Bristol-Myers Squibb’s BMS-986036 (Pegylated FGF21) Shows Consistent Improvement in Liver Fat, Liver Injury and Fibrosis in Patients with Nonalcoholic Steatohepatitis (NASH) in Phase 2 Trial

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Primary endpoint of significant reduction in liver fat achieved following 16 weeks of treatment with BMS-986036

PRINCETON, N.J.--(BUSINESS WIRE)--Bristol-Myers Squibb Company (NYSE:BMY) today announced data from a Phase 2 study of BMS-986036, an investigational pegylated analogue of human fibroblast growth factor 21 (FGF21), a key regulator of metabolism, in patients with biopsy-confirmed nonalcoholic steatohepatitis (NASH) (F1-F3). The study achieved its primary endpoint of significant reduction in liver fat versus placebo. Statistically significant improvements were also seen in prespecified exploratory endpoints including biomarkers of fibrosis, metabolic parameters and markers of liver injury. These data were presented at a late-breaking oral presentation at EASL: The International Liver Congress on April 22 at 4:15 p.m. CET in Amsterdam.

“These data suggest that BMS-986036 may be effective in patients with NASH, many of whom will experience disease progression due to the lack of available treatment options,” said Arun Sanyal, MBBS, M.D., professor, Departments of Medicine, Physiology, and Molecular Pathology, Virginia Commonwealth University. “The results of this study show that BMS-986036 had beneficial effects on three important components in the treatment of NASH: liver fat, liver injury and fibrosis.”

“We are encouraged by the improvements these data showed across multiple aspects of NASH, and that patients could be effectively evaluated through imaging rather than through invasive liver biopsy,” said Mike Burgess, head of Cardiovascular, Fibrosis and Immunoscience Development, Bristol-Myers Squibb. “These data, along with previously announced Phase 2 data in patients with type 2 diabetes, support further clinical research of BMS-986036 as a potential treatment for NASH. We look forward to sharing these data with health authorities to determine next steps for further study of this asset.”

Bristol-Myers Squibb exclusively licensed the rights to research, develop and commercialize BMS-986036 from Ambrx, Inc.

About MB130-045: A Phase 2 Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Multiple Dose Study to Evaluate the Safety, Pharmacokinetics and Pharmacodynamic Effects of BMS-986036 in Adults with Nonalcoholic Steatohepatitis

This was a multicenter, randomized (1:1:1), double-blind, placebo-controlled study in adults with body mass index ≥25 kg/m², biopsy-confirmed NASH (F1-F3), and hepatic fat fraction ≥10%, assessed by magnetic resonance imaging-proton density fat fraction (MRI-PDFF), a noninvasive measurement of liver fat. Randomization was stratified by diabetes status. Patients received subcutaneous injections of BMS-986036 10 mg daily (n=25), BMS-986036 20 mg weekly (n=23), or placebo (n=26) daily for 16 weeks. The primary efficacy endpoint was absolute change in MRI-PDFF at Week 16. Exploratory endpoints included serum Pro-C3 (N-terminal type III collagen propeptide, a fibrosis biomarker), enzymes alanine aminotransferase (ALT) and aspartate aminotransferase (AST), and, in a subset of patients, liver stiffness, assessed by MR elastography (MRE).

Among the 74 patients treated, 68 were assessed by MRI-PDFF at both Baseline and Week 16. Liver biopsy was conducted to confirm NASH at Baseline. At Week 16, both dosing regimens of BMS-986036 (10 mg daily or 20 mg weekly) significantly reduced liver fat as measured by MRI-PDFF versus placebo (6.8% and 5.2%, respectively, vs. 1.3%, p=0.0004 and p=0.008). The 10 mg daily dose resulted in 57% of patients (13/23) reaching ≥30% relative risk reduction. The 20 mg weekly dose resulted in 52% of patients (11/21) reaching ≥30% relative risk reduction. Both dosing regimens also improved Pro-C3 (a serum biomarker of fibrosis), magnetic resonance elastography (MRE, a measure of liver stiffness), as well as adiponectin, ALT and AST (markers of liver injury). Improvements in triglycerides, low density lipoprotein (LDL), and high density lipoprotein (HDL) were also observed in the treatment groups.

Overall, BMS-986036 had a favorable safety profile, with no deaths or serious adverse events related to treatment, and no discontinuations due to adverse events. The most frequent adverse events were diarrhea (13% and 22%, respectively, vs. 8% in placebo), nausea (16% and 13%, respectively, vs. 8%), and frequent bowel movements (20% and 0%, respectively, vs. 0%), none of which were severe.

About Fibrosis and NASH
Fibrotic diseases are characterized by chronic inflammation that leads to excess collagen deposition and scar formation in an organ or tissue. This scarring response compromises function and ultimately leads to organ failure. Nonalcoholic steatohepatitis (NASH) may progress to cirrhosis, hepatocellular carcinoma (liver cancer) and liver failure, and is expected to be the leading cause of liver transplant by 2020. The severity of liver fibrosis (scar tissue in the liver) is measured on a scale of F0 (normal) to F4 (cirrhosis) in a liver biopsy specimen. Approximately 20 million patients in the U.S. have NASH, and there are currently no approved pharmacological treatments.

About Fibrosis at Bristol-Myers Squibb

Bristol-Myers Squibb is committed to the discovery and development of medicines for the treatment of fibrosis, the buildup of scar tissue that impacts organ function. We are advancing a robust pipeline of investigational compounds to address areas of high unmet need in fibrosis, including nonalcoholic steatohepatitis (NASH), a condition with no approved treatment options that may lead to liver fibrosis and/or cirrhosis; and idiopathic pulmonary fibrosis (IPF), a progressive lung disease with a high mortality rate. We are researching multiple mechanisms and approaches to make the biggest impact on patients.

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 and Facebook.

Bristol-Myers Squibb Forward Looking Statement

This press release contains “forward-looking statements” as that term is defined in the Private Securities Litigation Reform Act of 1995 regarding the research, development and commercialization of pharmaceutical products. Such forward-looking statements are based on current expectations and involve inherent risks and uncertainties, including factors that could delay, divert or change any of them, and could cause actual outcomes and results to differ materially from current expectations. No forward-looking statement can be guaranteed. Among other risks, there can be no guarantee that the investigational compound discussed in this release will be successfully developed or approved for any of the indications described in this release. Forward-looking statements in this press release should be evaluated together with the many uncertainties that affect Bristol-Myers Squibb's business, particularly those identified in the cautionary factors discussion in Bristol-Myers Squibb's Annual Report on Form 10-K for the year ended December 31, 2016 in our Quarterly Reports on Form 10-Q and our Current Reports on Form 8-K. Bristol-Myers Squibb undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise.

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