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Interim Report H1 2016
Reporting period January – June 2016

Halle (Saale), 30 August 2016

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CMO

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Investment highlights

1	**Alzheimer's Disease: major burden, no cure**
2	**Attractive industry landscape**
3	**Clearly differentiated approach**
4	**Focused proprietary pipeline**
5	**Strong IP protection**
6	**Experienced management team and renowned investor base**

- Alzheimer's Disease ("AD") is the most common form of dementia, a devastating neurological disease affecting 46 million people world-wide*
- No cure or long-term beneficial treatment available
- No new drugs approved since 2007**

- After years of "drought" rising interest in AD / neurodegeneration
- Only few major pharma players in the field with clinical programs
- Limited number of innovative approaches available on the biotech side

- Developing a differentiated approach aimed to treat AD
- Building on proprietary know-how of AD biology, taking into account the latest insights in AD drug development

- A novel target in AD: pGlu-Abeta
  - PQ912: small molecule, first of its kind in clinical trials – Phase 2
  - PBD-C06: antibody, complementary mode of action – pre-clinical

- Extensive ownership of IP:
  - Granted composition of matter patents
  - Granted medical use patents

- Established drug development and CNS expertise
- Track record of monetizing cutting-edge science (diabetes/DP4-inhibitor drugs)
- Committed support from leading financial and strategic investors

* World Alzheimer Report 2015 ** FDA

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Longstanding track-record and renowned investor base

Brief history

- 1997: Foundation, pioneered a new class of anti-diabetics (gliptins) – partnerships with Merck & Co, Ferring and Novartis
- 2004: Sold diabetes franchise to OSI Pharmaceuticals – proceeds partially returned to shareholders and partially invested in AD
- 2007 - 2014: Series A and B financings round totalling appr. € 80m with top tier investors
- 2011: Progressed PQ912 in Phase 1 clinical development – first in class in clinical development
- Oct 27 2014: IPO at Euronext/ Amsterdam, raise of € 23.2m
- 2015: Initiation Phase 2 clinical development of PQ912
- Jun 2015: European Mediscience Award for Best Technology of the Year
- Nov 5 2015: Private Placement, raise of € 13.5m

EUROPEAN MEDISCIENCE AWARDS 2015

Major investors (> 3%)

BB BIOTECH
AVIVA INVESTORS
IBG
EDMOND DE ROTHSCHILD INVESTMENT PARTNERS
TVM | Capital
HBM Healthcare Investments
LSP Life Sciences Partners
CFH CFH Beteiligungsgesellschaft
Biogen
J.P.Morgan

Experienced management team

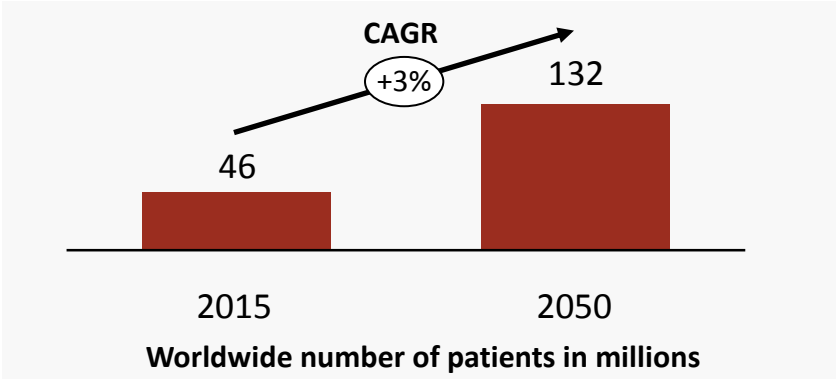
Management team		Biography
Konrad Glund, PhD CEO Co-founder Chairman of the management board		▪ Co-founder of Probiodrug, CEO since 2006 ▪ Led development of DP 4 inhibitors, transactions with Merck, Novartis, OSI and Ferring ▪ COO & VP business development OSI (Prosidion) in 2004-2006 ▪ > 10 deals at OSI, including phase 1 deal with pharma
Hendrik Liebers, PhD CFO Member of the management board		▪ Longstanding track record in venture and private capital, CFH and IBG ▪ Numerous board seats in biotech companies ▪ > 20 financing rounds, M&A transactions, trade sales
Inge Lues, PhD CDO Member of the management board		▪ Advisor to biotech companies and public research institutions ▪ Family office E. Merck KG ▪ EVP member of the Pharma Board, Merck KGaA ▪ Head Global Drug Discovery and Non-Clinical Development; Head, Business Area Team, CNS Pharma, Merck KGaA
Frank Weber MD, CMO		▪ Global Clinical Advisor of InterMune ▪ Chief Medical Officer at Merck KGaA ▪ Several medical affairs and clinical development management positions at American Cyanamid/Lederle, Synthelabo, Merck KGaA

