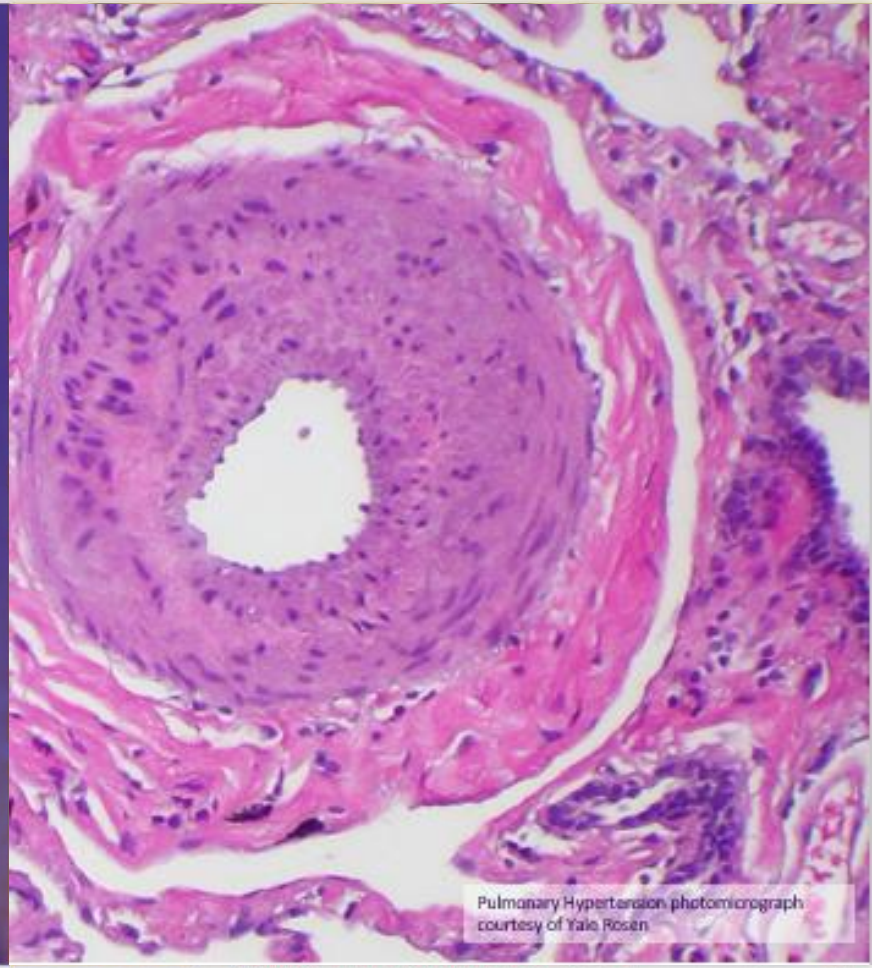
February 19, 2021

TPIP Phase 1 Topline Results

insmed®



Forward Looking Statements

This presentation contains forward-looking statements that involve substantial risks and uncertainties. "Forward-looking statements," as that term is defined in the Private Securities Litigation Reform Act of 1995, are statements that are not historical facts and involve a number of risks and uncertainties. Words herein such as "may," "will," "should," "could," "would," "expects," "plans," "anticipates," "believes," "estimates," "projects," "predicts," "intends," "potential," "continues," and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) may identify forward-looking statements.

The forward-looking statements in this presentation are based upon the Company's current expectations and beliefs, and involve known and unknown risks, uncertainties and other factors, which may cause the Company's actual results, performance and achievements and the timing of certain events to differ materially from the results, performance, achievements or timing discussed, projected, anticipated or indicated in any forward-looking statements. Such risks, uncertainties and other factors include, among others, the following: the risk that brensocatib does not prove to be effective or safe for patients in ongoing and future clinical studies, including the ASPEN study; the risk that TPIP does not prove to be effective or safe for patients in ongoing and future clinical studies; business or economic disruptions due to catastrophes or other events, including natural disasters or public health crises; impact of the novel coronavirus (COVID-19) pandemic and efforts to reduce its spread on our business, employees, including key personnel, patients, partners and suppliers; failure to successfully commercialize ARIKAYCE®, our only approved product, in the United States or European Union (amikacin liposome inhalation suspension and Liposomal 590 mg Nebuliser Dispersion, respectively), or to maintain U.S. or EU approval for ARIKAYCE; uncertainties in the degree of market acceptance of ARIKAYCE by physicians, patients, third-party payors and others in the healthcare community; the Company's inability to obtain full approval of ARIKAYCE from the FDA, including the risk that the Company will not timely and successfully complete the study to validate a PRO tool and the confirmatory post-marketing clinical trial required for full approval of ARIKAYCE; inability of the Company, PARI Pharma GmbH (PARI) or the Company's.other third-party manufacturers to comply with regulatory requirements related to ARIKAYCE or the Lamira® Nebulizer System; the Company's inability to obtain adequate reimbursement from government or third-party payors for ARIKAYCE or acceptable prices for ARIKAYCE; development of unexpected safety or efficacy concerns related to ARIKAYCE or the Company's product candidates; inaccuracies in the Company's estimates of the size of the potential markets for ARIKAYCE or its product candidates or in data the Company has used to identify physicians, expected rates of patient uptake, duration of expected treatment, or expected patient adherence or discontinuation rates; the Company's inability to create an effective direct sales and marketing infrastructure or to partner with third parties that offer such an infrastructure for distribution of ARIKAYCE or any of the company's product candidates that are approved in the future; failure to obtain regulatory approval to expand ARIKAYCE's indication to a broader patient population; failure to successfully conduct future clinical trials for ARIKAYCE, brensocatib, trepostinil palmitil inhalation powder (TPIP) and the Company's other product candidates, due to the Company's limited experience in conducting preclinical development activities and clinical trials necessary for regulatory approval and the Company's potential inability to enroll or retain sufficient patients to conduct and complete the trials or generate data necessary for regulatory approval, among other things; risks that the Company's clinical studies will be delayed or that serious side effects will be identified during drug development; failure to obtain, or delays in obtaining, regulatory approvals for ARIKAYCE outside the U.S. or European Union, including the United Kingdom as a result of its exit from the EU, or for the Company's product candidates in the U.S., Europe, Japan or other markets; failure of third parties on which the Company is dependent to manufacture sufficient quantities of ARIKAYCE or the Company's product candidates for commercial or clinical needs, to conduct the Company's clinical trials, or to comply with the Company's agreements or laws and regulations that impact the Company's business or agreements with the Company; the Company's inability to attract and retain key personnel or to effectively manage the Company's growth; the Company's inability to adapt to its highly competitive and changing environment; the Company's inability to adequately protect its intellectual property rights or prevent disclosure of its trade secrets and other proprietary information and costs associated with litigation or other proceedings related to such matters; restrictions or other obligations imposed on the Company by its agreements related to ARIKAYCE or the Company's product candidates, including its license agreements with PARI and AstraZeneca AB, and failure of the Company to comply with its obligations under such agreements; the cost and potential reputational damage resulting from litigation to which the Company is or may become a party, including product liability claims; the Company's limited experience operating internationally; changes in laws and regulations applicable to the Company's business, including any pricing reform, and failure to comply with such laws and regulations; inability to repay the Company's existing indebtedness and uncertainties with respect to the Company's ability to access future capital; and delays in the execution of plans to build out an additional third-party manufacturing facility approved by the FDA and unexpected expenses associated with those plans.

