



Allogene Therapeutics and SpringWorks Therapeutics Announce Clinical Collaboration to Evaluate ALLO-715 in Combination with Nirogacestat in Multiple Myeloma

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- Increasing BCMA Surface Expression with Gamma Secretase Inhibitor Nirogacestat May Enable Deep and Durable Responses to ALLO-715, an Investigational Anti-BCMA Allogeneic CAR T Therapy

SOUTH SAN FRANCISCO, Calif. and STAMFORD, Conn., Jan. 13, 2020 (GLOBE NEWSWIRE) -- Allogene Therapeutics, Inc. (Nasdaq: ALLO), a clinical-stage biotechnology company pioneering the development of allogeneic chimeric antigen receptor T cell (AlloCAR T™) therapies for cancer and SpringWorks Therapeutics, Inc. (Nasdaq: SWTX), a clinical-stage biopharmaceutical company focused on developing life-changing medicines for patients with severe rare diseases and cancer, today announced that they have entered into a clinical trial collaboration agreement. This agreement will evaluate ALLO-715, Allogene's investigational anti-B-cell maturation antigen (BCMA) AlloCAR T therapy in combination with SpringWorks' investigational gamma secretase inhibitor (GSI), nirogacestat, in patients with relapsed or refractory multiple myeloma.

Gamma secretase inhibition prevents the cleavage and shedding of BCMA from the surface of myeloma cells. In preclinical models, nirogacestat has been shown to increase the cell surface density of BCMA and reduce levels of soluble BCMA, thereby enhancing the activity of BCMA-targeted therapies.¹ In addition, emerging clinical data suggest that a GSI may increase antitumor efficacy of BCMA-targeted autologous CAR T therapy in patients with relapsed and refractory multiple myeloma.^{2,3}

"Autologous CAR T therapy has shown the potential for engineered cell therapy to treat multiple myeloma and provide significant benefits to patients. We believe allogeneic CAR T therapy is the next frontier in genetically engineered cell therapy for the treatment of cancer," said David Chang, M.D., Ph.D., President, CEO and Co-Founder of Allogene Therapeutics. "The search to find long-lasting and potentially curative therapies for patients with multiple myeloma continues to evolve. We are pleased with the progress of our ALLO-715 Phase 1 UNIVERSAL trial and are excited to explore the combination of ALLO-715 with nirogacestat as a means to further unlock the potential of allogeneic CAR T therapy in this disease."

Under the terms of the agreement, Allogene will sponsor and conduct the Phase 1 study to evaluate the safety, tolerability and preliminary efficacy of the combination, and will assume all development costs associated with the study. Allogene and SpringWorks will form a joint development committee to oversee the clinical study, which is expected to commence in the second half of 2020 pending discussions with regulators.

"Gamma secretase inhibition has emerged as a clinically validated mechanism to potentiate BCMA therapies and we believe that nirogacestat has the potential to become a cornerstone of BCMA combination therapy for patients with multiple myeloma," said Saqib Islam, Chief Executive Officer of SpringWorks Therapeutics. "We are delighted to partner with Allogene, a pioneer in the allogeneic cell therapy field, to further explore nirogacestat in combination with an 'off-the-shelf' CAR T therapy for these patients where the need for treatment options remains great."

SpringWorks is currently enrolling patients in a global Phase 3, double-blind, randomized, placebo-controlled clinical trial (the DeFi Trial) to evaluate nirogacestat in adults with progressing desmoid tumors.

About ALLO-715

ALLO-715, an AlloCAR T therapy targeting B-cell maturation antigen (BCMA), is currently in Phase 1 development as a potential novel treatment for multiple myeloma. Multiple myeloma is characterized by abnormalities in plasma cells that reproduce uncontrollably in the bone marrow of people with the disease,⁴ multiple myeloma is incurable for most patients, and most patients relapse despite the treatments available.⁵ Preclinical study results for ALLO-715 were published in the journal *Molecular Therapy* validating the potential for an AlloCAR T to treat multiple myeloma and demonstrating the ability for ALLO-715 to sustain potent anti-tumor responses in pre-clinical models. Allogene initiated the UNIVERSAL study in the third quarter of 2019.

