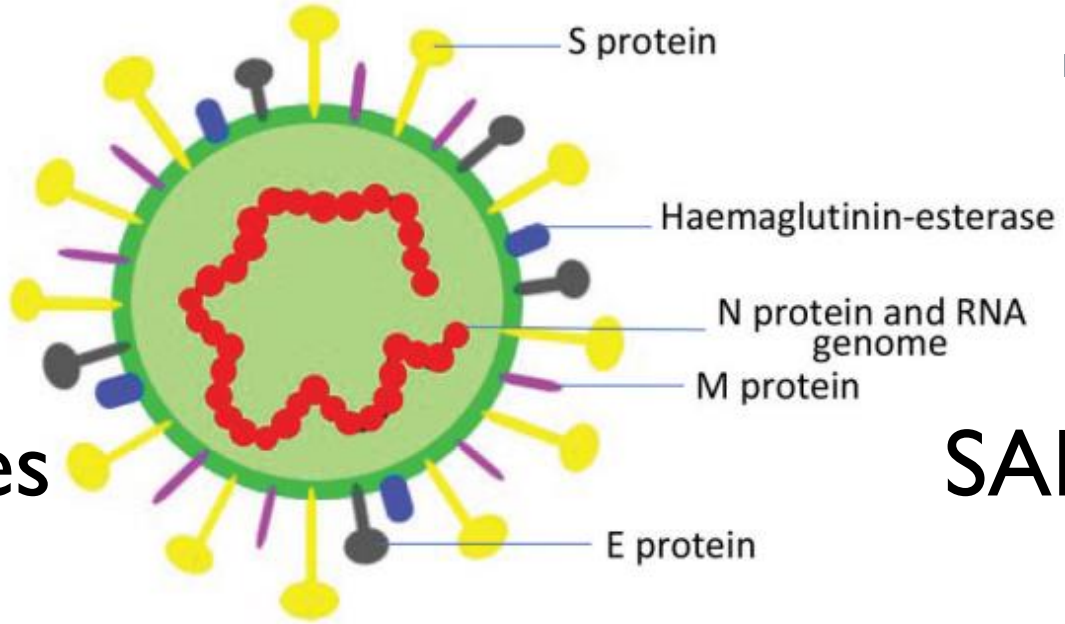
Sarbecoviruses closely related to SARS-CoV-2

Coronaviruses that are evolutionarily closest to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have been sampled in China, Cambodia, Japan, and Thailand (*5*). The phylogenetic tree, inferred from a genomic region minimized for recombination (*5*), shows sarbecoviruses closely related to SARS-CoV-2. Host species for each virus, horseshoe bat (*Rhinolophus*), human (*Homo sapiens*), and pangolin (*Manis javanica*) and the year of sample collection are shown in the key. Longquan140 is inferred from another genomic region (*5*) (dashed line). See supplementary table S1 for more details.



