ANNUAL REPORT 2022

European Vaccine Initiative

Contents

Message from the Chairman and Executive Director

The global health agenda continued to be heavily dominated by COVID-19 throughout 2022 but toward the end of the year we could see the light ahead of us. Vaccine roll-out, public health measurements and herd immunity in combination with the appearance of milder COVID-19 variants meant that society could slowly return to a state of normalisation. In doing so, it is key to remember some of the important lessons that we have learnt during the preceding two years. We should remember that vaccine research played an essential role in overcoming the pandemic, we should be inspired by the speed with which several new vaccines were developed, but we should also be concerned by the global inequalities in vaccine distribution and uptake that we witnessed. This is evidence that global health and pandemic preparedness goes hand in hand, and it underlines the importance of EVI's mission to develop safe, effective, and affordable vaccines for everybody.

The return to normal business for EVI meant that we could dedicate more time and resources to our long-term goals. EVI has historically been a champion of promoting malaria vaccines, and we continue to do so. In the EDCTP2 financed MVPE-CC project, EVI is supporting Kintampo Health Research Centre (KHRC) in Ghana to collect surveillance data for a safe roll-out of RTS,S/AS01, the first malaria vaccine to be recommended by WHO. EVI is also partner in the EDCTP2 funded MMVC and MIMVaC-Africa projects, which contribute, among other activities, to the development of R21, a promising new pre-erythrocytic malaria vaccine candidate that is being developed by University of Oxford and Serum Institute of India.

Meanwhile, EVI continues to support the development of several next generation malaria vaccines, with particular focus on underserved and neglected population groups. In the EVI-coordinated projects VAC4PM (financed by the GHIT Fund of Japan) and ADVANCE-VAC4PM (financed by EU), EVI is spearheading the development of a placental malaria vaccine. Such a vaccine would help prevent the detrimental effect on mother and foetus of contracting malaria during pregnancy. EVI has secured funding to initiate a phase II clinical trial of a vaccine against placental malaria.

EVI has continued its engagement in 2022 to support the development of new tools and technologies for vaccinology. The IMI2-funded VAC2VAC project (Vaccine batch to vaccine batch comparison by consistency testing), which came to a successful conclusion in February, resulted in the validation of two *in vitro* assays, the monocyte activation test (MAT) and the Tetanus Neurotoxin (TeNT) LC-MS/MS assay, which can replace animal testing in routine vaccine manufacturing. The MAT has thus been approved by the regulatory authorities and implemented in industry as a replacement of the Rabbit Pyrogen Test. EVI continues to engage passionately in developing new tests and research tools that can replace animal testing in vaccine research and production, for example through the Inno4Vac, a large public-private partnership that is funded by the Innovative Health Initiative (IHI) and coordinated by EVI.

Organisationally, EVI has evolved in 2022 and continues to adapt to a rapidly changing global health landscape. In May 2022 we complete a change in our legal status from a European Economic Interest Grouping (EEIG) to a non-profit Association under German law. This change will allow EVI to engage in a wider range of activities and collaborate with a broader range of stakeholders. We have also welcomed a number of new talented colleagues that share our passion for vaccines and global health and will be instrumental in achieving our ambitious agenda over the coming years.

Dr Clemens Kocken, Chairman of the EVI Board
Dr Ole F. Olesen, Executive Director

2022 in Highlights

Leading placental malaria vaccine development, mitigating risks to pregnancy.

Pioneering *in silico* modelling for antimicrobial resistance prevention and vaccine production.

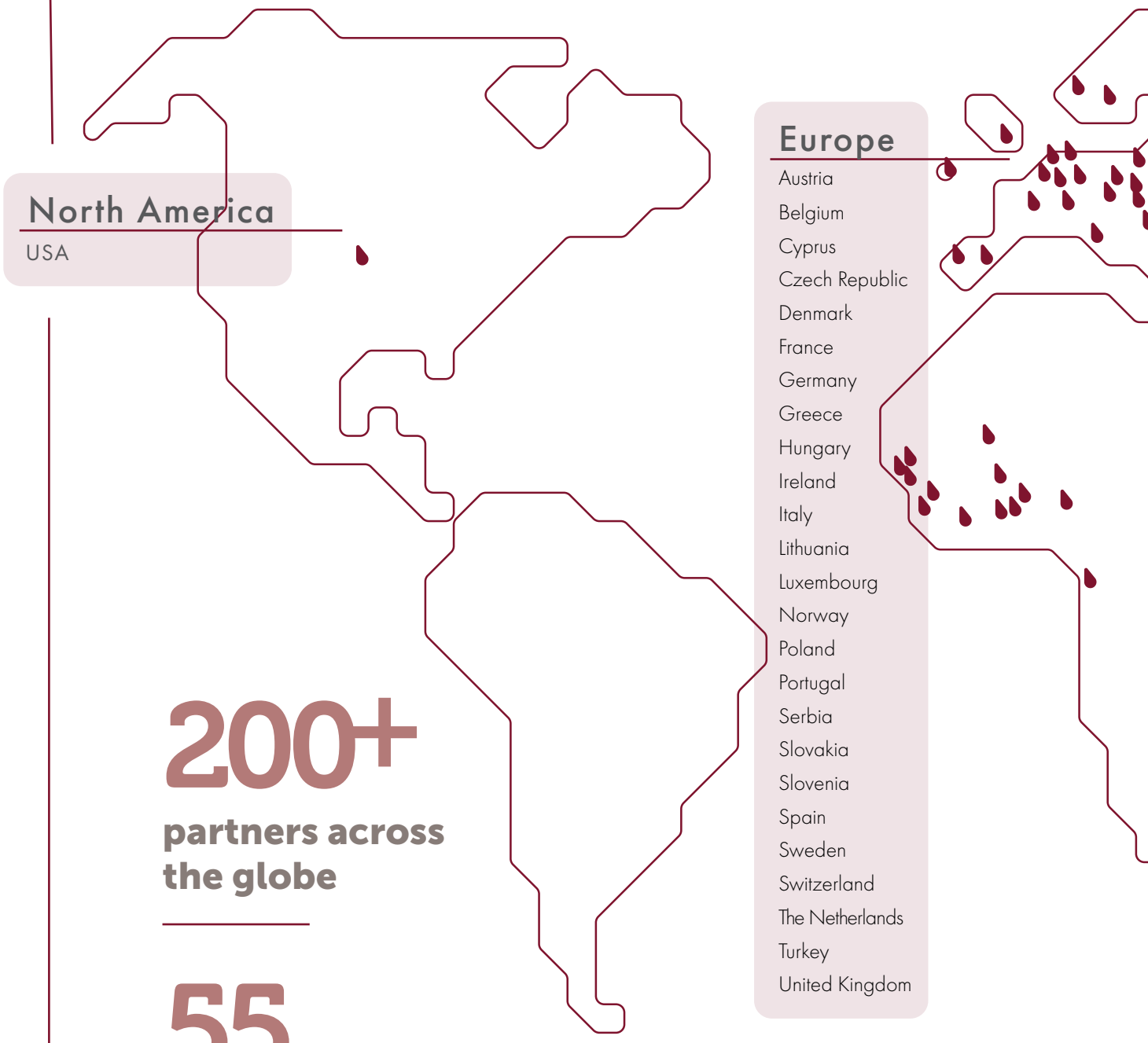
Backing R21/Matrix-M, a potent malaria vaccine in advanced stages.

Sustaining TRANSVAC network, Europe's vaccine development catalyst.

Replacing animal tests: EVI coordinated the development and validation of two *in vitro* assays for vaccine production.

EVI shifts its legal status to a non-profit Association for greater impact.

Global partners



North America

USA

Europe

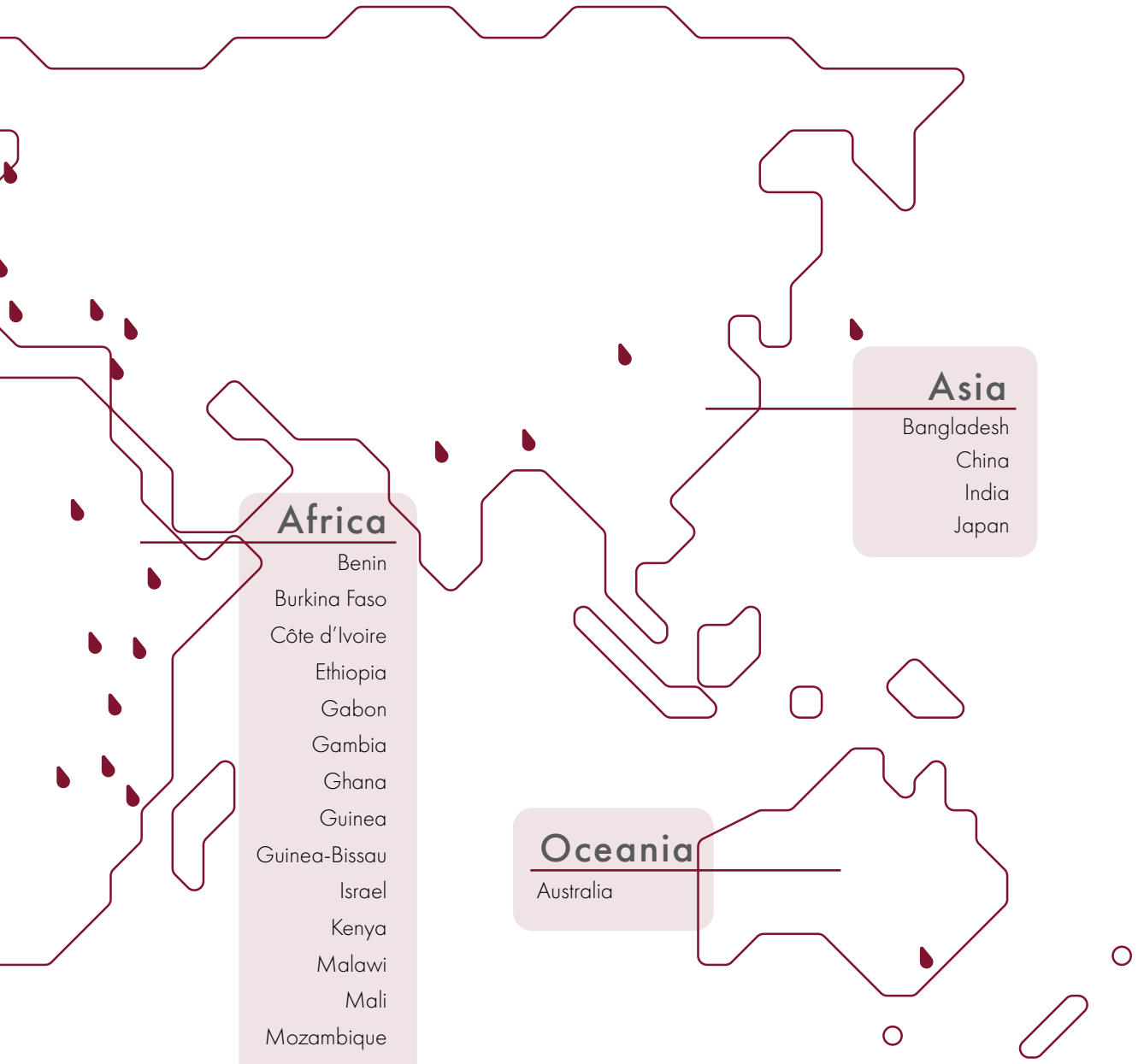
Austria
Belgium
Cyprus
Czech Republic
Denmark
France
Germany
Greece
Hungary
Ireland
Italy
Lithuania
Luxembourg
Norway
Poland
Portugal
Serbia
Slovakia
Slovenia
Spain
Sweden
Switzerland
The Netherlands
Turkey
United Kingdom

200+

partners across the globe

55

different countries



Asia

Bangladesh
China
India
Japan

Africa

Benin
Burkina Faso
Côte d'Ivoire
Ethiopia
Gabon
Gambia
Ghana
Guinea
Guinea-Bissau
Israel
Kenya
Malawi
Mali
Mozambique
Nigeria
Senegal
Sierra Leone
South Africa
Sudan
Tanzania
The Gambia
Togo
Uganda
Zambia

