STATISTICAL ANALYSIS PLAN

A phase 1/2a Clinical Trial to assess safety of a single IV infusion of autologous adipose-derived mesenchymal stem cells in adults with active Rheumatoid Arthritis

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Statistical Models and Methodology

1. General Methods:

Descriptive Statistics: Data variables will be subjected to descriptive analysis, including number of subjects, mean, standard deviation (SD), median, interquartile range (IQR) and percentages.

P values and Reporting Conventions: All applicable tests will be two-tailed and statistical significance of 0.05 will be used to determine p-values, with the confidence level of 95%, unless otherwise stated. P values will be reported to 4 decimal places. P values less than .0001 will be reported as <.0001. The mean, standard deviation, and any other statistics other than quantiles, will be reported to one decimal place greater than the original data. Quantiles, such as median, or minimum and maximum will use the same number of decimal places as the original data. Effect sizes will also be calculated to determine clinical significance of the results, wherever statistical significance will be observed.

All statistical analysis will be carried out using GraphPad Prism for Mac.

2. Data Normality and Statistical Test Selection:

Data variables for all safety and efficacy parameters will be analyzed for normality. For the normally distributed data, mixed effect analysis will be performed. For the variables that does not pass normality test, non-parametric tests will be used to analyze the changes from the baseline.

3. Handling Missing Data:

All patients who received at least a single dose of intervention will be included in the study analysis. Missing visit data or other missing data will not be imputed. Given the pathological nature of the disease, some extreme datapoints are both expected and informative, for which no outlier detection will be performed.

4. Interim Analysis:

All data will be subjected to analysis throughout the conduct of the trial, including but not limited to 4 weeks post infusion, 3 months post infusion, 6 months post infusion, 1 year from beginning of trial, and at End of Study time points.

5. Multiple Testing/Comparisons:

Clinical data is sometimes heavily skewed which is challenging to analyze. To account for skewed data that might be involved in efficacy analysis, non-parametric tests will be performed to analyze the changes from the baseline. Multiple comparisons will be performed where significance in efficacy parameters will be observed across various timepoints versus baseline. In

these types of analyses, data will be corrected using applicable tests (e.g., Bonferroni or Holm-Šídák correction) by adjusting the α-value when relevant.

6. Primary Safety Analyses:

To provide evidence of the safety of HB-adMSCs, the number of AEs and SAEs and overall occurrence rate in the treated patients will be calculated. AEs and SAEs will be assessed beginning with intervention 2 and when AEs or SAEs will be first noted. The AEs and SAEs will be summarized as percentages at each time point, calculated as a rate of occurrence.

Also, measures of hematologic, hepatic, and renal function will be examined as safety endpoints.

7. Secondary Efficacy Analyses:

Joint Counts measured on American College of Rheumatology (ACR) 66/68 will be examined. The initial score, captured at Intervention 2 will serve as the baseline for disease evaluation. Any improvement from treatment would be the difference from baseline to the score at different timepoints up to the final follow-up visit at 52 weeks (1 year). Also, inflammatory parameters including serum Tumor Necrosis Factor-alpha (TNF-α), Interleukin-6 (IL-6), C-reactive Protein (CRP) and Erythrocyte Sedimentation Rate (ESR) will be assessed as changes from the baseline levels.