SpringWorks Therapeutics Highlights Nirogacestat Clinical Data at the 2022 ASCO Annual Meeting

May 26, 2022

- Initial Data to be Presented from GSK-Sponsored Phase 1/2 Study Evaluating Nirogacestat in Combination with Low-Dose BLENREP in Patients with Relapsed or Refractory Multiple Myeloma -

- Long-Term Follow-up Data from NCI-Sponsored Phase 2 Study of Nirogacestat in Patients with Progressing Desmoid Tumors Also to be Presented -

STAMFORD, Conn., May 26, 2022 (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 initial clinical data from the Phase 1/2 study evaluating nirogacestat, SpringWorks' investigational gamma secretase inhibitor, in combination with BLENREP (belantamab mafodotin-blmf), GSK plc's (LSE/NYSE: GSK) antibody drug conjugate targeting B-cell maturation agent (BCMA), in patients with relapsed or refractory multiple myeloma (RRMM). In addition, SpringWorks also highlighted long-term follow-up data from a Phase 2 study sponsored by the National Cancer Institute (NCI) evaluating nirogacestat in patients with progressing desmoid tumors, which included follow-up on progression-free survival and long-term safety data.[2] These data sets will be shared in poster sessions at the 2022 American Society of Clinical Oncology (ASCO) Annual Meeting, June 3-7, 2022 in Chicago.

"We are encouraged by the emerging clinical profile of nirogacestat with low-dose BLENREP given the promising efficacy and safety profile that we have seen to date, and we look forward to the maturation of the Phase 2 portion of the study in parallel with the initiation of new sub-studies to evaluate this combination with standard of care treatments in multiple myeloma," said Saqib Islam, Chief Executive Officer of SpringWorks. "I would also like to thank the NCI for their commitment to evaluating nirogacestat in patients with progressing desmoid tumors. We were very pleased to recently report positive topline data from our Phase 3 DeFi trial and these follow-up data from the NCI-sponsored Phase 2 study provide valuable information on the long-term safety and efficacy profile of nirogacestat in desmoid tumor patients."

Synergistic Effects of Low-Dose Belantamab Mafodotin in Combination with a Gamma-Secretase Inhibitor (Nirogacestat) in Patients with Relapsed/Refractory Multiple Myeloma (RRMM): DREAMM-5 Study (Poster # 443)

The objective of this sub-study of GSK's DREAMM-5 platform trial (NCT04126200) is to determine if low-dose BLENREP in combination with nirogacestat results in similar efficacy with an improved ocular toxicity profile compared to single-agent BLENREP at its approved dose and schedule. The study opened with a dose-exploration (DE) arm evaluating 0.95 mg/kg BLENREP Q3W combined with 100 mg BID nirogacestat dosed continuously, and subsequently moved into a cohort expansion (CE) arm. The target enrollment for the CE arm of the study is 70 patients randomized either to BLENREP 2.5mg/kg Q3W monotherapy (control arm) or low-dose BLENREP plus nirogacestat combination using the same dose as the DE arm cohort.

The following results of the pre-planned interim analysis will be presented at ASCO:

- The study enrolled patients with relapsed or refractory multiple myeloma who have received at least 3 prior lines of therapy (median: 4.5), including an immunomodulatory agent, proteasome inhibitor, and anti-CD38 antibody. The poster being presented at ASCO includes data from a total of 24 patients treated with low-dose BLENREP + nirogacestat across the DE and CE cohorts (N=10 and N=14, respectively) and 14 patients treated with monotherapy BLENREP in the CE cohort.
- At the time of the March 4, 2022 data cut-off, the median (range) of follow-up in the low-dose BLENREP plus nirogacestat DE cohort was 34.5 weeks (5-88 weeks), with durations of response exceeding one year in some patients. Data from the CE cohorts are not yet mature with a median duration of follow-up of 12 weeks available at the time of data cut-off.
- The CE cohorts utilized the KVA ocular toxicity grading scale; Grade 3 ocular adverse events occurred in 1/14 (7%) patients in the low-dose BLENREP plus nirogacestat combination compared to 7/14 patients (50%) in the BLENREP monotherapy arm. The DE cohort utilized the CTCAE-5 ocular toxicity grading scale; the low-dose BLENREP plus nirogacestat combination demonstrated Grade 3 ocular adverse events in 2/10 (20%) patients.
- At the time of data cut-off, the objective response rate (ORR) of low-dose BLENREP plus nirogacestat across the DE and CE cohorts was 38%, with 17% of patients achieving a VGPR or better (N=24). The ORR of the BLENREP monotherapy control arm was 50%, with no patients achieving a VGPR or better (N=14).

