Kymera Therapeutics Announces Positive First-in-Human Results from Phase 1 Healthy Volunteer Clinical Trial of KT-621, a First-in-Class, Oral STAT6 Degrader

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Phase 1 healthy volunteer data of KT-621, a once-a-day STAT6 degrader, surpass Kymera's target product profile, significantly derisking program and further validating its oral, biologics-like profile

>90% mean STAT6 degradation in blood achieved at all doses above 1.5 mg

Complete STAT6 degradation achieved in both blood and skin at all MAD doses ≥50 mg

KT-621 impact on Th2 biomarkers in line or superior to dupilumab with median TARC reduction up to 37% and median Eotaxin-3 reduction up to 63%

KT-621 was well-tolerated with a safety profile undifferentiated from placebo, with no serious adverse events, no severe adverse events, no treatment related adverse events in more than one subject, and no clinically relevant changes in vital signs, lab tests or ECGs

KT-621 BroADen Phase 1b trial in moderate to severe atopic dermatitis (AD) actively recruiting, with data expected in 4Q25

Two parallel Phase 2b trials in AD and asthma planned to start in 4Q25 and 1Q26, respectively

Company to hold video conference call and webcast today at 8:00 a.m. ET

WATERTOWN, Mass., June 02, 2025 (GLOBE NEWSWIRE) -- Kymera Therapeutics, Inc. (NASDAQ: KYMR), a clinical-stage biopharmaceutical company advancing a new class of oral small molecule degrader medicines for immunological diseases, today announced positive clinical results from the Phase 1 healthy volunteer study of KT-621, its first-in-class, oral STAT6 degrader medicine.

"Our primary objective was to demonstrate that KT-621 could achieve robust STAT6 degradation in blood and skin that was well tolerated, and these results go well beyond our expectations. Building from the compelling preclinical data demonstrating a dupilumab-like profile, this impressive dataset, the first reported clinical data for a STAT6-targeted medicine, is a powerful demonstration of what we believe is an impeccable translation into humans. KT-621's degradation potency, tolerability and initial Th2 biomarker profile in healthy volunteers demonstrates its potential for the treatment of IL-4/IL-13-driven allergic diseases, and of Kymera's strategy and ability to develop revolutionary oral small molecules with the activity and safety of injectable biologics," said Nello Mainolfi, PhD, Founder, President and CEO, Kymera Therapeutics.

Dr. Mainolfi continued, "Across every measure, the KT-621 Phase 1 results were exceptional. We exceeded our 90% STAT6 degradation target even at single doses as low as 6.25 mg, which supports KT-621's excellent potency profile. Complete degradation was achieved by KT-621 in both blood and skin in all MAD cohorts at or above 50 mg. Importantly, KT-621 was well tolerated with a safety profile undifferentiated from placebo, with no serious adverse events in the trial and no treatment related adverse events in more than one patient. This safety profile was achieved at MAD dose levels up to and including 200 mg, which was 16-fold above the dose level at which 90% degradation in blood and skin was first achieved. The Th2 biomarker results were very encouraging as well, particularly given the limitation of these measures in healthy volunteers, and were comparable or superior to published dupilumab results. We are excited to advance the development of this innovative program in the ongoing BroADen Phase 1b study in AD patients and are on track to start the first Phase 2b studies in AD and asthma later this year and early next year, respectively."

Study Design

The KT-621 Phase 1 healthy volunteer trial was a double-blind, placebo-controlled study that enrolled a total of 118 subjects. The trial consisted of single ascending dose (SAD) and multiple ascending dose (MAD) cohorts. The trial objective was to evaluate the safety and tolerability of escalating single and multiple ascending daily oral doses of KT-621. The trial also included pharmacokinetic measures as secondary endpoints. Exploratory endpoints included STAT6 protein levels in blood (SAD and MAD) and skin (MAD) and Th2 biomarkers (MAD).