Alzheimer's Disease: growing burden, no cure

Alzheimer's Disease introduction

- Leading cause of dementia, ultimately leading to death
- Large burden on families
- Growing cost for society
- Available treatments marginally effective and focus on symptoms only
- Current symptomatic treatments generate ~$4bn p.a.**
- No disease modifying beneficial treatments available
- No new drugs approved since 2007***

Worldwide dementia population will triple in the next 30 years*



* WHO Alzheimer Report 2015 ** Datamonitor 2014 *** FDA Source picture: Alzheimers.org

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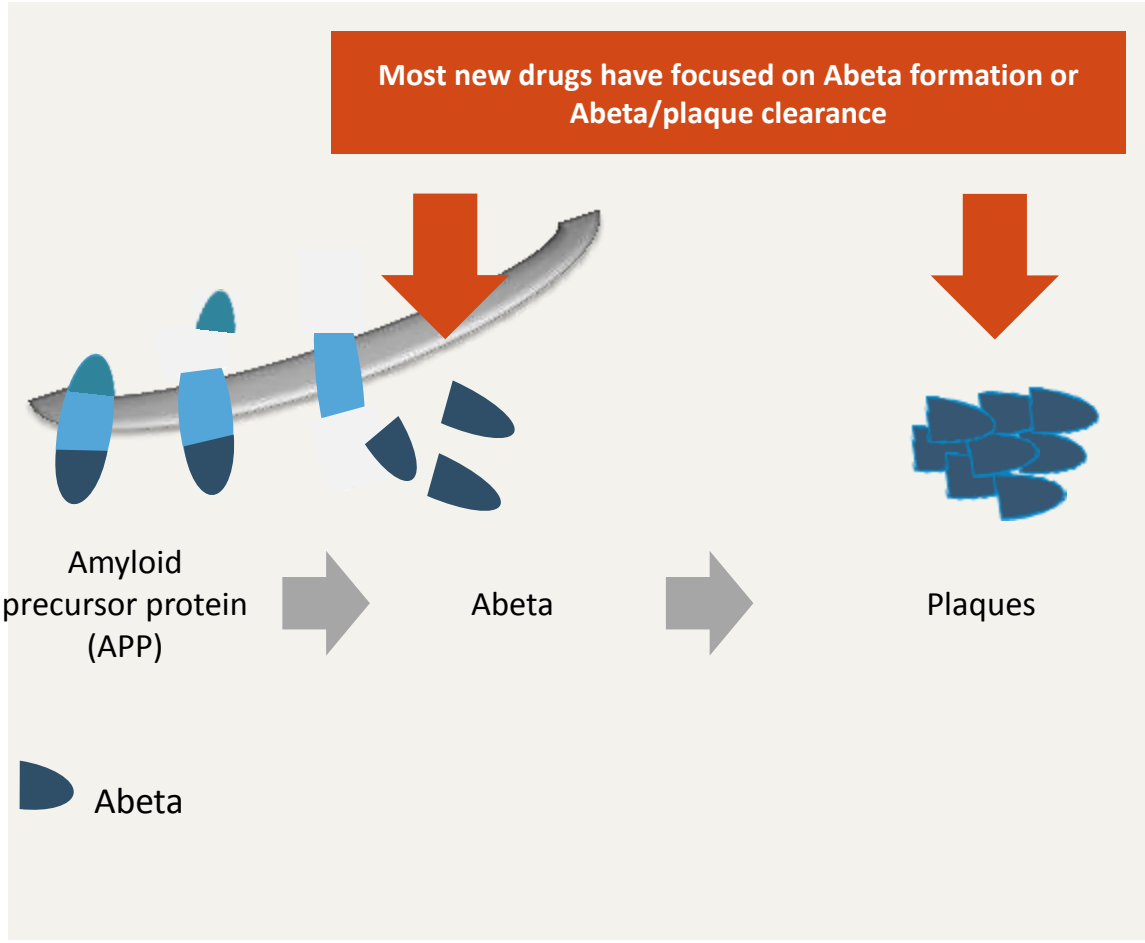
Original Abeta approach

Probiodrug targets toxic structures in Alzheimer's Disease



Considerations*

- Most new drug treatments have targeted Abeta or plaques
- Therapies have focused on:
  1. Reduction of Abeta formation
  2. Clearance of existing Abeta or plaque
- To date, several drug development attempts based on this original Abeta approach have failed – except one Abeta antibody in an early trial - others are ongoing and have yet to show benefit