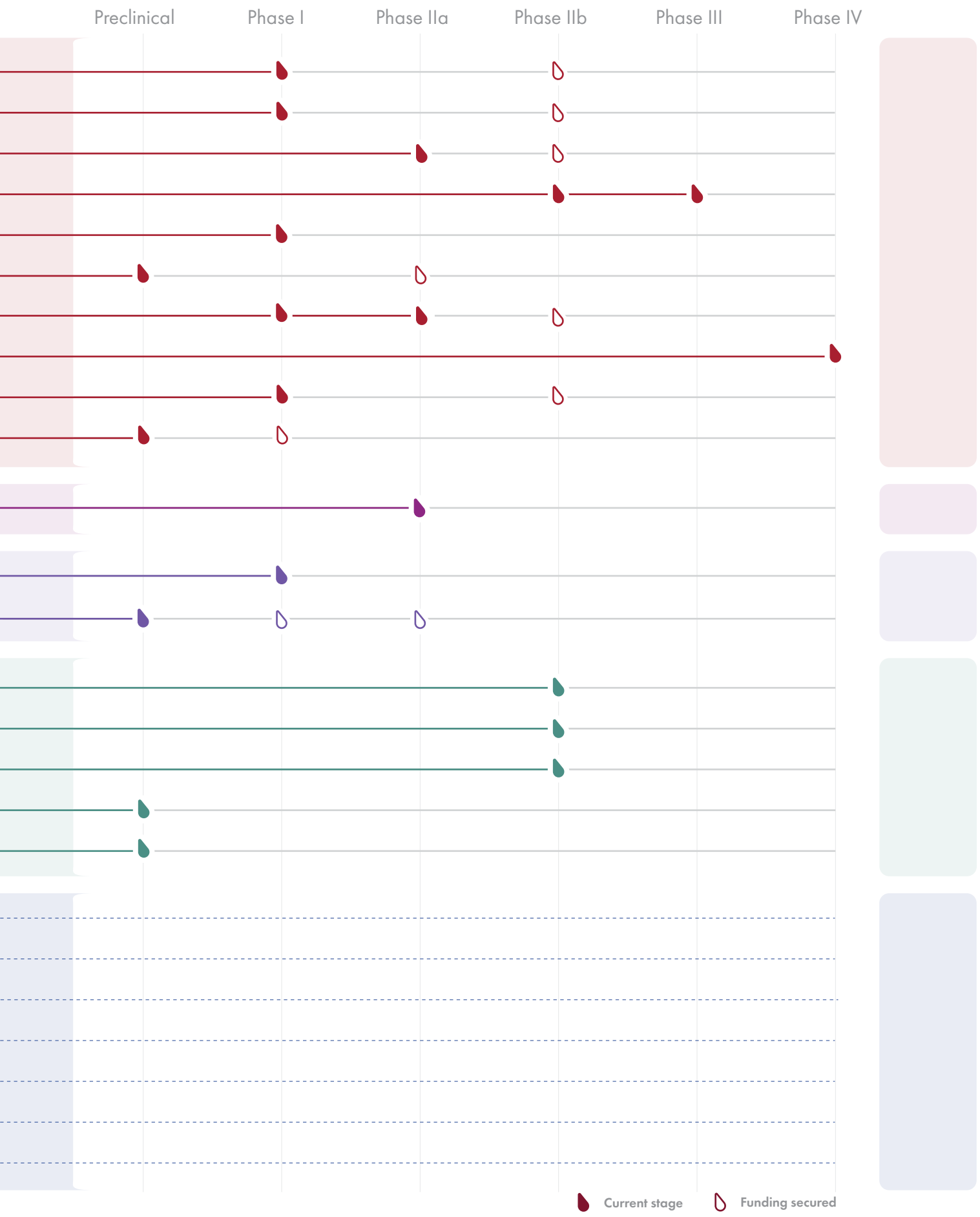
Oceania

Australia

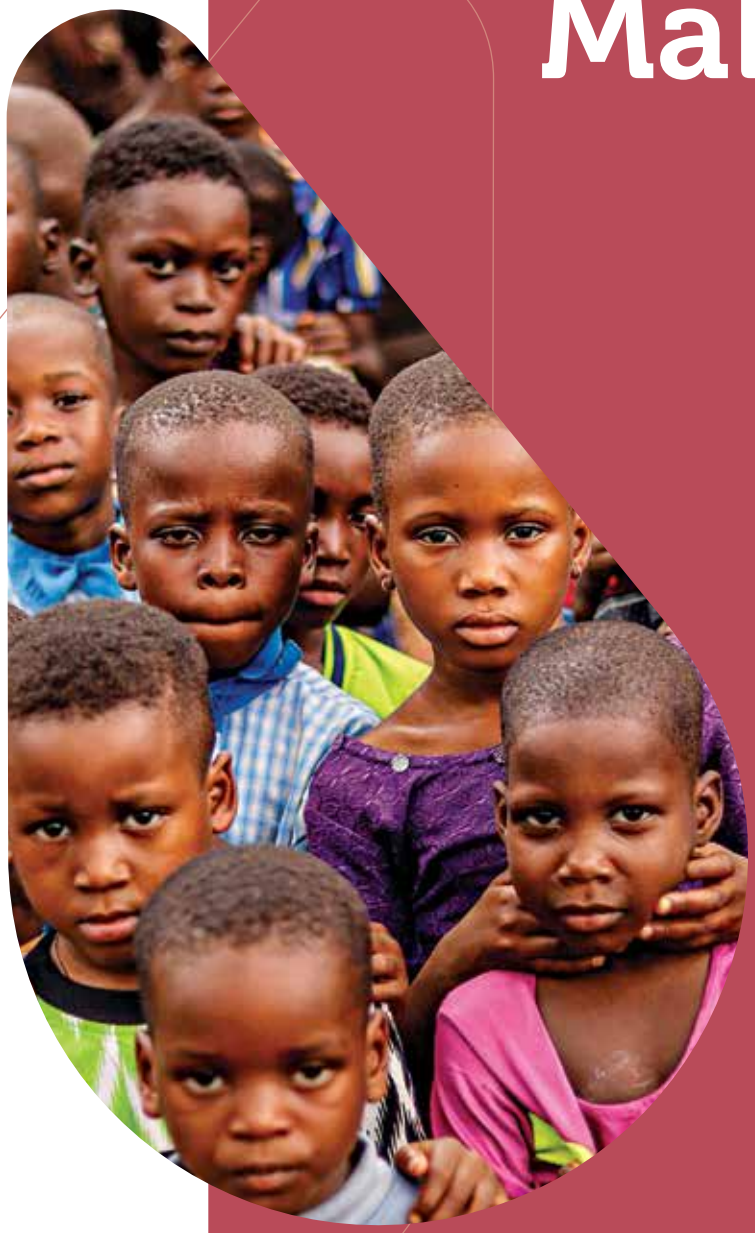
Pipeline in 2022

Area	Projects	Candidates
MALARIA	MMVC; MIMVaC-Africa	PfRH5
		Pfs25
		ME-TRAP
		R21
	SEmalvac2	BK-SE36/CpG
	SEmalvac4; MIMVac-Africa	NPC-SE36/CpG
	MIMVaC-Africa	PfSPZ-CVac
	MVPE-CC	RTS, S*
	VAC4PM / ADVANCE-VAC4PM	PRIMVAC
		PAMVAC-CLP
LEISHMANIASIS	PREV_PKDL	ChAd63-KH
DIARRHOEAL DISEASES	SHIGETECVAX	ShigETEC
	ShigaPlexIM	Invaplex$^{AR\text{-}Detox}$
COVID-19	VACCELERATE (COVID-19)	BNT162b2**
		mRNA-1273**
		ChAdOx-1-S**
	CEPI-Betacoronaviruses	Pan-Betacoronavirus
NIPAH VIRUS	CEPI-Nipah	MV-Nipah
CROSS-CUTTING ACTIVITIES	Inno4Vac	
	ISIDORe	
	PrIMAVeRa	
	TRANSVAC2	
	TRANSVAC-DS	
	VAC2VAC	
	WANETAM 3	

* WHO-recommended malaria vaccine
** Approved vaccine assessed for alternative administration schedules


Preclinical
Phase I
Phase IIa
Phase IIb
Phase III
Phase IV
Current stage
Funding secured

Malaria



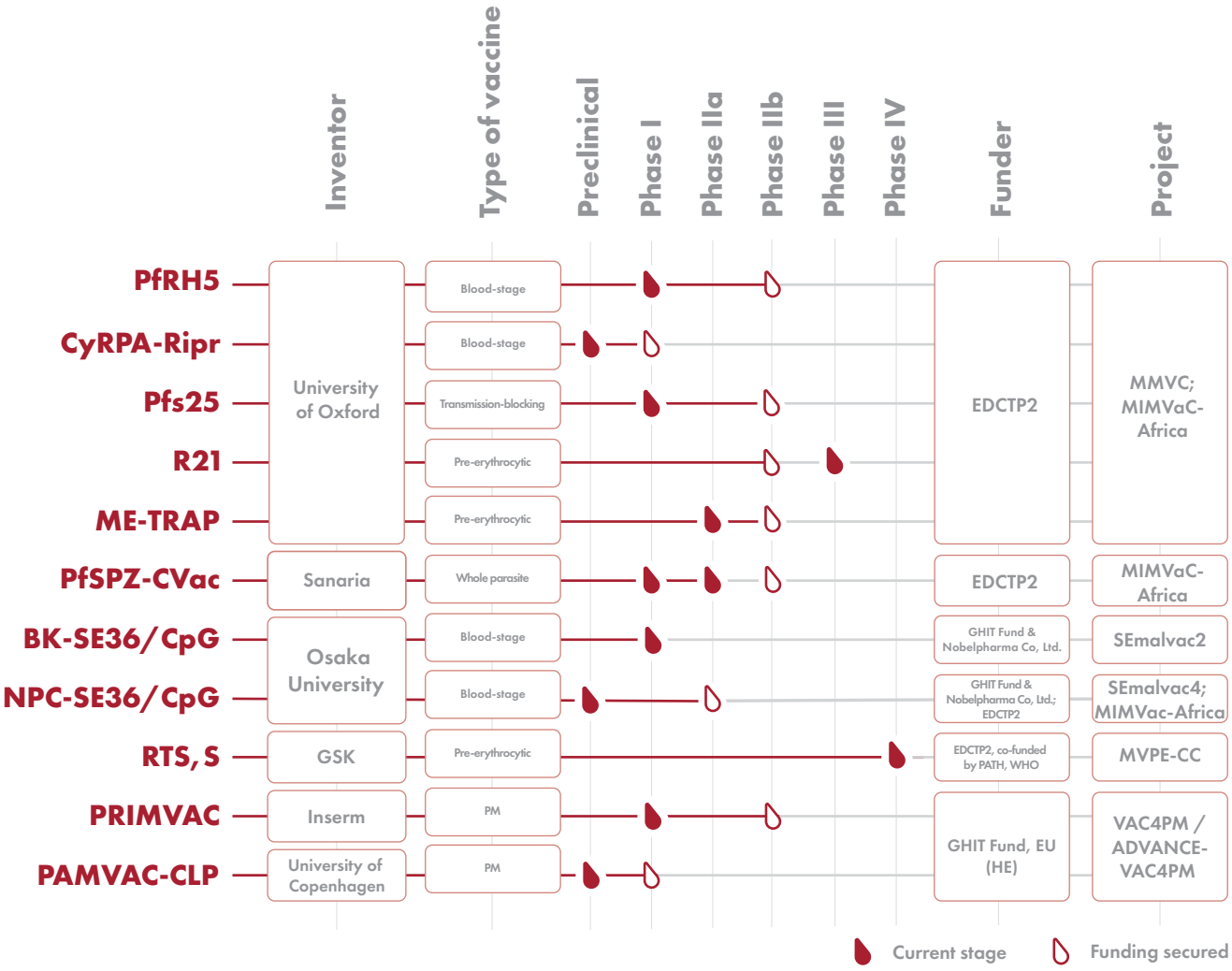
95%
of all cases occur in Africa

Nearly
50%
of the world's population is at risk

76%
of all deaths occur in children <5

619.000
malaria deaths worldwide (in 2021)

Malaria vaccine candidates



Malaria at a glance

Malaria is a mosquito-borne infectious disease. Symptoms typically include fever, chills, tiredness, vomiting, and headaches, ranging from no or very mild symptoms to severe disease and even death. Malaria is caused by five species of *Plasmodium* single-cell parasites, among which *P. falciparum* is responsible for most deaths. The rise and spread of drug resistant *P. falciparum* strains threatens the efficacy of the currently used malaria therapy. Natural immunity to *P. falciparum* malaria only develops slowly and leads to partial and short-lived immunity in response to repeated infections. Disruption to malaria prevention, diagnosis and treatment during the COVID-19 pandemic led to an increase in malaria burden in most moderate and high transmission countries, especially in sub-Saharan Africa (WHO World Malaria Report 2022). The development of vaccines targeting *P. falciparum* malaria would provide an extremely valuable, cost-effective tool to eliminate and ultimately eradicate malaria. The malaria vaccine, RTS,S/AS01, was recommended by WHO for widespread use among children in sub-Saharan Africa and in other regions with moderate to high *P. falciparum* malaria transmission following its pilot implementation in three African countries (Malawi, Ghana, Kenya). However, RTS,S/AS01 only confers partial protection waning over some months as antibody levels rapidly decline after vaccination. Therefore, more efforts are needed for the development of a second-generation malaria vaccine with greater efficacy and longevity in target populations.

Vaccines, the challenges ahead

The enormous complexity of the *P. falciparum* parasite and variability in the infections is a major challenge for vaccine development. These challenges include the antigenic polymorphism, the intricate immunological interplay between the host and the parasite, and heterogeneity in human immune response depending for example on the type of human leukocyte antigen (HLA), genetic traits such as haemoglobin type and red cell polymorphisms. In addition, to achieve sufficient coverage, a malaria vaccine should be suitable for deployment through existing immunisation programs (such as the Expanded Programme on Immunisation). Plasmodium has a complex life cycle with developmental stages in the mosquito vector and human host. Malaria vaccines are designed to target one or more of the parasite stages resulting in different outcomes. **Pre-erythrocytic vaccines** prevent infection of the liver by sporozoites or clear liver-stage parasites thereby rendering sterile immunity. On the other hand, **blood stage vaccines** prevent parasite multiplication in red blood cells thereby preventing clinical symptoms of malaria. In contrast, **transmission blocking vaccines** target parasite development in the mosquito vector thereby preventing transmission.

Malaria infection during pregnancy constitutes a particularly serious problem that can lead to the development of placental malaria (PM), affecting particularly vulnerable demographic groups, pregnant women and their babies in Africa. In 2021, approximately 13.3 million pregnant women were exposed to malaria infection, resulting in an estimated 961,000 children with low birthweight (WHO Malaria report 2022). An effective vaccine would be an attractive tool to control PM on its own or to complement the existing tools. The assessment of safety and efficacy of PM vaccines is challenged by the selection of the appropriate clinical trial design as well as the ethical and regulatory complexities associated with clinical studies in pregnant women.

DIVERSE APPROACHES FOR BETTER VACCINES

Development of asexual blood-stage malaria vaccine

SEmalvac2 and SEmalvac4

Serine repeat antigen-5 (SERA5) is indispensable during blood-stage growth and is suggested to be involved in parasite egress and in parasite immune evasion. SERA5 may overcome two major challenges for malaria vaccine antigens as it shows limited polymorphism and has immunodominant IgG epitopes not requiring strict tertiary structures to elicit protective antibodies. A recombinant form of SERA5 N-terminal domain (SE36), formulated with aluminium hydroxide gel, constitutes the BK-SE36 vaccine candidate. **The safety and immunogenicity of BK-SE36 has been demonstrated in phase I trials in Japan and Uganda, and 1 to 5 years old children in Burkina Faso under the EVI-coordinated SEmalvac project.** In the SEmalvac2 project, coordinated by EVI, the vaccine has been adjuvanted with CpG TLR9 ligand (BK-SE36/CpG) to improve its immunogenicity. BK-SE36/CpG has undergone testing in adults and children in Burkina Faso, where it showed a satisfactory safety profile and immunogenicity with high anti-SE36 IgG antibody titres. Trends towards reduced risk for malaria incidences were seen only in the 5 to 10 year-old children cohort; very few malaria episodes were reported in the other cohorts with no differences observed in the risk of malaria between BK-SE36/CpG vaccinees and control subjects.

Coordinated by EVI as well, the SEmalvac4 project has continued the clinical development of the SE36 vaccine toward with the manufacture and preclinical testing of a new vaccine batch (named NPC-SE36/CpG) and the preparation of the protocol and the selection of clinical trial sites for a phase IIb trial. In addition, the potential of a SE36-cVLP formulation where a capsid virus-like particle (cVLP) has been added as a backbone to improve immunogenicity, cross-reactivity and longevity of the induced immune response is being explored in collaboration with University of Copenhagen and AdaptVac. **Recombinant cVLP-SE36 has been prepared and pre-clinical immunogenicity studies were successfully conducted, confirming the potential of this novel platform.** Finally, a follow-up sero-epidemiology study to assess the persistence of the anti-SE36 antibodies in 5-10 year-old trial participants has been successfully conducted, showing that BK-SE36/

CpG induced high-level and long-lasting immunological responses in children that were naturally exposed to malaria infection.

Comparing approaches

MIMVaC-Africa, a multilateral initiative to foster the clinical development of effective malaria vaccine candidates in Africa

The MIMVaC-Africa consortium started in 2021 and evaluates a number of pre-erythrocytic and blood-stage vaccine candidates for safety, immunogenicity and efficacy with the aim of identifying the most promising candidates for further clinical development in phase III trials.

Five vaccine candidates are assessed in MIMVAC-Africa, namely three pre-erythrocytic vaccine candidates: R21 adjuvanted with Matrix-M, chemically attenuated whole sporozoite vaccine PfSPZ-CVac, and vectored ME-TRAP; and two blood-stage candidates: PfRH5 + CyRPA-Ripr adjuvanted with Matrix-M and NPC-SE36 adjuvanted with CpG. Candidate vaccines will first be tested in phase I/II trials using controlled human malaria infection (CHMI) platforms at the University Hospital Tübingen (Germany) and the Ifakara Health Institute (Tanzania) for pre-erythrocytic and blood-stage vaccine candidates, respectively (start planned for 2023). The most promising candidates from these trials will proceed into a multi-centre phase II trial in healthy African children in Burkina Faso, Gabon and Mozambique. In preparation for the phase II trial, a baseline sero-epidemiological study to assess the incidence of malaria in children in the three African (phase II) trial sites was started in 2021 and is still ongoing.

While the clinical trial preparations have been significantly delayed due to the COVID-19 pandemic, the trial protocols for the CHMI studies in Germany and Tanzania have been developed and submitted to local and national regulatory authorities for approval (trial start is planned for Q2/Q3 2023). The phase IIb trial protocol drafting has progressed. Auditors, selected by EVI, conducted a system audit of the phase II trial sites to independently evaluate site compliance with Good Clinical Practice (GCP), Good Clinical Laboratory Practice (GCLP), local and national regulatory requirements, as well as the robustness of the sites Quality Management System (QMS). This was done to ensure the safety and well-being of study participants and ensure reliability of data. The delay of clinical trials also affected networking activities led by EVI. Training capacities and needs have been mapped and the relief of COVID-19 restrictions will enhance the capacity building and networking activities in 2023.

