ZIKAVAX PARTNERSHIP

Today’s Catalyst For Tomorrow’s Vaccines

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DCVMN Seoul
26th September 2017
Product Development Partnership

The European Vaccine Initiative is a Product Development Partnership which aims to accelerate the development of vaccines for diseases of poverty.
First European PDP

Selected other public-private partnerships important for PDPs

Adapted from IAVI 2013
# About EVI

## Mission
To contribute to the global efforts to control diseases of poverty by supporting development and clinical assessment of vaccines for diseases of poverty

## What we do?
- **Support translational vaccine R&D with focus on preclinical to early clinical development**
  - Operational, managerial and financial support

- **Support capacity strengthening in low-income target regions**

- **Bringing together and aligning stakeholders**
Initiatives Address the Entire Pipeline

- Antigen Discovery Validation
- cGMP Manufacture
  Formulation, Fill & Finish
  Toxicology, Stability, Potency

Industrial Scale-up

Phase 1a/b
Safety
Immunogenicity

Phase II
Immunogenicity

Phase III
Efficacy

Licensure & Launch
Support in Vaccine Development

Antigen Discovery

Validation

Technical support & overview of process development, analytical procedures, GMP production, quality control, potency/nonclinical safety/stability studies etc

Selection of sub-contractors

Technical support and overview for adjuvant selection and testing

Development and review of the Investigational Medicinal Product Dossier (IMPD)

cGMP Manufacture

Formulation, Fill & Finish

Toxicology, Stability, Potency

Industrial Scale-up
Support in Vaccine Development

- Selection of sponsor and investigational site
- Development and review of the clinical development plan, clinical trial protocol, methodology etc
- Technical support for clinical trial application/review to ethic committee and regulatory agency
How is EVI addressing the global need for new vaccines?

- Feed the pipeline FIRST! - PDP
- Coordination – connecting the chain
- Harmonisation – guidelines, procedures
- Building European infrastructure with global network
  - TRANSVAC2 project
  - 1st call 15/10/2017
Public-Private Partnership for Product Development

- Heidelberg University
  Germany

- Stockholm University
  Sweden

- Royal College of Surgeons in Ireland
  Ireland

- Institute for Translational Vaccinology, Bilthoven
  The Netherlands

- Institut Pasteur, Paris
  France

- The Jenner Vaccine Foundation
  United Kingdom

- Biomedical Primate Research Centre
  The Netherlands

- EVI
  Headquarters

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Partnership Principles and Strategy for Success

• To involve affected population and their policy makers in strategy for development plan et setting priorities (diseases, products):
  ◦ objectives developed together
  ✓ product development (including analysis of the results (both safety and efficacy) AND
  ✓ capacity building – infrastructure and training) Need to call funding agencies to have a global portfolio management (as for malaria, tb and hiv vaccine) for PRND assessing gaps and defining priorities

• To call funding agencies to have a global portfolio management assessing gaps and defining priorities
  ◦ global portfolio management AND
  ◦ connecting the chain
Partnership Principles and Strategy for Success

• To have **sustainable pipeline** populated with enough candidate to increase chance of success

• To advocate for **pooled funding mechanisms** with FRESH funding to manage global portfolios.

✓ Funders should explicitly include product development aspect into their funding mechanism, as well as the requirement for the applicants to outline their access policies.
ZIKAVAX
Fast track development of a Zika vaccine based on measles vector

Duration: 48 months
Total grant: €4,918,137.50
EC-funded project under H2020
Objectives

1. To construct and characterise recombinant MV expressing Zika virus proteins as soluble secreted antigens

2. To demonstrate preclinical immunogenicity and protective efficacy of the recombinant MV-Zika vaccine candidate(s) in a mouse model and in a non-human primate (NHP) model of Zika virus infection

3. To manufacture a good manufacturing practice (GMP) clinical lot of the MV-Zika vaccine candidate using scalable platform technology

4. To assess the safety and immunogenicity of the MV-Zika vaccine candidate in a phase I dose-escalation clinical trial
**ZIKAVAX Methodology**

- Delivery platform technology: measles vaccine vector (live attenuated)
  - demonstrated proof of principle in clinical and pre-clinical studies.

  ➢ Rapid adaptability and effectiveness for a variety of pathogens (Chikungunya virus, West Nile virus, Ebola, *Plasmodium*, *Mycobacterium*)

- Optimised manufacturing process

  ➢ high yields and purity using standards equipment → **Rapid transfer to other manufacturers for any outbreak**

- Ultimate objective is the demonstration of safety and immunogenicity in adults in a Phase 1 clinical trial
MV genes are indicated: N (nucleoprotein), PVC (phoshoprotein and V/C proteins), M (matrix), F (fusion), H (hemagluttinin), L (polymerase), T7 (T7 RNA polymerase promoter), hh (hammerhead ribozyme), T7t (T7 RNA polymerase terminator), \( \partial \) (hepatitis delta virus ribozyme), red arrows (additional transcription units).
WHO DRAFT Target Product Profile:
A vaccine to protect against congenital Zika virus syndrome in neonates, for use during an emergency

Joachim Hombach, Initiative for Vaccine Research, WHO on behalf of the WHO PDVAC ZIKV vaccine working group

6th June 2016
Vaccine Pipeline: ~ 50 projects from 27 institutions/organisations

- 5 inactivated whole virus vaccines
- 5 live attenuated whole virus vaccines
- 11 recombinant sub-unit non VLP/VLP
- 11 recombinant viral vector vaccine
- 4 DNA or RNA or peptide
More to come
Issues and concerns for vaccine development

- Animal models

**ZIKV AG129 Mouse Model**
- Neurologic disease
- Conjunctivitis
- Hunching, lethargy, and excitability at late stage
- Measurable viremia
- Hindlimb paralysis

**A129 (IFNAR −/−) Mice Develop Neurological Disease and Succumb to Infection**

- AG129 (Aliota et al. 2016; Rossi et al., 2016; Zmurko, et al.; 2016; Julander et al., unpublished data; review by Sarathy et al. 2015 (Dengue))
Issues and concerns for vaccine development

- Animal models

- Macaque monkeys are susceptible to infection with Zika virus
- Pregnant monkeys are infected for an unusually long time
- A vaccine should work because monkeys resist reinfection
Further development needed for vaccine development

1. Human challenge models

**Validation & Feasibility**

1. Definition and validation of correlates/surrogates of protection

**Harmonisation & Standardisation of immuno-assays**

Further investigations needed for vaccine development

1. Cross reactivity with other flavivirus
2. Epidemiology pattern
# Acknowledgements

**EVI donors**
- DGIS (NL)
- Irish Aid (IE)
- BMBF via KfW (DE)
- BMBF (DE)
- FP6/FP7 (EC)
- EDCTP (EC & EU MS)
- IMI-IMI2
- GHIT
- Nobelpharma

**Scientific Community**
Europe, Africa, India, Japan, USA

**EVI EEIG members**
- Stockholm University, SE
- Heidelberg University, DE
- Royal College of Surgeon in Ireland, IE
- Jenner Vaccine Foundation-University of Oxford, UK
- Biomedical Primate Research Centre, NL
- Intravacc, NL
- Institut Pasteur, FR

**Subjects in EVI funded clinical trials**

**EVI sub-contractors, CMOs, CROs, Consultants**

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*Many thanks for your attention!*

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https://youtu.be/ToU9Pl4HyY4
You can
Contribute to make a better world free of diseases of poverty