

Positive results presented from pivotal Phase 3 trial of sutimlimab in people with cold agglutinin disease

- * Sutimlimab, a novel investigational C1s inhibitor, has the potential to be the first approved treatment for cold agglutinin disease, a serious, chronic, rare blood disorder
- * Results met the primary and secondary endpoints and demonstrated rapid inhibition of hemolysis and clinically significant improvements in anemia and fatigue within one week of treatment
- * U.S. FDA submission planned in the near future

PARIS – December 10, 2019 - A pivotal Phase 3 open-label, single-arm trial evaluating the safety and efficacy of sutimlimab in people with primary cold agglutinin disease (CAD) met its primary and secondary endpoints. These results were presented today at the Late-Breaking Abstracts Session of the 61st Annual Meeting of the American Society of Hematology in Orlando, FL.

Sutimlimab is the first investigational treatment designed to selectively target and inhibit C1s in the classical complement pathway, a part of the immune system that is responsible for activating the mechanism of hemolysis in CAD. It has the potential to be the first approved therapy for this rare autoimmune hemolytic anemia. Sanofi intends to submit a Biologics License Application for sutimlimab, for which it has received Breakthrough Therapy designation, to the US Food and Drug Administration in the near future.

“Cold agglutinin disease can be a debilitating condition, with many patients suffering from crippling fatigue and generally experiencing a poor quality of life,” says principal investigator and presenting author Alexander Röth, M.D., Department of Hematology, University Hospital, University of Duisburg-Essen, Germany. *“These positive data from the Phase 3 CARDINAL study provide clinically significant evidence that sutimlimab, by inhibiting hemolysis and improving anemia, has the potential to be an important new treatment for CAD and make a meaningful impact on patients’ lives.”*

The primary efficacy outcome was a responder rate based on a composite 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 and the absence of transfusions from Weeks 5 to 26, further, patients were not allowed to receive other CAD-related treatments. The secondary efficacy measures assessed improvement in key indicators of the disease process: hemoglobin, bilirubin (a measure of red blood cell destruction in CAD), Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue Score (a quality of life measure of fatigue), lactate dehydrogenase (LDH), and transfusion usage.

CARDINAL Phase 3 study data (final Part A) presented at the Late-Breaker Session at ASH

Twenty-four patients enrolled and received at least one dose of sutimlimab (mean age of 71.3 years). 62.5% of patients (n=15) had received ≥ 1 prior targeted therapy within the last 5 years. Two patients withdrew from the study early for reasons unrelated to study drug. All 22 patients who completed Part A of the study elected to continue sutimlimab in Part B, an ongoing safety and durability of response extension study.

Efficacy and Safety Data:

- The pre-specified primary endpoint was met. 54% (n=13) of patients met the composite endpoint criteria, with 62.5% (n=15) of patients achieving a hemoglobin ≥ 12 g/dL or an increase of at least 2 g/dL and 71% (n=17) of patients remaining transfusion-free after week 5.
- The study showed an overall mean increase in hemoglobin of 2.6 g/dL at treatment assessment timepoint; 83% (n=20) of the 24 patients enrolled achieved a clinically significant mean hemoglobin improvement of ≥ 1 g/dL.
- Hemoglobin improved rapidly, with a mean increase from baseline of ≥ 1 g/dL by week 1 and ≥ 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, a key marker of hemolysis in CAD, achieved near normalization after the first week of treatment (24.6 $\mu\text{mol/L}$; upper limit of reference range 20.5 $\mu\text{mol/L}$), with normalized bilirubin levels ($<$ upper limit of reference range) maintained from week 3 through the remainder of the study.
- Mean FACIT-Fatigue score demonstrated a clinically meaningful improvement in fatigue by week 1 of treatment with an increase of 7.2 points. The overall mean FACIT-Fatigue score increase from baseline at the 26-week treatment assessment timepoint was 10.9 points.
- 22 patients (91.7%) experienced at least 1 treatment-emergent adverse event.
- 7 patients (29.2%) experienced at least 1 treatment-emergent serious adverse event (TESAE) of which none were assessed by the investigator as related to sutimlimab.
- 2 patients (8.3%) experienced at least 1 TESAE of infection, of which none were assessed by the investigator as related to sutimlimab. No patient discontinued sutimlimab due to infection and there were no meningococcal infections identified.

“CAD is a disease in which the immune system attacks red blood cells and causes a cascade of symptoms for patients. In our study, sutimlimab achieved clinically meaningful results by impacting the central mechanism of CAD, bringing about marked improvements in patients’ hemolysis, anemia and fatigue,” said John Reed, M.D., Ph.D. Global Head of Research and Development at Sanofi. *“We are eager to share these results with regulatory authorities beginning with the U.S. FDA in the near*

future in an effort to provide patients with a first-in-class targeted therapy that we believe has the potential to change the treatment paradigm for CAD.”

Results from this trial will be submitted to regulatory authorities, starting with the U.S. Food and Drug Administration (FDA) in the near future. Sutimlimab has been granted Breakthrough Therapy designation by the U.S. Food and Drug Administration (FDA) and Orphan Drug status by the FDA, European Medicines Agency and the Pharmaceuticals and Medical Devices Agency in Japan. The efficacy and safety of sutimlimab has not been reviewed by any regulatory authority.

About the CARDINAL study

The CARDINAL trial is a pivotal, open-label, single-arm study to assess the efficacy and safety of sutimlimab in adult patients with primary CAD who received a recent blood transfusion. Patients received a fixed weight-based dose (6.5g or 7.5g) of sutimlimab via intravenous infusion on Day 0, Day 7 and then once every other week up to Week 26. For more information, please visit www.clinicaltrials.gov, study identifier number NCT03347396

About Cold Agglutinin Disease (CAD)

CAD is a serious, chronic rare blood disease in which a part of the body’s immune system called the complement system mistakenly attacks a person’s own healthy red blood cells. People with CAD suffer from chronic anemia, debilitating fatigue, acute hemolytic crisis and a poor quality of life. Retrospective analyses have also demonstrated other potential complications for CAD patients including an increased risk of thromboembolic events and early mortality. CAD occurs in approximately 16 people per millionⁱ, including an estimated 12,000 people in the United States, Europe and Japan.

About Sutimlimab

Sutimlimab is a potential first-in-class, investigational, humanized, monoclonal antibody that has been specifically designed to target C1s, a serine protease within the C1-complex, that is the first step in activating the classical complement pathway of the immune system. Activation of the classical complement pathway is the central mechanism of hemolysis in CAD and blocking it may potentially halt the CAD disease process. With a novel mechanism of action and high target specificity, sutimlimab is designed to selectively inhibit disease processes upstream in the classical complement pathway while leaving intact the alternative and lectin complement pathways and their immune surveillance functions.

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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ⁱ Berentsen S, et al. *Haematologica*. 2006;91(4):460-466