Probiodrug reports full year 2015 financial results

Phase 2a study of novel treatment for Alzheimer's disease initiated
Phase 1 PQ912 data, a first in class Glutaminyl Cyclase (QC) inhibitor for the treatment of AD, prominently published
Private Placement completed raising EUR 13.5 million

HALLE/SAALE, Germany, 15 March 2016 Probiodrug AG (Euronext Amsterdam: PBD), a biopharmaceutical company developing novel therapeutic solutions to treat Alzheimer's disease (AD), today announced its financial results for the twelve-month period ending 31 December 2015 prepared in accordance with German GAAP ("HGB") and, on a voluntary basis, in accordance with IFRS as endorsed by the European Union. The Annual Reports are available on the company website (http://www.probiodrug.de/investors/reports-and-presentations/).

KEY HIGHLIGHTS

- Phase 2a study of novel treatment for Alzheimer's disease, the SAPHIR trial, initiated
- Phase 1 PQ912 data, a first in class Glutaminyl Cyclase (QC) inhibitor for the treatment of AD, published in *Alzheimer's & Dementia: Translational Research & Clinical Interventions*
- Manufacturing process for PBD-C06, Probiodrug's anti-pGlu-Abeta targeting antibody, initiated
- Additional data on Glutaminyl Cyclases (QCs) in Alzheimer's disease published in *Acta Neuropathologica*
- Data on Probiodrug's anti-pGlu-Abeta monoclonal antibody presented at the 12th AD/PD™ 2015, Nice, France and at Neuroscience 2015, the 45th annual meeting of the Society for Neuroscience (SfN) in Chicago, USA
- Key patents on Glutaminyl Cyclase (QC) inhibition for the treatment of AD and for Probiodrug's antibody program targeting pGlu-Abeta granted in key territories
- Several high-caliber academic collaborations continued or initiated, e.g. with the Brigham and Women's Hospital, affiliated with Harvard Medical School and with University of Leipzig, Paul Flechsig Institute for Brain Research
- Winner of the European Mediscience Award 2015 for Best Technology
- Annual General Meeting held in June 2015, all resolutions proposed by Management and Supervisory Board approved
- New members of the Supervisory Board with distinguished industry expertise appointed
- Private placement raising EUR 13.5 million closed in November 2015
- Cash and cash equivalents of EUR 21.4 million as of 31 December 2015
- Net loss of EUR 13.5 million compared with EUR 11.4 million in 2014 - in line with company expectations

POST PERIOD HIGHLIGHTS

There were no significant events subsequent to the reporting period.

CONFERENCE CALL

Probiodrug will host a conference call open to the public today, March 15th, at 15:00 Central European Time (CET); the presentation will also be posted to the website. 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: **26484450#**

Country	Toll-Free	Toll/Local
Austria	0800301051 (EN) 0800301052 (DE)	+4319280492 (EN) +4319280494 (DE)
Belgium		+32 11500307
Canada (Toronto)		+1 4162164186
Finland	0800523161	+35 8981710496
France	0805110449	+33 170750705
Germany (Frankfurt)	08006270715	+49 69222229043 (EN) +49 69222229044 (DE)
Luxemburg	080040184	+35 227300157
Netherlands		+31 107137273
Sweden	0200883629	+46 850556469
Switzerland	0800005200 (EN) 0800005205 (DE)	+41 225805970 (EN) +41 225805971 (DE)
UK		+44 2030092452
USA		+1 8554027766

A Question and Answer session will follow the presentation of results.

Commenting on the results, Dr Konrad Glund, Chief Executive Officer of Probiodrug, said: "In its first year as a listed company, Probiodrug successfully continued to progress its innovative pGlu-Abeta therapeutic approach and reached important milestones. The start of the Phase 2 "SAPHIR" study of our lead product PQ912 for treating Alzheimer's disease, the initiation of the manufacturing process for our anti-pGlu-Abeta-antibody PBD-C06 and the publication of crucial data of our programs represent significant accomplishments. Our first private placement as a public company was very successful - with the money raised we also welcomed new bluechip investors. The achievements of 2015 would not have been possible without the support, commitment and trust of our employees, advisors, partners and shareholders - many thanks to all of you for the achievements of 2015."

