Preclinical Data from Kymera Therapeutics' Collaborations Demonstrate Therapeutic Potential of STAT3 Degraders in CTCL and IRAKIMiD Combination with BCL-2 Inhibitor in MYD88-Mutant DLBCL at the American Society of Hematology Annual Meeting

December 12, 2022

Activity of STAT3 degrader in preclinical model of cutaneous T-cell lymphoma (CTCL) validates selective STAT3 degradation as a potential therapeutic strategy for STAT3-driven T cell malignancies

Preclinical study highlights the potential of IRAKIMiDs combined with BCL-2 inhibitor as a therapeutic approach for the treatment of MYD88-mutant diffuse large B-cell lymphoma (DLBCL)

WATERTOWN, Mass., Dec. 12, 2022 (GLOBE NEWSWIRE) -- Kymera Therapeutics, Inc. (NASDAQ: KYMR), a clinical-stage biopharmaceutical company advancing targeted protein degradation to deliver novel small molecule protein degrader medicines, today announced that preclinical data from collaborations for its STAT3 and IRAKIMiD degraders was presented at the American Society of Hematology (ASH) Annual Meeting, taking place from December 10 - 13, 2022 in New Orleans, Louisiana.

The first presentation, "Leveraging Pre-Clinical Animal Model of CTCL to Explore Therapeutic Potential of a Novel STAT3 Degrader," conveys the results of a study conducted in collaboration with the NYU School of Medicine using a STAT3-dependent model of CTCL that shares many key features of human disease. Cutaneous T cell lymphoma (CTCL) is a type of mature T cell lymphoma characterized by the accumulation of malignant T cells in the skin with upregulation of the STAT3 signaling pathway as a key driver of disease pathogenesis. The model was used to evaluate the therapeutic potential of one of Kymera's potent and selective STAT3 heterobifunctional degraders for targeting this difficult-to-treat hematologic malignancy. A single intravenous infusion of a STAT3 degrader led to substantial reduction in STAT3 levels in lymph node T cells, circulating T cells, and skin-resident T cells. Chronic weekly dosing on a 4 weeks on/1 week off schedule resulted in the dramatic amelioration of disease and prevented development of characteristic skin pathology. These data provide a rationale for selective STAT3 degradation as a therapeutic strategy for T cell malignancies such as CTCL that are associated with constitutive activation of STAT3 signaling. Kymera's lead STAT3 degrader, KT-333, is currently being evaluated in a Phase 1 clinical trial in liquid and solid tumors, including CTCL.

The second presentation, "Precision Targeting of MYD88 Mutant DLBCL Using the Novel Combination of IRAKIMiDs and BCL2 Inhibition," was a research collaboration with the Department of Medicine, Lymphoma Service, at Memorial Sloan Kettering Cancer Center. Kymera has previously shown that IRAKIMiD degraders targeting IRAK4 and the IMiD substrates Ikaros and Aiolos have profound antitumor activity in CDX and PDX mouse models of MYD88-mutant DLBCL, where both the NF-kB and IRF4 pathways are upregulated by oncogenic MYD88 mutations. As BCL-2 upregulation has been seen in conjunction with NF-kB activation, the activity of BCL-2 inhibition combined with IRAKIMiDs was assessed in MYD88-mutant and -wild type DLBCL. Strong synergistic inhibition of cell growth and induction of apoptosis in vitro was seen with nanomolar concentrations of an IRAKIMiD combined with the BCL-2 inhibitor venetoclax in MYD88-mutant DLBCL cell lines. Weaker synergy with the combination was seen in wild-type MYD88 DLBCL. These data show the potential for IRAKIMiD/BCL-2 inhibitor combinations in MYD88-mutant DLBCL. Kymera's lead IRAKIMiD compound, KT-413, is currently being evaluated in a Phase 1 clinical trial in B cell lymphoma, including MYD88-mutant DLBCL.

"The results from these two preclinical studies show how our academic collaborations with investigators who have relevant disease models can provide key validation of indication selection, as with CTCL for our KT-333 STAT3 program, or help identify combinations that could be prioritized for testing in the clinic, as with venetoclax for our KT-413 IRAKID program," said Jared Gollob, M.D., Chief Medical Officer at Kymera Therapeutics.

Presentations at ASH Annual Meeting:

- Title: Leveraging Pre-Clinical Animal Model of CTCL to Explore Therapeutic Potential of a Novel STAT3 Degrader
  - Abstract Number: 1545
  - Session Time: 5:30 PM – 7:30 PM CT, December 10, 2022
  - Location: Ernest N. Morial Convention Center, Hall D
  - Presenter: Sergei Koralov, PhD, Department of Pathology, New York University School of Medicine
- Title: Precision Targeting of MYD88 Mutant DLBCL Using the Novel Combination of Irakimids and BCL2 Inhibition
  - Abstract Number: 3995
  - Session Time: 6:00 PM – 8:00 PM CT, December 12, 2022
  - Location: Ernest N. Morial Convention Center, Hall D
  - Presenter: Andre Grilo, PhD, Department of Medicine, Lymphoma Service, Memorial Sloan Kettering Cancer Center

About Kymera Therapeutics

Kymera Therapeutics (Nasdaq: KYMR) 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 therapies that 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 therapeutics designed to address the most intractable pathways and provide new treatments for patients. Kymera's initial programs target IRAK4, IRAKIMiD, and STAT3 within

the IL-1R/TLR or JAK/STAT pathways, providing the opportunity to treat patients with a broad range of immune-inflammatory diseases, hematologic malignancies, and solid tumors. For more information, visit www.kymeratx.com.

Founded in 2016, Kymera is headquartered in Watertown, Mass. Kymera has been named a “Fierce 15” biotechnology 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 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 the IRAK4, IRAKIMiD,STAT3 and MDM2 degrader programs; plans and timelines for the 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 clinical trials; the ability to initiate new clinical programs; and cash position and expected runway. 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 impact of COVID-19 on countries or regions in which we have operations or do business, as well as on 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 future clinical trials; 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; 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, 2021 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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