

HEALTHING AGING – PIONEERING INNOVATION

Beyond Tau and Abeta hypothesis – small molecule QPCT inhibitors as a disease modifying Alzheimer's Disease treatment

Cancer immune checkpoint modulation by QPCTL inhibitors

| Ulrich Dauer, January 2020



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ONE OF THE MOST ADVANCED DRUG CANDIDATES IN AD

Phase 2b ready
lead asset in
Alzheimer's disease



Further upside from
partnered oncology
program

morphosys

Opportunity to
monetize IP portfolio



- Building on strong safety package and first sign of improvement of cognition
- Well-informed Phase 2b trial could lead to results in 2022 in Europe and potential conditional approval by 2024

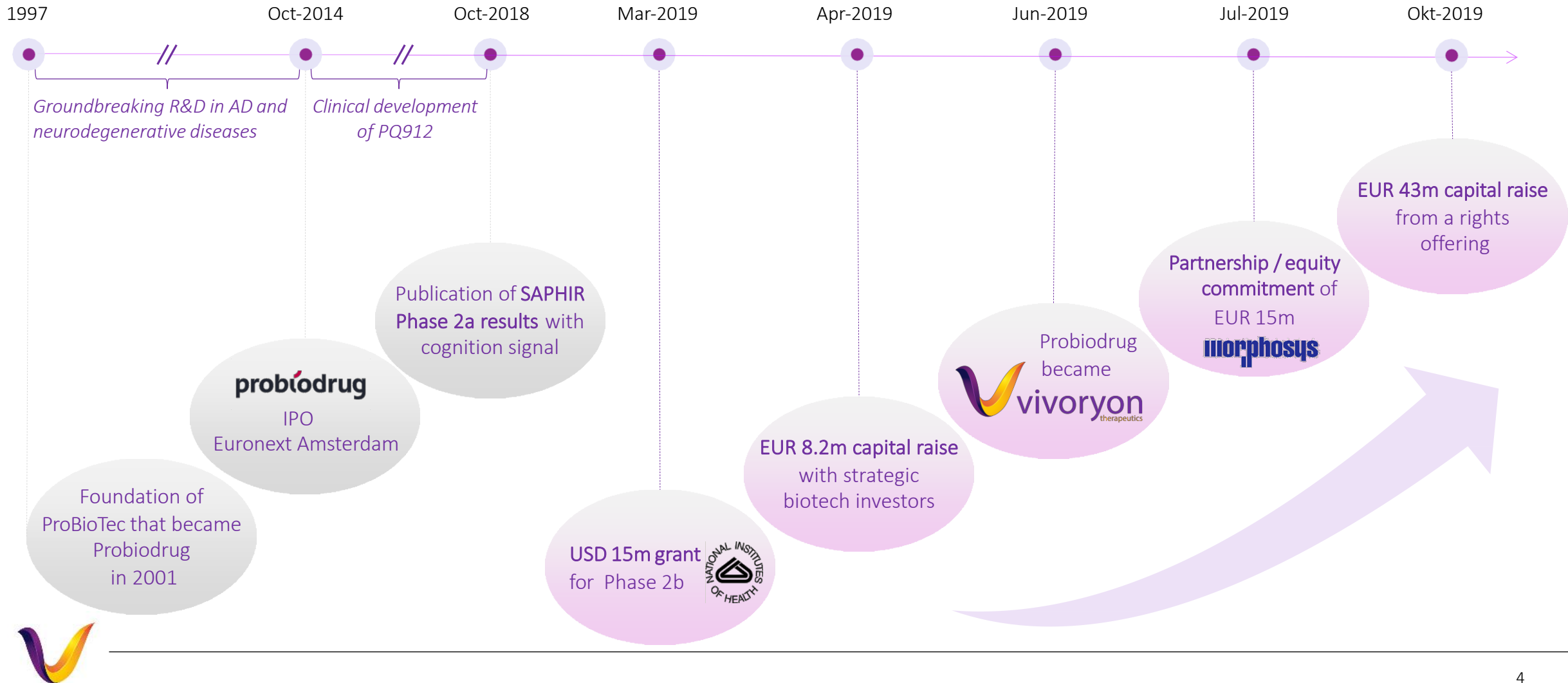
- Generated EUR 15m upfront equity commitment
- News flow expected to come from opt-in and clinical milestones

- Proven mode of action of glutaminyll inhibitors attracts potential partners
- Broad patent portfolio with global coverage on technology platform

What if all of us get a chance to age healthy...?