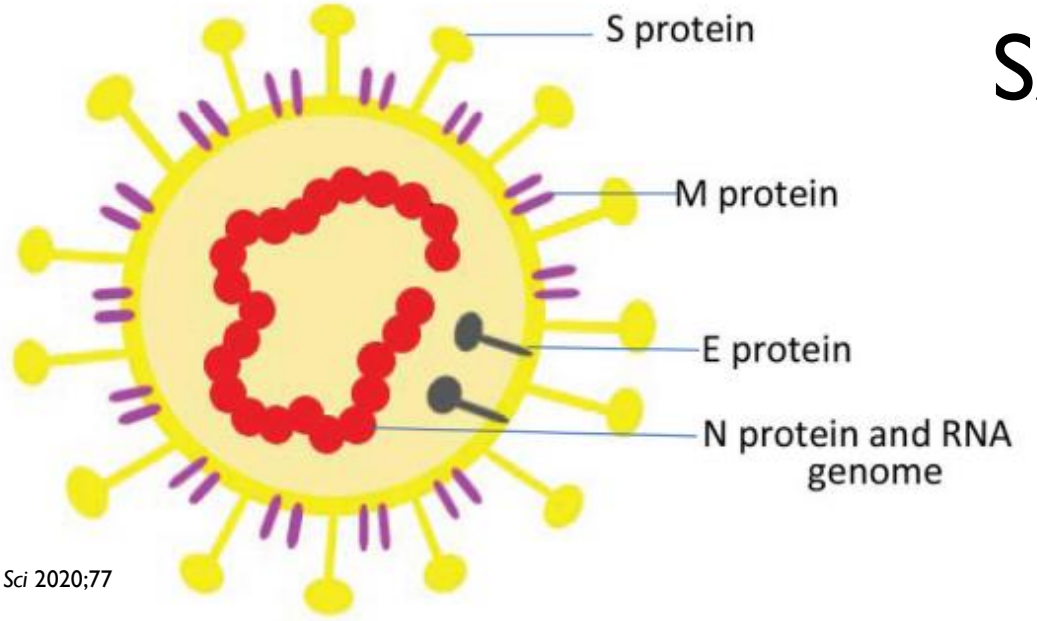
Lytras, S., et al, *Science* 373 2021

Structures of Coronaviruses



SARS-2

(A)