4 in 1, multi-component vaccine

The Multi-Stage Malaria Vaccine Consortium (MMVC)

The lifecycle of the malaria parasite is complex, and a highly efficacious vaccine may need to target more than one of the parasite's lifecycle stages. The Multi-Stage Malaria Vaccine Consortium (MMVC) is targeting such a multi-component, multistage approach using antigens that have shown promising results in clinical trials on their own. **MMVC is undertaking a tightly coordinated series of lead-in trials in the first years of the project building towards a phase IIb multi-stage vaccine efficacy trial in West and East African infants in the last years of the project, using a combination of the most promising vaccine candidates.**

In 2022, the MMVC clinical trials continued to progress successfully, although delays were caused due to the COVID-19 pandemic. Two phase I trials are ongoing in Tanzania: a phase Ib safety and immunogenicity assessment of the blood-stage vaccine RH5.1/Matrix-M in adults and infants (ClinicalTrials.gov Identifier: NCT04318002), and a phase Ib study assessing safety, immunogenicity and *ex vivo* efficacy of the transmission-blocking vaccine Pfs25-IMX313/Matrix-M in adults and children (ClinicalTrials.gov Identifier: NCT04271306). In Kenya, a phase 1b, open-label, age de-escalation, dose-escalation study to evaluate the safety and immunogenicity of different doses of R21/Matrix M in adults, young children and infants (ClinicalTrials.gov identifier: NCT03580824) is completed, and a phase IIb trial in Kenyan adults safety, immunogenicity, and efficacy of R21/Matrix-M and ChAd63/MVA-ME-TRAP in the context of controlled human malaria infection (ClinicalTrials.gov identifier: NCT03947190) is ongoing. Three further trials, including a phase Ib multi-stage trial with RH5.2 and R21 vaccines in Matrix-M are under preparation. **Most notably, published results of a phase II trial in Burkina Faso (ClinicalTrials.gov Identifier: NCT03896724) demonstrated high-level efficacy of R21/Matrix-M of 77% over 12-months of follow-up in children, making it the first vaccine to achieve the WHO-specified 75 % efficacy goal.**

EVI is leading the capacity strengthening and networking in MMVC. Capacity has been strengthened at IRSS-DRO in Burkina Faso where the direct membrane feeding assay (DMFA) at large scale was successfully validated, which will allow field efficacy testing of transmission-blocking vaccines. Three African PhD candidates have successfully continued their

training and made good progress on their trial-related research activities with one book chapter on controlled human malaria infection studies, and a review of the transmission-blocking malaria vaccine, Pfs25. One African MSc student has completed training in 2022 and the training of the second MSc student is progressing well. Networking and training activities were still hampered by the pandemic in 2022.

The first WHO-recommended malaria vaccine

MVPE-CC to further strengthen evidence for widespread use of RTS,S/AS01

RTS,S/AS01 (GSK) is the first malaria vaccine to receive a positive scientific opinion from the European Medicines Agency (in 2015) and to be recommended by WHO (in 2021) for broad use among children in sub-Saharan Africa and in other regions with moderate to high *P. falciparum* malaria transmission. The ongoing vaccine implementation in Ghana, Kenya and Malawi has been accompanied by an independent Malaria Vaccine Pilot Evaluation (MVPE). Embedded in MVPE, the MVPE-CC project is using case-control studies that take advantage of the community-based mortality surveillance and hospital-based disease surveillance systems that have been established as part of MVPE. The main objectives of MVPE-CC are to assess safety signals observed in the phase III trial of the vaccine, to estimate vaccine effectiveness in preventing malaria in children, to assess the incremental benefit of receiving a 4th vaccine dose, and to strengthen capacity in African countries to monitor the effectiveness of malaria vaccines after their introduction. **The findings of MVPE-CC will be instrumental for wider use of RTS,S/AS01 at global and country level, inform policy decisions, and will help to maximise acceptability, uptake and impact of the vaccine.**

Data collection began in October 2021 - within the catchment area of 18 sentinel hospitals across the three participating countries - and progressed well in 2022. Cases of severe malaria, meningitis, cerebral malaria and malaria related mortality, and age and location matched controls were identified and recruited into the case control study. Recruitment will continue in 2023. EVI is part of the project management team and has closely worked with Kintampo Health Research Centre (KHRC) in Ghana as a co-lead in the project management work package of the study, also aiming to transfer capacity between EVI and KHRC in this area.

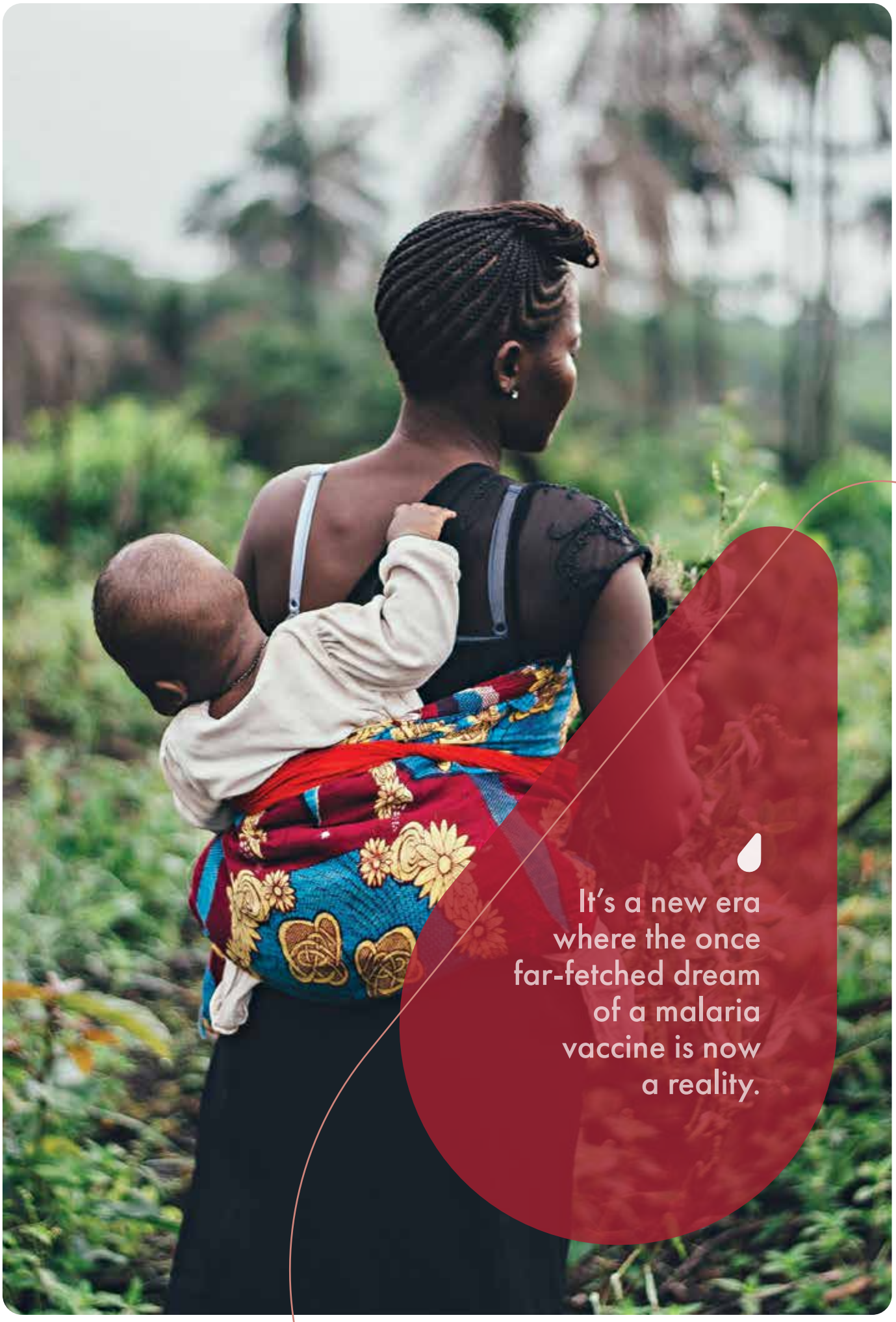
Protecting pregnant women and infants: placental malaria

VAR2CSA-based vaccine candidates against placental malaria (PM): PRIMVAC & PAMVAC

PM is caused by parasite-infected red blood cells adhering to the placental receptor Chondroitin Sulfate A (CSA), and their subsequent accumulation in the placenta. The prevalence of PM decreases sharply with successive pregnancies, suggesting that protective immunity can be naturally acquired. The cysteine-rich transmembrane multidomain surface protein, VAR2CSA, stands today as the leading candidate for developing a targeted vaccine that prevents PM and improves pregnancy outcomes. Vaccination should induce antibody responses to prevent massive sequestration of blood stage *P. falciparum* CSA-binding parasites in the placenta of pregnant women to protect the mother and fetus/newborn.

EVI has supported the development of two leading PM vaccine candidates: PRIMVAC, discovered by INSERM, France and PAMVAC from the University of Copenhagen, Denmark. Preclinical results for both PAMVAC and PRIMVAC have confirmed the feasibility of developing a PM vaccine, while clinical studies in Europe and Africa have demonstrated that PAMVAC and PRIMVAC are safe, well-tolerated and induce good homologous immune responses. As a next step, we are investigating the cross-reactivity against different VAR2CSA variants and the longevity of the immune response.

The longevity of the PRIMVAC immune response is examined in a follow-up study in women previously vaccinated with PRIMVAC (NCT05426187). This study started successfully in 2022 and study results are expected by end of 2023. In parallel, an improved version of PAMVAC on a capsid Virus-Like Particle (PAMVAC cVLP) have undergone pre-clinical immunogenicity studies with promising results in terms of immunogenicity and cross-reactivity of the immune response. In 2023, EVI will work towards bringing PAMVAC cVLP into early clinical testing, while also continuing the clinical testing of PRIMVAC. Finally, a research study is planned in Malawi to model the cost-effectiveness and evaluate the acceptability and feasibility of introducing a placental malaria vaccine *in P. falciparum* malaria-endemic regions.



It's a new era where the once far-fetched dream of a malaria vaccine is now a reality.

Leishmaniasis

There are over

20

***Leishmania* parasite species**

Post kala-azar dermal leishmaniasis (PKDL) appears in

5-10%

of patients who suffered from VL

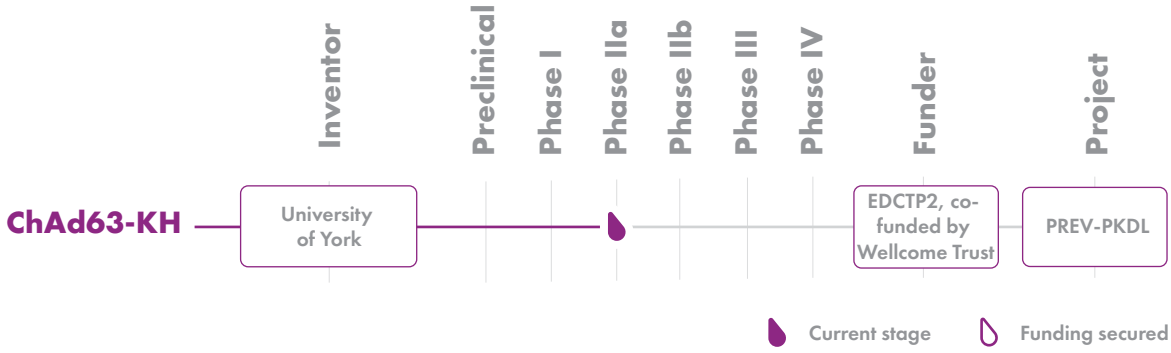
Poverty increases the risk for leishmaniasis

700,000 to 1,000,000

new cases occur annually

No vaccine for leishmaniasis is available for humans

Leishmaniasis vaccine candidates



Leishmaniasis at a glance

Leishmaniasis is one of the most neglected infectious diseases with very limited resources invested in diagnosis, treatment & control, and it has strong association with poverty. Leishmaniasis is caused by protozoan *Leishmania* parasites, transmitted by the bites of infected female phlebotomine sandflies. There are three main clinical forms of leishmaniasis: i) cutaneous, the most common form of the disease (CL); ii) visceral, also known as kala-azar and the most fatal (VL); and iii) mucocutaneous. Whereas cutaneous and mucocutaneous leishmaniases are chronic, non-life-threatening but highly stigmatising, visceral leishmaniasis is fatal in over 95% of cases if left untreated. Post kala-azar dermal leishmaniasis (PKDL) is a sequela of VL, which develops commonly after completing treatment for VL. It is mainly observed in Sudan and India and plays a central role in VL transmission as people with PKDL are reservoirs of Leishmania parasites.
There are currently no licensed vaccines for human use against leishmaniases, and control measures rely on chemotherapy to alleviate disease and vector control to reduce transmission.

Vaccines, the challenges ahead

The development of vaccines against leishmaniasis has been hampered by significant antigenic diversity, as well as the fact that parasites have a digenetic life cycle in at least two hosts, which includes the sandfly vector and human or animal reservoirs such as dogs. Furthermore, the immune reactions against leishmaniasis are highly complex, with some of them accelerating cure, while others seem to aggravate the disease. The type of response elicited depends on the particular stage of the disease, species of the infectious agent and host immune status.

FIGHTING NEGLECTED DISEASES WITH VACCINES

Clinical development of a therapeutic vaccine for prevention of visceral leishmaniasis (VL) and post-kala azar dermal leishmaniasis (PKDL)

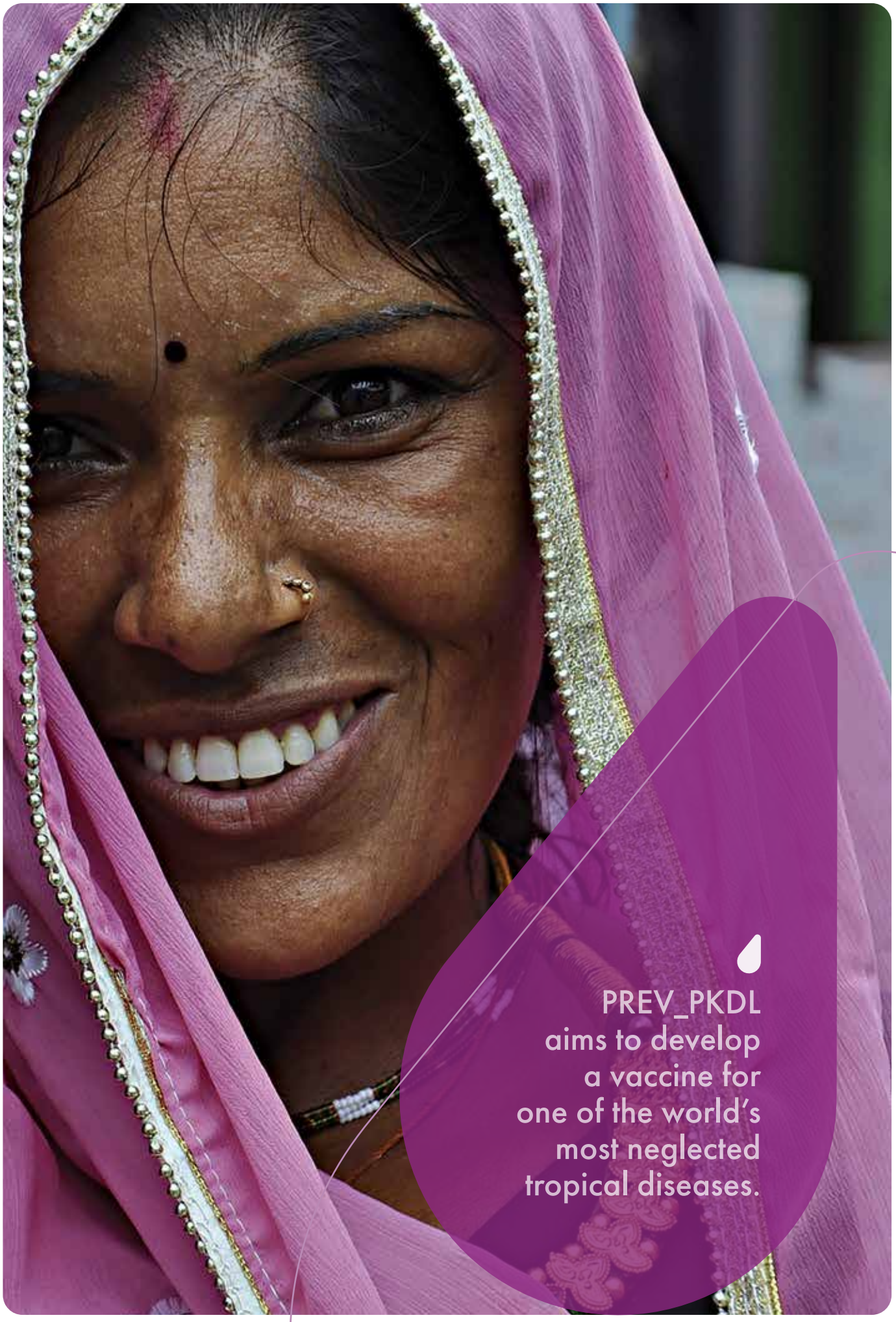
PREV_PKDL

The ChAd63-KH vaccine was invented at the University of York, United Kingdom, and is designed to target the induction CD8+ T cells immune response. The vaccine is based on a well-characterised simian adenovirus vector (ChAd63) expressing two Leishmania antigens, kinetoplastid membrane protein 11 (KMP-11) and hydrophilic acylated surface protein B (HASPB). The vaccine was shown to be safe and immunogenic as a prime-only single dose vaccine in a phase I trial in UK and is currently being tested for therapeutic efficacy in a phase IIb trial in Sudanese patients with persistent PKDL. The PREV_PKDL project will evaluate ChAd63-KH as a prophylactic vaccine to prevent VL, and consequently also PKDL.

