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### PEPTIDES AND THEIR DERIVATIVES

### INHIBITING EXTRACELLULAR RELEASE OF HIV-1 TAT PROTEIN AND HIV-1 REPLICATION

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**Summary:** the present invention relates to the medical and pharmacological field, in particular to the treatment of HIV/AIDS infection. The patent relates specifically to the discovery that certain peptides can target one of the HIV-1 proteins, Tat, and block its function. This discovery can lead to the development of innovative compounds blocking HIV-1 replication and HIV disease progression.

**Background of the invention:** in the AIDS therapy field, the introduction of highly active antiretroviral therapy (HAART) has dramatically changed the natural history of infection, transforming a lethal disease into a chronic one. HAART, however, is fraught with at least two major problems: on one hand, it appears unable to eradicate infection, while on the other, it has major toxicity problems that often determine poor compliance to therapy in patients. In addition, the emergence of viral escape mutants resistant to multiple drugs is often reported in patients treated for prolonged periods of time with HAART. Developing an innovative therapeutic strategy with an essential viral protein such as Tat, which acts both inside and outside the cells, thus appears an extremely attractive target. The Tat protein acts as an essential activator of viral gene expression and replication. Furthermore, since Tat is released outside the infected cells, mounting evidence indicates that it might be one of the determinants of HIV-1 disease pathogenesis, including the progressive development of immunodeficiency and the specific toxic damage to the brain in the course of AIDS-associated neuropathy, a very frequent condition that accompanies HIV-1 infection. In light of these considerations, the development of drugs able to block Tat function and extracellular Tat release appears highly desirable. To date, no drug has been developed to target HIV-1 Tat.

**Description of the invention:** the patent is based on the discovery that, in order to exit the infected cells, Tat binds a specific region of the cellular Na,K-ATPase membrane pump. Peptides, peptidomimetics or small molecules targeting this interaction prevent Tat release and might block Tat transcriptional activity, thus inhibiting HIV-1 replication and AIDS development.

**Applications/Suggested use:** the main application of this patent consists in the development of a novel class of compounds blocking HIV-1 replication and/or interfering with AIDS disease development by targeting the HIV-1 Tat protein.

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\*The patent is jointly owned with Scuola Normale Superiore di Pisa in the ratio ICGEB 80%, SNS 20%, and as per joint ownership agreement ICGEB is the commercializing agent.