MapKure, BeiGene and SpringWorks Announce Initiation of Phase 1 Clinical Trial of BGB-3245, a Selective Next-Generation B-RAF Inhibitor, in Adult Patients with Advanced or Refractory Solid Tumors

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-- Phase 1 Study Initiated in Australia with IND Cleared to Expand Study to the U.S.--

-- Industry-Leading Scientific Advisory Board Formed to Support Advancement of BGB-3245 --

CAMBRIDGE, Mass. and BEIJING and STAMFORD, Conn., Feb. 27, 2020 (GLOBE NEWSWIRE) -- MapKure, LLC, a clinical-stage company developing precision medicines for patients with life-threatening diseases, together with BeiGene, Ltd. (NASDAQ: BGNE; HKEX: 06160) and SpringWorks Therapeutics, Inc. (NASDAQ: SWTX), who are joint owners of MapKure, announced today that the first patient has been dosed in Australia in a Phase 1 clinical trial to evaluate BGB-3245, an investigational, next-generation B-RAF inhibitor, in patients with advanced or refractory solid tumors. The companies also announced that the U.S. Food and Drug Administration (FDA) has allowed the Investigational New Drug (IND) application submitted for BGB-3245 to proceed, which will enable study expansion to U.S. sites.

B-RAF gene mutations and fusions have been shown to play a key role in the development of certain cancers. BGB-3245 is designed to inhibit both monomeric and dimeric forms of activating B-RAF mutations including V600 and non-V600 mutations, and RAF fusions, and has shown potent preclinical activity against a range of B-RAF gene alterations, including those for which there are no approved targeted therapies and those associated with resistance to currently approved therapies.

“Preclinical data suggest that BGB-3245 could potentially address a range of B-RAF driven tumors, which represent a significant need for patients who currently lack targeted therapeutic options, as well as patients who have developed resistance to first generation B-RAF inhibitors,” said Neal Rosen, M.D., Ph.D., the Enid A. Haupt Chair in Medical Oncology at Memorial Sloan-Kettering Cancer Center and Chair of the MapKure Scientific Advisory Board. “If our hypothesis is correct, we believe that BGB-3245 could have meaningful, single agent antitumor activity in B-RAF-altered cancers through its ability to address key primary and resistance gene alterations that are currently unaddressed by approved therapies.”

The Phase 1 clinical trial is a first-in-human, open-label, dose escalation and expansion study to investigate the safety, pharmacokinetics (PK) and antitumor activity of BGB-3245 in adult patients with solid tumors, including those harboring specific B-RAF driver mutations and fusions that are likely to respond to a RAF dimer inhibitor, as well as in certain adult patients who have developed resistance to first-generation B-RAF V600 inhibitors. The trial is designed to define the dose and assess the tolerability of BGB-3245 and will capture early antitumor activity signals to allow for potential cohort expansion.

In addition, MapKure has completed the formation of its Scientific Advisory Board (SAB), comprised of renowned leaders in MAPK pathway biology and targeted oncology clinical development. The SAB will continue to collaborate with MapKure’s joint steering committee, consisting of representatives from BeiGene and SpringWorks, to support the advancement of BGB-3245. The composition of the SAB is as follows:

- Neal Rosen, M.D., Ph.D., the Enid A. Haupt Chair in Medical Oncology at Memorial Sloan-Kettering Cancer Center. Dr. Rosen is the founding member and Chair of the MapKure SAB.
- Antoni Ribas, M.D., Professor of Medicine, Professor of Surgery, and Professor of Molecular and Medical Pharmacology at the University of California Los Angeles.
- Kevin Koch, Ph.D., President and CEO of Edgewise Therapeutics; formerly Founder, President, and Chief Scientific Officer of Array BioPharma.
- Zhan Yao, Ph.D., Assistant Research Professor, Molecular Pharmacology Program, Memorial Sloan-Kettering Cancer Center.
- Dejan Juric, M.D., Program Director, Investigational Cancer Therapeutics Program and Attending Physician in Medical Oncology, Massachusetts General Hospital.

About the Phase 1 Trial

The Phase 1 trial (NCT04249843) of BGB-3245 is an open-label, dose-escalation trial of BGB-3245 in adult patients with advanced or refractory solid tumors, including those with B-RAF driver mutations and fusions that are likely to respond to a RAF dimer inhibitor. The study will enroll patients who have experienced disease progression during or after at least one prior line of systemic anticancer therapy or for which treatment is not tolerated or acceptable to the participants.

