

# THE 2018 FULL YEAR RESULTS & OUTLOOK 2019

Halle (Saale), March 28, 2019

Probiodrug AG

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# WELCOME TO PROBIODRUG

## - THE MANAGEMENT TEAM -



ULRICH DAUR

PhD / CEO

20 years experience in the biopharmaceutical industry

Has held CEO positions in several private and public entities

Achieved multiple licensing and M&A transactions

Strong track record of private and public capital raises

PhD in Chemistry from the Julius-Maximilians University of Wuerzburg



MICHAEL SCHAEFFER

PhD / CBO

18 years of life science industry experience in strategic business development, scientific project and alliance management

Founder, CEO and Managing Director of several biotech companies.

Integrated CRELUX into WuXi AppTec a world-leading Shanghai-based CRO with over 25,000 employees globally

PhD in Molecular Biology (cancer immunology) from Ludwig-Maximilians-University of Munich

## AGENDA

- 01 HIGHLIGHTS IN 2018
- 02 PORTFOLIO
- 03 FINANCIALS 2018
- 04 POST-PERIOD HIGHLIGHTS & OUTLOOK
- 06 Q&A

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# 01 HIGHLIGHTS IN 2018

# HIGHLIGHTS AND LOWLIGHTS 2018

## *Highlights*

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- Maturing product pipeline and progress towards goal of becoming a leader in the development of innovative drugs for Alzheimer's disease
- Strategy for the Phase 2b and proof of concept program has been defined and the set-up Phase of SAPHIR 2
- Successful Publication of PQ912 Phase 2a study SAPHIR

## *Lowlight*

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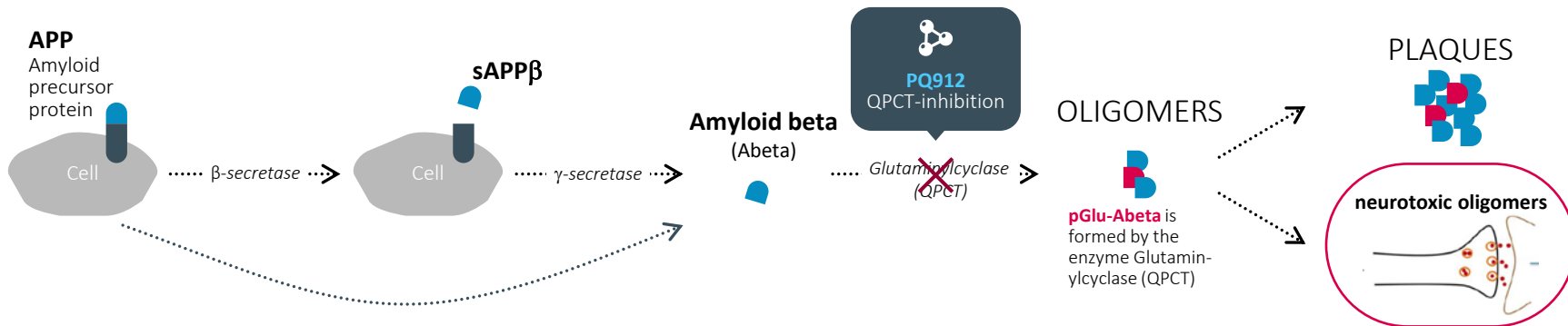
- Collapse of the stock price