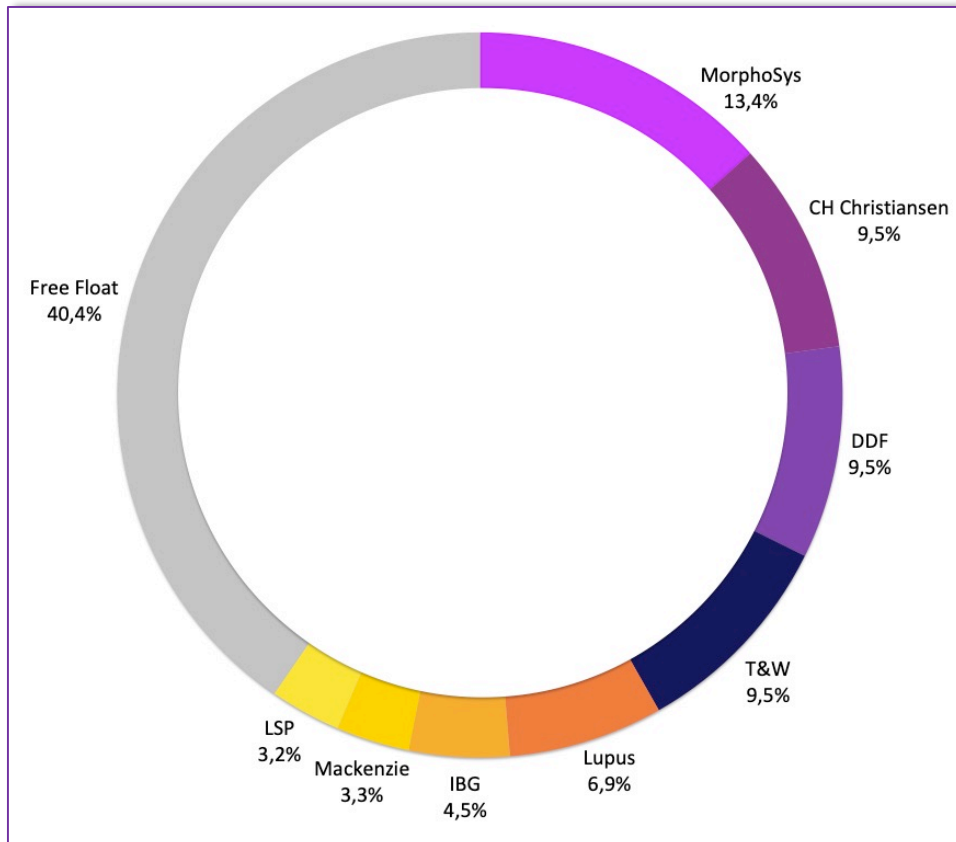


VIVORYON MADE SIGNIFICANT PROGRESS



SHAREHOLDERS AND STOCK

Shareholding structure¹



Stock

ISIN:	DE0007921835
WKN:	792183
Ticker symbol:	VVY
Types of shares:	Bearer shares
Number of shares	19,975,482
Stock exchange:	Euronext Amsterdam
Liquidity provider:	Kempen & Co. / NIBC
Listing agent:	Kempen & Co.
First trading day:	27 October 2014

Analyst Coverage

goetzpartners securities Limited

Brigitte de Lima

FMR Frankfurt Main Research AG

Christian Ehmann

NIBC

Anita Ye

Dylan van Haaften

Rx Securities

Samir Devani



ALZHEIMER'S REPRESENTS THE LARGEST UNMET MEDICAL NEED IN HEALTHCARE

11% of elderly is estimated to get Alzheimer's

Global AD healthcare costs are ~\$1 trillion/year

Only 4 Alzheimer's drugs are approved, which are only treating symptoms

There are 50m AD patients globally of which 5.5m in the US and 8m in the EU

\$290bn total cost estimation in 2019 of which \$195 paid by Medicare and Medicaid, which is 20% of the Medicare budget

0 disease modifying treatments are on the market

The number of AD patients is expected to 2x in 2040

Average onset is between 60-70 years with average death 5-10 years after diagnosis

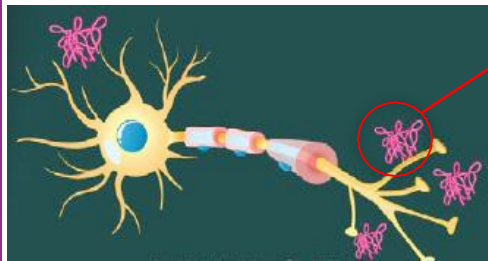
Alzheimer's is the 5th leading cause of death worldwide with 3m annual deaths



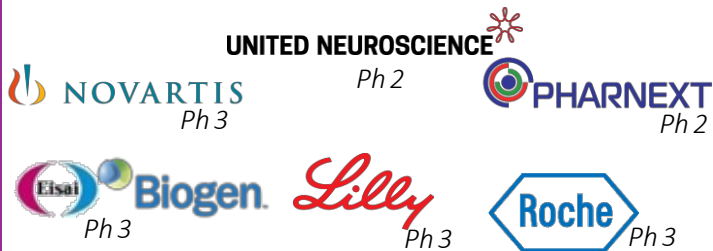
NOVEL APPROACHES BEYOND AB AND TAU

Traditional Aβ approaches

The last decades pharma focused on either reducing or stopping the formation of Aβ plaques. Whereas many showed the ability to reduce Aβ plaques, an effect on cognition was never achieved. In total hundreds of attempts failed during clinical development.

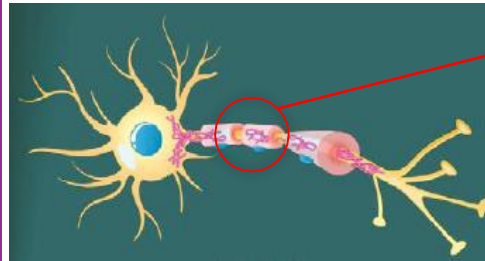


Aβ: Focus on Aβ plaque removal or production inhibition



Tau-related approaches

Over the last years Tau approaches, inhibiting neurofibrillary tangles gained popularity due to its improved correlation with the clinical onset and progression of AD as compared to Aβ. However, recent late stage candidates failed to show a cognition effect.