The trial is designed in two parts: the Phase 1a portion will consist of a dose-escalation and dose-finding component to establish the maximum tolerated dose and/or the recommended Phase 2 dose and to evaluate the pharmacokinetics of BGB-3245 in patients with MAPK pathway aberrations. The Phase 1b portion will consist of one or more expansion cohorts to further evaluate the pharmacokinetics, safety, and tolerability of BGB-3245 at the recommended Phase 2 dose and to assess the preliminary antitumor activity of the compound in patients with select tumor types and B-RAF status (B-RAF point mutations and gene fusions).

About BGB-3245

BGB-3245 is an investigational, oral, selective small molecule inhibitor of monomer and dimer forms of activating B-RAF mutations including V600 B-RAF mutations, non-V600 B-RAF mutations, and RAF fusions. These mutations and fusions have been identified in a number of solid tumors to be

drivers of cancer growth, including in non-small cell lung cancer, colorectal cancer, thyroid cancer, and brain tumors. Preclinical data have demonstrated that BGB-3245 has activity in patient-derived xenografts driven by B-RAF fusions and non-V600 mutations for which approved B-RAF inhibitors are ineffective. In addition, BGB-3245's preclinical activity in cancer models driven by V600 B-RAF mutations has suggested that it could provide an additional therapeutic option for patients with the potential to reduce dimer-driven resistance.

In addition to its intended use as a monotherapy in several genetically defined solid tumor types, BGB-3245 also has the potential to be used in rational combination therapies in the future.

About MapKure

MapKure is a clinical-stage company created in 2019 to develop precision medicines for patients with life-threatening diseases, with an initial focus on cancer. By focusing on genetically defined disease drivers, MapKure is positioned to advance the development of transformative medicines to patients whose unmet medical needs are largely unaddressed. MapKure is jointly owned by BeiGene, Ltd. and SpringWorks, and is currently developing BGB-3245 under exclusive license from BeiGene in solid tumor patients harboring specific B-RAF driver mutations and RAF fusions, as well as in patients who have developed resistance to first-generation B-RAF inhibitors.

About BeiGene

BeiGene is a global, commercial-stage research-based biotechnology company focused on molecularly-targeted and immuno-oncology cancer therapeutics. With a team of over 3,500 employees in the United States, China, Australia, and Europe, BeiGene is advancing a pipeline consisting of novel oral small molecules and monoclonal antibodies for cancer. BeiGene is also working to create combination solutions aimed to have both a meaningful and lasting impact on cancer patients. In the United States, BeiGene markets and distributes BRUKINSA™ (zanubrutinib) and in China, the Company has received approval to market its anti-PD-1 antibody tislelizumab and markets ABRAXANE® (nanoparticle albumin-bound paclitaxel), REVLIMID® (lenalidomide), and VIDAZA® (azacitidine) under a license from Celgene Logistics Sarl, a Bristol-Myers Squibb company[i], and plans to market XGEVA® (denosumab) under a license from Amgen[ii]. For more information please visit www.beigene.com.

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. For more information, please visit www.springworkstx.com.

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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 encouraging pre-clinical data and therapeutic potential of BGB-3245 and plans for the operations of MapKure and clinical development of BGB-3245. 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 products and drug candidates, if approved; BeiGene's ability to obtain and maintain protection of intellectual property for its technology and drugs; BeiGene's reliance on third parties to conduct drug development, manufacturing and other services; BeiGene's limited operating history and BeiGene's ability to obtain additional funding for operations and to complete the development and commercialization of its drug candidates, as well as those risks more fully discussed in the section entitled "Risk Factors" in BeiGene's most recent quarterly report on Form 10-Q, 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.

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, 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, statements regarding the development of BGB-3245 or other future research and development activities conducted by MapKure, the timing for completion of SpringWorks' clinical trials of its 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, competition from other biopharmaceutical companies, and other risks identified in the section entitled "Risk Factors" in Item 1A of Part II of SpringWorks' Quarterly Report on Form 10-Q for the quarter ended September 30, 2019, as well as discussions of potential risks, uncertainties and other important factors in SpringWorks' subsequent filings with the Securities and Exchange Commission. 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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Source: SpringWorks Therapeutics, Inc.