* Company analysis, Mullard A Nat Rev Drug Discov 2012

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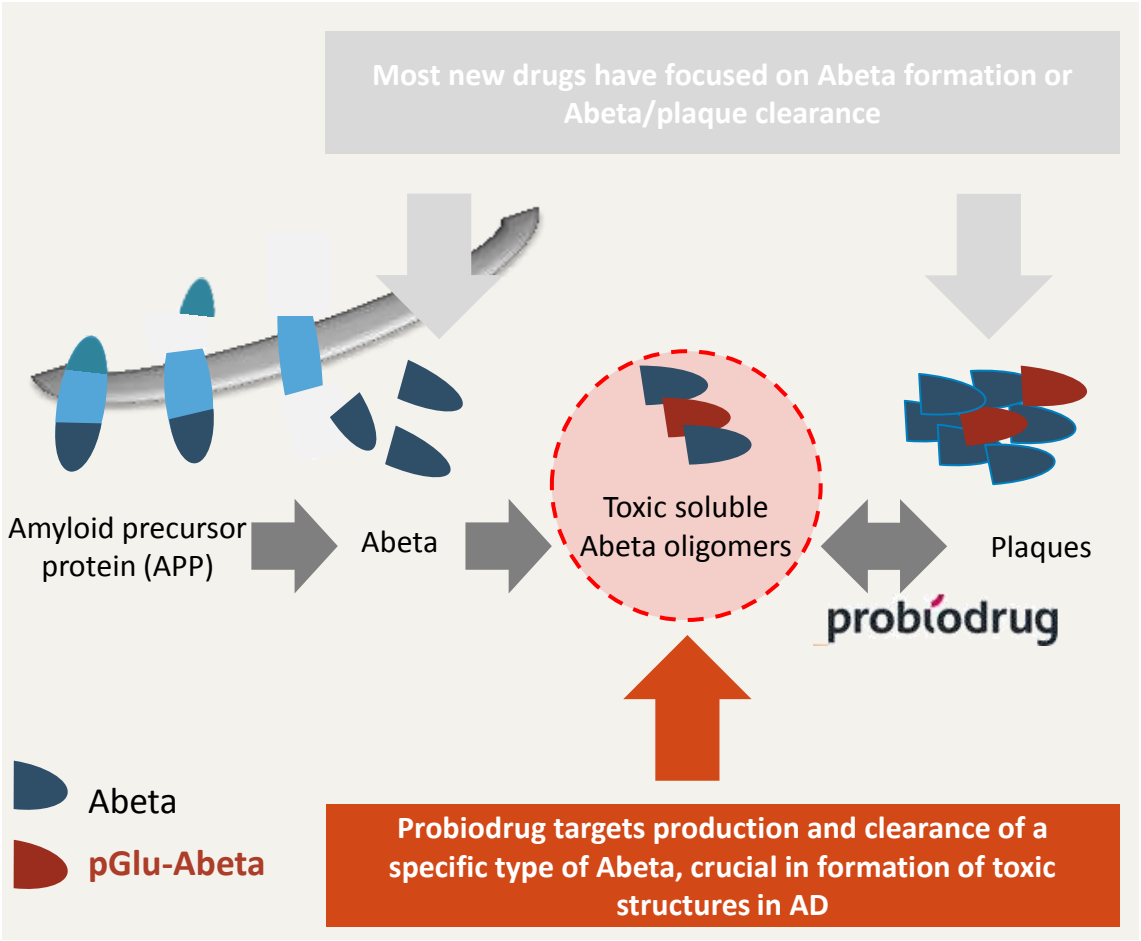
Probiodrug's **differentiated** approach

