

# FIRST HALF 2023 RESULTS WEBCAST AND CONFERENCE CALL

September 7, 2023

| Vivoryon Therapeutics N.V.

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# Vivoryon: Advancing a Uniquely Differentiated Potential Best-/First-in-Class Small Molecule Medicine to Treat Alzheimer's Disease



Unique first-in-class approach designed to overcome challenges in AD

- ◆ **Reduces brain damage:** blocks formation 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**



Phase 2 studies progressing well with no drug-related ARIA, very low AE-related discontinuations

- ◆ **Delivering on our promise:** post-positive PoC, orally available, favorable safety profile to date
- ◆ **VIVIAD (EU):** Fully recruited (259 pts), ~82 weeks of treatment, final data readout: Q1/2024
- ◆ **VIVA-MIND (US):** Cohort A fully recruited (60 pts), DSMB recommended to continue without modification



Senior management changes and funding support future success

- ◆ **New CEO** Frank Weber, new CS&IRO Anne Doering
- ◆ **New Board Members:** Kugan Sathiyandarajah and Morten Asser Karsdal
- ◆ **Healthy runway:** recent private placement (€25m) extending cash runway through key milestones into H2/2024

We believe that Vivoryon is uniquely positioned, to bring an oral, highly differentiated, post PoC molecule, with no ARIA liability to patients with Alzheimer's disease



# Experienced Leadership

Strengthened Management and Board Bring Key Drug Development Experience and Business Acumen

## MANAGEMENT



Frank Weber, MD  
*Chief Executive Officer / Chief Medical Officer*



Michael Schaeffer, PhD  
*Chief Business Officer, Executive Director*



Florian Schmid  
*Chief Financial Officer, Executive Director*



Anne Doering, CFA  
*Chief Strategy & Investor Relations Officer*



## NON-EXECUTIVE DIRECTORS

Erich Platzer, MD, PhD  
*Chairman of the Board*

Kugan Sathiyandarajah  
*Vice-Chairman & Chair Compensation Committee*



Prof. Morten Asser Karsdal  
MSc, PhD, mMBA



Charlotte Lohmann  
*Chair Nomination & Corporate Governance Committee*

Claudia Riedl, PhD  
*Chair Audit Committee*

Samir Shah, MD  
*Chair IR Committee*



# Highlights H1 2023 and Post-Period

## Progressing Trials

- ◆ **VIVIAD Phase 2b:** Independent DSMB decision to **continue without modification**; on track for **final data readout in Q1/2024**
- ◆ **VIVA-MIND Phase 2a/b:** **Completed recruitment of Cohort A** (60 patients, 600mg bid); study actively recruiting participants into Cohort B with 19 U.S. sites open; DSMB decision to **progress as planned**; next update **planned for Q4/2023**

## Advancing Science

- ◆ **AD/PD 2023:** VIVIAD blinded data **confirming varoglutamstat well-tolerated** in study to-date with **favorable safety profile**
- ◆ **AAIC 2023:** Presented data demonstrating **precision recruitment** of early AD target population into VIVIAD study

## Securing Financing

- ◆ **May 2023:** EUR 25M private placement; financing backed by **new and existing high-quality institutional investors**
- ◆ **Cash runway extended into H2/2024** through inflection points

## Investing in Long Term Growth

- ◆ **Management:** **Frank Weber, MD promoted to CEO**; Anne Doering, CFA, assumed new CS&IRO position
- ◆ **Board:** Appointed Kugan Sathiyandarajah and Morten Asser Karsdal, MSc, PhD, mMBA as Non-Executive Board members
- ◆ **IP:** Agreement with Scenic Immunology B.V., Vivoryon was granted a license to certain patent rights in the field of oncology



# Varoglutamstat: Rigorous Clinical Development Strategy

Carefully crafted strategy towards well-designed and well-powered placebo-controlled Phase 2b studies



## Preclinical research *In vitro and in vivo studies*

### Phase 1

*Assessment of safety and tolerability in 205 healthy volunteers*

### Phase 1

*Assessment of safety and tolerability in 60 healthy Chinese volunteers \**

### Phase 2a SAPHIR

*12-week Proof of Concept study in 120 patients with early AD*

- Statistically significant changes from baseline in working memory after 3 months of treatment
- Strong evidence of synaptic recovery
- High target occupancy detected at doses of 150mg BID and above

