OVERVIEW OF THE CURRENT RESEARCH, DEVELOPMENT AND USE, OF VACCINES AGAINST EBOLA

October 2019
SUMMARY

• Ebola virus disease is one of the most devastating infectious diseases in the world
• The global research and development community is rising to the challenge with a co-ordinated effort to fund, develop, test and utilise vaccines
• There are currently 8 candidate vaccines undergoing clinical evaluation at different research trial phases to combat Ebola
• One vaccine has completed all research trial phases

• 5 vaccines are intended for preventive use and 4 vaccines for reactive use during an outbreak
• All the vaccines are being developed and tested by the collaborative efforts of Governments and numerous organisations across the globe – in Africa, North America, Europe, Russia and China
• Please refer to the table at the end of the document which compares all of the vaccines in detail

TYPES OF CANDIDATE EBOLA VACCINES

Different kinds of Ebola vaccines have been developed, evaluated and used. They can be divided into 3 categories.

Category 1 & 2 - Non-replicative and replicative vector-based Ebola vaccines
• The first 2 categories utilise modified non-ebola viruses. These act as carriers (or vectors) for key elements of the vaccine to enter the body and stimulate the body’s immune response.
• This technology either employs live ‘replicating’ carrier viruses or modified ‘non-replicating’ carrier viruses
• Using live vaccines that replicate in the body generally provides a strong and long-lasting immune response, but they aren’t always recommended in immuno-compromised individuals
• An example of a live vaccine that has successfully completed many clinical trials uses a genetically engineered version of a live animal virus (vesicular stomatitis virus (rVSV)), to carry an Ebola virus gene. This is called recombinant EBOVAVP30
• Viral vectors that are adapted not to replicate in the body, while potentially safer, may require multiple doses to achieve optimal immunity

Category 3 - Other ebola vaccines
Other approaches include...
• using an inactivated Ebola virus
• using inactivated Ebola virus-like particles
• inserting Ebola virus (EBOV) genes into DNA that is introduced specifically into a patient’s muscle. The use of DNA vaccines can be advantageous as they can lead to an enhanced immune response
TYPES OF CANDIDATE EBOLA VACCINES

Ebola Vaccines

Non replicative vector-based Ebola vaccines
- MVA-vectored vaccine
- Ad26.ZEBOV & MVA-BN-Filo (2-dose regimen, VAC52150)
  - Janssen Vaccines & Prevention B.V, The Netherlands
- Ad vaccine
- Chimpanzees Ad vaccine

Replicative vector-based Ebola vaccines
- Ad5-EOBOV (monovalent)
  - CanSino Biologies Inc. & Beijing Institute of Biotechnology, China
- GamEvac-Combi and GamEvac-Lyo rSV-GP rAdS-GP
  - Gamaleya Research Institute of Epidemiology and Microbiology, Russia
- Ad26.ZEBOV & MVA-BN-Filo (2-dose regimen, VAC52150)
  - Janssen Vaccines & Prevention B.V, The Netherlands
- ChAd3 (monovalent Zaire)
  - Sabin Vaccines Institute / National Institute of Allergy and Infectious Diseases (NIAID), USA
- rSVVAG-ZEBOV-GP
  - Merck, USA

Other Ebola vaccines
- INO-4201 (DNA vaccine)
  - Inovio Pharmaceuticals, USA
- Nanoparticle recombinant Ebola GP vaccine
  - Novavax, USA
- EpivacEboV
  - FBRI SRC V8 VECTOR, Rospatrebnadzor, Russia
EBOLA VACCINES
According to the number of people who have received the vaccine in clinical trials or as part of expanded access and compassionate use protocols

- **rVSV-ZEBOV-GP**
  - >18,000 people in clinical trials

- Ad26.ZEBOV & MVA-BN-Filo
  - (2-dose regimen, VAC52150)
  - >6,500 people in clinical trials

- ChAd3
  - (monovalent Zaire)
  - >5,600 people in clinical trials

- GamEvac-Combi and GamEvac-Lyo
  - 2,200 people in clinical trials

- Ad5-EOBV (monovalent)
  - 681 people in clinical trials

- EpivacEbola
  - 300 people in clinical trials

>200,000 people
compassionate use/expanded access protocols

*Infographic represents total figures divided by 100*
EBOLA VACCINES
How far are they progressing in research testing?

