

Diversifying the TB Vaccine pipeline

 **7TH GLOBAL FORUM
ON TB VACCINES** | 8-10 October 2024
Rio de Janeiro, Brazil
Driving innovation from discovery to access

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8 October 2024



From discovery to access

Vaccine development pathway

Vaccine implementation pathway

HEALTH
IMPACT

Discovery

Preclinical

Clinical; FIH,
Phase 2, 3

Registration

- Demand
- Commercial attractiveness
- Delivery requirements
- Donor funding
- Legal framework for global access
- National policy development pathway

Proof-of-
Efficacy

Registration

NITAG*
review

Country
introduction

Phase
IV/effectiveness

- Global policy development pathway

Proof-of-
Efficacy

Registration

WHO policy
rec & PQ

Vaccine
financing

Vaccine
procurement

NITAG review

Country
introduction

Phase IV
studies

- Local access (logistics, cold chain)
- Vaccine acceptance

TB Vaccine Pipeline

Vaccine candidates under clinical development

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Platform

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Primary candidate indication

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Information reported by vaccine sponsors or found in clinical trial registries or other public sources

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Last update: 2 September 2024



Diversifying the pipeline; why?

Preferred Product Characteristics

Prevention of TB disease

Neonates and infants

> 80% efficacy vs baseline / better than BCG

>10 years protection after primary immunization

Prevention of active pulmonary TB disease

Adults and adolescents

> 50% efficacy preventing confirmed pulmonary TB

>10 years protection after primary immunization

Safety and reactogenicity profile favourable

Minimal number of doses

No interference with other vaccines recommended for same target population

Meets WHO criteria for vaccine presentation, packaging, thermostability, formulation and disposal

Cost of goods should not be a barrier to access in LMICs

Diversifying the pipeline; why?

