Kymera Therapeutics Presents Preclinical Data for KT-621, a Potent, Selective, First-In-Class, Oral STAT6 Degrader at the EADV Congress

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KT-621 has the potential to provide dupilumab-like activity with an oral small molecule profile for TH2 driven allergic and atopic disease

KT-621 demonstrated strong degradation of STAT6 in human sensory neurons resulting in inhibition of IL-13-induced itch- and pain-related gene transcripts with the potential to alleviate these symptoms in atopic dermatitis patients

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., Sept. 25, 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 preclinical data for KT-621, a potent, selective, oral degrader of STAT6, an essential transcription factor that is a central driver of TH2 inflammation. The featured data highlight the differentiated profile of KT-621 as a potential once daily, oral treatment for TH2 driven allergic and atopic diseases. The data were presented at the European Academy of Dermatology and Venereology (EADV) Congress being held September 25-28, 2024, in Amsterdam, Netherlands. The Company has completed IND-enabling studies and intends to initiate Phase 1 testing for KT-621 in the second half of 2024, with data from the Phase 1 trial expected to be reported in the first half of 2025.

“As we continue to demonstrate with disclosures of our preclinical characterization of KT-621, we believe STAT6 degradation has the potential to phenocopy upstream biologics, like dupilumab, but with the convenience of a once daily, oral medicine,” said Nello Mainolfi, PhD, Founder, President and CEO, Kymera Therapeutics. “Developing oral medicines with biologics-like activity and favorable safety profiles represents an enormous opportunity to expand patient access in many important disease areas that are currently dominated by injectable agents including atopic dermatitis, asthma and COPD, among other highly prevalent immune-inflammatory diseases. As a result, we believe Kymera has the potential to deliver differentiated therapeutic solutions to millions of patients suffering from these debilitating and chronic conditions around the world.”

In preclinical studies, KT-621 was exquisitely selective for STAT6 over other STAT proteins and fully blocked the function of IL-4/IL-13, critical cytokines in allergic and atopic inflammation, in key human TH2 cellular assays with picomolar potency that was comparable or 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 and was well-tolerated. In an MC903-induced atopic dermatitis mouse model, orally administered KT-621 demonstrated robust degradation of STAT6 in vivo and marked reduction of total serum IgE comparable to the activity of the IL-4RA saturating dose of dupilumab. In the intranasal house dust mite (HDM)-induced asthma model, KT-621 demonstrated similar robust degradation and reduced all cytokine, cell infiltration, and disease severity readouts in the lung and bronchoalveolar lavage fluid comparable or superior to dupilumab.

New data shared at EADV highlight the potential role of the STAT6 signaling pathway in the molecular mechanisms of TH2 inflammation causing itch and pain in the sensory neurons of the skin in atopic dermatitis. These findings further support the relevance of the STAT6 pathway to the clinical manifestations of the disease. KT-621 demonstrated strong degradation of STAT6 in human iPSC-derived sensory neurons and associated inhibition of IL-13-induced itch- and pain-related gene transcripts, showing the ability of KT-621 to fully block the IL-4/IL-13 pathways in these cells and the potential to alleviate these symptoms in atopic dermatitis patients by effectively targeting and modulating the STAT6 pathway.

A copy of the EADV poster presentation is available in the Resource Library section of Kymera's website. The Company will also present an overview of its KT-621 preclinical data at the American College of Allergy, Asthma, and Immunology (ACAAI) Annual Scientific Meeting being held October 24-28, 2024, in Boston, Massachusetts.

About STAT6 Degrader
STAT6 is a historically undrugged essential transcription factor in the IL-4/IL-13 signaling pathways and the central driver of T helper 2 (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 and atopic 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 heterobifunctional degrader with dupilumab-like activity and the potential to address multiple allergic and atopic diseases including atopic dermatitis, asthma, and chronic obstructive pulmonary disorder, among others. 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.

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 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; Sanofi’s intent to expand the Phase 2 clinical trials of KT- 474/SAR444656; 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 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- 474/SAR444656, KT-333 and KT-253 and its preclinical programs STAT6 and TYK2; 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, 2023, 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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