

DEMOCRACY AND PANDEMIC



13 — 15.11.25

Fondazione Giorgio Cini, Venezia

Preparing for the Unknown by Prototype Pathogens

Rino Rappuoli

Fondazione Biotechnopolo di Siena

DEMOCRACY AND PANDEMICS Symposium

Venice, San Giorgio Island

13 – 15 November 2025



Eight Emerging Infectious Diseases In 40 Years

Three Pandemics

Climate change, 8 billion people, Deforestation, Urbanization, Travel, accelerate their frequency

Covid 7 million deaths

HIV 43 million deaths



HIV



SARS-CoV-2

2019

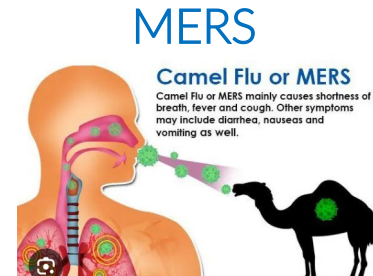
Impact on Health
Economy
National Security

1981



SARS

H1N1



MERS

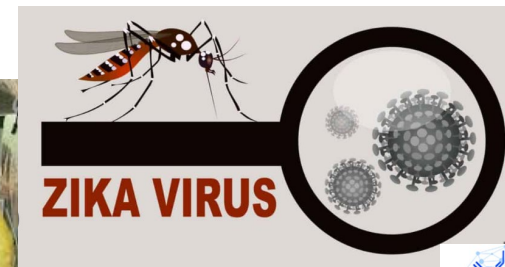


Ebola

Mpox



Zika



ZIKA VIRUS



CEPI, the Coalition for Epidemic Preparedness Innovations, a global partnership

Established after Ebola 2014

Mission supported by G7, G20, NIH, WHO

Negotiated Pandemic Treaty

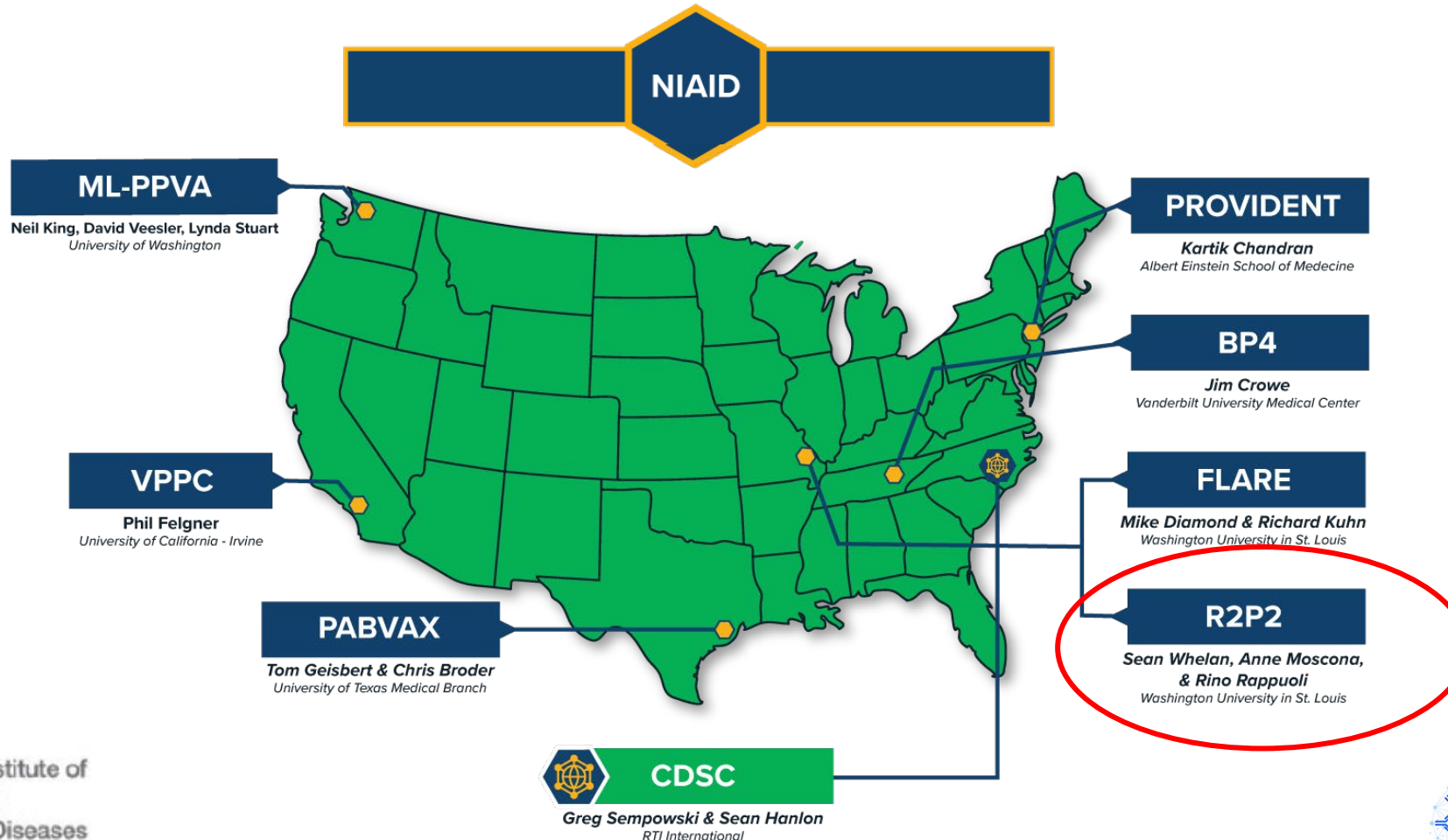
Prioritize pathogens with pandemic potential ..

