

Supplementary Material

2025 Annual Review of Pulmonary Arterial Hypertension Clinical Research

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Supplementary Table 1. Overview and classification of pulmonary arterial hypertension clinical trials registered in international clinical research platforms in 2025

Registry ID	Acronym	Study public title	Study design	Intervention category	Primary outcomes	Therapeutic pathway / domain	Investigational product / strategy	Study phase	Population focus	High-level study classification
ACTRN12625000340437	Not informed	The Effectiveness of Acceptance and Commitment Therapy (ACT) on Clinical and Psychological Outcomes among Patients with Pulmonary Arterial Hypertension (PAH) in National Heart Institute Malaysia	Interventional	Digital / Behavioral	Psychological flexibility, quality of life, and psychological distress (AAQ-II, PAH-SYMPACT, DASS-21)	Not informed	Behavioral intervention – Psychotherapy program	Not Applicable	Adults with pulmonary arterial hypertension with mental health focus	Interventional – non-pharmacological
ACTRN12625000563460	Not informed	Study to Evaluate the parameters of TRX-248 Transdermal System in Healthy Female Volunteers	Randomized controlled trial (crossover, open-label; pharmacokinetics endpoint)	Pharmacological	Pharmacokinetic parameters (C _{max} , T _{max} , t _{1/2} , AUC, clearance, volume of distribution)	Prostacyclin	Drug – TRX-248	Phase 1	Adults with pulmonary arterial hypertension (Group 1)	Observational
ACTRN12625000656437	Not informed	The Feasibility of Acceptance and Commitment Therapy (ACT) on Clinical and Psychological Outcomes among Patients with Pulmonary Arterial Hypertension (PAH) in National Heart Institute Malaysia	Non-randomized interventional trial	Digital / Behavioral	Feasibility of ACT intervention and study procedures	Digital and multidimensional endpoints	Behavioral intervention – Acceptance and Commitment Therapy (ACT)	Not Applicable	Adults with pulmonary arterial hypertension with mental health focus	Interventional – non-pharmacological
ChiCTR2500096676	Not informed	The Impact of Lobectomy and Segmentectomy on Pulmonary Vascular Resistance and Pulmonary Circulation, and Its Guiding Strategies for the Treatment of Pulmonary Arterial Hypertension	Cross-sectional study	Non-pharmacological	Pulmonary vein–left atrium angle	Not informed	Surgical comparator – Lobectomy / segmentectomy (no intervention)	Not informed	Adults with pulmonary arterial hypertension (Group 1)	Observational
ChiCTR2500096733	Not informed	An observational study of Phosphodiesterase inhibitor replacement therapy for congenital heart defect pulmonary hypertension in	Sequential study	Registry / observational	Six-minute walk distance (6MWD)	Nitric oxide – sGC – cGMP	Drug – Riociguat	Phase 4	Adults with pulmonary arterial hypertension associated with	Observational