The diagram depicts the most advanced research phase a specific vaccine has achieved so far - and the country where the study took place.

Phase I
- Nanoparticle recombinant Ebola GP vaccine
- INO-4201 (DNA vaccine)
- Non-particle recombinant Ebola GP vaccine

Phase II
- Ad5-EBOV (monovalent) (Sierra Leone)
- EpivacEbola (Russia)
- Ad26.ZEOBV & MVA-BN-Filo (2-dose regimen, VAC52150) (Europe, USA, Africa)
- ChAd3 (monovalent Zaire) (Cameroon, Senegal, Mali, Liberia, Nigeria)

Phase III
- rVSV-A-G-EBOV-GP (Guinea) - completed
- GamEvac-Combi and GamEvac-Lyo (Guinea)
- Phase IV also reported in Russia

Phase III
- These vaccines are licensed in their country of origin
  - Ad5-EBOV (monovalent) in China
  - EpivacEbola and GamEvac-Combi and GamEvac-Lyo rVSV-GP rAd5-GP in Russia

Phase I
- In this Phase vaccines are tested in a small group of people (often 20-80) to evaluate their safety, determine what a safe dosage might be, and identify any side effects.

Phase II
- This phase is primarily focused on analysing the preliminary efficacy of the vaccine. It involves, over several months, testing it with a larger group of people (often several hundred) to determine its efficacy and to evaluate its safety.

Phase III
- This phase is focused on finally confirming the vaccine’s safety and efficacy. It can take longer than Phase II - although timelines vary. It involves testing with large groups of people (typically up to 3,000) to evaluate the vaccine’s efficacy compared with others and monitor side effects.
EBOLA VACCINES

In the Democratic Republic of the Congo (DRC) outbreak, countries where they are being used under different protocols (expanded access and compassionate use) or in clinical trials.

rVSVΔG-ZEBOV-GP9 vaccine is currently being used under different protocols in DRC, Uganda, South Sudan, Rwanda and Burundi.
## EBOLA VACCINES

**According to doses currently available as of 30 August 2019**

<table>
<thead>
<tr>
<th>Vaccine Type</th>
<th>Manufacturer</th>
<th>Country</th>
<th>Doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>ChAd3 (monovalent Zaire)</td>
<td>Sabin Vaccines Institute / National Institute of Allergy and Infectious Diseases</td>
<td>USA</td>
<td>450,000 doses</td>
</tr>
<tr>
<td>rSVΔG-ZEBOV-GP</td>
<td>Merck, USA</td>
<td>USA</td>
<td>400,000 doses</td>
</tr>
<tr>
<td>Ad26 ZEBOV &amp; MVA-BN-Filo (2-dose regimen, VAC52150)</td>
<td>Janssen Vaccines &amp; Prevention B.V., The Netherlands</td>
<td>The Netherlands</td>
<td>45,000 labelled regimens</td>
</tr>
<tr>
<td>EpivacEbo</td>
<td>FBRI SRC VB VECTOR, Rospotrebnadzor, Russia</td>
<td>Russia</td>
<td>20,000 doses</td>
</tr>
<tr>
<td>Ad5-EOBV (monovalent)</td>
<td>CanSino Biologics Inc. &amp; Beijing Institute of Biotechnology, China</td>
<td>China</td>
<td>20,000 doses</td>
</tr>
<tr>
<td>GamEvac-Combi and GamEvac-Lyo</td>
<td>rSVV-GP rAd5-GP Gamaleya Research Institute of Epidemiology and Microbiology, Russia</td>
<td>Russia</td>
<td>No data</td>
</tr>
</tbody>
</table>

