

# HALF YEAR 2020 RESULTS WEBCAST AND CONFERENCE CALL

Halle (Saale) / Munich, August 27, 2020

| Vivoryon Therapeutics AG

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# TODAY ON THE CALL



Dr. Ulrich Dauer  
Chief Executive Officer



Dr. Michael Schaeffer  
Chief Business Officer





## AGENDA

- 01 FINANCIALS HALF YEAR 2020
- 02 OPERATIONAL REVIEW HALF YEAR 2020
- 03 OUTLOOK
- 04 Q&A

# SPOTLIGHT H1 2020

## Vivoryon Therapeutics and Nordic Bioscience Enter Research and Development Collaboration

HALLE (SAALE), Germany and Herlev, Denmark, 14 January 2020 – Vivoryon Therapeutics AG (Euronext Amsterdam: VVY, ISIN DE0007921835) and Nordic Bioscience, announced today an agreement to collaborate [...]

[READ MORE](#)

## Vivoryon Therapeutics Announces Update on Phase 2b Alzheimer's Clinical Trial, VIVIAD

Vivoryon has extended the trial protocol through the inclusion of exploratory parameters and plans to enroll patients in selected study sites in Denmark, Germany and the [...]

[READ MORE](#)

## Vivoryon Therapeutics Starts Development Program for Meprin Protease Inhibitors with Intended Therapeutic Use in Fibrosis, Cancer and Alzheimer's Disease

HALLE (SAALE) / MUNICH and LEIPZIG, Germany, 16 April 2020 – Vivoryon Therapeutics AG (Euronext Amsterdam: VVY, ISIN DE0007921835) announced today that the Company has entered [...]

[READ MORE](#)

## Vivoryon Therapeutics Announces Outcome of Exclusive Option Deal with MorphoSys

MorphoSys will not execute the option deal to license Vivoryon's small molecule QPCTL inhibitors for oncology. Vivoryon will continue to evaluate QPCTL inhibitors in oncology [...]

[READ MORE](#)

## Vivoryon Therapeutics Provides Update on US and EU Alzheimer's Clinical Trial Program with PQ912

Vivoryon and the Alzheimer's Disease Cooperative Study (ADCS) have developed a new trial design for Phase 2a Alzheimer's trial in the US; as a stage gate [...]

[READ MORE](#)



# POST PERIOD

Vivoryon Therapeutics Announces Enrollment of First Patient in VIVIAD, European Phase 2b Alzheimer's Disease Study with Varoglutamstat (PQ912)

HALLE (SAALE) / Munich, Germany, 15 July 2020 – Vivoryon Therapeutics AG (Euronext Amsterdam: VVY, ISIN DE0007921835) today announced that the first patient has been enrolled in [...]

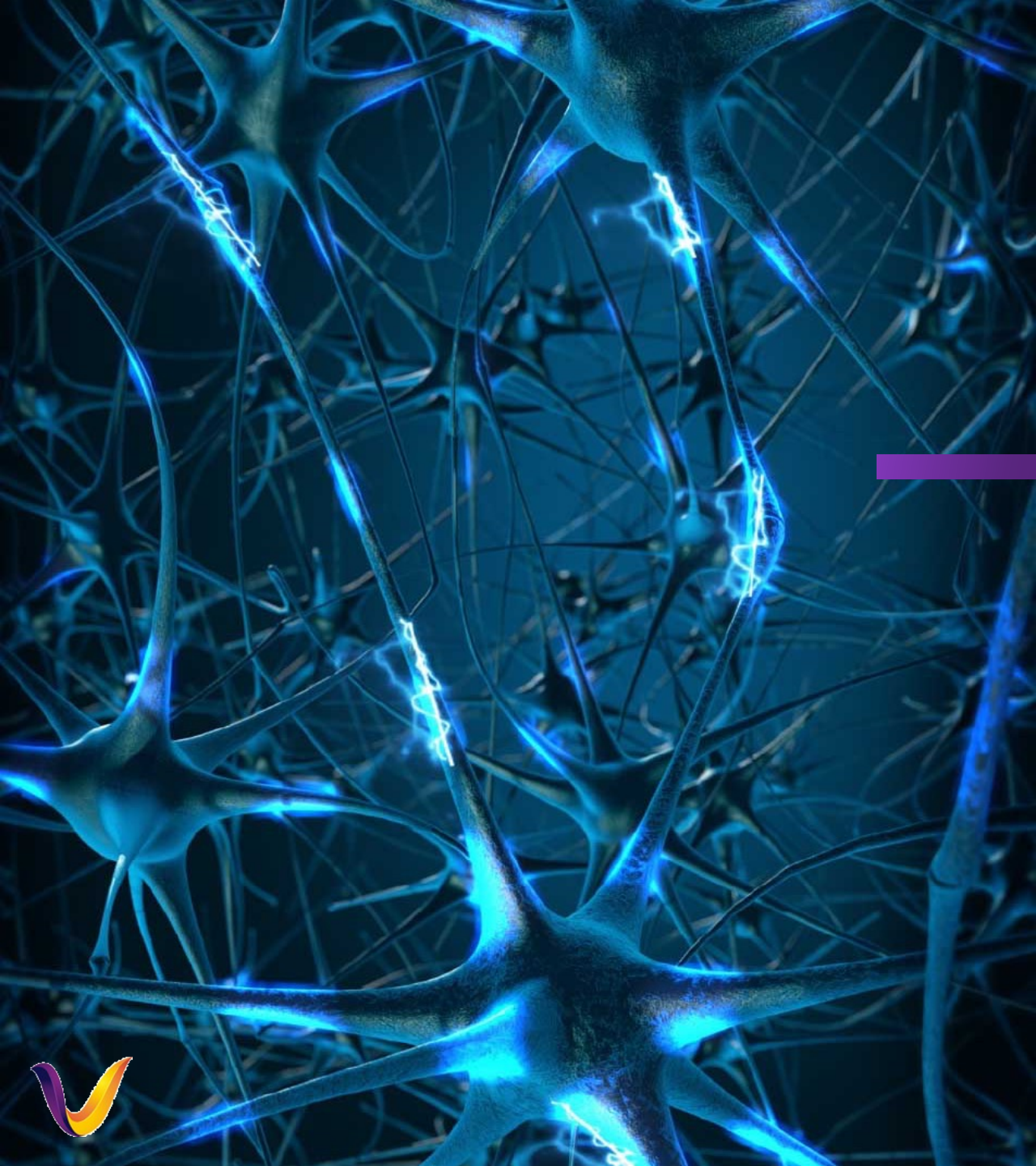
[READ MORE](#)

Vivoryon Receives IND Approval for Varoglutamstat's (PQ912) Phase 2 Study in Alzheimer's Disease

HALLE (SAALE) / Munich, Germany, 04 August 2020 – Vivoryon Therapeutics AG (Euronext Amsterdam: VVY, ISIN DE0007921835) today announced that the U.S. Food and Drug Administration (FDA) [...]

