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INTERIM REPORT H1 2018
REPORTING PERIOD JANUARY TO JUNE 2018

Halle (Saale), August 30, 2018

Ulrich Dauer
CEO

| Inge Lues
CDO

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AGENDA

01 CORPORATE INTRODUCTION

02 RESULTS JANUARY TO JUNE 2018

03 OUTLOOK

04 Q & A

PROBIODRUG'S LONGSTANDING TRACK-RECORD

Key Milestones

- 1997: Foundation, headquarter Halle (Saale), pioneered a new class of antidiabetics (gliptins) – partnerships with Merck & Co, Ferring and Novartis
- 2004: Sold diabetes franchise to OSI Pharmaceuticals
- Oct 27, 2014: IPO at Euronext/ Amsterdam (Symbol: PBD)
- June 2017: PQ912 delivers positive pharmacodynamic and efficacy results in SAPHIR trial in 'early AD' patients, presented in November 2017 at CTAD 2017

Probiodrug facility in Halle (Saale)

- Established: 1997
- Headquarter: Halle (Saale), Germany
- IPO: October 2014
- Listing: Euronext Amsterdam (Ticker: PBD)

MISSION

Developing a novel therapeutic approach to a disease modifying treatment for AD that bears the potential to make a true difference for patients suffering from this devastating disease

WHAT: Building on robust scientific data, Probiodrug's lead candidate is ready to start Phase 2b trials with a very convincing development program outlined for the EU and US

WHY:

Huge medical need in Alzheimer's Disease

AD is one of the largest medical challenges for our aging population

It is a neurological disorder and the most common form of dementia which currently can not be cured

Only a few symptomatic treatments are available

Today, 47 million people live with dementia worldwide, this number is projected to treble to more than 131 million by 2050.

Huge economic impact

AD has an estimated, global societal cost of US$ 818 billion, and it will become a trillion dollar disease by 2018

* World Alzheimer Report 2016

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KEY HIGHLIGHTS JANUARY TO JUNE 2018

- In February 2018 submission of NIH grant application for US Phase 2b study
- In March 2018 presentation of inhibition of Glutaminyl Cyclase as a new treatment concept for Alzheimer's Disease at the 255th ACS National Meeting & Exposition in New Orleans, USA
- In April 2018 detailed study design of PQ912 Phase 2b core program outlined
- In April 2018 appointment of Dr. Ulrich Dauer as Chief Executive Officer
- In May 2018 review publication co-authored - positioning of Probiodrug`s anti-pGlu-Abeta antibody in the field of Abeta antibodies
- In June 2018 Annual Shareholders' Meeting held
- Expenditures and corresponding liquidity position (June 30, 2018, EUR 6.7 million) in line with management expectations

KEY FINANCIAL FIGURES JANUARY TO JUNE 2018 (ACCORDING TO IFRS)

In EUR k	Jan - June 2018	Jan - June 2017	Jan - Dec 2017
Earnings, Financial and Net Assets Position			
Operating loss	-4,133	-6,262	-9,961
Finance income (expenses), net	13	856	856
Income tax gain	0	1,102	1,102
Net loss for the period	-4,120	-4,306	-8,009
Equity (end of the reporting period)	4,848	12,211	8,923
Equity ratio (end of the reporting period) (in %)	67.6%	81.6%	82.9 %
Balance sheet total (end of the reporting period)	7,169	14,971	10,762
Cash flows from operating activities (year)	-4,092	-7,508	-12,117
Cash flows from operating activities (monthly average)	-682	-1,251	-1,010
Cash flows from investing activities (year)	471	-4	459
Cash flows from financing activities (net)	0	0	127
Cash and cash equivalents at the end of the reporting period	6,686	14,385	10,291

KEY FINANCIAL FIGURES JANUARY TO JUNE 2018 (ACCORDING TO IFRS)

	June 30, 2018	June 30, 2017	Dec 31, 2017
Personnel			
Total number of employees (incl. Executive Board)	14	14	15

	June 30, 2018	June 30, 2017	Dec 31, 2017
Probiodrug-Share			
Loss per share (basic and diluted) (in EUR)	0,51	0,53	0,98
Number of shares issued (in EUR k)	8,208	8,187	8,208

DETAILS OF THE FINANCIAL RESULTS JANUARY TO JUNE 2018 (ACCORDING TO IFRS)

