1.1 PUBLISHABLE SUMMMARY (max 7,500 characters)

SUMMARY OF THE ACTION CONTEXT AND OBJECTIVES

The Ebolavirus Zaire (EBOV) outbreak of 2014 was the largest and most complex outbreak described since EBOV was first identified leading to >11,000 deaths in West Africa.

In August 2014, the WHO declared the Ebola outbreak as an international public health emergency and many organizations mobilized their efforts to control the epidemic.

This is when, to accelerate the clinical development of the GSK chimpanzee adenovirus type 3 Ebolavirus Zaire (ChAd3-EBOV) vaccine candidate (developed according to a joint effort between VRC/NIH and GSK), the EBOLAVAC consortium was created.

The specific project objectives were to:

1. Support a Ph1 CT of the ChAd3-EBOV vaccine sponsored by the Centre Hospitalier Universitaire Vaudois (CHUV) (WP2)

2. Evaluate the ChAd3-EBO-Z vaccine in the course of Ph2, randomized, observer-blind, controlled studies sponsored by GSK and performed in clinical study centers in Central/West Africa outside geographical zones where the epidemic was the most active (Guinea, Sierra Leone and Liberia) (WP3)

3. Evaluate in West Africans safety and immunogenicity of boosting a single dose of the ChAd3-EBO-V vaccine with a heterologous boost 1 week or 2 and 4 weeks later with the same EBOV insert expressed by a Modified vaccinia Virus Ankara (MVA) vector. Preclinical studies with the EBOV insert and clinical studies with other microbial antigens indicated that this could enhance the humoral and cellular immunogenicity of the vaccination leading to higher and more durable efficacy (WP4)

4. Accelerate the development of a suitable cGMP process for the biomanufacture of MVA-GSK-EBOV on a cell line (WP7).

In addition to the above, other activities included data management and analysis (WP5), results communication and dissemination (WP6) and project management/coordination (WP1).

WORK PERFORMED FROM THE BEGINNING OF THE ACTION TO THE END OF THE PERIOD COVERED BY THE REPORT AND MAIN RESULTS ACHIEVED SO FAR

The EBOLAVAC consortium achieved the following results:

1. Ph1/2 randomised-controlled study, Lausanne, Switzerland: Completion of a trial to assess safety, reactogenicity and immunogenicity of a single injection of ChAd3-EBO-Z when administered to healthy volunteers at 2 different doses. Between 24/10/14 and 22/06/15, 120 subjects were randomly assigned of whom 18 were potentially to be deployed to EBOV

transmission areas and 102 were not to deploy, to receive high dose vaccine (n=49), low dose vaccine (n=51) or placebo (n=20)

2. Ph2 expanded safety and immunogenicity studies in Africa: a. Completion of a multi-centre study in 4 African countries: Cameroon (2 centres), Mali (1 centre), Nigeria (1 centre) and Senegal (2 centres) to assess safety and immunogenicity of a single i.m dose of ChAd3-EBOV in adults 18 years of age and older- N of subjects vaccinated:3013 (1508 in the ChAd3-EBOV group- 1505 in the Placebo/ChAd3-EBO-Z group); b. Completion of a multi-centre study in 2 African countries: Mali (1 centre) and Senegal (1 centre) to assess safety and immunogenicity of a single i.m dose of ChAd3-EBOV in children 1-17 years of age -N of subjects vaccinated:600 (300 in the ChAd3-EBOV/MENACWY-TT group-300 in the MENACWY-TT/ChAd3-EBOV group)
3. Booster study with MVA-GSK-EBOV: Completion of a Ph1 study in Dakar, Senegal to assess safety and immunogenicity of heterologous prime-boost immunization with ChAd3-EBOV and MVA-GSK-EBOV received 7days after prime injection in healthy Senegalese adults (18-50 years). N of subjects vaccinated:40 (20 receiving prime and boost vaccination in the same arm, 20 in the opposite arm)
4. MVA-GSK-EBOV Advanced Cell Line Process Development: Process development completed by Emergent Biosolutions (activity partially funded by Wellcome Trust). Completion of GMP manufacture at 200L scale (drug substance for~25000 doses). Half of this was filled into 2500 multi-dose vials (5 doses/vial). A similar quantity remains in storage unfilled.
5. Communication, dissemination and exploitation: Several communication and dissemination materials, incl.press-releases, articles in press and TV/radio programs were produced and distributed;Publication of a major scientific manuscript (www.sciencedirect.com/science/article/pii/S1473309915004867); Confidential sharing of project results with governments and NGOs incl. WHO towards improved efforts to better prepare for recurring public health emergencies; Presentation at international congresses, meetings and workshops; Project website

PROGRESS BEYOND THE STATE OF THE ART AND EXPECTED POTENTIAL IMPACT (INCLUDING THE SOCIO-ECONOMIC IMPACT AND THE WIDER SOCIETAL IMPLICATIONS OF THE ACTION SO FAR)

The unedited nature of the West African 2014-2016 Ebola epidemic catalyzed unprecedented efforts, of which the EBOLAVAC program which generated new scientific information on the ChAd3-EBOV vaccine approach in a context of emergency response.

The path towards registration of ChAd3-EBOV is elusive in the absence of field efficacy data, with virtually no possibility to generate effectiveness data in the future. Nonetheless EBOLAVAC paved the way for the preparedness against future outbreaks.

The robust safety and immunogenicity data package generated in the program has substantially improved the knowledge on the ChAd platform which is key for regulator's confidence. Ongoing EBOV vaccine approaches looking at other filovirus species will capitalize on this robust dataset and enable future developments. These will be further facilitated by the many efforts deployed in improving the productivity and formulation of ChAd-based EBOV vaccines, as well as on collective efforts to generate widely accepted immunological read-outs. Clinical research expertise was developed/strengthened in the field and will be key to accelerate the set-up of potential future new

clinical programs, with the aim of capturing clinical evidence of efficacy for new filovirus vaccine candidates.

With regards to societal impacts, one visible example is that the 2014 West African Ebola epidemic triggered a global health emergency response where the role of social science-based initiatives was acknowledged at the very early stages for EBOV disease control in affected countries.

For instance anthropologists were invited in initial WHO workshops and their insights were translated into concepts and recommendations relevant for the public health of affected countries during the epidemic. Such interventions have not been limited to the beginning of the epidemic and have led to the creation of several platforms (e.g. www.shsebola.hypotheses.org;www.socialscienceinaction.org), active in post-epidemic questions like the continued social disruption caused by the epidemic or preparedness questions in order to strengthen rapid emergency responses in the future.

The adult and paediatric Ph2 trials were designed taking these early anthropological insights into account, in close collaboration with investigators involved in the studies. For instance, community-based communications were regularly dispensed at the Center for Vaccine Development in Bamako, Mali and were very beneficial for population adhesion and for study performance overall. Both studies led to the establishment of new, or to the strengthening of existing vaccine development capacities in Central/West Africa, be it specific to EBOV or to other infectious threats. We believe these capacities may fit with local ongoing preparedness efforts and assist African networks in advance of other epidemic, for instance in the preparation of mock-up research protocols or in the establishment of methodological guidelines.

Finally, the EBOV epidemic in West Africa also renewed government and NGO efforts to better prepare for recurring public health emergencies. One example is CEPI.

ADDRESS (URL) OF THE ACTION'S PUBLIC WEBSITE

www.ebolavac.eu

PUBLISHABLE SUMMARY'S ASSOCIATED IMAGES

EbolaVac