The Company may not actually achieve the results, plans, intentions or expectations indicated by the Company's forward-looking statements because, by their nature, forward-looking statements involve risks and uncertainties because they relate to events and depend on circumstances that may or may not occur in the future. For additional information about the risks and uncertainties that may affect the Company's business, please see the factors discussed in Item 1A, "Risk Factors," in the Company's Annual Report on Form 10-K for the year ended December 31, 2019, Quarterly Reports on Form 10-Q for the quarters ended March 31, 2020, June 30, 2020 and September 30, 2020, and any subsequent Company filings with the SEC.

The Company cautions readers not to place undue reliance on any such forward-looking statements, which speak only as of the date of this presentation. The Company disclaims any obligation, except as specifically required by law and the rules of the SEC, to publicly update or revise any such statements to reflect any change in expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements.

Powered By Purpose

Our commitment to transforming the lives of people with rare diseases drives what we do.

insmed®

Treprostinil Palmitil Inhalation Powder (TPIP)

Potentially Developing a Superior Treatment Paradigm

Current Therapies

Prostanoids have long been considered the “gold standard” therapy for PAH; however, this class of drugs has also been plagued by challenges

Treprostinil palmitil has demonstrated substantial promise for the treatment of pulmonary arterial hypertension

TPIP Phase 1

A Phase 1 study of TPIP in healthy volunteers has recently been **completed**

Encouraging Results

Topline results demonstrate that TPIP was **generally well tolerated**

The highest dose tested as a single dose was 675 µg, and the highest dose tested in repeated dosing was 225 µg

Further Development

Results support moving forward with development of TPIP with **once daily dosing**

TPIP may also have utility in treatment of Group 3 pulmonary hypertension (PH-ILD) and idiopathic pulmonary fibrosis (IPF)

We believe evidence of efficacy with Tyvaso® in these patient populations may translate to TPIP as well

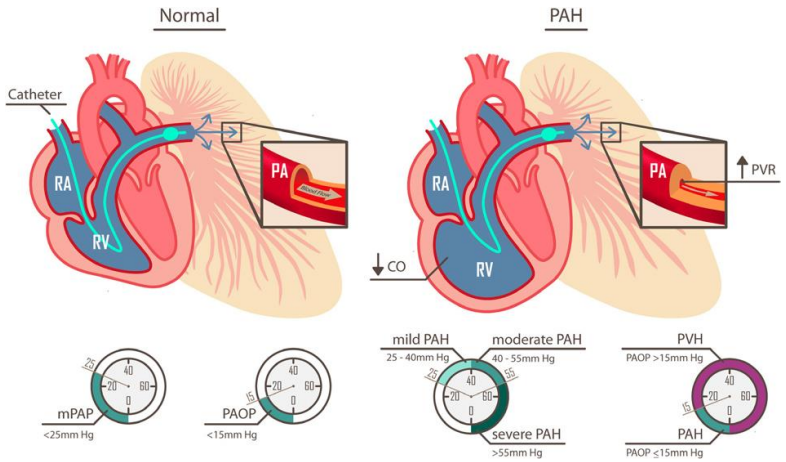
Treprostinil Palmitil

Harnessing the Full Potential of the Prostanoid Pathway

Prostanoids have long been a cornerstone therapy for PAH, but clinical use has faced challenges related to rapid metabolism and dose-limiting tolerability issues

TPIP could address the shortcomings of existing prostanoid therapies by potentially:

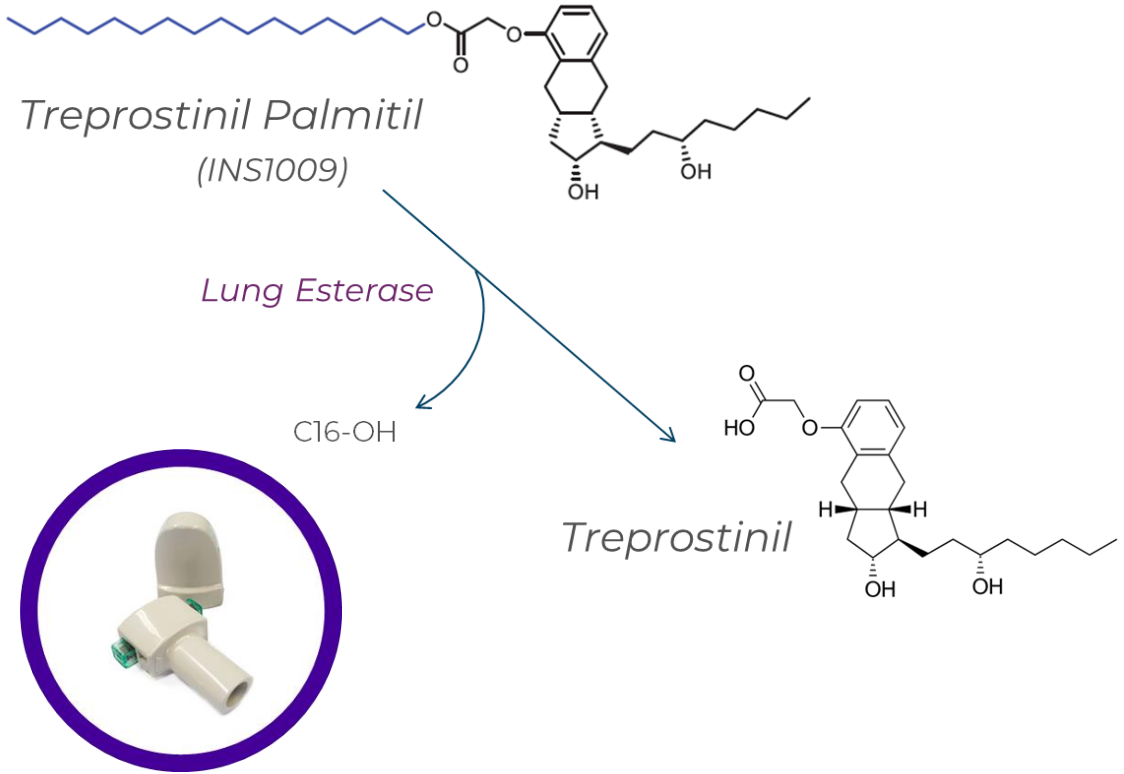
- Providing prolonged, localized pulmonary vasodilation
- Offering **improved tolerability**, with fewer prostanoid-related side effects
- Enabling higher dosing for superior efficacy with the potential for **disease-modifying effect**
- Simplifying dosing with **once daily administration**



PAH = pulmonary arterial hypertension; RA = right atrium; RV = right ventricle; PA = pulmonary artery; mPAP = mean pulmonary arterial pressure; PAOP = pulmonary artery occluded pressure; PVH = pulmonary venous hypertension

