

Valneva Reports Positive Phase 1/2 Data for Its Inactivated, Adjuvanted COVID-19 Vaccine Candidate, VLA2001

- VLA2001 was well tolerated with no safety concerns identified
- In the high dose group :
 - IgG seroconversion rate of 100%
 - Neutralizing antibody titres at or above levels generally seen in convalescent sera.

Saint-Herblain (France), April 6, 2021 – Valneva SE, a specialty vaccine company focused on the development and commercialization of prophylactic vaccines for infectious diseases with significant unmet medical need, today announced positive data for Part A of the Phase 1/2 clinical trial of its inactivated, adjuvanted COVID-19 vaccine candidate, VLA2001. Based on this data, the Company plans to commence a Phase 3 clinical trial by the end of April 2021, subject to regulatory approval.

In study VLA2001-201, three dose levels of VLA2001 (low, medium, high), based on a schedule of two doses with vaccinations three weeks apart, were evaluated in 153 healthy adults aged 18 to 55 years.

VLA2001 was generally safe and well tolerated across all dose groups tested, with no safety concerns identified by an independent Data Safety Monitoring Board. There were no statistically significant differences between dose groups and no differences between first and second vaccinations in terms of reactogenicity. The majority of Adverse Events (AEs) were mild or moderate and only two subjects reported severe solicited AEs (headache and fatigue). All solicited AEs were transient. Only 17.6% of unsolicited AEs up to day 36 were considered related to the vaccine and no severe unsolicited AEs were reported. No serious related AEs were reported.

VLA2001 was highly immunogenic with more than 90% of all study participants developing significant levels of antibodies to the SARS-CoV-2 virus spike protein across all dose groups tested. Seroconversion Rates (SCR) for S-protein binding IgG antibodies were 89.8% in the medium dose and 100% in the high dose group. Two weeks after completion of the two dose schedule, Geometric Mean Fold Rise (GMFR) from baseline were 26 in the medium dose and 86 in the high dose group.

Of note, the IgG antibody response was highly correlated with neutralization titres in a micro-neutralization assay (MNA50) ($r=0.79$, $p<0.001$).

VLA2001 induced a dose dependent response with statistically significant higher Geometric Mean Titres (GMTs) for both IgG and neutralizing antibodies in the high dose group compared to the low and medium dose groups. In the high dose group, the GMT of neutralizing antibody titres measured two weeks after completion of the two-dose schedule was at or above levels for a panel of convalescent sera (GMT 530.4 (95% CI: 421.49, 667.52)).



With a GMT ratio of vaccine vs. convalescent sera ≥ 1 , vaccine efficacy has been reported above 80% for other vaccines¹.

VLA2001 induced broad T-cell responses across participants with antigen-specific IFN-gamma producing T-cells against the S-protein, M and N protein detected in 75.6 %, 35.6% and 48.9% of study participants, respectively.

Thomas Lingelbach, Chief Executive Officer of Valneva, said: *“We are extremely pleased with these results which take us a step closer to providing an inactivated vaccine to help the global fight against COVID-19. The world needs multiple vaccines as well as booster options. Given the potential advantages often associated with inactivated whole virus vaccines, we believe that VLA2001 has an important role to play. This includes potential modifications to the vaccine to address variants, using our existing manufacturing process. I want to thank everyone involved in the ongoing work. We could not have achieved this milestone without them.”*

Health and Social Care Secretary, Matt Hancock said: *“The U.K. government has funded these clinical trials and it is fantastic to see Valneva’s vaccine produces a strong immune response. This vaccine will be made onshore in Livingston in Scotland, giving another boost to British life science, and if approved will play an important role in protecting our communities. I look forward to seeing the results of the upcoming phase 3 trial.”*

Vaccines Minister Nadhim Zahawi said: *“These results are very promising and provide renewed hope that a vaccine using a whole inactivated virus might provide strong protection against variants. If the results from the phase 3 clinical trials are positive and the vaccine meets the robust standards of safety, quality and effectiveness of our medicines regulator, the MHRA, this will be another powerful weapon in our arsenal to beat this pandemic. The government has funded the clinical trials for this promising vaccine and, if approved, it will be manufactured in Scotland, boosting the UK’s ability to become more self-sufficient in the future.”*

Clive Dix, Chair of the Vaccines Taskforce said: *“These are great results from Valneva, particularly around the antibody and cellular responses generated and low numbers of adverse events, as these indicate good levels of immune responses among the participants to date. The findings of 100% levels of immunogenicity against the viral spike protein in the high-dose group is also encouraging. Inactivated virus vaccines are proven technologies that are often able to induce wide-ranging immune responses, and these promising data indicate that VLA2001 may continue this trend. We are hopeful of seeing good results from the upcoming Phase 3 trials, and look forward to continuing working closely with Valneva on their vaccine.”*

Based on the data assessed, the Company has decided to advance the high dose into the Phase 3 clinical trial. Other trials, including booster trials, involving antigen sparing doses will also be evaluated.

The Company continues to work closely with the UK Government to review plans including potential variant vaccine development and supply as well as meeting the UK’s booster campaign requirements acknowledging the ongoing vaccine roll out in the UK. As a result, Valneva now believes that the timeline for delivery of 60 million doses of vaccine to the UK Government will extend into the first quarter

¹Earle et al. MedRxiv, March 2021, <https://doi.org/10.1101/2021.03.17.20200246>; Khoury et al. MedRxiv, March 2021, <https://doi.org/10.1101/2021.03.09.21252641>)



of 2022. Based on the Phase 1/2 data, the Company is also investigating antigen sparing options for booster strategies. Overall capacity and delivery schedule will be dependent on the UK's vaccine requirements and production related factors.

