Inhibikase Therapeutics

Corporate Overview

August 2025

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Experienced Leadership with Deep Expertise in PAH

MARK IWICKI
Chief Executive Officer

CHRIS CABELL, MD MHS FACC
Head of R&D, Chief Medical Officer

DAVID McINTYRE BEC CPA LLB MBA
Chief Financial Officer

JEFF KAGY
Chief Human Resource Officer

JOHN ADAMS, PHD
Chief Scientific Officer

CHAD OREVILLO, MPH
EVP, Development Operations

ALLISON WIDLITZ, MS, PA
VP, Clinical Development

Inhibikase and IKT-001: Pulmonary Arterial Hypertension (PAH)

Major unmet need with high mortality, poor QoL and high cost

- PAH is a rare, progressive and life-threatening disease with significant unmet need
- ~30% 5-year mortality(1), reduced quality of life and high economic burden
- $7.6 Billion market with limited treatments that address the underlying etiology

Imatinib has proven efficacy in Phase 3 in PAH

- Imatinib is an anti-proliferative TKI with potential best-in-class improvements in PVR and 6MWD (45 meters*) based on Phase 3 IMPRES and Phase 2 studies
- Imatinib hit primary efficacy endpoints in IMPRES but was not well tolerated at 400mg

Potential to be the 1st oral anti-proliferative agent

- IKT-001 is a pro-drug engineered to realize the potential of imatinib in PAH
- IKT-001 releases imatinib in the blood with potential to minimize GI side effects maximizing potential to achieve highly efficacious doses

Strong Leadership Executing Near Term Development

- IKT's Phase 2b is on track to initiate in the second half of 2025
- Long intellectual property runway through 2044
- Team with extensive PAH / CV experience

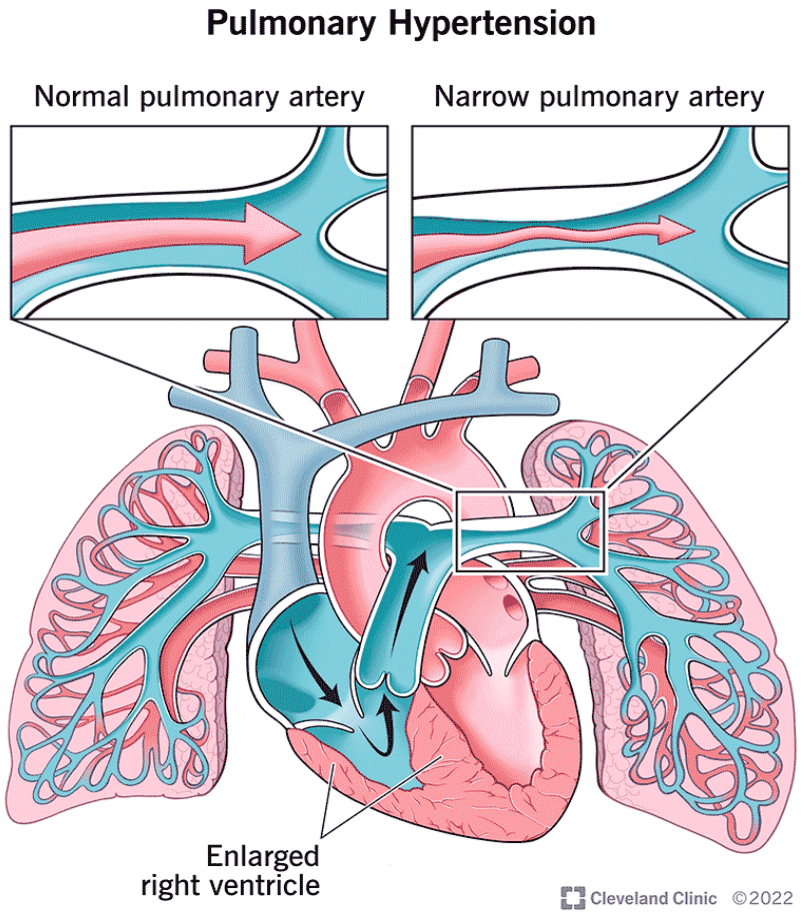
(1) Hoeper M, et al. Eur Respir J. 2017

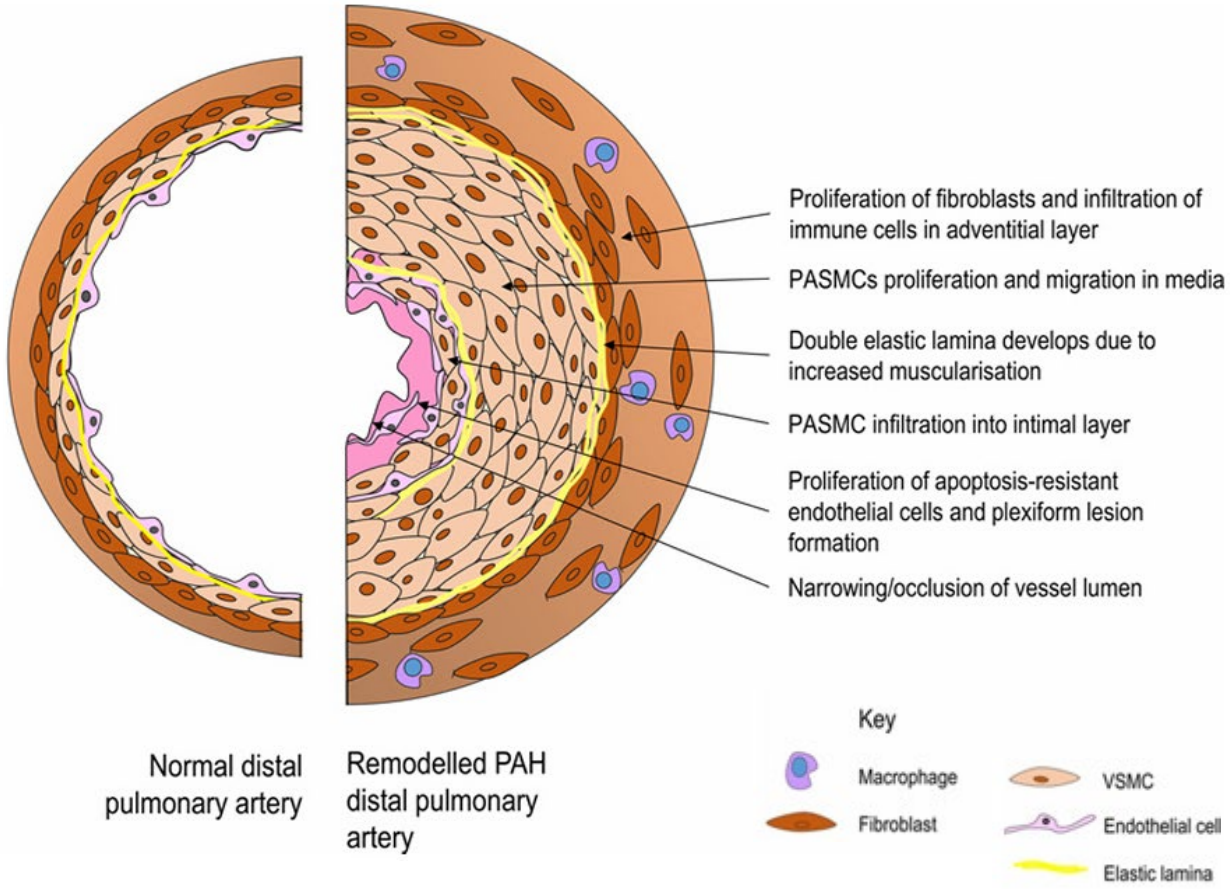
TKI = tyrosine kinase inhibitor; QoL= Quality of Life; PVR = pulmonary vascular resistance; 6MWD = 6-minute walk distance; GI= Gastrointestinal; CV = cardiovascular