**According to doses potentially available in 2020**

<table>
<thead>
<tr>
<th>Vaccine Type</th>
<th>Manufacturer</th>
<th>Country</th>
<th>Doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>ChAd3 (monovalent Zaire)</td>
<td>Sabin Vaccines Institute / National Institute of Allergy and Infectious Diseases</td>
<td>USA</td>
<td>No data</td>
</tr>
<tr>
<td>rSVΔG-ZEBOV-GP</td>
<td>Merck, USA</td>
<td>USA</td>
<td>1.3 million doses</td>
</tr>
<tr>
<td>Ad26 ZEBOV &amp; MVA-BN-Filo (2-dose regimen, VAC52150)</td>
<td>Janssen Vaccines &amp; Prevention B.V., The Netherlands</td>
<td>The Netherlands</td>
<td>Up to 1.5 million doses</td>
</tr>
<tr>
<td>EpivacEbo</td>
<td>FBRI SRC VB VECTOR, Rospotrebnadzor, Russia</td>
<td>Russia</td>
<td>1 million doses</td>
</tr>
<tr>
<td>Ad5-EOBV (monovalent)</td>
<td>CanSino Biologics Inc. &amp; Beijing Institute of Biotechnology, China</td>
<td>China</td>
<td>150,000 doses</td>
</tr>
<tr>
<td>GamEvac-Combi and GamEvac-Lyo</td>
<td>rSVV-GP rAd5-GP Gamaleya Research Institute of Epidemiology and Microbiology, Russia</td>
<td>Russia</td>
<td>100,000 doses</td>
</tr>
</tbody>
</table>

*Infographic represents total figures divided by 10,000*
# OVERVIEW OF CANDIDATE EBOLA VACCINES AS OF AUGUST 19, 2019

Eight candidate Ebola vaccines have undergone or are currently undergoing clinical evaluation at different trial phases. Three vaccines were licensed, three vaccines have completed or are in trials up to Phase 1 phase, two vaccines up to or in Phase 2 stage, and one vaccine has completed Phase 3 stage.

