vivoryon therapeutics

HALF YEAR 2020 RESULTS WEBCAST AND CONFERENCE CALL

September 21, 2021

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VIVORYON THERAPEUTICS

Overview

- **Enzyme inhibition for targeted intervention:** Modulating the activity of proteins altered in disease settings
- **Lead product candidate varoglutamstat in AD: Phase 2a evidence of disease-modifying activity**
  - Statistically significant improvement in working memory after 3-months treatment
  - Upstream intervention with dual MoA: Targeting the QPCT/L and CCL2 pathways
  - Targets all three major hallmarks of AD: Abeta aggregation, neuroinflammation and tau pathology, as well as synaptic function
- **Ongoing Phase 2b program** in AD designed to provide clear path to regulatory approval[1]
- **Oral small molecule**: Good blood-brain-barrier penetration, intracellular activity, attractive COGS
- **Large pharma partnership deals:** Simcere (QPCT/L in AD; Greater China regional partnership worth up to US$ 565 M), OSI/Astellas (DPP4), AstraZeneca (CDK9)
- Follow-up programs in **oncology, inflammatory diseases/NASH** and **AKI/fibrosis**
- **Strong IP** including composition of matter coverage beyond 2035

AD: Alzheimer's disease; CCL2: chemokine (C-C motif) ligand 2; CDK9: Cyclin-dependent kinase 9; COGs: cost of goods; DPP4: dipeptidyl peptidase-4; QPCT/L: glutaminyl cyclase and glutaminyl cyclase-like protein; [1]Cummings, Feldman and Scheltens, 2019

KEY UPDATES

- US Phase 2a/b VIVA-MIND study for varoglutamstat in patients with early AD being initiated as planned, with the first site now approved to initiate screening
- 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 M plus double-digit royalties on sales
- Enrollment into European Phase 2b VIVIAD study in patients with mild cognitive impairment and mild AD on track with additional study centers opened to balance effects of COVID-19 related patient and staff protection policies implemented at German study sites; study details recently published as *Vijverberg et al., Alzheimer's Research & Therapy (2021) 13:142*
- Significant expansion of patent portfolio with a total of 14 additional patents granted for Vivoryon's small molecule inhibitors and antibody-based medicines in development to treat AD and other diseases with exceptionally high medical need
- Florian Schmid joined Vivoryon as Chief Financial Officer
- AGM: shareholders approved all resolutions with large majority

