Third Quarter 2017 Business Update

HALLE (SAALE), Germany, 30 November 2017 – Probiodrug AG (Euronext Amsterdam: PBD), a biopharmaceutical company developing novel therapeutic solutions to treat Alzheimer's disease (AD), today announces its third quarter business update for the period ending 30 September 2017, in the form of an interim management report.

OPERATIONAL HIGHLIGHTS

- Unique binding mode of Probiodrug`s anti-pGlu-Abeta antibody PBD-C06 published in a peer reviewed journal
- Expenditures and corresponding cash position in line with management expectations
- As of 30 September 2017, Probiodrug held EUR 11.70 million in cash and cash equivalents, providing according to present projections a cash reach through 2018

POST PERIOD HIGHLIGHTS

- Phase 2b core program of PQ912 initiated and details of further strategy outlined
- Data of Probiodrug`s Phase 2a SAPHIR Study presented in November 2017 at CTAD in Boston, USA - the world congress for clinical trial results in AD
- Change at supervisory board

Commenting on the third quarter, Dr Konrad Glund, Chief Executive Officer of Probiodrug, said:
"Probiodrug is strongly engaged and committed to further progress its highly innovative and differentiated concept of targeting a toxic Abeta variant, pGlu-Abeta, for the treatment of AD with PQ912, a first in class small molecule Glutaminyl Cyclase inhibitor in Phase 2, and PBD-C06, a pGlu-Abeta specific monoclonal antibody in advanced preclinical development.

"As for PQ912, results of the phase 2a (SAPHIR) study, provided important guidance for designing a core Phase 2b program consisting of trials planned to be conducted in Europe and the US. The preparation of the European trial has been initiated. In parallel to initiating Phase 2b, we are continuing pharma interactions.

"PBD-C06, our pGlu-Abeta specific monoclonal antibody, has the potential of being a best in class compound. The molecule is designed to bind aggregated pGlu-Abeta with high affinity and specificity while having a reduced potential for side effects and immunogenicity. We recently published a unique binding mode of this antibody to pGlu-Abeta explaining its extraordinary affinity and specificity. Results have been obtained using crystal structure analysis within a collaboration of Probiodrug with academic groups."

OPERATIONAL REVIEW

probiodrug

Pipeline update

Probiodrug`s therapeutic approach targets pyroglutamate-Abeta (pGlu-Abeta, also called N3pG Abeta) as a therapeutic strategy to fight Alzheimer's disease (AD). 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 formation 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's lead product candidate, PQ912, is a highly specific and potent inhibitor of QC, which has shown therapeutic effects in AD-animal models. In a Phase-1-study with healthy young and elderly volunteers, PQ912 was shown to be safe and well tolerated and also revealed a dose dependent QC-inhibition in the CSF, reaching 90% at the highest dose used.

PQ912 is the first QC-inhibitor being tested in patients. The Phase-2a-study, the SAPHIR trial, was a randomized, double-blind multi-center study which enrolled a total of 120 patients with early stage Alzheimer's disease. The study was led by internationally renowned experts in AD in seven European countries at 21 sites, with the Alzheimer Center, VU Medical Center (VUmc), Amsterdam, NL being the lead center. The primary endpoint of the trial was 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 were used to evaluate the compound's effect on the pathology of AD, in particular the effect on synaptic impairment, an early pathological change in the early stages of AD.

The data of the Phase 2a SAPHIR Study were presented by Prof Philipp Scheltens, Principal Investigator of this study, at the CTAD in Boston, USA in November 2017. The presentation was entitled *"Phase 2a study results with the glutaminylcyclase inhibitor PQ912 in early Alzheimer's Disease".*

The SAPHIR trial used a high dose of PQ912 (which showed 90% QC-enzyme inhibition in CSF in Phase-1) in order to find both

- early-on tolerability signs and
- first signals on various sensitive secondary exploratory outcome measures in a relatively short time frame.

With respect to the primary endpoints there were no statistically significant differences of PQ912 vs placebo between the number of patients experiencing an adverse event or a serious adverse event. 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 and the total number of patients non-adherent to randomised treatment for any reason was higher in the treatment arm. 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. With a view on the high dose applied, Probiodrug is confident that with lower doses showing still quite high levels of QC-inhibition and a slower titration scheme the drug will be safe and well tolerated in AD patients.

With respect to the secondary exploratory endpoints PQ912 showed a very strong target engagement (QC inhibition), confirming the finding in Phase 1 in elderly healthy volunteers of more than 90%, significant improvements of one test of working memory (one back test) and a clear trend in detection test (attention domain). At the functional level a very significant positive effect was found on the EEG theta power. Regarding exploratory biomarkers in the spinal fluid, encouraging results in the right direction on synaptic and inflammatory CSF markers were obtained.

In summary, the positive effects 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. The next step is the Phase 2b core program, for which preparation started in October 2017.

