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Valneva Reports Further Positive Results for Its Chikungunya Vaccine Candidate

Phase 1 unblinded results up to month 7 showed an excellent immunogenicity and safety profile confirming Valneva´s unique, single-shot vaccine candidate.

These results strongly support further development acceleration

- **VLA1553 was generally safe in all dose groups**
  - **Well-tolerated in the low and medium dose. (Superior safety profile, including viremia, compared to the high dose group)**
  - **Excellent local tolerability**
- **Excellent immunogenicity profile in all dose groups after a single vaccination**
  - **100% Seroconversion[1] achieved at Day 14 after a single vaccination in all dose groups**
  - **Sustained at 100% after six months**

Saint Herblain (France), May 22, 2019 – Valneva SE ("Valneva" or "the Company"), a biotech company developing and commercializing vaccines for infectious diseases with major unmet medical needs, today announced further positive Phase 1 results for its chikungunya vaccine candidate, VLA1553.

The objectives of VLA1553-101 Phase 1 study were to assess the overall safety and immunogenicity profile after a single vaccination across three dose levels.
Today´s analysis (Part B) of the ongoing study includes the overall safety and immunogenicity results up to Month 7, unblinded on a group level and including first results from the "intrinsic human viral challenge".

VLA1553 was generally safe in all dose groups. The low and medium dose groups were well tolerated and showed a superior safety profile, including viremia, compared to the high dose.
No adverse events of special interest (e.g. chikungunya infection related) were reported up to month 7 and the product candidate´s local tolerability profile was excellent.

The results showed an excellent immunogenicity profile in all vaccinated dose groups after a single vaccination with a 100% Seroconversion[1] achieved at Day 14 after a single vaccination in all dose groups and fully sustained at 100% at Month 6.

A subset of study subjects were re-vaccinated after 6 months. For those subjects there was no anamnestic response observed which demonstrates that a single vaccination of VLA1553 is

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[1] *Seroconversion is defined as the proportion of subjects achieving a CHIKV-specific neutralizing antibody titer of* NT_{50} *≥20.*

sufficient to induce sustaining, high titer, neutralizing antibodies. Vaccinees were protected from vaccine induced viremia serving as “intrinsic human viral challenge“.

Wolfgang Bender, M.D., Ph.D., Chief Medical Officer of Valneva commented, “We are thrilled about these exciting results confirming that we have identified a highly immunogenic and safe final product candidate which we now aim to progress into pivotal trials as quickly as possible. In addition and as hoped, the data indicate that vaccinated subjects are protected from chikungunya viremia. This marks a very important milestone getting us a step closer to a highly competitively differentiated vaccine addressing a serious threat to public health.”

Valneva is committed to advancing its chikungunya vaccine candidate as quickly as possible and expects to be in a position to announce a plan, agreed with regulators, to licensure for its FDA fast tracked candidate VLA1553 at its planned R&D investor day, July 9th in New York (details to be announced at a later point in time)

About The Phase 1 Clinical Study VLA1553-101
This study is a randomized, observer-blinded, multicenter, dose-escalation Phase 1 clinical study investigating three dose levels of VLA1553 after a single immunization.
The study enrolled 120 healthy volunteers, 18 to 45 years of age, in the United States. Subjects were randomized in three different study groups to receive one of three dose levels (30 subjects in the low and medium and 60 subjects in the high dose group).
The protocol includes a re-vaccination at Month 6 or Month 12 to confirm that a single vaccination will be sufficient to induce high titer neutralizing antibodies and protect subjects from Chikungunya viremia (intrinsic viral challenge).
Study participants will be followed up until 13 months after initial vaccination.
An independent Drug Safety Monitoring Board (DSMB) continuously oversees the study and reviews data.
Additional information, including a detailed description of the study design, eligibility criteria and investigator sites, is available at ClinicalTrials.gov (NCT03382964).

About Chikungunya
Chikungunya is a mosquito-borne viral disease caused by the Chikungunya virus (CHIKV), a *Togaviridae* virus, transmitted by *Aedes* mosquitoes. Clinical symptoms include acute onset of fever, debilitating joint and muscle pain, headache, nausea and rash, potentially developing into long-term, serious health impairments. Chikungunya virus causes clinical illness in 72-92% of infected humans around 4 to 7 days after an infected mosquito bite. Complications resulting from the disease include visual, neurological, heart and gastrointestinal manifestations; fatalities have been reported (case fatality rates of 0.1% to 4.9% from epidemics)[2] in elderly patients at higher risk. Chikungunya outbreaks have been reported in Asia, Africa, the Americas and recently (2017) in Europe. As of 2017, there have been more than one million reported cases in the Americas[3] and the economic impact is considered to be significant (e.g. Colombia outbreak 2014: $73.6m[4]). The medical and economic burden is expected to grow as the CHIKV primary mosquito vectors continue to further spread geographically. There are no preventive vaccines

[2] *WHO, PAHO*
[3] *PAHO/WHO data: Number of reported cases of Chikungunya Fever in the Americas – EW 51 (December 22, 2017)*
[4] *Cardona-Ospina et al., Trans R Soc Trip Med Hyg 2015*

or effective treatments available and, as such, Chikungunya is considered to be a major public health threat.

About VLA1553

VLA1553 is a monovalent, single dose, live-attenuated vaccine candidate for protection against Chikungunya and was granted Fast Track designation by the U.S. Food and Drug Administration (FDA) in December 2018[5]. The vaccine candidate is designed for prophylactic, active, single-dose immunization against Chikungunya in humans over one year old. The vaccine targets long-lasting protection and an anticipated safety profile similar to licensed vaccines for active immunization in adults and children. The target population segments are travelers, military personnel and individuals at risk living in endemic regions. The global market for vaccines against Chikungunya is estimated at up to €500 million annually[6].

VLA1553 is based on an infectious clone (CHIKV LR2006-OPY1) attenuated by deleting a major part of the gene encoding the non-structural replicase complex protein nsP3, aiming for protection against various Chikungunya virus outbreak phylogroups and strains[7].

In pre-clinical development, a single-vaccine shot was shown to be highly immunogenic in vaccinated Non-Human Primates (NHP) (*cynomolgus* macaques) and showed no signs of viremia after challenge[8]. In NHPs, VLA1553 induced a strong, long lasting (more than 300 days) neutralizing antibody response comparable to wild-type CHIKV infections, combined with a good safety profile.

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

[5] *Valneva PR: Valneva Awarded FDA Fast Track Designation for Chikungunya vaccine candidate*
[6] *Company estimate support by an independent market study*
[7] *Hallengärd et al. 2013 J. Virology 88: 2858-2866*
[8] *Roques et al. 2017JCI Insight 2 (6): e83527*

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.