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Valneva Announces Positive Initial Results for Phase 2 Study of Lyme Disease Vaccine Candidate

- Phase 2 study VLA15-201 met its endpoints
- Compared to Phase 1, the higher doses used in this trial elicited higher antibody responses across all serotypes
- Encouraging immunogenicity profile confirmed, including older adults (50-65 years)
- VLA15 generally safe across all dose and age groups tested
    - No related Serious Adverse Events (SAEs) associated with VLA15

Saint-Herblain (France), July 22, 2020 – Valneva SE ("Valneva"), a specialty vaccine company focused on prevention of diseases with major unmet needs, today announced positive initial results for its first Phase 2 study (VLA15-201) of Lyme disease vaccine candidate VLA15.

VLA15 was immunogenic across all dose groups tested. Compared to Phase 1, the higher doses used in this trial elicited higher antibody responses across all serotypes. Seroconversion rates (SCR) in the highest dose ranged from 81.5% (ST1) to 95.8% (ST2). In the age group comparable to the age group investigated in Phase 1 (18-49 years), SCRs ranged from 85.6% to 97%. The immunological response in older adults, one of the main target groups for a Lyme vaccine, is particularly encouraging.
Results did not indicate that prior exposure to Lyme (sero-positivity) has an impact on immunogenicity or safety.
As part of further Phase 2 data to be released in a few months, an analysis of the functionality of the antibodies generated with VLA15 will be conducted. In close collaboration with regulatory authorities, Valneva has developed a Serum Bactericidal Antibody assay ("SBA") for that purpose.

VLA15 was generally safe across all dose and age groups tested. No related Serious Adverse Events (SAEs) were observed with VLA15 in this study in any treatment group. Reactogenicity decreased with subsequent vaccinations.
Overall, the tolerability profile including rates of fever appeared to be comparable to other lipidated recombinant vaccines or lipid-containing formulations.

Wolfgang Bender, MD, PhD, Chief Medical Officer of Valneva commented "*We are pleased to report a successful first Phase 2 trial of our vaccine candidate against Lyme disease, a severe infection which affects an increasing number of people each year. Further data from the ongoing Phase 2 trials in the coming months will support further dose and schedule decisions. We are closely working with Pfizer to advance the development of VLA15 expeditiously.*"

This first Phase 2 study, conducted in the EU and US, included 572 healthy adults aged 18 to 65 years. In the main study phase, 452 subjects received one of two dose levels (either 135µg or 180µg) of VLA15 (approximately 180 subjects each) in three injections (Days 1, 29 and 57) or placebo (approximately 90 subjects). Immunogenicity was measured by determining IgG antibodies against each of the six most prevalent Outer Surface Protein A serotypes of Lyme borreliosis in the US and Europe covered by the vaccine. The endpoint readout was immunogenicity at Day 85 (one month after finalization of primary immunization).

Valneva expects to report top-line results for the second Phase 2 study, VLA15-202, in a few months. In the VLA15-202 study, identical doses to the VLA15-201 study were tested using a longer vaccination schedule (Days 1, 57 and 180).

About VLA 15

VLA15 is the only active Lyme disease vaccine in clinical development today, and covers six serotypes that are prevalent in North America and Europe. This investigational multivalent protein subunit vaccine targets the outer surface protein A (OspA) of Borrelia, an established mechanism of action for a Lyme disease vaccine. OspA is one of the most dominant surface proteins expressed by the bacteria when present in a tick. VLA15 has demonstrated strong immunogenicity and safety data in pre-clinical and Phase 1 studies. The program was granted Fast Track designation by the U.S. Food and Drug Administration (FDA) in July 2017[1].

Valneva and Pfizer announced a collaboration for VLA15's development and commercialization at the end of April 2020[2]. The two companies are working closely together on the next development steps.

About Phase 2 Clinical Study VLA15-201

VLA15-201, the first of two parallel Phase 2 studies, is a randomized, observer-blind, placebo controlled study conducted in the US and Europe.

In a run-in Phase of the study, 120 subjects received one of three dosage levels of VLA15, or placebo. Following a positive review of safety data by an independent Data Safety Monitoring Board, 452 subjects received, in the main study phase, one of two selected dose levels of VLA15 (approximately 180 subjects each), or placebo (approximately 90 subjects).

VLA15 was tested as an alum-adjuvanted formulation and administered intramuscularly in three injections, given at Days 1, 29 and 57. Subjects, healthy adults 18 to 65 years of age, were followed for one year, with the main immunogenicity readout at Day 85 (Primary endpoint). Study centers for this study were located in areas where Lyme disease is endemic; subjects with a cleared past infection with *Borrelia burgdorferi*, the bacteria that cause Lyme disease, were also enrolled.

About Lyme Disease

Lyme disease is a systemic infection caused by *Borrelia* bacteria transmitted to humans by infected *Ixodes* ticks[3]. It is considered the most common vector borne illness in the Northern Hemisphere. According to the U.S. Centers for Disease Control and Prevention (CDC), approximately 300,000 Americans[4] are diagnosed with Lyme disease each year with at least a further 200,000 cases in Europe[5]. Early symptoms of Lyme disease (such as a gradually expanding erythematous rash called *Erythema migrans* or more unspecific symptoms like fatigue, fever, headache, mild stiff neck, arthralgia or myalgia) are often overlooked or misinterpreted. Left untreated, the disease can disseminate and cause more serious complications affecting the joints (arthritis), the heart (carditis) or the nervous system. The medical need for vaccination against Lyme disease is steadily increasing as the disease footprint widens[6].

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[1] *Valneva Receives FDA Fast Track Designation for its Lyme Disease Vaccine Candidate VLA15*

[2] *Valneva and Pfizer Announce Collaboration to Co-Develop and Commercialize Lyme Disease Vaccine, VLA15*

[3] *Stanek et al. 2012, The Lancet 379:461–473*

[4] *As estimated by the CDC, https://www.cdc.gov/lyme/stats/humancases.html.*

[5] *Estimated from available national data. Number largely underestimated based on WHO Europe Lyme Report as case reporting is highly inconsistent in Europe and many LB infections go undiagnosed; ECDC tick-borne-diseases-meeting-report*

[6] *New Scientist, Lyme disease is set to explode and we still don't have a vaccine; March 29, 2017 https://www.newscientist.com/article/mg23431195-800-lyme-disease-is-set-to-explode-and-you-cant-protect-yourself/*

About Valneva SE

Valneva is a specialty vaccine company focused on prevention of diseases with major unmet needs. 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 various vaccines in development including unique vaccines against Lyme disease and chikungunya. Valneva has operations in Austria, Sweden, the United Kingdom, France, Canada and the US with over 500 employees. For more information, visit www.valneva.com and follow the Company on LinkedIn.

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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.