TPIP: A Potentially Differentiated Prostanoid

- TPIP* is a dry powder formulation of **treprostinil palmitil**, a prodrug of the prostacyclin vasodilator treprostinil
- Treprostinil palmitil was formerly referred to as **INS1009**
- Once delivered to the lung, treprostinil palmitil is hydrolyzed by endogenous esterases to active treprostinil
- The inhalation device is a simple capsule-based dry powder inhaler (DPI) device manufactured by Plastiape and used with several approved products

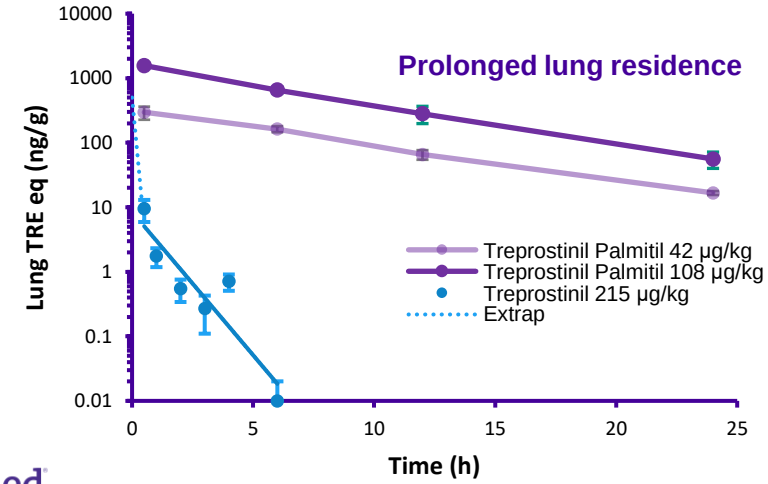


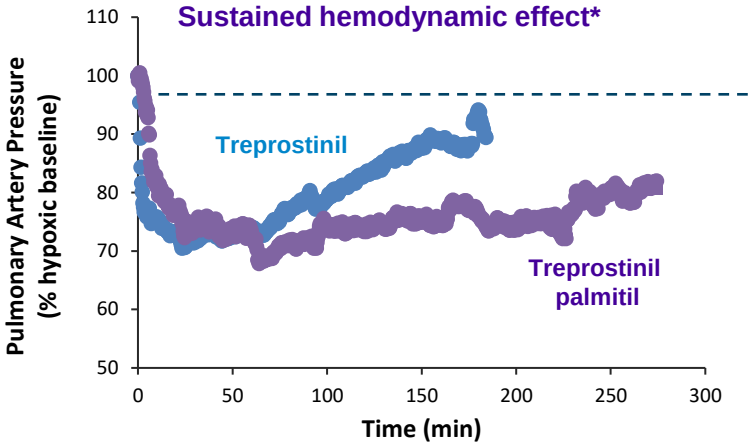
*Previously, treprostinil palmitil was formulated as a nebulized suspension (treprostinil palmitil inhalation suspension, or TPIS)

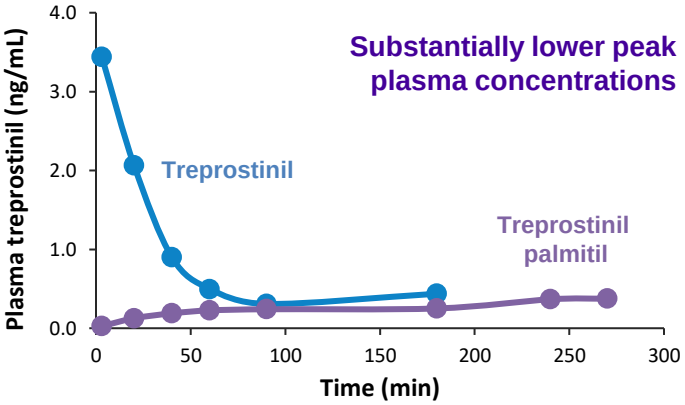

Insmed®
R&D DAY
September 30, 2020

Prolonged Lung Residence Translated to Sustained Efficacy with Low Systemic Treprostinil Concentrations

- Treprostinil palmitil and treprostinil delivered as nebulized inhalation suspension and inhalation solution, respectively
- Pulmonary vasodilator activity and plasma concentrations measured in anesthetized, ventilated rats under hypoxic conditions before and after nebulization of drugs; delivered pulmonary dose was 6 µg/kg treprostinil and the molar equivalent for treprostinil palmitil (~9.4 µg/kg); PAP is a percent of hypoxic baseline







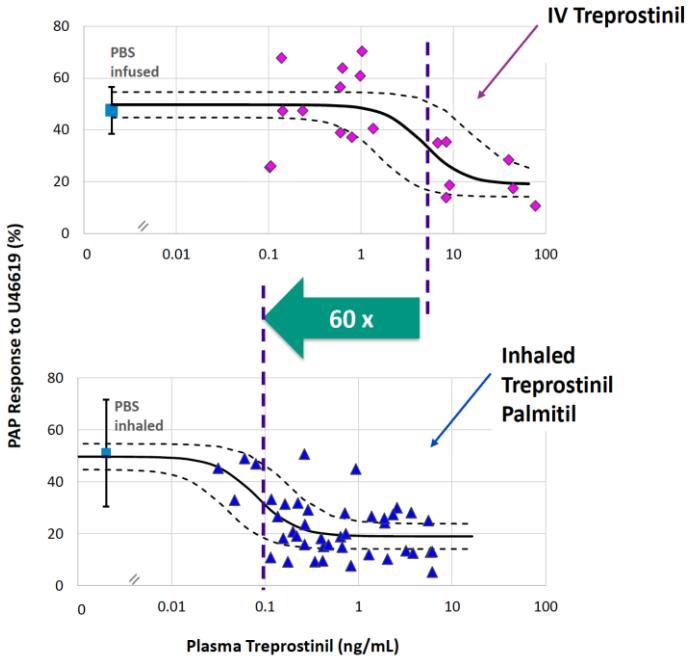
** Each data point represents an average of 20-seconds of data*

F.G. Leifer et al. (2018) Drug Res 68: 605-614

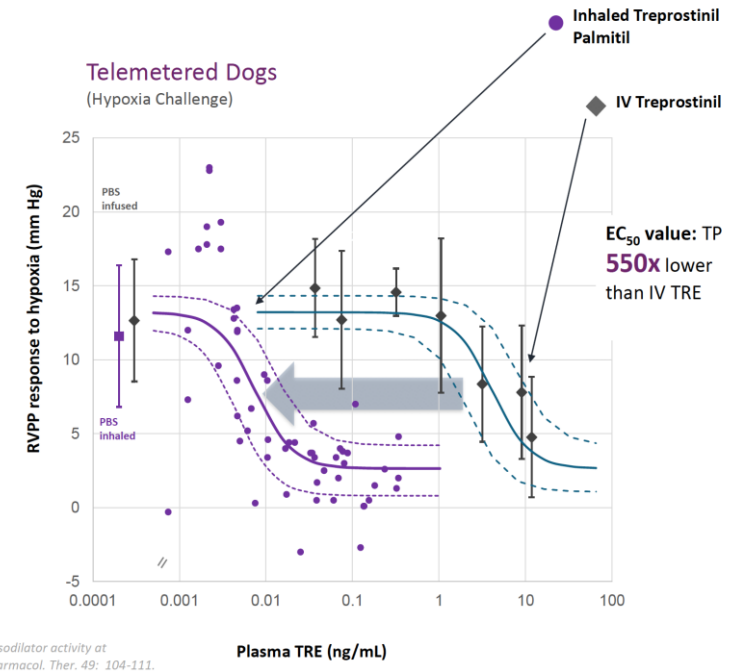
LOCAL PHARMACODYNAMIC EFFECT:

Treprostinil Palmitil Exhibited Local Vasodilatory Activity in the Lung, Beyond that which can be Attributed to the Circulating Treprostinil

RAT Thromboxane Mimetic Model



DOG Hypoxemia Model



*asodilator activity at
harmacol. Ther. 49: 104-111.*

TPIP at High Dose

Showed Superior Effect Overall in the Sugen-Hypoxia Rat Model for PAH

Parameter value = (Value – Value of Normal) /
(Value of Vehicle – Value of Normal)

- Normal
- TPIP LD
- TPIP HD
- TRE INH
- TRE IV
- Selexipag
- Vehicle

Fulton Index = weight ration
Right Ventricle / (Left Ventricle + Septum)

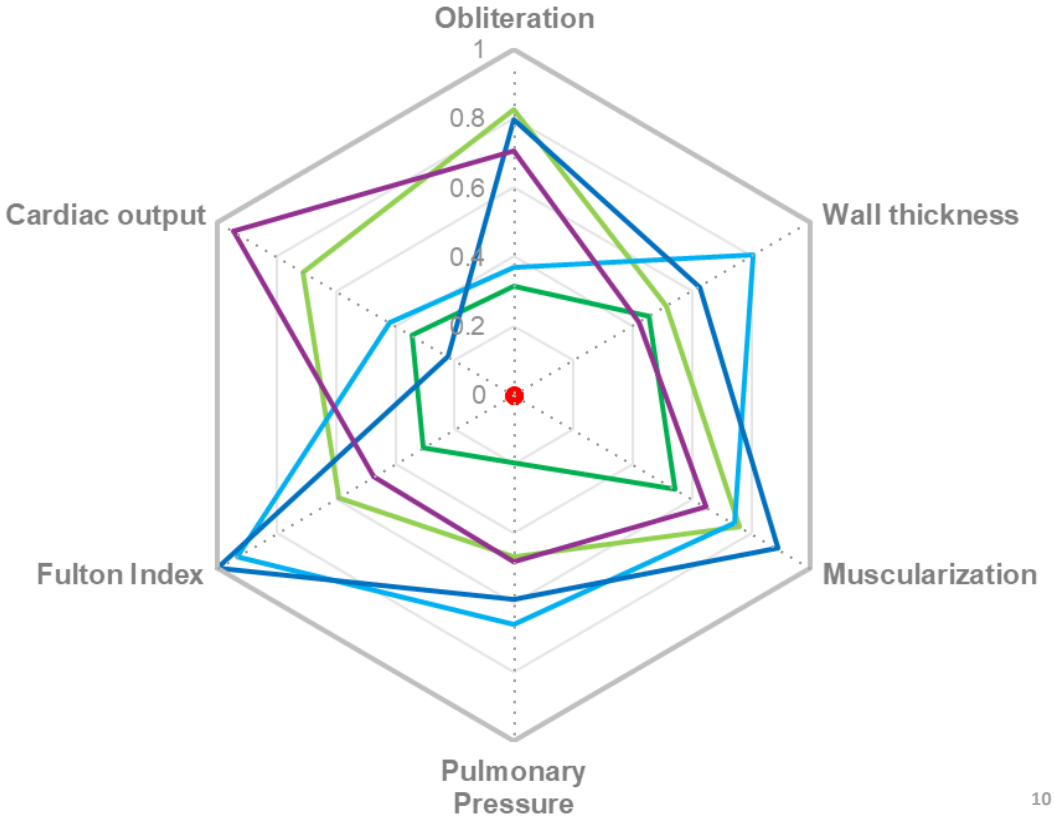
Pulmonary Pressure
mean Pulmonary Arterial Pressure

Obliteration
% of non-obliterated vessels

Wall thickness
Small vessel wall thickness

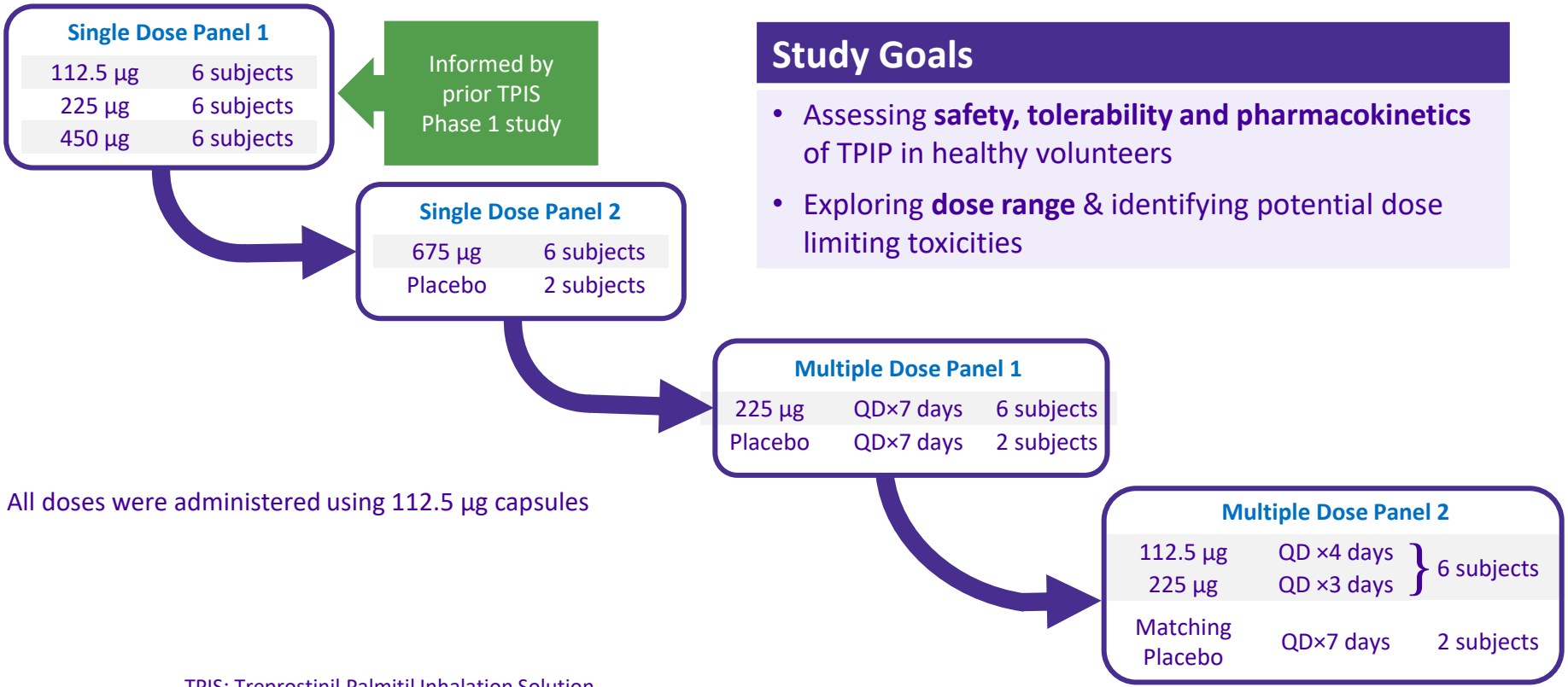
Muscularization
% of muscularized vessels

