

# THIRD QUARTER 2023 RESULTS WEBCAST AND CONFERENCE CALL

December 6, 2023

| Vivoryon Therapeutics N.V.

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# Vivoryon is Uniquely Positioned to Improve Health Outcome in Patients with Early Alzheimer's Disease



## Unique First-in-Class Approach

**Stops production of neurotoxic N3pE-amyloid**

- ◆ **Validated MOA:** targeting all key hallmarks of AD (amyloid, tau, neuroinflammation)
- ◆ **Avoids mAb constraints:** ARIA, imaging, infusions, costs
- ◆ **Large addressable market:** worldwide ~55m people living with dementia, of which estimated 60-70% is AD



## Robust Development Program

**Phase 2 studies progressing well**

- ◆ **VIVIAD (EU):** Fully recruited (259 pts), ~82 weeks of treatment, final topline data readout: during end of Q1/2024
- ◆ **VIVA-MIND (US):** recent DSMB decision for 600 mg BID - same dose as VIVIAD with faster titration



## Proven Team of Innovators

**Strong discovery and development**

- ◆ **Management:** track record of bringing multiple innovative drugs to market
- ◆ **Healthy runway:** cash through key value generating milestones into H2/2024
- ◆ **Leader** in oral QPCT/L inhibitor small molecule development



# Highlights Q3 2023 and Post-Period

## Progressing Trials: VIVIAD Phase 2b

- ◆ On track for final topline results during end of Q1/2024
- ◆ Confirms low discontinuation rate due to AE as well as low overall discontinuation rate
- ◆ Statistical power of the VIVIAD study is above 80%, confirming the design of the study
- ◆ Preparing end of Phase 2 meeting with FDA planned for H2/2024 leveraging VIVIAD data

## Unveiling Growth Strategy with Preparation for Future Value Generation in AD and Beyond

- ◆ Building a future of oral small molecules with focus on QPCT inhibitor platform
- ◆ Leveraging varoglutamstat and VIVIAD readout to provide foundation for future development programs
- ◆ Evaluating additional programs focused on kidney function, CKD, NASH, oncology and additional biomarkers related to AD

## Progressing Trials: VIVA-MIND Phase 2a/b

- ◆ Positive DSMB decision to progress at 600 mg twice daily through remainder of study
- ◆ Adaptive study design and positive DSMB decision support a potential expansion to Phase 3 contingent on VIVIAD results and regulatory feedback

## Developing Company and Organization

- ◆ Sell-side coverage initiated by several investment banks, increasing Street awareness of Vivoryon
- ◆ Healthy cash position beyond VIVIAD Phase 2b study readout into H2/2024
- ◆ Management and Board updates: transition of CFO from Florian Schmid to Anne Doering effective March 1, 2024, leveraging capital markets experience
- ◆ Approved appointment in Q3/2023 of Frank Weber, MD and Anne Doering to the Company's Board as executive directors



# VIVIAD Update: Discontinuation Rates are Favorable and Comparably Low

Metric	<u>Varoglutamstat</u> VIVIAD (blinded)	<u>Lecanemab</u> CLARITY AD (placebo/active)	<u>Donanemab</u> TRAILBLAZER ALZ 2 combined tau (placebo/active)
# of patients	259	1,734	1,736
Duration	~78 weeks*	72 weeks	76 weeks
Total Discontinuations	12.7%*	15.6% / 18.8%	19.7% / 26.9%
Discontinuations due to AE	3.5%*	2.9% / 6.9%	2.4% / 5.8%

## Observations:

- ◆ Total number of discontinuations remains low in VIVIAD throughout the study at <13%\* (blinded data)
- ◆ Safety update at recent data cut-off confirms low number of discontinuations due to AEs in VIVIAD throughout the study at <4%\* (blinded data)
- ◆ Studies are of comparable treatment duration



# VIVIAD Update: Study Progressing as Planned with Regard to Statistical Power and Timing

## Confirmation of statistical power

- Low level of discontinuations supports statistical power of study
- Statistical power to detect a potential treatment difference of Cohen's d of 0.35 between active and placebo is above 80% as assumed in the protocol
- Remains on track to detect potential treatment difference between placebo and active arms

## Status update: on track

- End of active treatment phase is estimated to occur by year end 2023, followed by a minimum period of four weeks of safety follow up visits with rigorous data and statistical analysis thereafter
- On track to share final topline data during end of Q1/2024



