# Prothena Announces Bristol Myers Squibb Opt-in of Anti-Tau PRX005 as the First Program from Global Neuroscience Research and Development Collaboration

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- Prothena to receive $80 million from Bristol Myers Squibb for exclusive US license to PRX005; Next option for worldwide rights following completion of Phase 1
- PRX005 is an investigational best-in-class anti-tau antibody targeting the microtubule binding region of tau for the treatment of Alzheimer's disease
- Phase 1 study has initiated

DUBLIN, Ireland, June 24, 2021 (GLOBE NEWSWIRE) -- Prothena Corporation plc (NASDAQ:PRTA), a late-stage clinical company with a robust pipeline of novel 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 enter into an exclusive U.S. license for PRX005 and will pay Prothena $80 million. PRX005 is designed to be a best-in-class anti-tau antibody by specifically targeting an area within the microtubule binding region (MTBR) for the potential treatment of Alzheimer's disease (AD). Phase 1 study with PRX005 has initiated.

"Our continued collaboration with Bristol Myers Squibb on PRX005 allows us to further leverage our combined expertise to accelerate the development of therapies with the potential to transform the lives of those affected by neurodegeneration," said Gene Kinney, PhD, President and Chief Executive Officer of Prothena. "Mounting scientific evidence suggests the MTBR of tau is most closely associated with the pathogenic spread of tau. The presence of MTBR fragments in cerebrospinal fluid have also been shown to correlate with dementia stages in Alzheimer's disease to a higher degree than fragments of other tau regions. These recent biological understandings support the further development of PRX005, which uniquely targets a key region within the MTBR of the tau protein. In our studies, we have found that targeting specific regions within the MTBR reduce pathogenic tau uptake into neurons, an attribute that was not achievable with antibodies targeting other regions of tau."

"We are pleased that our collaboration with Prothena has successfully identified and developed PRX005, a novel, differentiated anti-tau antibody that we believe has the potential to provide a meaningful disease modifying treatment option for the millions of patients that suffer from Alzheimer's disease," said Richard Hargreaves, Senior Vice President and Head of Bristol Myers Squibb's Neuroscience Thematic Research Center. "We look forward to our continued partnership with Prothena."

Tau is a microtubule associated protein, which aggregates and hyper-phospohrylates in the brains of individuals with AD to form pathological neurofibrillary tangles. Tau tangles, along with amyloid beta plaques represent the pathological hallmarks of AD. The presence of tau pathology strongly correlates with neurodegeneration and cognitive impairment in AD 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 tau "seeds" containing the MTBR of tau. 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 the Global Neuroscience Research and Development 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, where the Phase 1 study has initiated. With this payment, Prothena will have received a total of $230 million pursuant to the collaboration, and is eligible to receive up to an additional $160 million for U.S. rights, up to $165 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 plus potential tiered commercial sales royalties across multiple programs.

**About PRX005 for Alzheimer's Disease**

PRX005 is designed to be a best-in-class anti-tau antibody that specifically targets a key region within the microtubule binding region (MTBR), which 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 (AD). 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 AD. Recent publications suggest that during the course of AD 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 in AD 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 AD animal models. In these preclinical models, PRX005 demonstrated significant inhibition of cell-to-cell transmission and neuronal internalization in vitro and in vivo and slowed pathological progression in a tau transgenic mouse model.

**About Alzheimer's Disease**

Alzheimer's disease is a type of dementia that can cause increasingly serious symptoms, including confusion, disorientation, mood and behavioral changes, difficulty speaking, swallowing, and walking. Approximately 6.2 million Americans age 65 and older are currently estimated to be living with Alzheimer's disease, making it the most common neurodegenerative disorder. It is also the sixth leading cause of death among adults in the United States. 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, geared

toward building upon first generation treatments to advance the treatment paradigm.

**About Prothena**

Prothena Corporation plc is a late-stage clinical company with a robust pipeline of novel investigational therapeutics built on protein dysregulation expertise with the potential to change the course of devastating rare peripheral amyloid and neurodegenerative 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, and proposed mechanism of action of PRX005; 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" section of our Prospectus Supplement filed pursuant to Rule 424(b)5 with the Securities and Exchange Commission (SEC) on March 24, 2021, as well as 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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