



# The Miracle of COVID-19 Vaccines & the Trillion Dollar Gap

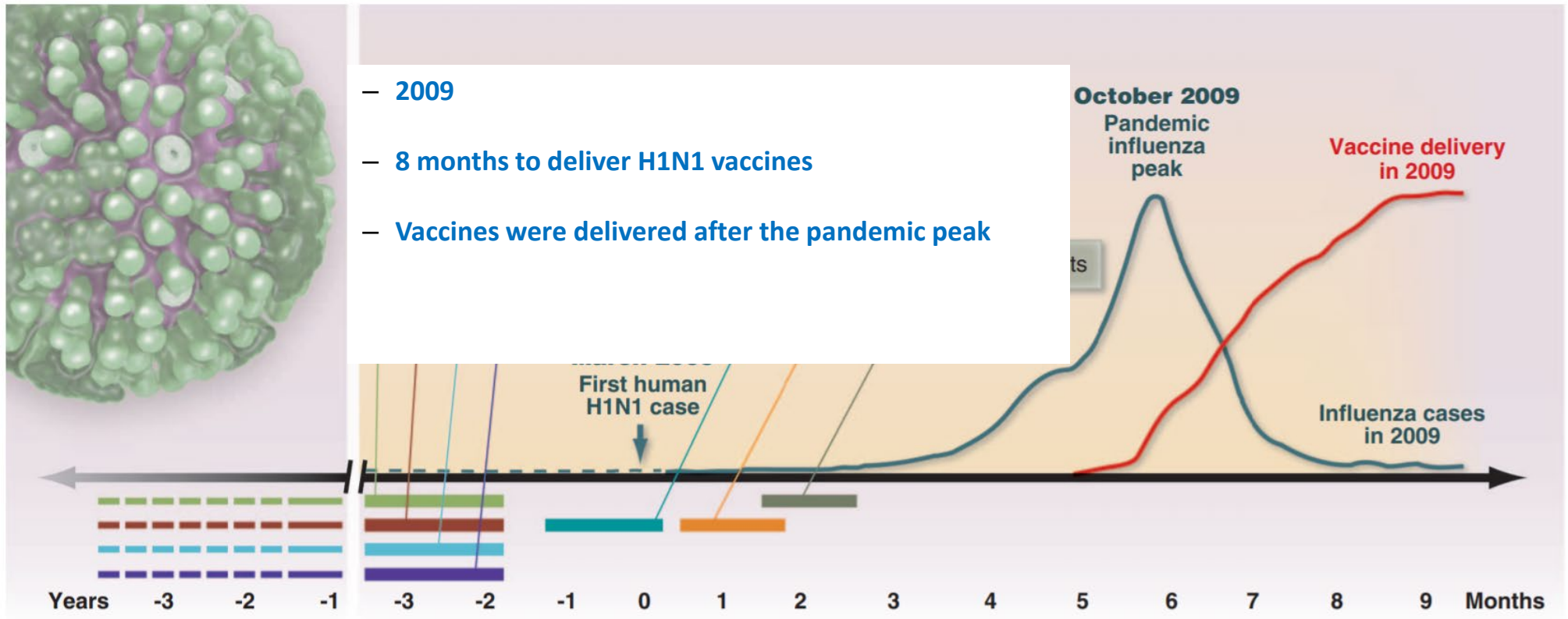
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**Rino Rappuoli**  
Rome November 29 2022

C: Institut Pasteur in Italy – Cenci Bolognetti Foundation

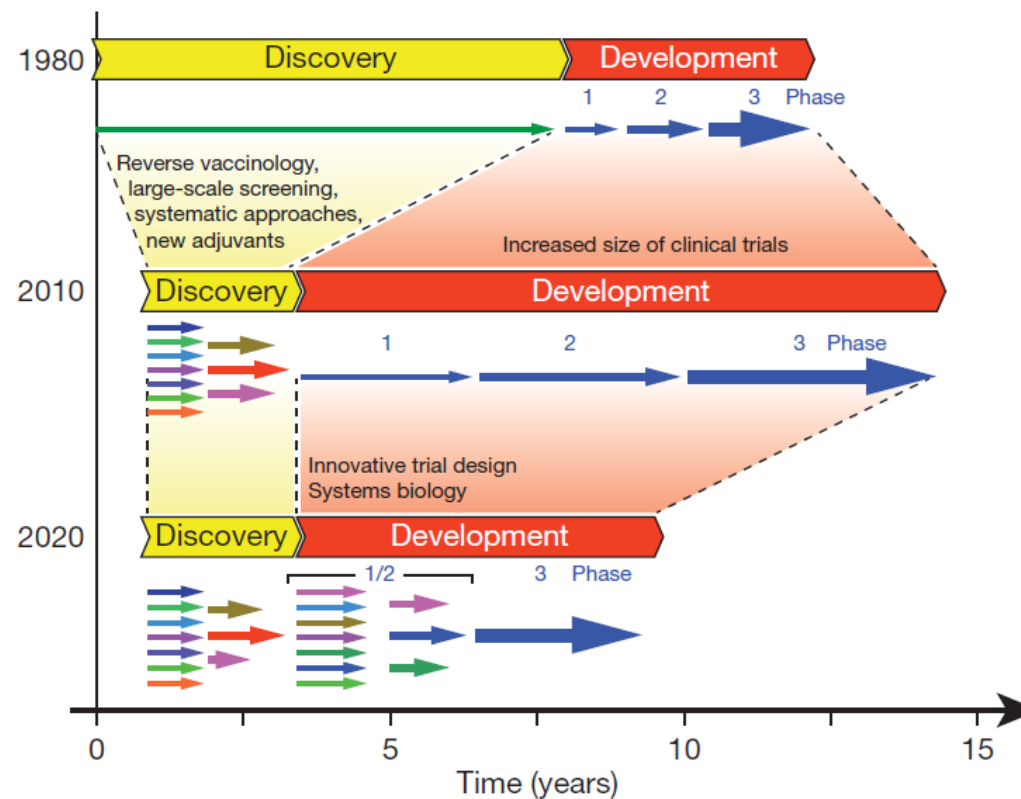
# Influenza: Options to Improve Pandemic Preparation

