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Valneva Completes Enrollment for Adolescent Phase 3 Trial of Single-Shot Chikungunya Vaccine Candidate

Saint-Herblain (France), February 14, 2023 – Valneva SE (Nasdaq: VALN; Euronext Paris: VLA), a specialty vaccine company, today announced that it completed enrollment and vaccination for a Phase 3 trial in adolescents, VLA1553-321, of its single-shot chikungunya vaccine candidate, VLA1553. First results of the trial are expected mid-2023.

Funded by the Coalition for Epidemic Preparedness Innovations (CEPI), the VLA1553-321 adolescent trial is intended to support the label extension in this age group following a potential initial regulatory approval in adults from the Food and Drugs Administration (FDA) in the United States (U.S).

Valneva completed rolling submission of the Biologics License Application (BLA) to the U.S. FDA for approval of VLA1553 in persons aged 18 years and above in December 2022[1]. If BLA filing is accepted and approved, VLA1553 could become the first chikungunya vaccine to be marketed in the U.S. Valneva reported final pivotal Phase 3 data for VLA1553 in March 2022[2] and final lot-to-lot consistency results in May 2022[3]. The Company also recently reported positive antibody persistence data with a 99% seroresponse rate 12 months after a single-dose vaccination[4].

The VLA1553-321 adolescent trial is also expected to support licensure of the vaccine in Europe and Brazil, which would be the first potential approval for use in endemic populations.

Conducted in collaboration between Instituto Butantan and Valneva, VLA1553-321 is a double-blinded, multi-center, randomized and placebo-controlled Phase 3 trial. 754 adolescents aged 12 to 17 years were vaccinated following randomization at a 2:1 ratio to receive either VLA1553 or placebo. The primary objective of the trial is to evaluate safety and immunogenicity 28 days following a single vaccination with VLA1553. Participants will be evaluated for the primary endpoint and followed up to twelve months. The study will also provide the first systematic safety and immunogenicity data in participants previously exposed to chikungunya.

Juan Carlos Jaramillo, M.D., Chief Medical Officer of Valneva, commented, "Recruitment completion in this study is an important milestone for the overall program. We reported compelling pivotal Phase 3 results in adults and in the elderly, and we are now looking forward to obtaining results in adolescents later this year. Chikungunya virus is a major, growing public health threat which has already impacted over 100 countries and affected millions worldwide, yet no vaccine or specific treatment is currently available to prevent this debilitating disease."

Dr. Esper Georges Kallas, President of Instituto Butantan, which will develop, manufacture and market VLA1553 in Low- and Middle-Income Countries, commented, "the achievement of this goal is a major milestone to expand the vaccine indication in adolescents. Based on a single-dose schedule, the VLA1553 chikungunya vaccine could become a key tool to prevent the chikungunya disease in endemics areas and fight the disease-induced public health burden."

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[1] *Valneva Completes BLA Submission to U.S. FDA for its Single-Shot Chikungunya Vaccine Candidate - Valneva*
[2] Valneva Successfully Completes Pivotal Phase 3 Trial of Single-Shot Chikungunya Vaccine Candidate
[3] Valneva Successfully Completes Lot-to-Lot Consistency Trial for its Single-Shot Chikungunya Vaccine Candidate
[4] *Valneva Reports Positive 12-Month Antibody Persistence Data for Single-Shot Chikungunya Vaccine Candidate - Valneva*

Dr. Melanie Saville, Director of Vaccine Research & Development at CEPI, which provided funding for this study, added, "Millions of people have been affected by chikungunya and, today, over a billion people live in areas where chikungunya outbreaks occur. The progress Valneva has made to date brings the world one step closer towards a safe and effective vaccine against this debilitating disease, for which there is currently no specific treatment nor vaccine licenced for human use. Data from this Phase 3 study will help to ensure that the people most affected by this virus can benefit from this product and help regulators assess this important vaccine candidate."

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[5]. The collaboration falls within the framework of the agreement signed between CEPI and Valneva in July 2019[6], which provides funding of up to $24.6 million with support from the European Union's Horizon 2020 program.

Brazil had an exponential increase of chikungunya cases in 2021 in comparison to 2020, according to data from the Brazilian Vigilance Health Secretary (SVS). At the beginning of December 2021, 90,147 chikungunya cases had been registered compared to 78,808 over the same period in the previous year. The three states that most registered cases of the disease were Pernambuco (29,700 cases), São Paulo (18,100 cases) and Paraíba (9,000 cases), respectively. In 2021, São Paulo which is the most populous state in the country, went from 468 cases to 18,156 cases compared to 2020[7].

