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PRESS RELEASE

TheraVectys announces IND clearance from the US FDA enabling Phase 1 initiation for its therapeutic vaccine candidate Lenti-HPV-07 against oropharyngeal and cervical cancers.

- Targeting to initiate dosing of Phase 1 clinical trial in Q1 2024 to evaluate Lenti-HPV-07 in patients having oropharyngeal or cervical cancers induced by HPV16 or 18.

- The multicenter, open-label Phase 1 trial will evaluate the safety of ascending doses of Lenti-HPV-07 in 36 patients

- Lenti-HPV-07 preclinical profile and clinical development carried out by the Pasteur-TheraVectys joint laboratory were published in EMBO Molecular Medicine journal on September 7, 2023

On November 27, 2023, TheraVectys a lentiviral vector immunotherapy company focused on developing vaccine candidates to drive the widespread treatment and prevention of cancer and infectious diseases, today announced that the U.S. Food and Drug Administration (FDA) has completed its safety review of the Investigational New Drug (IND) application and concluded that TheraVectys'proposed clinical study may proceed to evaluate the onco-therapeutic vaccine Lenti-HPV-07 for the treatment of human papillomavirus (HPV)-induced cancers.

The lentiviral vector-based intramuscular vaccine candidate has already demonstrated 100% preclinical efficacy against HPV-induced cancers. The results of the pre-clinical development work carried out by the Pasteur-TheraVectys joint laboratory were published in EMBO Molecular Medicine journal on September 7, 2023, in an article entitled : "Full eradication of pre-clinical human papilloma virus-induced tumors by a lentiviral vaccine"
https://www.embopress.org/doi/full/10.15252/emmm.202317723

The clinical trial, scheduled to begin in the first quarter of 2024, will be conducted in the U.S. at four cancer centers, including Florida's Moffitt Cancer Institute.

The multicenter, open-label Phase 1 trial will evaluate the safety of ascending doses of Lenti-HPV-07 and determine its immunogenicity profile. It will include 36 patients with oropharyngeal or cervical cancers induced by HPV16 or 18. Group A will consist of patients with recurrent/metastatic cancers who have received multiple lines of treatment, including immunotherapies, and Group B of patients with newly diagnosed, treatment-naïve, locally advanced cancers. Patients in Group B will receive a single intramuscular injection of Lenti-

HPV-07, while those in Group A will receive two intramuscular injections one month apart. They will be monitored clinically and immunologically for one year.

HPV causes almost all cervical cancers, as well as many oropharyngeal and anogenital cancers. The currently available HPV vaccines essentially induce HPV-neutralizing antibodies, and thus prevent infection, but have no effect on established tumors.

Using its non-integrative lentiviral vector vaccine platform, the Institut Pasteur-TheraVectys Joint Laboratory has developed an onco-therapeutic HPV vaccine candidate capable of inducing strong cellular responses against the E6 and E7 antigens of HPV16 and HPV18.

A single intramuscular administration of Lenti-HPV-07 to mice bearing small, medium or large HPV-induced tumors triggers a long-term effector and memory cellular immune response, notably based on anti-tumor cytotoxic $CD8^+$ T cells, accompanied by profound modulation of the tumor microenvironment, **total tumor eradication and complete elimination of metastases in 100% of animals. Importantly, a single administration of Lenti-HPV-07 also prevents long-term tumor relapse.**

By comparison, the immunotherapeutic potential of mRNA-based vaccine technology demonstrated efficacy against very small HPV-induced tumors, with early relapse in almost 50% of treated animals (Ramos da Silva *et al*, 2023). **Conversely, in the preclinical study conducted by the Institut Pasteur - TheraVectys Joint Laboratory, Lenti-HPV-07 immune therapy was active on large tumors, which are notoriously more difficult to control, demonstrating the superior efficacy of the lentiviral based vaccine platform.**

In addition, Lenti-HPV-07 oncotherapy can act synergistically with other immunotherapies, such as treatments with immune checkpoint inhibitors like anti-PD1 (Programmed cell death protein-1) antibodies. Lenti-HPV-07 therapy is emerging as a promising immuno-oncotherapy for HPV-induced tumors.

About TheraVectys

TheraVectys, with more than 20 years of research into lentiviral vectors, brings innovative technologies to the fields of immunotherapies and vaccinology.
Researches are conducted under the scientific leadership of **Pierre CHARNEAU**, inventor and pioneer of breakthrough lentiviral technologies (for which he received a prize from the French “Académie des Sciences” in 2004) and **Laleh MAJLESSI**, Research Director in Immunology, at the Institut Pasteur-TheraVectys Joint Laboratory.
Christian BRECHOT, the former Director General of Institut Pasteur and INSERM, is the Medical Director of TheraVectys.
Estelle BESSON, Director of Clinical Operations, coordinated and supervised all preparatory works required to obtain FDA approval, including vaccine production, pre-clinical studies, preparation of IND filing, in collaboration with TheraVectys' partners.
The biotech's work is based on a proprietary platform to deliver T-cell vaccines in response to critical unmet medical needs.
TheraVectys' technology, with its worldwide patents and licenses, is driving a silent revolution in prophylactic and therapeutic vaccination against infectious diseases and cancer.

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