Tau: Focus on Neurofibrillary tangles within the neuron



Novel disease-modifying approaches

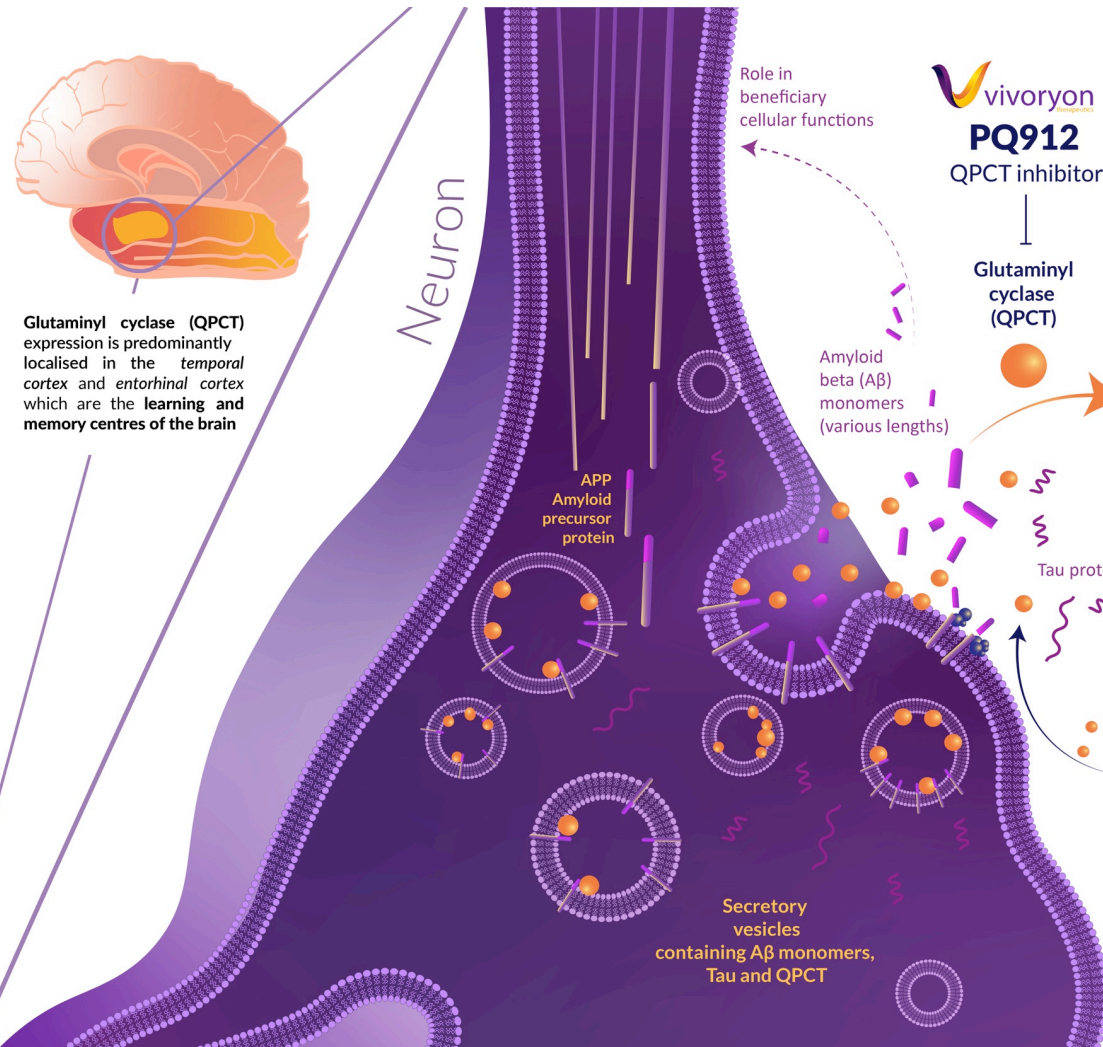
Recent developments and insights points towards a need for new AD strategies focusing on the aimed effect (improve cognition) instead of observable disease hallmarks / pathology.



