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Valneva Reports Positive Pivotal Phase 3 Immunogenicity Data in Adolescents for its Single-Shot Chikungunya Vaccine Candidate

Saint-Herblain (France), November 13, 2023 – Valneva SE (Nasdaq: VALN; Euronext Paris: VLA), a specialty vaccine company, today reported positive pivotal Phase 3 immunogenicity data in adolescents for its single-dose chikungunya virus (CHIKV) vaccine candidate VLA1553. These results complement the initial Phase 3 safety data the Company reported for the trial in August 2023[1].

Funded by the Coalition for Epidemic Preparedness Innovations (CEPI), with support from the European Union's Horizon 2020 program, and conducted in collaboration with Instituto Butantan, the VLA1553-321 adolescent trial is intended to support label extension in this age group following recent regulatory approval in adults from the Food and Drug Administration (FDA) in the United States (U.S)[2]. The trial is also expected to support licensure of the vaccine in Brazil, which would be the first potential approval for use in endemic populations. Additionally, the trial is expected to support regulatory approval in Europe and the initial safety data were included in the submission to the European Medicines Agency (EMA) in October 2023[3]. VLA1553-321 represents the first clinical trial Valneva is conducting in an endemic area and with individuals previously infected with CHIKV.

The pivotal immunogenicity data showed that a single-dose vaccination with VLA1553 induced a robust immune response in adolescents aged 12 to <18 years[4], confirming the excellent immunogenicity previously observed in adults[5].

Trial VLA1553-321 met its primary endpoint. VLA1553 induced levels of protective antibody titers[6] in 98.8% of participants 28 days after a single vaccination (seroresponse rate[7] of 98.8% (95% CI: 96.5, 99.8; 247 of 250 baseline seronegative participants from the per-protocol population), significantly exceeding the FDA's requirement for study success of the lower bound of the 95%CI for SRR >70%).

The vaccine was highly immunogenic with a Geometric Mean Titer (GMT) of 3890 in baseline seronegative participants. Neutralizing antibody GMTs at Day 29 in baseline seronegative participants were similar to GMTs observed in seropositive participants at baseline, indicating that VLA1553 induces levels of antibodies comparable to those in individuals with a history of CHIKV wild type infection.

As reported previously, VLA1553 administered as a single-dose was generally well tolerated in adolescents aged 12 to <18 years, irrespective of previous CHIKV infection and showed a similar safety profile as reported in adults[8].

754 individuals were vaccinated in trial VLA1553-321, and the present analysis includes data up to Day 29 (primary endpoint). An independent Data Safety Monitoring Board has continuously evaluated safety

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[1] *Valneva Reports Positive Initial Phase 3 Safety Data in Adolescents for its Single-Shot Chikungunya Vaccine Candidate - Valneva*
[2] *Valneva Announces U.S. FDA Approval of World's First Chikungunya Vaccine, IXCHIQ® - Valneva*
[3] *Valneva Submits Chikungunya Vaccine Marketing Application to EMA and Announces CHMP Accelerated Assessment*
[4] Valneva Reports Positive Initial Phase 3 Safety Data in Adolescents for its Single-Shot Chikungunya Vaccine Candidate - Valneva
[5] *Lancet Paper: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(23)00641-4/fulltext*
[6] µPRNT50/ seroresponse reasonably likely to predict protection as per the accelerated approval pathway
[7] *Defined as µPRNT50 antibody titer ≥ 150 agreed with the FDA as surrogate of protection to support accelerated approval*
[8] *Lancet Paper: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(23)00641-4/fulltext*

data during the trial and has not identified any safety concerns. The majority of solicited adverse events observed following VLA1553 administration were mild or moderate and resolved within three days. Importantly, the initial data suggest a favorable safety profile in seropositive participants, confirming the observations following re-vaccination of individuals in Phase 1 trial VLA1553-101[9].

Juan Carlos Jaramillo M.D., Chief Medical Officer of Valneva, said, "These new data in a younger population and in individuals previously infected with the chikungunya virus confirm the robust immunity and safety profile we previously observed in adults and the elderly. Given the significant threat that chikungunya poses to individuals living in or traveling to endemic areas, it is crucial to make the vaccine accessible to all age groups. By doing so, we can enhance the protection and reduce the impact of this debilitating disease."

The recent U.S. FDA approval[10] was based on final pivotal Phase 3 data in 4,115 adults aged 18 years and above reported in March 2022[11], and the *Lancet* subsequently published these results in June 2023[12]. Final lot-to-lot consistency results were published in May 2022[13] and positive twelve-month persistence data in December 2022[14].

About Phase 3 study VLA1553-321

VLA1553-321 is a prospective, double-blinded, multicenter, randomized, placebo-controlled pivotal Phase 3 trial conducted in 754 adolescents aged 12 to 17 years old in Brazil. The VLA1553-321 clinical trial was initiated in January 2022 and Valneva reported enrollment and vaccination completion in February 2023. VLA1553 or placebo was administered as a single intramuscular immunization to participants who were randomized into two study groups at a 2:1 ratio. The primary objective is to evaluate the immunogenicity and safety of the adult dose of VLA1553 28 days following a single vaccination. Secondary objectives of the trial include assessment of safety and immunogenicity up to twelve months following a single vaccination with VLA1553. Additional information, including a detailed description of the study design, eligibility criteria and investigator sites, is available at ClinicalTrials.gov (Identifier: NCT04650399).

