MACAQUE STUDY DESIGN

**T-CELL RESPONSE**
A demonstrable increase in CD4+ and CD8+ T-cell activity as well as polyfunctionality in animals receiving JVR-S-100 adjuvant vaccine

**HEMMAGGLUTINATION INHIBITION (HAI)**
Results show an increase of geometric mean HAI antibody titers in animals receiving JVR-S-100 adjuvant vaccines compared to Fluzone® alone

**MICRONUTRALIZATION**
Results demonstrate an enhancement of geometric mean viral neutralizing antibody titers in animals receiving JVR-S-100 adjuvant vaccines compared to Fluzone® alone

**PHASE 1 CLINICAL STUDY DESIGN**

**OBJECTIVES:** Study is designed to assess safety, tolerability and immunogenicity of four dose levels of Fluzone® adjuvant compared to Fluzone® vaccine alone in healthy adults 18 to 65 years of age. Primary end point and other evaluation comparisons are designed to assess safety, tolerability in the primary efficacy population, with a secondary endpoint comparing the primary efficacy population to the control group.

Methods:

- Single-center, open-label, randomized, three-period, parallel-group design.
- Volunteer participants: 18 to 65 years of age, healthy adults with normal sensory, mental, and physical health.
- Volunteers are randomized to one of four dose groups: 25 µg Fluzone®, 22.5 µg Fluzone®/22.5 µg JVR-S-100, 15 µg Fluzone®/22.5 µg JVR-S-100, and 12.5 µg Fluzone®/22.5 µg JVR-S-100.
- Participants receive one dose of the study vaccine at least 28 days apart.
- Efficacy endpoints include geometric mean titers (GMTs) for in vitro neutralization and intracellular cytokine staining for antibody-specific T cells.

**CONCLUSIONS**
Influenza A infection causes annual substantial morbidity and mortality worldwide, particularly for infants, the elderly, and the immunocompromised. Current vaccines, such as the parenterally administered trivalent inactivated vaccine (TVV) are administered either unadjuvanted or adjuvanted with aluminum or steel hydrolate (alum). The efficacy of these vaccines is highly dependent on close matching of the hemagglutinin (HA) and neuraminidase (NA) surface proteins of the vaccine with currently circulating viruses. Should neutralizing antibody fail to prevent infection of the respiratory tract, subsequent clearance of viral infection is mainly dependent on T cells, particularly cytotoxic T lymphocytes (CTLs) of the CD8+ T-cell subset. Thus, it would be ideal for new vaccines used with existing flu vaccines to induce both high levels of antibody and T-cell immunity. Cationic lipid DNA complexes (JVR-S-100) are a unique adjuvant that is particularly promising for vaccines that require induction of both high levels of antibody and T-cell immunity including TVV. The adjuvant is based on a cationic-neutral lipid carrier and non-coding DNA complex. Inclusion of protein antigens with JVR-S-100 results in an extremely robust humoral, CD4+, and CD8+ immune response. The JVR-S-100 adjuvant combined with split vaccine (Fluzone®-solved Pasteur) resulted in increased antibody and T-cell responses in non-human primates and is currently being tested in a human phase I clinical trial. This could be critically important in vaccination of populations that show a decreased response to vaccination (i.e., children or immunocompromised)