MVA PLATFORM PARTNERSHIP
ACCELERATING VACCINE DEVELOPMENT FOR WHO PRIORITY PATHOGENS

CONSORTIUM MEMBERS:
GERMAN CENTRE FOR INFECTION RESEARCH
PUBLIC HEALTH ENGLAND
BAVARIAN NORDIC
MVA Platform Partnership

Consortium Members

German Centre for Infection Research (DZIF) - Publicly funded legal association of 35 cross-sectoral German non-for-profit institutions collaborating in the field of human infectious diseases.

Public Health England (PHE) - Executive Agency of the UK Department of Health, with a broad public health remit to “Protect and improve the nations health”. PHE Porton has a track record of over 65 years’ experience working in infectious diseases research.

Bavarian Nordic (BN) - International biotechnology company specialized in the research, development and manufacturing of vaccines based on viral vectors for the delivery of antigens targeting infectious diseases and cancers.
MVA Platform Partnership

A Public-Private Partnership combining the disease expertise housed in governmental laboratories with the advanced development and manufacturing capabilities of industry to accelerate development of a portfolio of MVA-based vaccines for use in future epidemics.

MVA-PP will manage a portfolio of vaccine development programs that will include:

- vaccine design and optimization
- preclinical testing and evaluation
- cGMP manufacturing & IND-enabling studies
- Phase I clinical studies
- PD studies for commercial scale manufacturing
- production of a mixed stockpile of Final Drug Product and Bulk Drug Substance suitable for deployment in an emergency.
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THE MODIFIED VACCINIA ANKARA VACCINE PLATFORM

- High capacity to accommodate foreign genes: at least 29,000 base pairs
- Triggers high level foreign gene expression
- Multiple B- and T-cell target antigens from an infectious agent - broad spectrum epitope coverage
- Multiple antigens from different microorganisms, or from different strains of a microorganism - multivalent
MVA Platform Partnership

MVA-BN: Licensed Vaccine Platform

Indicated for:

- EU: Active immunization against smallpox for entire adult population

- CANADA: Active immunization against smallpox for adults with immune deficiencies or skin disorders

- US: 20M+ doses stockpiled under Emergency Use Authorization

Trade name: IMVANEX®
Approved August 2013

Trade name: IMVAMUNE®
Approved November 2013
MVA PLATFORM PARTNERSHIP
MVA-BN: LEVERAGING A DECADE OF DEVELOPMENT

Developing, producing, supplying liquid frozen IMVAMUNE

- RFP-1 IMVAMUNE Smallpox Vaccine $14M NIH
- RFP-2 IMVAMUNE Smallpox Vaccine $100M NIH
- RFP-3 IMVAMUNE Smallpox Vaccine $500M BARDA
- RFP-2 Expansion IMVAMUNE Smallpox Vaccine $16M NIH
- RFP-3 Expansion IMVAMUNE Smallpox Vaccine $49M BARDA
- Delivery Contract IMVAMUNE Smallpox Vaccine $228M BARDA

Developing freeze dried vaccine
- RFP Freeze Dried IMVAMUNE Smallpox Vaccine $40M BARDA
- RFP Freeze Dried Expansion $55M BARDA
- Bulk Order IMVAMUNE Smallpox Vaccine $133M BARDA

Expanding MVA-BN platform
- MVA-BN Marburg $18M NIH
- MVA-BN Foot-and-Mouth Disease $1M DHS
- MVA-BN Burkholderia $500K DOD DTRA
- MVA-BN Marburg Expansion $15M NIH
# MVA Platform Partnership

**The Modified Vaccinia Ankara Vaccine Platform**

<table>
<thead>
<tr>
<th>MVA VACCINE PLATFORM</th>
<th>Features of the Platform</th>
<th>Benefits to Partnership</th>
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<tr>
<td>Large genome capable of accommodating multiple protein and/or peptide antigens.</td>
<td>suitable for development of complex multi-antigen vaccines.</td>
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<td>Induces a durable and balanced cellular and humoral immune response.</td>
<td>Supports development of long-lasting vaccines with B- and T-cell dependent modes of action.</td>
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<td>Utilized in homologous and heterologous prime boost vaccination regimes.</td>
<td>Allows combinations with other vaccine technologies if advantageous.</td>
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<td>Vector licensed in Europe and Canada as a stand-alone smallpox vaccine.</td>
<td>Reduced development risk due to regulatory agency familiarity.</td>
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<td>Clinical development included healthy subjects, HIV positive individuals, geriatric and pediatric populations.</td>
<td>New development efforts can reference excellent safety profile in healthy and at-risk populations.</td>
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<td>28+M doses of MVA-BN stockpiled by USG.</td>
<td>Commercially validated manufacturing facility routinely producing MVA-BN.</td>
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<tr>
<td>On-going development of freeze-dried formulation.</td>
<td>Offers operational benefits (no cold chain) and cost savings (longer shelf-life)</td>
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MVA PLATFORM PARTNERSHIP

CONSORTIUM PROPOSAL

- Focus on vaccine development not platform improvement.
- Include disease expertise and preclinical testing capabilities, vaccine development experience and established manufacturing capacity.