Preferred Product Characteristics

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Neonates and infants

> 80% efficacy vs baseline / better than
>10 years protection after

Prevention of active pulmonary TB disease
Adults and adolescents

> 50% efficacy prevented
>10 years protection after

Cold chain independent

Reducing cost

Improving vaccine efficacy

Preventing Infection, Disease, Recurrence

Addressing target groups; safety and immunogenicity

Improve longevity of protection



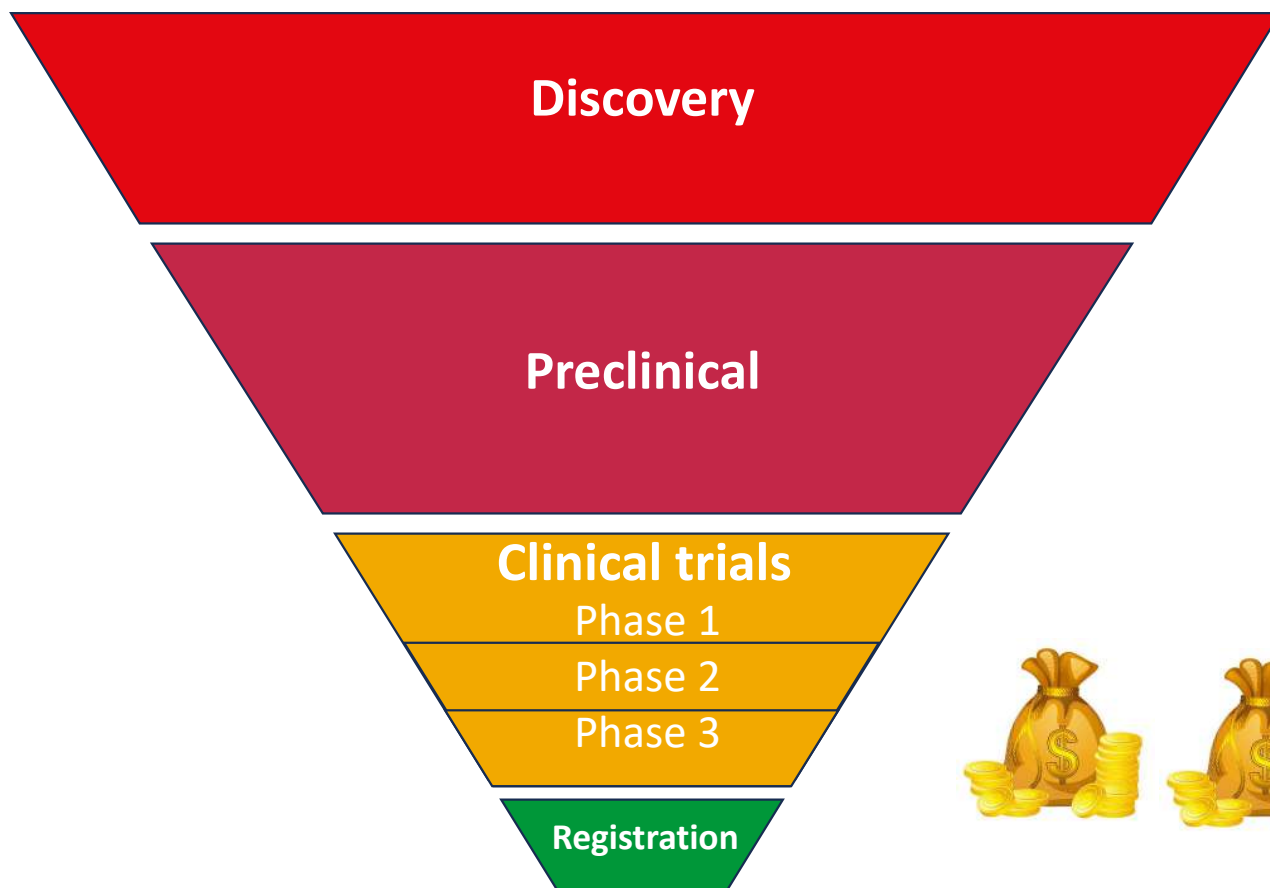
No interference

Meet...

