SpringWorks Therapeutics Announces Initiation of Phase 1/2 Clinical Trial of Mirdametinib in Children and Young Adults with Low-Grade Glioma

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STAMFORD, Conn., June 16, 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 the initiation of a Phase 1/2 clinical trial to evaluate mirdametinib, an investigational MEK inhibitor, for the treatment of children, adolescents, and young adults with low-grade glioma (LGG). The study is sponsored by St. Jude Children's Research Hospital. More information on the trial can be found on www.clinicaltrials.gov under the identifier NCT04923126.

Pediatric LGG can harbor genetic alterations that upregulate the MAPK pathway and promote tumor growth. Prior studies of therapeutic agents that target the MAPK pathway have demonstrated promising results in patients with pediatric LGG.[1] Mirdametinib is an oral, allosteric, brain-penetrant small molecule designed to inhibit MEK1 and MEK2, which are proteins that occupy pivotal positions in the MAPK pathway. To date, over 250 subjects have been exposed to treatment with mirdametinib across clinical trials, with preliminary evidence of clinical activity against tumors driven by over-activated MAPK signaling.[2]

"Children with LGG who do not achieve a cure following surgery can face years of increasingly aggressive chemotherapy, which can have lasting negative effects on learning, cognition and quality of life," said L. Mary Smith, Ph.D., Chief Development Officer of SpringWorks. "Recently, it has been recognized that most cases of pediatric LGG have genetic alterations that upregulate the MAPK pathway. Given its brain-penetrant properties, we look forward to studying mirdametinib to evaluate whether our MEK inhibitor can provide meaningful antitumor activity and clinical benefit in patients with LGG."

This trial is being conducted pursuant to a research agreement that SpringWorks entered into with St. Jude Children's Research Hospital whereby St. Jude sponsors the trial and SpringWorks provides partial funding, study drug and other non-financial support.

About the Phase 1/2 LGG Trial

The open-label, multi-center Phase 1/2 trial will evaluate the safety, tolerability and pharmacokinetics of mirdametinib in children, adolescents and young adults with LGG. The study plans to enroll up to 130 patients between the ages of 2 years and 24 years of age. Patients will receive mirdametinib twice daily on a continuous schedule for up to two years.

The primary objective of the Phase 1 portion of the trial will be to evaluate the safety, tolerability, and pharmacokinetics of mirdametinib. The Phase 2 portion of the trial is designed to measure the objective response rate and duration of response to mirdametinib. Patients in the Phase 2 portion will be stratified into one of three treatment cohorts based on tumor status and history of MEK inhibitor exposure: Cohort 1: Patients with newly diagnosed LGG; Cohort 2: Patients with progressive or recurrent LGG without previous exposure to a MEK inhibitor; Cohort 3: Patients with progressive or recurrent LGG with previous exposure to a MEK inhibitor.

About Low-Grade Glioma

Pediatric LGG is a type of tumor that affects the brain and spinal cord. LGG is the most common central nervous system (CNS) tumor in children, accounting for approximately 30% of all childhood CNS tumors.[3] LGG can arise in several different areas of the CNS including the cerebellum, cerebrum, brainstem, hypothalamus, visual pathway, optic nerve, and spinal cord.[3] Low-grade gliomas are associated with significant morbidity including seizures and cognitive decline, and recurrent gliomas often undergo malignant transformation.[4]

Optimal management of LGG remains uncertain.[3] While most children with LGG survive their cancer, children with progressive residual disease following surgery and those not amenable to surgery can oftentimes face years of increasingly aggressive cytotoxic therapies that can have lasting effects on learning, cognition, and quality of life.[3] There are no FDA approved therapies for pediatric LGG and current treatments being used off-label can be associated with significant acute and life-long adverse effects.[3] As a result, the unmet medical need for these patients remains high.

About Mirdametinib

Mirdametinib is an investigational, oral, potent, allosteric small molecule MEK1/2 inhibitor with clinical validation and over 250 subjects exposed to date. It is 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 is being evaluated in a Phase 2b trial for pediatric and adult patients with NF1-associated plexiform neurofibromas (NF1-PN), which are tumors that grow in an infiltrative pattern along the peripheral nerve sheath.

In addition to the monotherapy trials in NF1-PN and LGG, 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 advancing 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, 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.

SpringWorks Media/Investor Contact:
Kim Diamond
Vice President, Communications and Investor Relations
203-561-1646
kdiamond@springworkstx.com

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