Probiodrug targets toxic structures in Alzheimer's Disease

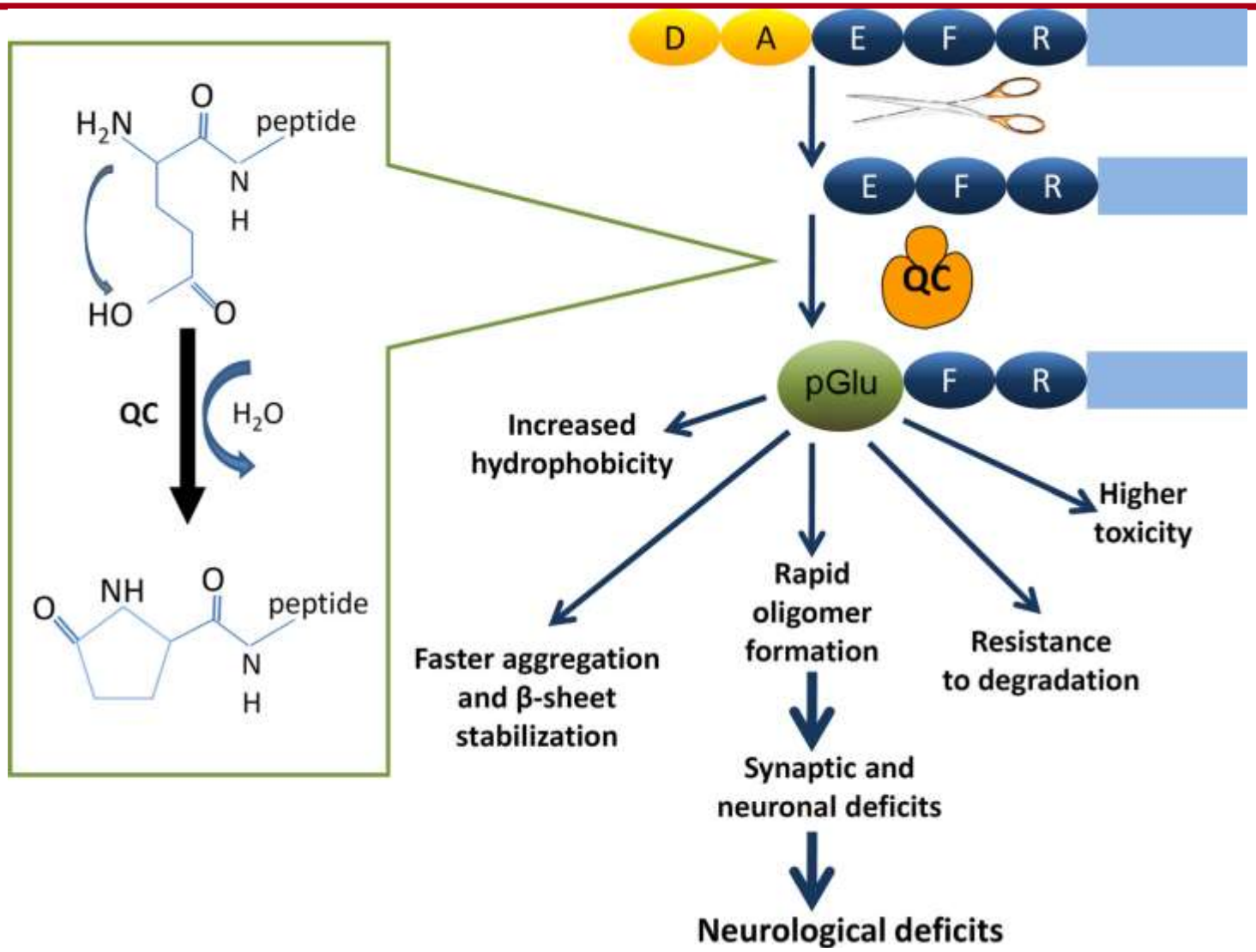


Considerations*

- Probiodrug and others have progressed insights on Abeta and its role in AD
- Abeta has a physiological function
- Plaques are not the primary toxic culprit
- In fact, an oligomer structure is most toxic and relevant from a clinical perspective
- Probiodrug targets a specific type of Abeta, **pGlu-Abeta**, which is crucial in the formation of these toxic oligomers

