SpringWorks and BeiGene Present Clinical Data on Lifirafenib in combination with Mirdametinib in Patients with Advanced or Refractory Solid Tumors with MAPK Pathway Aberrations at the American Association for Cancer Research Annual Meeting 2023

April 17, 2023

STAMFORD, Conn. and BASEL, Switzerland and BEIJING and CAMBRIDGE, Mass., April 17, 2023 (GLOBE NEWSWIRE) -- SpringWorks Therapeutics, Inc. (NASDAQ: SWTX), and BeiGene, Ltd. (NASDAQ: BGNE; HKEX: 06160; SSE: 688235), today announced that they will present updated clinical data from the Phase 1b trial of BeiGene's RAF dimer inhibitor, lifirafenib, in combination with SpringWorks' MEK inhibitor, mirdametinib, in patients with advanced or refractory solid tumors with RAS mutations, RAF mutations and other MAPK pathway aberrations. The data are being presented today in an oral presentation at the American Association for Cancer Research (AACR) Annual Meeting 2023, taking place in Orlando, Florida.

"The lifirafenib plus mirdametinib combination represents a novel targeted approach to treat solid tumors driven by RAS/RAF mutations, and other MAPK pathway aberrations. The early clinical data reported here demonstrate the potential of this vertical combination strategy in addressing the substantial unmet medical need represented by patients with tumors driven by these genetic alterations," said Lusong Luo, Ph.D. Senior Vice President, External Innovation at BeiGene. "We are very excited about our continued study of this combination with its advancement into dose expansion this year."

"We are pleased by the progress of our collaboration with BeiGene on the lifirafenib and mirdametinib combination," said Saqib Islam, CEO of SpringWorks. "We view vertical inhibition approaches, such as this novel combination, as a promising strategy to improve outcomes in biomarker-defined subgroups of patients that lack efficacious treatments for their cancers."

Oral Presentation at the AACR Annual Meeting 2023:

Safety, pharmacokinetics, and antitumor activity findings from a phase 1b, open-label, dose-escalation and expansion study investigating RAF dimer inhibitor lifirafenib in combination with MEK inhibitor mirdametinib in patients with advanced or refractory solid tumors

Presenter: Benjamin Solomon, M.D., Peter MacCallum Cancer Centre, Melbourne, Australia
Session Title: Mini-symposium Session CTMS02 - Targeting the KRAS Pathway in the Clinic
Abstract #: CT033
Session Date and Time: Monday, April 17, 2023, 3:50-4:00 PM ET

This ongoing Phase 1b trial (NCT03905148) is an open-label, dose escalation and expansion study to investigate the safety, pharmacokinetics (PK) and antitumor activities of mirdametinib in combination with lifirafenib, BeiGene's RAF dimer inhibitor, in patients with advanced or refractory solid tumors harboring RAS mutations, RAF mutations, and other MAPK pathway aberrations.

Results from the Part A dose-escalation and dose-finding study are being presented at AACR. This portion of the study was designed to evaluate the safety, tolerability, and pharmacokinetics of the combination, and determine the maximum tolerated dose and/or recommended Phase 2 dose.

As of the data cut-off of January 20, 2023, 71 patients were treated across 9 dose levels evaluating different dosing regimens. Results suggest that lifirafenib in combination with mirdametinib demonstrated a favorable safety profile, with low incidence of dose limiting toxicities and treatment-emergent adverse events that led to dose discontinuations. The most common treatment-related adverse events related to lifirafenib and/or mirdametinib (>15%) were dermatitis acneiform (42%), fatigue (32%), diarrhea (27%), platelet count decreased (18%), alopecia (18%), nausea (17%) and alanine aminotransferase increased (16%).

The combination showed antitumor activity in patients with various KRAS, NRAS, and BRAF mutations across several solid tumor types, including low-grade serous ovarian cancer (LGSOC), non-small cell lung cancer (NSCLC), and endometrial cancer. Among 62 efficacy-evaluable patients, 14 patients (23%) had confirmed objective responses. Of 17 patients with LGSOC treated, 10 patients (59%) had objective responses, with median duration of treatment of approximately 26 months. Of the 4 endometrial cancer patients treated, 2 (50%) had objective responses in tumors that harbor BRAF fusion mutation or KRAS mutation, respectively. Of the 11 patients with NSCLC treated, 2 (18%) had objective responses in tumors that harbor NRAS mutation or BRAF V600E mutation, respectively. These data support the advancement of this combination into the dose-expansion portion of the study, which will focus on a biomarker selected patient population with a tumor agnostic approach. The expansion is expected to start in the second half of 2023.

"Our findings indicate that the combination of lifirafenib and mirdametinib treatment demonstrated antitumor activity in patients with various KRAS, NRAS, and BRAF mutations across several solid tumor types known to be driven by the MAPK pathway and for which current treatment options are limited," said Benjamin Solomon, MBBS, PhD, FRACP, medical oncologist at Peter MacCallum Cancer Centre in Melbourne, Australia. "We are pleased with the risk-benefit profile seen to date with this combination and look forward to the further clinical investigation in the dose-expansion portion of the study."