SARS-1

Salvamani, S., et al, *Brit Jour of Bio Medi Sci* 2020;77

Classification of circulating genetic variants of SARS-CoV-2

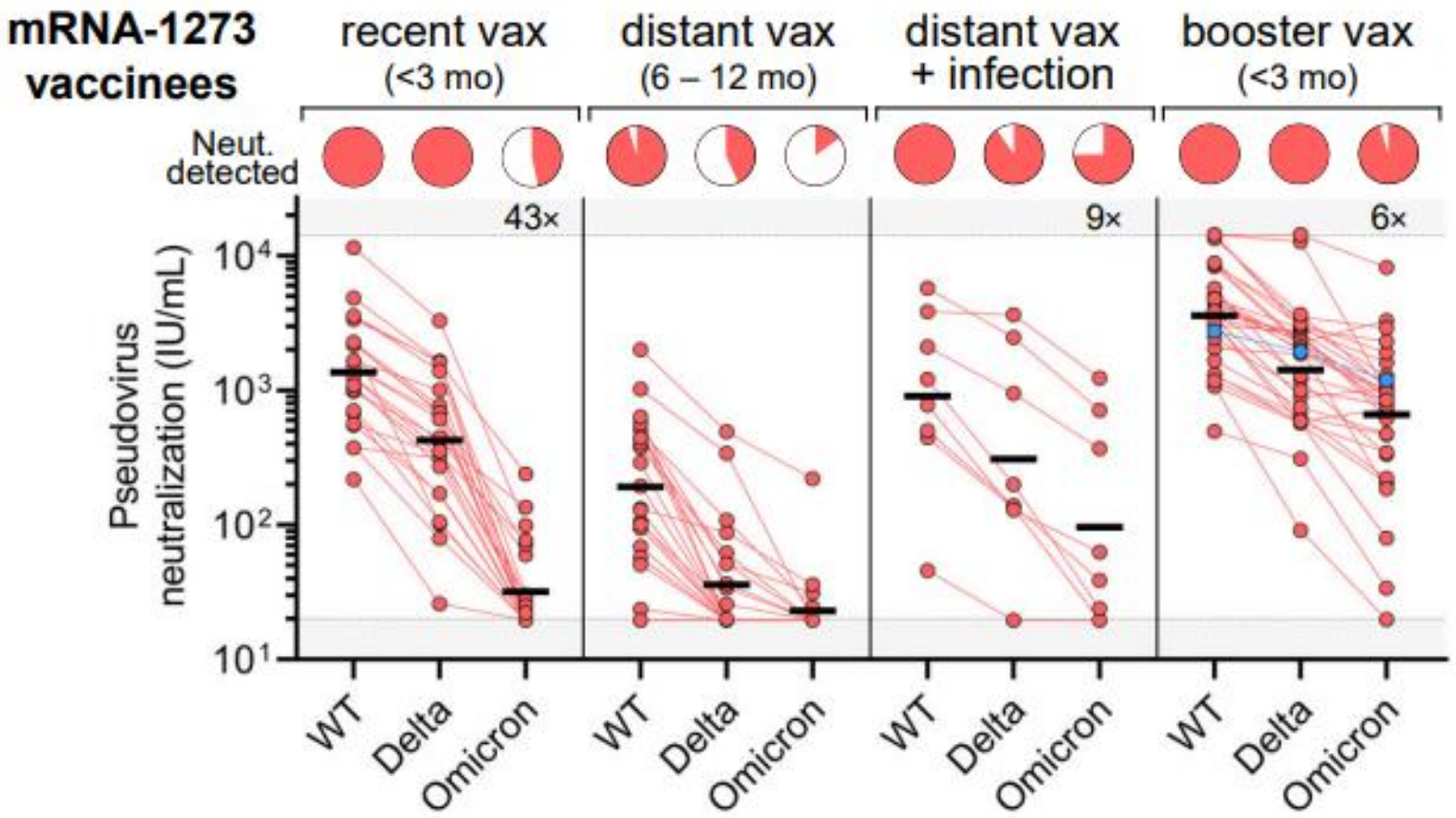
Lineage	Label	First detected in	Earliest samples
B.1.1.7	Alpha	United Kingdom	September 2020
B.1.1.7 + E484K	Alpha	United Kingdom	February 2021
B.1.351	Beta	South Africa	May 2020
B.1.1.28.1 (P.1)	Gamma	Brazil	November 2020
B.1.1.28.2 (P.2)	Zeta	Brazil	April 2020
B.1.1.28.3 (P.3)	Theta	Philippines	January 2021
B.1.617.1	Kappa	India	October 2020
B.1.617.2	Delta	India	October 2020
B.1.617.3		India	October 2020
B.1.427/B.1.429	Epsilon	USA	March 2020
B.1.525	Eta	Nigeria	December 2020
B.1.526	Iota	USA	November 2020
B.1.620		Lithuania	February 2021
B.1.621		Colombia	January 2021
B.1.1.318		United Kingdom	February 2021
A.23.1 + E484K		United Kingdom	February 2021
AV.1		United Kingdom	May 2021
C.36.3		Thailand/Egypt	May 2021
C.37	Lambda	Peru	December 2020

Trimpert et al., *Sci. Adv.* 7 2021

Currently designated variants of concern (VOCs)

