Janssen Ebola Vaccine
Emergency Track Program

Review of ebola vaccines in phase 1 clinical evaluation

WHO Meeting, January 8, 2015

Infectious Diseases and Vaccines

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Janssen R&D

Melinda, Goddess of Healing
Melinda’s artwork reflects her journey living with HIV.
Agenda

• Janssen Ebola Vaccine Regimen
  • Key attributes
  • Supply situation

• Clinical Development Plan

• Summary
Janssen/BN Filovirus vaccine
Proof of concept in highly stringent NHP model

- Multivalent vaccine developed with funding from DMID
- Heterologous prime boost schedule 0 - 2 months

<table>
<thead>
<tr>
<th>PRIME</th>
<th>BOOST</th>
<th>Original FIH Timelines</th>
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<tbody>
<tr>
<td>Ad26.ZEBOV</td>
<td>Ad35.ZEBOV</td>
<td>Q3 2016</td>
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<tr>
<td>Ad26.SUDV</td>
<td>Ad35.SUDV</td>
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<td>Ad26.MARVA</td>
<td>Ad35.MARVA</td>
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<tr>
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<td>Ad26.SUDV</td>
<td>Q1 2016</td>
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<tr>
<td>Ad26.SUDV</td>
<td>MVA-BN-Filo</td>
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<tr>
<td>Ad26.MARVA</td>
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100% Protection After Vaccination In NHP Using Stringent Ebola Challenge Model

Ad26/MVA-BN, MVA-BN/Ad26
Ad26/Ad35: 100% survival, no symptoms after challenge

MVA-BN-Filo: one single vector expressing 4 filovirus antigens (Ebola, Sudan and Marburg GP and Tai Forest NP)
A prophylactic Ebola Zaire vaccine leveraging on two existing platforms

AdVac® vector

Ad26.ZEBOV Vaccine

Production on complementing PER.C6® cells

Ad26.ZEBOV (prime)

MVA-BN® vector

MVA-BN-Filo

Production on permissive primary Chicken Embryo Fibroblasts

MVA-BN-Filo (Boost)

Synthesized gene encoding Filo virus glycoproteins

Vaccine

Ad26.filo and MVA-BN-Filo deliver the Ebola GP transgenes inside human cells that then produce Ebola GP which elicits an immune response

Day 0 (prime)  Day 56 (boost)
Ad26.ZEBOV – technical characteristics

Manufacturability

- Established high yield process (PER.C6®-based)
- >400,000 doses (bulk) produced and released to date
- Final product available to date is 20,000 doses; remaining to be released March (250,000) through May (total of 400,000)
- Capacity for 2015 up to 5 million, if needs are confirmed

Stability Final Product

- Based on experience with Ad26 containing other inserts:
  - ≥ 3 years expected at -65°C
  - 2-8°C > 12 months
- Ad26.ZEBOV:
  - As of Q1 2015, minimally 3 months at 2-8°C
  - Later on in 2015: 6 months – 1 year at 2-8°C
  - Long-term perspective (>2016): Minimal 2 years stability at 2-8°C
Ad26.ZEBOV – clinical characteristics

• **Ad26 & Ad35 based vaccines (with other inserts)**
  • HIV (Ad26, N=230)
  • TB and malaria (Ad35; N≥700; incl. children age 4-9 months)
  • Optimal Ad26 immunogenicity profile found at 5x10^{10}
  • Tolerability profile is driven by vector dose; similar, independent of inserts

• **Phase I, Ad26.ZEBOV/MVA-BN-Filo FIH study ongoing at Oxford**:
  • Four sentinel subjects dosed; no AEs reported to date
Ad26.ENVA.01 prototype HIV vaccine candidate was safe and immunogenic at all doses tested

- Ad26.ENVA.001 elicited HIV env-specific antibodies in 100% of volunteers within two weeks after priming
- Cell mediated immunity peaked between days 28-56 and was stable for at least 6 months


Infectious Diseases and Vaccines
MVA-BN-Filo - vaccine characteristics

Manufacturability
- Leverage established smallpox vaccine process (≈30M doses produced)
- Bulk available to date > 400 K, release pending
- Final product to be released March (250 K) through May (total of 400K)
- 700 doses available for use in phase I
- Capacity for 2015: up to 5 million, if needs are confirmed

Clinical Safety:
- Backbone licensed as smallpox vaccine in EU and Canada
  - In addition U.S. Strategic National Stockpile
- Acceptable safety profile in >7500 subjects immunized at clinical dose including HIV patients and children (age 0.5 – 6 years)

