Kymera Therapeutics Presents Positive Late-Breaking Data from Non-Interventional Study in Patients with Hidradenitis Suppurativa at the Society for Investigative Dermatology 2021 Annual Meeting

May 3, 2021

Data provide further evidence for the central role of IRAK4 in inflammation in hidradenitis suppurativa and support both the degrader rationale for targeting IRAK4 and KT-474 development

KT-474 is in Phase 1 clinical development as a first-in-class oral IRAK4 degrader for the treatment of immune-inflammatory diseases, such as atopic dermatitis, hidradenitis suppurativa, rheumatoid arthritis, and potentially others

WATERTOWN, Mass., May 03, 2021 (GLOBE NEWSWIRE) -- Kymera Therapeutics, Inc. (NASDAQ: KYMR), a clinical-stage biopharmaceutical company advancing targeted protein degradation to deliver novel small molecule protein degrader medicines, today presented positive late-breaking data in patients with hidradenitis suppurativa (HS) from its non-interventional study of patients with HS or atopic dermatitis (AD). The non-interventional study is evaluating expression of IRAK4 and other mediators of inflammation in the skin and blood of patients with HS or AD and the *ex vivo* effect of the IRAK4 degrader KT-474. The late-breaking data presentation is available at the Society for Investigative Dermatology (SID) 2021 Annual Meeting, being held virtually May 3-8, 2021 (LB819: Multiple mediators of inflammation correlate with IRAK4 expression in the skin of hidradenitis suppurativa patients and are blocked by the IRAK4 protein degrader KT-474 in TLR-activated monocytes).

The non-interventional study is designed to characterize IRAK4 expression and its relationship to inflammatory biomarkers in diseased tissues of HS or AD patients, as well as demonstrate *ex vivo* proof of mechanism with KT-474. Conducted in collaboration with Afsaneh Alavi, MD, at York Dermatology Clinic and Research Center in Ontario, Canada, the non-interventional trial enrolled 30 patients with HS and 10 patients with AD. Interim data from HS patients, including IRAK4 expression in the skin and blood of HS patients and *ex vivo* treatment of whole blood with KT-474, were previously presented at the 5th Annual Symposium on Hidradenitis Suppurativa Advances (SHSA) in October 2020. The presentation at the SID Annual Meeting includes the full HS dataset for IRAK4 and inflammatory gene transcripts in skin, as well as data from healthy subject skin and from healthy monocytes treated *ex vivo* with KT-474 prior to toll-like receptor (TLR) stimulation. Additional study results, including data from patients with AD, are expected to be presented later this year.

“IRAK4 plays a central role in inflammation through its control of TLR and IL-1R signaling, and these data from our non-interventional study showing upregulation of gene transcripts for multiple mediators of inflammation in active HS skin lesions that correlates with IRAK4 protein expression support the relevance of the IRAK4 signaling pathway in HS,” said Jared Gollob, MD, Chief Medical Officer at Kymera Therapeutics. “The ability of KT-474 to inhibit TLR-mediated upregulation of many of these same genes in monocytes, a key driver of inflammation in HS with overexpression of IRAK4 relative to other immune cell subsets, further points to the central role of IRAK4 in HS skin lesions and underscores the potential of an IRAK4 degrader to impact the clinical manifestations of HS.”

Data highlights include:

- IRAK4 protein, as measured by both immunofluorescence and mass spectrometry, was overexpressed in HS skin lesions relative to skin from healthy subjects due to an increase in the number of IRAK4-positive dermal immune cells and epidermal keratinocytes
- Gene expression profiling showed upregulation of multiple mediators of inflammation in HS skin lesions that correlated with IRAK4 protein overexpression, including genes involved in TLR/myddosome signaling, inflammasome activity, prostaglandin generation, Th1 and Th17 inflammation, and monocyte/neutrophil migration and activation
- IRAK4 degrader KT-474 inhibited TLR-stimulated upregulation of HS-overexpressed inflammatory genes (such as IL-1b, IL-6, TNF-a, CXCL8 and PTGS2) in monocytes from healthy subjects

“HS is a chronic and debilitating inflammatory skin disease with critical unmet medical needs that call for the development of new and better treatments,” said Dr. Alavi, Principal Investigator and currently at Mayo Clinic in Rochester, MN. “These new results linking IRAK4 protein expression to the pleiotropic inflammation in HS skin lesions suggest that selective IRAK4 targeting with KT-474 could have a broad anti-inflammatory effect with the potential to improve patient outcomes.”

