IAVI Vesicular Stomatitis Virus Sudan Virus Vaccine (VSV-SUDV) Program Update

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Vice President – Emerging Infectious Diseases and Epidemiology

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IAVI is Advancing Multiple VSV-Vectored Vaccines throughout the Development Continuum

**VSVΔG-SARS-CoV-2**
Funded by DTRA, Japan MOF/World Bank

- Preclinical studies underway for IN Administration

**VSVΔG-SUDV**
Funded by Biomedical Advanced Research and Development Authority (BARDA)

- Preclinical studies complete

**VSVΔG-LASV**
Funded by Coalition for Epidemic Preparedness Innovation (CEPI) and European & Developing Countries Clinical Trials Partnership (EDCTP)

- Ph1 in U.S. and W. Africa

**VSVΔG-MARV**
Funded by US Defense Threat Reduction Agency (DTRA)

- Preclinical studies complete

**VSVΔG-SARS-CoV-2**
Funded by Merck, BARDA, DTRA, Japan MOF

- Ph1 Trial Complete – IM Administration

Licensed through the Public Health Agency of Canada
IAVI VSV-SUDV Program Starts in October 2021 with BARDA

IAVI and the Biomedical Advanced Research and Development Authority partner to advance filovirus vaccine candidates

NEW YORK – OCTOBER 27, 2021 – IAVI announced today the award of up to US$126 million from the Biomedical Advanced Research and Development Authority (BARDA) at the U.S. Department of Health and Human Services to develop two recombinant vesicular stomatitis virus (rVSV)-vectored filovirus vaccine candidates. This award supports preclinical activities and includes options for clinical development up to and inclusive of a Phase II clinical trial of IAVI’s rVSV Sudan ebolavirus vaccine candidate (rVSVΔG-SUDV-GP). Optional work that would continue the development of IAVI’s Marburg virus vaccine candidate (rVSVΔG-MARV-GP) that is currently supported by the Defense Threat Reduction Agency of the U.S. Department of Defense could be funded at a later date.

BARDA VSV-SUDV Program Includes:

- Preclinical development
- NHP dose-finding study
- Manufacturing for Phase 1 clinical trial material
- Clinical trial preparations
- Nonclinical NHP studies
- Phase 1 trial
- Phase 2 clinical trial manufacturing
- Phase 2 trial
IAVI’s Vesicular Stomatitis Virus Sudan Vaccine (VSV-SUDV) Program and Acceleration Steps

- IAVI licensed the VSV Sudan vaccine from the Public Health Agency of Canada in March 2019, following the return of Merck’s exclusive licensing rights to PHAC
- Preclinical research has been completed on VSV-SUDV (including a NHP efficacy study)
- Program acceleration started after reports of SUDV outbreak in Uganda (September 2022) and WHO convening of filovirus vaccine development group, focused on two parallel development paths:
  - Accelerating VSV-SUDV clinical trial material manufacturing with IAVI partner Batavia Biosciences
  - Leveraging VSV-SUDV manufactured by Merck for initial clinical trial material availability and stockpile
- IAVI has delivered investigational doses to Uganda for inclusion in the ring vaccination trial in an outbreak situation, and has doses vialled to be used for additional clinical trials in Africa (outside of an outbreak situation).
- IAVI VSV-SUDV program was evaluated as the priority candidate for evaluation during the SUDV outbreak by the WHO Vaccine Prioritization Working Group
- A VSV-SUDV vaccine has not been evaluated in humans; however, IAVI VSV-SUDV is built on the identical platform to ERVEBO®, a licensed EBOV vaccine with multiple safety studies completed; Phase 1 study will start soon.
- IAVI is continuing to accelerate the manufacturing of VSV-SUDV with Batavia Biosciences and anticipates possible bridging studies between the manufacturing processes used at Merck and at Batavia
Preclinical studies show that VSVΔG-SUDV-GP is efficacious in macaques like the VSVΔG-ZEBOV-GP and VSVΔG-MARV-GP vaccines

1. Prophylactic vaccination with a mixture of VSVΔG-ZEBOV-GP, VSVΔG-SUDV-GP, and VSVΔG-MARV-GP protected from SUDV (Boniface), ZEBOV, or MARV challenge as well as heterologous TAFV challenge

2. Vaccination with VSVΔG-SUDV-GP shortly after SUDV (Boniface) challenge (30 mins) was protective

3. VSVΔG-SUDV-GP prime and VSVΔG-ZEBOV-GP boost protected from heterologous BDBV challenge

4. Macaques vaccinated with VSVΔG-EBOV-GP survive EBOV challenge after which vaccination with VSVΔG-SUDV-GP(Gulu) protects from SUDV (Gulu) challenge

5. VSVΔG-SUDV-GP(IAVI) preMVS dose-range/immunogenicity/efficacy study is ongoing – preliminary data indicates the vaccine material prepared from the preMVS is efficacious against challenge with the Gulu isolate

6. VSV-SUDV material manufactured by Merck (identical to material being filled as DP) was immunogenic when used to vaccinate rats and mice, animals were healthy after vaccination

5. IAVI, UTMB, et al., Ongoing
6. Merck internal technical reports
IAVI VSVΔG-SUDV-GP is efficacious at multiple doses against high dose, heterologous Gulu challenge in NHPs