Rino Rappuoli<sup>1\*</sup> and Philip R. Dormitzer<sup>2</sup>



# Transforming Vaccine Development

## Vaccine Vision in 2011



Rino Rappuoli<sup>1</sup> & Alan Aderem<sup>2</sup>

26 MAY 2011 | VOL 473 | NATURE | 467



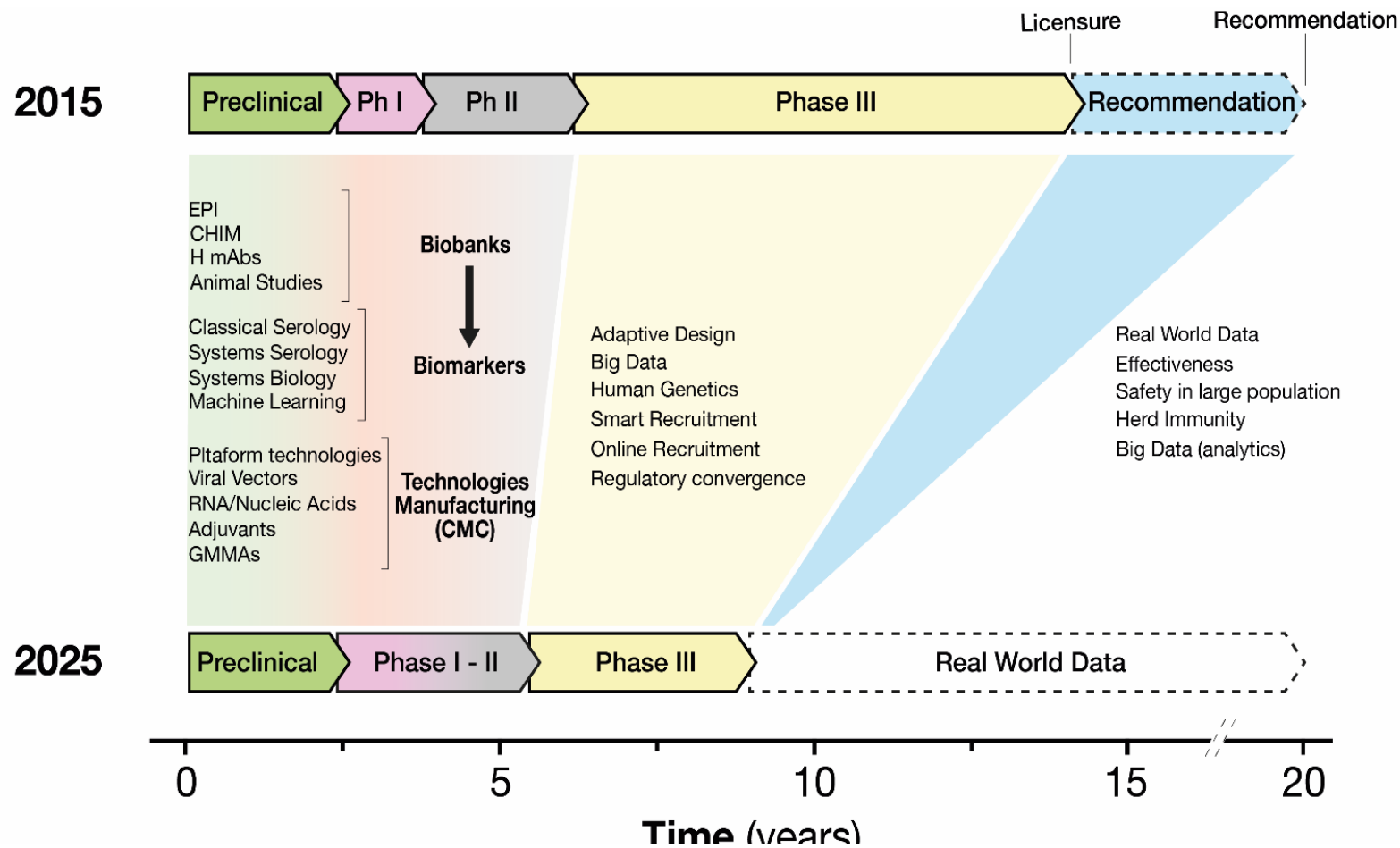


# Transforming Vaccine Development to Make Vaccines Available Faster

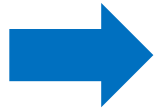


Palio meeting, Rockville, July 1<sup>st</sup> 2019

Seminar at Stanford University January 17<sup>th</sup> 2020



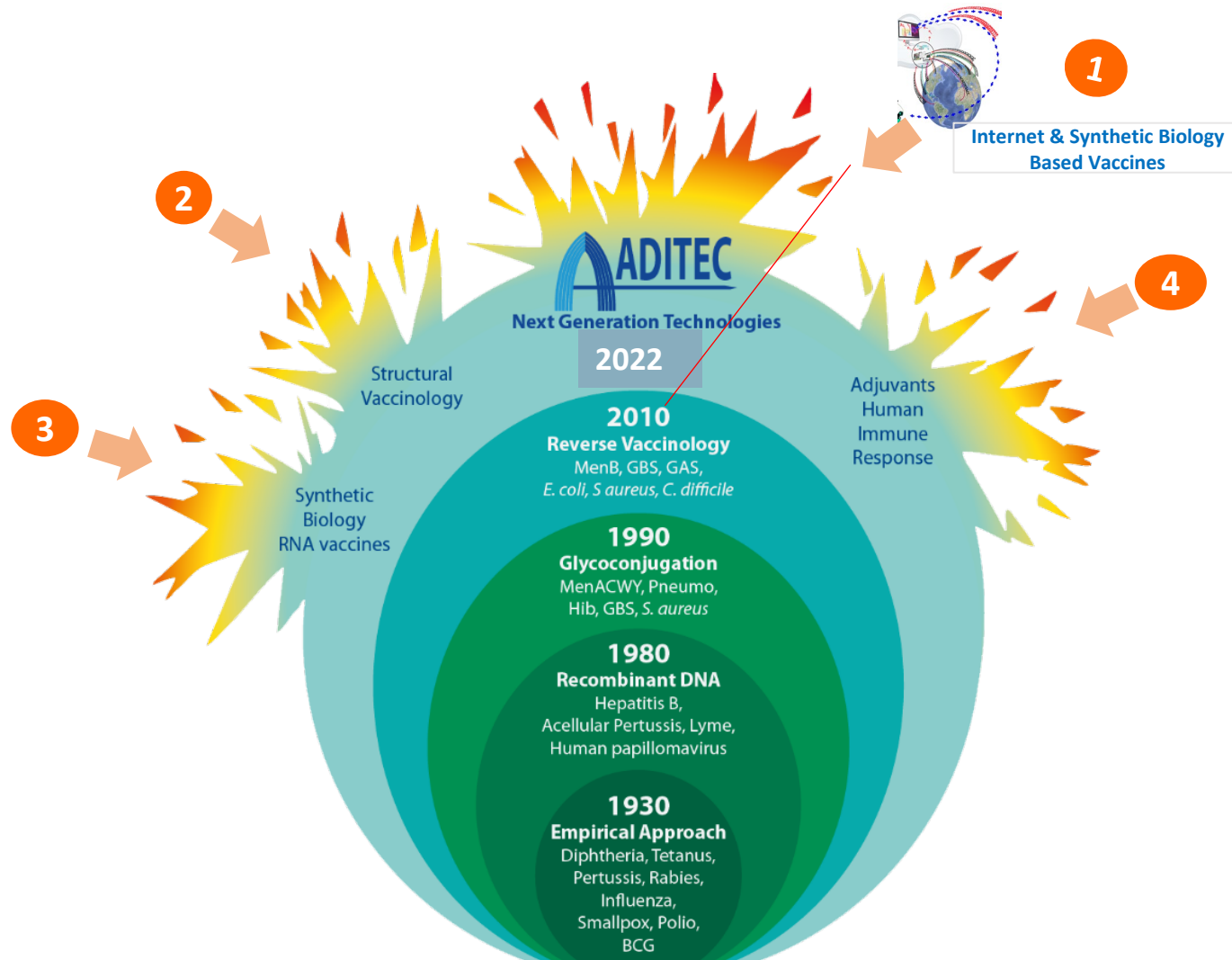
# Vaccines in 10 Months



- Technology
- Unprecedented investment by the public sector

# Technologies

4 technologies allowed fast development of Covid-19 vaccines



## Sunday March 31<sup>st</sup> 2013 Easter day

- Chinese CDC postes the sequence of an H7N9 avian influenza virus
- The virus had already killed 3 people, high risk of influenza pandemic
- Race for vaccine developement starts
- Virus had to be sent from China to CDC in Atlanta



### Synthetic Generation of Influenza Vaccine Viruses for Rapid Response to Pandemics

Philip R. Dormitzer *et al.*

*Sci Transl Med* **5**, 185ra68 (2013);

DOI: 10.1126/scitranslmed.3006368

**Emerging Microbes and Infections (2013) 2**, e52; doi:10.1038/emi.2013.54

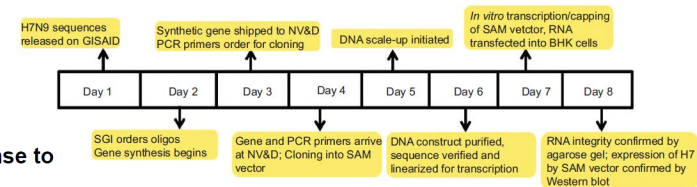
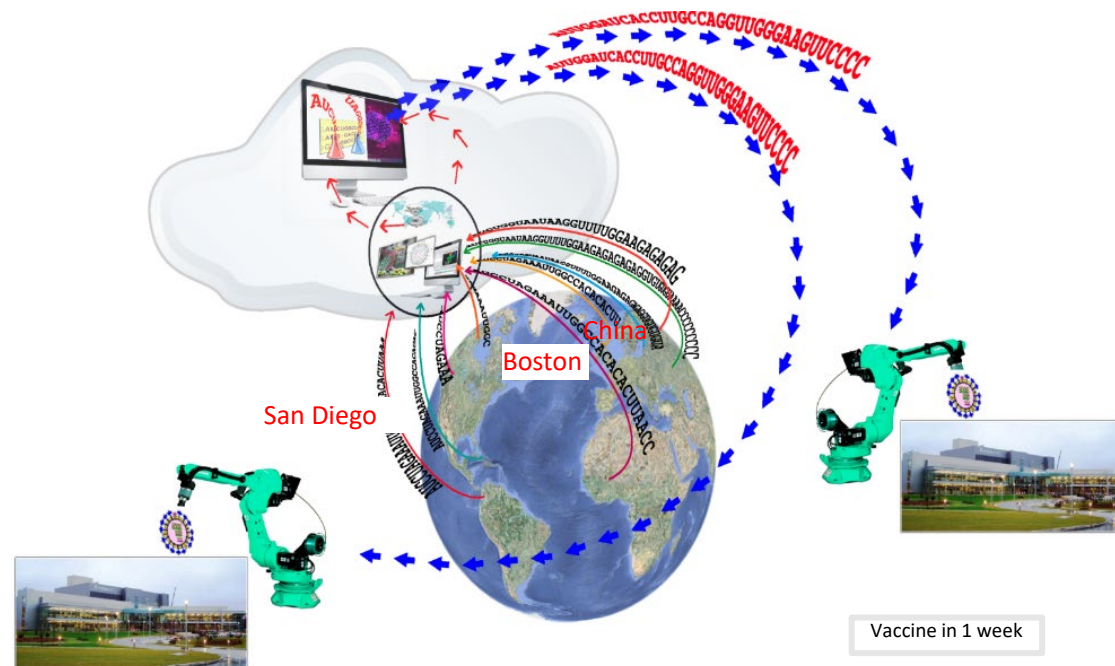
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[www.nature.com/emi](http://www.nature.com/emi)

# 2013: Internet & Synthetic Biology-based Vaccines in One Week

In 2013 an RNA vaccine and a virus seed in one week  
using information teleported by internet



Timeline from electronic gene sequence posting to production of RNA prior to formulation with the LNP delivery system. GISAID, Global Initiative for Sharing Data; PCR, polymerase chain reaction.



