Evaluation of NOVAVAX NVX-CoV2373 vaccine

1. **Description of the vaccine**
   The vaccine consists of trimers of the full-length spike protein, including the transmembrane domain, stabilized in the prefusion state. The trimers were formulated in 0.01% polysorbate 80, leading to nanoparticles that contain multi-trimer rosettes. The antigen is adjuvanted with saponin based Matrix-M. (Ref.d).
2. **Preclinical data**
   The vaccine induces anti-S antibodies, hACE2-receptor inhibiting antibodies and SARS-CoV-2 neutralizing antibodies in mice and baboons. In addition it induced CD4+ and CD8+ T cell responses. It protected mice against SARS-CoV-2 challenge (ref. e). The vaccine protected cynomolgus macaques against upper and lower respiratory infection, i.e. virus replication and against pulmonary disease after challenge with. SARS-CoV-2 (ref. f).
3. **Clinical data phase 1-2**
   Ref. g describes a study where 5 and 25 µg vaccine was tested with or without 50 µg adjuvant. Ages varied from 18 to 59. There were only mild adverse effects of short duration. The adjuvant significantly enhanced immune responses. A boost vaccination after 21 day enhanced the immune responses (antibodies, neutralizing antibodies and T cell responses). Both doses elicited, after two injections, neutralizing antibodies that exceed the mean responses in convalescent sera from COVID-19 sera with clinically significant illnesses. T cell responses were mostly of the Th1 phenotype.
   Q: ADE? A: Unlikely, in view of strong functional antibody responses and predominant Th1 response (ref. h).
4. **Planning phase 3 study**
   A phase 2/3 study is planned to start in September/October. The final vaccine will probably consist of two doses of 5 µg antigen and 50 µg adjuvant. However, 25 µg antigen is still under consideration. During the presentation on August 11 a planning (not in slide deck) was shown indicating that the phase 3 studies will run through halfway 2021. Higher ages will be part of the study.
5. **Test methods**
   a. Neutralization of wild type SARS-CoV-2 was carried out by the University of Maryland, details in supplementary material ref. g.
   b. ELISA units, details in supplementary material ref. g.
6. **Production**
   a. Process. The vaccine is produced by a baculovirus expression system in insect cells lines.
   b. Time scale and quantities. Production facilities are still under development in the Czech Republic https://ir.novavax.com/news-releases/news-release-details/novavax-expands-large-scale-global-manufacturing-capacity
   c. Availability. By the end of 2020 about 100 million doses of vaccine will be available, but since phase 3 trials will still ongoing by that time they can probably not be used. By 2021 a production capacity of 1 billion is expected.
7. **Formulation**
   Liquid, in vials ready to use, stable at 2°C to 8°C
8. **Information/literature**

a. Powerpoint presentation August 4 2020
b. Powerpoint presentation August 11 2020
c. Press release August 2020
d. Paper Bangaru et al. on description of vaccine
   https://www.biorxiv.org/content/10.1101/2020.08.06.234674v1
e. Tian et al. on preclinical data in mice and baboons.
   https://www.biorxiv.org/content/10.1101/2020.06.29.178509v1
f. Guebre-Xabier et al. on protection of cynomolgus macaques
   https://www.biorxiv.org/content/10.1101/2020.08.18.256578v1
g. Keech et al. on phase 1 trial.
   https://www.medrxiv.org/content/10.1101/2020.08.05.20168435v1
h. Q&A during webex meeting on August 11 2020