		intermediate-high-risk patients							congenital heart disease	
ChiCTR2500100718	Not informed	The role and mechanism of deoxycholic acid in pulmonary hypertension and pulmonary vascular remodeling	Case-control study	Non-pharmacological	All-cause mortality	Not informed	No active intervention / observational	Not Applicable	Adults with pulmonary arterial hypertension (Group 1)	Observational
ChiCTR2500100857	Not informed	A modified 4-strata risk assessment instrument in Chinese patients with pulmonary arterial hypertension based on a retrospective database	Cross-sectional study	Observational	Four-strata risk assessment and risk change	Digital and multidimensional endpoints	No active intervention / observational	Not Applicable	Adults with pulmonary arterial hypertension (Group 1)	Observational
ChiCTR2500103552	Not informed	A single-dose, randomized, open, crossover, fasting four-cycle and postprandial three-cycle human bioequivalence trial of bosentan tablets in healthy adult male subjects	Crossover study	Pharmacological	Pharmacokinetic exposure (Cmax, AUC)	Endothelin	Drug – Bosentan	Not Applicable	Men with pulmonary arterial hypertension (Group 1)	Observational
ChiCTR2500105323	Not informed	An Observational Study of Genomics and Clinical Characteristics in Chinese PAH Patients	Observational study	Registry / observational	Risk stratification and mortality	Not informed	No active intervention / observational	Not Applicable	Adults with pulmonary arterial hypertension (Group 1)	Observational
ChiCTR2500110083	Not informed	A Multicenter, Randomized, Double-blind, Positive-controlled Clinical Study to Evaluate the Pharmacodynamic Effects, Safety, Tolerability, and Pharmacokinetics of Multiple Doses of DDCI-01 in Patients with Pulmonary Arterial Hypertension	Parallel study	Pharmacological	Hemodynamic parameters	Nitric oxide – sGC – cGMP	Drug – DDCI-01	Phase 2	Adults with pulmonary arterial hypertension (Group 1)	Interventional – pharmacological
CTIS2024-513613-12-00	Not informed	A Study to Learn About the Treatment LTP001 in Healthy Participants (Part A) and in Participants With PAH (Part B)	Uncontrolled observational study	Pharmacological	Safety and tolerability (AEs, labs, ECG, vital signs)	Activin-TGF- β / BMP signaling	Drug – LTP001	Phase 2	Adults with pulmonary arterial hypertension (Group 1)	Observational

CTIS2024-517009-99-00	EmPAH	Proof-of-concept study of Empagliflozin in patients with pulmonary arterial hypertension (EmPAH)	Uncontrolled observational study	Pharmacologic al	Right ventricular diastolic function (S'/RAAi by echocardiography)	Metabolic–cardiorenal	Drug – Empagliflozin	Phase 2	Adults with pulmonary arterial hypertension (Group 1)	Observational
CTIS2024-518687-12-00	Not informed	A clinical study of sotatercept in people with pulmonary arterial hypertension	Uncontrolled observational study	Pharmacologic al	Safety and tolerability (Part A); change in pulmonary vascular resistance (PVR) (Part B)	Activin–TGF-β / BMP signaling	Drug – Sotatercept	Phase 2	Adults with pulmonary arterial hypertension (Group 1)	Observational
CTIS2025-521694-14-00	REVIDAH	REstoration with calcifediol of Vitamin D deficiency in pulmonary Arterial Hypertension patients (REVIDAH study)	Uncontrolled observational study	Pharmacologic al	Clinical improvement without clinical worsening	Sympathetic & hormonal–metabolic	Drug – Vitamin D (calcifediol)	Phase 4	Adults with pulmonary arterial hypertension (Group 1)	Observational
CTIS2025-521970-33-00	Not informed	A clinical study of sotatercept in people with pulmonary arterial hypertension (MK-7962-038)	Open-label, long-term follow-up study	Pharmacologic al	Long-term safety and tolerability	Activin–TGF-β / BMP signaling	Drug – Sotatercept	Phase 3	Adults with pulmonary arterial hypertension (Group 1)	Interventional – pharmacologic al
IRCT20120520009801N18	Not informed	Effects of empagliflozin on pulmonary hypertension	Randomized controlled trial (parallel, single-blind, placebo-controlled)	Pharmacologic al	Change in 6-minute walk distance and invasive RV function	Metabolic–cardiorenal	Drug – Empagliflozin	Phase 3	Adults with pulmonary arterial hypertension (Group 1)	Interventional – pharmacologic al
ISRCTN94603622	REPIPAH	Investigating the use of oral imatinib as a treatment for pulmonary arterial hypertension	Phase II open-label clinical trial (safety and efficacy)	Pharmacologic al	Pulmonary vascular resistance (CardioMEMS-derived)	Tyrosine kinase signaling	Drug – Imatinib	Phase 2	Adults with pulmonary arterial hypertension (Group 1)	Interventional – pharmacologic al
JPRN-jRCT1071250069	SuMILE	A Study of Sotatercept for Patients with Eisenmenger Syndrome or Unrepaired Shunt-Associated PAH Resistant to Vasodilator Therapy	Randomized controlled trial (open-label)	Pharmacologic al	Change in 6MWD at Week 24	Activin–TGF-β / BMP signaling	Drug – Sotatercept	Phase 4	Adults with pulmonary arterial hypertension associated with congenital heart disease (Eisenmenger syndrome)	Interventional – pharmacologic al
JPRN-jRCT2031240628	Not informed	Phase II/III study of MD-712	Single-arm interventional study (open-label, treatment)	Pharmacologic al	Change in pulmonary vascular resistance index	Prostacyclin	Drug – Treprostinil	Phase 2/Phase 3	Mixed pulmonary hypertension (PAH and PH associated with	Interventional – pharmacologic al

