HUTCHMED and Epizyme Announce Strategic Collaboration to Develop and Commercialize TAZVERIK® (tazemetostat) in Greater China

Collaboration designed to accelerate global development and investigate TAZVERIK® combinations with HUTCHMED's novel oncology medicines portfolio

Epizyme to receive US$25 million upfront payment and up to US$285 million in potential milestone payments, together with additional tiered royalties; HUTCHMED to receive development and commercial rights to TAZVERIK® in Greater China

HUTCHMED to host a webcast and call on Monday August 9, at 9:30 a.m. EDT / 2:30 p.m. BST / 9:30 p.m. HKT – see www.hutch-med.com/event for details

Hong Kong, Shanghai, Florham Park, N.J. and Cambridge, Mass—Monday, August 9, 2021: HUTCHMED (China) Limited ("HUTCHMED") (Nasdaq/AIM:HCM; HKEX:13) and Epizyme, Inc. ("Epizyme") (Nasdaq: EPZM), a fully integrated, commercial-stage biopharmaceutical company developing and delivering novel epigenetic therapies, today announce a collaboration to research, develop, manufacture and commercialize TAZVERIK® in Greater China, including mainland China, Hong Kong, Macau and Taiwan (the "Territory").

TAZVERIK® is a methyltransferase inhibitor of EZH2 developed by Epizyme that is approved by the U.S. Food and Drug Administration ("FDA") for the treatment of certain patients with epithelioid sarcoma ("ES") and certain patients with follicular lymphoma ("FL"). It was approved under FDA accelerated approval based on overall response rate ("ORR") and duration of response ("DOR") in January and June 2020 for ES and FL, respectively.

"We are thrilled to be able to launch this collaboration designed to bring TAZVERIK® to patients in Greater China and to have HUTCHMED participate in the global development of TAZVERIK®," commented Mr. Robert Bazemore, Epizyme President and CEO. "HUTCHMED is an ideal partner for us in Greater China, given their development and commercial expertise and shared commitment to expanding the value of TAZVERIK® through new clinical trials that complement Epizyme's development plans." Mr. Bazemore continued, "Through this collaboration we anticipate TAZVERIK® to become the first EZH2 inhibitor brought to market in Greater China, and we believe the involvement of HUTCHMED in the global development of TAZVERIK® can allow for a more rapid, resource-efficient, and geographically inclusive development plan for the U.S. confirmatory EZH-302 trial of TAZVERIK® in second line follicular lymphoma (2L FL) in combination with Revlimid plus rituximab ('R²')."

"We view the activity of TAZVERIK® and its epigenetic mechanism in controlling the expression of certain genes as highly complementary and potentially synergistic with our broad portfolio of novel oncology assets," said Mr. Christian Hogg, CEO of HUTCHMED. "TAZVERIK®'s potential for broad applicability and favorable safety profile may provide further inhibition of tumor growth and metastasis when used in combination therapy. This collaboration will accelerate the exploration of the clinical potential of EZH2 inhibition in multiple tumor types, including both hematological malignancies and solid tumors. We believe that Epizyme and HUTCHMED are uniquely positioned to realize these opportunities and thereby rapidly benefit as many patients, both inside and outside China, as possible."

Under the terms of the agreement, HUTCHMED will be responsible for the development and commercialization of TAZVERIK® in greater China. Epizyme will receive a US$25 million upfront payment and is eligible to receive up to an additional US$110 million in development and regulatory milestone payments, across up to eight potential indications, and up to an additional US$175 million in sales milestone payments. Epizyme is also eligible to receive tiered royalties of mid -teen to low-twenties-percent based on annual net sales of TAZVERIK® in Greater China. In addition, HUTCHMED receives a four-year warrant to acquire up to US$65 million of Epizyme shares at US$11.50 per share. The upfront payment will be funded by HUTCHMED from existing cash resources, and potential milestone payments and royalties are expected to be funded from future cash resources including cash from the sales of TAZVERIK®.

HUTCHMED plans to develop and seek approval for TAZVERIK® in various hematological and solid tumors, including ES, FL and diffuse large b-cell lymphoma ("DLBCL") in its Territory. HUTCHMED will also participate in Epizyme's global registrational study of TAZVERIK® in combination with R² in second line FL, the EZH-302

study, and lead the study in Greater China. The parties also intend to conduct additional global studies jointly. HUTCHMED will generally be responsible for funding all clinical trials of TAZVERIK® in its Territory including the portion of global trials conducted therein. Upon any approvals HUTCHMED will be responsible for commercialization in its designated Territory. HUTCHMED will also hold rights to research and manufacture TAZVERIK® in the Territory.

