European Commission Grants Orphan Drug Designation for SpringWorks Therapeutics' MEK Inhibitor, Mirdametinib, for the Treatment of Neurofibromatosis Type 1

STAMFORD, Conn – July 30, 2019 – SpringWorks Therapeutics, Inc., a clinical-stage biopharmaceutical company focused on developing life-changing medicines for patients with severe rare diseases and cancer, today announced that the European Commission has granted Orphan Drug Designation for mirdametinib (formerly PD-0325901), an oral, small molecule inhibitor of MEK1 and MEK2, for the treatment of neurofibromatosis type 1 (NF1).

NF1 is a rare genetic disorder characterized by mutations in the MAPK pathway. Throughout their lifetime, up to half of NF1 patients progress to develop plexiform neurofibromas, which are peripheral nerve sheath tumors that cause significant pain, disfigurement and morbidity. NF1-associated plexiform neurofibromas (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.[1-3] There are currently no therapies approved for the treatment of NF1-PN.

"This orphan designation in the European Union is another important recognition of the significant need for an effective treatment for patients with NF1, and follows the orphan drug and fast-track designations already granted for mirdametinib in the U.S. by the FDA," said Saqib Islam, Chief Executive Officer of SpringWorks. "We expect to initiate our Phase 2b trial of mirdametinib in children and adults with NF1-PN this quarter and look forward to working closely with regulatory authorities throughout our development program."

The European Commission grants orphan medicinal status for products intended for the treatment, prevention or diagnosis of life-threatening or very serious conditions that affect no more than 5 in 10,000 people in the European Union, and where the product represents a significant benefit over existing treatments. Orphan designation provides companies with certain benefits and incentives in the EU, including a 10-year period of market exclusivity after product approval, reduced regulatory fees and protocol assistance.[4]

Mirdametinib previously received Orphan Drug Designation from the FDA for the treatment of neurofibromatosis type 1 and Fast Track Designation from the FDA for the treatment of patients ≥ 2 years of age with neurofibromatosis type 1-associated inoperable plexiform neurofibromas that are progressing or causing significant morbidity. SpringWorks expects to initiate the ReNeu trial, a Phase 2b open-label, single-arm trial with mirdametinib that will enroll both pediatric and adult NF1-PN patients, in the third quarter of 2019.

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.[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. Patients with NF1 have an eight to 15-year mean reduction in their life expectancy compared to the general population.[5]

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.[2,3] 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.[1,2,5]

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.[6] There are no therapies currently approved for the treatment of NF1-PN.

About Mirdametinib

Mirdametinib is an oral, small molecule inhibitor of 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/m^2 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 in 53% (10/19), fatigue in 26% (5/19) and nausea in 21% (4/19) of patients.

In addition to the Phase 2b monotherapy trial in NF1-associated 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

At SpringWorks, a clinical-stage biopharmaceutical company, we are driven to develop life-changing medicines for patients with severe rare diseases and cancer. Since our launch in 2017, we have worked to identify and advance promising science, beginning with our licensed clinical therapies from Pfizer Inc. We pioneer efficient pathways for drug development, leveraging shared-value partnerships with patient advocacy groups, innovators in industry and academia, and investors so that together, we can unlock the potential of science and bring new therapies to underserved patients. Nirogacestat, our gamma secretase inhibitor for the treatment of desmoid tumors is currently in a Phase 3 clinical trial, and SpringWorks expects to initiate a Phase 2b clinical trial of mirdametinib, our MEK 1/2 inhibitor for neurofibromatosis type 1 patients with plexiform neurofibromas, in the third quarter of 2019. Mirdametinib also holds promise as the backbone for combination therapies to treat metastatic solid tumors. At SpringWorks, we ignite the power of promising science to unleash new possibilities for patients. For more information, please visit www.springworkstx.com.

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