“The dataset generated in HS patients continues to validate the role of IRAK4 as a key focal mediator of inflammation in this serious disease and derisks both our target selection, as well as our development strategy, for KT-474, the first IRAK4 degrader and first heterobifunctional small molecule protein degrader to enter clinical development outside of oncology. Our ongoing Phase 1 trial in healthy volunteers and patients with HS or AD provides us with the opportunity to generate one of the most robust datasets in the targeted protein degradation field to date, including proof-of-biology in TLR/IL-1R-driven skin diseases using the same biomarker assays established in the non-interventional study,” said Nello Mainolfi, PhD, Co-Founder, President and CEO, Kymera Therapeutics.

Presentation Details:

- Abstract: LB819
- Title: Multiple mediators of inflammation correlate with IRAK4 expression in the skin of hidradenitis suppurativa patients

and are blocked by the IRAK4 protein degrader KT-474 in TLR-activated monocytes
- Session: Translational Studies
- Session Time: 2:30 PM-4:00 PM ET on Thursday, May 6, 2021
- Presenter: Afsaneh Alavi, MD, Mayo Clinic (Principal Investigator)

The presentation is available on demand from May 3-31, 2021 and is available for download at https://www.kymeratx.com/scientific-resources/.

About IRAK4 and KT-474

IRAK4 is a key protein involved in inflammation mediated by the activation of toll-like receptors (TLRs) and IL-1 receptors (IL-1Rs). Aberrant activation of these pathways is the underlying cause of multiple immune-inflammatory conditions. KT-474, a potential first-in-class, orally bioavailable IRAK4 degrader, is being developed for the treatment of TLR/IL-1R-driven immune-inflammatory diseases with high unmet medical need, such as atopic dermatitis, hidradenitis suppurativa, rheumatoid arthritis, and potentially others. KT-474 is designed to block TLR/IL-1R-mediated inflammation more broadly compared to monoclonal antibodies targeting single cytokines, and to enable pathway inhibition that is superior to IRAK4 kinase inhibitors by abolishing both the kinase and scaffolding functions of IRAK4. In February 2021, Kymera initiated dosing of healthy volunteers in a first-in-human Phase 1 single and multiple ascending dose trial designed to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of orally administered KT-474 in adult healthy volunteers and patients with atopic dermatitis or hidradenitis suppurativa.

Kymera is collaborating with Sanofi on the development of degrader candidates targeting IRAK4, including KT-474 (SAR444656), outside of the oncology and immuno-oncology fields.

About Pegasus™

Pegasus™ is Kymera Therapeutics' proprietary protein degradation platform, created by its team of experienced drug hunters to improve the effectiveness of targeted protein degradation and generate a pipeline of novel therapeutics for previously undruggable diseases. The platform consists of informatics-driven target identification, novel E3 ligases, proprietary ternary complex predictive modeling capabilities, and degradation tools.

About Kymera Therapeutics

Kymera Therapeutics is a clinical-stage biopharmaceutical company focused on advancing the field of targeted protein degradation, a transformative new approach to address previously intractable disease targets. Kymera's Pegasus™ targeted protein degradation platform harnesses 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 is accelerating drug discovery with an unmatched ability to target and degrade the most intractable of proteins, and advance new treatment options for patients. Kymera's initial programs are IRAK4, IRAKIMiD, and STAT3, which each address 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. For more information, visit www.kymeratx.com.

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: beliefs regarding the potential clinical impact of KT-474, including resulting datasets, and plans to present new data; strategy, business plans and objectives for the IRAK4, IRAKIMiD and STAT3 degrader programs; beliefs regarding the roles of IRAK4 and the potential of an IRAK4 degrader to improve patient outcomes; 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, including the resolution of the current partial clinical hold for KT-474; 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 Annual Report on Form 10-K for the period ended December 31, 2020, filed on March 11, 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.

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