There were 48 healthy participants enrolled in SAD, with 8 per cohort randomized 6:2 (KT-621:placebo). The SAD doses, which were administered as a single dose, ranged from 6.25 to 800 mg. There were 70 healthy subjects enrolled in MAD, with 12 per cohort randomized 9:3 (KT-621:placebo) except for the 12.5 mg cohort which randomized 10 participants (7:3). The MAD doses, which were administered once daily for 14 days, ranged from 1.5 to 200 mg.

Pharmacokinetics (PK)

KT-621 demonstrated a favorable plasma PK profile after single and multiple doses. Rapid absorption was demonstrated with a median t_{max} of 2-4 hours and a mean half-life of 9-36 hours. There was a dose-proportional increase in exposure after multi-dosing and steady-state was achieved by Day 4.

Pharmacodynamics (PD)

KT-621 demonstrated rapid, deep and prolonged STAT6 degradation in blood after single doses of KT-621 and in blood and skin after multiple doses of KT-621.

STAT6 levels in blood and skin were measured using a highly sensitive and quantitative mass spectrometry assay. Complete degradation within a cohort is defined as either a mean reduction of ≥95% or when most subjects' STAT6 levels are reduced below the Lower Limit of Quantification (LLOQ), or both.

In SAD, maximal degradation was achieved in blood as quickly as the first collected timepoint of 4 hours after a single dose, with mean STAT6 degradation reaching >90% across all SAD doses starting at 6.25 mg. All SAD cohorts at doses of 75 mg or greater achieved >95% mean STAT6 degradation with STAT6 levels below LLOQ in multiple subjects.

In MAD, robust STAT6 degradation was observed in blood at the first timepoint measured (8 hours) for doses above 1.5 mg. Steady-state, complete degradation, associated with STAT6 reductions below the LLOQ in the majority of subjects, was achieved at doses ≥50 mg with recovery starting as

early as 4 days post-last dose.

In MAD, robust STAT6 degradation was observed in skin at the first timepoint measured (Day 7) for doses above 1.5 mg. Steady-state, complete degradation, associated with ≥95% mean STAT6 degradation with STAT6 levels below LLOQ in multiple subjects, was achieved at doses ≥50 mg.

Th2 Biomarkers

The impact of STAT6 degradation on Th2 biomarkers was assessed in the MAD cohorts, despite the low baseline levels typically seen in healthy volunteers. TARC reduction was observed for all KT-621 dose groups, with median reduction of up to 37% at Day 14. We believe these results are comparable or superior to what was seen in the dupilumab healthy volunteer study. In line with the dupilumab study in healthy volunteers, minimal IgE reductions were observed given the low levels of IgE at baseline and the short duration of treatment. Eotaxin-3, a highly specific downstream cytokine of the IL-4/IL-13 pathway, was also measured. Eotaxin-3 reduction was observed for all KT-621 dose groups with a median reduction of 63% at Day 14. These results are superior to what has been reported with dupilumab in asthma or chronic rhinosinusitis with nasal polyps (CRSwNP) patients even at 52 weeks.

Safety and Tolerability

The safety profile of KT-621 was undifferentiated from placebo. There were no serious adverse events (SAEs), no severe AEs, no treatment related adverse events (TRAEs) in more than one subject, no TRAEs leading to discontinuation, and no clinically relevant changes in vital signs, laboratory tests and ECGs.

Next Steps

The Company's KT-621 BroADen Phase 1b trial in moderate to severe AD patients is ongoing, with data expected to be reported in the fourth quarter of 2025. Two parallel Phase 2b trials in AD and asthma are planned to start in 4Q25 and 1Q26, respectively. These studies are intended to accelerate KT-621 development and enable dose selection for subsequent parallel Phase 3 registration studies across multiple Th2 dermatology, gastroenterology and respiratory indications.

Event Details

Kymera will host a video conference call today, June 2, 2025, at 8:00 a.m. ET. To join the video call or view the livestreamed webcast please register via this **link** or visit "News and Events" in the Investors section of Kymera's website at www.kymeratx.com. A replay of the webcast and the presentation will be available following the event.

