Press Release

HUTCHMED Highlights Presentation of Phase III Data on Fruquintinib in Second-Line Gastric Cancer at ASCO Plenary Series Session

Hong Kong, Shanghai & Florham Park, NJ — Wednesday, February 7, 2024: HUTCHMED (China) Limited ("HUTCHMED") (Nasdaq/AIM:HCM; HKEX:13) today announces that data from FRUTIGA, HUTCHMED's Phase III trial of fruquintinib in combination with paclitaxel for the treatment of second-line advanced gastric cancer in China, were presented at the American Society of Clinical Oncology ("ASCO") Plenary Series Session on February 6, 2024. The full presentation can be found here. Fruquintinib is a selective oral inhibitor of vascular endothelial growth factor receptors ("VEGFR") -1, -2 and -3, which play a pivotal role in blocking tumor angiogenesis.

The ASCO Plenary Series was established to feature practice-changing and clinically relevant studies on the latest advances in cancer care.[1]

The FRUTIGA trial (clinicaltrials.gov identifier NCT03223376) was a 1:1 randomized, double-blind, Phase III study conducted at 35 sites in China to evaluate fruquintinib combined with chemotherapy, paclitaxel, compared with paclitaxel monotherapy for second-line treatment of 703 patients with advanced gastric or gastro-esophageal junction adenocarcinoma. The dual primary endpoints were progression-free survival ("PFS") and overall survival ("OS"), and the study was declared positive as the PFS endpoint met statistical significance at a pre-defined alpha level.

Median PFS for patients who received fruquintinib plus paclitaxel was 5.6 months, compared to 2.7 months for those who received paclitaxel monotherapy, a statistically significant improvement (stratified hazard ratio ["HR"] = 0.569; $p < 0.0001$). The objective response rate ("ORR") was significantly higher in the fruquintinib combination group (42.5% vs. 22.4%).

There was an improvement in OS with median OS of 9.6 months vs. 8.4 months, however this was not statistically significant. There was an imbalance of patients receiving subsequent antitumor therapies across the two groups, with 52.7% in the fruquintinib plus paclitaxel group vs. 72.2% in the paclitaxel monotherapy group. Pre-specified sensitivity analyses showed that in patients without these subsequent antitumor therapies, OS improvement was statistically significant. Median OS for patients who received the combination therapy was 6.9 months compared to 4.8 months for those receiving the placebo, with a HR of 0.72 ($p = 0.0422$).

Fruquintinib demonstrated a statistically significant improvement in multiple other endpoints, including disease control rate ("DCR") at 77.2% vs. 56.3%, and duration of response ("DoR") at 5.5 vs. 3.7 months. The most common (at least 5%) grade 3 or above treatment-emergent adverse events were neutropenia (60.0% vs. 36.4%), leukopenia (42.9% vs. 23.5%), anemia (11.7% vs. 10.6%) and palmar-plantar erythrodysesthesia syndrome (8.9% vs. 4.9%). As such, fruquintinib plus paclitaxel was well-tolerated with a safety profile consistent with expectations.

The presentation concludes that fruquintinib plus paclitaxel could be a promising second-line treatment option for patients with advanced gastric or gastroesophageal adenocarcinoma who have failed fluoropyrimidine- or platinum-containing chemotherapy.

Presentation title	Presenter & Lead author	Presentation details
Fruquintinib plus paclitaxel versus paclitaxel as second-line therapy for patients with advanced gastric or gastroesophageal junction adenocarcinoma (FRUTIGA): a randomized, multicenter, double-blind, placebo-controlled, phase 3 study	Rui-Hua Xu, MD, PhD	February ASCO Plenary Series Session Abstract 438730 Tuesday, February 6, 2024 3 pm ET (8pm GMT, 4am HKT)

The New Drug Application ("NDA") for fruquintinib in combination with paclitaxel for the treatment of second-line advanced gastric or gastroesophageal junction adenocarcinoma in China was accepted for review by the China National Medical Products Administration in April 2023. Fruquintinib is approved in China and the United States for the treatment of certain patients with metastatic colorectal cancer ("mCRC").

About the ASCO Plenary Series

According to ASCO, the ASCO Plenary Series was established to feature practice-changing and clinically relevant studies on the latest advances in cancer care. Up to two abstracts are presented in each session, and accompanied by a discussant presentation and a live question and answer session. It was developed by ASCO so that researchers and clinicians can stay current on cutting-edge research in oncology in between meetings, providing faster dissemination of practice-changing science to better help clinicians deliver the most up-to-date care and treatments to patients.