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## 02 PORTFOLIO

# PROBIODRUG'S TARGET FOCUSED APPROACH: PQ912 TARGETS QPCT

## Targeting QPCT to inhibit formation of pGlu Abeta



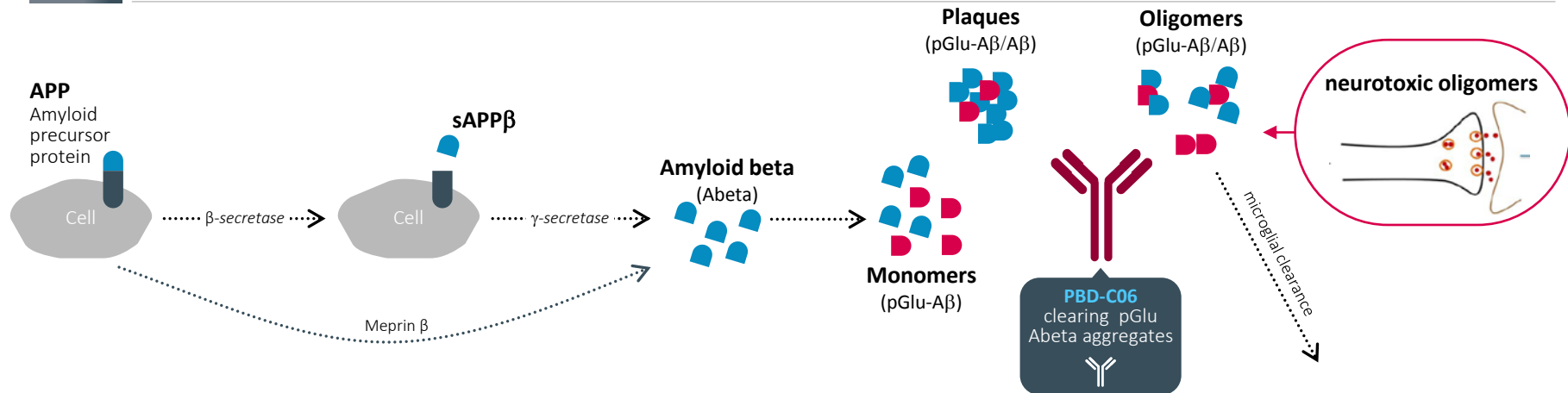
**pGlu-Aβeta** is crucial in the formation of synapto-/neurotoxic toxic oligomers

- **PQ912** (small molecule) inhibits QC and thereby the production of pGlu-Aβeta



# AD THERAPY BEYOND TAU AND Abeta: CLEARANCE OF NEUROTOXIC OLIGOMERS BY PBD-C06

## Antibody mediated pGlu-Abeta clearance



- **PBD-C06** specific monoclonal antibody, for the clearance of neurotoxic pGlu-Abeta containing oligomers
  - | prevents aggregation of A $\beta$  and neurotoxic pGlu-Abeta oligomers |
  - | clears these neurotoxic aggregates via Fc-mediated phagocytosis |
  - | exclusive expression of pGlu-Abeta in brain prevents potential PBD-C06 systemic off-target toxicity |

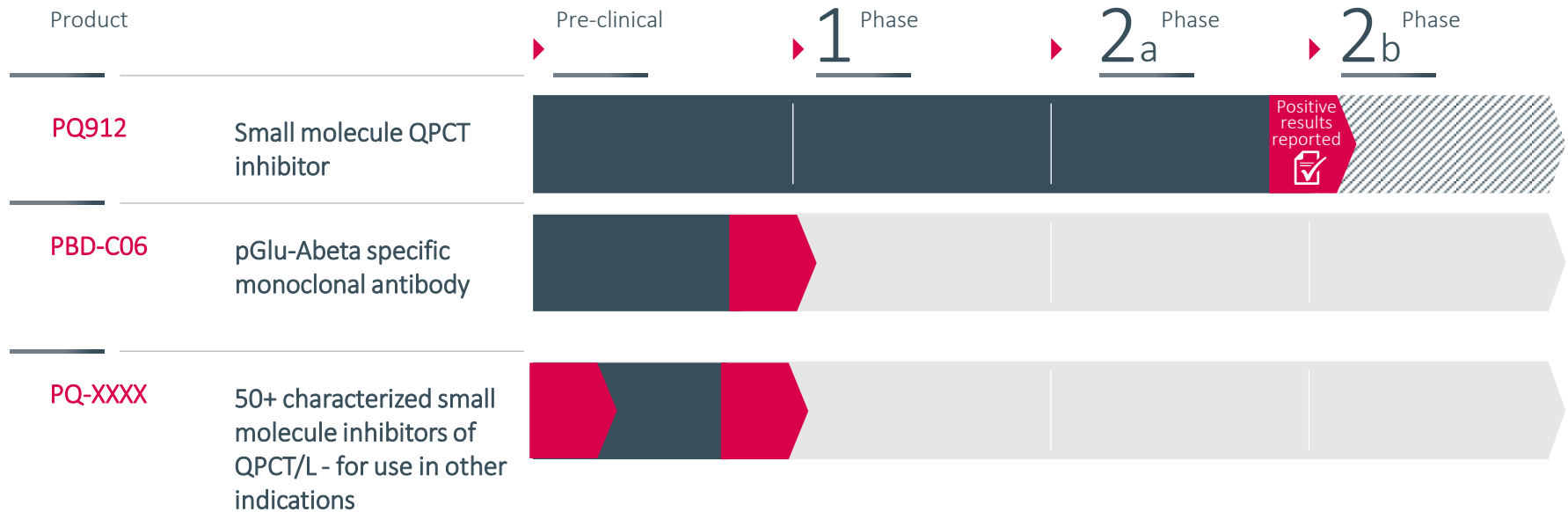


# WHY TARGETING Abeta IS NOT A GOOD IDEA

....but pGlu-Abeta/QPCT is!

