WHO/MPP mRNA Technology Transfer Programme
Follow-up regional meeting in South-East Asia
Establishing R&D consortia

Establishing an mRNA R&D Consortium for Dengue

Proposal by International Vaccine Institute (IVI)

International Vaccine Institute

Goal and objectives for mRNA dengue vaccine development consortium

Goal: To establish research consortium to advance mRNA dengue vaccine development up to proof of concept

A consortium on dengue mRNA vaccine product development to be led by the International Vaccine Institute (IVI), in collaboration with Chula VRC, Chulalongkorn University and mRNA manufacturing partners from Bangladesh and Indonesia.

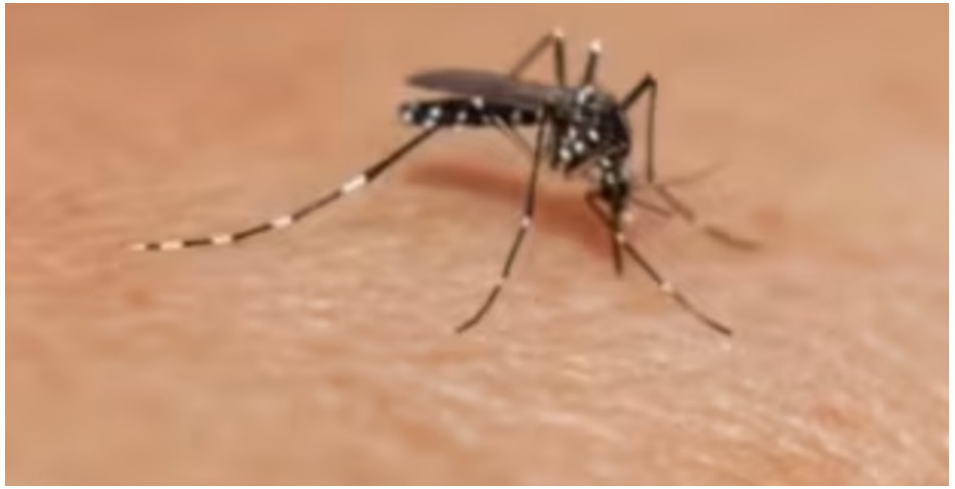
Objectives:

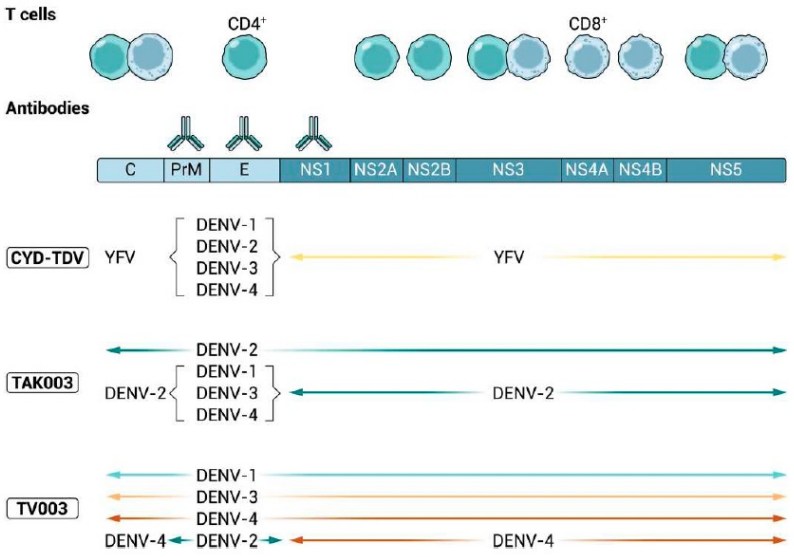
1) Review key scientific and technical considerations for mRNA vaccine development against dengue
2) Discuss key roles and responsibilities of partners engaged in proposed consortium to advance mRNA vaccine development up to proof of concept early phase clinical development
3) Discuss terms of MoU that will form the basis of the R&D consortium
4) Discuss investment opportunities to support regional R&D collaboration

CAVEAT: These are notional and have not been discussed with partners. These are subject to change.

Challenges

- 3 vaccines, two WHO PQ'd, a 3d on the way (1 not usable, 1 with partial coverage, 1 with unknown D3 and D4 coverage)
- Existence of 4 DENV types, each capable of causing infections, disease, and death, each with differences that may be distinctive and quantitative
- No validated immune CoP
- Animal models do not fully mimic human dengue infection or disease
- Immunological assays are unable to precisely define DENV type-specific (homotypic) immune responses
- Requirement for very large efficacy trials to demonstrate benefit across diverse populations and clinical endpoints – CHIM, effectiveness (maybe this is a separate issue that requires funding)
- Procurement, implementation insight





Timelines and Budget proposal

Project Timeline																					
Project name	mRNA dengue vaccine development	Year 1				Year 2				Year 3				Year 4				Year 5			
		2024		2025				2026				2027				2028				2029	
Version #	1.0	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2
Version date	18 March 2024																				
Work area 1:	Preclinical development																				
Work area 2:	Technology transfer and batch manufacturing																				
Work area 3:	First in Human (FIH) clinical trial																				
Work area 4:	Phase 2 clinical trial conduct (out of scope)																				

Functional Domain	Estimated budget (USD)*
Process development	$0.3M
Pre-clinical	$0.2M
Tech transfer	$0.8M
Tox study	$0.8M
Manufacturing	$1.5M
Phase I clinical trial (incl. CRO)	$2.5M
Clinical immunology assay development	$0.5M
Consortium management and coordination	$0.5M
Budget total (est.)	$7.1M

*Budget assumption is only up to early clinical trial (phase 1).