Develop vaccines in 100 days

Equity

350 million \$ for a Network of 7 Research Centers

to make **Prototype Vaccines** against most important viral families



Prototype Vaccines

Using Genome-Based Vaccine Discovery & Design

Image from NIH ReVAMPP

Virus families



Prototype Vaccines



100 days delivery

Pandemic Potential

High

Moderate

High

<ul style="list-style-type: none"> Orthomyxoviridae Coronaviridae 	<ul style="list-style-type: none"> Retroviridae Poxviridae* Papillomaviridae* Hepadnaviridae*
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Moderate

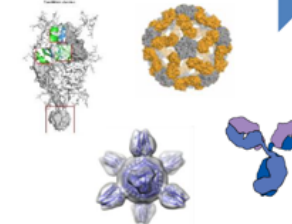
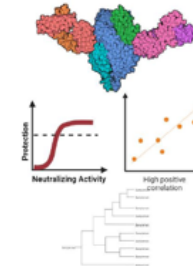
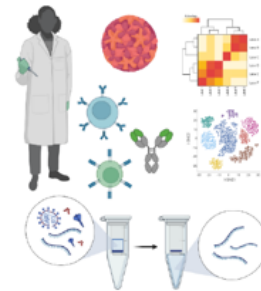
<ul style="list-style-type: none"> Bunyavirales order <ul style="list-style-type: none"> Arenaviridae Phenuiviridae Peribunyaviridae Hantaviridae Nairoviridae Filoviridae Flaviviridae Paramyxoviridae Togaviridae Picornaviridae 	<ul style="list-style-type: none"> Arteriviridae Pneumoviridae Herpesviridae Bornaviridae Rabdoviridae Adenoviridae Anelloviridae Astroviridae Caliciviridae Hepeviridae Parvoviridae Picobirnaviridae Reoviridae Polyomaviridae
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The **prototype pathogen** approach enables rapid response to new threats

Research on Known Prototype

Foundational Knowledge

Generalizable Vaccine/mAb Strategies



Genomes
Antibodies →

Structures → Structure-based vaccine design



A Decree to create a National Center for Pandemic Preparedness (CNAPS) Funded by the Italian Government was Published on August 26th 2022

Fondazione
Biotecnopolo
di Siena

Biotecnopolo di Siena
National Center
for Pandemic Preparedness

*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

SI PUBBLICA TUTTI I
GIORNI NON FESTIVI

DIREZIONE E REDAZIONE PRESSO IL MINISTERO DELLA GIUSTIZIA - UFFICIO PUBBLICAZIONE LEGGI E DECRETI - VIA ARENULA, 70 - 00186 ROMA
AMMINISTRAZIONE PRESSO L'ISTITUTO POLIGRAFICO E ZECCA DELLO STATO - VIA SALARIA, 691 - 00138 ROMA - CENTRALINO 06-85081 - LIBRERIA DELLO STATO
PIAZZA G. VERDI, 1 - 00198 ROMA

DECRETO DEL PRESIDENTE DEL CONSIGLIO DEI
MINISTRI 11 luglio 2022.

Approvazione dello statuto della Fondazione «Biotecnopolo di Siena».