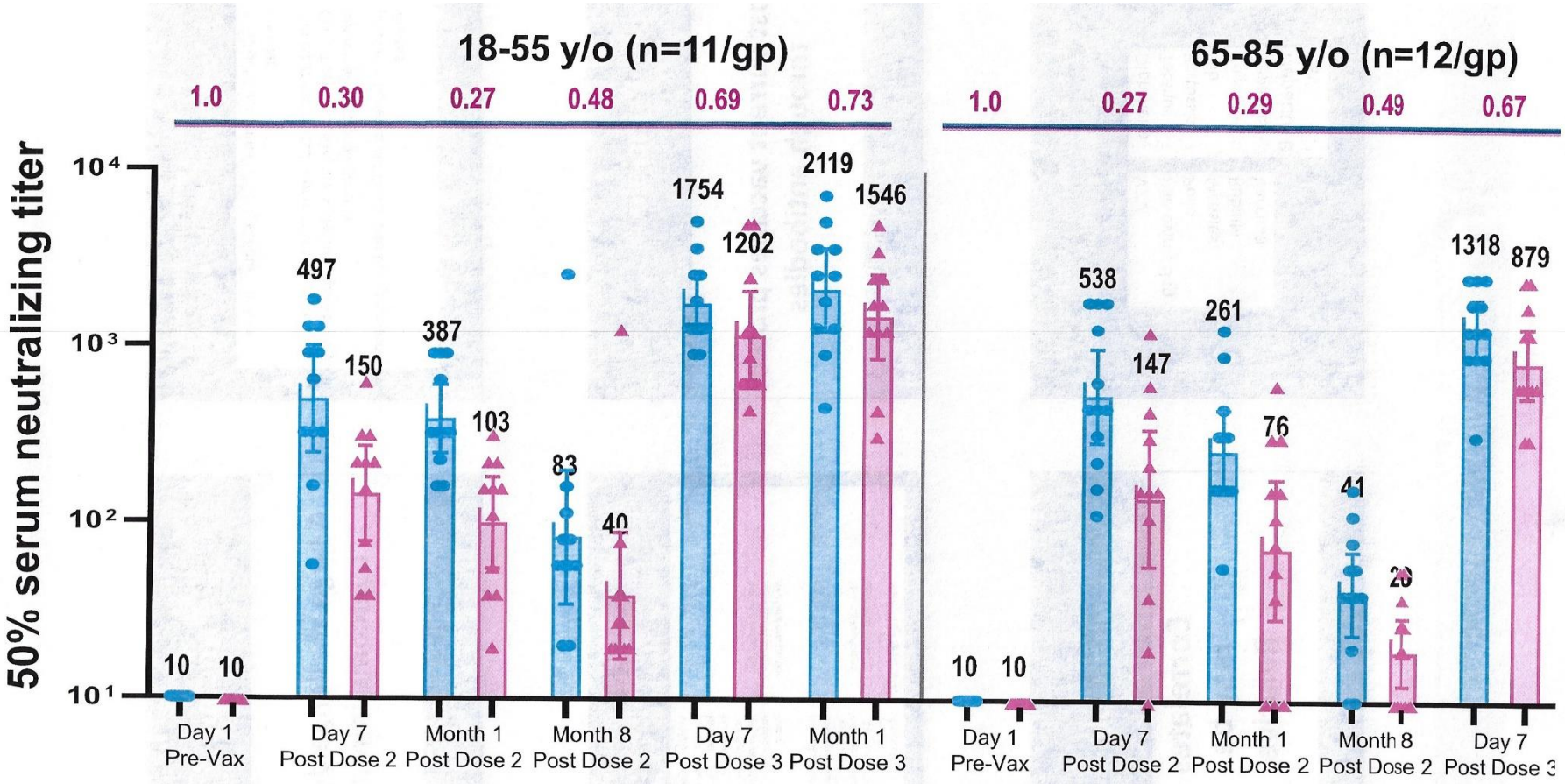
WHO Label	Pango Lineage	Earliest Documented Samples
Alpha	B.1.1.7	United Kingdom Sept. 2020
Beta	B.1.351	South Africa May 2020
Gamma	P.1	Brazil Nov. 2020
Delta	B.1.617.2	India Oct. 2020
Omicron	B.1.1.529	Multiple Countries Nov. 2021

https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/



Garcia-Beltran, W., et al, Cell 185 2022

Covid-19 Vaccine: Neutralization Titers Much Higher Post 3rd Than Post 2nd for Wild Type and Beta Variants[1,2]