Assumptions considered for initial plan

- Preclinical & process development will be in parallel with manufacturing partner selection process
- Produce batches for tox and phase I clinical trial
- Tox and stability results will be submitted to the country NRA where a clinical trial is conducted, once available
- Preparation of FIH will be proceeded in parallel with batch production and tox & stability studies.
- Phase I clinical trial will be 80 adults with 2 doses

Gantt Chart for mRNA dengue vaccine development consortium [1]

Project Gantt Chart																									
Projet name	***mRNA dengue vaccine development***	Year 1				Year 2				Year 3				Year 4				Year 5							
		2024		2025				2026				2027				2028				2029			
Version #	*1.0*	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2
Version date	*18 March 2024*																								
Work area 1:	**Preclinical development**																								
Activity 1.1: Preclinical development																									
1.1.1	Lead candidate(s) identified (e.g. formulation of 4 valent or 5 valent)																								
1.1.2	Safety and immunogenicity and challenge/efficacy assessed in animal models																								
Activity 1.2: Process development																									
1.2.1	Process optimization																								
1.2.2	QC assay development																								
1.2.3	SOP, tech transfer packaging documents preparation																								
Milestone 1.1	Preclinical data in animal model readiness																								
Milestone 1.2	Process development and optimization completion for tech transfer																								
Work area 2:	**Technology transfer and batch manufacturing**																								
Activity 2.1: Partner selection																									
2.1.1	Partner selection plan in place																								
2.1.2	Due diligence																								
2.1.3	Selection of manufacturing partners																								
Activity 2.2: Technology transfer to manufacturing partners																									
2.2.1	Technology Transfer Agreement in place																								
2.2.2	Technology transfer to the selected manufacturing partner																								
Activity 2.3: Manufacturing for tox study and clinical lot for phase 1																									
2.3.1	Batch manufacturing (GLP or GMP by CDMO)																								
2.3.2	Conduct of toxicology study																								
2.3.3	Stability testing, etc.																								
Activity 2.4: Global Access Agreement																									
2.4.1	Global Access Agreement in place																								
2.4.2	Preliminary COGs analysis																								
Milestone 2.1	Partner selected for batch manufacturing																								
Milestone 2.2	Tech transfer agreement signed and completion of tech transfer																								
Milestone 2.3	Tox data readiness																								
Milestone 2.4	GAA signed																								

Gantt Chart for mRNA dengue vaccine development consortium [2]

Project Gantt Chart																							
Projet name	***mRNA dengue vaccine development***	Year 1				Year 2				Year 3				Year 4				Year 5					
		2024		2025				2026				2027				2028				2029			
Version #	*1.0*	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2		
Version date	*18 March 2024*																						
Work area 3:	**First in Human (FIH) clinical trial**																						
Activity 3.1: Pre-activity for FIH																							
3.1.1	Finalization of clinical development plan																						
3.1.2	Study site selection																						
3.1.3	Pre-IND meeting with NRA																						
3.1.4	IND submission and approval (incl. EC approval)																						
Activity 3.2: Conduct of FIH																							
3.2.1	Study conduct																						
3.2.2	Data analysis and dissemination																						
Milestone 3.1	Clinical readiness for site selection and initiation	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Milestone 3.2	Clinical POC (safety and immunogenicity) readiness	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Work area 4:	**Phase 2 clinical trial conduct**																						
Activity 4.1: Pre-activity for phase 2 clinical trial																							
4.1.1	Study site selection																						
4.1.2	IND submission and approval (incl. EC approval)																						
Activity 4.2: Phase 2 clinical trial conduct																							
4.2.1	Study conduct																						
4.2.2	Data analysis and dissemination																						
Milestone 4.1	Clinical readiness for site selection and initiation	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Milestone 4.2	Efficacy POC readiness	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

List of stakeholders, R&R, and engagement plan

Key product development areas	Potential stakeholders	Expected R&R
Preclinical & process development	Chula VRC	Perform pre-clinical and process development of the mRNA dengue vaccine candidate
Technology transfer	?IVI, Hilleman	Transfer the technology of mRNA dengue vaccine to the selected manufacturing partner(s)
Global access		Subaward terms / CEPI / Gates
Manufacturing	BioFarma, Incepta, Thai?	Produce batch for toxicology study and early phase clinical trial lot
Toxicology		Conduct toxicology study as required by the country NRA of the manufacturer and WHO PQ
Regulatory	Companies / IVI support	Responsible for the regulatory affairs for a conduct of clinical trial
Clinical trial conduct	Chula, IVI, NVI, others?	Lead and conduct the clinical trial as performing selection & managing study site(s) and CRO, data collection, analysis and dissemination
Clinical immunology assay	IVI?	Develop clinical immunology assay and perform the immunology testing with phase 1 human samples
Consortium partner management	IVI	Coordinate and manage the consortium efforts among the partners

Next steps

1. MoU (forming the basis of the consortium)
2. Funding opportunities (preparation of consortium proposal)
3. Consortium agreement in place with partners (defining Roles and Responsibilities, scope of work, timeline, budget, etc.)
4. CDP/IPDP (Clinical Development Plan / Integrated PDP)
5. Agreement with manufacturing partners (tech & know-how transfer, IP, timeline, etc.)
6. Regulatory strategy / pathway
7. Establish Joint Steering Committee (JSC) & Technical Advisory Committee
    - Governance structure setup for the consortium
    - Review the progress of the collaborative activities, milestones, results
    - Facilitating communications and decision-making process between the partners

Science

- Qualification of assays
- Work on CoP (or a cellular composite testable hypothesis)
- Cost effectiveness
- Effectiveness
- National / Regional KOLs and stakeholders

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