IL PRESIDENTE
DEL CONSIGLIO DEI MINISTRI



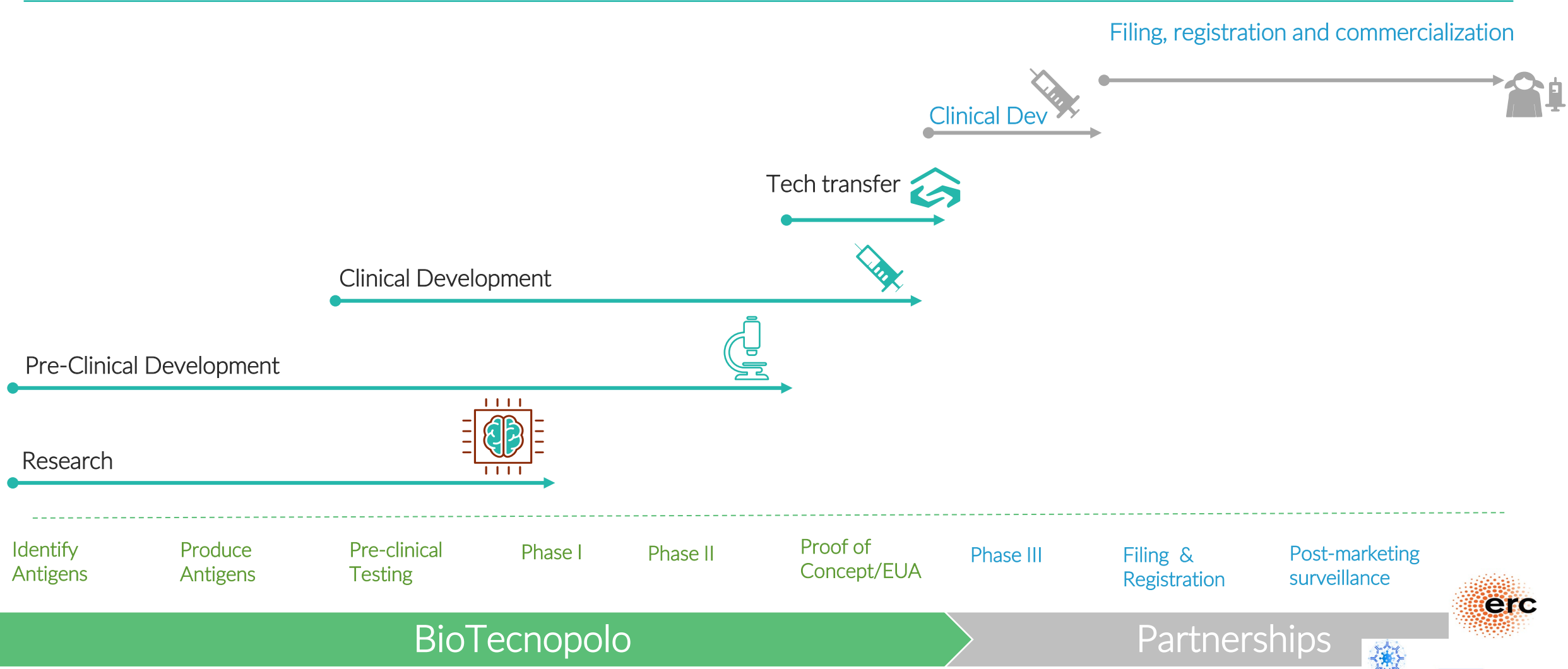
Co-funded by the
European Union

An Italian Center for Pandemic Preparedness

- A National Center, funded by the Italian Government
- 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, HERA, NIH, CARBX, BMGF, Wellcome Trust, IVI, Pasteur Network, etc..)
- Focus on **Vaccines and Monoclonal Antibodies**
- Target: **Emerging Viruses and Antibiotic Resistant bacteria (AMR)**
- Discovery, GMP up to phase 2B, for emergency approval

From discovery to phase 2b

Sustainable vaccine development model



Co-funded by the European Union

EVH European Vaccines Hub for Pandemic Readiness

Call for proposal EU4H-2024-PJ-01-1 (CP-g-24-10)

Contract signed May 21st 2025!!!!