About Chikungunya

Chikungunya is a mosquito-borne viral disease caused by the chikungunya virus (CHIKV), a Togaviridae virus, transmitted by Aedes mosquitoes. Infection leads to symptomatic disease in up to 97% of humans after four to seven days following the mosquito bite. While mortality with CHIKV is low, morbidity is high, and the global market for vaccines against chikungunya is estimated to exceed $500 million annually by 2032[15]. Clinical symptoms include acute onset of fever, debilitating joint and muscle pain, headache, nausea, rash and chronic arthralgia. Chikungunya virus often causes sudden large outbreaks with high attack rates, affecting one-third to three-quarters of the population in areas where the virus is circulating. The high-risk areas of infection for travelers are places where chikungunya virus-carrying mosquitos are endemic, including the Americas, parts of Africa, and Southeast Asia, and the

[9] *Chikungunya vaccine: a single shot for a long protection? - The Lancet Infectious Diseases*
[10] *Valneva Announces U.S. FDA Approval of World's First Chikungunya Vaccine, IXCHIQ® - Valneva*
[11] *Valneva Successfully Completes Pivotal Phase 3 Trial of Single-Shot Chikungunya Vaccine Candidate*
[12] *Valneva Announces Publication of its Chikungunya Vaccine Candidate Phase 3 Data in The Lancet*
[13] *Valneva Successfully Completes Lot-to-Lot Consistency Trial for its Single-Shot Chikungunya Vaccine Candidate*
[14] *Valneva Reports Positive 12-Month Antibody Persistence Data for Single-Shot Chikungunya Vaccine Candidate*
[15] *VacZine Analytics Chikungunya virus vaccines Global demand analysis. February 2020*

virus has spread to more than 110 countries[16]. As of July 2022, more than three million cases have been reported in the Americas[17] and the economic impact is considered to be significant. The medical and economic burden is expected to grow as the CHIKV primary mosquito vectors continue to spread geographically. There are no preventive vaccines or effective treatments available and, as such, chikungunya is considered to be a major public health threat.

About VLA1553

VLA1553 is a live-attenuated, single dose investigational vaccine candidate targeting the chikungunya virus, which has spread to over 110 countries[18]. It has been designed by deleting a part of the chikungunya virus genome.

Valneva reported final data from the pivotal Phase 3 trial of VLA1553 in March 2022[19], final lot-to-lot consistency results in May 2022[20] and positive twelve-month persistence data in December 2022[21].

To make VLA1553 more accessible to Low- and Middle-Income Countries (LMIC), Valneva and Instituto Butantan in Brazil signed an agreement in January 2021 for the development, manufacturing and marketing of VLA1553[22]. The collaboration falls within the framework of the agreement signed between CEPI and Valneva in July 2019[23], which provides funding of up to $24.6 million with support from the European Union's Horizon 2020 program.

VLA1553 received FDA approval in November 2023 under the brand name IXCHIQ® and is indicated for the prevention of disease caused by CHIKV in individuals 18 years of age and older who are at increased risk of exposure to CHIKV. VLA1553 was also granted PRIority MEdicine (PRIME) designation and accelerated assessment by the European Medicines Agency (EMA) in 2020 and 2023 respectively.

The Company intends to commercialize this vaccine, leveraging its existing manufacturing and commercial operations.

About Valneva SE

We are a specialty vaccine company that develops, manufactures, and commercializes prophylactic vaccines for infectious diseases addressing unmet medical needs. We take a highly specialized and targeted approach, applying our deep expertise across multiple vaccine modalities, focused on providing either first-, best- or only-in-class vaccine solutions.

We have a strong track record, having advanced multiple vaccines from early R&D to approvals, and currently market two proprietary travel vaccines as well as certain third-party vaccines leveraging our established commercial infrastructure.

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[16] *https://www.who.int/news-room/fact-sheets/detail/chikungunya*
[17] *PAHO/WHO data: Number of reported cases of chikungunya fever in the Americas (Cumulative Cases 2018-2022 and Cases per year 2013-2017). https://www.paho.org/data/index.php/en/mnu-topics/chikv-en/550-chikv-weekly-en.html. Last accessed 25 Jul 2022.*
[18] *https://www.who.int/news-room/fact-sheets/detail/chikungunya*
[19] *Valneva Successfully Completes Pivotal Phase 3 Trial of Single-Shot Chikungunya Vaccine Candidate*
[20] *Valneva Successfully Completes Lot-to-Lot Consistency Trial for its Single-Shot Chikungunya Vaccine Candidate*
[21] *Valneva Reports Positive 12-Month Antibody Persistence Data for Single-Shot Chikungunya Vaccine Candidate - Valneva*
[22] *Valneva and Instituto Butantan Sign Final Agreement on Single-Shot Chikungunya Vaccine for Low and Middle Income Countries*
[23] *CEPI awards up to $23.4 million to Valneva for late-stage development of a single-dose Chikungunya vaccine*

Revenues from our growing commercial business help fuel the continued advancement of our vaccine pipeline. This includes the only Lyme disease vaccine candidate in advanced clinical development, which is partnered with Pfizer, potentially the world's first vaccine against the chikungunya virus, as well as vaccine candidates against the Zika virus and other global public health threats.

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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, to regulatory approval of product candidates and review of existing products. 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 and delays 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.