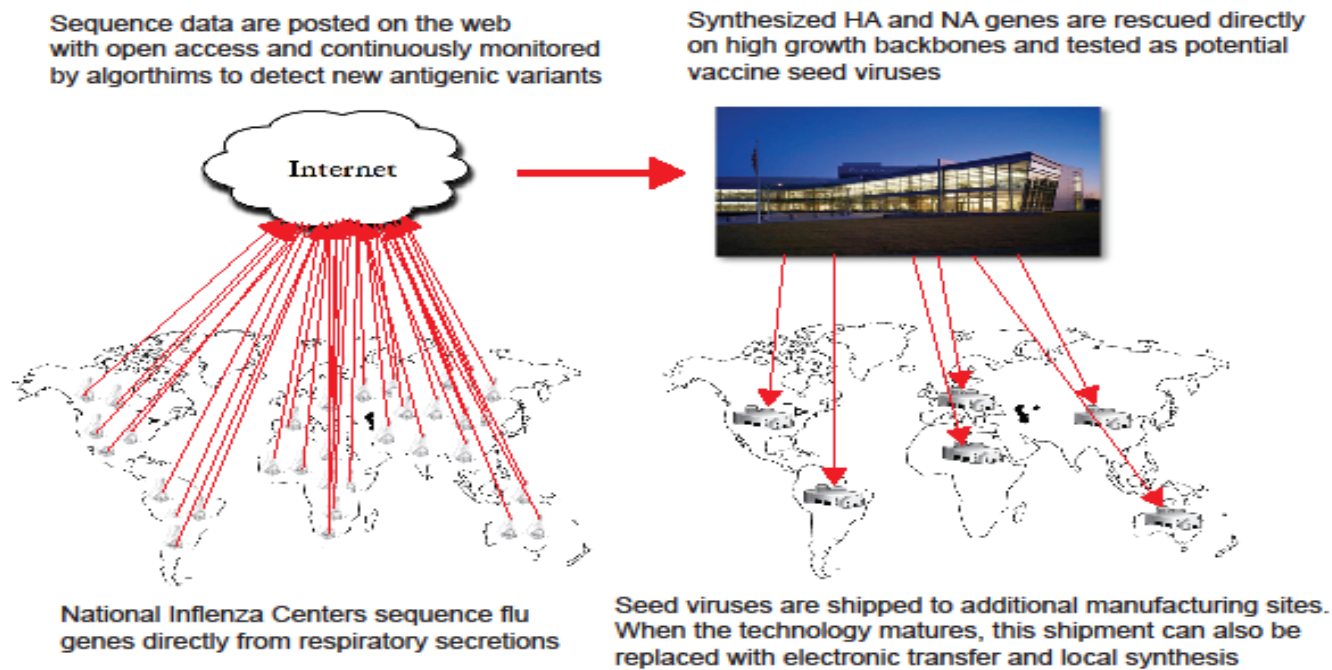
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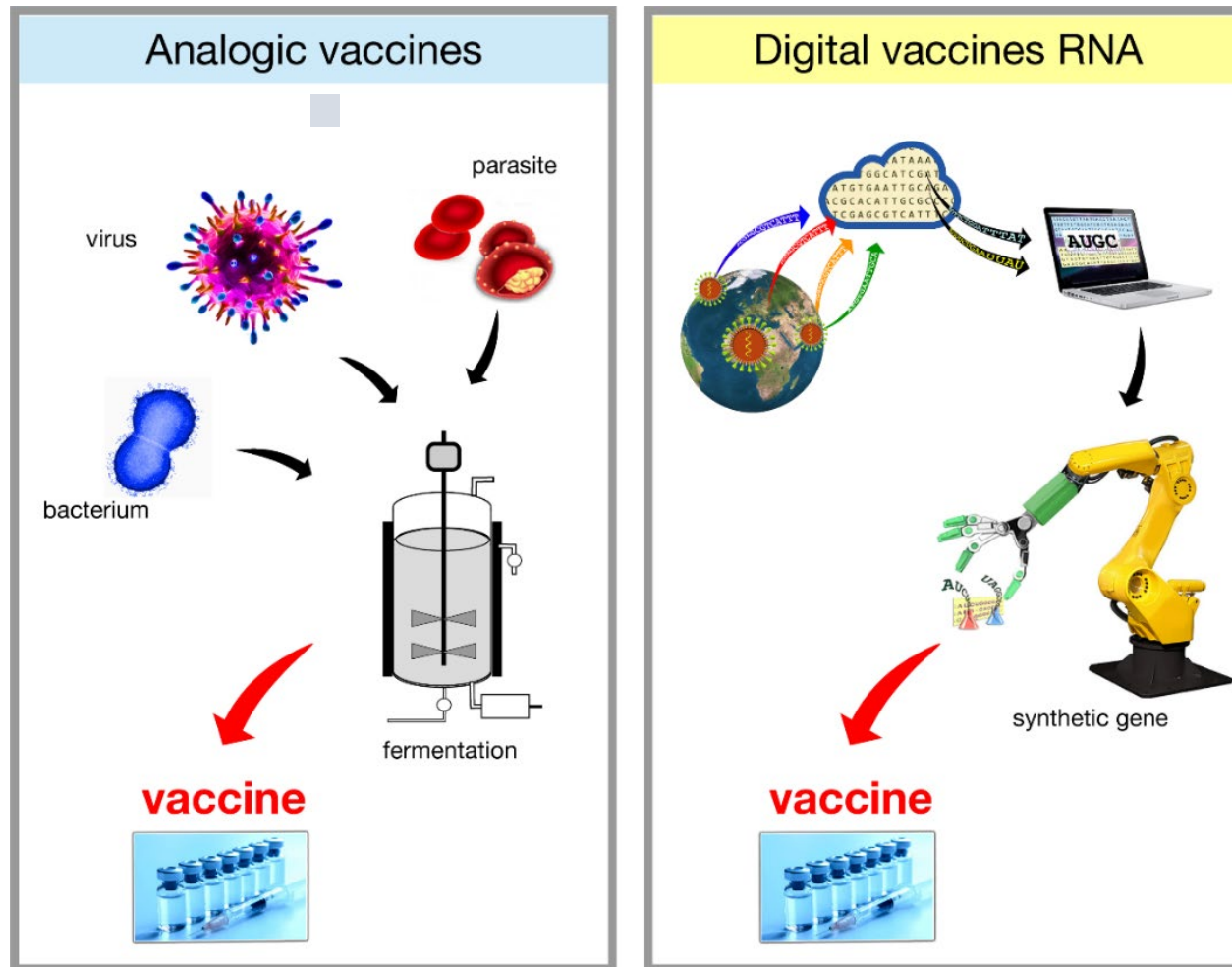
[www.nature.com/emi](http://www.nature.com/emi)



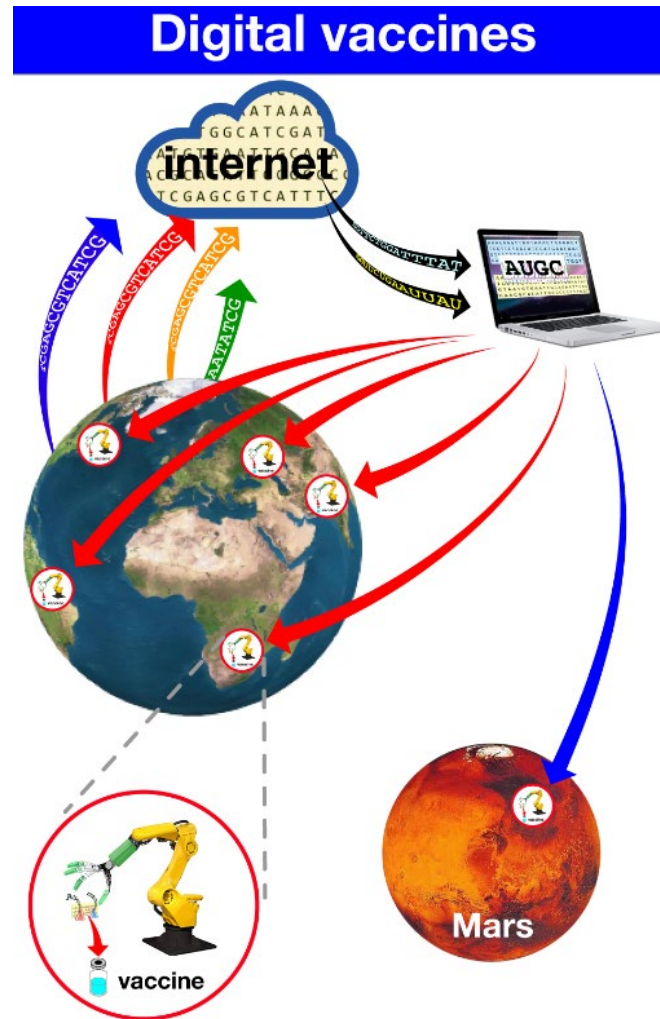
# Shipping Information Instead of Viruses



## from Analog to Digital vaccines

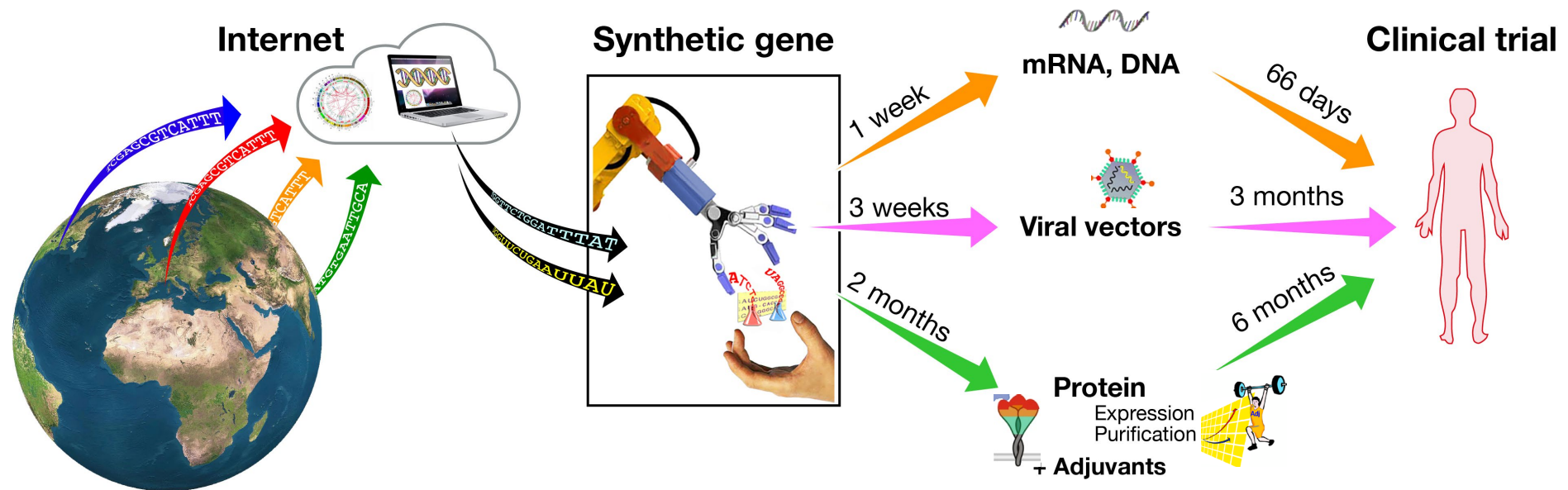


# Accessible Vaccines Globally and even in Mars



# January 10<sup>th</sup> 2020 SARS-CoV-2 Sequence Posted in Internet

350 labs worldwide used the sequence to make synthetic genes



PNAS 2021 Vol. 118 No. 3 e2020368118

<https://doi.org/10.1073/pnas.2020368118> | 1

## Vaccinology in the post–COVID-19 era

Rino Rappuoli<sup>a,1</sup>, Ennio De Gregorio<sup>a</sup>, Giuseppe Del Giudice<sup>a</sup>, Sanjay Phogat<sup>a</sup>, Simone Pecetta<sup>a</sup>,