Cardiac Output
amount of blood pumped by the heart per minute



TPIP Phase 1 Study

INS1009-102 Study Design



Study Goals

- Assessing **safety, tolerability and pharmacokinetics** of TPIP in healthy volunteers
- Exploring **dose range** & identifying potential dose limiting toxicities

All doses were administered using 112.5 µg capsules

TPIS: Treprostinil Palmitil Inhalation Solution
TPIP: Treprostinil Palmitil Inhalation Powder
QD: Quaque Die or Once-a-day

SAD Cohorts: Treatment Emergent Adverse Events (TEAEs)

TEAEs were Consistent with Inhaled Prostanoid and Mostly Mild

	112.5 µg (6)	225 µg (6)	450 µg (6)	675 µg (6)	Placebo (2)	Total (26)
Completed (%)	6 (100)	6 (100)	6 (100)	6 (100)	2 (100)	26 (100)
TEAEs (%)	4 (66.7)	3 (50.0)	4 (66.7)	6 (100)	0 (0.0)	17 (65.4)
Moderate TEAEs (%)	0 (0.0)	1 (16.7)	0 (0.0)	3 (50.0)	0 (0.0)	4 (15.4)
Prostanoid-Related AEs						
Dizziness (%)	1 (16.7)	1 (16.7)	2 (33.3)	3 (50.0)	0 (0.0)	7 (26.9)
Nausea (%)	0 (0.0)	1 (16.7)*	2 (33.3)	1 (16.7)	0 (0.0)	4 (15.4)
Hypotension (%)	0 (0.0)	1 (16.7)	1 (16.7)	2 (33.3)*	0 (0.0)	4 (15.4)
Headache (%)	0 (0.0)	0 (0.0)	1 (16.7)	1 (16.7)	0 (0.0)	2 (7.7)
Vomiting (%)	0 (0.0)	1 (16.7)*	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.8)
Respiratory / Other Notable AEs						
Cough (%)	2 (33.3)	2 (33.3)	3 (50.0)	4 (66.7)	0 (0.0)	11 (42.3)
Throat Irritation (%)	2 (33.3)	2 (33.3)	1 (16.7)	0 (0.0)	0 (0.0)	5 (19.2)
Chest Discomfort (%)	1 (16.7)	0 (0.0)	1 (16.7)	1 (16.7)*	0 (0.0)	3 (11.5)
Low O_2 Saturation	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)*	0 (0.0)	1 (3.8)
Dyspnea	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	1 (3.8)

* Moderate TEAEs: 225 µg – 1 subject with nausea and vomiting; 675 µg – 2 subjects with hypotension, 1 subject with chest discomfort, low oxygen saturation and dyspnea

Includes all AEs that occurred in more than two subjects, as well as others of interest

MAD Cohorts: Subject Disposition, TEAEs

Lower TEAE Frequency with Titration and Mostly Mild

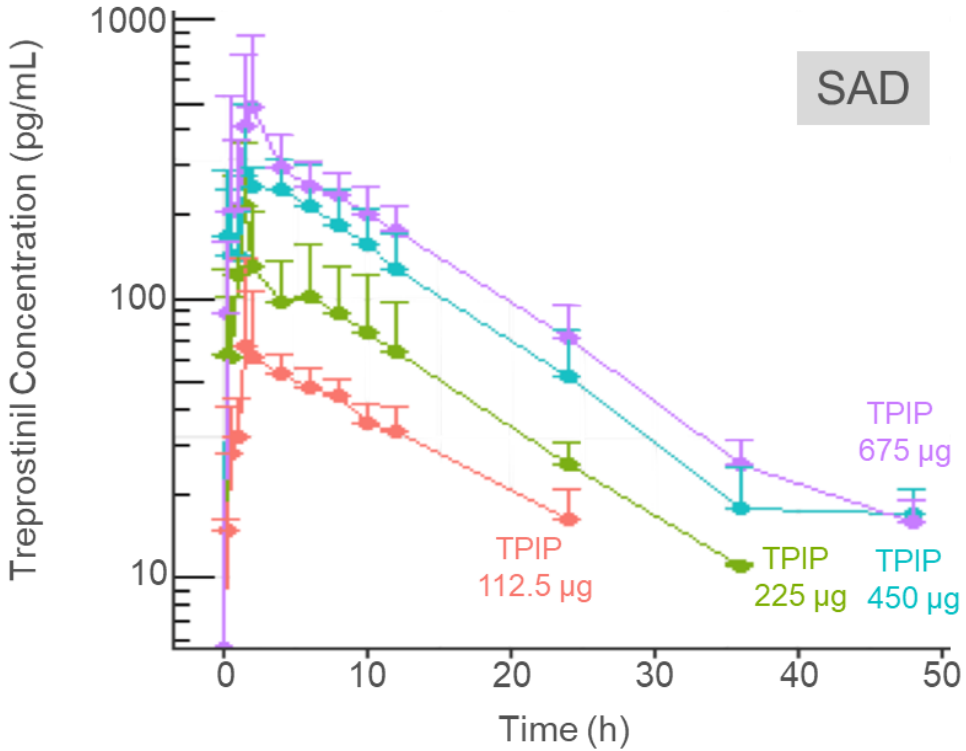
	225 µg (6)	112.5 – 225 µg (6)	Placebo (4)	Total (15)
Completed (%)	5 (83.3)	6 (100)	4 (100)	15 (93.8)
TEAEs (%)	6 (100.0)	4 (66.7)	2 (50.0)	12 (75.0)
Moderate TEAEs (%)	3 (50.0)	0 (0.0)	0 (0.0)	3 (18.8)
Prostanoid-Related AEs				
Headache (%)	4 (66.7)	2 (33.3)	0 (0.0)	6 (37.5)
Nausea (%)	3 (50.0)	1 (16.7)	0 (0.0)	4 (25.0)
Dizziness (%)	2 (33.3)	1 (16.7)	0 (0.0)	3 (18.8)
Syncope (%)	1 (16.7)*	0 (0.0)	0 (0.0)	1 (6.3)
Diarrhea (%)	1 (16.7)	0 (0.0)	0 (0.0)	1 (6.3)
Abdominal Pain (%)	1 (16.7)	0 (0.0)	0 (0.0)	1 (6.3)
Hypotension (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Respiratory AEs				
Cough (%)	6 (100.0)	1 (16.7)	2 (50.0)	9 (56.3)
Throat Irritation (%)	1 (16.7)*	0 (0.0)	0 (0.0)	1 (6.3)
Chest Discomfort (%)	1 (16.7) | 1 (16.7)*	2 (33.3)	0 (0.0)	4 (25.0)