### Phase 2b VIVIAD

*Assessment of safety, tolerability and efficacy in 250 patients with MCI or mild AD*

Fully recruited  
Final readout Q1/2024

- ◆ Endpoints: safety, efficacy (NTB, attention/ working memory, biomarkers)
- ◆ Fully enrolled (259 pts); planned to allow for mean treatment duration of ~82 weeks

### Phase 2a/b VIVA-MIND

*Assessment of efficacy and safety in 180/414 patients with early AD*

Expanded treatment duration in Phase 2a portion (72 weeks)  
Study status update in Q4/2023

- ◆ Endpoints: safety, efficacy (attention/working memory, CDR-SB, biomarkers)

## Pivotal study or accelerated approval

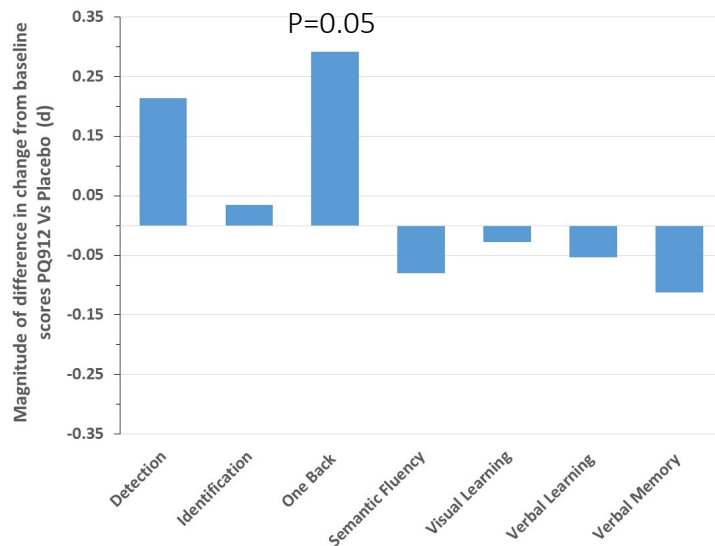
- FDA Fast Track designation granted in 2021
- Two possible scenarios for late-stage development
  - Application for accelerated approval (based on consistent / positive data of Phase 2b studies)
- Phase 3 clinical development





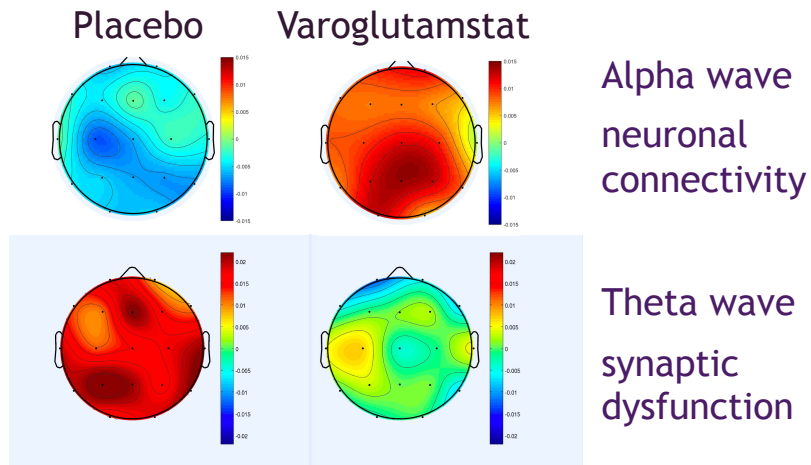
# Phase 2a SAPHIR Study: Evidence of Significant Changes in Working Memory and Synaptic Recovery After Only 12w Treatment

