Scientific Presentation by Sanofi-GSK to Experts from EU27 Nominated by the Steering Board

9 September 2020

11:00-12:00 CET

Subject: Scientific Presentation on the Sanofi-GSK vaccine candidate

The Chair opened the meeting and welcomed all participants. [redacted] gave the presentation, indicating that their candidate subunit vaccine has the technology adapted from that developed for one of their seasonal influenza vaccines (technology acquired from Protein Sciences).

The antigen used is based on the SARS-CoV-2 Spike protein without transmembrane or intracytoplasmic domains. Mutated S protein (2 Prolines and furin cleavage site) to achieve better stabilisation and promote the formation of trimers. The antigen is administered with a squalene-containing adjuvant (GSK AS03 – used in GSK's Pandemrix Pandemic H1N1 vaccine). [redacted]

Preclinical studies have started and Sanofi presented the first data in mice and NHP.

Clinical Development:

- Phase 1/2: [redacted]. Dose levels tested: 5µg and 15µg. The AF03 and AS03 adjuvants were compared.
- Phase 3: [redacted], once intermediate data from phase 1/2 is available. Adults >18 years; age stratification (young and elderly volunteers). Global study, inclusions planned in several countries.

Production capacity, presentation and storage: purification of antigens from insect cells infected with a recombinant baculovirus encoding the SARS-CoV-2 S protein (a well-controlled procedure adapted from that developed for seasonal influenza vaccine). Sanofi-Pasteur has the necessary infrastructure to ensure very large-scale production. Discussions to extend production to other countries are ongoing. Phase II study in 11 sites in the US. Phase III (study size 30.000-35.000 subjects scheduled for December 2020, site selection not yet completed). The study is funded by BARDA operation Warp Speed. GSK is a very important collaborator and Sanofi has been working diligently with these colleagues. Cooperation with NIH for the NHP and clinical studies.

Q&A

The Chair thanked for the presentation and opened the Q&A session.

[redacted] asked about the requirements for needles and syringes for the application of the vaccine, specifically regarding the volume that needs to be administered. Sanofi replied

that the antigen and the adjuvant are both in ten-dose vials. One would need to draw up the adjuvant from the vial, inject it into the vial of antigen and draw out the formulation for 10 subjects – i.e. 0.5ml per vaccinee/ vaccination.

[redacted] enquired why Sanofi chose the AS03 adjuvant instead of AS04. Sanofi answered that they used AS03 in the pandemic influenza vaccine and [redacted] AS03 was the most beneficial to protect against infection and against severity of disease based on their latest assessment.

[redacted] enquired about the pre-existing prevalence of HLA-DQB haplotypes in the choice of Sanofi's trial sites. The narcolepsy post-Pandemrix strongly associated with genetic predisposition may raise the question of the safety of the product in trial sites with high prevalence of such genes. Sanofi replied that [redacted] have been addressing the safety of AS03 in response to the narcolepsy observation in the pandemic influenza vaccine produced by GSK in 2009. Sanofi pointed to the safety of the adjuvant formulation and that the bulk of the narcolepsy incidence related to genetic predisposition and the specific sequence of the pandemic influenza vaccine candidate. Safety protocols looking at sentinel cohorts are one way of investigating the safety profile of the adjuvant.

[redacted] enquired about the design of the immunogenicity studies and specifically their duration. [redacted] further remarked that convalescents' sera (studies) are not standardised and within a few months, subjects previously diagnosed with COVID-19 were re-infected. Sanofi agreed, convalescent sera studies are not standardised. They used [redacted] subjects for the broad panel – some mild, some moderate and some severe diseased. In terms of the protocol for the trial, the primary endpoint is modulation of disease severity. Sanofi will be looking at severe disease profiles of convalescent sera. The second endpoint is protection against disease acquisition. It is therefore important to look at asymptomatic, infected subjects and whether they would be able to block acquisition and transmission. The six month durability of the immune response is as important as efficacy. There is still considerable uncertainty as regards how durable the response is – Sanofi is still learning what the durable response is and what is the patient durability to natural exposure.

[redacted] asked about EMA submission timelines. Sanofi replied that meetings in view of obtaining and following up scientific advice have already taken place. The rolling submission is [redacted] and the last package of the rolling submission is planned in [redacted] when the last key tables from Phase III studies are expected.

[redacted] enquired whether adjuvant MF59 was envisaged at all. Sanofi replied that site selection played a key role. For their Phase I/II studies, Sanofi intends to enrol 18-55 year-olds and then 55 and older adults. [redacted] Furthermore, unlike MF59, AS03 has already been administered to tens of millions of human subjects already. [redacted].

[redacted] asked about plans to enrol patients with comorbidities (preferably a significant contingent) for the Phase III trials. Sanofi confirmed that for Phase III, 30.000 patients including seropositives and seronegatives are included, the primary endpoint being seronegatives. Elderly and patients with comorbidities are included in Phase III.

