GH Research Announces Global Pivotal Program Plans and Further Development Updates

July 23, 2025

- **Engagement with FDA on GH001 IND complete response ongoing**
- **The fully completed Open-Label Extension analysis confirms a 73% remission rate at 6 months with infrequent treatment visits and no psychotherapy**
- **Treatment was well tolerated and no treatment related serious adverse events were reported. There was no evidence of treatment-emergent suicidal ideation or behavior**
- **Global pivotal program initiation on track for 2026**

DUBLIN, July 23, 2025 (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 provided updates on its business and key upcoming milestones.

GH001 Update

We have recently announced that we submitted a complete response to the previously announced clinical hold on our Investigational New Drug Application (IND) for GH001 with the U.S. Food and Drug Administration (FDA). We have now received a response from the FDA with only one hold topic remaining. The FDA requested that we either provide additional data or further justification related to the previously announced respiratory tract histology findings in rats. We strongly believe, based on scientific evidence, that the respiratory tract histology findings are rat specific. There are no additional requests related to dog toxicology. There are no device related issues remaining.

Engagement with FDA on IND complete response is ongoing. We are actively working to address the remaining issue.

Final Data from Fully Completed Phase 2b TRD

Previously we reported on the initial results from the phase 2b clinical trial of GH001 in treatment-resistant depression (TRD). This included part of the open-label extension (OLE) phase. Today we can report on the full dataset.

The primary endpoint was met with a highly significant placebo adjusted reduction from baseline of -15.5 points in Montgomery-Åsberg Depression Rating Scale (MADRS) total score on Day 8 ($p<0.0001$).

The full analysis of the OLE confirms a 73% remission rate at 6 months with infrequent treatment visits and no mandated psychotherapeutic intervention. GH001 delivered consistent MADRS reduction with re-treatments as needed. 57.5% of patients achieved remission at day 8 and 90% of those were also in remission at month 6.

Safety analysis confirmed that 100% of patients from the double-blind (DB) part continued in the OLE and there were no treatment related serious adverse events across the full 6-month duration of the trial. No treatment-emergent events of suicidal intent or suicidal behaviour occurred throughout the 6-month duration of the trial and lower rates of suicidal ideation were observed during the study in comparison to baseline. The psychoactive experience had a median duration of 11 minutes across the DB and OLE parts of the trial.

Across the DB and OLE, patients were deemed discharge ready by 1 hour from dose administration at 99% of treatment visits. A majority of patients needed 1-2 doses of GH001 suggesting a 2-hour visit or less in a commercial setting.

GH002 Update

We have previously announced the completion of a Phase 1, dose-ranging clinical pharmacology trial of GH002, our proprietary intravenous mebufotenin HBr product candidate, in healthy volunteers.

Top-line results demonstrate that GH002 was well-tolerated with no severe or serious adverse events and produced ultra-rapid psychoactive effects. The pharmacokinetic profile of GH002 was equivalent to that of GH001. We expect to submit an IND with the FDA for GH002 in Q4 2025.

Global Pivotal Program Plans

Pivotal program planning has been ongoing since Q1 2025:

- We have established a steering committee with KOLs to review Phase 2b results and assist with design of pivotal program;
- CRO and site selection process is ongoing and we are ramping up the team with laser focus on execution; and
- We are in the process of getting regulatory input on phase 3 requirements and preparation for end-of-phase 2 meeting is underway.

On that basis, we expect to initiate our global pivotal program in 2026.

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 treatment-resistant depression (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 potential to change the way TRD is treated today.

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 the clinical hold on GH001, including plans and expectations for progressing any nonclinical programs and any other work needed to lift the continuing clinical hold and the timing required for the FDA to lift such clinical hold; our plans and expectations with respect to progressing development of GH002 including with respect to the timing, scope and likelihood of IND submission and approval with the FDA; our targets regarding the initiation of our first global pivotal program; our future results of operations and financial position, business strategy, product candidates, medical devices required to deliver these product candidates, research pipeline, ongoing and currently planned preclinical studies and clinical trials, regulatory submissions and approvals and their effects on our business strategy, our expectations related to commencing trials in the US, research and development costs, cash runway, timing and likelihood of success, as well as plans and objectives of management for future operations, 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, the risk that the FDA does not accept our responses to the clinical hold issues and that we will be unable to fully address the FDA's concerns and lift the clinical hold on GH001; the risk that we may not be able to submit an IND for GH002, or to commence clinical trials in the United States on the timelines we are targeting; those described in our filings with the U.S. Securities and Exchange Commission. No assurance can be given that such future results, plans, or expectations or targets 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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