Net loss

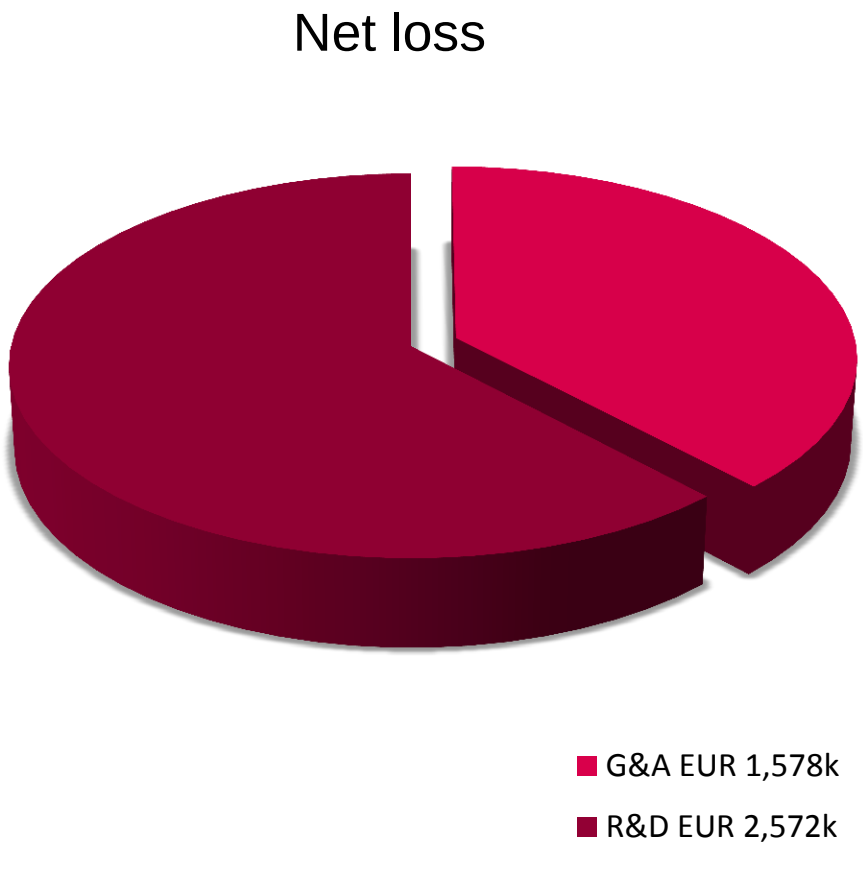
- Expenditures in line with company`s projections
- Net loss primarily driven by R&D expenses and G&A expenses and in line with expectations
- Other operating income/Finance income EUR 30k (Jan-June 2017: EUR 860k)

Equity

- Equity amounts to EUR 4,848k (Dec. 31 , 2017: EUR 12,211k), corresponding to an equity ratio of 67.6% (Dec 31, 2017: 82.9%)

Cash

- Cash and cash equivalents were EUR 6,686k compared with EUR 10,291k as at December 31, 2017
- Cash Flow from investing activities:
  EUR 475k resulting from proceeds from the expiration of a pension liabilities insurance



PQ912 - CLINICAL DEVELOPMENT STRATEGY AD

- Phase 1: Comprehensive single and multiple dose studies

  Focus on mechanism based biomarker, PK / PD model, safety
  Delivered target occupancy model, good safety margins, drug formulation strategy, drug metabolism

- Phase 2a: Pilot double blind study in target AD population

  Focus on safety of high dose, efficacy : CSF, imaging and functional outcomes
  Delivered dosing strategy for long-term studies, proof of principle of target engagement and positive functional AD outcomes for next study

- Phase 2b: Clinical proof of concept study program powered for cognition endpoint

  Focus on clinical efficacy in cognition
  Will deliver clinical proof of concept, using sensitive cognition endpoints according to latest FDA guideline, upside for early approval

