FDA Grants Priority Review to SpringWorks Therapeutics' New Drug Application for Mirdametinib for the Treatment of Adults and Children with NF1-PN

August 28, 2024

– PDUFA target action date of February 28, 2025 –

– EU Marketing Authorization Application also validated by European Medicines Agency –

STAMFORD, Conn., Aug. 28, 2024 (GLOBE NEWSWIRE) -- SpringWorks Therapeutics, Inc. (Nasdaq: SWTX), a commercial-stage biopharmaceutical company focused on severe rare diseases and cancer, announced today that the U.S. Food and Drug Administration (FDA) has accepted the Company's New Drug Application (NDA) for mirdametinib, an investigational MEK inhibitor, for the treatment of adult and pediatric patients with neurofibromatosis type 1-associated plexiform neurofibromas (NF1-PN). The NDA was granted Priority Review and has been given a Prescription Drug User Fee Act (PDUFA) action date of February 28, 2025. In addition, the FDA has stated that it is not currently planning to hold an advisory committee meeting to discuss the application. SpringWorks also announced today that 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. Mirdametinib has the potential to be the first approved therapy for the treatment of adult patients and a best-in-class therapy for children with NF1-PN.

"These significant milestones bring us closer to our goal of delivering a transformative medicine to both adults and children with NF1-PN in the U.S. and Europe," said Saqib Islam, Chief Executive Officer of SpringWorks. "People living with NF1-PN are in need of new advances and we look forward to working with the FDA and EMA during their review processes as we prepare to bring our second medicine to patients suffering from devastating diseases."

The FDA grants Priority Review to applications for medicines that offer, if approved, significant improvements over available options or that provide a treatment option where no adequate therapy currently exists. The FDA and the European Commission have 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.

"Plexiform neurofibromas may sit next to or surround vital organs and can cause serious medical complications for patients. While progress has been made, there remains a pressing need for more treatment options, particularly for adults who currently have no approved therapy," said Annette Bakker, Ph.D., Chief Executive Officer of the Children's Tumor Foundation (CTF) and Board Chair of CTF Europe. "CTF is dedicated to deploying its time, talent and funding towards accelerating the development of new treatments. We congratulate our long-term partner SpringWorks on this important milestone and we are thrilled that patients in the United States and Europe could soon have a new therapy available to them."

Both submissions include data from the pivotal Phase 2b ReNeu trial, which evaluated mirdametinib in patients ≥ 2 years of age with NF1-associated PN causing significant morbidity. Results were presented in an oral presentation at the 2024 American Society of Clinical Oncology Annual Meeting and demonstrated that mirdametinib treatment resulted in robust objective response rates confirmed by blinded independent central review, deep and durable responses, improvement in pain and health-related quality of life as well as a manageable safety profile across both the adult and pediatric cohorts.[1]

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 ≥ 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 assessed by proportion of patients with ≥ 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 loss-of-function variants in the NF1 gene, which encodes for neurofibromin, a key suppressor of the MAPK pathway.[2,3] 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.[4,5] The clinical course of NF1 is heterogeneous and manifests as a variety of symptoms across numerous organ systems, including abnormal skin pigmentation, skeletal deformities, tumor growth, and neurological complications such as cognitive impairment.[6] 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.[7,8] NF1-PNs are most often diagnosed in the first two decades of life.[7] These tumors can be aggressive and are associated with clinically significant morbidities; typically, they grow more rapidly during childhood.[9,10] 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.[11] MEK inhibitors have emerged as a validated class of treatment for NF1-PN.[12]

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 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 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, 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 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) 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, (ii) interactions with the FDA or EMA, including reviews and inspections, the timing related thereto and the outcome thereof, (iii) our expectations regarding the potential therapeutic benefits, safety profile and effectiveness of mirdametinib for patients with NF1-PN (iv) whether the NDA or the MAA will be approved, and (v) if approved, whether mirdametinib will be commercially successful.

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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