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<td>Vaccine Available</td>
<td>2,000 Doses</td>
<td>200,000 Doses</td>
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- Large Scale manufacturing
- BDS and FDP production
- Long-term stability studies
MVA PLATFORM PARTNERSHIP

DISEASE EXPERTISE / PRE-CLINICAL TESTING – DZIF & PHE

GERMAN CENTRE FOR INFECTION RESEARCH

Gerd Sutter
Stephan Becker

Vaccine Assets
MERS-CoV
MVA-based w/ preclinical efficacy & planned Phase 1

Disease Expertise
Lassa / Nipah / MERS

Containment Facilities
Biosafety Level 4

PUBLIC HEALTH ENGLAND

Miles Carroll
Roger Hewson

Vaccine Assets
Crimean Congo Hemorrhagic Fever
MVA-based vaccine w/ preclinical efficacy

Disease Expertise
Lassa / Nipah / CCHF

Containment Facilities
Biosafety Level 4
MVA Platform Partnership

Clinical Testing – DZIF & African Partner Institutions

DZIF Clinical Trial Units (CTU)

A nationwide network of Clinical Trial Units that combines expertise in all clinical ID indications. Utilization of the existing DZIF clinical trial infrastructure will reduce costs while providing rapid recruitment potential and generating high-level data quality and performance rates.

African Partner Institutions

A network of partner sites based on long-lasting collaborations between these centres and DZIF.

Kumasi Centre for Collaborative Research in Tropical Medicine, Ghana
Albert Schweitzer Hospital, Lambaréné, Gabon
Centre de Recherche en Santé de Nouna, Burkina Faso
NIMR - Mbeya Medical Research Center, Tanzania

The MVA-PP will integrate these institutions in the conduct of clinical trial work for infectious diseases with high prevalence in African countries.
About DZIF...

The German Federal Ministry of Education and Research has founded the German Center for Infection Research (DZIF) with the aim to make translation of basic research faster and more effective. The DZIF is a multicentre structure consisting of “Thematic Translational Units” (TTUs) and “Translational Infra-structures” (TIs). The Ti “German-African Partnerships in Infectious Disease Research (GAPID)” has the objective to establish an international network, to strengthen high quality infectious disease-related research in low-income countries and to build capacity and expertise exchange.

Nouna and Heidelberg
Public Health, Epidemiology and Clinical Research

The “Centre de Recherche en Santé de Nouna (CRSN)” in Burkina Faso and Heidelberg University, in particular the Institute of Public Health and the section “Clinical Tropical Medicine, Department of Infectious Diseases”, have successfully been cooperating since almost two decades. CRSN today covers a wide range of health research including a Health and Demographic Surveillance System. CRSN was a founding member and is a leading partner in the Africa-Asia research network INDEPTH.

With the support of a large 12 years DFG grant (SFB 544 “Control of Tropical Infectious Diseases”), of the European Union, the Volkswagen Foundation, other research funding and the core support of the Ministry of Science, Education and Art of Baden-Württemberg, the Medical Faculty of the University of Heidelberg and the Ministry of Health of Burkina Faso, CRSN made a big step forward and is today among the leading health research centres in the region. CRSN focuses in public health research on treatment seeking behaviour, quality of care, health financing, poverty reduction, environment & health research and in clinical and biomedical research on malaria, bacterial meningitis and sepsis as well as HIV/AIDS. With increasing experience with phase II and III clinical trials, CRSN meets international trial standards.