Webcast and Conference Call

Analysts and investors are invited to join a webcast and conference call scheduled today – Monday, August 9 – at 9:30 a.m. Eastern Daylight Time / 2:30 p.m. British Summer Time (BST) / 9:30 p.m. Hong Kong Time (HKT). Investors may participate in the call as follows: +1 646 722 4977 (U.S.) / +44 20 3194 0569 (U.K.) / +852 3027 6500 (Hong Kong), or access a live audio webcast of the call via HUTCHMED's website at www.hutch-med.com/event/. Please use participant access code "**85770452#**."

About Epigenetics, EZH2, Its Role in Cancer and TAZVERIK®'s Complementary Role with HUTCHMED's Portfolio of Drug Candidates

Epigenetics refers to a broad regulatory system that controls gene expression without altering the sequence of the genes themselves. EZH2 is one member of a class of histone methyltransferases ("HMTs"). It catalyzes the methylation of histone H3 at lysine 27 (H3K27) which controls expression of various genes and in turn plays a role in the normal physiology of many cell types.

Dysregulation of EZH2 has been seen in a wide range of cancers and is associated with poor clinical prognosis and outcomes.[1,2] It is associated with follicular lymphoma and diffuse large B-cell lymphoma, B-cell malignancies that are estimated to respectively account for approximately 17% and 32% of the estimated 544,000 new cases of non-Hodgkin Lymphoma (NHL) worldwide in 2020.[3,4] EZH2 dysregulation has been described in the five most common solid tumors (breast, lung, colorectum, prostate and stomach) with an estimated combined incidence of over 1 million in 2020 globally.

TAZVERIK® inhibits EZH2 which allows transcription of genes involved in functions such as cell cycle control and terminal differentiation and thus TAZVERIK® action inhibits cancer cell proliferation. This mechanism of action is highly complementary and potentially synergistic with HUTCHMED's portfolio of cancer drug candidates. For solid tumors, these include fruquintinib, a highly selective inhibitor of vascular endothelial growth factor receptor, and surufatinib, a unique compound that inhibits angiogenesis and promotes the body's immune response against tumor cells.[5] For hematological malignancies, these include many assets including inhibitors of the B-cell signaling pathway such as the highly selective and potent PI3Kδ inhibitor HMPL-689, the Syk inhibitor HMPL-523 and third generation BTK inhibitor HMPL-760[6], as well the IDH1/2 inhibitor HMPL-306, the ERK inhibitor HMPL-295, the FGFR inhibitor HMPL-453 and the CD47 antibody HMPL-A83. The potential for broad applicability and favorable safety profile of TAZVERIK® may provide more effective inhibition of tumor growth and metastasis when used in combination therapy.

About TAZVERIK® (tazemetostat)

TAZVERIK® is a methyltransferase inhibitor indicated in the United States for the treatment of:

- Adults and pediatric patients aged 16 years and older with metastatic or locally advanced epithelioid sarcoma not eligible for complete resection.
- Adult patients with relapsed or refractory follicular lymphoma whose tumors are positive for an EZH2 mutation as detected by an FDA-approved test and who have received at least two prior systemic therapies.
- Adult patients with relapsed or refractory follicular lymphoma who have no satisfactory alternative treatment options.

These indications are approved under accelerated approval by the U.S. FDA based on overall response rate and duration of response. Continued approval for these indications may be contingent upon verification and description of clinical benefit in confirmatory trials.

View the U.S. Full Prescribing Information here: www.Tazverik.com

About TAZVERIK® Accelerated Approval in FL

TAZVERIK® was approved in the U.S. for the above relapsed/refractory FL indications in June 2020, based on FL cohort efficacy and safety data in a Phase II trial (Study E7438-G000-101, clinicaltrials.gov identifier: NCT01897571).

The efficacy of TAZVERIK® was evaluated in an open-label, single-arm, multi-center Phase II clinical trial in patients with histologically confirmed FL whose disease had progressed following at least two prior systemic treatment regimens. Patients were enrolled into two cohorts: one cohort enrolled 45 patients with EZH2 activating mutations and a second cohort enrolled 54 patients with wild-type EZH2. All patients were treated with 800 mg of tazemetostat, administered orally twice a day. The major efficacy outcome measures were ORR and DOR according to the International Working Group Non-Hodgkin Lymphoma (IWG-NHL) criteria (Cheson 2007) as assessed by Independent Review Committee. Median duration of follow-up was 22 months for patients with EZH2 activating mutations and 36 months for patients with wild-type EZH2.

