Kymera Therapeutics Presents New Clinical Data from Ongoing Phase 1 Trial of MDM2 Degrader KT-253 at ASCO Annual Meeting

June 1, 2024

KT-253 demonstrates initial clinical proof of concept in patients with tumor types shown to be sensitive in preclinical models, including responses in MCC and AML

Evidence of target engagement and potent upregulation of p53 pathway biomarkers even at the lowest dose levels in solid tumor and AML patients

KT-253 was generally well tolerated without hematologic adverse events seen with traditional MDM2 small molecule inhibitors

KT-253 Phase 1 study ongoing with additional data expected in the second half of 2024

WATERTOWN, Mass., June 01, 2024 (GLOBE NEWSWIRE) -- Kymera Therapeutics, Inc. (NASDAQ: KYMR), a clinical-stage biopharmaceutical company advancing a new class of small molecule medicines using targeted protein degradation (TPD), today shared new clinical data from its ongoing KT-253 Phase 1 trial. KT-253, a potent, selective heterobifunctional small molecule degrader of MDM2, demonstrated preliminary signs of efficacy across tumor types at doses that were generally well-tolerated. The data were presented at the American Society of Clinical Oncology (ASCO) Annual Meeting, taking place from May 31 – June 4, 2024. Results released in an ASCO poster today include a data cut-off of April 9, 2024.

“We’re encouraged by the data emerging from the KT-253 Phase 1 dose escalation trial, showcasing the potential of TPD to address this clinically proven but inadequately drugged cancer mechanism. We have demonstrated strong proof of mechanism as well as preliminary signs of efficacy in both solid tumors and AML, with translation from our preclinical models to patient populations, without the hematological toxicity typically seen with traditional small molecule inhibitors,” said Jared Gollob, MD, Chief Medical Officer, Kymera Therapeutics. “These findings continue to support our therapeutic hypothesis for MDM2 degradation and the potential to improve the therapeutic index compared to small molecule inhibitors. We look forward to sharing the full Phase 1 data set, as well as our biomarker strategy and guidance on the program’s next development steps, later this year.”

“I am pleased to see responses in both liquid and solid tumor patients being treated with KT-253 at doses that do not cause neutropenia or diarrhea,” said Naval Daver, MD, of The University of Texas MD Anderson Cancer Center and clinical investigator of the KT-253 Phase 1 study. “The responses in post-MPN AML are especially encouraging, as these patients are often refractory to multiple different therapies and therefore represent a subset of AML with high unmet medical need.”

KT-253 Clinical Update

The Phase 1 study of KT-253 is evaluating the safety, tolerability, pharmacokinetics (PK)/pharmacodynamics (PD), and clinical activity of KT-253 in patients with relapsed or refractory high grade myeloid malignancies, including acute myeloid leukemia (AML), acute lymphocytic leukemia (ALL), lymphomas, and solid tumors.

The poster provides a clinical update from the ongoing KT-253 Phase 1 trial from 24 patients including 16 patients in Arm A (solid tumors and lymphomas) at dose levels (DL) 1-5, and 8 patients in Arm B (high grade myeloid malignancies) at DL1-3 as of April 9, 2024. The most common solid tumor types treated were Merkel cell carcinoma (MCC) in 3 patients, adenoid cystic carcinoma (ACC) in 2 patients, melanoma in 2 patients, and uveal melanoma in 2 patients. Highlights include:

- Disease Response Assessments:
  - Arm A: One partial response confirmed in a MCC patient in DL1. Additionally, 4 stable diseases were reported for patients with fibromyxoid sarcoma, ACC, and renal cell cancer in DL1-3, respectively.
  - Arm B: One confirmed complete response in DL2 and one confirmed partial response in DL1, both in patients with post-myeloproliferative neoplasm (MPN) AML.
- KT-253 treatment resulted in upregulation of p53 pathway activation biomarkers, including plasma GDF-15 protein and CDKN1A and PHLDA3 mRNA levels in blood, even at the lowest dose levels in solid tumor and AML patients, providing proof of mechanism for MDM2 target engagement.
- KT-253 demonstrated dose-dependent increase in plasma exposure with levels approximating projected efficacious doses.
- KT-253 was generally well-tolerated with the most common adverse events (AEs) considered related to KT-253 including nausea, fatigue, and decreased appetite. There was 1 dose-limiting toxicity of AEs leading to discontinuation that included Grade 2 fatigue and arthralgia in Arm A DL4. There were no neutropenia or thrombocytopenia AEs in either Arm. In Arm A, KT-253 related serious adverse events (SAEs) included Grade 3 hypotension in a patient with decreased oral intake at DL1 and Grade 3 ventricular tachycardia leading to treatment discontinuation in one patient at DL3. No SAEs were observed in Arm B.