# Three Main Vaccine Types for Covid-19

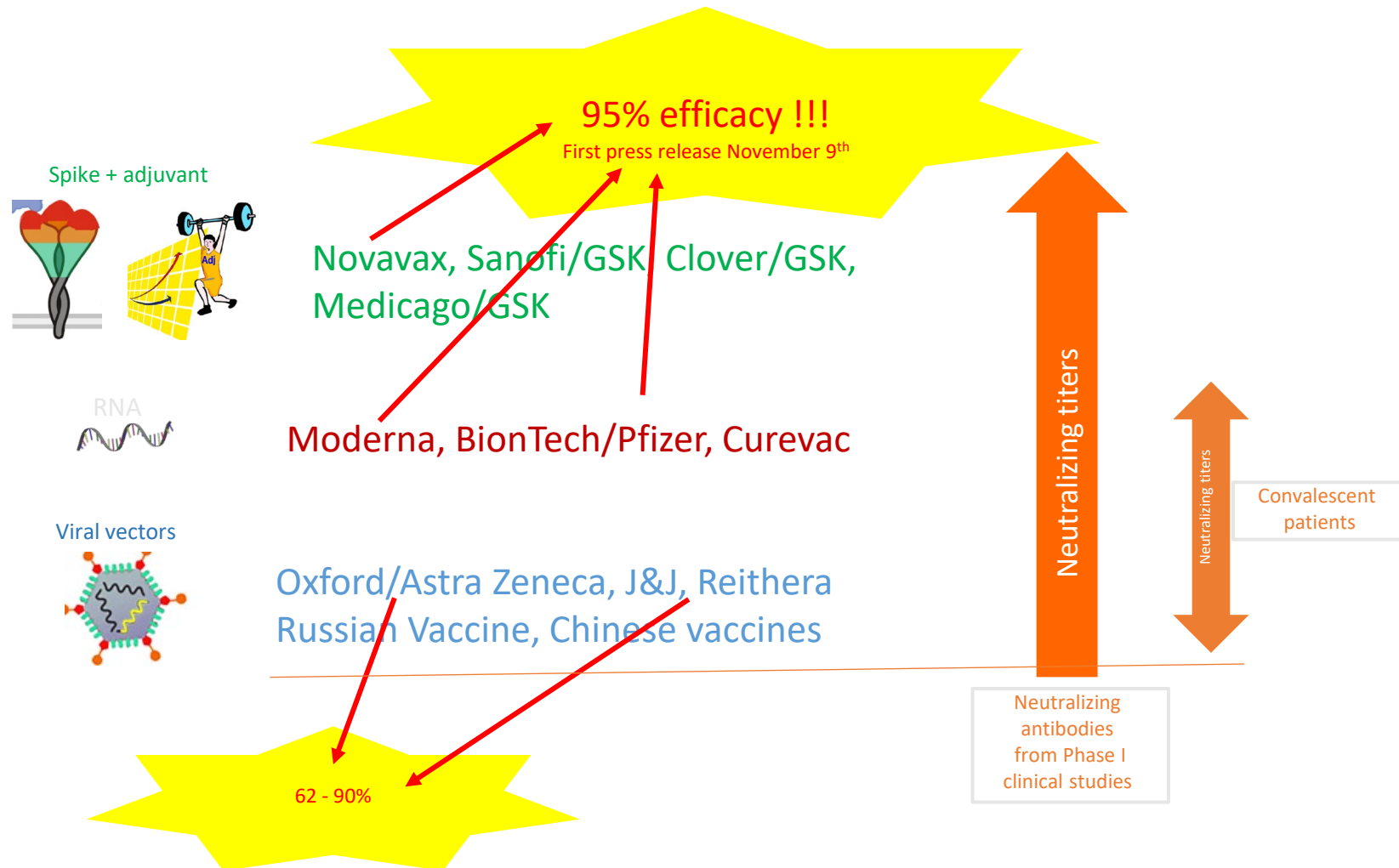
## *Immunogenicity*





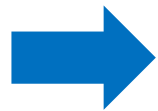
# Three Main Vaccine Types for Covid-19

## *Efficacy*



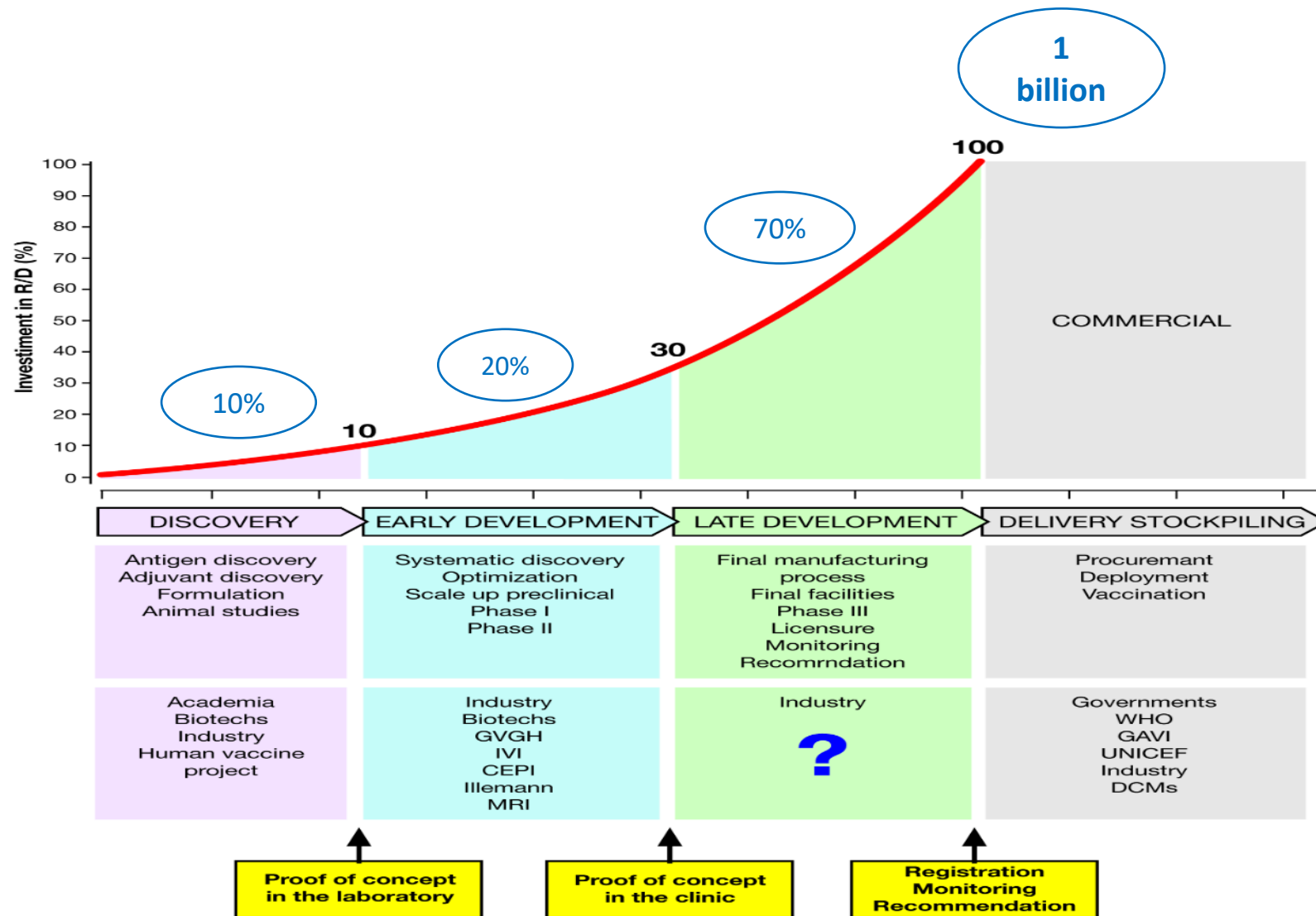
# Vaccines in 10 Months

- Technology



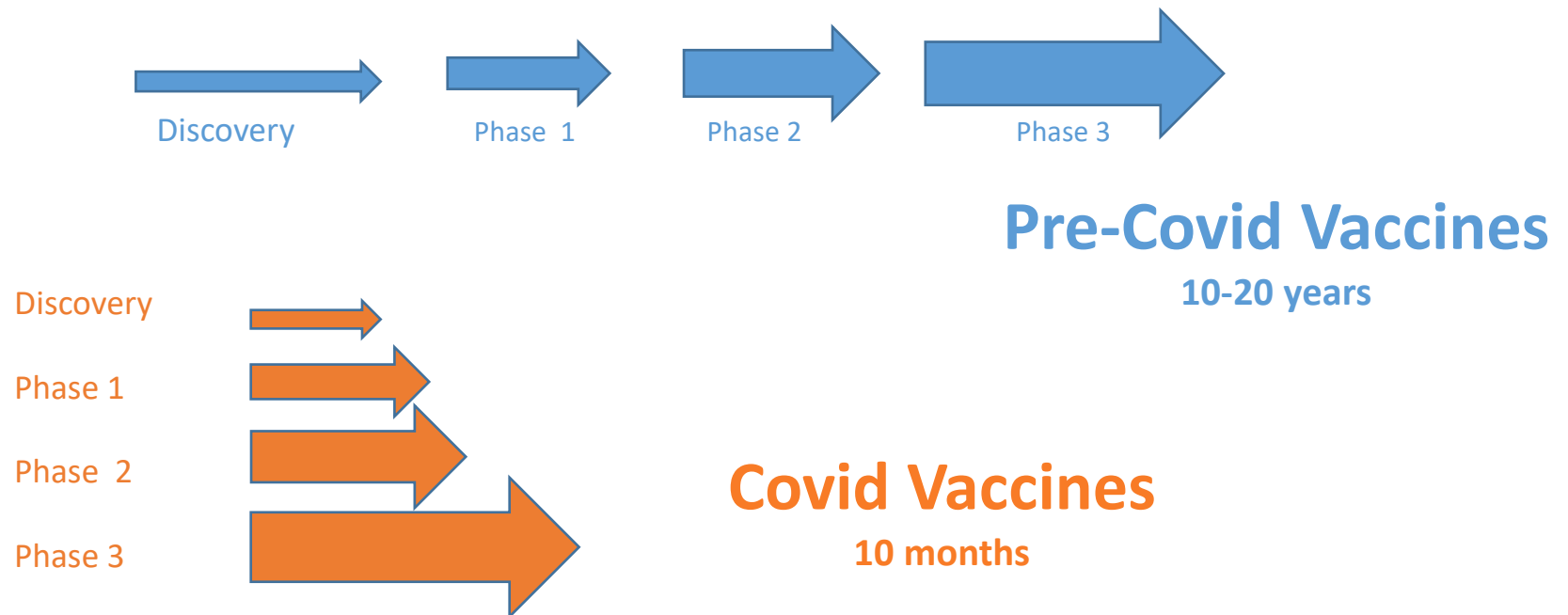
- Unprecedented investment by the public sector

