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WHO/MPP mRNA Technology Transfer Programme
Regional meeting in South-East Asia

Shangri-la hotel, *Bangkok, Kingdom of Thailand*
31 Oct-1 Nov 2023

Executive Summary

In the context of the mRNA technology transfer Programme, The World Health Organization (WHO) and the Medicines Patent Pool (MPP) convened a meeting in Bangkok, Kingdom of Thailand, with the regional partners of the Programme (Bangladesh, India, Indonesia, Vietnam) and key research and development (R&D) stakeholders from the R&D and manufacturing ecosystem of the SEARO and WPRO regions, including IVI (Republic of Korea) , A*STAR, Hilleman Labs, and NUS (Singapore) and Chulalongkorn University. Other partners, including the mRNA technology transfer hub Afrigen, and academic groups, were also invited.

The primary objective of this meeting was to promote collaboration among the stakeholders in the region to advance the development of novel mRNA-based products, in order to sustain the regional mRNA manufacturing capacity that is being built. Discussions were focused on mRNA product development against four infectious diseases of public health importance the region: dengue, malaria caused by *plasmodium vivax* (P. vivax), hand-food-and-mouth disease (HFMD), and therapeutic vaccines against human papillomavirus (HPV). These disease topics had been selected as priority targets by the regional manufacturers. In addition, key innovations and research questions around technological improvements to existing mRNA technology to make it adapted to the disease target were discussed as well as reducing cost of goods (COGS), improving risk/benefit profile, enhancing stability, and ensuring freedom to operate (FTO).

Key considerations for mRNA dengue vaccine development –

Dengue will continue to pose significant public health burden and better dengue vaccines are needed. Dengue poses a significant public health burden in endemic countries, particularly in South-East Asia, and is anticipated to increase further both in terms of incidence and geographic expansion. Dengue virus has four serotypes which can cause severe disease in all age groups and disease incidence generally peaks between 5 and 14 years old, typically upon second exposure with a heterotypic serotype. Antibody-dependent enhancement (ADE) is the major underlying mechanism leading to increased severity in secondary dengue infection. The risk of ADE is thought to be serotype-specific and could also be induced by closely related flaviviruses such as Zika. Further exposure to the virus is generally associated with less risk of severe disease.

There are currently two licensed dengue vaccines (Dengvaxia™ and Qdenga™) and a candidate vaccine (TV003) is currently in late-stage clinical trial. These vaccines are all based on tetravalent live-attenuated platforms, which differ in their backbone and extent of chimerization, and which translate into differential overall and serotype-specific vaccine performance. These observed differences may arise from vaccine interferences which results in imbalanced serotype-specific immune responses.

Current vaccine approaches do not fully meet current public health needs: Dengvaxia™ was shown to put seronegative children at higher risk of severe dengue and is not currently used and the potential accrued risk of enhanced disease due to serotypes 3 and 4 in seronegative vaccinated children cannot be currently ruled out with the use of Qdenga™ and TV003. For this reason, the WHO SAGE[1] recommended in September 2023 that Qdenga™ be considered for introduction in settings with high dengue disease burden and high transmission intensity to maximize the public health impact and minimize any potential risk in seronegative persons. Additional clinical data from TV003 as well as post-marketing data from Qdenga™ are expected in years to come to better inform current policy recommendations and to provide further insights on our understanding of correlates of protection and correlates of disease enhancement, which would significantly accelerate the development of next-generation dengue vaccines.

An ideal dengue vaccine should provide long-lasting and balanced neutralizing antibody response against all four serotypes as well as robust T-cell response.

Neutralizing antibodies titers measured by plaque reduction neutralization tests (PRNT) has historically been the main driver in dengue vaccine development. However, data from clinical trials and cohort studies suggest that neutralizing antibodies titers measured by PRNT do not systematically correlate with protection, suggesting that other immune parameters may contribute to protection. Furthermore, it is thought that the level of immunity required for protection is also serotype-specific, which further challenges the interpretation on vaccine performance. Because PRNT assays measure neutralizing activity from a mixture of homotypic and heterotypic antibodies, additional assays, such as antibody depletion assays, should be also considered to better understand serotype-specific immunity.