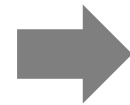
# VIVA-MIND Update: Recent DSMB Decision Leads to Progress and Enables Further Study Design Flexibility

- ❖ Ongoing Phase 2 study running in parallel to VIVIAD to provide clear picture of cognitive changes and support Vivoryon's regulatory strategy
- ❖ Adaptive study design involving titration, futility and expanded efficacy evaluation following VIVIAD

600 mg 2x daily | Treatment duration = 72 weeks | 1:1 Randomization

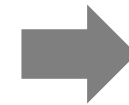
## Phase 2a

- Adaptive dose-finding portion of study: DSMB recommended 600 mg BID
- n=180 patients



## Phase 2b

- Seeks to enroll an additional 234 patients at 600 mg BID



## Option to Amend to Phase 3

- Based on adaptive design of study
- Contingent on VIVIAD study results and regulatory discussions

### Primary Endpoint:

- Clinical dementia rating scale - sum of boxes (CDR-SB)

### Key Secondary Endpoints:

- ABC score
- Quantitative EEG-relative theta wave power
- FAQ (Functional Activities Questionnaire)
- Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog-13)
- Neuropsychiatric Inventory



# Monoclonal Antibodies Demonstrate Slowing of Disease Progression in Early AD, Although Not in All Patients

- ❖ Multiple scales used for assessing slowing of disease progression in early AD
- ❖ Based on MOA, varoglutamstat offers potential to slow disease progression, in high and low tau patients, and avoid treatment-related ARIAs

Drug	Drug Class	Tau Patient Subtype	Slowing of Disease Progression	Scale/Endpoint
Lecanemab <sup>1</sup>	mAb	Not specified	27% (p<0.001)	CDR-SB
Donanemab <sup>2</sup>	mAb	Low/Medium Tau	35% (p<0.001)	iADRS
Donanemab <sup>2</sup>	mAb	Combined Tau	22% (p<0.001)	iADRS
Donanemab <sup>3</sup>	mAb	High Tau	6% (p=0.415; ns)	iADRS
Varoglutamstat VIVIAD	Small Molecule	Tau+ *	VIVIAD Phase 2b readout Q1/2024	Cogstate NTB, A-IADL-Q
Varoglutamstat VIVA-MIND	Small Molecule	Tau+ *	VIVA-MIND Phase 2a/b	CDR-SB

## Observations:

- Tolerability and incidence of ARIAs affects also patients in early, slower progressing AD stages
- Donanemab achieved statistical significance in low/medium and combined tau populations, but not in high tau population

\* All patients are tau positive, tau to be measured in the CSF (cerebral spinal fluid)





# Despite Recent AD Treatment Successes Early AD Unmet Need Remains High

## Unmet Need Remains High for Early AD Patients

- Improved safety and higher efficacy in early (MCI) patients
- Robust efficacy in more progressive/advanced mild AD patients with elevated tau levels
- Avoidance of ARIAs (H+E)
- Convenient administration and no infusion-related reactions

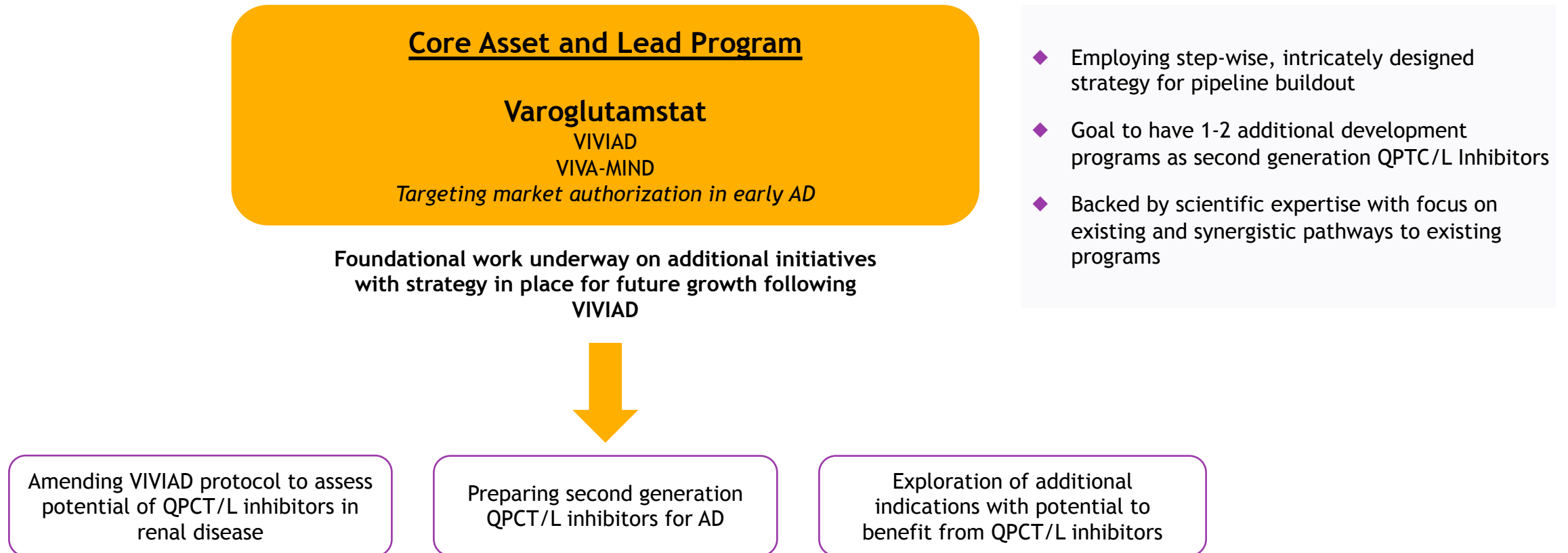
## Varoglutamstat Has Potential to Fill the Gaps