Synaptic functioning: Focus on interaction between neurons

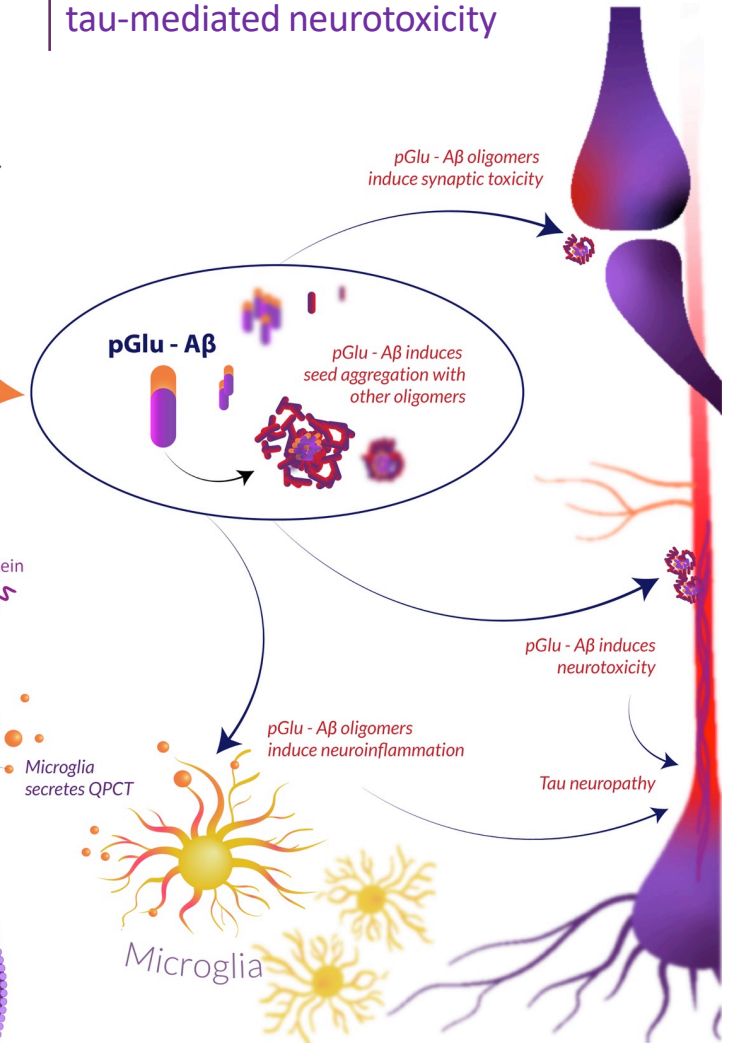


PQ912 A FIRST-IN-CLASS QPCT INHIBITOR TARGETING COGNITION



Glutaminy cyclase (QPCT) expression is predominantly localised in the temporal cortex and entorhinal cortex which are the learning and memory centres of the brain

Toxic pGlu species drive multiple AD-associated pathways, including oligomer aggregation, neuro-inflammation and tau-mediated neurotoxicity



DE-RISKED PHASE 2B

Well-informed Phase 2b design with similar endpoints

- Randomized placebo controlled
- Dose escalation up to 600 mg
- MMSE 20-30
- CSF amyloid positive
- Primary endpoint: cognitive function
- Estimated costs: EUR 30-50m (depending on parallel US trial)



NIH grant of USD 15m supports US trial

probiodrug

ALZHEIMER'S DISEASE
ADCS
COOPERATIVE STUDY



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

Parameter	European Phase 2b expects data mid 2022	US Phase 2b has a treatment duration of 78 weeks
Principal investigator	Prof. Dr. Scheltens, VU Amsterdam	Prof. Dr. Feldman, San Diego
# Patients / Clinical sites	250 / 10	462 / 55
Treatment duration	Min of 48w up to 96w	78w
Primary endpoint	Cognitive function as measured by neuropsychological test battery	Cognitive function as measured by CDR SOB
Patient flow	<p>Q1 2020 Q1 2021 Q1 2022 Mid 2022</p>	<p>Q2 2020 Q1 2022 Q4 2023 Q1 2024</p>



PARTNER MORPHOSYS WILL DRIVE ONCOLOGY

Exclusive option agreement on PQ912 and QPCTL platform in oncology

EUR 15m commitment in the ongoing rights issue:

- Commitment in the rights issue of up to EUR 15m, regardless of option exercise
- Acquisition of exclusive option to license QPCTL inhibitors for use in oncology

Upfront, milestone and royalty payments if the option is exercised:

- During the option period MorphoSys will conduct preclinical studies
- Vivoryon retains rights to develop the compounds in AD and other indications Opportunity to leverage close to market

Augmenting efficacy of Tafasitamab and other anti-tumor antibodies:

- FDA breakthrough designation Tafasitamab (MOR208) is a monoclonal antibody against CD19, expressed on B-cell related blood cancers:
- Diffuse large B cell lymphoma (DLBCL) – Phase 3 ongoing
- Chronic lymphocytic leukemia (CLL) – Phase 2 ongoing



MorphoSys and Vivoryon Therapeutics Enter Agreement on Small Molecule Inhibitors of CD47-SIRP alpha Signaling in Immuno-Oncology

HALLE (SAALE) and PLANEGG/MUNICH, Germany, 8 July 2019: Vivoryon Therapeutics AG (Euronext Amsterdam: VVY) and MorphoSys AG (FSE: MOR; Prime Standard Segment; MDAX & TecDAX; Nasdaq: MOR) today announced that they have entered into an agreement under the terms of which MorphoSys has obtained an exclusive option to license Vivoryon's small molecule QPCTL inhibitors in the field of oncology. The option covers worldwide development and commercialization for cancer of Vivoryon's family of inhibitors of the glutaminyl-peptide cyclotransferase-like (QPCTL) protein, including its lead compound PQ912. In exchange, MorphoSys has committed to investing up to EUR 15 million in a minority stake in Vivoryon Therapeutics as part of a capital raise planned for later this year.