* Company analysis, Mullard A Nat Rev Drug Discov 2012

pGlu-Abeta - N-modified Abeta



Jawhar, S., Wirths, O., Bayer, T.A. JBC 286, 45, 2011

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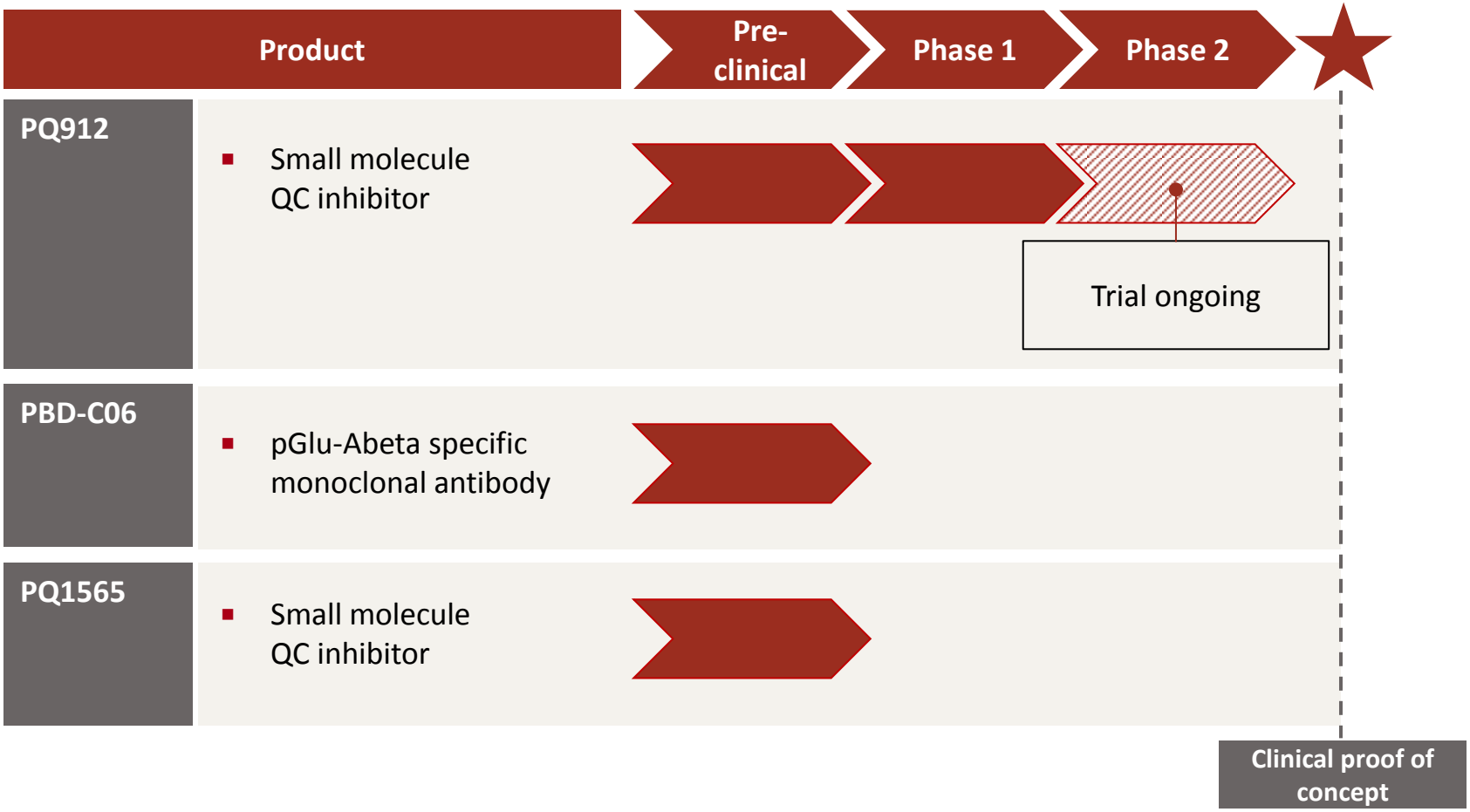
Focused proprietary pipeline

