Novavax Ebola/Makona Glycoprotein (GP) Nanoparticle Vaccine Candidate Update: NHP and Clinical Data

July 21, 2015
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Novavax Ebola GP Nanoparticle Vaccine

• Ebola Zaire Makona GP Nanoparticle Vaccine
  ▪ Recombinant, full length EBOV/Makona GP trimers
  ▪ 30 – 40 nm spherical nanoparticles

• Matrix-M™ adjuvant
  ▪ Nano-particulate saponin-based adjuvant
    o Promising stability in long-term pre-formulation with ZEBOV GP
  ▪ EBOV-H-101 represents 8\textsuperscript{th} clinical trial using Matrix-M
  ▪ Most recently with flu H7N9-well tolerated, dose sparing, robust HAI
    o Adjuvant-induced cross-protection in avian influenza
  ▪ Toxicology study completed prior to study initiation
    o Transient injection site, draining lymph node inflammatory response
    o No distant tissue findings
Novavax EBOV-H-101 Protocol

- Randomized, placebo-controlled, dose-escalating design with safety monitoring committee oversight

- **Primary Objectives:**
  - To accumulate a safety profile based on 7-day solicited reactogenicity, 84-day all AE profile, 1-year MAE and SAE profile, selected clinical labs
  - To demonstrate Matrix-M adjuvant effect on anti-GP IgG responses
  - To select the lowest antigen dose yielding a anti-EBOV GP IgG response not < the maximum feasible unadjuvanted dose

- **Secondary Objectives:**
  - To describe serum immune responses in terms of antibody titers competitive with known-neutralizing EBOV GP mab (13C6)
  - To describe antibody response kinetics in response to 1 and 2-dose regimens through one year
  - To compare Novavax anti-GP IgG with ELISA and neutralizing antibody responses from an external lab (University of Marburg)
## Novavax EBOV-H-101

### Study Design

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Day 0 Vaccination</th>
<th>Day 21 Vaccination</th>
<th>Subjects per Group</th>
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<tr>
<td></td>
<td>EBOV GP Antigen Dose</td>
<td>Matrix-M™ Adjuvant Dose</td>
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<tr>
<td>A</td>
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<td>0µg (Placebo)</td>
</tr>
</tbody>
</table>

**Total Subjects per Stage**: 40, 75, 115

**Total Subjects**: 230
Novavax EBOV-H-101 Status

• Clinical trial material for phase I released Dec 2014
• 230 healthy young adults 18 to < 50 y.o., male and non-pregnant female; recruited in Australia.
• First subject dosed 10 Feb 2015
  ▪ No stopping rules triggered during dose escalation
• Last subject received second dose April 2015
• Current data span days 0 – 35
  ▪ Safety – all subjects
  ▪ Novavax Makona GP ELISA – all per-protocol subjects
  ▪ Inactivated Makona whole-virus capture ELISA provided by Dr. V. Krähling, Univ. Marburg. 100-subject randomly selected panel at day 35 spanning placebo and 10 of 12 active groups
• Pending, ~ 24 July, neutralization data on same 100 serum panel from University of Marburg (Dr. Becker).
Novavax ZEBOV Makona IgG ELISA
Preliminary Results

Novavax Makona GP ELISA

- 2-dose adjuvanted regimens
- 1-dose adjuvanted regimens
- Unadjuvanted regimens

SAB TC bovine hyperimmune serum std. set to 1,000 EU
Whole Virus ELISA Results

Day 35 Makona Whole Virus ELISA Titers
Dr. V. Krähling, Phillips Univ. Marburg

2-dose adjuvanted regimens
Novavax EBOV-H-101 Safety to Date

• Dose escalation completed without triggering stopping rules
• No attrition due to AE
• Local injection site pain
  ▪ 8.3% of placebo recipients
  ▪ 21.6% of unadjuvanted vaccine recipients
  ▪ 60.0% of 1-dose adjuvanted vaccine recipients and 91.6% of 2-dose adjuvanted vaccine recipients
    ▪ Predominantly mild
    ▪ Transient
• Fever in 1 placebo recipient (2.1%), no 1-dose adjuvanted vaccine recipients and 3 in 2-dose adjuvanted vaccine recipients (5.0%)
  ▪ None >38.9°C
• Mild to moderate headache, myalgia, arthralgia and fatigue
• One SAE – active vaccinee with trauma secondary to auto accident
• Rates of severe; severe and related unsolicited AEs closely similar in active and placebo subjects
Preclinical NHP *Cynomolgus macaque* Challenge Summary

1. Texas Biomedical NOV2014-001- Complete
   - 5µg EBOV GP + Matrix
   - Immunization Day 0 and 21 (n=3)
   - 100% survival, challenged with 100 pfu wt ZEBOV Kikwit

2. OBRA/DMID/NIAID Stage one C25 - Complete
   - 5µg EBOV GP + Matrix
   - Immunization Day 0 and 42 (n=2) or Day 21 and 42 (n=2)
   - 100% survival, challenged with 100 pfu wt ZEBOV Kikwit

3. OBRA/DMID/NIAID Stage two C29 - Challenge result pending
   - 5µg or 1µg EBOV GP + Matrix (n=8)
   - 5µg EBOV GP + 5µg SUDV GP + Matrix (n=2)
   - Immunization Day 7 and 28
   - Challenged with 100 pfu wt virus ZEBOV Kikwit, 14 July 2015
Baboon Modeled Anti-EBOV GP IgG Response

Anti-EBOV/Makona GP IgG ELISA - EC$_{50}$

- 5 µg EBOV GP + Matrix
- 60 µg EBOV GP + Matrix
- 60 µg EBOV GP + AlPO$_4$
- 60 µg EBOV GP

- Adjuvant effect
- Dose sparing
- Durability
- 13C6-like antibodies

Welliver et al, Univ. of Oklahoma
Summary

• Full-length Recombinant Makona GP with Matrix-M adjuvant
• 100% protection against mortality in 2 NHP challenges to date, third in progress to identify failing dose
• Sustained IgG anti-GP responses in baboons
• Phase 1 data to date:
  ▪ Adjuvant increases local and systemic reactogenicity, but symptoms are predominantly mild-moderate and transient
  ▪ Approx. 3% vaccine-attributable incidence of mild-to-moderate fever in 2-dose adjuvanted vaccine groups
  ▪ Approximately 10-fold antigen dose-sparing with Matrix-M (6.5 vs 50µg)
  ▪ Two-dose adjuvanted regimens strongly immunogenic
  ▪ Similar findings with Univ. Marburg Whole Virus ELISA
  ▪ One-dose regimens readily detected, lower compared to two-dose
  ▪ Neutralization data pending
• Further development of this vaccine is warranted