KEY FIGURES (ACCORDING TO IFRS)

in EUR k, unless otherwise stated	2015	2014
Earnings, Financial and Net Assets Position		
Revenues	0	0
Operating loss	-13,393	-11,267
Net loss for the period	-13,505	-11,437
Equity (end of the year)	16,133	15,971
Equity ratio (end of the year) (in %)	73.8 %	74.4 %
Balance sheet total (end of the year)	21,866	21,480
Cash flows used in operating activities (year)	-12,147	-10,589
Cash flows used in operating activities (average)	-1,012	-882
Cash flows provided by financing activities (net)	12,598	25,762

Cash and cash equivalents at the end of period	21,361	20,920

Personnel		
Total number of employees (incl. Board of management) (end of the year)	16	12
Average number of employees (incl. Board of management)	15.8	12.0

Probiodrug-Share		
Loss per share (basic and diluted) (in EUR)	-1.97	-2.35
Number of shares issued (end of the year)	7,442	6,766

DETAILS OF THE FINANCIAL RESULTS (ACCORDING TO IFRS)

Net loss
The net loss amounts to EUR 13,505k (2014: EUR 11,437k), thereof EUR 13,393k (2014: EUR 11,267k) are to be attributed to the operating loss and EUR 112k (2014: EUR 170k) to the financial loss, all in line with the expectations of Probiodrug. The operating loss is primarily driven by the research and development expenses amounting to EUR 10,158k (2014: EUR 8,008k) and to a lesser degree by the general and administrative expenses of EUR 3,279k (2014: EUR 3,319k). The increase in research and development expenses reflects primarily an increase in the purchased services within the scope of the phase 2 clinical study.

Equity
The equity amounts to EUR 16,133k (2014: EUR 15,971k), corresponding to an equity ratio of 73.8%.

Cash
Cash and cash equivalents were EUR 21,361k, compared with EUR 20,920k as at the end of 2014. As a result of the capital increase in November 2015, net cash proceeds of EUR 12,598k were realised.

Noncurrent/ current liabilities
The noncurrent liabilities amount to EUR 822k (2014: EUR 929k), consisting completely of the net commitment (defined benefit liability) of the pension commitments (defined benefit obligations) of EUR 1,522k (2014: EUR 1,564k). The current liabilities amount to EUR 4,911k (2014: EUR 4,580k), consisting primarily of the tax liabilities of EUR 2,641k (comprising the Company's payment obligations as a result of the tax audit for the period 2002 through 2005 including interest for late payment) and trade payables. The trade payables amounted to EUR 1,629k (2014: EUR 1,036k) resulting from of the ordinary course of business. They have a remaining term of up to one year.

OPERATIONAL REVIEW

Pipeline update
Probiodrug's development approach targets pyroglutamate-Abeta (pGlu-Abeta, also called N3pG Abeta) as a therapeutic strategy to fight Alzheimer's disease. This modified Abeta is considered to be linked with disease initiation and progression by seeding the formation of soluble neurotoxic amyloid oligomers. Probiodrug is developing proprietary product

candidates to target toxic pGlu-Abeta via two modes of action: by (i) inhibiting the production of pGlu-Abeta; and (ii) clearing existing pGlu-Abeta from the brain.

Probiodrug's innovative approach is based on the development of specific inhibitors for the enzyme Glutaminyl Cyclase (QC), which is instrumental in the creation of pGlu-Abeta. In addition, the company is developing a monoclonal antibody targeting pGlu-Abeta to enhance its clearance.

To date, Probiodrug's pipeline consists of two small molecule inhibitors of the QC-enzyme, PQ912 and PQ1565, and a monoclonal antibody, PBD-C06, targeting pGlu-Abeta.

PQ912
In 2015, Probiodrug initiated a Phase 2a study, the "SAPHIR" study, of its lead product candidate PQ912. In a preceding Phase 1 study with healthy young and elderly volunteers, PQ912 was shown to be safe and well tolerated and revealed high QC-inhibition.