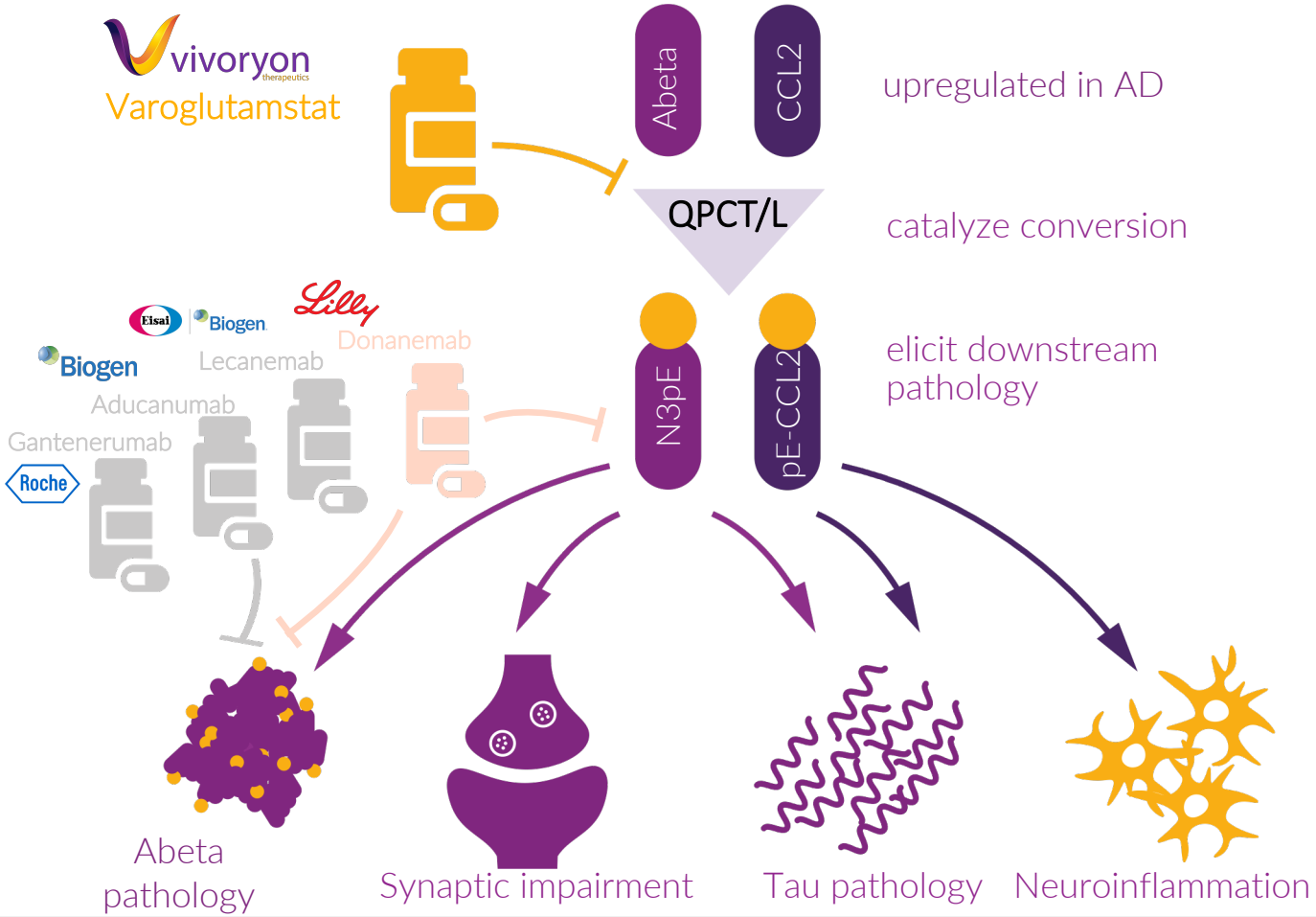
THERAPEUTIC INTERVENTIONS IN AD

Varoglutamstat Inhibits Formation of Toxic Abeta Species Upstream of Other Approaches

ROLE OF QPCT/L IN AD PATHOLOGY

- Increased activity of glutaminyl cyclase (QPCT) is associated with AD pathology[1]
- QPCT catalyzes formation of neurotoxic N3pE amyloid by cyclization of N-terminal glutamate on Abeta[2]
- N3pE amyloid correlates with QPCT expression and MMSE status in AD patients and is not found in healthy individuals[3]
- N3pE amyloid is a validated target: Phase 2 data from VVY's small molecule varoglutamstat and Lilly's mAb donanemab
- Targeting QPCTL:
  - Inhibits neuroinflammation by modulating CCL2 activity
  - Increased levels of QPCTL and high pE-CCL2 levels correlate strongly with low MMSE scores[4]

VAROGLUTAMSTAT TARGETS UPSTREAM PATHOGENESIS



[1]Gunn et al., J.Neurochem 2021; [2] Schilling et al., Nat. Med. 2008; [3]Morawski et. al., JAD 2014; Nussbaum et al., Nature 2012; [4]Hartlage-Rübsamen et al., Acta Neuropathol, 2015

CLINICAL DEVELOPMENT STRATEGY

Clear Path To Regulatory Approval with Upside Potential for Accelerated Approval

Preclinical research
In vitro and in vivo studies

COMPLETED

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

Phase 1
Safety and tolerability in 205 healthy volunteers

COMPLETED

- Varoglutamstat is well-tolerated
- No DLT at single dose (up to 3.6 g daily) or multiple dose (2x800 mg)

Phase 2a SAPHIR
Safety and tolerability in 120 patients with early AD

COMPLETED

- 3-month treatment improved working memory/attention (as measured by CogState)
- High target occupancy confirmed at doses of 150 mg and above

Phase 2b VIVIAD
Safety, tolerability and efficacy in 250 Patients MCI and mild AD