About Lifirafenib

Lifirafenib (BGB-283) is an investigational novel small molecule designed to inhibit both monomeric and dimeric RAF kinase. Lifirafenib has demonstrated antitumor activity in preclinical models and in cancer patients with tumors harboring BRAF V600E mutations and non-V600E BRAF mutations, in which the monomeric form of RAF is implicated, as well as KRAS/NRAS mutations, in which the dimeric form of RAF is implicated.

About Mirdametinib

Mirdametinib is an investigational, oral, allosteric small molecule MEK inhibitor. Mirdametinib is designed to inhibit MEK1 and MEK2, which occupy pivotal positions in the MAPK pathway. The MAPK pathway is a key signaling network that regulates cell growth and survival and that plays a central role in multiple oncology and rare disease indications when genetically altered.

Mirdametinib is in development as a monotherapy treatment for neurofibromatosis type 1-associated plexiform neurofibromas (NF1-PN) and low-grade glioma (LGG), and as a combination therapy for the treatment of several subsets of biomarker-defined metastatic solid tumors. To date, over 300 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.

The U.S. Food and Drug Administration (FDA) and the European Commission granted Orphan Drug designation for mirdametinib for the treatment of NF1, and the FDA granted Fast Track designation for the treatment of patients ≥ 2 years of age with NF1-PN that are progressing or causing significant morbidity.

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 pipeline spanning solid tumors and hematological cancers, including two late-stage clinical trials in rare tumor types as well as several 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 unlock the full potential for its portfolio and create more solutions for patients with cancer. For more information, please visit www.springworkstx.com and follow @SpringWorksTx on Twitter and LinkedIn.

About BeiGene

BeiGene is a global biotechnology company that is developing and commercializing innovative and affordable oncology medicines to improve treatment outcomes and access for far more patients worldwide. With a broad portfolio, we are expediting development of our diverse pipeline of novel therapeutics through our internal capabilities and collaborations. We are committed to radically improving access to medicines for far more patients who need them. Our growing global team of more than 9,000 colleagues spans five continents, with administrative offices in Basel, Beijing and Cambridge, Mass. To learn more about BeiGene, please visit www.beigene.com and follow us on Twitter at @BeiGeneGlobal.

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 plans, our preclinical and clinical results, 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 and timing of our product development activities, including the initiation and completion of SpringWorks' clinical trials, (ii) the fact that topline or interim data from a clinical study may not be predictive of the final or more detailed 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) the timing of our planned regulatory submissions and interactions, including the timing and outcome of decisions made by the U.S. Food and Drug Administration (FDA) and other regulatory authorities, investigational review boards at clinical trial sites and publication review bodies; (v) whether FDA or other regulatory authorities will require additional information or further studies, or may fail or refuse to approve or may delay approval of our drug candidates, (vii) our ability to obtain and maintain regulatory approval of any of our product candidates, (viii) our plans to research, discover and develop additional product candidates, (ix) our ability to maintain adequate patent protection and successfully enforce patent claims against third parties, (x) our ability to enter into collaborations for the development of new product candidates, (xi) our ability to establish manufacturing capabilities, and our and our collaboration partners' abilities to manufacture our product candidates and scale production, (xii) our ability to meet any specific milestones set forth herein, and (xiii) 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' Annual Report on Form 10-K for the year ended December 31, 2022, as well as discussions of potential risks, uncertainties and other important factors in SpringWorks' subsequent filings.

BeiGene Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 and other federal securities laws, including statements regarding the potential for a combination of lifirafenib and mirdametinib to address the unmet medical needs from patients with tumors with RAS mutations, RAF mutations and other MAPK pathway aberrations; the future development and regulatory filing and approval of lifirafenib; and BeiGene's plans, commitments, aspirations, and goals under the heading "About BeiGene." Actual results may differ materially from those indicated in the forward-looking statements as a result of various important factors, including BeiGene's ability to demonstrate the efficacy and safety of its drug candidates; the clinical results for its drug candidates, which may not support further development or marketing approval; actions of regulatory agencies, which may affect the initiation, timing and progress of clinical trials and marketing approval; BeiGene's ability to achieve commercial success for its marketed medicines and drug candidates, if approved; BeiGene's ability to obtain and maintain protection of

intellectual property for its medicines and technology; BeiGene's reliance on third parties to conduct drug development, manufacturing and other services; BeiGene's limited experience in obtaining regulatory approvals and commercializing pharmaceutical products and its ability to obtain additional funding for operations and to complete the development of its drug candidates and achieve and maintain profitability; and the impact of the COVID-19 pandemic on BeiGene's clinical development, regulatory, commercial, manufacturing, and other operations, as well as those risks more fully discussed in the section entitled "Risk Factors" in BeiGene's most recent annual report on Form 10-K, as well as discussions of potential risks, uncertainties, and other important factors in BeiGene's subsequent filings with the U.S. Securities and Exchange Commission. All information in this press release is as of the date of this press release, and BeiGene undertakes no duty to update such information unless required by law.

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