

## First Quarter 2016 Business Update

**HALLE/SAALE, Germany, 12 May 2016** – 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 2016, in the form of an interim management report.

### OPERATIONAL HIGHLIGHTS

- Key patents for Probiodrug's pGlu-Abeta targeting monoclonal antibody program for the treatment of Alzheimer's disease granted in the US and in Japan
- Probiodrug's pGlu-Abeta approaches presented at 14<sup>th</sup> AAT Symposium on Advances in Alzheimer Therapy in Athens/ Greece
- Mark Booth appointed as Chief Business Officer
- Expenditures and corresponding cash position in line with management expectations
- As of 31 March 2016, Probiodrug held EUR 17.5 million in cash and cash equivalents

### POST PERIOD HIGHLIGHTS

- Probiodrug announced results of the chronic toxicology studies with PQ912, its 'first in class' Glutaminyl Cyclase (QC) inhibitor for the treatment of Alzheimer's disease in April 2016

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

"In the first quarter 2016 we continued to progress our programs, mainly the ongoing SAPHIR study of PQ912 and related activities. The long term toxicology data of PQ912, announced early April 2016, mark an important derisking event for this molecule and provide a sound basis for longer term treatments of AD patients. With that we concluded a successful first quarter 2016."

### 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.

### **CORPORATE REVIEW**

Probiodrug appointed Mark Booth as Chief Business Officer and member of the Management Board. Mr. Booth brings over 30 years of biopharmaceutical experience to Probiodrug.

He most recently served as the Chief Commercial Officer at Orexigen Therapeutics, Inc. where he also played a leadership role in all business development and investor relations activities.

Prior to Orexigen Therapeutics, Inc., Mr. Booth served as the President of Takeda Pharmaceuticals North America (TPNA). Under his leadership TPNA became one of the fastest growing pharmaceutical companies in the U.S. with sales of over \$4 billion. Prior to his role at TPNA, Mr. Booth was the Senior Vice President, General Manager at Immunex Corporation. Previously, Mr.



Booth was at Abbott Laboratories where he held multiple positions, in his last role at Abbott, he held the title of Division Vice President, General Manager for the anti-infective franchise.

Mark Booth holds a BS in Biology from Northern Illinois University and an MBA from Northwestern University Kellogg School of Management.

### **Financials**

The first quarter of 2016 showed a decrease of research and development expenses to EUR 1,974k as compared to EUR 2,528k in the first quarter of 2015, reflecting mainly an intrayear shift of costs for external research and development. General and administrative expenses amounted to EUR 597k compared to EUR 657k in the first quarter of 2015, which is in line with the expectation of the company. In the first quarter 2016 the Company has not generated any revenues, also in line with the corporate planning. Correspondingly, the comprehensive loss of the reporting period was EUR 2,596k, compared to EUR 3,026k in the first quarter of 2015.

All results are in line with management expectations.

Probiodrug held EUR 17.5 million in cash and cash equivalents as of 31 March 2016.

### **POST PERIOD UPDATE**

#### **Results of chronic toxicology studies with PQ912, Probiodrug's 'first in class' Glutaminyl Cyclase (QC) inhibitor for the treatment of Alzheimer's disease announced**

On 04 April 2016 Probiodrug announced the results of the chronic toxicology studies with PQ912. The results showed that the toxicology profile of PQ912 in the 6-month rat and 9-month dog studies was absolutely comparable to the results of the previously available 3-month toxicology studies conducted in the same species. No new findings were observed and the minimal to slight non-adverse or questionable changes seen in both the 1-month – and the 3 month-studies were not aggravated after prolonged treatment, thus providing an excellent basis for a sound preclinical safety assessment. In conclusion, the comfortable safety margin was retained.

Based on these favourable outcomes, Probiodrug is exploring opportunities for longer-term clinical studies in AD, which may be run either as separate trials or as an extension of the SAPHIR trial.

PQ912, Probiodrug's lead product candidate, is a highly specific and potent inhibitor of Glutaminyl Cyclase (QC), which has shown therapeutic benefit in Alzheimer's animal models.

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PQ912 is the first QC-inhibitor being tested in AD 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.

**Invitation to Probiodrug's Ordinary General Meeting of Shareholders on May 19, 2016**

On 05 April 2016 Probiodrug invited its shareholders to its ordinary general meeting of shareholders to be held on Thursday, 19 May 2016 at 11.00 am (CEST), in the Leonardo Royal Hotel Berlin Alexanderplatz, Otto-Braun-Straße 90, 10249 Berlin, Germany. The relevant documents can be found at <http://www.probiodrug.de/investors/annual-shareholders-meeting-2016/>.

**Halle (Saale), 12 May 2016**

**Management Probiodrug**