SpringWorks Therapeutics Reports Interim Data from Phase 2b ReNeu Trial of Mirdametinib for Patients with NF1-PN and Provides Trial Update

February 25, 2021

- Interim Data Reported from First 20 Adult Patients Enrolled with January 22, 2021 Data Cutoff -

- 10/20 Patients (50%) Had Achieved an Objective Response by Blinded Independent Central Review (BICR) and 16/20 (80%) Remain on Study -

- Mirdametinib Continues to Show a Potentially Differentiated Safety and Tolerability Profile -

- Trial is Approximately 70% Enrolled and With Full Enrollment Expected in 2H2021 -

- Conference Call and Webcast Scheduled for Today at 8:30 a.m. Eastern Time -

STAMFORD, Conn., Feb. 25, 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 reported interim data from the first 20 adult patients enrolled in the ongoing Phase 2b ReNeu trial evaluating mirdametinib, an investigational MEK inhibitor, in adult and pediatric patients with NF1-associated plexiform neurofibromas (NF1-PN). As of the January 22nd data cutoff date, 10/20 (50%) of these patients had achieved an objective response, as assessed by blinded independent central review (BICR), 16/20 (80%) remained on study, and the median time on treatment was 10.1 cycles (approximately 10 months). Mirdametinib was also generally well tolerated, with the majority of treatment related adverse events (TRAE) being Grade 1 or 2 and only one Grade 3 TRAE; there have been no Grade 4 or 5 adverse events (AE). SpringWorks also provided an update on the enrollment status of ReNeu, highlighting that the trial has reached approximately 70% of its target enrollment of 100 patients and that full enrollment is expected in the second half of 2021.

“We are very encouraged by these emerging data from our ongoing ReNeu trial, as they reaffirm our belief that mirdametinib has the potential to be a best-in-class treatment for patients with NF1-PN,” said Saqib Islam, Chief Executive Officer of SpringWorks. “The robust response rate, which was assessed by blinded independent central review, and the very encouraging tolerability profile observed in these interim data are particularly compelling given the unmet need among NF1-PN patients for a therapy that can provide durable efficacy while maintaining a safety profile that is suitable for long-term dosing. We look forward to completing enrollment in the ReNeu trial in the second half of this year and sharing additional data from the study at a future medical conference in 2021.”

Interim Phase 2b Data from ReNeu Trial:

The interim Phase 2b ReNeu data set for the first 20 adult patients enrolled utilized a January 22, 2021 data cutoff. Objective responses were defined as a ≥ 20% reduction in target tumor volume measured by MRI and were assessed by BICR. Patients received mirdametinib at a dose of 2 mg/m^2 twice daily (maximum dose: 4 mg twice daily) without regard to food on a three weeks-on, one week-off intermittent schedule, with patients being allowed to stay on treatment for up to 24 cycles (approximately two years). The median time on treatment for the 20 adult patients evaluated for this analysis was 10.1 cycles (approximately 10 months), with an initial efficacy assessment performed following cycle five and then every four cycles thereafter.

The preliminary efficacy and safety analysis showed:

- 10/20 (50%) of patients had achieved an objective response by BICR.
- For seven of the 10 patients who achieved an initial objective response, subsequent scheduled scans were available, and six of these seven patients had confirmed responses.
- 16/20 (80%) of these patients remain on study and only one patient required a dose reduction due to an AE. Reasons for discontinuation included one each of progressive disease, participant decision, AE (Grade 1 diarrhea), and a patient being unable to undergo required MRI imaging due to a titanium rod implant from non-treatment-related worsening of scoliosis.
- A generally well-tolerated safety profile. The majority of TRAEs were Grade 1 or 2 with only one Grade 3 TRAE reported. No Grade 4 or 5 AEs have been reported. The most common TRAEs were rash, nausea and diarrhea.

Conference Call and Webcast:
SpringWorks will host a conference call and webcast today, Thursday, February 25, 2021, at 8:30 a.m. Eastern Time to discuss the ReNeu trial data and program update. Participants can listen to the call by dialing +1 (800) 708-4539 (domestic) or +1 (847) 619-6396 (international) and providing the confirmation number 50110177. A live webcast presentation can be accessed through the “Investors & Media” section of the Company’s website at https://ir.springworkstx.com/. A replay of the webcast will be available on the SpringWorks website for a limited time following the event.

About the ReNeu Trial
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. The study will enroll approximately 100 patients in the United States. Patients receive mirdametinib at a dose of 2 mg/m^2 twice daily (maximum dose of 4 mg twice daily, calculated based on body surface area) without regard to food. Mirdametinib is administered in a three-weeks on, one-week off dosing schedule.

The primary endpoint is objective response rate, defined as ≥ 20% reduction in target tumor volume as measured by MRI and assessed by BICR.

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.

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 small molecule designed to inhibit MEK1 and MEK2. MEK proteins occupy a pivotal position in the MAPK pathway, a key signaling network that regulates cell growth and survival, and that plays a central role in multiple oncology and rare disease indications.

Mirdametinib has been evaluated in several Phase 1 and Phase 2 clinical trials, with over 200 subjects having been exposed to treatment. A Phase 2 trial was conducted by the Neurofibromatosis Clinical Trial Consortium and evaluated mirdametinib in 19 adolescent and adult patients with inoperable and symptomatic or growing plexiform neurofibromas. Patients received an oral dose of 2 mg/m^2 BID with a maximum dose of 4 mg BID on a four-week cycle of three weeks-on, one week-off. Eight patients (42%) achieved an objective response by cycle 12, prospectively defined as volumetric reduction in their target PN of at least 20%. Mirdametinib was generally well-tolerated in this trial. The most commonly reported treatment-emergent Grade 2 or higher AEs were acneiform rash, fatigue and nausea.

In addition to the Phase 2b monotherapy trial in NF1- PN, and given the critical role that the MAPK pathway plays in the growth and proliferation of a large number of tumor types, SpringWorks is also pursuing mirdametinib in combination with other rational anti-cancer agents across a range of solid tumors.

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.

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, the interim data of the ReNeu clinical trial, including its interim primary efficacy, safety and tolerability data, 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 presentation 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 presentation, including, without limitation, risks relating to: (i) the success and timing of our ongoing DeFi and ReNeu 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 product development activities and initiating clinical trials, (iv) the success and timing of our collaboration partners' ongoing and planned clinical trials, (v) our ability to obtain and maintain regulatory approval of any of our product candidates, (vi) our plans to research, discover and develop additional product candidates, (vii) our ability to enter into collaborations for the development of new product candidates, (viii) our ability to establish manufacturing capabilities, and our and our collaboration partners' abilities to manufacture our product candidates and scale production, (ix) our ability to meet any specific milestones set forth herein, and (x) 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" section(s) of our filings with the Securities and Exchange Commission.

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