Abstracts at the ASCO Plenary Series are expected to address novel scientific questions, detail clinical observations, and contain primary scientific data in the form of a randomized phase II and III trial, or be original research studies that highlight novel and high-impact research with practice-changing implications. Presented studies are also expected to be placed in an oral presentation at the ASCO Annual Meeting.

About the Phase III FRUTIGA Trial

FRUTIGA is a randomized, double-blind, Phase III study in China to evaluate fruquintinib combined with paclitaxel compared with paclitaxel monotherapy, for second-line treatment of advanced gastric cancer. The study enrolled 703 patients. Its dual-primary endpoints were PFS and OS. The trial met the PFS endpoint at a statistically and clinically meaningful level. While there was an improvement in median OS, the OS endpoint was not statistically significant per the pre-specified statistical plan. Fruquintinib also demonstrated a statistically significant improvement in secondary endpoints including objective response rate (ORR), DCR and DoR. The safety profile of fruquintinib in FRUTIGA was consistent with previously reported studies. Additional details may be found at clinicaltrials.gov, using identifier NCT03223376.

About Gastric Cancer

Gastric cancer is a cancer that starts in the stomach. It is the fifth most common cancer worldwide in 2020. It was estimated to have caused approximately 770,000 deaths worldwide.[2] In China, it was estimated that over 478,000 people were diagnosed with gastric cancer, and approximately 374,000 people died from gastric cancer.[3]

About Fruquintinib

Fruquintinib is a selective oral inhibitor of VEGFR-1, -2 and -3. VEGFR inhibitors play a pivotal role in inhibiting tumor angiogenesis. Fruquintinib was designed to have enhanced selectivity that limits off-target kinase activity, allowing for high drug exposure, sustained target inhibition, and flexibility for the potential use as part of combination therapy. Fruquintinib has demonstrated a manageable safety profile and is being investigated in combinations with other anti-cancer therapies.

About Fruquintinib Approval in China

Fruquintinib is approved for marketing in China, where it is co-marketed by HUTCHMED and Lilly under the brand name ELUNATE®. It was included in the China National Reimbursement Drug List (NRDL) in January 2020. The approval was based on data from the FRESCO study, a Phase III pivotal registration trial of fruquintinib in 416 patients with mCRC in China, which were published in The Journal of the American Medical Association, JAMA. Since its launch in China, fruquintinib has benefited more than 80,000 colorectal cancer patients as of mid-2023.

About Fruquintinib Approval in the United States

Fruquintinib received approval in the United States in November 2023, where it is marketed by Takeda under the brand name FRUZAQLA™. The approval was based on data from two large Phase III trials: the multi-regional FRESCO-2 trial, data from which were published in *The Lancet*, along with the FRESCO trial conducted in China. The trials investigated fruquintinib plus best supportive care versus placebo plus best supportive care in patients with previously treated mCRC. Both FRESCO and FRESCO-2 met their primary and key secondary efficacy endpoints and showed consistent benefit among a total of 734 patients treated with fruquintinib. Safety profiles were consistent across trials.

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 approximately 5,000 personnel across all its companies, at the center of which is a team of about 1,800 in oncology/immunology. Since inception it has focused on bringing cancer drug candidates from in-house discovery to patients around the world, with its first three medicines marketed in China, the first of which is also marketed in the U.S. 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 fruquintinib for the treatment of patients with advanced gastric cancer and the further clinical development of fruquintinib in this and other indications. Forward-looking statements involve risks and uncertainties. Such risks and uncertainties include, among other things, assumptions regarding the sufficiency of clinical data to support NDA approval of fruquintinib for the treatment of patients with advanced gastric cancer in China, the U.S., Europe, Japan, Australia or other jurisdictions, its potential to gain expeditious approvals from regulatory authorities, the safety profile of fruquintinib, HUTCHMED's ability to fund, implement and complete its further clinical development and commercialization plans for fruquintinib, the timing of these events, and the impact of the COVID-19 pandemic on general economic, regulatory and political conditions. In addition, as certain studies rely on the use of other drug products such as paclitaxel, tislelizumab and sintilimab as combination therapeutics with fruquintinib, such risks and uncertainties include assumptions regarding the safety, efficacy, supply and continued regulatory approval of these therapeutics. 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, on AIM and on The Stock Exchange of Hong Kong Limited. 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.

Medical Information

This press release contains information about products that may not be available in all countries, or may be available under different trademarks, for different indications, in different dosages, or in different strengths. Nothing contained herein should be considered a solicitation, promotion or advertisement for any prescription drugs including the ones under development.

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[1] Plenary Series FAQs | ASCO. Accessed January 31, 2024.
[2] The Global Cancer Observatory, Stomach Cancer Fact Sheet. Accessed April 6, 2023.
[3] The Global Cancer Observatory, China Fact Sheet. Accessed April 6, 2023.