starting date: **1 March 2025**

Total Project cost: **€ 169.992.330**

EU Contribution: **€ 101.995.398**



Co-funded by the
European Union

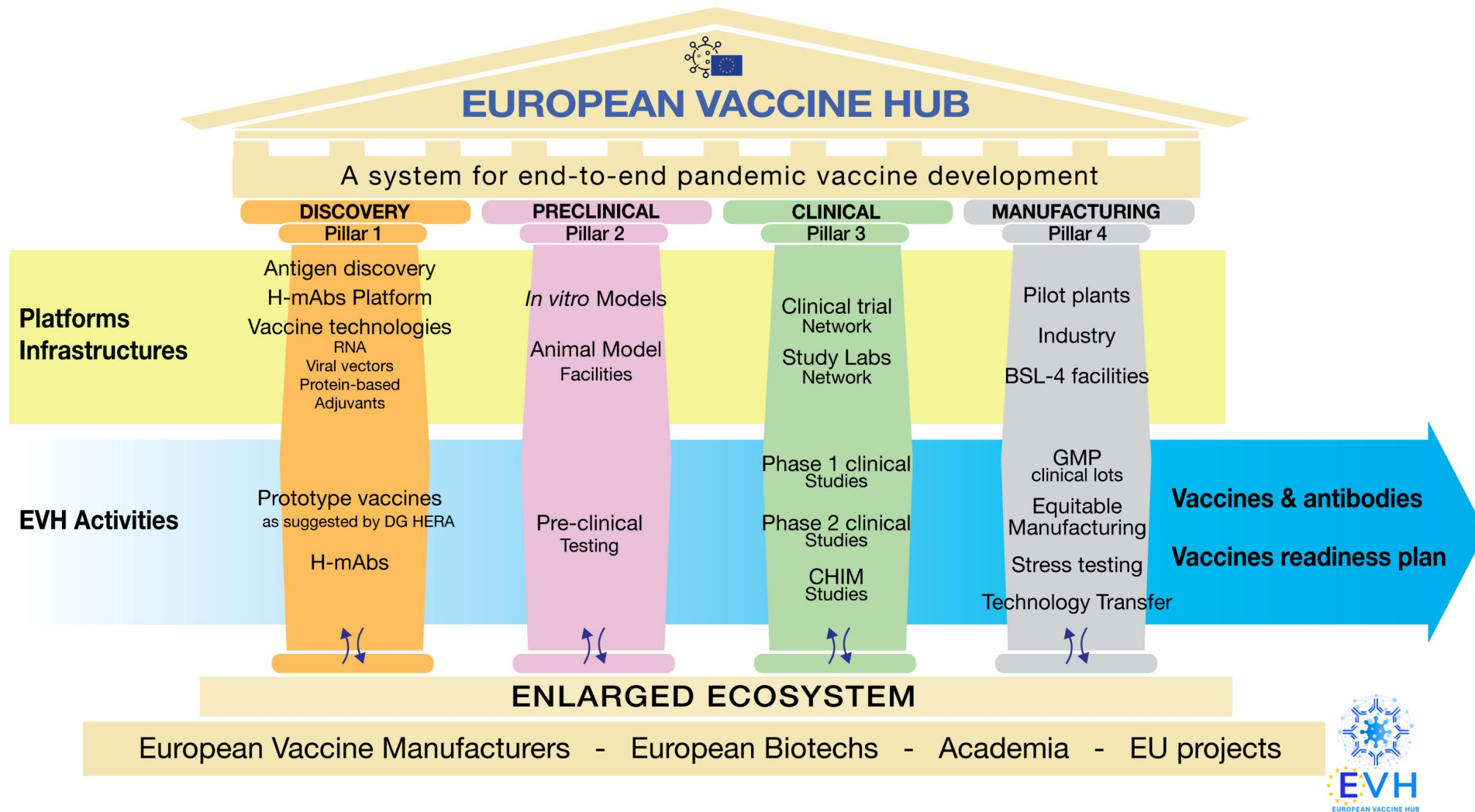
EVH Vision

- 1) **An Hub with permanent structure**, with 40% co-founding (National Institutes cofounded by their Member State) and **sustainable beyond the four years** funding of the present HERA call. **Agile management** structure able to make quick decisions to respond to emerging threats and pandemics.
- 2) An Hub **able to reach all European partners that can contribute** with a *technology, physical facilities, containment labs BSL-4, serology and immunology capacities, epidemiology networks, clinical trial infrastructures, pilot plants, industrial manufacturing facilities and technologies* etc).

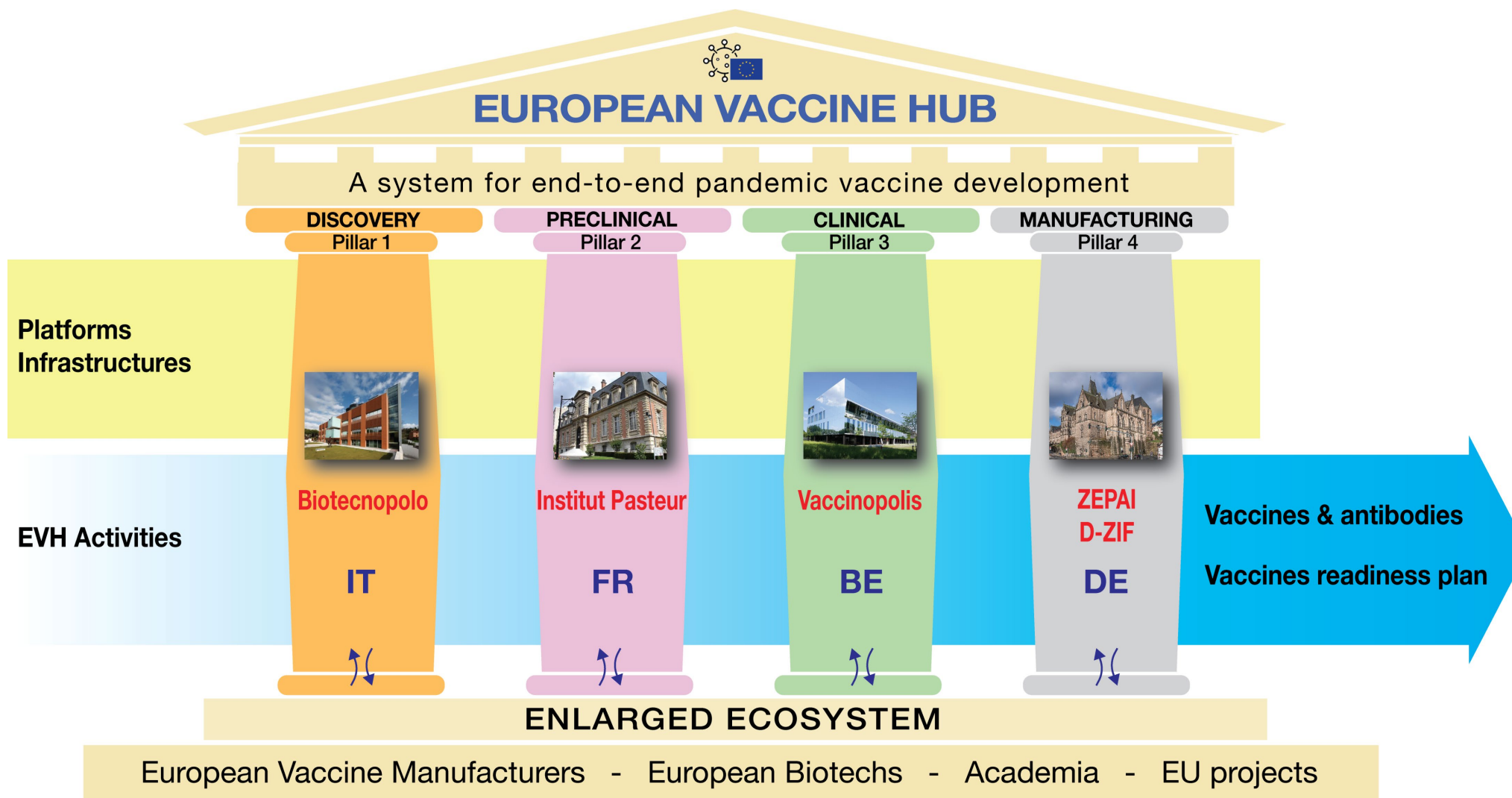
Meeting the requirements described in point **1** requires an **Hub composed by few, key partners**.
Meeting the requirements of point **2** requires to **potentially include a very large number of partners**.
How can the hub be simple, agile and inclusive?