# Classical Vaccine Development



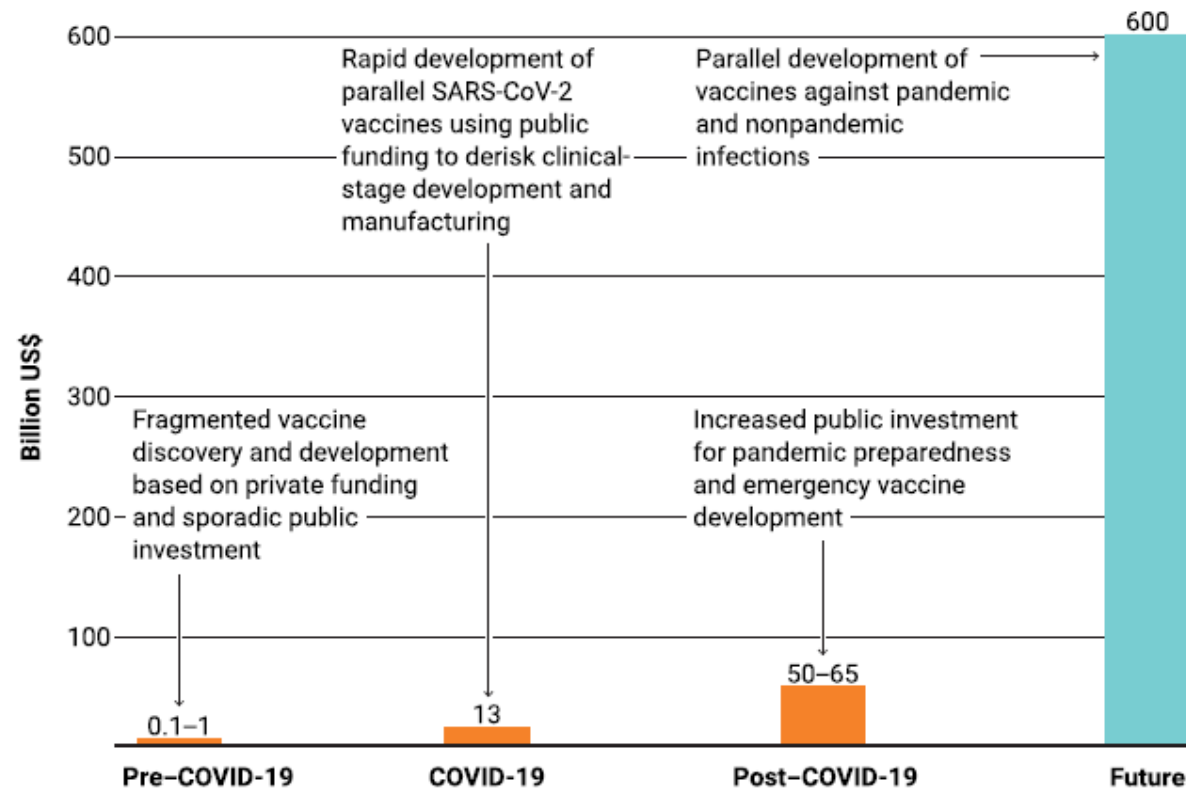
# Unprecedented Acceleration of Vaccine Development

**Investment > 15 billion** investment from the public sector (>10 billion USA alone) in vaccine Development and Manufacturing allowed at risk development (parallel investment in discovery, early and late development)



# The trillion dollar vaccine gap

## A Investment in vaccine development



### The trillion dollar vaccine gap

Simone Pecetta<sup>1</sup>, Daniel Tortorice<sup>2</sup>, Francesco Berlanda Scorza<sup>3</sup>, Mariagrazia Pizza<sup>3</sup>, Gordon Dougan<sup>4</sup>, Richard Hatchett<sup>5</sup>, Steve Black<sup>6</sup>, David E. Bloom<sup>7</sup>, Rino Rappuoli<sup>1\*</sup>

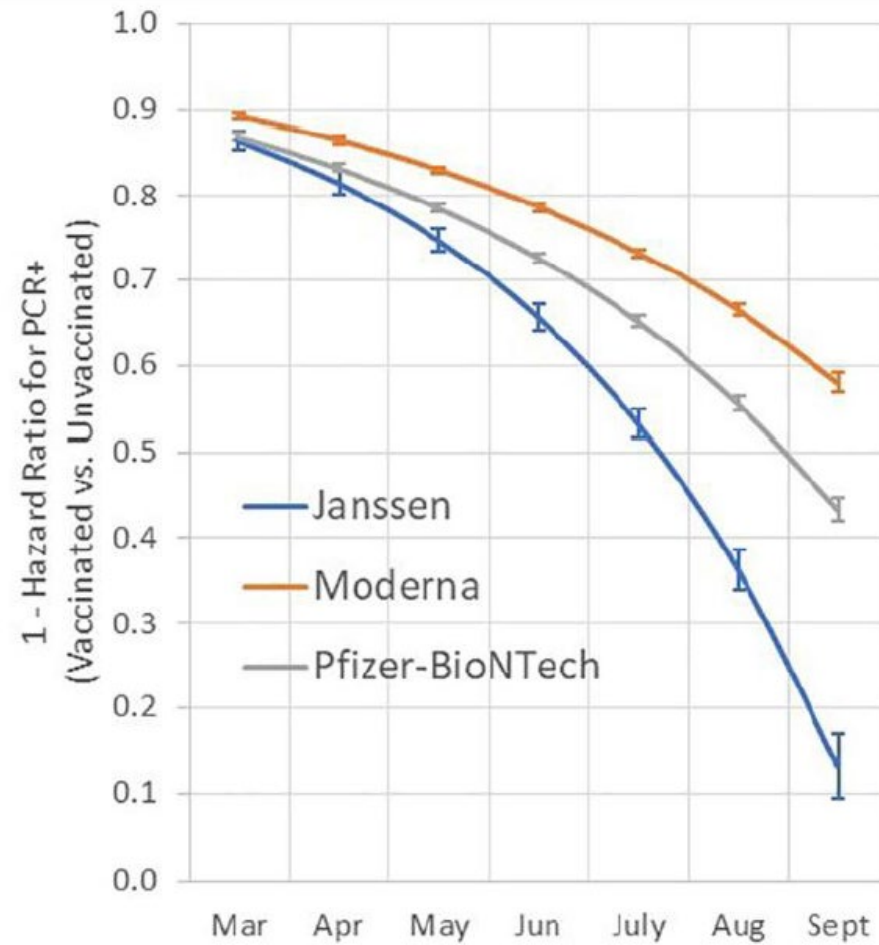
Pecetta et al., *Sci. Transl. Med.* 14, eabn4342 (2022) 30 March 2022



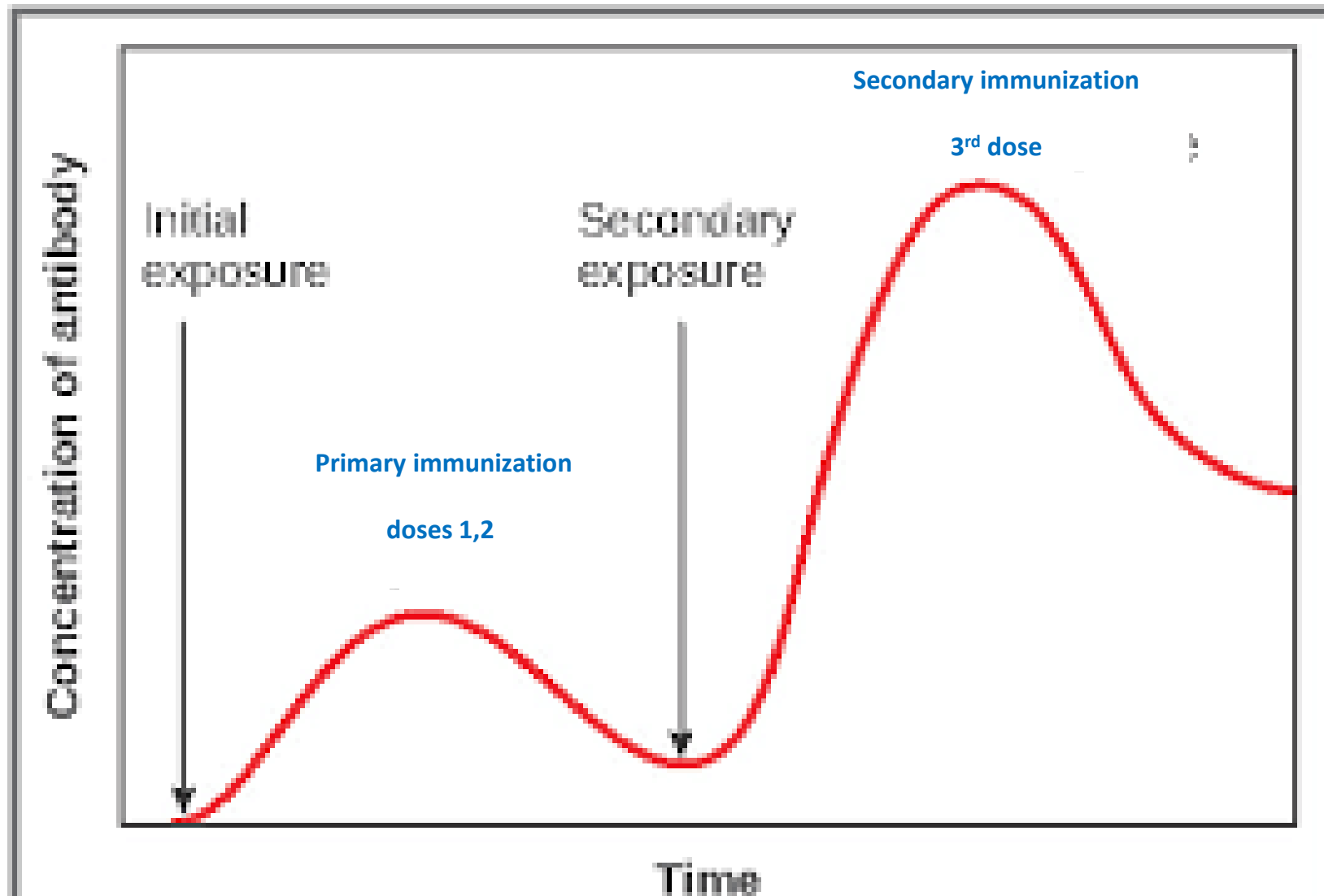
Cite as: B. A. Cohn *et al.*, *Science*  
10.1126/science.abm0620 (2021).

