Upstream intervention to address multiple hallmarks of AD

Tackling AD at the roots

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Vivoryon Uniquely Positioned to Bring Oral, Highly Differentiated, Post PoC Small Molecule to Patients with 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 Sathiyanandarajah and Morten Asser Karsdal
- **Healthy runway:** recent private placement (€25m) extending cash runway through key milestones into H2/2024

Recent Management and Board Changes Strengthen Development Experience, Enhance Business Acumen and Prepare Company for Next Phase

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 Sathiyanandarajah
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

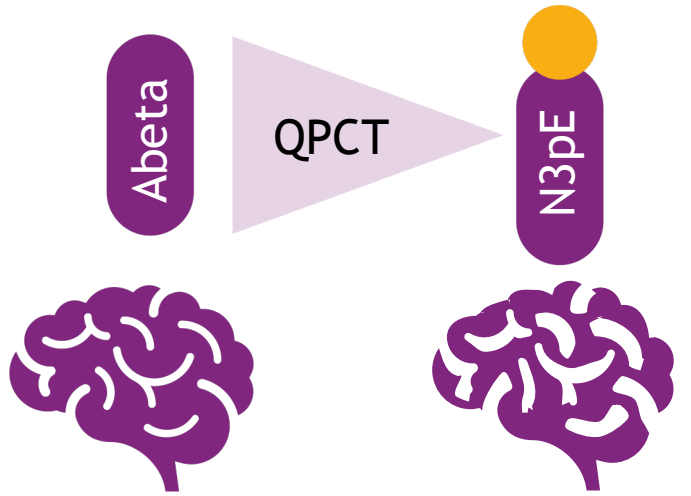
Vivoryon Pioneering Small Molecule-Based Therapies Designed to Prevent N3pE-Abeta Formation Rather Than Aiming to Clear Existing Plaques

ONGOING CHALLENGES IN AD

- **~30 million** people worldwide and expected to double by 2050, with ~12.7 million in the US alone
- Recent advances with **mAbs** (e.g. lecanemab, donanemab) show promise, but come with **significant limitations**
- **Multitude of clinical studies, but statistical significance** does **not necessarily** imply a **meaningful drug** to individual patients and their caregivers
- **Lack of meaningful endpoints** to enable reliable evaluation of study data for correlation to real-life benefit
- **Meaningful trial design** is needed to leverage existing data to select the right patients/appropriate treatment duration
- **New modalities** are needed to address hallmarks of AD beyond Abeta

VIVORYON'S APPROACH

- Discovered QPCT-mediated formation of a neurotoxic Abeta variant, N3pE-Abeta (pGlu-Abeta), as driver of AD pathology[1,2]
- Pioneering small molecule-based therapies designed to prevent N3pE-Abeta formation - rather than aiming to clear existing plaques[3]



