Serotonergic targets in the treatment of pulmonary arterial hypertension (PAH) and idiopathic pulmonary fibrosis (IPF)

Pulmonary arterial hypertension (PAH) and idiopathic pulmonary fibrosis (IPF) are two progressive, debilitating, and fatal lung diseases. Both diseases are limited in treatment options and have no cure. Pulmonary hypertension, inflammation, and structural remodeling, all with varying degrees of severity, are the most common and significant underlying pathophysiologic factors associated with these conditions. Although the pathogenesis is not clearly understood, increased levels of inflammatory cytokines, including growth factors and dysfunctional endothelial vasoactive mediators (e.g., serotonin, 5-HT; endothelin, ET; nitric oxide, NO; and prostacyclin, PGI2), are found in the lungs of PAH and IPF patients. The 5-HT receptor signaling pathway appears to play a central role in the pathobiology of both conditions. RP5063, a new chemical entity, is a potent modulator of 5-HT signaling that involves specifically the 5-HT2A/2B/7 receptors within the lung. The signal transduction pathways involving these 5-HT receptors mediate significant underlying pathophysiology (vasoconstriction, and vascular/alveolar inflammation, fibrosis, and proliferation) for PAH and IPF. RP5063 has demonstrated proof of concept in translational animal models that emulate IPF and PAH in humans. The U.S. FDA has granted an Orphan Drug Designation to RP5063 for the treatment of PAH and IPF, in which clinical phase 2 studies are planned to start soon. This presentation will briefly review approved therapies and unmet medical needs for PAH and IPF. It will segue to the current understanding of 5-HT receptor signaling pathways in the pathobiology of these two diseases, and will then discuss RP5063 pharmacology and preclinical efficacy for PAH and IPF. It will close by delineating the clinical pharmacokinetic/pharmacodynamic and safety profiles of this compound.

Recent Publications

Biography
Laxminarayan Bhat, PhD, is the Founder, President, and Chief Executive Officer of Reviva Pharmaceuticals, Inc. Dr. Bhat founded Reviva in 2006 and since its inception, the company has advanced rapidly under his leadership with a portfolio of propriety compounds at different stages in a pipeline encompassing central nervous system (CNS), cardiovascular, and inflammatory diseases. Dr. Bhat has over 20 years of experience in drug discovery and development, and prior to founding Reviva, he held research positions at XenoPort, ARYx Therapeutics, and Higuchi Biosciences Center in the United States. Dr. Bhat conducted extensive graduate and post-graduate training in medicinal chemistry in India, France, Germany, and USA. Dr. Bhat has published over 25 research papers in peer reviewed international journals and has given several invited lectures/presentations in national and international conferences. Dr. Bhat is an inventor with over 60 granted patents and contributed to one approved drug currently in the market worldwide.