CEPI-WHO LASSA Workshop
INO-4500 and CELLECTRA™ 2000

Bonaventure Orizu, MD
Director, Clinical Development

25 October 2022
INO-4500 Program Overview

• INO-4500 is INOVIO's DNA vaccine candidate against Lassa virus infection.

• Composed of an optimized DNA plasmid encoding the glycoprotein precursor (GPC) gene from Josiah strain virus formulated in Saline Sodium-Citrate, INO-4500 is delivered ID via a Mantoux injection immediately followed by ID Electroporation.

• The vaccine was shown to be immunogenic, generating cellular and humoral responses in various animals, and providing protection against lethal Lassa challenge in a nonhuman primate model.

• Since the initiation of this CEPI-funded program 3.5 years ago, the INO-4500 FIH Phase 1a study was completed in the U.S.

• Enrollment, dosing and all follow-up visits for the Phase 1b dose selecting study in Ghana are completed.
• **Program goals:** Advance the Lassa DNA vaccine candidate (INO-4500) into a demographically relevant population-based Phase 2a clinical trial with the eventual goal of preparation of Lassa vaccine stockpiles (investigational stockpile and optional stockpile for efficacy studies).

• **Overall Status**
  • LSV-001 Phase 1 study in the US: Last Subject Last Visit achieved 21Oct2022
  • LSV-002 Phase 1b study in Ghana: Last Subject Last Visit achieved 27Sep2022

• **Next Phase**
  • LSV-201 Phase 2a study in West Africa: In planning
INO-4500 Preclinical Results Align with WHO TPP Criteria

• Preclinical immunogenicity
  Demonstrated in mouse, guinea, pig, and NHP models

• Efficacy in a standardized and relevant animal model
  100% protection lethality and severe disease in 3 independent cynomolgus macaque lethal Lassa (Josiah) challenge studies

• Durability of protection (5 years preferred & 3 years minimal, can be maintained by booster doses)
  100% protection up to 1 year after immunization; boostable immune responses

• Coverage against Lassa virus lineages I to IV
  Cross-reactive immunogenicity against Lassa Clades I-IV, VII

• No Lassa-induced hearing loss was observed for INO-4500 immunized NHPs

• Analyses of correlates of INO-4500 mediated protection ongoing
Protection from Lassa Fever disease is associated with cell-mediated immunity and not dependent on humoral responses

- In humans CD4+ and CD8+ T-cell responses during early infection have been associated with recovery from Lassa Fever
- Neutralizing antibodies are rarely detected in the acute phase of disease. Lassa Fever patients develop neutralizing antibodies after the virus has been eliminated
- Protection appears to be associated with cell-mediated immunity induced by DNA, as well as several viral vector-based vaccines, ML29 and modified vaccinia and CD8 restricted epitopes
- Antibody responses in vaccinated rhesus monkeys (γ-irradiated LASV) did not correlate with protection.
  - Protection with INO-4500 was observed in the absence of neutralizing antibody responses in some NHPs

**Based on these findings, cell-mediated immune response rate was considered an important criterion**

GROUP A*
Regimen: 1 inj/visit
N = 6
4 Active (1mg INO-4500)
2 Placebo (SSC-0001)

GROUP B
Regimen: 2 inj/visit
N = 54
36 Active (1mg INO-4500)
18 Placebo (SSC-0001)

*The study had a safety run (N=6) in with 1mg or placebo prior to opening the 2mg dose group.

ClinicalTrials.gov Identifier: NCT03805984
LSV-001: Summary of Safety & Immunology

• Safety profile
  ✓ No safety concerns
  ✓ No treatment related SAEs

• Immunology summary
  ✓ Overall immune response based on interim, blinded immunology data
  ✓ Met Decision Point Go/No-Go Criteria
  ✓ Approval to move to LSV-002
LSV-002: Study Design

- There were no enrollment pauses
- Week 6 group-level unblinding for safety and immunology data has been completed
- Complete unblinding at End of Study

**ACTIVE (INO-4500)**
- Regimen A (1mg, 1 injection) N = 88
- Regimen B (1mg, 2 injections) N = 88

**PLACEBO (SSC-0001)**
- Regimen C (1 injection) N = 22
- Regimen D (2 injections) N = 22

ClinicalTrials.gov Identifier: NCT04093076
Go/No Go Criteria to Advance into Phase 2a Clinical Study

Go/No-Go Criteria

Safety Profile:
- No safety concerns from Inovio/DSMB safety review
- No treatment related SAEs

Immunology:
- Met target response rate at Week 6 (post dose 2)
Go/No Go Criteria to Advance into Phase 2a Clinical Study

Go/No-Go Criteria

Safety Profile:
• No safety concerns from Inovio/DSMB safety review
• No treatment related SAEs

Immunology:
• Met target response rate at Week 6 (post dose 2).
LSV-201 High Level Proposed Study Design

- Randomized, double-blind, placebo-controlled
- Selected dose and regimen from LSV-001 and LSV-002
- Enrollment open to all sites/countries
- Randomization will occur across both groups (i.e., all groups open for enrollment simultaneously)
- First DSMB meeting one month post-first dose
- Quarterly DSMB meetings until study completion
- No enrollment pauses for DSMB reviews unless a Stopping Rule has been met
- Projected 6-month enrollment
Thank you