- Phase 3: Confirmation of Phase 2b results

GOOD NEWS AFTER A CHAIN OF LATE STAGE FAILURES - (CAUTIOUS OPTIMISM IN) ABETA IS BACK -

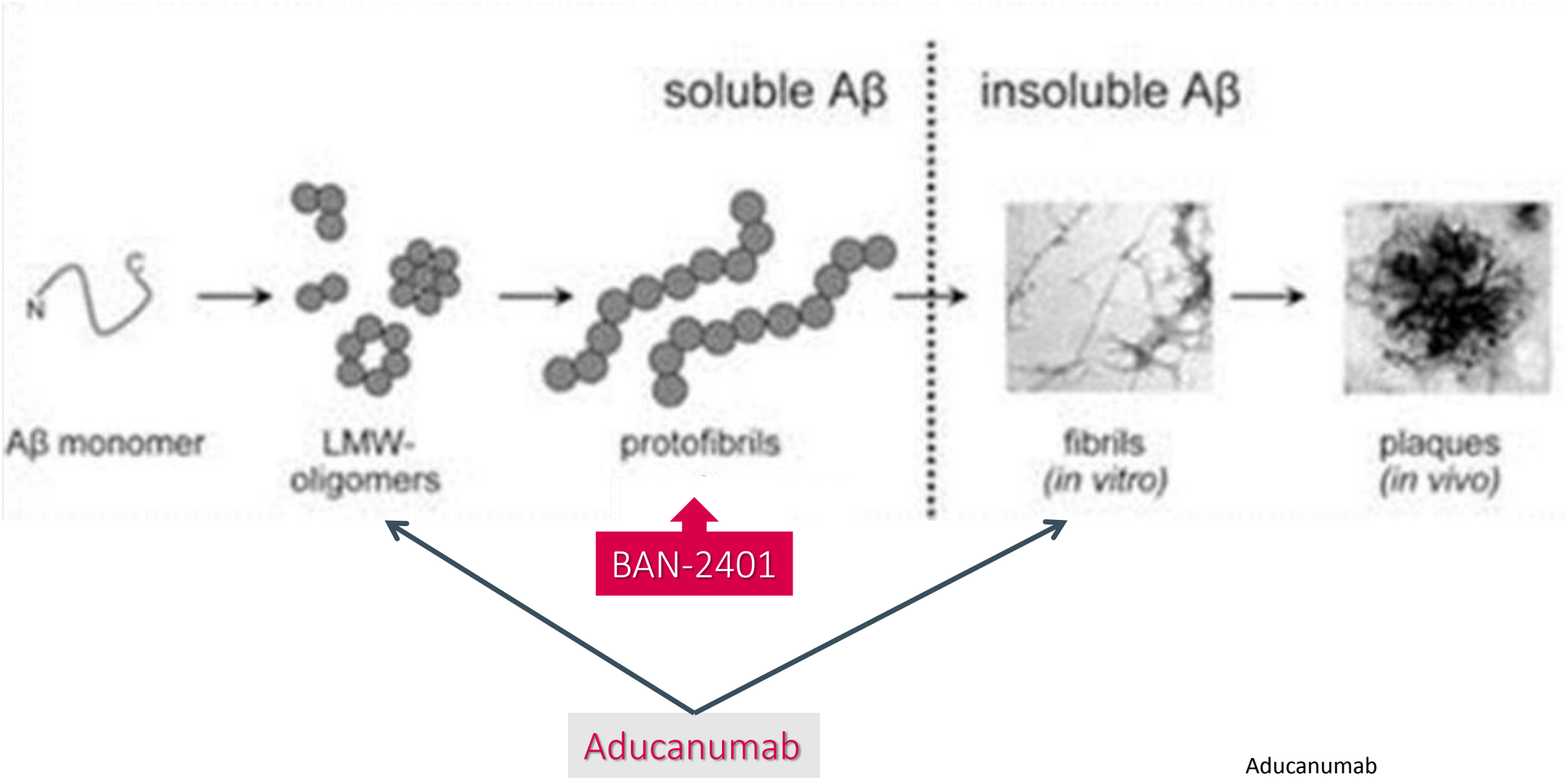
- More recent data move the needle - Abeta approaches showing positive results:
- **Aducanumab** Biogen – (in) Phase 3 – binding Abeta-oligomers and plaques.
  - **Reduced progression of clinical symptoms**
  - **Dose dependent reduction of plaques (TO)**
  - **Effect due to reducing also** Abeta oligomers

- NEW: **BAN2401** Eisai/Biogen/Bioarctic

  - Monoclonal Abeta Antibody **targeting soluble protofibrils (big oligomers)**
  - The Phase 2b trial - mild cognitive impairment due to AD or mild AD (60/40) and who had evidence of brain amyloid pathology by cerebrospinal fluid analysis or PET
  - **Significant effects on plaque load and cognition**
    - *Caveat:* Need to be more data parsing into groups with an uneven distribution of APOE4 carriers (triples the risk for AD) between placebo and TX – (result of Reg Agency request for safety reasons)

The overarching take-home message:
targeting Abeta and oligomers seem to work - the centerpiece of PBD's approach

BINDING ABETA (SOLUBLE) AGGREGATES



Aducanumab
Discovery, Preclinical Studies and Phase 1 Trials

WHY SO MANY FAILURES IN AD CLINICAL DEVELOPMENT?