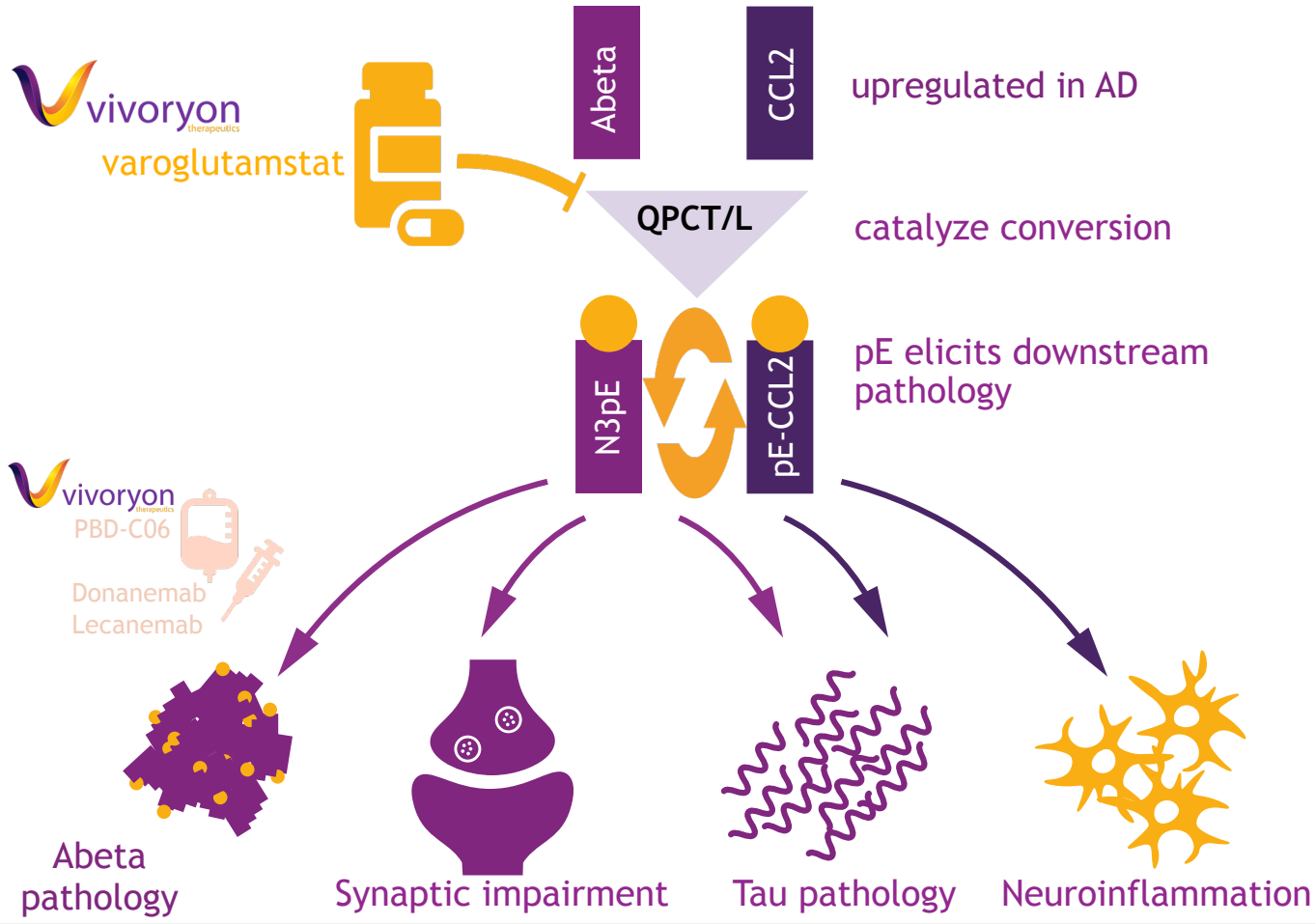
[1] *Schilling et al., Nat. Med. 2008;* [2]*Grochowska et al., EMBO 2017;* [3]*Buchholz et al., J. Med. Chem 2006, Nussbaum et al., Nature 2012*

Our Lead Product Candidate, Varoglutamstat, Targets Multiple Key Hallmarks of Alzheimer's Disease Early in Pathological Process

ROLE OF QPCT/L IN AD PATHOLOGY

- Increased activity of glutaminyl cyclase (QPCT) is associated with AD pathology in humans[1]
- QPCT catalyzes formation of neurotoxic N3pE-Abeta- which is not found in healthy individuals. [2,3]
- Varoglutamstat efficiently inhibits QPCT, thus targeting N3pE-Abeta monomer formation and all of its aggregation states[4]
- Varoglutamstat also efficiently inhibits QPCTL (isoform of QPCT) leading to decreased neuro-inflammation by attenuating CCL2 activity[5]
- Low MMSE scores correlate with high N3pE-Abeta, high QPCT levels, high pE-CCL2 and high QPCTL levels in AD patients[3,5]
- QPCT/L activity is the key driver of a pathologic cycle involving neuroinflammation, pE-CCL2 and N3pE-Abeta[5]

VAROGLUTAMSTAT TARGETS AD PATHOGENESIS EARLY-ON



[1]Gunn et al., J.Neurochem 2021; [2] Schilling et al., Nat. Med. 2008; [3]Morawski et al., JAD 2014; [4]Upadhaya et al., Brain 2014; [5]Hartlage-Rübsamen et al., Acta Neuropathol, 2015;

