GH Research Announces Publication of Phase 2b Results for Mebufotenin (GH001) in JAMA Psychiatry and Reports New Finding of Severity-Independent Efficacy in TRD

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- Phase 2b results for GH001 in TRD now published and peer-reviewed in *JAMA Psychiatry*
- New peer-reviewed article in forthcoming issue of *Psychopharmacology Bulletin* demonstrates that GH001 efficacy is independent of prior antidepressant treatment failures

DUBLIN, March 25, 2026 (GLOBE NEWSWIRE) -- GH Research PLC (Nasdaq: GHRS), a clinical-stage biopharmaceutical company dedicated to transforming the lives of patients by developing a practice-changing treatment in depression, today announced two peer-reviewed publications from its Phase 2b clinical program of GH001 in treatment-resistant depression (TRD): the primary trial results in *JAMA Psychiatry*, and a new analysis demonstrating that efficacy is independent of the number of prior lifetime treatment failures in a forthcoming issue of *Psychopharmacology Bulletin*.

***JAMA Psychiatry* Publication**

The peer-reviewed article, titled "GH001 vs Placebo in Patients with Treatment-Resistant Depression" has been published today in *JAMA Psychiatry* (DOI: 10.1001/jamapsychiatry.2026.0096). The publication includes the complete results from the randomized, double-blind, placebo-controlled Phase 2b trial of mebufotenin in patients with TRD, including all primary and secondary efficacy endpoints, safety and tolerability data, and initial results from the 6-month open-label extension. These results were previously reported in topline form.

"Publication in JAMA Psychiatry *provides independent peer-reviewed validation of our Phase 2b findings,"* said Dr. Velichka Valcheva, Chief Executive Officer. *"This supports our ongoing efforts to advance GH001 into global pivotal trials."*

New Finding: GH001 Efficacy Is Independent of Prior Treatment Failures

A supporting peer-reviewed article, titled "GH001 Efficacy is Independent of Prior Antidepressant Treatment Failures in Treatment-Resistant Depression: A Post Hoc Analysis of a Phase 2b Randomized Controlled Trial," will be published in a forthcoming issue of *Psychopharmacology Bulletin*.

In TRD, a well-established finding across multiple treatment modalities is that remission rates decline significantly with each successive antidepressant treatment failure. This pattern, first quantified in the landmark STAR*D trial (see *About STAR*D* below), represents a fundamental challenge in treating patients with extensive treatment histories. The new analysis of Phase 2b data demonstrates that GH001 does not follow this pattern:

- Day 8 remission rates ranged from 53.9% to 63.6% across patients with 2 to ≥5 prior lifetime antidepressant failures, with no decline at higher failure counts;
- End of trial/Month 6 remission rates ranged from 61.5% to 85.7% across the same subgroups; and
- No meaningful correlation was observed between the number of prior lifetime treatment failures and Montgomery-Åsberg Depression Rating Scale (MADRS) improvement at Day 8 ($r=-0.13$; $P=0.44$) or among those who completed the 6-month OLE ($r=-0.10$; $P=0.60$).

*"One interesting, unanticipated finding from this trial is that the benefit of GH001 appeared to be independent of the number of prior lifetime antidepressant failures. Remission rates were consistently high across subgroups – in contrast to the decline seen with each successive treatment that we observed in the STAR*D trial. This suggests patients who have not responded to three or more prior courses of antidepressant therapy might benefit from this novel therapy,"* said Michael E. Thase, MD, Professor of Psychiatry, Perelman School of Medicine at the University of Pennsylvania.

Consistent with the findings of this article, GH001 efficacy is also independent from prior treatment failures within the current depressive episode in this Phase 2b trial.

About GH Research PLC

GH Research PLC is a clinical-stage biopharmaceutical company dedicated to transforming the lives of patients by developing a practice-changing treatment in depression. GH Research PLC's initial focus is on developing its novel and proprietary mebufotenin therapies for the treatment of patients with TRD. Based on the observed clinical activity in our Phase 2b trial, where the primary endpoint was met with a MADRS reduction from baseline of −15.5 points compared with placebo on Day 8 ($P<0.0001$), we believe that our mebufotenin product candidates have the potential to change the way TRD is treated today.

About GH001

Our lead product candidate, GH001, is formulated for mebufotenin administration via a proprietary inhalation approach. Based on the observed clinical activity in our Phase 2b GH001-TRD-201 trial, where the primary endpoint was met with a MADRS reduction from baseline of −15.5 points compared with placebo on Day 8 ($P<0.0001$), we believe that GH001 has the potential to change the way TRD is treated today.

About STAR*D

The Sequenced Treatment Alternatives to Relieve Depression (STAR*D) trial was the largest and most comprehensive prospective study of depression treatment outcomes ever conducted. Funded by the National Institute of Mental Health (NIMH), the trial enrolled 4041 outpatients with major depressive disorder across 41 U.S. clinical sites between 2001 and 2004. The study used a sequential design in which patients who did not

achieve remission on an initial antidepressant (citalopram) were moved through up to four successive treatment steps, each involving a switch to or augmentation with a different medication.

STAR*D's central finding was that remission rates declined progressively with each treatment step: 36.8% achieved remission after the first course, 30.6% after the second, 13.7% after the third, and just 13.0% after the fourth (Rush et al., *American Journal of Psychiatry*, 2006). Cumulatively, after all four steps, approximately one-third of patients had still not achieved remission. This pattern of diminishing returns with increasing treatment resistance has been widely replicated and is now considered a defining characteristic of TRD.

Forward-Looking Statements

This press release contains statements that are, or may be deemed to be, forward-looking statements. All statements other than statements of historical fact included in this press release, including statements regarding our plans and expectations with respect to our global Phase 3 pivotal program for GH001, strategies and prospects for our business, including the development and therapeutic potential of mebufotenin and GH001, are forward-looking statements. Forward-looking statements appear in a number of places in this press release and include, but are not limited to, statements regarding our intent, belief or current expectations. Forward-looking statements are based on our management's beliefs and assumptions and on information currently available to our management. Such statements are subject to risks and uncertainties, and actual results may differ materially from those expressed or implied in the forward-looking statements due to various factors, including, but not limited to, those described in our filings with the U.S. Securities and Exchange Commission from time to time. No assurance can be given that such future results will be achieved. Such forward-looking statements contained in this press release speak only as of the date hereof. We expressly disclaim any obligation or undertaking to update these forward-looking statements contained in this press release to reflect any change in our expectations or any change in events, conditions, or circumstances on which such statements are based unless required to do so by applicable law. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements.

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