[READ MORE](#)





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# 01 FINANCIALS HALF YEAR 2020

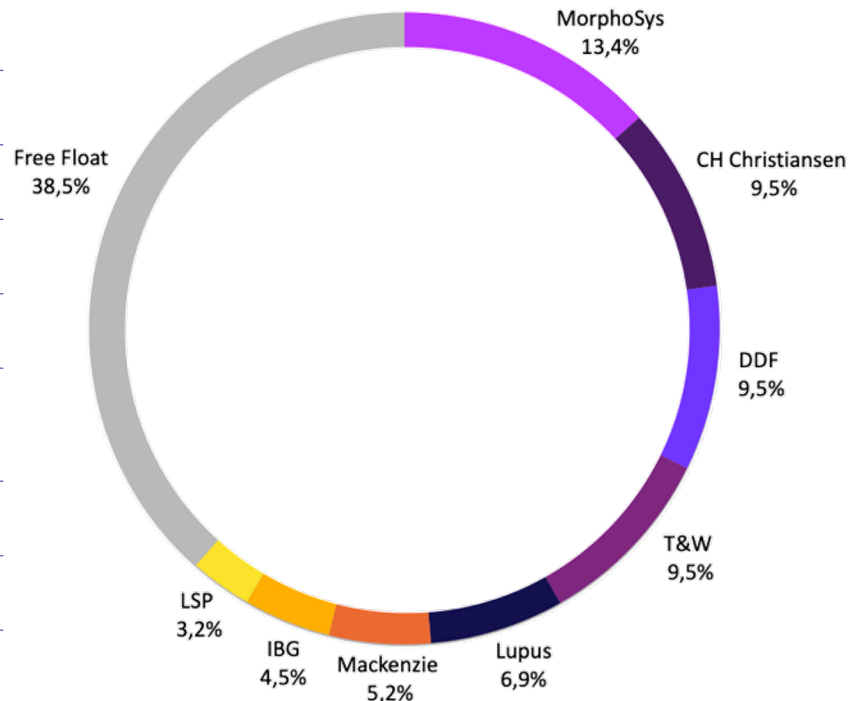


# SHARE

## KEY INFORMATION

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.
Listing agent:	Kempen & Co.
First trading day:	October 27, 2014

## SHAREHOLDER STRUCTURE\*



## SHARE PRICE



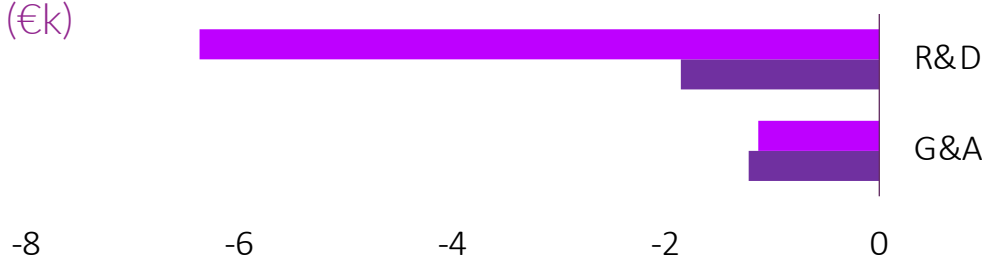


# KEY FINANCIAL HIGHLIGHTS, P&L (IFRS)

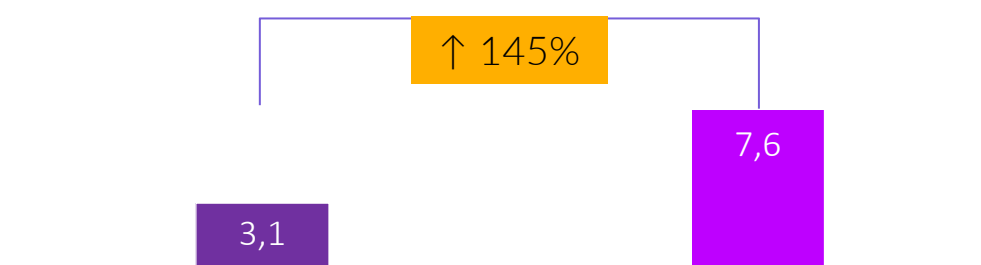
IN €k

	H1 2020	H1 2019	Variance in %
Research and development expenses	-6,380	-1,862	70,8
General and administrative expenses	-1,138	-1,223	7,5
Other operating income	38	8	78,9
Operating loss	-7,480	-3,077	58,8
Finance income	0	0	0
Finance expenses	-92	-15	83,69
<b>Net loss for period</b>	<b>-7,572</b>	<b>-3,091</b>	<b>59,2</b>

## OPERATING LOSS (€k)



## NET LOSS (€k)



■ 2019 ■ 2020



# KEY FINANCIAL FIGURES (IFRS)

In €k	June 30, 2020	June 30, 2019	Dec 31, 2019
Earnings, Financial and Net Assets Position			
Operating loss	-7,480	-3,077	-7,715
Finance income /loss	-92	-15	-108
Net loss for the period	-7,572	-3,091	-7,823
Equity (end of the reporting period)	35,075	5,636	42,665
Equity ratio (end of the reporting period) (in %)	92.5	60.8	93,0
Balance sheet total (end of the reporting period)	37,900	9,269	45,861
Cash flows from operating activities (cum.)	-6,274	-3,428	-11,608
Cash flows from operating activities (monthly average)	-1,029	-571	-967
Cash flows from investing activities	-31,501	-4	-47
Cash flows from financing activities	-45	7,644	49,354
Cash and equivalents	3,623	7,999	41,524
Current securities and short-term time deposits	30,848	0	0
Vivoryon Therapeutics-Share			
Loss per share (basic/diluted) (in EUR)	-0.38	-0.31	-0.62



