

## FULL YEAR 2021 RESULTS WEBCAST AND CONFERENCE CALL

April 28, 2022

Vivoryon Therapeutics N.V.

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## VIVORYON'S APPROACH TO OVERCOMING THE CHALLENGES OF AD DRUG DEVELOPMENT

Oral small molecule inhibitor varoglutamstat targeting multiple hallmarks of AD

#### QPCT/L AS KEY TARGET IN AD

#### High unmet medical need in AD despite recent advances

- Despite approval in the U.S., Aducanumab is not broadly available to patients outside the clinical study setting
- Uncertainties around regulatory path to approval for other Abeta-antibody-based approaches
- Varoglutamstat is designed as an alternative to overcome challenges of AD drug development
  - Phase 2b-stage oral small molecule with unique, dual mode of action that is truly differentiated from the other approaches in clinical development
  - Prevents formation of toxic Abeta species upstream of other approaches, thereby also targeting tau pathology, neuroinflammation and synaptic impairment
  - Development strategy rooted in promising Ph 1 and Ph 2a results (well-tolerated, statistically significant changes in working memory after only 3 months of treatment)
  - Protected by strong patent estate

#### VAROGLUTAMSTAT TARGETS UPSTREAM PATHOGENESIS



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## 2021 CLINICAL PORTFOLIO HIGHLIGHTS

- Fast Track designation granted by the U.S. Food and Drug Administration (FDA) for varoglutamstat as an investigational oral small molecule medicine for the potential treatment of early AD
- VIVA-MIND U.S. Ph 2a/b study of varoglutamstat initiated and currently enrolling patients into the Ph 2a adaptive dose finding part; coordinated by ADCS and on track for interim futility analysis planned for H1/2023
- VIVIAD European Ph 2b study of varoglutamstat ongoing and consistently meeting recruitment objectives, with number of study sites more than doubled to balance the effects of the ongoing pandemic; on track for interim safety analysis planned for mid-2022
- Preclinical evidence published supporting rationale for evaluating varoglutamstat in combination with monoclonal Abeta antibodies to treat AD (Hoffmann et al., *Int. J. Mol. Sci. 2021*, 22(21), 11791; https://doi.org/10.3390/ijms222111791)
- Expansion of manufacturing capabilities for API production to ensure sustainable study drug supply with varoglutamstat for ongoing and future studies, also increasing flexibility to react to global challenges such as the ongoing pandemic
- Clinical Trial Application submitted by partner Simcere for the development of varoglutamstat in Greater China approved by China's Center for Drug Evaluation (CDE); Simcere intends to start clinical development in China in H1/2022

## 2021 CORPORATE DEVELOPMENT HIGHLIGHTS

- Strategic regional licensing partnership with Simcere to develop and commercialize N3pE amyloid-targeting medicines to treat AD in Greater China; Vivoryon to receive combined upfront and milestone payments of up to US\$ 565 million plus double-digit royalties on sales
- Extraordinary General Meeting re-appointed Dr. Ulrich Dauer as CEO and appointed Florian Schmid as CFO (March 2021); Ordinary Annual General Meeting re-appointed Dr. Michael Schaeffer as CBO, all items presented for resolution by the Board of Directors approved with large majority (June 2021)
- Significant expansion of patent portfolio with a total of 55 additional patents granted in 2021 for Vivoryon's small molecule inhibitors and antibody-based medicines in development to treat AD and other diseases with exceptionally high medical need
- Vivoryon plans to expand and diversify its Non-Executive Board, intending to propose two additional candidates for nomination at its 2022 Annual General Meeting to be held later this year, in line with the Company's efforts to meet international best practice standards (post-period)
- EUR 21 million raised in successful private placement to support ongoing clinical development; capital raise supported by a number of high-quality institutional investors from Europe and the U.S. as well as members of Vivoryon's Executive and Non-Executive Boards (post-period, April 1, 2022)

### CLINICAL DEVELOPMENT STRATEGY

Clear Path To Potential Regulatory Approval 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*





Assessment of safety and tolerability in 205 healthy volunteers

#### COMPLETED

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



# Phase 2a SAPHIR

Assessment of safety and tolerability in 120 patients with early AD

#### COMPLETED

- Statistically significant changes from baseline in working memory after only 3 months of treatment (as measured by CogState)
- High target occupancy detected at doses of 150 mg BID and above



#### Phase 2b VIVIAD

Assessment of safety, tolerability and efficacy in 250 Patients MCI and mild AD

Interim safety readout mid-22; final readout H2/2023

 Endpoints: safety, attention/working memory, NTB, biomarkers

Phase 2a/b VIVA-MIND Assessment of efficacy and safety in 414 patients with early AD

#### Stage-gate to Ph2b H1/2023

#### Endpoints: safety, 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

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BID: twice daily; CDR-SB: clinical dementia rating scale-sum of boxes; DLT: dose-limiting toxicity; NTB: neuropsychological test battery 6

## VAROGLUTAMSTAT CLINICAL MILESTONES 2022/2023 outlook



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  - Phase 2b study in 250 patients with MCI/mild AD

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Endpoints: safety, attention/working memory, NTB, biomarkers

- ◆ 22 sites in 5 countries active
  - No pandemic-related delays
- >90 patients randomized 1:1:1 (placebo/ 300 mg / 600 mg, all BID)
  - On track for interim safety analysis
  - ◆ >90 patients to be included in DSMB decision

MID-22 INTERIM SAFETY AND DSMB DECISION safety/final dose selection

- ◆ All patients randomized 1:1 (placebo/ final dose)
  - On track for final readout in H2/2023



Phase 2a/b study in 414 patients with early AD

Endpoints: safety, ABC scores/ cognition & EEG , CDR-SB, biomarkers

NIH Run by ADCS, supported by NIH grant

ADOS

FDA

- Significant support and visibility
- ◆ FDA Fast Track designation
  - Opportunity to benefit from more frequent engagement with the FDA
- Ph 2a part ongoing with 11 active sites
  - Randomizing and treating patients despite pandemic and weather-related challenges in the U.S.
  - On track for interim futility analysis

H1/2023 STAGE GATE DECISION safety/efficacy, transition to Ph 2b



- Clinical Trial Application approved in China
- Ph 1 study planned for H1/2022, Ph2 to follow

Several key milestones in 2022/23; overall data set intended to support clear path to approval



## CONDENSED STATEMENT OF PROFIT AND LOSS

In €k	2021	2020	%
Gross profit	9,196	0	
Research and development expenses	(17,452)	(13,210)	32 %
General and administrative expenses	(4,549)	(2,807)	62 %
Operating loss	(12,798)	(16,011)	(20) %
Finance result	575	(499)	>100%
Income taxes	(432)	0	
Net loss for period	(12,655)	(16,510)	(23) %
Loss per share (basic and diluted) (in EUR)	(0.63)	(0.83)	



## KEY FINANCIAL FIGURES

In €k	Dec 31, 2021	Dec 31, 2020
Cash and cash equivalents	14,661	26,306
Total assets	24,520	29,751
Total equity	16,557	26,221
Shares (number)	20,050,482	19,975,482
In €k	2021	2020
Cash flows used in operating activities	(11,257)	(14,012)
Cash flows used in investing activities	(28)	(640)
Cash flows used in by financing activities	(827)	(90)
Cash and cash equivalents at the end of period	14,661	26,306

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