AELIX Therapeutics presents positive results from randomized placebo-controlled phase IIa therapeutic HIV vaccine and immune modulator combination clinical trial

- **Investigational AELIX HTI vaccine in combination with Gilead's investigational Toll-Like Receptor 7 (TLR7) agonist, vesatolimod, enabled an extended period without antiretroviral treatment (ART) in people with HIV on antiretroviral therapy**
- **Robust levels of HTI-specific T-cell immunity were observed following vaccination with HTI and vesatolimod treatment**
- **Vaccinees with a high viral reservoir were able to reach 24 weeks without ART; in contrast, all placebo participants with a high viral reservoir initiated ART within the first 12 weeks**
- **These data support the continued evaluation of HTI in investigational combination cure regimens**

Barcelona, Spain, February 21, 2023 – AELIX Therapeutics S.L. ('AELIX'), a clinical-stage biotechnology company specialized in the discovery and development of immunotherapies for HIV infection, today announced positive topline results from the AELIX-003 trial.

The study evaluated the safety, tolerability, immunogenicity and efficacy of AELIX's HTI T-cell therapeutic HIV vaccine in combination with Gilead's investigational Toll-Like Receptor 7 (TLR7) agonist, vesatolimod (VES), in people with HIV on antiretroviral therapy. VES is an immune modulator being evaluated as part of an investigational combination regimen that could potentially lead to viral remission.

The results of the trial were presented today at the 2023 Conference on Retroviruses and Opportunistic Infections (CROI).

The study met its primary and secondary endpoints for safety, tolerability and immunogenicity. The trial also evaluated the efficacy of HTI vaccines in combination with VES to avoid, delay or contain viral rebound compared to a placebo group. For this evaluation, participants underwent an analytical treatment interruption (ATI) in their antiretroviral therapy (ART) for up to 24 weeks. During this time, plasma viral load was monitored weekly.

The data show that a higher proportion of HTI+VES-treated participants remained off ART for the full 24 weeks. The combination of the HTI vaccine and VES as part of an HIV cure strategy in early treated people with HIV was safe and well tolerated.

Preliminary immune data suggest that HTI vaccines given in combination with VES induce high levels of HTI-specific T-cell responses; VES consistently induced pharmacodynamic response over multiple doses in combination therapy with the HTI vaccine. A lower pre-intervention reservoir was associated with better viral outcomes during the ATI, but only in the placebo group. The magnitude and breadth of vaccine response correlated with better viral outcomes. Importantly, HTI vaccines were highly immunogenic in a simpler regimen than in previous AELIX-002 study, and the vaccine-induced responses were associated with higher time off ART, supporting the contribution of the HTI vaccines to better viral control.

"These encouraging efficacy data demonstrate that the HTI vaccine in combination with VES may be able to modulate an individual's HIV-specific immune response in a way that can potentially contribute to a better HIV control in the absence of ongoing ART. The AELIX-003 data are exciting, and confirm what we have seen in the AELIX-002 study, where the HTI vaccine alone also extended the time off ART for the vaccinated participants," **said Dr. Christian Brander, Chief Scientific Officer of AELIX.** *"The HTI vaccine is aimed at refocusing the immune response to especially vulnerable sites in HIV. The vaccine contains antigenic regions of HIV that are more commonly targeted by individuals who naturally control the virus. Maintenance of viral remission without ART represents the next frontier in HIV infection treatment and an important step towards HIV eradication."*

About the AELIX-003 clinical trial

AELIX-003 (NCT04364035) was a randomized, multi-center, placebo-controlled trial to evaluate the safety, immunogenicity, and antiviral efficacy of the MVA.HTI (M)/ChAdOx1.HTI (C) vaccines and VES 6 mg in early-treated PLWH. Participants on ART were randomized 2:1 to active placebo treatment. During a 24-week ATI, plasma viral load (pVL) was monitored weekly, and ART was resumed if pVL >100,000 copies/mL (c/mL), or >10,000 c/mL for eight consecutive weeks, and/or CD4<350 cells/μL. Key results include:

- 50 participants enrolled into the study and 47 entered the ATI period (CCMM+VES (n=30) or placebo (n=17).
- HTI immunizations and VES were well-tolerated with one unrelated SAE.
- Currently available immune data demonstrated strong HTI-focused T-cell immunogenicity after vaccination.
- The proportion of CCMM+VES participants who remained off ART for 24 weeks was 33% (10/30) compared to 24% (4/17) of placebo participants.
- VES increased the production of circulating antiviral cytokines and chemokines.

"The AELIX-003 data are exciting, and confirm what we have seen in the AELIX-002 study, where the HTI vaccine alone also extended the time off-ART for the vaccinated participants. Both AELIX's HIV cure studies (AELIX-002 and AELIX-003) have shown that the HTI vaccines have the potential to enhance immune control. It is clear that they should be considered as a backbone for future HIV cure eradication trials," **said Dr. José Ramon Arribas, AELIX-003 Coordinating Investigator, Hospital Universitario La Paz, CIBERINFEC, Madrid, Spain.**

About the HTI immunogen

The HTI immunogen was designed at IrsiCaixa by Dr. Christian Brander, CSO at AELIX and Head of the IrsiCaixa Host Genetics and Cellular Immunity Group, and his colleagues. It is based on the observation that T-cell responses to certain parts of HIV are enriched in individuals with a non-progressor clinical phenotype. The HTI immunogen combines these regions in a vaccine immunogen.

The HTI sequence design is driven by functional immune data from close to 1,000 individuals from four different cohorts on three continents (Mothe et al. 2011). It does not rely solely on sequence conservation, density of HLA binding motifs or gene expression levels and kinetics as other vaccine candidates do. The predictive power of HTI directed T-cell responses on in vivo

virus control has been validated in unrelated cohorts and through sub-studies in samples from earlier vaccine trials, including the STEP trial.

About AELIX Therapeutics

AELIX, a clinical-stage biotechnology company based in Barcelona, Spain, is focused on the development of a therapeutic HIV vaccine to be included in cure/eradication strategies. AELIX is a spin-off of HIVACAT, the Catalan public-private consortium conducting cutting-edge research in the HIV vaccine field, and the support of Fundació Glòria Soler. AELIX holds a worldwide, exclusive license for the development and commercialization of the HTI immunogen. The company is backed by a syndicate of experienced Spanish and international investors including Ysios Capital, Caixa Capital Risc, 10K Lakes Capital, and the Centro para el Desarrollo Tecnológico e Industrial (CDTI).

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