Kymera Therapeutics Announces Publication of Phase 1 Trial Results for KT-474 (SAR444656), a First-in-Class IRAK4 Degrader, in Nature Medicine

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KT-474 showed evidence of robust target degradation and pathway inhibition with a favorable safety profile in healthy volunteers and patients

Trial showed encouraging impact on disease burden and symptoms in Hidradenitis Suppurativa (HS) and Atopic Dermatitis (AD), with a systemic anti-inflammatory effect observed in patients with moderate-to-severe disease

Study is first published clinical trial using a heterobifunctional degrader

Kymera's partner Sanofi conducting Phase 2 clinical trials of KT-474 (SAR444656) in HS and AD

WATERTOWN, Mass., Nov. 13, 2023 (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 results from the positive Phase 1 clinical trial from its lead program, KT-474 (SAR444656), a potent, highly selective, orally bioavailable IRAK4 degrader, were published in *Nature Medicine*. The results showed a reduction of disease-relevant inflammatory biomarkers in the blood and skin of HS and AD patients associated with improvement in skin lesions and symptoms. The full manuscript, "IRAK4 degrader in hidradenitis suppurativa and atopic dermatitis: a phase 1 trial," was published online on November 13, 2023, on the *Nature Medicine* website.

The data reported in the publication show that KT-474 administered to HS and AD patients had safety, pharmacokinetics and pharmacodynamics similar to healthy volunteers (HVs), achieved robust IRAK4 degradation in blood and skin lesions associated with a systemic anti-inflammatory effect, and showed activity in HS and AD. The Company previously reported Phase 1 results in December 2022 and at the European Academy of Dermatology and Venereology Symposium in May 2023. The publication also highlights preclinical data on KT-474, including the first publication of the compound's chemical structure.

"The Phase 1 results published in *Nature Medicine* highlight the transformative potential of IRAK4 degradation in TLR/IL-1R-driven, high unmet need inflammatory diseases, with KT-474 demonstrating a favorable safety profile, broad anti-inflammatory effect including downregulation of disease-relevant gene transcripts in skin lesions, and promising impact on skin lesions and symptoms in HS and AD patients after only 28 days of dosing," said Jared Gollob, M.D., Chief Medical Officer, Kymera Therapeutics. "These positive data show TPD's unique ability to unlock this critical pathway, and we look forward to sharing additional updates as our partner Sanofi advances the Phase 2 clinical trials of KT-474 in HS and AD."

Highlights from the Nature Medicine Publication

KT-474 (SAR444656) was studied in a Phase 1 randomized, placebo-controlled, single and multiple ascending dose trial to assess safety, pharmacokinetics, pharmacodynamics and clinical activity (NCT04772885). 105 healthy volunteers (HVs) were enrolled in the placebo-controlled single and multiple ascending dose escalation cohorts (SAD and MAD) and 21 HS and AD patients were enrolled into an open-label patient cohort. KT-474 was administered as a single dose and then daily for 14 days in the fasted state in HVs followed by dosing for 28 days in the fed state in patients with HS or AD. Degradation of IRAK4 was observed in HV blood, with mean reductions after a single dose of ≥93% at 600–1600 mg and after 14 daily doses of ≥95% at 50–200 mg. In patients treated with 75 mg of KT-474, similar IRAK4 degradation was achieved in blood, and IRAK4 was normalized in skin lesions where it was overexpressed relative to HVs. Reduction of disease-relevant inflammatory biomarkers was demonstrated in the blood and skin of HS and AD patients associated with improvement in skin lesions and symptoms. KT-474 was well-tolerated with no drug-related infections. These results from the first published clinical trial using a heterobifunctional degrader provide initial proof of concept for KT-474 in HS and AD to be further confirmed in placebo-controlled Phase 2 trials.

About KT-474 (SAR444656)
KT-474 (SAR444656) is a first-in-class IRAK4 degrader in development for the treatment of immune-inflammatory diseases with significant patient need, such as hidradenitis suppurativa (HS), atopic dermatitis (AD), and potentially others. IRAK4 is a key protein of the myddosome complex that mediates signaling through IL-1 and toll-like receptors, which play a crucial role in initiating the immune response against invading pathogens. IRAK4 is a scaffolding kinase that acts at the interface of the innate and adaptive immune responses with a variety of functions depending on its kinase activity and scaffolding function. Eliminating IRAK4 completely through degradation impacts both the kinase and scaffolding functions, therefore having the potential to achieve a broad, well-tolerated, anti-inflammatory effect providing a novel therapeutic approach for a variety of immune-inflammatory diseases. Sanofi, which is collaborating with Kymera on the development of KT-474 (SAR444656) outside of the oncology and immuno-oncology fields, is conducting Phase 2 clinical trials of KT-474 in both HS and AD.

More information on the Phase 2 studies in HS (NCT06028230) and AD (NCT06058156) can be found at www.clinicaltrials.gov.

About Kymera Therapeutics
Kymera is a biopharmaceutical company pioneering the field of targeted protein degradation, a transformative approach to address disease targets and pathways inaccessible with conventional therapeutics. Kymera's Pegasus platform is a powerful drug discovery engine, advancing novel small molecule programs designed to harness the body's innate protein recycling machinery to degrade dysregulated, disease-causing proteins. With a focus on undrugged nodes in validated pathways, Kymera is advancing a pipeline of novel therapeutic candidates designed to address the most promising targets and provide patients with more effective treatments. Kymera's initial programs target IRAK4 and STAT3 within the IL-1R/TLR or JAK/STAT pathways, and the MDM2 oncoprotein, providing the opportunity to treat patients with a broad range of immune-inflammatory diseases, hematologic malignancies, and solid tumors.

Founded in 2016, Kymera is headquartered in Watertown, Mass. Kymera has been named a "Fierce 15" company by Fierce Biotech and has been recognized by both the Boston Globe and the Boston Business Journal as one of Boston's top workplaces. For more information about our people, science and pipeline, 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 second half of 2025. 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); 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 Contact:

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

Media Contact:

Todd Cooper
Senior Vice President, Corporate Affairs
media@kymeratx.com
857-285-5300