Press release
Nantes, June 9th, 2022

#immunosuppressant #transplantation #LIS1

Safety and efficacy results of LIS1, a new induction treatment in organ transplantation by the French biotech XENOTHERA

Results from the clinical trial of LIS1, XENOTHERA's polyclonal glyco-humanised antibody and induction immunosuppressant in solid organ transplantation, were presented at the American Transplant Congress (ATC) (ATC) held in Boston (USA) from 4 to 8 June 2022.

At the American Transplant Congress, Professor Ondrej Viklicky from the IKEM Institute - one of Europe's leading kidney transplant centers for several decades (Prague, Czech Republic) - principal investigator of the NCT04431219 trial, presented the first results of the LIS1 Phase I/II First In Human (FIH) clinical trial, which ran from September 5, 2019 to March 28, 2022 (last patient visit).

The clinical trial of the transplant dedicated immunosuppressant LIS1 consisted of two cohorts of first-time kidney transplant patients with limited immunological risk who received 5 consecutive administrations of LIS1 starting the day after transplantation. The AD[1] cohort of 5 patients received escalating doses of LIS1 ranging from 0.6 to 8 mg/kg. The TD[2] cohort of 5 patients received therapeutic doses of LIS1.

The primary endpoint was product safety, LIS1 was well tolerated. The majority of adverse events were mild or moderate, and all recovered.
All ten patients, 4 females and 6 males, recovered their renal function within the usual time frame after transplantation. No side effects such as leucopenia or thrombocytopenia were observed. In total, the study results of this trial provide **a reassuring global safety profile for LIS1.**

In parallel, the first pharmacokinetic and pharmacodynamic results are promising. Pharmacokinetic analyses showed a long half-life and no anti-drug antibodies (ADA[3]) were detected. The pharmacodynamics show a unique new mechanism of action, combining lymphocyte depletion and inhibition of alloreactivity, which gives **LIS1 a promising status as a new induction treatment in solid organ transplantation**.

XENOTHERA is the sponsor of **the first human clinical study of LIS1, a product issued from its glyco-humanized antibody platform, indicated for the prevention of acute rejection in transplantation**.

[1] Ascending Dose
[2] Therapeutic Dose
[3] Anti-Drug Antibodies

"This is a major milestone for XENOTHERA and for the entire team. It has been almost eight years since the company was born, and today we are reaping the fruits of our research. This is excellent news for the Nantes ecosystem, and I am thinking of the Transplantation and Immunology Research Center, which is the cradle of the LIS1 technology, and of the entire ecosystem, namely Atlanpole, which incubated the company in its early days. Transplantation is a major public health issue, and these encouraging results show that XENOTHERA might bring innovation to patients either transplanted or in waiting lists, which is something we would be extremely proud of," comments **Odile Duvaux, CEO and co-founder of XENOTHERA.**

The induction therapies available today have either safety issues or efficacy limitations. LIS1 aims to **combine better efficacy than anti-IL2Rs and better safety than conventional depleting agents, the two main types of induction therapy in transplantation**. As such, this treatment might be considered by transplanters who are facing the risk of toxicity of depleting agents used in induction, particularly the increased risk of infection in the first year after transplantation.
LIS1, through the controlled depletion allowed, will provide transplant patients with **a gain in comfort of life, while providing them with the same effectiveness in preventing acute graft rejection**.

The biotech is preparing the next phase of LIS1's clinical development, with **a confirmatory trial (phase II/III) planned for 2023** and to be conducted in several transplant centers in Europe and the United States.

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About solid organ transplantation:
There are 130,000 solid organ transplants per year, including 36,000 in the US and 23,000 in France, with an annual growth rate of 3%. The demand is constantly increasing, especially in emerging countries, particularly in China. The ageing of the population and the increase in chronic diseases are impacting the demand for transplants. In France, 12,500 people are on the waiting list. 50% of kidney transplants are rejected after 15 years, and this period is reduced to 8 years for lung transplants.

About LIS1:
LIS1 is one of the innovative immunotherapy approaches developed by XENOTHERA, based on technology from INSERM and the University of Nantes. This polyclonal depleting antibody is potentially aimed at the 130,000 people who receive solid organ transplants each year and at a market estimated at over one billion dollars. This new induction therapy for LIS1 transplantation is an intravenous solution administered immediately after transplantation.

About XENOTHERA:
Founded in 2014, XENOTHERA is a Nantes-based biotech that develops new therapeutic modes in many fields (immunology, oncology, viral infections...). The company develops treatments based on a unique proprietary technology for the production of "glyco-humanised" polyclonal antibodies. Its technological platform is built on a dual expertise in genetics and immunology.
The biotech has a complete portfolio of products, including three products in the clinic: LIS1, an immunosuppressant for solid organ transplantation; XAV-19, an anti-Covid treatment for patients with moderate disease; and XAB05, which entered the clinic ((phase I trial) in January 2022 and is intended for the prevention and treatment of multi-drug resistant bacterial infections.
XENOTHERA, a member of the Atlanpole Biotherapies competitiveness cluster, is part of the scientific and medical environment of the Pays de la Loire (France). The company has been supported since its creation by private investors, by the Pays de la Loire Region, by BPI France and by the European EIC Fund.
More information: www.xenothera.com
Follow XENOTHERA on social networks: LinkedIn Twitter

Media Relations:
IZsoGOOD
Ingrid Zémor
+33 6 73 72 99 92
xenothera@izsogood.co