PQ912 is the first QC-inhibitor being tested in patients. The Phase 2a study is a randomized, double-blind multi-center study which plans to enrol a total of 110 patients with early stage Alzheimer's disease. The study is led by internationally renowned experts in AD in six European countries at about 18 sites, with the Alzheimer Center, VU Medical Center (VUmc), Amsterdam being the lead center. The primary endpoint of the trial is the safety and tolerability of PQ912 compared with placebo over a three-month treatment period. Additionally, a set of exploratory read-outs comprising cognitive tests, functional assessments by EEG and functional MRI and new molecular biomarkers in CSF will be used to evaluate the compound's effect on the pathology of the disease.
Patient enrolment started in March 2015.

SAPHIR is now in full swing. To respond to several challenges such as high competition in getting access to treatment naïve patients we have taken various measures, in particular adding more sites in various countries while keeping quality at high level. Additional sites are activated, all are highly motivated and enrolling. Primary endpoint data are expected to be available end of 2016, while the full picture of all exploratory results are expected to be finally evaluated about 3 to 4 months thereafter.

PBD-C06
PBD-C06 is a monoclonal antibody, currently in preclinical stage. PBD-C06 targets pGlu-Abeta, aiming to selectively clear the brain of pGlu-Abeta while leaving non-toxic forms of Abeta untouched. PBD-C06 has been successfully humanized and also de-immunized to avoid detection by the patient's endogenous immune system. For the first time for an anti-pGlu-Abeta approach PBD-C06 has not only shown the ability to reduce Abeta/plaques but also to significantly improve cognitive deficits in aged Alzheimer's mice. Moreover, no evidence was found of increased microhemorrhages after treatment with PBD-C06.

The manufacturing process of this molecule started in October 2015.

PQ1565
PQ1565 is a QC-inhibitor, currently in preclinical stage. The product candidate has shown attractive drug-like properties in preclinical studies. The GMP process for this molecule is being implemented.

Publications/ Presentations
In March 2015, additional data on Glutaminyl Cyclases (QCs) in its relation to Alzheimer's disease was published in the journal *Acta Neuropathologica 2015 Apr, 129(4), Pages 565-83*. The study provides further evidence of the strong correlation between QCs and AD pathology in human brain biopsies underlining QC-inhibition as a therapeutic approach.

Also in March 2015, Probiodrug presented the poster "Anti-pGlu-3 Abeta mab ig isotype affects plaque clearance" on its specific pGlu-Abeta mouse antibody 17/1 at the 12th International Conference on Alzheimer's and Parkinson's Diseases and Related Neurological Disorders (AD/PDTM 2015) in Nice, France. The data resulted from a collaboration between Probiodrug and the research team led by Professor Cynthia Lemere from the Center for Neurologic Diseases at the Brigham and Women's Hospital and Harvard Medical School, Boston, MA. The study addressed specifically the effect of the antibody's Ig isotype on microglia-mediated Abeta plaque clearance in an in-vitro phagocytosis assay using brain tissues from 20-month-old APP dE9 mice. It was found that the mouse pGlu-Abeta IgG2a antibody was the most efficient, followed by the mutated IgG2a form while the IgG1 was the least effective in clearing Abeta plaques.

In October 2015, Probiodrug during an oral presentation entitled "Preclinical in vivo Effects of an anti-PyroGlu-3 Abeta Antibody" presented data on its specific anti pGlu-Abeta monoclonal antibody at Neuroscience 2015, the 45th annual meeting of the Society for Neuroscience (SfN) in Chicago, USA. The data presented resulted from a collaboration between Probiodrug and the research team led by Associate Professor Cynthia Lemere from the Center for Neurologic Diseases at the Brigham and Women's Hospital and Harvard Medical School, Boston, USA. This was the first report that an anti-pGlu-Abeta antibody approach not only reduced Abeta/plaques but also significantly improved cognitive deficits in aged Alzheimer's mice. Moreover no evidence was found for increased microhemorrhages after treatment.

In December 2015, the data from an extensive phase 1 study with PQ912, Probiodrug's lead QC inhibitor for the treatment of AD, was published in *Alzheimer's & Dementia: Translational Research & Clinical Interventions, Volume 1, Issue 3 Pages 182-195*. PQ912 is a first-in-class competitive inhibitor of Glutaminyl Cyclase, essential for the formation of pyroglutamate-Amyloid-beta (pGlu-Abeta). PGlu-Abeta seeds Abeta oligomers which, due to their hypertoxicity, are regarded as the key culprits behind AD. In the published data, over 200 young and elderly healthy volunteers were included in a single-and multiple-ascending dose design. PQ912 was found to be safe and well tolerated; the maximum tolerated dose was not reached. The study also evaluated pharmacokinetic parameters of the compound as well as the extent of QC inhibition in the cerebral spinal fluid (CSF), which is a measure for QC-inhibition in the brain. Based on the data obtained in CSF, the dose dependent target inhibition could be reliably determined and was used for dose selection in the current phase 2a trial. The study was conducted with Covance in Switzerland and the UK.

