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Targeting RNA binding proteins: A versatile platform for the discovery and development of new antivirals

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ABX464 is a first-in-class, novel, small molecule inhibiting HIV replication through an entirely new mechanism of action. For the first time in the treatment of HIV, this molecule could reduce or eliminate the viral reservoirs, and thus potentially deliver a long lasting reduction in the viral load of HIV-patients., ABIVAX designed ABX464 with the goal of targeting the viral reservoirs of immune cells with integrated genetic material from the HIV-virus. These reservoirs are not affected by current antiretroviral therapies, and lead to viral load rebound once treatment is stopped. ABX464 inhibits the biogenesis of viral RNA required for the replication of the HIV virus by targeting the Cap Binding Complex (CBC). During replication HIV RNA is first spliced to give rise to spliced RNA from which essential auxiliary proteins, like Rev and Tat proteins, are synthesized but later during infection unsliced viral RNA are produced to generate structural protein and viral genome. ABX464 by stabilizing CBC complex on HIV RNA prevent the synthesis of unspliced RNA.

This unique mode of action and the preclinical data to-date suggest that ABX464 has the potential to:

Reduce or eliminate the viral reservoirs in patients with HIV

Induce long term control of the viral load

Prevent the emergence of HIV mutants that are resistant to treatment

Be less frequently administered over a shorter period than standard treatments

Reduce healthcare costs and offer broader access to treatment.

ABX464 is the first candidate molecule coming from ABIVAX's proprietary antiviral platform and chemical library. This library of more than one thousand small molecules targets the formation of RNP's in the nucleus or the cytoplasm of the infected cell during viral infection. Indeed, to replicate, viruses need to generate RNA-Protein complexes (RNP) from the host cell material. RNP complexes are composed of viral RNA and cellular and viral proteins. Those complexes can "hijack" the cellular machinery of the host cells to express viral RNA and generate new viruses. This approach can be applied to any type of viruses.

ABX311 is the second molecule coming from the ABIVAX antiviral platform. ABX311 is a small molecule able to inhibit Chikungunya viral replication in vitro with an IC50 in the nanomolar range. ABX311 will enter preclinical development Q4 2017.

Biography

Jamal Tazi is Professor of Functional Genomics at the University of Montpellier and Deputy Director of the Health Centre Biology "Rabelais" responsible for education and training. For 20 years, he led the team "messenger RNA metabolism in metazoans" within the Institute for Molecular Genetics in Montpellier (IGMM) where he made important contributions to understand the fundamental mechanisms of the expression of our genes and editing of their products. These discoveries are used today in the medical field through the development of a new therapy based on the use of small molecules to fight against viral infections. To ensure the transition between basic and applied research, and also to support these innovative projects to clinical stage, Hel founded in 2008 the company Splicos and established its partnership with public institutions as a cooperative laboratory where, he became the Scientific Director

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