Interim safety mid-22; final data 2H23

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

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

Stage-gate to Ph2b 1H23; final Ph2b data 2H24*

- Endpoints: safety, attention/ working memory, CDR-SB, biomarkers

Pivotal study or accelerated approval

- Two possible scenarios
  - Application for accelerated approval (based on consistent/ positive data from both Phase 2b studies)
  - Phase 3 clinical development

**CDR-SB: clinical dementia rating scale-sum of boxes; DLT: dose-limiting toxicity; NTB: neuropsychological test battery; *pts moving into Ph2b prior to stage-gate*

PHASE 2A/B STUDY - ONGOING

Efficacy and Safety of Varoglutamstat in Patients With Early AD[1]

START 2H21

Site visits: 4, 8, 12, 16, 24, 36, 48, 60, 72

INTERIM DATA 1H23

w 1-24

PHASE 2A ADAPTIVE DOSE FINDING

180 patients

Placebo/ 600 mg/ 300 mg/ 150 mg

Inclusion

- MCI/mild AD
- Confirmed with AD biomarkers
- 50-89 years old
- On stable dose of FDA-approved AD medication

FUTILITY/STAGE GATE TO 2B

Safety/Final Dose Selection/Cognition (ABC Score)/EEG

w 25 – 72

PHASE 2B

Additional 234 patients on dose carried forward/ Placebo, 1:1

ENDPOINTS

Primary efficacy:

CDR-SB over 72w

Secondary efficacy:

ABC score, quantitative EEG-relative theta wave power, FAQ, ADAS-Cog-13, Neuropsychiatric Inventory

Exploratory efficacy:

MRI, MMSE, MOCA, qEEG connectivity measures, CSF biomarkers, AD Composite Score, ADAS Cog Exec, Relative QPCT activity in CSF

ADAS-Cog: Alzheimer's Disease Assessment Scale-Cognitive Subscale; ADNI ABC: neuropathologic assessment; CDR-SB: CFC2: cognitive- functional composite; *MRI: magnetic resonance imaging;* [1]*https://clinicaltrials.gov/ct2/show/NCT03919162; **

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CONDENSED STATEMENT OF PROFIT AND LOSS

In €k	Jan – June 2021	Jan – June 2020	%
Research and development expenses	9,456	6,380	48
General and administrative expenses	2,337	1,138	>100
Other operating income	(5)	(38)	>100
Operating loss	11,788	7,480	58
Finance result	(117)	92	>(100)
Loss for period	11,671	7,572	54
Loss per share (basic and diluted) (in EUR)	0.58	0.38	53

KEY FINANCIAL FIGURES

In €k	June 30, 2021	Dec 31, 2020
Cash and cash equivalents	19,832	26,306
Total assets	23,041	29,751
Total equity	15,471	26,221
Shares (number)	19,975,482	19,975,482

In €k	Jan – June 2021	Jan – June 2020
Cash flows used in operating activities	(6,540)	(6,353)
Cash flows used in investing activities	(24)	(574)
Cash flows provided by financing activities	(45)	(45)
Cash and cash equivalents at the end of period	19,832	34,471

MULTIPLE AVENUES TO VALUE GENERATION

Diverse Pipeline of Oral Small Molecule Inhibitors to Address Exceptionally High Medical Need

ALZHEIMER'S DISEASE

- Small molecule oral QPCT/L inhibitors with good blood-brain barrier penetration
- Inhibits production of N3pE amyloid (pGlu-Abeta): neurotoxic, glutaminylated, soluble Abeta peptides
- Significant effects on CSF biomarkers, synaptic function & working memory after 12w treatment

INFLAMMATION/NASH

- Small molecule QPCTL inhibitors to modulate the CCL2-CCR2 axis
- *In vivo* proof of concept in NAFLD mice
- Investigated as single agent and in combination with meprin inhibitors

