Allogene Therapeutics and SpringWorks Therapeutics Announce Dosing of First Patient in Phase 1 Study Evaluating ALLO-715 in Combination with Nirogacestat in Patients with Relapsed or Refractory Multiple Myeloma

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SOUTH SAN FRANCISCO, Calif. and STAMFORD, Conn., April 12, 2021 (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 the first patient has been dosed in a Phase 1 trial evaluating ALLO-715, Allogene's investigational anti-B-cell maturation antigen (BCMA) AlloCAR T therapy, in combination with nirogacestat, SpringWorks' investigational gamma secretase inhibitor (GSI), in patients with relapsed or refractory multiple myeloma.

"We are pleased to have initiated this portion of the UNIVERSAL trial and look forward to investigating ALLO-715 in combination with nirogacestat as part of our comprehensive anti-BCMA strategy aimed at bringing an off-the-shelf cell therapy to patients with relapsed or refractory multiple myeloma," said David Chang, M.D., Ph.D., President, CEO and Co-Founder of Allogene Therapeutics.

Gamma secretase inhibition prevents the cleavage and shedding of BCMA from the surface of multiple myeloma cells. In preclinical models, nirogacestat has been shown to increase the cell surface density of BCMA and reduce levels of soluble BCMA, which may enhance 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]

"Multiple myeloma is incurable for the overwhelming majority of patients diagnosed with this cancer and those who have relapsed or are refractory to current treatments have very limited therapeutic options available to them," said Saqib Islam, Chief Executive Officer of SpringWorks Therapeutics. "SpringWorks is advancing nirogacestat as a cornerstone of BCMA combination therapy across modalities, with the goal of potentiating BCMA therapies to provide better outcomes for patients. This study represents the first clinical trial combining nirogacestat with a CAR T therapy and we are delighted that the milestone of dosing the first patient has been achieved."

The Phase 1 trial (NCT04093596), which is part of the ongoing UNIVERSAL trial being conducted by Allogene, is an open-label study evaluating the safety, tolerability and preliminary efficacy of ALLO-715 in combination with nirogacestat in patients with relapsed or refractory multiple myeloma. The trial is being advanced pursuant to a clinical trial collaboration agreement between Allogene and SpringWorks. Under the terms of the agreement, Allogene is sponsoring and conducting the Phase 1 study. Allogene and SpringWorks have formed a joint development committee to oversee this portion of 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.4 Multiple myeloma is incurable for most patients, as relapses occur despite most treatments available. 5 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 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 evaluating nirogacestat as a BCMA potentiator and has five collaborations with industry -leading BCMA developers to evaluate nirogacestat in combinations across modalities, including with an antibody-drug conjugate, two CAR T cell therapies and two bispecific antibodies. In addition, SpringWorks and Fred Hutchinson Cancer Research Center have entered into a sponsored research agreement to further characterize the ability of nirogacestat to modulate BCMA and potentiate BCMA directed therapies using a variety of preclinical and patient-derived multiple myeloma models developed by researchers at Fred Hutch.

Nirogacestat has received Orphan Drug Designation from the U.S. Food and Drug Administration (FDA) for the treatment of desmoid tumors and from the European Commission for the treatment of soft tissue sarcoma. 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.

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.

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, and follow @SpringWorksTx on Twitter 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 ability to progress the UNIVERSAL trial and combination of ALLO-715 with nirogacestat; the ability of ALLO-715 in combination with nirogacestat to provide better outcomes for patients; 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-K for the year ended December 31, 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.

AlloCAR T™ is a trademark of Allogene Therapeutics, Inc.

SpringWorks Forward-Looking Statements
This press release contains “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995 relating to our business, operations, and financial conditions, including but not limited to current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, our development plans, our preclinical and clinical results, and other future conditions. Words such as, but not limited to, “look forward to,” “believe,” “expect,” “anticipate,” “estimate,” “intend,” “plan,” “would,” “should” and “could,” and similar expressions or words, identify forward-looking statements. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. 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, risks relating to: (i) the success and timing of our product development activities, including the initiation and completion of SpringWorks' clinical trials, (ii) the fact that interim data from a clinical study may not be predictive of the final results of such study or the results of other ongoing or future studies, (iii) the success and timing of our collaboration partners' ongoing and planned clinical trials, (iv) our ability to obtain and maintain regulatory approval of any of our product candidates, (v) our plans to research, discover and develop additional product candidates, (vi) our ability to enter into collaborations for the development of new product candidates, (vii) our ability to establish manufacturing capabilities, and our and our collaboration partners' abilities to manufacture our product candidates and scale production, (viii) our ability to meet any specific milestone s set forth herein, and (ix) uncertainties and assumptions regarding the impact of the COVID-19 pandemic on SpringWorks' business, operations, clinical trials, supply chain, strategy, goals and anticipated timelines. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise. Although we believe the expectations reflected in such forward-looking statements are reasonable, we can give no assurance that such expectations will prove to be correct. Accordingly, readers are cautioned not to place undue reliance on these forward-looking statements. For further information regarding the risks, uncertainties and other factors that may cause differences between SpringWorks' expectations and actual results, you should review the “Risk Factors” in Item 1A of Part I of SpringWorks' Annual Report on Form 10-K for the year ended December 31, 2020, as well as discussions of potential risks, uncertainties and other important factors in SpringWorks' subsequent filings.

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