OVERVIEW OF EBOLA I STUDY DESIGN

This is a Phase 1, randomized, placebo-controlled, observer-blind study evaluating the safety, tolerability and immunogenicity of 4 regimens using MVA-BN-Filo at a dose of $1x10^8$ TCID50 and Ad26.ZEBOV at a dose of $5x10^{10}$ vp: 2 regimens will have MVA-BN-Filo as prime and Ad26.ZEBOV as boost at a 28- or 56-day interval and 2 regimens will have Ad26.ZEBOV as prime and MVA-BN-Filo as boost at a 28- or 56-day interval. The study will be conducted in approximately 72 healthy adult subjects who never received an experimental Ebola candidate vaccine before and have no known exposure to or diagnosis of Ebola disease.

The study consists of a screening period of up to 28 days, a vaccination period in which subjects will be vaccinated at baseline (Day 1) followed by a boost on Day 29 or 57, and a post-boost follow-up until all subjects have had their 21-day post-boost visit (Day 50 or Day 78) or discontinued earlier. At that time the study will be unblinded. Subjects who received placebo will be contacted to communicate that they have completed the study and do not need to contact the site any longer. Subjects who received active vaccine will enter a long-term follow-up, with visits on Days 180 (±15 days), 240 (±30 days) and 360 (±30 days) post-prime.

The blinded Principal Investigator will be responsible for the safety monitoring of the study. If at least one pre-specified pausing rule is met, study vaccinations will be paused and an Independent Data Monitoring Committee (IDMC) meeting will be convened. Subjects will be enrolled into 4 different groups, comprising 18 healthy subjects each. Overall, subjects will be randomized within group in a 5:1 ratio to receive either active vaccine or placebo (0.9% saline) through intramuscular (IM) injections (0.5 mL) as follows:

- MVA-BN-Filo ($1x10^8$ TCID50) administered on Day 1, followed by a booster of Ad26.ZEBOV ($5x10^{10}$ vp) on Day 29 (Group 1) or Day 57 (Group 2), or

- Ad26.ZEBOV ($5x10^{10}$ VP) administered on Day 1, followed by a booster of MVA-BN-Filo ($1x10^8$ $TCID^{50}$) on Day 29 (Group 3) or Day 57 (Group 4).

Enrollment of subjects in Groups 1 and 3 will start with vaccination of 1/1 subjects (active vaccine/placebo; Sentinel Cohort) to assess the tolerability of the 2 study vaccines over a 24-hour period before exposing larger cohorts of subjects to the vaccines. At least 24 hours (but no more than 30 hours) after the prime vaccination, subjects will come to the site (or be visited at home) to verify the absence of any predefined events (i.e., a serious adverse event considered to be related to any of the study vaccines, signs of anaphylaxis or generalized urticaria clearly attributable to study vaccination, a severe [grade 3] systemic adverse event considered to be related to any of the study vaccines, a severe [grade 3] solicited local [injection site] adverse event, a severe [grade 3] solicited systemic adverse event considered to be related to any of the study vaccines, or death). Enrollment of the next cohorts will be as follows:

- Groups 1 and 3: 4/1 subjects (active vaccine/placebo; Cohort 1) followed, in the absence of any of the above-mentioned events, confirmed during a visit (at the site or at the

subject's home) for each subject at least 24 hours (but no more than 30 hours) after prime vaccination, by 10/1 subjects (active vaccine/placebo; Cohort 2)

- Groups 2 and 4: 5/1 subjects (active vaccine/placebo; Cohort 1) followed, in the absence of any of the above-mentioned events, confirmed during a visit (at the site or at the subject's home) for each subject at least 24 hours (but no more than 30 hours) after prime vaccination, by 10/2 subjects (active vaccine/placebo; Cohort 2)

The enrollment of all subjects of Cohort 1 will be carried out ideally on the same day. Also the enrollment of all subjects of Cohort 2 will be carried out ideally on the same day. If the enrollment of Cohort 1 is carried out over more than 1 day, enrollment of Cohort 2 in that group may only begin after the safety of the last subject in Cohort 1 has been assessed (i.e., 24 to 30 hours after the prime vaccination).