* See Page 17

PAH is a Progressive Disease Driven by Uncontrolled Cell Proliferation

Proliferation of vascular cells drive vascular remodeling, raising pulmonary artery pressure and leading to progressive right ventricular heart failure and ultimately death





PASMCs = Pulmonary artery smooth muscle cells; Vascular smooth muscle cells

PAH: An Orphan Disease with ~30% 5-Year Mortality Despite Aggressive Treatment

~50,000
People with PAH in the US[1]

52 years
Average age at diagnosis[2]

~26,000
People with PAH in the EU5[1]

15
Approved vasodilators
(across the prostacyclin, nitric oxide, and endothelin pathways)

~80%
Female[2]

1
Approved anti-proliferative

High Unmet Medical Need

Progressive and Life Threatening

- ~30% 5-year mortality[3] despite aggressive treatment with vasodilator therapies
- Progressively worsening symptoms

Reduced Quality of Life

- Chronic breathlessness, and fatigue
- Significant limitation on activities of daily living
- Dizziness, chest pain, anxiety and depression

High Economic Burden[4]

- Average monthly healthcare costs ~$6,850-$15,650
- Acute all cause hospitalization rate of 700 per 1000 patients per year among Medicare or Medicaid patients
- Substantial indirect costs due to work loss, caregiver time and disability

(1) CVrG Market Strategies report Jun 2025; (2) Badlam et al; CHEST 2021; (3) Hoeper M, et al. Eur Respir J. 2017; (4) Watzger et al; Pharmacoeconomics 2025

PAH: Patient and Treatment Journey

Progressive pulmonary vasculopathy driving right heart failure (RHF)

	ESC/ERS 4 Risk Strata (Risk of 1 year Mortality)[1]			
	Low (0-3%)	**Intermediate Low (2-7%)**	**Intermediate High (9-19%)**	**High (>20%)**
WHO Functional Class	**Class 1** No limitation of physical activity **Class 2** Slight limitation of physical activity. Ordinary physical activity causes dyspnea, fatigue, chest pain, or near syncope		**Class 3** Marked limitation in physical activity. Less than ordinary activity causes undue dyspnea, fatigue, chest pain or near syncope	**Class 4** Inability to carry out any physical activity without symptoms. Signs of RHF. Discomfort increased by any physical activity. Dyspnea and fatigue present at rest
6MWD	>440 meters	320 – 440 meters	165 - 319 meters	<165 meters
NT-ProBNP	<300ng.L^{-1}	300-649ng.L^{-1}	650-1100ng.L^{-1}	>1100ng.L^{-1}

1st Line of Therapy → **Add On Therapy With Declining Health Status** →

Initiate PDE-5i +ERA Combo		Oral/Inhaled Prostacyclin	Activin Signaling Inhibitor	Infused Prostacyclin
PDE-5i or •NO Pathway Sildenafil; Tadalafil; Riociguat*	**ERA's** Bosentan; Ambrisentan Macitentan	Selexipag; Oral Remodulin; Tyvaso, Tyvaso DPI; Yutrepia	Sotatercept	Remodulin IV; Remodulin Sub-Q; Flolan, Veletri

ERS=European Respiratory Society; ESC=European Society of Cardiology; WHO=World Health Organization; 6MWD= 6 Minute Walk Distance Test; NT-ProBNP= Biomarker of cardiac strain; NO = Nitric Oxide; * Riociguat is a soluble guanylate cyclase stimulator (sGC)

(1) Humbert et al; ERJ 2023

$7.6B Market Driven by Vasodilators Which Don't Treat Underlying Causes of PAH

Novel antiproliferative agents with disease modifying properties expected to revolutionize treatment

Vasodilators

Prostacyclin Pathway ($3.7B)

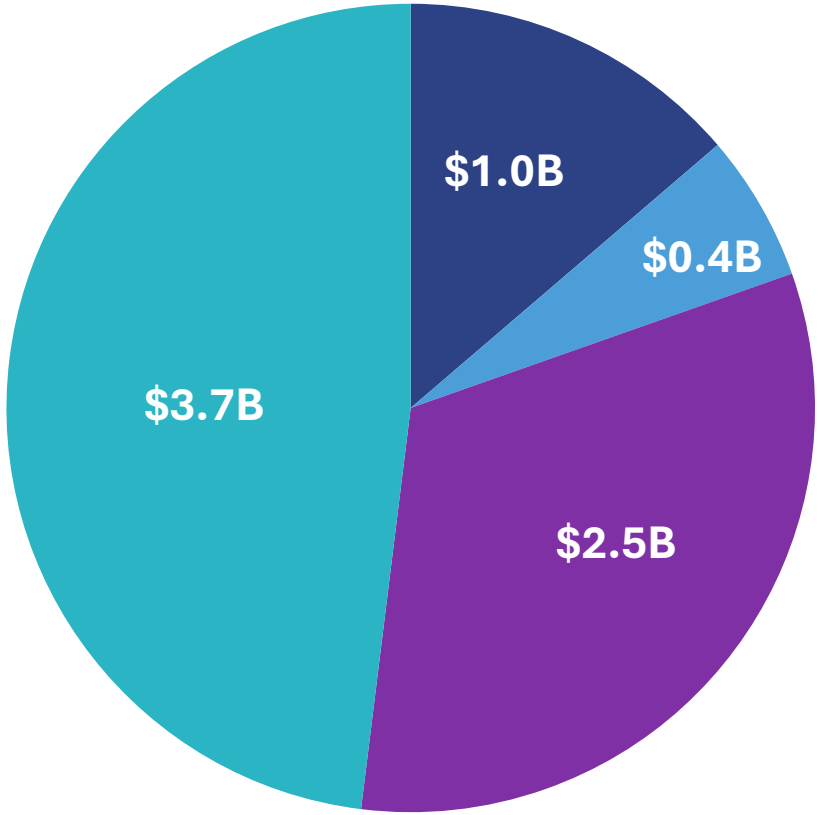
Epoprostenol, Treprostinil, Iloprost, Selexipag

Endothelin Pathway ($2.5B)

Ambrisentan, Bosentan, Macitentan

Nitric Oxide Pathway ($1.0B)

Sildenafil, Tadalafil, Riociguat



Anti-proliferative Agents

Activin Signaling Pathway ($0.4B)

