# SpringWorks Therapeutics Announces Dosing of First Patient in Phase 1b Combination Study Evaluating Nirogacestat and GlaxoSmithKline's Belantamab Mafodotin for the Treatment of Relapsed or Refractory Multiple Myeloma

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STAMFORD, Conn., June 22, 2020 (GLOBE NEWSWIRE) -- 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 1b clinical trial evaluating SpringWorks Therapeutics' investigational gamma secretase inhibitor, nirogacestat, in combination with GlaxoSmithKline's (GSK) investigational anti-B-cell maturation antigen (BCMA) antibody-drug conjugate, belantamab mafodotin, in patients with relapsed or refractory multiple myeloma. The nirogacestat and belantamab mafodotin combination is being evaluated as a sub-study in GSK's ongoing DREAMM-5 platform trial.

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 to reduce levels of soluble BCMA, thereby enhancing the activity of BCMA-targeted therapies. Further, preclinical data evaluating the combination of nirogacestat and belantamab mafodotin demonstrated synergistic increases in human multiple myeloma cell killing as compared to belantamab mafodotin alone, with an up to ~3,000-fold improvement in cytotoxicity with the combination.[1]

"SpringWorks is focused on advancing a comprehensive strategy to evaluate the ability of nirogacestat to potentiate BCMA-directed therapies across modalities with the goal of making nirogacestat a cornerstone of BCMA combination therapy for patients with multiple myeloma," said Saqib Islam, Chief Executive Officer of SpringWorks Therapeutics. "We are delighted to have reached this important milestone of dosing the first patient in this collaborative trial with GSK, an industry leader committed to advancing BCMA therapies. We look forward to generating clinical data to test the hypothesis that adding nirogacestat to belantamab mafodotin could lead to better clinical outcomes for patients."

The Phase 1b combination trial is being advanced pursuant to a global clinical trial collaboration agreement that SpringWorks and GSK entered into in June 2019. Under the terms of the agreement, GSK is sponsoring and conducting the Phase 1b 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. SpringWorks and GlaxoSmithKline have formed a joint development committee to help manage and oversee the clinical study.

**About the Phase 1b Trial**
The Phase 1b trial (NCT04126200), which is a sub-study of GSK's DREAMM-5 Phase 1/2 platform study, is an open-label study to evaluate the safety, tolerability and preliminary efficacy of nirogacestat in combination with belantamab mafodotin in patients with relapsed or refractory multiple myeloma. The study will include two parts, a dose exploration phase and a cohort expansion phase. The dose exploration phase will evaluate the safety and tolerability profile of GSK's belantamab mafodotin when administered in combination with nirogacestat and will identify a recommended Phase 2 dose for each drug in combination. The cohort expansion phase will evaluate the clinical activity of the combination in comparison to belantamab mafodotin monotherapy in additional patients with relapsed or refractory multiple myeloma.

**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 soluble BCMA from the cell surface. By inhibiting gamma secretase, membrane-bound BCMA can be preserved, increasing target density while reducing levels of soluble BCMA, which may serve as a decoy receptor 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 GSK'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 in November 2018 and August 2019, respectively.

**About belantamab mafodotin (GSK2857916)**
Belantamab mafodotin is an investigational antibody drug conjugate comprising a humanized anti-B cell maturation antigen (BCMA) monoclonal antibody conjugated to the cytotoxic agent auristatin F via non-cleavable linker.[2] The drug linker technology is licensed from Seattle Genetics; monoclonal antibody is produced using POTELLIGENT Technology licensed from BioWa.

Belantamab mafodotin is not currently approved for use anywhere in the world.

**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.

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**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, those related to SpringWorks' financial results, 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, uncertainties and assumptions regarding the impact of the COVID-19 pandemic on SpringWorks' business, operations, clinical trials, supply chain, strategy, goals and anticipated timelines, 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 March 31, 2020, 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, S., Shelton, C., Gupta, I., Krueger, J., Blackwell, C., & Bojczuk, P. M. (2019, December). *4401 Synergistic Activity of Belantamab Mafodotin (anti-BCMA immuno-conjugate) with PF-03084014 (gamma-secretase inhibitor) in Bcma-Expressing Cancer Cell Lines*. Poster session presented at the 61st American Society of Hematology Annual Meeting & Exposition, Orlando, FL.

[2] NCI Drug Dictionary - Anti-BCMA Antibody-Drug Conjugate GSK2857916. National Cancer Institute. https://www.cancer.gov/publications/dictionaries/cancer-drug/def/anti-bcma-antibody-drug-conjugate-gsk2857916. Accessed May 2020.