Pooled Individual Patient Data Analysis of Three Phase 2 Trials Supports Vasopressin V1b Receptor Antagonism (BH-200 250 mg BID) as an Antidepressant Mechanism for the Treatment of Major Depressive Disorder (MDD)

Lars Arvastson[1], Daniel Gehrlach[1], Evangelos Papanastasiou[1], Meline Gevergyan[1], Christine zu Eulenburg[1,2], **Hans Eriksson**[1]

[1]HMNC Holding GmbH, Wilhelm-Wagenfeld-Straße 20, 80807 Munich, Germany
[2]University Medical Center Hamburg-Eppendorf, Martini-Straße 52, 21049 Hamburg, Germany

Lars.Arvastson@hmnc-brainhealth.com

American Society of Clinical Psychopharmacology
Annual Meeting 2026; May 26-29, 2026; Miami, FL, USA

HMNC BRAIN HEALTH PRECISION THERAPEUTICS

MAIN TAKEAWAYS

- Pooled analysis of 3 trials demonstrated antidepressant efficacy of BH-200 vs placebo.
- Favorable benefit/risk ratio of BH-200, with transient and reversible liver enzyme elevations.
- Vasopressin V1b receptor antagonism is a viable antidepressant mechanism in MDD, supporting further evaluation in harder-to-treat populations such as treatment-resistant depression.

Background

Lack of novel pharmacological mechanisms to address symptoms of MDD is the main reason behind the unmet medical need in those clinical populations showing suboptimal response to existing treatments. Vasopressin V1b receptor antagonism as a modulator of hypothalamic–pituitary–adrenal stress axis has therapeutic potential, but clinical evidence has been inconsistent across trials in MDD. Two trials in MDD (DFI 5878 and OLIVE) demonstrated a separation between patients treated with BH-200 (250 mg BID) and those treated with placebo at Week 8 ($p<0.05$); the third trial (DFI 5879) showed no separation.

Here, we conducted a pooled analysis of three clinical trials to estimate the overall antidepressant efficacy of BH-200 250 mg BID and evaluate consistency across studies.

Methods

This retrospective analysis included three randomized, double-blind, placebo-controlled phase 2 studies in MDD with a similar design: DFI 5878, DFI 5879, and OLIVE. Individual Patient Data (IPD) were pooled in an intention-to-treat framework (randomized participants with ≥1 post-baseline assessment). The endpoint was the change from baseline to Week 8 in Hamilton Depression Scale total score (HAM-D17). A mixed model for repeated measures (MMRM) included baseline, visit, treatment, study, visit-by-treatment, visit-by-study, and treatment-by-study, with covariates (sex, age, baseline BMI) and random effects for country and subject-level visit slope/intercept. Primary estimates focused on the overall treatment effect at Week 8 and on the assessment of heterogeneity via a treatment-by-study interaction.

Results – Efficacy

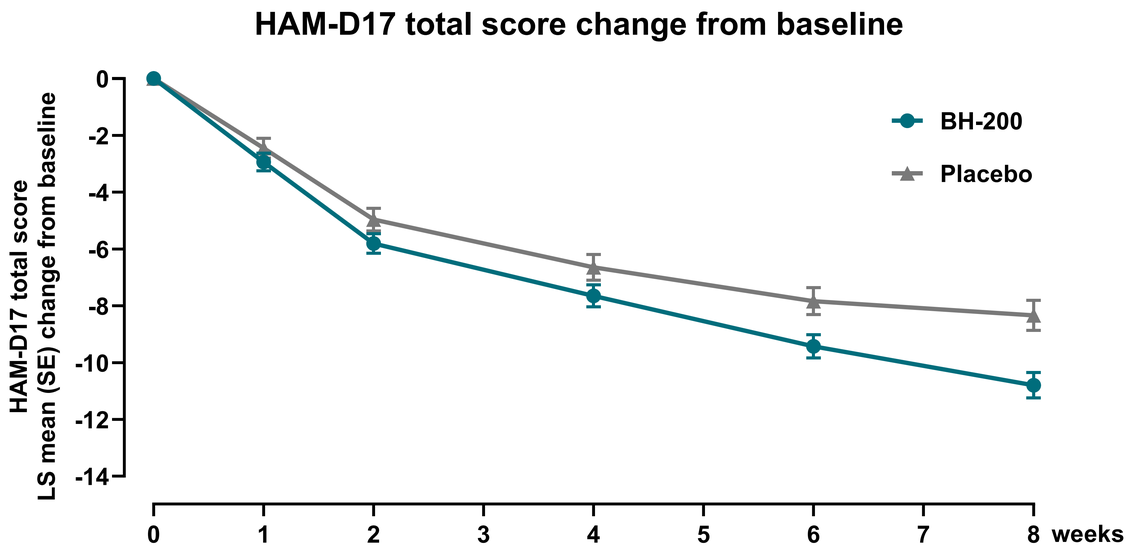
The pooled dataset included 610 MDD patients (DFI 5878: n=139, DFI 5879: n=145, and OLIVE: n=326). 362 patients were treated with BH-200, 249 patients received placebo.