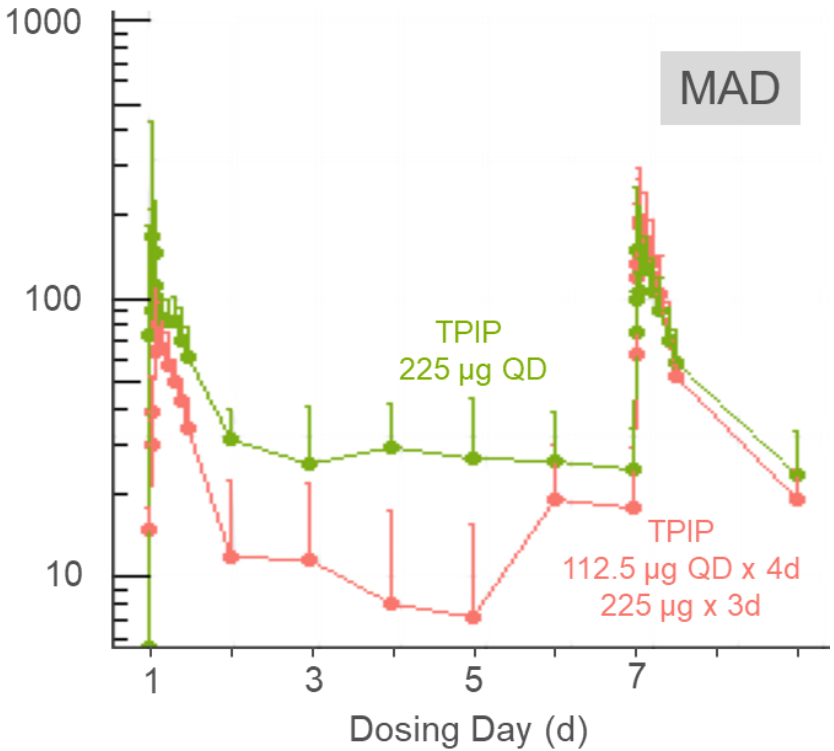
* Moderate TEAEs: 225 µg – 1 subject with chest discomfort (subject discontinued day 2), 1 subject with throat irritation (day 2-7), 1 subject with syncope (day 1)

Includes all AEs that occurred in more than two subjects, as well as others of interest

INS1009-102 Study Plasma Treprostinil Concentrations

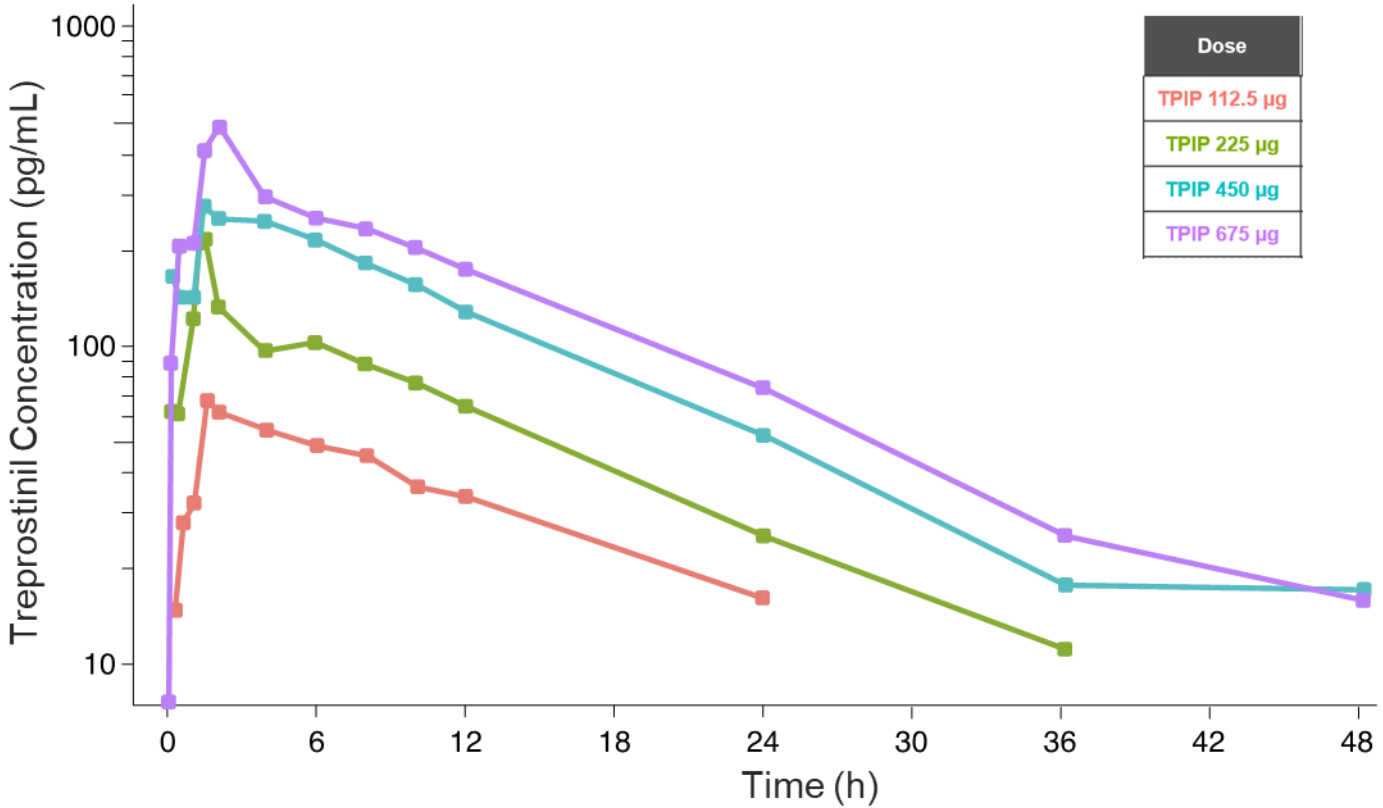
Dose proportional C_{max} and AUC





TPIP showed substantially lower C_{max} and longer half-life

Supports the potential for improved tolerability, efficacy and convenience



TPIP from Study INS1009-102, Tyvaso from Han Tyvaso from Han D, et al. Eur Respir J 2016 48: PA2403

