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Valneva Reports Successful Outcome of Phase 2 Run-In for its Lyme Disease Vaccine Candidate

Based on DSMB clearance, two lead dosage levels have been selected for ongoing Phase 2 clinical development

Saint-Herblain (France), June 12, 2019 – Valneva SE ("Valneva" or "the Company"), a biotech company developing and commercializing vaccines for infectious diseases with major unmet medical needs, today announced progress of its ongoing Phase 2 study for its leading, unique Lyme disease vaccine candidate, VLA15, into the main study phase. An independent Data Safety Monitoring Board (DSMB) has cleared two dosage levels to be used for clinical development.

Valneva has previously reported initial booster data and final Phase 1 follow-up data for VLA15, confirming that the vaccine candidate has a favorable safety profile and was immunogenic in all doses and formulations tested. VLA15 elicited an excellent anamnestic response following a booster vaccination in a time window of 12 to 15 months after initial primary immunization[1].

As part of the VLA15-201 run-in Phase, 120 subjects received one of three alum adjuvanted dose levels of VLA15 (90µg, the high dose from Phase 1, 135µg or 180µg) or placebo. The DSMB has reviewed safety data from those subjects and has cleared the 135µg and 180µg dosage levels for further investigation in the main study phase.

Valneva has commenced preparations to initiate a further Phase 2 study (VLA15-202) to evaluate an alternative immunization schedule. The Company expects this study to commence in the third quarter of this year.

Wolfgang Bender, MD, PhD, Chief Medical Officer of Valneva, commented, "*We are pleased that the run-in safety data confirm our hypothesis that we can proceed with higher doses than initially studied in Phase 1. Given the well-understood mode of action, high anti-OspA antibody titers are key to deliver a highly effective vaccine that will address the significant unmet medical need arising from the increasing spread of Lyme disease".*

Preliminary Phase 2 results (primary endpoint) are anticipated – as previously announced – mid-2020.

About The Phase 2 Clinical Study VLA15-201
VLA15-201 is the first of two planned, parallel Phase 2 studies. It is a randomized, observer-blind, placebo controlled trial conducted at trial sites in the US and Europe.
In the run-in Phase, 120 subjects received one of three dosage levels of VLA15, or placebo. Following review of safety data by an independent Data Safety Monitoring Board, 450 subjects

[1] *Valneva PR: Valneva Reports Positive Initial Booster Data and Final Phase 1 Data for its Lyme Disease Vaccine Candidate*

in the main study phase will receive one of two selected dose levels of VLA15 (180 subjects each), or placebo (90 subjects).
VLA15 will be tested as alum adjuvanted formulation and will be administered intramuscularly in three injections, given one month apart at Days 1, 29 and 57. Subjects will be followed for one year, with the main immunogenicity readout one month after the third immunization on Day 85 (Primary Endpoint). The study is enrolling healthy adults 18 to 65 years of age. Study centers will be located in areas where Lyme disease is endemic; subjects with a cleared past infection with *Borrelia burgdorferi*, the bacteria that cause Lyme disease, will also be enrolled.

About Lyme Disease
Lyme disease is a systemic infection caused by *Borrelia* bacteria transmitted to humans by infected *Ixodes* ticks[2]. 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[3] are diagnosed with Lyme disease each year with at least a further 200,000 cases in Europe[4]. 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[5].

About VLA15
Valneva's vaccine candidate, VLA15, is currently the only active vaccine program in clinical development against Lyme disease. The program was granted Fast Track designation by the U.S. Food and Drug Administration (FDA) in July 2017[6] and Valneva reported positive Phase 1 results in March 2018[7]. VLA15 showed a favourable safety profile and was immunogenic in all doses and formulations tested with good OspA-specific IgG antibody responses against all OspA serotypes.
VLA15 is a multivalent, protein subunit vaccine that targets the outer surface protein A (OspA) of *Borrelia*. It is designed for prophylactic, active immunization against Lyme disease aiming for protection against the majority of human pathogenic *Borrelia* species. VLA15 is designed to confer protection by raising antibodies that prevent *Borreliae* from migrating from ticks to humans after a bite. The safety profile is expected to be similar to other lipidated protein based vaccines that are approved for active immunization in adults and children
The target population includes individuals at risk above 2 years of age living in endemic areas, people planning to travel to endemic areas to pursue outdoor activities and people at risk who have a history of Lyme disease (as infection with *Borrelia* does not confer protective immunity against all pathogenic *Borrelia* species).

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[2] *Stanek et al. 2012, The Lancet 379:461–473*
[3] *As estimated by the CDC, https://www.cdc.gov/lyme/stats/humancases.html.*
[4] *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*
[5] *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/*
[6] *http://www.valneva.com/en/investors-media/news/2018;*
[7] Valneva Press Release March 19, 2018: Valneva Reports Positive Phase I Interim Results for Its Lyme Vaccine Candidate VLA15.

Vaccination with OspA was already proven to work in the 1990s and VLA15 pre-clinical data showed that the vaccine has the potential to provide protection against the majority of the *Borrelia* species pathogenic for humans[8].

About Valneva SE

Valneva is a biotech company developing and commercializing vaccines for infectious 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. The Company has various vaccines in development including a unique vaccine against Lyme disease. Valneva has operations in Austria, Sweden, the United Kingdom, France, Canada and the US with approximately 480 employees. More information is available at www.valneva.com.

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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

[8] *http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0113294.*

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.