| hallmarks                               | A-beta  | pGlu-Abeta/QPCT                                     |
|---|---|---|
| expression pattern                      | brain, plasma, peripheral organs  | only brain, only in disease                         |
| upstream enzymes                        | $\beta$ & $\gamma$ -secretases, meprin $\beta$                              | only one crucial enzyme: QPCT                       |
| physiological function                  | synaptic function, bbb integrity, antimicrobial activity, tumor suppression | no physiological function of pGlu-Abeta             |
| abundance                               | does not correlate with disease progression                                 | correlates with disease progression                 |
| QPCT is upregulated during inflammation | Full-length Abeta is not a substrate of QPCT, but Abeta 3-40/42 is          | QPCT upregulation generates highly toxic pGlu-Abeta |

# PROBIODRUG'S FIRST-IN-CLASS DRUG PIPELINE



# PQ912 – SAPHIR CLINICAL DEVELOPMENT STRATEGY IN AD



|              | <b>Comprehensive single and multiple dose studies</b>   | <b>Pilot double blind study in target AD population</b>   | <b>Clinical proof of concept study program powered for cognitive endpoints</b>   | Confirmation of Phase 2b results (if required) |
|--------------|---|---|--|--|
| FOCUS        | Mechanism based biomarker, PK / PD model, safety  | Safety of high dose, efficacy: cerebrospinal fluid (CSF), imaging and functional outcomes   | Clinical efficacy in cognition   |  |
| DELIVERABLES | Delivered target occupancy model, satisfactory safety margins, drug formulation strategy, drug metabolism | Delivered dosing strategy for long-term studies, proof of principle of target engagement and positive functional AD outcomes for next study | Will deliver clinical proof of concept, using sensitive cognitive endpoints according to latest FDA guideline, upside for early conditional approval |  |

# SAPHIR PHASE 2B TRAIL DEVELOPMENT STRATEGY

EU STUDY

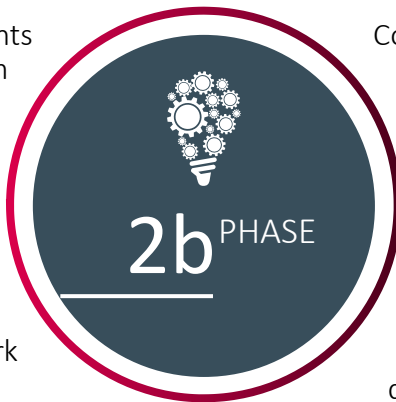


US STUDY

Cognitive and functional endpoints  
create a solid base for Phase 3 program

Innovative design with sufficiently long  
treatment to enable predictive cognitive  
read-outs and short enough to allow for  
the earliest Phase 3 commencement

Highly cost effective, builds on existing  
structure and trial network



Complementary to EU study  
with longer treatment duration

Powered for cognition read-out

Builds on Alzheimer's Disease Cooperative  
Study (ADCS) competence network

Allows, if both studies (EU + US) positive  
on primary and key secondary endpoints,  
discussion of conditional approval

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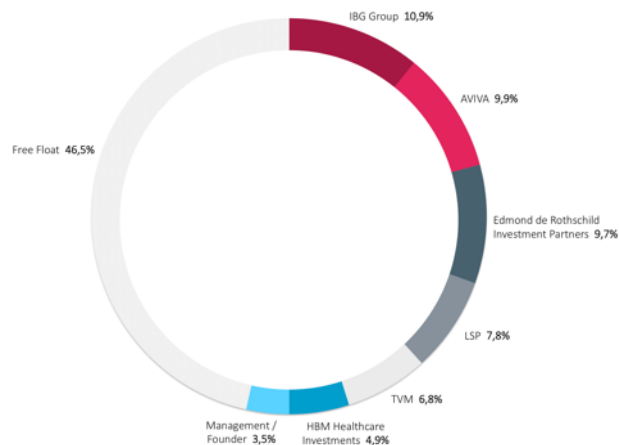
## 03 FINANCIALS 2018

