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EudraCT Number	2020-002306-12
Sponsor's Study Number	GB004-2101
Study Title	A Phase 2, randomized, double-blind, placebo-controlled, multi-center study to evaluate GB004 in adult subjects with mild-to-moderate active ulcerative colitis.

To whom it may concern,

GB004, Inc., as the sponsor of the above-mentioned clinical trial, terminated the study prematurely for lack of treatment benefit.

The global study completion date (last patient, last visit) was 01 June 2022.

Results of the study are summarized in the following pages.

For more information, please contact regaffairs@gossamerbio.com

Discussion of Study Results

This Phase 2 study in adult subjects with mild-to-moderate active ulcerative colitis (UC) who had disease activity despite treatment with 5-acetylsalicylic acid with or without systemic corticosteroids was terminated prematurely by the Sponsor for lack of treatment benefit based on the totality of results available at the time of the placebo-controlled period (PCP) Week 12 Analysis.

The primary objective of the PCP was to evaluate the effect of GB004 compared to placebo on clinical remission at PCP Week 12, and the primary objective of the OLE was to evaluate the safety and tolerability of GB004.

A total of 236 subjects were randomized and treated, with the PCP safety population consisting of 78, 76, and 82 subjects in the Placebo, GB004 480 mg QD, and GB004 480 mg BID groups, respectively.

A higher percentage of subjects completed PCP Week 12 on study treatment in the Placebo group (87.2%) than the two GB004 groups (80.8% in the GB004 480 mg QD group and 83.8% in the GB004 480 mg BID group). Higher percentages of subjects discontinued study treatment prior to PCP Week 12 due to AE in the two GB004 groups relative to placebo (9.0% in the GB004 480 mg QD group and 7.5% in the GB004 480 mg BID group, versus 1.3% in placebo).

The majority of subjects (69.1%) did not complete PCP study treatment, primarily due to lack of efficacy (31.4%) and study termination by the Sponsor (19.1%). The majority of subjects (69.2%) did not complete OLE study treatment, primarily due to study termination by the Sponsor (52.3%).

Neither GB004 treatment group demonstrated statistically significant or clinically meaningful results for the primary analysis of the PCP primary endpoint of the proportion of subjects with clinical remission at PCP Week 12 in the PCP Week 12 Analysis. The proportions of subjects with clinical remission at PCP Week 12 were 17.9% in the Placebo group, 15.4% in the GB004 480 mg QD group (p-value versus placebo = 0.6694), and 22.5% in the GB004 480 mg BID group (p-value versus placebo = 0.4719). Similarly, neither GB004 treatment group demonstrated statistically significant or clinically meaningful results for any of the primary analyses of PCP secondary efficacy endpoints at PCP Week 12 (clinical response, histologic remission, endoscopic improvement, and mucosal healing) in the PCP Week 12 Analysis. Additionally, an assessment of available results for PCP secondary efficacy endpoints at PCP Week 36 at the time of the PCP Week 12 Analysis did not show any meaningful differences for either GB004 treatment group versus placebo.

The overall incidence of AEs in the PCP was higher in both GB004 treatment groups (60.5% in the GB004 480 mg QD group and 56.1% in the GB004 480 mg BID group) than in the Placebo group (44.9%). Of the AEs with an incidence ≥ 2% higher in either GB004 treatment group relative to placebo, the following events had an incidence ≥ 5% in either GB004 treatment group: dizziness, nausea, somnolence, fatigue, headache, and anaemia.

The incidence of SAEs in the PCP excluding UC SAEs was higher in the GB004 480 mg BID group (4.9%) than in the placebo (1.3%) or GB004 480 mg QD (0%) groups. No treatment-related SAEs were reported in the PCP.

The incidence of severe AEs in the PCP was higher in both GB004 treatment groups (6.6% and 8.5% in the GB004 480 mg QD and GB004 480 mg BID groups, respectively) than in placebo (1.3%). The incidence of treatment-related AEs in the PCP was higher in both GB004 treatment groups (30.3% and 31.7% in the GB004 480 mg QD and GB004 480 mg BID groups, respectively) than in placebo (9.0%). The incidence of AEs leading to an action taken with PCP study treatment in the PCP was higher in both GB004 treatment groups (18.4% and 19.5% in the GB004 480 mg QD and GB004 480 mg BID groups, respectively) than in placebo (1.3%). The incidence of AEs leading to discontinuation of PCP study treatment was higher in both GB004 treatment groups (11.8% and 9.8% in the GB004 480 mg QD and GB004 480 mg BID groups, respectively) than in placebo (1.3%).

The overall incidence of AEs in the OLE was 32.3%. The only AE PT with an overall incidence ≥ 5% in the OLE was COVID-19 (6.2%). The overall incidence of SAEs in the OLE excluding UC SAEs was 3.8%. No treatment-related SAEs were reported in the OLE. There was 1 death during the OLE; the fatal SAE of COVID-19 pneumonia was not considered treatment-related.

The GB004 treatment groups had higher incidences than placebo of shifts from baseline to low hematocrit (17.9% in placebo, 26.9% in GB004 480 mg QD, and 28.1% in GB004 480 mg BID) and shifts from baseline to low erythrocytes (13.1% in placebo, 36.4% in GB004 480 mg QD, and 31.8% in GB004 480 mg BID) in the PCP.

The incidence of transaminase elevations to ≥ 3 x ULN in the PCP was higher in both GB004 groups (3.9%, 3 subjects in GB004 480 mg QD and 6.2%, 5 subjects in GB004 480 mg BID) than in placebo (1.3%, 1 subject). All of these subjects met the criteria for Temple's Corollary, with the exception of one subject in the GB004 480 mg BID group who met the biochemical criteria for possible Hy's law but was not considered a Hy's law case due to a confounding AE of cholelithiasis.

Neither GB004 group had clinically significant differences from placebo in urinalysis, plasma and serum markers, vital signs, or ECG parameters in the PCP.

Overall, GB004 failed to demonstrate efficacy in adult subjects with mild-to-moderate UC. Relative to placebo, both GB004 groups had higher incidences of AEs leading to PCP treatment discontinuation, higher incidences of the AEs of dizziness, nausea, and somnolence, and higher incidences of transaminase elevations to ≥ 3 x ULN.

Overall Conclusion

This study in mild-to-moderate UC subjects did not meet primary or secondary efficacy endpoints at Week 12 of the PCP for either GB004 treatment group relative to placebo.

Based on the totality of results available at the time of the PCP Week 12 Analysis, the study was terminated prematurely by the Sponsor for lack of treatment benefit.