European Vaccine Hub (EVH)

Provide EU with a self sustainable and independent ability to discover, develop and manufacture vaccines and monoclonal antibodies against infectious diseases of epidemic and pandemic potential

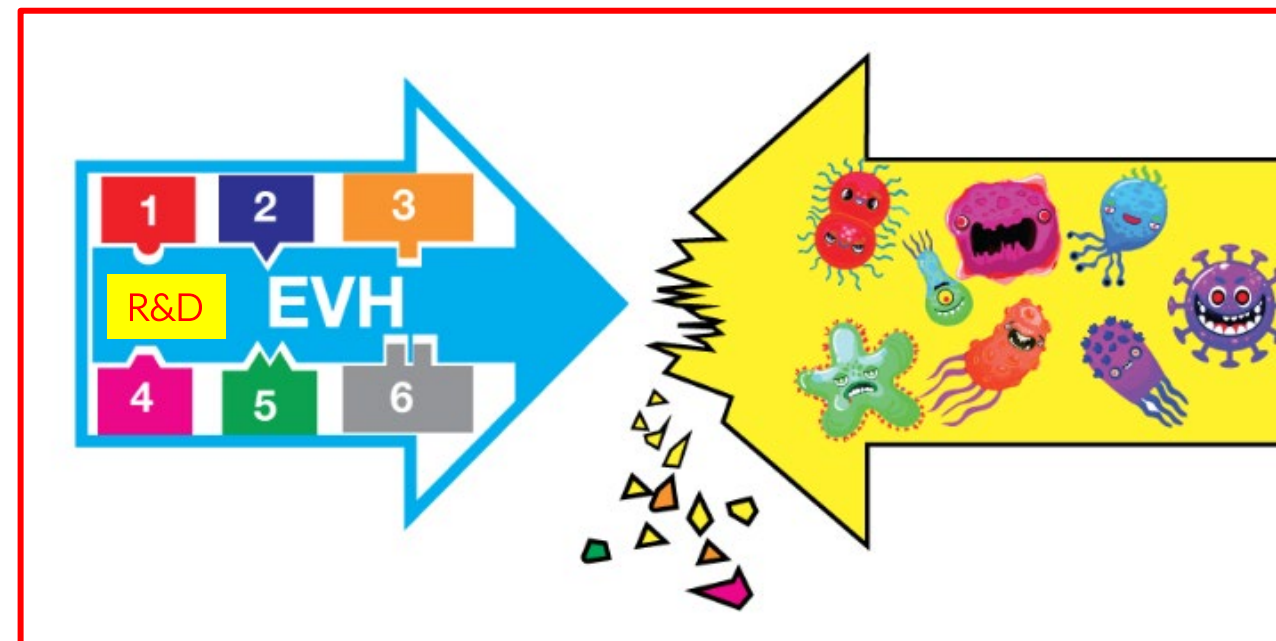
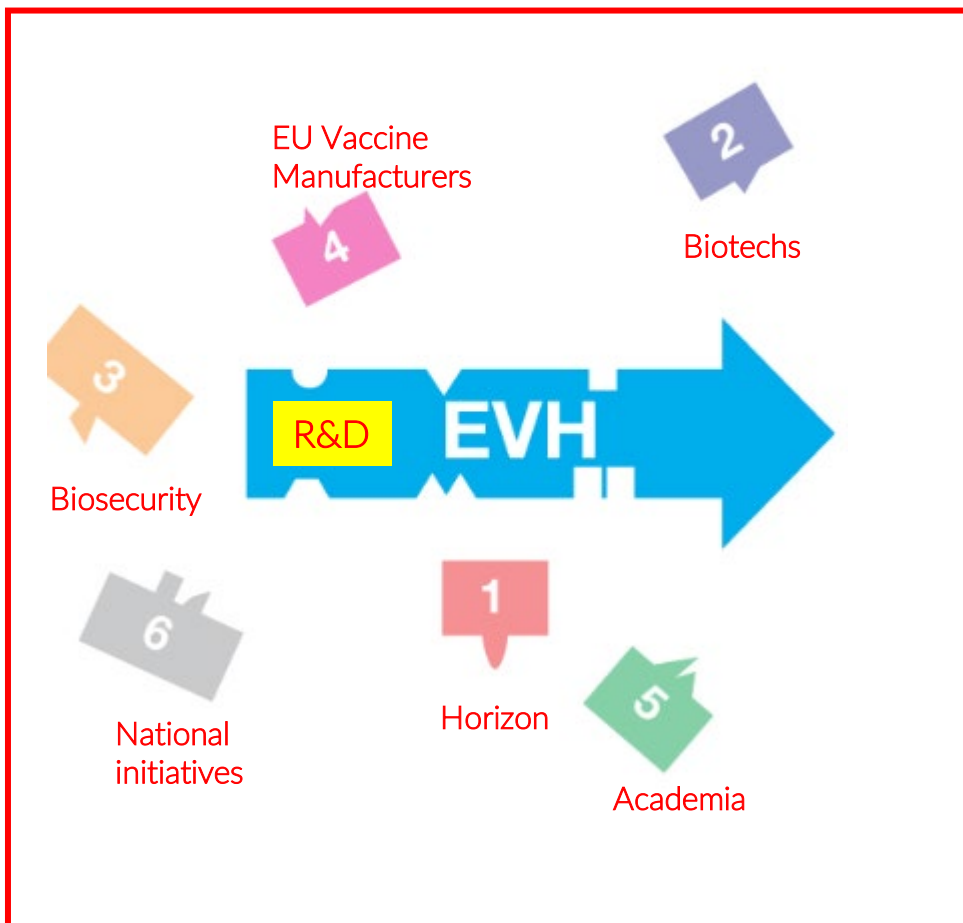


