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Valneva Reports Further Positive Phase 2 Safety and Immunogenicity Results for Lyme Disease Vaccine Candidate

- *Strong immune response after third yearly booster dose in children and adults*
- *Significant anamnestic antibody response across all six serotypes*
- *No safety concerns observed in any age group by independent Data Monitoring Committee (DMC), consistent with previous booster results.*

Saint-Herblain (France), September 3rd, 2025 – Valneva SE (Nasdaq: VALN; Euronext Paris: VLA) announced positive immunogenicity and safety data from the ongoing Phase 2 study of Lyme disease vaccine candidate, VLA15. The strong anamnestic immune response and favorable safety profile following a third booster dose were consistent with those reported after receiving previous annual booster doses[1,2] further demonstrating compatibility with the anticipated benefits of a yearly vaccination prior to each Lyme season.

There are currently no approved human vaccines for Lyme disease, and VLA15 has advanced the furthest in clinical development, with two Phase 3 trials nearing completion. The Centers for Disease Control and Prevention (CDC) estimates that approximately 476,000 people in the U.S. are diagnosed and treated for Lyme disease each year, and 132,000 cases are reported annually in Europe.[3,4] Vaccination has been completed in the pivotal Phase 3 study of VLA15[5], and subject to positive data, Pfizer aims to submit a Biologics License Application (BLA) to the U.S. Food and Drug Administration (FDA) and Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) in 2026.

Juan Carlos Jaramillo M.D., Chief Medical Officer of Valneva, said, "These latest data further reinforce the potential benefits of booster doses across all evaluated age groups. There are currently no approved human vaccines for Lyme disease, and as the disease continues to expand geographically, it remains a pressing unmet medical need affecting communities across the Northern Hemisphere. Each set of positive results moves us closer to the possibility of making this vaccine available to both adults and children living in Lyme-endemic areas."

These latest results from the VLA15-221 Phase 2 study - measured one month after vaccination at month 42 - again demonstrated a significant anamnestic antibody response across all six serotypes covered by the vaccine candidate in pediatric (5 to 11 years of age) and adolescent (12 to 17 years of age) participants, as well as in adults (18 to 65 years of age). A high proportion of participants seroconverted after the third booster dose, yielding seroconversion rates* (SCRs) at 100% (confidence interval 96.7%, 100%) for all outer surface protein A (OspA) serotypes in all age groups, in-line with SCRs after the first and second booster. Geometric Mean Titers at one month post first and second booster (i.e. month 19 vs. month 31) were comparably high.

The safety and tolerability profile of VLA15 after the third booster dose was similar to the profile observed after the previous booster doses. To date, no safety concerns have been observed by the independent DMC in any treatment or age group.

Pfizer and Valneva entered into a collaboration agreement in April 2020 for the development and commercialization by Pfizer of VLA15.

Participants in this Phase 2 study received VLA15 or placebo during the primary vaccination phase in two immunization schedules (month 0-2-6 or month 0-6), followed by yearly vaccinations at months 18, 30 and 42. In August 2022, Pfizer and Valneva initiated the currently ongoing Phase 3 clinical study, Vaccine Against Lyme for Outdoor Recreationists (VALOR) (NCT05477524), to investigate the efficacy, safety and immunogenicity of VLA15 in participants five years of age and older in highly endemic regions in North America and Europe.[6] Dosing of all subjects was recently completed as announced by Pfizer. A second Phase 3 trial (C4601012), aiming to provide further evidence on the safety profile of VLA15 in the pediatric population between 5 and 17 years of age also completed vaccination.

About VLA15

There are currently no approved human vaccines for Lyme disease, and VLA15 is the Lyme disease vaccine candidate which has advanced the furthest along the clinical development timeline, 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 Clinical Study VLA15-221

VLA15-221 is a randomized, observer-blind, placebo-controlled Phase 2 study. It is the first clinical study with VLA15 which enrolled a pediatric population (5-17 years old). 560 healthy participants received either VLA15 in two immunization schedules (month 0-2-6 [N=190] or month 0-6 [N=181]) or placebo (month 0-2-6 [N=189]). Vaccine recipients received VLA15 at a dose of 180 µg, which was selected based on data generated in two previous Phase 2 studies. The main safety and immunogenicity readout (primary endpoint) was performed one month after completion of the primary series vaccination schedule. All eligible subjects received yearly booster doses of VLA15 or placebo at Months 18, 30 and 42. Antibody persistence will be followed up to six months post third annual booster.

VLA15 is tested as an alum-adjuvanted formulation and administered intramuscularly. The study is being conducted at U.S. sites located in areas where Lyme disease is endemic and has enrolled both volunteers with a prior infection with *Borrelia burgdorferi* as well as *Borrelia burgdorferi*-naïve volunteers.

About Lyme Disease

Lyme disease is a systemic infection caused by Borrelia burgdorferi bacteria transmitted to humans by the bite of infected Ixodes ticks.7 It is considered the most common vector-borne illness in the Northern Hemisphere.8,9 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 132,000 cases are reported annually in Europe. 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 paints) 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. The medical need for vaccination against Lyme disease is steadily increasing as the geographic footprint of the disease widens.[10]

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 three proprietary travel vaccines.

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, the world's most clinically advanced tetravalent Shigella vaccine candidate as well as vaccine candidates against the Zika virus and other global public health threats.

Valneva 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 and the timing for submission of such product candidates for regulatory approval. In addition, even if the actual results or developments 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 in this press release will in fact be realized. Valneva is providing this information as of the date of this press release and disclaims any intention or obligation to publicly update or revise any forward-looking statements, whether as a result of new information, future events, or otherwise.

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