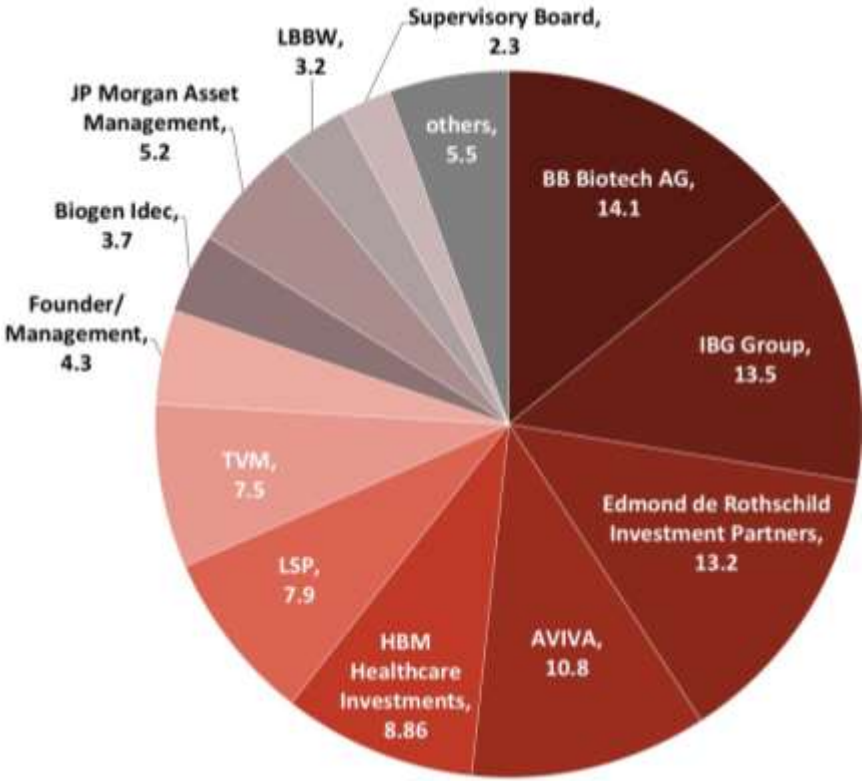


The Probiodrug Share

KEY INFORMATION

- ISIN: DE0007921835
- WKN: 792183
- Ticker Symbol: PBD
- Type of shares: Bearer shares
- Number of shares: 7,442,487
- Stock exchange: Euronext Amsterdam
- Liquidity Provider: Kempen & Co.
- Listing Agent: Kempen & Co.
- First trading day: 27 October 2014

SHAREHOLDER (> 3%)



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Key Highlights January to June 2016

- Announcement of favourable results of chronic toxicology studies with PQ912, Probiodrug`s 'first- in-class' Glutaminyl Cyclase (QC) inhibitor for the treatment of AD
- Annual Shareholders' Meeting held on May 19, 2016
- Key patents for Probiodrug's pGlu-Abeta targeting monoclonal antibody program for the treatment of AD granted in the US and in Japan
- Two key patents on Glutaminyl Cyclase (QC) inhibition for the treatment of AD granted in Japan
- Probiodrug's pGlu-Abeta approaches presented at the 14th AAT Symposium on Advances in Alzheimer Therapy in Athens/ Greece
- Probiodrug and Crossbeta Biosciences enter into a partnership in the field of AD biomarkers
- Expenditures and corresponding cash position in line with management expectations
- As of 30 June 2016, Probiodrug held EUR 14.2 million in cash and cash equivalents

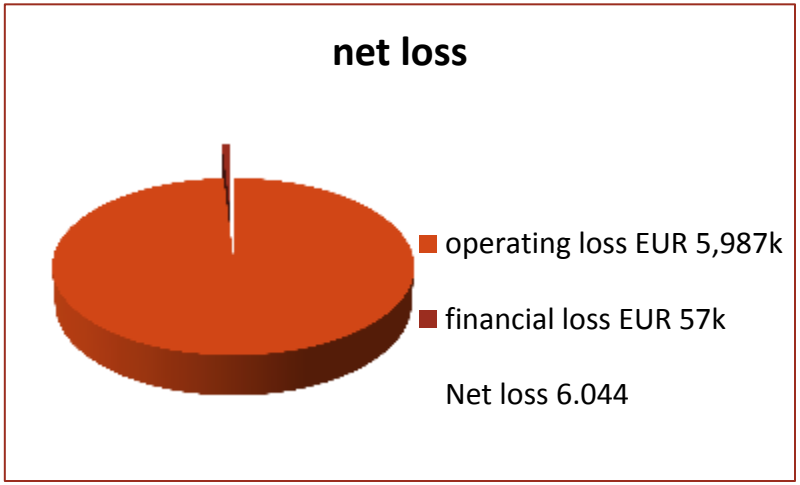
Key financial figures January – June 2016 (according to IFRS)

In EUR k, unless otherwise stated	Jan - June 2016	Jan - June 2015	Jan - Dec 2015
Earnings, Financial and Net Assets Position Revenues	0	0	0
Operating loss	-5,987	-6,177	-13,393
Net loss for the period	-6,044	-6,233	-13,505
Equity (end of the reporting period)	10,465	10,160	16,133
Equity ratio (end of the reporting period) (in %)	66.6%	66.0 %	73.8 %
Balance sheet total (end of the reporting period)	15,740	15,383	21,866
Cash flows from operating activities (cum.)	-7,000	-6,119	-12,147
Cash flows from operating activities (monthly average)	-1,167	-1,020	-1,012
Cash flows from financing activities (net)	0	0	12,598
Cash and cash equivalents at the end of the reporting period	14,245	14,793	21,361
Personnel Total number of employees (incl. Board of management) (end of the reporting period)	16	16	16
Probiodrug-Share Loss per share (basic/diluted) (in EUR)	-0,81	-0.92	-1.97
Number of shares issued (end of the reporting period)	7,442	6,766	7,442

Details of the Financial Results January – June 2016 (according to IFRS)

Net loss

- Net loss in line with expectations
- Operating loss primarily driven by R&D expenses, in particular the SAPHIR study
- Increase in operating expenses reflects primarily the development activities with respect to PQ912.