Sotatercept - subcutaneos injection

(FDA approval March 2024)

IKT-001 has the potential to be the first oral anti-proliferative agent for the treatment of PAH

2024 annual reports from Janssen, United Therapeutics, Bayer, and Merck

Our Solution: An Oral Pro-Drug of Imatinib Optimized for PAH

Engineered to realize imatinib's best-in-class efficacy potential in PAH

Gleevec (Imatinib)

NOVARTIS

IKT-001 (Imatinib Pro-Drug)

IkT

History
First Approved in 2001; 25 years of real-world experience
Indicated for: Leukemia, Soft Tissue Sarcoma, Myelodysplastic Syndromes, Mastocytosis and GIST

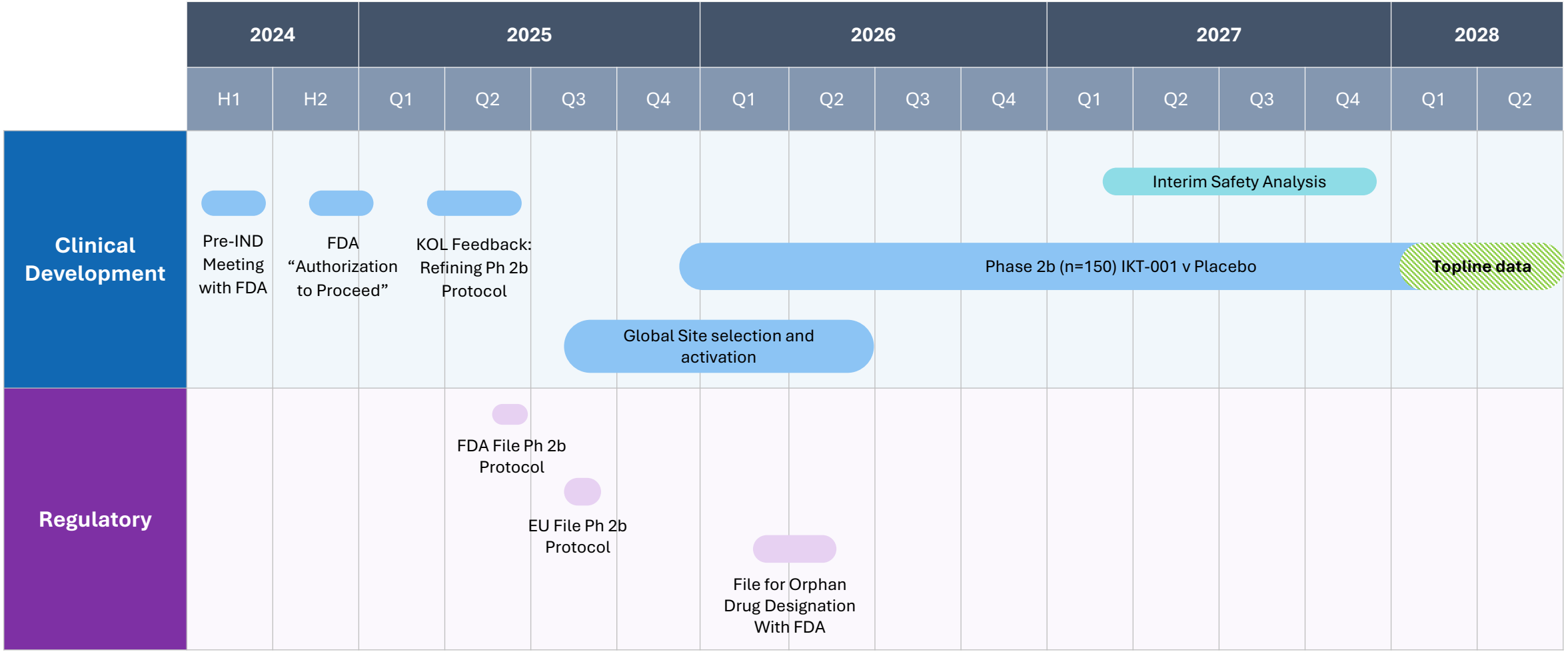
IKT-001 is a novel pro-drug of imatinib designed for better GI tolerability allowing optimal efficacy

PAH Data
Best-in-class improvements in PVR and 6MWD in Phase 2 & 3
Greatest efficacy at 400mg but not clinically tolerated
Contemporary study supports 400mg efficacy/tolerability findings

Potential to be the first and only once-daily oral anti-proliferative tyrosine kinase inhibitor (TKI) for PAH

PVR = Pulmonary Vascular Resistance; 6MWD= 6 Minute Walk Distance test; GI = Gastrointestinal; GIST = Gastrointestinal Stromal Tumor

Development and Regulatory Timeline



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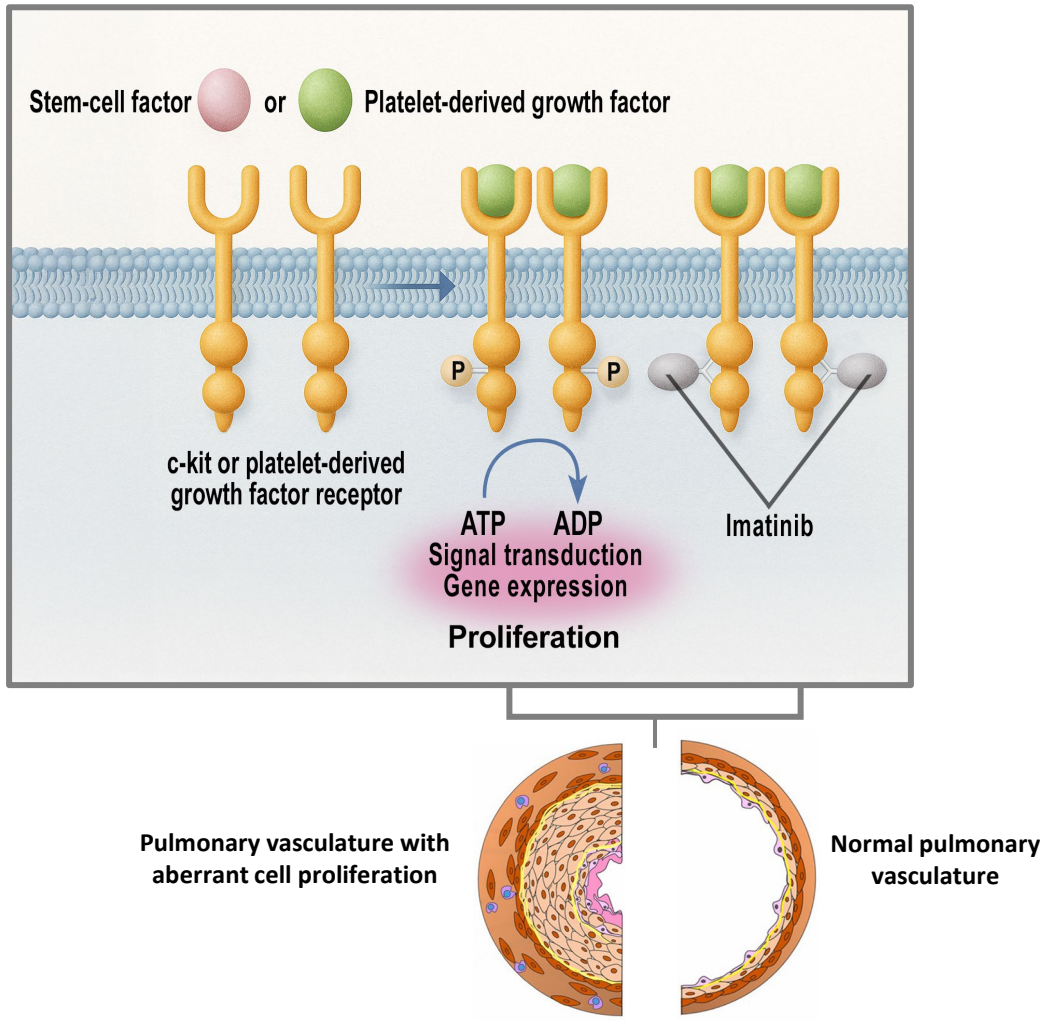
Scientific and Clinical Rationale

