Data on Bristol-Myers Squibb’s Investigational Treatment for Alzheimer’s Disease Demonstrate Potential Therapeutic Window at Doses Below 100 mg in Phase II Safety and Tolerability Study

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Study Conducted in Patients with Mild-to-Moderate Alzheimer’s Disease

Data Presented at 2011 Alzheimer’s Association International Conference

PARIS--(BUSINESS WIRE)--Bristol-Myers Squibb Company (NYSE: BMY) today announced the results of a Phase II study evaluating the safety and tolerability of the investigational gamma secretase inhibitor BMS-708163 in patients with mild-to-moderate Alzheimer’s disease. The randomized, double-blind, placebo-controlled study (CN156-013) demonstrated that BMS-708163 doses below 100 mg/day provide a potential therapeutic window for further evaluation in Phase III registrational studies. The study results were presented at the 2011 Alzheimer’s Association International Conference (AAIC).

Of the four BMS-708163 doses evaluated in the study (25 mg, 50 mg, 100 mg and 125 mg/day), doses below 100 mg/day demonstrated acceptable tolerability profiles for further development and were associated with discontinuation rates comparable with placebo. BMS-708163 doses at or above 100 mg were associated with higher discontinuation rates, most commonly due to gastrointestinal and dermatological side effects.

BMS-708163 is an oral gamma secretase inhibitor designed for selective inhibition of amyloid beta (Aβ) synthesis. Aβ is hypothesized to play a central role in the development of Alzheimer’s disease. In healthy people, Aβ breaks down and is eliminated; but in people with Alzheimer’s disease, Aβ accumulates and forms “amyloid plaques” in the brain. While the chain of events that lead to the development of Alzheimer’s is still unclear, the accumulation of Aβ and the resulting formation of amyloid plaques are considered hallmarks of the disease pathology.

“The safety and tolerability results of this Phase II study in mild-to-moderate Alzheimer’s disease support the further clinical evaluation of Bristol-Myers Squibb’s gamma secretase inhibitor. The data also provide clear direction to continue testing of the amyloid hypothesis as we look for ways to address this devastating illness,” said Stephen Salloway, MD, professor of Neurology and Psychiatry, Brown University, and director, The Butler Hospital Memory and Aging Program, Providence, RI.

Study Results

This Phase II study (CN156-013) in mild-to-moderate Alzheimer’s disease met its primary objective of identifying safe and tolerable doses of BMS-708163, providing a potential therapeutic window for intervention at doses less than 100 mg/day that warrants testing in Phase III registrational studies. The study was not adequately powered to determine the efficacy of BMS-708163.

For treated patients, the discontinuation rates for any reason were placebo: 19%, BMS-708163 25 mg: 21%, 50 mg: 28%, 100 mg: 41%, and 125 mg: 48%. The most common gastrointestinal adverse events observed in this study were diarrhea (placebo: 7%, 25 mg: 24%, 50 mg: 12%, 100 mg: 27%, 125 mg: 20%) and nausea (placebo: 0%, 25 mg: 5%, 50 mg: 2%, 100 mg: 27%, 125 mg: 13%). The most common skin-related adverse events observed in this study were rash (placebo: 0%, 25 mg: 2%, 50 mg: 12%, 100 mg: 27%, 125 mg: 43%) and pruritis (placebo: 0%, 25 mg: 0%, 50 mg: 2%, 100 mg: 10%, 125 mg: 20%).

Signals that occurred at greater rates in treatment groups compared to placebo and that were identified for ongoing monitoring included: reversible glucosuria with no changes in serum glucose, asymptomatic MRI findings (amyloid-related imaging abnormalities), gastrointestinal ulcers, rash, pruritis, and non-melanoma skin cancer. The overall incidence of serious adverse events was similar across placebo and all treatment groups (placebo: 19%; 25 mg: 17%; 50 mg: 16%; 100 mg: 15%; 125 mg: 15%). There were no deaths reported in the study.

About the Study

CN156-013 was a multicenter, randomized, double-blind, placebo-controlled, 24-week phase II study in patients with mild-to-moderate Alzheimer’s disease. The purpose of CN156-013 was to determine the safety and tolerability of BMS-708163 at
A total of 209 patients were randomly assigned to one of five study arms: placebo (n=42), or BMS-708163 at 25 mg (n=42), 50 mg (n=41), 100 mg (n=42) or 125 mg/day (n=42). Patients assigned to the 100 mg and 125 mg treatment groups were treated with 50 mg/day for the first two weeks and subsequently titrated to their final fixed dose during their Week 2 visit. Dose adjustments due to tolerability were not allowed. Safety was assessed every two weeks during the treatment period.

About Alzheimer's Disease

Alzheimer's disease is a progressive brain disease that impairs memory, interferes with thinking and ultimately destroys the ability of an individual to carry out simple tasks. The disease is a continuum, with damage to the brain starting long before the onset of dementia. Alzheimer's affects 24 million people worldwide and the prevalence is projected to significantly increase over the coming decades due to the aging population. While there are medicines available to help treat the symptoms of Alzheimer’s disease, there remains a significant unmet medical need for therapies that slow or prevent the progression of underlying disease.

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 www.bms.com, or follow us on Twitter at http://twitter.com/bmsnews.