QPCT/L Inhibition Has Significant Potential in Humans with Alzheimer's Disease: Translating *In Vivo* Evidence into Proof of Concept in AD Patients

Abeta Pathology	QPCT is essential for N3pE amyloid formation *in vivo*[1] 5XFAD mice, QPCT ko and tg	QPCT/ N3pE	Dose-dependent reduction of QPCT activity in CSF & serum (Ph1 + Ph2a)
Neuroinflammation Tau Pathology	CCL2 activity promotes neuroinflammation and accelerates tau pathology[2] rTg45105 mice, CCL2 AAV	CCL2/ Tau	Dose-dependent decrease of pE-CCL2 in serum (Ph1)
Cognition	QPCT inhibition improves cognitive parameters in AD mouse models[3] hAPPSLxhQPCT mice, MWM	Cognition/ Memory	Statistically significant changes from baseline in working memory as measured by CogState (Ph2a)

[1]*Jawhar et al., 2011;* [2]*Joly-Amado et al. 2020; Hartlage-Rübsamen et al., 2015;* [3]*Hoffmann et al., 2017*

Varoglutamstat Clinical Development Strategy

Clear Path To Potential Regulatory Approval Based on Well-Informed, Extensive Phase 1 and Phase 2 Trials

Preclinical research
In vitro and in vivo studies

COMPLETED

- QPCT inhibition improves cognitive parameters in AD mouse models
- QPCT is essential for N3pE amyloid and pE-CCL2 formation *in vivo*

Phase 1
Assessment of safety and tolerability in 205 healthy volunteers

COMPLETED

- Varoglutamstat is well-tolerated – no DLT at 800mg twice daily or up to 3.6g once daily

Phase 1
*Assessment of safety and tolerability in 60 healthy Chinese volunteers**

IN PREPARATION

Phase 2a SAPHIR
12-week Proof of Concept study in 120 patients with early AD

COMPLETED

- 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)

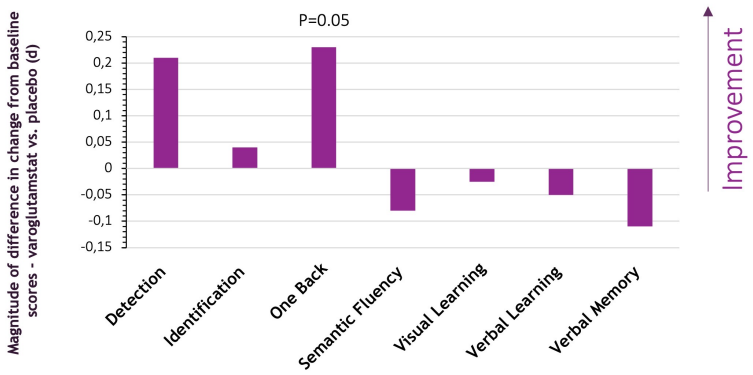
Pivotal study or accelerated approval

- 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

*BID: twice daily; CDR-SB: clinical dementia rating scale-sum of boxes; DLT: dose-limiting toxicity; NTB: neuropsychological test battery. *Regional license, Simcere Pharmaceuticals responsible for clinical development in Greater China*

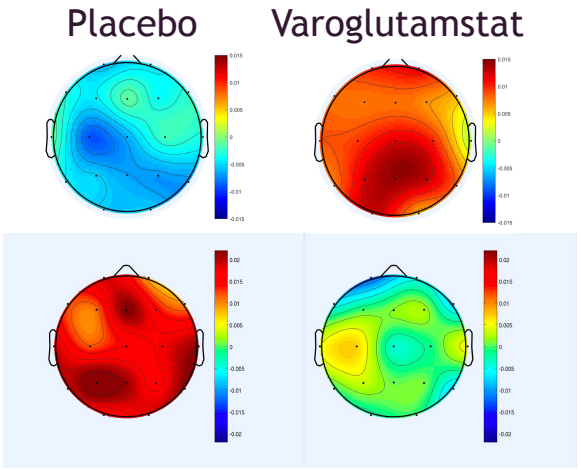
Phase 2a SAPHIR Study Provides Evidence of Significant Changes in Working Memory and Synaptic Recovery After Only 12 Weeks of Treatment

