Krystal Biotech Announces Pipeline Expansion into Oncology and FDA Acceptance of IND Application for Lead Oncology Candidate KB707

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PITTSBURGH, July 26, 2023 (GLOBE NEWSWIRE) -- Krystal Biotech, Inc. (the “Company”) (NASDAQ: KRYS), a commercial-stage biotechnology company focused on the discovery, development and commercialization of genetic medicines to treat diseases with high unmet medical needs, announced today that it has expanded its R&D pipeline to oncology and that the US Food and Drug Administration (FDA) has accepted its Investigational New Drug (IND) application of its lead oncology drug candidate KB707 for the treatment of locally advanced or metastatic solid tumor malignancies. The Company will host an investor conference call and webcast, Thursday, July 27, 2023, at 8:00 am ET, to discuss the KB707 program. To join the investor conference call, please see the instructions below. The presentation for the investor conference call is attached to the Company’s Form 8-K.

“The KB707 program leverages our learnings and clinical experience in two tissue areas, the skin and the lung, and underscores the broader potential of our HSV-1 platform to deliver all types of exogenous genetic material and improve outcomes for patients with debilitating diseases,” said Krish S. Krishnan, Chairman and CEO of Krystal Biotech.

KB707 is a modified HSV-1 vector designed to deliver genes encoding both human IL-12 and IL-2 to the tumor microenvironment and promote systemic immune-mediated tumor clearance. Two formulations of KB707 are in development, a solution formulation for transcutaneous injection and an inhaled (nebulized) formulation for lung delivery.

“We believe KB707 is a unique and highly differentiated drug candidate with the potential to unlock the capabilities of cytokine-based immunotherapy,” said Suma Krishnan, President of Research & Development at Krystal Biotech. “By enabling localized and sustained cytokine expression within a treated tumor, KB707 has the potential to maximize therapeutic efficacy while avoiding the tolerability challenges of systemic cytokine treatments.”

The FDA has accepted the Company’s IND to evaluate intratumoral KB707 in patients with solid tumors accessible by transcutaneous injection, and the Company expects to initiate a Phase 1 study in the second half of 2023. The Company is planning to file an amendment to the KB707 IND in the second half of 2023 to evaluate inhaled KB707 in a clinical trial in the first half of 2024.

Interleukin-2 (IL-2) and interleukin-12 (IL-12) are secreted cytokines with complementary functions promoting cell-mediated immunity in humans. Both IL-2 and IL-12 have been shown to elicit anti-tumor immune responses in preclinical or clinical models and have been extensively studied for their potential in cancer immunotherapy. Despite promising signs of efficacy, it has proven difficult to effectively harness IL-2 and IL-12 for therapeutic benefit, as systemic administration is often poorly tolerated, and their inherently short half-lives necessitate high dose levels and extremely frequent dose intervals. KB707 leverages the Company’s modified HSV-1 vector – and its ability to efficiently deliver a durable DNA payload without active replication and minimal cytotoxicity – to drive local and sustained cytokine expression within the tumor microenvironment and maximize the therapeutic window and benefit of IL-2 and IL-12.

“There remains an urgent unmet need for new therapies in cutaneous oncology, including for patients that do not respond to current first-line options and for the many who eventually progress on available therapy,” said Jason Luke, MD, Associate Professor of Medicine in the Division of Hematology/Oncology and Director of the Cancer Immunotherapeutic Center within UPMC Hillman Cancer Center Immunology and Immunotherapy Program in Pittsburgh, PA. “As the lead investigator on multiple practice changing immunotherapy trials, I have seen first-hand the benefits that can be realized through effective immune modulation and am excited about the potential of Krystal's approach for localized, sustained cytokine delivery.”