- Potential for higher safety and better efficacy compared to SOC
- Novel MOA to address efficacy gap (tau pathology downstream of pE-Abeta synthesis)
- Favorable safety profile established with no evidence of ARIAs in clinical setting
- Oral small-molecule that can be taken in outpatient setting

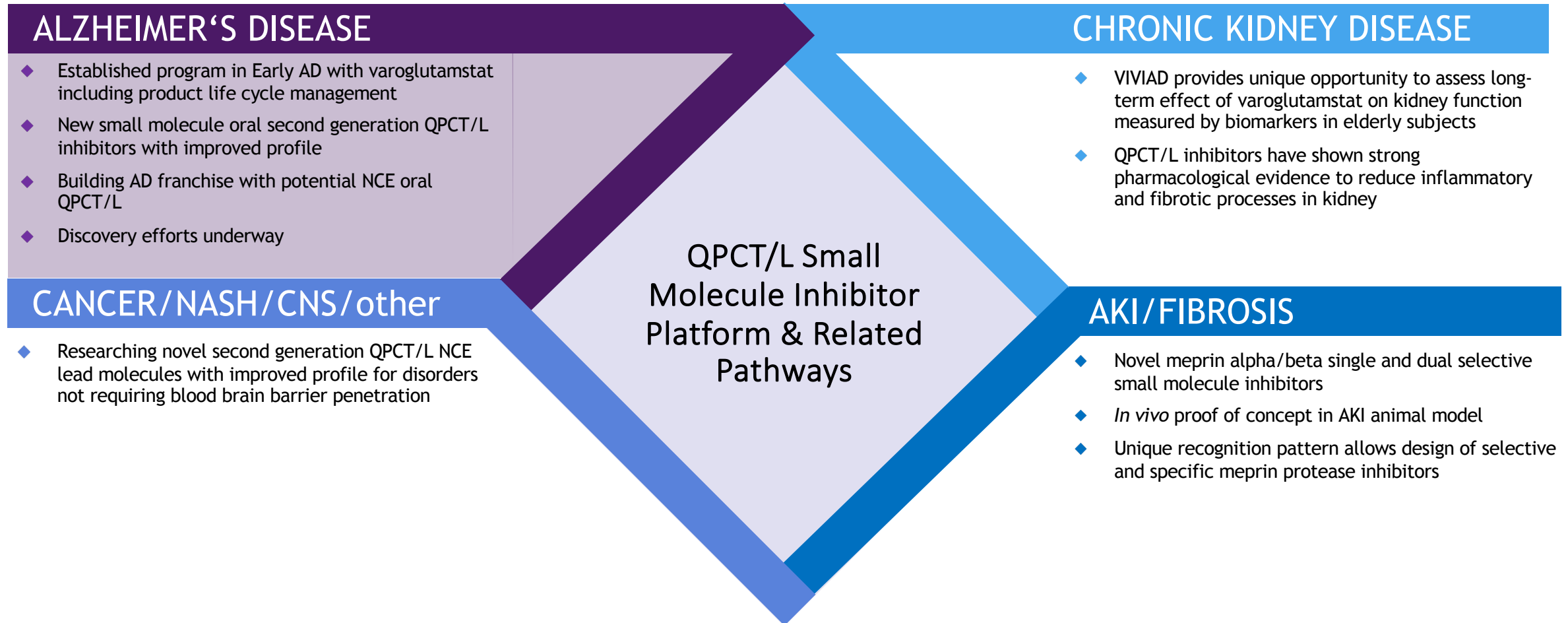


# Unveiling Focused Growth Strategy Rooted in Core Asset and Expertise

Positions Vivoryon for robust future by leveraging Varoglutamstat and VIVIAD data



# Leveraging Core Expertise in QPCT/L Oral Small Molecule Inhibitors to Generate Multiple Avenues of Addressing Unmet Need



# Announcing an Additional Area of Focus: Chronic Kidney Disease

VIVIAD to provide key biomarker data on kidney function to be utilized for future development of QPCT/L compound

## SCIENTIFIC FOUNDATION

Inflammatory and fibrotic pathways require pyroglutamization for full effect:

- QPCT-Inhibitor improved kidney function and reduced inflammation in glomerulonephritis CKD rat model via CCL2/CCR2 axis<sup>1</sup>
- Wealth of research indicates pathogenic role for the CX3CL1- CX3CR1 axis during both acute and chronic renal diseases<sup>2</sup>

## DEVELOPMENT RATIONALE

Integrated biomarker into VIVIAD to assess long-term effect of varoglutamstat on kidney function:

- Monitoring kidney function has been integral in varoglutamstat design to-date
- Cost-effective and efficient opportunity: multiple fibrotic disease markers to be added into VIVIAD protocol provide head start on

Comprehensive assessment of opportunity in CKD



# Condensed Statement of Profit and Loss

In €k	Sep 30, 2023	Sep 30, 2022	YoY in %
Research and development expenses	(10,449)	(16,054)	(35) %
General and administrative expenses	(6,803)	(4,243)	60 %
