Excellent ABNCoV2 safety data confirmed in Phase 3, while latest variant requires vaccine update

Copenhagen, Denmark, September 1, 2023 –The safety data for the ABNCoV2 phase 3 clinical trial from 4,205 individuals followed up for 2 months post vaccination showed that ABNCoV2 to be well-tolerated with no serious adverse events being reported. Additional safety data will be report for 6-month post vaccination at a later time point. Also, the primary endpoint was met by demonstrating non-inferiority to the market leader Pfizer/BioNtech Comirnaty® for the original SARS-CoV-2 variant (Wuhan index virus). However, ABNCoV2 and the comparator vaccine demonstrated a significantly reduced level of neutralizing antibodies against a circulating variant (Omicron XBB.1.5). This dictates that an update would be required to address the currently circulating and very distantly related Omicron variants, as is currently required for all marketed COVID-19 vaccines.

"It is a strong validation of the platform to have confirmation of the excellent safety profile of the cVLP based ABNCoV2 vaccine in more than 4000 persons. Together with meeting the study's primary endpoint of non-inferiority to market leader Pfizer/BioNtech Comirnaty® and the exceptional 12-month durability shown in Phase 2, this clearly demonstrates the strength of our cVLP vaccine platform to target infectious diseases. We aim to build on the significant governmental support as well as Ph3 validation of the cVLP platform and will continue to work with Bavarian Nordic on vaccines for pandemic preparedness ", said Wian de Jongh, AdaptVac's CEO.

As previously reported, two weeks post booster vaccination with non-adjuvanted ABNCoV2, the levels of neutralizing antibodies against the original SARS-CoV-2 variant (Wuhan index virus) were non-inferior to those stimulated in people vaccinated with Comirnaty® and this result met the primary objective of the Phase 3 study. The Wuhan variant is no longer the primary concern, as the virus has mutated creating new circulating variants, such as Omicron XBB.1.5. In a follow-up analysis, which looked at a more distant variant, the levels of neutralizing antibodies induced by ABNCoV2 were lower than those stimulated by the non-adapted Wuhan-based Comirnaty, and fewer people had detectable antibodies following ABNCoV2 (64%) versus Comirnaty (85%). The levels of neutralizing antibodies induced by both vaccines were much lower than against the Wuhan variant.

A 6-month follow-up analysis will be conducted to evaluate the durability of the antibody responses from booster vaccination with ABNCoV2 and Comirnaty. If the Phase 2 durability results for ABNCoV2 are confirmed in the Phase 3 study, it would confirm an advantage over the comparator vaccine.

"It is important to highlight that in the broader context of vaccines, generation of durable antibody responses remains a fundamental challenge, which has only been achieved by traditional live-attenuated viral vaccines and the HPV cVLP vaccine. Thus, the data generated by the ABNCOV2 vaccine may be the first proof of a vaccine platform technology with this unique ability" said Adam Bertelsen, AdaptVac's CSO.

While safety data from the Phase 3 study will continue to be collected for 6 months. Additionally, safety data from 4,205 individuals followed up for 2 months post vaccination showed ABNCoV2 to be well-tolerated with no serious adverse events being reported.

Requirements for ABNCoV2 update

The cVLP platform is infinitely adaptable to novel antigens and variants, with the speed dictated only by the production of the disease specific antigen, as the cVLP is unchanged and can be stockpiled. The current position of the US regulator (FDA) is to request variant-specific COVID vaccines that will likely have to be adapted each year like flu vaccines. The breath of protection afforded by a ABNCoV2 update would need to be investigated to understand if the broad protection demonstrated in Phase 2 would support less frequent updates. It would, however, be challenging to update a protein-based vaccine yearly within the seasonal timeframe of approximately 3 months currently required by the FDA. This challenge will be clarified by the progress of

approved protein based COVID-19 vaccines, such as those of Novavax in the US, and Hipra in EU. However, Bavarian has stated that they will no longer pursue ABNCoV2 commercially.

"*Our technology has succeeded in demonstrating pandemic preparedness regarding production and safety as well as durability and level of immunity, that is remarkable for a novel technology within such a short time span. The best in class cross neutralization against early variants of concern demonstrated in phase 2, suggests that ABNCoV2 potentially does not need to be updated with the same frequency as competing technologies. The regulatory challenge may be to explain the potential for technologies like ours, which may require less frequent updates, while providing longer-term protection*", said Prof. Morten Nielsen, Chairman of the board.