These data will be presented in a poster discussion session at ASCO on June 4, 2022 from 5:30 - 7:00 p.m. EDT by Sagar Lonial, MD, FACP, Professor and Chair Department of Hematology and Medical Oncology, Winship Cancer Institute, Emory University.

Extended Progression-Free Survival and Long-Term Safety of Nirogacestat in Patients with Desmoid Tumors (Poster #449)

The primary objective of this open-label, NCI-sponsored Phase 2 study (NCT01981551) was to assess the RECIST 1.1-determined objective response rate of nirogacestat in patients with progressing desmoid tumors. Seventeen adult patients received 150 mg BID of nirogacestat dosed continuously.

The following results will be presented at ASCO:

- Of the 16 evaluable patients, no disease progression has been observed for any patient while on study.

- The median time on treatment for all evaluable patients was 4.4 years (range 0.17-7.99 years) with 4/16 patients remaining on treatment over 7 years. At the time of the Kummar, et. al publication,[3] the median time on treatment was >25 months (range: 3-30 months), with 10/16 patients remaining on treatment as of the publication.
- The adverse event profile was generally consistent with what was previously reported by Kummar, et. al. Long-term follow-up data reported one new Grade 3 adverse event of diarrhea and one new Grade 3 adverse event of fatigue.

These data will be presented in a poster session on June 5, 2022 from 9:00a.m.-12:00p.m. EDT by Geraldine Helen O'Sullivan Coyne, MD, PhD, Developmental Therapeutics Clinic/Early Clinical Trials Development Program, Division of Cancer Treatment and Diagnosis, National Cancer Institute.

About Multiple Myeloma

Multiple myeloma is the second most common blood cancer in the U.S. and is generally considered treatable, but not curable.[4,5] It originates in the bone marrow and is characterized by abnormalities in plasma cells that reproduce uncontrollably in the bone marrow and other disease sites. In the U.S., more than 34,000 people are estimated to be diagnosed with multiple myeloma this year and nearly 13,000 people will die from the disease.[6] New therapies are needed as multiple myeloma commonly becomes refractory to available treatments.[7]

About Desmoid Tumors

Desmoid tumors are rare, aggressive, locally invasive, potentially morbid tumors of the soft tissues.[8,9] While they do not metastasize, desmoid tumors are associated with a high rate of recurrence.[9,10,11] Sometimes referred to as aggressive fibromatosis, or desmoid fibromatosis, these soft tissue tumors can be serious, debilitating, and in rare cases when vital organs are impacted, they can be life-threatening.[9,12]

Desmoid tumors are most commonly diagnosed in patients between the ages of 20 to 44 years, with a two-to-three times higher prevalence in females.[11,13,14] It is estimated that there are 1,000-1,650 new cases diagnosed per year in the United States.[14,15]

Historically, desmoid tumors were treated with surgical resection, but this approach has become less favored due to a high recurrence rate after surgery.[8,11,16] There are currently no FDA-approved therapies for the treatment of desmoid tumors.

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 eight collaborations with industry-leading BCMA developers to evaluate nirogacestat in combinations across modalities, including with an antibody-drug conjugate, two CAR T cell therapies, four bispecific antibodies and a monoclonal antibody. SpringWorks has also formed research collaborations with Fred Hutchinson Cancer Research Center and Dana-Farber Cancer Institute to further characterize the ability of nirogacestat to modulate BCMA and potentiate BCMA-directed therapies using a variety of preclinical multiple myeloma models.

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 SpringWorks Therapeutics

SpringWorks is a clinical-stage biopharmaceutical company applying a precision medicine approach to acquiring, developing and commercializing life-changing medicines for patients living with severe rare diseases and cancer. SpringWorks has a differentiated targeted oncology portfolio of small molecule product candidates and is advancing 18 development programs, including two potentially registrational clinical trials in rare tumor types as well as several 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 innovators in industry and academia to expand its portfolio and create more solutions for patients with cancer. For more information, visit www.springworkstx.com and follow @SpringWorksTx on Twitter and LinkedIn.

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 the timing for initiation, enrollment, progress and completion of SpringWorks' clinical trials or third-party clinical trials of its product candidates, the timing for expected data readouts from partners and partners' clinical trials, the expected benefits of collaborations, the fact that interim results from a clinical study may not be predictive of the final results of such study or the results of other ongoing or future studies, 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 involving its product candidates, supply chain, strategy, goals and anticipated timelines, competition from other biopharmaceutical companies, and other risks identified in SpringWorks' SEC filings.

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' Quarterly Report on Form 10-Q for the quarter ended March 31, 2022, as well as discussions of potential risks, uncertainties and other important factors in SpringWorks' subsequent filings.

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