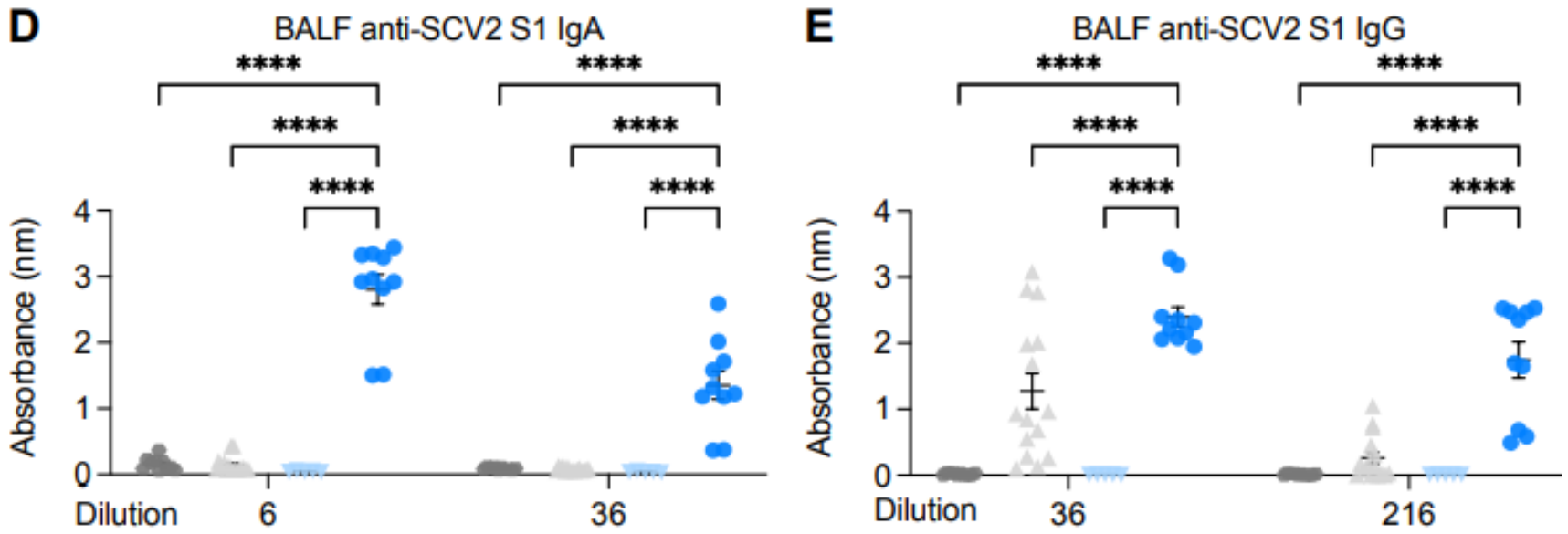
1. Initial data, Phase 1 sentinel subjects received dose 1 & 2 of 30mcg BNT162b2 21 days apart, subjects then came back and received BNT162b2 30 mcg as a 3rd
2. Samples were tested against each variant separately; PRNT: Plaque Reduction Neutralizing Test; GMR: Geometric Mean Ratio; WT: Wild Type; LOD: Limit of

Pfizer

Second Quarter 2021 Earnings

Data submitted for publication

IN boosting with stabilized SARS-CoV-2 spike induces mucosal humoral memory.



Mao T, et al, bioRxiv [Preprint]. 2022 Jan 26:2022.