European Vaccine Hub (EVH)



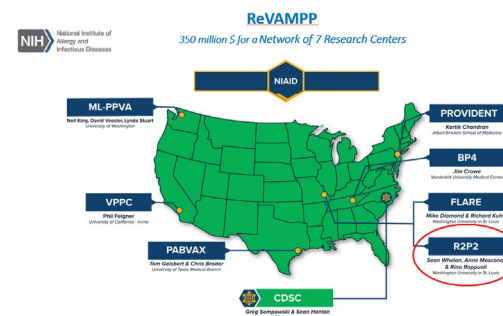
One strong Europe United by EVH

to fight pandemics and emerging infections



A Global Alliance

to fight emerging infections and pandemics



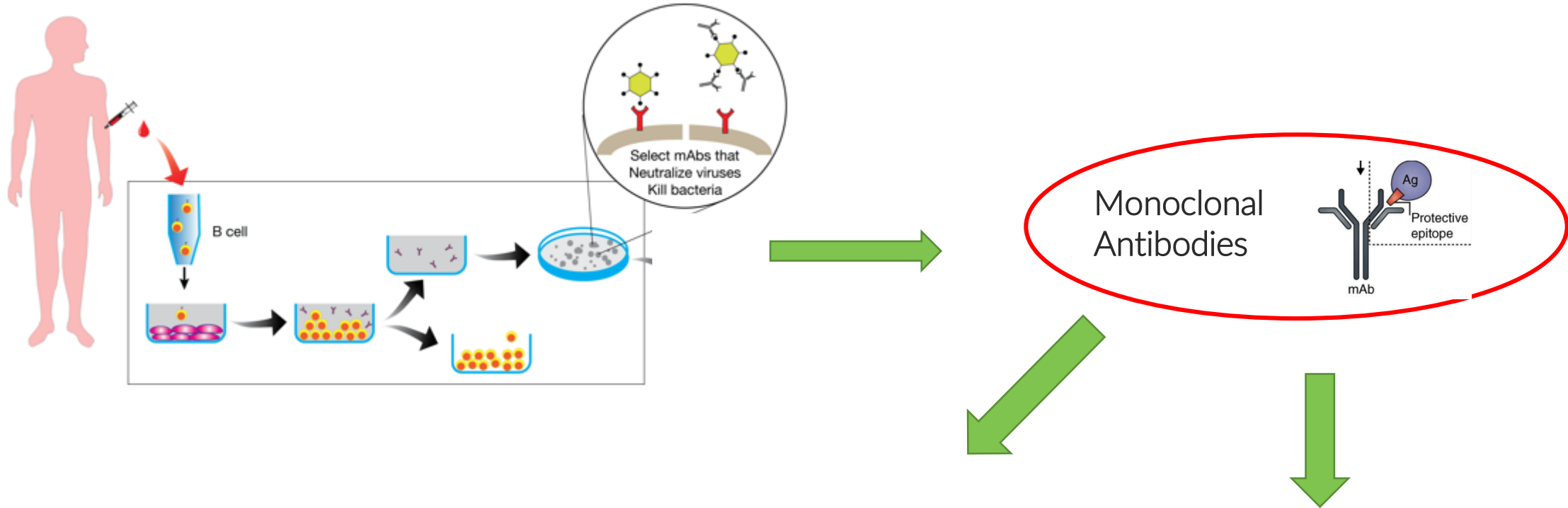
WHO,
PREPARE
SCARDA,
BARDA



IAVI, CARBX,
BMGF, Wellcome
Trust, IVI
AFRICA,

Reverse Vaccinology 2.0

Genomics enhanced by Immunology and Artificial Intelligence



Prototype Vaccines
discovery of protective antigens
antigen structure
structure-based design

