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Valneva Reports Positive Initial Booster Data and Final Phase 1 Data for its Lyme Disease Vaccine Candidate

Saint-Herblain (France), January 31, 2019 – Valneva SE ("Valneva"), a biotech company developing and commercializing vaccines for infectious diseases with major unmet needs, today announced positive initial booster data and final Phase 1 data for its leading, unique Lyme disease vaccine candidate VLA15.

To investigate whether a VLA15 booster will elicit an anamnestic response[1], Valneva amended its Phase 1 study protocol during 2018, adding a booster dose in a sub-cohort of the Phase 1 study population. At the same time the full Phase 1 study population has been followed-up across all doses for up to one year, providing the final Phase 1 data.

The final Phase 1 data confirmed the safety and tolerability profile observed at all time-points, as reported in the interim analysis. VLA15 demonstrated a favorable safety profile and had no associated safety concerns. In addition, the final Phase 1 immunogenicity results indicated that the alum-adjuvanted formulations elicit higher immune-responses at all time-points, confirming the interim data findings. As expected, based on the interim Phase 1 data, antibody titres declined post Day 84 across all groups, trending towards baseline at approximately one year post initial vaccination.

To evaluate the benefit of a booster dose, 64 subjects across the two higher dose groups (48µg and 90µg, both with and without alum) from Phase 1 received a booster in the period 12 to 15 months after their initial dose in the primary immunization. These single re-vaccinations resulted in a significant immune-response, yielding OspA antibody titres at levels 2.7-fold (ST3[2]) – 5.8-fold (ST1) over the initial titres observed at Day 84 (geometric mean fold rise (GMFR)). These results are in line with published data from other OspA-based Lyme vaccines that had previously been in development.

Wolfgang Bender, M.D., Ph.D., Chief Medical Officer of Valneva, commented, *"These encouraging results support our current development plans and hypothesis for our leading vaccine candidate, VLA15. As a result of these findings, we have included a VLA15 booster in the Phase 2 program that is now underway. Addressing the significant, and growing, unmet medical need caused by Lyme disease is our top priority, VLA15 remains the only Lyme vaccine candidate in clinical development worldwide."*

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[1] An anamnestic response is a renewed rapid production of an antibody on the second (or subsequent) encounter with the same antigen.
[2] ST = serotype specific anti-OspA antibody response.

Valneva announced primary endpoint (interim) data from its Phase 1 trial of VLA15 (VLA15-101) in March 2018[3].
Given the range of immune response and the variability across the different serotypes (seroconversion rates at Day 84 were between 71.4% (ST1) and 96.4%(ST2)), the ongoing Phase 2 study (VLA15-201) includes two higher doses (135 µg and 180µg, both adjuvanted with alum) and a study evaluating an alternative vaccination schedule (VLA15-202) is scheduled to commence mid-2019.

The complete Phase 2 study is expected to be approximately two years in duration with interim data (primary endpoint) expected 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.
Initially, 120 subjects will receive one of three dosage levels of VLA15, or placebo, followed by a Data Safety Monitoring Board (DSMB) review of safety data. Thereafter, 450 subjects will receive one of two dose levels of VLA15 (180 subjects each), or placebo (90 subjects), in the main study phase.
VLA15 will be tested as alum adjuvanted formulation and will be administered intramuscularly in three injections, at Days 1, 29 and 57. Subjects will be followed for one year, with the main immunogenicity readout 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[4]. 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[5] are diagnosed with Lyme disease each year with at least a further 200,000 cases in Europe[6]. 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[7].

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

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[3] Valneva's press release: "Valneva Reports Positive Phase I Interim Results for Its Lyme Vaccine Candidate VLA15"
[4] Stanek et al. 2012, The Lancet 379:461–473
[5] As estimated by the CDC, https://www.cdc.gov/lyme/stats/humancases.html.
[6] 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
[7] 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/

U.S. Food and Drug Administration (FDA) in July 2017[8] and Valneva reported positive interim Phase 1 results in March 2018[9]. 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 *Borrelia* from migrating from ticks to humans after a bite. The safety profile is expected to be similar to other vaccines using the same technology that have been 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).
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[10].

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 over 450 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

[8] *http://www.valneva.com/en/investors-media/news/2018;*
[9] Valneva Press Release March 19, 2018: Valneva Reports Positive Phase I Interim Results for Its Lyme Vaccine Candidate VLA15.
[10] *http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0113294.*

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.