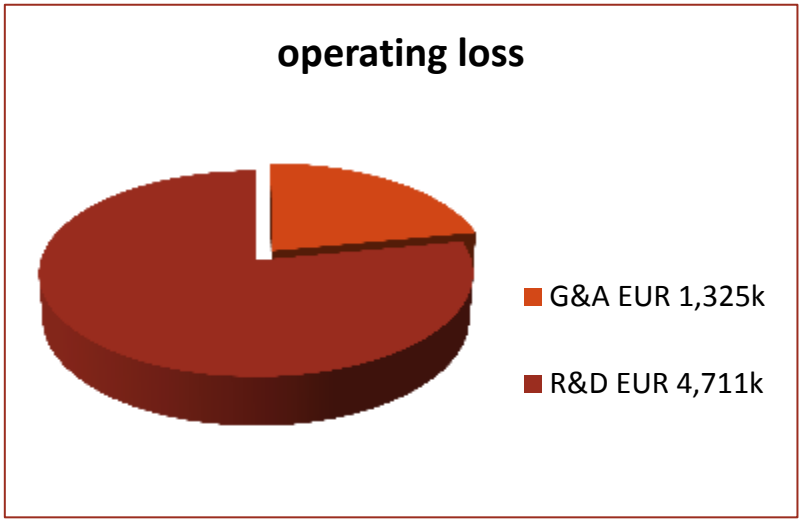


Equity

- The equity amounts to EUR 10,465k (Year 2015: EUR 16,133k), corresponding to an equity ratio of 66.6% (Year 2015: 73.8%).

Cash

- Cash and cash equivalents were EUR 14,245k compared with EUR 21,361k as at 31 December 2015.



Operational Review (1)

Pipeline Update PQ912

- PQ912 has been evaluated in rats and dogs in 4 weeks, 3 months and 6/9 months studies
  - In April 2016 data of the chronic tox studies announced:
    - No new findings were observed and the minimal to slight, non-adverse changes seen in both the 4-week and the 13-week studies were without any aggravation by the prolonged treatment
    - The adverse and dose- limiting effects for both species are determined by local effects due to strong taste aversion reactions of the animals to the test item and stayed at the same dose level
    - The comfortable safety margin, which was the basis for the SAPHIR Phase 2a study is maintained

Operational Review (2)

Pipeline Update PQ912

- In preceding Phase 1 study with healthy young and elderly volunteers shown to be safe, well tolerated and revealed high QC-inhibition
- SAPHIR is a randomized, double-blind multi-center Phase 2a study in early AD patients
  - Led by internationally renowned experts in AD
  - Run in seven European countries at about 20 sites
  - Plans to enrol a total of 110 patients with early stage Alzheimer's disease
  - Primary endpoint safety and tolerability compared with placebo over a three-month treatment period
  - Set of exploratory read-outs comprising cognitive tests, functional assessments by EEG and functional MRI and new molecular biomarkers in CSF to evaluate the compound's effect on the AD pathology
  - Headline data expected to be available end of 2016
  - Full picture of all results expected to be finally evaluated about 3 to 4 months thereafter

Operational Review (3)

PBD-C06

- Monoclonal antibody targeting pGlu-Abeta, while leaving non-toxic forms of Abeta untouched
- Currently in preclinical stage
- Successfully humanized and de-immunized
- For the first time for an anti-pGlu-Abeta-antibody 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

- Second QC-inhibitor with attractive drug-like properties
- Currently in preclinical stage
- GMP process for this molecule is being implemented

Operational Review (4)

Publications/ Presentations

- March 2016: pGlu-Abeta Approaches being presented at 14th AAT Symposium on Advances in Alzheimer Therapy, Athens, Greece
  - Presentation entitled “The pyroglutamate modification of toxic A-beta resulted in new therapeutic approaches: Inhibitors of glutaminyl cyclase and highly specific antibodies – A status report” was held by Prof Dr Hans-Ulrich Demuth
  - Presentation entitled “Phagocytic characterization and therapeutic efficacy of an Anti-PyroGlutamate-3 A-beta IgG2a antibody in aged APP/PS1dE9 mice” was held by Prof Dr Cynthia Lemere

- May 2016: Poster presentation “Quantitative Analysis of truncated Aβ peptide substrates of glutaminyl cyclase in human CSF samples using LC-MS/MS” and “Determination of Aβ Oligomers using a Flow Cytometry-Förster Resonance Energy Transfer (FRET) method” at the 1st Meeting of The Society for CSF analysis and Clinical Neurochemistry, Gothenburg, Denmark
  - Probiodrug is evaluating and establishing new concept-related molecular biomarkers to be used in their ongoing Phase 2a study (SAPHIR). The emphasis is regarded as an important and key cornerstone in the read out hierarchy in clinical studies.