Valneva plans to initiate a pivotal, comparative immunogenicity Phase 3 clinical trial by the end of April 2021 with the aim of making a regulatory licensure submission to the Medicines and Healthcare products Regulatory Agency (MHRA) in the United Kingdom in the autumn 2021. Discussions with other regulatory bodies are ongoing.

In parallel, Valneva has initiated the development of new variant based viral seed banks.

About the Novel Coronavirus SARS-CoV-2 and COVID-19 Disease

SARS-CoV-2 is a new coronavirus identified in late 2019 and belongs to a family of enveloped RNA viruses that include MERS and SARS, both of which caused serious human infections of the respiratory system. The virus, which causes a disease named COVID-19, has never before been found in humans. Since this outbreak was first reported, the virus has caused millions of deaths globally². It has been declared a pandemic by the World Health Organization (WHO).

About VLA2001-201

VLA2001-201 is a randomized, dose-finding study to evaluate the safety, tolerability and immunogenicity of the inactivated, adjuvanted SARS-CoV-2 virus vaccine candidate VLA2001, against COVID-19 in healthy subjects. VLA2001-201 is the first-in-human Phase 1/2 study evaluating three dose levels of VLA2001 (low, medium, high) for safety, tolerability and immunogenicity in a two-dose schedule with intra muscular vaccinations three weeks apart. Overall, 153 healthy young adults aged 18 to 55 years have been recruited in the study. VLA2001-201 is being conducted in two parts: Part A (Day 1 to Day 36) and Part B (Day 37 to Day 208).

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About VLA2001

VLA2001 is currently the only whole virus, inactivated, adjuvanted vaccine candidate in clinical trials against COVID-19 in Europe. It is intended for active immunization of at-risk populations to prevent carriage and symptomatic infection with COVID-19 during the ongoing pandemic and potentially later for routine vaccination including addressing new variants. VLA2001 may also be suited for boosting, as repeat booster vaccinations have been shown to work well with whole virus inactivated vaccines. VLA2001 is produced on Valneva's established Vero-cell platform, leveraging the manufacturing technology for Valneva's licensed Japanese encephalitis vaccine, IXIARO[®]. VLA2001 consists of inactivated whole virus particles of SARS-CoV-2 with high S-protein density, in combination with two adjuvants, alum and CpG 1018. This adjuvant combination has consistently induced higher antibody levels in preclinical experiments than alum-only formulations and shown a shift of the immune response towards Th1. CpG 1018 adjuvant, supplied by Dynavax Technologies Corporation (Nasdaq: DVAX), is a component of the US FDA- and EMA-approved HEPLISAV-B[®] vaccine. The manufacturing process for VLA2001, which has already been upscaled to final industrial scale, includes inactivation with BPL

² <https://www.worldometers.info/coronavirus/>





to preserve the native structure of the S-protein. VLA2001 is expected to conform with standard cold chain requirements (2 degrees to 8 degrees Celsius).

About Valneva SE

Valneva is a specialty vaccine company focused on the development and commercialization of prophylactic vaccines for infectious diseases with significant unmet medical need. We take a highly specialized and targeted approach to vaccine development, beginning with the identification of deadly and debilitating infectious diseases that lack a prophylactic vaccine solution and for which there are limited therapeutic treatment options. We then apply our deep understanding of vaccine science, including our expertise across multiple vaccine modalities, as well as our established vaccine development capabilities, to develop prophylactic vaccines to address these diseases. We have leveraged our expertise and capabilities both to successfully commercialize two vaccines and to rapidly advance a broad range of vaccine candidates into and through the clinic, including candidates against Lyme disease, the chikungunya virus and COVID-19.

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Valneva Forward-Looking Statements

This press release contains certain forward-looking statements relating to the business of Valneva, including with respect to the progress, timing, results and completion of research, development and clinical trials for product candidates, timing and volume expectations with respect to the manufacture of our product candidates; the ability to market, commercialize and achieve market acceptance for product candidates, the ability to protect intellectual property and operate the business without infringing on the intellectual property rights of others, estimates for future performance and estimates regarding anticipated operating losses, future revenues, capital requirements and needs for additional financing. In addition, even if the actual results or development of Valneva are consistent with the forward-looking statements contained in this press release, those results or developments of Valneva may not be sustained in the future. In some cases, you can identify forward-looking statements by words such as "could," "should," "may," "expects," "anticipates," "believes," "intends," "estimates," "aims," "targets," or similar words. These forward-looking statements are based largely on the current expectations of Valneva as of the date of this press release and are subject to a number of known and unknown risks and uncertainties and other factors that may cause actual results, performance or achievements to be materially different from any future results, performance or achievement expressed or implied by these forward-looking statements. In particular, the expectations of Valneva could be affected by, among other things, uncertainties involved in the development and manufacture of vaccines, unexpected clinical trial results, unexpected regulatory actions or delays, competition in general, currency fluctuations, the impact of the global and European credit crisis, and the ability to obtain or maintain patent or other proprietary intellectual property protection. Success in preclinical studies or earlier clinical trials may not be indicative of results in future clinical trials. In light of these risks and uncertainties, there can be no assurance that the forward-looking statements made during this presentation will in fact be realized. Valneva is providing the information in these materials as of this press release, and disclaim any intention or obligation to publicly update or revise any forward-looking statements, whether as a result of new information, future events, or otherwise.