Pandemic preparedness
Despite the significant decrease in neutralization against the latest distant and less virulent variant, the data generated in the overall development of ABNCoV2 demonstrating broad and exceptionally long-lived neutralization supports the use of the cVLP platform in future pandemics. Bavarian Nordic will discuss with the authorities how best to leverage the learnings from this development program.

ABNCoV2 Phase 3 validates capsid Virus-Like Particle (cVLP) vaccine platform
The cVLP technology was developed to be a highly efficacious, cost-effective, heat stable and versatile to enable production and distribution also in under-developed regions globally. In addition to the COVID-19 vaccine, AdaptVac has recently initiated a cVLP displayed malaria vaccine development program as part of a €10M EU funded consortium.

Our EU funded COVID-19 PhI study demonstrated exceptionally high neutralizing antibody levels without the need for adjuvant in a primary vaccine setting. The only protein-based vaccine to achieve protective levels without the need for an adjuvant. It was also demonstrated that these levels could be further increased by addition of an adjuvant. This demonstrates the strength of the platform and our ability to additionally boost the immune response if ever required for protection against a future disease outbreak.

The overall COVID-19 Phase 2 results confirmed the ability of non-adjuvanted ABNCoV2 to boost neutralizing antibodies to levels reported to be highly efficacious against SARS-CoV-2, both when used for primary vaccination and when used as a booster in subjects previously vaccinated with mRNA- or Adeno-based vaccines. A similar fold increase was observed for all SARS-CoV-2 variants of concern tested (Wuhan, Alpha, Beta, Delta and Omicron) following the booster vaccination with ABNCoV2. While the neutralizing antibody titers against Omicron were the lowest when compared to all other variants of concern tested, they were boosted to levels reported to be associated with a high level of protection (>90%). The vaccine was generally well-tolerated, with no related serious adverse events reported and no relevant difference in the safety profile between subjects receiving either the low (50 µg) or high dose (100 µg) of ABNCoV2.

The Phase 3 study demonstrated non-inferiority of ABNCoV2 to Comirnaty® measured by neutralizing antibodies against the SARS-CoV-2 virus (Wuhan wild type). The study enrolled a total of 4,205 adults who either previously completed primary vaccination or had already received one booster dose of a licensed COVID-19 vaccine. The active, controlled part enrolled 622 participants who were randomized to receive either a single 100 µg dose of ABNCoV2, or a single 30 µg adult booster dose of Comirnaty. The second part of the study evaluated the safety and tolerability of a single 100 µg dose of ABNCoV2 in 3,583 participants.

The Phase 3 development of ABNCoV2 was partly funded through an agreement with the Danish State.

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About the PREVENT-nCoV consortium

The consortium is funded by an EU Horizon 2020 grant to develop a COVID-19 vaccine (Grant agreement 101003608 https://cordis.europa.eu/project/id/101003608). Further the vaccine development at University of Copenhagen is supported by the Carlsberg Foundation, the Danish research councils and Gudbjørg og Ejnar Honorés Fond. The consortium members are world-leading experts in their respective fields, covering all relevant areas of viral research and vaccine development required for rapid clinical development of a COVID-19 vaccine. This includes pre-clinical and clinically validated experience from working with similar Coronaviruses such as MERS and SARS, ExpreS^{2}ion Biotechnologies' *Drosophila* S2 insect cell expression system, and AdaptVac's capsid virus-like particle (cVLP) technology. In addition to ExpreS^{2}ion and AdaptVac, the consortium members are Leiden University Medical Center (LUMC), Institute for Tropical Medicine (ITM) at University of Tübingen, The Department of Immunology and Microbiology (ISIM) at University of Copenhagen, the Laboratory of Virology at Wageningen University, and Radboud University Medical Center. Through the Carlsberg foundation grant the Prevent-nCoV consortium works closely together with Department of Biomedicine at Aarhus University.

About AdaptVac

AdaptVac is a joint venture between ExpreS^{2}ion Biotechnologies and NextGen Vaccines, owned by the inventors of the novel proprietary and ground-breaking viral capsid-like virus particle (cVLP) platform technology spun out from the University of Copenhagen. The Company aims to accelerate the development of highly efficient therapeutic and prophylactic vaccines within high value segments of oncology, infectious diseases, and immunological disorders. Please visit: www.AdaptVac.com

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