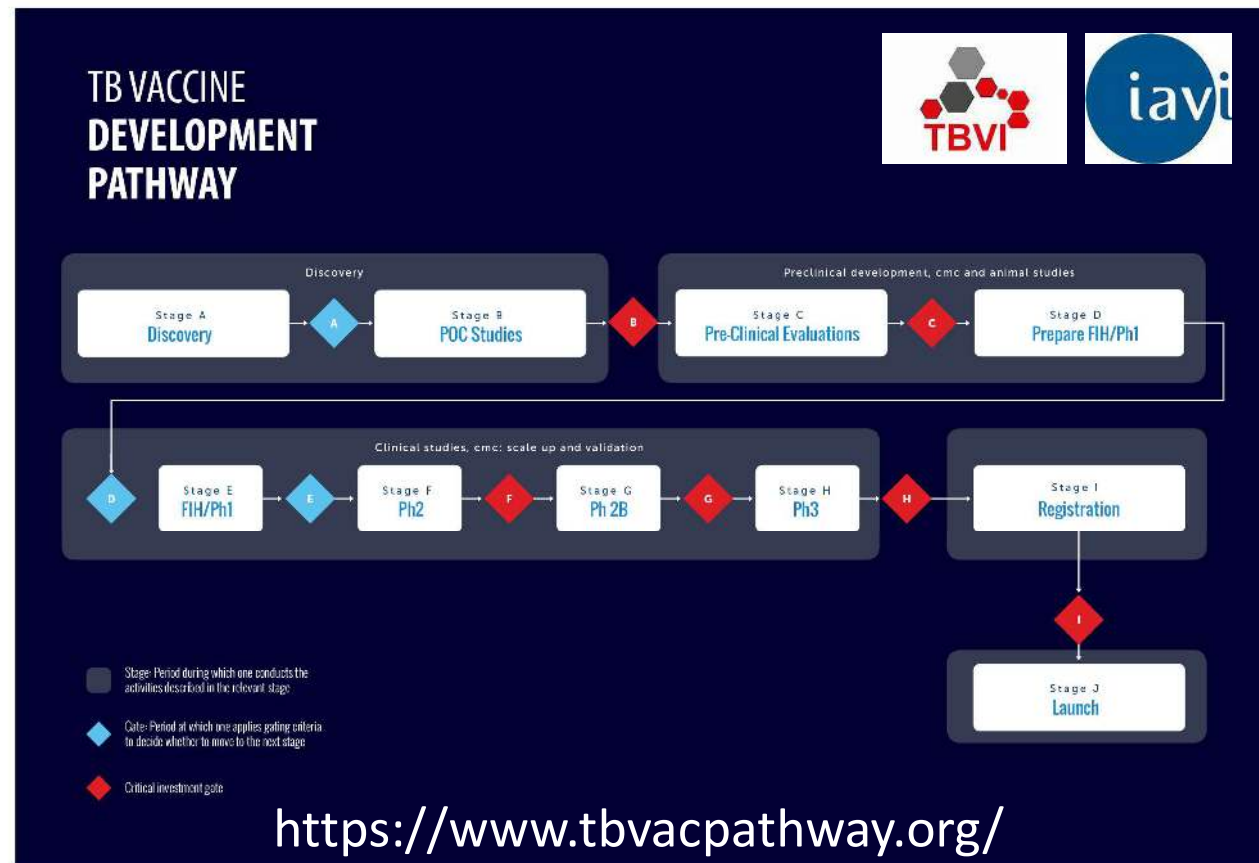
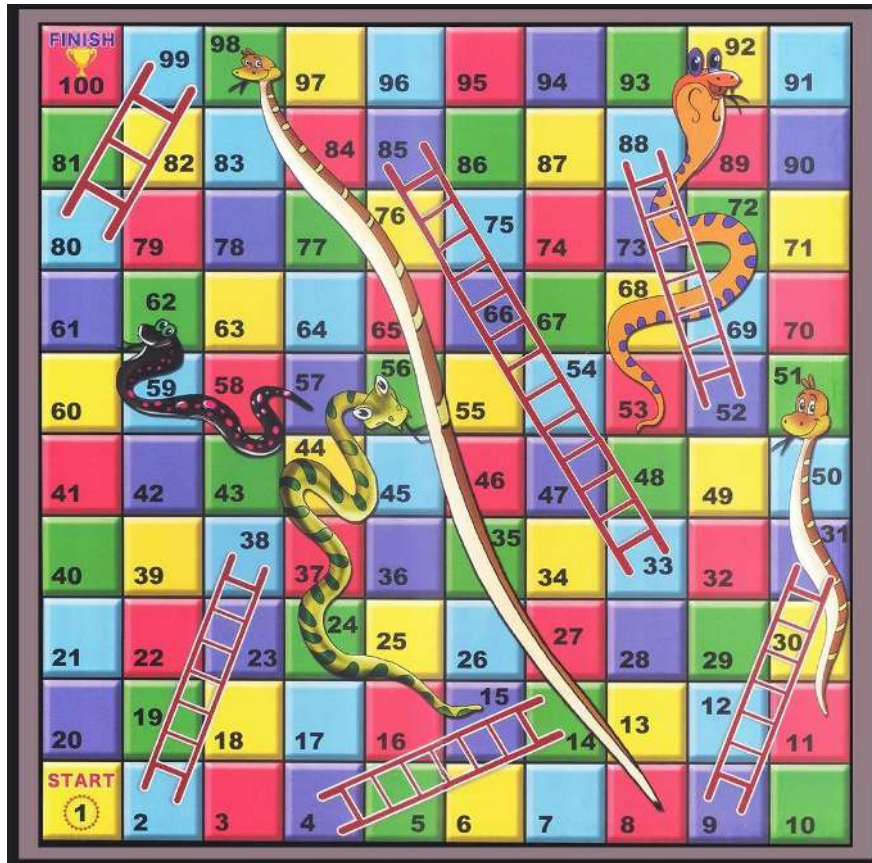
relation
on and disposal

