Kymera Therapeutics Presents Interim Results from STAT3 Degrader Phase 1 Clinical Trial at American Society of Hematology Annual Meeting

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STAT3 Degrader KT-333 showed early signs of antitumor activity across liquid and solid tumors, including major responses in cutaneous T-cell lymphoma (CTCL) and Hodgkin's lymphoma

Robust STAT3 knockdown and positive immunomodulatory effect demonstrated in tumor as well as blood

KT-333 was generally well-tolerated with dose escalation continuing

WATERTOWN, Mass., Dec. 10, 2023 (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 data from its ongoing KT-333 Phase 1 trial. KT-333, a first-in-class, potent, highly selective, heterobifunctional small molecule degrader of STAT3, demonstrated early signs of antitumor activity at doses that were generally well-tolerated and associated with substantial STAT3 knockdown in blood and tumor. The data were presented at the American Society of Hematology (ASH) 65th Annual Meeting and Exposition taking place from December 9-12, 2023, in San Diego, California.

"We're encouraged by the data from the Phase 1 trial showing consistent fidelity of translation from preclinical models to patients, including STAT3 degradation in blood and tumor, induction of IFN-γ response signature, and antitumor responses in CTCL and Hodgkin's lymphoma, which we believe supports the potential of KT-333 to address both hematological malignancies as a single agent and solid tumors as a potential novel combination partner with anti-PD-1 drugs," said Jared Gollob, M.D., Chief Medical Officer, Kymera Therapeutics. "We look forward to completing the dose escalation portion of the Phase 1 study in 2024 and sharing additional updates on this first-in-class program across a range of indications at future medical meetings."

KT-333 STAT3 Clinical Update

KT-333 degrades STAT3, a transcriptional regulator that has been linked to numerous cancers, as well as to inflammatory and autoimmune diseases, and is being developed for the treatment of STAT3-dependent hematological malignancies and solid tumors. The Phase 1 clinical trial is evaluating the safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD) and clinical activity of KT-333 dosed weekly on 28-day cycles in adult patients with relapsed and/or refractory lymphomas, leukemias and solid tumors.

The poster provides an interim update with a data cut-off as of October 18, 2023. Twenty-nine patients were treated across five dose levels (DL1-5) with a mean of eight doses, including five with cutaneous T-cell lymphoma (CTCL), two with large granular lymphocytic leukemia (LGL-L), one each with peripheral T-cell lymphoma (PTCL), B-cell and Hodgkins's lymphoma, and nineteen with a variety of solid tumor malignancies. Dose escalation is ongoing at DL5 in solid tumor/lymphoma patients and at DL3 in leukemia patients. Dr. Aditi Shastri from Montefiore Medical Center and Albert Einstein College of Medicine, a lead investigator in the study, presented the interim Phase 1 findings. Highlights from the poster presentation include:

- A partial response (PR) was observed in one patient with Hodgkin's lymphoma, and two PRs and one stable disease were reported among the five CTCL patients treated. Stable disease was observed in four patients with advanced solid tumors, including two head and neck cancer patients as well as patients with cholangiocarcinoma and renal cell cancer.
- KT-333 was generally well tolerated with primarily Grade 1 and 2 adverse events which included constipation, fatigue, nausea and anemia. The only KT-333 related adverse events that were Grade 3 or higher were stomatitis, arthralgia, and decreased weight in one patient each. Two dose-limiting toxicities (DLTs), stomatitis and arthralgia, occurred in LGL-L patients at DL5 and no DLTs were observed in solid tumor/lymphoma patients. Based on these findings, the study protocol was revised to continue dose escalation in solid tumor and lymphoma patients separately from patients with leukemia, including LGL-L and T-cell prolymphocytic leukemia (T-PLL) patients. The study continues to enroll solid tumor/lymphoma patients at DL5 and LGL-L/T-PLL patients at DL3.
- KT-333 achieved maximum degradation up to 96% in peripheral blood mononuclear cells at DL4-5 and with evidence of STAT3 pathway inhibition and downregulation of inflammatory biomarkers in peripheral blood.
- A critical cytokine involved in anti-tumor immunity, IFNγ, as well as IFNγ-stimulated genes, were induced in peripheral blood showing functional engagement of the JAK/STAT pathway, similar to preclinical studies.
- KT-333 resulted in substantial reduction of STAT3, pSTAT3 and SOCS3 in a CTCL patient tumor with concomitant induction of IFNγ-stimulated genes, suggestive of positive immunomodulatory response in the tumor microenvironment that both clinically and preclinically has been shown to enhance the activity of anti-PD-1 drugs, supporting potential expansion into combinations of KT-333 and anti-PD-1 agents.

Preclinical data demonstrating the potential of STAT3 protein degraders as a therapeutic approach in venetoclax-resistant Acute Myeloid Leukemia was also presented at the meeting.

A copy of the poster presentation, entitled "Preliminary Safety, Pharmacokinetics, Pharmacodynamics and Clinical Activity of KT-333, a Targeted Protein Degrader of STAT3, in Patients with Relapsed or Refractory Lymphomas, Large Granular Lymphocytic Leukemia, and Solid Tumors" is available in the Scientific Resources section of Kymera's website.

More information on the Phase 1 study can be found at www.clinicaltrials.gov, identifier NCT05225584.

About Kymera Therapeutics
Kymera is a biopharmaceutical company pioneering the field of targeted protein degradation, a transformative approach to address disease targets and pathways inaccessible with conventional therapeutics. Kymera's Pegasus platform is a powerful drug discovery engine, advancing novel small

molecule programs designed to harness the body's innate protein recycling machinery to degrade dysregulated, disease-causing proteins. With a focus on undrugged nodes in validated pathways, Kymera is advancing a pipeline of novel therapeutic candidates designed to address the most promising targets and provide patients with more effective treatments. Kymera's initial programs target IRAK4 and STAT3 within the IL-1R/TLR or JAK/STAT pathways, and the MDM2 oncoprotein, providing the opportunity to treat patients with a broad range of immune-inflammatory diseases, hematologic malignancies, and solid tumors.

Founded in 2016, Kymera is headquartered in Watertown, Mass. Kymera has been named a "Fierce 15" company by Fierce Biotech and has been recognized by both the Boston Globe and the Boston Business Journal as one of Boston's top workplaces. For more information about our people, science and pipeline, 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, including those for KT-333; expectations regarding timing, success and data announcements of current ongoing preclinical and clinical trials, including those for KT-333; the ability to initiate new clinical programs; and Kymera's financial condition and expected cash runway into the second half of 2025. 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 those for KT-333; 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, 2022, and most recent Quarterly Report on Form 10-Q, 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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