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HALLE (SAALE), Germany, 11 June 2017 - Probiodrug AG (Euronext Amsterdam: PBD), a biopharmaceutical company developing novel therapeutic solutions to treat Alzheimer's disease (AD), today announced first line results of its Phase 2a SAPHIR study in early AD patients.

The SAPHIR study is the first clinical trial to investigate the Glutaminylcyclase (QC) inhibitor PQ912 in patients with early AD over a treatment period of 12 weeks. The highest dose of 800mg bid PQ912 used in the Phase 1 multiple dose study and showing a very high target occupancy was compared to placebo to identify early efficacy and safety signals to optimally plan future long-term dose ranging studies.

The primary objective of the SAPHIR study was to investigate the safety and the tolerability of PQ912. Secondary objectives were to assess early effects of PQ912 on the exploratory endpoints NTB, EEG, cerebro-spinal fluid (CSF) biomarkers related to the QC-inhibition (mechanism of action) and to the AD pathology.

Methodology: The SAPHIR study is a double-blind, placebo controlled randomised study carried out in 7 European countries at 21 study sites in treatment naïve patients with early AD disease. The statistical analysis of the endpoints was based on two-sided tests with a significance level of alpha 0.05 and not corrected for multiplicity. Results presented in this press release are for the Intention to treat (ITT) population based on a 'complete case' analysis.

Results: A total of 120 patients were randomised in the SAPHIR study, 60 to the placebo arm and 60 to PQ912 arm. Treatment arms were well balanced with respect to age, gender, disease severity and APOE4 status. The mean MMSE (Mini-Mental State Examination) score at baseline was 25.5 (min-max 21-30).

Safety and tolerability results (primary objective): There were no statistically significant differences of PQ912 vs placebo between the number of patients experiencing an adverse event (PQ912 n=49, placebo n=45) or the number of patients with a serious adverse event (PQ912 n=8; placebo n=5). Patients in the treatment arm did show a significantly higher discontinuation rate due to SAE or grade 3 adverse events compared to patients in the placebo arm (PQ912 n=6; placebo n=0, p=0.027) and the total number of patients non-adherent to randomised treatment for any reason was higher in the treatment arm (PQ912 n=26; placebo n= 2; $p<0.01$). Skin and gastrointestinal organ system related adverse events were observed in a higher frequency in the PQ912 arm compared to placebo and occurred in the majority in the first half of the treatment period. Dose reductions prescribed by the investigator were identical in the treatment and the placebo arm (both n=5).

Results of the secondary exploratory endpoints:
Molecular biomarkers in the CSF: CSF analyses showed a highly significant QC inhibition (p=0.001), corresponding to a calculated target occupancy of 92% (median), which was achieved

in patients with last drug intake within 24 hours before CSF sampling. A decrease in pGlu-Abeta oligomers in the CSF was observed in the treatment arm whereas pGlu-Abeta oligomers increased in the placebo arm. This directional change demonstrates, together with the significant QC-enzyme inhibition, a strong and robust target engagement.

There was a strong trend for reduction in the level of neurogranin, a marker of synaptic dysfunction in the ITT population in the treatment arm compared to placebo (p=0.1), which became significant if 3 patients starting prohibited concomitant medication during the study were excluded (p=0.046, a 5% absolute reduction of baseline in neurogranin observed in the treatment arm). There was also a strong trend in the mean reduction of YKL 40, a biomarker of inflammation, in the PQ912 arm compared to placebo (p= 0.07, 5% absolute reduction of baseline-level in the treatment arm).

EEG: The analysis of the EEG power spectra showed a significant reduction of theta power in the PQ912 arm compared to placebo (p=0.002). Slow wave theta activity is reported to increase with the onset and progression of AD. Further analysis of functional connectivity and EEG network parameters is pending.

Neuropsychological test battery (NTB): Patients in the placebo arm showed overall a stable performance with no or marginal change between baseline and week 12. Performance on the 'One Card Back Test', an assessment of working memory showed a statistically significant effect in favour of PQ912 (p=0.05, Cohen's d = 0.24) while the 'Detection Test' an assessment of attention, also showed a meaningful improvement under PQ912 (Cohen's d=0.20) although not sufficient to reach statistical significance. Performance on the five other cognitive assessments, as well as on their aggregate scores, were not influenced by treatment with PQ912 for 12 weeks (Cohen`s d < 0.2).

Additional analysis comprising all endpoints, further CSF biomarker and subpopulations will continue during the next several months and the full results of the SAPHIR study are intended to be reported at scientific congresses and published in scientific journals.

Philip Scheltens, Director of the Alzheimer Center VU University Medical Center Amsterdam, and Principal Investigator of the SAPHIR study commented: The population studied was very representative of patients with early AD. The primary objective of the SAPHIR study was safety and tolerance. Although differences between treatment arms were observed we are confident that the drug is safe and well tolerated in the AD population. We set out to detect small signals on the various sensitive secondary exploratory outcome measures in a relatively short time frame and were happy to see very strong target engagement, significant effects on a working memory task and EEG theta power and encouraging results in the right direction on synaptic and inflammatory CSF markers. These results point to a direct effect on pGlu-Abeta with beneficial effects on synaptic function, even in such a short treatment period.

Inge Lues, Chief Development Officer at Probiodrug commented: We are very positively encouraged by the outcome of the SAPHIR trial and look forward to the results of further analyses. The results observed support our hypothesis of pGlu-Abeta being synaptotoxic. The SAPHIR study was designed to guide the future development of PQ912 in AD. In this first in-patient study, we used a high dose achieving about 90% QC occupancy to meet two goals: to

get a first picture of frequency and types of safety and tolerability events and at the same time to test for early signals of efficacy in a relatively short treatment period of 12 weeks.

The results will guide the design of future studies of PQ912 and support the use of lower doses of PQ912 still reaching relevant target occupancy of the QC enzyme, as well as the option to introduce a titration phase for the 800 mg bid dose. We are encouraged by having observed early indicators of response to PQ912 in the CSF, the EEG and the NTB. The results we have today in our hand are tremendously useful to deliver a tailored future development program.

CONFERENCE CALL
Probiodrug will host a conference call open to the public Monday, June 12th, at 15:00 Central European Summer Time (CEST). The conference will be held in English. To participate in the conference call, please call one of the following numbers ten minutes prior to commencement:

Please dial one of the following access numbers,
then enter the PIN Code: **17625824#**

Country	Toll-Free	Toll/Local
Austria	0800 301 051 (EN) 0800 301 052 (DE)	+43 192 804 92 (EN) +43 192 804 94 (DE)
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A Question and Answer session will follow the presentation of results.

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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 was evaluated 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.

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.