SpringWorks Therapeutics Announces Mirdametinib Data to be Presented at the 2024 Society for Neuro-Oncology (SNO) Annual Meeting

November 11, 2024

– Data from the pivotal Phase 2b ReNeu trial demonstrate that patients with NF1-PN achieved deep responses and improvements in health-related quality of life over the course of mirdametinib treatment –

– Encouraging results from Phase 1/2 study of mirdametinib in pediatric patients with low-grade glioma also to be presented in oral session at SNO –

STAMFORD, Conn., Nov. 11, 2024 (GLOBE NEWSWIRE) -- SpringWorks Therapeutics, Inc. (Nasdaq: SWTX), a commercial-stage biopharmaceutical company focused on severe rare diseases and cancer, today announced that three abstracts from the pivotal Phase 2b ReNeu trial of mirdametinib, an investigational MEK inhibitor, in adults and children with neurofibromatosis type 1-associated plexiform neurofibromas (NF1-PN) will be presented in oral and poster sessions at the 29th Annual Meeting & Education Day of the Society for Neuro-Oncology (SNO), being held November 21-24, 2024.

ReNeu (NCT03962543) is a multicenter, single-arm trial and the largest study conducted to date in patients with NF1-PN. As previously reported, data from the ReNeu trial demonstrated deep and sustained reductions in tumor volume as well as improvement in pain and health-related quality of life (HRQoL) in both the adult and pediatric cohorts. New data being presented at SNO show that the deep responses in tumor volume reduction were achieved regardless of baseline characteristics, and suggest a trend between deep response and both earlier achievement of a first confirmed response and longer treatment duration. In addition, the improvements in HRQoL were clinically meaningful, early, and sustained over the course of mirdametinib treatment.

Data from the Phase 1/2 trial of mirdametinib in pediatric and young adult patients with low-grade gliomas (LGG) will also be presented in an oral presentation at SNO and suggest that mirdametinib is well-tolerated and has promising clinical activity in this patient population, including a 63% objective response rate in patients with measurable tumors and a median time to response of 5.4 months.

“We are very pleased that new data analyses from our ReNeu trial continue to support the potentially differentiated profile of mirdametinib for patients with NF1-PN, including deeper responses in target tumors for those who were on treatment for a longer duration, and meaningful improvements across quality-of-life measures,” said Jim Cassidy, M.D., Ph.D., Chief Medical Officer of SpringWorks Therapeutics. “We are also encouraged by the data in children and young adults with LGG treated with mirdametinib and look forward to the phase 2 portion of the trial to further evaluate the efficacy and safety of mirdametinib in this patient population.”

A New Drug Application (NDA) for mirdametinib in adults and children with NF1-PN was granted Priority Review designation by the U.S. Food and Drug Administration (FDA), with a Prescription Drug User Fee Act action date of February 28, 2025. In addition, the European Medicines Agency (EMA) has validated the Marketing Authorization Application (MAA) for mirdametinib for the treatment of adult and pediatric patients with NF1-PN.

Oral and Poster Presentations at 2024 SNO Annual Meeting

Pivotal, phase 2b ReNeu trial of mirdametinib in children and adults with neurofibromatosis type-1 associated plexiform neurofibroma (NF1-PN): A spotlight on patients achieving deep response
Poster Presentation
Abstract #: CTNI-21
Date and Time: November 22, 7:30-9:30 p.m. CST (8:30-10:30 p.m. EST)

As previously reported at the 2024 American Society of Clinical Oncology Annual Meeting, the Phase 2b ReNeu trial met its primary endpoint of confirmed objective response rate, as assessed by blinded independent central review, in both adults and children. Tumor volume reductions were deep and durable over the course of the study. The data being presented at SNO demonstrate that the deep responses in target tumors were achieved regardless of different baseline characteristics and also show that patients with a deep response had longer treatment duration with mirdametinib. The SNO data include:

- Of the 41% (24/58) of adults and 52% (29/56) of children who experienced a confirmed objective response during the 24-cycle treatment phase (approximately 22 months), 62% (15/24) of adults and 52% (15/29) of children achieved deep response (defined as >50% best reduction from baseline in target PN volume).
- Of those with a deep response in the total cohort, 35% of adults (6/17) and 72% of children (13/18) were investigator-defined as having progressing PN at baseline.
- Patients achieved deep response regardless of age, sex, target PN volume, tumor location, or progression status at baseline.
- The median time to best percent change from baseline in PN volume for patients achieving deep response was 25 months for adults and 22 months for children. For patients with ≥20% to ≤50% PN volume reduction, the median time to best percent change from baseline was 15 months for adults and 15 months for children.

