ATYR1923 Ameliorates Dermal and Pulmonary Fibrosis in a Murine Model of Sclerodermatous Chronic Graft vs. Host Disease

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Abstract

Objective: During the analysis of antibody repertoires, although bleomycin sensitized animals were exposed to high resolution and genome-wide sequencing analysis methods have been developed to identify antibody sequences specific to bleomycin. However, the relationship between bleomycin-induced lung fibrosis and human fibrosis is not well understood. In this study, we investigated whether ATYR1923, a novel antibody that modulates immune responses, could reduce bleomycin-induced fibrosis.

Methods: Male BALB/c mice received intravenous (IV) antibody or vehicle and were exposed to bleomycin to induce fibrosis. Skin and lung tissues were collected at designated time points and histological and biochemical assessments were performed.

Results: ATYR1923 treatment reduced fibrosis in both skin and lung tissues compared to vehicle-treated controls. ATYR1923 treatment reduced collagen deposition and myofibroblast counts in lung tissues.

Conclusions: ATYR1923 is efficacious in a murine model of sclerodermatous chronic GvHD.

EXHIBIT 99.2

Sclerodermatous cGvHD Model

Hydroxyproline Content

Histological evaluation

Myofibroblast Counts

Lung

Dermal Thickness

Skin

Experimental Protocol

Introduction

ATYR1923

Modulator domain

Fc domain

Mouse Bleomycin

Rat Bleomycin

ATYR1923

Kd domain of HARS

• Encoded by a splice variant that is enriched in human lung.
• Inhibits human T cell activation.
• Eosinophil administration reduces fibrosis in rat
• Bleomycin-induced lung fibrosis
• ATYR1923 is administered once weekly at 0.4 mg/kg intravenously
• Nintedanib administered once daily at 60 mg/kg orally

Histological evaluation

Skin

Myofibroblast Counts

Hydroxyproline Content

CONCLUSIONS

• ATYR1923 has robust activity, comparable to nintedanib when treatment initiated at Day 7.
• ATYR1923 activity did not reach significance at 0.4 mg/kg weekly when treatment was initiated at Day 21.

Data are consistent with our hypothesis that ATYR1923 modulates immune responses and inflammation following tissue injury. Based on the pre-clinical data, including in vitro, in vivo and toxicological experiments, a clinical trial with ATYR1923 for treatment of intestinal and lung diseases is planned to initiate later this year.