SpringWorks Therapeutics Announces Presentation of Updated Interim Data from the Phase 2b ReNeu Trial at the 2021 Children's Tumor Foundation NF Conference

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Additional Follow-up of First 20 Adult Patients Enrolled Continues to Show Encouraging Efficacy and Tolerability of Mirdametinib in Patients with NF1-PN

STAMFORD, Conn., June 15, 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 an update on the previously reported interim data from the first 20 adult patients enrolled in the ongoing Phase 2b ReNeu trial evaluating mirdametinib, an investigational MEK inhibitor being studied in adult and pediatric patients with NF1-associated plexiform neurofibromas (NF1-PN), was presented at the 2021 Children's Tumor Foundation NF Conference being held June 14-16, 2021. The data were presented by Christopher Moertel, M.D., Professor and Medical Director of the Pediatric Neuro-Oncology and Neurofibromatosis Programs at the University of Minnesota Medical School and Principal Investigator of the ReNeu trial.

In February 2021, SpringWorks reported results from the first 20 adult patients enrolled utilizing a January 22, 2021 data cutoff date and showed that 50% of these patients had achieved an objective response as assessed by blinded independent central review (BICR), that 80% remained on study, and that the median time on treatment for these patients was 10.1 cycles (approximately 10 months). The NF Conference presentation utilized a March 23, 2021 data cutoff date and showed durable efficacy in these same 20 patients, with the median time on treatment now having reached 13 cycles (approximately 12 months), the objective response rate remaining at 50%, and 80% of these patients still remain on study. Among these patients, there had been no further dose reductions as of the later data cutoff date and mirdametinib continued to be generally well tolerated, with the majority of treatment-related adverse events (TRAE) being Grade 1 or 2, with only one Grade 3 TRAE and no Grade 4 or 5 adverse events (AE) reported in these 20 patients.

"Plexiform neurofibromas are tumors that can cause serious disfigurement and significant pain," said Dr. Moertel. "These interim data from the ReNeu trial are promising for patients who are in need of new treatment options and the availability of a pediatric formulation of mirdametinib, along with a dosing schedule that does not require fasting, may also be meaningful for patients, many of whom are children and young adults that require long-term treatment in order to control tumor growth and its associated morbidities."

"We remain encouraged by these interim data, which 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 ReNeu trial is on track to complete enrollment in the second half of 2021 and we look forward to sharing additional updates as the trial progresses."

Interim Phase 2b Data from ReNeu Trial:

The interim Phase 2b ReNeu data set presented at the Children's Tumor Foundation NF Conference included the first 20 adult patients enrolled and utilized a March 23, 2021 data cutoff date. 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: 4mg twice daily) without regard to food on a 3 weeks-on, 1 week-off intermittent schedule, with patients being allowed to stay on therapy for up to 24 cycles (approximately two years). The median time on treatment for the 20 adult patients evaluated for this analysis was 13 cycles (approximately 12 months), with an initial efficacy assessment performed following cycle five and then every four cycles thereafter.

The preliminary efficacy and safety analysis presented showed:

- 10/20 (50%) of patients had achieved an objective response by BICR, seven of which have been confirmed at a subsequent scan.
- Responders had a median tumor volume reduction of 45%.
- 16/20 (80%) of these patients remained on study as of the data cutoff 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; there was only one Grade 3 TRAE reported and no Grade 4 or 5 AEs reported in these 20 patients. The most common TRAEs were rash, nausea and diarrhea.

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 3-week on, 1-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 investigational, oral, potent, allosteric small molecule MEK1/2 inhibitor 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 250 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, 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 patients living with severe rare diseases and cancer. SpringWorks has a differentiated targeted oncology portfolio of small molecule product candidates and is advancing two potentially registrational clinical trials in rare tumor types as well as eight 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 March 31, 2021, as well as discussions of potential risks, uncertainties and other important factors in SpringWorks' subsequent filings.

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References

1. Yap YS, McPherson JR, Ong CK, et al. The NF1 gene revisited - from bench to bedside. *Oncotarget*. 2014;5(15):5873-5892. doi:10.18632/oncotarget.2194.
2. Rasmussen S, Friedman J. NF1 Gene and Neurofibromatosis 1. *Am J Epidemiol*. 2000;151(1):33-40. doi:10.1093/oxfordjournals.aje.a010118.
3. Prada C, Rangwala F, Martin L, et al. Pediatric Plexiform Neurofibromas: Impact on Morbidity and Mortality in Neurofibromatosis Type 1. *J Pediatr*. 2012;160(3):461-467. doi:10.1016/j.jpeds.2011.08.051.
4. Ferner R. Neurofibromatosis 1 and neurofibromatosis 2: a twenty first century perspective. *The Lancet Neurology*. 2007;6(4):340-351. doi:10.1016/s1474-4422(07)70075-3.
5. Weiss BD, Wolters PL, Plotkin SR, et al. NF106: A Neurofibromatosis Clinical Trials Consortium Phase II Trial of the MEK Inhibitor Mirdametinib (PD-0325901) in Adolescents and Adults With NF1-Related Plexiform Neurofibromas. *Journal of Clinical Oncology*. 2021;JCO.20.02220.doi.org/10. 1200/JCO.20.02220.
6. Hirbe A, Gutmann D. Neurofibromatosis type 1: a multidisciplinary approach to care. *The Lancet Neurology*. 2014;13(8):834-843. doi:10.1016/s1474-4422(14)70063-8.
7. Gross A, Singh G, Akshintala S, et al. Association of plexiform neurofibroma volume changes and development of clinical morbidities in neurofibromatosis 1. *Neuro Oncol*. 2018;20(12):1643-1651. doi:10.1093/neuonc/noy067.
8. Nguyen R, Dombi E, Widemann B, et al. Growth dynamics of plexiform neurofibromas: a retrospective cohort study of 201 patients with neurofibromatosis 1. *Orphanet J Rare Dis*. 2012;7(1):75. doi:10.1186/1750-1172-7-75.
9. Needle M, Cnaan A, Dattilo J, et al. Prognostic signs in the surgical management of plexiform neurofibroma: The Children's Hospital of Philadelphia experience, 1974-1994. *J Pediatr*. 1997;131(5):678-682. doi:10.1016/s0022-3476(97)70092-1.