VIVORYON'S GLUTAMINYL CYCLASE PLATFORM IS UNIQUELY POSITIONED IN IMMUNO-ONCOLOGY

Glutaminyl cyclase inhibitors have beneficial properties for IO

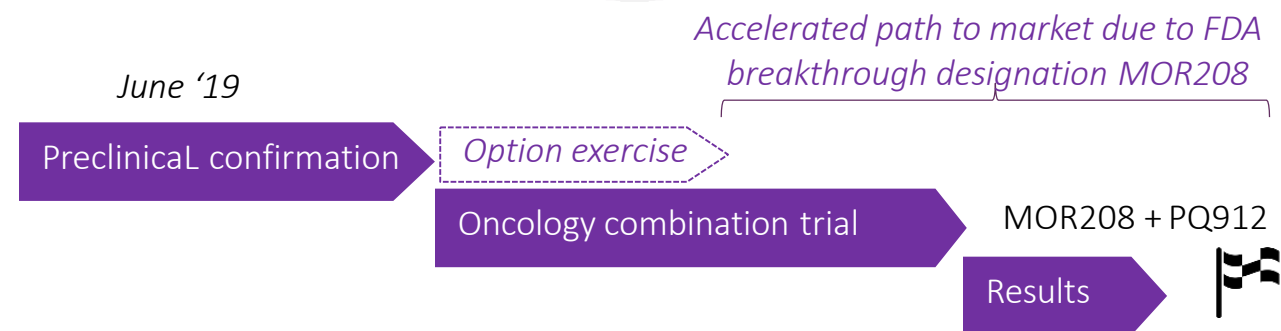
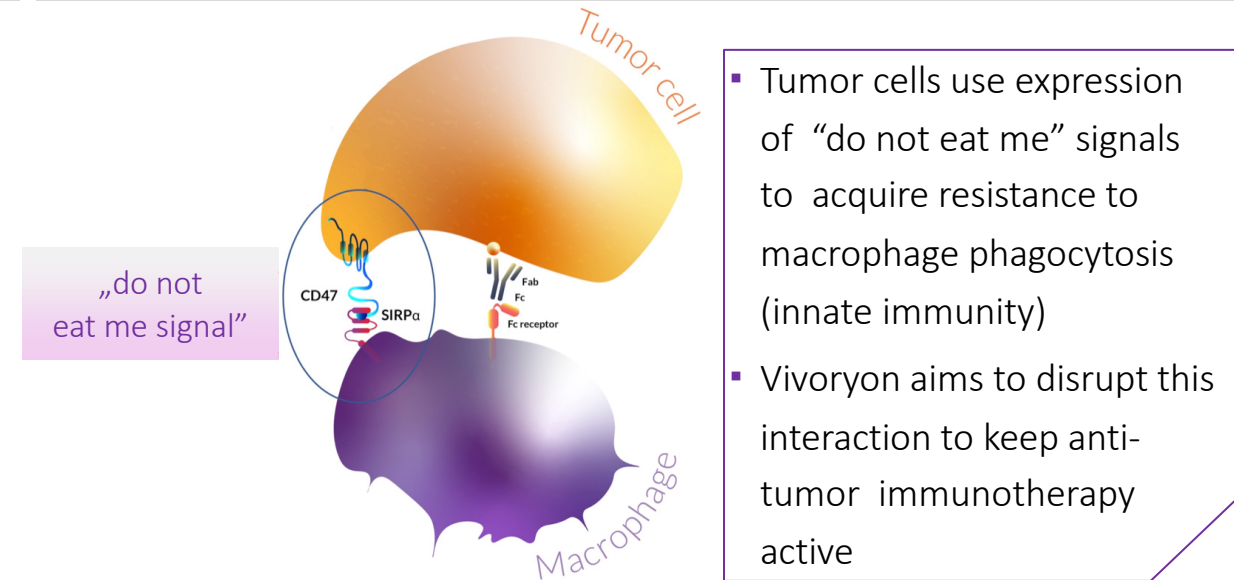
Vivoryon owns first-in-class QPCTL small molecule inhibitor platform:

- QPCTL have improved tumor penetration and targeting due to small molecule based compounds
- Small molecule approach circumvents antibody sink problem caused by red blood cells
- Extended patent portfolio including both composition of matter and indication coverage with expirations beyond 2034

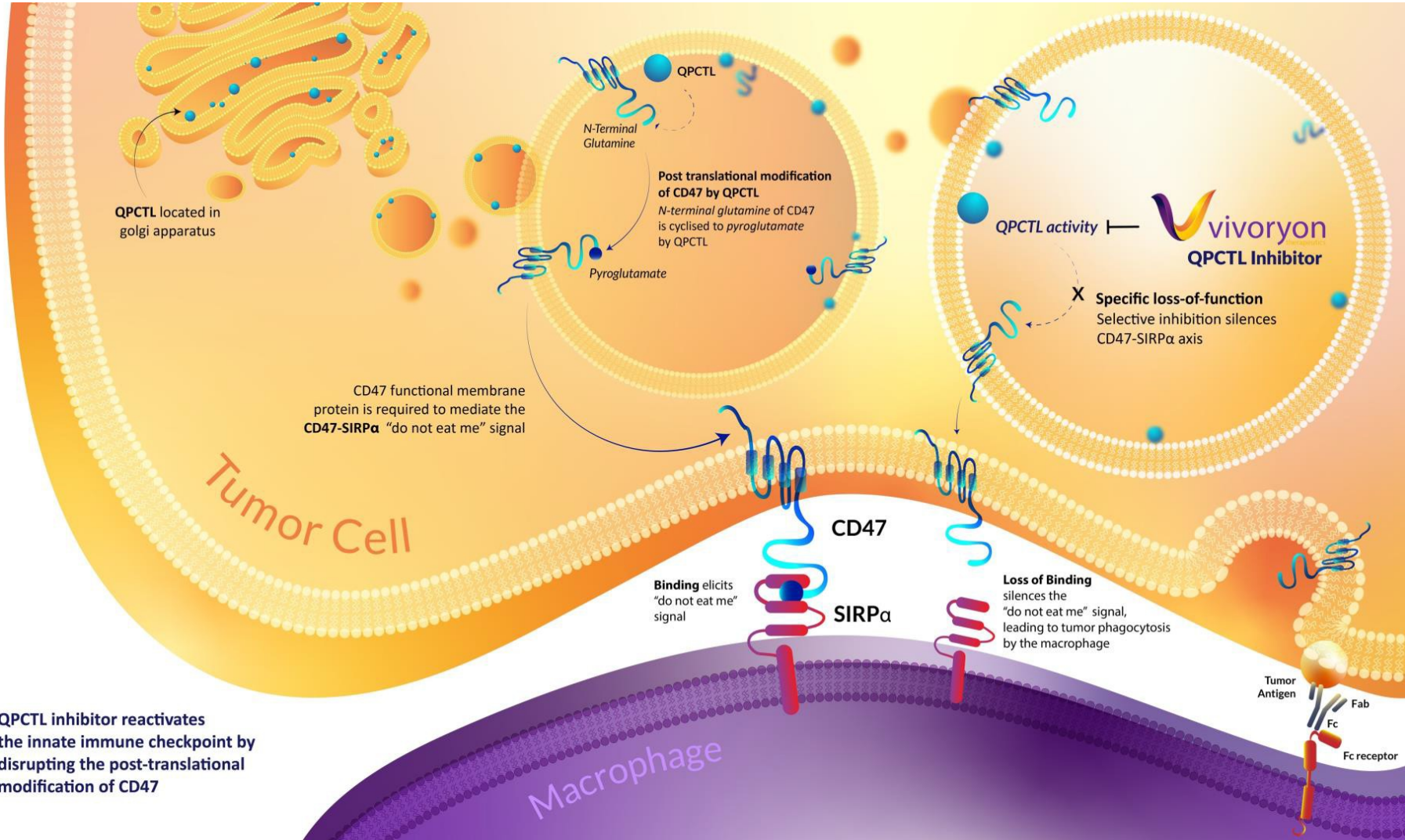
Results demonstrate potential upside in oncology:

- Lead compound PQ912 did not induce anemia and is well tolerated in young and elderly
- Compounds showed in vivo (monkey) plasma target occupancy (QPCTL) over 80%

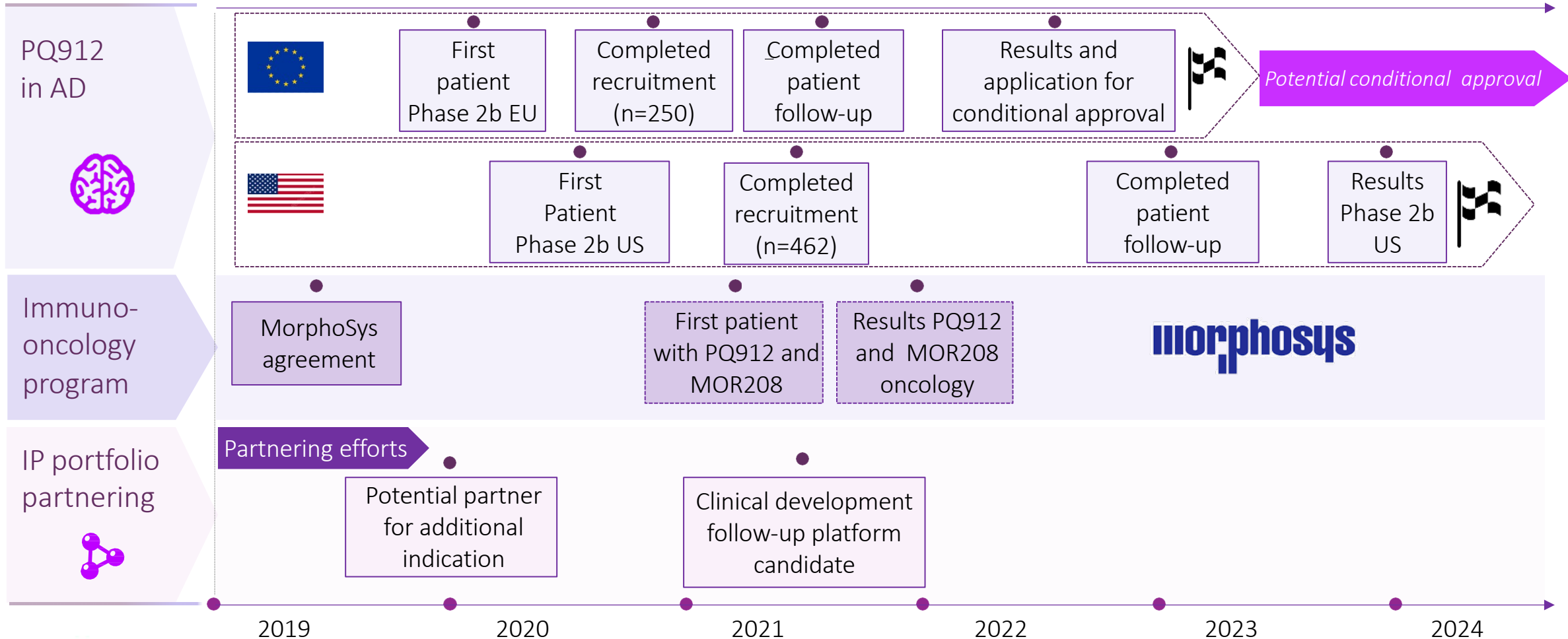
PQ912 blocks tumor escape and resensitizes tumors



DIFFERENTIATED MODE OF ACTION OF QPCTL INHIBITORS IN ONCOLOGY



NEAR TERM NEWS FLOW COMING FROM PQ912



UNIQUE POTENTIAL FOR VALUE CREATION



FIRST-IN-CLASS
QPCT/L INHIBITORS
FOR ALZHEIMER'S
DISEASE THERAPY &
CANCER IMMUNE
CHECKPOINT
INHIBITION

Leading innovator in Alzheimer's Disease Targeting pGlu-species - the most neurotoxic driver of disease initiation and progression