Derisking vaccine development; fast fail

Diversification

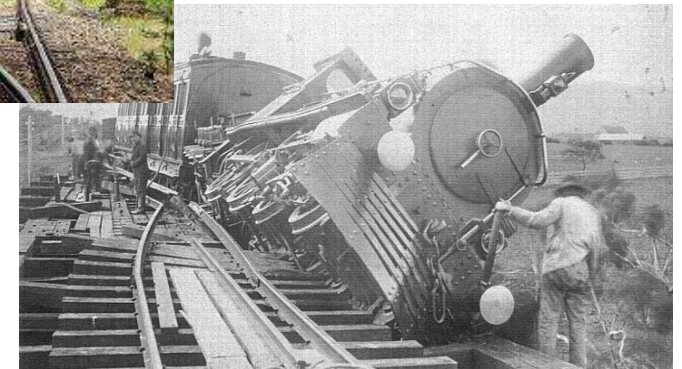
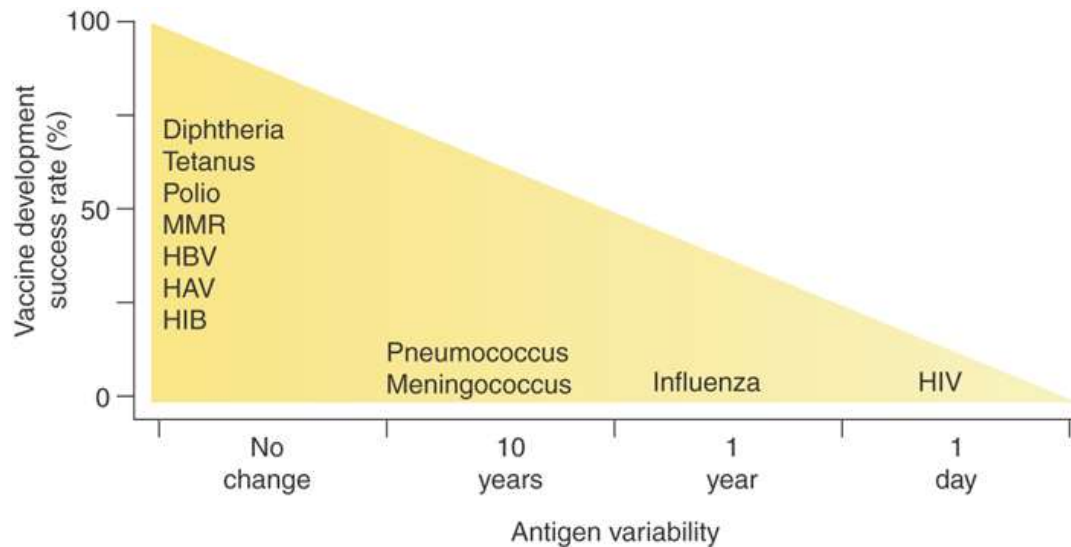