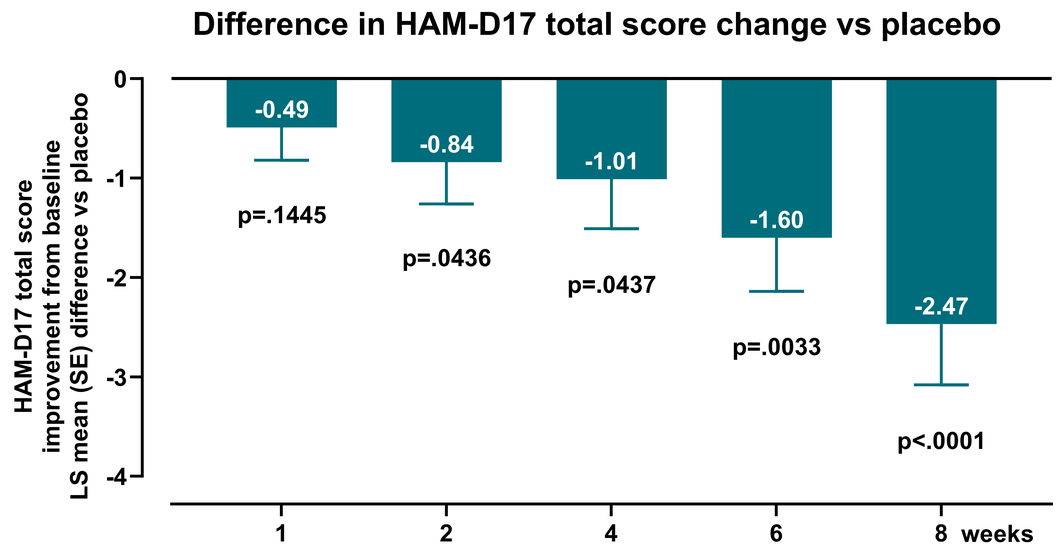
BH-200 demonstrated robust improvement over placebo, with a separation beginning in Week 2 and increasing over time through Week 8. The least-squares mean difference (between BH-200 and placebo) was −2.47 (SE=0.61) HAM-D17 points (p=.000063).

A follow-up assessment 4 weeks after the end of the trial treatment (i.e., at week 12 from baseline) demonstrated a sustained treatment effect for BH-200.

Treatment effects were directionally consistent across studies, with no evidence of treatment-by-study heterogeneity (treatment-by-study interaction: p=.38, Type III fixed-effect test from the MMRM).

In MMRM analysis, older age was statistically significantly associated with a lower antidepressant efficacy (p=.0068) while gender and BMI had no effect.





Results – Safety

Transient liver enzyme elevations (ALT or AST ≥ 3× the upper limit of normal) were observed, and occurred in 5.9% of patients, with variation across studies. Overall adverse event rates appeared comparable between placebo and BH-200, with a generally favorable tolerability profile.

Funding: This analysis and the OLIVE trial were sponsored by HMNC Holding GmbH.

Disclosures: LA, DG, EP, MG, CzE, and HE are employed by or serve as consultants to HMNC Holding GmbH and may own shares in the company.