CRISPR Therapeutics Presents Positive Data on Allogeneic CRISPR-based CAR-T Cell Therapies at AACR 2018

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-Off-the-shelf CAR-T candidates against BCMA and CD70 address both hematologic malignancies and solid tumors -

-New data demonstrate high editing rates, consistent expression, selective and potent cell killing-

ZUG, Switzerland and CAMBRIDGE, Mass., April 16, 2018 (GLOBE NEWSWIRE) -- CRISPR Therapeutics (NASDAQ:CRSP), a biopharmaceutical company focused on creating transformative gene-based medicines for serious diseases, today announced the presentation of new data from the company's allogeneic chimeric antigen receptor T cell (CAR-T) program at the American Association for Cancer Research (AACR) Annual Meeting 2018. The data presented today demonstrate the generation of CAR-T cells targeted to BCMA and CD70 through CRISPR/Cas9 gene editing that have high editing rates, consistent expression, and selective and potent cell killing. These data confirm and expand on the work already completed on CTX101, CRISPR's lead allogeneic CAR-T cell therapy in development for CD19+ malignancies.

"In the studies presented today, we used multiplexed CRISPR gene editing to modify healthy donor T cells to make CAR-T cells that selectively and potently target the tumor antigen of choice," said Tony Ho, MD, Head of R&D, CRISPR Therapeutics. "These data provide further evidence that CRISPR/Cas9 can play a major role in enabling the creation of next-generation CAR-T cell therapies that may work for a broader population of patients including those with solid tumors."

In Poster 1540, allogeneic CAR-T cells targeting B cell maturation antigen (BCMA) were evaluated as a potential approach for the treatment of multiple myeloma (MM). Using the CRISPR/Cas9 system, allogeneic CAR-T cells targeting the BCMA receptor were generated by disrupting the beta-2-microglobulin (B2M) and TCR alpha constant region (TRAC) genes and inserting an anti-BCMA CAR into the TRAC locus. Over 60% of the cells contained all three of the targeted edits. The study found that the CAR-T cells selectively and potently killed BCMA+ cells *in vitro* and eradicated MM cells in *in vitro* and *in vivo* models.

To address the need for effective and durable therapies for both hematologic and solid tumors, allogeneic CAR-T cells targeting the CD70 antigen were generated by CRISPR/Cas9 genome editing. CD70 is expressed in both hematologic malignancies as well as in solid tumors such as renal cell carcinoma (RCC), while its expression in normal tissues is restricted. In Poster 2551, the B2M and TRAC genes from healthy donor cells were disrupted and the CAR was introduced into the TRAC locus, similar to other allogeneic CAR-T cell therapies in CRISPR's portfolio. Data showed that over 60% of the cells contained all three of the targeted edits. The study found that the CD70 CAR-T cells displayed potent cell killing function *in vitro* against CD70 expressing lymphoid and renal cancer derived cell lines across a broad range of antigen expression levels. These cells also secreted IFNg, released granzyme B and proliferated in a CD70 specific manner, all indications of potent anti-tumor activity. The CD70 targeting CAR-T cells eradicated RCC cells in an *in vivo* murine model.

"The future of cell therapies lies in the ability to create more sophisticated versions of CAR-Ts by incorporating multiple modifications with precision and consistency. We believe that CRISPR-based gene editing will be the engine to enable this next generation of CAR-Ts," said Samarth Kulkarni, Chief Executive Officer of CRISPR Therapeutics. "We continue to make rapid progress on our first CAR-T program, CTX101, directed towards CD19+ malignancies, and aim to file an IND for this program by the end of this year."

These results were presented at the American Association for Cancer Research Annual Meeting on April 16th, 2018 in two poster sessions entitled *Allogeneic chimeric antigen receptor T cells targeting B cell maturation antigen* and *Allogeneic CRISPR engineered anti-CD70 CAR-T cells demonstrate potent preclinical activity against both solid and hematological cancer cells.*

About CRISPR-Based Allogeneic CAR-T Programs
CRISPR has a wholly owned portfolio of CRISPR-based allogeneic CAR-T cell therapies. The lead program in CRISPR's immuno-oncology portfolio, CTX101, is an allogeneic CD19 CAR-T product that has several potential advantages over other approaches in the clinic due to the ability of the CRISPR/Cas9 system to achieve efficient and specific multiplexed editing. First, the CD19 chimeric antigen receptor, or CAR, is inserted into a specifically chosen locus rather than the random insertion common in current-generation products. Second, the T cell receptor (TCR) is eliminated to enable off-the-shelf use of a single batch of product in many patients. Finally, the class 1 major histocompatibility complex (MHC I) is eliminated to improve durability. CTX101 is based on healthy donor cells that are edited *ex vivo* using CRISPR/Cas9, a process that the company has optimized and successfully transitioned to a GMP-capable CMO. CRISPR has additional CAR-T cell therapies including those targeting BCMA and CD70 in preclinical development.

About CRISPR Therapeutics
CRISPR Therapeutics is a leading gene editing company focused on developing transformative gene-based medicines for serious diseases using its proprietary CRISPR/Cas9 platform. CRISPR/Cas9 is a revolutionary gene editing technology that allows for precise, directed changes to genomic DNA. The Company has established a portfolio of therapeutic programs across a broad range of disease areas including hemoglobinopathies, oncology and rare diseases. To accelerate and expand its efforts, CRISPR Therapeutics has established strategic collaborations with leading companies including Bayer AG and Vertex Pharmaceuticals. CRISPR Therapeutics AG is headquartered in Zug, Switzerland, with its wholly-owned U.S. subsidiary, CRISPR Therapeutics, Inc., and R&D operations based in Cambridge, Massachusetts, and business offices in London, United Kingdom. For more information, please visit www.crisprtx.com.

CRISPR Forward-Looking Statement

Certain statements set forth in this press release constitute "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, but not limited to, statements concerning: the timing of filing of clinical trial applications and INDs, any approvals thereof and timing of commencement of clinical trials, the intellectual property coverage and positions of the Company, its licensors and third parties, the sufficiency of the Company's cash resources and the therapeutic value, development, and commercial potential of CRISPR/Cas-9 gene editing technologies and therapies. You are cautioned that forward-looking statements are inherently uncertain. Although the Company believes that such statements are based on reasonable assumptions within the bounds of its knowledge of its business and operations, the forward-looking statements are neither promises nor guarantees and they are necessarily subject to a high degree of uncertainty and risk. Actual performance and results may differ materially from those projected or suggested in the forward-looking statements due to various risks and uncertainties. These risks and uncertainties include, among others: uncertainties regarding the intellectual property protection for our technology and intellectual property belonging to third parties; uncertainties inherent in the initiation and completion of preclinical studies for the Company's product candidates; availability and timing of results from preclinical studies; whether results from a preclinical trial will be predictive of future results of the future trials; expectations for regulatory approvals to conduct trials or to market products; and those risks and uncertainties described under the heading "Risk Factors" in the Company's most recent annual report on Form 10-K, and in any other subsequent filings made by the Company with the U.S. Securities and Exchange Commission (SEC), which are available on the SEC's website at www.sec.gov. Existing and prospective investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date they are made.

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