# GH Research Announces Successful Outcome of the Phase 2 part of its Phase 1/2 Clinical Trial of GH001 in Treatment-Resistant Depression

December 6, 2021

- Primary endpoint met in Phase 2 part of clinical trial for GH001 in TRD
  - *7 of 8 patients (87.5%) were in remission (MADRS ≤10) at day 7 after dosing (p<0.0001)*
- Secondary endpoints met
  - *Mean change from baseline in MADRS at day 7 after dosing was -24.4 points (-76%) (p<0.0001)*
  - *GH001 was well tolerated and no serious adverse events were reported*
- In addition, we announce positive preliminary safety results from a Phase 1 clinical pharmacology trial of GH001 in 46 healthy volunteers with 30-day follow-up supporting the safety profile of GH001 beyond day 7.

DUBLIN, Ireland, Dec. 06, 2021 (GLOBE NEWSWIRE) -- GH Research PLC (Nasdaq: GHRS), a clinical-stage biopharmaceutical company dedicated to transforming the treatment of psychiatric and neurological disorders, today reported the successful outcome of the Phase 2 part of a Phase 1/2 clinical trial of GH001, an inhalable 5-MeO-DMT product candidate, in patients with treatment-resistant depression (TRD) (GH001-TRD-102).

The primary endpoint of the Phase 2 part of the trial was met with 7 of 8 patients (87.5%) in remission (Montgomery–Åsberg Depression Rating Scale (MADRS) ≤10) at day 7 after dosing (p<0.0001). According to FDA Guidance for Industry, a 7-day endpoint is an appropriate primary efficacy endpoint for rapid-acting antidepressants.

The Phase 2 part of the clinical trial recruited 8 patients. The median age was 34 years. The median baseline severity of depression by MADRS was 32.

Patients followed a proprietary GH001 individualized dosing regimen administered on a single day with up to three increasing doses of GH001 (6 mg, 12 mg and 18 mg). The second and third doses were only administered in the event that the patient did not achieve a peak experience[1] (PE) at the previously administered dose. Based on this trial design, 6 patients received 6 mg and 12 mg doses of GH001 and 2 patients received 6 mg, 12 mg and 18 mg doses of GH001. 7 patients were able to achieve a PE at their final dose, and at this final dose the mean PE total score was 90.4.

Of the 7 patients who had a remission at day 7, all were in remission beginning on day 1, with 5 in remission as early as 2 hours after dosing. The single patient who did not achieve a remission at day 7, also improved on day 7 versus baseline. 6 of the 7 patients in remission had achieved a PE at their final dose. The mean MADRS change from baseline for all 8 patients at day 7 was -24.4 points (-76%) (p<0.0001).

Compared with the single dose results in the previously reported Phase 1 part of the trial (12 mg, n=4; 18 mg, n=4), the proprietary GH001 individualized dosing regimen increased the rate of MADRS remission at day 7, increased the mean MADRS absolute change from baseline at day 7, increased the rate of PE, and increased the mean PE score achieved.

In accordance with the trial protocol, a study safety group (SSG) was established, including external experts, to evaluate the safety data for the clinical trial. All patients completed all planned visits. No serious adverse events (SAE) were reported. 7 of 8 patients (87.5%) experienced at least one adverse drug reaction (ADR), all of which were mild (81%) or moderate (19%) in intensity, and all of which resolved spontaneously. The ADRs reported were: headache, sensory disturbance (each in 3 patients), anxiety, flashback, nausea (each in 2 patients), muscle discomfort, abdominal discomfort, paresthesia, depressive symptom (each in 1 patient). Based on the full safety results of the trial, the SSG concluded that no unexpected or severe adverse effects and no clinically significant changes were observed in any of the safety laboratory analyses, vital signs, psychiatric safety assessments or measures of cognitive function and that no signal for suicidal ideation or behavior was observed.

**Safety Results from Phase 1 Clinical Pharmacology Trial in Healthy Volunteers**

In addition, we also reported positive preliminary safety results from a Phase 1 clinical pharmacology trial in healthy volunteers (GH001-HV-103).

This trial enrolled 46 healthy volunteers with 30-day safety follow-up. The trial investigated three different single doses of GH001 in a double-blind, placebo-controlled design (6 mg (n=8), 12 mg (n=8), 18 mg (n=8), placebo (n=2 in each dose group)) and a proprietary GH001 individualized dosing regimen with intra-subject dose escalation within a single day in an open-label, non-randomized design in two groups with two different intervals between doses (1 hour (n=8), 2 hours (n=8)).

All subjects completed all planned visits. No SAEs were reported. 11 of 24 subjects (45.8%) who received GH001 in the single-dose part and 0 of 6 subjects (0%) who received placebo in the single-dose part experienced at least one ADR. In the multiple-dose part, 7 of 16 subjects (43.8%) who received GH001 experienced at least one ADR. All ADRs were mild and all ADRs resolved spontaneously. In the single-dose part, the ADRs reported were: headache (in four participants), tachycardia, crying (each in two participants), chest discomfort, dizziness, dry mouth, dyskinesia, fatigue, hypoesthesia oral, retching, somnolence, tremor (each in one participant). In the multiple dose part, the ADRs reported were: fatigue (in three participants), headache (in two participants), abnormal dreams, paresthesia oral, crying, tension (each in one participant). No clinically relevant changes were observed for vital parameters, peak expiratory flow rate, safety laboratory analyses, ECG and psychiatric safety assessments.

The preliminary results of this 30-day trial support the safety profile of GH001 single doses and the proprietary GH001 individualized dosing regimen with intra-subject dose escalation within a single day. Final source data verification, the pharmacokinetic analyses and analyses of various secondary

endpoints are still ongoing. The full results from this trial are intended to support the selection of the optimal dosing interval for the individualized dosing regimen in future studies of GH001.

[1]*The occurrence of peak experiences (PE) is assessed using a proprietary visual analogue scale (PE scale), which averages answers scored by the patient from 0 to 100 for three parameters of the experience: intensity, feelings of loss of control and profoundness. A PE is defined as a total score of at least 75 on this scale.*

**About GH Research PLC**

GH Research PLC is a clinical-stage biopharmaceutical company dedicated to transforming the treatment of psychiatric and neurological disorders. GH Research PLC's initial focus is on developing its novel and proprietary 5-MeO-DMT therapies for the treatment of patients with treatment-resistant depression (TRD).

**About GH001**

Our lead product candidate, GH001, is formulated for 5-MeO-DMT administration via a proprietary inhalation approach. With GH001, we have completed two Phase 1 healthy volunteer clinical trials and a Phase 1/2 clinical trial in patients with treatment-resistant depression (TRD). Based on the observed clinical activity, where 87.5% of patients with TRD were brought into an ultra-rapid remission with our GH001 individualized single-day dosing regimen in the Phase 2 part of the trial, we believe that GH001 has potential to change the way TRD is treated today. Across the GH001 program, no serious adverse events have been reported and GH001 was well tolerated at the investigated single dose levels and in the individualized dosing regimen.

**Forward-Looking Statements**

This press release contains statements that are, or may deemed to be, forward-looking statements. All statements other than statements of historical fact included in this press release, including statements regarding our future results of operations and financial position, business strategy, product candidates, research pipeline, ongoing and currently planned preclinical studies and clinical trials, regulatory submissions and approvals, research and development costs, 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, those described in our filings with the U.S. Securities and Exchange Commission. No assurance can be given that such future results will be achieved. Such forward-looking statements contained in this document speak only as of the date of this press release. 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.

**Investor Relations**
Julie Ryan
GH Research PLC
investors@ghres.com