# SHARE

## KEY INFORMATION

|                     |                       |
|---------------------|-----------------------|
| ISIN:               | DE0007921835          |
| WKN:                | 792183                |
| Ticker symbol:      | PBD                   |
| Types of shares:    | Bearer shares         |
| Number of shares    | 8,208,009             |
| Stock exchange:     | Euronext<br>Amsterdam |
| Liquidity provider: | Kempen & Co.          |
| Listing agent:      | Kempen & Co.          |
| First trading day:  | October 27, 2014      |
| 52 week high/low    | € 17.00 / € 2.56      |

## SHAREHOLDER STRUCTURE



## SHARE PRICE

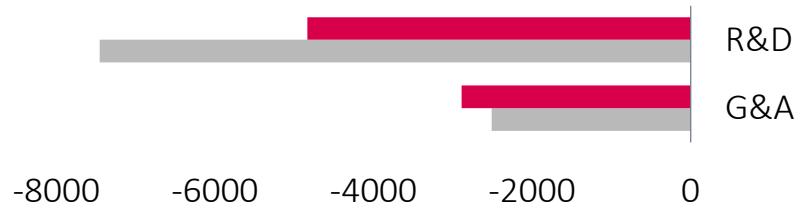


# KEY FINANCIAL HIGHLIGHTS (P&L): ACCORDING TO IFRS

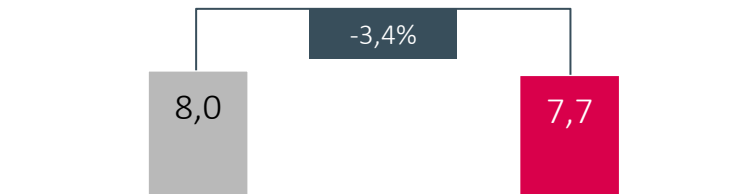
## IN €k

|                                     | 2018   | 2017   | %     |
|-------------------------------------|--------|--------|-------|
| Research and development expenses   | -4,836 | -7,454 | -35,1 |
| General and administrative expenses | -2,891 | -2,511 | 15,1  |
| Other operating income              | 29     | 4      | 86,2  |
| Operating loss                      | -7,698 | -9,961 | -22,7 |
| Finance income                      | 2      | 862    | -99,8 |
| Finance expenses                    | -41    | -12    | 70,7  |
| Income tax gain                     | 0      | 1,102  | -     |
| Net loss for period                 | -7,737 | -8,009 | -3,4  |

## OPERATING LOSS (€k)



## NET LOSS (€k)



■ 2017 ■ 2018



# KEY FINANCIAL FIGURES (ACCORDING TO IFRS)

| In €k   | Dec 31, 2018 | Dec 31, 2017 |
|---|--------------|--------------|
| Earnings, Financial and Net Assets Position               |              |              |
| Operating loss  | -7,698       | -9,961       |
| Finance income/loss                                       | -39          | 850          |
| Income tax gain   | 0            | 1,102        |
| Net loss for the period                                   | -7,737       | -8,009       |
| Equity (end of the year)                                  | 1,230        | 8,923        |
| Equity ratio (end of the year) (in %)                     | 30.4         | 82.9         |
| Balance sheet total (end of the year)                     | 4,048        | 10,762       |
| Cash flows used in operating activities (year)            | -6,994       | -12,117      |
| Cash flows used in operating activities (monthly average) | -583         | -1,010       |
| Cash flows used in investing activities (year)            | 460          | 459          |
| Cash flows provided by financing activities (net)         | 0            | 127          |
| Cash and cash equivalents at the end of period            | 3,783        | 10,291       |
| Probiodrug-Share  |              |              |
| Loss per share (basic and diluted) (in EUR)               | -0.94        | -0.98        |

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## 04 POST-PERIOD HIGHLIGHTS & OUTLOOK

# NIH GRANTS 15M US-\$ TO SUPPORT US PHASE 2B TRIAL



**Probiodrug and Alzheimer's Disease Cooperative Study (ADCS) Receive 15 Million USD National Institutes of Health (NIH) Grant for U.S. Phase 2b Core Program for PQ912**

***Study to Evaluate Safety and Efficacy of Drug Seeking to Treat Those with Mild Cognitive Impairment or Mild Dementia***

**HALLE (SAALE), Germany and San Diego, CA - USA, 20 March 2019** – Probiodrug AG, a clinical stage biopharmaceutical company developing novel therapeutic solutions to treat Alzheimer's disease (AD) (Euronext Amsterdam: PBD) and the Alzheimer's Disease Cooperative Study (ADCS), announced today that the National Institutes of Health (NIH) is funding in part a US Phase 2b core program to evaluate the efficacy and safety of Probiodrug's PQ912 in patients with mild cognitive impairment (MCI) or mild dementia due to AD with an NIH Research Project (R01) grant expected to total 15 million USD over four years.