									interstitial lung disease)	
JPRN-jRCT2031250407	UNK	A Study to Learn About the Study Medicine (Called PF-07868489) in People With Pulmonary Arterial Hypertension Who Have Previously Participated in a Clinical Study With PF-07868489	Single-arm interventional study (open-label, treatment)	Pharmacologic al	Safety: treatment-emergent AEs and SAEs	Activin-TGF- β / BMP signaling	Drug – PF-07868489	Phase 2	Mixed pulmonary hypertension	Interventional – pharmacologic al
JPRN-jRCT2051240238	Not informed	Open-label Extension Study of Seralutinib in Adult Subjects with PAH	Single-arm interventional study (open-label, treatment)	Pharmacologic al	Incidence of treatment-emergent adverse events	Prostacyclin	Drug – Inhaled therapy (dry powder inhaler)	Phase 3	Adults with pulmonary arterial hypertension (Group 1)	Interventional – pharmacologic al
JPRN-UMIN000056065	Not informed	The study on phenotyping and predicting prognosis of patients with pulmonary arterial hypertension with cardiopulmonary comorbidities	Observational study	Observational	All-cause mortality	Not applicable	No active intervention / phenotyping and prognostic assessment	Not informed	Adolescents and adults with pulmonary arterial hypertension (Group 1)	Observational
NCT06804122	PAHexercise	Exercise-based Rehabilitation in Patients With Pulmonary Arterial Hypertension	Single-group interventional study (open-label, treatment)	Digital / Behavioral	Change in six-minute walk distance	Digital and multidimension al endpoints	Behavioral intervention – Exercise training ($\pm$ medication)	Not Applicabl e	Adults with pulmonary arterial hypertension (Group 1)	Interventional – non-pharmacologic al
NCT06819059	Not informed	Safety and Effectiveness of a Virtual Pediatric Cardiac Rehabilitation Program or Telerehabilitation in Children with Heart Disease	Randomized interventional study (parallel, open-label)	Digital / Behavioral	Intervention adherence (sessions completed)	Digital and multidimension al endpoints	Behavioral intervention – Pediatric cardiac telerehabilitation / fitness tracker	Not Applicabl e	Pediatric and young adults with congenital heart disease–associated PAH	Interventional – non-pharmacologic al
NCT06846554	ViTAL-PH	A Trial of "APL-9796" in Adults With Pulmonary Hypertension	Non-randomized interventional study (sequential, open-label)	Pharmacologic al	Treatment-emergent adverse events	Inflammation / ECM remodeling	Drug – APL-9796	Phase 2	Adults with pulmonary arterial hypertension (Group 1)	Interventional – pharmacologic al
NCT06850792	OPENLINE	imprOving Adherence to Pulmonary artErial hypertENsion Treatment With telEmedicIne and patieNt guidaNce	Single-group interventional study (open-label, treatment)	Digital / Behavioral	Medication adherence (MBG scale)	Digital and multidimension al endpoints	Behavioral intervention – Telemedicine-based	Not Applicabl e	Adults with pulmonary arterial hypertension (Group 1)	Interventional – non-pharmacologic al

