NEWS RELEASE

Prothena Announces Bristol Myers Squibb Opt-in for Worldwide Rights of PRX005, a Novel Anti-MTBR-Tau Antibody

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- Prothena to receive $55 million from Bristol Myers Squibb for exclusive worldwide license to PRX005, building on exclusive U.S. license which was optioned in June 2021
- Bristol Myers Squibb will be responsible for development, manufacturing, and commercialization going forward

DUBLIN--(BUSINESS WIRE)-- Prothena Corporation plc (NASDAQ:PRTA), a late-stage clinical biotechnology company with a robust pipeline of investigational therapeutics built on protein dysregulation expertise, today announced that Bristol Myers Squibb exercised its option under the global neuroscience research and development collaboration to obtain the exclusive worldwide commercial rights for PRX005 and will pay Prothena $55 million. PRX005, which is designed to be a best-in-class anti-tau antibody, specifically targets an area within the microtubule binding region (MTBR) of tau for the potential treatment of Alzheimer's disease.

"Earlier this year, as part of our collaboration with Bristol Myers Squibb, we announced topline data from the single ascending dose portion of the Phase 1 clinical trial showing that PRX005 across three dose cohorts was safe and well tolerated with expected pharmacokinetic properties, meeting the primary objectives of the study. We are proud of our pioneering role in targeting this key region within the MTBR of tau and excited that Bristol Myers Squibb have exercised their option for worldwide rights to PRX005," said Gene Kinney, PhD, President and Chief Executive Officer, Prothena. "At Prothena, we will continue advancing our broad portfolio of product candidates for Alzheimer's disease, including PRX012, our next-generation antibody targeting amyloid beta, a well-validated

disease pathway, and PRX123 an amyloid beta/tau dual-targeting vaccine with the potential to prevent Alzheimer's disease. We believe that our portfolio is well-positioned to revolutionize the care of patients suffering from this devastating disease."

"PRX005, identified and developed by Prothena through our partnership, has the potential to provide a meaningful disease-modifying treatment option for the millions of people that suffer from Alzheimer's disease," said Richard Hargreaves, Senior Vice President and Head of Bristol Myers Squibb's Neuroscience Thematic Research Center. "PRX005 becomes a key component of our commitment to the Alzheimer's disease community and our neuroscience portfolio, and we look forward to continuing its development."

The multiple ascending dose (MAD) portion of the Phase 1 clinical trial for PRX005 is ongoing. All program updates, including results from ongoing and any future PRX005 clinical studies, will be reported by Bristol Myers Squibb going forward.

About the Global Neuroscience R&D Collaboration

This global neuroscience research and development collaboration is focused on three proteins implicated in the pathogenesis of several neurodegenerative diseases, including tau, TDP-43 and an undisclosed target. PRX005 is designed to be a best-in-class anti-tau, MTBR-specific antibody for the potential treatment of Alzheimer's disease and is the first program to advance to the clinic from this collaboration. Prothena is eligible to receive up to an additional $160 million for U.S. rights, up to $110 million for global rights, and up to $1.7 billion for regulatory and commercial milestone payments for a total of up to $2.2 billion, which also includes amounts received to date.

About Tau

Tau is a microtubule associated protein, which hyper-phosphorylates and aggregates in the brains of individuals with Alzheimer's disease to form pathological neurofibrillary tangles. Tau tangles and amyloid beta plaques represent the pathological hallmarks of Alzheimer's disease. The presence of tau pathology strongly correlates with neurodegeneration and cognitive impairment in Alzheimer's disease and its pattern of progression throughout the brain suggests that tau pathology spreads through anatomically connected pathways via cell-to-cell transmission, a hypothesis supported by multiple preclinical studies. This propagation of pathology is thought to be mediated by MTBR-tau "seeds". PRX005 has demonstrated superior ability to bind, intercept and block cellular internalization of pathogenic tau, and mitigate downstream neurotoxicity compared to other anti-tau antibodies in multiple preclinical studies.

About PRX005

PRX005 is designed to be a best-in-class anti-tau antibody that specifically binds with high affinity the R1, R2, and R3 repeats within the MTBR of tau and targets both 3R and 4R tau isoforms. MTBR tau has been shown in preclinical studies to be involved in the pathological spread of tau. Neurofibrillary tangles composed of misfolded tau proteins, along with amyloid beta plaques, are pathological hallmarks of Alzheimer's disease. Cell-to-cell transmission of pathogenic extracellular tau and the accumulation of pathogenic tau also correlate with the progression of symptomatology and clinical decline in patients with Alzheimer's disease. Recent publications suggest that during the course of Alzheimer's disease progression, tau appears to spread throughout the brain via synaptically-connected pathways; this propagation of pathology is thought to be mediated by tau "seeds" containing the MTBR of tau. Additionally, it has been recently reported that the presence of MTBR fragments in cerebrospinal fluid correlate with dementia stages and tau tangles in Alzheimer's disease to a higher degree than fragments of other tau regions. In preclinical research, antibodies targeting this region of tau were superior in blocking tau uptake and neurotoxicity, which has been associated with efficacy in Alzheimer's disease animal models. In these preclinical models, PRX005 demonstrated significant reduction of intraneuronal tau pathology and protection against behavioral deficit in a tau transgenic mouse model and complete blockade of neuronal tau internalization in vitro.

About Alzheimer's Disease

Alzheimer's disease is a fatal disease and the most common form of dementia causing increasingly serious symptoms, including confusion, disorientation, mood and behavioral changes, and difficulty speaking, swallowing, and walking. Approximately 50 million people worldwide are estimated to be living with Alzheimer's disease or other dementias. Alzheimer's disease is the most common neurodegenerative disorder. There is an urgent need for therapies that slow the progression and ultimately prevent Alzheimer's disease to address this global healthcare crisis. Prothena's Alzheimer's disease portfolio spans next generation antibody immunotherapy, small molecule, and vaccine approaches, all geared toward building upon first generation treatments to advance the treatment paradigm.

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 AL amyloidosis, ATTR amyloidosis, 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 Twitter @ProthenaCorp.

Forward-Looking Statements

This press release contains forward-looking statements. These statements relate to, among other things, the treatment potential, design, proposed mechanism of action, and potential administration of PRX005; attributes of epitopes and PRX005 we have identified; the timing for advancement of our PRX005 program, including the ongoing multiple ascending dose (MAD) portion of the Phase 1 study; and amounts we might receive under our collaboration with BMS. 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 May 4, 2023, 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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