Significant Changes in Working Memory[1]



- 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[1,2]

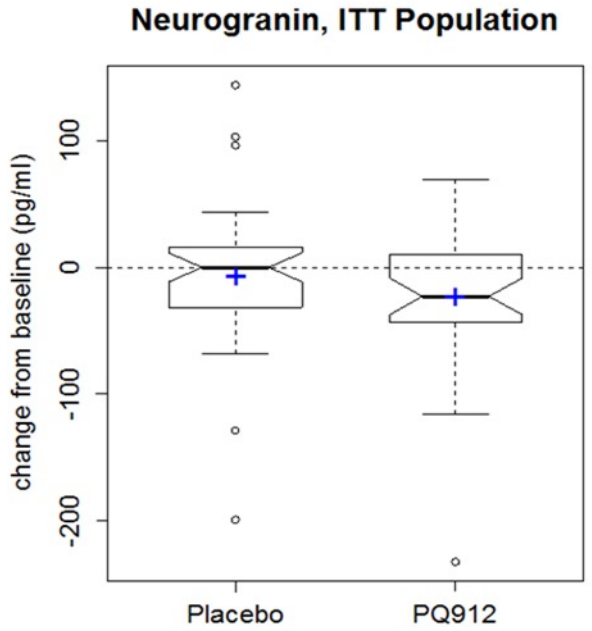


Alpha wave neuronal connectivity

Theta wave synaptic dysfunction

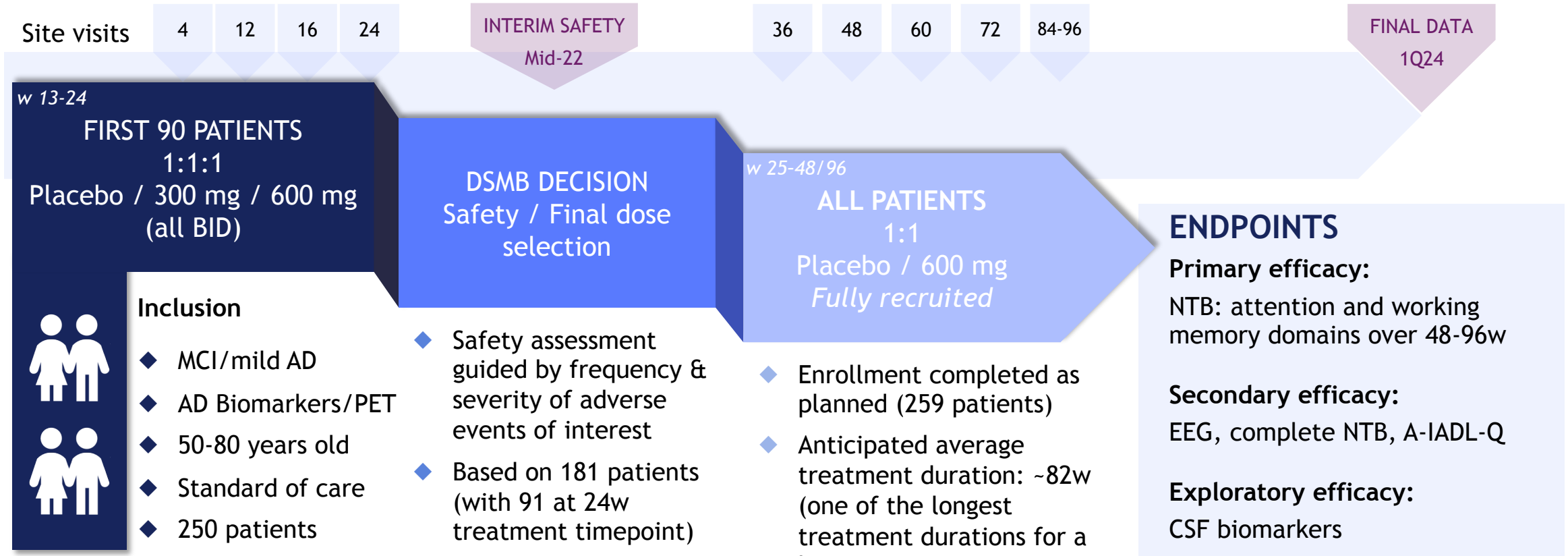
- Significant (p=0.002, ITT and PP) decrease in theta power
- Post hoc analysis of alpha wave: significant increase on connectivity - amplitude envelope correlation (AEC) p=0.025