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of Animals</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>VSVΔG-SUDV-GP</td>
<td>8</td>
<td>2x10^7 PFU</td>
</tr>
<tr>
<td>VSVΔG-SUDV-GP</td>
<td>6</td>
<td>2x10^4 PFU</td>
</tr>
<tr>
<td>VSVΔG-SUDV-GP</td>
<td>6</td>
<td>2x10^2 PFU</td>
</tr>
<tr>
<td>Negative control (Saline)</td>
<td>4</td>
<td>NA</td>
</tr>
</tbody>
</table>

Key Finding / Notes

• Vaccine efficacy was 90% for the complete study
• Larger than typical group size was used to provide increased confidence in efficacy evaluation
• Younger animals were used due to animal availability
• Immunogenicity, cytokine expression, and blood transcriptome analyses are ongoing using samples collected after vaccination – the data will be valuable for understanding the individual high-dose and low-dose breakthrough cases
Future Efforts: Clinical and NHP Studies Program for VSV-SUDV

- IAVI’s VSV-SUDV program includes the initiation of a clinical trial as soon as possible to obtain safety and immunogenicity data on VSV-SUDV in the United States
  - High to low doses of vaccine to be evaluated
  - Potential comparisons between VSV-SUDV drug product manufactured in different processes
- Phase 1/2 studies in Uganda in health care workers are also being discussed with experts in-country
- Data acquisition on safety and immunogenicity at different dose levels will aid in the dose selection for future clinical trials in Africa – either during a public health emergency or outside of outbreak scenarios
- Doses are now vialled and available for larger scale trials in addition to the initial amounts sent to Uganda in December
- IAVI is also pursuing NHP studies to:
  - Further refine dose-range and expand data on SUDV challenge outcomes
  - Determine onset of protection after VSV-SUDV in SUDV challenged animals
Phase I Clinical Trials Planned for IAVI VSV-SUDV

A Phase 1, Single-blind, Placebo-controlled, Dose-escalation Clinical Trial to Rapidly Evaluate the Safety and Immunogenicity of rVSV\textgreek{AG}-SEBOV-GP Vaccine at 3 Dose Levels in Adults in Good General Health

<table>
<thead>
<tr>
<th>Study Group</th>
<th>rVSV\textgreek{AG}-SEBOV-GP Vaccine Dosage (pfu), intramuscularly Day 1</th>
<th>N (Vaccine/Placebo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single Blind Dose</td>
<td></td>
<td></td>
</tr>
<tr>
<td>escalation</td>
<td>1</td>
<td>$2 \times 10^6$</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>$2 \times 10^7$</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>$2 \times 10^8$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Total = 36 (30/6)</td>
</tr>
</tbody>
</table>

**Objectives**

**Endpoints**

**Primary**

**Safety**
- To evaluate the safety and tolerability of rVSV\textgreek{AG}-SEBOV-GP vaccine
  - Proportion of participants with Grade 3 or higher reactogenicity (ie, solicited AEs) during the 14 days after vaccine administration
  - Proportion of participants with Grade 2 or higher vaccine-related unsolicited AEs, including safety laboratory parameters, within 14 days of vaccine administration
  - Proportion of participants with Grade 2 or higher unsolicited AEs, including safety laboratory parameters, within 14 days of vaccine administration
  - Proportion of participants with vaccine-related SAEs throughout the study period

**Secondary**

**Immunogenicity**
- To determine SEBOV-GP-specific antibody responses induced by rVSV\textgreek{AG}-SEBOV-GP vaccine
  - Proportion of participants with binding antibody responses to SEBOV-GP
  - Magnitude of binding antibody responses to SEBOV-GP
  - Proportion of participants with neutralizing antibody responses against SEBOV
  - Magnitude of neutralizing antibody responses against SEBOV
Approaches to infer effectiveness of a VSV-SUDV vaccine in the absence of field efficacy studies

Clinical Immunobridging

Studies by which the effectiveness of a new vaccine candidate is inferred by comparing the vaccine-induced immune response (e.g., neutralizing antibody titer) to that induced by a comparator vaccine for which efficacy was previously demonstrated

i. Clinical immunobridging using anti-GP antibody titers as an endpoint could be used to infer effectiveness of filovirus vaccine candidates by comparing them to licensed Zaire Ebolavirus vaccines based on the same platform, i.e. ERVEBO (VSV vectored vaccine)

ii. Anti-GP antibody titers should be similar in proportion to cellular and other protective immune responses induced by the vaccine candidate and the licensed comparator vaccine

iii. Supportive data derived from challenge/protection studies (and/or passive transfer studies) in NHP demonstrating that the filovirus vaccine candidate protects animals from challenge with Marburg or Sudan viruses are needed

iv. In addition, data demonstrating similarity of immune pathogenesis and the roles of T cells in the protective immune response against filoviruses would be needed.
Thank you
IAVI gratefully acknowledges the generous support provided by the following major funders:

Biomedical Advanced Research and Development Authority (BARDA) | Foundation for the National Institutes of Health | National Institute of Allergy and Infectious Diseases | amfAR, The Foundation for AIDS Research | Broadway Cares/Equity Fights AIDS | Cancer Research UK | The City of New York, Economic Development Corporation | Congressionally Directed Medical Research Program (DoD) | GSK | The Hearst Foundations | Keith Haring Foundation | Merck & Co., Inc., Kenilworth, NJ, USA (known as MSD outside the USA and Canada) | And many other generous individuals and partners around the world

As of April 2022