Additionally, multidimensional, multiparameter phenotyping on patient cohorts recruited across the countries of the Leishmaniasis East Africa Platform (Ethiopia, Kenya, Sudan and Uganda) will help to better understand the disease as well as drug and vaccine responses.

In 2022, the project has focused on preparing a GMP batch of the vaccine candidate and revising the clinical trial design. Required ethical and regulatory approvals were secured by Ethiopia, Kenya, Sudan and Uganda, and renovation works were completed to enable the start of the multicentre research study (ImmStat@Cure, NCT04342715). Key to the success of the study is the setting up of flow cytometry capacity at each site that will allow investigation and monitoring of changes in the immune response status. Particularly for multicentre studies, flow cytometry brings challenges including access to expertise, equipment support, protocol harmonisation / standardisation and data management. The project has created a network of Flow Cytometry Centres across the research sites, linked in real time to a support centre based at University of York.

In 2022, the project has prepared a GMP batch of the vaccine candidate and revised the clinical trial design.



PREV_PKDL aims to develop a vaccine for one of the world's most neglected tropical diseases.

Diarrehoeal disease

2nd
leading cause of death in children under five years old

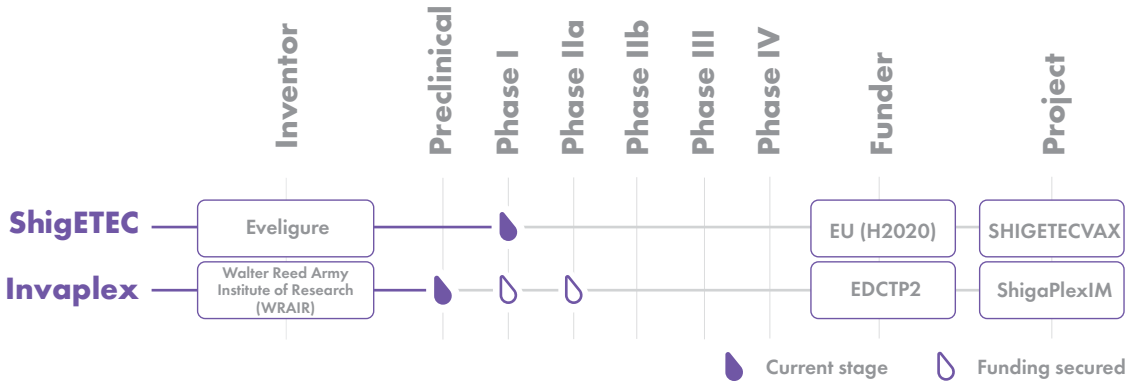
525,000
deaths annually, under 5 years old

Nearly
1.7 billion
cases each year

Most of the cases occur in South Asia and sub-Saharan regions of Africa

Leading cause of malnutrition in children under five

Diarrhoeal diseases vaccine candidates



Diarrhoeal diseases at a glance

According to the World Health Organization (WHO), diarrhoeal disease is the second leading cause of death and high morbidity in children under five years old. As diarrhoeal episodes usually follow the ingestion of contaminated food or water, children and individuals living in low- and middle-income countries (LMICs) are particularly at risk. The African and Southeast Asian regions have the highest percentage of Enterotoxigenic *E. coli* (ETEC) episodes, while most *Shigella* cases occur in Africa, the Eastern Mediterranean and Southern Asia. In addition to posing an immediate and serious health risk, prolonged and/or repeated symptomatic episodes of diarrhoea in childhood can have long-term consequences such as reduced cognitive development, physical stunting, antimicrobial resistance, poorer educational outcomes, reduced wages, and increased risk of non-communicable diseases in adulthood. Conventional treatment includes rehydration therapy and the use of antibiotics. However, given the emergence of multi-drug resistant strains of ETEC and *Shigella*, the development of vaccines is becoming increasingly imperative.

Vaccines, the challenges ahead

Although vaccination is an effective way to reduce the huge disease burden associated with diarrhoea caused by enteric pathogens, many attempts to develop vaccines for shigellosis and ETEC infections have failed, and current approaches are too complex and costly to provide an adequate solution for LMICs.

The absence of defined correlates of protective immunity along with the lack of good small animal models that fully recapitulate the disease, represent additional challenges to the development of a safe and effective vaccine. As Shigella and ETEC are antigenically diverse pathogens, the vaccine should provide broad coverage.

The potential of inadvertently inducing reactive arthritis, the perception that other interventions (including water and sanitation) are more appropriate, and insufficient funding to accelerate and complete the clinical development also pose major challenges in the path forward towards a vaccine against Shigella and ETEC.

STOPPING THE CYCLE OF DIARRHOEAL DISEASES

Early clinical development of oral vaccines

ShigaPlexIM

The ShigaPlexIM project intends to test an intramuscular vaccine candidate, the Invaplex$_{AR\text{-}detox}$ antigen in combination with dmLT adjuvant, in a phase Ia/b clinical trial in European and African adults followed by an age de-escalating phase IIa trial in Burkina Faso. During the year 2022, a sero-epidemiological study conducted in Burkina Faso and Zambia to evaluate the incidence of Shigella disease among children under five (NCT04312906) has been completed. In Zambia, the overall observed Shigella incidence was 30.6 per 1,000 children per month. The incidence was highest in younger children (< one year old) and among malnourished, stunted and wasted children. Among the cases that could be speciated, the most prevalent serotype was *Shigella flexneri*. A low Shigella incidence (8,35%) was observed in the study conducted in Burkina Faso; this could potentially be attributable to the culture detection methods used for Shigella diagnosis, which are less sensitive than molecular tools. The most prevalent subtype detected was *Shigella flexneri*. The preparation of the combined phase Ia/b clinical trial in Europe and Africa was initiated.

SHIGETECVAX

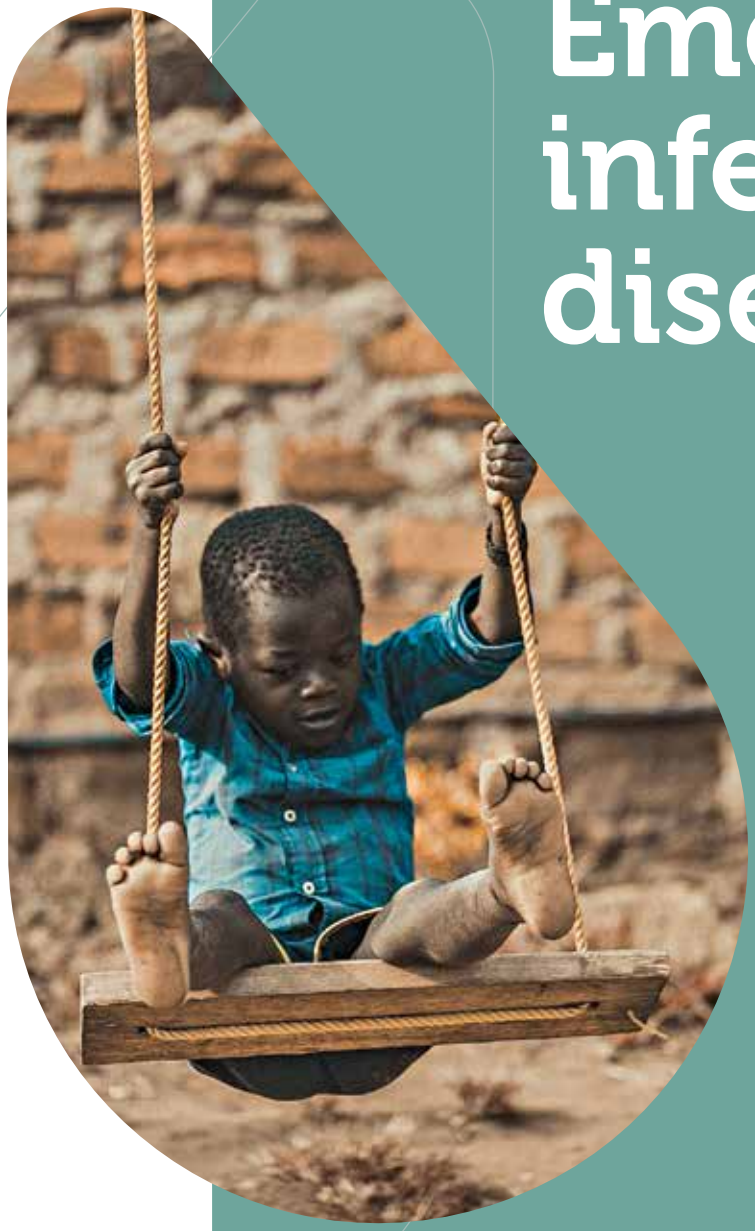
SHIGETECVAX is developing a novel oral vaccine against two closely-related bacteria that are leading causes of diarrhoea: *Shigella* and ETEC. The ShigETEC vaccine candidate is based on a live attenuated Shigella vaccine strain able to induce broad protection against shigellosis thanks to targeted genetic mutations introduced into the Shigella strain. ShigETEC also expresses a tandem repeat of a fusion protein of LTB and an ST toxoid that induces neutralising antibodies and thus protective immunity against both toxins of ETEC strains.

Following the promising safety and immunogenicity data of the phase Ia trial conducted in Hungary[1], the preparation of an age-descending phase Ib clinical trial in Bangladeshi adults and three paediatric age groups down to 6-11 month-old infants is ongoing. The aim of the study will be to demonstrate safety and immunogenicity of three escalating doses of the ShigETEC vaccine candidate in the endemic population. The study documents were successfully submitted and approved by the icddr,b Ethical Review Commission (ERC) and Research Review Commission (RRC) during 2022, while approval from the Directorate General of Drug Administration (DGDA) of the government in Bangladesh is expected in the first half of 2023.

The preparation of clinical trials for Invaplex and ShigETEC continued in 2022.

[1] Girardi, P., Harutyunyan, S., Neuhauser, I., Glaninger, K., Korda, O., Nagy, G., Nagy, E., Szijártó, V., Pall, D., Szarka, K., Kardos, G., Henics, T., & Malinoski, F. J. (2022). Evaluation of the Safety, Tolerability and Immunogenicity of ShigETEC, an Oral Live Attenuated Shigella-ETEC Vaccine in Placebo-Controlled Randomized Phase 1 Trial. Vaccines, 10(2), 340. https://doi.org/10.3390/vaccines10020340

The development of a vaccine against *Shigella* and ETEC is a pressing global public health need.



Emerging infectious diseases

SARS-COV-2 VIRUS KEY FIGURES

5.44m
deaths confirmed in 2021

36.7m
cases in 2021

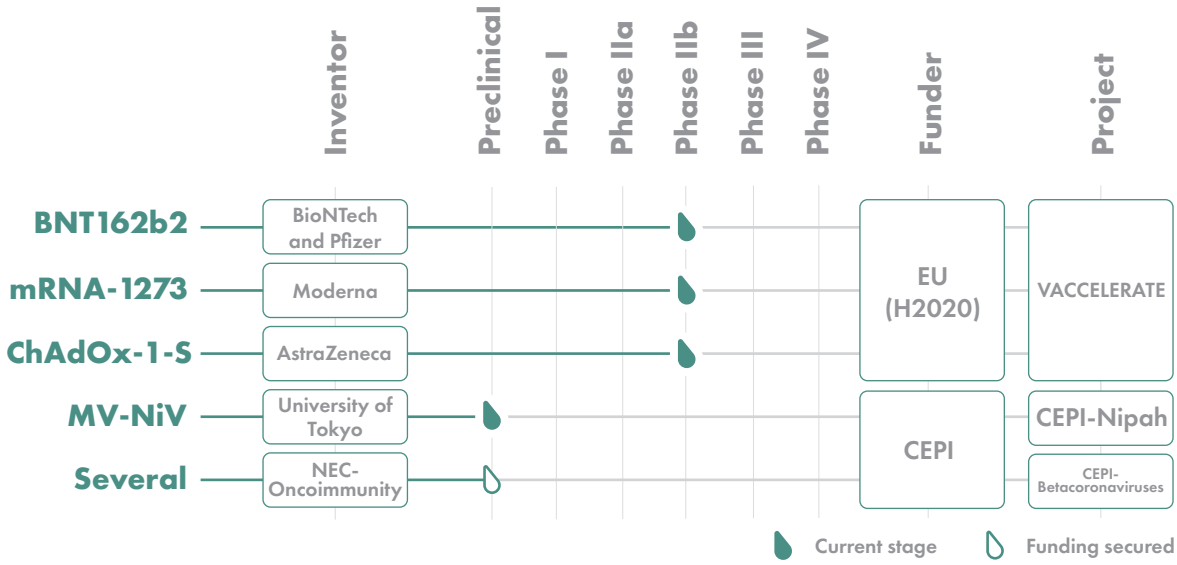
5%
of people infected develop critical symptoms

NIPAH VIRUS KEY FIGURES

2 Billion
people at risk

40-75%
estimated case fatality rate

Emerging infectious diseases vaccine



Emerging infectious diseases vaccine at a glance

Coronavirus disease (COVID-19) has reminded the world of the impact that emerging, and pandemic-prone pathogens can have in society. Similar to COVID-19, many emerging infectious diseases (EIDs) are zoonotic in origin, and often humans may have little or no natural immunity to them, making it difficult to predict their impact on health, society, and the economy. WHO has developed a list of priority diseases and pathogens for R&D in public health emergency contexts. The list includes 10 priority diseases: COVID-19, Crimean-Congo haemorrhagic fever, Ebola virus disease and Marburg virus disease, Lassa fever, Middle East respiratory syndrome coronavirus (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS), Nipah and henipaviral diseases, Rift Valley fever, Zika and "Disease X". **EVI is supporting vaccine R&D on COVID-19, Nipah and Zika virus.**

Vaccines, the challenges ahead

Safe and effective vaccines against COVID-19 were developed and made available in record time, but major challenges remain when tackling the threat of future pandemic outbreaks of COVID-19 and other emerging pathogens. The current vaccines against COVID-19 have been remarkably effective protecting against severe disease, however their impact on preventing the spread of the disease is limited. The efficacy of approved vaccines against new COVID-19 variants is also variable, so a second generation of vaccines that address cross-variant protection is urgently required. Investigator-driven clinical trials are also critical to further understand how specific population groups (e.g., elderly, immunocompromised patients, children, infants, pregnant and lactating people) respond to the currently approved vaccines, as well as to optimise and test administration schedules.

Several different vaccines have been developed against COVID-19 using a variety of different vaccine technologies.

However, many of the emerging pathogens on the WHO priority list have so far escaped attempts to develop vaccines against them. This includes both Zika and Nipah virus, where challenges remain in determining a well-documented target for an immune response, as well as a lack of basic research tools like the correlates of protection, choice of assays for serum neutralising antibodies and predictive animal challenge models.

TACKLING (RE)EMERGING DISEASES AND OUTBREAKS

VACCELERATE

VACCELERATE

Is a clinical research network for the coordination and conduct of COVID-19 vaccine trials. The network is led by the University Hospital Cologne, Germany, and comprises academic and non-profit institutions from all over Europe, including EVI. VACCELERATE is funded by the European Commission's activities for future pandemic preparedness, the HERA Incubator, and aims at becoming the single entry-point for phase 2 & 3 vaccine trials for COVID-19 vaccines in Europe. One of VACCELERATE's main goals is to accelerate and increase the quality of vaccine development during pandemics by establishing a pan-European clinical trial platform, enhancing capacity mapping and building on clinical trial sites, providing easy access to all citizen-volunteers including underserved minorities and interconnecting them with the trial sites, as well as privileged access to vaccine researchers. Beyond the COVID-19 pandemic, it will be an established pandemic preparedness network, ready to face emerging future pandemics, as well as a pivot in Europe's capacity to develop vaccines.