TPIP showed substantially lower C_{max} and longer half-life

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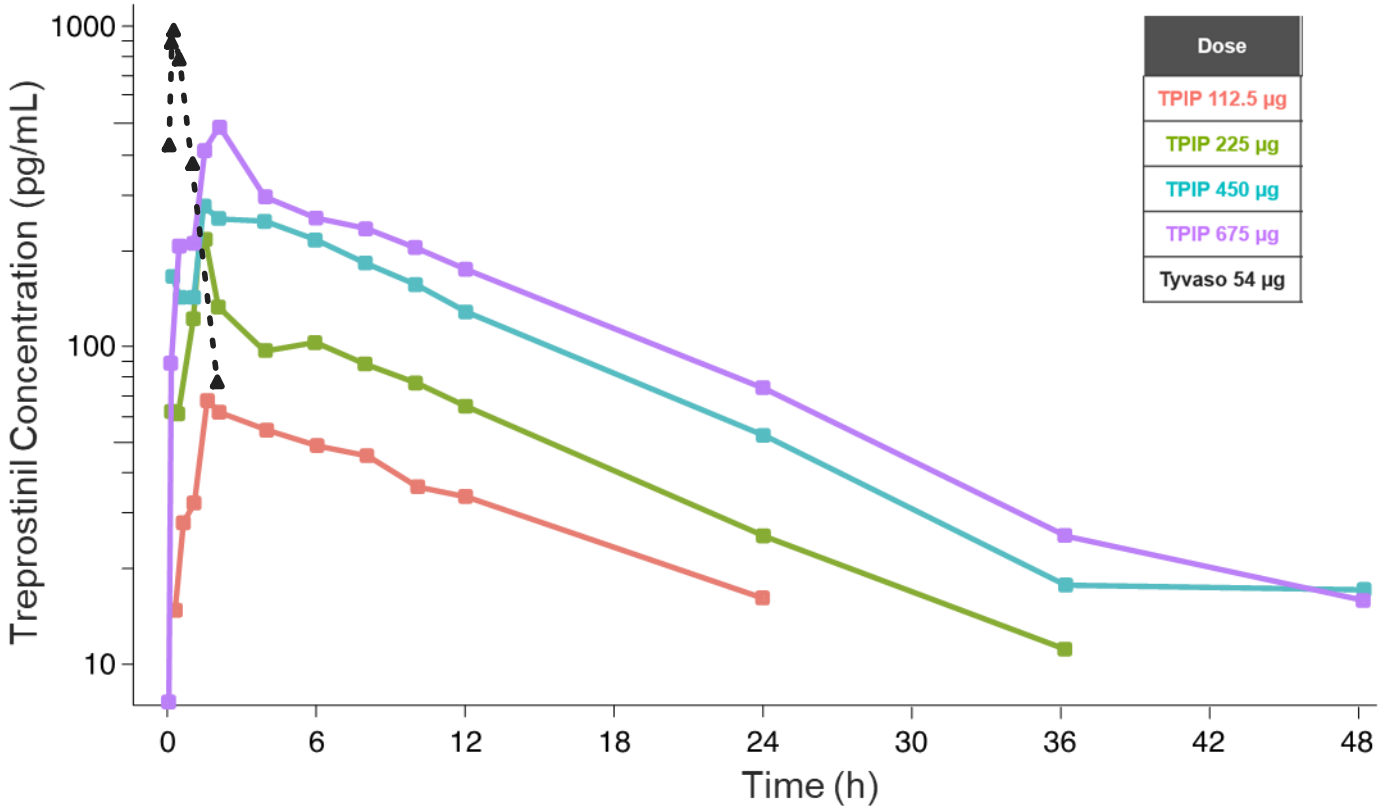

TPIP from Study INS1009-102, Tyvaso from Han Tyvaso from Han D, et al. Eur Respir J 2016 48: PA2403

Key Takeaways from TPIP Phase 1 study

1. Safety profile was generally **well tolerated,** AEs were mild and **consistent with inhaled prostanoid**
2. Tolerability was improved with **an up-titration approach**
3. Findings suggest TPIP may be safely **dosed at nominal doses far in excess of Tyvaso**
4. PK supports development of TPIP with **once daily dosing**
5. TPIP showed substantially **lower C_{max} and longer half-life** than that of Tyvaso
6. Future studies would use an up-titration dosing schedule to the maximum individual tolerated dose **exceeding 600 µg once daily**

Inhaled Treprostinil

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doi:10.1016/j.jacc.2006.06.062

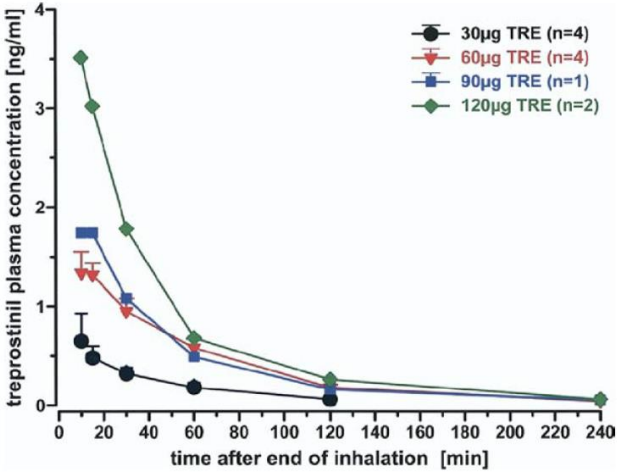
Pulmonary Vascular Disease

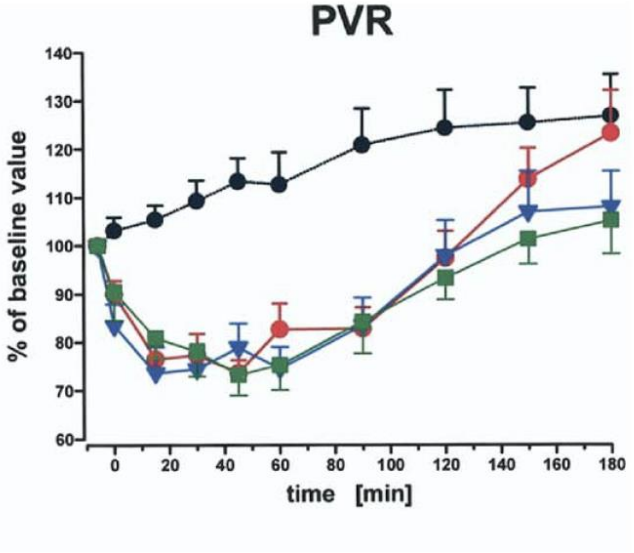
Favorable Effects of Inhaled Treprostinil in Severe Pulmonary Hypertension

