SpringWorks Therapeutics Announces FDA Approval of GOMEKLI™ (mirdametinib) for the Treatment of Adult and Pediatric Patients with NF1-PN

February 11, 2025

– GOMEKLI is the first and only medicine approved for both adults and children with NF1-PN –

– Approval based on positive data from Phase 2b ReNeu trial, which showed GOMEKLI treatment resulted in robust ORR, deep and durable reductions in tumor volume, and a manageable safety profile –

– SpringWorks granted rare pediatric disease priority review voucher by the FDA –

Photos accompanying this announcement are available at:
https://www.globenewswire.com/NewsRoom/AttachmentNg/8eb8effc-49a5-4b24-911f-d3e6dfa9c8a9
https://www.globenewswire.com/NewsRoom/AttachmentNg/f1041678-3f79-43b7-a101-2390fb8cb86b
https://www.globenewswire.com/NewsRoom/AttachmentNg/7d8cb318-e5f8-4944-8736-24cb19a5dec9
https://www.globenewswire.com/NewsRoom/AttachmentNg/072d748b-3237-48ad-8d83-1c6c23dda65f

STAMFORD, Conn., Feb. 11, 2025 (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 approved GOMEKLI™ (mirdametinib), SpringWorks' MEK inhibitor, for the treatment of adult and pediatric patients 2 years of age and older with neurofibromatosis type 1 (NF1) who have symptomatic plexiform neurofibromas (PN) not amenable to complete resection.[1] With the approval, SpringWorks was granted a rare pediatric disease priority review voucher (PRV) by the FDA.

"The NF1-PN patient community has a great need for more treatment options. With today's approval, we are honored to serve both adults and children with NF1-PN and provide them with a therapy that has the potential to shrink their tumors and offer meaningful symptomatic relief," said Saqib Islam, Chief Executive Officer of SpringWorks. "We are grateful to each clinical trial participant, their families, the investigators, and the patient advocacy groups involved in the journey towards making GOMEKLI available in the U.S. I am proud that we are delivering on our commitment to patients with devastating diseases with our company's second FDA approval in less than 18 months."

NF1 is a genetic disorder that currently affects approximately 100,000 children and adults in the United States.[2,3] Patients with NF1 have approximately a 30-50% lifetime risk of developing plexiform neurofibromas, or PNs, which are tumors that grow in an infiltrative pattern along the peripheral nerve sheath and that can cause severe disfigurement, pain and functional impairment.[2,4] There are approximately 40,000 people in the United States living with NF1-PN, the majority of whom are adults that have not had an approved medicine until GOMEKLI.[5] Plexiform neurofibromas can transform into malignant peripheral nerve sheath tumors, an aggressive and potentially fatal disease.[6] Surgical removal can be challenging due to the infiltrative tumor growth pattern of plexiform neurofibromas along nerves, and up to approximately 85% of plexiform neurofibromas are considered not amenable to complete resection.[7,8,9]

"Patients with NF1-PN often face significant challenges with their health and have had limited treatment options to manage this devastating condition," said Christopher Moertel, M.D., Medical Director Pediatric Neuro-Oncology and Neurofibromatosis Programs and Kenneth and Betty Jayne Dahlberg Professor of Pediatrics, University of Minnesota, and lead investigator of the ReNeu trial. "It was very encouraging in the ReNeu trial to see that GOMEKLI provided deep and durable responses, with a manageable safety profile that enabled patients to stay on therapy. This approval represents an important advance, especially for adults who previously did not have an approved treatment."

GOMEKLI was approved under Priority Review and SpringWorks received a rare pediatric disease priority review voucher from the FDA. GOMEKLI was previously granted Orphan Drug and Fast Track designations for the treatment of NF1-PN.