In preclinical studies, KB707 has been shown to efficiently transduce mammalian cells *in vitro* leading to the secretion of bioactive IL-2 and IL-12 and can drive localized, durable cytokine expression in mouse skin after intradermal injection. Furthermore, in stringent checkpoint inhibitor refractory ‘cold’ syngeneic mouse models, HSV-1 vector based delivery of murine equivalent *IL2* and *IL12* elicited robust antitumor responses and survival benefits, including via intratumoral injection in single and dual flank B16F10 melanoma models, as well as via intratracheal delivery in a metastatic K7M2 osteosarcoma model, with evidence of protection from tumor rechallenge in both models suggestive of prolonged adaptive immunity.

The intratumoral KB707 Phase 1/Opal 1 study is an open-label, multi-center, monotherapy, dose escalation and expansion study, enrolling patients with locally advanced or metastatic solid tumors, who relapsed or are refractory to standard of care, with at least one measurable and injectable tumor accessible by transcutaneous route. The primary objective of the study is to evaluate safety and tolerability of KB707. Efficacy will also be assessed by multiple measures including overall response rate, progression free survival, and overall survival, and the immune effects of KB707 monotherapy will be assessed in tumor tissue, lymph nodes, and blood.

Investor Conference Call, Webcast and Presentation Information

The Company will host an investor conference call and webcast, Thursday, July 27, at 8:00 am ET, to discuss the KB707 program.

The conference call will include management’s overview of the Company’s expanded pipeline and research and development focus in oncology and discuss potential target indications as well as a summary of preclinical data and clinical development plans. External speakers will include Samuel Broder, M.D., former Director of the National Cancer Institute where he oversaw the development of numerous anti-cancer therapeutic agents, and Jason Luke, M.D., F.A.C.P., Associate Professor of Medicine in the Division of Hematology/Oncology and Director of the Cancer Immunotherapeutic Center within UPMC Hillman Cancer Center Immunology and Immunotherapy Program in Pittsburgh, PA.

To register and join the conference call, please go to: https://www.netroadshow.com/events/login?show=6a3175e6&confId=53637

For those unable to listen to the live conference call, a replay will be available on the Investor’s section of the Company’s website at www.krystalbio.com.

About Krystal Biotech, Inc.
Krystal Biotech, Inc. (NASDAQ: KRYS) is a commercial-stage biotechnology company focused on the discovery, development and commercialization of genetic medicines to treat diseases with high unmet medical needs. VYJUVEK™ is the Company's first commercial product, the first-ever redosable gene therapy, and the only medicine approved by the FDA for the treatment of dystrophic epidermolysis bullosa. The Company is rapidly advancing a robust preclinical and clinical pipeline of investigational genetic medicines in respiratory, oncology, dermatology, ophthalmology, and aesthetics. Krystal Biotech is headquartered in Pittsburgh, Pennsylvania. For more information, please visit http://www.krystalbio.com, and follow @KrystalBiotech on LinkedIn and Twitter.

Forward Looking Statements
Any statements in this press release about future expectations, plans and prospects for Krystal Biotech, Inc., including statements about the potential of the Company's proprietary HSV-1 platform, the Company's beliefs about the clinical utility of KB707 and its potential therapeutic capabilities, the Company expectations regarding the timing of a Phase 1 study of the transcutaneous injection formulation of KB707, the Company's plans to file an amendment to the KB707 IND in the second half of 2023 to evaluate inhaled KB707 in a clinical trial in the first half of 2024, and other statements containing the words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "likely," "will," "would," "could," "should," "continue," and similar expressions, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including: uncertainties associated with regulatory review of clinical trials and applications for marketing approvals, the availability or commercial potential of product candidates including KB707, the sufficiency of cash resources and need for additional financing and such other important factors as are set forth under the caption "Risk Factors" in the Company's annual and quarterly reports on file with the U.S. Securities and Exchange Commission. In addition, the forward-looking statements included in this press release represent the Company's views as of the date of this release. The Company anticipates that subsequent events and developments will cause its views to change. However, while the Company may elect to update these forward-looking statements at some point in the future, it specifically disclaims any obligation to do so. These forward-looking statements should not be relied upon as representing the Company's views as of any date subsequent to the date of this release.

Disclosures
Dr. Jason Luke is a consultant for Krystal Biotech, Inc.

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