Reduction of Neuronal Injury Biomarker[1]



[1]Scheltens et al., Alzheimer's Research & Therapy, 2018; [2]Briels et.al., Clinical Neurophysiol. 2020

VIVIAD Assesses Safety, Tolerability and Efficacy of Varoglutamstat in Patients with MCI and Mild AD[1,2]



ENDPOINTS

Primary efficacy:

NTB: attention and working memory domains over 48-96w

Secondary efficacy:

EEG, complete NTB, A-IADL-Q

Exploratory efficacy:

CSF biomarkers

Correlation of CSF with serum biomarkers

Winterlight Speech Assessment

A-IADL-Q: Amsterdam IADL Questionnaire; *BID: twice daily; DSMD: data safety monitoring board: PET: positron emission tomography;*
[1]*https://clinicaltrials.gov/ct2/show/NCT04498650,* [1]*Vijverberg et al.; Alzheimer's Research & Therapy 2021,* [2]*Weber et al., AAIC 2022, poster P1-403, abstract 69290*

VIVIAD Inclusion Criteria Enabled 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:

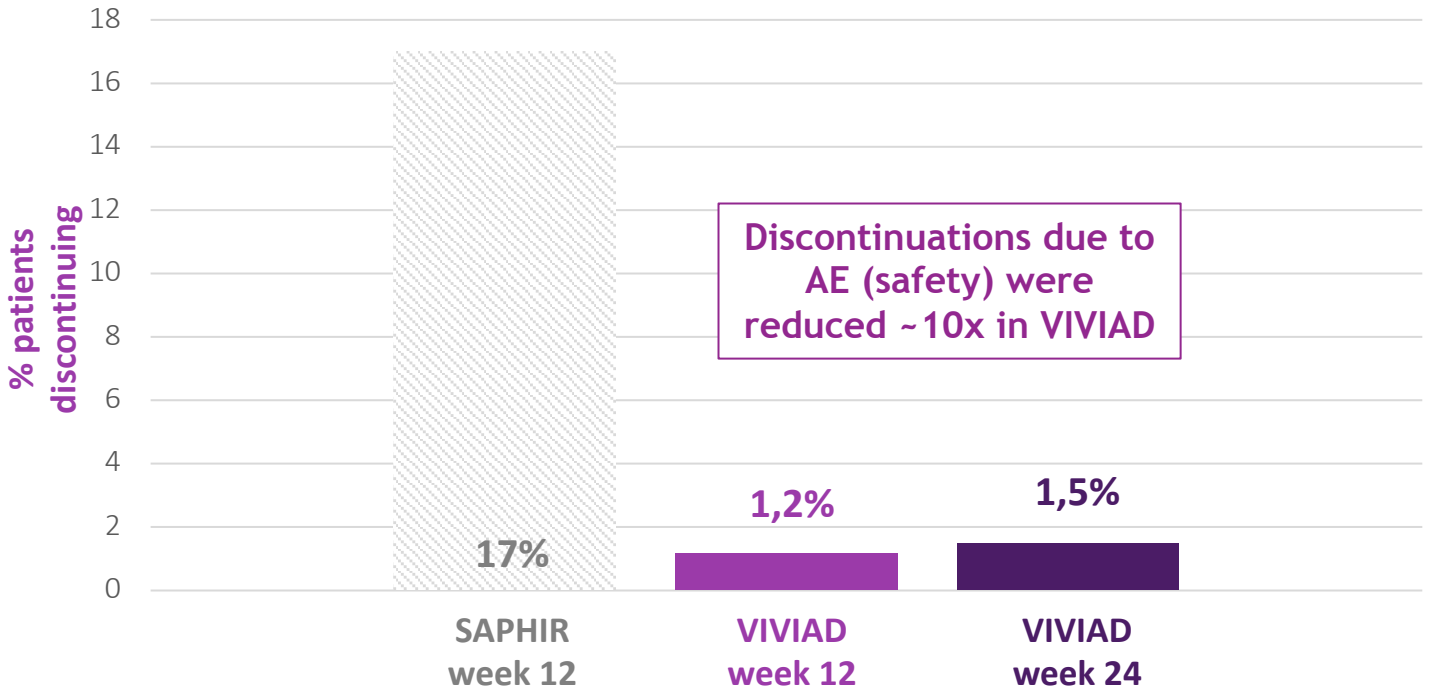
- Precision recruitment of individuals with at least minimal cognitive impairment by using the WAIS IV inclusion criterion (at least half a standard deviation worse than age and education matched healthy population)
- Baseline mean value of MMSE in VIVIAD is 24.5