Key Achievements

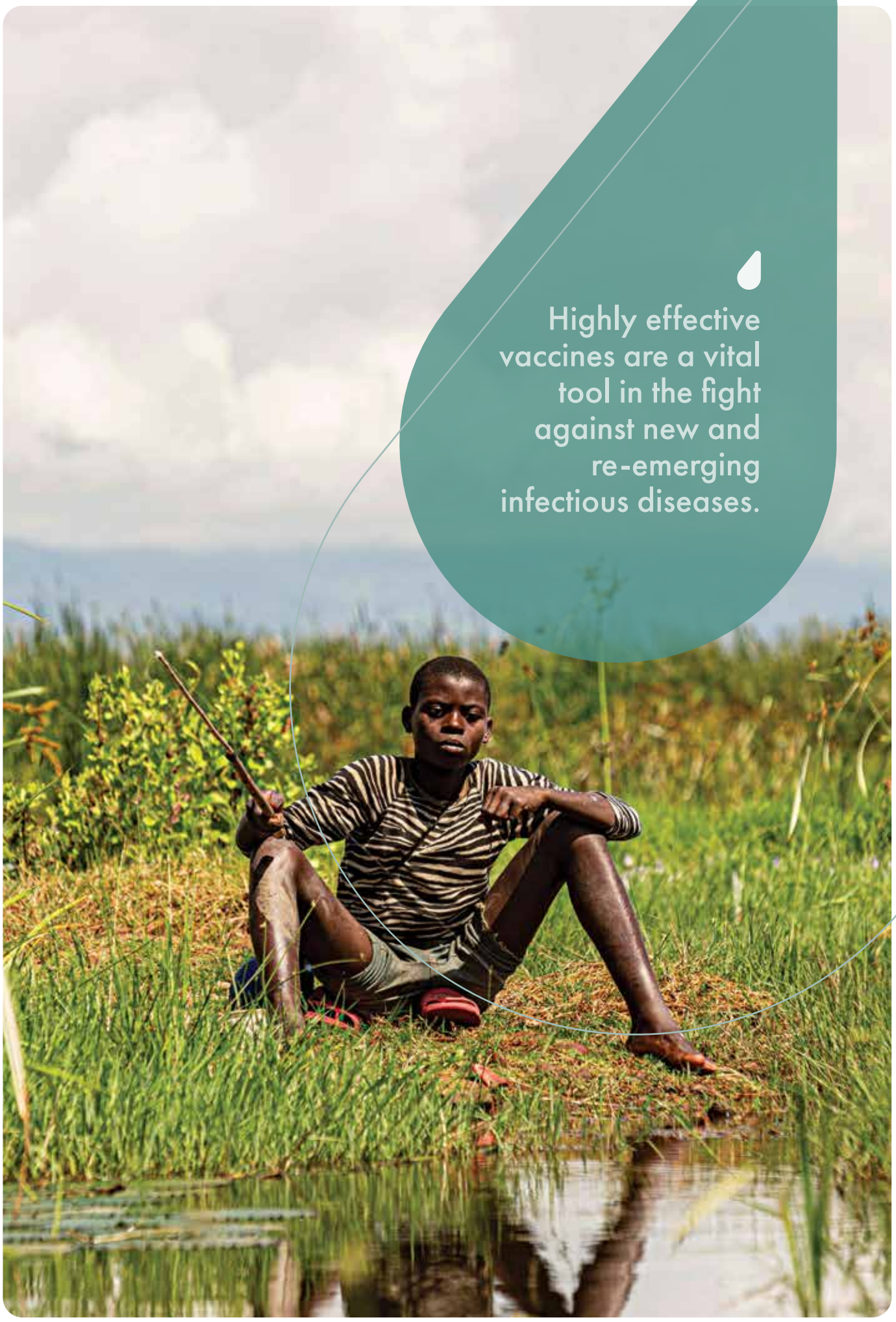
VACCELERATE has established the first transnational European registry of volunteers for participation in future clinical trials, and the recruitment of clinical trial volunteers has continued across different European countries during 2022. Along with volunteer registration, nearly 500 clinical trial sites across Europe have been identified by the VACCELERATE network.

EVI co-leads the activities on Immune Monitoring, which aims to identify a core set of immune assays to be validated and used across the VACCELERATE network in order to ensure standardised testing of all samples collected in COVID-19 clinical trials. High priority assays for measuring both the humoral immune response and the cellular immune response were identified within VACCELERATE at the beginning of the project and standardised protocols and associated standard operating procedures (SOP's) were prepared, validated, and made available to the scientific community at large.

EVI is also deeply involved in the Communication and Outreach activities. In this context, EVI developed an 'Inventory and gap analysis report of existing public outreach material' to identify and tackle existing gaps in public information material on COVID-19 vaccine trials in Europe, with special emphasis on identifying informational, promotional and educational material for underserved groups. This information is freely available on EVI website, and a publication was published in August 2022 (doi.org/10.22323/2.21050205).

Nipah vaccine development

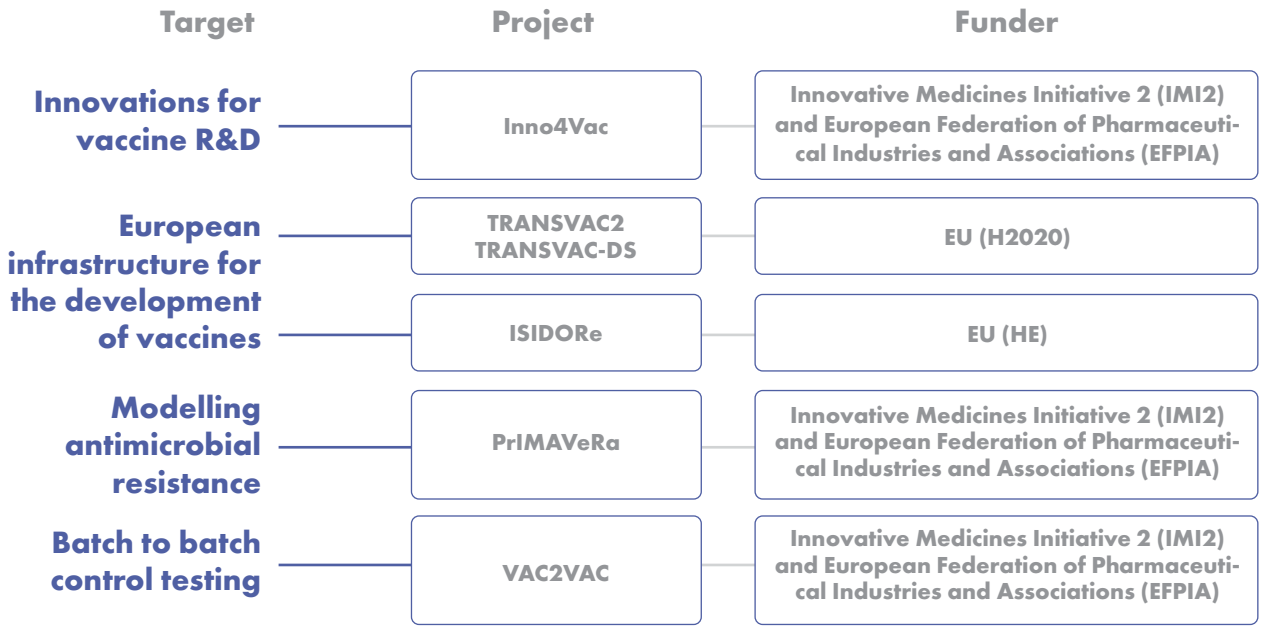
The MV-NiV vaccine candidate is a live attenuated measles vector-based vaccine containing the Nipah-virus G gene (Malaysia strain). The recombinant vaccine candidate was developed at the Institute of Medical Science, University of Tokyo, and has shown to induce strong humoral responses in a preclinical study. The vaccine has also demonstrated protection against lethal Nipah virus infection in hamster and non-human primate models. A GMP compliant manufacturing process for the vaccine candidate has been successfully established, and 12 months and in-use stabilities studies have been completed. A proof-of-concept study in the hamster NiV infection model has confirmed the protective efficacy of the vaccine candidate, while cross neutralizing antibody production against the NIV Bangladesh strain has also been demonstrated in 2022. **These results suggest that the MV-NiV vaccine could be effective against the NiV-Malaysia as well as the NiV-Bangladesh strains and support the initiation of the First-in-Human (FIH) clinical trial.**



Highly effective vaccines are a vital tool in the fight against new and re-emerging infectious diseases.

Cross-cutting activities

EVI coordinates and promotes a number of disease-overarching research projects that aim to provide better tools and technologies for vaccinology in general.



Innovations to accelerate vaccine development and manufacture

Inno4Vac

Inno4Vac is a public-private partnership that addresses scientific bottlenecks in vaccine development. The project is developing predictive biological and mathematical models of vaccine performance and bio-manufacturing. Artificial intelligence combined with big data and computational modelling is being used to build an open-access and cloud-based platform for *in silico* vaccine efficacy assessment and development. Controlled human infection models and cell-based human *in vitro* 3D models are being developed to enable early evaluation of vaccine efficacy and prediction of immune protection. Finally, for vaccine bio-manufacturing, an open-source *in silico* simulation platform for guiding the production of vaccine candidates and associated stability testing is being established.

Key achievements

Inno4Vac project activities are progressing in line with expectations, and the forward momentum continues into the new year. **Fourteen deliverables were submitted in 2022 including the data management plan, the project communication policy and plan for dissemination and exploitation, the first impact assessment report, developing strategies and roadmaps for positioning the newly developed models in the regulatory framework,** as well as numerous deliverables with a scientific-technical focus as described below. The Scientific and Ethics Advisory Committee (SEAC) was formed, comprised of international experts covering all project-related disciplines to ensure high quality of scientific outputs. Additionally, approximately 120 consortium members participated in the first annual meeting, held on 5-6 October in Siena, Italy. The annual meeting included the presentation and discussion of data and developments, celebrated the initial achievements, and drove the project forward as a strong consortium. Inno4Vac had a vibrant year in terms of communication and dissemination; the consortium issued 35 press releases and published 34 social media posts featuring project events, news, and achievements. These items were published across several platforms including LinkedIn, Facebook, and Twitter. As a result of publication on certain high traffic websites including several regional European newspapers, as well as 3 television spots, the consortium estimates to have reached nearly 223,000 people with these activities. In terms of outreach, project partners advanced engagement with regulatory authorities to discuss strategies to increase the likelihood of acceptance of the developed models in the regulatory framework.

The project management structure is in full effect as activities within SubTopics begin to produce tangible outputs, and the consortium members anticipate further advancement of project goals through 2023.

ST1: ST1 (VAXPRED) progressed in developing methods for modelling and quantifying the heterogeneous baseline of

human adaptive immunity and for the prediction of antigen & pathogen features.

ST2: The end goal of ST2 (CHIMICHURRI) is to develop new and improved controlled human infection models (CHIMs) for three pathogens (Influenza, RSV and *C. difficile*) and facilitate the implementation of CHIMs within the vaccine development pipeline and regulatory framework. CHIMICHURRI has worked intensely in 2022 to identify suitable candidate strains for challenge agent manufacturing. Key experts in regulatory affairs and CHIMs assembled in two workshops in 2022 to address pathogen-specific issues, to build scientific consensus for improvements to each of the challenge models to be accepted by regulators as part of the licensure for new vaccines. In January an Influenza and RSV workshop focused on strain selection, immunoassays development and viral isolates access/sourcing for in depth characterisation. Evaluated participants the best approach to pre-select suitable viral strain candidates, and discussed what current key aspects of the vaccine production and validation processes should be given close attention. In October, a Chemistry, Manufacturing and Controls (CMC) regulatory workshop focused on aspects of GMP manufacturing of challenge agents to offer guidance and clarification in the development (challenge strains selection, characterisation), manufacture, and control strategy of challenge agents. The working highlighted key aspects that may be critical for regulatory acceptance and ultimately the support of the implementation of CHIMs within the vaccine development pipeline on a global scale. The ST2 partners proactively identified a clinical data sharing platform in 2022 for all data that will be generated from all Inno4Vac trials, and to allow data sharing according to FAIR principles (Findable, Accessible, Interoperable, Reusable) moving forward.

ST3: The goal of ST3 (MERMAID) is the development of next-generation human *in vitro* 3D models for gastro-intestinal, respiratory and urovaginal mucosae that include relevant immune-system components in combination with selected pathogens (or toxins produced by a pathogen). Design of various models for each of the mucosae was discussed by all partners during an early workshop in November in the Netherlands. It was decided that seven different cellular model types and seven pathogens (16 models total) would be explored in the "Development Phase" (*i.e.*, in the first two years of the project, the so-called Stage Gate 1 period): two cell models based on gastro-intestinal cell sources (organ-on-chip, organoid) with Norovirus and *C. difficile,* three cell models on respiratory cell sources (Air-liquid-Interface, organ-on-chip, organoid) with influenza virus and respiratory syncytial virus (RSV), and two on uro-vaginal cell sources (Air-liquid-Interface, organ-on-chip) with herpes simplex virus type-2, *C. trachomatis* and *N. gonorrhoea*. Good progress was made for all model types, and preparations were made for several models to add relevant immune components, such as innate immune cells, or T-cell lines genetically engineered to be relevant in the models. To work on a road map for regulatory use and acceptance of next-generation human *in vitro* 3D models in de-risking vaccine development, a workshop with experts in the regulatory space and from the 3D model field was held in June in Brussels.

ST4: As the ST4's (VaXinS) objective to establish a one-stop cloud-based platform for computational modelling of vaccine biomanufacturing processes and stability requires a high level of coordination to bring all necessary components into a single platform, all partners met face to face in Lyngby, Denmark, in February 2022, in addition to regular meetings for each Work Package. To develop *in silico* models for protein vaccine stability prediction, datasets were defined and exchanged between partners and modelling progressed. To develop *in silico* models of fermentation (upstream processing), a compartment model approach for different reactor scales, based on computational fluid dynamics (CFD), was established and documented in a report. Additionally, microbial metabolism models that will be integrated with those mixing models were refined. For the *in silico* models for centrifugation and chromatography (downstream processing), data was exchanged, initial model simulations were run, and implementation of process control began. To generate additional necessary centrifugation data, an ultra scale-down approach was implemented at a partner site. The implementation of an open-access cloud based platform to integrate all necessary components is ongoing and builds on an established software of the consortium. Importantly, an expert panel of regulators was assembled in Brussels in March 2022 where each Work Package outlined the modelling approaches and engaged in a dialogue to gain regulatory feedback and guidance, and compiled a structured report for follow-up.

Predicting the Impact of Monoclonal Antibodies & Vaccines on Antimicrobial Resistance

PrIMAVeRa

The goal of PrIMAVeRa (**Pr**edicting the **I**mpact of **M**onoclonal **A**ntibodies & **V**accin**e**s on Antimicrobial **R**esist**a**nce) is to develop an open-source, web-based platform combining mathematical models with a comprehensive epidemiological repository (*i.e.*, with data referring to health, economic outcomes and frequency measures). This platform aims to enable policymakers to reach data-driven decisions regarding the prioritisation of specific vaccines and monoclonal antibodies (mAbs), informing the strategic allocation of limited resources.

Key achievements

In 2022, work was concentrated mainly on the literature search. Protocols for 4 systematic reviews (SR) were developed and uploaded to the International Prospective Register of Systematic Reviews (PROSPERO): 1) frequency measures of healthcare-associated infections and antimicrobial resistance (AMR), 2) AMR-associated health outcomes, 3) AMR-associated economic outcomes, and 4) existing mathematical models for AMR. Additionally, a protocol for a systematic review of the grey literature was developed and registered in PROSPERO and focused on obtaining individual-level data. Potential databases have been identified and database owners are being contacted for the exchange of their data.