## TABLE 1. OVERVIEW OF CANDIDATE EBOLA VACCINE

<table>
<thead>
<tr>
<th>Type of candidate vaccine</th>
<th>Developer</th>
<th>Strain(s) aimed to protect against</th>
<th>a. Current stage of clinical evaluation</th>
<th>b. Number of subjects with data analysed to date</th>
<th>c. Regulatory status</th>
<th>Proposed vaccination schedule</th>
<th>Proposed indication</th>
<th>Proposed target population for the label indication</th>
<th>Current storage specifications*</th>
<th>Current formulation and presentation (doses per vial)</th>
<th>Number of clinical research grade doses available</th>
<th>Forecasted production capacity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PROPOSED INDICATION: REACTIVE USE DURING OUTBREAKS</strong>&lt;br&gt;Licensed in country of origin</td>
<td></td>
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<tr>
<td>AD5-EBOV (monovalent)1</td>
<td>CanSino Biologics Inc. &amp; Beijing Institute of Biotechnology, China</td>
<td>Zaire ebolavirus (Makona)</td>
<td>a. Phase 1 in China and Phase 2 in Sierra Leone</td>
<td>b. ≈681 people enrolled</td>
<td>c. Licensed obtained from CFDA in October 2017 to use under national reserves by National Medical Products Administration (NMPA). China in the event of Ebola outbreak. Submitted to WHO for Emergency Use Assessment and Listing (EUAL) in July 2018.</td>
<td>1 dose Reactive</td>
<td>18 to 60 years</td>
<td>-2°C to +8°C for 12 months</td>
<td>Final Formulation: Lyophilized</td>
<td>Presentation: Single dose vial + diluent</td>
<td>20,000 doses</td>
<td>Can produce 150,000 doses per year and potentially scale-up to 500,000 doses/year.</td>
</tr>
<tr>
<td>MV-SAVVIEBOV (multiple)2</td>
<td>Merck, USA</td>
<td>Monovalent Zaire (Kikwit 1995)</td>
<td>a. Phase 3 completed in Guinea (2016).</td>
<td>b. ≈200,000 people Over 18,000 people enrolled in clinical trials. Ongoing expanded access protocol in DRC with over 200,000 people vaccinated in affected areas in DRC.</td>
<td>c. Granted Breakthrough Therapy Designation by the US FDA and PRIME status by the European Medicines Agency (EMA) since 2016.</td>
<td>1 dose Active immunization (reactive use) of at-risk subjects ≥18 years of age to protect against disease caused by Zaire ebolavirus. (When the required paediatric data are available, will seek an indication for use in subjects ≥1 year of age).</td>
<td>60°C to -80°C for 36 months And.</td>
<td>2°C – 8°C for 14 days</td>
<td>Final Formulation: Liquid frozen</td>
<td>Presentation: 10 dose vials. After licensure single dose vials</td>
<td>380,000 doses currently available for dosing recommended by SAGE = 2x10⁷ pfu/mL (Guinea dose). (Corresponds to ~190,000 doses available for dosing proposed for licensure).</td>
<td>For 2020, planned replenishments targets are set to be displayed as Guinea dose (2x10⁷pfu/mL): Jan 2020: Approx. 340,000 additional doses April/May: Approx 600,000 June-Dec: Approx 900,000 additional doses Total: Approx. 1300,000</td>
</tr>
<tr>
<td>Ongoing clinical evaluation</td>
<td></td>
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</tr>
<tr>
<td>INO-4201 (DNA vaccine)3</td>
<td>Inovio Pharmaceuticals, USA</td>
<td>Plasmid of Ebola outbreak strains from 1976-2006</td>
<td>a. Phase 1</td>
<td>b. &gt;200 people enrolled</td>
<td></td>
<td>2 doses Reactive</td>
<td>≥18 years</td>
<td>-2°C to +8°C for 3 years and 28°C for 1 year 37°C for 1 month 60°C for several days</td>
<td>Final Formulation: Liquid frozen</td>
<td>Presentation: Single-dose vials</td>
<td>Potentially have 10,000 doses in bulk remaining of INO-4201.</td>
<td>No information available</td>
</tr>
<tr>
<td>CHAd3 (monovalent Zaire)4</td>
<td>Sabin Vaccine Institute / National Institute of Allergy and Infectious Diseases (NIAID), USA</td>
<td>Monovalent: Zaire (Mayinga)</td>
<td>a. Phase 2 in Cameroon, Senegal, Mali, Liberia, Nigeria</td>
<td>b. &gt;5,600 people enrolled</td>
<td>c. GSK has sublicensed the investigational product to Sabin (press release)</td>
<td>1 dose Reactive</td>
<td>Adults and Children</td>
<td></td>
<td>Final Formulation: Unknown</td>
<td>Presentation: Single dose vials</td>
<td>450,000 doses</td>
<td>No data</td>
</tr>
<tr>
<td>Type of candidate vaccine</td>
<td>Developer</td>
<td>Strain(s) aimed to protect against</td>
<td>a. Current stage of clinical evaluation</td>
<td>b. Number of subjects with data analysed to date</td>
<td>c. Regulatory status</td>
<td>Proposed vaccination schedule</td>
<td>Proposed indication</td>
<td>Proposed target population for the label indication</td>
<td>Current storage specifications*</td>
<td>Current formulation and presentation (doses per vial)</td>
<td>Number of clinical research grade doses available</td>
<td>Forecasted production capacity</td>
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</tr>
<tr>
<td>PROPOSED INDICATION: PREVENTIVE USE</td>
<td>Licensed in country of origin</td>
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</tr>
<tr>
<td>EpivacEbola</td>
<td>FBRG SRC VB/VECTOR, Rospatrebnadzor, Russia</td>
<td>Monovalent Zaire (Makona)</td>
<td>Phase 1 and 2/3 in Russia</td>
<td>300 people enrolled</td>
<td>Licensed in Russia since 2016</td>
<td>2 doses (prime + boost on 28 days)</td>
<td>Preventive</td>
<td>18 to 55 years</td>
<td>2-8°C for 1 year</td>
<td>Final Formulation: Liquid</td>
<td>20,000 doses currently available</td>
<td>Can produce 1,000,000 doses in a few weeks, no additional data</td>
</tr>
<tr>
<td>GamEvac-Combi and GamEvac-Lyo</td>
<td>Gamaleya Research Institute of Epidemiology and Microbiology, Russia</td>
<td>Monovalent Zaire (Makona)</td>
<td>Ongoing Phase 1/2 in Russia and Phase 3 in Guinea (Kindia)</td>
<td>2,000 people enrolled</td>
<td>Licensed in Russia for emergency use in the event of an EVD outbreak</td>
<td>2 doses (prime + boost on 21 days)</td>
<td>Preventive</td>
<td>18 to 55 years</td>
<td>16°C to 20°C for 12 months</td>
<td>Final Formulation: Liquid and Lyophilized</td>
<td>No information available</td>
<td>Can produce 20,000 doses per year and potentially scale-up to 100,000 doses/year</td>
</tr>
<tr>
<td>Ad26.ZEOBV &amp; MVA-BN-Filo (2-dose regimen, VAC52150)</td>
<td>Janssen Vaccines &amp; Prevention B.V, The Netherlands</td>
<td>Zaire ebolavirus (Mayinga)</td>
<td>Phase 1: Four studies completed in Europe, the United States and Africa Phase 2/3: Six Phase 2/3 studies in Europe, USA and Africa (partially) unblinded; two Phase 2/3 studies in Africa ongoing</td>
<td>6,500 people enrolled</td>
<td>Orchestrating with the US FDA to obtain licensure using the Animal Rule Filing at EMA under conditional approval or approval under exceptional circumstances Collaborative review with WHO (PO) and African NRAs planned Submitted file to WHO for EUAL. Received request for additional evidence.</td>
<td>2 doses</td>
<td>Preventive</td>
<td>Adults and children ≥ 1 year of age</td>
<td>20°C or 60°C for up to 60 months and +2 to +8°C for up to 12 months MVA-BN-Filo: 20°C or 60°C for up to 60 months and +2 to +8°C for up to 6 months</td>
<td>Final Formulation: Liquid</td>
<td>50,000 labelled regimens ready to be used. 1.5 million regimens in vials, QC-released, need to be labelled. Depending on urgency 45,000 or more additional regimens available each month</td>
<td>500,000 per year depending on the demand</td>
</tr>
<tr>
<td>Nanoparticle recombinant Ebola GP vaccine</td>
<td>Novavax, USA</td>
<td>Monovalent Zaire (Makona)</td>
<td>Phase 1</td>
<td>&gt;182 people enrolled</td>
<td></td>
<td>2 doses with planned boosts for HCW in potential epidemic areas</td>
<td>Preventive</td>
<td>≥ 18 years</td>
<td>N.A.</td>
<td>Final Formulation: Liquid</td>
<td>N.A.</td>
<td>N.A.</td>
</tr>
</tbody>
</table>
Table 1 - Notes