# TARGETING PATHOLOGICAL POST-TRANSLATIONAL MODIFICATION

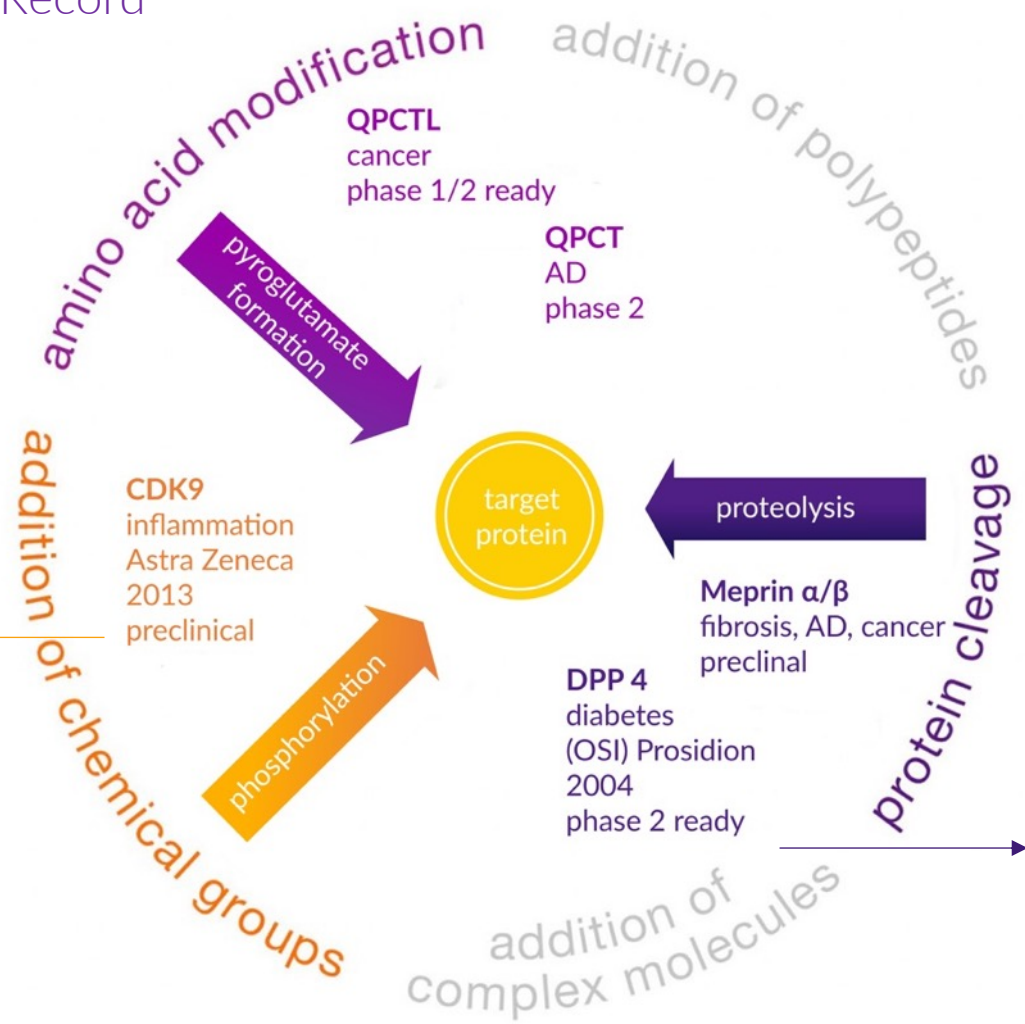
Leading European Biotech - Track Record

physiological functions of pyroglutamate formation

chemokine and peptide protection against proteolysis

mediation of protein-protein interactions

Successfully sold in 2013 to



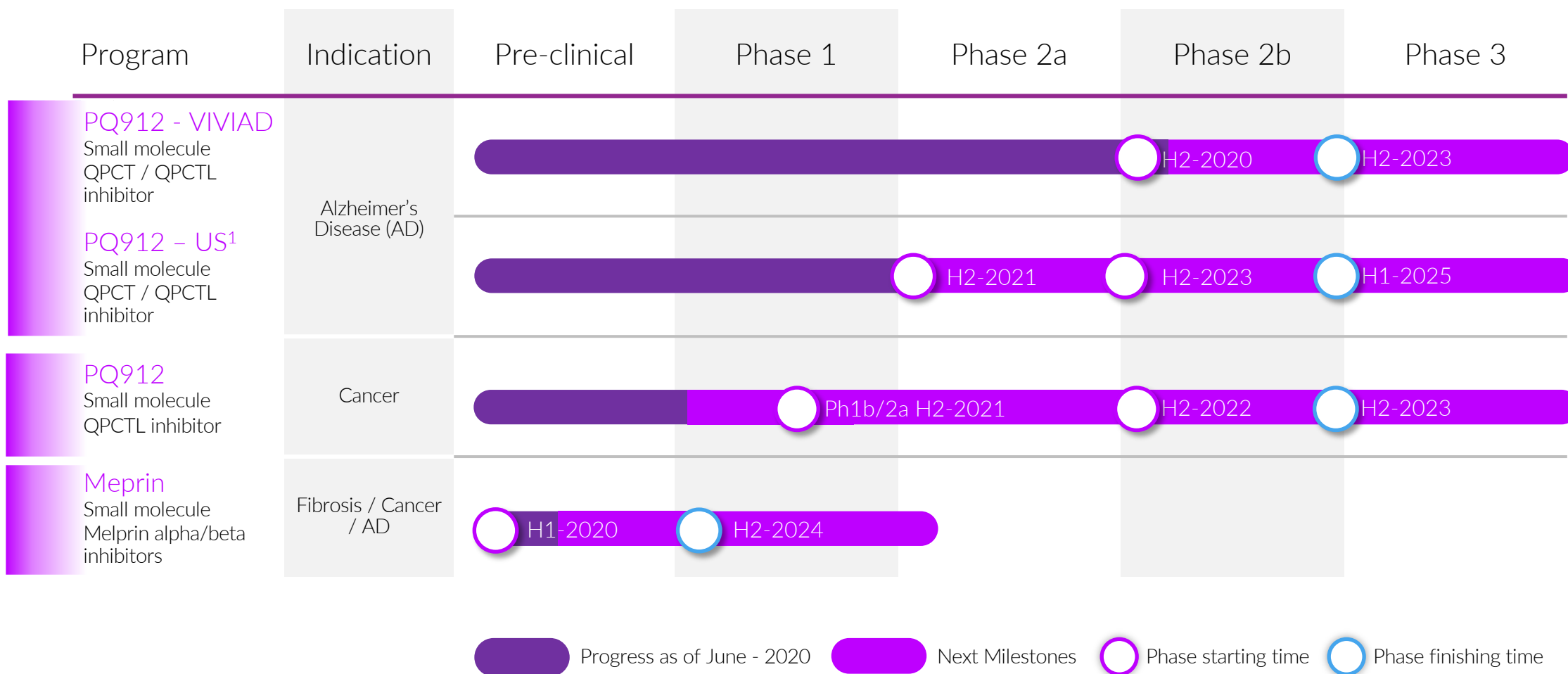
post-translational modifying enzymes are therapeutic targets

