Kymera Therapeutics Presents Preclinical Data for STAT6 and TYK2 First-In-Class, Oral Degrader Immunology Programs at the American Academy of Dermatology Annual Meeting

March 8, 2024

KT-621 (STAT6) and KT-294 (TYK2) have the potential to provide biologics-like activity with oral small molecule profiles

KT-621 (STAT6) expected to start Phase 1 in second half of 2024 and KT-294 (TYK2) expected to start Phase 1 in first half of 2025, both with Phase 1 data in 2025

WATERTOWN, Mass., March 08, 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 that its preclinical data demonstrating the therapeutic potential of its potent and selective heterobifunctional degraders of STAT6 (KT-621) and TYK2 (KT-294) are being presented in the poster session at the American Academy of Dermatology's Annual Meeting in San Diego, California. Kymera's oral STAT6 and TYK2 degraders have the potential to address multiple immune-mediated diseases and overcome the limitations of existing technologies and agents. Today's poster presentations mark the first time that data from a STAT6 targeted agent and a TYK2 degrader have been shared at a major medical meeting. Based on the results generated to date, Kymera intends to initiate Phase 1 testing for KT-621 and KT-294 in the in the second half of 2024 and the first half of 2025, respectively. Data from both Phase 1 trials are expected to be reported in 2025.

"Our differentiated strategy to targeted protein degradation has resulted in an industry-leading immunology pipeline of oral degrader medicines, each with the potential to treat multiple complex immuno-inflammatory diseases. Our preclinical findings demonstrate the potential advantage of using oral degraders over other technologies to effectively drug critical signaling nodes driving inflammation in a variety of diseases," said Nello Mainolfi, PhD, Founder, President and CEO, Kymera Therapeutics. "Importantly, we believe our STAT6 and TYK2 degraders provide the convenience of oral medicines with the potential for biologics-like activity and in doing so reach broader patient populations compared to injectable biologics or other standards of care."

The findings presented today demonstrate that in preclinical studies, KT-621, Kymera's first-in-class oral STAT6 degrader, 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. 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. In a MC903-induced atopic dermatitis mouse model, KT-621 demonstrated robust degradation of STAT6 in spleen and marked reduction of total serum IgE comparable to the activity of dupilumab. These data demonstrate the potential of KT-621 for the treatment of atopic dermatitis and other allergic diseases with best-in-pathway potential given its dupilumab-like activity profile and the convivence of an oral pill.

Additionally, in preclinical studies, KT-294, Kymera's first-in-class highly selective oral TYK2 degrader, demonstrated picomolar degradation potency and potent inhibition of the IL-23, IL-12 and Type I IFN pathways, showing its potential to recapitulate the biology of human TYK2 loss-of-function profile. KT-294, does not impact any of the other Janus kinase (JAK) proteins and in doing so spares IL-10, unlike the TYK2 small molecule inhibitor, deucravacitinib, which is important in inflammatory bowel disease. In addition, TYK2 degradation leads to superior inhibition of the Type 1 IFN pathway compared to TAK-279[1], which is relevant to the treatment of interferonopathies. The biological differentiation of the TYK2 degrader, KT-294, combined with the ability to provide deep and sustained TYK2 knockdown *in vivo* with low daily oral doses, has the potential to deliver a best-in-class TYK2 profile with broad activity across multiple IL-12/IL-23- and IFN-driven immune-inflammatory diseases potentially reaching pathway biologics activity.

The company plans to share additional preclinical data for KT-621 and KT-294 at upcoming medical meetings in 2024.

Copies of both poster presentations entitled "*Potent and Selective Oral STAT6 Degraders Inhibit IL-4 and IL-13 Functions in Human Cells and Block TH2 Inflammation in a Mouse Model of Atopic Dermatitis*" and " *Potent and Selective TYK2 Degraders, Devoid of JAK Activity, Potently and Completely Suppress IL-12/23 and Type I IFN Signaling Pathways*" 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 a potential biologics-like efficacy profile, to address multiple diseases including atopic dermatitis, asthma, and chronic obstructive pulmonary disorder, among others.

About TYK2 Degrader
TYK2 is a member of the JAK family of kinases that binds the IL-12, IL-23 and interferon (IFN) receptors to recruit and phosphorylate STAT transcription factors. A loss of function variant is protective in autoimmune diseases and an allosteric inhibitor of TYK2, as well as biological agents targeting IL-12, IL-23 and Type I IFN, have been approved for the treatment of multiple autoimmune diseases, making TYK2 a highly validated target. TYK2 has a well-established scaffolding function that plays a key role in cytokine receptor surface expression and activation. By blocking both the catalytic and scaffolding functions, degradation of TYK2 has the potential to recapitulate the human loss-of-function biology of near full pathway inhibition of Type I IFN, IL-12 and IL-23, while also sparing IL-10/IL-22 and the ability to overcome the challenges of small molecule inhibitors, which have limitations due to lack of selectivity, limited target engagement, and/or lack of potent activity against Type I IFN. KT-294 is a once daily, oral TYK2 degrader with a potential biologics-like efficacy profile, to address conditions such as inflammatory bowel disease, psoriasis, psoriatic arthritis, and lupus, among others.

[1]Gangolli et al., SID 2022

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 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-621 and KT-294; 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, 2022, 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.

Investor & Media Contact:

Justine Koenigsberg
Vice President, Investor Relations
investors@kymeratx.com
media@kymeratx.com
857-285-5300