Jeune Aesthetics Announces Positive Clinical Phase 1 (PEARL-1 Study) Efficacy Results for KB301, an Investigational Gene-based Treatment Designed to Address the Underlying Biology of Aging Skin

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- *Positive proof-of-concept efficacy data supports advancing into Phase 2 studies*
- *Adverse events, associated with injection site reactions, were mild and transitory*
- *Conference call to discuss results scheduled for Tuesday, March 22, 2022 at 8:00 a.m. ET*

PITTSBURGH, March 22, 2022 (GLOBE NEWSWIRE) -- Jeune Aesthetics, Inc. ("Jeune Aesthetics"), a wholly-owned subsidiary of Krystal Biotech, Inc. ("Krystal") (NASDAQ: KRYS) today announced positive proof-of-concept efficacy data from Cohort 2 of the PEARL-1 study of KB301, Jeune Aesthetics' lead candidate for the treatment of aesthetic skin conditions.

"We are pleased to see results supporting the clinical benefits afforded by KB301, especially improvement of fine lines and texture in the cheek and improved thickness results in the knee, with only minimal adverse events across all injection sites," said Bhushan Hardas, M.D., President of Jeune Aesthetics. "We look forward to advancing KB301 into Phase 2 testing later this year, as well as progressing the rest of the Jeune Aesthetics' pipeline as we work to create a new category of aesthetic medicine designed to address – and potentially reverse – biological changes in aging skin."

Skin aging is caused by both intrinsic and extrinsic factors, leading to progressive loss of dermal collagen and other proteins. KB301 is designed to address declining levels of collagen by delivering the human *COL3A1* gene to increase production of normal type III collagen at the site of administration. KB301 leverages Krystal's proprietary gene delivery platform to restore protein production and rebuild the underlying extracellular matrix structure.

About the PEARL-1 Trial

The Phase 1 dose-ranging trial evaluated the safety, tolerability, and initial efficacy of intradermal injections of KB301 in adult subjects aged 18-75 (NCT04540900). Complete results from Cohort 1 focused on safety were presented at the 2021 Society for Investigative Dermatology (SID) Annual Meeting.

In Cohort 1, three different dose levels of KB301 were evaluated in seven healthy subjects who received two intradermal injections into healthy buttock tissue spaced 30 days apart (day 0, day 30). KB301 injected areas were compared to uninjected or saline injected control tissue within the same subject. Treatment and control sites were biopsied at day 2 or day 32. KB301 was shown to be well tolerated for *COL3A1* supplementation in healthy human subjects, supporting clinical progression of KB301 for the treatment of aesthetic skin conditions.

Cohort 2 is a randomized, double-blind, placebo-controlled clinical trial that evaluated the safety and efficacy of KB301 for the improvement of fine lines and skin texture in the lower and upper cheek and for improvement in skin thickness in the knee. Cohort 2 enrolled 27 subjects across two trial sites. Bilateral treatment areas included the neck behind the ear to assess initial safety and on the cheek below and above the zygomatic arch (lower and upper cheek), and around the knee. Subjects were randomized 2:1 to receive low dose KB301 or placebo in the upper cheek and knee as multiple micro depot injections over the selected treatment area with a 33 G needle. Subjects receiving KB301 in the lower check were randomized 2:1 to receive either low dose KB301, high dose KB301 or placebo. Four patients dropped out of the Cohort 2 study – one subject following the initial safety assessment behind the ear, two subjects for unspecified reasons, and one subject due to unevenness in face between active and placebo during the study.

Above the Knee Safety and Efficacy Results

Low dose KB301 was well tolerated by subjects. Subjects were not administered high dose of KB301 above the knee. Adverse events observed were injection site reactions (ISRs) with 100% of the adverse events categorized as mild. The adverse events were transitory and dramatically reduced during follow-on injections.

Efficacy at Visit 6 was clinically meaningful across Subject Satisfaction Scores, Blinded Independent Reviewer Assessment, and Mean Change in Skin Thickness:

- Subject Satisfaction Scores showed a 21.9% responder rate difference between KB301 and placebo (41.9% for KB301 and 20% for placebo, Odds Ratio: 2.95);
- Blinded Independent Reviewer Assessment showed a 21.5% response rate difference (54.8% for KB301 and 33.3% for placebo, Odds ratio 2.47); and
- The Mean Change in Skin Thickness was 1.07mm between KB301 and placebo (KB301: 1.74mm, placebo: 0.67mm).

Lower Cheek (below zygomatic arch) Safety and Efficacy Results

Both the high and the low dose of KB301 were well tolerated by subjects. Adverse events were injection site reactions with 91% of the adverse events categorized as mild and 9% moderate. The adverse events were transitory and dramatically reduced during follow-on injections.

