HUTCHMED (China) Limited

和黃醫藥（中國）有限公司

(Incorporated in the Cayman Islands with limited liability)

(Stock Code: 13)

VOLUNTARY ANNOUNCEMENT

HUTCHMED Highlights Presentations at the 2023 ASCO Annual Meeting

HUTCHMED (China) Limited ("HUTCHMED") today announces that new and updated clinical data related to HUTCHMED's novel investigational cancer therapies fruquintinib, surufatinib and HMPL-453 in 21 abstracts that will be presented at the upcoming American Society of Clinical Oncology (ASCO) Annual Meeting, taking place June 2-6, 2023 in Chicago, IL and online.

Fruquintinib: further analyses from the FRESCO-2 study and exploratory combination studies

Fruquintinib is a highly selective and potent oral inhibitor of vascular endothelial growth factor receptor ("VEGFR")-1, -2 and -3.[1] Fruquintinib has been generally well tolerated in patients to date and is being investigated as a single agent and in combination with other anti-cancer therapies. 13 presentations and publications, including several investigator-initiated-trials ("IITs"), are listed in the table below.

Additional FRESCO-2 analyses: New analyses from the FRESCO-2 multi-regional clinical trial (MRCT) are being presented. FRESCO-2 is a key study supporting ongoing and upcoming submissions to the U.S., European and Japanese regulatory authorities for the treatment of previously treated metastatic colorectal cancer ("CRC"). FRESCO-2 results were first presented at the European Society for Medical Oncology Congress 2022. These new analyses add to the understanding of fruquintinib efficacy by specific lines of therapy as well as adverse events of special interest ("AESI"). In subgroup analyses by prior lines of therapies up to six or more and by prior treatment with approved agents, fruquintinib improved overall survival ("OS") and progression free survival ("PFS") for all subgroups and prior therapies, consistent with those of the intent-to-treat ("ITT") population. Furthermore, during the study AESIs led to low rates of dose reduction (13.6% for patients who received fruquintinib vs 0.9% for patients who received placebo) and dose discontinuation (8.3% for patients who received fruquintinib vs 6.1% for patients who received placebo).

CRC real-world data: Results from a prospective, 3,005-patient Phase IV study to evaluate the safety of fruquintinib in real-world clinical practice in China are consistent with the fruquintinib safety profile observed in existing clinical studies, with no new or significant safety signals identified.

PD-1 combination in ccRCC: PFS results from an exploratory study of the fruquintinib and sintilimab (an anti-programmed cell death protein-1 ["PD-1"] antibody) combination in metastatic clear cell renal cell carcinoma ("ccRCC") are available with longer term follow-up. At data cut-off on November 30, 2022, median PFS was 15.9 months in 20 previously treated patients. Median PFS was not reached when results from this study were initially presented at the 2021 Chinese Society of Clinical Oncology Annual Meeting (data cut-off on August 31, 2021). No new safety signals were observed. A Phase II/III trial of fruquintinib in combination with sintilimab as second-line treatment for locally advanced or metastatic ccRCC was initiated in October 2022 (NCT05522231).

IIT in 2L MSS CRC: A number of IITs are being presented, including initial results of an IIT for fruquintinib in combination with investigator's choice of chemotherapy in second-line metastatic CRC with microsatellite-stable (MSS) phenotype. At median follow up of 8.4 months, median PFS was not reached in 31 efficacy evaluable patients, disease control rate (DCR) was 90.3% and objective response rate (ORR) was 48.4%. Five patients received reduced doses of fruquintinib.

Surufatinib: exploratory results in combination with other agents

Surufatinib is a small-molecule inhibitor of VEGFR-1, -2 and -3, fibroblast growth factor receptor ("FGFR")-1 and colony-stimulating factor 1 receptor (CSF-1R). Seven related presentations and publications, including IITs, are listed in the table below.

PD-1 combinations: We conducted an open-label, multi-cohort, single-arm Phase II study of surufatinib plus toripalimab (an anti-PD-1 antibody) in several advanced solid tumors. We reported the results from the advanced thyroid cancer and endometrial cancer cohorts (NCT04169672). Amongst efficacy evaluable radioactive iodine-refractory differentiated thyroid cancer patients, median PFS was 10.9 months and median OS was not reached (median follow-up duration was 22.1 months). Amongst efficacy evaluable endometrial cancer patients, median PFS was 5.4 months and 12-month OS rate was 71.0% (median follow-up duration was 16.8 months). In both cohorts, the combination showed a tolerable safety profile.

Combo IITs: A number of IITs are being presented for surufatinib in combination with other agents, including with chemotherapy as well as with camrelizumab (an anti-PD-1 antibody) plus different chemotherapy regimens.

Preliminary results in an ongoing IIT in treatment of patients with naïve metastatic pancreatic adenocarcinoma (PDAC) showed median PFS of 8.8 months in patients who received a combination of surufatinib, camrelizumab, nab-paclitaxel and S-1, compared to 5.8 months in patients who received gemcitabine in combination with nab-paclitaxel. Markers of immune cells were observed in an analysis of tissue samples from 13 (out of 20) patients who received S-1 in combination with surufatinib, camrelizumab and nab-paclitaxel. The combination safety profiles were manageable.