The Consortium has also selected the pathogen-infection combinations of interest an important step for data gathering and model development. The Consortium also advanced discussions on how to make project data publicly available through the EPI-Net repository.

The Consortium management structure was established and is currently in operation. A workshop was held where AMR case studies were discussed, and the first annual meeting of the project was held in hybrid format on 29-30 November 2022 in Verona, Italy. The Consortium had a vibrant year in Communication and Dissemination: the project website was launched and multiple social media posts featuring the project were published on LinkedIn, Twitter, the project website, and other platforms. The consortium finalised the communication plan as well as the first Data Management Plan, and the Scientific Advisory Committee was established.

Building a European infrastructure for the development of vaccines

TRANSVAC

TRANSVAC is a collaborative infrastructure to accelerate European vaccine research and training in vaccinology. TRANSVAC was established in 2009 by the European Vaccine Initiative (EVI), and initially funded by the European Union under the 7th Framework Programme (FP7) and subsequently under Horizon 2020 as TRANSVAC2. The collaboration is a joint effort of leading European groups working in the field of vaccine development, and TRANSVAC catalyses vaccine development through three types of activities: (i) Transnational Access (TNA), (ii) Joint Research Activities (JRA) and (iii) Networking Activities.

TNA is a wide range of scientific-technical services that are offered to support the development of vaccines, the majority of which can be accessed free-of-charge. The services are orgnised in four different platforms: Technology, Immunocorrelates and System Biology, Animal Models, and Clinical Trial Support.

JRAs are conducted by the consortium partners to improve and support the scientific-technical services. The TRANSVAC research activities have focussed on improving adjuvants, predictive assays, systems biology and animal models.

Networking Activities have been used to set-up training modules at leading European centres with the aim to train the next generation of scientists in vaccine research and development.

In 2022, TRANSVAC2 launched the final calls for applications for TNA services. **A total of 5 new TRANSVAC2 services were awarded to 4 different research groups from SMEs and public institutions to help speed-up the vaccines development for malaria, *C. difficile* and COVID-19. In addition, 8 different vaccine development projects were completed by TRANSVAC2 service providers, including work focused on *C. difficile, H. pylori,* and multiple COVID-19 projects.**

Additionally, TRANSVAC2 integrated into the novel ISIDORe framework (see in page 32). As part of this initiative, TRANSVAC2 updated the service catalogue, harmonised with other RIs, and began accepting and reviewing applications for TNA services within ISIDORe.

5 training modules were held in 2022: clinical vaccine development and biomanufacturing; adjuvants and vaccine formulations; validity and comparison of animal models; statistics of vaccine evaluation; and regulatory aspects of vaccine development. 215 applications were received for a 90 total training spots. In addition to the TRANSVAC2-funded spots, the support of Coalition for Epidemic Preparedness Innovations (CEPI) funded additional spots for their personnel to attend the courses. In 2022, the foundation was laid for the long-term continuation of these courses after the conclusion of TRANSVAC2 as an EU-supported project, supported by a combination of registration fees, continued CEPI participation, and sponsorships.

As part of the JRAs, methods and platforms developed in various JRA programs were used to support numerous vaccine research projects. Utilised JRA-derived services included adjuvant profiling services, cross-linking mass spectrometry techniques, and platforms for cytokine/ chemokine analysis, transcriptomics/ next-generation sequencing, and computational modelling.

Building on the great success of the TRANSVAC infrastructure, the TRANSVAC-DS project is a design study to propose a business model for a permanent and stable vaccine infrastructure and develop detailed business and implementation plans for its further preparation, implementation, and operation.

A business model was developed that integrates and relies on two different models under the same umbrella. On one hand, this includes a branch dedicated to the provision of high-value scientific-technical vaccine R&D services, on the other hand there will be a business incubator-type of venture that will focus on the direct development of selected vaccine candidates within the vaccine infrastructure.

During 2022, detailed business and implementation plans have been developed. Various legal entity options have been assessed to identify the best option for a sustainable vaccine infrastructure. This is accompanied by stakeholder engagement and advocacy activities to ensure that the proposed infrastructure can count on the necessary political and financial support from relevant funders and policy and decision makers.

ISIDORe is a consortium of 16 European research infrastructures and coordinated networks, including TRANSVAC, that are integrated together into a single framework for conducting research and providing a diverse range of TNA services. The ISIDORe consortium was formed in response to the SARS-CoV-2 pandemic to provide a single interface to users of various TNA providers from different European infrastructures. Additionally, Joint Research Activities (JRAs) will promote coordination and integration between the different networks while developing novel scientific capabilities to address gaps in current capacities and offer cutting-edge services to future TNA applicants.

In 2022, ISIDORe opened dedicated calls for TNA applications for SARS-CoV-2 and monkeypox. Moreover, a broader Preparedness call was launched to address specific needs in several disease categories: risk-group 4 pathogens; respiratory pathogens with epidemic potential; vector-borne pathogens; and Pathogen X.

Reducing the use of animals in vaccine research and manufacturing

VAC2VAC

Current quality control approaches when manufacturing vaccines rely mostly on *in vivo* methods. VAC2VAC aimed to develop and validate quality testing approaches for human and veterinary vaccines using nonanimal methods. VAC2VAC involved experts from the veterinary and human vaccine industries in a partnership with official medicines control laboratories, academia, translational research organisations, and vaccinology alliances. The project partners developed, optimised, and evaluated physicochemical methods, immunochemical methods, cell-based assays and multiparametric and bioinformatics assays for routine control testing of vaccines. This effort was conducted in collaboration and consultation with regulatory agencies. The project period concluded officially in early 2022, but EVI and consortium partners have continued disseminating the results of VAC2VAC, while exploring funding opportunities for continuing the important task of promoting *in vitro* replacement of *in vivo* methods.

Key achievements

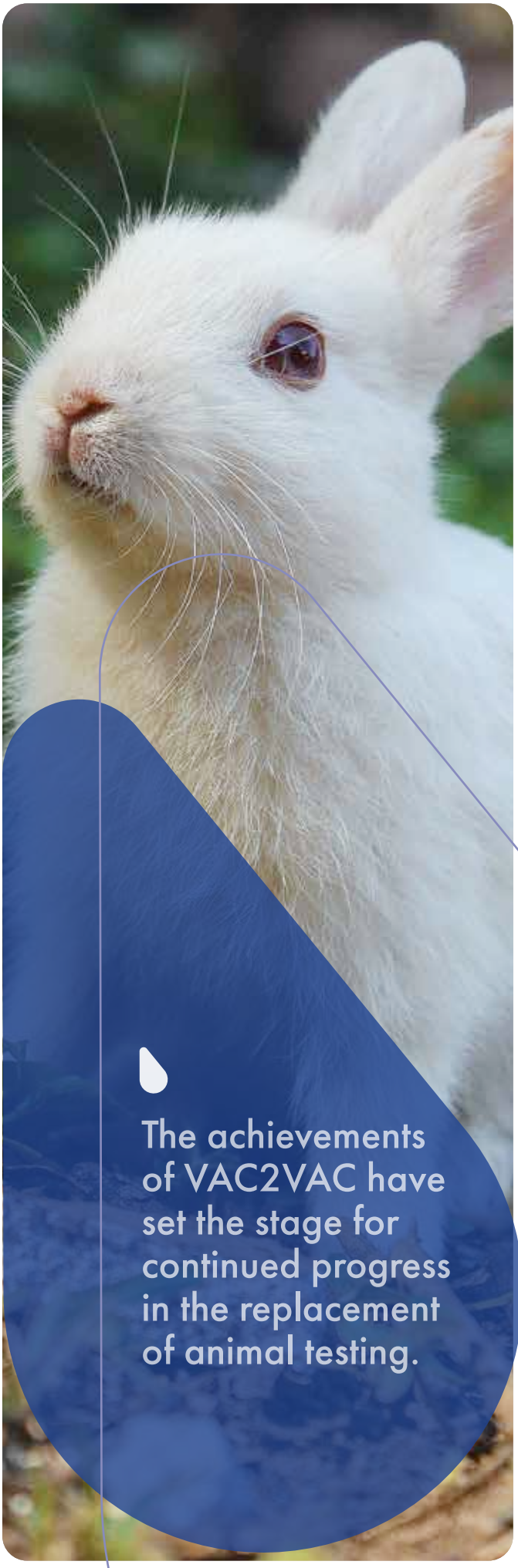
Two *in vitro* assays have been validated by the VAC2VAC consortium: the monocyte activation test (MAT) and the Tetanus Neurotoxin (TeNT) LC-MS/MS assay.

The MAT has been validated, approved by the competent regulatory authorities, and implemented in industry as a replacement of the Rabbit Pyrogen Test (RPT). A proposal to revise Ph. Eur. monograph 1375 on tick-borne encephalitis virus (TBEV) by replacing the RPT with the MAT was submitted, acknowledged, and included in the more extensive revision of all monographs to replace the RPT.

The TeNT LC-MS/MS is an antibody free method that is

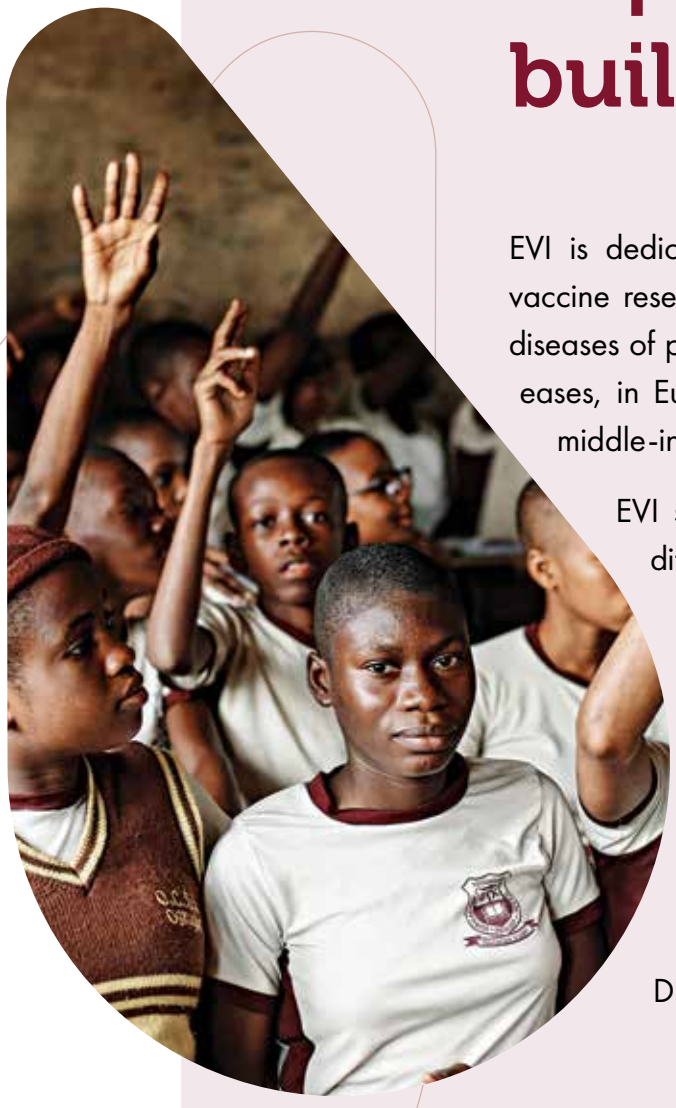
able to identify and quantify the amount of TeNT present in the bacterial medium during the different production time points.
In addition to the validated MAT and TeNT assays, seven ELISA assays have been qualified, including diphtheria, tetanus, and TBEV ELISAs that have been transferred to the industry partners for further product-specific optimisation and validation. Furthermore, 11 *in vitro* assays have reached proof of principle, and have been transferred to industry partners.
VAC2VAC has not only been very successful in the development of new assays: during the VAC2VAC project, over 13 young scientists were able to further their education and refine their skills through graduate degrees and internships at consortium members.

VAC2VAC has implemented a sustainability plan to make critical reagents widely available following the conclusion of the official project period. To do so, NIBSC has been entrusted to manage the handling, distribution, and future production of monoclonal antibodies needed in DTaP ELISA and Luminex assays developed in VAC2VAC. Depositor agreements between NIBSC and other owners of the monoclonal antibodies that are used in the assays (GSK, Sanofi, and Intravacc B.V) have been signed whereby depositors agreed to supply the material and hybridoma information to NIBSC. NIBSC has made the monoclonal antibodies available to the public subject to a handling fee to cover operational costs and future replacement of antibody batches.



The achievements of VAC2VAC have set the stage for continued progress in the replacement of animal testing.

Capacity building



EVI is dedicated to strengthening clinical and vaccine research capacities in the fight against diseases of poverty and emerging infectious diseases, in Europe and particularly in low- and middle-income countries (LMICs).

EVI supports capacity building through different activities such as **fellowships, short-term courses, networking, workshops, and stakeholder meetings,** and has served for almost a decade as hosting institution for the EDCTP Clinical Research and Development Fellowship Scheme and the WHO/TDR Special Programme on Tropical Diseases Research.

Master and Doctoral Fellowships

As part of the EDCTP2-supported Multi-Stage Malaria Vaccine Consortium (MMVC), EVI has been able to offer Masters and PhD Fellowships to a handful of talented African scientists wishing to pursue a career in malaria research and vaccinology:

Caroline Bundi
MMVC PhD fellow at Ifakara Health Institute Clinical Trial Facility, Bagamoyo Research and Training Centre, Tanzania. Sep 2019 to Nov 2023

Vaccine dosing and vaccination schedule are key in determining immunogenicity, longevity, and vaccine efficacy. *P. falciparum* reticulocyte-binding protein homolog 5 (PfRH5) and R21 are malaria vaccine candidates targeting the blood-stage and sporozoite-stage, respectively, that have been tested in malaria-endemic countries. Using samples from two clinical trials conducted using these vaccines in Tanzania and Kenya, I aim to evaluate how the following four factors affect the vaccine response. A) Previous malaria exposure (high malaria intensity vs low malaria intensity), B) Age (compare adults, children, and infants) C) Vaccine dose (different combination of the vaccine and adjuvant dose) D) Vaccine regime (a monthly dose versus a last dose delayed to 6 months). I will model how these factors interact with each other with the aim to identify the best vaccine regime.

Elizabeth Kibwana
MMVC PhD fellow at KEMRI-Wellcome Trust Research programme, Kilifi, Kenya. Oct 2019 to Oct 2023

My study is part of a clinical trial to determine the efficacy of R21/MM in semi-immune adults, using the controlled human malaria infection (CHMI) model. CHMI studies involve infecting healthy volunteers with malaria parasites, monitoring parasitemia and treating them when a set threshold is reached. Malaria remains a public health concern, and the development of a malaria vaccine remains a priority. My project seeks to identify and characterise responses induced by R21/Matrix MTM malaria vaccine that may correlate with or confer protection. To do this, I carry out a variety of immunological assays to tease out vaccine induced antibody, and cell mediated immune responses that are associated with protection post infection in a CHMI study. The study looks to further understand the vaccine induced immunity, efficacy and potentially identify *in vitro* immune cell populations that correlate with protection for a novel malaria vaccine.

Prisca Yamaego
MMVC MSc fellow at IRSS- Clinical Research Unit of Nanoro (CRUN). Sep 2021 to Aug 2023.

Vaccination has been shown to be one of the most effective public health interventions worldwide. Immunogenicity of vaccines administered to infants could be modulated by several factors such as age, previous exposure to malaria parasite and malnutrition. In my MSc project, I will first look at the effect of these factors on the immunogenicity of both EPI vaccines and the novel malaria vaccine candidate (R21/Matrix MTM) in children participating in clinical trial in Nanoro, Burkina Faso. In the second analysis, I will assess whether children who respond poorly to R21/Matrix MTM vaccine also respond poorly to EPI vaccines. My findings will have public health significance by providing a better understanding on factors that modulate immune responses to vaccines intended for children in malaria endemic settings.

Lamin Camara
MMVC MSc fellow at MRC Gambia. Sep 2020 to August 2022.