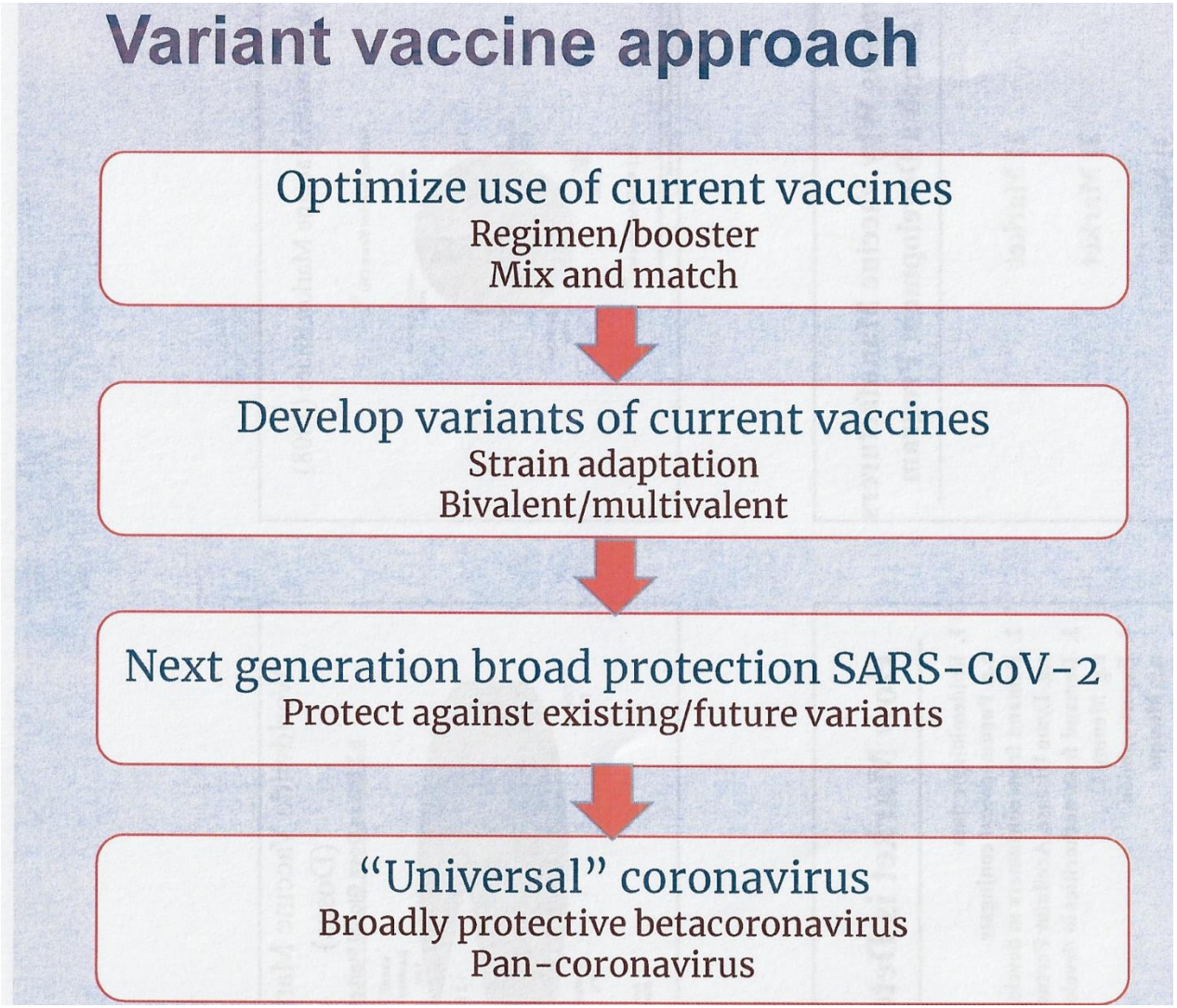
We Need a Pan Sarbecovirus Vaccine Because:

Variants of SARS-2 beta coronavirus may continue to escape neutralizing antibodies induced by vaccines against prior variants

The reservoir of beta coronaviruses in bats is large and new crossovers to humans is likely

