SpringWorks Therapeutics Announces Initiation of Phase 1b Clinical Trial of MEK Inhibitor PD-0325901 in Combination with BeiGene's RAF Dimer Inhibitor Lifirafenib in Advanced or Refractory Solid Tumors

STAMFORD, Conn – May 6, 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 first patient has been dosed in a Phase 1b study to evaluate the combination of SpringWorks Therapeutics' investigational MEK inhibitor, PD-0325901, and BeiGene, Ltd.'s (Nasdaq: BGNE; HKEX: 06160) investigational RAF dimer inhibitor, lifirafenib (BGB-283), in patients with advanced or refractory solid tumors.

The Phase 1b clinical trial, being conducted by BeiGene, is an open-label, dose-escalation and expansion study to investigate the safety, pharmacokinetics (PK) and antitumor activity of PD-0325901 in combination with lifirafenib in patients with advanced or refractory solid tumors that harbor RAS mutations, RAF mutations and other MAPK pathway aberrations. The trial is designed to define the dose and tolerability of the combination as well as to capture early efficacy signals to allow for rapid cohort expansion.

"We are excited to explore this combination therapy approach in collaboration with BeiGene, as it could address the approximately one-fourth of solid tumor patients whose cancers are driven by RAS mutations, as well as those with RAF mutations and other MAPK pathway aberrations, which occur in many of the most devastating tumor types," said Saqib Islam, Chief Executive Officer of SpringWorks Therapeutics. "Despite decades of research, no anti-RAS therapies have been approved to-date. This trial has the potential to meet a critical need for patients and is an important evolution for SpringWorks as it provides the opportunity to study our MEK inhibitor in patients with more commonly occurring tumors."

The rationale for the Phase 1b study is supported by data presented by BeiGene at the 2015 Annual Meeting of the American Association for Cancer Research (AACR)[1], which demonstrated that the combination of PD-0325901 and lifirafenib led to antitumor activity in preclinical models of RAS-mutated cancers. Vertical inhibition of the MAPK pathway, enabled by the combination of a MEK inhibitor with a RAF dimer inhibitor, has been further validated preclinically by multiple academic and industry investigators, and has the potential to overcome the drug resistance mechanisms that have impeded previous attempts to develop therapies for tumors with MAPK mutations and aberrations.

In addition to this Phase 1b study, SpringWorks Therapeutics is preparing to initiate a Phase 2b single-arm, open-label study of PD-0325901 as a monotherapy in patients with

neurofibromatosis type 1-associated plexiform neurofibromas (NF1-associated PN). NF1-associated PN is a rare genetic disorder characterized by the growth of painful, disfiguring and debilitating tumors along peripheral nerves throughout the body.

About the Phase 1b Trial in Advanced or Refractory Solid Tumors

The Phase 1b trial is a multicenter, open label, dose-escalation trial of PD-0325901 in combination with lifirafenib in adult patients with advanced or metastatic, unresectable tumors harboring K-RAS/N-RAS or B-RAF mutations, or any other MAPK pathway aberration. The study will enroll patients who have experienced disease progression during or after at least one line of systemic therapy or for which treatment is not available, not tolerated or refused.

The trial is designed in two parts; the first part will consist of a dose-escalation and dose-finding study to assess the safety and tolerability of combining PD-0325901 and lifirafenib, and to determine the maximum tolerated dose and/or the recommended Phase 2 dose for the combination. The second part is a multiple-group, noncomparative, indication expansion study to assess the preliminary antitumor activity of the combination in patients with selected tumor types, in addition to further assessing the safety, tolerability and PK of the combination.

The trial is being conducted under a global clinical collaboration agreement between SpringWorks Therapeutics and BeiGene, which was entered into in September 2018. Under the terms of the agreement, BeiGene is responsible for administering the Phase 1b clinical trial, with all costs of the clinical studies and governance responsibilities to be shared equally among both parties. More information about the study is available at www.clinical trials.gov under the identifier NCT03905148.

About PD-0325901

PD-0325901 is an investigational, selective, orally bioavailable small molecule inhibitor of MEK1 and MEK2, proteins that play key roles in the MAPK pathway. The MAPK pathway is critical for cell survival and proliferation, and overactivation of this pathway has been shown to help enable tumor growth. By blocking activity of the MAPK pathway, PD-0325901 may help arrest uncontrolled cellular growth associated with many types of tumors.

PD-0325901 has been tested in several Phase 1 and Phase 2 clinical trials, and approximately 260 subjects have been exposed to treatment. SpringWorks is evaluating PD-0325901 as a monotherapy for the treatment of patients with neurofibromatosis type 1-associated plexiform neurofibromas and is also pursuing PD-0325901 in combination with other rational anti-cancer agents across a range of solid tumors.

About Lifirafenib

Lifirafenib was discovered in BeiGene's research facilities in Beijing, China, and is an investigational small molecule kinase inhibitor with RAF monomer and dimer inhibition activities. Lifirafenib has shown antitumor activities in preclinical models and in cancer patients with tumors harboring BRAF V600E mutations, non-V600E BRAF mutations, non-

small cell lung cancer and endometrial cancer harboring KRAS mutations. To date, lifirafenib has been dosed in more than 150 patients globally.

About SpringWorks Therapeutics

At SpringWorks Therapeutics, 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. Two of our therapies will be entering potentially pivotal studies this year: nirogacestat, a gamma secretase inhibitor for the treatment of desmoid tumors, and PD-0325901, a MEK 1/2 inhibitor for neurofibromatosis type 1 patients with plexiform neurofibromas. PD-0325901 also holds promise as the backbone for combination therapies to treat metastatic solid tumors. At SpringWorks Therapeutics, we ignite the power of promising science to unleash new possibilities for patients. For more information, please visit www.springworkstx.com.

References

[1] Yuan, X., Tang, Z., Du, R., et al. BGB-283 Effectively Enhances MEK Inhibitor Induced Tumor Suppression in RAS Mutant Cancers. Poster (Abstract 669) presented at the American Association for Cancer Research Annual Meeting 2015.

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