Several cohort studies have highlighted a key role of T-cells in immune protection, particularly in controlling infection and clearing dengue virus, although its role needs to be better understood. Unlike with the spike protein of SARS-CoV-2, dengue immunodominant targets for neutralizing antibodies (primarily targeted at the pre-membrane and envelope proteins prM/E) do not significantly overlap with immunodominant dengue epitopes recognized by CD4 and CD8-T-cells. In particular, it was shown that Qdenga™ and TV003 primarily elicit CD8-T-cell response against conserved epitopes from the NS3 and NS5 region. It is therefore thought that a mRNA vaccine should ideally also encode for relevant non-

[1] Strategic Advisory Group of Experts

structural epitopes in addition to prM/E in order to elicit both robust humoral and cell-mediated immunity.

Preclinical research suggest that mRNA dengue vaccines is a feasible approach, though additional work is critically needed on antigen design and optimization.
Several groups of researchers designed mRNA constructs to explore novel approaches to try to overcome some of the limitations faced by live-attenuated tetravalent vaccines. One major advantage of using mRNA against flaviviruses is that mRNA encoding prM/E has been shown to induce and secrete virus-like particles (VLP) associated with protective immune response in animal models. The flexibility of mRNA further allows for tailored antigen design to enhance immunogenicity or eliminate undesired side effects. For instance, researchers from the University of Illinois at Chicago tested a monovalent mRNA construct encoding for prM/E proteins with fusion loop deletion, as antibodies targeting the highly conserved fusion loop epitope primary drive ADE. Researchers from the Institute Pasteur of Shanghai tested different monovalent mRNA constructs using different portions on the envelope protein. At the meeting, researchers from the Chulalongkorn university presented unpublished data from four mRNA monovalent constructs and one tetravalent mRNA construct encoding the prM/E tested in a immunocompromised AG129 mice model and now plan to incorporate non-structural proteins in their construct. Despite overall promising results, it is however worth noting that some of the key observations have limited reproducibility across the three laboratories studies, raising some concerns around the relevance of small animal models for dengue. Further work is needed to optimize each monovalent immunogen design and dosing in preparation of a tetravalent mRNA formulation.

Large-scale efficacy trials are still required to evaluate novel dengue vaccines.
In the absence of immunological correlates of protection and correlates of disease enhancement, WHO recommends conducting large-scale Phase 3 efficacy trials to test novel dengue vaccines. Such trials should be designed to capture disease incidence from all four serotypes, and up to five years to provide insights on long-term protection and allow the detection of potential enhanced disease-related signals. Blood sample collection at baseline is also required to allow the evaluation of vaccine performance by serostatus. Given the availability of at least one approved vaccine, conduct of placebo-controlled efficacy studies will be difficult, and non-inferiority trials would be massive. A potential route to efficacy testing would be to perform placebo-controlled trials in settings where current dengue vaccines are not introduced, such as settings with moderate dengue transmission, however due to lower transmission rates large sample sizes would be required to achieve statistically significant results. In addition, it was noted that a majority of baseline participants would be expected to be seronegative. Human challenge models (CHIM) may also be considered to guide vaccine development, while acknowledging current limitations on the relevance of challenge strains and study design to inform safety issues.

A consortium with regional research centers should be established to accelerate and guide mRNA product development against dengue. Given the lack of strong R&D at the vaccine manufacturers, and a strong dengue expertise at the academic and translational research groups in the region, it was proposed that a consortium should be established to undertake product development. This consortium would address some of the numerous basic science research questions around dengue vaccine development and be responsible for coordinating mRNA product development pathway including enabling access to key assays and models for preclinical and clinical research. The experience of IVI in coordinating the Dengue Vaccine Initiative as well as a track record of successful vaccine development, and the preclinical dengue and mRNA expertise at Chulalongkorn, NUS and A*Star, and the demonstrated interest of Incepta and Biofarma were proposed as the basis for a regional consortium.

Key considerations for mRNA hand-foot-and-mouth disease (HFMD) vaccine development –

In South East Asia, HFMD causes seasonal epidemics associated with significant DALY-losses and socio-economic burden. HFMD mainly affects young children, from six months to six years old, and is commonly caused by enterovirus A71 (EV-A71) and other enteroviruses, such as coxsackie A viruses CV-A16, CV-A10 and CV-A6 as well as echoviruses. These enteroviruses are associated with various degrees of virulence and often co-circulate during HFMD outbreaks where co-infection and recombination events can occur. Very few relapses upon re-exposure to the same enterovirus serotype have been observed and which provide good rationale for HFMD vaccine development.