The FDA approval of GOMEKLI is based on results from the Phase 2b ReNeu trial, which enrolled 114 patients with NF1-PN ≥2 years of age (58 adults and 56 pediatric patients).[10] GOMEKLI met the primary endpoint of confirmed objective response rate (ORR), as assessed by blinded independent central review, demonstrating a 41% ORR (N= 24/ 58) in adults and 52% in children (N=29/56).[10] Tumor volume reductions were deep and durable; the median best percentage change in target PN volume was -41% (range: -90 to 13%) in adults and -42% (range: -91 to 48%) in children.[10] Eighty-eight percent of adults and 90% of children with a confirmed response had a response of at least 12 months duration, and 50% and 48%, respectively, had a response of at least 24 months duration.[10] Patients in both cohorts also experienced early and sustained significant improvements from baseline in pain, and quality of life, as assessed across multiple patient-reported outcome tools.[10]

GOMEKLI demonstrated a manageable safety and tolerability profile.[1] The most common adverse events (>25%) reported in adults receiving GOMEKLI were rash, diarrhea, nausea, musculoskeletal pain, vomiting and fatigue.[1] The most common adverse events (>25%) occurring in children were rash, diarrhea, musculoskeletal pain, abdominal pain, vomiting, headache, paronychia, left ventricular dysfunction, and nausea.[1] Please see additional Important Safety Information below, including Warnings & Precautions relating to ocular toxicity, left ventricular dysfunction, dermatologic adverse reactions, and embryo-fetal toxicity.[1]

"We are excited to celebrate the extraordinary milestone of our partners and long-term friends at SpringWorks for the NF1-PN community. This FDA approval shows the power of collaboration to advance innovative science for drugs that may otherwise not have been taken forward," said Annette Bakker, Ph.D., Chief Executive Officer of the Children's Tumor Foundation. "When industry, researchers, and organizations like ours driving treatment

innovation join forces, scientific progress moves faster, and patients gain access to the therapies they need. Every treatment approval is hard-won, built on research, persistence, and partnership. Today, that work delivers a critical new option for NF patients of all ages."

"NF1-PN is a complex, devastating disease that affects not only individual patients, but entire families. Treatment advances are crucial to achieving better outcomes for patients and this FDA approval offers hope for NF patients and their families," said Kim Bischoff, Executive Director, NF Network.

SpringWorks is dedicated to helping patients with NF1-PN access GOMEKLI and to providing support throughout their treatment journey. The SpringWorks CareConnections™ program is a comprehensive patient support program that offers personalized support services and resources to eligible GOMEKLI patients, including insurance coverage information and access support, financial assistance and personalized educational and emotional support. Physicians and patients can contact 1-844-CARES-55 (1-844-227-3755) or visit www.springworkstxcares.com for more information.

GOMEKLI is available in 1 and 2 mg capsules and in a 1mg tablet for oral suspension, which dissolves easily in water. GOMEKLI is expected to be available through a specialty pharmacy and specialty distributor network in the United States within two weeks.

SpringWorks' Marketing Authorization Application for mirdametinib for the treatment of children and adults with NF1-PN was validated by the European Medicines Agency (EMA) and is currently under review; a decision is expected from the European Commission in 2025.

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.[11,12] NF1 is the most common form of neurofibromatosis, with an estimated global birth incidence of approximately 1 in 2,500 individuals, and there are approximately 100,000 patients living with NF1 in the United States.[2,3] 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.[13] Patients with NF1 have an 8 to 15-year mean reduction in their life expectancy compared to the general population.[14]

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.[2,4,6] NF1-PNs are most often diagnosed in the first two decades of life.[2] These tumors can be aggressive and are associated with clinically significant morbidities; typically, they grow more rapidly during childhood.[15,16]

Surgical removal of these tumors can be challenging due to the infiltrative tumor growth pattern along nerves and can lead to permanent nerve damage and disfigurement.[6] Up to approximately 85% of plexiform neurofibromas are considered not amenable to complete resection.[7,8,9]

About GOMEKLI™ (mirdametinib)

GOMEKLI™ is an oral, small molecule MEK inhibitor approved in the United States for the treatment of adult and pediatric patients 2 years of age and older with neurofibromatosis type 1 (NF1) who have symptomatic plexiform neurofibromas (PN) not amenable to complete resection.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Ocular Toxicity: GOMEKLI can cause ocular toxicity including retinal vein occlusion (RVO), retinal pigment epithelium detachment (RPED), and blurred vision. In the adult pooled safety population, ocular toxicity occurred in 28% of patients treated with GOMEKLI: 21% were Grade 1, 5% were Grade 2 and 1.3% were Grade 3. RVO occurred in 2.7%, RPED occurred in 1.3%, and blurred vision occurred in 9% of adult patients. In the pediatric pooled safety population, ocular toxicity occurred in 19% of patients: 17% were Grade 1 and 1.7% were Grade 2. Conduct comprehensive ophthalmic assessments prior to initiating GOMEKLI, at regular intervals during treatment, and to evaluate any new or worsening visual changes such as blurred vision. Continue, withhold, reduce the dose, or permanently discontinue GOMEKLI as clinically indicated.