Results of this study were published in *The Lancet Oncology*.[7] Data from the label is below. Among the 45 FL patients with an EZH2 activating mutation who received TAZVERIK®, the median age was 62 years (range 38 to 80); 42% were male; 42% had early progression following front-line therapy ("POD24"); and all had an Eastern Cooperative Oncology Group ("ECOG") performance status ("PS") of 0 or 1. The median number of lines of prior systemic therapy was 2.0 (range 1 to 11); 49% were refractory to rituximab and 49% were refractory to their last therapy. In the 42 patients treated with at least 2 prior systemic therapies, the ORR (95% confidence interval) was 69% (53%, 82%), with 12% of patients achieving a complete response and 57% achieving a partial response. The median DOR was 10.9 months and ongoing.

Among the 54 FL patients with wild-type EZH2 who received TAZVERIK®, the median age was 61 years (range 36 to 87); 63% were male; 59% had POD24; and 91% had an ECOG PS of 0 or 1. The median number of lines of prior systemic therapy was 3.0 (range 1 to 8); 59% were refractory to rituximab and 41% were refractory to their last therapy. In the 53 patients treated with at least 2 prior systemic therapies, the ORR (95% confidence interval) was 34% (22%, 48%), with 4% of patients achieving a complete response and 30% achieving a partial response. The median DOR was 13.0 months.

Serious adverse reactions, irrespective of attribution, occurred in 30% of patients receiving TAZVERIK®. Serious adverse reactions in ≥2% of patients who received TAZVERIK® were general physical health deterioration, abdominal pain, pneumonia, sepsis, and anemia. The most common (≥20%) adverse reactions are fatigue, upper respiratory tract infection, musculoskeletal pain, nausea and abdominal pain.

Eight patients (8%) discontinued due to adverse reaction during the trial. There were no reported deaths on study, and no black box warnings or contraindications.

The most common (≥20%) adverse reactions in patients with follicular lymphoma are fatigue, upper respiratory tract infection, musculoskeletal pain, nausea and abdominal pain.

EZH-302 is a global, randomized, double-blind, active-controlled, biomarker enrichment, adaptive design Phase Ib/III confirmatory trial (clinicaltrials.gov identifier: NCT04224493) assessing the combination of TAZVERIK® with R² (REVLIMID® plus rituximab), an approved chemotherapy-free treatment regimen, compared with R² plus placebo for relapsed or refractory FL patients followed by maintenance TAZVERIK or placebo in the second-line or later treatment setting. The trial is expected to enroll approximately 500 FL patients.

About TAZVERIK® Accelerated Approval in ES

TAZVERIK® was approved in the U.S. for the above ES indication in January 2020, based on ES cohort 5 efficacy and safety data in a Phase II trial (Study EZH-202, clinicaltrials.gov identifier: NCT02601950).

The efficacy of TAZVERIK® was evaluated in an open-label, single-arm cohort (Cohort 5) of a multi-center study in patients with histologically confirmed, metastatic or locally advanced epithelioid sarcoma. Patients were required to have INI1 loss, detected using local tests, and an ECOG PS of 0-2. Patients received TAZVERIK® 800 mg orally twice daily until disease progression or unacceptable toxicity. Tumor response assessments were performed every 8 weeks. The major efficacy outcome measures were confirmed ORR according to Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 as assessed by blinded independent central review (BICR) and DOR. Median duration of follow-up was 14 months (range 0.4 to 31).

Results of this study were published in *The Lancet Oncology*.[8] Data from the label is below. Among the 62 patients who received TAZVERIK®, median age was 34 years (range 16 to 79); 63% were male, 76% were White, 11% were Asian, 44% had proximal disease, 92% had an ECOG PS of 0 or 1, and 8% had an ECOG PS of 2. Prior surgery occurred in 77% of patients; 61% received prior systemic chemotherapy.

In the total 62 patients treated, the ORR (95% confidence interval) was 15% (7%, 26%), with 1.6% of patients achieving a complete response and 13% achieving a partial response. Among responders in the trial, 67% had a duration of response of six months or longer.

Serious adverse reactions occurred in 37% of patients receiving TAZVERIK®. Serious adverse reactions in ≥3% of patients who received TAZVERIK® were hemorrhage, pleural effusion, skin infection, dyspnea, pain, and respiratory distress.

One patient (2%) permanently discontinued TAZVERIK® due to an adverse reaction of altered mood.