There are currently four monovalent EV-A71 vaccines (based on genogroup C4 or B4) available for broad use in infants. These licensed products are formalin-inactivated vaccines adjuvanted with alum, which differ in their vaccine strain, manufacturing cell substrate, and antigen dose. In clinical trials, these vaccines were proven safe and highly effective against EV-A71–associated HFMD in infants and showed sustained neutralizing antibody response in long-term follow-up studies as well as robust cross-neutralization activity across several EV-A71 genogroups. Furthermore, these trials helped to inform correlates of protection for EV-A71 inactivated vaccines where relatively low neutralizing antibodies titers are considered to be protective. However, these vaccines did not confer cross-protection for HFMD caused by non–EV-A71 enteroviruses, such as CV-A16. As a consequence, the introduction of the first EV-A71 vaccines in 2015 has resulted in a significant reduction of EV-A71-caused HFMD epidemics in endemic regions. In addition, data points towards replacement with different enterovirus serotypes. Recently, the emergence of a EV-A71 genotype C1 in China raised concerns as no detectable cross-neutralization activity was observed in serum collected from vaccinated children.

The potential for EV-A71 gradual replacement with other enteroviruses from different serotypes prompts the need for multivalent HFMD vaccines, and also raises the need for continued surveillance and molecular epidemiology studies to inform the right vaccine targets. Several multivalent approaches have been tested in preclinical models, based on inactivated, live-attenuated, subunit and VLP vaccine platforms. The development of multivalent vaccines was attempted via the simple combination of potent monovalent vaccines or the construction of chimeric vaccines comprised of epitopes derived from different virus serotypes. Like with dengue, significant differences in immune responses against antigens have been observed in tetravalent formulations, possibly due to vaccine interference and/or immune biases. The potential emergence of new variants also challenges the development of multivalent vaccine. Representative strains for each enterovirus serotype, containing viral protein VP1 or VLPs, could be designed to mitigate this concern. Including conserved cross-reactive immunodominant T-cell epitopes from non-structural proteins could potentially help develop broadly-protective vaccines. So far, mRNA technology has not been used against enteroviruses but could play a role in developing multivalent HFMD vaccines and in rapidly testing different antigens in humans, particularly as current animal models have serious limitations in recapitulating HFMD disease. Additional work on antigen mapping is needed to better inform mRNA vaccine design to induce both humoral and cellular immunity. Researchers from the National University of Singapore have initiated a program to screen mRNA HFMD vaccines in human organoids models with immune cells. Finally, multi-country pediatric clinical trials will be required to test multivalent HFMD vaccines against the most important serotypes.

Key considerations for mRNA *P. vivax* vaccine development –

P. vivax, transmitted by female Anopheline mosquitoes, is the second most common cause of malaria after P. falciparum. Nearly 5 million P. vivax cases have been reported globally in 2021, though there are specific challenges in P. vivax case detection. In South East Asia, as P. falciparum cases continue to decline, P. vivax has emerged as the dominant species within the region. Myanmar and Indonesia reported the highest P. vivax case incidence in 2021. Similar to P. falciparum, P. vivax parasite undergo a complex life cycle. However, P. vivax causes a milder form of malaria that can remain dormant as hypnozoites in hepatocytes, and which can cause relapses of malaria disease several months after infection. There is a need to develop P. vivax vaccines to add to the other interventions designed to control and eliminate malaria, although P. vivax vaccine development has received significant less attention than P. falciparum.

P. vivax vaccine pipeline is relatively scarce: there is currently no licensed vaccine and the most advanced candidates are in Phase 1/2, and for which a majority are derived from P. falciparum vaccine research. Lessons learned from P. falciparum vaccine development may help accelerate P. vivax vaccine development and the licensure and broad use of P. falciparum pre-erythrocytic vaccines provides good rationale to the technical and regulatory feasibility of P. vivax pre-erythrocytic vaccines, although blood-stage and transmission-blocking vaccines are also needed. As with P. falciparum, the major challenge in developing P. vivax vaccines is the wide array of antigens across the parasite life cycle, associated with different protective immune mechanisms, assay development, as well as the high levels of parasite genetic diversity that may lead to variant-specific immunity. Specifically, P. vivax displays two types of circumsporozoite protein (CSP) and attempts to design pre-erythrocytic vaccines would need to express the two CSP types.