Derisking vaccine development; asking the right questions



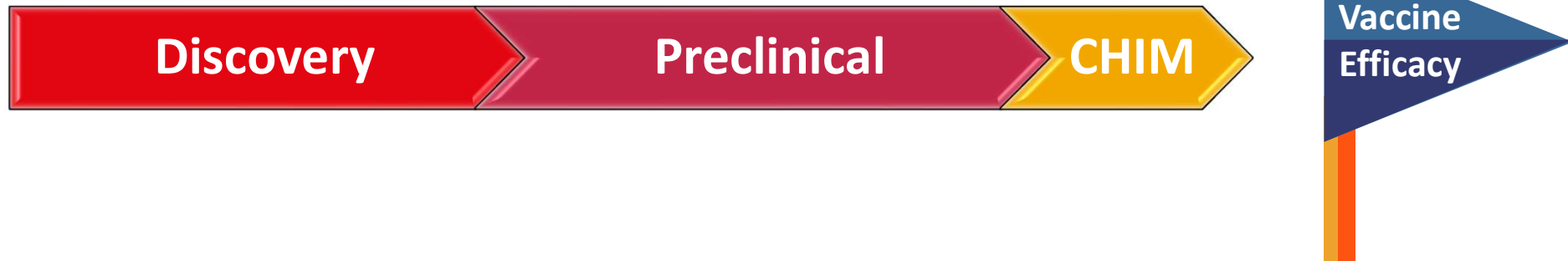
Not all vaccines work equally well

Pathogen-survival-kit:
disguise, hide-and-seek, sabotage,...



From: Rappuoli, *Nature Biotechnol.* 25:1361, dec 2007

Vaccine design and evaluation



TB vaccine design

Antigens
Adjuvants
Administration routes
Platforms

TB vaccine evaluation

TB vaccine design: Antigens

Culture filtrate; secreted proteins
Serological screening
Genome wide in silico approach
T-cell expression cloning / single cell T cell receptor sequencing
Immunoepitidomics

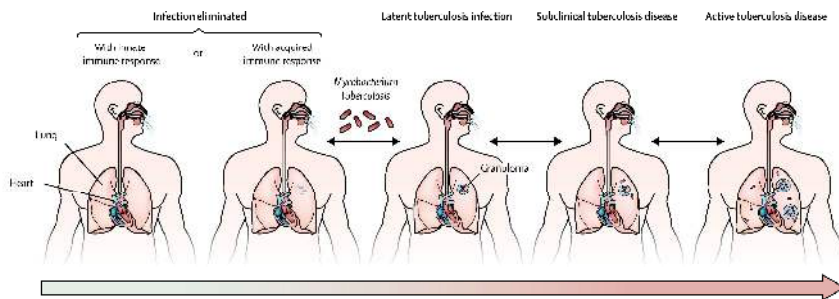


Stages of TB;

Active disease antigens

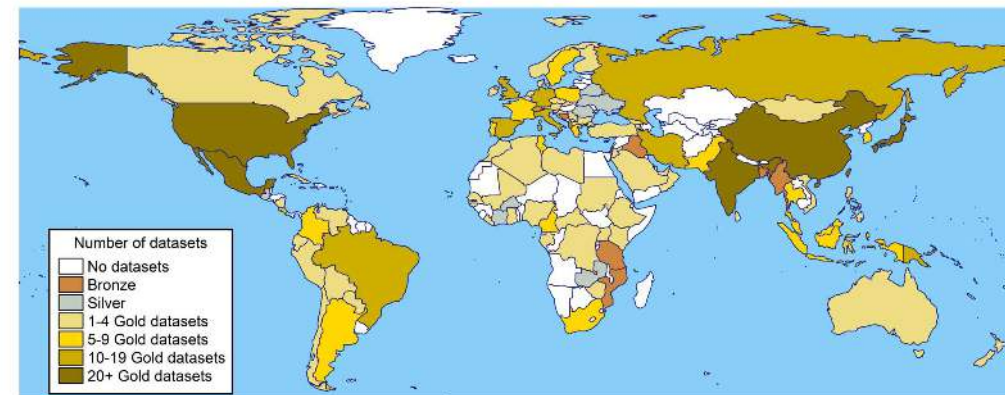
Latency antigens

Resuscitation-promoting factors



DOI: [10.1016/S0140-6736\(19\)30308-3](https://doi.org/10.1016/S0140-6736(19)30308-3)

