May 22, 2023
StemRIM Inc.

StemRIM Announces Results from Phase 2 Clinical Trial of Redasemtide in Patients with Chronic Liver Disease (Additional Report)

Osaka, Japan, May 22, 2023 – StemRIM Inc. (TSE: 4599, Chairman and CEO: Kensuke Tomita; "StemRIM") announced today, that the results of the analysis of the investigator-initiated Phase 2 clinical trial conducted by Niigata University for patients with chronic liver disease. The preliminary results have already been published as a flash report on April 10, 2023.

In this study, Redasemtide was administered to two groups, Cohort A (5 cases) and Cohort B (5 cases), with different administration methods. After a 3-month pre-observation period for both cohorts, Cohort A received weekly administration of 1.5 mg/kg of Redasemtide for 4 weeks (a totally 4 administrations), while Cohort B received daily administration for 4 consecutive days in the first week and weekly administration in the 2nd to 4th weeks (a totally 7 administrations). Subsequently, a follow-up observation of approximately 6 months was conducted to evaluate safety as the primary endpoint and effectiveness, including fibrosis indicators using MR Elastography (MRE)*1, as secondary endpoints. There were no cases of discontinuation or dropout, and all cases were completed.

Regarding the safety evaluation, which was set as the primary endpoint, 2 cases out of the 10 participants in both cohorts experienced adverse events (dysphonia and fever) that could not be ruled out as being related to the investigational drug. However, both adverse events were mild in nature and the patients have since recovered. Furthermore, one case of a serious adverse event (bleeding during a liver biopsy) occurred during the follow-up period. However, the event was resolved without intervention, and the causality with the investigational drug was ruled out. Therefore, the tolerability of the study drug is considered to be good.

Regarding the exploratory efficacy evaluation, which was set as a secondary endpoint, a trend of improvement in liver stiffness measured by MRE was observed in Cohort A (5 cases) at 78 days and 162 days after the start of administration. The average reduction rates were found to be 12% and 8%, respectively, compared to the baseline measurements. In addition to the improvement in liver stiffness measured by MRE, several cases demonstrated an accompanying improvement trend in other fibrosis indicators, including fibrosis index*2, fibrosis markers*3, and fibrosis stage value based on modified HAI*4.

Based on the comprehensive evaluation conducted by the principal investigator considering these various efficacy assessment results, it is speculated that there was an indication of improvement in liver fibrosis in 3 out of 5 cases (60%) in Cohort A and 2 out of 5 cases (40%) in Cohort B.

Based on the results of this trial, we are currently considering the future development strategy for the treatment of chronic liver diseases.

An overview of this study can be found in the Japan Registry of Clinical Trials (jRCT2031200232), a clinical research database.

This matter is progressing as planned and has no impact on our financial results for the fiscal year ending July 31, 2023.

*1; MR Elastography is one of the diagnostic techniques used to measure the stiffness of the liver. Liver stiffness is related to the degree of liver fibrosis. MRE involves the use of a vibrator placed on the liver, which generates mechanical vibrations. The speed of these vibrations is measured using MRI, allowing for the quantitative assessment of liver stiffness.

*2; The Fibrosis Index is a scoring system used to evaluate the progression of liver fibrosis by using blood test data. Two commonly used scoring systems are FIB-4 and APRI. FIB-4 = (Age x AST) / (Platelet count x $\sqrt{}$ALT). APRI = (AST / Upper limit of normal) / (Platelet count in 10^9/L) x 100.

*3; Fibrosis markers are biological indicators used to evaluate the degree of fibrosis in organs such as the liver, lungs, and heart. They refer to proteins, enzymes, and other biomolecules present in the blood. In this clinical trial, the following fibrosis markers were evaluated: P-III-P (Type III Procollagen Peptide), Type IV Collagen-7S, Hyaluronic Acid, M2BPGi, and ATX.

*4; Modified HAI (Histologic Activity Index) is one of the histopathological evaluation indicators for the liver. It is assessed by staining and microscopic observation of liver tissue sections. HAI is used to evaluate histopathological changes in liver diseases such as hepatitis and liver fibrosis. Modified HAI consists of three evaluation items: 1) Inflammatory Cell Infiltration, 2) Mononuclear/Kupffer Cell Proliferation, and 3) Fibrosis. Each item is scored on a scale of 0 to 4 and based on the comprehensive evaluation of the Modified HAI score, the progression of liver disease and treatment efficacy can be assessed.

About StemRIM Inc.

StemRIM Inc. is a biotech venture which began at Osaka University to realize a new type of medicine called "Regeneration-Inducing Medicine™". The overall aim is to achieve regenerative therapy effects equivalent to those of regenerative medicine, solely through drug administration, without using living cells or tissues. Living organisms have inherent self-organizing abilities to repair and regenerate tissues that have been damaged or lost due to injury or disease. This ability arises from the presence of stem cells in the body that exhibit pluripotency i.e., can differentiate into various types of tissues. When tissues are damaged, these cells, therefore, exhibit proliferative and differentiative capabilities, promoting functional tissue regeneration. "Regeneration-Inducing Medicine™" is aimed at maximizing the tissue repair and regeneration mechanisms already present in the body. With this aim, StemRIM is currently developing one of its most advanced regenerative medicine products. Specifically, this product is designed to release (mobilize) mesenchymal stem cells from the bone marrow into the peripheral circulation upon administration, thus increasing the number of stem cells circulating throughout the body and promoting their accumulation in damaged tissues. Here, these stem cells should accelerate tissue repair and regeneration.
Certain disease areas expected to benefit from "Regeneration-Inducing Medicine™" include epidermolysis bullosa (EB), acute phase cerebral infarction, cardiomyopathy, osteoarthritis of the knees, chronic liver disease, myocardial infarction, pulmonary fibrosis, traumatic brain injury, spinal cord injury, atopic dermatitis, cerebrovascular disease, intractable skin ulcers, amyotrophic lateral sclerosis (ALS), ulcerative colitis, non-alcoholic steatohepatitis (NASH),

systemic sclerosis, and any other areas where treatment with extrapulmonary mesenchymal stem cells is promising.

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For more information, please visit the StemRIM website (https://stemrim.com/english/)