## SARS-CoV-2 vaccine protection and deaths among US veterans during 2021

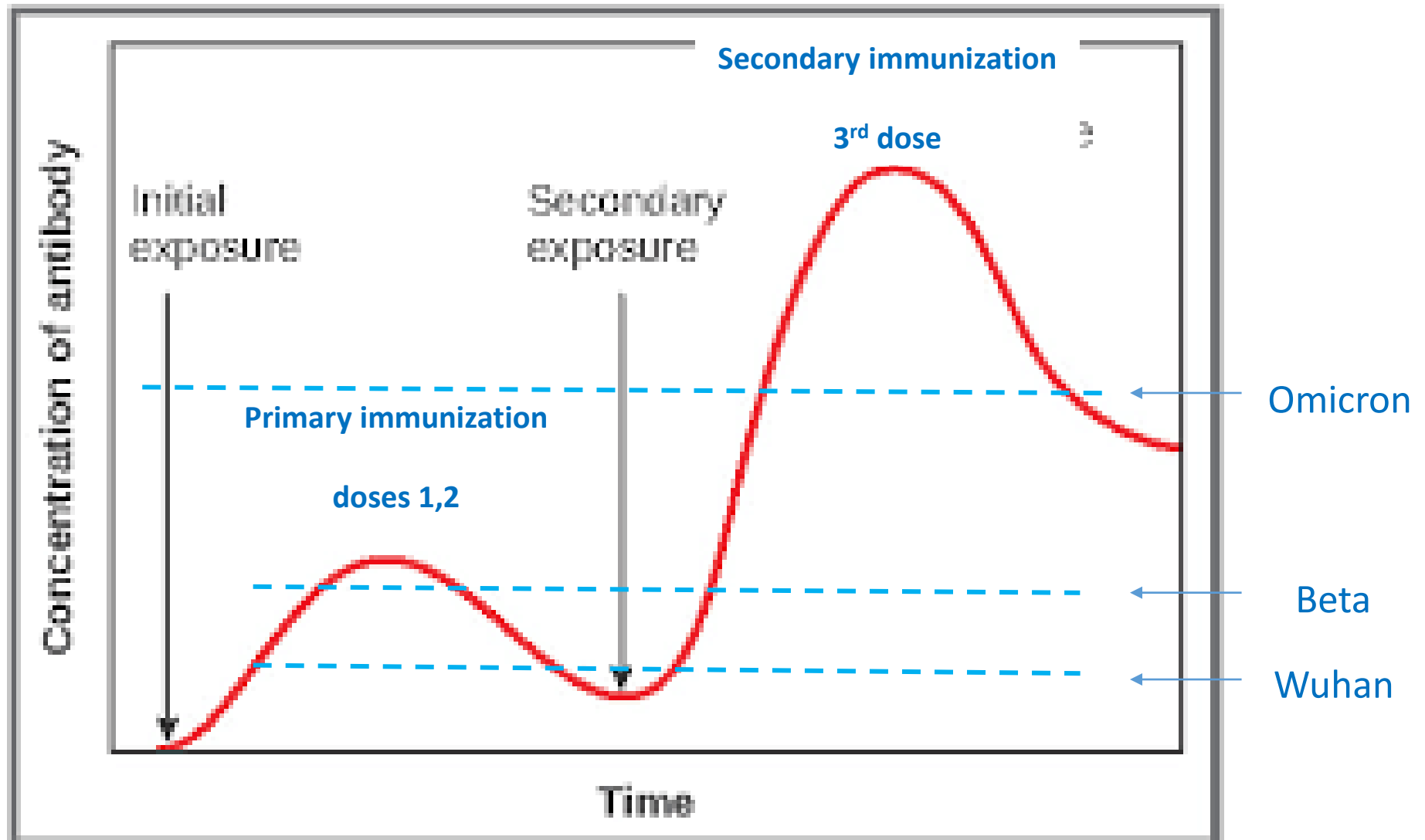
Barbara A. Cohn<sup>1†</sup>, Piera M. Cirillo<sup>1,2†</sup>, Caitlin C. Murphy<sup>3†</sup>, Nickilou Y. Krigbaum<sup>1,2</sup>, Arthur W. Wallace<sup>2,4\*</sup>



