NEWS RELEASE

Prothena's Partner Bristol Myers Squibb Obtains Fast Track Designation from the U.S. FDA for BMS-986446 (PRX005), an Anti-MTBR-Tau-Targeting Antibody, for the Treatment of Alzheimer's Disease

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- Anti-microtubule binding region-tau antibody being investigated as a potential disease-modifying therapy to slow or delay progression of disease
- Fast Track Designation recognizes the potential of anti-MTBR tau to be an important treatment option for patients with Alzheimer's disease

DUBLIN--(BUSINESS WIRE)-- Prothena Corporation plc (NASDAQ:PRTA), announced today that Bristol Myers Squibb communicated in a press release that the U.S. Food and Drug Administration (FDA) has granted Fast Track Designation to BMS-986446, a potential best-in-class anti-microtubule binding region-tau (anti-MTBR-tau) antibody currently in Phase 2 development for the treatment of early Alzheimer's disease. Fast Track Designation is intended to facilitate the development and expedite the review of investigational drugs that treat serious conditions and fill an unmet medical need.

Alzheimer's disease — the most common type of dementia in adults — is a progressive, multifaceted and devastating neurodegenerative disease in which significant changes occur in the brain that cause neurons to die over time. These changes include the accumulation and spread of pathological tau, an abnormal form of the tau protein. Pathological tau protein fragments containing the microtubule binding region (MTBR) appear to have a key role in the underlying pathology of Alzheimer's disease. By neutralizing the spread and promoting the clearance of pathological tau, BMS-986446 aims to modify the underlying course of the disease with the ultimate goal of slowing or delaying disease progression.

In preclinical models, BMS-986446 demonstrated significant reductions in tau uptake and spread, protection against behavioral deficits and was localized with tau pathology in Alzheimer's brain tissue. BMS-986446 was also shown to be safe and well tolerated across three dose cohorts in a Phase 1 study of healthy participants. Bristol Myers Squibb also announced that the ongoing Phase 2 study is fully enrolled and includes several biomarkers of tau and amyloid-beta biology, as well as clinical outcome measures, to evaluate the impact of BMS-986446 on disease progression.

As part of the BMS-986446 global license with Bristol Myers Squibb, Prothena is eligible to receive additional regulatory and sales milestone payments of up to $562.5 million. Prothena also is eligible to receive tiered royalties on net sales. Bristol Myers Squibb is responsible for all communication, development, manufacturing, and commercialization for BMS-986446.

About BMS-986446 (PRX005)

BMS-986446 is a humanized monoclonal antibody that targets multiple domains of the microtubule binding region of tau, a highly pathogenic tau fragment associated with neurofibrillary tangle formation and cognitive decline in Alzheimer's disease. BMS-986446 binds to specific regions of the tau protein (R1–R3 within the microtubule-binding domain) to prevent the cell-to-cell spread of tau and tau uptake into cells. It also activates microglia—the brain's immune cells—through its Fc receptor function, promoting the clearance of tau via phagocytosis.

About the TargetTau-1 Phase 2 Trial (**NCT06268886**)

TargetTau-1 is a randomized, double-blind, placebo-controlled, global Phase 2 proof-of-concept study designed to evaluate the efficacy, safety and tolerability of multiple doses of BMS-986446 in participants with early Alzheimer's disease. The study aims to determine whether targeting MTBR-tau can modify disease progression. In addition to clinical outcome measures, the trial integrates a comprehensive biomarker strategy to assess tau and amyloid-beta biology.

About Alzheimer's Disease

Alzheimer's disease is a progressive, multifaceted and devastating neurodegenerative disease and the most common type of dementia in adults. Changes in the brain disrupt communication between neurons, impacting memory, cognition and behavior. As a result, Alzheimer's disease has a significant impact on the day-to-day lives of those it directly affects, as well as on their families, caregivers and friends, resulting in considerable shifts in interpersonal relationships. There remains a critical need for disease-modifying therapies that can slow or delay the progression of Alzheimer's disease as well as therapies that manage and ease neurobehavioral symptoms.

About Prothena

Prothena Corporation plc is a late-stage clinical biotechnology company with expertise in protein dysregulation and a pipeline of investigational therapeutics with the potential to change the course of devastating neurodegenerative and rare peripheral amyloid diseases. Fueled by its deep scientific expertise built over decades of research, Prothena is advancing a pipeline of therapeutic candidates for a number of indications and novel targets for which its ability to integrate scientific insights around neurological dysfunction and the biology of misfolded proteins can be leveraged. Prothena's pipeline includes both wholly-owned and partnered programs being developed for the potential treatment of diseases including ATTR amyloidosis with cardiomyopathy, Alzheimer's disease, Parkinson's disease and a number of other neurodegenerative diseases. For more information, please visit the Company's website at **www.prothena.com** and follow the Company on X (formerly Twitter) @ProthenaCorp.

Forward-Looking Statements

This press release contains forward-looking statements. These statements relate to, among other things, the treatment potential, design, and proposed mechanism of action BMS-986446; plans for ongoing clinical trials of BMS-986446; and amounts we might receive under our agreement with Bristol Myers Squibb. These statements are based on estimates, projections and assumptions that may prove not to be accurate, and actual results could differ materially from those anticipated due to known and unknown risks, uncertainties and other factors, including but not limited to those described in the "Risk Factors" sections of our Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on August 4, 2025, and discussions of potential risks, uncertainties, and other important factors in our subsequent filings with the SEC. We undertake no obligation to update publicly any forward-looking statements contained in this press release as a result of new information, future events, or changes in our expectations.

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