Left Ventricular Dysfunction: GOMEKLI can cause left ventricular dysfunction. GOMEKLI has not been studied in patients with a history of clinically significant cardiac disease or LVEF <55% prior to initiation of treatment. In the ReNeu study, decreased LVEF of 10 to <20% occurred in 16% of adult patients treated with GOMEKLI. Five patients (9%) required dose interruption, one patient (1.7%) required a dose reduction, and one patient required permanent discontinuation of GOMEKLI. The median time to first onset of decreased LVEF in adult patients was 70 days. Decreased LVEF of 10 to <20% occurred in 25%, and decreased LVEF of ≥20% occurred in 1.8% of pediatric patients treated with GOMEKLI. One patient (1.8%) required dose interruption of GOMEKLI. The median time to first onset of decreased LVEF in pediatric patients was 132 days. All patients with decreased LVEF were identified during routine echocardiography, and decreased LVEF resolved in 75% of patients. Before initiating GOMEKLI, assess ejection fraction (EF) by echocardiogram. Monitor EF every 3 months during the first year and then as clinically indicated. Withhold, reduce the dose, or permanently discontinue GOMEKLI based on severity of adverse reaction.

Dermatologic Adverse Reactions: GOMEKLI can cause dermatologic adverse reactions including rash. The most frequent rashes included dermatitis acneiform, rash, eczema, maculo-papular rash and pustular rash. In the pooled adult safety population, rash occurred in 92% of patients treated with GOMEKLI and required permanent discontinuation in 11% of adult patients. In the pooled pediatric safety population, rash occurred in 72% of patients treated with GOMEKLI and resulted in permanent discontinuation of GOMEKLI in 3.4% of patients. Initiate supportive care at first signs of dermatologic adverse reactions. Withhold, reduce the dose, or permanently discontinue GOMEKLI based on severity of adverse reaction.

Embryo-Fetal Toxicity: GOMEKLI can cause fetal harm when administered to a pregnant woman. Verify the pregnancy status of females of reproductive potential prior to the initiation of GOMEKLI. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Also advise patients to use effective contraception during treatment with GOMEKLI and for 6 weeks after the last dose (females) or 3 months after the last dose (males).

ADVERSE REACTIONS

The most common adverse reactions (>25%) in adult patients were rash (90%), diarrhea (59%), nausea (52%), musculoskeletal pain (41%), vomiting

(38%), and fatigue (29%). Serious adverse reactions occurred in 17% of adult patients who received GOMEKLI. The most common Grade 3 or 4 laboratory abnormality (>2%) was increased creatine phosphokinase.

The most common adverse reactions (>25%) in pediatric patients were rash (73%), diarrhea (55%), musculoskeletal pain (41%), abdominal pain (39%), vomiting (39%), headache (34%), paronychia (32%), left ventricular dysfunction (27%), and nausea (27%). Serious adverse reactions occurred in 14% of pediatric patients who received GOMEKLI. The most common Grade 3 or 4 laboratory abnormalities (>2%) were decreased neutrophil count and increased creatine phosphokinase.

USE IN SPECIFIC POPULATIONS

Pregnancy & Lactation. Verify the pregnancy status of patients of reproductive potential prior to initiating GOMEKLI. Due to the potential for adverse reactions in a breastfed child, advise patients not to breastfeed during treatment with GOMEKLI and for 1 week after the last dose.

You are encouraged to report negative side effects of prescription drugs to the FDA. To report suspected adverse reactions, contact SpringWorks Therapeutics at 1-888-400-SWTX (1-888-400-7989) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see accompanying full **Prescribing Information** for more information.

About SpringWorks Therapeutics

SpringWorks is a commercial-stage biopharmaceutical company dedicated to improving the lives of patients with severe rare diseases and cancer. We developed and are commercializing OGSIVEO® (nirogacestat) as the first and only FDA-approved medicine for adults with desmoid tumors and GOMEKLI™ (mirdametinib) as the first and only FDA-approved medicine for both adults and children with neurofibromatosis type 1 associated plexiform neurofibromas (NF1-PN). We are also advancing a diverse portfolio of novel targeted therapy product candidates for patients with both solid tumors and hematological cancers.

