Kymera Therapeutics Presents New Clinical Data from the Ongoing Phase 1 Trial of STAT3 Degrader KT-333 at EHA Annual Meeting

June 14, 2024

KT-333 demonstrated initial clinical proof of concept across multiple hematological malignancies, including complete responses in two patients with Hodgkin's lymphoma

Robust STAT3 knockdown and positive immunomodulatory effect achieved in blood and tumor

KT-333 was well-tolerated with Phase 1 dose escalation ongoing and additional data expected in the second half of 2024

WATERTOWN, Mass., June 14, 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 shared new clinical data from its ongoing KT-333 Phase 1 trial. KT-333, a first-in-class, potent, highly selective, heterobifunctional small molecule degrader of STAT3, demonstrated antitumor responses in hematological malignancies with high unmet need, including relapsed/refractory classic Hodgkin's lymphoma (cHL), cutaneous T-cell lymphoma (CTCL), and NK-cell lymphoma, at doses that were well-tolerated. The data were presented at the European Hematology Association (EHA) Annual Meeting, taking place from June 13-16, 2024, in Madrid, Spain. Results released in an EHA poster today include a data cut-off of June 3, 2024.

"The complete responses we've shown in Hodgkin's lymphoma demonstrate the transformative therapeutic potential of STAT3 degradation, with two heavily pretreated cHL patients in the KT-333 trial moving to potentially curative stem cell transplants after treatment," said Jared Gollob, MD, Chief Medical Officer, Kymera Therapeutics. "We continue to be encouraged by the data generated in the ongoing Phase 1 trial showing clinical translation of our degrader's profile across multiple hematological malignancies including cHL, CTCL and NK-cell lymphoma and the potential to improve patients' lives. With dose escalation continuing, we look forward to completing the Phase 1 study and sharing the full data set later this year."

KT-333 Clinical Update

The KT-333 Phase 1 clinical trial is evaluating the safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD) and clinical activity of KT-333 dosed weekly on 28-day cycles in adult patients with relapsed and/or refractory lymphomas, leukemias and solid tumors.

The poster provides a clinical update as of June 3, 2024, from the ongoing KT-333 Phase 1 trial from 47 patients enrolled through seven dose levels (DLs) with a mean of 9.1 doses. This includes patients with cHL, B-cell non-Hodgkin's lymphoma, CTCL, peripheral T-cell lymphoma (PTCL), large granular lymphocytic leukemia (LGL-L), T-cell prolymphocytic leukemia (T-PLL), NK-cell lymphoma, as well as solid tumors. Highlights from the poster include:

- Antitumor activity in patients with hematological malignancies evaluable for response:
  - In cHL, complete responses were achieved in two of three patients at DL4. Both responders, who had received prior treatment with at least one regimen containing a check point inhibitor as well as brentuximab vedotin, have subsequently undergone stem cell transplantation. Additionally, stable disease was observed in a third cHL patient at DL6.
  - In NK-cell lymphoma, one complete response was achieved at DL7 in a patient with STAT3 mutation.
  - Among nine patients with CTCL, partial responses were achieved in four patients at DL2 and DL4-6, and stable disease was observed in one patient at DL4.
  - In solid tumors, stable disease was observed in four of fourteen patients, including two head and neck tumor types as well as patients with cholangiocarcinoma and renal cell cancer, at DL3-4.
- Strong proof of mechanism with KT-333 achieving up to 95% mean maximum STAT3 degradation in peripheral blood mononuclear cells at DL7 with evidence of STAT3 pathway inhibition and downregulation of inflammatory biomarkers in whole blood. Notably, KT-333 resulted in robust reduction of STAT3, pSTAT3, and SOCS3 expression in a CTCL tumor biopsy in DL4.
- Induction of an IFN-γ stimulated gene signature predictive of sensitivity to anti-PD1 was seen in both peripheral blood and tumor as previously shown, suggestive of favorable immunomodulatory response in the tumor microenvironment following KT-333 treatment and supporting a potential novel combination partner with anti-PD-1 drugs in solid tumors.
- Dose dependent increases in KT-333 plasma exposure were observed, achieving levels predicted to be efficacious.
- KT-333 was well tolerated with primarily Grade 1 and 2 adverse events, including stomatitis and fatigue. Two dose-limiting toxicities (DLTs), Grade 3 stomatitis and arthralgia, occurred in LGL-L patients at DL5 and one DLT, Grade 3 fatigue, was observed in a lymphoma patient treated at DL7.

The Phase 1a trial for KT-333 is currently ongoing. The Company expects to complete the study and share additional clinical data to inform the program's next development steps in 2024 at an upcoming medical meeting.

A copy of the EHA poster presentation is available in the Resource Library section of Kymera's website.

About KT-333 STAT3 Degrader
KT-333 is a potent, highly selective degrader of STAT3 in development for the treatment of multiple STAT3-dependent pathologies, including hematological malignancies and solid tumors. STAT3 is an undrugged transcription factor activated through a variety of different cytokine and growth factor receptors via Janus kinases (JAKs), as well as through oncogenic fusion proteins and mutations in STAT3 itself. In certain malignant cells, STAT3 activation is set into overdrive, leading to a dampened immune response, tumor progression, and metastasis. STAT3's role as a cancer driver and tumor microenvironment modulator has been validated in a multitude of studies, making it a strong candidate to target in the treatment of cancer. KT-333 was the first degrader against an undrugged transcription factor to enter the clinic and the Phase 1 clinical trial is designed to evaluate the

safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD), and clinical activity of KT-333 dosed weekly in adult patients with relapsed and/or refractory lymphomas, leukemias, and solid tumors. Clinical data from the KT-333 Phase 1 trial has shown evidence of STAT3 targeted protein degradation in humans with associated STAT3 pathway inhibition, along with early signs of antitumor activity, highlighting the potential of heterobifunctional degraders for targeting this previously undruggable transcription factor. The Phase 1a trial for KT-333 is currently ongoing. More information on the Phase 1 study can be found at www.clinicaltrials.gov, identifier NCT05225584.

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 for KT-333; 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, 2023, 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 and Media Contact:

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