Innovative small molecule myeloid immune checkpoint inhibitors

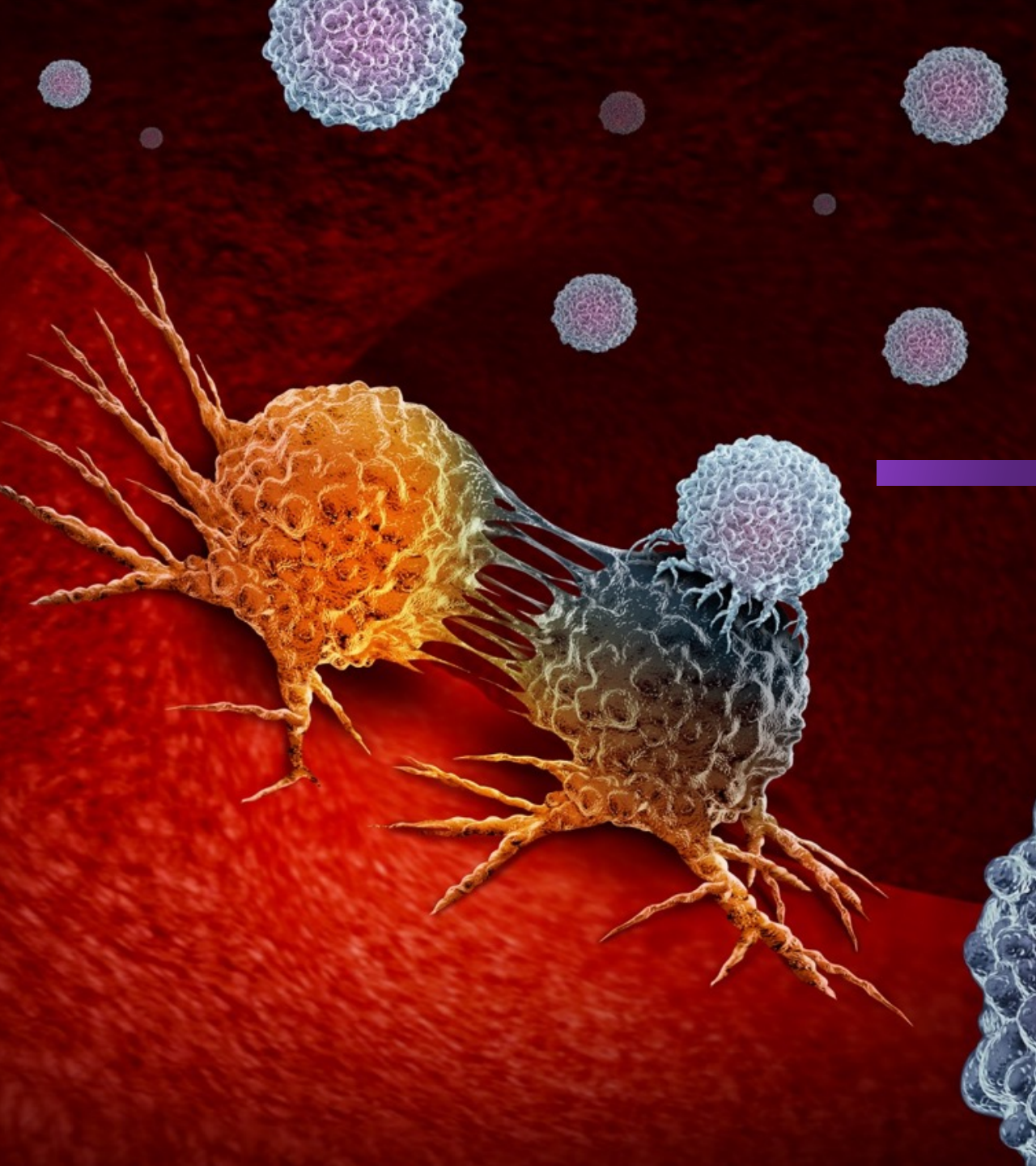
Strong Balance sheet with EUR 43m capital increase

Excellent in-house clinical expertise and **network with top key opinion leaders**

Strong IP estate based on composition of matter and medial use claims

Well defined development path with potential for conditional approval upon completion of Phase 2b in AD and near term option to start clinical Phase 1 co-medication trails in cancer immunotherapy