Imatinib Mechanism of Action in PAH Targets the Underlying Cause of PAH



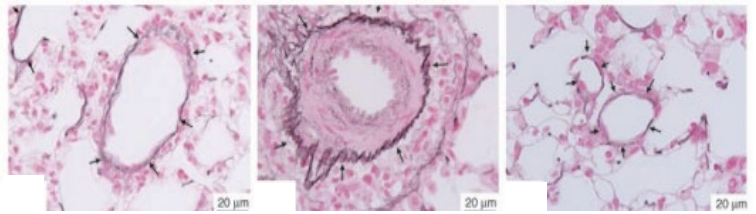
Overactive kinases implicated in aberrant cell proliferation and migration in the pulmonary vasculature

Imatinib inhibits the tyrosine kinase activity of PDGFR and c-kit , blocking cell signaling that drives vascular remodeling

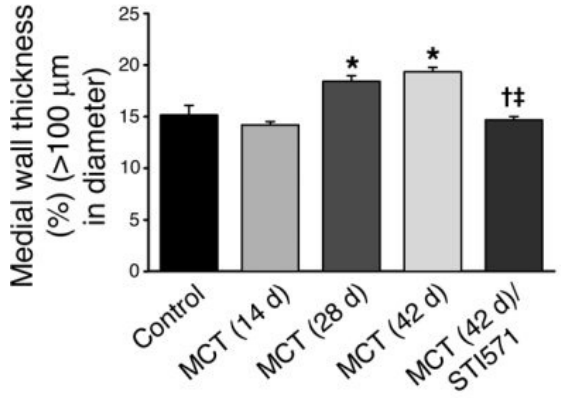
Modified from Savage and Antman, 2005 and Barst, R J Clin Invest 2005

Imatinib Demonstrated Reversal of PAH in Standard Animal Model

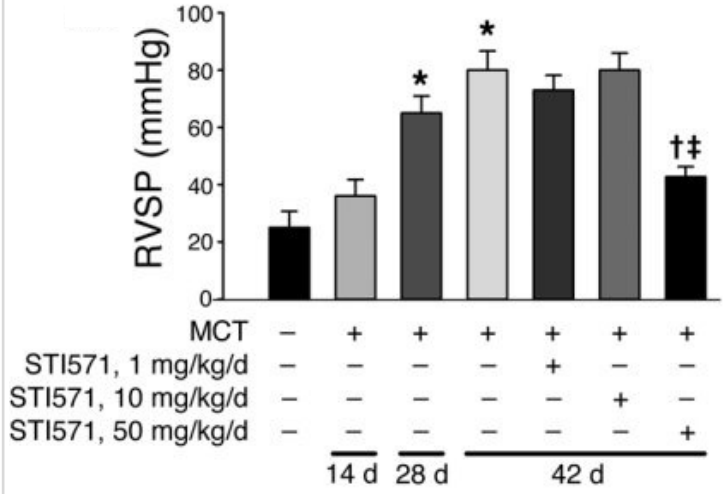
Reversal of vascular remodeling



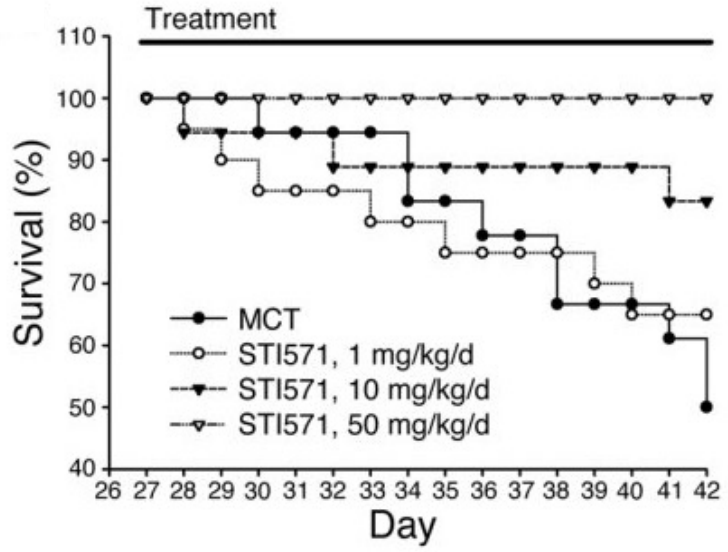
Day 0 MCT d42 MCT d42/+imatinib



Reversal of right ventricular pressure



Improved survival



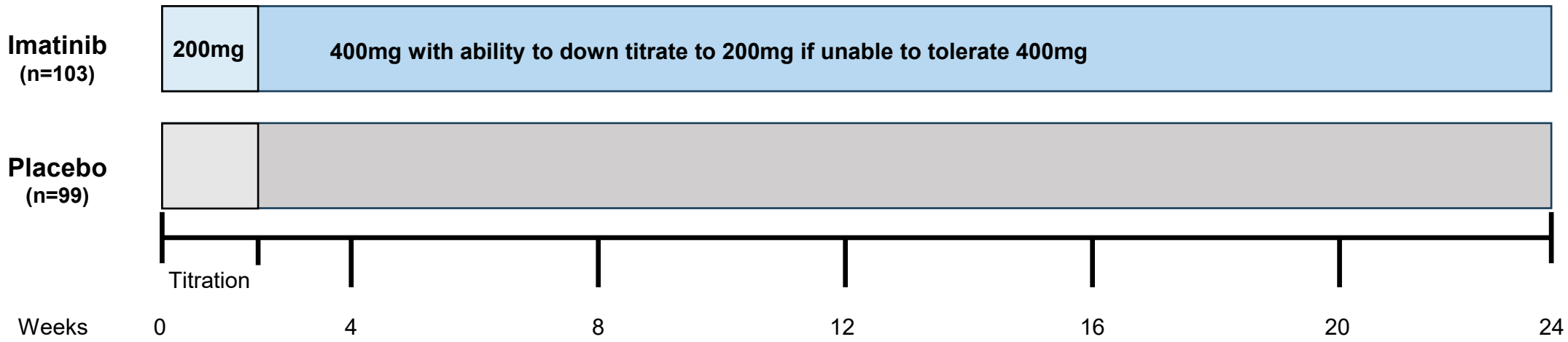
Imatinib reverses pulmonary vascular remodeling, right ventricular pressure / remodeling and improves survival

STI571 = imatinib; MCT = monocrotaline
*P < 0.05 versus control; †P < 0.05 versus MCT at day 28 or hypoxia at day 21; ‡P < 0.05 versus MCT at day 42 or hypoxia at day 35.