- Wrong targets?
  - especially Amyloid beta under siege
- Flaws in the concept?
  - based on scientific knowledge of the late 90s
- Too late?
  - effective only if preventive or start at preclinical stage?
- Too little?
  - Antibodies - low amount crossing BBB - limited safety - IgG1 induces ARIAs
- Too fast?
  - Rushing from preliminary MoA data to Phase 3
- Inappropriate cognitive/functional readouts used for early AD patients?
- Combination needed? e.g. Lilly pGlu-Abeta Antibody and BACE-inhibitor

- Bandwagon effect- Pharma restarts with other unprecedented targets

Probiodrug:

- Targeting pGlu-Abeta, though bearing the Abeta name - a different and specific approach- based on today's enhanced understanding of pathology, double pronged – Abeta oligomers and inflammation
- Pursuing an innovative and success-oriented , DILIGENT AND SOUND clinical development strategy

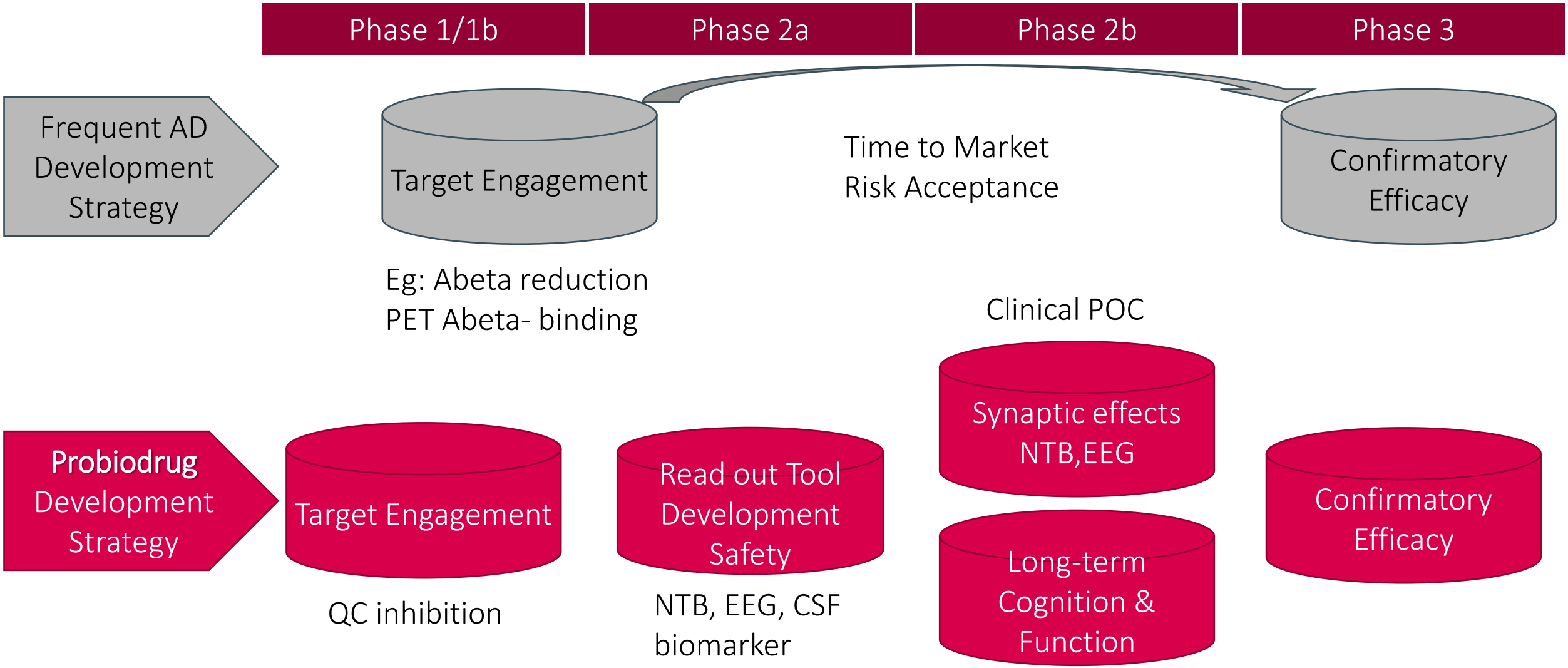
WHAT ARE THE IMPLICATIONS OF THE RECENT ABETA ANTIBODY PHASE 2 RESULTS ON THE PQ912 DEVELOPMENT AND INVESTMENT OPPORTUNITY?