The Phase 1a trial for KT-253 is currently ongoing. The Company expects to complete the study and share additional clinical data to inform the program’s next development steps in 2024 at an upcoming medical meeting. Kymera is also developing a biomarker-based patient selection strategy for subsequent development beyond Phase 1a and is expected to present data at a medical meeting this year.

A copy of the ASCO poster presentation is available in the Resource Library section of Kymera's website.

About KT-253 MDM2 Degrader
KT-253 targets MDM2, the crucial regulator of the most common tumor suppressor, p53. P53 remains intact (wild type) in close to 50% of cancers, meaning that it retains its ability to modulate cancer cell growth. While small molecule inhibitors (SMIs) have been developed to stabilize and upregulate p53 expression, they have been unable to show meaningful clinical benefits of p53 stabilization, with acceptable safety margins, likely due to their inability to overcome a feedback loop that increases MDM2 protein levels when p53 is upregulated. In preclinical studies, KT-253 has shown the ability to overcome the MDM2 feedback loop and rapidly induce cancer cell death with brief exposures, providing the opportunity for an improved

efficacy and safety profile. The Phase 1 study of KT-253 will evaluate the safety, tolerability, pharmacokinetics/pharmacodynamics, and clinical activity of KT-253 in patients with relapsed or refractory high grade myeloid malignancies, including acute myeloid leukemia (AML), acute lymphocytic leukemia (ALL), lymphomas, and solid tumors. KT-253 has achieved clinical proof-of-mechanism in the Phase 1 trial and shown early signs of anti-tumor activity and the Phase 1a trial is currently ongoing. More information on the Phase 1 study can be found at www.clinicaltrials.gov, identifier NCT05775406.

About Kymera Therapeutics
Kymera is a clinical-stage biotechnology company pioneering the field of targeted protein degradation (TPD) to develop medicines that address critical health problems and have the potential to dramatically improve patients' lives. Kymera is deploying TPD to address disease targets and pathways inaccessible with conventional therapeutics. Having advanced the first degrader into the clinic for immunological diseases, Kymera is focused on delivering oral small molecule degraders to provide a new generation of convenient, highly effective therapies for patients with these conditions. Kymera is also progressing degrader oncology programs that target undrugged or poorly drugged proteins to create new ways to fight cancer. Founded in 2016, Kymera has been recognized as one of Boston's top workplaces for the past several years. For more information about our science, pipeline and people, please visit www.kymeratx.com or follow us on X (previously Twitter) or LinkedIn.

Cautionary Note Regarding Forward-Looking Statements
This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, implied and express statements by Kymera Therapeutics regarding its: strategy, business plans and objectives for its clinical programs; plans and timelines for the preclinical and clinical development of its product candidates, including the therapeutic potential, clinical benefits and safety thereof; expectations regarding timing, success and data announcements of current ongoing preclinical and clinical trials; the ability to initiate new clinical programs; and Kymera's financial condition and expected cash runway into the first half of 2027. The words "may," "might," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "expect," "estimate," "seek," "predict," "future," "project," "potential," "continue," "target" and similar words or expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements in this press release are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this press release, including, without limitation, risks associated with: the timing and anticipated results of our current and future preclinical studies and clinical trials, supply chain, strategy and future operations; the delay of any current and future preclinical studies or clinical trials or the development of Kymera Therapeutics' drug candidates; the risk that the results of current preclinical studies and clinical trials may not be predictive of future results in connection with current or future preclinical and clinical trials, including for KT-253; Kymera Therapeutics' ability to successfully demonstrate the safety and efficacy of its drug candidates; the timing and outcome of the Kymera Therapeutics' planned interactions with regulatory authorities; obtaining, maintaining and protecting its intellectual property; the risks associated with pandemics or epidemics; and Kymera Therapeutics' relationships with its existing and future collaboration partners. These and other risks and uncertainties are described in greater detail in the section entitled "Risk Factors" in the Annual Report on Form 10-K for the period ended December 31, 2023, as well as discussions of potential risks, uncertainties, and other important factors in Kymera Therapeutics' subsequent filings with the Securities and Exchange Commission. In addition, any forward-looking statements represent Kymera Therapeutics' views only as of today and should not be relied upon as representing its views as of any subsequent date. Kymera Therapeutics explicitly disclaims any obligation to update any forward-looking statements. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements.

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