A microscopic image of a cell, possibly a myeloid cell, with a complex, textured surface. The cell is primarily orange and yellow, with some darker, brownish spots. It has several long, thin, branching processes extending outwards. The background is a deep red color. The overall appearance is that of a biological specimen under a microscope.

probiodrug

# FIRST-IN-CLASS SMALL MOLECULES AS MYELOID IMMUNE- CHECKPOINT INHIBITORS

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augmenting cancer immunotherapy by blocking  
the CD47-SIRPa axis with QPCTL inhibitors

# QPCTL: A NOVEL TARGET FOR CANCER IMMUNOTHERAPY

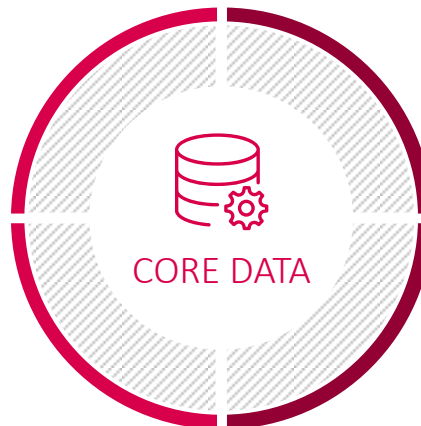


## Glutaminyl cyclase is an enzymatic modifier of the CD47- SIRP $\alpha$ axis and a target for cancer immunotherapy

Meike E. W. Logtenberg<sup>1</sup>, J. H. Marco Jansen<sup>1,2</sup>, Matthijs Raaben<sup>1,3</sup>, Mireille Toebes<sup>1,3</sup>, Katka Franke<sup>4</sup>, Arianne M. Brandsma<sup>1</sup>, Hanke L. Matlung<sup>1</sup>, Astrid Fauster<sup>1</sup>, Raquel Gomez-Eerland<sup>1</sup>, Noor A. M. Bakker<sup>1</sup>, Simone van der Schot<sup>1</sup>, Koen A. Marijt<sup>1</sup>, Martijn Verdoes<sup>1,4</sup>, John B. A. G. Haanen<sup>1</sup>, Joost H. van den Berg<sup>1</sup>, Jacques Neefjes<sup>1,5</sup>, Timo K. van den Berg<sup>1</sup>, Thijn R. Brummelkamp<sup>1</sup>, Jeanette H. W. Leusen<sup>1,6</sup>, Ferenc A. Scheeren<sup>1,6</sup> and Ton N. Schumacher<sup>1,4,7\*</sup>

interference with the CD47-SIRP $\alpha$  interaction potentially synergizes with cancer therapeutic antibodies used to opsonize tumor cells.

QPCTL inhibition enhances antibody-dependent cellular phagocytosis tumor cells.



## CD47-signal regulatory protein- $\alpha$ (SIRP $\alpha$ ) interactions form a barrier for antibody-mediated tumor cell destruction

Xi Wen Zhao<sup>1</sup>, Ellen M. van Beek<sup>1</sup>, Karin Schornagel<sup>1</sup>, Hans Van der Maaden<sup>1</sup>, Michel Van Houdt<sup>1</sup>, Mariëtte A. Otten<sup>1</sup>, Pascal Finetti<sup>1</sup>, Marjolijn Van Egmond<sup>1</sup>, Takashi Matozaki<sup>1</sup>, Georg Krahl<sup>1</sup>, Daniel Birnbaum<sup>1</sup>, Andrea van Elbas<sup>1</sup>, Taco W. Kuijpers<sup>1,2</sup>, Francois Bertucci<sup>1</sup>, and Timo K. van den Berg<sup>1,3\*</sup>

<sup>1</sup>Sankin Research and Landsteiner Laboratory, Academic Medical Center, University of Amsterdam, 1066 CX Amsterdam, The Netherlands; <sup>2</sup>Departments of Immunotherapeutics and Molecular Pharmacology, Merck Sharp and Dohme Research, 5342 CC, Oss, The Netherlands; <sup>3</sup>Immunotherapy Laboratory,