## From basic Immunology textbooks



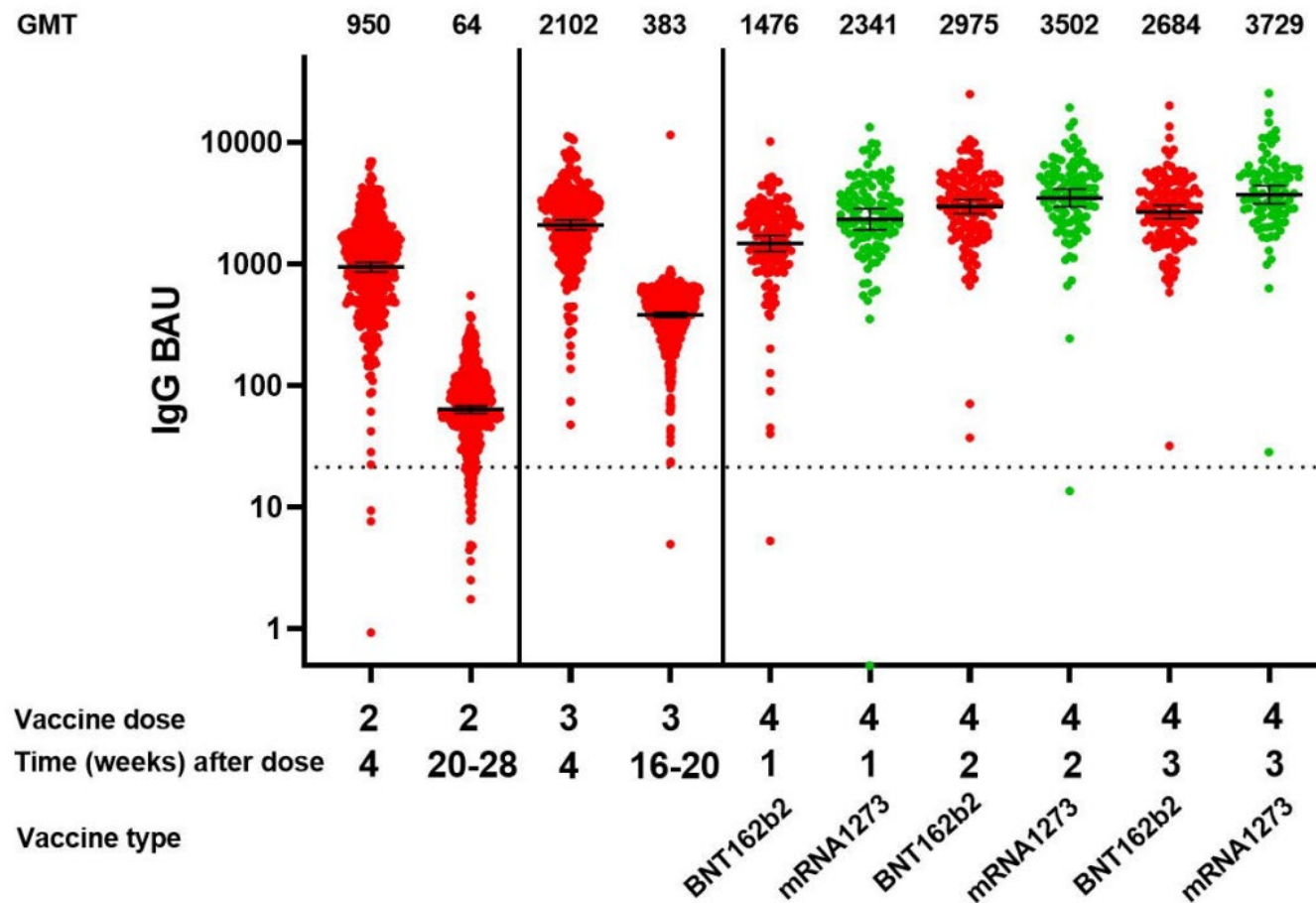
## From basic Immunology textbooks



# 4th Dose COVID mRNA Vaccines' Immunogenicity & Efficacy Against Omicron VOC

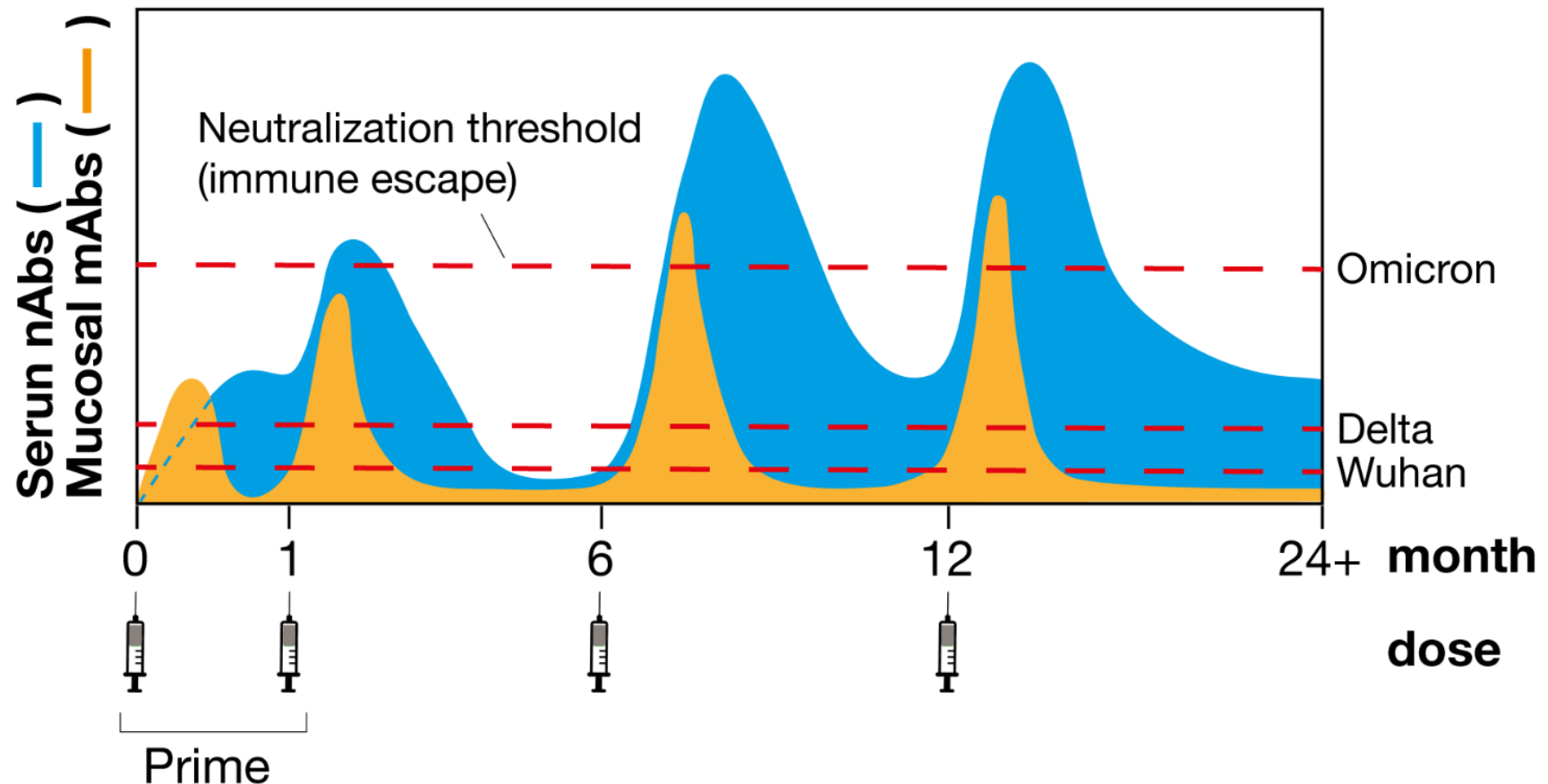
Gili Regev-Yochay<sup>1,2</sup>, Tal Gonen<sup>1,2</sup>, Mayan Gilboa<sup>1,2</sup>, Michal Mandelboim<sup>2,3</sup>, Victoria Indenbaum<sup>3</sup>, Sharon Amit<sup>4</sup>, Lilac Meltzer<sup>1,2</sup>, Keren Asraf<sup>6</sup>, Carmit Cohen<sup>1</sup>, Ronen Fluss<sup>6</sup>, Asaf Biber<sup>1,2</sup>, Itai Nemet<sup>3</sup>, Limor Kliker<sup>2,3</sup>, Gili Joseph<sup>1</sup>, Ram Doolman<sup>5</sup>, Ella Mendelson<sup>2,3</sup>, Laurence S. Freedman<sup>6</sup>, Dror Harats<sup>7</sup>, Yitshak Kreiss<sup>\*7</sup> and Yaniv Lustig<sup>\*2,3</sup>

medRxiv preprint doi: <https://doi.org/10.1101/2022.02.15.22270948>; 1



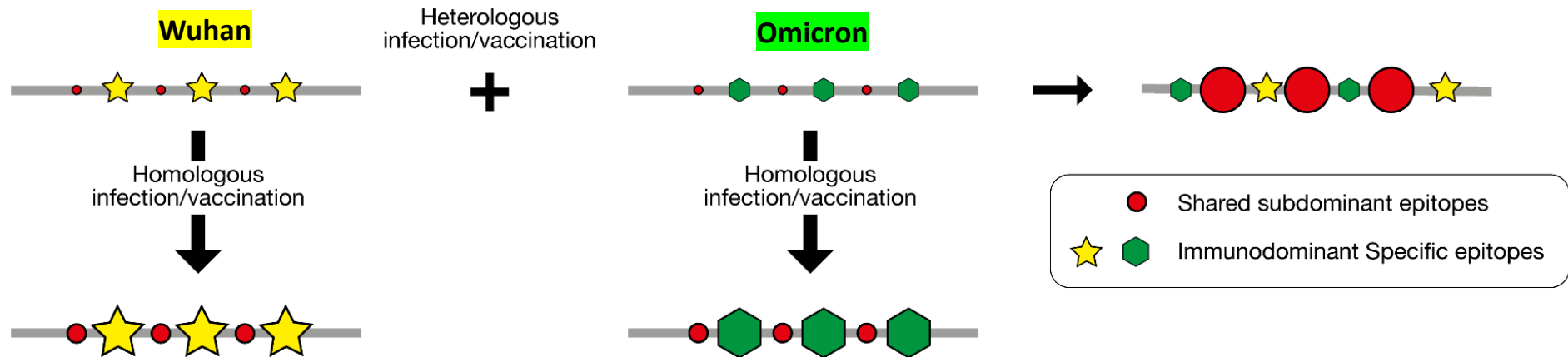
# Why Vaccines Protect Poorly from Infection but Protect Well from Severe Disease and Long Covid