Schermuly et al., JCI 2005

IMPRES – Imatinib Phase 3 Study

Randomized, double blind, placebo controlled study to assess the efficacy, safety and tolerability of 400mg imatinib once daily (n=202)



Primary Endpoint

- Change in 6MWD at 24 weeks

Secondary Endpoints

- Changes in hemodynamics (PVR, CO, mPAP, RAP) at 24 weeks
- Time to clinical worsening

Key Inclusion Criteria

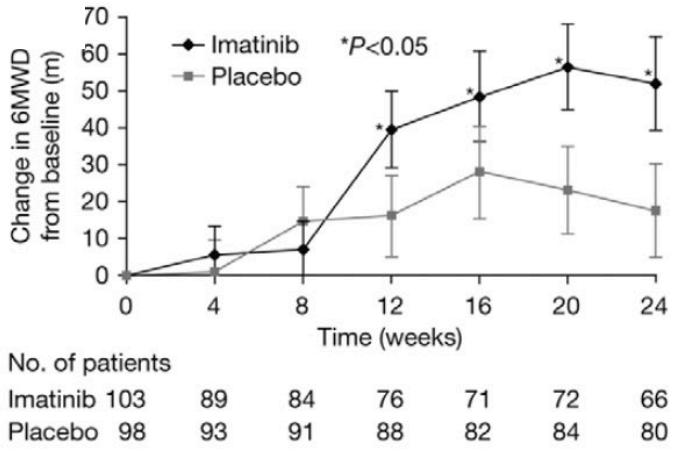
- Functional Class II-IV
- 2 or more background PAH therapies
- PVR ≧ 800 dynes.s.cm^{-5}
- 6MWD ≥150 meters and ≤ 450meters

PVR = pulmonary vascular resistance; CO = cardiac output; mPAP = mean pulmonary arterial pressure; RAP = right arterial pressure; 6MWD = 6-minute walk distance

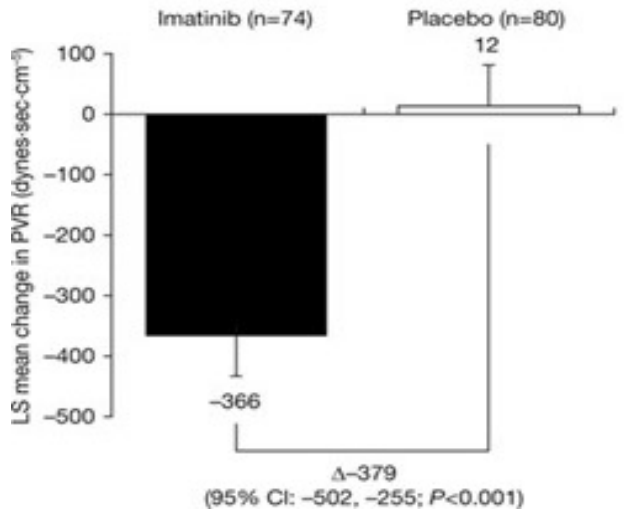
Phase 3 IMPRES: Statistically Significant Improvement in Function & Hemodynamics

32-meter improvement in 6WMD and 32% reduction in PVR at week 24

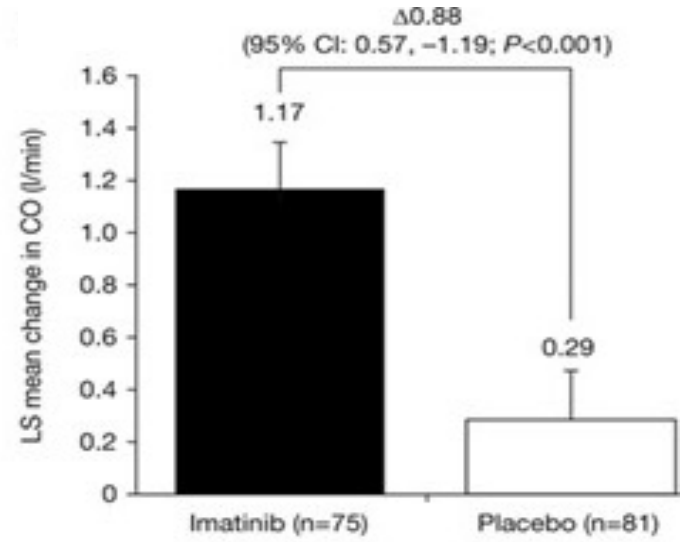
Change in 6MWD



Change in Pulmonary Vascular Resistance



Change in Cardiac Output



Phase 3 IMPRES study hit its primary endpoint along with key clinically relevant secondary endpoints

PVR = Pulmonary Vascular Resistance; 6MWD= 6 Minute Walk Distance test

Hoeper et al; Circulation 2013

Phase 3 IMPRES: 3 of the Top 5 AEs were GI Related

Majority of patients were unable to maintain 400 mg target dose of imatinib

	Imatinib n=103 (%)	Placebo n=98 (%)
Adverse Events	100 (97)	94 (96)
Nausea	57 (55)	23 (24)
Peripheral edema	45 (44)	20 (20)
Diarrhea	36 (35)	19 (19)
Vomiting	31 (30)	10 (10)
Periorbital edema	30 (29)	7 (7)

- The AE profile in IMPRES was similar to the established AE profile of imatinib in other indications
- Poor tolerance prevented most patients from maintaining the target dose of 400 mg of imatinib

Phase 3 IMPRES hit its primary endpoint DESPITE only 48/103 participants maintaining 400mg dose for at least half of the treatment period

IKT-001 is a novel pro-drug of imatinib designed for better GI tolerability allowing optimal efficacy