Operating loss	(17,252)	(20,278)	(15) %
Finance result	95	1,484	
Income taxes	37	(151)	
Net loss for period	(17,120)	(18,945)	(10) %
Loss per share (basic and diluted) (in EUR)	(0.69)	(0.89)	

Careful and selected spending until VIVIAD read-out during end of first quarter of 2024



# Key Financial Figures

In €k	Sep 30, 2023	Dec 31, 2022
Cash and cash equivalents	16,979*	26,555
Total assets	40,589	31,378
Total equity	36,963	26,506
Shares (number)	26,066,808	24,105,278
In €k	Sep 30, 2023	Sep 30, 2022
Cash flows used in operating activities	(33,259)*	(14,740)
Cash flows used in investing activities	(511)	(2)
Cash flows from financing activities	24,181	19,070

**Cash runway into second half of 2024**



# Leadership Transition

Florian Schmid



Anne Doering, CFA



- ◆ Seamless hand-off; remain on track for key value driving inflection points
- ◆ Effective March 1, 2024
- ◆ Future executive team includes Frank Weber, CEO & CMO, Michael Schaeffer, CBO and Anne Doering, CFO



# Multiple Value-Generating Catalysts and Events Ahead

## Recent Robust Execution

- ◆ Hosted successful R&D Day with KOLs<sup>1</sup>
- ◆ Sell-side coverage initiated by several investment banks, increasing Street awareness of Vivoryon
- ◆ Positive DSMB decisions for both VIVIAD and VIVA-MIND

## Clinical Progress

- ◆ VIVIAD European Phase 2b final topline results during end of Q1/2024
- ◆ Continue recruitment of VIVA-MIND at 600 mg twice daily post recent DSMB decision

## Regulatory Strategy

- ◆ End of Phase 2 meeting with FDA planned leveraging VIVIAD data
- ◆ Positioning varoglutamstat as potential first line treatment option for early AD





# Core Asset Varoglutamstat Well-Positioned to be a Leader in QPCT/L for Early AD, Future Opportunities Build on AD and Go Beyond