The IIT in previously treated CRC study completed the dose escalation phase of the study in 12 patients and enrolled a further 36 patients in the dose expansion phase of the study. The investigators found the combination of surufatinib with camrelizumab, irinotecan and GM-CSF to be well tolerated with a manageable safety profile. Median PFS was 7.2 months (95% CI 3.7-10.7).

The IIT in previously treated, advanced driver-gene negative, non-squamous, non-small cell lung cancer ("NSCLC") in combination with chemotherapy. This study complements Phase II results previously presented for the surufatinib and toripalimab combination in patients with treatment naïve advanced NSCLC with positive PD-L1 expression.

HMPL-453: first in human results

FGFRs regulate numerous cellular processes. Dysregulation of FGFR signaling due to receptor fusion, mutation or amplification is observed across multiple cancer types, making activated FGFRs an important therapeutic target. HMPL-453 is a highly potent and selective inhibitor of FGFR-1, -2, and -3. Preclinical data presented at the American Association for Cancer Research Annual Meeting 2023 (AACR 2023) showed that it has strong activity against FGFR-deregulated tumors, supporting investigation in patients with FGFR alterations (such as fusion and mutation) either as a single agent or in combination with PD-1 blockade.

Here we present first-in-human data for HMPL-453 in patients with previously treated advanced intrahepatic cholangiocarcinoma (IHCC) harboring FGFR2 fusions. A Phase II registration intent cohort is currently enrolling such patients (NCT04353375).

Further details including the full abstracts are available at meetings.asco.org, as summarized below.

ABSTRACT PRESENTATION DETAILS

Abstract title	Presenter / Lead author	Presentation details
FRUQUINTINIB		
Subgroup analyses of safety and efficacy by number and types of prior lines of treatment in FRESCO-2, a global phase III study of fruquintinib in patients with refractory metastatic colorectal cancer	Arvind Dasari, MD Anderson Cancer Center	Abstract # 3604 Poster Session Gastrointestinal Cancer–Colorectal and Anal Monday, June 5, 2023, 8 am CDT, Hall A
Analysis of fruquintinib adverse events of special interest from phase 3 of the FRESCO-2 study	Cathy Eng, Vanderbilt-Ingram Cancer Center	Abstract # 3601 Poster Session Gastrointestinal Cancer–Colorectal and Anal Monday, June 5, 2023, 8 am CDT, Hall A
A phase IV study to evaluate the safety of fruquintinib in Chinese real-world clinical practice	Jin Li, Tongji University Shanghai East Hospital	Abstract # e15568 Publication Only Gastrointestinal Cancer–Colorectal and Anal
Fruquintinib plus sintilimab in patients with either treatment-naive or previously first line treated metastatic clear-cell renal cell carcinoma (ccRCC): Results from a multicenter, single-arm phase 2 study	Dingwei Ye, Fudan University Shanghai Cancer Center	Abstract # e16514 Publication Only Genitourinary Cancer—Kidney and Bladder
Efficacy and safety of fruquintinib plus investigator's choice of chemotherapy as second-line therapy in metastatic colorectal cancer: A multicenter, single-arm phase 2 trial	Wensi Zhao, Renmin Hospital of Wuhan University	Abstract # 3582 Poster Session Gastrointestinal Cancer–Colorectal and Anal Monday, June 5, 2023, 8 am CDT, Hall A
Fruquintinib plus oxaliplatin combined with S-1 (SOX) as neoadjuvant therapy for locally advanced gastric adenocarcinoma (FRUTINEOGA): a multicenter, phase II study.	Liucheng Wu, Guangxi Medical University Cancer Hospital	Abstract # e16063 Publication Only Gastrointestinal Cancer—Gastroesophageal, Pancreatic, and Hepatobiliary
Association of neutrophil/lymphocyte ratio and IFN-γ with clinical response and survival in patients with MSS/pMMR mCRC treated with anti-PD-1 and VEGF inhibitors	Zhuqing Liu, Tongji University School of Medicine	Abstract # e14610 Publication Only Developmental Therapeutics—Immunotherapy
Efficacy and safety of radiation therapy combined with anti-angiogenic agents and immunotherapy for MSS/pMMR metastatic colorectal cancer: A real-world study	Zhenyu Lin, Tongji Medical College	Abstract # e15559 Publication Only Gastrointestinal Cancer—Colorectal and Anal
A phase II study of fruquintinib in the first- (1L) or second-line (2L) treatment of unresectable metastatic soft tissue sarcoma	Zhiguo Luo, Fudan University Shanghai Cancer Center	Abstract # e23547 Publication Only Sarcoma
Quality of life, effectiveness, and compliance of fruquintinib in the treatment of metastatic colorectal cancer: Results from a prospective real-world study.	Jun Zhang, Reijin Hospital	Abstract # e15557 Publication Only Gastrointestinal Cancer–Colorectal and Anal
Fruquintinib versus fruquintinib combined with PD-1 inhibitors for metastatic colorectal cancer: Real-world data	Lina He, Shanghai Jiao Tong University	Abstract # e15592 Publication Only Gastrointestinal Cancer–Colorectal and Anal
Phase II study of fruquintinib as second or further-line therapy for patients with advanced biliary tract cancer	Pengfei Zhang, West China Hospital	Abstract # e16161 Publication Only Gastrointestinal Cancer—Gastroesophageal, Pancreatic, and Hepatobiliary
A phase I/IIa study of cetuximab combined with fruquintinib in the previously treated RAS/BRAF wild-type metastatic colorectal cancer: Results of the CEFRU study	Yong Li, Traditional Chinese Medicine Hospital of Guangdong	Abstract # e15558 Publication Only Gastrointestinal Cancer–Colorectal and Anal
SURUFATINIB		
A multicenter, single-arm phase 2 study of surufatinib plus toripalimab for patients with locally advanced or metastatic radioactive iodine-refractory differentiated thyroid cancer	Dongmei Ji, Fudan University Shanghai Cancer Center	Abstract # 6089 Poster Session Head and Neck Cancer Monday, June 5, 2023, 1:15 pm CDT, Hall A
A multicenter, single-arm, phase 2 study of surufatinib plus toripalimab for patients with advanced endometrial cancer	Guangwen Yuan, Cancer Hospital Chinese Academy of Medical Sciences	Abstract # 5609 Poster Session Gynecologic Cancer Monday, June 5, 2023, 1:15 pm CDT, Hall A