Efficacy at Visit 6 was clinically meaningful across Subject Satisfaction Scores and before - after pictures:

- Subject Satisfaction Scores demonstrated a mean clinical score change of 1.0 between active and placebo for KB301 high dose. The mean score change from baseline to Visit 6 was 1.9 for KB301 and 0.9 for placebo;

- Before and after picture evaluations showed clear improvement in both fine lines and skin texture in patients administered with high dose KB301; and
- Blinded independent reviewer assessments using Jeune's Skin Roughness Score (JASRS) and Fine Lines Score (JAFLS) did not show clinical separation between active and placebo. These scales, developed specifically for this skin area, will be adapted specifically for KB301 by Jeune Aesthetics prior to advancing development.

Upper Cheek (above zygomatic arch) Results

Low dose KB301 was well tolerated by subjects. Subjects were not administered high dose of KB301 in the upper cheek. Adverse events were injection site reactions with 98% of the adverse events categorized as mild and 2% moderate. The adverse events were transitory and dramatically reduced during follow-on injections.

Efficacy at Visit 6 was clinically meaningful across Subject Satisfaction Scores and before - after pictures:

- Subject Satisfaction Scores demonstrated a mean clinical score change of 0.6 between active and placebo for KB301 low dose. The mean score change from baseline to Visit 6 was 1.3 for KB301 and 0.7 for placebo;
- Before and after picture evaluations showed clear improvement in both fine lines and texture in patients administered with low dose of KB301; and
- Blinded independent reviewer assessments using JASRS and JAFLS did not show clinical separation between active and placebo. These scales, developed specifically for this skin area, will be further developed, validated, and adapted by Jeune Aesthetics specifically for KB301 prior to advancing development.

"KB301 has the potential to address not just the look of aging skin, but the aging process itself," said Steve G. Yoelin, M.D., an ophthalmologist with a medical aesthetics private practice in Newport Beach, California, and a distinguished researcher, clinician, corporate strategic advisor, and speaker. "Currently, there are no aesthetic treatment options that truly rebuild the architecture of the dermis to address the fundamental biology of aging. In my view, KB301 complements existing medical aesthetics and has the potential to change the field of aesthetic medicine."

Next Steps

Subjects from the PEARL-1 Cohort 2 trial will be enrolled in a durability trial to look for duration of effect, reduction of the unevenness in placebo treated sites, and for long term safety monitoring. Based on the results from Cohort 2, Jeune Aesthetics is currently planning for two Phase 2a trials – one to improve skin quality attributes in the lower cheek and a second to evaluate the potential of improving the aesthetic appearance in a subject's hand by increasing skin thickness on the back of the subject's hands. A third Phase 2 trial, to evaluate the improvement of skin quality attributes of KB301 in the upper cheek, will be initiated, following development and validation of Jeune Aesthetics' scales in the upper cheek, specific to KB301.

Investor Conference Call, Webcast and Presentation Information
Jeune Aesthetics and Krystal Biotech will host an investor conference call and webcast today, Tuesday, March 22, at 8:00 a.m. ET, to discuss the Phase 1 PEARL-1 study data and the KB301 clinical development program. To participate in the conference call, please dial 1-877-407-4018 (domestic) or 1-201-689-8471 (international) and refer to conference ID 13727826. The webcast, which will include presentation slides, will be available live and for replay on Krystal's website at www.krystalbio.com in the Investors section.

About Jeune Aesthetics, Inc.
Jeune Aesthetics, Inc., a subsidiary of Krystal Biotech, is a biotechnology company leveraging a clinically validated gene-delivery platform to fundamentally address – and reverse – the biology of aging and/or damaged skin. For more information, please visit http://www.jeuneinc.com.

About Krystal Biotech, Inc.
Krystal Biotech, Inc. (NASDAQ:KRYS) is a pivotal-stage gene therapy company leveraging its proprietary, redosable gene therapy platform and in-house manufacturing capabilities to potentially bring life-changing treatment options to patients with serious diseases, including rare diseases in skin, lung, and other areas. 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., or its wholly-owned subsidiary, Jeune Aesthetics, Inc., including but not limited to statements about the development of Jeune Aesthetics' product candidates, such as plans for the design, conduct and timelines of ongoing clinical trials of KB301, the clinical utility of KB301, the ability of KB301 to fundamentally address and potentially reverse the biology of aging or damaged skin, 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: the uncertainties inherent in the initiation and conduct of clinical trials, availability and timing of data from clinical trials, whether results of early clinical trials or trials will be indicative of the results of ongoing or future trials, uncertainties associated with regulatory review of clinical trials and applications for marketing approvals, the availability or commercial potential of product candidates including KB301 and such other important factors as are set forth under the caption "Risk Factors" in Krystal'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 Krystal's and Jeune Aesthetics' views as of the date of this release. Krystal and Jeune Aesthetics anticipate that subsequent events and developments will cause their views to change. However, while Krystal and Jeune Aesthetics may elect to update these forward-looking statements at some point in the future, they specifically disclaim any obligation to do so. These forward-looking statements should not be relied upon as representing Krystal's and Jeune Aesthetics' views as of any date subsequent to the date of this release.

CONTACTS:

Investor Contact:
Whitney Ijem
Krystal Biotech

wijem@krystalbio.com

Media:
Tiffany Hamilton
Krystal Biotech
thamilton@krystalbio.com