A deeper understanding of immune mechanisms is needed to design highly effective malaria vaccines. Clinical trials data suggest that neutralizing antibodies do not systematically correlate with protection. T-cell immunity as well as functional antibodies, through interactions with their Fcγ receptor and complement fixation, can mediate immune functions which may also play a role in protection against malaria. For instance, RTS,S was shown to induce short-lived complement-fixing antibodies which mirrors the declining vaccine efficacy of RTS,S over time. A cohort study of children developing P. vivax malaria allowed researchers from the Burnet Institute to identify antigens that elicit polyfunctional antibodies responses which were associated with control of malaria disease. Whether these antigens work as well in a vaccine context as in a natural infection context and whether they can achieve long-term polyfunctional responses remain critical questions to inform vaccine design. The fact that several antigens contributed to protection highlights the need for multi-antigen vaccines, across several stages.

Controlled human malaria infection trials (CHMI) have also been established for P. vivax infection. CHMI studies are expected to play a key role in screening target antigens, vaccine regimen and downselect candidate vaccines for late-stage trials. For instance, a recent CHMI study from Oxford researchers revealed the impact of vaccine schedules on parasite growth inhibition in blood, using a blood-stage candidate vaccine. Sporozoite challenge models using mosquitoes bites are also being established. However, specific challenges to the sourcing and culture of sporozoites has been identified as a hurdle in the use of CHMI studies, particularly in endemic countries. The Mahidol Vivax Research Unit has established the capacity to perform CHMI studies for pre-erythrocytic and blood-stage vaccines in Thailand.

Several mRNA constructs have been tested in preclinical models against malaria in South-East Asia. Noting that natural killer T cells, largely present in the liver and spleen, can act as cellular adjuvant to drive T-cell response, researchers from the Doherty Institute and the Victoria University of Wellington tested a mRNA construct encoding a P. berghei sporozoite protein adjuvanted with a chemically-modified natural killer T cell agonist which elicited a robust resident CD8 T-cell response in the liver associated with sterile protection after P. berghei challenge in a mice model. This approach could also be applied to P. vivax vaccines. Based on their immunogen discovery study, highlighted more above, the Burnet Institute will test several multi-antigen mRNA constructs for liver and blood stages in mice models before going to human trials. The Mahidol Vivax Research Unit is developing a transmission-blocking mRNA vaccine encoding for Pvs25 which showed durable immune response in mice and will be further evaluated in a non-human primate model. Biofarma, a WHO/MPP manufacturing Partner, aims to develop mRNA vaccine targeting the CSP of P. falciparum and P. vivax using a common strain in the South-East region, with plans to start first in humans clinical trials in 2026. Regional partnerships are needed to enable synergies between these different vaccine development efforts.

It was considered that the available data on epidemiology and low-hanging candidates was insufficient to justify the creation of a consortium for P. vivax mRNA vaccines at this moment.

Key considerations for human papillomavirus (HPV) therapeutic vaccine development –

Cervical cancer, caused almost exclusively by sexual transmission of oncogenic types of HPV, is an important public health problem globally. In 2020, an estimated 604,000 women were diagnosed with cervical cancer, and approximately 342,000 women died from the disease. HPV16 and HPV18 are the most common cause of HPV-mediated cancers and nearly 90% of cervical cancer-associated deaths occurred in women in LMICs, largely due to inequitable access to effective cervical cancer prevention and management measures, including licensed HPV preventive vaccines, and which provide a rationale for the development of HPV therapeutic vaccines, particularly for use in LMICs. In many parts of the world a highly effective prophylactic vaccine has been introduced for adolescents, however women in other countries, or those who were infected prior to the introduction of the vaccine have a high risk of being chronically infected with the virus and therefore at risk of cervical cancer. It is thought that therapeutic vaccines that clear the viral infection, or optimally clear both viral infection and early neoplasias, could have a significant impact on the future cervical cancer disease burden.

Therapeutic HPV vaccines are currently in early clinical development and might offer an additional tool to address gaps in cervical cancer programmes. Unlike existing prophylactic HPV vaccines, which prevent new infections, therapeutic vaccines would be designed to clear or treat existing HPV infections, HPV-associated precancers, or invasive cervical cancer. WHO has recently developed a preferred product characteristics to provide guidance to vaccine developers, policy-makers and programme implementers on preferences for HPV therapeutic vaccines designed to clear HPV 16 and 18 infections as well as to treat cervical precancers. Clinical trials results, using different vaccine platforms, provided proof of concept that the development of HPV therapeutic vaccines may be feasible to clear infection or to induce regression of cervical precancers. Treating advanced, recurring, or metastatic cancers may be more difficult to achieve. More recently, a DNA vaccine failed to achieve its biomarker-based primary endpoint, despite significantly improving grade-3 precancerous lesions regression and viral clearance

rates, highlighting the need for more appropriate biomarkers, more predictive of local protective immunity.