Abstract title	Presenter / Lead author	Presentation details
A phase 1b/2 study of surufatinib plus camrelizumab, nab-paclitaxel, and S-1 (NASCA) as first-line therapy for metastatic pancreatic adenocarcinoma (mPDAC)	Guanghai Dai, The Fifth Medical Center of the PLA General Hospital	Abstract # 4142 Poster Session Gastrointestinal Cancer—Gastroesophageal, Pancreatic, and Hepatobiliary Monday, June 5, 2023, 8:00 am CDT, Hall A
A phase Ib/II study to evaluate surufatinib combined with camrelizumab and chemotherapy in the second-line treatment of advanced colorectal cancer: Phase Ib results	Sheng Li, Department of Oncology, Jiangsu Cancer Hospital	Abstract # 3555 Poster Session Gastrointestinal Cancer–Colorectal and Anal Monday, June 5, 2023, 8 am CDT, Hall A
Phase 1b/2 study of surufatinib in combination with docetaxel as second-line treatment of advanced driver-gene negative non-squamous non-small cell lung cancer (NSCLC)	Wei Jiang, Guangxi Medical University Cancer Hospital	Abstract # e21087 Publication Only Lung Cancer—Non-Small Cell Metastatic
Pathologic exploration of neuroendocrine differentiation in carcinomas	Yaru Wen, Cancer Hospital Chinese Academy of Medical Sciences	Abstract # e16238 Publication Only Gastrointestinal Cancer—Gastroesophageal, Pancreatic, and Hepatobiliary
A phase II study of surufatinib in patients with osteosarcoma and soft tissue sarcoma who have failed in standard chemotherapy	Xing Zhang, Sun Yat-sen University Cancer Center	Abstract # e23540 Publication Only Sarcoma
HMPL-453		
A phase 2 study of HMPL-453, a selective FGFR tyrosine kinase inhibitor (TKI), in patients with previously treated advanced cholangiocarcinoma containing FGFR2 fusions	Jianming Xu, Fifth Medical Center, Chinese PLA General Hospital	Abstract # e16118 Publication Only Gastrointestinal Cancer—Gastroesophageal, Pancreatic, and Hepatobiliary

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 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 announcement 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, surufatinib, and HMPL-453, the further clinical development for fruquintinib, surufatinib, and HMPL-453, its expectations as to whether any studies on fruquintinib, surufatinib and HMPL-453 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 fruquintinib, surufatinib and HMPL-453, 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 fruquintinib, surufatinib and HMPL-453 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 announcement, whether as a result of new information, future events or circumstances or otherwise.

[1] Sun Q, et al. (2014) Discovery of fruquintinib, a potent and highly selective small molecule inhibitor of VEGFR 1, 2, 3 tyrosine kinases for cancer therapy, *Cancer Biol Ther*. 2014 15:12, 1635-1645. Doi: 10.4161/15384047.2014.964087

By Order of the Board

Edith Shih
Non-executive Director and Company Secretary

Hong Kong, May 29, 2023

As at the date of this announcement, the Directors of the Company are:

Executive Directors:
Mr TO Chi Keung, Simon
(Chairman)
Dr Weiguo SU
(Chief Executive Officer and Chief Scientific Officer)
Mr CHENG Chig Fung, Johnny
(Chief Financial Officer)

Non-executive Directors:
Dr Dan ELDAR
Ms Edith SHIH
Mr Lefei SUN

Independent Non-executive Directors:
Mr Paul Rutherford CARTER
(Senior Independent Director)
Mr Graeme Allan JACK
Professor MOK Shu Kam, Tony