ALLO-715 utilizes TALEN® gene-editing technology pioneered and owned by Collectis. Allogene has an exclusive license to the Collectis technology for allogeneic products directed at the BCMA target. Allogene holds 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 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 receptors for BCMA-directed therapies. Nirogacestat's ability to enhance the activity of BCMA-directed therapies has been observed in preclinical models of multiple myeloma. SpringWorks is pursuing a combination therapy approach to evaluate nirogacestat as a BCMA potentiator across modalities by collaborating with industry leaders. To date, SpringWorks has entered into two clinical collaborations to evaluate nirogacestat in combination with GlaxoSmithKline's BCMA antibody-drug conjugate belantamab mafodotin and with Allogene's allogeneic BCMA CAR-T cell therapy ALLO-715.

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 world-class 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.

About SpringWorks Therapeutics

SpringWorks is a clinical-stage biopharmaceutical company applying a precision medicine approach to acquiring, developing and commercializing life-changing medicines for underserved patient populations suffering from devastating rare diseases and cancer. SpringWorks has a differentiated portfolio of small molecule targeted oncology product candidates and is advancing two potentially registrational clinical trials in rare tumor types, as well as several other programs addressing highly prevalent, genetically defined cancers. SpringWorks' strategic approach and operational excellence in clinical development have enabled it to rapidly advance its two lead product candidates into late-stage clinical trials while simultaneously entering into multiple shared-value partnerships with industry leaders to expand its portfolio. For more information, please visit www.springworkstx.com. Follow SpringWorks Therapeutics on social media: @SpringWorksTx and LinkedIn.

Allogene 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 timing and ability to initiate and advance a combination trial for nirogacestat and ALLO-715, the potential benefits of the combination trial, including the ability of nirogacestat to increase BCMA surface expression to enable a deep and durable response of ALLO-715, the ability to develop allogeneic CAR T therapies for cancer 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 Securities and Exchange Commission (SEC), including without limitation in its Form 10-Q for the quarter ended September 30, 2019. 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.

SpringWorks Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, statements regarding SpringWorks' clinical trials and its strategy, business plans and focus. The words "may," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "project," "potential," "continue," "target" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements in this press release are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this press release, including, without limitation, statements regarding the future research and development activities under the agreement with Allogene, the timing for completion of SpringWorks' clinical trials of its product candidates, whether and when, if at all, SpringWorks' product candidates will receive approval from the U.S. Food and Drug Administration, or FDA, or other foreign regulatory authorities, competition from other biopharmaceutical companies, and other risks identified in the section entitled "Risk Factors" in Item 1A of Part II of SpringWorks' Quarterly Report on Form 10-Q for the quarter ended September 30, 2019, as well as discussions of potential risks, uncertainties and other important factors in SpringWorks' subsequent filings with the Securities and Exchange Commission. SpringWorks cautions you not to place undue reliance on any forward-looking statements, which speak only as of the date they are made. SpringWorks disclaims any obligation to publicly update or revise any such statements to reflect any change in expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements. Any forward-looking statements contained in this press release represent SpringWorks' views only as of the date hereof and should not be relied upon as representing its views as of any subsequent date.

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1 Eastman et al., Abstract #4401 "Synergistic Activity of Belantamab Mafodotin (anti-BCMA immuno-conjugate) with Nirogacestat (PF-03084014, gamma-secretase inhibitor) in BCMA-Expressing Cancer Cell Lines", ASH 2019.

2 Cowan et al., Abstract #204 "Efficacy and Safety of Fully Human BCMA CAR T Cells in Combination with a Gamma Secretase Inhibitor to Increase Bcma Surface Expression in Patients with Relapsed or Refractory Multiple Myeloma", ASH 2019.

3 Blood. 2019 Nov 7;134(19):1585-1597. doi: 10.1182/blood.2019000050

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

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



Source: Allogene Therapeutics, Inc.