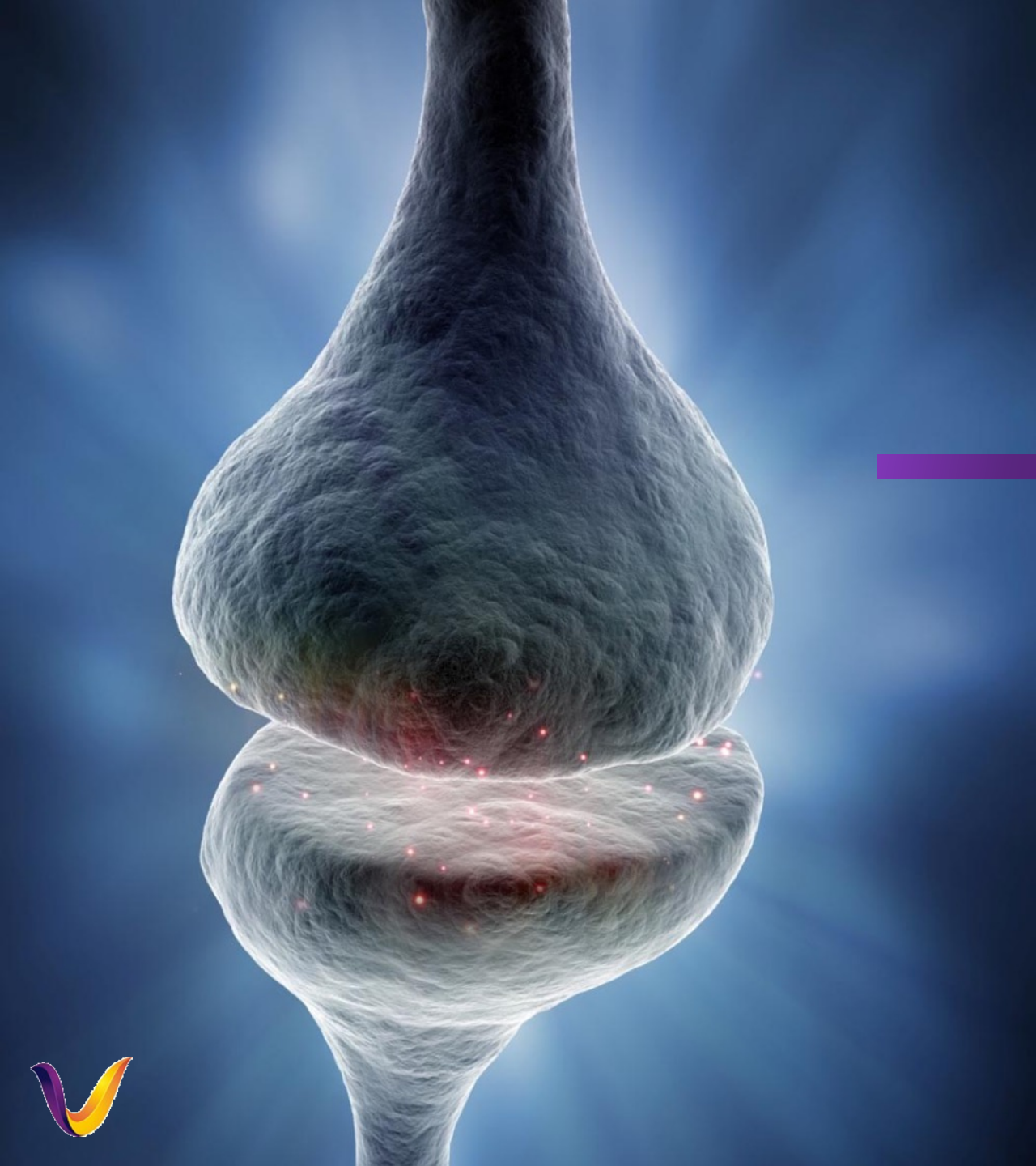
- Kinases
- Phosphatases
- Proteases
- Methylases
- Ligases
- Acetylases
- ...

Successfully sold in 2004 to **(OSI) pharmaceuticals / **



# VIVORYON'S FIRST-IN-CLASS DRUG PIPELINE





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## 02 OPERATIONAL REVIEW HALF YEAR 2020



# BROAD & DIVERSIFIED PROJECT PORTFOLIO

1

Phase 2  
lead asset in  
Alzheimer's disease



- Ongoing well-informed Phase 2b trial with final results in Europe expected in 2023
- US Phase 2 study supported by significant NIH grant – starts 2021, read-out expected in 2023

2

Clinical trial ready  
program: Oncology



- Potential for a combination therapy with a broad range of tumor antibodies
- Program available for clinical development partnerships
- Alternatively, own clinical Phase 1b trial in planning

3

Preclinical program:  
Meprin protease inhibitors



- Targeting acute kidney injury, fibrosis and cancer
- Proven mode of action in animal model
- Clear path towards clinical Phase 1 stage

4

Exploring other therapeutic  
areas for QC inhibitors



- With varoglutamstat (PQ912): a molecule with validated safety profile available
- Exploring other applications for QPCT/L inhibitors disease areas include inflammation, HD, NASH

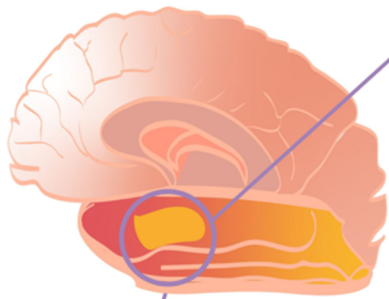
What if...