[redacted] enquired about storage conditions. Sanofi answered that short-term storage is possible at room temperature up to a week. Whilst there is some confirmed stability at 2-8° Celsius, further stability testing is underway and not confirmed yet.

[redacted] had a question about the location of the production facilities. [redacted]

[redacted] asked how many animals were used per group in NHP studies and whether challenge studies were performed. Sanofi replied that three different species were used, i.e. six animals per group in NHP, in cooperation with the VRC (Vaccine Research Centre) and a second study completed by Sanofi-Pasteur also used six NHP per group.

[redacted] enquired what age groups would be enrolled in Phase III clinical trials. Sanofi replied that Phase III CTs are mainly targeted at adults, with the paediatric part having a tailored plan. The priority is to focus first on high-risk patients and adults with comorbidities, in a balanced cohort group of adults aged 18 and older, with no age limit. Staging is also key. [redacted]

[redacted] remarked that the platform resembles the Flublok® one and enquired whether any potential interactions between the COVID-19 vaccine and the Flublok® vaccine were expected. Sanofi replied that in view of immunological interference, the vaccines should be administered a minimum of two weeks apart.

[redacted]

[redacted] enquired whether any data was expected on the onset of immunity. Sanofi replied that GMT titers were demonstrated post-administration after the first dose, with neutralisation titers picking up after the second dose. The data is strongly supporting a two-dose regimen administration, although certain levels of antibodies are elicited already after the first administration.

[redacted] asked about plans to study the compatibility of this vaccine candidate with common adult vaccines. Sanofi welcomed the question and replied that more time is needed to get a proper handle on the pandemic. [redacted]

[redacted] was interested in exploring what the VE% and the lower end of 95% CI Sanofi is planning to consider for the primary endpoint in Phase III. Sanofi replied that they are seeking to harmonise on endpoints and therefore consulting with other manufacturers on their endpoints.

[redacted] enquired whether animal challenge studies were done after vaccination and if so, whether there were any results in protection against infection versus disease. Sanofi replied that efficacy data on three studies [redacted] was expected at [redacted].

The Chair thanked Sanofi for the presentation and the participating experts for the good discussion and closed the meeting.

Participants

Sanofi-GSK:

[redacted] Public Affairs for Vaccines Europe, Sanofi Pasteur

[redacted] External Research And Development, Sanofi Pasteur

[redacted] Human Resources, Sanofi Pasteur

[redacted] Medical Health, Sanofi Pasteur

[redacted] Regulatory affairs, Sanofi Pasteur

Member States:

[redacted] (AT)

[redacted] (AT)

[redacted] (AT)

[redacted] (BE)

[redacted] (BE)

[redacted] (CZ)

[redacted] (DE)

[redacted] (DK)

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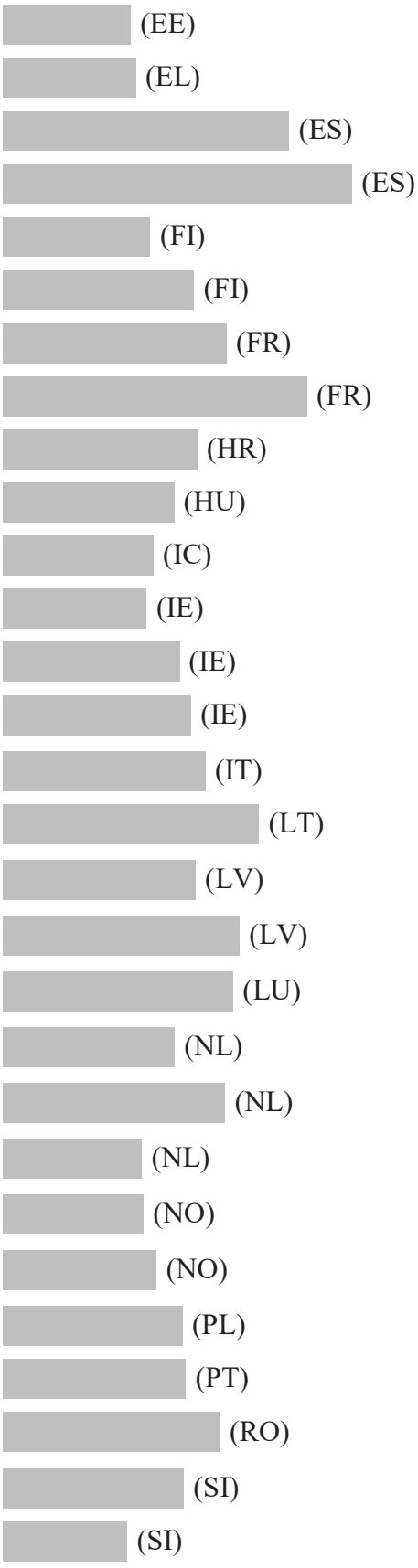
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[redacted] (SK)

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European Commission:

[redacted] (EC, Chair)

[redacted] (EC)

[redacted] (EC)

[redacted] (EC)

[redacted] (EC)

[redacted] (EC, Minutes)