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# First Quarter 2015 Business Update

**HALLE/SAALE, Germany, 13 May 2015** – Probiodrug AG (Euronext Amsterdam: PBD), a biopharmaceutical company developing novel therapeutic solutions to treat Alzheimer's disease (AD), today announces its interim management report including the first quarter 2015 business update.

# **Operational Highlights**

- Enrolment of first patient in Phase 2a "SAPHIR" study at leading Alzheimer Center in Amsterdam
- Key patents on Glutaminyl Cyclase (QC) inhibition for the treatment of AD granted in Japan
- Additional data on Glutaminyl Cyclases (QCs) in its relation to AD published in Acta Neuropathologica
- Data on Probiodrug's Anti-pGlu-3 Abeta monoclonal Antibody presented at the 12th International Conference on Alzheimer's and Parkinson's Diseases (AD/PDTM 2015), Nice
- Expenditures and corresponding cash position in line with management expectations
- As at March 31st, 2015 Probiodrug held EUR 18.7 million in cash and cash equivalents

#### **OPERATIONAL UPDATE**

## Pipeline update

The development approaches of Probiodrug are targeting pyroglutamate-Abeta (pGlu-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 approaches comprise 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 2014, Probiodrug prepared its lead product candidate PQ912 for a Phase 2a study, the "SAPHIR" study. 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, doubleblind multi-center study, which plans to enrol a total of 110 patients with early stage Alzheimer's disease. Led by internationally renowned experts in AD in so far five European countries at about 14 sites with ongoing activities to further increase the number of sites, the primary endpoint of the trial

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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. First data of the "SAPHIR" study are expected mid-2016.

In March 2015, the first patient was enrolled in the Phase 2a study at the Alzheimer Center, VU Medical Center (VUmc), Amsterdam.

## 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. Probiodrug selected PBD-C06 with a IgG2 backbone for development.

#### PQ1565

PQ1565 is a QC-inhibitor, currently in preclinical stage. The product candidate has shown attractive drug-like properties in preclinical studies. Regulatory toxicology studies are in preparation and production of this molecule is being scaled up.

#### Publications

In January 2015, additional data on Glutaminyl Cyclases (QCs) and its potential role in AD was published in the journal Acta Neuropathologica. The study provides further evidence of the strong correlation between QCs and AD pathology underlining QC-inhibition as a therapeutic approach.

#### Patents

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

- JP 5690463 (Use of inhibitors of Glutaminyl Cyclases for the treatment of Alzheimer's disease)
- JP 5677297 (Glutaminyl Cyclase as a diagnostic/prognostic indicator for neurodegenerative diseases)
- JP 5688745 (Heterocyclic inhibitors of Glutaminyl Cyclase, covering chemical space)

In addition, a Notice of Allowance was released for Japanese patent application no. P2007-508347A (Use of inhibitors of Glutaminyl Cyclases for the treatment of Familial British Dementia and Familial Danish Dementia).

## CORPORATE UPDATE

#### Financials

In the first quarter 2015, the Company has not generated any revenues. The first quarter of 2015 shows an increase of research and development expenses to TEUR 2,528 as compared to TEUR 1,302 in the first quarter of 2014 mainly due to the preparation and initiation of the SAPHIR trial. General and administrative expenses in the first quarter of 2015 show an increase to TEUR 657 as compared to TEUR 391 in the first quarter of 2014 resulting mainly from increased administration costs in the course of addressing post listing requirements, preparation of the first annual shareholders meeting as a public company and costs of the options issued in October/ November 2014. Overall, the comprehensive loss of the Company was TEUR 3,026 in the first quarter of 2015 compared to TEUR



1,717 in the first quarter of 2014. Expenditures for the first quarter 2015 have been in line with management expectations.

As at March 31st, 2015 Probiodrug held EUR 18.7 million in cash and cash equivalents.

# POST Q 1 2015 Update

After March 31, 2015 until the date of this interim management statement, Probiodrug conducted its business in the ordinary course. There were no further special events or topics to be reported.

Halle, 13 May 2015

Management Probiodrug