	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. 1st in patient study SAPHIR

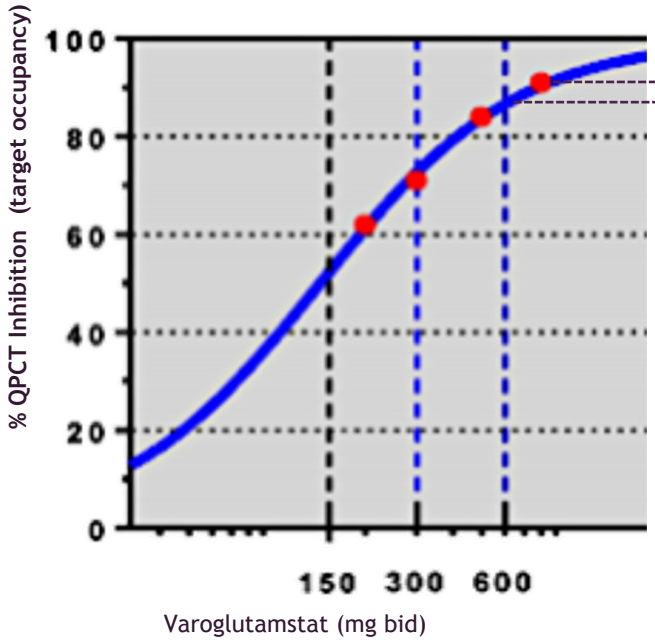
- Total number of discontinuations remains low in VIVIAD throughout the study, today 10%
- Number of discontinuations due to AE remain low in VIVIAD throughout the study, today < 4%
- Titration phase of VIVIAD is through week 12
- High dose of 600mg twice daily with nearly 90% target occupancy

Informed Design of VIVIAD vs. SAPHIR: Slower Titration and Lower Final Dose While Maintaining Level of Target Inhibition

Dose and titration varoglutamstat mg

Weeks	1	2	3&4	5 to 8	9 to 12	After 12
SAPHIR	400 BID	800 BID	800 BID	800 BID	800 BID	STOP
VIVIAD	50 OD	50 OD	50 BID	150 BID	300 BID	600 BID