## Aiming for first line single agent treatment of patients with early AD

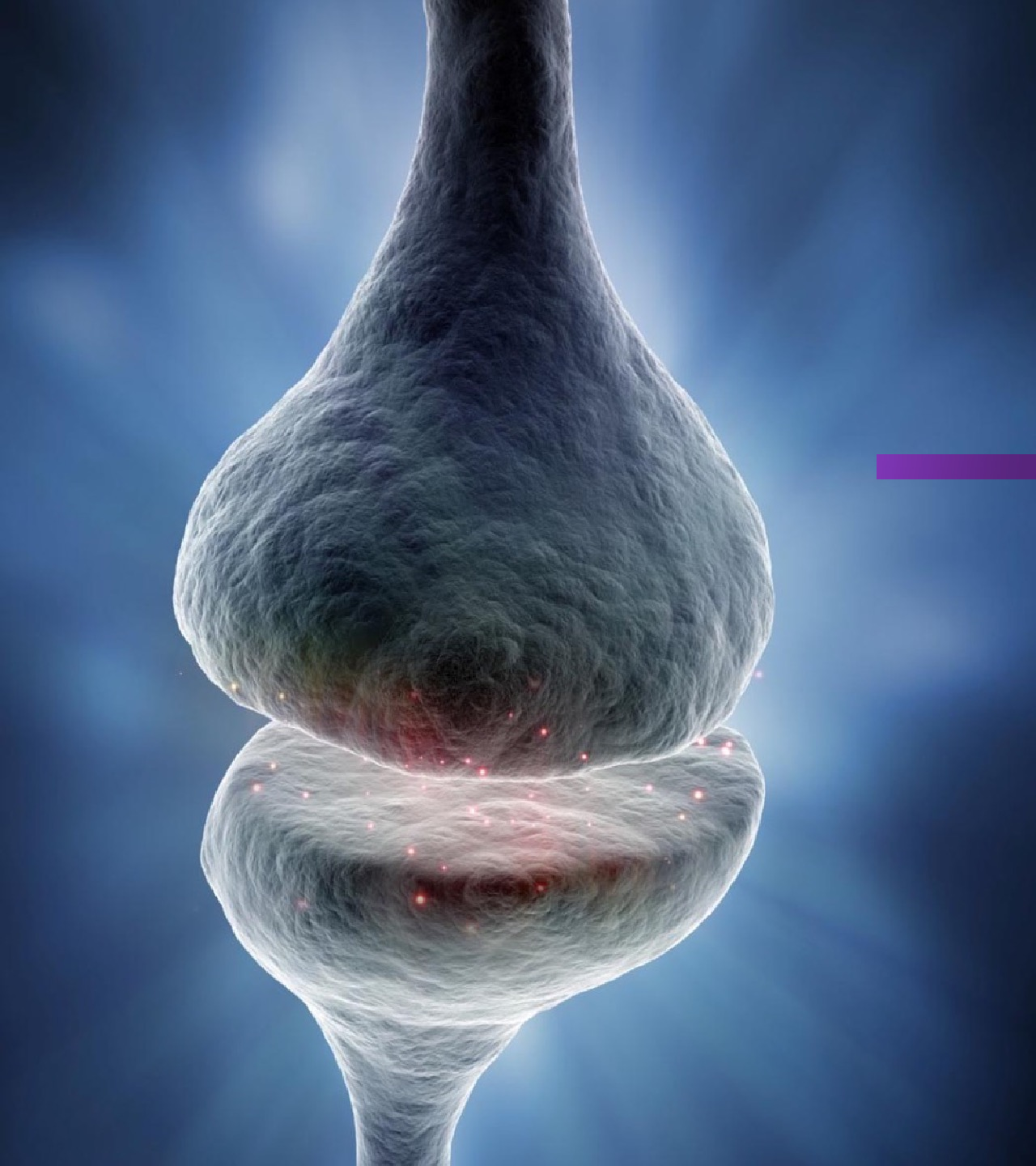
- ◆ Only product in late-stage development addressing neurotoxic N3pE-Abeta formation<sup>1</sup>
- ◆ Not limited to clearing existing plaques
- ◆ Well-tolerated
- ◆ No signs of product related ARIA in clinical setting
- ◆ Convenient oral administration
- ◆ Maintaining synaptic and neuronal functionality



## VIVIAD learnings to inform future opportunities in AD and additional indications

- ◆ Varoglutamstat future opportunities:
  - ◆ Expand target patient population to capture asymptomatic and moderate AD patients
  - ◆ Combination with / follow-on to mAbs in AD
  - ◆ Development in Greater China with Simcere
- ◆ Unveiled growth strategy with activities to further advance broader pipeline of discovery-stage QPCT/L inhibitors and related pathways





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Q&A



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