Allogene Therapeutics Receives IND Clearance from the U.S. Food and Drug Administration for ALLO-715 in Combination with Nirogacestat in Relapsed/Refractory Multiple Myeloma

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- Combination Represents One of Allogene's Three Strategies to Target BCMA for Multiple Myeloma
- Phase 1 Clinical Trial Expected to Begin in the First Quarter of 2021

SOUTH SAN FRANCISCO, Calif., Dec. 23, 2020 (GLOBE NEWSWIRE) -- Allogene Therapeutics, Inc. (Nasdaq: ALLO), a clinical-stage biotechnology company pioneering the development of allogeneic CAR T (AlloCAR T™) therapies for cancer today announced that the U.S. Food & Drug Administration (FDA) has cleared an Investigational New Drug (IND) application to study ALLO-715, Allogene's investigational BCMA AlloCAR T therapy, in combination with nirogacestat, SpringWorks Therapeutics' investigational gamma secretase inhibitor (GSI), in patients with relapsed or refractory multiple myeloma. This combination is part of the company's multi-pronged strategy to develop a treatment for multiple myeloma and will be deployed in the ongoing UNIVERSAL trial. Enrollment in this cohort is expected to begin in the first quarter of 2021.

"We are delighted that the FDA has cleared our IND application for ALLO-715 in combination with nirogacestat," said Rafael Amado, M.D., Executive Vice President of Research & Development and Chief Medical Officer of Allogene. "We look forward to investigating this combination as part of our comprehensive anti-BCMA strategy aimed at optimizing cell therapy for patients with relapsed/refractory multiple myeloma."

Gamma secretase is an enzyme that cleaves BCMA from the surface of myeloma cells. In preclinical models, nirogacestat has been shown to prevent the cleavage and shedding of BCMA, leading to an increase in the cell surface density of BCMA and reduced levels of soluble BCMA.[1] Increasing BCMA surface expression with gamma secretase inhibitor may enable deeper and more durable responses to ALLO-715 in patients with multiple myeloma.

Multiple myeloma is the second most common hematological malignancy in the United States, with 32,270 new cases and 12,830 deaths estimated in 2020.[2]

The Phase 1 combination trial is being advanced pursuant to a clinical trial collaboration agreement that Allogene and SpringWorks entered into in January 2020. Under the terms of the agreement, Allogene is sponsoring and conducting the Phase 1 study to evaluate the safety, tolerability and preliminary efficacy of the combination, and is assuming all development costs associated with the study, other than expenses related to the manufacturing of nirogacestat and certain expenses related to intellectual property rights. Allogene and SpringWorks have formed a joint development committee to oversee the clinical study.

About ALLO-715
ALLO-715, an AlloCAR T therapy targeting B-cell maturation antigen (BCMA), is a potential novel treatment for multiple myeloma and other BCMA-positive malignancies. Multiple myeloma originates in the bone marrow and it is characterized by abnormalities in plasma cells that reproduce uncontrollably in the bone marrow and other disease sites.[3] Multiple myeloma is incurable for most patients, as relapses occur despite most treatments available.[4] Initial results from the Phase 1 UNIVERSAL study of ALLO-715 in relapsed/refractory multiple myeloma were presented at an oral session of the American Society of Hematology (ASH) annual meeting in December 2020. This study also uses ALLO-647, Allogene's anti-CD52 monoclonal antibody (mAb), as a part of its differentiated lymphodepletion regimen.

ALLO-715 utilizes the TALEN® gene-editing technology pioneered and owned by Cellectis. Allogene has an exclusive license to the Cellectis technology for allogeneic products directed at the BCMA target. Allogene holds the global development and commercial rights for this investigational candidate.

About Nirogacestat
Nirogacestat is an investigational, oral, selective, small molecule gamma secretase inhibitor in Phase 3 clinical development for desmoid tumors, which are rare and often recurrent, debilitating and disfiguring soft-tissue tumors. Gamma secretase cleaves multiple transmembrane protein complexes, including Notch, which is believed to play a role in activating pathways that contribute to desmoid tumor growth.

In addition, gamma secretase has been shown to directly cleave membrane-bound BCMA, resulting in the release of the BCMA extracellular domain, or ECD, from the cell surface. By inhibiting gamma secretase, membrane-bound BCMA can be preserved, increasing target density while reducing levels of soluble BCMA ECD, which may serve as decoy binding molecules for BCMA-directed therapies. Nirogacestat's ability to enhance the activity of BCMA-directed therapies has been observed in preclinical models of multiple myeloma.

Nirogacestat has received Orphan Drug Designation from the U.S. Food and Drug Administration (FDA) for the treatment of desmoid tumors (June 2018) and from the European Commission for the treatment of soft tissue sarcoma (September 2019). The FDA also granted Fast Track and Breakthrough Therapy Designations for the treatment of adult patients with progressive, unresectable, recurrent or refractory desmoid tumors or deep fibromatosis (November 2018 and August 2019).

About Allogene Therapeutics
Allogene Therapeutics, with headquarters in South San Francisco, is a clinical-stage biotechnology company pioneering the development of allogeneic chimeric antigen receptor T cell (AlloCAR T™) therapies for cancer. Led by a management team with significant experience in cell therapy, Allogene is developing a pipeline of "off-the-shelf" CAR T cell therapy candidates with the goal of delivering readily available cell therapy on-demand,

more reliably, and at greater scale to more patients. For more information, please visit www.allogene.com, and follow @AllogeneTx on Twitter and LinkedIn.

Forward-Looking Statements
This press release contains forward-looking statements for purposes of the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. The press release may, in some cases, use terms such as "predicts," "believes," "potential," "proposed," "continue," "estimates," "anticipates," "expects," "plans," "intends," "may," "could," "might," "will," "should" or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements. Forward-looking statements include statements regarding intentions, beliefs, projections, outlook, analyses or current expectations concerning, among other things: the ability and timing to initiate a clinical trial of ALLO-715 in combination with nirogacestat; ability to manufacture ALLO-715; the ability of ALLO-715 in combination with nirogacestat to enable deeper or more durable responses; and the potential benefits of AlloCAR T™ therapy. Various factors may cause differences between Allogene's expectations and actual results as discussed in greater detail in Allogene's filings with the SEC, including without limitation in its Form 10-Q for the quarter ended September 30, 2020. Any forward-looking statements that are made in this press release speak only as of the date of this press release. Allogene assumes no obligation to update the forward-looking statements whether as a result of new information, future events or otherwise, after the date of this press release.

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1 Eastman S, Shelton C, Gupta I, Krueger J, Blackwell C, Bojczuk. Synergistic activity of belantamab mafodotin (anti-BCMA immuno-conjugate) with PF-03084014 (gamma-secretase inhibitor) in Bcma-expressing cancer cell lines. Blood. 2019;134(supplement_1):4401. doi.org/10.1182/blood-2019-123705.

2 https://www.cancer.org/cancer/multiple-myeloma/about/what-is-multiple-myeloma.html

3 Multiple myeloma - Genetics Home Reference - NIH. Retrieved from https://ghr.nlm.nih.gov/condition/multiple-myeloma#

4 Sonneveld P, Broijl A. Treatment of relapsed and refractory multiple myeloma. Haematologica. 2016;101(4):396-406

Source: Allogene Therapeutics, Inc.