SpringWorks Therapeutics Announces Initiation of Phase 2b ReNeu Clinical Trial of Mirdametinib in Children and Adults with Neurofibromatosis Type 1 (NF1)-Associated Plexiform Neurofibromas (NF1-PN)

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STAMFORD, Conn., Oct. 24, 2019 (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 the first patient has been dosed in the Phase 2b ReNeu clinical trial evaluating mirdametinib (formerly PD-0325901), an oral, small molecule designed to inhibit MEK1 and MEK2, in children and adult patients with neurofibromatosis type 1 (NF1)-associated plexiform neurofibromas (NF1-PN).

NF1 has a global birth incidence of approximately one in every 3,000 individuals, with an estimated 100,000 patients living with NF1 in the United States. The disorder is characterized by mutations in the NF1 gene, which affects the MAPK pathway. Throughout their lifetime, approximately 30% to 50% of NF1 patients progress to develop plexiform neurofibromas, which are peripheral nerve sheath tumors that cause significant pain, disfigurement and morbidity. NF1-PN are most often diagnosed in the first two decades of life and are characterized by aggressive tumor growth, which is typically more rapid during childhood. There are currently no therapies approved for the treatment of NF1-PN.

“Unfortunately, up to half of all NF1 patients are at risk of developing plexiform neurofibromas, a more severe form of NF1 that causes painful tumors to grow on nerves throughout the body,” said Saqib Islam, Chief Executive Officer of SpringWorks. “While there are no therapies currently approved for these patients, several prior studies, including a Phase 2 study evaluating mirdametinib, have provided support for the mechanism of MEK inhibition in plexiform neurofibromas. We look forward to continuing to enroll patients in the ReNeu trial to further evaluate the clinical benefits of mirdametinib for children and adults with these devastating tumors.”

The U.S. Food and Drug Administration (FDA) and the European Commission have granted Orphan Drug Designation for mirdametinib for the treatment of neurofibromatosis type 1. The FDA has also granted Fast Track Designation for mirdametinib for the treatment of patients ≥ 2 years of age with neurofibromatosis type 1-associated inoperable plexiform neurofibromas that are progressing or causing significant morbidity.

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 will 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. Mirdametinib will be administered in a 3-week on, 1-week off dosing schedule.

The primary endpoint is objective response rate using centrally read MRI volumetric analysis. 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 Neurofibromatosis Type 1

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. 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. 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. Patients with NF1 have an eight to 15-year mean reduction in their life expectancy compared to the general population.

NF1 patients have an approximately 30% to 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. NF1-PN are most often diagnosed in the first two decades of life. These tumors are characterized by aggressive growth, which is typically more rapid during childhood.

The only definitive treatment for NF1-PN is surgical removal of the tumors, however, because NF1-PN arise from nerve cells and grow in an infiltrative pattern, it is challenging to successfully resect tumors without severe comorbidities, such as permanent nerve damage and disfigurement. There are no therapies currently approved for the treatment of NF1-PN.

About Mirdametinib

Mirdametinib is an oral small molecule 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 200 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/m2 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 percent. 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 to the Phase 2b monotherapy trial in NF1- PN, 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 underserved patient populations suffering from devastating rare diseases and cancer. SpringWorks has a differentiated portfolio of small molecule targeted oncology product candidates and is advancing two potentially registrational clinical trials in rare tumor types, as well as several other 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 industry leaders to expand its portfolio.

At SpringWorks, we ignite the power of promising science to unleash new possibilities for patients. For more information, please visit www.springworkstx.com. Follow SpringWorks on social media: @SpringWorksTx and LinkedIn.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, statements regarding SpringWorks' clinical trials and its strategy, business plans and focus. The words "may," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "project," "potential," "continue," "target" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. 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, those related to the timing for completion of our clinical trials of our product candidates, whether and when, if at all, SpringWorks' product candidates will receive approval from the U.S. Food and Drug Administration, or FDA, or other foreign regulatory authorities, the potential benefits of receiving Orphan Drug Designation from the FDA or other foreign regulatory authorities, competition from other biopharmaceutical companies, and other risks identified in SpringWorks' SEC filings, including its final prospectus for its initial public offering and subsequent filings with the SEC. SpringWorks cautions you not to place undue reliance on any forward-looking statements, which speak only as of the date they are made. SpringWorks disclaims any obligation to publicly update or revise any such statements to reflect any change in expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements. Any forward-looking statements contained in this press release represent SpringWorks' views only as of the date hereof and should not be relied upon as representing its views as of any subsequent date.

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