Kymera Therapeutics Presents Late-Breaking Preclinical Data Highlighting Superiority of Dual-Targeting Activity of IRAKIMiD Degrader KT-413 at AACR Annual Meeting 2021

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KT-413-mediated degradation of IRAK4 and IMiD substrates has synergistic effect on MYD88-NFkB and IRF4-Type 1 Interferon pathways resulting in superior antitumor activity in MYD88-mutant DLBCL models compared to IMiDs or selective IRAK4 targeting alone

Company anticipates IND submission and, if cleared, initiation of Phase 1 trial of KT-413 in relapsed/refractory B cell lymphomas, including MYD88-mutant DLBCL, in 2H 2021

WATERTOWN, Mass., April 10, 2021 (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 presented late-breaking preclinical data showing how the dual targeting of IRAK4 and IMiD substrates by KT-413, its IRAKIMiD degrader currently in preclinical development, synergizes to impact signaling and cell killing in MYD88-mutant diffuse large B cell lymphoma (DLBCL) in a manner that is distinct from IMiDs or selective IRAK4 targeting alone. The data were presented today in a poster session at the American Association of Cancer Research (AACR) Annual Meeting 2021 (LB118: Mechanisms underlying synergistic activity in $MYD88^{MT}$ DLBCL of KT-413, a targeted degrader of IRAK4 and IMiD substrates).

IRAKIMiDs are novel heterobifunctional degraders designed to degrade both IRAK4 and IMiD substrates, including Ikaros and Aiolos, with a single small molecule. IRAKIMiDs synergistically target both the MYD88-NFkB and IRF4-Type 1 interferon pathways to enhance and broaden anti-tumor activity in MYD88-mutant DLBCL. KT-413 is being developed initially for the treatment of relapsed/refractory MYD88-mutant DLBCL, with the potential to expand into other MYD88-mutant indications and IL-1R/NFkB-driven malignancies. KT-413 is currently in preclinical development and Kymera plans to submit an Investigational New Drug Application (IND) to the U.S. Food and Drug Administration (FDA) and, if cleared, initiate a Phase 1 clinical trial in relapsed/refractory B cell lymphomas, including MYD88-mutant DLBCL, in the second half of 2021.

“KT-413 combines IRAK4 degradation with potent IMiD activity in a single agent in order to simultaneously target two signaling pathways central to the malignant phenotype of aggressive, poor prognosis MYD88-mutant DLBCL,” said Jared Gollob, MD, Chief Medical Officer at Kymera Therapeutics. “KT-413 has demonstrated broad activity against MYD88-mutant lymphomas *in vitro* and in mouse xenograft models, leading to rapid, complete and sustained tumor regressions, even when dosed intermittently. Our understanding of the molecular mechanism driving this remarkable antitumor activity allows us to further differentiate this dual-degrader approach from either IMiDs or selective IRAK4 targeting alone.”

Data highlights include:

- KT-413 showed superior cell killing compared to the potent IMiD CC-220 or the IRAK4-selective degrader KTX-545 across MYD88-mutant DLBCL cell lines.
- In an *in vivo* MYD88-mutant mouse xenograft model, intermittent dosing of KT-413 induced deep and sustained tumor regressions, whereas the IMiDs pomalidomide or CC-220 showed only tumor stasis or slight regressions.
- KT-413 uniquely inhibited both IRAK4-dependent MYD88-NFkB signaling and IMiD substrate-dependent IRF4 upregulation and Type 1 interferon response suppression, whereas CC-220 and KTX-545 affected only IRF4-Type 1 interferon or MYD88-NFkB signaling, respectively.
- Global transcriptomics analysis showed KT-413 induced significantly greater downregulation of NFkB, cell cycle and DNA replication pathways, as well as greater activation of interferon and apoptosis pathway signaling, compared to CC-220 or KTX-545.

“We believe this will be the first precision medicine in DLBCL to target a genetically defined population, which accounts for at least 25% of DLBCL patients, and we are excited to begin clinical development of this compound with Phase 1 initiation planned for the second half of this year,” said Nello Mainolfi, PhD, Co-Founder, President and CEO, Kymera Therapeutics. “We are also excited about the potential of this dual mechanism in areas where IMiDs and IRAK4 targeting alone are insufficient to drive profound clinical benefits.”

The AACR poster presentation is available for download at: https://www.kymeratx.com/scientific-resources/?cat=13&tag=all.

About Kymera Therapeutics

Kymera Therapeutics is a clinical-stage biopharmaceutical company focused on advancing the field of targeted protein degradation, a transformative new approach to address previously intractable disease targets. Kymera’s Pegasus™ targeted protein degradation platform harnesses the body’s natural protein recycling machinery to degrade disease-causing proteins, with a focus on undrugged nodes in validated pathways currently inaccessible with conventional therapeutics. Kymera is accelerating drug discovery with an unmatched ability to target and degrade the most intractable of proteins, and advance new treatment options for patients. Kymera’s initial programs are IRAK4, IRAKIMiD, and STAT3, which each address high impact targets within the IL-1R/TLR or JAK/STAT pathways, providing the opportunity to treat a broad range of immune-inflammatory diseases, hematologic malignancies, and solid tumors. For more information, visit www.kymeratx.com.

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 regarding its: strategy, business plans and objectives for the IRAK4, IRAKIMiD and STAT3 degrader programs; and plans and timelines for the clinical development of Kymera Therapeutics' product candidates, including the therapeutic

potential and clinical benefits thereof. 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 preclinical studies and future clinical trials, strategy and future operations; the delay of any current preclinical studies or future clinical trials or the development of Kymera Therapeutics' drug candidates; the risk that the results of current preclinical studies 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 Company’s planned interactions with regulatory authorities, including the resolution of the current partial clinical hold for KT-474; and obtaining, maintaining and protecting its intellectual property. 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, 2020, filed on March 11, 2021, 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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