1 Ad5-EBOV (monovalent)
   - Ad5-EBOV is a replication-defective recombinant human type 5 adenovirus expressing Zaire (Makona, 2014) Ebola virus envelope glycoprotein.
   - After re-constitution, each dose includes two vials (0.5ml/vial) with a total volume of 1ml, containing 8 x 10^10 VP of the replication-defective recombinant human type 5 adenovirus expressing the Ebola virus envelope glycoprotein.
   - Three clinical studies of Ad5-EBOV were completed, including a randomized, double-blinded, placebo-controlled Phase I clinical trial of 120 Chinese subjects, an open Phase Ib clinical trial of 61 Africans in China (PMID: 25817373, 28017642, 28709622) and a Phase 2 clinical trial of 500 Africans in West Africa (PMID: 28017399). Total 156 subjects were inoculated according to the registration specification (8 x 10^10 VP/dose), 78 subjects were inoculated by 4 x 10^10 VP/dose and 355 subjects were inoculated by 1.6 x 10^11 VP/dose.
   - Two Phase 1 trials in China (120 and 61 healthy adults) and one Phase 2 trial in Sierra Leone (500 healthy adults) were completed. The investigators reported good safety (the most common adverse events (AEs) reported included fever and mild injection site pain and no vaccine-related serious adverse events (SAEs) recorded) and immunogenicity profile (the geometric mean titre (GMT) of anti GP antibody peaked around 28 days after vaccination with a responder rate of 96% (95% CI: 91%-99%) but the vaccine-elicted antibody responses decreased on 186 days with a responder rate of 76% (95% CI: 67%-83%)) of Ad5-EBOV (PMID: 28017399).
   - This vaccine is licensed to use under national reserves by NCPA, China in the event of Ebola outbreak or emergency to prevent the Ebola virus disease caused by the Ebola virus (Zaire).
   - EUAL application was submitted to WHO in July 2018 and is currently under review.