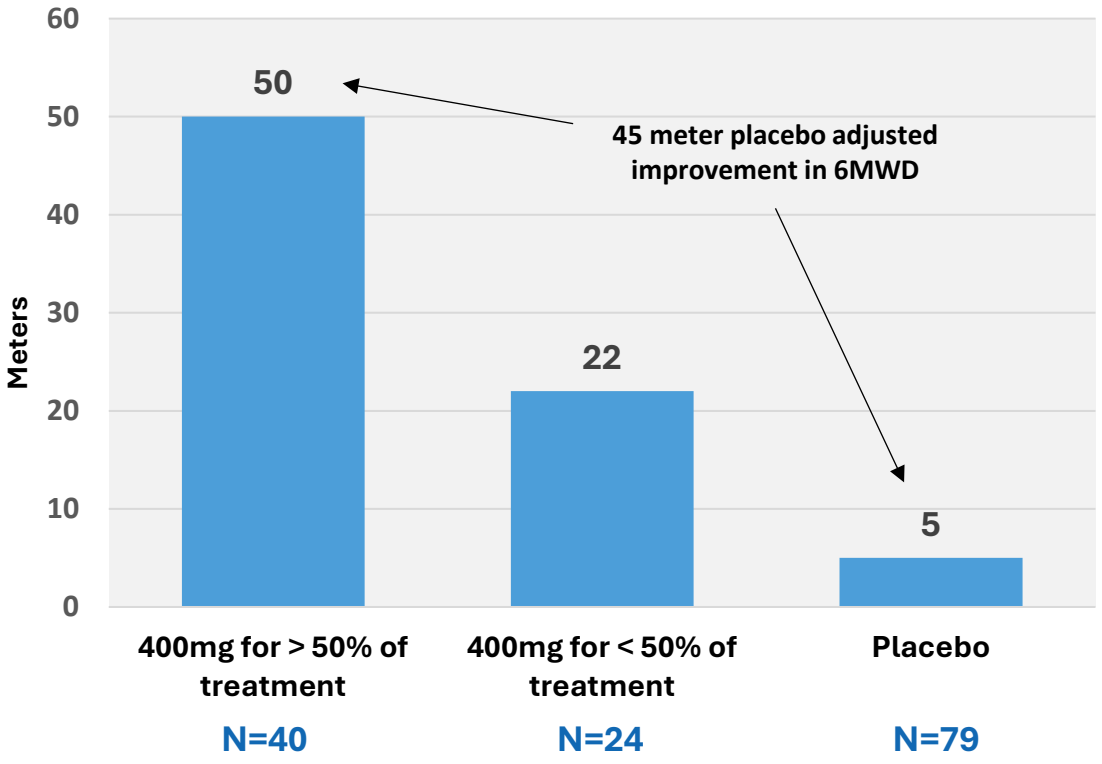
AE = Adverse event; GI = Gastrointestinal

Hoeper et al; Circulation 2013

IMPRES: Efficacy Impacted by Tolerability of 400mg Per Day

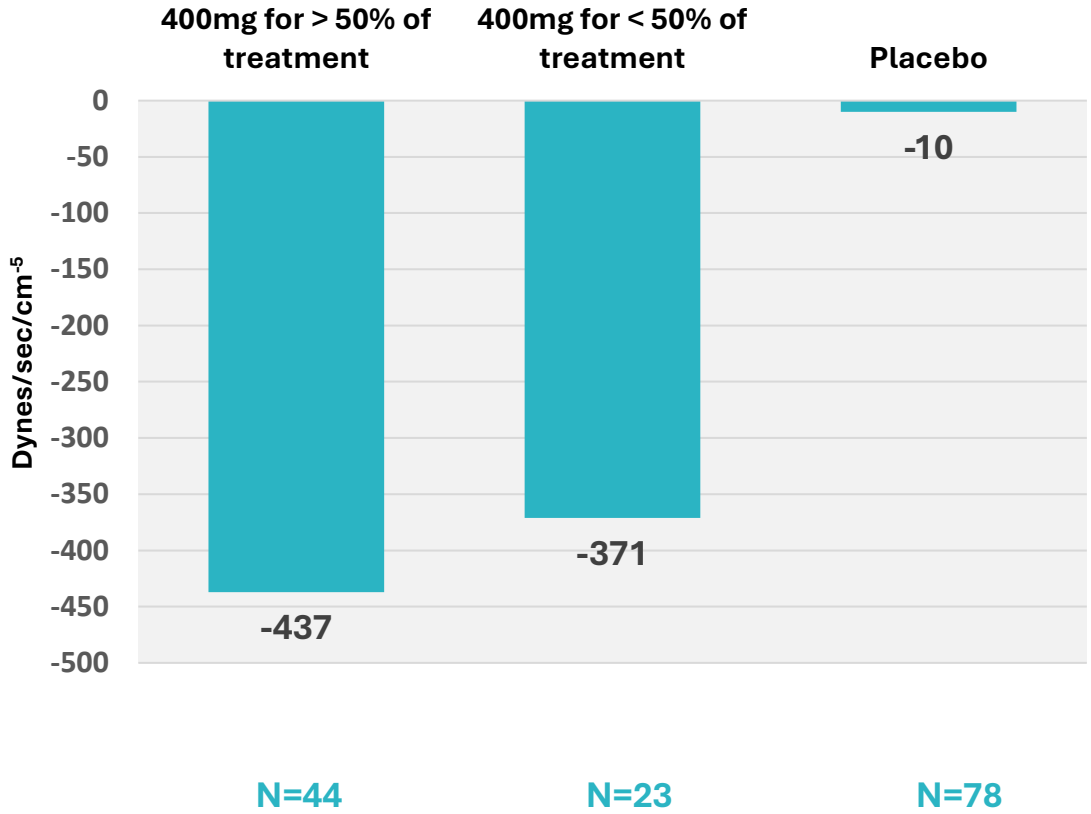
Patients able to sustain 400mg dose showed greater improvements in 6MWD and PVR

Changes in 6MWD at Week 24



(Baseline*: 355 meters imatinib; 366 meters placebo)

Changes in PVR at Week 24



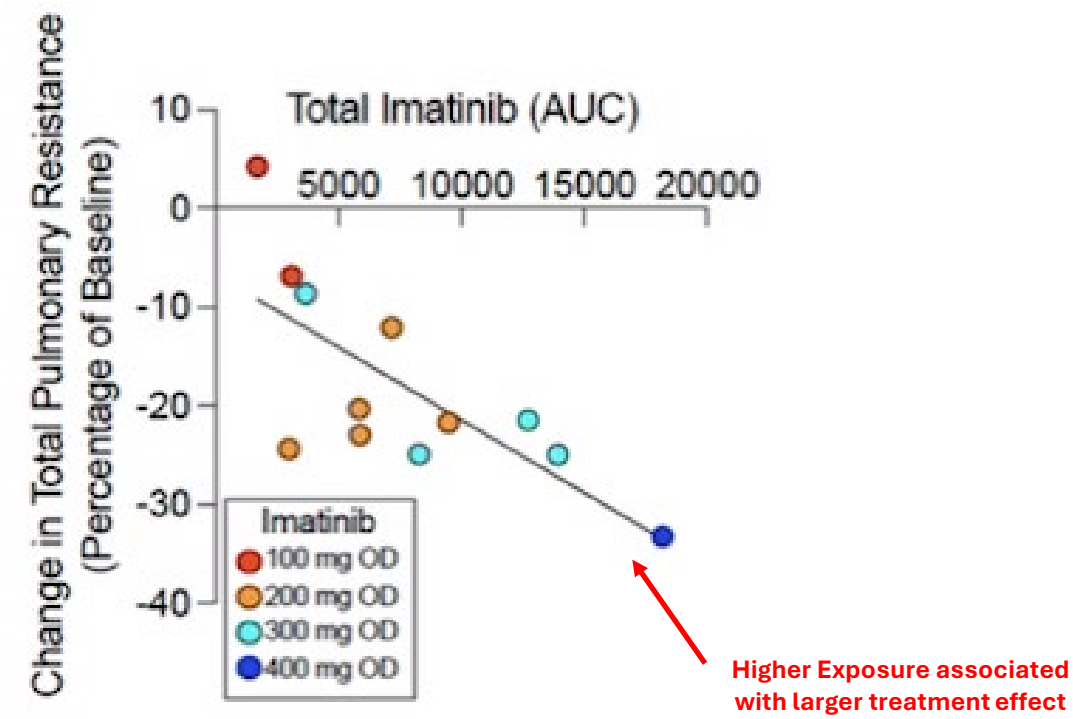
(Baseline*: 1202 dynes/sec/cm^{-5} imatininb; 1181 dynes/sec/cm^{-5} placebo)