“It is very encouraging to see such deep tumor volume reductions across subgroups of patients, and the trend we observed between deep response and longer treatment duration suggests that patients can benefit from prolonged therapy with mirdametinib,” said Timothy R. Gershon, M.D., Ph.D., professor in the Department of Pediatrics at Emory University School of Medicine, Director of the Children’s Center for Neurosciences Research at

Emory University, and ReNeu trial investigator. “The collective findings from the ReNeu trial support the potential for mirdametinib to be a much-needed therapy for patients with this debilitating disease.”

Health-related quality-of-life (HRQoL) in adults and children with neurofibromatosis type-1 associated plexiform neurofibroma (NF1-PN) treated with mirdametinib: Pivotal, phase 2b ReNeu trial
Oral Presentation
Abstract #: QOL-08
Date and Time: November 24, 10:25-10:35 a.m. CST (11:25-11:35 a.m. EST)

In the ReNeu trial, change in HRQoL in adults and children was assessed by the Pediatric QoL Inventory (Peds QL) Total Score; change from baseline at Cycle 13 was a prespecified secondary endpoint. Results showed clinically meaningful, early, and sustained benefits in HRQoL, including:

- Improvement (least-squares mean, LSM [SE] change) from baseline at Cycle 13 was 3.9 (1.6; P=.018; n=34) for adults, 4.0 (2.4; P=.096; n=38) for children by patient-report, and 5.6 (1.9; p=0.005; n=43) by parent proxy-report.
- Improvements for adults and children by parent proxy-report were observed early (at Cycle 5 and Cycle 3, respectively) and sustained at most time points through Cycle 13.
- Clinically meaningful improvement from baseline at Cycle 13 was achieved by 37% (10/27) of adults, 45% (13/29) of children by patient-report, and 47% (15/32) of children by parent proxy-report (among patients who could have achieved a clinically meaningful change from baseline).

“Patients with NF1-PN experience pain and other symptoms that negatively impact their functioning and quality of life,” said Rene Y. McNall-Knapp, M.D., a pediatric hematologist-oncologist at the Jimmy Everest Center at Oklahoma Children’s Hospital OU Health and ReNeu study investigator. “In the ReNeu trial, both adults and children experienced early and sustained improvements in health-related quality of life over the course of treatment with mirdametinib, which is an important outcome of treatment for those living with this devastating disease.”

Addressing skin adverse events (AEs) during mirdametinib treatment in patients with neurofibromatosis type-1 associated plexiform neurofibroma (NF1-PN): Guidance from a multidisciplinary group of experts on the management of MEK inhibitor-associated skin AEs
Poster Presentation
Abstract #: CTNI-20
Date and Time: November 22, 7:30-9:30 p.m. CST (8:30-10:30 p.m. EST)

Skin adverse events (AEs) are commonly seen with MEK inhibitors as a class and were common in the ReNeu trial. To prevent and manage skin AEs, a multidisciplinary team retrospectively reviewed skincare practices at one high-enrolling ReNeu trial site and provided a series of recommendations to healthcare professionals to support treatment adherence.

Results from the Phase 1 and Phase 1 expansion cohorts of SJ901: A Phase 1/2 trial of single-agent mirdametinib (PD-0325901) in children, adolescents, and young adults with low-grade glioma
Oral Presentation
Abstract #: CTNI-70
Date and Time: November 22, 11:50-11:55 a.m. CST (12:50-12:55 p.m. EST)

Data from the Phase 1 and Phase 1 expansion cohorts of an ongoing Phase 1/2 trial (NCT04923126) evaluating mirdametinib in patients ages 2 to 24 with pediatric and young adult low-grade gliomas (LGG) suggest that mirdametinib, which has high blood brain barrier penetration, is well tolerated and has promising clinical activity in patients with recurrent/progressive LGG across a variety of MAPK pathway aberrations. Results demonstrated:

- Of the 23 patients enrolled in the trial, 17 (74%) completed or remain on-therapy; 4 (17%) stopped for progression, and two discontinued for toxicities.
- Twelve (63%) of the 19 patients with measurable tumors achieved an objective response (one major, six partial, and five minor responses).
- The median time to an objective response was 5.4 months (range: 1.7 to 7.3).
- Mirdametinib was well-tolerated in the Phase 1 portion of the trial.