- Preliminary conclusions of the Abeta Antibody results
  - Best-in-class Abeta Antibodies show a 25 -40% reduction of decline of progression of cognition: even if confirmed - further large medical need
  - Induce ARIAs - microhemorrhage vascular edema to different degrees – dose-limiting
  - Effective Abeta Antibodies bind to existing neuro-toxic oligomers, they do not prevent the production of new neuro-toxic oligomers (limitation of concept)
  - A beta Antibodies require every 2-4 weeks i.v. applications and show efficacy only at the highest dose (economical and convenience burden)

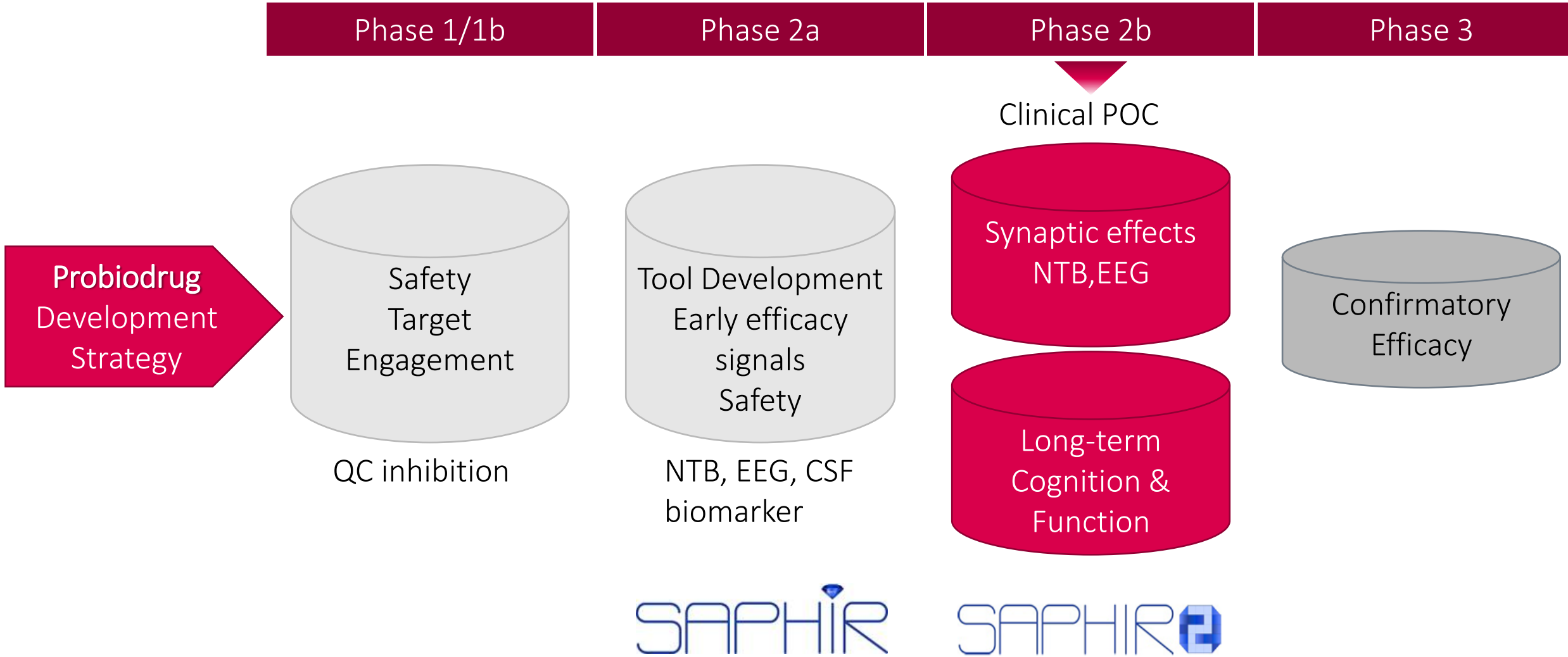
WHAT ARE THE IMPLICATIONS OF THE RECENT ABETA ANTIBODY PHASE 2 RESULTS ON THE PQ912 DEVELOPMENT AND INVESTMENT OPPORTUNITY?