Populations



<https://allelefrequencies.net/>

Adjuvants - enhancing vaccine efficacy

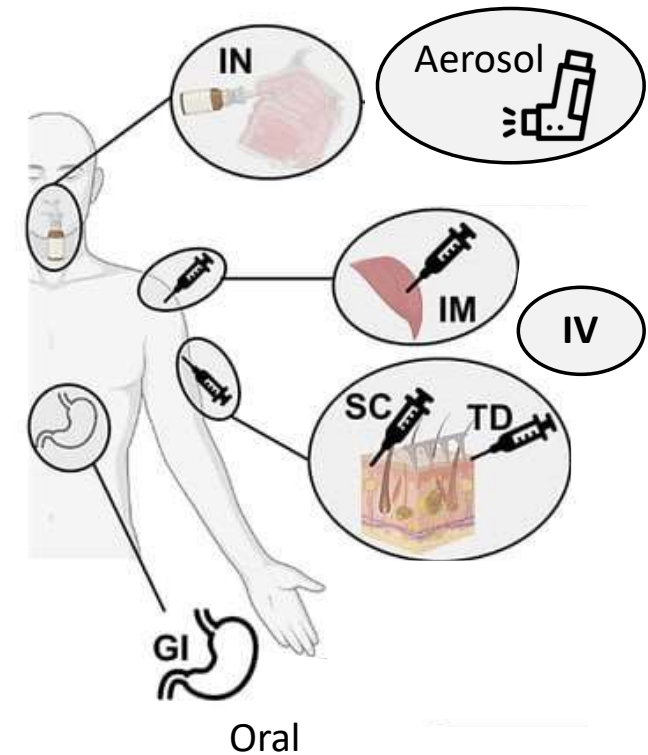
Activation of innate immunity:

- Danger signal
- Direct ligand for pathogen recognition receptor
- Depot (enhanced retention & sustained release)

Leading to:

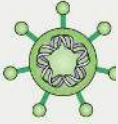

- Immune targeting (Lymph node, DC activation)
- Immune polarization (T helper cell, antibodies)
- Sustained adaptive immune memory


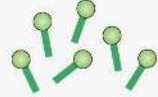
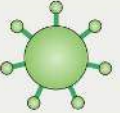
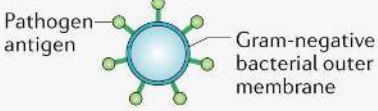
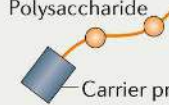
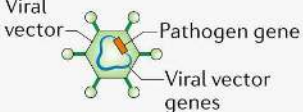

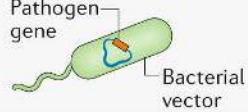
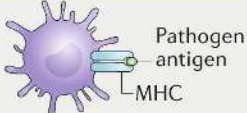
Administration routes





Platforms

Type of vaccine	Licensed vaccines using this technology	First introduced
Live attenuated (weakened or inactivated)	 Measles, mumps, rubella, yellow fever, influenza, oral polio, typhoid, Japanese encephalitis, rotavirus, BCG, varicella zoster	1798 (smallpox)
Killed whole organism	 Whole-cell pertussis, polio, influenza, Japanese encephalitis, hepatitis A, rabies	1896 (typhoid)

Toxoid		Diphtheria, tetanus	1923 (diphtheria)
Subunit (purified protein, recombinant protein, polysaccharide, peptide)		Pertussis, influenza, hepatitis B, meningococcal, pneumococcal, typhoid, hepatitis A	1970 (anthrax)
Virus-like particle		Human papillomavirus	1986 (hepatitis B)
Outer membrane vesicle		Group B meningococcal	1987 (group B meningococcal)
Protein-polysaccharide conjugate		<i>Haemophilus influenzae</i> type B, pneumococcal, meningococcal, typhoid	1987 (<i>H. influenzae</i> type b)
Viral vectored		Ebola SARS-CoV-2	2019 (Ebola)
Nucleic acid vaccine		SARS-CoV-2	2020 (SARS-CoV-2)
Bacterial vectored		Experimental	–
Antigen-presenting cell		Experimental	–

From: Pollard, A.J., Bijker, E.M. *Nat Rev Immunol* **21**, 83–100 (2021). <https://doi.org/10.1038/s41577-020-00479-7>

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Vaccine evaluation



Several images from flaticon.com

CORRELATES that predict Vaccine Efficacy in the target population

Current diversification of the pipeline



Panel discussions (Wednesday 17:00)

