

Non-clinical development of novel target PRDX-based treatment for pulmonary arterial hypertension

VASTHERA Co. Ltd.

Disease Area	Cardiovascular disease (CVD)
Product Type	Small-molecule compound (VTB-10)
Indication	Pulmonary Arterial Hypertension (PAH)
Target	Peroxiredoxin II (PRDX2)
Mechanism of Action	VTB-10 is an enzyme mimetic (Nanozyme) that replaces the activity of inactivated or deficient peroxiredoxin (Enzyme replacement) and represents a novel therapeutic mechanism to restore symptoms and function of pulmonary arterial hypertension by simultaneously and oppositely modulating key RTK receptor signaling systems in vascular smooth muscle and endothelial cells.
Competitiveness	<p>Competitor : Sotatercept; MSD</p> <ul style="list-style-type: none"> - PAH is a rare vascular disease where three receptor signaling pathways, i.e. PDGF, VEGF, and TGF-β, are dysregulated. Sotatercept is a protein drug that targets TGF-β, family ligands (Activin/GDF-11) and retards the progression of late-stage PAH. - In contrast, VTB-10 is a small-molecule compound that doubly targets PDGF and VEGF and reverse the PAH.
Development Stage	IND-enabling study
Route of Administration	Oral

Pathogenesis

Arterial Disease (PAH, Restenosis, Atherosclerosis) leads to an Occluded artery. This is associated with EC dysfunction, SMC hyperplasia, and EndoMT. This process leads to Prx Inactivation.

Mechanism of Action

VEGFR2 and PDGFRβ signaling pathways are involved. H₂O₂ levels are elevated, leading to Disease Progression. VTB-10, derived from a Redoxzyme platform, acts as an antioxidant to reverse this process.

Key Data

1 VTB-10 reduces right ventricle hypertrophy/systolic pressure in the SU/Hx-induced rat PAH model. (PO administration once daily at 0.1 mpk for five-weeks treatment)

2 VTB-10 reverses the occlusion of pulmonary arteries and normalizes structure and function of pulmonary arteries.

Group	RVSP (mmHg)
Normal	~30
Vehicle	~65
VTB-10 0.1mpk	~45

Group	Fulton's index
Normal	~0.25
Vehicle	~0.45
VTB-10 0.1mpk	~0.30