- Opportunities for the PQ912 Glutaminyl Cyclase program
  - PQ912 prevents the production of new synapto/neurotoxic Abeta oligomers – complementary approach to AB; combination of pGlu-AB and QC-I resulted in additive effects in pre-clinical models of AD
  - **Small molecule, orally available, convenient twice daily dosing**, very well established PK/PD model with well achievable target occupancy range (50-80%)
  - Development program tailored to most recent paradigms in AD: patients with early AD, sensitive validated cognitive scales (Cogstate), target effect size 35%

DILIGENT DEVELOPMENT STRATEGY MAKES A DIFFERENCE



DILIGENT DEVELOPMENT STRATEGY



THE UNIQUE PHASE 2B PROGRAM OF PQ912

Designed according to newest regulatory EU and US guidelines and state of the art scientific concepts.

In collaboration with world class leading experts

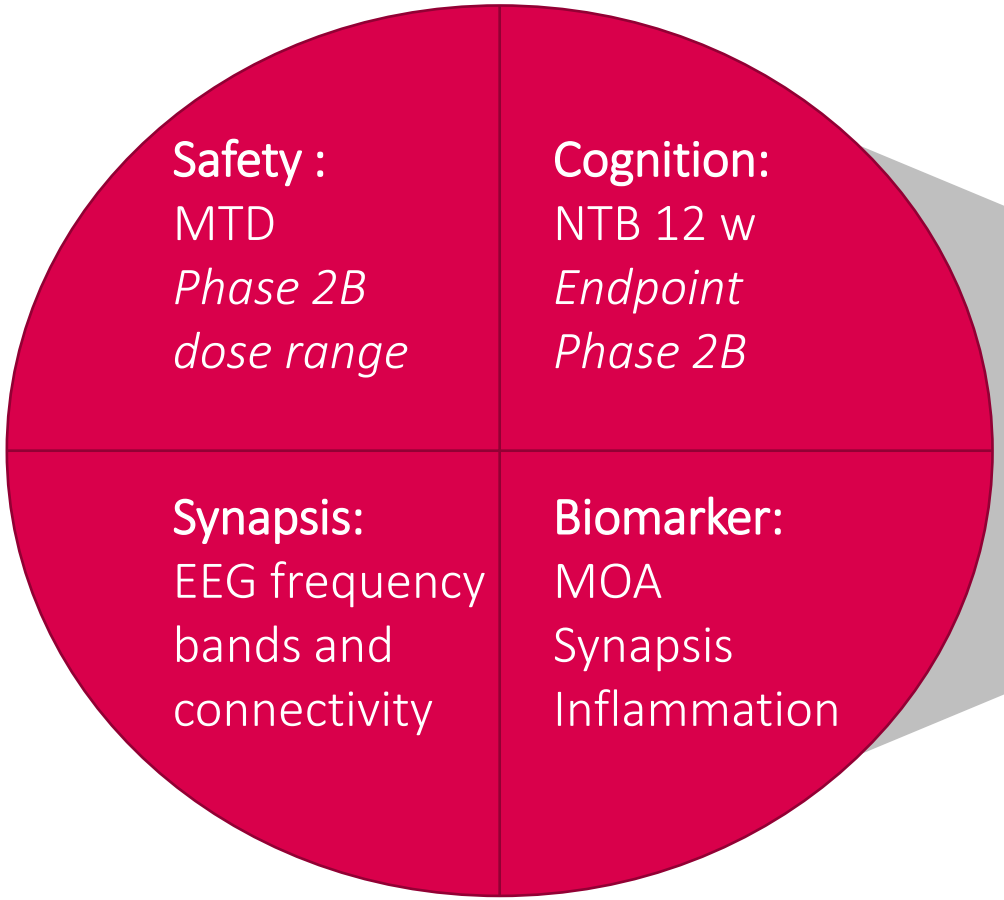
- P. Scheltens, J. Harrison, P. Maruff – Cogstate, F. Barkhof, A. Gouw
- H. Feldman and US Protocol Steering Committee consisting of highly renowned Neurologists

Integrated development strategy informed by Phase 2a results.

