PRELIMINARY EFFICACY SUMMARY

Efficacy objective:
Secondary: Preliminary efficacy. To evaluate clinical and biological efficacy parameters following HepaStem infusion up to Day 28, up to Month 3 and up to Year 1 post first HepaStem infusion.

Efficacy endpoints:
Secondary:

- Clinical efficacy parameters assessed on Day 28, and up to Year 1 including mortality, liver transplantation and disease scoring. Disease scores encompassed the European Foundation for the study of the Chronic Liver Failure (EF-CLIF) organ failure (OF) score, CLIF-C ACLF score, CLIF ACLF grade, CLIF-C AD score, MELD score and Child-Pugh score.
- Biological efficacy parameters (bilirubin, creatinine, INR and albumin).

Preliminary efficacy results:

Clinical efficacy

The HE grade was assessed by the investigator using the West Haven classification system. At baseline, 11 (45.8%) participants had HE, with grade 2 being the maximal grade reported (one participant each in Cohorts 1 and 5). During the active study period, the status either improved or remained stable for most of the participants over time. However, 4 participants developed or showed a deterioration of HE, with the worst grade reported being grade 4 for a participant in Cohort 5 on Day 8, who deceased few days later from a septic shock. On Month 2, the HE was resolved in all participants and remained so until the end of the study.

At baseline, the CLIF-C score for organ failure (CLIF-C OF) ranged between 7 and 12 with 9 participants having a score ≥ 10. At the end of the active study period, the score was above 10 for 2 participants. One of them, reported an increase of 6 points on Day 12 (this participant underwent liver transplantation shortly after). Furthermore, for 6 participants, a decrease of 3 points was reported. These participants reached a score of 6 or 7 up to the end of the active study period (Day 21 or Day 28). Overall, the percentage of participants with a CLIF-C OF score of 6, increased from none at baseline to 41% (7 out of 17 participants) on Day 28, to 85% (11 out of 13 participants) on Month 3 with 2 participants (enrolled in Cohort 2) among those evaluable for CLIF-C OF score having undergone liver transplantation. On Year 1, 12 out of 15 participants with available data had a score of 6, 2 had a score of 7 and one had a score of 8. Thus, the CLIF-C OF score suggests a long-lasting improvement.

A decrease in the number of participants with liver failure was observed during the study (17 out of 24 participants at baseline versus 5 out of 18 participants on Day 28 and none on Month 3 and Year 1). Over the mid-term and the long-term follow-up periods, no organ failure was documented, whereas 2 hospitalizations due to condition worsening and one fatal outcome were reported.

The evolution of participants' prognosis was assessed by means of the CLIF-C ACLF, CLIF-C AD, New MELD, Child-Pugh. The CLIF-C ACLF score was derived for 15 participants at baseline and ranged from 33.9 to 58.9 (score > 50 mainly observed in Cohorts 1, 4 and 5). On Days 14 and 28, the CLIF-C ACLF score was derived for fewer participants (none in Cohort 1) and remained within the same range. The prognosis assessed using the CLIF-C AD score for all participants at baseline, ranged from 40.1 to 82.2, and tended to decrease during the active study period. In addition, the number of participants with a score above 60 decreased over time. On Month 3 and up to Year 1, none of the participant still in the study and for whom the score was available had a score above 60.

A decrease in the mean New MELD score from baseline to Day 28 was observed (from 27.2 [SD: 4.2] to 20.9 [SD: 8.0]). On Day 1 before infusion, all participants had a score > 15. On Day 28, of the 19 participants with available data, 5 (26.3%) had a New MELD score < 15. On Month 3, the mean New MELD score was further decreased compared to baseline for all participants for whom the score was calculated (13.1 [SD: 5.2]), with 10 (58.8%) participants having a New MELD score < 15. The remaining 7, had a New MELD score > 15. These participants had a score between 25 and 30 at baseline which decreased below 20 on Month 3 except for one participant (this participant was hospitalized for progressive ACLF condition about 2.5 months after the first HepaStem infusion). At the end of the study, the mean New MELD score was 12.3 (SD: 4.6), with one more participant having a score < 15 and with the remaining participants being stable. When considering participants who had not undergone liver transplantation up to Month 3, the New MELD score, was lower throughout the follow-up period compared to baseline.

The Child-Pugh score remained within the same ranges throughout the active study period (5.0-12.0) and the mean score by cohort tended to decrease. About half of the participants (9 out of 17 participants) still followed up on Month 3 had a Child-Pugh Class A, compared to the Class C or B reported at baseline. At the end of the study, only one participant was reported with a Class C. When scores were considered for participants who had

not undergone liver transplantation during the first 3 months of the study, the mean score, was lower throughout the follow-up period compared to baseline.

Biological efficacy

Leukocyte and neutrophil counts appeared stable throughout the study, with a slight reduction during the follow-up period. When cell counts were considered for participants who did not receive a liver transplant, the reduction in the cell counts during the follow-up was more pronounced. Similarly, mean levels of CRP seemed to slightly decrease in all participants, and liver transplantation did not seem to have an impact.

Bilirubin was high at baseline for all participants (20.5 [SD: 10.0] mg/dL) and seemed to decrease over time (9.6 [SD: 10.9] mg/dL on Day 28). Three months after the first HepaStem infusion, 17 participants were alive and still followed-up; mean bilirubin levels further improved (from 9.6 [SD: 10.9] mg/dL on Day 28 to 2.4 [SD: 2.0] mg/dL at the end of the mid-term follow-up period), with all participants with available data, except one, having a level below 5 mg/dL. At the end of the study, mean bilirubin levels had stabilized (2.6 [SD: 2.5]) and only two participants were reported with levels above 5 mg/dL.

In addition, albumin values remained within the same range throughout the study. Compared to baseline, a slight increase in the mean albumin concentration in some participants could be detected during the active study period, as well as during the follow-up period.

Furthermore, creatinine and sodium levels appeared to be generally stable throughout the study suggesting that the kidney condition did not worsen.

Taken together, these results are suggestive of an improvement of liver function and are in line with the decrease observed in the New MELD score.

Conclusion: Preliminary efficacy results suggested an improvement of liver function on Day 28, which seemed to persist on Month 3 and up to Year 1.