Monoclonal Antibodies
for prevention and
therapy

Reverse vaccinology 2.0: Human immunology instructs vaccine antigen design

Rino Rappuoli, Matthew J. Bottomley, Ugo D'Oro, Oretta Finco, and Ennio De Gregorio

J Exp Med (2016) 213 (4): 469–481.

Klebsiella pneumoniae K64 hypervirulent and pan-resistant

Protection from 100% lethal sepsis

Nature October 30th 2025

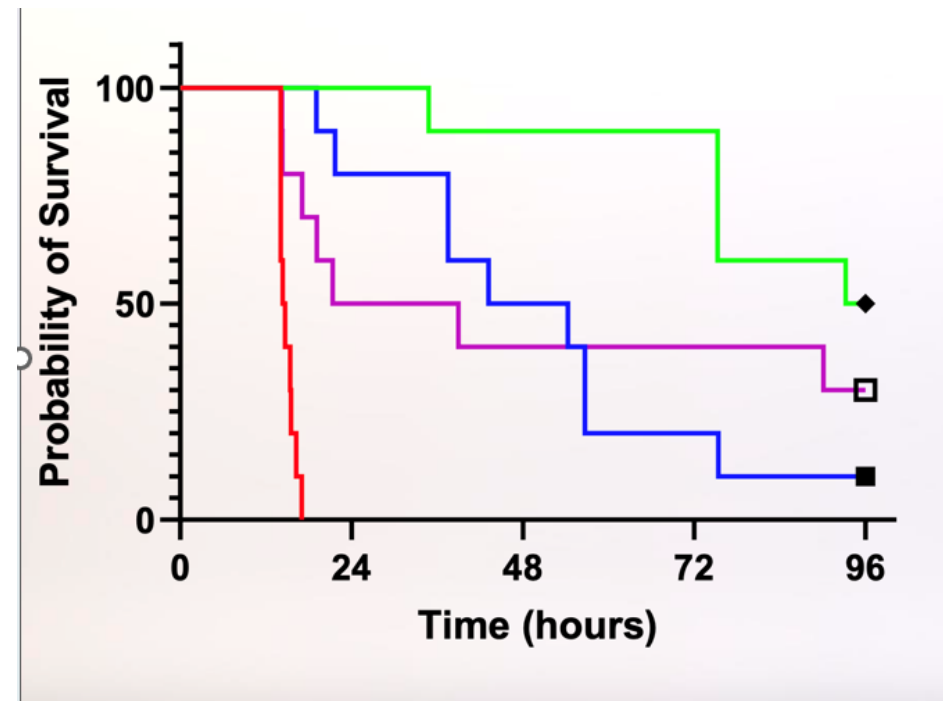
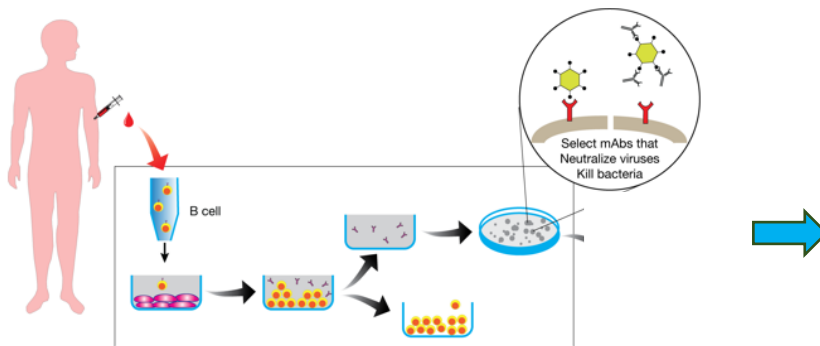
KL64 genomes till December 2010 (n=84)



KL64 genomes till December 2016 (n=822)



KL64 genomes till December 2022 (n=3111)



The International Journal of Science | 30 October 2025

Article
Monoclonal antibodies protect against pandrug-resistant *Klebsiella pneumoniae*