I studied the immune response to a malaria vaccine called ChAd63 MVA ME-TRAP. This vaccine showed promising results in previous studies, stimulating T cell and antibody responses. My objective was to investigate the differences in immunogenicity in individuals who received this vaccine and identify patterns associated with a strong immune response. I also examined the differences in immune response between different age groups. To achieve this, I used flow cytometry to characterise a specific type of immune cell called circulating follicular helper T cells (cTfh) which play crucial role in coordinating the activity of antibody-producing B cells and improving the effectiveness of vaccinations. My work provided proof-of-concept for new approaches in malaria vaccine research that could be employed in LMICs, such as the Gambia.

Charles Mulamba
MMVC PhD fellow at Ifakara Health Institute Clinical Trial Facility, Bagamoyo Research and Training Centre, Tanzania. Sep 2019 to August 2023.

Malaria control relies heavily on the use of anti-malarial drugs and insecticides against malaria parasites and vectors, respectively. Drug and insecticide resistance threatens the effectiveness of conventional malaria interventions; alternative control approaches are therefore needed. The development of transmission-blocking vaccines that target the sexual stages in humans or mosquito vectors is among new approaches being pursued. Transmission-blocking vaccines induce antibodies that prevent malaria parasite development in the mosquito vector after a blood meal consequently blocking onward transmission. My project sets out to evaluate the capability of a new vaccine (Pfs25-IMX313/Matrix MTM) to induce transmission blocking antibodies in individuals living in malaria endemic areas.

Networking

EVI participates as European partner in the West African Network for TB, AIDS, and Malaria (WANETAM), which provides an important opportunity to network and exchange knowledge and skills with the scientific community in West Africa. WANETAM has evolved from the first EDCTP grant in 2009-2013, over the consolidation phase in 2016-2019 (WANETAM-2), and into the present WANETAM-3 (2021-2024). Coordinated by Professor Souleymane Mboup from the Reseau Africain de Recherche sur le SIDA in Senegal and comprising 30 institutions from 4 European and 12 West African countries, **the overall goal of WANETAM is to strengthen regional, national, institutional, and individual capacities to conduct clinical trials in line with the International Conference on Harmonization guidelines for Good Clinical Practice (ICH-GCP).**

WANETAM-3 builds on the activities of disease-defined work packages on TB, malaria, HIV, neglected tropical diseases, and emerging infections, together with Cross-Cutting Trainings to strengthen capacity of individuals in specialised skills needed in clinical research and the capacity of supporting infrastructure. EVI is mainly involved in WP6 that covers cross-cutting training and platform building.

Short Courses

As part of its capacity building activities, EVI provides a number of customised short-term courses and trainings in vaccinology and related topics. In 2022, EVI added training in science communication to its portfolio of short-term courses.

The EVI Communication Team contributed thus to the BactiVax European Training Network (www.bactivax.eu), a scientific research-based programme involving identification of new vaccine antigens and optimisation of immune responses, with a workshop on **'Vaccine education: tools & tactics',** tackling vaccine advocacy and its effective communication, for Early Stage Researchers and PhD students from across all Europe.

We strongly believe that vaccine advocacy is important and all researchers in the field **should be trained in how to be effective advocates for immunisation,** particularly with the increasingly vocal anti-immunisation lobby.

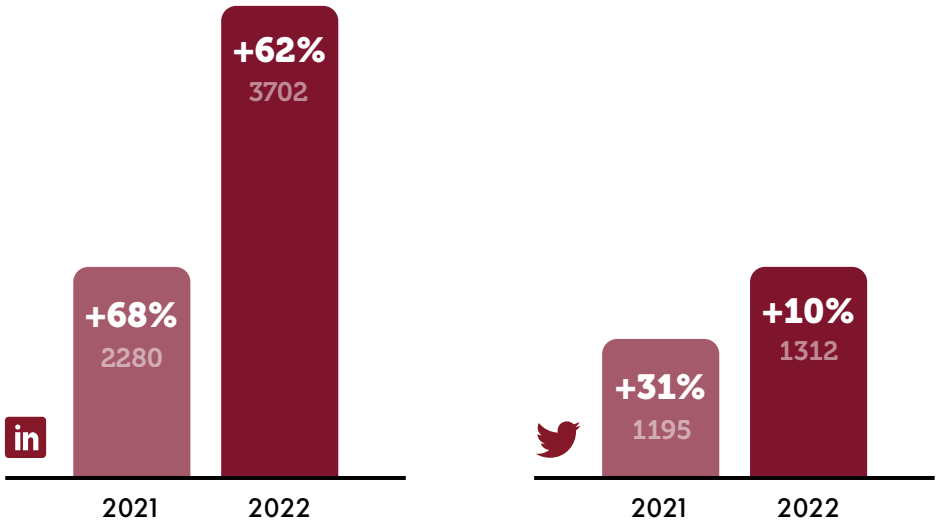
The workshop was given on site in Ischia, Naples, Italy, in the context of BactiVax Summer School.

Corporate communications

During 2022 the EVI Communications Team has continued to expand and strengthen the organisational network and profile, both offline by assuring conference and webinar participations from colleagues and employees, and/or by giving on site trainings, and online by maintaining a sustainable digital community growth through social media channels as well as in the newsletter subscribers list.

Digital community

The digital community on LinkedIn grew another 62% compared to 2021 (in 2021 the growth rate was +68% vs 2020), while on Twitter the numbers showed a slower yet sustained growth of 10% compared to 2021 (2021 vs 2020 was +31%).



Newsletter

The number of newsletter subscribers grew by 33%, which is double the growth of last year (2021 vs 2020 growth was 15%). The Communications team ensures that all new email addresses gathered comply with the EU general data protection regulation (GDPR).

Website development

In 2022 EVI launched two new websites for the projects PrIMAVeRa (www.primavera-amr.eu, in January 2022) and ADVANCE-VAC4PM (www.advance-vac4pm.eu, in August 2022), and continued reflecting updates on another seven websites for old and currently open projects.

Financial Performance Report 2022

The year 2022 has, from a financial perspective, consolidated EVI significantly. The year brought funding to EVI for cross-cutting activities and especially malaria activities. We are proud to welcome DGIS (Directorate-General for International Cooperation of the Netherlands) and BMBF (Federal Ministry of Education and Research of Germany) among our largest funders.

EVI came out of 2022 with a small surplus on the Profit and Loss, improved solvency (increased ability to meet long-term obligations), and at the same time greatly increased the operating budget for the next 5 years. This puts EVI in a solid financial position with an operating budget of €44.9 million to be used for the mission of EVI.

EVI Expenditures

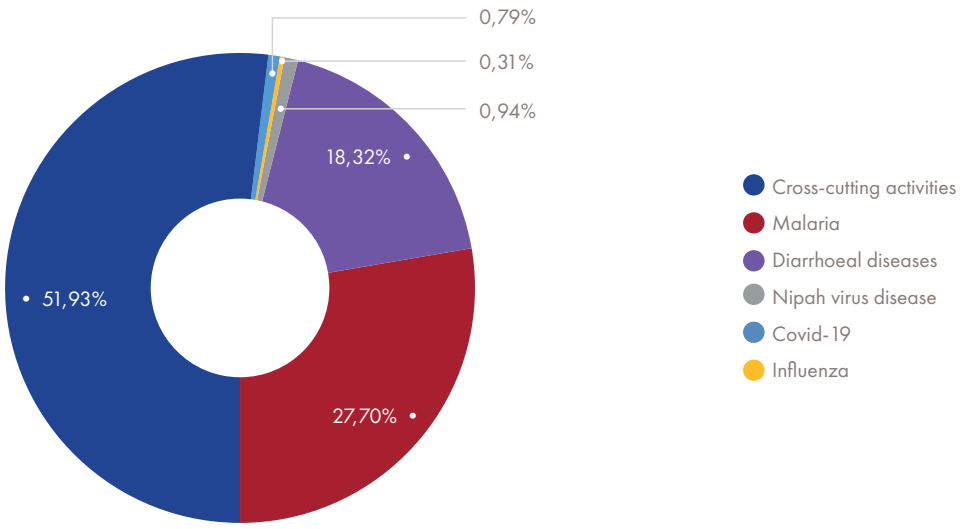


Figure 1: EVI Expenditure per area

Fundraising

EVI is sincerely grateful for the continued support from its long-term funders, as well as an increasing number of new funders. EVI's activities over the current reporting period were covering a broad portfolio of EU, EDCTP, CEPI, IMI, GHIT and now also including DGIS and BMBF.

Currently almost €386 million have been raised by EVI (past and current entities) since its inception in 1998. 2022 was a successful year for fundraising, in which the EVI PDP corporation was expanded while approaching new funders. EVI successfully applied for competitive research grants in the field of PDP vaccine development and was selected for funding by BMBF and DGIS with a grand total of €25.2 million.

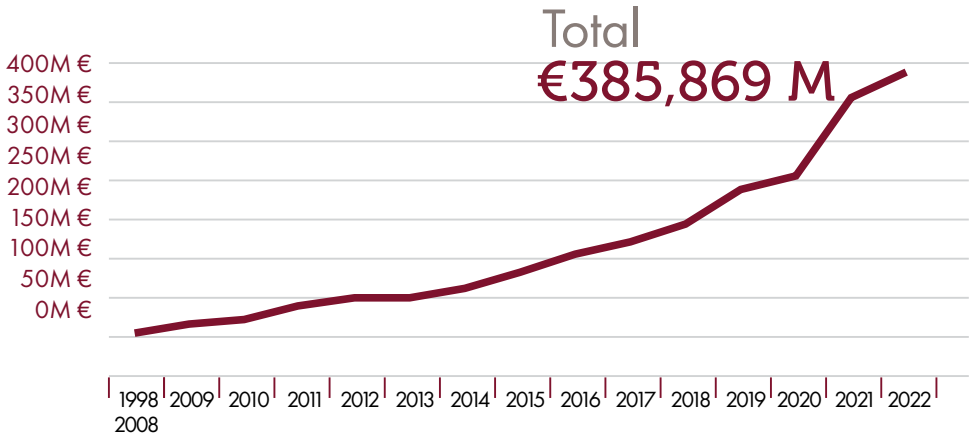


Figure2: Grants signed and projected (incl. cofunding) 2009-2022

Statement of comprehensive income for the year as of 31 December 2022

	EUR 2022
Income	
Turnover from sales	**28,000.00**
Public institutional funding:	
Governmental & International Organisations	196,896.14
EU & IHI	9,780,534.54
EDCTP	2,461,096.44
Total public institutional funding	**12,438,527.12**
Other income net	274,422.73
Total income	**12,740,949.85**
Social mission expenditure	
Research & vaccine development expenditure:	
Malaria	3,530,886.19
Diarrhoeal diseases	2,335,124.58
Nipah virus disease	119,759.00
Influenza	40,069.54
Covid-19	100,515.30
Cross-cutting activities	6,618,874.56
Advocacy & communications expenses	2,599.92
Total social mission expenditure	**12,747,829.09**
Supportive social mission expenditure	
Training, quality assurance and project development	796.54
Fundraising	403.61
Governance	4,824.80
Total supportive social mission expenditure	**6,024.95**
Non-social mission expenditure	
General executive administration	196,121.74
Overhead income	(237,581.02)
Total non-social mission expenditure	**(41,459.28)**
Total expenditure	**12,712,394.76**
Operating surplus / (deficit)	28,555.09

Statement of financial position as of 31 December 2022

	EUR 2022
Current assets	
Cash and cash equivalents:	
Cash and banks - key accounts	10,251,450.03
Total cash and cash equivalents	**10,251,450.03**
Current accounts and receivables:	
Other receivables	986.45
Financial and debtor receivables	1,081.52
Total current accounts and receivables	**2,067.97**
Total current assets	**10,253,518.00**
Non-current assets	
Tangible fixed assets, net	6,231.00
Long term securities	1,000,000.00
Deferred Expenses	65,436.34
Total non-current assets	**1,071,667.34**
Total assets	**11,325,185.34**
Current liabilities	
Creditors	1,844,091.85
Accrued expenses	242,293.63
Other liabilities	45,348.78
Deferred income	7,120,411.27
Total current liabilities	**9,252,145.53**
Equity of organisation	
Operating result	28,555.09
Operating funds	2,044,484.72
Total equity of the organisation	**2,073,039.81**
Total equity and liabilities	**11,325,185.34**

For more detailed information about EVI's financial statements and related indicators the '2022 EVI. Financial and Performance Report' is available upon request (www.euvaccine.eu/contact-us). The above figures are for the performance of EVI Association. As of 1st May 2022, EVI changed its legal status from an European Economic Interest Grouping (EEIG) to an Association (e.V) under German law. The figures for the EEIG from 1st January to 30th April 2022 can be requested using the above contact us link.

Governance

AS OF 31 DECEMBER 2022

During 2022 the legal status of EVI was changed. EVI was formerly organised as an European Economic Interest Grouping (EEIG), which proved inconsistent with its goals and future ambitions. EVI has therefore changed its legal registration to become a German Association (e.V) with non-profit status and registered with its official headquarters in Heidelberg. The change has not affected any ongoing activities but will open new possibilities to engage in new activities in the future.

The change in legal status, which took effect in May 2022, has led to a streamlining in EVI's governance structure. The highest decision-making body, the EVI Board, has been renamed to the EVI General Meeting, but remains otherwise unchanged. The General Meeting continues to be advised on financial and legal matters by the EVI Finance and Risk Management Committee (FRMC), which also remains unchanged.

EVI Board

Clemens Kocken
Biomedical Primate Research Centre, The Netherlands CHAIR

Samuel McConkey
Royal College of Surgeons in Ireland, Ireland VICE-CHAIR

Christiane Gerke
Institut Pasteur, France
BOARD MEMBER

Michael Lanzer
Heidelberg University
BOARD MEMBER

David Salisbury
Jenner Vaccine Foundation, United Kingdom
BOARD MEMBER

EVI Finance and Risk Management Committee (FRMC)

Clemens Kocken
Biomedical Primate Research Centre, Rijswijk, The Netherlands

Steffen Ahrens
Falk & Co., Heidelberg, Germany

Vacant position to be filled

EVI Secretariat

Ole Olesen
Executive Director

Sten Larsen Finnsson
Director of Finance & Administration

Sophie Houard
Director of Vaccine Development

Stefan Jungbluth
Head of Business Development

Thorsten Kohaut
Head of Accounting

Nicoletta Corti
Project Manager Consultant

Flavia D'Alessio
Senior Project Manager

Romina Di Marzo
Communications & Advocacy Manager

Roland Frank
Project Manager

Sandra Hauenstein
Financial Accountant & Travel Manager

Mandeep Kaur
Project & Communication Assistant

Reinhard Liebers
Project Manager

Catarina Luis
Communication & Senior Project Manager

Candice Marion
Vaccine Development Manager

William Martin
Project Manager

Irina Meln
Senior Innovation Manager

Irene N. Nkumama
Malaria Programme Manager

Daniel Reem
Project Manager Assistant

Aicha Sayeh
Clinical Project Manager

Monika Slezak
Project Manager Consultant

Kimberly Veenstra
Project Manager

Acknowledgments

During our more than twenty years of existence, EVI has succeeded in securing the support of a large number of partners, funders, and other individuals and organisations. We would like to sincerely thank everyone for their backing and collaboration and gratefully acknowledge the financial and other support received from the following organisations.

- All4Cloud
- Austrian Federal Ministry of Science and Research, Austria
- Boehringer Ingelheim Animal Health, France, previously known Merial Boehringer Ingelheim (BI), Germany
- Centre National de la Recherche Scientifique (CNRS), France
- Centre National de Recherche et de Formation sur le Paludisme (CNRFP), Burkina Faso
- Co-funding was kindly provided by the following organisations:
- Coalition for Epidemic Preparedness Innovations (CEPI), Norway
- Danida, Denmark's development cooperation, Denmark
- Danish National Advanced Technology Foundation, Denmark
- Department of Foreign Affairs, Irish Aid, Ireland
- Dutch Ministry of Foreign Affairs, Directorate-General for International Cooperation (DGIS), The Netherlands
- Dutch Research Council, The Netherlands
- European & Developing Countries Clinical Trials Partnership (EDCTP), The Netherlands, with co-funding from EU Member
- States and other countries
- European Union, Belgium
- Federal Ministry of Education and Research (BMBF) through KfW, Germany
- Global Health Innovative Technologies (GHIT) Fund, Japan
- GSK Biologicals (GSKBio), Belgium
- Innovative Medicines Initiative (IMI), Belgium
- Inserm, France
- Institut National de la Transfusion Sanguine (INTS), France
- Intervet International B.V., also known as MSD Animal Health, Netherlands
- NIH – NIAID, United States of America
- Nobelpharma Co., Ltd., Japan
- Research Institute for Microbial Diseases (RIMD), Japan
- Sanofi Pasteur, France
- SAP
- Sumitomo Pharma Co., Ltd
- Swedish Ministry of Foreign Affairs, Swedish International Development Cooperation Agency (Sida), Sweden
- Takeda Pharmaceuticals International AG, Switzerland
- University of Copenhagen, Denmark
- University of Oxford, United Kingdom
- Wellcome Trust, United Kingdom
- World Health Organization - Special Programme for Research and Training in Tropical Diseases (WHO-TDR), Switzerland
- Zoetis Belgium SA (Zoetis), Belgium

Partners

EVI thanks all its collaborators that support our common goal of developing vaccines that create health and equity for all people.

