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Valneva Reports Positive Phase II Results for its Clostridium Difficile Vaccine Candidate

+ Vaccine candidate was highly immunogenic in all age groups tested and induced strong immune responses to both *Clostridium difficile* Toxins A and B (primary endpoint met)

+ Good safety and tolerability profile of vaccine candidate confirmed (secondary endpoint met)

+ Next development steps to be announced after final study close-out in Q2 2016 and consultations with regulators and partner

Lyon (France), November 30, 2015 – Valneva SE ("Valneva"), a leading pure-play vaccine company, announced today, positive Phase II results for its prophylactic vaccine candidate against *Clostridium difficile* (*C. difficile*) infection (CDI).

The key objectives of this Phase II trial have been met, the vaccine candidate generated strong immune responses against *C. difficile* toxins A and B, and the safety and tolerability profile was good.

Valneva´s vaccine candidate is targeting the prevention of primary symptomatic *C.difficile* infection (CDI). The vaccine is designed to produce an immune response to neutralize the effects of *C. difficile* toxins A and B, considered to be largely responsible for CDI, which is emerging as a leading cause of life-threatening, healthcare-associated infections (HAIs) worldwide.

Thomas Lingelbach, President and CEO and Franck Grimaud, Deputy CEO of Valneva, commented, "*C. difficile* has become the most frequent hospital-acquired infection and is now linked to almost 30 thousand deaths every year in the US alone[1]. Our Phase II results provide a strong basis for the further development of a much needed vaccine for the prevention of C. difficile infection (CDI) in a growing target population of older patients"

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 study design was agreed with regulators in Europe and the U.S. with the aim of potentially supporting a subsequent progression into Phase III.

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

The trial was conducted in Germany and the United States under an Investigational New Drug application (IND) and included 500 volunteers who were randomized in several study groups: low-dose vaccine without adjuvant, high-dose vaccine with or without adjuvant (Aluminiumhydroxid), or placebo.

Valneva´s vaccine candidate was immunogenic at all doses and formulations tested, in that IgG and functional (neutralizing) antibody responses were seen.

The study met its primary endpoint in terms of identifying the dose/formulation with the highest seroconversion rate[2] against both toxins A and B on Day 56. The high-dose without adjuvant vaccine formulation generated a superior immune response.

The observed seroconversion rate in this difficult to vaccinate older adults population, was considered at an appropriate response level and broadly in-line with published data from comparable prophylactic *C. difficile* vaccine trials.

The vaccine was generally safe and well tolerated in all treatment groups and there were no severe local reactions noted in any group. The adverse events (AE profile) of all tested doses / formulations appear in a range comparable to other well tolerated vaccines.

Immune response and safety parameters will now be monitored until Day 210 and final study close-out is expected in the second quarter of 2016.

Valneva's *C. difficile* vaccine program is part of the Strategic Alliance Agreement (SAA) which was signed between Valneva Austria GmbH (Intercell AG at that time) and Novartis in 2007 and was transferred to GlaxoSmithKline (GSK) at the beginning of 2015.

Valneva estimates that the total market potential for prophylactic *C. difficile* products may exceed USD 1 billion annually.

About Clostridium Difficile

C. difficile is a bacterium that causes diarrhea and sometimes can lead to serious intestinal conditions or complications. 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[3]. Beyond the substantial morbidity and mortality, CDI is associated with significant economic burden

[2] *Four-fold increase of IgG from baseline*

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

due to prolongation of hospitalization, estimated at approximately USD 5 billion for U.S. acute care facilities alone[4].
C. difficile rarely causes infections in healthy persons, but if the gut microflora is disrupted by antibiotic treatment, the bacteria can overgrow the gut and release toxins, leading to symptoms of *Clostridium Difficile* Infection (CDI). CDI can be a significant threat for patients, especially those of advanced age with underlying conditions.
Most often, *C. difficile* is acquired in healthcare settings: it is the single most common pathogen of acute healthcare-associated infections in the U.S.[5] However, about one third of cases are acquired outside healthcare settings, indicating need for prevention beyond the hospital[6].
Currently, no vaccine against *C. difficile* exists, and antibiotic treatment of the established disease has significant limitations with recurrence in ~20% of cases[7]. The incidence of nosocomial infections is steadily increasing due to the growing number of medical interventions.
Valneva aims at developing a vaccine for the prevention of primary *C. difficile* infection using an age-and risk-based vaccination approach, in persons of advanced age with upcoming hospitalizations or underlying chronic conditions, and eventually for community-wide prophylaxis on an age-based vaccination strategy.

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: one for the prevention of Japanese Encephalitis (IXIARO®) and the second (DUKORAL®) indicated for the prevention of cholera and, in some countries, prevention of diarrhea caused by ETEC (*Enterotoxigenic Escherichia coli)*. The Company has proprietary vaccines in development including candidates against *Pseudomonas aeruginosa*, *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 incorporated in Lyon, France, listed on Euronext-Paris and the Vienna stock exchange and has operations in France, Austria, Scotland and Sweden with approximately 400 employees. More information is available at www.valneva.com.

[4] *Dubberke ER, Clinical Infectious Diseases 55, no. suppl 2 (2012): S88-S92.*
[5] *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*
[6] *Lessa et al, Burden of Clostridium difficile Infection in the United States. N Engl J Med 2015;372:825-34*
[7] *Lessa et al, Clostridium difficile infection. N Engl J Med 2015;372:1539-48).*

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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.