Target occupancy / QPCT inhibition in CSF

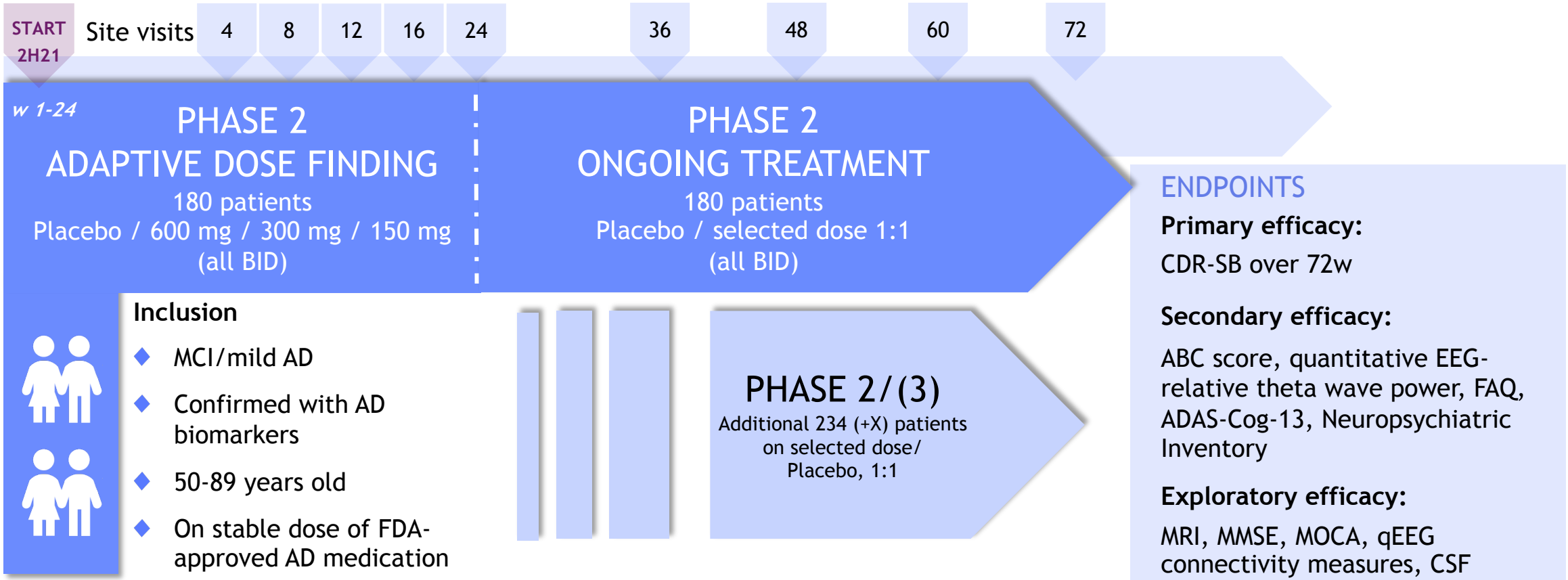


~93% with 800 mg BID
~87% with 600 mg BID
70% with 300 mg BID
>50% with 150 mg BID

maintained level of target inhibition

Translational models show robust activity starting at 50% target occupancy

VIVA-MIND Recruiting into Cohort B and Has Option to Transform into Confirmatory Phase 3



ADAS-Cog: Alzheimer's Disease Assessment Scale-Cognitive Subscale; ADNI ABC: neuropathologic assessment; BID: twice daily; CFC2: cognitive- functional composite; MRI: magnetic resonance imaging; https://clinicaltrials.gov/ct2/show/NCT03919162

Vivoryon's Pipeline Focused on Alzheimer's Disease with Potential Follow-on Programs

	Program	Approach	Discovery Preclinical	Phase 1 Phase 2a Phase 2b Phase 3	Status
AD	Varoglutamstat (PQ912)	SMI QPCT/L	*VIVIAD - Ph2b in EU*		Fully recruited; Final readout Q1/2024
AD	Varoglutamstat (PQ912)	SMI QPCT/L	*VIVA-MIND - Ph2a/b in US*		Ph 2a ongoing; expanded treatment duration of 72 weeks
AD	Varoglutamstat (SIM0408, PQ912)	SMI QPCT/L	*CTA approval in China*		Partnered with Simcere in Greater China; Clinical development in preparation
AD	PBD-C06	mAb N3pE amyloid			Pre-IND; Partnered with Simcere in Greater China
Cancer		SMI QPCTL			Pre-IND
NASH		SMI QPCTL			Pre-IND
Fibrosis		SMI Meprin			Pre-IND

mAb: monoclonal antibody; SMI: small molecule inhibitor; CTA: Clinical Trial Application

Multiple Value-Generating Catalysts and Events Ahead

Upcoming Events	◆ R&D Day with KOLs[1] 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