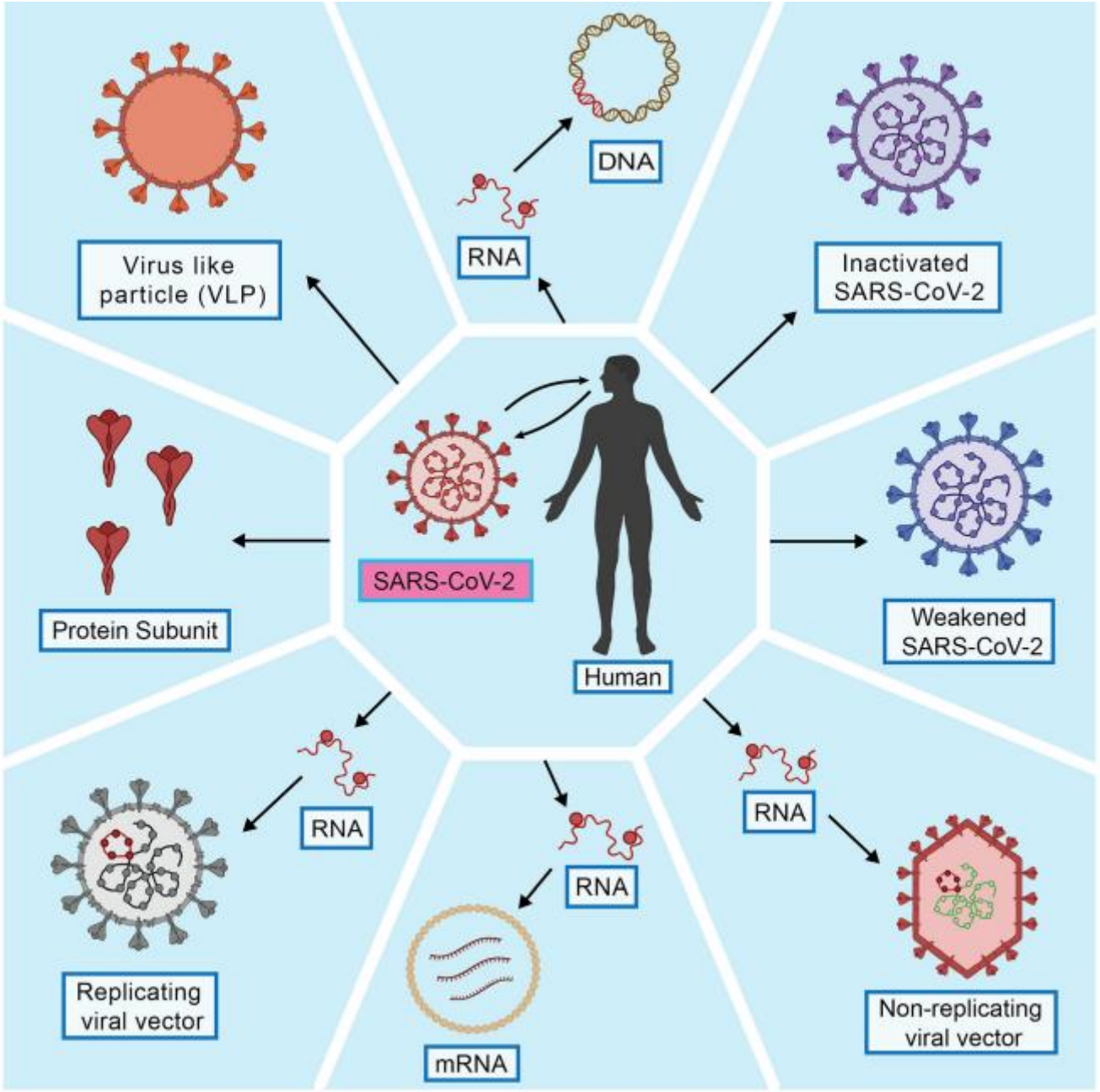
If we prepare now, the time required for large scale vaccine manufacture will be reduced and lives will be saved

Variant vaccine approach



The technology to make pan-sarbecovirus vaccines appears to be available. A supply of such a vaccine might be able to stifle a small outbreak of a new coronavirus. Once developed, shown to be safe and immunogenic, a large amount of a new vaccine can be manufactured quickly and used to deal with the adaptation of a new beta coronavirus to humans.

Fig. 1
Types of different COVID-19 vaccines and their manufacturing features.



Rahman, M., et al, *VirusDis.* Feb. 2022