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Media Update

Positive results from the sutimlimab pivotal trial for people with cold agglutinin disease published in *New England Journal of Medicine*

- Data from the pivotal Phase 3 CARDINAL study demonstrated sutimlimab inhibited C1-activated hemolysis (abnormal destruction of healthy red blood cells) within one week of treatment and had a sustained treatment effect over the course of the study
- Sutimlimab met primary and secondary endpoints, which measured hemoglobin, bilirubin and fatigue
- Sutimlimab, a first-in-class investigational C1s inhibitor, has the potential to be the first approved treatment for hemolysis in adults with cold agglutinin disease, a serious and chronic autoimmune hemolytic anemia

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The *New England Journal of Medicine (NEJM)* today published the final results of Part A of the pivotal Phase 3 CARDINAL open label, single-arm study evaluating the safety and efficacy of sutimlimab for 26 weeks in people with primary cold agglutinin disease (CAD). Sutimlimab, a first-in-class investigational C1s inhibitor, met the primary and secondary endpoints in the study and demonstrated sustained inhibition of classical complement pathway mediated hemolysis with improvements in anemia within one week of treatment.

> *"The New England Journal of Medicine's publication of these pivotal results underscore the clear and clinically meaningful treatment effect of sutimlimab on classical complement pathway activation, which triggers chronic hemolysis and anemia experienced by people living with cold agglutinin disease,"* said principal investigator and author Alexander Röth, MD, Department of Hematology and Stem Cell Transplantation, West German Cancer Center, University Hospital, University of Duisburg-Essen, Germany. *"These results are promising because of patients' sustained response to sutimlimab over the duration of the study. Sutimlimab has the potential to address a major unmet medical need for people with cold agglutinin disease."*

CAD is a chronic autoimmune hemolytic anemia that causes the body's immune system to mistakenly attack healthy red blood cells and cause their rupture (hemolysis). CAD patients may experience chronic anemia, profound fatigue, acute hemolytic crisis, and other potential complications, including an increased risk of thromboembolic events and early

death.[1,2,3] CAD impacts the lives of an estimated 12,000 people in the U.S., Europe, and Japan.[4]

The *NEJM* publication of the Phase 3 Pivotal Study Results

The *NEJM* publication included efficacy and safety results from Part A of the Phase 3 CARDINAL study, a 26-week, open label, single arm study of patients with CAD (n=24) who had a recent history of blood transfusions. The study demonstrated sutimlimab met its pre-specified primary composite endpoint of an increase in hemoglobin ≥2 g/dL from baseline or reaching a hemoglobin level ≥12 g/dL at the 26-week treatment assessment timepoint; the absence of transfusions from Weeks 5 to 26; and patients were not allowed to receive other CAD-related treatment. In the study, 54 percent (n=13) of patients met the composite endpoint criteria with 62.5 percent (n=15) of patients achieving a hemoglobin ≥ 12 g/dL or an increase of at least 2 g/dL and 71 percent (n=17) of patients remaining transfusion-free after week 5.

Key secondary endpoints were also met and indicate improvements in hemoglobin and normalization of bilirubin. The study showed an overall mean increase in hemoglobin of 2.6 g/dL at treatment assessment timepoint. Hemoglobin improved with a mean increase from baseline of ≥2 g/dL by week 3. Mean hemoglobin levels were maintained at >11 g/dL (from a mean baseline 8.6 g/dL) after week 3, demonstrating a sustained effect throughout the remainder of the treatment period. Mean total bilirubin was 55 µmol/L (2.7-fold ULN) at baseline and 15 µmol/L (0.8-fold ULN) at the treatment assessment time point. The study also measured the Functional Assessment of Chronic Illness Therapy-Fatigue Score.

In the completed 26-week core treatment period (Part A) of the CARDINAL study, 22 of 24 patients (91.7%) experienced at least one treatment-emergent adverse event. The most common adverse events were increase in blood pressure and infusion-related reactions. Seven patients (29.2%) experienced at least one treatment-emergent serious adverse event (TESAE), including 2 patients (8.3%) that experienced at least one TESAE of infection and 1 death in a patient due to an unrelated event of hepatic cancer. There were no events of meningococcal infections reported, and no patients developed systemic lupus erythematosus. Following the completion of the Part A (26-week) treatment period of the CARDINAL study, eligible patients continue to receive sutimlimab in an on-going extension study for an additional 24 months (Part B) to evaluate the long-term safety and durability of response.

Sutimlimab, a targeted C1s inhibitor

Sutimlimab is an investigational, humanized monoclonal antibody that is designed to selectively target and inhibit C1s in the classical complement pathway, which is part of the innate immune system. By blocking C1s, sutimlimab inhibits the activation of the classical complement pathway with the goal of halting C1-activated hemolysis in CAD to prevent the abnormal destruction of healthy red blood cells. Sutimlimab, by selectively inhibiting classical pathway upstream at C1s, did not alter C1q levels and does not inhibit the lectin and alternative complement pathways.

Sutimlimab has been granted Breakthrough Therapy and Orphan Drug designations by the U.S. Food and Drug Administration (FDA). Sutimlimab is currently under clinical investigation and its safety and efficacy have not been reviewed by any regulatory authority.

1. Broome C, et al. Increased risk of thrombotic events in cold agglutinin disease: A 10-year retrospective analysis. *Res Pract Thromb Haemost*. 2020;00:1–8.
2. Quentin A. Hill, Rajeshwari Punekar, Jaime Morales Arias, Catherine M Broome, Jun Su; Mortality Among Patients with Cold Agglutinin Disease in the United States: An Electronic Health Record (EHR)-Based Analysis. *Blood* 2019; 134 (Supplement_1): 4790.
3. Lauren C. Bylsma, Anne Gulbech Ording, Adam Rosenthal, Buket Öztürk, Jon P. Fryzek, Jaime Morales Arias, Alexander Röth, Sigbjørn Berentsen; Occurrence, thromboembolic risk, and mortality in Danish patients with cold agglutinin disease. *Blood Adv* 2019; 3 (20): 2980–2985.
4. Berentsen S, et al. Haematologica. 2006;91(4):460-466

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

Sanofi, Empowering Life

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of such product candidates, the fact that product candidates if approved may not be commercially successful, the future approval and commercial success of therapeutic alternatives, Sanofi's ability to benefit from external growth opportunities, to complete related transactions and/or obtain regulatory clearances, risks associated with intellectual property and any related pending or future litigation and the ultimate outcome of such litigation, trends in exchange rates and prevailing interest rates, volatile economic and market conditions, cost containment initiatives and subsequent changes thereto, and the impact that COVID-19 will have on us, our customers, suppliers, vendors, and other business partners, and the financial condition of any one of them, as well as on our employees and on the global economy as a whole. Any material effect of COVID-19 on any of the foregoing could also adversely impact us. This situation is changing rapidly and additional impacts may arise of which we are not currently aware and may exacerbate other previously identified risks. The risks and uncertainties also include the uncertainties discussed or identified in the public filings with the SEC and the AMF made by Sanofi, including those listed under "Risk Factors" and "Cautionary Statement Regarding Forward-Looking Statements" in Sanofi's annual report on Form 20-F for the year ended December 31, 2020. Other than as required by applicable law, Sanofi does not undertake any obligation to update or revise any forward-looking information or statement-s.