About KT-621
KT-621 is an investigational, first-in-class, once daily, oral degrader of STAT6, the specific transcription factor responsible for IL-4/IL-13 signaling and the central driver of Th2 inflammation. STAT6 degradation has the potential to provide the convenience of an oral medicine with the potential for biologics-like activity and in doing so reach broader patient populations compared to injectable biologics or other standards of care. In the Phase 1 clinical study in healthy volunteers, KT-621 demonstrated robust STAT6 degradation in blood and skin following low daily oral doses, reductions of multiple Th2 disease-relevant cytokines, and a favorable safety profile. KT-621, the first STAT6 directed medicine to enter clinical evaluation, has the opportunity to transform treatment paradigms for more than 130 million patients around the world, including children and adults, suffering from Th2 diseases such as AD, asthma, chronic obstructive pulmonary disease (COPD), prurigo nodularis (PN), chronic rhinosinusitis with nasal polyps (CRSwNP), eosinophilic esophagitis (EoE), bullous pemphigoid (BP), and chronic spontaneous urticaria (CSU), among others.

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 building an industry-leading pipeline of oral small molecule degraders to provide a new generation of convenient, highly effective therapies for patients with these conditions. 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.

Availability of Other Information About Kymera Therapeutics
For more information, please visit the Kymera website at https://www.kymeratx.com/ or follow Kymera on X (@KymeraTx) and LinkedIn (Kymera Therapeutics). Investors and others should note that Kymera communicates with its investors and the public using the Company website, including, but not limited to, corporate disclosures, investor presentations, FAQs, Securities and Exchange Commission (SEC) filings, and press releases, as well as on X and LinkedIn. The information that Kymera posts on its website or on X or LinkedIn could be deemed to be material information. As a result, Kymera encourages investors, the media and others interested to review the information that Kymera posts there on a regular basis. The contents of Kymera's website or social media shall not be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended.

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 about our expectations regarding strategy, business plans and objectives on the development of KT-621, including the therapeutic potential, clinical benefits and safety thereof, the Phase 1b data readout of KT-621 in AD patients in the fourth quarter of 2025, the initiation of Phase 2b studies of KT-621 in patients with AD and asthma in the fourth quarter of 2025 and first quarter of 2026, respectively, the effect of initial parallel development of Phase 2b studies in AD and asthma patients on acceleration of late parallel development and dose selection across multiple indications, and the preliminary cross-study assessments comparing non-head-to-head clinical data of KT-621 to published data for dupilumab. The words "may," "might," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "expect," "estimate," "seek," "predict," "future," "project," "potential," "continue," "target," "upcoming" 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 any forward-looking statements contained in this press release, including, without limitation, risks associated with: the risk that cross-trial comparisons may not be reliable as no head-to-head trials have been conducted comparing KT-621 to dupilumab, and Phase 1 clinical data for KT-621 may not be directly comparable to dupilumab's clinical data due to differences in molecule composition, trial protocols, dosing regimens, and patient populations and characteristics, that the results from the Phase 1b KT-621 trial may differ from the Phase 1 KT-621 data, that preclinical and clinical data, including the results from the Phase 1 trial of KT-621, is not predictive of, may be inconsistent with, or more favorable than, data generated from future or ongoing clinical trials of the same product candidate, uncertainties inherent in the initiation, timing and design of future clinical trials, the availability and timing of data from ongoing and future clinical trials and the results of such trials, the ability to successfully demonstrate the safety and efficacy of drug candidates, the timing and outcome of planned interactions with and submissions to regulatory authorities, the availability of funding sufficient for our operating expenses and capital expenditure requirements and other factors. These risks and uncertainties are described in greater detail in the section entitled "Risk Factors" in the most recent Quarterly Report on Form

10-Q and in subsequent filings with the SEC. In addition, any forward-looking statements represent our views only as of today and should not be relied upon as representing our views as of any subsequent date. We explicitly disclaim 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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