VPM1002
A new TB prime vaccine on the horizon

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Serum Institute of India Ltd
Who We Are...

• Founded 2002 as a private company
• Currently 10 employees
• VPM team members represent core competences along the entire value chain – from bench to market authorization and product launches in global market
Serum Institute of India Limited
Serving Mankind by ensuring good health through vaccines

"It is our endeavour to make quality vaccines more affordable around the world because we firmly believe that health should be the right of every child."

Dr. Cyrus Poonawalla, Chairman and Managing Director
Development of a safe, well tolerated and efficacious vaccine (rBCGΔureC:Hly/VPM1002) against tuberculosis for residents in endemic areas and persons at risk in non-endemic areas
The Idea behind

VPM1002

S.H.E. Kaufmann et al.
VPM1002 Antigen Presentation

CD4+ & CD8+ T-cells

S.H.E. Kaufmann et al.
Target Product Profile

- No interference with TB diagnostics
- Induction of CD4+ and CD8+ Immune response
- Induction of multifunctional T-cells (IL-2; IFN-γ; TNF-α)
- Safer than BCG in immunocompromised species/vaccinees
Autophagy induced by VPM1002

Autophagy Controls BCG-Induced Trained Immunity and the Response to Intravesical BCG Therapy for Bladder Cancer

Kathrin Buffen¹,², Marije Oosting¹,², Jessica Quintin¹,², Aylwin Ng³,⁴, Johanneke Kleinnijenhuis¹,²,

The Recombinant BCG ΔureC::hly Vaccine Targets the AIM2 Inflammasome to Induce Autophagy and Inflammation

Hiroyuki Saiga, Natalie Nieuwenhuizen, Martin Gengenbacher, Anne-Britta Koehler, Stefanie Schuerer, Pedro Moura-Alves, Ina Wagner, Hans-Joachim Mollenkopf, Anca Dorhoi and Stefan H. E. Kaufmann

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SCID mice survive when immunized with VPM1002

Intravenous Innocula
- BCG 4x10^8
- rBCG-hly 3.5x10^7
- rBCG-hly-delta urea 1.5x10^6
Rapid Clearance of VPM1002

Alexis Vogelzang et al., 2014
Cost efficient Product

Manufacturing:
VPM1002 is manufactured by submerse fermentation in minimal medium. The final product is a lyophilised cake of live bacteria. Establishment of a GMP process is completed. The process has been designed to offer full scalability.

- Modern submers 30 liter fermentation
  - Theoretically ~1-3 Million doses from one 30 liter batch

- Lyophilization
  - The pilot lyophilization currently gives ~3000 GMP vials which adds-up to ~60 000 doses

Each vial contains 20 human doses (~5x10e6 CFU/vial)
Stability >42 months (>2x10e6 CFU/vial)
Fast Translational Product Development

Vibalogics

AURIGON

TBVAC/PDT

BioReg Cons

FOCUS CDD

Vaccine and Pharma industry

!!! < 4 years !!!

MPI

Infection biology

Tb Reference Center Borstel

Reconstruction

process dev.

+ manufacture

Preclinical Devel.

2004

2005

2006

2007

2008-9

2010

2011

GMP-Material

CTA

FIM

Ph Ib

Ph II
VPM1002 in Phase Ia in Germany

First Vaccinee enrolled on Sep 08, 2008

Last Vaccinee enrolled on June 2, 2009

Clinical Trials Summary

VPM study no.: VPM1002-GE-1.01TB

Phase Ib Open Label, Randomized, Controlled, Dose-Escalation Study to Evaluate Safety and Immunogenicity of VPM1002 in Comparison with BCG in Healthy Volunteers in Germany

- **Test item:** VPM1002: three escalating doses of VPM1002 were investigated (5x10^3 CFU, 5x10^4 CFU, 5x10^5 CFU) and BCG
- **Observation period:** 6 months
- **Inclusion criteria:** 80 healthy male Caucasian adult volunteers with or without pre-exposure to BCG were vaccinated with VPM1002 (N=30 + 30) or BCG (N=10 + 10)
- **Primary objective** of this study was to investigate the safety of single doses of VPM1002
- **The secondary objective** of this study was to investigate the immunogenicity of single doses of VPM1002

**Results:**

- This study revealed that a single vaccination with VPM1002 up to 5x10^5 CFU was safe and well tolerated
- VPM1002 was highly immunogenic; it induced multifunctional CD4+ and CD8+ T cell subsets which are thought to play a crucial role in protection against tuberculosis
- VPM1002 showed a trend of superiority over BCG with regard to multifunctional CD8+ T cells, at a comparable dosage
- Shedding of the live vaccine, microbiological surveillance of VPM1002 in the first clinical trial was investigated in blood, urine, saliva and stool samples of vaccinees throughout the study. All of the samples were negative for VPM1002
VPM1002 in Phase Ib in South Africa