THE NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

## CD47 Blockade by Hu5F9-G4 and Rituximab in Non-Hodgkin's Lymphoma

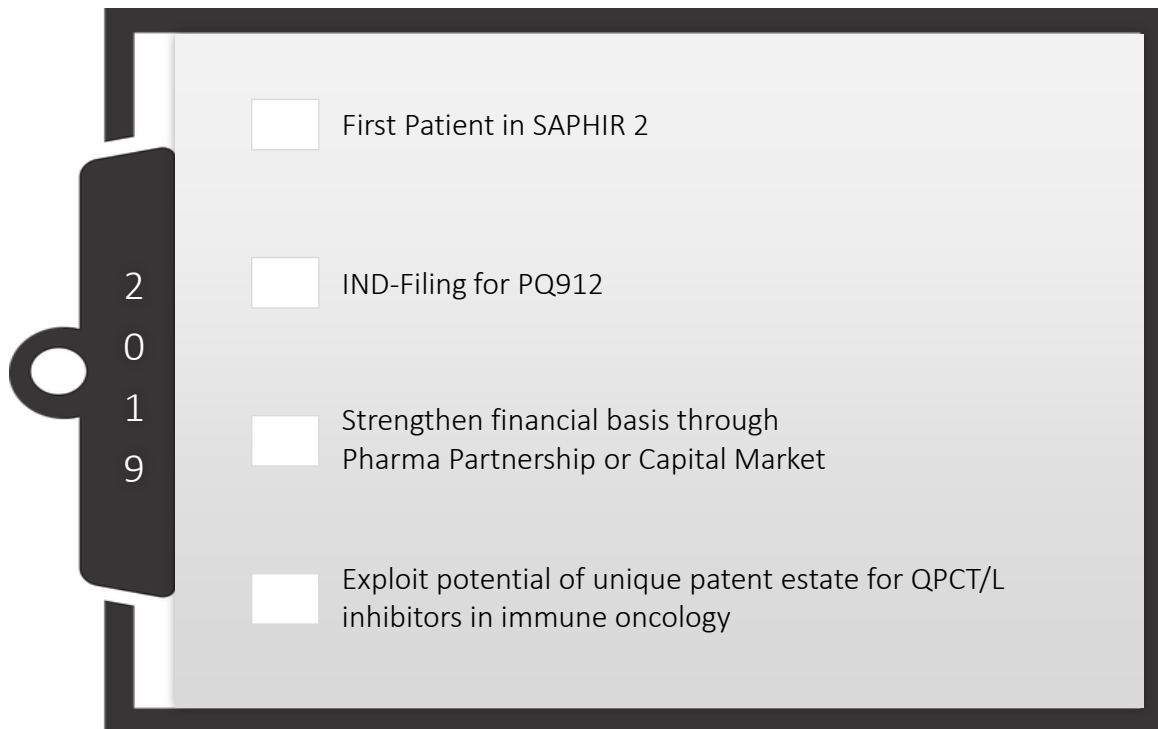
Ranjana Advani, M.D., Ian Flinn, M.D., Ph.D., Leslie Popplewell, M.D., Andres Forero, M.D., Nancy L. Bartlett, M.D., Nilanjan Ghosh, M.D., Ph.D., Justin Kline, M.D., Mark Roschewski, M.D., Ann LaCasce, M.D., Graham P. Collins, M.D., Thu Tran, B.S., Judith Lynn, M.B.A., James Y. Chen, M.D., Ph.D., Jens-Peter Volkmer, M.D., Balaji Agoram, Ph.D., Jie Huang, Sc.D., Ravindra Majeti, M.D., Ph.D., Irving L. Weissman, M.D., Chris H. Takimoto, M.D., Ph.D., Mark P. Chao, M.D., Ph.D., and Sonali M. Smith, M.D.

# MYELOID IMMUNE-CHECKPOINT INHIBITOR: PROBIODRUG'S UNIQUE POSITION

- Lead compound PQ912 did not induce anemia and is well tolerated in young and elderly\*.
- First-in-class small molecule approach circumvents antibody sink problem caused by red blood cells.
- Probiodrug owns a number of compounds with in vivo (monkey) plasma target occupancy of over 80% and patent expirations beyond 2035.
- QPCTL resides in the Golgi and CD47 molecules that newly arrive at the cell surface upon its inhibition already lack the pGlu modification - this may be an advantage relative to antagonistic antibodies that need to compete with SIRPa in the tumor microenvironment.