Patents

In 2015, Probiodrug's IP position was further strengthened by important patent applications being granted. These include:

- Patent no. US 9,156,907 and JP 5,828,762, covering method as well as composition of matter claims for Probiodrug's antibody program targeting pGlu-Abeta, were granted in the US and in Japan, respectively
- Patent nos. JP 5690463, covering the use of QC inhibitors for the treatment of Alzheimer's disease, JP 5688745, covering a chemical space of heterocyclic QC inhibitors, and Patent no. JP2007-508347A, covering the use of QC inhibitors for the treatment of Familial British Dementia and Familial Danish Dementia, were granted in Japan
- Patent no. JP 5677297, covering Glutaminyl Cyclase as a diagnostic/prognostic indicator for neurodegenerative diseases, was granted in Japan.

CORPORATE REVIEW

Execution of a private placement
On November, 5, 2015 Probiodrug announced an increase in its share capital from EUR 6,765,898 to EUR 7,442,487, by issuing 676,589 new shares with a notional par value of EUR 1.00 per share generating gross proceeds of EUR 13.5 million. The order book was well covered based on strong demand from European and US investors. The new shares were placed with selected qualified institutional investors at a price of EUR 20 per share. The issued shares represented approximately 10% of the Company's issued share capital at the time of the placing.

Supervisory Board
The general shareholder meeting on June, 10, 2015, elected Ms Charlotte Lohmann and Mr Kees Been, two industry experts with an extensive background in drug development and public markets respectively, as new members of the Supervisory Board. Dr Hubert Birner and Prof Georg Frank, who contributed significantly in establishing Probiodrug as a successful public biopharmaceutical company, did not apply for a new term. Probiodrug would like to thank them again for their valuable contribution to the growth of the company.

European Mediscience Award for Best Technology 2015
In June 2015, Probiodrug won the 2015 European Mediscience Award for Best Technology 2015. This Award is presented for an innovative technology that is well funded and capable of significant commercial success. The jury believed that Probiodrug was the clear winner in this category, with its innovative and differentiated approach to treating Alzheimer's disease and the Company's recent achievements.

OUTLOOK

The mid-term focus of Probiodrug's business activities can be summarised as follows:

- Continue the clinical development of PQ912 in particular generate initial patient study data and start long-term treatment,
- Completion of the production development of PBD-C06 and conduction of regulatory tox as preparation for first in man study,
- Continuation of the development of PQ 1565,
- Further scientific analysis of potential additional indications for the use of QC inhibitors,
- Continuation of work to better understand the pGlu Abeta mediated pathologies,
- Further increasing visibility and acceptance as an important prerequisite for obtaining additional capital as well as for an industrial transaction,
- Further strengthening Probiodrug's financial resources.

As a result of the additional costs being incurred for development activities, the Company estimates a net loss for the financial year 2016, which may be in excess of that incurred in 2015.

ANNUAL FINANCIAL REPORT 2015

Probiodrug has finalized its financial statements for the year ended 31 December 2015 according to German GAAP ("HGB") and IFRS. The auditor KPMG has issued an unqualified auditors report for both statements. The reports are available on the company website (http://www.probiodrug.de/investors/reports-and-presentations/).

FINANCIAL CALENDAR

12 May 2016	Interim Management Statement Q1 2016
19 May 2016	Annual General Meeting 2016
30 August 2016	Interim Report, Half Year Results 2016
10 November 2016	Interim Management Statement Q3 2016

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Notes to Editors:

About Probiodrug AG
Headquartered in Halle, 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.
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, over 46 million people worldwide currently live with the condition and this number is expected

to increase to 132 million by 2050. Alzheimer's also has an estimated, global societal cost of US$ 818 billion (World Alzheimer Report 2015).

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.