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



- 1
- 2
- 3



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

Neuron

Role in beneficiary cellular functions

**vivoryon**  
**PQ912**  
QPCT inhibitor

Glutaminyl cyclase (QPCT)

Amyloid beta (Aβ) monomers (various lengths)

**pGlu - Aβ**

pGlu - Aβ induces seed aggregation with other oligomers

pGlu - Aβ oligomers induce synaptic toxicity

pGlu - Aβ induces neurotoxicity

pGlu - Aβ oligomers induce neuroinflammation

Tau neuropathy

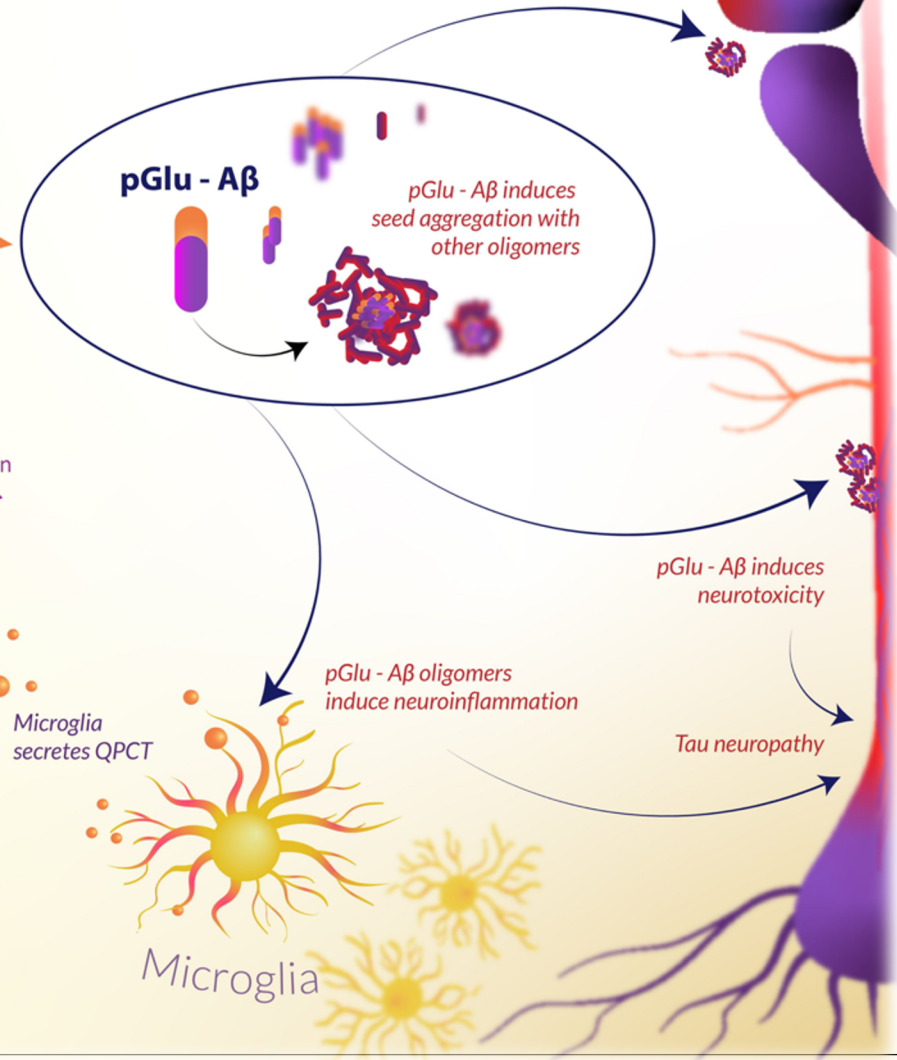
Microglia secretes QPCT

Microglia

APP  
Amyloid precursor protein

Tau protein

Secretory vesicles containing Aβ monomers, Tau and QPCT

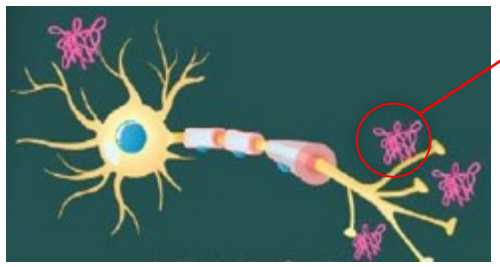


Toxic pGlu species drive crucial AD-associated pathways, including oligomer aggregation, neuro-inflammation and tau-mediated neurotoxicity








# TARGETING COGNITION & DISEASE PATHWAYS- APPROACHES BEYOND CLASSICAL Abeta & 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.

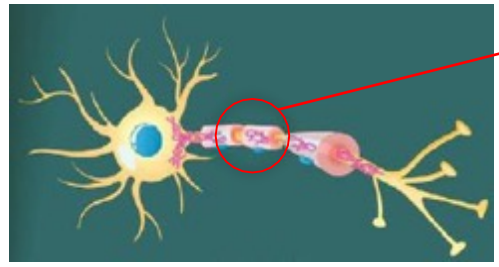


Aβ: Focus on Aβ plaque removal or production inhibition


 **NOVARTIS** Ph 3  
 **UNITED NEUROSCIENCE** Ph 2  
 **PHARXENT** Ph 2  
 **Eisai** Ph 3  
 **Biogen** Ph 3  
 **Lilly** Ph 3  
 **Roche** Ph 3

## 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

 **abbvie** Ph 2  
 **axon** NEUROSCIENCE Ph 2  
 **AC Immune** Ph 2

## Novel disease-modifying approaches

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



Synaptic functioning: Focus on Interaction between neurons

 **Neurim** PHARMACEUTICALS  
 **COXGRX**  
 **Denovo** Biopharma  
 **anavex** LIFE SCIENCES Corp  
 **Lilly**  
 **EIP** PHARMA  
 **CASSAVA** sciences





1

2

3

# VIVORYON'S EU PHASE 2B AD TRIAL

The logo features a large, 3D-style 'V' in shades of blue and purple, followed by the word 'ivoryon' in a lowercase, blue, sans-serif font.

