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Valneva Successfully Completes Pivotal Phase 3 Trial of Single-Shot Chikungunya Vaccine Candidate

- **VLA1553-301 six-month follow-up completed – all endpoints met**
- **Seroprotection (protective CHIKV neutralizing antibody levels) in 98.9% of participants after one month and 96.3% after six months**
- **Good safety and tolerability profile confirmed**
- **Valneva expects to commence pre-submission process**

Saint Herblain (France), March 8, 2022 – Valneva SE (Nasdaq: VALN; Euronext Paris: VLA), a specialty vaccine company, today announced the successful completion of the Phase 3 pivotal trial of its single-shot chikungunya vaccine candidate, VLA1553. The positive final analysis included six-month follow-up data and confirmed the topline results reported in August 2021. Valneva now expects to commence the pre-submission process with the U.S. Food and Drug Administration (FDA) in the second quarter of 2022.

The VLA1553-301 trial, which enrolled 4,115 adults aged 18 years and above across 44 sites in the U.S., met all primary and secondary endpoints. The final analysis confirmed the very high level of seroprotection, with 98.9% of participants achieving protective levels of chikungunya virus (CHIKV) neutralizing antibodies one month after receiving a single vaccination (263 of 266 subjects from the per-protocol subgroup tested for immunogenicity, 95% CI: 96.7-99.8). The excellent immunogenicity profile was maintained over time, with 96.3% of participants showing protective CHIKV neutralizing antibody titers six months after receiving a single vaccination (233 of 242 subjects from the per-protocol subgroup tested for immunogenicity, 95%CI: 93.1-98.3). The reported levels of seroprotection far exceeded the 70% threshold (for non-acceptance) based on a surrogate of protection agreed with the FDA under the accelerated approval pathway[1].

VLA1553 was also confirmed to be highly immunogenic in elderly study participants (65 years of age or older), who achieved equally high seroprotection rates and neutralizing antibody titers over time as younger adults. A dedicated antibody persistence trial (VLA1553-303) will monitor a subset of participants from study VLA1553-301 for a period of at least five years to confirm the anticipated long-term protection after a single vaccination.

The six-month safety profile was also consistent with previous results across all age groups. VLA1553 was generally well tolerated among the 3,082 subjects evaluated for safety. An independent Data Safety Monitoring Board continuously monitored the study and identified no safety concerns. The majority of solicited adverse events were mild or moderate and resolved within three days. 2.0% of study participants reported severe solicited adverse events, most commonly fever. Approximately 50% of study participants experienced solicited systemic adverse events, most commonly headache, fatigue and myalgia.

[1] *Valneva Announces Positive Phase 3 Pivotal Results for its Single-Shot Chikungunya Vaccine Candidate – Valneva*

Juan Carlos Jaramillo, M.D, Chief Medical Officer of Valneva commented, "These final pivotal Phase 3 results confirm the compelling profile of our single-shot vaccine candidate across all age groups. Delivering these first-ever final Phase 3 results for a chikungunya vaccine candidate means that we are a step closer to addressing a major, growing and unmet public health threat. We would like to thank everyone who participated in the trial and who continued to advance the trial during the pandemic."

Valneva previously reported positive topline lot-to-lot manufacturing consistency results for VLA1553[2]. This is one of the standard requirements for vaccine licensure, and final lot-to-lot results are expected in the second quarter of 2022. Valneva also recently initiated a Phase 3 trial in adolescents conducted in Brazil by Instituto Butantan to support the label extension in this age group following a potential initial regulatory approval in adults in the U.S[3]. Funded by the Coalition for Epidemic Preparedness Innovations (CEPI), this trial is also expected to support licensure of the vaccine in Brazil, which would be the first potential approval for use in an endemic region.

Valneva's chikungunya vaccine program was awarded Breakthrough Therapy Designation by the FDA in July 2021. This followed the FDA Fast Track designation and the European Medicines Agency (EMA)'s PRIME designations, which the Company received in December 2018 and in October 2020, respectively. The sponsor of the first chikungunya vaccine approved in the U.S. will be eligible to receive a Priority Review Voucher (PRV).

About Chikungunya

Chikungunya is a mosquito-borne viral disease caused by the chikungunya virus (CHIKV), a *Togaviridae* virus, transmitted by *Aedes* mosquitoes. 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. There are no preventive vaccines or effective treatments available and, as such, chikungunya is considered to be a major public health threat. As of September 2020, there were more than 3 million reported cases in the Americas[4] 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. Infection leads to symptomatic disease in 72-92% of humans after four to seven 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, rash and chronic arthralgia. High risk areas of infection are places where chikungunya virus-carrying mosquitos are currently endemic, including the Americas, parts of Africa, and Southeast Asia.

About VLA1553

VLA1553 is a live-attenuated, single dose vaccine candidate targeting the chikungunya virus, which has spread to over 120 countries. It has been designed by deleting a part of the chikungunya virus genome.

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[2] *Valneva Announces Positive Lot-to-Lot Consistency Trial Results for its Single-Shot Chikungunya Vaccine Candidate*

[3] *Valneva Announces Initiation of Adolescent Phase 3 Trial for its Single-Shot Chikungunya Vaccine Candidate – Valneva*

[4] *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.*

VLA1553 would expand Valneva's existing commercial vaccines 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[5].

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[6]. The collaboration falls within the framework of the agreement signed between CEPI and Valneva in July 2019[7], which provides funding of up to $23.4 million with support from the European Union's Horizon 2020 program.

About Phase 3 trial VLA1553-301

VLA1553-301 Phase 3 trial was initiated in September 2020. It is a prospective, double-blinded, multicenter, randomized, pivotal Phase 3 trial evaluating 4,115 participants aged 18 years or above. Lyophilized VLA1553 or placebo were administered as a single intramuscular immunization. The primary objective of the trial was to evaluate the immunogenicity and safety of VLA1553 at one month following a single immunization. Additional information, including a detailed description of the trial design, eligibility criteria and investigator sites, is available at ClinicalTrials.gov (Identifier: NCT04546724).

About Valneva SE

Valneva is a specialty vaccine company focused on the development, production and commercialization of prophylactic vaccines for infectious diseases with significant unmet medical need. The Company takes a highly specialized and targeted approach to vaccine development and then applies its deep understanding of vaccine science to develop prophylactic vaccines addressing these diseases. Valneva has leveraged its 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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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, clinical trials, and regulatory review of VLA1553. 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

[5] *VacZine Analytics Chikungunya virus vaccines Global demand analysis. February 2020*
[6] *Valneva and Instituto Butantan Sign Final Agreement on Single-Shot Chikungunya Vaccine for Low and Middle Income Countries*
[7] *CEPI awards up to $23.4 million to Valneva for late-stage development of a single-dose Chikungunya vaccine*

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.