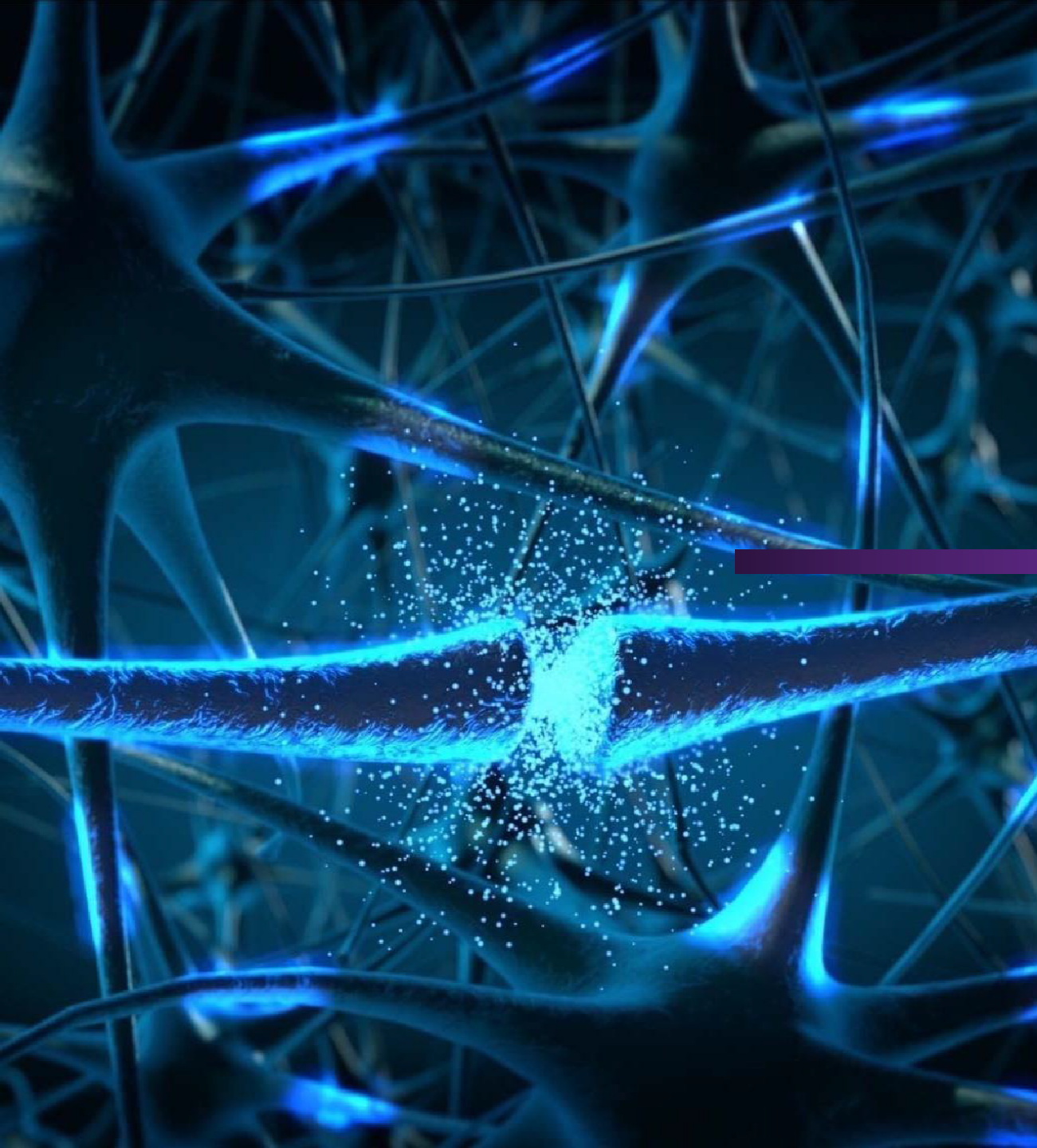
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APPENDIX

VIVORYON'S MANAGEMENT BOARD



ULRICH DAUER, PhD
CEO

- More than 20 years experience in the biotech industry
- Successfully closed multiple licensing deals, M&A transactions and public capital raises
- PhD in Chemistry from the Julius-Maximilians University of Würzburg
- Has held CEO and Chief Strategy Officer positions in several private and public entities:



MICHAEL SCHAEFFER, PhD
CBO

- More than 15 years experience in life sciences industry
- Strong background in strategic and corporate development
- PhD in Molecular Biology from Ludwig-Maximilians-University of Munich
- Has held several biotech founder and C-level positions:



SAPHIR PHASE 2A: TRIAL DESIGN



OBJECTIVES

Primary objective:

Using a high dose of PQ912 to assess safety and tolerability when compared with a placebo

Exploratory secondary objectives:

Scientifically most advanced biomarker and pharmacodynamic endpoints selected

- Molecular biomarkers in CSF:
 - Abeta pattern, Neurogranin and inflammatory markers
- Physiological function assessments:
 - EEG and rested state functional MRI to measure synaptic plasticity and neuronal connectivity
- Cognitive read-outs:
 - Neuropsychological Test Battery (NTB) to test short-term memory improvements



SAPHIR PHASE 2A TRIAL DESIGN



DESIGN

7 EU countries,

21 sites, principal investigator,
Prof. Dr. Philip Scheltens, Amsterdam

1:1 randomization

12 week treatment, week one: 400 mg bid,
weeks 2-12: 800 mg bid

4 week follow up

120 Total number of patients:

→ Early stage (3&4) Alzheimer's Disease

- MMSE*: 21-30 inclusive
- Abeta level in CSF below cutoff 638 ng / L
- T-tau level in CSF above cutoff 375 ng/L or p-tau level in CSF above cutoff >52 ng / L
- Tau / Abeta ratio in CSF >0,52
- Positive amyloid PET if available

→

“Treatment naive”: no other Alzheimer drugs as co-medication



SAPHIR PHASE 2A TRIAL: NO MAJOR SAFETY CONCERNS

Under high dosing only very minor differences in the number of adverse events (AE) and serious adverse events (SAE) between active and control arm

Significantly higher number of patients discontinuing treatment within initial weeks of treatment with PQ912 800mg twice daily (bid) compared to a placebo

- Clinically relevant differences in number of patients with skin and GI effects
- Events appeared early in the study and were fully reversible



Overall no major safety concern associated with PQ912

Safety and tolerability are likely to be improved by a lower dose and a slower titration regimen while maintaining a high enzyme inhibition

MAXIMUM TOLERATED
DOSE IDENTIFIED



SAPHIR PHASE 2A TRIAL: SIGNIFICANT IMPROVEMENT OF COGNITION PARAMETER WITHIN 3 MONTHS



CLEAR PROOF OF MECHANISM OF ACTION

Molecular biomarkers in cerebrospinal fluid (CSF):

Strong QC-inhibition, target occupancy approximately 90 %

Significant reduction of the synaptic marker neurogranin*, and the inflammatory marker YKL40**, which are both enhanced in early AD



SIGNIFICANT EFFECTS ON SYNAPTIC FUNCTION

Physiological function assessment with electroencephalography (EEG):

Significant effect on 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), $p=0.025$, Cohen's $d=0.45$



IMPROVEMENT OF A COMPONENT OF WORKING MEMORY

Cognition using the Neuropsychological Test Battery (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.”

– Prof. Dr. Philip Scheltens,
Principal Investigator