Operational Review (5)

IP

- January and June 2016: IP position further strengthened by important patent applications being granted:
  - Japanese Patent Office has granted the company two important patents.
    - 5.934.645 Heterocyclic derivatives as inhibitors of glutaminyl cyclase
    - 5.930.573 cover the general use of QC inhibitors for the treatment of Mild Cognitive Impairment
  - 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

Collaborations

- June 2016: Partnership in the field of Alzheimer's disease biomarkers with Crossbeta
  - Provides Probiodrug a unique technology for validating sensitive and specific assays for Abeta- and pGlu-Abeta-oligomers to be used in the clinical studies of Probiodrug's lead candidate.

Corporate Review

Annual Shareholders' Meeting 2016 on 19 May, 2016

- All resolutions proposed by the Company's Management and Supervisory Board were approved at the meeting including:
  - Adoption of a resolution on the approval of the actions of the management board members for the financial year 2015
  - Adoption of a resolution on the approval of the actions of the supervisory board members for the financial year 2015
  - Election of the financial statements auditor for the financial year 2016
  - Elections to the supervisory board
  - Remuneration of the supervisory board
  - Adoption of a resolution on the increase of the Authorized Capital 2014 as well as the corresponding amendments to the articles of association
  - Adoption of a resolution on the adjustment of the Stock Option Program 2014 and the Conditional Capital 2014/I as well as the corresponding amendments to the articles of association
  - Adoption of a resolution on the extension of the exercise periods for the Option Programs 2007/2008 and 2010

Post Period Highlights

Eli Lilly presented data of LY3002813 its antibody targeting pGlu-Abeta

- At the Alzheimer's Association International Conference 2016 (AAIC) held in Toronto in July 2016, Eli Lilly presented data from a patient trial of LY3002813, its antibody targeting pGlu-Abeta.
- LY3002813 (also referred to as N3pG) significantly **reduced Abeta plaques by approximately 40% at the highest dose of 10mg/kg**, while lower doses were ineffective.
- These **results represent the first patient data from an approach targeting pGlu-Abeta** and **provide encouraging support for the emerging anti pGlu-Abeta field**.
- Eli Lilly has meanwhile advanced LY3002813 into a patient study with longer treatment duration (NCT02624778).

Supervisory Board and Management

- Olivier Litzka, partner at Edmond de Rothschild Investment Partners (EdRIP) and member of the Supervisory Board since October 2009, will step down effective 12 September 2016.
- Mark Booth, Chief Business Officer has left the company for personal reasons as of 15 August 2016.

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Outlook 2016

- Further preclinical and clinical testing of the development candidate PQ912, in particular completion of the first patient study in a Phase 2a trial in 2017 and the evaluation and design of a long -term treatment.
- Compiling further supporting data and securing intellectual property protection for the therapeutic concept of QC inhibition as a novel approach for the treatment of AD and other diseases.
- Further progression of the development of the anti pGlu-Abeta specific antibody (PBD-CO6) as well as of PQ1565.
- Progressing preclinical studies to further evaluate the potential of Probiodrug's therapeutic candidates in combinations for the treatment of AD and for use in other indications.

Guidance

- 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.

Anticipated news flow *(selection)*

2015

- ✔ First patient enrolled in PQ912 Phase 2a "SAPHIR" study at leading Alzheimer Center in Amsterdam
- ✔ Additional data on Glutaminyl Cyclases (QCs) in AD published in Acta Neuropathologica
- ✔ Key patents on Glutaminyl Cyclase (QC) inhibition for treatment of AD granted in Japan
- ✔ 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)
- ✔ PBD-C06 start of development activities to prepare for Phase 1
- ✔ PQ912 Publication of complete Phase 1 results

2016

- ✔ PQ912 results of long term tox studies
- ☐ PQ912 POP* combination therapy with BACE Inhibitor; and with PBD-C06
- ☐ PQ912 Preclinical assessment of potential in Down syndrome and in age-related macular degeneration (AMD)

2017

- ☐ PQ912 Phase 2a SAPHIR results

* Pre-clinical proof of Principle
Please note: timing of news flow is indicative

Financial Calendar

May 12th, 2016	Interim Management Statement Q1 2016
May 9th, 2016	Annual General Meeting of Shareholders in Berlin
August 23rd, 2016	Interim Report, half year results 2016
November 10th, 2016	Interim Management Statement Q3 2016

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Q & A