Simone Pecetta and Rappuoli in preparation



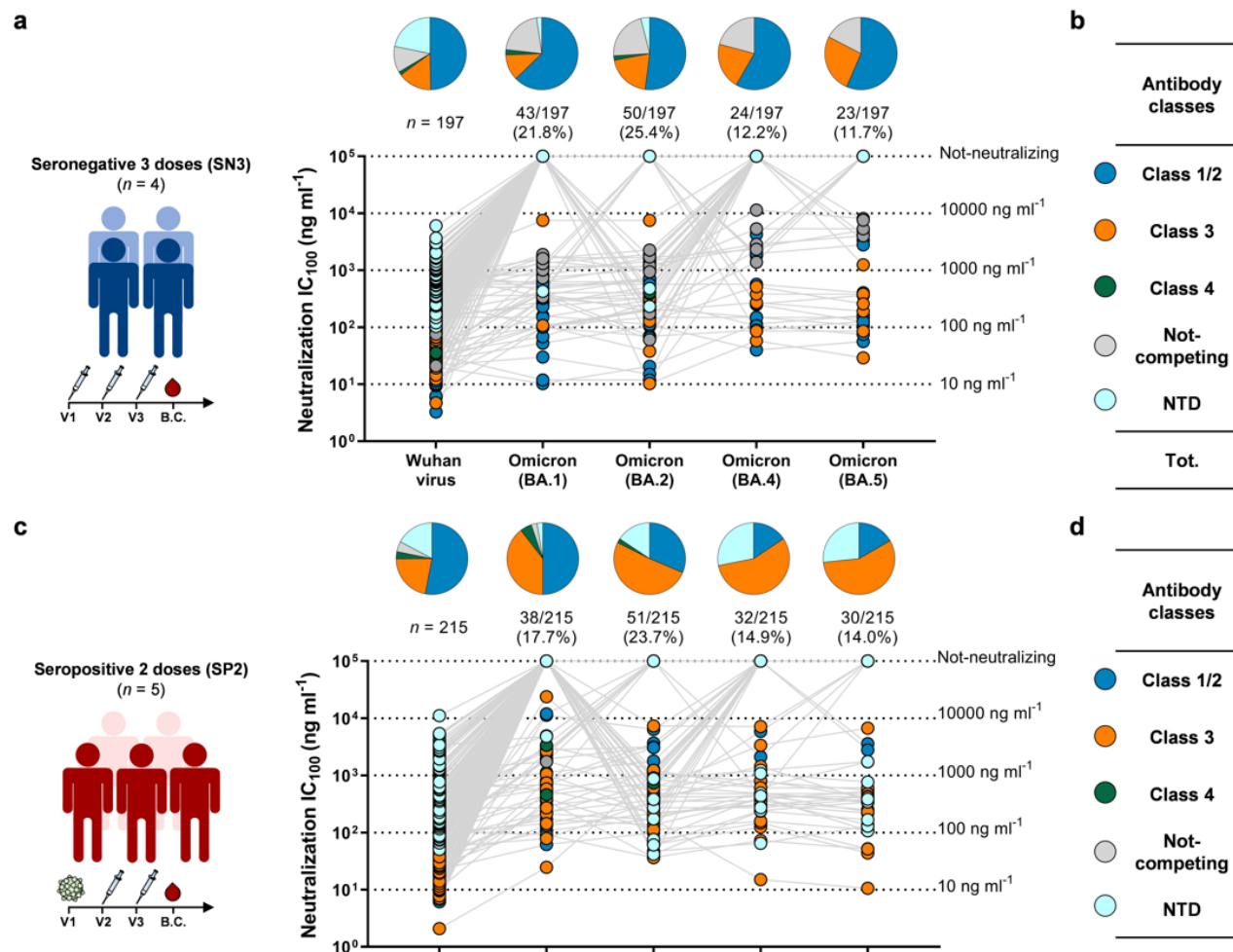


# Omicron Infection or Vaccination is Expected to Boost Immunity to Subdominant Crossreactive Epitopes



# Vaccination and Infection Induce Different Classes of Omicron Neutralizing Antibodies

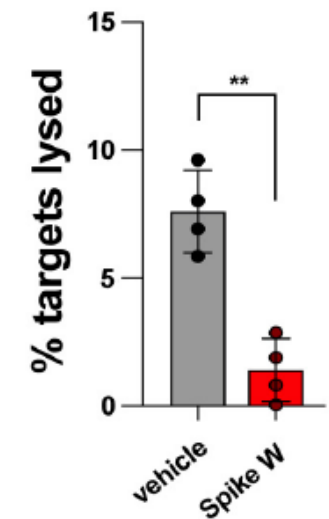
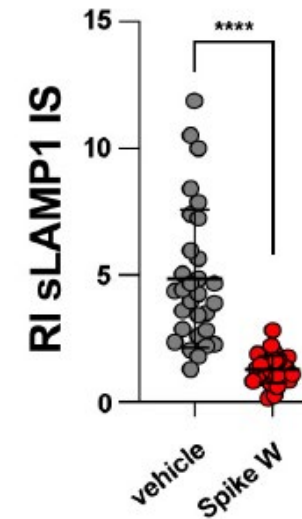
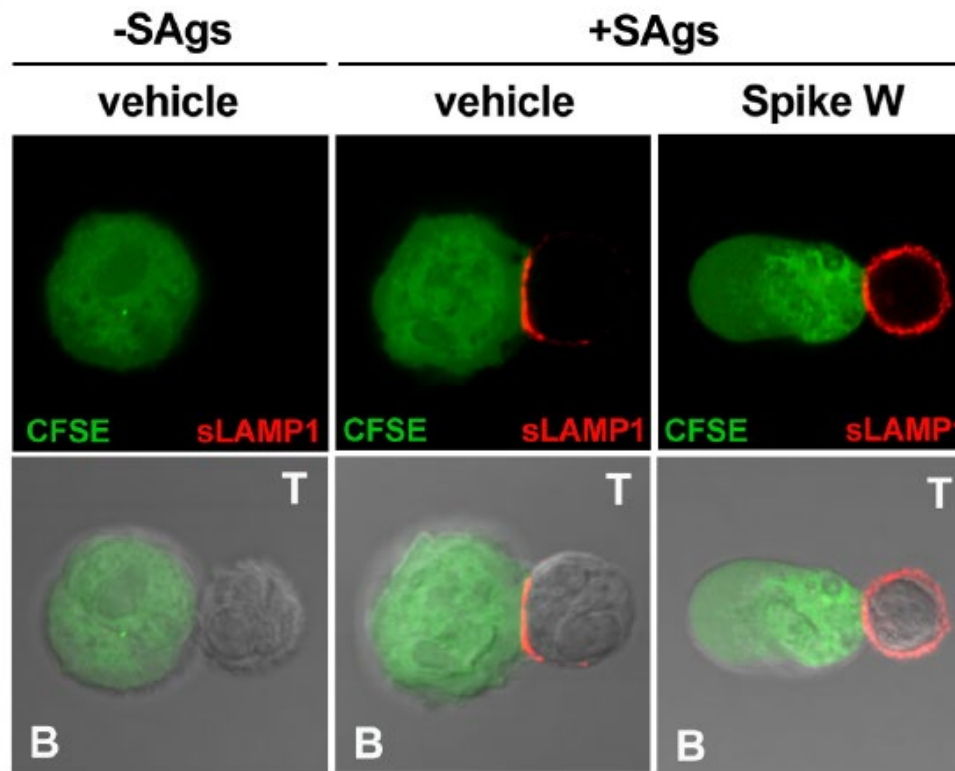
*Emanuele Andreano submitted*



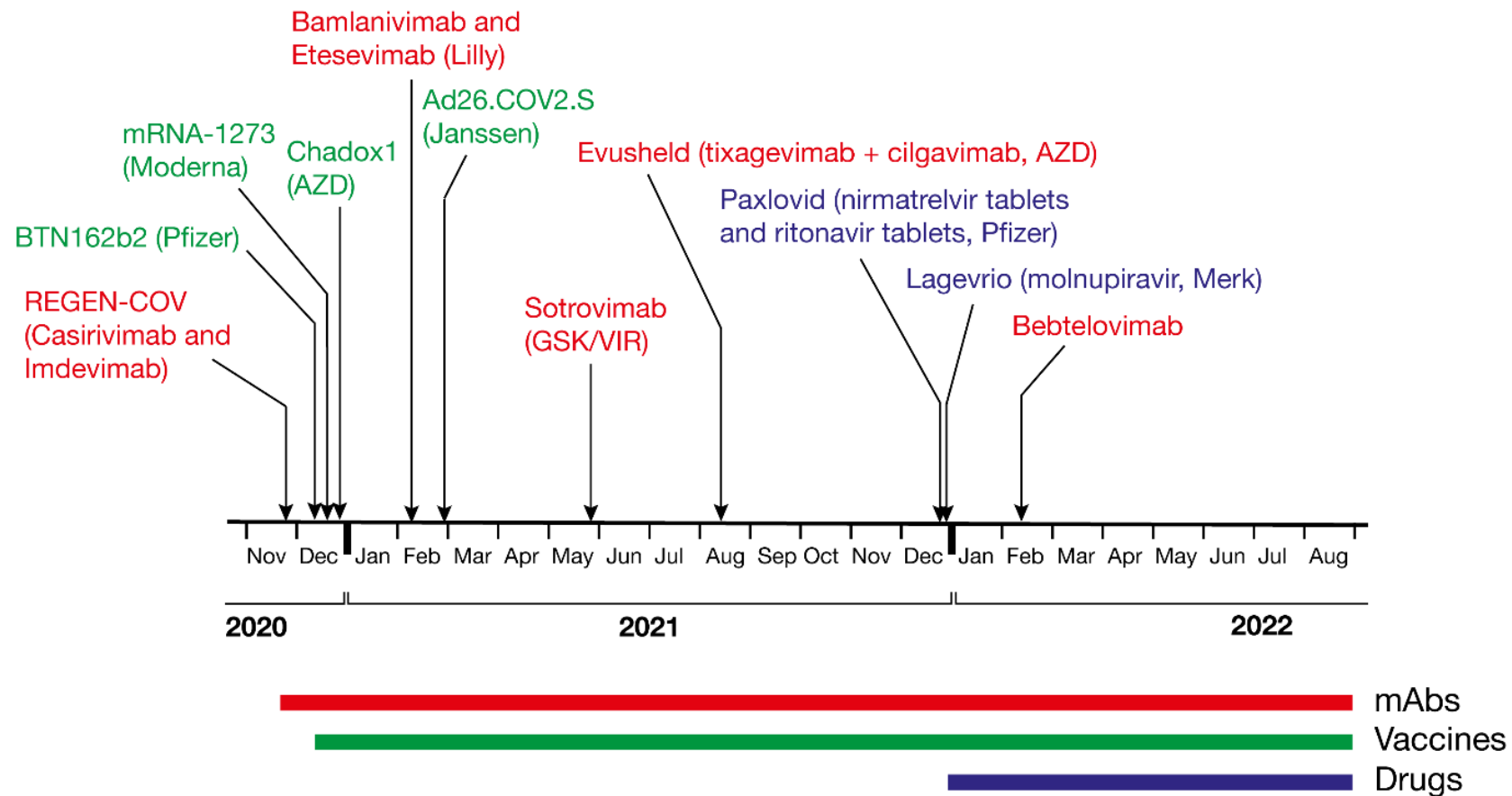
# SARS-CoV-2 Spike Suppresses CTL-Mediated Killing

SARS-CoV-2 Spike protein suppresses CTL-mediated killing by inhibiting immune synapse assembly

Anna Onnis<sup>1</sup>, Emanuele Andreano<sup>2</sup>, Chiara Cassioli<sup>1</sup>, Francesca Finetti<sup>1</sup>, Elisa Pantano<sup>2</sup>, Valentina Abbiento<sup>2</sup>, Giuseppe Marotta<sup>3</sup>, Rino Rappuoli<sup>2,4</sup>, Cosima T Baldari<sup>1</sup>



# Monoclonal and Vaccines Provide the Fastest Response for a Pandemic



## Governments Invested but not Enough

- 12.5 billion warp speed paid itself by anticipating vaccination by just 12 hours (Micheal Kremer)
- More investments would have had high returns
- Additional manufacturing capacity in early 2021 was needed
- Early manufacturing capacity necessary to improve equity
- Developing one vaccine requires more than 34 billion



# A Center for Pandemic Preparedness in Siena, Italy

*Spediz. abb. post. - art. 1, comma 1  
Legge 27-02-2004, n. 46 - Filiale di Roma*

Anno 163° - Numero 199

## GAZZETTA UFFICIALE DELLA REPUBBLICA ITALIANA

*PARTE PRIMA*

Roma - Venerdì, 26 agosto 2022

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PIAZZA G. VERDI, 1 - 00198 ROMA

DECRETO DEL PRESIDENTE DEL CONSIGLIO DEI  
MINISTRI 11 luglio 2022.

Approvazione dello statuto della Fondazione «Biotecno-  
polo di Siena».

IL PRESIDENTE  
DEL CONSIGLIO DEI MINISTRI

## A center for Pandemic Preparedness in Siena, Italy

- A National Center, well funded by the Italian Government up to the end of 2026
- The ambition to be a resource for Europe and for the world
- To be part of a global network of Institutes preparing the world for new pandemics (collaborate with CEPI, CARBX, BMGF, NIH, Wellcome Trust, etc..) including antimicrobial resistance
- Discovery, GMP up to phase 2B, for emergency approval
- To be started in 2022



Thank you !