Editas Medicine Reports Preclinical Data Demonstrating Robust Tumor Reduction and Clearance Using Novel, Engineered iNK Cells at the American Society of Hematology Annual Meeting

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Preclinical data demonstrating Editas-engineered AsCas12a multiplexed editing of iPSCs enhances iNK tumor killing ability, supporting promise as a potential therapeutic approach for solid tumors

iNKs with double knock-in of CD16 and mbIL-15 in combination with monoclonal antibody significantly reduce tumor burden

iNKs with double knock-out of CISH and TGFβR2 substantially reduce tumor burden

CAMBRIDGE, Mass., Dec. 12, 2021 (GLOBE NEWSWIRE) -- Editas Medicine, Inc. (Nasdaq: EDIT), a leading genome editing company, today reported *in vitro* and *in vivo* preclinical data on the enhanced tumor killing capacity of two modified induced pluripotent stem cell (iPSC)-derived natural killer (or iNK) cell therapies using Editas Medicine's proprietary AsCas12a gene editing. The Company reported these findings in a presentation today at the 63rd Annual Meeting and Exposition of the American Society of Hematology (ASH), being held in Atlanta and virtually.

The research evaluated two strategies to generate engineered iPSC clones, which were then differentiated into iNK cells and evaluated *in vitro* and *in vivo* to determine anti-tumor activity. These approaches have the potential to create allogeneic, investigational NK cell therapy medicines with enhanced activity against solid tumors.

CD16$^{+/+}$/mbIL-15$^{+/+}$ Double Knock-in (DKI) Approach
IPSC's were edited at the GAPDH locus using the Company's proprietary SLEEK (SeLection by Essential-gene Exon Knock-in) technology and engineered AsCas12a nuclease to knock-in both CD16 and membrane-bound IL-15 (mbIL-15). CD16$^{+/+}$/mbIL-15$^{+/+}$ edits were designed to increase antibody-dependent cellular cytotoxicity (ADCC) when combined with tumor-targeting antibodies and prolong iNK cell persistence.

DKI iNK cells, as monotherapy or in combination with trastuzumab, showed significantly enhanced tumor killing compared with wild type (WT) iNKs in an *in vitro* 3D SKOV-3 ovarian tumor spheroid assay. Evaluation in an *in vivo* mouse SKOV-3 cancer model confirmed that DKI iNKs combined with trastuzumab exerted greater anti-tumor activity compared to WT iNKs with trastuzumab, or trastuzumab alone. A single dose of DKI iNKs combined with three doses of trastuzumab induced complete tumor clearance in 50 percent of mice (n=4/8). Importantly, DKI iNKs were detected in the peritoneum of the treated mice for greater than three (3) months, demonstrating that the mbIL-15 maintained iNK survival for a prolonged period in the absence of exogenous cytokine support.

CISH$^{-/-}$/TGFβR2$^{-/-}$ Double Knock-out (DKO) Approach
In a separate study, iPSCs were edited with Editas-engineered AsCas12a to knock out both the CISH and TGFβ-receptor 2 (TGFβR2) genes. CISH$^{-/-}$/TGFβR2$^{-/-}$ edits were designed to improve iNK cell effector function and provide resistance to TGFβ-mediated NK suppression in the tumor microenvironment. DKO iNKs induced enhanced tumor killing against *in vitro* 3D SKOV-3 ovarian tumor spheroids compared to WT iNKs. Following stimulation, DKO iNKs produced elevated levels of inflammatory cytokines, including IFN-γ and TNF-α. The DKO iNK cells also induced significant reduction in tumor burden compared with WT iNK treatment when tested *in vivo* in a SKOV-3 ovarian cancer mouse model.

"In this promising research, we demonstrate the use of our proprietary engineered AsCas12a nuclease and SLEEK technology with its high efficiency, multi-transgene editing capability to enable the efficient development and evaluation of multiple iNK therapeutic approaches. Using selective, double knock-in and double knock-out strategies, we have developed allogenic iNK cell lines with substantially enhanced *in vitro* and *in vivo* anti-tumor activity, reducing or eliminating tumors in tumor-bearing mice. The potency of both modified iNK cell therapeutic approaches supports their continued development as novel cell-based medicines for the treatment of cancer," said Mark S. Shearman, Ph.D., Executive Vice President and Chief Scientific Officer, Editas Medicine. "We believe that NK cells are attractive candidates for off-the-shelf immunotherapy medicines given their high tumor killing capacity and their low propensity for graft-versus-host disease. Furthermore, our approach builds in safeguards by screening and selecting iPSC clones that are fully characterized, eliminating those with chromosomal abnormalities and ensuring a pure final population of cells. These data reinforce our view of the potential for our gene editing platform to optimize NK cell function, providing a promising approach to treat a wide range of solid tumors."

At ASH, the Company also presented preclinical data on EDIT-301 supporting its differentiated approach to develop a transformative medicine for people living with transfusion-dependent beta-thalassemia (TDT). AsCas12a edited TDT erythroid cells had improved maturation, health, and higher total hemoglobin content per cell when compared to unedited controls. The EDIT-301 Phase 1/2 RUBY trial for the treatment of sickle cell disease is currently enrolling study participants and the Company expects to begin dosing in the first half of 2022.

Full details of the Editas Medicine presentations can be accessed in the **Posters & Presentations** section on the Company's website.

About SLEEK Gene Editing
SLEEK (SeLection by Essential-gene Exon Knock-in) gene editing is an optimized approach to developing the next generation of cell therapy medicines for cancer and other serious diseases. Utilizing Editas Medicine's proprietary engineered AsCas12a nuclease, SLEEK enables high efficiency, multi-transgene knock-in of induced pluripotent stem cells (iPSCs), T cells, and natural killer (NK) cells while ensuring robust, transgene expression. Editas Medicine is currently leveraging SLEEK technology in its oncology programs.

About Editas Medicine
As a leading genome editing company, Editas Medicine is focused on translating the power and potential of the CRISPR/Cas9 and CRISPR/Cas12a

(also known as Cpf1) genome editing systems into a robust pipeline of treatments for people living with serious diseases around the world. Editas Medicine aims to discover, develop, manufacture, and commercialize transformative, durable, precision genomic medicines for a broad class of diseases. For the latest information and scientific presentations, please visit www.editasmedicine.com.

Forward-Looking Statements

This press release contains forward-looking statements and information within the meaning of The Private Securities Litigation Reform Act of 1995. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "target," "should," "would," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. The Company may not actually achieve the plans, intentions, or expectations disclosed in these forward-looking statements, and you should not place undue reliance on these forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in these forward-looking statements as a result of various factors, including: uncertainties inherent in the initiation and completion of preclinical studies and clinical trials and clinical development of the Company's product candidates; availability and timing of results from preclinical studies and clinical trials; whether interim results from a clinical trial will be predictive of the final results of the trial or the results of future trials; expectations for regulatory approvals to conduct trials or to market products and availability of funding sufficient for the Company's foreseeable and unforeseeable operating expenses and capital expenditure requirements. These and other risks are described in greater detail under the caption "Risk Factors" included in the Company's most recent Annual Report on Form 10-K, which is on file with the Securities and Exchange Commission, as updated by the Company's subsequent filings with the Securities and Exchange Commission, and in other filings that the Company may make with the Securities and Exchange Commission in the future. Any forward-looking statements contained in this press release speak only as of the date hereof, and the Company expressly disclaims any obligation to update any forward-looking statements, whether because of new information, future events or otherwise.

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