Advancing disease modifying treatment and non-invasive diagnostics for  
Alzheimer's disease



# VIVIAD – FOCUS ON LOW-INVASIVE ANALYSIS

## EEG:

- Brain waves are measured in an eyes closed task free 15-minute session
- Theta power as an indicator for communication between brain regions

## Speech analysis :

- Using speech pattern to monitor cognitive health
- Syntactic, semantic, informative and coherence patterns are analyzed using AI

## Blood-based biomarkers:

- Exploratory blood-based biomarkers are reducing invasive CSF sampling
- Blood based measurements of: NFL, QC activity, Tau, ECM, GFAP



# PHASE 2 STRATEGY

## Well-informed Phase 2b trial design in Europe

- Randomized placebo-controlled
- Dose escalation up to 600 mg
- MMSE 20-30
- CSF amyloid positive
- Primary endpoint: cognitive function
- Estimated costs: EUR 30m-35m



## NIH grant of USD 15m supports US Phase 2 trial

- Randomized placebo-controlled Phase 2a
- Designed as a stage-gate to Phase 2b
- Cognitive outcome after 24w
- CSF amyloid positive
- Primary endpoint: safety/tolerability (DAE-I proportion)
- Estimated costs: EUR 3-4m (in addition to NIH grant)



Parameter	European Phase 2b expects data mid 2023	US Phase 2a expects data mid 2023
Principal investigator	Prof. Dr. Scheltens, VU Amsterdam	Prof. Dr. Feldman, San Diego
# Patients / Clinical sites	250 / 10	180 / 30
Treatment duration	Min of 48w up to 96w	24w
Primary endpoint	Cognitive function as measured by NTB	Cognitive function as measured by ADNI scores
Patient flow		



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# OUR GLUTAMINYL CYCLASE PLATFORM IS UNIQUELY POSITIONED IN CANCER THERAPY

Two disease relevant pathways are hit by QC inhibitors

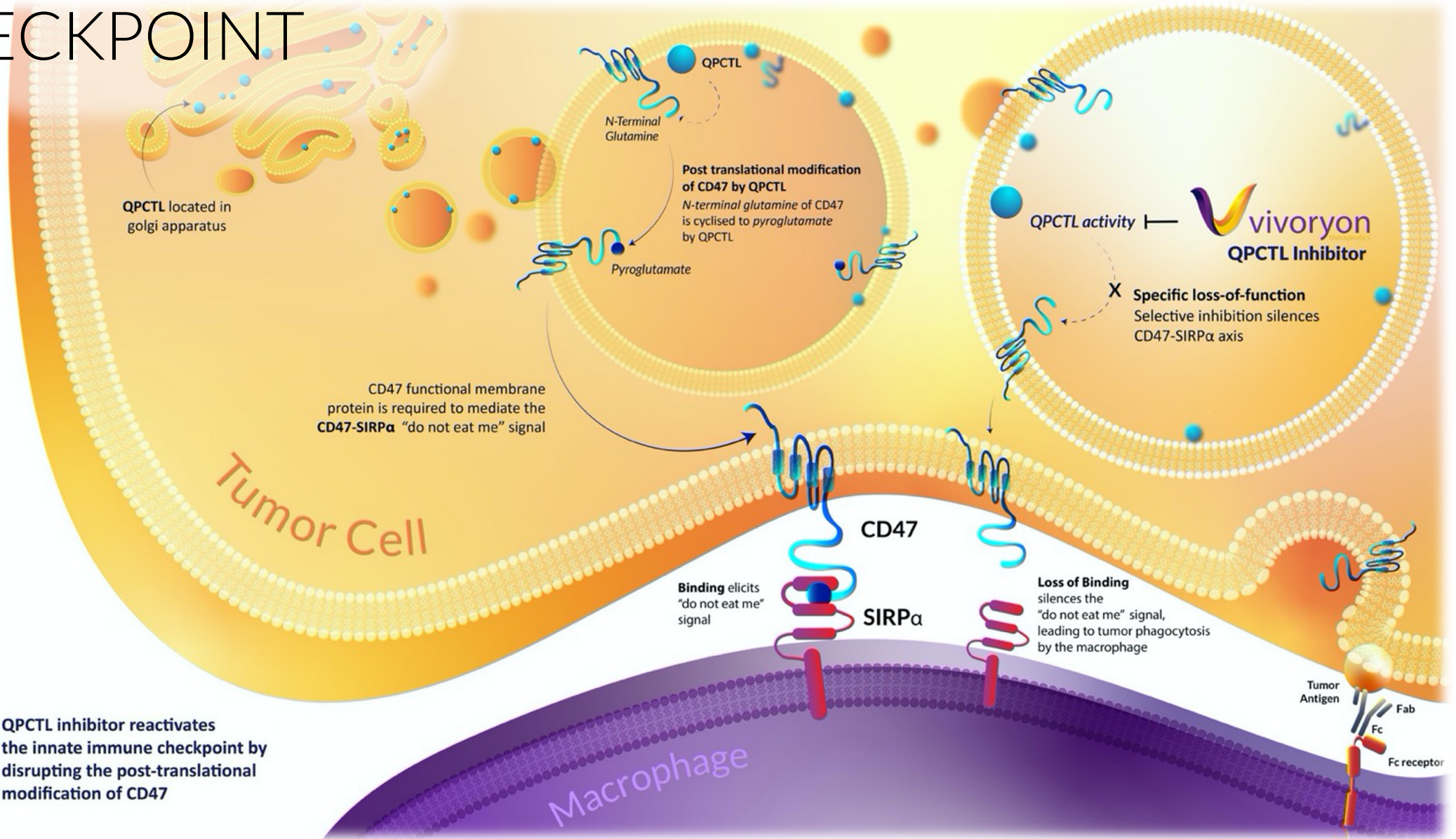
- Clinical Phase 1/2 ready compound with varoglutamstat (PQ912)
- Good tox profile: mild to moderate and reversible AEs in clinical trials
- Targeting the **CD47-SIRP $\alpha$**  innate immune system checkpoint. First-in-class small molecule approach, circumvents antibody sink problem caused by red blood cells
- Labeling of the tumorigenic chemokine **CCL2** for faster degradation.
- Extended patent portfolio including both composition of matter and indication coverage with expirations beyond 2034

Vivoryon owns 40 patent families around QC inhibitors and is constantly strengthening its platform with additional patents



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# VAROGLUTAMSTAT MODULATES THE CD47-SIRP $\alpha$ CHECKPOINT



QPCTL inhibitor reactivates the innate immune checkpoint by disrupting the post-translational modification of CD47