PD1: Defining correlates of protection

PD2: feeding the pipeline: New vaccines and platforms

Presentations in plenary 5 (Thursday 9:00)

Innovative approaches to TB vaccine development

Oral abstract session 3 (Thursday 11:30)

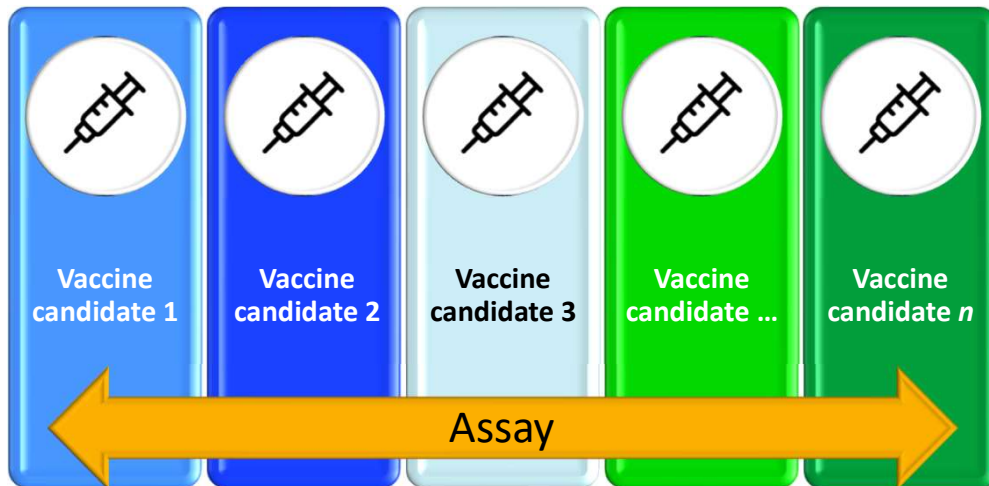
Improved formulation and delivery platforms, preclinical research



Moving towards the future

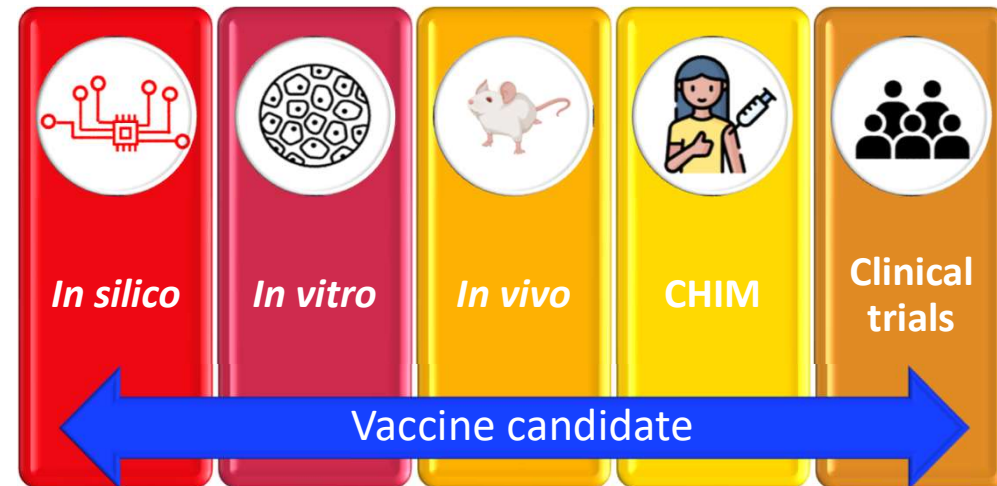


<https://newtbvaccines.org/tb-vaccine-pipeline-form/>



Images from flaticon.com

Head-to-head testing



Feedback



Let's take the next steps!



<https://newtbvaccines.org/tb-vaccine-pipeline-form/>

<https://www.tbvacpathway.org/>

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