U.S. Food and Drug Administration Accepts for Priority Review Bristol Myers Squibb's Application for Repotrectinib for the Treatment of Patients with Locally Advanced or Metastatic ROS1-Positive Non-Small Cell Lung Cancer

May 30, 2023

Application based on results from the registrational TRIDENT-1 trial, in which repotrectinib demonstrated high response rates and durable responses in patients with* ROS1*-positive locally advanced or metastatic non-small cell lung cancer

If approved, repotrectinib will provide a potential best-in-class option for patients with* ROS1*-positive NSCLC who are TKI-naïve and a potential first-in-class treatment for patients who have been treated with prior TKI

The U.S. Food and Drug Administration assigned a target action date of November 27, 2023

PRINCETON, N.J.--(BUSINESS WIRE)--Bristol Myers Squibb (NYSE: BMY) today announced that the U.S. Food and Drug Administration (FDA) has accepted the New Drug Application (NDA) for repotrectinib, a next-generation tyrosine kinase inhibitor (TKI), for the treatment of patients with *ROS1*-positive locally advanced or metastatic non-small cell lung cancer (NSCLC), based on results from the TRIDENT-1 trial. The FDA granted the application Priority Review and assigned a Prescription Drug User Fee Act (PDUFA) goal date of November 27, 2023. "Patients with *ROS1*-positive non-small cell lung cancer face a rare disease with a significant unmet medical need given the limited durability of benefit and emergence of resistance to approved therapies," said Jonathan Cheng, M.D., senior vice president and head of oncology development, Bristol Myers Squibb. "The FDA's acceptance of this application marks an exciting milestone on our journey to bring this next-generation tyrosine kinase inhibitor to patients. If approved, this would represent a potential best-in-class option for TKI-naïve patients and a potential first-in-class option for patients with *ROS1*-positive NSCLC who have been previously treated with TKI, and for whom there are currently no approved targeted therapies available. We are eager to continue working closely with the FDA on the review of this precision medicine, which has shown unprecedented level of durability of responses and robust intracranial responses in patients with *ROS1*-positive NSCLC."

The filing was based on results from the registrational TRIDENT-1 study. In the trial, repotrectinib demonstrated high response rates and clinically meaningful durability of benefit in both TKI-naïve and TKI-pretreated patients, including those with *ROS1* resistance mutations. The safety profile of repotrectinib was well characterized and manageable. Results from TRIDENT-1 were most recently presented at the 2022 EORTC-NCI-AACR (ENA) Symposium. The study remains ongoing to assess long-term outcomes and additional endpoints across patient populations with *ROS1*-positive locally advanced or metastatic NSCLC and *NTRK*-positive advanced solid tumors. Bristol Myers Squibb thanks the patients and investigators involved with the TRIDENT-1 clinical trial.

Turning Point Therapeutics is a wholly owned subsidiary of the Bristol-Myers Squibb Company. As of August 2022, Bristol Myers Squibb acquired the leading clinical stage precision oncology company and its pipeline of investigational drugs across precision oncology and advanced solid tumors, including repotrectinib.

About TRIDENT-1

TRIDENT-1 is a Phase 1/2 open-label, global, multi-center, first-in-human clinical trial evaluating the safety, tolerability, pharmacokinetics and anti-tumor activity of repotrectinib (TPX-0005, BMS-986472) in patients with advanced solid tumors, including non-small cell lung cancer (NSCLC). Phase 1 of the trial includes several primary and secondary safety and pharmacokinetics endpoints. Phase 2 of the trial has a primary endpoint of overall response rate (ORR) as assessed by Blinded Independent Central Review (BICR) using RECIST v1.1 and key secondary endpoints including duration of response (DOR), time to response (TTR), progression-free survival (PFS), overall survival (OS) and clinical benefit rate (CBR) in six distinct expansion cohorts, including tyrosine kinase inhibitor (TKI)-naïve and TKI-pretreated patients with *ROS1*-positive locally advanced or metastatic NSCLC and *NTRK*-positive advanced solid tumors.

About Lung Cancer

Lung cancer is the leading cause of cancer deaths globally. Non-small cell lung cancer (NSCLC) is one of the most common types of lung cancer, representing up to 84% of diagnoses. Survival rates vary depending on the stage and type of the cancer when diagnosed. ROS1 fusions are rare and occur in about 1-2% of patients with NSCLC. Patients with tumors that are *ROS1*-positive tend to be younger than the average patient with lung cancer, more often female and may have little to no smoking history. Per international treatment guidelines, ROS1 targeted agents are preferred in patients with a tumor harboring this alteration.

