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Valneva Initiates Phase 3 Clinical Lot Consistency Study for its Single-Shot Chikungunya Vaccine Candidate

Saint-Herblain (France), February 22, 2021 –Valneva SE ("Valneva" or "the Company"), a specialty vaccine company focused on prevention of infectious diseases with significant unmet medical need, today announced that it has initiated the clinical lot-to-lot consistency Phase 3 study for its single-shot chikungunya vaccine candidate, VLA1553.

This study will run in parallel to the ongoing, pivotal Phase 3 study, VLA1553-301, which includes the determination of seroprotection based on an immunological surrogate[1].

The objective of this study is to show manufacturing consistency of the vaccine by demonstrating that three consecutively manufactured lots elicit equivalent immune responses measured by neutralizing antibody titers on Day 29 after vaccination. Study volunteers will be followed for a total of six months.

Juan Carlos Jaramillo, M.D., Chief Medical Officer of Valneva, commented, "This study initiation signifies another important step in the development of VLA1553 towards licensure. The chikungunya virus continues to represent a major public health threat, and we are working as fast as we can to bring a preventive solution to those who need it most. We would like to thank our employees, partners and study participants for making this trial possible despite the ongoing COVID-19 pandemic."

VLA1553 is the only chikungunya vaccine candidate in Phase 3 clinical trials. The sponsor of the first chikungunya vaccine Biologics License Application (BLA) to be approved in the U.S. will be eligible to receive a Priority Review Voucher (PRV)[2].

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 72-92% of humans after 4 to 7 days following the mosquito bite. While mortality with CHIKV is low, morbidity is high. Clinical symptoms include acute onset of fever, debilitating joint and muscle pain, headache, nausea and rash. 4.1%-78.6% of infections develop into chronic arthralgia (> 3 months). 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 highest risk areas of infection for travelers are places where chikungunya virus-carrying mosquitos are endemic, including the Americas, parts of Africa, and Southeast Asia. As of September 2020, there have been more than 3 million reported cases in the Americas[3] and the economic impact is considered to be significant (e.g. Colombia outbreak 2014: $73.6

[1] *Valneva Initiates Phase 3 Clinical Study for its Chikungunya Vaccine Candidate VLA1553*
[2] *https://priorityreviewvoucher.org/*
[3] *PAHO/WHO data: Number of reported cases of chikungunya fever in the Americas. https://www.paho.org/data/index.php/en/mnu-topics/chikv-en/550-chikv-weekly-en.html. Last accessed 13 Oct 2020.*

million[4]). The medical and economic burden is expected to grow as the CHIKV primary mosquito vectors continue to further 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 vaccine candidate for protection against chikungunya disease and currently tested in clinical Phase 3. VLA1553 has been designed by deleting a part of the chikungunya virus genome. As a live-attenuated vaccine, VLA1553 is particularly well suited to target long-lasting protection.

Valneva is the first company to advance a chikungunya vaccine candidate into Phase 3. The sponsor of the first chikungunya vaccine Biologics License Application (BLA) to be approved in the U.S. will be eligible to receive a Priority Review Voucher (PRV) [5].

VLA1553 would expand Valneva's existing travel vaccine portfolio and as such, Valneva intends to commercialize this vaccine, if approved, leveraging its existing manufacturing and commercial operations. The global market for vaccines against chikungunya is estimated to exceed $500 million annually by 2032[6].

VLA1553 Phase 1 data in 120 volunteers were published in *The Lancet Infectious Diseases*[7]. The vaccine was well tolerated at the dose level selected for Phase 3. No vaccine-related serious adverse events were reported during 12 months of follow-up. Neutralizing antibodies were developed in 100% of volunteers within 14 days after a single vaccination and were maintained up to one year. Based on these encouraging results, Phase 3 testing was initiated in September 2020. The program was granted Fast Track designation by the U.S. Food and Drug Administration (FDA) in December 2018[8] and PRIME designation by the European Medicines Agency (EMA) in October 2020[9].

To make VLA1553 also accessible to Low and Middle Income Countries (LMIC), Valneva and Instituto Butantan in Brazil signed an agreement for the development, manufacturing and marketing of VLA1553. The collaboration falls within the framework of the funding agreement between Valneva and the Coalition for Epidemic Preparedness Innovations (CEPI) in July 2019, which provides for funding of up to $23.4 million.

About Phase 3 study VLA1553-302

VLA1553-302 clinical lot-to-lot consistency Phase 3 study is a prospective, multicenter, randomized, pivotal Phase 3 study comprising approximately 400 participants aged 18 to 45 years. Lyophilized VLA1553 will be administered as a single intramuscular immunization. Equivalence of immune responses will be determined based on neutralizing antibody titers. The primary objective of the study is to evaluate a pair-wise comparison of the 95% CI on the ratio of GMTs on Day 29 after vaccination in the three vaccine lots. The two-sided 95% CI on the GMT ratio should be within 0.67 and 1.5.

Study volunteers will be followed for a total of six months and overall, the study is expected to last approximately eight months. Additional information, including a detailed description of the study design, eligibility criteria and investigator sites, will be published on ClinicalTrials.gov.

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[4] *Cardona-Ospina et al. 2015, Trans R Soc Trip Med Hyg 109:793-802.*
[5] *https://priorityreviewvoucher.org/*
[6] *VacZine Analytics Chikungunya virus vaccines Global demand analysis. February 2020*
[7] *Wressnigg et al. 2020, Lancet ID;20(10):1193-1203.*
[8] *Valneva PR: Valneva Awarded FDA Fast Track Designation for Chikungunya vaccine candidate*
[9] *Valneva's Chikungunya Vaccine Candidate Awarded EMA Prime Designation*

About Valneva SE

Valneva is a specialty vaccine company focused on prevention of infectious diseases with significant unmet medical need. The Company has several vaccines in development including unique vaccines against Lyme disease, COVID-19 and chikungunya. Valneva's portfolio includes two commercial vaccines for travelers: IXIARO®/JESPECT® indicated for the prevention of Japanese encephalitis and DUKORAL® indicated for the prevention of cholera and, in some countries, prevention of diarrhea caused by ETEC. Valneva has operations in Austria, Sweden, the United Kingdom, France, Canada and the U.S. with over 500 employees.

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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 and completion of research, development and clinical trials for product candidates, the ability to manufacture, 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 indicative of their 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. 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.