Vandria Reports Positive Phase 1 Target Engagement Data for VNA-318, Supporting Further Development in Alzheimer's Disease

Results presented at the 18th Clinical Trials in Alzheimer's Disease (CTAD) meeting, San Diego, December 1-4

- VNA-318, an oral brain-penetrant small molecule therapeutic modulates a novel target to reduce inflammation and improve mitochondrial function
- First-in-human trial showed a highly favourable safety profile, with VNA-318 well tolerated across all dose levels without any safety concerns
- Single doses of VNA-318 resulted in a statistically significant ($p<0.001$) and dose-dependent change in a key plasma target engagement biomarker
- Pharmacokinetic data showed exposure to VNA-318 at concentrations predictive of therapeutic efficacy based on pre-clinical studies in both acute pro-cognitive and long-term disease-modifying models of Alzheimer's disease pathophysiology
- Given its broad mode of action VNA-318 has potential to treat other CNS diseases beyond Alzheimer's disease
- Vandria is planning the next stage of development, including Phase 2 proof-of-concept trials for VNA-318 and continued pipeline expansion for multiple systemic indications

Lausanne, Switzerland – 2 December 2025 – Vandria SA, a clinical stage biotech company developing small molecule therapeutics to restore mitochondrial function and reduce inflammation for the treatment of age-related and chronic diseases, today announces topline results from its first-in-human clinical trial of its lead Central Nervous System (CNS) compound VNA-318.

VNA-318 is a first-in-class, orally bioavailable, and brain-penetrant small molecule targeting a novel protein with a dual mode of action (MoA). Initially, VNA-318 is being developed to address the major unmet medical needs facing patients with Alzheimer's disease: cognitive impairment and the debilitating loss of function associated with it. Given its broad MoA, VNA-318 has potential to treat other CNS diseases.

The novel target of VNA-318 has genetic associations with several human diseases including Alzheimer's disease. In pre-clinical mouse models of neurodegeneration and cognitive impairment, VNA-318's dual MoA resulted in both immediate pro-cognitive and long-term disease-modifying benefits. More specifically, VNA-318 showed an immediate improvement

in memory, learning, and cognitive function, as well as long-term reduction in neuroinflammation, reduced toxic protein aggregation, and improved mitochondrial function.

Topline results from the first-in-human trial of VNA-318 are being presented today at the annual meeting of the 18th Clinical Trials in Alzheimer's Disease (CTAD) meeting, being held in San Diego December 1-4. The Phase 1 trial, VNA-318-01, is a randomized, double-blind single and multiple ascending dose study designed to assess safety, tolerability, pharmacokinetic (PK) and pharmacodynamic parameters in 92 healthy male subjects [VNA-318-01| ClinicalTrials.gov]. Interim results show excellent safety and tolerability of VNA-318 with no severe or serious adverse events and no adverse events leading to trial discontinuation. The PK data demonstrate a long half-life supportive of once-daily oral dosing and a predictable, dose-linear increase of exposure with low variability. Already with single dosing, a statistically significant ($p<0.001$) and dose-dependent change in a key target engagement biomarker has been observed. The availability of an easily accessible target engagement biomarker in plasma will be leveraged in VNA-318's future clinical development.

VNA-318 levels in the cerebrospinal fluid measured during the trial in one cohort confirm that the brain penetration seen in pre-clinical studies translates to humans.

Klaus Dugi M.D., CEO of Vandria, said: "We are very excited about the results of our first-in-human trial of VNA-318, which ticks all the boxes for a Phase 1 trial – and more. The statistically significant dose-dependent change in a key target engagement biomarker is a very important finding and will be valuable for our Phase 2 clinical development strategy. This, coupled with safety, tolerability and demonstrated brain penetration, as well as pre-clinical data strongly support VNA-318's advancement in Alzheimer's disease.

"We believe that VNA-318 has the potential to address unmet medical needs like mild cognitive impairment associated with Alzheimer's and Major Depressive Disorder, as well as other CNS disorders."

Steven Arnold M.D., Professor of Neurology at Harvard Medical School and EGC Endowed Chair in Alzheimer Therapeutic Sciences at Massachusetts General Hospital said "VNA-318 modulates a novel target with genetic associations with Alzheimer's disease and related neurodegenerative diseases. It is very exciting to see the compelling data from Vandria's pre-clinical and clinical studies, and the progress VNA-318 is making as it gets closer to being tested in patients."

Vandria is planning to raise a Series B in 2026 to fund proof-of-concept Phase 2 trials. The global market for Alzheimer's alone is estimated at $6 billion and is expected to grow at a CAGR of 12% to 2035, driven by an aging population, improved diagnosis, and a growing awareness and understanding of the condition and its implications.

The planned Series B will also be used to progress Vandria's pre-clinical pipeline of compounds in non-CNS indications such as muscle, lung, and liver diseases.

- ends -

For further information contact:
Vandria
info@vandria.com

Media Enquiries
Charles Consultants
Sue Charles – Sue@charles-consultants.com +44 (0)7968 726585

About Vandria
Vandria is a clinical stage biotech company developing first-in-class, small molecule precision therapeutics to restore mitochondrial function and reduce inflammation for the treatment of age-related and chronic diseases.

The company's lead CNS asset, VNA-318, is an orally bioavailable, first-in-class, brain-penetrant, patent-protected small molecule with a dual mode of action designed to improve short term memory and learning, and to have long term disease-modifying effects, as demonstrated in models of neurodegenerative disease such as Alzheimer's and Parkinson's disease. The company has a wider portfolio of small molecule modulators against its novel target across a broad range of age-related and chronic diseases of the muscle, lung and liver.

Based at the Biopôle campus in Lausanne Switzerland, the company has raised $32M (CHF28M) in venture finance from +ND Capital, Hevolution Foundation, Dolby Family Ventures and private investors.

Read more: https://vandria.com/
Follow us on LinkedIn: https://www.linkedin.com/company/vandria-sa/about/


Vandria