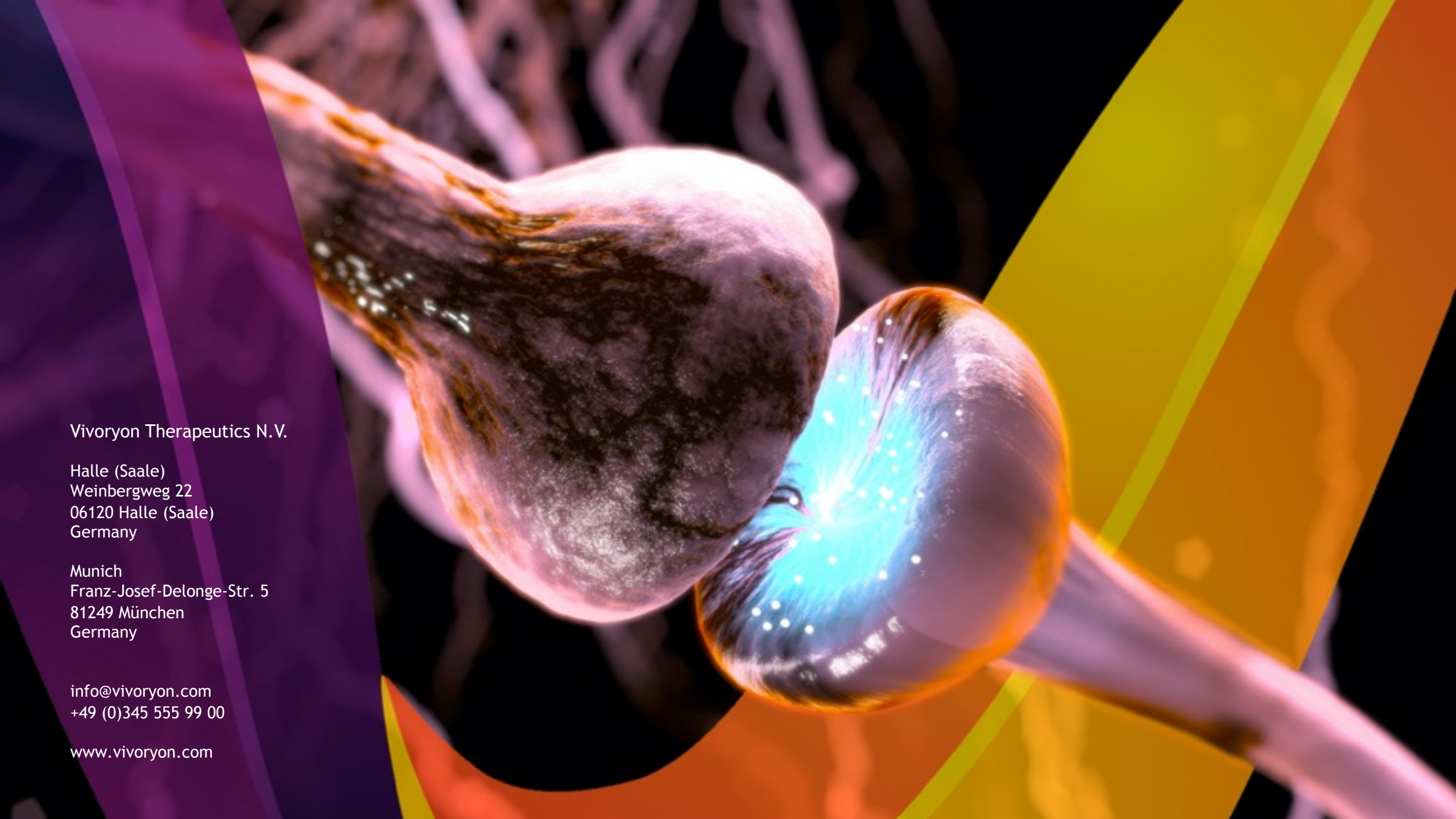
[1]*KOL: Key opinion leader*

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[1,2]
- 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% ?

[1]*Scheltens et al., Alzheimer's Research & Therapy, 2018;* [2]*Sims et.al., JAMA, 2023*



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