Probiodrug is open to enter into discussions on co-development programs  
in cancer indications

# OUTLOOK



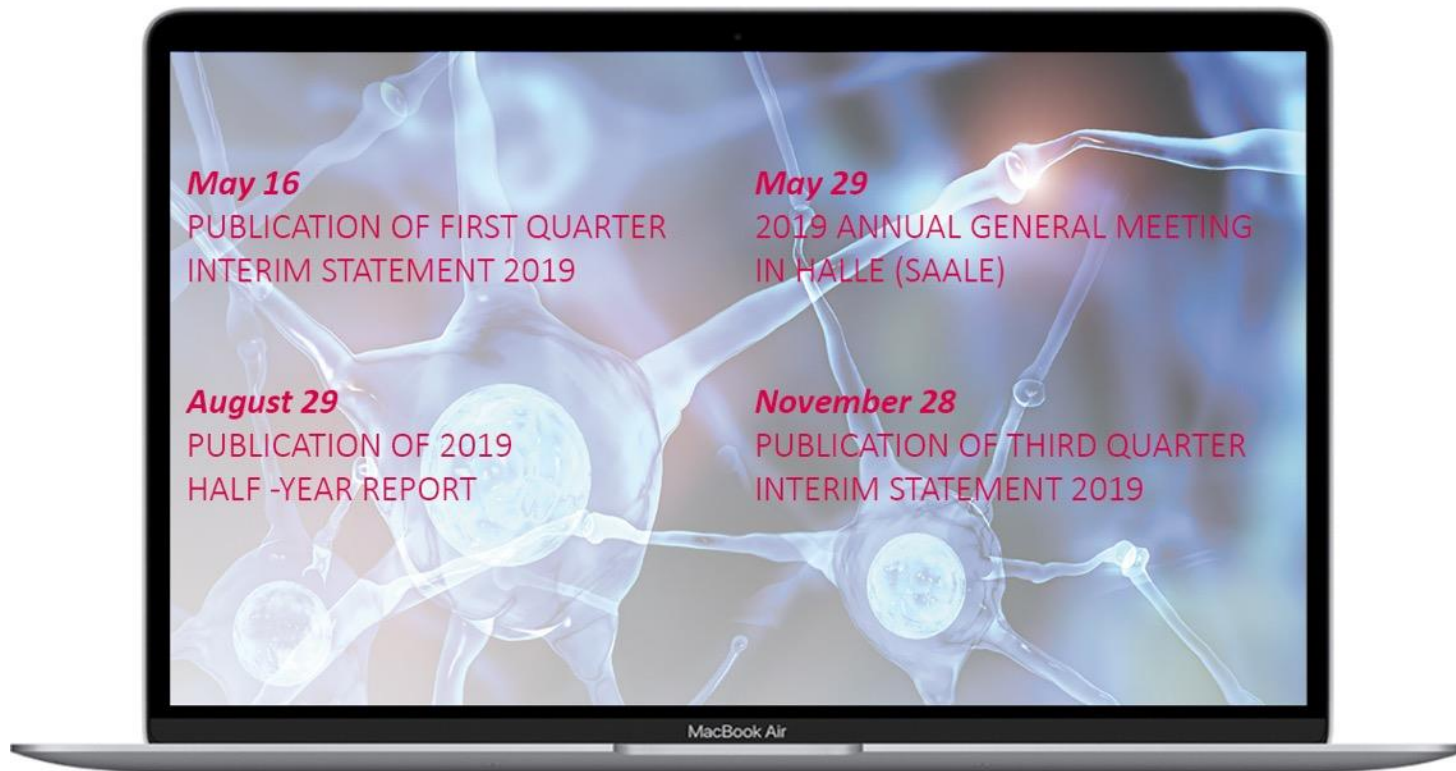
# OUTLOOK

## Mid-term focus of Probiodrug's business activities

- Execution of the Phase 2b clinical study program for PQ912,
- Continuing partner discussions with PBD-C06,
- Conclusion of one or more industrial partnerships,
- Further scientific analysis of potential second indications for the use of QC-inhibitors,
- Further strengthening Probiodrug's financial resources



# FINANCIAL CALENDAR 2019





probiobdrug

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## 05 Q&A



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THANK YOU!

# CONTACT



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