Bristol Myers Squibb: Creating a Better Future for People with Cancer

Bristol Myers Squibb is inspired by a single vision — transforming patients' lives through science. The goal of the company's cancer research is to deliver medicines that offer each patient a better, healthier life and to make cure a possibility. Building on a legacy across a broad range of cancers that

have changed survival expectations for many, Bristol Myers Squibb researchers are exploring new frontiers in personalized medicine, and through innovative digital platforms, are turning data into insights that sharpen their focus. Deep scientific expertise, cutting-edge capabilities and discovery platforms enable the company to look at cancer from every angle. Cancer can have a relentless grasp on many parts of a patient's life, and Bristol Myers Squibb is committed to taking actions to address all aspects of care, from diagnosis to survivorship. Because as a leader in cancer care, Bristol Myers Squibb is working to empower all people with cancer to have a better future.

About Repotrectinib

Repotrectinib (TPX-0005, BMS-986472) is a next-generation, potential best-in-class tyrosine kinase inhibitor (TKI) targeting *ROS1*- or *NTRK*-positive locally advanced or metastatic solid tumors, including non-small cell lung cancer (NSCLC), where there remain significant unmet medical needs for patients. Repotrectinib was designed to improve durability of response and with favorable properties for human brain penetration to enhance intracranial activity. It is being studied in a registrational Phase 1/2 trial primarily in adults and a Phase 1/2 trial in pediatric patients.

In June 2017, repotrectinib was granted an Orphan Drug designation by the U.S. Food and Drug Administration (FDA). Since then, repotrectinib has demonstrated clinically meaningful results and was granted three Breakthrough Therapy Designations (BTDs) by the FDA for the treatment of patients with: *ROS1*-positive metastatic NSCLC who have not been treated with a ROS1 TKI; *ROS1*-positive metastatic NSCLC who have been previously treated with one ROS1 TKI and who have not received prior platinum-based chemotherapy; and advanced solid tumors that have an *NTRK* gene fusion who have progressed following treatment with one or two prior tropomyosin receptor kinase (TRK) TKIs (with or without prior chemotherapy) and have no satisfactory alternative treatments.

Repotrectinib was also previously granted four fast-track designations in patients with: *ROS1*-positive advanced NSCLC who have been treated with disease progression following one prior line of platinum-based chemotherapy and one prior line of a ROS1 TKI; *ROS1*-positive advanced NSCLC who have not been treated with a ROS1 TKI; *ROS1*-positive advanced NSCLC who have been previously treated with one ROS1 TKI and who have not received prior platinum-based chemotherapy; and advanced solid tumors that have an *NTRK* gene fusion who have progressed following treatment with at least one prior line of chemotherapy and one or two prior TRK TKIs and have no satisfactory alternative treatments.

About Bristol Myers Squibb

Bristol Myers Squibb is a global biopharmaceutical company whose mission is to discover, develop and deliver innovative medicines that help patients prevail over serious diseases. For more information about Bristol Myers Squibb, visit us at BMS.com or follow us on LinkedIn, Twitter, YouTube, Facebook and Instagram.

Cautionary Statement Regarding Forward-Looking Statements

This press release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 regarding, among other things, the research, development and commercialization of pharmaceutical products. All statements that are not statements of historical facts are, or may be deemed to be, forward-looking statements. Such forward-looking statements are based on current expectations and projections about our future financial results, goals, plans and objectives and involve inherent risks, assumptions and uncertainties, including internal or external factors that could delay, divert or change any of them in the next several years, that are difficult to predict, may be beyond our control and could cause our future financial results, goals, plans and objectives to differ materially from those expressed in, or implied by, the statements. These risks, assumptions, uncertainties and other factors include, among others, that repotrectinib may not receive regulatory approval for the indication described in this release in the currently anticipated timeline or at all, that any marketing approvals, if granted, may have significant limitations on their use, and, if approved, whether such product candidate for such indication described in this release will be commercially successful. No forward-looking statement can be guaranteed. Forward-looking statements in this press release should be evaluated together with the many risks and uncertainties that affect Bristol Myers Squibb's business and market, particularly those identified in the cautionary statement and risk factors discussion in Bristol Myers Squibb's Annual Report on Form 10-K for the year ended December 31, 2022, as updated by our subsequent Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and other filings with the Securities and Exchange Commission. The forward-looking statements included in this document are made only as of the date of this document and except as otherwise required by applicable law, Bristol Myers Squibb undertakes no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events, changed circumstances or otherwise.

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Contacts

Bristol Myers Squibb

Media Inquiries:
media@bms.com

Investors:
investor.relations@bms.com