PQ912 - PHASE 2 STRATEGY

Phase 2a

Exploration and short-term outcome



Outcome informs design of Phase 2b

Phase 2b

Clinical Proof of Concept

EU Study

Focus on Synaptic function @ 9-12 m:
NTB working memory / attention,
EEG, Biomarker

US Study

Focus on cognition @ 18m:
In depth analysis of effect on
cognition, and function

PQ912 - PHASE 2B DEVELOPMENT STRATEGY

EU study

- Cognitive and functional endpoints creates solid base for Phase 3 program
- Innovative design with long enough treatment to enable predictive cognitive read-outs and short enough study to allow earliest Phase 3 start
- Highly cost effective builds on existing structure and trial network

US study

- Complementary to EU study with longer treatment duration
- Powered for Cognition read out
- Builds on ADCS competence network
- Allows, if both studies (EU, US) positive on primary and key secondary endpoints discussion of conditional approval

PQ912 - CLINICAL PROOF OF CONCEPT STRATEGY

EU Phase 2b study focus on synaptic effects with tools investigated in Phase 2a

- Midterm drug exposure : treatment 36 -84 weeks (mean 12 months)
- 250 patients
- Primary endpoint working memory / attention composite (Cogstate)
- Secondary endpoint EEG / network, total Cogstate and IADL
- Exploratory Biomarker

US Phase 2b study focus on cognitive effects across domains and daily function

- Long-term drug exposure : 18 months
- 460 patients
- Early AD patents – FDA stage 3+4 Primary endpoint
- Endpoints CDR-SB and Composite Cognitive Functional Measure
- Further secondary and exploratory outcome parameter

THE NEW REGULATORY FRAMEWORK IN EARLY AD

- FDA issued updated draft guideline for the treatment of early AD Allows claim of treatment before onset of overt dementia
  - Clear classification of population
  - Suggestions for endpoints and trial methodology with strong focus on cognition
  - Invitation to enter discussion and dialogue

- EU updated clinical investigation for AD guideline (EMA)
  - Phase 1: Kinetics in elderly and drug-drug interaction
  - Exploratory trial showing target engagement, PK/ PD relationship and maximal tolerated dose
  - NTB considered to assess cognition in early AD
  - Clinical meaningfulness to be shown by relevance of cognition findings and or selective activities of daily living

The regulatory EU and US framework is fully considered with no short cuts

EMA GUIDANCE - EXPLORATORY (POC) TRIALS 2/2018

"Unfortunately the field of AD drug development has witnessed many failures and it is noted that in many cases, exploratory trials did not provide 'proof of concept' to inform Phase 3

Consequently the large Phase 3 trials often failed to be confirmatory.

Exploratory trials in well-characterized patient populations are therefore strongly encouraged to be conducted prior to Phase 3".

Exploratory studies may have the following objectives:	PBD PQ912 status
Demonstration of target engagement	✓
Assessment of short-term adverse reactions from a clinical and laboratory standpoint	✓
Determination of pharmacokinetic characteristics	✓
Determination of maximal tolerated doses	✓
Determination of PK/PD relationship	✓
Determination of dose-response	✓ (TO)
Preliminary evaluation of efficacy	✓
Proof of concept	**in preparation**
Identification of subsets of patients able to benefit from treatment and population selection for confirmatory trials	

STATUS, TIMELINES AND FINANCIALS OF THE EU STUDY

- EU Phase 2b study protocol completed
- CRO the same as for SAPHIR - in close collaboration with Amsterdam UMC
- sites currently in assessment –
  - 54 CDAs, 50 selected for SSV, 30 conducted (target: 12 countries / 48 sites)
- FPFV planned for End 2018 (depending on financing)
- Recruitment duration 16 months
- Study closes 40 weeks after LPI (date)
- Total cost about 25 million

US 2B STUDY: SEAMLESS PHASE A AND PHASE B TRIAL

WORK IN PROGRESS

Trial matrix and design

- US/Canada: PI H. Feldman ADCS/UCSD
- Total projected: 462 patients (55 sites)
  - Early Alzheimer's Disease
    - MMSE: 21-30 inclusive
    - CSF AD pathophysiology amyloid + and pTau & tau/A-beta ratio +
  - Patients on SoC or treatment naïve
- Phase A: Group sequential dose design: groups on 150, 300, and 600 mg bid for at least 8 weeks for initial safety read out in first 180 patients
- Following DSMB reviews, trial will continue highest tolerated dose through Phase 2b
- Phase B: Treatment duration per patient 72 weeks (primary endpoint of CDR-SOB)