* Baseline data is not available for the sub-population of patients on 400mg of imatinib for > 50% of treatment so baseline data above reflects entire study population. PVR= Pulmonary vascular resistance; 6MWD = 6-minute walk distance

Hoeper et al; Circulation 2013 Suppl. Appendix

Contemporary Study of Imatinib Supports 400mg Dose for Best Efficacy

Higher Exposure = Larger Improvement



Percentage change in total pulmonary resistance from baseline at 60 days in relation to plasma level (area under curve in µg*h/L) of imatinib at steady state (red-100md QD, orange-200mgQD, cyan-300mg QD, blue-400mg QD)

Doses over 200mg per day were poorly tolerated

More than 50% of subjects who completed the study were on 200mg per day or less

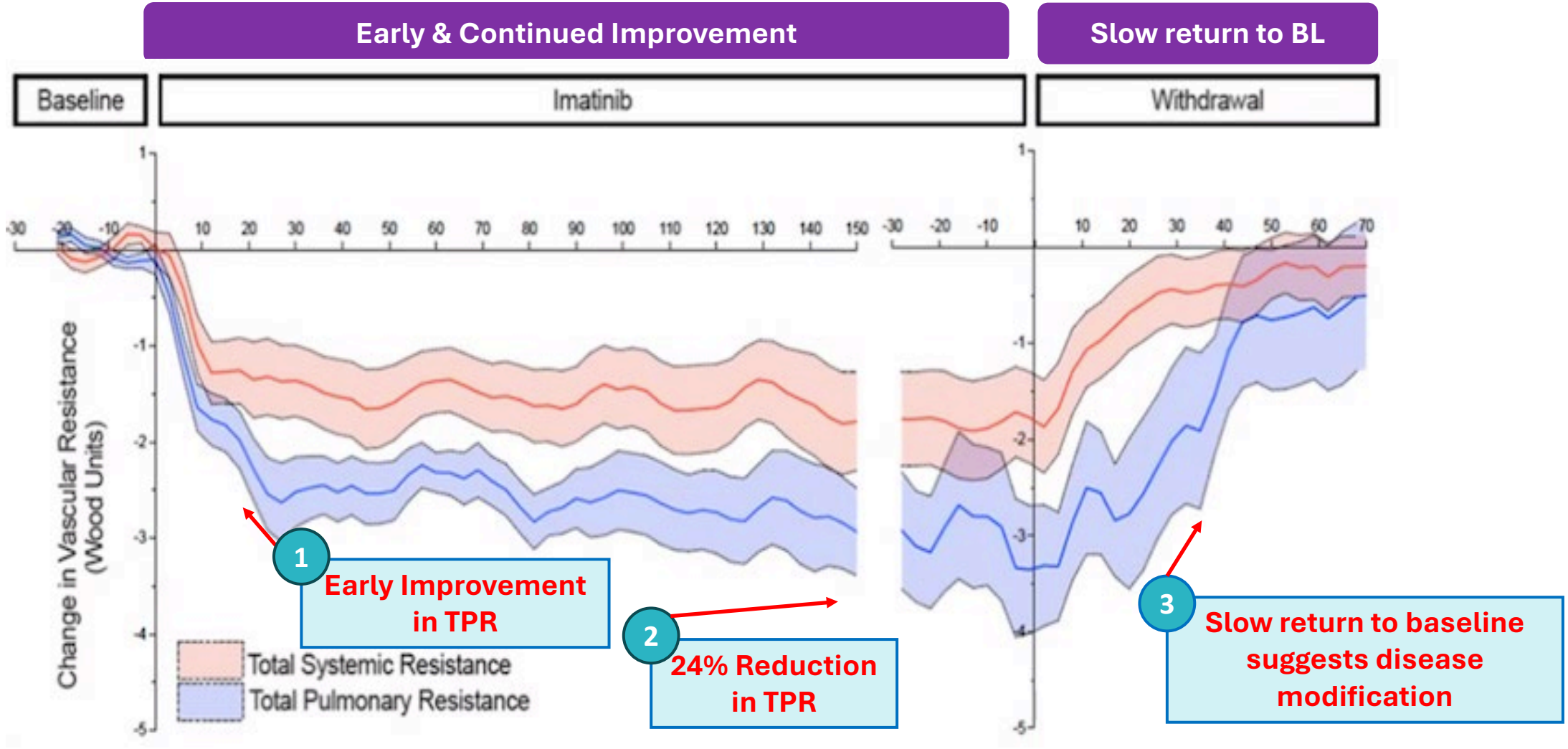
One-third of patients who started the study at either 300mg or 400mg had dose-limiting toxicity at Week 4 and subsequent dose reduction

Only 5 patients completed the study at 300mg or 400mg per day

* Rothman et al., AJRCCM 2025. 17 patient open-label study. Patients were implanted with the CardioMEMS HF System which is a small, wireless sensor implanted in the pulmonary artery to monitor pulmonary artery pressure. Patients remained in the study for up to 24 weeks.

Rapid and Sustained Hemodynamic Effect & Disease Modification of Imatinib in PAH

24% reduction in Total Pulmonary Resistance (TPR); Patients at 200mg or less leaves “efficacy on the table”