2 Ad26.ZEBOV & MVA-BN-Filo (2-dose regimen, VACS2150)
   - Ad26.ZEBOV is a monovalent replication-incompetent adenoaviral vector serotype 26 (Ad26) vaccine, which encodes the full-length GP of the EBOV Mayinga variant, and is produced in the human PER.C6 cell line. MVA-BN-Filo is a multivalent Modified Vaccinia Ankara (MVA)-BN vaccine, which encodes the EBOV Mayinga GP, the Sudan virus (SUDV) Gulu GP, the Marburg virus (MARV) Musoke GP, and the Tai Forest virus (TAFV, formerly known as Côte d'Ivoire ebolavirus) nucleoprotein (NP). It is manufactured in chicken embryonated eggs. 
   - The proposed target population of Ad26.ZEBOV, MVA-BN-Filo is liquid frozen. The vaccine regimen consists of an immunization with Ad26.ZEBOV (5 x 10^11 VP) as the first dose, followed by MVA-BN-Filo (1 x 10^10 Inf U) as a second dose 56 days later. The proposed target population includes adults and children aged ≥ 1 year.
   - Efficacy of the vaccine was demonstrated in an EBOV animal model where vaccination with the clinical dose provided 100% protection. Partial protection was observed when the doses of the vaccines were reduced. A shorter interval between doses as well as an inverted dose-order were also associated with lower protective efficacy rates.
   - Four Phase 1 trials were completed: 87 healthy adults in Europe (PMID: 27092831, 28019182), 164 healthy adults in the United States (NCT02926052) and 72 and 72 healthy adults in Africa (NCT02937426, NCT02937640). Three Phase 2 trials were completed: 423 healthy adults in Europe (NCT02116465), 200 healthy adults and 200 HIV-infected adults in the United States and Africa (NCT02958386), and 669 healthy adults, 142 HIV-infected adults, 132 healthy adolescents and 132 healthy children in African countries (NCT02564523). Two Phase 3 trials in the United States (144 and 329 healthy adults) (NCT02453267, NCT02543268) and 17 countries in the United States, Europe and Africa (NCT02681464) are ongoing. One additional trial was started in 2017, PREVAC (in partnership with NIAID, INSERM, LSHTM). 
   - Efficacy of Ad26.ZEBOV was demonstrated in two Phase 2 trials, one in Africa and another in the United States, with 164 healthy adults in the United States and 132 healthy adults in African countries (NCT02564523). Two Phase 1 trials in the United States (144 and 329 healthy adults) (NCT02453267, NCT02543268) were completed. One Phase 3 study in an Ebola-affected region (Sierra Leone) (445 healthy adults, 192 healthy adolescents and 193 healthy children) (PMID: 27821112) with the aim of establishing safety and immunogenicity in adults, followed by an expanded safety and immunogenicity study in adults and children was partially unblinded. In addition, one Phase 1/2/3 trial on healthy children and adults aged less than 71 years in multi-countries in the United States, Europe and Africa (NCT02681464) are ongoing. One additional trial was started in 2017, PREVAC (in partnership with NIAID, INSERM, LSHTM). 
   - To date more than 6,500 people have been enrolled. The available (partially) unblinded and analyzed clinical studies (4 Phase 1, 3 Phase 2, and 3 Phase 3) evaluating the 2-dose Ad26.ZEBOV, MVA-BN-Filo regimen in different intervals (14 to 84 days) in adults did not reveal any safety concerns. An unblinded safety review on pooled data from 1932 adults (of which 118 HIV+) revealed only mild to moderate AEs of short duration with no sequelae. Unblinded pediatric safety data are available for 649 children aged ≥1 year receiving active vaccination (253 adolescents 12-17 years old; 252 children 4-11 years old and 144 toddlers 1-3 years old) and 189 children receiving at least one dose of placebo/control. Overall, the safety profile complies with studies in a support of WHO EUAL was submitted to WHO in a rolling manner including CMC, non-clinical and clinical Phase 1/2/3 data in July/September 2016 and in subsequent annual updates.