[1] Cognitive-Functional Component 2
[2] Raghavan N et al *Alz & Dem* 2013

Objectives and read-outs

- Primary objective: efficacy of PQ912 on cognition and function (CDR-SOB)

- Key secondary objective: efficacy on composite measure of cognition and function (CFC2) [1,2]
- Other secondary efficacy objectives: QC inhibition, ADAS-Cog 13, ADNI NTB, FAQ, NPI, and qEEG spectral analysis
- Secondary safety objectives: AEs/SAEs, Drug AEs of Interest (GI, skin), Sheehan Suicidality

- Exploratory readouts: CSF and plasma based biomarkers, MRI imaging, EEG network connectivity

Tentative timelines

- NIH funding submission: Q1 2018, final Protocol ready: Q3 2018, NIH funding decision Q3 2018
- FPI Q2 2019; start subject to funding
- LPI: Q3 2020, LPO: Q1 2022 ; Dose decision: Q1 2020; key results Q3 2022

SUMMARY PQ912 CLINICAL DEVELOPMENT

- Stepwise rational development with essential learning and de-risking strategies implemented
- Program designed according to most recent regulatory AD guidelines and input from world-class leaders in the AD field
- Next step of Phase 2b studies has been well prepared and represents a big value inclination by demonstrating effect on cognition
- EU study is the base case which will allow high value exit and smooth transition into Phase 3
- US study broadens PQ912 global footprint and includes upside of an early approval

SUMMARY OF EXPLORATORY EFFICACY RESULTS IN SAPHIR 2A TRIAL

Molecular Biomarkers in CSF:

- Strong QC-inhibition, target occupancy about 90%
- Strong trends to reduce the synaptic marker neurogranin, and the inflammatory marker YKL40, which are both enhanced in early AD

Physiological function assessment with EEG:

- Significant effect at the first level of EEG analysis: strong reduction in theta power which is increased in AD
- Post-hoc analysis: significant positive effect on functional connectivity as measured by AEC (amplitude envelope correlation) , p= 0.025, Cohens's d=0.45

Cognition using NTB:

- Significant improvement in 'one card back', (p=0.050, Cohen's d=0.23) a test to assess working memory
- The 'Detection' test, a measure of attention, showed a meaningful trend towards improvement (Cohen's d=0.2)

"These results point to a direct effect on pGlu-Abeta with beneficial effects on synaptic function, even in such a short treatment period." P. Scheltens, PI

Clear proof of Mechanism of Action

↓

Significant effects on synaptic function

↓

Improvement of a component of working memory

CORPORATE REVIEW

Dr. Ulrich Dauer appointed as CEO

- On April 23, 2018 Probiodrug announced that effective May 1, 2018, Dr. Ulrich Dauer is appointed to the position of Chief Executive Officer.
- He teamed up with long-serving Chief Development Officer, Dr. Inge Lues, who has borne key responsibility for development of Probiodrug's pipeline.
- Dr. Konrad Glund and Dr. Hendrik Liebers left the management board of the company effective April 30, 2018.

CORPORATE REVIEW

Annual Shareholders' Meeting held on June 21, 2018

- 38.26 % of the voting shares were represented at the 2018 Probiodrug AG AGM. All resolutions proposed by the Company's Management and Supervisory Board were approved at the meeting with a large majority.

Supervisory Board

- The Shareholders` meeting on June 21, 2018, re-elected Dr. Erich Platzer, Charlotte Lohmann, Dr. Dinnies von der Osten and Dr. Jörg Neermann as members of Supervisory Board.

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OUTLOOK

Mid-term focus of Probiodrug' s business activities are summarized as follows:

- Execution of the Phase 2b clinical study program for PQ912
- Identifying industrial partners
- Further strengthening Probiodrug's financial resources

Probiodrug projects a net loss for the financial year 2018 which, based on the current budget, is expected to be lower than that of 2017.

FINANCIAL CALENDAR 2018

April 03, 2018	Annual report, full year results 2017
May 15, 2018	Interim Management Statement Q1 2018
June 21, 2018	Annual General Meeting of Shareholders in Berlin
August 30, 2018	Interim Report, half year results 2018
November 29, 2018	Interim Management Statement Q3 2018

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