This trial is being conducted pursuant to a research agreement that SpringWorks entered into with St. Jude Children’s Research Hospital. These data were previously presented at the 21st International Symposium on Pediatric Neuro-Oncology (ISPNO 2024). The Phase 2 portion of the trial is ongoing and recruiting patients.

About the ReNeu Trial

ReNeu (NCT03962543) is an ongoing, multi-center, open-label, single arm, Phase 2b trial evaluating the efficacy, safety, and tolerability of mirdametinib in patients ≥2 years of age with an inoperable NF1-associated PN causing significant morbidity. The study enrolled 114 patients to receive mirdametinib at a dose of 2 mg/m2 twice daily (maximum dose of 4 mg twice daily) without regard to food. Mirdametinib was administered orally in a 3-week on, 1-week off dosing schedule as either a capsule or dispersible tablet. The primary endpoint is confirmed objective response rate defined as the proportion of patients with a ≥ 20% reduction in target tumor volume on consecutive scans during the 24-cycle treatment phase, as measured by MRI and assessed by blinded independent central review. Secondary endpoints include safety and tolerability, duration of response, and changes in patient reported outcomes from baseline to Cycle 13. The treatment phase of the trial is complete, and results were presented at the 2024 American Society of Clinical Oncology Annual Meeting. Patients who completed the treatment phase were eligible to continue receiving treatment in the optional long-term follow up portion of the study, which is ongoing.

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 2,500 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 8 to 15-year mean reduction in their life expectancy compared to the general population.[3]

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.[6,7] NF1-PNs are most often diagnosed in the first two decades of life.[6] These tumors can be aggressive and are associated with clinically significant morbidities; typically, they grow more rapidly during childhood.[8,9]

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.[10] MEK inhibitors have emerged as a validated class of treatment for NF1-PN.[11]

About Mirdametinib

Mirdametinib is a potent, oral, CNS-penetrant, 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 an investigational drug for which safety and efficacy have not been established.

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 plays a central role in multiple cancers and rare diseases when genetically altered.

The U.S. Food and Drug Administration (FDA) has accepted a New Drug Application (NDA) for mirdametinib in adults and children with NF1-PN. The NDA was granted Priority Review designation and has been given a Prescription Drug User Fee Act (PDUFA) action date of February 28, 2025. The European Medicines Agency (EMA) has validated the Marketing Authorization Application (MAA) for mirdametinib for the treatment of adult and pediatric patients with NF1-PN.

In addition, the FDA and the European Commission previously 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 and Rare Pediatric Disease designation for the treatment of NF1.

About SpringWorks Therapeutics

SpringWorks is a commercial-stage biopharmaceutical company applying a precision medicine approach to developing and delivering life-changing medicines for people with severe rare diseases and cancer. OGSIVEO® (nirogacestat), approved in the United States for the treatment of adult patients with progressing desmoid tumors who require systemic treatment, is the Company's first FDA-approved therapy. SpringWorks also has a diversified targeted therapy pipeline spanning solid tumors and hematological cancers, with programs ranging from preclinical development through advanced clinical trials. In addition to its wholly owned programs, SpringWorks has also entered into multiple collaborations with innovators in industry and academia to unlock the full potential for its portfolio and create more solutions for patients in need.

For more information, visit www.springworkstx.com and follow @SpringWorksTx on X (formerly Twitter), LinkedIn, and YouTube.

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 and commercialization plans, our preclinical and clinical results, whether the preclinical and clinical results of the mirdametinib studies will meet the regulatory requirements for an approval by the FDA or by the EMA of mirdametinib for the treatment of pediatric and adult patients with NF1-PN, 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, 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) our limited experience as a commercial company, (ii) the success and timing of our product development activities, including the initiation and completion of our clinical trials, (iii) the fact that topline or interim data from clinical studies 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 timing of our planned regulatory submissions and interactions, including the timing and outcome of decisions made by the FDA, EMA, and other regulatory authorities, investigational review boards at clinical trial sites and publication review bodies, (v) 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, (vi) our ability to obtain regulatory approval of any of our product candidates or maintain regulatory approvals granted for our products, (vii) our plans to research, discover and develop additional product candidates, (viii) our ability to enter into collaborations for the development of new product candidates and our ability to realize the benefits expected from such collaborations, (ix) our ability to maintain adequate patent protection and successfully enforce patent claims against third parties, (x) our ability to establish manufacturing capabilities, and our and our collaboration partners' abilities to manufacture our 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 June 30, 2024, as well as discussions of potential risks, uncertainties and other important factors in SpringWorks' subsequent filings.

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