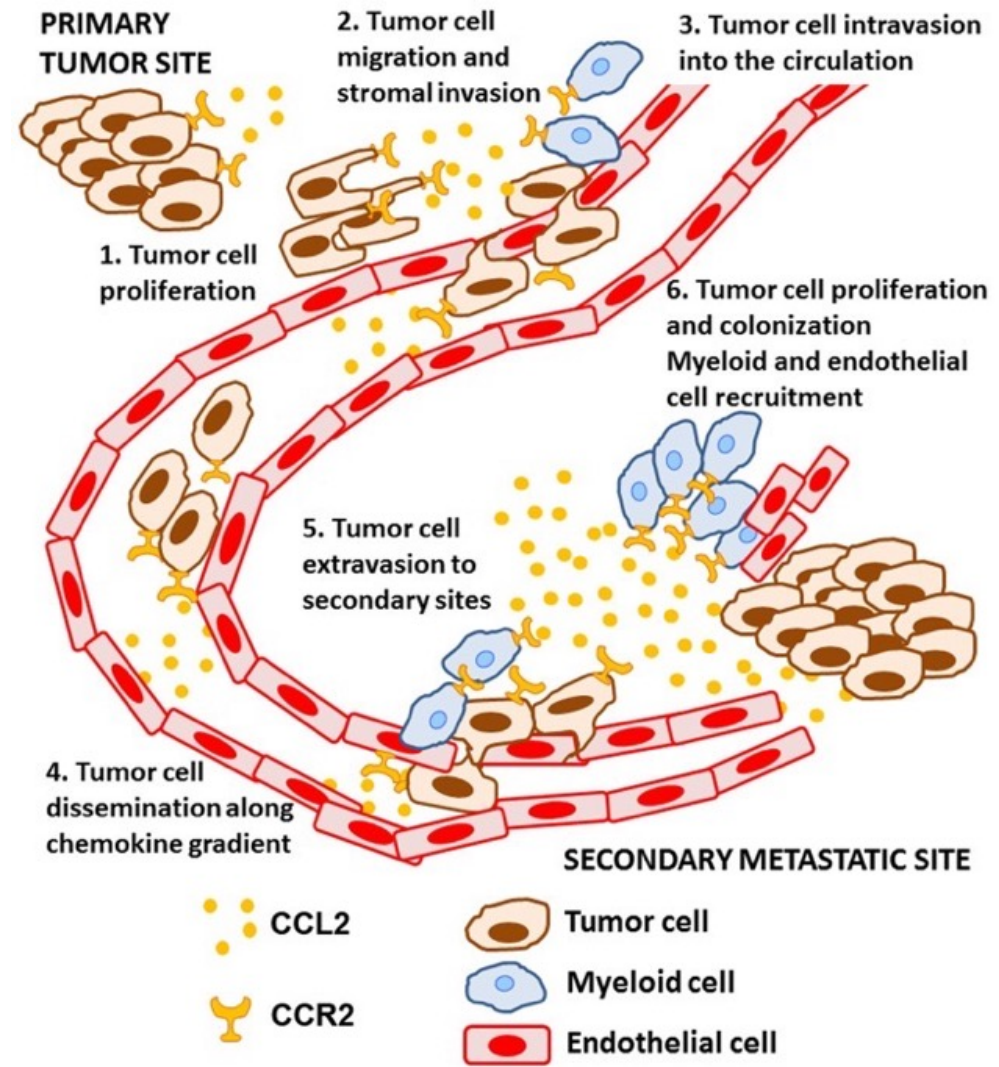


# VAROGLUTAMSTAT TARGETS METASTASIS BY DECREASING CCL2 STABILITY

- The CCL2-CCR2 axis has been described as being critical for the metastatic process
- QPCTL catalyzes the modification of CCL2 into of N-terminal pyroglutamate pE-CCL2
- pE-CCL2 is much more resistant to degradation by aminopeptidases
- N-terminally degraded forms of CCL2 have markedly diminished biological activity

pE-CCL2 is a strong activator of the CCL2-CCR2 axis

QPTCL inhibitors block pE-CCL2 formation and thus could act as anti-metastatic compounds