## Significant Changes in Working Memory<sup>1</sup>



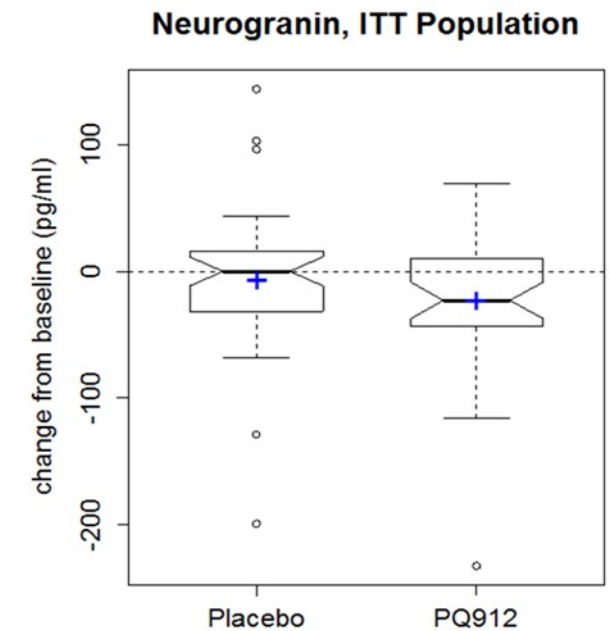
- Statistically significant changes from baseline in working memory (One Back Test,  $p = 0.05$ ,  $d = 0.23$ , ITT) in AD patients after 12 weeks of treatment

## Recovery EEG Synaptic Activity<sup>1,2</sup>



- Significant ( $p=0.002$ , ITT and PP) decrease in theta power
- Post hoc analysis of alpha wave: significant increase on connectivity - amplitude envelope correlation (AEC)  $p=0.025$

## Reduction of Neuronal Injury Biomarker<sup>1</sup>



# VIVIAD: Study Design to Enable Precision Recruitment

**Lessons learned: Recruiting the right patients with early AD is a critical success factor for VIVIAD**

## **BASIC REQUIREMENT:**

- ◆ Mandatory sampling for inclusion: all patients included had low Abeta and high p-tau CSF values

## **RETHINKING MCI ASSESSMENT:**

- ◆ Precision recruitment of individuals with at least minimal cognitive impairment by using the WAIS IV inclusion criterion (at least half a standard deviation worse than age and education matched healthy population)
- ◆ Baseline mean value of MMSE in VIVIAD is 24.5

	N	Mean	Median	SD	Value
Age	259	68,44	70	7,40	63 to 74
MMSE total score - V1	259	24,51	25	2,73	22 to 27
WAIS-IV total score - V1	259	27,75	28	12,36	19 to 37

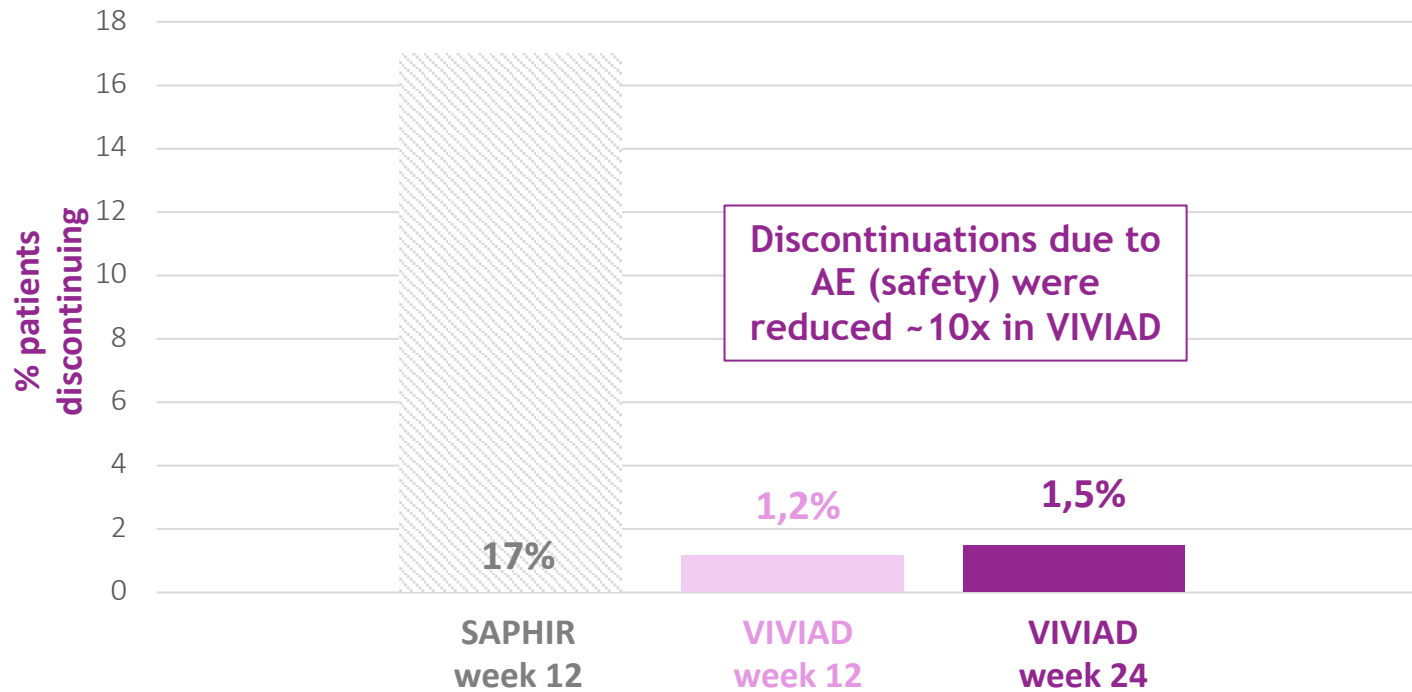
➤ Study population exactly represents early AD population