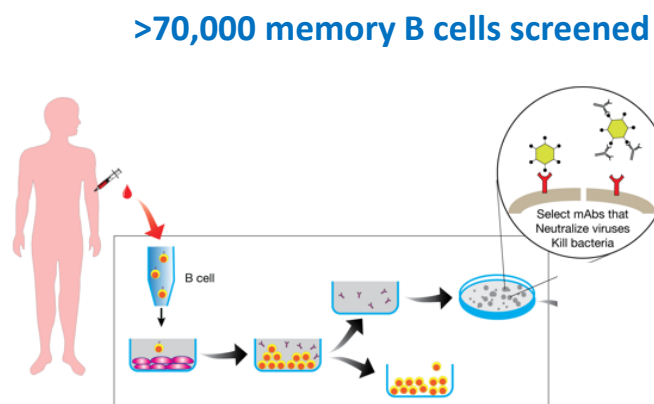
<https://doi.org/10.1038/s41596-025-06391-3>
 Received: 24 June 2024
 Accepted: 6 July 2025
 Published online: 01 October 2025
 Check for updates

Emanuele Roscillo¹, Vittoria Zucconi Galili Fonseca^{1,2}, Soraya Soledad Bosch^{1,3}, Ida Paciello¹, Giuseppe Maccari¹, Giulia Cardinali^{1,3}, Giampiero Batani¹, Samuele Stazzoni¹, Olusy Ylase¹, Cosira Giordano¹, Shen Yuwei¹, Laura Caspocchia¹, Dario Cardamone¹, Matteo Sidoti¹, Marco Trisoli¹, Noreni Mangano¹, Chiara Magagnoli¹, Concetta De Santis¹, Annalisa Ciabattini¹, Linda Cerofolini¹, Marco Fraga¹, Danilo Licastro¹, Kelly Wyres^{1,4}, Laurent Dortet^{1,5}, Simona Barmini¹, David P. Nicolau¹, Francesco Menichetti¹, Marco Falcomi¹, Kamelia Abdelrazek¹, Claudia Tala^{1,6}, Anna Kabanova^{1,7,8}, Rino Rappuoli^{1,9,10}

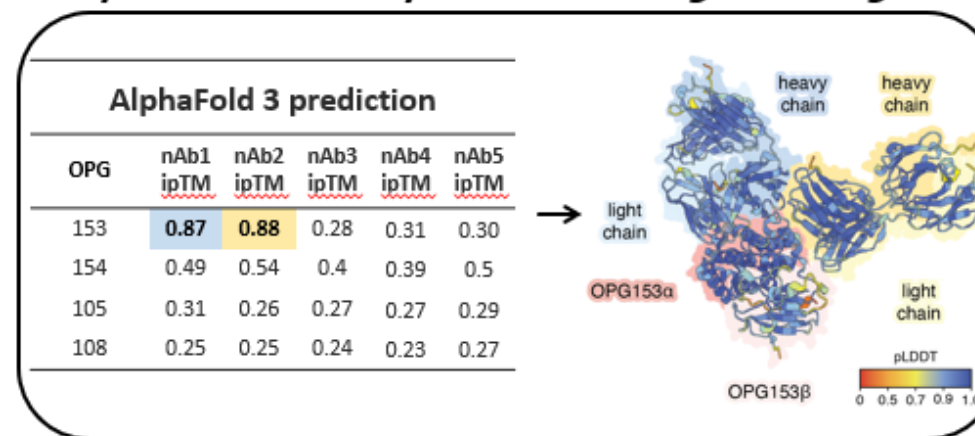


Monkeypox a new pan-pox protective antigen discovered by Reverse Vaccinology 3.0

Science Translational Medicine accepted for publication



Alpha fold 3-based prediction of targeted antigens



Cryo-EM confirmed AI prediction

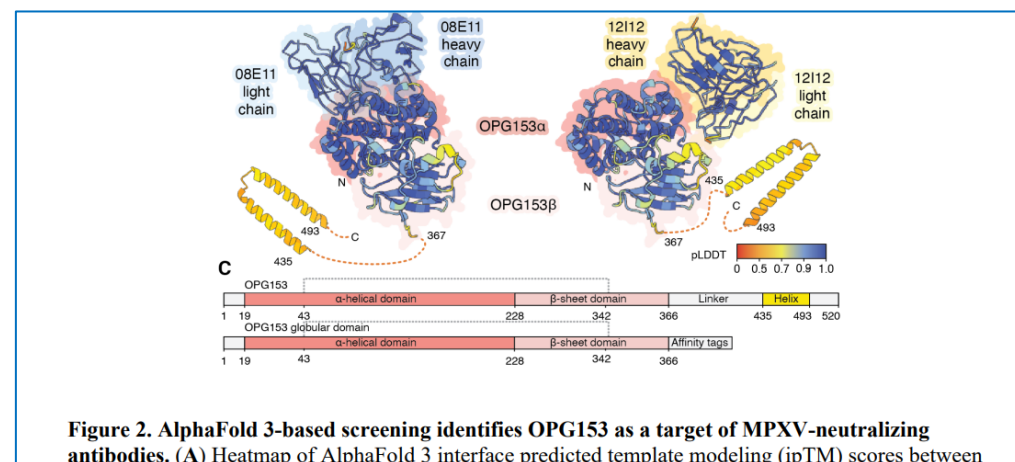


Figure 2. AlphaFold 3-based screening identifies OPG153 as a target of MPXV-neutralizing antibodies. (A) Heatmap of AlphaFold 3 interface predicted template modeling (ipTM) scores between

THANK YOU