

Press Release

HUTCHMED Initiates a Phase II/III Trial of Sovleplenib for Warm Antibody Autoimmune Hemolytic Anemia in China

Hong Kong, Shanghai & Florham Park, NJ — Monday, October 10, 2022: HUTCHMED (China) Limited (“[HUTCHMED](#)”) (Nasdaq/AIM:HCM; HKEX:13) today announces that it has initiated a Phase II/III trial of soveplenib in adult patients with warm antibody autoimmune hemolytic anemia (“wAIHA”) in China. wAIHA is an autoimmune disorder that can lead to anemia and has limited treatment options. The first patient received the first dose on September 30, 2022.

This is a randomized, double blind, placebo-controlled clinical trial. The Phase II stage of the study is to evaluate the safety and preliminary efficacy of soveplenib in adult patients with wAIHA. If results of the Phase II stage are positive, the Phase III stage will be initiated to confirm such efficacy and safety. The primary endpoint for the Phase II study is the proportion of patients with overall hemoglobin (“Hb”) response by Week 24, whereas the primary endpoint for the Phase III study would be the proportion of patients who achieve a durable Hb response by Week 24. Approximately 110 patients are expected to be enrolled. The lead principal investigators are Dr. Liansheng Zhang of Lanzhou University Second Hospital, Dr. Fengkui Zhang of Chinese Academy of Medical Sciences Blood Diseases Hospital and Dr. Bing Han of Chinese Academy of Medical Sciences Peking Union Medical College Hospital. Additional details may be found at clinicaltrials.gov, using identifier [NCT05535933](#).

About Sovleplenib

Sovleplenib is a novel, investigational, selective small molecule inhibitor for oral administration targeting the spleen tyrosine kinase, also known as Syk. Syk is a major component in B-cell receptor and Fc receptor signaling and is an established target for the treatment of multiple subtypes of B-cell lymphomas and autoimmune disorders.

HUTCHMED currently retains all rights to soveplenib worldwide. In addition to wAIHA, soveplenib is also being studied in immune thrombocytopenia ([NCT05029635](#)), indolent non-Hodgkin’s lymphoma and multiple subtypes of B-cell malignancies in China, the U.S. and Europe ([NCT02857998](#); [NCT03779113](#)).

About wAIHA and Syk

AIHA is an autoimmune disorder characterized by the destruction of red blood cells (“RBCs”) due to the production of antibodies against RBC. The incidence of AIHA is estimated to be 0.8-3.0/100,000 adults per year with an estimated prevalence of 17 per 100,000 adults and a death rate of 8%-11%.^{1 2} wAIHA is the most common of the autoimmune hemolytic diseases,³ accounting for about 75-80% of all adult AIHA cases.⁴

The accelerated clearance of antibody-coated RBCs by immunoglobulin Fc receptor (“FcR”) bearing macrophages is thought to be the pathogenic mechanism in wAIHA.⁵ Activation of the FcR is associated with a signaling subunit, FcRγ, whose phosphorylation subsequent to receptor binding results in the recruitment and activation of Syk.⁶ Activated Syk mediates downstream signaling of the activated FcRs in phagocytic cells, resulting in phagocytosis of RBCs.⁷ In addition, activation of Syk through the B-cell receptor mediates activation and differentiation of B-lymphocytes into antibody secreting plasma cells.⁸ Therefore, inhibition of Syk may have potential effects in the treatment of wAIHA through inhibition of phagocytosis and reduction of antibody production.

About HUTCHMED

HUTCHMED (Nasdaq/AIM:HCM; HKEX:13) is an innovative, commercial-stage, biopharmaceutical company. It is committed to the discovery and global development and commercialization of targeted therapies and immunotherapies for the treatment of cancer and immunological diseases. It has more than 4,900 personnel

across all its companies, at the center of which is a team of over 1,800 in oncology/immunology. Since inception it has advanced 13 cancer drug candidates from in-house discovery into clinical studies around the world, with its first three oncology drugs now approved and marketed in China. For more information, please visit: www.hutch-med.com or follow us on [LinkedIn](#).

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the “safe harbor” provisions of the U.S. Private Securities Litigation Reform Act of 1995. These forward-looking statements reflect HUTCHMED’s current expectations regarding future events, including its expectations regarding the therapeutic potential of sovreplenib for patients for the treatment of wAIHA and other indications, its expectations as to whether any studies on sovreplenib would meet their primary or secondary endpoints, and its expectations as to the timing of the completion and the release of results from such studies. Forward-looking statements involve risks and uncertainties. Such risks and uncertainties include, among other things, assumptions regarding enrollment rates and the timing and availability of subjects meeting a study’s inclusion and exclusion criteria; changes to clinical protocols or regulatory requirements; unexpected adverse events or safety issues; the ability of sovreplenib, including as a combination therapy, to meet the primary or secondary endpoint of a study, to obtain regulatory approval in different jurisdictions and to gain commercial acceptance after obtaining regulatory approval; the potential market of sovreplenib for a targeted indication; the sufficiency of funding; and the impact of the COVID-19 pandemic on general economic, regulatory and political conditions. Existing and prospective investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. For further discussion of these and other risks, see HUTCHMED’s filings with the U.S. Securities and Exchange Commission, The Stock Exchange of Hong Kong Limited and on AIM. HUTCHMED undertakes no obligation to update or revise the information contained in this press release, whether as a result of new information, future events or circumstances or otherwise.

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- ¹ Eaton WW, Rose NR, Kalaydjian A, Pedersen MG, Mortensen PB. Epidemiology of autoimmune diseases in Denmark. *J Autoimmun.* 2007; 29 (1):1-9.
- ² Roumier M, Loustau V, Guillaud C, et al. Characteristics and outcome of warm autoimmune hemolytic anemia in adults: new insights based on a single-center experience with 60 patients. *Am J Hematol.* 2014; 89 (9):E150-5.
- ³ Cotran Ramzi S, Kumar Vinay, Fausto Nelson, Nelso Fausto, Robbins Stanley L, Abbas Abul K. Robbins and Cotran pathologic basis of disease. St. Louis, Mo: Elsevier Saunders; 2005. p. 637.
- ⁴ Gehrs BC, Friedberg RC. Autoimmune haemolytic anemia. *Am J Hematol.* 2002; 69:258–271. doi: 10.1002/ajh.10062.
- ⁵ Barros MM, Blajchman MA, Bordin JO. Warm autoimmune hemolytic anemia: recent progress in understanding the immunobiology and the treatment. *Transfus Med Rev.* 2010; 24(3):195 - 210. doi: 10.1016/j.tmr.2010.03.002.
- ⁶ Braselmann S, Taylor V, Zhao H, et al. R406, an orally available spleen tyrosine kinase inhibitor blocks fc receptor signaling and reduces immune complex - mediated inflammation. *J Pharmacol Exp Ther.* 2006; 319(3):998 - 1008. doi: 10.1124/jpet.106.109058.
- ⁷ Barcellini W, Fattizzo B, Zaninoni A. Current and emerging treatment options for autoimmune hemolytic anemia. *Expert Rev Clin Immunol.* 2018; 14(10):857 - 872. doi: 10.1080/1744666x.2018.1521722.
- ⁸ Davidzohn N, Biram A, Stoler - Barak L, Grenov A, Dassa B, Shulman Z. SYK degradation restrains plasma cell formation and promotes zonal transitions in germinal centers. *J Exp Med.* 2020; 217(3):e20191043. doi: 10.1084/jem.20191043.