SpringWorks Therapeutics Announces Positive Topline Results from the Phase 2b ReNeu Trial of Mirdametinib in NF1-PN

November 16, 2023

– Confirmed objective response rate of 52% in pediatric patients and 41% in adult patients, as assessed by Blinded Independent Central Review –

– Mirdametinib treatment resulted in deep and durable responses and significant improvements in key secondary patient-reported outcome measures –

– Mirdametinib was generally well tolerated with low rates of Grade 3+ adverse events –

– Additional data expected to be presented at medical conference and NDA submission to the U.S. FDA planned in the first half of 2024 –

– Company to host conference call today at 8:30 a.m. Eastern Time –

STAMFORD, Conn., Nov. 16, 2023 (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 positive topline results from the pivotal Phase 2b ReNeu trial evaluating mirdametinib, an investigational MEK inhibitor, in pediatric and adult patients with neurofibromatosis type 1-associated plexiform neurofibromas (NF1-PN).

The ReNeu trial enrolled 114 patients in two cohorts (pediatric and adult) across 50 sites in the U.S. The primary endpoint was confirmed objective response rate (ORR), defined as ≥ 20% reduction in target tumor volume as measured by MRI and assessed by Blinded Independent Central Review (BICR). As of the data cutoff date of September 20, 2023, 52% (29/56) of pediatric patients and 41% (24/58) of adult patients had BICR confirmed objective responses within the 24-cycle treatment period (cycle length: 28 days). An additional pediatric patient and two additional adult patients achieved confirmed objective responses after Cycle 24 in the long-term follow up phase of the trial, where patients continue to receive mirdametinib treatment. Median best percent change from baseline in target tumor volume was -42% and -41% in the pediatric and adult cohort, respectively. As of the data cut-off, the median duration of treatment was 22 months in both the pediatric and adult cohorts. Median duration of response was not reached in either cohort. Pediatric and adult patients in the ReNeu trial also experienced statistically significant improvements from baseline in pain, quality of life, and physical function, as assessed across multiple patient-reported outcome tools.

Mirdametinib was generally well tolerated in the ReNeu trial, with the majority of adverse events (AEs) being Grade 1 or Grade 2. The most frequently reported AEs were rash, diarrhea, and vomiting in the pediatric cohort and rash, diarrhea, and nausea in the adult cohort. Twenty-five percent of pediatric patients and 16% of adult patients experienced a Grade 3 or higher treatment-related AE. Additional data are expected to be presented at an upcoming medical conference in the first half of 2024 and to be submitted for publication in a peer-reviewed journal.

“Plexiform neurofibromas can grow aggressively along peripheral nerves and lead to extreme pain, disfigurement and other morbidities that have a significant impact on the lives of patients and their families,” said Saqib Islam, Chief Executive Officer of SpringWorks. “We are extremely pleased that the results of our ReNeu trial demonstrate a compelling clinical profile across measures of both safety and efficacy. Our data indicates that mirdametinib has the potential to be the best-in-class therapy for children and the first approved treatment for adults with NF1-PN and we are working with urgency to bring this differentiated medicine to patients.”

The U.S. Food and Drug Administration (FDA) and the European Commission have granted Orphan Drug designation for mirdametinib for the treatment of NF1. The FDA has also granted Fast Track designation for the treatment of patients ≥ 2 years of age with NF1-PN that are progressing or causing significant morbidity. In July 2023, FDA granted mirdametinib Rare Pediatric Disease Designation for the treatment of NF1, and as such, if approved, mirdametinib will be eligible to receive a priority review voucher. SpringWorks plans to submit a New Drug Application (NDA) for mirdametinib to the FDA in the first half of 2024.

About the ReNeu Trial

ReNeu (NCT03962543) is an ongoing, 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. The study enrolled 114 patients to 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 orally in a 3-week on, 1-week off dosing schedule and has a pediatric formulation (dispersible tablet) for patients who cannot swallow a pill. The primary endpoint of the ReNeu trial is confirmed 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, duration of response, and changes from baseline in patient reported outcomes.

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 a potent, 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.

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.

Conference Call and Webcast Information

SpringWorks will host a conference call and webcast to discuss the ReNeu topline data today, November 16, at 8:30 a.m. ET. To join the live webcast and view the corresponding slides, please click here. To access the live call by phone, please pre-register for the call here. Once registration is complete, participants will be provided with a dial-in number and conference code to access the call. A replay of the webcast will be available for a limited time following the event on the Investors and Media section of the Company's website at https://ir.springworkstx.com.

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 pipeline spanning solid tumors and hematological cancers, including two late-stage 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 unlock the full potential for 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, as amended, 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, the potential for the results of the Phase 2b ReNeu clinical trial to support an NDA submission for mirdametinib, the potential for mirdametinib to become an important new treatment for patients with NF1-PN, our plans for seeking regulatory approval for and making mirdametinib available for NF1-PN patients, if approved, the potential for SpringWorks to receive a priority review voucher following an FDA approval of mirdametinib, as well as relating to 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) our expectations regarding the potential clinical benefit of mirdametinib for patients with NF1-PN, (iii) the fact that topline or interim data from a clinical study may not be predictive of the final or more detailed results of such study, or the results of other ongoing or future studies, (iv) the success and timing of our collaboration partners' ongoing and planned clinical trials, (vi) the timing of our planned regulatory submissions and interactions, including our planned NDA submission for mirdametinib in the first half of 2024, and the timing and outcome of decisions made by the FDA, the European Medicines Agency (EMA) and other regulatory authorities, investigational review boards at clinical trial sites and publication review bodies; (vi) whether FDA, EMA or other regulatory authorities will require additional information or further studies, or may fail or refuse to approve or may delay approval of our product candidates, (vii) our ability to obtain and maintain regulatory approval of any of our product candidates, (viii) our plans to research, discover and develop additional product candidates, (ix) our ability to enter into collaborations for the development of new product candidates and our ability to realize the benefits expected from such collaborations, (x) our ability to maintain adequate patent protection and successfully enforce patent claims against third parties (xi) our ability to establish and maintain manufacturing capabilities, and our and our collaboration partners' abilities to manufacture our products and product candidates and scale production, and (xii) our ability to meet any specific milestones set forth herein.

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 II of SpringWorks' Quarterly Report on Form 10-Q for the quarter ended September 30, 2023, as well as discussions of potential risks, uncertainties and other important factors in SpringWorks' subsequent filings.

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