# VIVIAD: Low Number of Discontinuations Due to AE

SAPHIR (active and placebo groups) vs. blinded VIVIAD data



## Safety profile of varoglutamstat strongly improved vs. 1<sup>st</sup> in patient study SAPHIR

- ◆ Total number of discontinuations remains low in VIVIAD throughout the study, today 10%
- ◆ Number of discontinuations due to AE remain low in VIVIAD throughout the study, today < 4%
- ◆ Titration phase of VIVIAD is through week 12
- ◆ High dose of 600mg twice daily with nearly 90% target occupancy



# Condensed Statement of Profit and Loss

In €k	June 30, 2023	June 30, 2022	YoY in %
Research and development expenses	(6,259)	(11,067)	-43 %
General and administrative expenses	(4,433)	(2,311)	92 %
Operating loss	(10,692)	(13,378)	-20 %
Finance result	(69)	884	
Income taxes	45	(89)	
Net loss for period	(10,716)	(12,583)	-15%
Loss per share (basic and diluted) (in EUR)	(0.44)	(0.60)	



# Key Financial Figures

In €k	June 30, 2023	December 31, 2022
Cash and cash equivalents	29,582*	26,555
Total assets	45,355	31,378
Total equity	41,534	26,506
Shares (number)	25,961,892	24,105,278
In €k	June 30, 2023	June 30, 2022
Cash flows used in operating activities	(20,283)*	(10,237)
Cash flows used in investing activities	(9)	(2)
Cash flows from financing activities	23,400	19,581
Cash and cash equivalents at the end of period	29,582*	24,383

**Cash runway into second half of 2024**



# Multiple Value-Generating Catalysts and Events Ahead

## Upcoming Events

- ◆ R&D Day with KOLs<sup>1</sup> in Q4/2023 on varoglutamstat, scientific approach and study design
- ◆ Multiple investor interactions throughout Q4/2023 to update on progress

## Clinical Progress

- ◆ VIVA-MIND U.S. Phase 2a/b status update Q4/2023
- ◆ VIVIAD European Phase 2b final readout Q1/2024

## Regulatory Strategy

- ◆ End of Phase 2 meeting with FDA

## Future Opportunities

- ◆ Potential to develop varoglutamstat in combination with mAbs in AD (own and external assets)
- ◆ Follow-up programs into the clinic beyond AD
- ◆ Development opportunities in Greater China with Simcere