For more information, visit www.springworkstx.com and follow @SpringWorksTx on X, LinkedIn, Facebook, Instagram, 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, the potential for GOMEKLI to become an important new treatment for adult and pediatric NF1-PN patients, expectations regarding the timing and results of the review by the EMA of the MAA for mirdametinib for the treatment of adult and pediatric NF1-PN patients, 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 of our commercialization efforts with respect to GOMEKLI, (ii) our limited experience as a commercial company, (iii) our ability to obtain or maintain adequate coverage and reimbursement for GOMEKLI, (iv) the success and timing of our product development activities, including the initiation and completion of our clinical trials, (v) our expectations regarding the potential clinical benefit of GOMEKLI for adult and pediatric NF1-PN patients, (vi) our expectations regarding the market potential for GOMEKLI, (vii) our expectations regarding when GOMEKLI will become available, (viii) 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, (ix) the success and timing of our collaboration partners' ongoing and planned clinical trials, (x) 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, (xi) 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, (xii) our ability to obtain regulatory approval of any of our product candidates or maintain regulatory approvals granted for our products, (xiii) our plans to research, discover and develop additional product candidates, (xiv) our ability to enter into collaborations for the development of new product candidates and our ability to realize the benefits expected from such collaborations, (xv) our ability to maintain adequate patent protection and successfully enforce patent claims against third parties, (xvi) the adequacy of our cash position to fund our operations through any time period indicated herein, (xvii) our ability to establish manufacturing capabilities, and our and our collaboration partners' abilities to manufacture our product candidates and scale production, and (xviii) 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, 2024, as well as discussions of potential risks, uncertainties and other important factors in SpringWorks' subsequent filings.

Contacts:

Media
Media@Springworkstx.com

Investors
Investors@Springworkstx.com

References

1. GOMEKLI. Prescribing Information. SpringWorks Therapeutics, Inc.
2. 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.
3. 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.
4. Miller DT, et al. Health supervision for children with neurofibromatosis Type 1. Pediatrics. 2019;143(5):e20190660.
5. Data on File.
6. Kamaludin, Siti Nurhazwani et al. “Plexiform neurofibromatosis with peripheral malignant nerve sheath tumor and scoliosis - more surveillance imaging needed?.” Radiology case reports vol. 17,7 2388-2393. 6 May. 2022, doi:10.1016/j.radcr.2022.03.111.
7. 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.
8. Ejerskov, C., Farholt, S., Nielsen, F.S.K. et al. Clinical Characteristics and Management of Children and Adults with Neurofibromatosis Type 1 and Plexiform Neurofibromas in Denmark: A Nationwide Study. Oncol Ther 11, 97–110 (2023). https://doi.org/10.1007/s40487-022-00213-4.
9. Wolkenstein, P. et al. (2023) ‘French cohort of children and adolescents with neurofibromatosis type 1 and symptomatic inoperable plexiform neurofibromas: Cassiopea study’, European Journal of Medical Genetics, 66(5), p. 104734. doi:10.1016/j.ejmg.2023.104734.
10. Moertel CL, Fisher MJ, Weiss BD, et al. ReNeu: A pivotal, Phase IIb trial of mirdametinib in adults and children with symptomatic neurofibromatosis type 1-associated plexiform neurofibroma. J Clin Oncol. 2024;JCO.24.01034. doi.org/10.1200/JCO.24.01034.
11. 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.
12. Rasmussen S, Friedman J. NF1 Gene and Neurofibromatosis 1. Am J Epidemiol. 2000;151(1):33-40. doi:10.1093/oxfordjournals.aje.a010118.
13. 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. J Clin Onc. 2021;JCO.20.02220.doi.org/10. 1200/JCO.20.02220.
14. Lee: Lee TJ, et al. Incidence and prevalence of neurofibromatosis type 1 and 2: a systematic review and meta-analysis. Orphanet J Rare Dis. 2023;18(1):292. doi:10.1186/s13023-023-02911-2.
15. 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.
16. 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.