

Probiodrug AG reports First Quarter 2017 Business Update

HALLE (SAALE), Germany, 12 May 2017 - Probiodrug AG (Euronext Amsterdam: PBD), a biopharmaceutical company developing novel therapeutic solutions to treat Alzheimer's disease (AD), today announces its first quarter business update for the period ending 31 March 2017, in the form of an interim management report.

The interim management report for the first quarter 2017 is available for download on the company website (<http://www.probiodrug.de/investors/reports-and-presentations/>).

OPERATIONAL HIGHLIGHTS

- New, promising results from pharmacological studies with PQ912 and PBD-C06 in AD animal models and an evaluation of new biomarkers in cerebrospinal fluid (CSF) from AD patients presented
- Expenditures and corresponding cash position in line with management expectations
- As of 31 March 2017, Probiodrug held EUR 18.7 million in cash and cash equivalents

POST PERIOD HIGHLIGHTS

- Last Patient Last Visit (LPLV) reached in the SAPHIR Study
- The Glutaminyi Cyclase (QC) inhibitor PQ912 demonstrates beneficial effects in a preclinical Huntington's disease model

Commenting on the first quarter, Dr Konrad Glund, Chief Executive Officer of Probiodrug, said:

"In the first quarter of 2017 we successfully continued to execute on our corporate strategy. The Last Patient Last Visit (LPLV) represents an important step towards the conclusion of our first patient trial with PQ912. The promising data obtained with PQ912 and PBD-C06 in AD animal models further demonstrates the potential of the pGlu-Abeta treatment concept. Positive treatment results with PQ912 in a Huntington's disease animal model provide support for evaluating PQ912 in patients with Huntington's disease (HD) in the future, another neurological disease based on misfolded proteins."

OPERATIONAL REVIEW

Pipeline update

Probiodrug's therapeutic 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 Glutaminyi 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

Probiodrug is running a Phase 2a trial, 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 seven European countries at 21 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.

In this study Mini-Mental State Examination (MMSE) and the Cogstate neuro-psychological test battery (NTB) are monitored blindly every 30 patients to ensure consistency and reliability of ratings. First blinded results at baseline show that the mean MMSE scores from the 120 randomised patients is 25.3, the mean age is 73 years and gender distribution is 64 female and 56 male. Current results indicate a low variability and therefore the high quality of the assessments being used.

Recruitment has been completed in mid-December 2016. A total of 120 patients have been randomised, surpassing the 110 patients planned in the study protocol. Full unblinded results of the SAPHIR study are expected in the second quarter of 2017.

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 development of the manufacturing process of this molecule is running.

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.

The next development steps are in preparation and respective decisions would be made in connection with the readout of the SAPHIR trial.

Operational Update

New promising results from pharmacological studies with PQ912 and PBD-C06 in AD animal models and an evaluation of new biomarkers in cerebrospinal fluid (CSF) from AD patients presented

Three updates on the advancement of its product candidates and the results of a Biomarker research collaboration have been presented at the 13th International Conference on Alzheimer's and Parkinson's Diseases (AD/PD™ 2017), Vienna, Austria. The conference took place from 29th March to 2nd April 2017.

| Program | Presentations |
|---|---|
| QC- enzyme/CSF Biomarker Collaborator: VUmed Center Amsterdam, The Netherlands | <ul style="list-style-type: none">• Cerebrospinal fluid glutaminy cyclase (QC) activity correlates with Alzheimer's disease biomarkers and inflammation molecules in AD patients• <i>In CSF from AD patients a high correlation of QC activity with AD related biomarkers and inflammatory molecules was found</i> |

QC-Inhibitor PQ912
Collaborator:
Fraunhofer
Institute, Halle
(Saale), Germany

- Glutaminyl cyclase inhibition by PQ912 in transgenic mice with Alzheimer-like pathology-translation to clinics
- *Based on PKPD analysis in animal studies, a 50% inhibition of QC activity in the brain leads to a robust effect - an important translational guidance for therapeutic dosing in clinical studies*

Anti-pGlu-Abeta
MAB/QC-I
Collaborator:
Harvard, BWH,
Boston, USA

- Murine anti-pyroglutamate-3 Abeta MAB, 07/2a, spares cognition, reduces plaques, and, in combination with glutaminyl cyclase inhibitor PQ912, further improves efficacy
- *Selective targeting of pGlu-Abeta with an IgG2a isotype of an anti-pyroglutamate-3-Abeta Antibody in tg mice is effective in lowering plaque pathology and improving cognition. A combination of a QC-inhibitor and a pGlu-Abeta specific antibody showed superior efficacy compared to the single entities*

CORPORATE REVIEW

Financials

The first quarter of 2017 showed an increase of research and development expenses to EUR 2,268k compared to EUR 1,974k in the first quarter of 2016, reflecting mainly the costs for the Phase 2 trial (SAPHIR Study) of PQ912. General and administrative expenses amounted to EUR 507k compared to EUR 597k in the first quarter of 2016, reflecting more intrayear shifts than actual savings. In the first quarter 2017 the Company has not generated any revenues, also in line with the corporate planning. Correspondingly, the comprehensive loss of the reporting period was EUR 2,798k, compared to EUR 2,596k in the first quarter of 2016.

All results are in line with management expectations.

Probiodrug held EUR 18.7 million in cash and cash equivalents as of 31 March 2017.

POST PERIOD UPDATE

Last Patient Last Visit (LPLV) accomplished in the SAPHIR Study

On 07 April 2017 Probiodrug announced that the Last Patient's Last Visit (LPLV) occurred on 05 April 2017 in the currently running Phase 2a SAPHIR study investigating the QC-inhibitor PQ912.

PQ912 demonstrates beneficial effects in a preclinical Huntington's disease model

On 10 April 2017 Probiodrug announced results of a preclinical study targeting Glutaminyl Cyclases (QCs) in Huntington's disease (HD). The results have been 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 poly-glutamine amino acid sequence is expanded in a protein called huntingtin (HTT). There is currently no disease modifying therapy for this condition.

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.

Data were generated in collaboration with Stephan von Hörsten of the University Hospital Erlangen, part of Friedrich-Alexander-University (FAU), Erlangen, Germany.

Invitation to Probiodrug's Ordinary General Meeting of Shareholders on 13 June 2017

On 03 May 2017 Probiodrug invited its shareholders to its ordinary general meeting of shareholders to be held on Tuesday, 13 June 2017 at 11:00 am (CEST), at the Mercure Hotel MOA Berlin, Stephanstraße 41, 10559 Berlin, Germany. The relevant documents can be found at <http://www.probiodrug.de/investors/annual-shareholders-meeting-2017/>.

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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-Aβeta (pGlu-Aβeta) 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-Aβeta- 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 Glutaminyi 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.

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.