Kymera Therapeutics Presents New Preclinical Data on STAT3 Degraders at the Society for Immunotherapy of Cancer's (SITC) 36th Annual Meeting

November 12, 2021

WATERTOWN, Mass., Nov. 12, 2021 (GLOBE NEWSWIRE) -- Kymera Therapeutics, Inc. (NASDAQ: KYMR), a clinical-stage biopharmaceutical company advancing targeted protein degradation (TPD) to deliver novel small molecule protein degrader medicines, today presented new preclinical data from its STAT3 degrader program at the Society for Immunotherapy of Cancer's (SITC) 36th Annual Meeting, taking place from November 10 - 14, 2021 in Washington, D.C. and virtually.

The results reveal Kymera's potent and selective STAT3 degraders exhibited anti-tumor activity in multiple preclinical animal models of solid and hematologic malignancies that respond poorly to immunotherapies. Administration of a tool STAT3 degrader, KTX-201, led to molecular and cellular changes in the tumor microenvironment that were predictive of favorable responses to checkpoint inhibition. Consistent with these findings, KTX-201 sensitized these tumors to anti-PD1 treatment when administered in combination, leading to durable anti-tumor responses and development of long-term immunological memory.

"These encouraging findings underscore the potential power of targeted protein degradation (TPD) to address a range of cancers driven by STAT3, an undruggable transcription factor with effects on both tumor cells and the tumor microenvironment," said Jared Gollob, MD, Chief Medical Officer at Kymera Therapeutics. "We believe our novel data offer critical insights into the antitumor activity of Kymera's STAT3 degraders, particularly their potential to synergize with immunotherapies such as checkpoint blockade – which only work in a small percentage of patients – thereby providing a rationale for selectively degrading STAT3 to sensitize cancers to immune checkpoint inhibition in the clinic."

STAT3 is a transcription factor activated through a variety of different cytokine and growth factor receptors via Janus kinases (JAKs), as well as through oncogenic fusion proteins and mutations in STAT3 itself. Long considered an "undruggable" target, STAT3 hyperactivation is prominent in numerous liquid and solid tumors, including clinically aggressive lymphomas. Kymera is developing selective STAT3 degraders for the treatment of hematological malignancies and solid tumors, as well as autoimmune diseases and fibrosis. Kymera's STAT3 degraders have previously demonstrated strong anti-tumor effects in mouse xenograft and syngeneic models of liquid and solid cancers.

"Research presented to date on Kymera's STAT3 degraders has bolstered our knowledge of the mechanisms underlying the anti-tumor and immunomodulatory effects associated with STAT3 degradation," said Nello Mainolfi, PhD, Co-Founder, President and CEO, Kymera Therapeutics. "We are eager to advance KT-333, a first-in-class selective STAT3 degrader for liquid and solid tumors into Phase 1 clinical trials by the end of 2021."

Additional Research Highlights:

- Treatment of CT-26 (colorectal cancer) and A20 (B-cell lymphoma) tumor-bearing mice with a STAT3 degrader resulted in significant tumor growth inhibition compared to controls, with loss of STAT3 protein in both tumor cells and TME.
- Treatment of CT-26 and A20 tumor-bearing mice with a STAT3 degrader led to a decrease in M2 polarized macrophages and concomitant increases in M1 polarized macrophages and tumor infiltrating lymphocytes.
- Gene expression profiling of STAT3 degrader-treated CT-26 tumors showed marked increases in proinflammatory genes including T cell and M1 macrophage activation markers, compared to controls.
- Induction of an *Ifnγ*-responsive gene signature (*Ifnγ*, *Stat1, Cxcl9, Cxcl10, Ido1*) in CT-26 tumors showed that STAT3 degradation results in a T cell inflamed phenotype associated with responsiveness to immune checkpoint therapy.
    - On-treatment tumors showed an upregulation of genes such as *Pdl1, Ctla4, Lag3* which reflect T cell activation as well as counterregulatory mechanisms.
- STAT3 degradation in combination with anti-PD1 resulted in robust synergy in the CT-26 model with 60% complete responses and development of immunological memory as confirmed by tumor rechallenge studies.
- Studies are underway to ascertain the applicability of this combination therapy in different tumor immune contextures, and to elucidate the mechanistic basis of synergy.

Presentation at SITC Annual Meeting:

- Title: Targeted STAT3 Degradation Leads to Remodeling of an Immunosuppressive Tumor Microenvironment and Subsequent Sensitization to Immune Checkpoint Therapy
    - Abstract Number: 603
    - Session Time: 7:00 a.m. – 8:30 a.m. ET on Friday, Nov. 12, 2021
    - Location: Poster Hall (Hall E), Walter E. Washington Convention Center, Washington, D.C.
    - Presenter: Joyoti Dey, Associate Director, Translational Medicine, Kymera Therapeutics

About Kymera Therapeutics
Kymera Therapeutics (Nasdaq: KYMR) is a clinical-stage biopharmaceutical company founded with the mission to discover, develop, and

commercialize transformative therapies while leading the evolution of targeted protein degradation, a transformative new approach to address previously intractable disease targets. Kymera's Pegasus™ platform enables the discovery of novel small molecule degraders designed to harness 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's initial programs are IRAK4, IRAKIMiD, and STAT3, each of which addresses 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. Kymera's goal is to be a fully integrated biopharmaceutical company at the forefront of this new class of protein degrader medicines, with a pipeline of novel degrader medicines targeting disease-causing proteins that were previously intractable.

Founded in 2016, Kymera is headquartered in Watertown, Mass. Kymera has been named a "Fierce 15" biotechnology company by FierceBiotech and has been recognized by the Boston Business Journal as one of Boston's "Best Places to Work." 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 regarding its: strategy, business plans and objectives for the STAT3 degrader program; 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; 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 Quarterly Report on Form 10-Q for the period ended September 30, 2021, filed on November 10, 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.

Investor Contact:
Bruce Jacobs
Chief Financial Officer
investors@kymeratx.com
857-285-5300

Chris Brinzey
Managing Director, Westwicke
chris.brinzey@westwicke.com
339-970-2843

Media Contact:
Tyler Gagnon
Director, Corporate Communications
tgagnon@kymeratx.com
508-904-9446