MDI Therapeutics Initiates Phase 1 Clinical Study of MDI-2517, Investigational Inhibitor of Plasminogen Activator Inhibitor 1 (PAI-1)

Study supports development of potential new treatment of systemic sclerosis and interstitial lung disease

NOVI, MI — June 10, 2024 — MDI Therapeutics, Inc., a pharmaceutical company developing novel therapies for the treatment of fibrosis and fibroproliferative diseases, today announced that it has dosed the first participants in a Phase 1 clinical study evaluating the safety, tolerability, pharmacokinetics, and pharmacodynamics of MDI-2517, a potent small molecule inhibitor of plasminogen activator inhibitor 1 (PAI-1).

"Based on comprehensive preclinical studies, this first in human study of MDI-2517 will inform continued development of our novel, proprietary compound for the potential treatment of systemic sclerosis and interstitial lung disease, conditions where disability is significant and survival rates are poor," said Mark Weinberg, MD, MBA, Chief Medical Officer of MDI Therapeutics. "Beyond these initial indications, the outcomes of the Phase 1 trial will also support the potential evaluation of MDI-2517 in other chronic fibrotic and inflammatory diseases that have been associated with excessive PAI-1 activity."

The ascending single oral dose phase of this randomized, double-blind, placebo-controlled study will enroll up to 48 healthy participants. The primary endpoint is the assessment of the safety and tolerability of MDI-2517, and the study also includes evaluation of pharmacokinetics and exploratory assessments of changes to total and active PAI-1.

About MDI-2517
MDI-2517 is a potent small molecule inhibitor of plasminogen activator inhibitor-1 (PAI-1), a key regulator of pro-inflammatory and pro-fibrotic processes. Under normal physiological conditions, PAI-1 plays an important role in regulating wound healing. However, excessive PAI-1 activity promotes fibrosis by disrupting the ordered process of wound healing at several potential steps. First, by inhibiting fibrinolysis, PAI-1 supports the persistence of the pro-inflammatory provisional fibrin matrix. Second, PAI-1 enhances inflammatory cell infiltration through direct interaction with cellular integrins. This latter process may be particularly relevant to the development of pulmonary fibrosis as PAI-1 has been shown to promote the recruitment of exudate macrophages to the lung and to induce pro-fibrotic polarization in macrophages. PAI-1 has also been reported to directly promote myofibroblast differentiation and collagen synthesis, and to interact synergistically with TGF-β to sustain the fibrotic response. In preclinical studies, MDI-2517 functions in a rheostat-like mode to reduce pathologic levels of PAI-1 to normal physiologic levels, delivering therapeutic reductions in pro-inflammatory and pro-fibrotic processes.

About MDI Therapeutics
MDI Therapeutics Inc. is a pharmaceutical company developing novel therapies for the treatment of fibrosis and fibroproliferative diseases. Fibroproliferative diseases, which include pulmonary fibroses, systemic sclerosis (scleroderma), liver cirrhosis, cardiovascular disease and progressive kidney disease, are a leading cause of morbidity and mortality and can affect all tissues and organ systems. MDI's mission is to unlock the therapeutic potential of PAI-1 biology for the benefit of people diagnosed with chronic fibrotic and inflammatory diseases. The Company was founded on key enabling drug discovery technologies developed at the University of Michigan in the labs of co-founder Daniel A. Lawrence, PhD, Professor of Cardiovascular Medicine. MDI's lead candidate MDI-2517 is a potent small molecule inhibitor of plasminogen activator inhibitor-1 (PAI-1), a key regulator of pro-inflammatory and pro-fibrotic processes. For more information, please visit www.mditherapeutics.com.

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