Unique binding mode of PBD-C06 to pGlu-Abeta peptides identified

Probiodrug publishes mechanism of target binding for its lead anti-pGlu-Abeta monoclonal antibody PBD-C06

HALLE (SAALE), Germany, 29 August 2017 - Probiodrug AG (Euronext Amsterdam: PBD), a biopharmaceutical company developing novel therapeutic solutions to treat Alzheimer's disease (AD), announced today that results from a collaboration between Probiodrug, the Fraunhofer Institute for Cell Therapy and Immunology (IZI), Department of Drug Design and Target Validation (IZI-MWT, HalleS.) and a team led by Dr. Milton T. Stubbs at the Martin-Luther-Universität Halle-Wittenberg (MLU) were published in the Journal of Biological Chemistry (*Piechotta et al,. J. Biol. Chem. 2017 292:12713*). In these studies, the binding characteristics of a murine version of Probiodrug's lead therapeutic antibody (PBD-C06) against its designated target pGlu-Abeta was analyzed at the molecular level applying co-crystallization and X-ray structure analysis. The studies revealed a unique binding mode of PBD-C06 to pGlu-Abeta peptides, which are believed to catalyze the seeding of synapto/neurotoxic Abeta oligomers, a key culprit in the pathology of AD. Furthermore, the data provide a rationale for the high target specificity of PBD-C06 and suggest low binding to off-targets, such as unmodified, less toxic Abeta peptides.

These insights reveal a differentiating biological property of PBD-C06 compared to other anti-Abeta antibodies and further support the development of PBD-C06. PBD-C06 is a humanized and deimmunized monoclonal antibody selected based on an optimal safety and pharmacological profile. CMC development for PBD-C06 has been initiated.

Prof. Dr. Milton T. Stubbs from the Institute for Biochemistry und Biotechnology at the MLU commented: "The results explain why the unique structure of pGlu-Abeta can facilitate enhanced aggregation of Abeta oligomers. Specific targeting of pGlu-Abeta with antibodies could eliminate neurotoxic pGlu-Abeta containing oligomers in the brain. PBD-C06 thus has a promising therapeutic potential".

Dr. Inge Lues, PBD's Chief Development Officer, added: "These results provide differentiating insights into the biology of PBD-C06, allowing a better understanding of how PBD-C06 interacts with its target at the molecular level. Importantly, they support the nomination of PBD-C06 as an optimal candidate for further development.

Probiodrug is progressing two complementary strategies for tackling pGlu-Abeta with two candidates in development: PQ912, a small molecule inhibitor of Glutaminyl Cyclase, now in Phase 2, and PBD-C06, a pGlu-Abeta-specific monoclonal antibody in preclinical stage.

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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 (AD). Probiodrug has identified a new therapeutic concept linked to disease initiation and progression. The development approaches are targeting a key neuro/synaptotoxic component of the pathology, pyroglutamate-Abeta (pGlu-Abeta, N3pG) as a therapeutic strategy.

Probiodrug's lead product candidate, PQ912, is a highly specific and potent inhibitor of Glutaminyl Cyclase (QC), which has shown therapeutic effects in AD animal models. A Phase 1 study in healthy young and elderly volunteers revealed a dose dependent exposure and showed good safety and tolerability up to the highest dose showing >90% target occupancy in the spinal fluid. In June 2017 Probiodrug announced top-line data of the Phase 2a SAPHIR trial of its lead candidate (Probiodrug announces encouraging results of the Phase 2a SAPHIR Study). The positive effects seen on secondary exploratory efficacy markers are strongly supporting (a) the hypothesis of pGlu-Abeta being synaptotoxic and (b) the therapeutic concept pursued by Probiodrug. The study revealed a positive benefit risk ratio of PQ912 and provides important guidance how to move forward in the development of PQ912 as a disease-modifying drug for AD. Altogether, the results make the program highly attractive for further development.

Complementary to the small molecule PQ912 inhibiting the formation of the synaptotoxic agent pGlu-Abeta, the company is developing PBD-C06, an anti-pGlu-Abeta-specific monoclonal antibody.
The Company has medical use and composition of matter patents related to the inhibition of QC and anti-pGlu-Abeta-specific monoclonal antibodies, and has, in the Company's view, a leading position in this field of research.

Founded in 1997 by Hans-Ulrich Demuth and Konrad Glund, 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 aims to become a leading company in the development of AD treatments and to thereby provide a better life for Alzheimer's disease patients.

www.probiodrug.de

About Alzheimer's disease
Alzheimer's disease is a neurological disorder, which is the most common form of dementia, and ultimately leads to death. Because Alzheimer's disease cannot be cured and is degenerative, the affected patients must increasingly rely on others for assistance. Today, 47 million people live with dementia worldwide, and this number is projected to treble to more than 131 million by 2050, as populations age.

Dementia also has a huge economic impact. Alzheimer's has an estimated, global societal cost of US$ 818 billion, and it will become a trillion dollar disease by 2018. (World Alzheimer Report 2016).

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.