

Interim late-breaking clinical data validate not-alpha profile of THOR-707 (SAR444245), Sanofi's novel investigational IL-2

- * Early clinical results are consistent with preclinical studies and suggest THOR-707 (SAR444245) may promote an anti-tumor immune response without alpha-mediated side effects, both alone and in combination with anti-PD-1
- * THOR-707, a precisely PEGylated, engineered version of IL-2 built on Sanofi's Synthorin™ technology platform, is being studied in a trial of adults with advanced or metastatic solid tumors

PARIS – April 9, 2021 – Interim data from a first-in-human trial evaluating the safety, therapeutic activity and maximum tolerable dose of THOR-707 (SAR444245), a highly differentiated not-alpha interleukin-2 (IL-2) candidate, as a monotherapy and in combination with anti-PD-1, will be presented Saturday, April 10 as a late-breaking poster presentation at the American Association for Cancer Research (AACR) Annual Meeting. The Saturday late-breaking poster session will include additional updated data.

Interim safety, anti-tumor activity and biomarker data further validate the not-alpha IL-2 profile seen preclinically. In both the combination and monotherapy settings, initial activity was observed, with three confirmed partial responses, which includes patients who have received prior anti-PD-1 therapeutics.

"THOR-707 has a potentially best-in-class profile and reinforces the promise of our Synthorin technology platform to overcome difficult targets with precision biology," said John Reed, M.D. Ph.D., Global Head of Research & Development, Sanofi. *"The activity observed both as single agent and with an anti-PD-1 further strengthens our belief that as a unique not-alpha IL-2, THOR-707 could become a backbone of future immunology therapies. We will continue to explore the molecule's potential for best-in-disease combinations."*

THOR-707 is a precisely PEGylated version of IL-2, where the PEG chain is attached to a novel amino acid inserted at a location on IL-2 that prevents it from engaging the alpha-receptor and binding to immune receptors that cause drug toxicities (IL-2R-alpha, CD25). The engineered IL-2 retains near-native binding to the beta-gamma receptors that selectively expand tumor-killing T effector cells and Natural Killer (NK) cells without the alpha-mediated immunosuppressive effects of regulatory T cells or eosinophil-mediated vascular leak syndrome.

Interim results indicate a similar pattern where CD8+ T cells and NK cells increased after the first dose of THOR-707 and sustained throughout the entire cycle, with a dose escalating effect; this effect was enhanced when combined with KEYTRUDA® (pembrolizumab). No significant increases in CD4+ regulatory T cells or eosinophils were observed, indicative of not-alpha IL-2 receptor selectivity.

No dose-limiting toxicities were observed for THOR-707 at reported doses, up to 24 µg/kg as monotherapy and 16 µg/kg in combination. The most common treatment emergent adverse events (TEAEs) following the first dose included flu-like symptoms, fever, vomiting/nausea and chills. Symptoms were transient and resolved with standard supportive care. Among G3-4 related toxicities was a transient decrease in lymphocyte count, which preceded T cell expansion.

No eosinophilia or vascular leak syndrome was reported at any doses tested. IL-5 levels remained at or below the lowest level of detection, suggesting a rationale for the lack of IL-5 associated toxicity observed during treatment.

“Novel approaches, such as not-alpha IL-2, seek to activate this powerful immune pathway while mitigating current challenges with dosing and safety to potentially expand the patient population who could benefit from treatment,” said Filip Janku, M.D. Ph.D., Associate Professor, Department of Investigational Cancer Therapeutics, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX. *“Preclinically, THOR-707 appeared to activate an anti-tumor immune response without an increased risk of alpha-mediated toxicities, such as eosinophilia or vascular leak syndrome. While early, the interim clinical data at AACR align very closely to what we saw in preclinical research and suggest further study of this not-alpha IL-2 molecule is warranted, both alone and in combination with a synergistic treatment such as anti-PD-1.”*

THOR-707 dose escalation has progressed beyond projected monotherapy RP2D of 24 µg/kg Q3W to 32 µg/kg Q3W to further characterize the upper bounds of the dose range.

In addition to testing THOR-707 in combination with KEYTRUDA, Sanofi is planning to evaluate the activity of this novel biologic in combination with other

anti-PD-1 antibodies, including Libtayo^{®1}, (cemiplimab) anti-CD38 antibody Sarclisa[®] (isatuximab) and anti-EGFR.

Editor's Note: Sanofi previously entered into an agreement with Merck & Co. Inc., Kenilworth, NJ, USA (known as MSD outside the U.S. and Canada) to conduct a Phase 2 trial evaluating THOR-707 combined with or in sequenced administration with KEYTRUDA.

About THOR-707 (SAR444245)

THOR-707 is a precisely PEGylated engineered version of IL-2 with an increased half-life being investigated for the treatment of many types of malignancies. Additionally, pharmacology is being assessed to determine if THOR-707 may allow for less frequent dosing. In pre-clinical experiments, THOR-707 exhibited the ability to induce the expansion of CD8+T-cells suggesting potential for anti-tumor effects both as single agent as well as in combination with an anti-PD-1 monoclonal antibody. THOR-707 is not approved by any regulatory authority.

THOR-707 is the first molecule from the Synthorin[™] technology platform. Synthorins are novel proteins built on Sanofi's unique Expanded Genetic Alphabet platform, which allows scientists to fill important gaps in protein therapeutics by vastly expanding the variety of building blocks available to bioengineers. Used on its own or in combination with other Sanofi technologies, the Expanded Genetic Alphabet platform is enabling the company's scientists and bioengineers to develop novel biologics for cancer and other diseases.

About Sanofi

Sanofi is dedicated to supporting people through their health challenges. We are a global biopharmaceutical company focused on human health. We prevent illness with vaccines, provide innovative treatments to fight pain and ease suffering. We stand by the few who suffer from rare diseases and the millions with long-term chronic conditions.

With more than 100,000 people in 100 countries, Sanofi is transforming scientific innovation into healthcare solutions around the globe.

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¹ Libtayo[®] is being jointly developed by Regeneron and Sanofi under a global collaboration agreement.

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