AELIX Therapeutics presents positive results from randomized placebo-controlled phase I/IIa therapeutic HIV vaccine clinical trial

- **Investigational AELIX HTI vaccine leads to prolonged period without antiretroviral treatment (ART)**
- **Vaccine-induced immune T cell responses significantly correlate with prolonged time off ART**
- **Results support development of combination strategies based on HTI vaccine to control HIV - without the need for ongoing antiretroviral medication**

Barcelona, Spain, March 10, 2021 - AELIX Therapeutics S.L. ('AELIX'), a clinical-stage biotechnology company specialized in the discovery and development of immunotherapies for HIV infection, today announces positive topline results in the AELIX-002 trial. The study evaluated the safety, tolerability, immunogenicity and efficacy of AELIX's HTI T-cell therapeutic HIV vaccine, within early-treated people living with HIV. The results of the trial were presented today at the 2021 Conference on Retroviruses and Opportunistic Infections (CROI) – abstract link.

The study met its primary and secondary endpoints for safety, tolerability and immunogenicity. The trial also evaluated the efficacy of HTI vaccines 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 a higher proportion of participants off ART in the treated group. This signal is strongest among participants without a favorable genetic background, i.e. participants without specific HLA class I alleles, which have been associated with spontaneous control of HIV. In these participants, 8 (40%) vaccinated participants were able to remain off ART treatment for over 22 weeks, compared to only 1 (8%) in the placebo group.

Strong data supporting a breakthrough development in the field

"These encouraging efficacy data demonstrate that the HTI vaccine was able to modulate an individual's HIV-specific immune response, in a way that can contribute to a better HIV control in the absence of ongoing antiretroviral therapy," said Dr Beatriz Mothe, principal investigator of the study at Fundació Lluita contra la Sida i les Malalties Infeccioses (FLS) and associate researcher at the IrsiCaixa AIDS Research Institute, located at the Hospital Germans Trias i Pujol, in Badalona, Spain.

"We wish to express our deep gratitude to all the participants for their altruism and commitment to this long clinical trial, as well as to our colleagues at FLS, IrsiCaixa and BCN-Checkpoint, especially for their courage in finalizing the study under the stressful conditions of the COVID-19 pandemic," said Dr José Moltó, subinvestigator at FLS. "Their collective effort has been rewarded with this important milestone towards improving health care for people living with HIV."

The AELIX-002 study was a randomized, single-center, double-blind and placebo-controlled trial to evaluate the safety, tolerability, immunogenicity and antiviral effect of AELIX's therapeutic HIV vaccine - after discontinuation of ART in 45 early-treated people living with HIV (PLWH). The vaccine used in the study included a DNA vector (DNA.HTI -

D), a Modified Vaccinia Ankara virus vector (MVA.HTI - M) and an adenoviral vaccine vector (ChAdOx1.HTI - C). Participants were randomized (2:1) to receive heterologous prime-boost vaccination regimens consisting of DDDMM followed by CCM, or matched placebo (P), followed by a 24-week ATI.

Key results of the AELIX-002 Phase I/IIa trial include:

- A total of 45 participants received DDDMM (n=30) or PPPPP (n=15). Of the 45 participants, 41 further completed the CCM (n=26) or PPP (n=15) regimen and entered the ATI
- Immunizations were well tolerated, with neither unexpected nor related serious adverse events (SAEs), and were immunogenic in 97% of vaccine recipients (defined by a >2-fold increase in HTI-specific T cell responses compared to baseline)
- For participants without beneficial HLA class I alleles (32 of the 41); 8 of the 20 vaccinees (40%) versus 1 (8%) of the 12 placebo recipients were able to remain off ART for 22 weeks (Δ 32%, 80% CI [7.6; 55.7]); with pVL <2,000 copies/mL being observed in 5 vaccine and 1 placebo recipient, respectively
- Magnitude of HTI-specific responses at the time of ATI start correlated with time off ART in vaccinees (Rho 0.65, $p<0.01$)

"The HTI vaccine is aimed at refocusing the immune response to especially vulnerable sites in HIV. The vaccine contains antigenic regions of HIV such as the ones that are more commonly targeted by individuals who naturally control the virus," said Dr Christian Brander, chief scientific officer at AELIX. "Maintenance of viral remission without antiretroviral therapy represents the next frontier in HIV infection treatment."

"The AELIX-002 data are super exciting, this is the first time we have seen this impact on viral replication. I think the study has convincingly shown that the HTI vaccines can generate immune control; it is clear that they should be considered as a backbone for future HIV cure eradication trials," said Prof Sharon Lewin, director of the Peter Doherty Institute for Infection and Immunity (Melbourne, Australia) and professor of medicine at the University of Melbourne.

Results support AELIX's plans for larger combination trials and financing round

"With these promising data, AELIX's first-in-class HTI lead candidate could be a game-changer in HIV cure strategies," said Dr José Luis Cabero, CEO of AELIX. "Developing a cure for HIV is a global priority. An intervention that can immunologically control the virus would be of great interest to individuals living with HIV and to the HIV research community. We have shown for the first time that a T-cell vaccine can help control HIV. This supports our vision to position HTI as the backbone for future cure strategies, where it can be combined with other agents. In this sense, AELIX is a front-runner in the race to achieve a 'functional cure', or long-term viral suppression in the absence of ART, for people living with HIV. We are looking forward to moving ahead with the next financing round and working on larger combination trials."

The AELIX-002 study was conducted in the context of a clinical collaboration agreement between AELIX and Gilead Sciences. HTI-based vaccines as a component of combination cure regimens are being evaluated in the ongoing AELIX-003 clinical trial testing HTI in combination with Gilead's investigational TLR7 agonist vesatolimod (NCT04364035), in people living with HIV on ART.

Further details on AELIX-002: 'Safety and Immunogenicity Study of DNA.HTI, MVA.HTI and ChAdOx1.HTI in HIV-1-positive Patients' (NCT 03204617) can be found here.

About the HTI immunogen

The HTI immunogen was designed by Dr Christian Brander, chief scientific officer at AELIX Therapeutics 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. 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. Preclinical data shows that immunization with HTI in mice and macaques elicits strong and broad T-cell responses (Mothe *et al.* 2015).

About AELIX Therapeutics

AELIX Therapeutics is a clinical-stage biotechnology company based in Barcelona, Spain. It is focused on the development of a therapeutic HIV vaccine to be included in cure/eradication strategies. AELIX Therapeutics is a spin-off of HIVACAT, the Catalan public-private consortium conducting cutting-edge research in this field. 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.
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