1 SECONDARY EFFICACY ENDPOINT – FIBROSIS BIOMARKERS AND SCORES

1.1 FIBROSIS BIOMARKERS

Hyaluronic acid (**HA**), tissue inhibitor of metalloproteinase-1 (**TIMP-1**), and N-terminal propeptide of Type III collagen (**P3NP**) were measured as fibrosis biomarkers and were part of the ELF score.

Most patients (69.6%) had baseline HA levels within normal range; 30.4% of patients (mostly F4 patients) had baseline HA levels above ULN (i.e., 100 µg/L). All patients had baseline TIMP-1 levels within normal range (i.e., 39 to 279 ng/L). Most patients (82.6%) had baseline P3NP levels above ULN (i.e., 0.8 U/mL); the remaining patients 17.4%) had baseline P3NP levels within normal range.

From baseline up to Month 6, no significant change was observed in mean HA, TIMP-1, and P3NP levels by dose cohort, by fibrosis stage, by number of cells administered, and by number of injections. Several patients presented peaks in HA levels throughout the study, but for most of these patients, the levels at the latest time point lowered to baseline levels.

1.2 FIBROSIS SCORES

Fibrosis scores as non-invasive tests based on serum markers have limited value for definitive diagnosis of liver fibrosis; however, they help to rule-in or rule-out advanced fibrosis especially in combinations with TE.

At baseline, the means of simple non-patented fibrosis scores for most patients were in the range of indeterminate risk for advanced fibrosis which could indicate moderate fibrosis. Six patients (26.1%) had a baseline **NALFD score** > 0.675 and 2 patients (8.7%) had a baseline **FIB-4** > 3.25, which both have a predictive value of the presence of significant advanced fibrosis. FIB-4 was significantly higher in F4 patients compared to F3 patients which confirms that FIB-4 performs better for staging of NASH fibrosis among other simple fibrosis scores. Most patients (56.5%) had a baseline **APRI** score ≥ 0.5 and ≤ 1.5; 39.1% of patients had a baseline APRI score < 0.5; and the remaining patient (4.3%) had a baseline APRI score > 1.5. From baseline up to Month 6, no change was observed in mean NAFLD scores by dose cohort, by fibrosis stage, by number of cells administered, and by number of injections, and FIB-4 and APRI scores tended to decrease slightly in F3 patients and remained unchanged in F4 patients.

Patented fibrosis scores identified 7 patients (38.9%) with baseline **MACK-3** score ≥ 0.55 and none with **ELF score** ≥ 9.8 (which were indicative of high risk of advanced fibrosis). No change was observed in mean MACK-3 and ELF scores from baseline up to Month 6 by dose cohort, by fibrosis stage, by number of cells administered, and by number of injections.

Due to the shortness of the follow-up period, no significant changes were expected for fibrosis markers. However, a favorable tendency was noted in FIB-4 and APRI scores, particularly in F3 patients.