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Valneva Announces Successful Completion of Phase II for Clostridium Difficile Vaccine Candidate

+ Final Phase II results of Valneva's *Clostridium difficile* vaccine candidate confirm positive initial Phase II data that were released at the end of 2015
+ The Phase II study design, which enrolled 500 subjects, had been agreed with regulators with the aim of supporting a progression into Phase III
+ Valneva reaffirms its expectation to enter into a partnering agreement for *C. difficile* program by the end of year

Lyon (France), July 25, 2016 – Valneva SE ("Valneva" or "the Company"), a leading pure play vaccine company, today announced the successful completion of its Phase II study for its prophylactic vaccine candidate VLA84 targeting primary prevention of *C. difficile* infection (CDI), which is emerging as a leading cause of life-threatening, healthcare-associated infections (HAIs) worldwide.

Valneva previously announced positive top-line data from the Phase II study at the end of 2015. These initial results, which included data up to Day 56 following initial vaccination, were presented at the American Society of Microbiology's annual meeting, ASM Microbe 2016, on June 17 in Boston. VLA84 was immunogenic at all doses and formulations tested, in that Immunoglobulin G (IgG) and functional (neutralizing) antibody responses were observed. The study met its primary endpoint in terms of identifying the dose/formulation with the highest seroconversion[1] rate against both toxins A and B and confirmed the favorable safety profile observed in Phase I.

Final Phase II results included the follow-up of study participants until Day 210. This long-term data confirmed the optimal vaccine dose and formulation that had been previously identified (high-dose formulation without adjuvant) with an immunogenicity profile at Day 210 in line with expectations. Long-term safety concerns were not seen in any of the different vaccine doses tested.

Thomas Lingelbach, President and CEO, and Franck Grimaud, Deputy CEO of Valneva, commented, "We are pleased with the positive final data generated in this Phase II trial and believe that our *C. difficile* candidate has the potential to address a growing unmet medical need. Infections caused by *C. difficile* are responsible for almost 30 thousand deaths every year in the US alone[2]. There is currently no vaccine on the market that can protect patients and we are determined to find a partner to advance our vaccine candidate further."

[1] A level of antibodies in the blood directed against the two C. difficile Toxins A and B that is at least 4 times higher after vaccination than before vaccination
[2] Lessa *et al*, *Burden of Clostridium difficile Infection in the United States*. N Engl J Med 2015;372:825-34

Valneva's *C. difficile* Phase II trial was a randomized, placebo-controlled, observer-blind multi-center trial designed to further study and confirm the candidate vaccine's safety, immunogenicity and proposed doses of immunizations in two different age groups (50 to 64 years of age and 65 years of age and older). The trial was conducted in Germany and the United States under an Investigational New Drug application (IND) and enrolled 500 volunteers who were randomized in several study groups: low-dose vaccine without adjuvant, high-dose vaccine with or without adjuvant (Aluminium hydroxide), or placebo.

Valneva confirmed Phase III readiness through an independent Scientific Advisory Board (SAB) and is ready to support an end-of Phase II meeting (EOP2 meeting) with the regulatory authorities once the final Phase III design has been agreed with a partner. As announced previously, Valneva expects to enter into a partnering agreement for this program by year end 2016.

Currently, no vaccine against *C. difficile* is approved and antibiotic treatment of the established disease has significant limitations with recurrence in approximately 20% of cases[3]. The incidence of nosocomial infections is steadily increasing due to the growing number of medical interventions. Valneva estimates that the total market potential for prophylactic *C. difficile* products may exceed $1 billion annually.

This program is supported by the Vienna Business Agency.

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About Clostridium Difficile

C. difficile is a potentially life-threatening bacterium that causes diarrhea and can lead to serious intestinal diseases. It is estimated that 450,000 cases occur annually in the US, and close to 30.000 patients die within 30 days of the diagnosis[4].
Beyond the substantial morbidity and mortality, CDI is associated with significant economic burden (approximately $5 billion for U.S. acute care facilities alone[5]) due to prolongation of hospitalization.
Most often, *C. difficile* is acquired in healthcare settings: it is the single most common pathogen of acute healthcare-associated infections in the US[6]. However, about one third of

[3] Lessa et al, Clostridium difficile infection. N Engl J Med 2015;372:1539-48).
[4] Lessa et al, Burden of Clostridium difficile Infection in the United States. N Engl J Med 2015;372:825-34
[5] Dubberke ER, Clinical Infectious Diseases 55, no. suppl 2 (2012): S88-S92.
[6] Magill S, Edwards J R, Bamberg W et al. Multistate Point-Prevalence Survey of Health Care–Associated Infections. New England Journal of Medicine 2014;370:1198-208

cases are acquired outside healthcare settings, indicating need for prevention beyond the hospital[7].

About Valneva SE

Valneva is a fully integrated vaccine company that specializes in the development, manufacture and commercialization of innovative vaccines with a mission to protect people from infectious diseases through preventative medicine.

The Company seeks financial returns through focused R&D investments in promising product candidates and growing financial contributions from commercial products, striving towards financial self-sustainability.

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 proprietary vaccines in development including candidates against *Clostridium difficile* and Lyme Borreliosis. A variety of partnerships with leading pharmaceutical companies complement the Company's value proposition and include vaccines being developed using Valneva's innovative and validated technology platforms (EB66® vaccine production cell line, IC31® adjuvant).

Valneva is listed on Euronext-Paris and the Vienna stock exchange and has operations in France, Austria, Great Britain, Sweden, Canada and the US with over 400 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

[7] Lessa et al, Burden of Clostridium difficile Infection in the United States. N Engl J Med 2015;372:825-34

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.