							adherence support			
NCT06865118	Nor-SScCare	Home-Based Clinical Management of Cardiac Complications in Systemic Sclerosis	Observational study	Digital / behavioral	Feasibility of home monitoring (adherence, technical performance, agreement with hospital measures)	Digital and multidimensional endpoints	Behavioral intervention – home-based monitoring and digital follow-up	Not informed	Pulmonary arterial hypertension associated with systemic sclerosis	Observational
NCT06872112	STOP-PAH	A Study Evaluating the Safety and Tolerability of Artesunate in Patients With Pulmonary Arterial Hypertension	Single-group interventional study (open-label, treatment)	Pharmacologic al	Treatment-related adverse events and SAEs	Inflammation / ECM remodeling	Drug – Artesunate	Phase 1	Adults with pulmonary arterial hypertension (Group 1)	Interventional – pharmacologic al
NCT06907693	Not informed	The Effects of Drug Candidate CS1 on Lung Structure and Function Utilizing FRI	Interventional (diagnostic imaging study)	Diagnostic test	Pulmonary vascular imaging ratio (BV5A/BV10A)	Diagnosis / imaging	Diagnostic procedure – CT pulmonary angiography	Not informed	Pulmonary arterial hypertension (population not specified)	Interventional – non-pharmacologic al
NCT06917196	PROMPTLY	PROOF OF CONCEPT STUDY ON THE EFFICACY OF INHALATORY TARGETED IMATINIB NANOFORMULATIONS IN PULMONARY HYPERTENSION AND POST-INFLAMMATORY FIBROSIS.	Interventional (preclinical / early translational)	Pharmacologic al	Chemical synthesis and characterization (XHALIP)	Tyrosine kinase signaling	Drug – inhaled imatinib nanoformulation (XHALIP)	Not informed	Mixed pulmonary hypertension (PAH and interstitial lung disease)	Interventional – pharmacologic al
NCT06932198	Not informed	Bioequivalence Study to Compare Selexipag 400mcg Film Coated Tablets (400 mcg Selexipag) Versus Upravi® 400mcg Film Coated Tablets (400 mcg Selexipag)	Randomized interventional study (crossover, open-label, non-treatment purpose)	Pharmacologic al	Pharmacokinetic exposure (Cmax, AUC0–t)	Prostacyclin	Drug – Selexipag (Upravi®)	Phase 1	Adults with pulmonary arterial hypertension (Group 1)	Observational
NCT06939647	Not informed	An Expanded Access Study to Assess Treprostinil Palmitil Inhalation Powder (TPIP) for Participants With Pulmonary Arterial Hypertension (PAH) and Pulmonary Hypertension	Expanded access study	Pharmacologic al		Prostacyclin	Drug – Treprostinil palmitil	Not informed	Mixed pulmonary hypertension (PAH and PH associated with interstitial lung disease)	Expanded access

