# Kymera Therapeutics Expands Industry Leading Immunology Pipeline with New First-in-Class, Oral IRF5 Degrader Program with Potential to Address Multiple Immuno-Inflammatory Diseases

May 9, 2025

*IRF5 program strengthens Kymera's oral immunology pipeline with a complementary mechanism to expand into rheumatic and other autoimmune diseases with a potential best-in-class oral drug*

*IRF5, a historically undrugged transcription factor and master regulator of immunity, has strong genetic and clinical pathway validation across multiple diseases including RA, SLE, IBD and others*

*KT-579, a potent, selective, oral degrader of IRF5 with an excellent profile in preclinical safety studies, has demonstrated activity comparable or superior to approved and clinically active drugs in multiple efficacy animal models of lupus and RA*

*IND-enabling studies are ongoing with Phase 1 testing expected to begin in early 2026*

*Company to hold video webcast today at 10:00 a.m. ET as part of the release of first quarter 2025 results*

WATERTOWN, Mass., May 09, 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 unveiled a new wholly-owned program within its industry-leading oral immunology pipeline. KT-579, a highly potent, selective, first-in-class development candidate, targets IRF5, an essential signaling node in genetically and clinically validated immune pathways driving inflammation in many diseases with no or suboptimal oral options. The new program serves as a valuable addition to the Company's current portfolio, positioned to target multiple common immuno-inflammatory diseases with the potential to expand access to oral systemic advanced therapies for broader patient populations. Kymera will share preclinical data and outline upcoming milestones for KT-579 during a video webcast this morning.

"We're excited to unveil KT-579 as the latest addition to our paradigm-shifting oral immunology portfolio, providing a complementary immunoregulatory mechanism to our existing pipeline. IRF5 is a master regulator of immunity, and we believe blocking its activity with our degrader has the potential to deliver a transformative oral option in multiple chronic, debilitating rheumatic and autoimmune diseases," said Nello Mainolfi, PhD, Founder, President and CEO, Kymera Therapeutics. "The compelling data we have generated demonstrating activity in human primary cells, patient cell samples, and preclinical animal models showcases, for the first time in industry, that targeting IRF5 can lead to correcting immune dysregulation in a disease specific way while generally sparing normal cells."

Historically an undrugged transcription factor, IRF5 is a master regulator of innate and adaptive immune response pathways involving pro-inflammatory cytokines (TNFα, IL-6, IL-12, IL-23), B cell activation (autoantibody production), and Type I Interferon (IFN). IRF5 is selectively expressed and activated in specific cell types such as dendritic cells, monocytes, macrophages, and B cells. Its cell- and disease activation-specific profile has the potential to block cell-specific immune dysregulation while sparing normal cell function. IRF5 has been challenging to drug using traditional small molecule inhibitors due to multiple complex activation steps and the high degree of IRF family member homology.

KT-579, a potent, selective and oral degrader has the potential to be the first IRF5-targeted therapy to deliver a completely novel and potentially transformative treatment option, in many cases superior to pathway biologics, in rheumatic and autoimmune diseases such as lupus, Sjögren's, RA, IBD, among others. Currently in IND-enabling studies, the Company intends to advance KT-579 into Phase 1 clinical testing in early 2026.

In preclinical studies, KT-579 demonstrated an encouraging profile in human primary cells, patient derived cells, and *in vivo* disease models generally superior to existing standards of care:

- **Selectivity and Potency:** KT-579 was highly selective for IRF5 over all other proteins in the detectable proteome including other IRF family proteins. KT-579 also demonstrated picomolar to nanomolar potencies across all relevant human cell types evaluated, including B cells, dendritic cells, macrophages, and monocytes. KT-579 demonstrated potent inhibition of proinflammatory cytokines downstream of TLR4, TLR7, TLR8 and TLR9 activation in cellular assays and blocked Type I IFN production and response.
- ***In Vivo* Profile:** KT-579 achieved robust degradation (>90%) across multiple preclinical species *in vivo* and in all disease-relevant tissues with low oral doses. In preclinical safety studies, KT-579 did not show any adverse effects at concentrations up to 200-fold the projected human efficacious levels, demonstrating a favorable safety profile.
- **Efficacy Models:** In several preclinical efficacy models of lupus and RA, KT-579 was generally more efficacious than clinically active or marketed small molecule inhibitors and injectable biologics, phenocopying IRF5 knockout studies. In a lupus model, KT-579 demonstrated sustained and near complete reduction of proteinuria and circulating autoantibodies superior to the current standard of care. Additionally, in lupus patient PBMC samples, KT-579 effectively blocked TLR7- and TLR8-induced pro-inflammatory cytokines and IFNβ production and TLR9-induced IgG levels. In a mouse RA model, treatment with KT-579 led to significant reduction in joint swelling.

**Event Details**
Kymera will host a video webcast today, May 9, 2025, at 10:00 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 the Company's website at www.kymeratx.com. A replay of the webcast and the presentation will be available following the event.

**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, the Company 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 our clinical and preclinical pipeline, including the therapeutic potential, clinical benefits and safety thereof, and the advancement of KT-579 into Phase 1 clinical testing in early 2026. 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: uncertainties inherent in the initiation, timing and design of future clinical trials, the availability and timing of data from ongoing and future trials and the results of such trials, whether preclinical results will be indicative of the results of clinical trials, the ability to successfully demonstrate the safety and efficacy of drug candidates, the timing and outcome of planned interactions with 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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