Results from Early-Stage Trials of Inhaled Mebufotenin (GH001) in Healthy Volunteers and Patients with Treatment-Resistant Depression

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SUBMISSION DETAILS

Request for Proposals Psychedelics

Abstract: Background: Treatment-resistant depression (TRD) affects approximately 30% of patients with major depressive disorder (MDD) and is associated with higher rates of comorbidity, hospitalization, mortality, suicide and a reduced quality of life compared to patients with non-treatment-resistant depression. Only two pharmacotherapies are approved for TRD, highlighting the need for fast-acting, effective, and safe treatments. Mebufotenin (5-methoxy-N,N-dimethyltryptamine [5-MeO-DMT]) is a highly potent natural psychoactive substance from the tryptamine class. GH001 is a synthetic form of mebufotenin for pulmonary inhalation that has been evaluated in Phase 1 and Phase 2 clinical trials in healthy volunteers and patients with TRD, postpartum depression, and bipolar II disorder with a current major depressive episode. Results are presented herein for three early-stage clinical trials in healthy volunteers and patients with TRD.

Methods: Completed early-stage trials include two Phase 1 trials in 68 healthy volunteers (HVs; GH001: N=62; placebo: N=6]) and one Phase 1/2 trial in 16 patients with TRD (GH001: N=16). GH001 was administered via inhalation as single doses (2, 6, 12, 18 mg) or as an individualized dosing regimen (IDR) whereby up to three escalating doses (6, 12, 18 mg) were administered within a single day at intervals of 1-3 hours. Administration of subsequent doses was based on the patient’s subjectively reported psychoactive effects and the safety and tolerability at the previous dose. Psychotherapeutic intervention was not a component in these trials, but psychological support per standard of care was available to participants. These trials evaluated the safety, pharmacokinetic, and pharmacodynamic profile of GH001 in HVs, and the safety and antidepressant effects in patients with TRD.

Results: Data from three completed early-stage trials demonstrated that GH001 induces psychoactive effects with an ultra-rapid onset (commonly within seconds) and short duration (commonly 5-30 minutes). Inhalation of GH001 was well tolerated across trials with no severe or

serious adverse events reported. Among the 78 patients who received GH001, one or more treatment-emergent adverse events (TEAEs) were observed in 50 patients (64.1%) with a similar incidence in the single dose and IDR groups. The most frequently reported TEAEs across the trials included headache, anxiety, and nausea. No noteworthy changes in vital signs were observed; transient increases in heart rate and blood pressure immediately after GH001 administration were not clinically significant. Safety assessments, including laboratory analyses, psychiatric scales, electrocardiogram, and cognitive function tests, showed no clinically meaningful changes. The safety profile of GH001 broadly aligns with that observed for other serotonergic psychedelic drugs. In patients with TRD, remission (Montgomery-Åsberg Depression Rating Scale [MADRS] total score of ≤10) was achieved in 7/8 (87.5%) of patients in the IDR group at Day 8, compared to 3/8 (37.5%) patients in the single-dose group. This suggests that intraindividual dose escalation within a single day may increase the MADRS remission rate compared to single doses of GH001, whilst avoiding exposing the patient to unnecessarily high doses.

Conclusion: GH001 may represent an ultra-rapid, convenient, effective treatment for TRD and other depressive disorders without requirements for psychotherapeutic intervention before or after dosing.

Learning Objectives:

Learning Objective 1 Our objective is to educate attendees on results from three early-stage clinical trials of inhaled mebufotenin (GH001) that are part of a clinical development program seeking to deliver new treatment options to patients with depressive disorders.

Learning Objective 2 Our objective is to educate attendees on the significant potential of GH001 to induce ultra-rapid, remissions in patients with depression.

DISCLOSURE

Financial Relationships

Disclosure Yes, I do have a financial relationship(s) to disclose.

Financial Relationships Details

Ineligible Company	Type of Financial Interest
GH Research	Employee