Kymera Therapeutics Presents New Preclinical Data for KT-621, a First-In-Class, Oral STAT6 Degrader at the ATS Annual Meeting

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KT-621, a potent, selective, oral STAT6 degrader, demonstrated comparable or superior activity to dupilumab in preclinical studies including an asthma model shared at the ATS Annual Meeting

Additional KT-621 preclinical data was also featured in a poster presentation at Digestive Disease Week

KT-621 expected to start Phase 1 in the second half of 2024, with Phase 1 data in the first half of 2025

WATERTOWN, Mass., May 22, 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 announced the presentation of additional preclinical data for KT-621, a potent, selective, oral heterobifunctional degrader of STAT6, at the American Thoracic Society (ATS) Annual Meeting in San Diego, California. The featured data demonstrate activity of KT-621 comparable to a saturating dose of the IL-4Rα antibody, dupilumab, in an asthma efficacy model which demonstrated that KT-621 robustly inhibited all the tested cytokines, chemokines, and cell infiltrates involved in TH2 inflammation in asthma. The Company shared additional new histology data showing amelioration of lung remodeling after low, daily oral doses of KT-621 that was comparable to dupilumab. These data highlight the compelling profile of KT-621 as a potential oral treatment for asthma and other TH2 respiratory diseases. Kymera intends to initiate Phase 1 testing for KT-621 in the second half of 2024 and expects data from the Phase 1 trial to be reported in the first half of 2025.

“Having advanced the first degrader into the clinic for immunological diseases with KT-474, we’re now focused on delivering additional oral small molecule degraders with biologics-like activity to help as many patients as possible with these conditions,” said Nello Mainolfi, PhD, Founder, President and CEO, Kymera Therapeutics. “KT-621 has the potential to address multiple TH2 immune-mediated diseases and overcome the limitations of existing technologies and agents, such as biologics and traditional small molecule inhibitors. We believe KT-621 can provide the convenience of a once daily oral medicine with the potential to deliver dupilumab-like activity in highly prevalent allergic diseases like asthma, and in doing so has the promise to transform current treatment paradigms and reach broader patient populations.”

The company previously presented data showing its first-in-class oral STAT6 degrader, KT-621, was exquisitely selective for STAT6 over other STATs and fully blocked IL-4/IL-13 functions in key human TH2 cellular assays with picomolar potency that was superior to dupilumab. In addition, at low daily oral doses, preclinical studies with KT-621 demonstrated near full *in vivo* STAT6 degradation in disease-relevant tissues that was well-tolerated. New data shared at ATS show that in the intranasal house dust mite (HDM)-induced asthma model in hIL4/hIL4RA humanized mice, orally administered KT-621 was well tolerated with daily dosing for 30 days and demonstrated excellent *in vivo* efficacy comparable to an IL-4Rα saturating dose of dupilumab included in the same study. KT-621 robustly blocked TH2 inflammation including B cell activation, eosinophil recruitment, serum IgE and HDM-specific IgG1 induction, and reduced disease severity in the lung in this mouse model. Overall, the preclinical data generated to date demonstrate the potential of KT-621 for the treatment of TH2 allergic diseases with best-in-pathway potential given its dupilumab-like activity profile and the convenience of an oral pill.

KT-621 preclinical data was also presented at Digestive Disease Week in Washington, D.C. The data demonstrated reversal of IL-13 stimulatory effects on esophageal smooth muscle cells, an important cell type involved in the pathophysiology of eosinophilic esophagitis. The company plans to share additional preclinical data for KT-621 at upcoming medical meetings in 2024.

Copies of both the ATS and DDW poster presentations are available in the Resource Library section of Kymera's website.

About STAT6 Degrader
STAT6 is an essential transcription factor in the IL-4/IL-13 signaling pathways and the central driver of TH2 inflammation in allergic diseases. Multiple gain of function mutations of STAT6 were identified to cause severe allergic diseases in humans. Dupilumab, an injectable monoclonal antibody that blocks IL-4/IL-13 signaling, is an approved therapy for multiple allergic diseases. STAT6 targeting is therefore supported by both human genetics and clinical pathway validation. STAT6 functions through protein-protein and protein-DNA interactions, and it has been challenging to selectively and potently inhibit STAT6 with small molecule inhibitors. However, it is well suited for a targeted protein degradation approach, where a binding event is sufficient to drive degradation. KT-621 is a once daily, oral STAT6 degrader with dupilumab-like activity and the potential to address multiple diseases including atopic dermatitis, asthma, and chronic obstructive pulmonary disorder, among others. Kymera intends to initiate Phase 1 testing for KT-621 in the in the second half of 2024 and expects data from the Phase 1 trial to be reported in the first half of 2025.

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 KT-621; 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-621; 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. 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, 2024, 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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