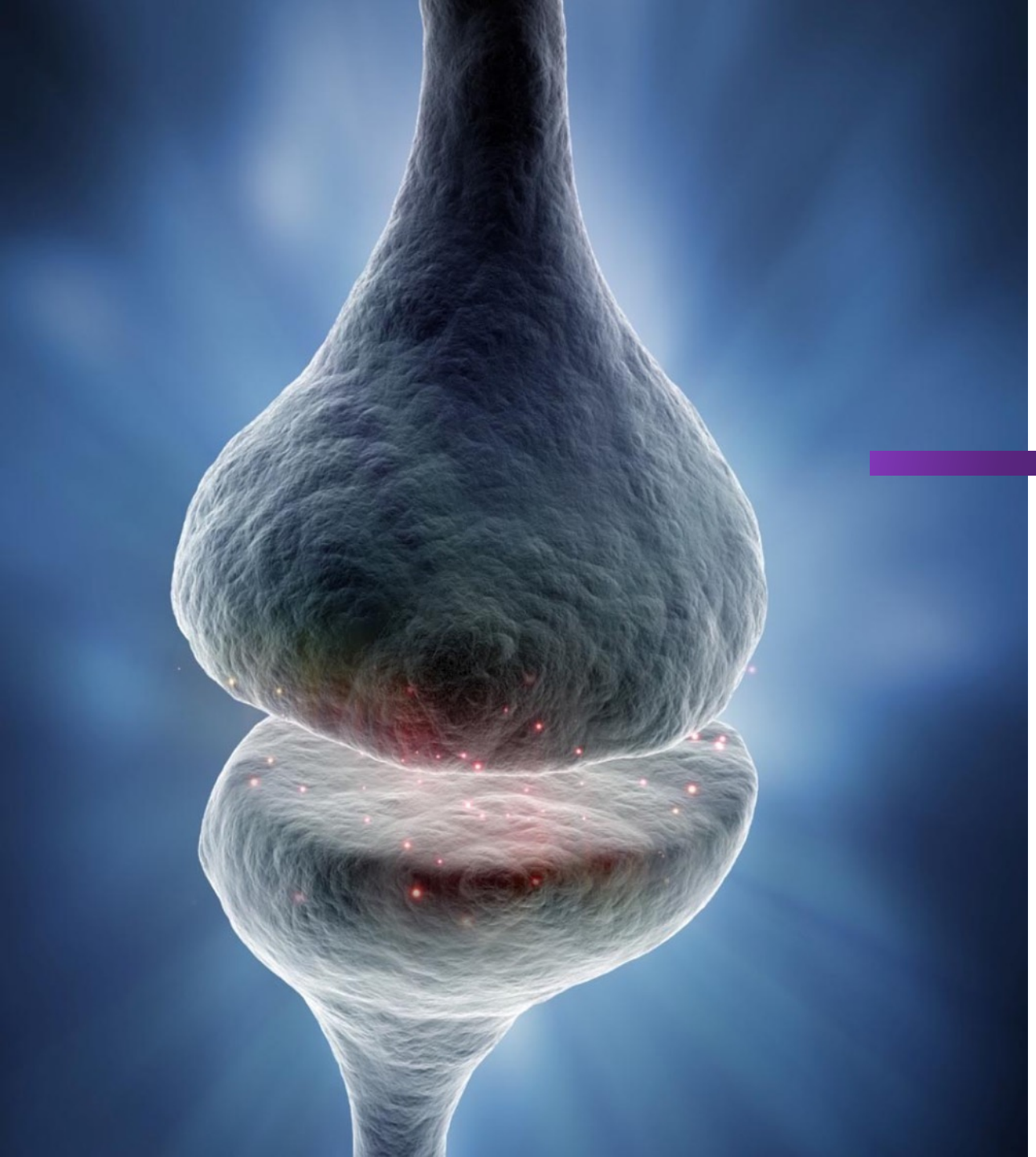
CANCER

- Small molecule QPCTL inhibitors to modulate cancer immune checkpoint activity
- Precision intervention to modulate the activity of pro-metastatic chemokines of the CCL family
- Opportunity for combination therapies

AKI/FIBROSIS

- First-in-class meprin alpha/beta single and dual selective small molecule inhibitors
- *In vivo* proof of concept in AKI animal model
- Unique recognition pattern allows design of selective and specific meprin protease inhibitors

AKI: acute kidney injury; CCL2: chemokine (C-C motif) ligand 2; CCR2: C-C chemokine receptor type 2; NASH: nonalcoholic steatohepatitis; NAFLD: nonalcoholic fatty liver disease; QPCT: glutaminyl cyclase; QPCTL glutaminyl cyclase-like protein; QPCT/L glutaminyl cyclase and glutaminyl cyclase-like protein



Q&A