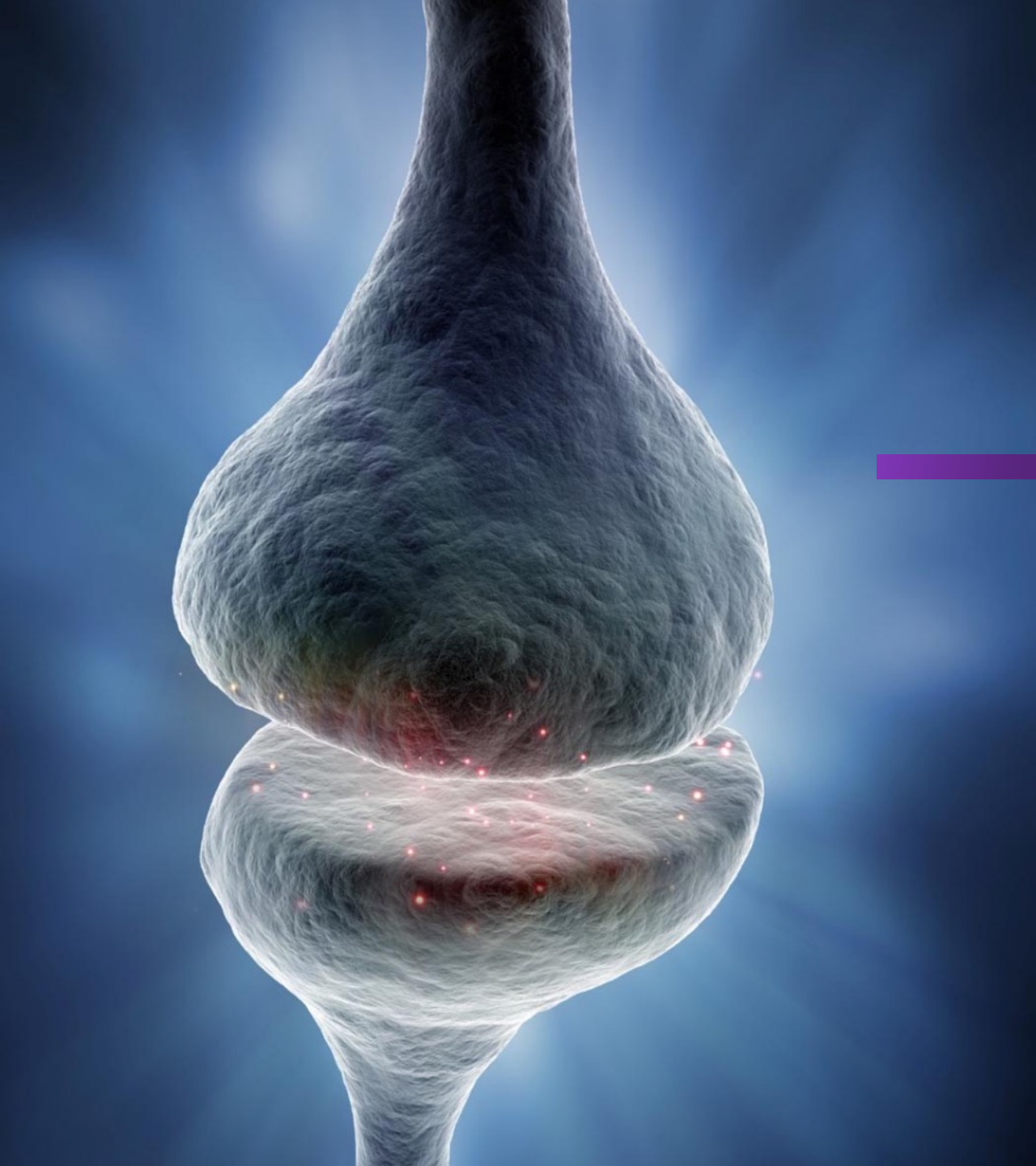
# Varoglutamstat Positioned for Continued Value Generation



## Differentiated Phase 2 Asset with Unique Potential in AD

- ◆ N3pE-Abeta is a validated target in AD; reducing pE concentration has shown to reduce progression of cognitive decline in early AD<sup>1,2</sup>
- ◆ Glutaminylcyclase QPCT is required for N3pE-Abeta production
- ◆ Inhibition of QPCT shown to stop N3pE-Abeta production and improve cognition in Phase 2a study of varoglutamstat (SAPHIR)
- ◆ VIVIAD results impact R&D strategy in early AD by answering key questions:
  - ◆ Are small molecules with additional intracellular effects more effective than antibodies?
  - ◆ Can targeting N3pE-Abeta show effect sizes > 30% ?





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Q&A





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