First Vaccinee enrolled on April, 2010

Last Vaccinee enrolled on July, 2010
Clinical Trials Summary

VPM study no.: VPM1002-ZA-1.10TB
Phase Ib Open Label, Randomized, Controlled, Dose-Escalation Study to Evaluate Safety and Immunogenicity of VPM1002 in Comparison with BCG in Healthy Volunteers in South Africa

- **Inclusion**: BCG vaccination > 10 years pre participation
- **24 healthy adults**, aged 18-45, resident in TB endemic area, min 12 females & 8 males
- **Test item**: VPM1002: a dose-escalation using three dose groups (5x10e3 CFU, 5x10e4 CFU, 5x10e5 CFU) and BCG
- 4 cohorts of 6, BCG cohort recruited in parallel with other cohorts
- **Primary Objective**: To investigate the safety and tolerability of single doses of VPM1002
- **Secondary Objective**: To investigate the immunogenicity of single doses of VPM1002 for vaccination against Tuberculosis
- **Observation period**: 6 months
- **Results**: safety data concurred with the German clinical trial
  - A single vaccination with VPM1002 up to a dose of 5x10e5 CFU
  - A single vaccination with VPM1002 (2-8 x 10e5 CFU) results in an immune response to mycobacterium antigens that is at least equivalent to that precipitated by a single vaccination with an equivalent dose of BCG was shown to be safe and well tolerated
VPM1002 Phase IIa in South Africa

First Vaccinee enrolled on November 22, 2011

Last Vaccinee on May 29th, 2012
Clinical Trials Summary

• **Inclusion:** 48 infants (36 VPM1002, 12 BCG), HIV-unexposed, BCG naive newborn infants in a region with a high burden of tuberculosis
• Vaccinated within 8 days of birth
• **Test item:** VPM1002 (1-4 x 10e5 CFU) and BCG Danish Strain, SSI (1-4 x 10e5 CFU)
• Observation period: 6 months
• **Primary Objective:** to investigate the safety and tolerability of a single dose of the recombinant BCG vaccine, VPM1002
• **Secondary Objective:** to investigate the immunogenicity of a single dose of the recombinant BCG vaccine, VPM1002
Unexpected Role for IL-17 in Protective Immunity against Hypervirulent *Mycobacterium tuberculosis* HN878 Infection

Radha Gopal¹, Leticia Monin¹, Samantha Slight¹, Uzodinma Uche¹, Emmeline Blanchard¹, Beth A. Fallert Junecko², Rosalio Ramos-Payan³,⁴, Christina L. Stallings⁵, Todd A. Reinhart², Jay K. Kolls⁶, Deepak Kaushal⁷, Uma Nagarajan⁸, Javier Rangel-Moreno⁴, Shabaana A. Khader¹,⁵*
Phase II double-blinded, randomized, controlled study to evaluate safety, tolerability and immunogenicity of VPM1002 in comparison with BCG VACCINE SSI in HIV-exposed and HIV-unexposed, BCG-naive newborn infants
### VPM1002-ZA-2.13TB

#### Project Team

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<thead>
<tr>
<th>Role</th>
<th>Details</th>
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<td>Manufacturer of IMP</td>
<td>SIIL</td>
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Study cohort (n=416)

Randomization
New born babies
(0-12 days old)

Allocated to BCG (n=104)

HIV-unexposed (n=52)
HIV-exposed (n=52)

Allocated to VPM1002 (n=312)

HIV-unexposed HmR (n=52)
HIV-unexposed HmS (n=104)
HIV-exposed HmS (n=156)

12 months follow-up

Primary objective
Safety & tolerability: VPM1002 (total) vs. BCG (total)

Secondary objective
1. Safety & tolerability: VPM1002 (HIV-exposed) vs. VPM1002 (HIV-unexposed)
2. Immunogenicity

24 months structured medical surveillance period
Clinical Development Plan

- 2009
- 2010
- 2013
- 2015
- 2016
- 2017
- 2018
- 2019

**Newborns World Wild clinical trials**

- Booster vaccine devel. India and ZA Phase III
- MAA

- **Newborns ZA, HIV-exposed**
  - Phase II
  - Phase III

- **Phase II a**
  - Newborns ZA
  - HIV-unexposed

- **Phase Ib**
  - Adults ZA

- **Phase Ia**
  - Adults GE

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Mark Hatherill, SATVI

Victor Strugo, Tracy Southwood

Triclinium

Partner of the
Stop TB Partnership

Max-Planck-Institut für Infektionsbiologie

UNIVERSITEIT STELLENBOSCH UNIVERSITY

VPD
Vaccine Preventable Diseases

RMPRU
Respiratory & Meningeal Pathogens Research Unit

TBVI
Tuberculosis Vaccine Initiative

Bundesministerium für Bildung und Forschung