3 ChAd3 (monovalent Zaire)
   - ChAd3 (monovalent Zaire) vaccine consists of ChAd3-EBOZ glycoprotein Zaire drug substance
   - ChAd3 (monovalent Zaire) has been administered to over 5000 adults and children
   - A Phase 1 trial was conducted in Mali (91 healthy adults) (NCT02287108). A Phase 1/1b trial has been completed in 143 adults in the U.S. (NCT02231866). A Phase Ib trial has been completed in 90 adults in Uganda (NCT02354404). The investigators reported acceptable safety profile of ChAd3 (monovalent Zaire).
   - A Phase 1/2 trial was conducted in 120 healthy adults in Switzerland (NCT0289027).
   - Three Phase 2 trials were conducted and completed in Cameroon, Nigeria, Senegal, Mali (3013 adults and 600 children), and Liberia (1500 adults) (NCT02485301; NCT02548078; NCT02344407). The investigators reported acceptable safety profile of ChAd3 (monovalent Zaire)
   - ChAd3 (monovalent Zaire) has been licensed to GSK and sublicensed to Sabin Vaccine Institute (press release).
No EUAL submission was initiated and no WHO prequalification has been obtained.

4 EpiVacEbola
- EpiVacEbola is a polyepitope vaccine, for the prevention of Ebola fever, based on peptide antigens conjugated to a carrier protein and adsorbed to an aluminium-containing adjuvant.
- The vaccine contributes to the development of protective immunity against the Zaire strain of Ebola virus following two subcutaneous administrations, spaced 21 to 28 days apart.
- A Phase 1 trial was conducted in Russian (60 healthy adults). A Phase 2-3 trial has been completed in 240 healthy adults in Russia.
- Two subcutaneous 100-μg doses (0.5 mL) given 28 days apart are well tolerated by adults aged 18-60. Low frequency of local and systemic reactions suggests good tolerance and low reactivity of the vaccine.
- Physical examinations as well as clinical and biochemical assays of blood and urine demonstrated no pathologic changes, which suggest a high safety profile of the vaccine. The vaccine induced Ebola-specific antibodies and virus-neutralizing antibodies in 78% and 71% of cases, respectively.

GamEvac-Combi and GamEvac-Lyo
- GamEvac-Combi and GamEvac-Lyo consist of live-attenuated recombinant vesicular stomatitis virus (VSV) and adenovirus serotype-5 (Ad5) expressing Ebola envelope GP of Zaire Ebola virus species (Makona).
- The formulation of GamEvac-Combi is liquid frozen but that of GamEvac-Lyo is lyophilized. The vaccine regimen consists of a priming immunization with VSV followed by a boosting immunization with Ad5 21 days later. The proposed dose of VSV and Ad5s are 0.5ml per dose targeting adults aged 18 to 55 years.
- One Phase I/II trial in Russia (84 healthy adults) (PMID: 28152326) and one Phase IV trial in Russia (60 healthy adults) (NCT02911415) were completed for GamEvac-Combi. The investigators reported good safety (the most common AE reported was injection site pain and no vaccine-related SAEs recorded) and immunogenicity profile (antigen-specific response was detected in 93% (half dose) and 100% (full dose) on 28 days after vaccination, and 100% on 42 days) of GamEvac-Combi (PMID: 28152326).
- There is one Phase 3 trial of GamEvac-Combi in Guinea, Africa (2000 healthy adults) (NCT03072030) and one Phase I/II trial of GamEvac-Lyo in Russia (220 healthy adults) (NCT03333538) ongoing.
- GamEvac-Combi has been licensed by the Ministry of Health of the Russian Federation for emergency use in the territory of the Russian Federation in December 2015 (registration number: LP-003390). The emergency license was based on Phase 1 and II clinical data of safety and immunogenicity (PMID: 28152326).
- No EUAL submission was initiated.
- Regarding WHO prequalification the company stated that a decision to submit will be made after completion of the Phase 3 GamEvac-Combi clinical trial in Guinea.