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[7] 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 up to 97% of humans after three 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. It is estimated that over three quarters of the world's population live in areas at-risk of CHIKV transmission[8]. High risk areas of infection are places where chikungunya virus-carrying mosquitos are currently endemic, including the Americas, parts of Africa, and Southeast Asia.

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[5] *Valneva and Instituto Butantan Sign Final Agreement on Single-Shot Chikungunya Vaccine for Low and Middle Income Countries*

[6] *CEPI awards up to $23.4 million to Valneva for late-stage development of a single-dose Chikungunya vaccine*

[7] *https://www.gov.br/saude/pt-br/assuntos/noticias/2021-1/novembro/sao-paulo-e-o-estado-com-o-maior-aumento-do-numero-de-casos-de chikungunya.*

[7] *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.*

[8] CDC 2022, Puntasecca CJ 2021

About VLA1553

VLA1553 is a live-attenuated, single dose investigational vaccine candidate targeting the chikungunya virus, which has spread to over 100 countries. 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[9] and final lot-to-lot consistency results in May 2022[10].

If approved, VLA1553 would expand Valneva's existing commercial vaccines portfolio and as such, Valneva intends to commercialize this vaccine, leveraging its existing manufacturing and commercial operations.

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[11]. The collaboration falls within the framework of the agreement signed between CEPI and Valneva in July 2019[12], which provides funding of up to $24.6 million with support from the European Union's Horizon 2020 program.

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. VLA1553 or placebo will be administered as a single intramuscular immunization to participants who will be 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 will include assessment of safety and immunogenicity up to twelve months following a single vaccination with VLA1553. The study will also provide safety and immunogenicity data in participants previously exposed to chikungunya.

Additional information, including a detailed description of the study design, eligibility criteria and investigator sites, is available at ClinicalTrials.gov (Identifier: NCT04650399).

About Valneva SE

Valneva is a specialty vaccine company focused on the development, manufacturing 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 commercialize three vaccines and to rapidly advance a broad range of vaccine candidates into and through the clinic, including candidates against Lyme disease and the chikungunya virus.

About Instituto Butantan

Instituto Butantan is the main producer of immunobiological products and vaccines in Brazil. Instituto Butantan carries out scientific missions domestically and abroad through the Pan American Health Organization, the World Health Organization, UNICEF and the United Nations.

[9] *Valneva Successfully Completes Pivotal Phase 3 Trial of Single-Shot Chikungunya Vaccine Candidate*
[10] *Valneva Successfully Completes Lot-to-Lot Consistency Trial for its Single-Shot Chikungunya Vaccine Candidate*
[11] *Valneva and Instituto Butantan Sign Final Agreement on Single-Shot Chikungunya Vaccine for Low and Middle Income Countries*
[12] *CEPI awards up to $23.4 million to Valneva for late-stage development of a single-dose Chikungunya vaccine*

The Institute collaborates with other agencies of the São Paulo State Secretariat of Health and the Brazilian Ministry of Health for the improvement of overall health in Brazil. It acts in partnership with various universities and entities such as the Bill & Melinda Gates Foundation for the achievement of its institutional objectives. For more information please visit the Institute website at www.butantan.gov.br or contact the press office at (+55 11) 2627-9606 / 9428 or email to imprensa@butantan.gov.br

About CEPI

CEPI is an innovative partnership between public, private, philanthropic, and civil organizations, launched at Davos in 2017, to develop vaccines to stop future epidemics. Before the emergence of COVID-19 CEPI's priority diseases included Ebola virus, Lassa virus, Middle East Respiratory Syndrome coronavirus, Nipah virus, Rift Valley Fever and chikungunya virus. CEPI also invested in platform technologies that can be used for rapid vaccine and immunoprophylactic development against unknown pathogens (Disease X).

CEPI has moved with great urgency and in coordination with WHO in response to the emergence of COVID-19. CEPI has initiated 9 partnerships to develop vaccines against the novel coronavirus. The programmes will leverage rapid response platforms already supported by CEPI as well as new partnerships. The aim is to advance COVID-19 vaccine candidates into clinical testing as quickly as possible.

CEPI, alongside Gavi and the World Health Organisation, co-leads the vaccines pillar of the ACT Accelerator – known as COVAX – which is working to develop, distribute and deploy COVID-19 vaccines to the world. Learn more at **http://www.cepi.net**. Follow CEPI at **@CEPIvaccines**.

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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 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.