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may@bni.trm.de

www.hd-nouna.org
www.crsn-nouna.bf
MVA Platform Partnership

Commercial Manufacturing Capabilities — Bavarian Nordic

Commercial Production Facility
- Inspected by the EMA and the FDA
- 28M doses of IMVAMUNE delivered to US national stockpile
- Over 2M doses of MVA-BN Filo (Ebola) delivered to Janssen

Multi-Product Facility
- Highly scalable, fully integrated, reduces dependency on sub-contractors
- Fill/Finish established to support commercial launch of PROSTVAC
- Production of all clinical trial material

Poxvirus Manufacturing Expertise
- Commercial partnerships in place with Janssen & BMS
- All manufacturing performed by BN
- Company has developed IP and extensive know-how in the production of poxvirus based vaccines
**MVA PLATFORM PARTNERSHIP**

**CONSORTIUM PROPOSAL**

## Proposed Scope of Work

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### Project Activities:

- Vaccine Available
- 2,000 Doses
- 200,000 Doses

### Project Goals (6+ Vaccine Candidates)

- Demonstrated efficacy (preclinical)
- Demonstrated immunogenicity (clinical)
- Dose selection
- Clinical assays
- Demonstrated manufacturability
- Stockpiled FDP and BDS
- On-going stability studies
**MVA Platform Partnership**

**Consortium Proposal**

**Proposed Scope of Work**

**Preclinical Activities**
- Selection and Optimization of Viral Antigens (Lassa/Nipah/Zika)
- Construct Generation & Research Grade Material (RGM) Production (MERS/Lassa/Nipah/Zika)
- Assay Development, Immunogenicity Studies and Efficacy Studies (MERS/Lassa/Nipah/Zika)
- Master Virus Bank (MVB) Production (MERS/CCHF/Lassa/Nipah/Zika)

**Clinical Activities (GLP Toxicity & Phase I)**
- GLP-compliant Toxicity Study to Support Clinical Phase I (MERS/Lassa/Nipah/Zika)
- Phase I Clinical Study (MERS/Lassa/Nipah/Zika)

**GMP Manufacturing (Clinical Trial Material & BDS/FDP Stockpile)**
- Production of Master Seed Virus (MSV) (MERS/CCHF/Lassa/Nipah/Zika)
- Production of Bulk Drug Substance (BDS) for Phase I (MERS/Lassa/Nipah/Zika)
- Production of FDP for Phase I (MERS/Lassa/Nipah/Zika)
- Production of BDS/FDP Stockpile (MERS/CCHF/Lassa/Nipah/Zika)
- Stability Program (MERS/CCHF/Lassa/Nipah/Zika)
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PORTFOLIO MANAGEMENT

• Portfolio-based vaccine development
  – Mitigate risks associated with vaccine R&D by ensuring a pipeline of candidates for transitioning into clinical study and manufacturing efforts.
  – Mitigate the lack of market-driven incentives for vaccine R&D by providing funding that is sustainable and predictable.
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**GO / NO GO CRITERIA**

- **Clinical Trial Material Production and Phase 1 Clinical Study**: Demonstration of efficacy in appropriate animal model(s) of disease.

- **Commercial Scale Manufacturing and Production of BDS/FDP Stockpile**: Demonstration of an immune response observed by an immunological assay that suggests the vaccine might be protective.
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CONSORTIUM MANAGEMENT AND MECHANICS

ESC: Governance

JPC: Implementation

Project: Execution

Manufacturing and portfolio management
Lead: BN

Preclinical development
Lead: PHE

Early clinical development
Lead: DZIF

MVA-MERS-S (Clinical Trial Application)

MVA-BN FILO (Manufacturing CTM)

MVA CCHF (Preclinical)

MVA-Nipah (Research)

MVA-Lassa (Planned)

MVA-Zika (Planned)

Decisions
Priorities
Networks
Funding

Coordination
Integration
Supervision
Reporting

Spending
Progress
Reporting
• Designed to induce immune responses to Marburg, Ebola Zaire and Sudan.
• Initial development efforts begun in 2011
• Combination vaccine regimen of Bavarian Nordic’s multivalent MVA-BN Filovirus vaccine and Janssen’s AdVac® technology demonstrated complete protection against Ebola in preclinical studies in mid-2014
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EPIDEMIC RESPONSE – A CASE STUDY

- MVA-BN-Filo manufacturing begins less than five weeks after entering into the supply agreement with Janssen.
- MVA-BN-Filo manufacturing is initiated using the IMVANEX production process.
- MVA-BN-Filo manufacturing required minimal changes to the production process, utilized existing raw materials and required minimal employee training to initiate.

