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PRESS RELEASE

Biotech TheraVectys: first promising results on the treatment of chronic infection of the hepatitis B virus (HBV) in humans using lentiviral vectors

Hepatitis B remains a major global public health problem.

More than 250 million of individuals are chronically infected by the hepatitis B virus (HBV) globally and at risk of developing serious liver diseases, in particular cirrhosis and liver cancer. Although the treatment of this infection has been significantly improved by the new direct-acting antivirals such as entecavir and tenofovir, which are effective in stopping viral multiplication, the virus persists in the liver with the HBV covalently closed circular DNA (cccDNA) and the integrated genomes of HBV that produce the hepatitis B surface antigen (HBsAg). The detection and quantification of the HBsAg in the plasma of HBV carriers is therefore the mark of this viral persistence. However, if some new direct-acting antivirals can have certain effect in reducing HBsAg, their action is not sustainable because HBV specific T-cells in chronic carriers are inadequate for controlling the replication of HBV. Consequently, the discontinuation of antivirals leads in most cases to reactivation of viral multiplication, which implies a life-long treatment with potential side effects and a very high treatment cost, with only a partial reduction in the risk of serious hepatic complications.

New approaches must therefore be designed to complement strategies based on direct-acting antivirals by stimulating the host immune response to the virus and eliminating HBV infected liver cells. Several candidate therapies are being evaluated for this immunotherapy-based strategy, but none of them has so far given convincing results.

It is in this context that TheraVectys and its Chinese partner Jinwei Bio jointly presented to the American Association for the Study of the Liver Diseases (AASLD) on November 7, 2022 the very promising results of the use of lentiviral vectors in immunotherapy of chronic infection with HBV. A close collaboration between TheraVectys and Jinwei Bio has made it possible to develop a lenti-HBV viral vector capable of producing HBsAg and to stimulate the host immune response to HBsAg. An experimental model in mice has clearly demonstrated the capacity of such therapy to decrease the levels of serum HBsAg, even cause HBsAg-negative, as well as to reduce very significantly the quantity of residual HBV in the liver. The capacity of the lentiviral-HBV vector to break the immune tolerance (inhibition of the immune response) induced by the HBV has also been established.

Based on the exciting results of preclinical studies, TheraVectys and its partner Jinwei Bio initiated a collaboration with the Department of Infectious Diseases of Huashan Hospital, which supported Changzhi hospital in Changzhi hospital's exploratory studies in humans. The preliminary results obtained in patients chronically infected by HBV confirmed the

safety of the lenti-HBV protocol after a six-month follow-up. The results have also shown a significant and lasting reduction in HBsAg in the patients' serum, as well as the detection of the T-cell's immune response against the virus.

“Even if these results in human carriers must be extended, the effectiveness of this lentiviral strategy is strongly suggested. The approach of our lentiviral technology therefore appears as a major therapeutic possibility for the treatment of chronic infection with HBV”, underlines Christian Bréchet, medical director of TheraVectys.

The therapeutic results obtained in humans reported by TheraVectys are consistent with those obtained in mice. These results confirm that the use of lentiviral vectors has an enormous potential in the treatment of many indications.

About TheraVectys

The Biotech TheraVectys, specialized in immunotherapy, is based on more than 20 years of research on lentiviral vectors and provides an innovative technology in the field of vaccinology.

The research is conducted under the scientific direction of **Pierre CHARNEAU**, inventor and pioneer of the lentiviral technology, and **Laleh MAJLESSI**, research director in immunology within the Institut Pasteur-TheraVectys Joint Laboratory.

Christian BRECHOT, former General Director of Institut Pasteur and INSERM, is the Medical Director of TheraVectys.

The biotech's work is based on an exclusive platform delivering T-cell vaccines (cytotoxic cells) in response to critical unmet medical needs. The technology used is at a clinical stage.

TheraVectys holds an exclusive worldwide license on this technology from Institut Pasteur in the field of prophylactic and therapeutic vaccines against infectious diseases, cancers and cancers of viral origin.

TheraVectys' technology and its global authorization range involve many infectious diseases, cancers and cancers of viral origin, and are at the origin of a real revolution in the field of vaccination.

Our goal: To profoundly improve global health.

Our approach: To establish strategic industrial partnerships to take our vaccine candidates from proof-of-concept to clinical trials and commercialization.

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