This Phase 2b core program will consist of two clinical trials, to be executed in the European Union (EU) and the USA, respectively. The first Phase 2b study is intended to investigate the safety and efficacy of the optimal dose range of PQ912 in early AD patients. This trial will build on the excellent and efficient infrastructure which was established for the Phase 2a SAPHIR study. Moreover, it is based on the valuable results of the SAPHIR study and has been designed with the guidance of international KOLs in the Alzheimer's field. Prof Philip Scheltens, MD PhD, Director of the Alzheimer Center VU University Medical Center Amsterdam, NL will once again serves as Principal Investigator and Chairperson for this study, which is to be conducted in the EU. A second complementary study is currently in the planning phase and is intended to be carried out in the USA and will also be chaired by a highly renowned Principal Investigator.

Probiodrug is also working on potential combination therapies. Here, new positive results with PQ912 and PBD-C06 alone and in combination in AD animal models have been presented at the 13th International Conference on Alzheimer's and Parkinson's Diseases (AD/PDTM 2017), Vienna, Austria, in March 2017.

Probiodrug is exploring potential second indications for its QC inhibitors. PQ912 demonstrated beneficial effects in a preclinical Huntington´s disease (HD) model; the data of this study have been presented at the 12th Annual HD Therapeutics Conference of the CHDI Foundation, Malta, in April 2017. 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 changes, metabolic and neuropathological signs of the disease become visible. 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, the energy metabolism as well as of several mRNA levels coding for HSPs in BACHD mice at 24 weeks of age.

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.

PBD-C06 revealed a unique binding mode, which was published in August 2017 in the Journal of Biological Chemistry (*Piechotta et a,. J. Biol. Chem. 2017 292:12713*).

PQ1565
PQ1565 is a QC-inhibitor, currently in preclinical stage. The product candidate has shown attractive drug-like properties in preclinical studies. The compound is ready for regulatory toxicology studies.

CORPORATE REVIEW

Operational Update

Unique binding mode of PBD-C06 to pGlu-Abeta published in August 2017
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.

The results from a collaboration between Probiodrug, the Fraunhofer Institute for Cell Therapy and Immunology (IZI), Department of Drug Design and Target Validation (IZI-MWT, Halle(S)) 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 August 2017.

Financials
Research and development expenses in the third quarter of 2017 were EUR 1,127k, lower than the corresponding numbers in 2016 (EUR 1,776k) due to the completion of the Phase 2 study (SAPHIR study) of PQ912. General administrative expenses amounted to EUR 526k compared to EUR 588k in the third quarter of 2016, which is in line with the company's expectations. As expected, the company did not generate any revenue in the third quarter of 2017. Overall, the company's loss is EUR 1,656k in the third quarter of 2017, compared to EUR 2,383k in the third quarter of 2016, mainly due to lower research and development expenses.

The corresponding comprehensive loss for the 9-month period from 1 January to 30 September 2017 amounts to EUR 5,962k, which is significantly lower than for the same period of 2016 (EUR 8,427k). The difference of EUR 2,465k is mainly driven by the release of tax provisions (EUR 1,964k) following the agreement with the relevant authorities about the corporate income and trade tax claim for the assessment period 2004.

As of 30 September 2017, Probiodrug held EUR 11.7 million in cash and cash equivalents, providing according to present projections a cash reach through 2018.

All numbers are in line with management expectations.

POST PERIOD UPDATE

Probiodrug provided update regarding its Phase 2b core program of PQ912 and further corporate strategy in October 2017
Probiodrug initiated the preparation of the Phase 2b core program of PQ912 in October 2017. This Phase 2b core program will consist of two clinical trials, to be executed in the European Union (EU) and the USA, respectively.

The first Phase 2b study is intended to investigate the safety and efficacy of the optimal dose range of PQ912 in early AD patients. This trial will build on the excellent and efficient infrastructure which was established for the Phase 2a SAPHIR study. Moreover, it is based on the valuable results of the SAPHIR study and has been designed with the guidance of international KOL`s in the Alzheimer's field. Prof. Philip Scheltens MD PhD, Director of the Alzheimer Center VU University Medical Center Amsterdam, NL will once again serves as Principal Investigator and Chairperson for this study, which is to be conducted in the EU.

A second complementary study is currently in the planning phase and is intended to be carried out in the USA and will also be chaired by a highly renowned Principal Investigator.

Probiodrug is in parallel progressing with its interaction with potential pharma partners to secure one or more transactions around its pipeline.

Prof Philipp Scheltens, Principal Investigator of the Phase 2a SAPHIR Study, presented the data of this study at CTAD 2017 - the world congress for clinical trial results in Alzheimer`s Disease (AD) - in Boston, USA in November 2017
Prof Philip Scheltens, MD, PhD, Principal Investigator of the study, presented during the Late Breaking Oral Communications session at the CTAD in Boston, USA in November 2017. The presentation was entitled "*Phase 2a study results with the glutaminylcyclase inhibitor PQ912 in early Alzheimer's Disease*".

Supervisory Board changes
Mr Kees Been resigned from his board position in November 2017 for personal reasons. The management and supervisory board expressed their gratitude for Kees´ contribution and support in the last two years.

Halle (Saale), 30 November 2017
Management Probiodrug