HPV infections are restricted to the epithelial layer of the mucosa and express different viral proteins at different stages of disease. Current HPV therapeutic vaccine approaches use E6/E7 as main antigen targets and clinical trials results have highlighted the role of E6/E7-specific T-cell response, and particularly of CD8 T-cell response, in regression or clearance of precancers lesions. Additional antigens, such as E2, could also play a role in clearing persistent infection and precancer regression. Observational data also suggest that current prophylactic VLP vaccines could also play a role in reversing lesions, suggesting a potential role for L1 antigen which could also serve to prevent re-infection. The inclusion of additional antigens in a HPV therapeutic vaccine would need to be evaluated in well-designed clinical trials. Different administration routes, such as thigh administration, could be tested to explore whether local (inguinal) immunity is further enhanced, and potentially vaginal delivery could explore the benefit of local mucosal response. Better animal models for persistent infection and precancerous lesions are needed in order to address these key research questions and better inform screening of candidate vaccines to enter clinical trials. Researchers from the Chulalongkorn university are developing a combined preventive and therapeutic HPV mRNA vaccine which has shown to be associated with robust T-cell response in a mice model and is looking at how immune response can be further optimized testing different mRNA leading sequences that promote MHC-I presentation and CD8 induction. The use of unmodified mRNA, or a mix of unmodified with nucleotide-modified mRNA, will be explored to see whether these different constructs can lead to optimal CD8 T-cell response while balancing antibody response.

A consortium to undertake the preclinical development, GMP manufacturing and clinical evaluation needs to be established. It was proposed that the University of Chulalongkorn could take the lead in building the consortium.

Innovations in mRNA-based research and manufacturing –

Despite the widespread use of the mRNA COVID-19 vaccine, there are still a number of key limitations and research questions that need to be addressed in order to fully unlock the potential of mRNA lipid nanoparticles (LNP) technology for broader use, including infectious diseases, cancers and chronic diseases. Different applications require different types of immune response (e.g. antibodies vs CD4 vs CD8 T-cell) and mRNA design can be tailored to deliver the desired immune response while also meeting the programmatic needs of cost, route of delivery, thermostability, reactogenicity etc.

From a product development perspective, some of the key mRNA vaccine design elements that may affect product cost, safety, immunogenicity and efficacy, were discussed. These include:

- Target antigen (e.g. stabilized protein vs native sequence)
- Plasmid and mRNA design (e.g. sequence optimization, leader sequence choice, mRNA structure)
- Protein expression (e.g. excreted monomers vs membrane-bound vs self-assembling multimeric VLP structures)
- Nucleotide-modifications (e.g. N1-methylpseudouridine vs pseudouridine vs uridine as well as % use in the mRNA)
- Lipids and LNP composition (e.g. which ionizable lipid, single-lipid formulation)
- Immunomodulators incorporated into the LNP or mRNA (e.g. NKT cell agonist, cytokines)

- Targeted LNP delivery (e.g. site of injection and lymph node distribution, ligand conjugation (e.g. mannose to target APCs))
- Priming or boosting regimen (e.g. boosting on top of naturally acquired prime response such as RSV in elderly, shingles) and duration of protection

While organoid and animal models remain important, it is essential to demonstrate a new concept in humans leveraging mRNA unique potential to accelerate translational research.

Researchers from the Wits university are addressing key research questions related to some of the above elements:
On the basis that single-component ionizable may be a feasible approach for lipid nanoparticle (LNP) encapsulation and mRNA delivery, they developed new ionizable lipids through a semi-synthetic approach starting from a cashew nutshell extract. Studies using these new ionizable lipids both as four-component and single-component formulations showed efficient mRNA encapsulation and protein expression localized at the site of injection in a mice model. This provides proof of concept that these novel lipids could be used in mRNA-LNP vaccines. Additional studies including toxicology need to be performed to evaluate potential for clinical use. Since cashew nutshell is an abundant resource the lipids from this will have a relatively low cost.
SARS-CoV-2 immunogenicity studies in mice showed comparing the immune responses induced my mRNA comprising uridine, pseudouridine or N1-methylpseudouridine demonstrated slight superiority of the non-methylated pseudouridin. Studies are lower doses will be performed to further identify any potential true differences resulting from the two types of nucleotide-modification. These studies are particularly important to address some of the current patent issues.
Finally, key considerations leading the design of a proprietary plasmid backbone designed to fast-track mRNA preclinical research were discussed. Using this backbone and pseudouridine, studies in mice were performed using four tuberculosis antigens expressed in either individual mRNA vaccines or polyprotein mRNA vaccines, to assess the efficiency of the plasmid backbone and the feasibility of a tuberculosis mRNA vaccine, and which yielded promising results. Further animal studies are planned to identify the best mRNA construct that will lead to the clinical development of a novel tuberculosis mRNA vaccine.