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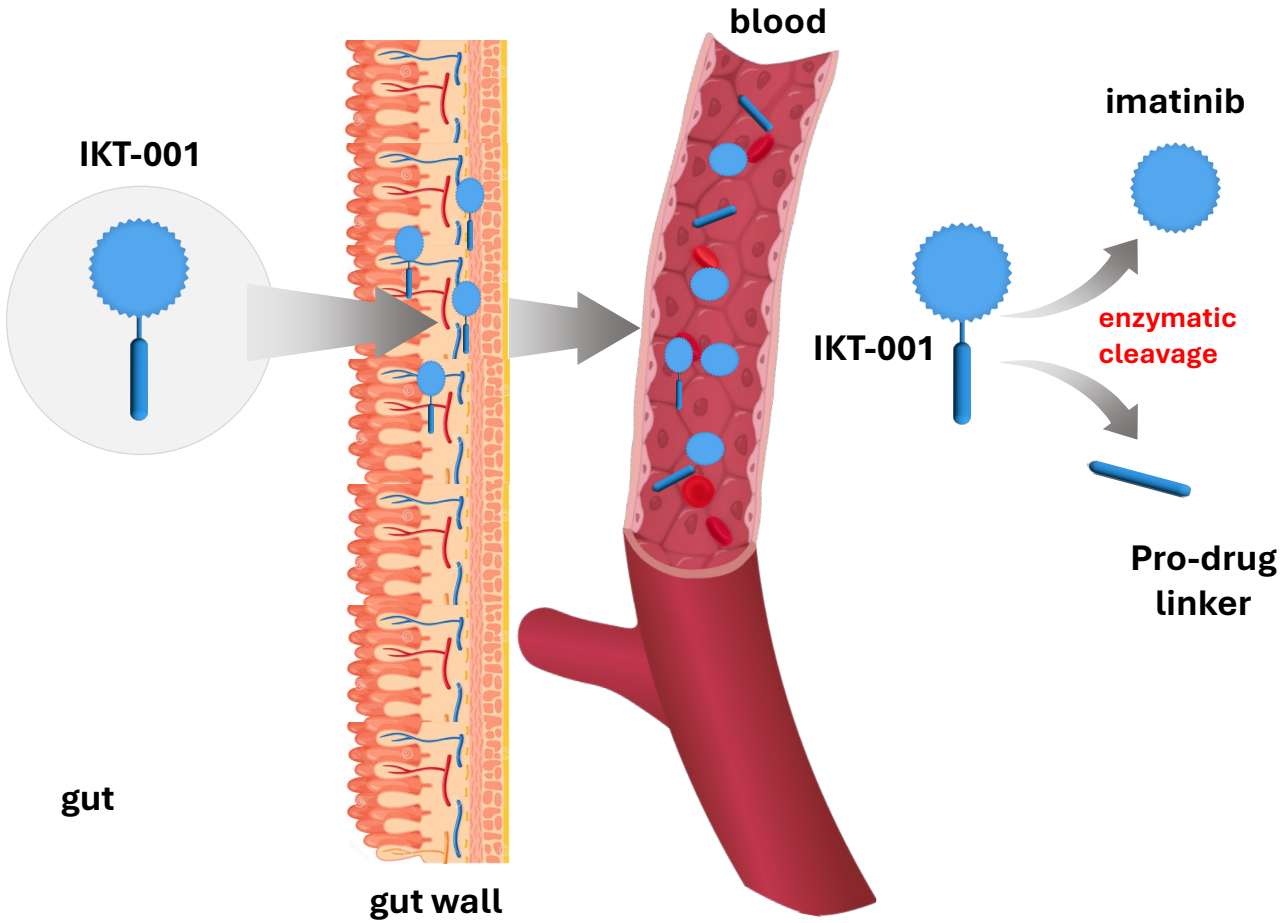
IKT-001

IKT-001 Minimizes GI Imatinib Exposure to Drive Increased Tolerability

28 Day non-human primate study documents improved GI tolerability



>2.5x Improvement in GI Tolerability

Dose Associated with GI Toxicity

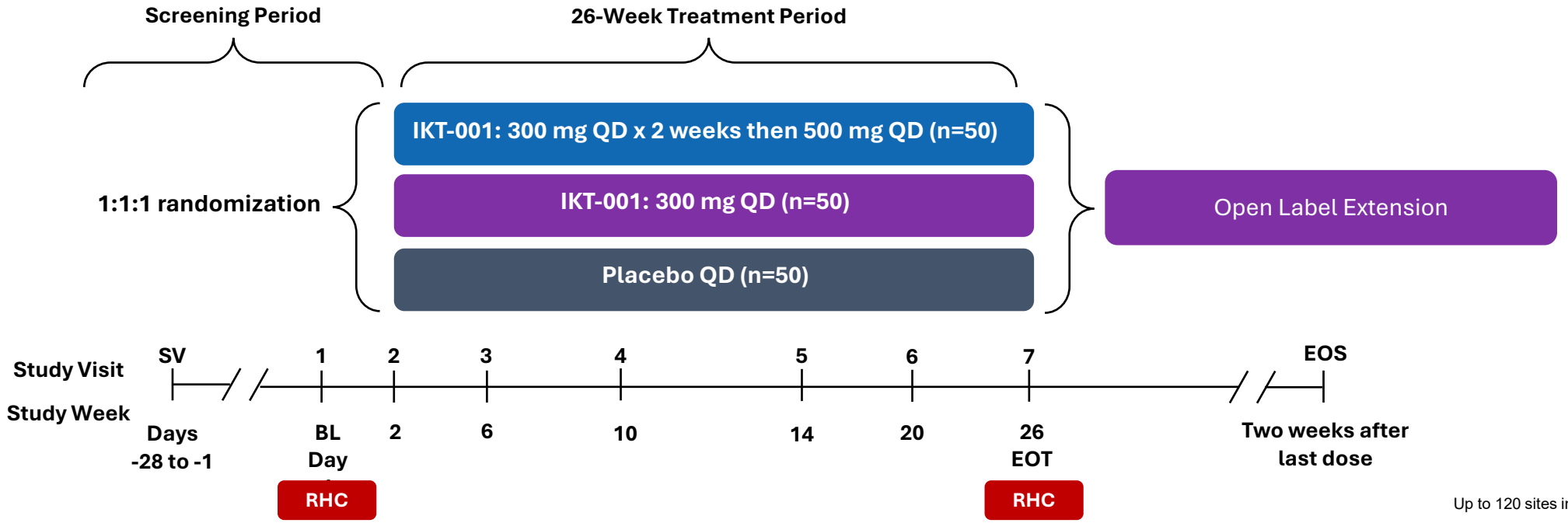
Imatinib: **75 mg per kg per day**

IKT-001: **200 mg per kg per day**

GI = gastrointestinal

IKT-001-201: A Phase 2b Study of IKT-001 in PAH

Randomized double-blind, placebo-controlled study to evaluate efficacy and safety of once daily IKT-001



Up to 120 sites in 18 countries

Primary Endpoints:

PVR at week 26, change from baseline

Safety and tolerability

Secondary Endpoints:

6MWD

WHO Functional Class

Pharmacokinetics

Inclusion / Stratification:

WHO Group 1 PAH with New York Heart Association Functional Class II / III symptoms

Baseline Right Heart Catheter performed during screening period:

- PVR of ≥400 dynes/sec/cm^{-5} ; PCWP ≤15 mmHg; mPAP >20 mmHg
- PVR enrichment criteria to ensure population baseline PVR >700 dynes/sec/cm^{-5}

6MWD ≥100 and ≤500 meters

Previous sotatercept allowed if discontinued 6 months prior to screening and no history of serious bleeding events

Stratification by number of background therapies and ERS/ESC Risk Score

PVR = pulmonary vascular resistance; 6MWD = 6-minute walk distance; RHC = right heart catheter; PCWP = pulmonary capillary wedge pressure; mPAP = mean pulmonary arterial pressure; BL = baseline; SV = screening visit; EOT = end of treatment; EOS = end of study

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Thank You