6 INO-4201 (DNA vaccine)
- DNA vaccine INO-4201 is a synthetic DNA plasmid construct expressing Ebola GP designed from consensus DNA sequences of Ebola outbreak strains from 1976-2006.
- The formulation of INO-4201 is liquid; two doses with proposed 2mg per dose intradermally administered in an interval of 4 weeks; targeting to adults aged over 18 years.
- One Phase 1 trial in the United States (75 healthy adults in the initial study) (NCT02464670) was completed. Final analysis (JID) showed acceptable safety profile (the most common AEs reported included injection site pain, redness, swelling and itching and no vaccine-related SAEs recorded). Humoral and cellular levels were similar to the rVSV vaccine (Tebas et al, JID 2019)
- No EUAL submission was initiated and no WHO prequalification has been obtained.

7 Nanoparticle recombinant Ebola GP vaccine
- The nanoparticle vaccine is based on purified recombinant full-length and unmodified 2014 Guinea EBOV GP trimers that self-assemble into distinct nanoparticle structures of approximately 30 to 40 nm diameter. The baculovirus/Sf9 insect cell system was used to clone and express the recombinant EBOV GP protein.
- A Phase 1, randomized, observer-blinded, dose-ranging study to evaluate the immunogenicity and safety of EBOV GP Vaccine with or without Matrix-M1 adjuvant in healthy subjects (≥ 18 to < 50 years of age) in Australia and completed through 1 year follow-up in April 2016 (NCT02570689). This study demonstrated the safety of single (Day 0) and repeat doses (Days 0 and 21) of the EBOV GP Vaccine (antigen doses of 6.5, 13, 25, or 50 μg) administered IM alone or in combination with Matrix-M1 adjuvant (50 μg) in healthy volunteers.
- No EUAL submission was initiated and no WHO prequalification has been obtained.

8 rSVAg-ZEBOV-GP
- rSVAg-ZEBOV-GP consists of a live, attenuated recombinant vesicular stomatitis virus-based vector expressing the envelope GP gene of Zaire Ebola virus (Kikwit 1995 strain).
- The formulation of rSVAg-ZEBOV-GP is liquid frozen; one dose with proposed 1ml per dose targeting adults. In the context of the ongoing outbreak in DRC, SAGE recommended to administer 0.5 mL per dose to increase the number of doses available.
- Eight Phase 1 trials in Europe and Africa (115 and 185 healthy adults and 40 healthy children aged 6 to 17 years) (PMID: 26248510, 29627147, 26831036, 28985293), Canada (40 healthy adults) (PMID: 28630456), and the United States (79 and 512 healthy adults) (PMID: 29830332, 28665931), one Phase 2 trial in Africa (1000 healthy adults) (NCT02344407), one Phase II/III trial in Russia (8673 healthy adults) (PMID: 27387995, 29788345), and two Phase 3 trials in Russia (5837 healthy adults) (PMID: 26215666, 26248676, 28017403), and in the United States, Canada and Europe (1197 healthy adults) (PMID: 28549145). The investigators reported acceptable safety profile (the most common AEs reported included injection site pain, headache, pyrexia, fatigue, myalgia and chills and few vaccine-related SAEs recorded) and 100% (95% CI: 69%-100%) efficacy (PMID: 28017403) of rSVAg-ZEBOV-GP in the ring-vaccination Guinea trial. The GMT were sustained with minimal change through 360 days after vaccination (PMID: 28606591).
- Two Phase 2 trials on populations aged from 13 to 65 years in Africa and Canada (NCT03031912) and older than 1 year in Africa (NCT02876328) are ongoing.
- Granted Breakthrough Therapy Designation from FPA and PRIME status from EMA since 2016.
- The developer submitted an application for licensure to the US FDA and the EMA; the expected timeline to obtain regulatory approval is early 2020. There is ongoing discussion with both regulatory authorities to shorten the timelines.
- EUAL application was submitted to WHO in 2015, and is currently under review.
- No WHO prequalification has been obtained.