From a manufacture perspective, mRNA-LNP innovations and process optimization is needed to increase freedom-to-operate, minimize cost of goods and footprint, while fully exploiting the flexibility offered by mRNA production in terms of scale and multi-product design.
Several scalable and automated approaches for mRNA-LNP production are now available on the market and several other fully integrated solutions, independent of mRNA product, with improved manufacturing parameters will reach the market in years to come. For instance, a sequential-staggered process consisting of scaling-out small individual batches was shown to lead to significant reduction in footprint and costs, while enabling multi-product production at different scales. Cost of goods analysis suggest that it is possible to significantly bring down the cost of a 50 ug vaccine dose down to 0.25 cents, in a scenario of large-scale production where all key raw materials and reagents are produced in-house.
WHO highlighted that while automated processes are ideal for manufacture in LMICs as it reduces the risk of user error, it is however essential that mRNA manufacturing partners acquire and understand the manual process of mRNA-LNP manufacturing developed by Afrigen prior to selecting and acquiring automated systems. Partners interested in acquiring automated systems for mRNA manufacturing are advised to conduct a detailed analysis of such systems including compatibility with plasmids being provided from the central hub, long-term supply of proprietary agents, maintenance, and scalability in the event of a pandemic.

The Bill and Melinda Gates Foundation and the Wellcome Trust have made a series of investments to enable access to low-cost and modular R&D and GMP mRNA-LNP manufacturing equipment. The deployment of mRNA manufacturing equipment also raises the need to secure access to raw materials, particularly in the event of a pandemic. A network of suppliers should be established to ensure there is a continuous supply of quality raw materials and reagents compatible with R&D and GMP mRNA-LNP manufacturing equipment already established. Besides, manufacturers and product developers would benefit from the development of in-silico bioinformatics tools, such as codon optimization algorithms, to advance product design as well as manufacturing verification of a given product. Finally, innovations leading to improved thermostability of mRNA-LNPs products, such as new formulations or micro-array patches, are needed to allow broader use of mRNA vaccines, particularly in LMICs.

Next Steps –

The WHO/MPP mRNA Technology Transfer Programme, established in 2021, is building mRNA manufacturing capacity in 15 LMICs around the world, including four countries in South-East Asia (Bangladesh, India, Indonesia, Vietnam). The driving force behind establishing these mRNA manufacturing facilities is primarily to be able to respond in the event of a future pandemic, however in order to be able to respond to a future pandemic these newly established mRNA facilities need to be operational and producing products that are commercially viable. Since the market for Covid vaccines is rapidly declining, WHO is seeking development partnerships to advance other mRNA vaccine candidates.

WHO and MPP aim to establish consortia of academic research groups, translational research groups, and manufacturers. In such consortia, a translational research group ideally with experience of successful vaccine development would coordinate preclinical activities and facilitate pilot-scale GMP production and preparation of necessary regulatory dossiers. Vaccine design and preclinical research would be undertaken by academic groups, and phase III and commercial production would be undertaken by the manufacturers under non-exclusive rights.

Based on the outcomes of the meeting, WHO and MPP are looking to establish the following research consortia:

- A consortium on dengue mRNA vaccine product development to be led by IVI, in collaboration with Chulalongkorn University and mRNA manufacturing partners from Bangladesh and Indonesia.
- A consortium on HFMD mRNA product development to be led by Hilleman labs in collaboration with Chula University, National University of Singapore and mRNA manufacturing partners from Vietnam.
- A consortium on therapeutic HPV to be led initially by Chulalongkorn University.

In parallel, WHO and MPP will also help establishing a global lipid consortium to advance development on novel lipids and LNP formulation to be used in mRNA applications.

A meeting of interested partners to finalise these consortia will be held in March 2024.