		Associated With Interstitial Lung Disease (PH-ILD)								
NCT06941441	Not informed	PAH Exercise Study	Single-group interventional study (open-label, treatment)	Digital / Behavioral	Recruitment, adherence, completion, and remote 6MWT feasibility metrics	Digital and multidimensional endpoints	Behavioral intervention – Home exercise program	Phase 3	Adults with pulmonary arterial hypertension (Group 1)	Interventional – non-pharmacological
NCT06954727	CHA-RHC	China Pulmonary Vascular Disease Intervention Diagnosis and Management Study-right Heart Catheterization	Observational study	Registry / observational	Three-month all-cause mortality	Not informed	No active intervention / observational	Not informed	Mixed pulmonary hypertension	Observational
NCT06987097	ALEPH	Ambrisentan for Early Low-Risk Pulmonary Arterial Hypertension	Randomized controlled trial (parallel, quadruple-blind)	Pharmacological	Pulmonary hypertension progression (composite endpoint)	Endothelin	Drug – Ambrisentan vs placebo	Not Applicable	Adults with pulmonary arterial hypertension (Group 1)	Interventional – pharmacological
NCT06992440	EmPATH	Empagliflozin to Improve Right Ventricular Function in Pulmonary Arterial Hypertension	Randomized controlled trial (parallel, quadruple-blind)	Pharmacological	Right ventricular ejection fraction (CMR)	Metabolic–cardiorenal	Drug – Empagliflozin vs placebo	Phase 2	Adults with pulmonary arterial hypertension (Group 1)	Interventional – pharmacological
NCT06998329	PANDORA	Pulmonary hypertension Diagnosis: a National cohort research	Observational study	Registry / observational	Time from symptom onset to confirmed PAH diagnosis	Not informed	No active intervention / observational	Not informed	Adults with pulmonary arterial hypertension (Group 1)	Observational
NCT07013149	ACTION	The Impact of ERA Switching on Risk Stratification in Pulmonary Arterial Hypertension	Observational study	Pharmacological	Change in risk category	Endothelin	Drug – Bosentan	Not Applicable	Adults with pulmonary arterial hypertension (Group 1)	Observational
NCT07039604	Not informed	Real-World Study of PADN for the Treatment of PAH	Observational study	Device	Clinical worsening	Sympathetic & hormonal–metabolic	Device-based intervention – Pulmonary artery denervation (Enhancor™ RF catheter)	Not informed	Mixed pulmonary hypertension	Observational
NCT07073820	Not informed	A Study to Learn About the Study Medicine (Called PF-07868489) in People With PAH	Single-group interventional study (open-label)	Pharmacological	Safety outcomes (AEs, labs, vital signs)	Activin–TGF-β / BMP signaling	Drug – PF-07868489	Phase 2	Mixed pulmonary hypertension	Interventional – pharmacological

		Previously Exposed to PF-07868489								
NCT07082933	Not informed	Long-term Survival and Influencing Factors of Patients With Pulmonary Arterial Hypertension and Diabetes	Observational study	Observational	Overall survival	Not informed	No active intervention / observational	Not informed	Adults with pulmonary arterial hypertension (Group 1)	Observational
NCT07120789	SAVOIR	Validation of a Patient Knowledge Questionnaire for Pulmonary Hypertension	Single-group study (open-label, health services research)	Digital / Behavioral	Questionnaire validity, clarity, and internal consistency	Digital and multidimensional endpoints	Behavioral intervention – Questionnaire-based assessment	Not Applicable	Mixed pulmonary hypertension	Interventional – non-pharmacological
NCT07140484	Not informed	Sotatercept in Pulmonary Arterial Hypertension	Single-arm interventional study (open-label)	Pharmacological	Lung diffusing capacity and pulmonary capillary blood volume	Activin–TGF- β / BMP signaling	Drug – Sotatercept	Phase 4	Adults with pulmonary arterial hypertension (Group 1)	Interventional – pharmacological
NCT07143448	Not informed	A Study of HS235 for Treatment of Pulmonary Arterial Hypertension (PAH) in Adults	Randomized interventional study (sequential, quadruple-blind)	Pharmacological	Incidence and number of adverse events	Activin–TGF- β / BMP signaling	Drug – HS235	Phase 1	Adults with pulmonary arterial hypertension (Group 1)	Interventional – pharmacological
NCT07164157	Not informed	The Risk of Adverse Pregnancy Outcomes for Long-term Exposure to Air Pollution in Pregnant Patients With Pulmonary Hypertension	Observational study	Observational	Primary maternal outcome	Not informed	No active intervention / observational	Not informed	Women with pulmonary arterial hypertension (maternal and air pollution focus)	Observational
NCT07172334	EXPOSPAHA	What is the Role of the Exposome in Pulmonary Hypertension	Observational study	Digital / Behavioral	Environmental exposure profiling (exposome)	Digital and multidimensional endpoints	Behavioral intervention – Questionnaire-based assessment	Not informed	Mixed pulmonary hypertension (PAH and CTEPH)	Observational
NCT07173738	Not informed	Pharmacokinetics, Safety and Tolerability of Concurrent Doses of BIA 5-1058 and Furosemide	Randomized interventional study (sequential, open-label)	Pharmacological	Pharmacokinetic parameters (C _{max} , T _{max} , t _{1/2} , AUC, CL/F, Vz/F)	Sympathetic & hormonal–metabolic	Combined drug therapy – BIA 5-1058 $\pm$ furosemide	Phase 1	Adults with pulmonary arterial hypertension (Group 1)	Interventional – pharmacological
NCT07175038	ROCSTAR	A Study of ROC-101 in Patients With Pulmonary Arterial Hypertension (PAH) and Pulmonary Hypertension Associated With Interstitial Lung Disease (ILD-PH) (ROCSTAR STUDY)	Single-group interventional study (open-label, treatment)	Pharmacological	Change in pulmonary vascular resistance and safety	Tyrosine kinase signaling	Drug – ROC-101	Phase 2	Mixed pulmonary hypertension (PAH and PH associated with interstitial lung disease)	Interventional – pharmacological

