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Promedior Announces Publication of New Research Demonstrating Pentraxin-2/SAP is a Potent Inhibitor of Pulmonary Fibrosis

Novel Therapeutic Approach Regulates All Fibrotic Pathologies Driven by TGF-beta1, a Major Mediator of Idiopathic Pulmonary Fibrosis (IPF)

MALVERN, Pa.--(BUSINESS WIRE)-- Promedior, Inc., a clinical stage biotechnology company developing novel therapies to treat fibrotic and inflammatory diseases, announced today the publication of collaborative research in the International Journal of Biochemistry and Cell Biology entitled, "*TGF-beta driven lung fibrosis is macrophage dependent and blocked by Serum amyloid P.*" The research showed that human Pentraxin-2 (PTX-2), also called human Serum amyloid P (SAP), potently inhibits all undesirable pro-fibrotic pathologies driven by $TGF\beta_1$ and represents a novel therapeutic approach for the treatment of diseases that involve lung fibrosis, including idiopathic pulmonary fibrosis (IPF). This research validates that PTX-2/SAP can have therapeutic effects even in conditions driven by $TGF\beta_1$ growth factor, and builds on the body of research showing the unique role of PTX-2/SAP in activating the body's natural ability to resolve tissue damage in disease processes that cause fibrosis and inflammation.

In this study, researchers examined the effects of PTX-2/SAP in the lung specific $TGF\beta_1$ transgenic mouse model, since many of the pathogenic mechanisms observed in lung fibrosis can be stimulated by the growth factor $TGF\beta_1$. Highlights of the results from this study validating the potential therapeutic effects of PTX-2/SAP in pulmonary fibrosis included:

- PTX-2/SAP inhibited all of the pathologies driven by $TGF\beta_1$ including apoptosis, airway inflammation, pulmonary fibrocyte and M2 macrophage accumulation and collagen deposition, without affecting the levels of $TGF\beta_1$ in the lung;
- An abbreviated therapeutic dose schedule was equally efficacious and demonstrated a sustained durability of effect following cessation of drug dosing, suggesting that intermittent dosing may be feasible in human patients;
- PTX-2/SAP levels were reduced in the serum of IPF patients when compared to closely matched healthy control subjects and the levels of SAP in IPF patient serum directly correlated with lung function;
- PTX-2/SAP directly inhibited M2 macrophage differentiation of monocytes obtained from IPF patients, suggesting that IPF patient monocytes would be responsive to PTX-2 therapy.

The findings regarding the effects of PTX-2/SAP in the lung specific TGFβ_1 transgenic mouse model expand on previous preclinical studies, in which Promedior investigators determined that PTX-2/SAP potently inhibited lung fibrosis in both acute bleomycin-induced pulmonary fibrosis models and chronic asthma models through an inhibition of pulmonary fibrocyte and pro-fibrotic (M2) macrophage activation and accumulation, associated with increased macrophage production of the regulatory cytokine IL-10.

"Our research clearly shows the beneficial anti-fibrotic effects of Pentraxin-2 in TGFβ_1-induced lung disease," said lead author Erica L. Herzog, M.D., Ph.D., Assistant Professor of Medicine (Pulmonary), Yale School of Medicine. "These findings highlight the potential of Pentraxin-2 to be a potent and durable inhibitor at a pivotal point in the disease pathway of progressive pulmonary fibrotic diseases."

Based on this research and other clinical and preclinical studies, Promedior is developing a pipeline of drugs based upon recombinant forms of PTX-2/SAP for the treatment and prevention of fibrotic and inflammatory diseases. The company is conducting human clinical studies to evaluate Pentraxin-2 therapeutics for a number of fibrotic diseases, including IPF and post-surgical scarring in glaucoma patients.

"These new findings further support our confidence in Pentraxin-2 as a novel therapeutic for many severe and chronic inflammatory and fibrotic diseases, including IPF," said Mark L. Lupher, Jr., Ph.D., Chief Scientific Officer, Promedior. "By showing that PTX-2/SAP has dominant therapeutic effects even downstream of TGFβ_1 pathways through the ability to inhibit pathologic fibrocytes and macrophages and promote regulatory macrophage function, these results further confirm that Pentraxin-2 regulates fundamental mechanisms of the innate immune system, opening an exciting new approach to treat inflammatory and fibrotic diseases."

About IPF

Idiopathic pulmonary fibrosis (IPF) is a progressive, debilitating and fatal disease that affects approximately 200,000 people in Europe and the United States combined, with approximately 30,000 new cases reported annually in each region.

IPF is characterized by inflammation and fibrosis in the lungs, hindering the ability to process oxygen and causing shortness of breath. IPF is a progressive disease, meaning that over time, lung scarring and related respiratory symptoms increase in severity. The median survival time from diagnosis is two to five years, with a five-year survival rate of approximately 20%. There are no medicines approved in the United States or Europe for the treatment of IPF.

About Pentraxin Therapeutics

Promedior's proprietary platform of pentraxin therapeutics is based upon breakthrough discoveries in how the body's innate response to injury results in pathologic fibrosis and

the loss of tissue and organ function. Promedior's novel therapeutics are designed to treat and prevent fibrotic pathology by regulating the common cellular mechanisms that control the initiation and progression of fibrosis across a variety of tissues and organ systems. Promedior's initial drug products are based upon the unique structure of Pentraxin-2, a naturally-occurring protein which has demonstrated a unique role in targeting monocytes at sites of tissue damage. Promedior's approach leverages the natural role of Pentraxin-2 in regulating the response of important immune and inflammatory processes in the body. Promedior has built a comprehensive patent estate for Pentraxin therapeutics, including recombinant human Pentraxin-2 (rhPTX2 or rhSAP), for a broad range of therapeutic applications in fibrosis and other inflammatory diseases.

About Promedior

Promedior has developed a novel drug discovery platform to regulate the monocyte-derived cell populations that play key roles in fibrotic, inflammatory and autoimmune diseases. By specifically targeting these cells at the site of injury, Promedior is able to treat the source of aberrant immune system responses, promote tissue healing and resolution, and greatly reduce the risk of systemic side effects inherent in current therapeutic approaches. Utilizing this novel approach, Promedior is initially developing drugs to address the most severe and difficult-to-treat fibrotic and inflammatory conditions of the eye, lung and kidney such as glaucoma, age-related macular degeneration, and diabetic retinopathy (eye); pulmonary fibrosis, scleroderma and COPD (lung); and acute and chronic nephropathy (kidney). For additional information about Promedior, please visit http://www.promedior.com.

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