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Valneva Announces Publication of Lyme Disease Phase 2 Trials in the Lancet Infectious Diseases

Saint-Herblain (France), June 3, 2024 – Valneva SE (Nasdaq: VALN; Euronext Paris: VLA), a specialty vaccine company, today announced that the results of two Phase 2 clinical trials of Lyme disease vaccine candidate, VLA15, were published in the peer-reviewed medical journal, *The Lancet Infectious Diseases*. These trials, as well as a third Phase 2 trial in pediatric participants, supported the design of the current pivotal Phase 3 trial, 'Vaccine Against Lyme for Outdoor Recreationists' (VALOR).

Juan Carlos Jaramillo M.D., Chief Medical Officer of Valneva, said*, "*We are pleased that these results are now fully available to the broader infectious disease community. Lyme disease is the most prevalent vector-borne infectious disease in North America and Europe, and we are excited about the ongoing trials and progress towards potentially offering a vaccine against this unmet medical need."

The article, titled "Optimization of Dose Level and Vaccination Schedule for the VLA15 Lyme Borreliosis Vaccine Candidate Among Healthy Adults: Two Randomized, Phase 2 Studies" provides a detailed analysis of the VLA15-201 and VLA15-202 trial results, which investigated different dose levels and vaccination schedules of VLA15, a hexavalent Lyme disease vaccine candidate targeting most prevalent *Borrelia* species (serotype 1-6) in North America and Europe.

VLA15 was shown to be immunogenic across all dose groups and vaccination schedules tested. Strongest antibody responses across all six serotypes were exhibited at the highest dose (180 µg) and broader vaccination intervals (Month 0,2,6). VLA15 has shown a favorable safety and tolerability profile across all trials to date. No safety concerns were observed by an independent Data Safety Monitoring Board (DSMB)[1,2], in any treatment group.

Valneva and Pfizer entered into a collaboration agreement in April 2020 to co-develop VLA15, with updates to the terms within this agreement made in June 2022[3]. The companies previously reported positive results for the booster phase of trial VLA15-202[4] and a third Phase 2 trial, VLA15-221[5], providing further evidence on VLA15's safety profile and its potential to provide immunity against Lyme disease in adult, pediatric and adolescent populations. The companies also aim to publish these results in a peer-reviewed medical journal.

[1] *Valneva and Pfizer Report Positive Phase 2 Pediatric Data for Lyme Disease Vaccine Candidate - Valneva*
[2] *Valneva and Pfizer Report Six-Month Antibody Persistence Data in Children and Adults for Lyme Disease Vaccine Candidate - Valneva*
[3] *Valneva and Pfizer Enter into an Equity Subscription Agreement and Update Terms of Collaboration Agreement for Lyme Disease Vaccine Candidate VLA15 - Valneva*
[4] *Valneva and Pfizer Report Further Positive Phase 2 Results, Including Booster Response, for Lyme Disease Vaccine Candidate - Valneva*
[5] *Valneva and Pfizer Report Positive Pediatric and Adolescent Phase 2 Booster Results for Lyme Disease Vaccine Candidate - Valneva*

The Phase 3 clinical trial, VALOR, is currently ongoing to investigate the efficacy, safety and immunogenicity of VLA15 in participants five years of age and older in highly endemic regions in the United States, Canada and Europe. Enrollment of 9,437 participants for the trial was completed in December 2023.

Subject to positive data, Pfizer aims to submit a Biologic License Application to the Food and Drug Administration and Marketing Authorization Application to the European Medicines Agency in 2026.

About VLA15

There are currently no approved human vaccines for Lyme disease, and VLA15 has advanced the furthest of any Lyme vaccine candidates currently in clinical development, with two Phase 3 trials in progress. This investigational multivalent protein subunit vaccine uses an established mechanism of action for a Lyme disease vaccine that targets the outer surface protein A (OspA) of *Borrelia burgdorferi*, the bacteria that cause Lyme disease. OspA is a surface protein expressed by the bacteria when present in a tick. Blocking OspA inhibits the bacterium's ability to leave the tick and infect humans. The vaccine candidate covers the six most prevalent OspA serotypes expressed by the *Borrelia burgdorferi sensu lato* species in North America and Europe.

About Lyme Disease

Lyme disease is a systemic infection caused by *Borrelia burgdorferi* bacteria transmitted to humans by the bite of infected Ixodes ticks[6]. It is the most common vector-borne illness in the Northern Hemisphere[7,8]. While the true incidence of Lyme disease is unknown, the Centers for Disease Control and Prevention (CDC) has estimated that approximately 476,000 people in the U.S. are diagnosed and treated each year and 129,000 cases are reported annually in Europe[9,10]. Early symptoms of Lyme disease (such as a gradually expanding erythematous rash called Erythema migrans or other nonspecific symptoms like fatigue, fever, headache, mild stiff neck, muscle and joint pains) are often overlooked or misinterpreted. Left untreated, the disease can disseminate and cause more serious chronic complications affecting the skin, joints (arthritis), the heart (carditis) or the nervous system[9,10]. The medical need for vaccination against Lyme disease is steadily increasing as the geographic footprint of the disease widens[11].

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 first-, best- or only-in-class vaccine solutions.

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[6] *Stanek, et al. Lyme Borreliosis. 2012. The Lancet 379:461–473.*
[7] *Burn L, et al. Incidence of Lyme Borreliosis in Europe from National Surveillance Systems (2005–2020). 2023. Vector Borne and Zoonotic Diseases. 23(4):156–171.*
[8] *Kugeler KJ, et al. Estimating the frequency of Lyme disease diagnoses—United States, 2010-2018. 2021. Emergency Infectious Disease. 27(2).*
[9] *Centers for Disease Control and Prevention. Lyme disease. Signs and Symptoms. Available from: https://www.cdc.gov/lyme/signs_symptoms/index.html. Accessed September 2022.*
[10] *Steere AC, Strle F, Wormser GP, et al. Lyme borreliosis. Nature Reviews Disease Primers. 2016;2:16090.*
[11] *Centers for Disease Control and Prevention. Understanding Lyme and Other Tickborne Diseases. May 2022. Available from: https://www.cdc.gov/ncezid/dvbd/media/lyme-tickborne-diseases-increasing.html. Accessed April 2024.*

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