AdaptVac APS (AdaptVac)	Denmark
African Research Collaboration for Health Limited Kenya	Kenya
Ares Genetics GmbH	Austria
Association Internationale de Standardisation Biologique pour L´Europe	France
Batavia Biosciences B.V.	The Netherlands
Bavarian Nordic	Denmark
BIOASTER - Fondation de Cooperation Scientifique	France
Biobanks And Biomolecular Resources Research Infrastructure Consortium (BBMRI-ERIC)	Austria
Biomedical Primate Research Centre	The Netherlands
Biomedical Research Center of the Slovak Academy of Sciences	Slovakia
Boehringer Ingelheim Animal Health France	France
Boehringer Ingelheim	Germany
Centre de Recherches Médicales de Lambaréné (CERMEL)	Gabon
Centre for Infectious Disease Research in Zambia (CIDRZ)	Zambia
Centre National de Recherche Scientifique et Technologique (CNRST)/Institut de Recherche en Science de la Santé (IRSS)	Burkina Faso
Centre National Hospitalier de Pneumo - Phtisiologie	Benin
Centro Hospitalar Universitário do Porto	Portugal
Collaborative Center for Clinical Epidemiology and Outcomes Research (CLEO)	Greece
College of Medicine - University of Ibadan	Nigeria
College of Medicine and Allied Health Sciences (COMAHS), University of Sierra Leone (USL)	Sierra Leone
College ter Beoordeling van Geneesmiddelen	The Netherlands
Commissariat a l'energie atomique et aux energies alternatives (CEA/IDMIT)	France
CureVac AG	Germany
Danmarks Tekniske Universitet	Denmark
Eberhard Karls Universität Tübingen (EKUT), linked third party: Universitätsklinikum Tübingen	Germany
Eberhard Karls Universität Tübingen	Germany
Ehime University	Japan
Enpicom BV	The Netherlands
Epicentre	France
ETH Zürich	Switzerland
Euro-Bioimaging	Finland

European Clinical Research Infrastructure Network (ECRIN)	France
European Commission, Joint Research Centre	Italy
European Infrastructure for Translational Medicine (EATRIS)	The Netherlands
European Infrastructure Of Open Screening Platforms For Chemical Biology / European Research Infrastructure Consortium (EU-OPENSCREEN ERIC)	Germany
European life-sciences Infrastructure for biological Information (ELIXIR)	United Kingdom
European Marine Biological Resource Centre European Research Infrastructure Consortium (EMBRC)	France
European Research Infrastructure On Highly Pathogenic Agents (ERINHA-ERIC)	France
European University Cyprus	Cyprus
European Vaccine Initiative	Germany
European Vaccine Research and Development Infrastructure (TRANSVAC)	Germany (EVI)
European Virus Archive – Global (EVAg)	France
Eveliqure Biotechnologies GmbH	Austria
Flanders Vaccines	Belgium
Fondation mondiale Recherche et Prévention Sida	Côte d'Ivoire
Fondation pour la Recherche Scientifique (FORS)	Benin
Forschungszentrum Borstel Leibniz-Zentrum fur Medizin und Biowissenschaften (FZB)	Germany
Forschungszentrum Jülich GmbH	Germany
Foundation for Appropriate Technology in Health (FATH)	Switzerland
Fraunhofer Institute for Molecular Biology and Applied Ecology	Germany
Fundação Manhiça	Mozambique
GenIbet Biopharmaceuticals S.A.	Portugal
GlaxoSmithKline Biologicals SA	Belgium
Goeteborgs Universitet	Sweden
Groupe de Recherche Action en Santé (GRAS)	Burkina Faso
GSK Biologicals	Belgium
Hacettepe University	Turkey
Helmholtz Center for Infection Research GmbH (HZI)	Germany
Hôpital National (DONKA)	Guinea
Hospital of Lithuanian University of Health Sciences Kauno Klinikos	Lithuania
icddr,b	Bangladesh
Ifakara Health Institute (IHI)	Tanzania
Imperial College of Science Technology and Medicine London	United Kingdom
Infrafrontier Gmbh	Germany
infraVec-2	France
Institut de Recerca i Tecnologia Agroalimentàries (IRTA)	Spain

Institut de Recherche en Sciences de la Santé (IRSS)	Burkina Faso
Institut de Recherche pour le Développement (IRD)	France
Institut de Salut Carlos III (ISCIII)	Spain
Institut National de la Recherche Agronomique (INRA)	France
Institut National de la Santé et de la Recherche Médicale (Inserm)	France
Institut National de Santé Publique	Burkina Faso
Institut Pasteur	France
Institut Pasteur de Dakar	Senegal
Institute des Sciences et Techniques (INSTech)	Burkina Faso
Institute of Endemic Diseases (IEND), University of Khartoum	Sudan
Institute of Human Virology Nigeria	Nigeria
Institute of Research in Health Sciences (IRSS-DRO), Bobo-Dioulasso	Burkina Faso
Institute of Research in Health Sciences, Clinical Research Unit of Nanoro (IRSS-URCN)	Burkina Faso
Instituto de Biologia Experimental e Tecnológica (iBET)	Portugal
Instituto de Engenhariade Sistemas e Computadores, Tecnologia e Ciencia	Portugal
Instruct Academic Services Limited	United Kingdom
Instruct-ERIC	UK
International Alliance for Biological Standardization for Europe	France
Intravacc B.V.	The Netherlands
Istituto Superiore di Sanità	Italy
Janssen Vaccines & Prevention B.V.	The Netherlands
Jos University Teaching Hospital	Nigeria
Julius-Maximilians-Universität Würzburg	Germany
Karolinska Institutet	Sweden
Kenya Medical Research Institute (KEMRI)	Kenya
Kintampo Health Research Centre (KHRC)	Ghana
Klinikum der Universität zu Köln	Germany
Leiden University Medical Center (LUMC)	The Netherlands
Leiden University Medical Center, Dept. Infectious Diseases (LUMC)	The Netherlands
Life Science Network GmbH	Germany
London School of Hygiene and Tropical Medicine (LSHTM)	United Kingdom
Lund University, Department of Chemical Engineering	Sweden
Luxembourg Institute of Health (LIH)	Luxembourg
Makerere University	Uganda
Malawi University of Science and Technology (MUST)	Malawi

Masaryk University, Faculty of Medicine	Czech Republic
MCT Bioseparation	Denmark
Medical Center for Translational Research, Osaka University Hospital	Japan
Medical Research Council Unit, The Gambia at London School of Hygiene and Tropical Medicine, UK (MRCG at LSHTM)	United Kingdom
Medical University of Bialystok	Poland
Medical University of Vienna	Austria
Medicines & Healthcare products Regulatory Agency (MHRA)	United Kingdom
Merck Sharp & Dohme	The Netherlands
Microbial Resource Research Infrastructure (MIRRI)	Portugal
Ministry of Health	Israel
National Institute for Biological Standards and Control	United Kingdom
National Institute for Public Health and the Environment	The Netherlands
National University of Ireland Galway	Ireland
Nigerian Institute of Medical Research (NIMR)	Nigeria
Nobelpharma Co, Ltd.	Japan
Noguchi Memorial Institute for Medical Research (NMIMR)	Ghana
Nova ID FCT – Associação para a Inovação e Desenvolvimento de FCT	Portugal
Novavax AB	Sweden
Országos Korányi Pulmonológiai Intézet (OKPI)	Hungary
Osaka University	Japan
Österreichische Agentur für Gesundheit und Ernährungssicherheit GmbH (Austrian Agency for Health and Food Safety)	Austria
PATH	USA
Paul-Ehrlich-Institut	Germany
Pfizer	United Kingdom
Pfizer	Austria
Pharmalex Belgium	Belgium
Public Health England (PHE)	United Kingdom
Region Hovedstaden	Denmark
Region Stockholm, Karolinska University Hospital	Sweden
Research Institute for Microbial Diseases (RIMD), Osaka University	Japan
Réseau Africain de Recherche sur le SIDA	Senegal
Rijksinstituut voor Volksgezondheid en Milieu	The Netherlands
Sanofi Pasteur SA	France
Sciensano	Belgium

Sclavo Vaccine Association	Italy
Serum Institute of India Pvt. Ltd.	India
Servicio Andaluz de Salud	Spain
Servicio Madrileño de Salud	Spain
Sonar Global	France
Stanford University School of Medicine	USA
Statens Serum Institut (SSI)	Denmark
Stichting Centre for Human Drug Research	The Netherlands
Stichting Radboud Universitair Medisch Centrum (Radboudumc)	The Netherlands
Stiftung Tierärztliche Hochschule Hannover	Germany
Takeda Pharmaceuticals International AG	Switzerland
Technical University of Denmark	Denmark
The Chancellors, Masters and Scholars of the University of Oxford (UOXF)	UK
The National Institute for Biological Standards and Control (NIBSC)	United Kingdom
The University of Nottingham	United Kingdom
UK Health Security Agency	United Kingdom
Universidade Nova de Lisboa (NOVA)	Portugal
Universita Degli Studi di Siena	Italy
Universitätsklinikum Jena	Germany
Université Cheikh Anta Diop de Dakar	Senegal
Université de Lomé	Togo
Université de Paris	France
Université des Sciences, des Techniques et des Technologies de Bamako	Mali
Université Grenoble Alpes	France
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Universitetet I Bergen	Norway
Universitetet I Oslo	Norway
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University College London	United Kingdom
University Hospital Cologne	Germany
University Medical Center Groningen	The Netherlands
University Medical Center Utrecht	The Netherlands
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Vaccine Formulation Institute (VFI)	Switzerland
Veterinary Biocontained research facility Network (VetBioNet)	France
Vilnius University Hospital Santaros klinikos	Lithuania
Viroclinics Biosciences BV	The Netherlands
Wageningen Bioveterinary Research, Wageningen University & Research	The Netherlands
Yokogawa Insilico Biotechnology GmbH (formerly Insilico Biotechnology AG)	Germany
Zoetis Belgium SA	Belgium

Project Index

Project	Funder	Project Title	Timeline
MMVC	EDCTP	The Multi-Stage Malaria Vaccine Consortium (MMVC)	01 April 2018 – 31 March 2025
SEmalvac2	GHIT Fund and Nobelpharma Co, Ltd.	Safety evaluation of BK-SE36/CpG in the malaria endemic population	01 November 2016 – 31 January 2022
SEmalvac4	GHIT Fund and Nobelpharma Co, Ltd.	Preparatory phase II for the malaria vaccine candidate NPC-SE36/CpG	01 April 2020 – 31 December 2022
MIMVaC-Africa	EDCTP	A multilateral initiative to foster the clinical development of effective malaria vaccine candidates in Africa (MIMVaC-Africa)	01 February 2020 – 31 January 2025
MVPE-CC	EDCTP	The Malaria Vaccine Pilot Evaluation-Case Control (MVPE-CC) Project	01 April 2021 – 30 June 2024
VAC4PM	GHIT Fund	Clinical development of placental malaria vaccine candidates	25 October 2021 – 30 September 2023
ADVANCE-VAC4PM	European Union	Advancing the clinical development of placental malaria vaccines in the context of capacity building and use of digital health technologies	01 June 2022 – 31 May 2027
PREV-PKDL	EDCTP2, co-funded by Wellcome Trust	Clinical development of a therapeutic vaccine for prevention of post-kala azar dermal leishmaniasis	01 April 2018 – 31 December 2025
SHIGETECVAX	European Union (Horizon 2020 Programme)	Early clinical development of a live, attenuated combination vaccine against Shigella and ETEC diarrhoea	01 September 2019 – 28 February 2025
ShigaPlexIM	EDCTP2	Early clinical development of an injectable shigella vaccine through phase I and descending age studies with and without an adjuvant in Africa	01 October 2019 – 31 December 2025
VACCELERATE	European Union (Horizon 2020 Programme)	European Corona Vaccine Trial Accelerator Platform	28 January 2021 - 27 January 2024
CEPI-NIPAH	Coalition for Epidemic Preparedness Innovations (CEPI)	Development of a Nipah measles vector vaccine (MV-NIV) to be used in outbreaks situation in children and adults exposed population.	01 March 2019 – 31 March 2023
CEPI-Betacoronaviruses	Coalition for Epidemic Preparedness Innovations (CEPI)	Preclinical proof of concept for broadly protective mRNA vaccine against betacoronaviruses.	01 April 2022 – depending on stage gate criteria
TRANSVAC2	European Union (Horizon 2020 Programme)	European Vaccine Research and Development Infrastructure	01 May 2017 – 30 April 2023
TRANSVAC-DS	European Union (Horizon 2020 Programme)	Design study for a European vaccine infrastructure	01 June 2020 – 28 February 2023
ISIDORe	European Union (Horizon Europe Programme)	Integrated Services for Infectious Diseases Outbreak Research	01 February 2022 – 31 December 2024
VAC2VAC	Innovative Medicines Initiative (IMI) and European Federation of Pharmaceutical Industries and Associations (EFPIA)	Vaccine batch to vaccine batch comparison by consistency testing	01 March 2016 – 28 February 2022
FLUCOP	Innovative Medicines Initiative (IMI) and European Federation of Pharmaceutical Industries and Associations (EFPIA)	Standardization and Development of Assays for Assessment of Influenza Vaccines Correlates of Protection	01 March 2015 – 28 February 2022
WANETAM 3	EDCTP	West African Network for TB, AIDS and Malaria	01 August 2021- 31 July 2024
PrIMAVeRa	Innovative Medicines Initiative (IMI) and European Federation of Pharmaceutical Industries and Associations (EFPIA)	Predicting the Impact of Monoclonal Antibodies & Vaccines on Antimicrobial Resistance	01 November 2021 – 31 October 2026
Inno4Vac	Innovative Medicines Initiative (IMI) and European Federation of Pharmaceutical Industries and Associations (EFPIA)	Innovations to accelerate vaccine development and manufacture	01 September 2021 – 28 February 2027

Report Sources

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Malaria

Key Figures:

- WHO – World malaria report (2022) https://www.who.int/publications/i/item/9789240064898

Images:

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Leishmaniasis

Key Figures:

- WHO - Leishmaniasis Key Facts (January 2023) - https://www.who.int/news-room/fact-sheets/detail/leishmaniasis
- Kaye, P., & Scott, P. (2011). Leishmaniasis: complexity at the host-pathogen interface. Nature reviews. Microbiology, 9(8), 604–615. https://doi.org/10.1038/nrmicro2608
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Diarrhoeal Diseases

Key Figures:

- WHO - Diarrhoeal disease Key Facts (2017) - https://www.who.int/news-room/fact-sheets/detail/diarrhoeal-disease
- UNICEF 'One is too many' (2016) https://data.unicef.org/resources/one-many-ending-child-deaths-pneumonia-diarrhoea/

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Emerging Infectious Diseases

Key Figures:

- World Health Organization – COVID-19. https://www.who.int/health-topics/coronavirus
- World Health Organization. Regional Office for South-East Asia. (2014). A brief guide to emerging infectious diseases and zoonoses. WHO Regional Office for South-East Asia. https://apps.who.int/iris/handle/10665/204722
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- Aditi, & Shariff, M. (2019). Nipah virus infection: A review. Epidemiology and infection, 147, e95. https://doi.org/10.1017/S0950268819000086

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Cross-cutting Activities

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Capacity building

Images:

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