The European Hematology Association (EHA) Deadline: March 1, 2021

Title: Efficacy and Safety of Efgartigimod PH20 Subcutaneous in Adult Patients with Primary Immune Thrombocytopenia (ITP): ADVANCE SC, a Global Phase 3 Clinical Trial in Progress

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Background: Immunoglobulin G (IgG) autoantibodies against platelet surface antigens are found in most patients with immune thrombocytopenia (ITP). These autoantibodies accelerate platelet clearance, can inhibit platelet production, and may impair platelet function. IgG homeostasis is regulated by the neonatal Fc receptor (FcRn). Efgartigimod, a human IgG1-derived Fc-fragment, binds with high affinity to FcRn in a pH dependent way, resulting in degradation of IgG by blocking recycling of endogenous IgG. In a Phase 2 trial (n=38), efgartigimod was well tolerated in patients with primary ITP[1] and induced a rapid reduction of total IgG levels. This was associated with clinically relevant increases in platelet counts, and a reduced proportion of patients with bleeding.

Study Design: ADVANCE SC, a Phase 3, multicenter, randomized, double-blinded, placebo-controlled trial (NCT04687072), will evaluate the efficacy and safety of a subcutaneous (SC) formulation of efgartigimod (PH20) in adults with persistent or chronic ITP. Eligible patients must have a mean platelet count $<30\times10^9$/L over ≥3 platelet evaluations and have received ≥2 prior ITP treatments, or 1 prior and 1 concurrent treatment, with response to ≥1. Patients enter a 24-week treatment period receiving efgartigimod PH20 or matching placebo (randomization 2:1). Efgartigimod PH20 or placebo PH20 is given weekly from visits 1 to 4 and then weekly or every other week from visit 5 to 16, determined by platelet counts. Dosing schedule is fixed from visit 17 to 24. The primary endpoint is the proportion of patients with a sustained platelet count response. Secondary endpoints include overall platelet count response, safety and tolerability, bleeding severity, use of rescue therapy, quality of life, patient-reported outcome measures, and immunogenicity and pharmacokinetic/pharmacodynamic effects of efgartigimod PH20.

Recruitment target is 117 patients with chronic ITP and ≤39 patients with persistent ITP across 170 international sites. Participants are eligible for ADVANCE SC[+], a long-term open-label extension.

1. Newland AC. *Am J Hematol*. 2020;95:178-187. NCT03102593

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WG:s fees for participation in Advisory board from Amgen, Novartis, Pfizer, Principia Biopharma Inc- a Sanofi Company, Sanofi, SOBI, Griffols, UCB, Argenx. Lecture honoraria from Amgen, Novartis, Pfizer, Bristol Myers Squibb, SOBI, Griffols, Sanofi. Research grants from Bayer, and BMS/Pfizer