The most common (≥20%) adverse reactions in patients with epithelioid sarcoma are pain, fatigue, nausea, decreased appetite, vomiting and constipation.

EZH-301 is a global, randomized, double-blind, placebo-controlled controlled Phase Ib/III confirmatory trial (clinicaltrials.gov identifier: NCT04204941) assessing TAZVERIK® in combination with doxorubicin compared with doxorubicin plus placebo as a front-line treatment for ES. The trial is expected to enroll approximately 150 patients.

About Other TAZVERIK® Clinical Development

In addition to the studies in FL and ES, TAZVERIK® is also being developed in DLBCL and in prostate cancer and ovarian cancer.

About Epizyme, Inc.

Epizyme, Inc. is a fully integrated, commercial-stage biopharmaceutical company committed to its mission of rewriting treatment for cancer and other serious diseases through novel epigenetic medicines. In addition to an active research and discovery pipeline, Epizyme has one U.S. FDA approved product, TAZVERIK® (tazemetostat), for the treatment of adults and pediatric patients aged 16 years and older with metastatic or locally advanced epithelioid sarcoma (ES) who are not eligible for complete resection; adult patients with relapsed or refractory follicular lymphoma (FL) whose tumors are positive for an EZH2 mutation as detected by an FDA-approved test and who have received at least two prior systemic therapies; and adult patients with relapsed or refractory follicular lymphoma who have no satisfactory alternative treatment options. These indications are approved under accelerated approval based on overall response rate and duration of response. Continued approval for these indications may be contingent upon verification and description of clinical benefit in confirmatory trials(s). Epizyme is also exploring the treatment potential of tazemetostat in investigational clinical trials in other solid tumors and hematological malignancies, as a monotherapy and combination therapy in both relapsed and front-line disease settings. By focusing on the genetic drivers of disease, Epizyme seeks to match medicines with the patients who need them. For more information, visit www.epizyme.com.

TAZVERIK® is a registered trademark of Epizyme, Inc.

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. A dedicated organization of over 1,400 personnel has advanced eleven cancer drug candidates from in-house discovery into clinical studies around the world, with its first three oncology drugs now approved and marketed. For more information, please visit: www.hutch-med.com or follow us on LinkedIn.

Cautionary Note on 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 and Epizyme's current expectations regarding future events, including their expectations regarding the therapeutic potential of TAZVERIK® for the treatment of patients with epithelioid sarcoma or follicular lymphoma, the further clinical development of TAZVERIK® in this and other indications, their expectations as to whether clinical studies of TAZVERIK® would meet their primary or secondary endpoints or will warrant meetings with regulatory authorities, submissions for regulatory approval or review by governmental authorities under the accelerated approval process and their 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 regulatory approvals, including accelerated approval, to conduct trials or to market products (including the sufficiency of data to support the New Drug Application approval of TAZVERIK® for the treatment of patients in China and whether TAZVERIK® will receive marketing approval for epithelioid sarcoma or follicular lymphoma in other jurisdictions, full approval in the United States or approval in any other indication), its expectations that preclinical studies or earlier clinical studies are predictive of the results of future trials, such as the ongoing confirmatory trials, the safety profile of TAZVERIK®, the potential for TAZVERIK® to become a new standard of care for epithelioid sarcoma or follicular lymphoma patients, each company's ability to implement and complete its further clinical development plans for TAZVERIK®, the potential commercial launch of TAZVERIK® in China and other jurisdictions in the approved indications, the sufficiency of each company's cash resources to fund its foreseeable and unforeseeable operating expenses and capital expenditure requirements, the timing of these events, and the impact of the COVID-19 pandemic on each company's business, results of operations and financial condition and on general economic, regulatory and political conditions. In addition, as certain studies rely on the use of other drug candidates as combination therapeutics with TAZVERIK®, such risks and uncertainties include assumptions regarding the safety, efficacy, supply and regulatory approval of such drug candidates. Existing and prospective investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. HUTCHMED and Epizyme anticipate that subsequent events and developments will cause their views to change; however, neither company undertakes any obligation to update or revise the information contained in this announcement, whether as a result of new information, future events or circumstances or otherwise. For a further discussion of these and other risks, see HUTCHMED's filings with the U.S. Securities and Exchange Commission, on AIM and with The Stock Exchange of Hong Kong Limited and Epizyme's filings with the U.S. Securities and Exchange Commission.

Inside Information

This announcement contains inside information for the purposes of Article 7 of Regulation (EU) No 596/2014 (as it forms part of retained EU law as defined in the European Union (Withdrawal) Act 2018).

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