- ~500,000 doses produced in the December campaign.
- Over 2M doses produced in less than 9 months.
- Successfully switched between IMVAMUNE and MVA-BN-Filo production.
MVA Platform Partnership

Conclusion & Summary

- Focus is on product development not platform improvement.
- Goal is not just capacity building but ensuring specific vaccine assets are available
  - in order to be able to fully evaluate candidates during an outbreak
  - to have be able to mitigate future disease outbreaks
- Cross-discipline collaboration by bringing together disease expertise found at DZIF and PHE with the manufacturing and production experience of BN.
- Centralizes vaccine development efforts around BN’s manufacturing infrastructure in order to reduce the operational risks associated with the vaccine development efforts (manufacturing, regulatory, safety) allowing programmatic emphasis on scientific challenges (design, immunogenicity, efficacy).
- Portfolio-based vaccine development can mitigate risks associated with vaccine R&D and provide sustainable and reliable funding.
- Vaccine candidates developed under the MVA Platform Partnership can be evaluated in combination with other vaccine platforms (viral vectored, DNA, protein etc.)
MVA Platform Partnership

DZIF

Public Health England

BAVARIAN NORDIC
Kumasi and Hamburg
Epidemiology and Biomedical Research
The Kumasi Centre for Collaborative Research in Tropical Medicine (KCCR) was founded in 1998 as a joint venture of the Ghanaian Ministry of Health, Kwame Nkrumah University of Science and Technology (KNUST) and Bernhard Nocht Institute for Tropical Medicine (BNITM), Hamburg. Designed as an African research and training platform, KCCR hosts projects jointly conducted by Ghanaian and international principal investigators. Training of Ghanaian and other African team members is provided at all levels from technicians to leading scientists and includes staff of collaborating university departments, hospitals and health centres. KCCR is run by a Ghanaian scientist. The staff serves international researchers in partnering with Ghanaian colleagues, recruitment of personnel, project management, submissions for ethical clearance, transport services, immigration and customs formalities, and other organizational issues.
Current Projects include clinical and epidemiological studies on malaria, tuberculosis, HIV/AIDS, filariasis, typhoid fever, Buruli ulcer and other infectious diseases as well as studies on vectors and reservoir hosts. KCCR has been nominated a Centre of Excellence of the African Network for Diagnosis and Drug Discovery Innovation (ANDI) for applied biomedical research.

www.kccr-ghana.org/kccr
www.bnitm.de

Lambaréné and Tübingen
Malaria and Clinical Research
The “Centre de Recherches Médicales de Lambaréné (CERMEL)” is located at the Albert-Schweitzer Hospital in Lambaréné, Gabon, and was part of the Albert-Schweitzer Foundation until it became an autonomous institution in 2012. The centre collaborates with national and international partners, particularly close with the Institute of Tropical Medicine of the University of Tübingen, a Centre of Excellence in Baden-Württemberg, Germany. CERMEL mainly focuses on clinical and biomedical studies on parasitic diseases such as malaria, schistosomiasis and intestinal helminth infections. During the last 20 years numerous Phase I to III clinical studies for the development of new drugs and vaccines have been conducted. Some of those studies had a strong impact on the treatment of malaria and malaria-related complications or were critical for the registration of new medical interventions.
Projects of local and global importance are realized dealing with tuberculosis and bacterial infections. Modern facilities, professional management, exciting, internationally visible projects in clinical research and experienced staff from all over the world, including many African countries, make CERMEL a nationally and internationally recognized magnet for young researchers.

www.cermel.org
www.medizin.uni-tuebingen.de

Mbeya and Munich
Clinical Research on HIV and TB
The NIMR-MMRC is located on the premises of a tertiary hospital in Mbeya city, serving a population of two million in South-Western Tanzania. The heterogeneous topography and socio-economic characteristics of the Mbeya region create an ideal environment for research on a variety of infectious pathogens, with HIV/AIDS and tuberculosis, being the most relevant. The MMRC has been a pioneer in research in Tanzania, studying the epidemiology of HIV in the nineties. The fundamental philosophy of MMRC is to enable direct translation of basic research findings into applicable local health interventions. Within the past 10 years, MMRC has grown to one of the most active clinical trial sites for HIV vaccines as well as TB drugs and diagnostics, including international, industry standard registration trials. The highly sophisticated immunology, TB and safety laboratories are internationally accredited and perform state of the art diagnostic tests as well as basic research activities. Further, it is the aim of MMRC to provide health care directly to the communities with a mobile laboratory, which conducts a comprehensive programme of near-patient point-of-care screening and staging for HIV and TB. This includes a training and quality assessment programme for local health facilities, to serve underprivileged and remote populations of Mbeya region.

www.mmrp.org
www.klinikum.uni-muenchen.de