Probiodrug to present at Huntington's Disease Therapeutics Conference

The Glutaminyl Cyclase (QC) inhibitor PQ912 demonstrates beneficial effects in a preclinical Huntington's disease model

HALLE (SAALE), Germany, 10 April 2017 - Probiodrug AG (Euronext Amsterdam: PBD), a biopharmaceutical company developing novel therapeutic solutions to treat Alzheimer's disease (AD) and other neurodegenerative disorders, today announced results of a preclinical study targeting Glutaminyl Cyclases (QCs) in Huntington's disease (HD). The results will be presented at the 12th Annual HD Therapeutics Conference of the CHDI Foundation on 23rd of April in St. Julian's, Malta. HD is the most common inherited neurodegenerative disorder, where due to a mutation, the glutamine amino acid sequence is expanded in a protein called huntingtin (HTT). There is currently no disease modifying therapy for this condition.

The QC inhibitor PQ912 clearly improved several signs of the disease in a well characterized BACHD mouse model of HD. BACHD mice carry the human gene for mutant HTT (mHTT). At six weeks old, parallel to the onset of first behavioral, metabolic and neuropathological signs of the disease, the BACHD mice were treated for 18 weeks with food pellets containing PQ912. PQ912 treatment for 18 weeks caused a significant reduction (approximately 30%) in brain mHTT levels. These lowered mHTT levels were associated with reduced levels of the inflammation/gliosis marker GFAP-protein, a striking normalization of the abnormal body weight gain and energy metabolism as well as a normalization of several mRNA levels coding for HSPs in BACHD mice at 24 weeks of age.

It is important to emphasize that these beneficial effects may result from inhibition of similar molecular mechanisms, as already proven for beta-amyloid toxicity in models of AD. Firstly, pyroglutamate (mutant) HTT fragments may be formed by QC activity. Secondly, subclinical neuro-inflammation and gliosis may be triggered and sustained in HD similar to AD via QC-dependent maturation of specific pro-inflammatory chemokines. Thirdly, the QC-mediated induction of HSP levels may inhibit mHTT toxicity.

In independent pre-studies PQ912 showed very good tolerability across a wide range of doses. In this study, efficacy of a medium dose of PQ912 was compared to treated wild-type mice as well as to sham-treated wild-type and BACHD mice. Pharmacodynamic effects on human mHTT were captured by mHTT TR-FRET assay in brain samples from treated and sham-treated BACHD mice. Data were generated in collaboration with Stephan von Hörsten of the University Hospital Erlangen, part of Friedrich-Alexander-University (FAU), Erlangen, Germany.

Commenting on the announcement, Dr Inge Lues, CDO of Probiodrug said: "Considering the complex pathology behind neurodegenerative disorders, this novel therapeutic approach will likely intensify further research on QC-mediated effects also in other disease entities, including but not limited to HD. Maybe even more important, our results are very exciting as they clearly indicate an attractive approach for lowering toxic mutant HTT levels including several downstream pathological effects in this devastating disease. Considering that PQ912 is already in clinical studies in AD, the way for interventional studies in human HD gene carriers and patients may be not that long anymore."

Stephan von Hörsten, Scientist at FAU, added: "These data are exciting because they indicate that specific pharmacotherapy of HD conditions may well be capable in lowering mHTT levels, and thus, this QC inhibitor based intervention acts very close at the disease-inducing agent."

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Notes to Editors:
About Probiodrug AG
Headquartered in Halle (Saale), Germany, Probiodrug AG (Euronext Amsterdam: PBD) is a biopharmaceutical company focused on the development of new therapeutic products for the treatment of Alzheimer's disease.

Founded in 1997, the company successfully developed a novel therapeutic concept for diabetes - the DP4 inhibitors - which provided the basis for a novel class of antidiabetics - the gliptins. Its core capabilities are based on its long-standing expertise in the elucidation of the structure and function of enzymes involved in the modification of proteins and peptides, which play a central role in pathological conditions.

Today Probiodrug's aim is to become a leading company in the development of Alzheimer's disease treatments and to thereby provide a better life for Alzheimer's disease patients. It has identified a new therapeutic concept linked to disease initiation and progression. The development approaches are targeting pyroglutamate-Abeta (pGlu-Abeta) as a therapeutic strategy to fight Alzheimer's disease. The Company has medical use and composition of matter patents related to the inhibition of Glutaminyl Cyclase (QC) and anti-pGlu-Abeta- specific monoclonal antibodies, providing it, in the Company's view, with a leading position in this field of research.

Probiodrug's lead product candidate, PQ912, is a highly specific and potent inhibitor of Glutaminyl Cyclase (QC), which has shown therapeutic effects in Alzheimer's animal models. PQ912 is currently in a Phase 2a study, the SAPHIR trial. In a preceding Phase 1 study with healthy young and elderly volunteers, PQ912 has shown to be safe and well tolerated and also revealed high QC-inhibition.

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About Huntington's disease
Huntington's disease (HD) is the most common inherited neurodegenerative disorder, with a prevalence of 5 to 8 cases per 100,000 and prominent clinical manifestations, including motor dysfunction, psychiatric disturbance, and dementia, ultimately, after decades of progression, leading to death. HD is one of nine autosomal dominant polyglutamine (polyQ) diseases characterized by a CAG/polyQ repeat expansion in ubiquitously expressed proteins. Because Huntington's disease cannot be cured and is degenerative, the affected patients must increasingly rely on others for assistance.

There are approximately 30,000 patients with overt Huntington's in the US. Estimates of the number who have the mutation but have not yet become symptomatic range up to 200,000. Today, estimates of the overall costs attributable to HD in the US are in the $2.5 billion range annually. (Neuroperspective 256/257, March/April 2017, p3)

Forward Looking Statements
Information set forth in this press release contains forward-looking statements, which involve a number of risks and uncertainties. The forward-looking statements contained herein represent the judgment of Probiodrug AG as of the date of this press release. Such forward-looking statements are neither promises nor guarantees, but are subject to a variety of risks and uncertainties, many of which are beyond our control, and which could cause actual results to differ materially from those contemplated in these forward-looking statements. We expressly disclaim any obligation or undertaking to release publicly any updates or revisions to any such statements to reflect any change in our expectations or any change in events, conditions or circumstances on which any such statement is based.