SpringWorks Therapeutics Announces Full Enrollment of Phase 2b ReNeu Trial Evaluating Mirdametinib in Adult and Pediatric Patients with NF1-Associated Plexiform Neurofibromas

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STAMFORD, Conn., Nov. 29, 2021 (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 it has achieved full enrollment in its Phase 2b ReNeu trial evaluating mirdametinib, an investigational MEK inhibitor, in adult and pediatric patients with NF1-associated plexiform neurofibromas (NF1-PN). The study enrolled over 50 adults and over 50 pediatric patients with NF1-PN. SpringWorks expects to provide an update on anticipated ReNeu trial timelines and milestones at an upcoming company-sponsored R&D Day.

“Plexiform neurofibromas can cause severe disfigurement, pain, and functional impairment, and patients living with these devastating tumors are in need of new treatments. We are very pleased to have reached another important milestone on behalf of the NF1-PN patient community by completing enrollment in the ReNeu study,” said Saqib Islam, Chief Executive Officer of SpringWorks. “We believe that mirdametinib has the potential to be a best-in-class treatment for NF1-PN based on its clinical activity, tolerability profile, ability to be taken without regard to food, and expected availability of a pediatric formulation. We look forward to providing further updates on the trial at our R&D Day.”

The ReNeu trial is a multi-center, open-label Phase 2b trial evaluating the efficacy, safety, and tolerability of mirdametinib in patients two years of age and older with an inoperable NF1-associated PN causing significant morbidity. Patients receive mirdametinib at a dose of 2 mg/m^2 twice daily (maximum dose of 4 mg twice daily) without regard to food. Mirdametinib is administered in a 3-week on, 1-week off dosing schedule. The primary endpoint of the ReNeu trial is objective response rate defined as ≥ 20% reduction in target tumor volume as measured by MRI and assessed by blinded independent central review. Secondary endpoints include safety and tolerability measures, duration of response, and changes from baseline in patient reported outcomes. More information about the ReNeu trial is available at www.clinicaltrials.gov under the identifier NCT03962543.

As previously disclosed, interim data from the first 20 adult patients enrolled in the ReNeu trial were presented at the 2021 Children’s Tumor Foundation NF Conference and showed encouraging efficacy and tolerability. As of the March 23, 2021 data cutoff date, 50% of patients had achieved an objective response as assessed by blinded independent central review, 80% remained on study, and median time on treatment was 13 cycles (approximately 12 months). Among these patients, mirdametinib was generally well tolerated, with the majority of treatment-related adverse events (TRAE) being Grade 1 or 2; only one Grade 3 TRAE and no Grade 4 or 5 adverse events (AE) were reported in these 20 patients.

About NF1-PN

Neurofibromatosis type 1 (NF1) is a rare genetic disorder that arises from mutations in the NF1 gene, which encodes for neurofibromin, a key suppressor of the MAPK pathway.[1,2] NF1 is the most common form of neurofibromatosis, with an estimated global birth incidence of approximately 1 in 3,000 individuals, and approximately 100,000 patients living with NF1 in the United States.[3,4] The clinical course of NF1 is heterogeneous and manifests in a variety of symptoms across numerous organ systems, including abnormal pigmentation, skeletal deformities, tumor growth and neurological complications, such as cognitive impairment.[5] Patients with NF1 have an eight to 15-year mean reduction in their life expectancy compared to the general population.[2]

NF1 patients have approximately a 30-50% lifetime risk of developing plexiform neurofibromas, or PN, which are tumors that grow in an infiltrative pattern along the peripheral nerve sheath and that can cause severe disfigurement, pain and functional impairment; in rare cases, NF1-PN may be fatal.[3,4,6] Patients with NF1 can also experience additional manifestations, including neurocognitive deficits and developmental delays.[4] NF1-PNs are most often diagnosed in the first two decades of life.[3] These tumors can be aggressive and are associated with clinically significant morbidities; typically, they grow more rapidly during childhood.[7,8]

Surgical removal of these tumors is challenging due to the infiltrative tumor growth pattern along nerves and can lead to permanent nerve damage and disfigurement.[9] MEK inhibitors have emerged as a validated class of treatment for NF1-PN.[4]

About Mirdametinib

Mirdametinib is an oral, allosteric small molecule MEK inhibitor in development as a monotherapy treatment for neurofibromatosis type 1-associated plexiform neurofibromas (NF1-PN) and low-grade glioma (LGG), and as a combination therapy for the treatment of several subsets of biomarker-defined metastatic solid tumors. To date, over 250 subjects have been exposed to treatment with mirdametinib across clinical trials, with preliminary evidence of clinical activity against tumors driven by over-activated MAPK signaling.[5]

Mirdametinib is designed to inhibit MEK1 and MEK2, which occupy pivotal positions in the MAPK pathway. The MAPK pathway is a key signaling network that regulates cell growth and survival and that plays a central role in multiple oncology and rare disease indications when genetically altered.

The U.S. Food and Drug Administration (FDA) and the European Commission granted Orphan Drug designation for mirdametinib for the treatment of NF1, and the FDA granted Fast Track designation for the treatment of patients ≥ 2 years of age with NF1-PN that are progressing or causing significant morbidity.

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 16 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, please visit www.springworkstx.com, and follow @SpringWorksTx on Twitter and LinkedIn.

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 milestones 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' Quarterly Report on Form 10-Q for the quarter ended September 30, 2021, as well as discussions of potential risks, uncertainties and other important factors in SpringWorks' subsequent filings.

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