NCT07177703	Ter-ImPAH	Efficacy and Safety of Treprostinil in Intermediate-Risk Pulmonary Arterial Hypertension	Single-group interventional study (open-label, treatment)	Pharmacologic al	Change in right ventricular stroke volume	Prostacyclin	Drug – Treprostinil	Phase 2	Adults with pulmonary arterial hypertension (Group 1)	Interventional – pharmacologic al
NCT07184814	CAPTAIN	Clinical Features and Prognosis of Takayasu's Arteritis With Pulmonary Arteries Involvement	Observational study	Observational	All-cause mortality	Not informed	No active intervention / observational	Not informed	Pulmonary arterial hypertension associated with connective tissue disease	Observational
NCT07245680	COMMODITIES	COMMODITIES Trial: Initial Dual Oral Therapy vs Monotherapy in PAH With Cardiovascular Comorbidities	Randomized interventional study (parallel, triple-blind)	Pharmacologic al	Non-invasive four-strata risk profile	Nitric oxide – sGC – cGMP	Combined drug therapy – Tadalafil ± ambrisentan ± placebo	Phase 3	Adults with pulmonary arterial hypertension and cardiovascular comorbidities	Interventional – pharmacologic al
NCT07266012	VExUS in PAH	Integration of Venous Excess Ultrasound Score (VEXUS) Into the ESC/ERS 2022 Simplified Risk Model in Pulmonary Arterial Hypertension: A Prospective Observational Study	Observational study	Observational	Correlation of VExUS score with invasive hemodynamics	Digital and multidimensional endpoints	Diagnostic / imaging-based risk stratification (VExUS score)	Not Applicable	Adults with pulmonary arterial hypertension (Group 1)	Observational
NCT07266519	SIRIUS	Sotatercept in treatment-naïve pulmonary arterial hypertension (SIRIUS)	Uncontrolled study	Pharmacologic al	Pulmonary vascular resistance	Activin–TGF-β / BMP signaling	Drug – Sotatercept	Phase 2	Adults with pulmonary arterial hypertension (Group 1)	Interventional – pharmacologic al
NCT06968962	ORIENTATION	Comparison of Sequential to Initial Combination Therapy in PAH	Randomized controlled trial (parallel, quadruple-blind)	Pharmacologic al	Change in 6-minute walk distance at 12 months	Nitric oxide – sGC – cGMP	Combined drug therapy – Tadalafil / ambrisentan (factorial design)	Not informed	Adults with pulmonary arterial hypertension (Group 1)	Interventional – pharmacologic al