Stability Final Product
- ≥ 3 years expected at -65°C (current available MVA-BN-Filo GMP DP batch)
- ≥ 2 years expected at -20°C (based on MVA-BN with other inserts)
- > 3 months at 2-8°C after Q1 2015
- Mid-term up to 1 year
- Long-term perspective (>2016): Minimal 2 years stability at 2-8°C
High level clinical strategy (1/2)

- Partners for clinical development are:
  - Oxford University, UK (phase I and II)
  - National Institutes of Health (Phase I)
  - London School of Hygiene and Tropical Medicine, UK (phase I and III)
  - INSERM, France (phase II)
High level clinical strategy (2/2)

- **Phase I studies in UK and US**
  - Establish preliminary safety and immunogenicity
  - Identify optimal short schedule* (2 week to 2 month intervals)
  - One year follow up:
    - Investigate durability of immune responses
    - Late boost possibilities

- **Phase I studies in UG, KE, TZ**
  - Repeat of UK study
  - To be initiated based on preliminary EU/US safety data
  - Confirm preliminary safety and immunogenicity

- **Phase II studies (EU/Africa)**

- **Collaborative Study** with GSK to assess possibility of using various combinations of Ebola vectors as prime and boost. (design under discussion)

- **Efficacy study under discussion** (with a lead in safety/immuno study, RCT)
Overall Phase I studies

- Establish safety and immunogenicity of various prime boost schedules

### Phase I studies, healthy adults

<table>
<thead>
<tr>
<th>Study</th>
<th>Total N</th>
<th>N of subjects with candidate vaccines</th>
<th>Safety</th>
<th>Immuno</th>
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<tbody>
<tr>
<td>-1001</td>
<td>72</td>
<td>60</td>
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<tr>
<td>-1002</td>
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<tr>
<td>-1004</td>
<td>72</td>
<td>60</td>
<td>60</td>
<td>60</td>
</tr>
<tr>
<td>Total</td>
<td>308</td>
<td>258</td>
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Phase II studies, N > 2000 (under discussion)

- Enter Ph II based on Phase I post prime data
  - Focus on single regimen that is ‘outbreak responsive’
  - Africa: expanded safety + immuno of selected regimen; n=1200
  - EU: expanded safety + immuno of selected regimen; n=600
  - Timing: April 2015

- Special populations to be evaluated:
  - Children, aged 1 to 17 years
  - Elderly/older adults (50-70 years)
  - HIV+ adults
  - Western-based HCW, planning to work in the affected areas

- Countries under consideration:
  - FR, UK, US, Ghana, Côte d’Ivoire, Burkina Faso
- Study designs and populations to be agreed upon with Health Authorities
How to assess efficacy?

• We continue to look for opportunities to join any of the planned efficacy trials, especially if the ramp up of these is protracted
• London School of Hygiene and Tropical Medicine is our partner for efficacy testing of our vaccine candidate
• Potential for demonstrating efficacy is situation dependent:
  • Status of epidemic by time of study start
  • If not possible: consider potential for immune bridging, or application of animal rule?
# Janssen Ebola Vaccine – Preliminary Timeline

<table>
<thead>
<tr>
<th>2015</th>
<th>2016</th>
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<tr>
<td>Q1</td>
<td>Q2</td>
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**Phase I (N=258)**  
Adults 18-50  
UK, US, TZ, KE, UG

**Phase II EU**  
N=600 Adults Prime  
N=1200 (incl childr) Prime

**Phase II EU Boost**  
**Phase II Afr Prime**  
**Phase II Afr Boost**

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**Sierra Leone – (draft proposal, under discussion)**

**Phase III – Lead in:**  
- Safety and immunogenicity in adults/children  
- Population TBD, N = 1000 adults, 200 children

**Phase III – large scale:**  
Methodology, TBD, options:  
- RCT  
- Wedge approach:  
  - Stepwise by region/district

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*Avail. of post prime data S/I*  
*Full Regimen Safety and Immuno available*
Janssen Ebola Vaccine - Executive Summary

• High yield manufacturing platforms (Ad26-PerC6 // MVA)
  • 450 K regimens to be released starting end March 2015
  • Production capacity 2015 up to 5 million doses (if needed).

• ≥ 1 year thermostability for backbone vectors
  • Anticipated 3 months at 2 – 8 °C by start of use
  • At country level: central storage frozen (-20°C) - Distribution through normal ‘vaccine supply chain’ channels (2 - 8°C)

• Substantial human experience with both vectors
  • Ad26 post dose 1 (HIV) : robust humoral and CD8+ T cell responses

• Conduct a lead in safety (and immuno study) in Sierra Leone, prior to large scale (efficacy) trial, based on post dose 1 safety/immunogenicity in phase 1.
Thank you