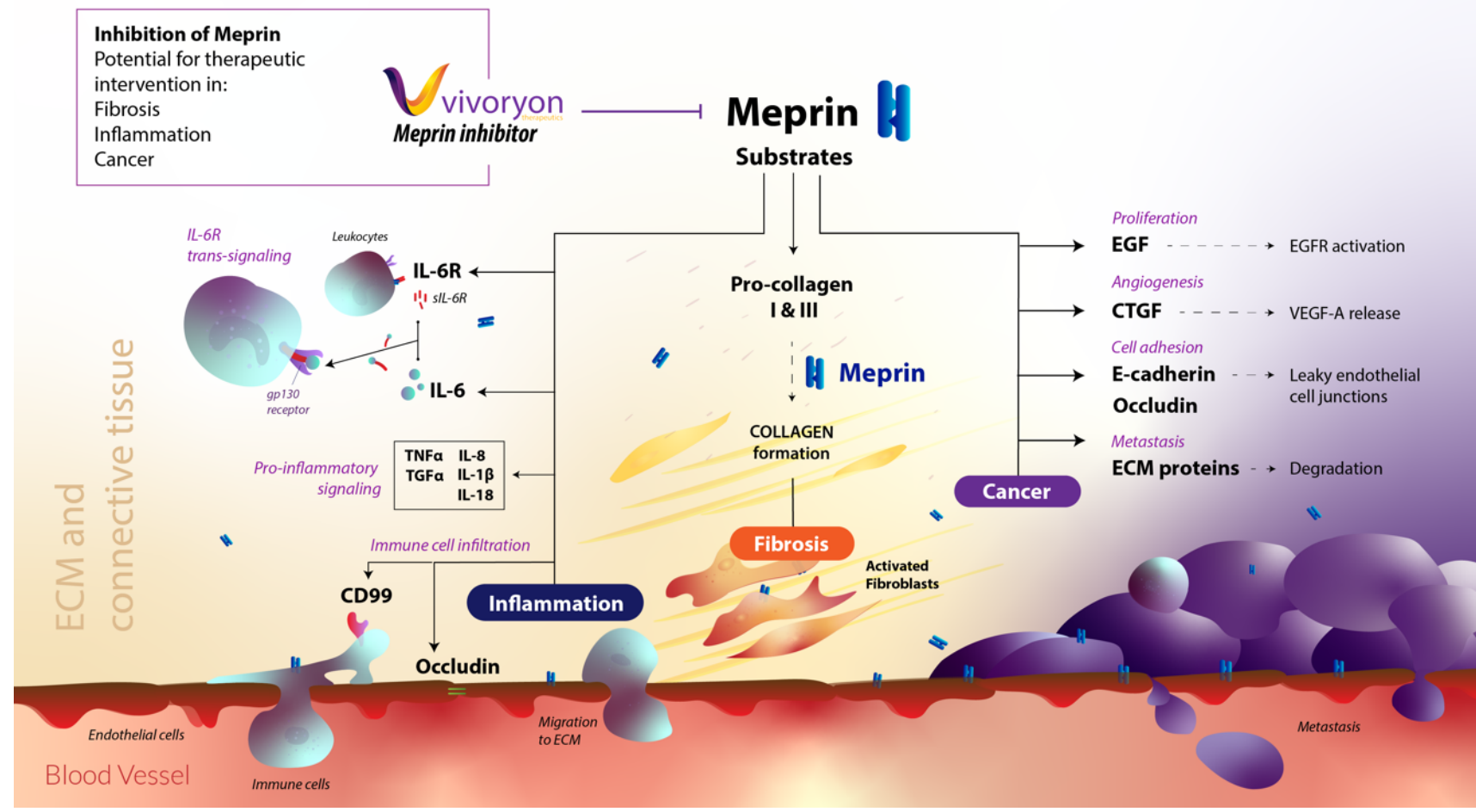


# MEPRIN: UNIQUE IP POSITION ON EMERGING TARGET

Focus on pathologic post-translational modification ACUTE KIDNEY INJURY - FIBROSIS - CANCER

Metalloproteases, crucial for ECM remodeling and activation of cytokines & signaling receptors

- Acquired IP from FhG Leipzig
- Lead compound with animal proof-of-concept in AKI model
- Portfolio of nanomolar inhibitors selective for Meprin a and b.
- PCTs 2017, 2018, & later





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## 03 OUTLOOK





# NEAR-TERM INFLECTION POINTS

- All sites fully recruiting H2 2020
- Interim safety data analysis (dose finding) of VIVIAD trial in AD 2021
- Start of a Phase 2 AD Study in US in 2021
- Potential to start clinical combination trial in oncology in 2021
- Advancing Meprin inhibitors towards clinical stage testing - in collaboration with FhG
- Partnership discussions with respect to Vivoryon's pipeline programs expected to come into fruition

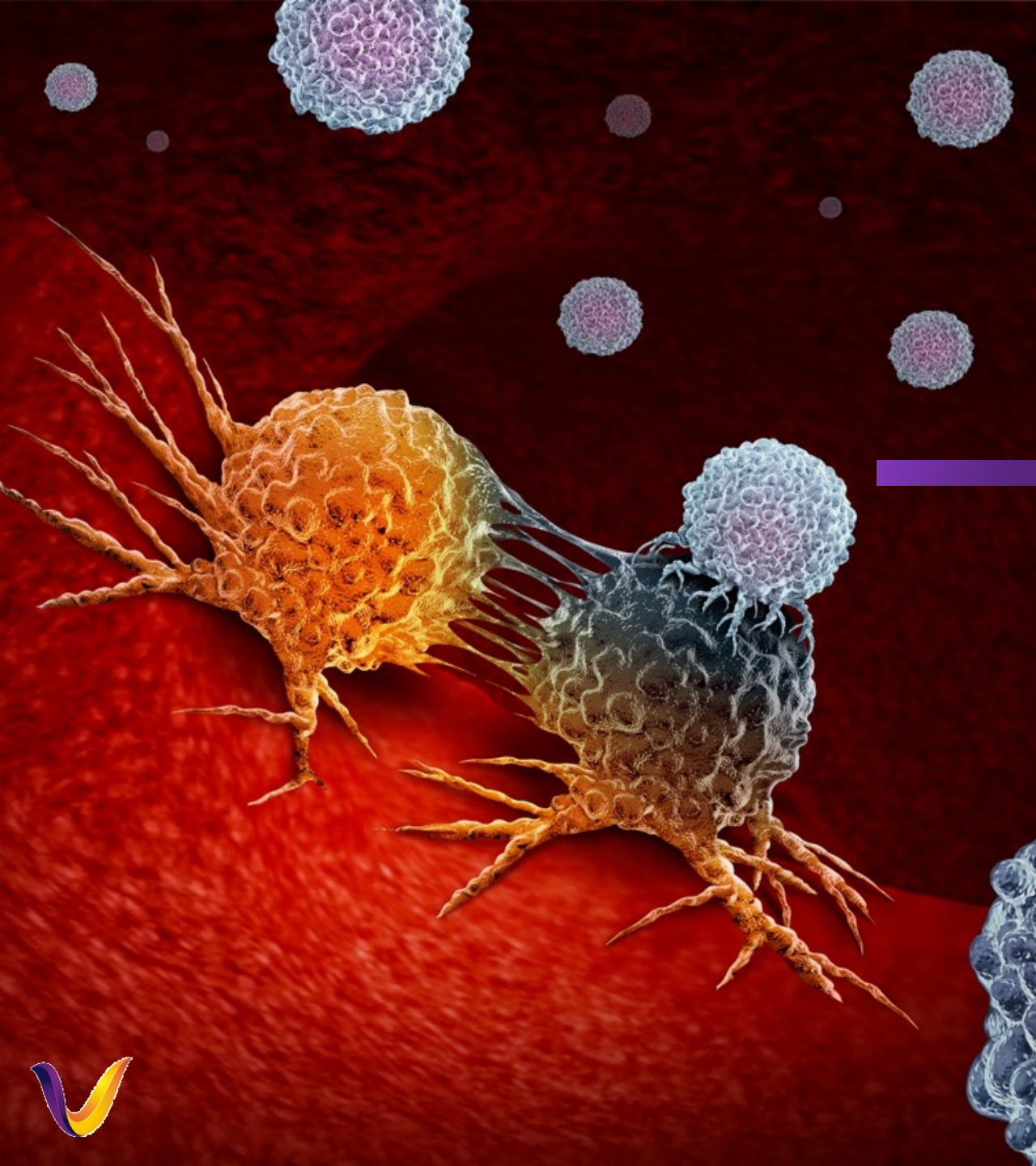




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## 04 Q&A





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