Results From Randomized Controlled Pilot Studies

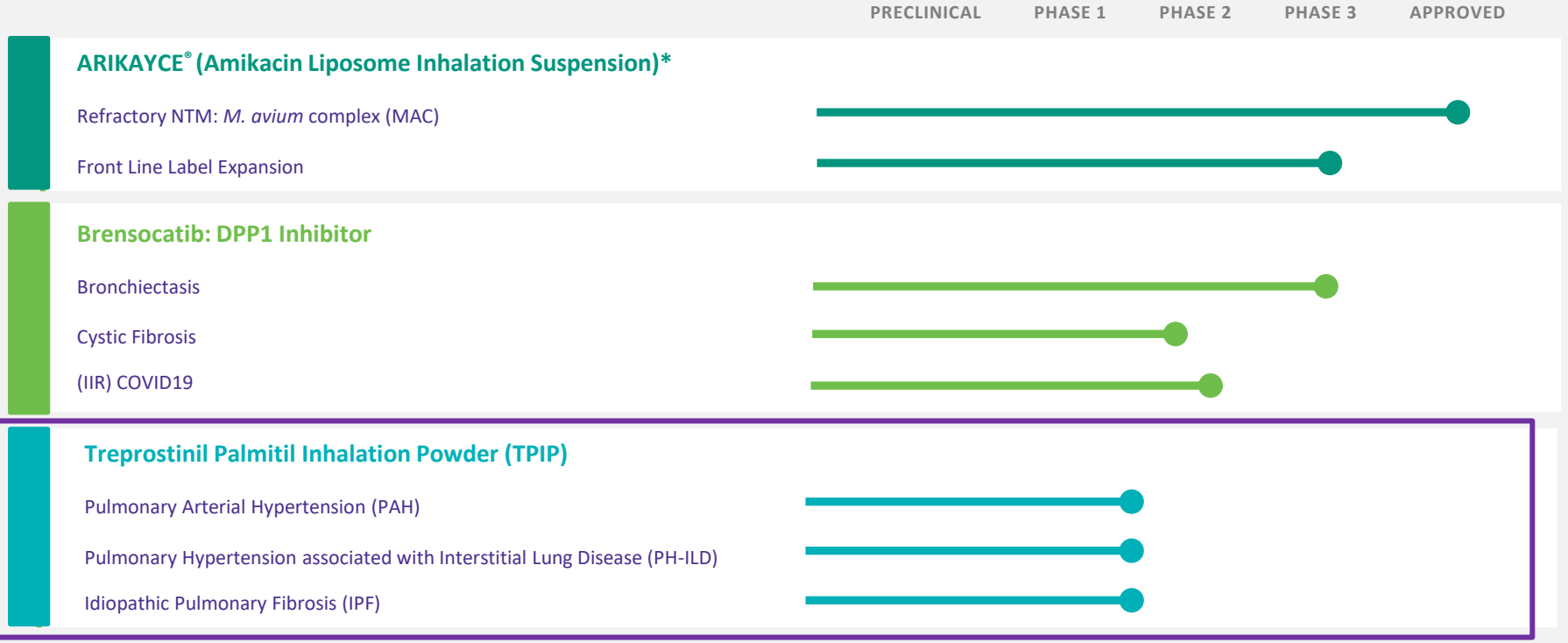
Robert Voswinckel, MD,* Beate Enke, MD,* Frank Reichenberger, MD,* Markus Kohstall, MD,* Andree Kreckel, MD,* Stefanie Krick, MD,* Henning Gall, MD,* Tobias Gessler, MD, PHD,* Thomas Schmehl, PHD,* Hossein A. Ghofrani, MD,* Ralph Theo Schermuly, PHD,* Friedrich Grimminger, MD, PHD,* Lewis J. Rubin, MD,† Werner Seeger, MD,* Horst Olschewski, MD*‡

Giessen, Germany; La Jolla, California; and Graz, Austria





Three Pillars of Value Creation



** In the U.S., as a condition of accelerated approval, Insmed is conducting an additional clinical study to support full approval. Full approved has been granted by the European Commission.*

Comparison of Prostacyclin Analogs/Agonists

Approved Therapies vs. TPIP (investigational product candidate)

	Remodulin®	Tyvaso®	Orenitram®	Uptravi®	TPIP
Route of administration	IV or Subcutaneous	Inhaled (nebulized)	Oral	Oral	Inhaled **(dry powder)**
Dosing frequency	Continuous	4x per day	2x or 3x per day	2x per day	**Once daily**
Dose-limiting side effects	Yes	Yes	Yes	Yes	To be evaluated in Phase 2 (encouraging preclinical & P1 data)
Efficacy in PAH (WHO Group 1)	Yes	Yes	Yes	Yes	
Proven to slow disease progression in PAH	No	No	Yes (but only as add-on to monotherapy)	Yes	To be evaluated in Phase 3 (encouraging Preclinical & P1 data)
Efficacy in PH-ILD (WHO Group 3)	No data	Yes	No data	No data	Potential to pursue in parallel to PAH
Efficacy in IPF	No data	TBC in upcoming TETON study	No data	No data	

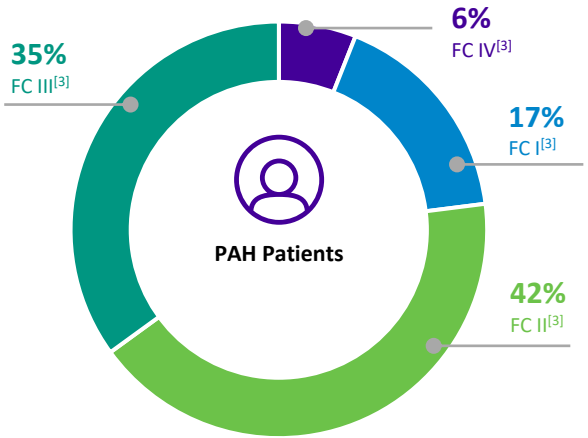
Market Opportunity

United Therapeutics' Viewpoint… Building On Their Precedent

Innovate → Grow → Expand

Current PAH Landscape

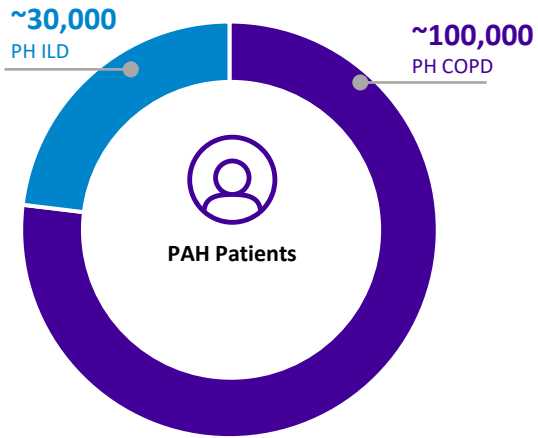
Prevalence of PH[1]
WHO Group 1[2]
[in U.S. as of 2019]



>45,000 Patients in U.S.

New PH Opportunities

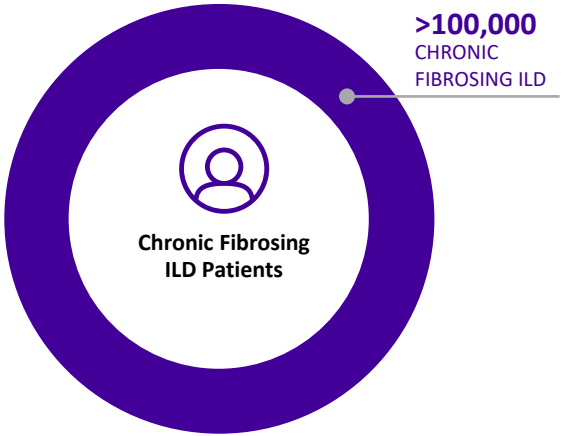
Prevalence of PH ILD[4]
& PH COPD[5] in WHO Group 3[2]
[in U.S. as of 2019]



>130,000 Patients in U.S.

Opportunities Beyond PH

Prevalence of Chronic
Fibrosing ILD[2]
[in U.S. as of 2019]



>100,000 Patients in U.S.

Slide information sourced from United Therapeutics November 2020 Corporate Presentation

[1] PH – Pulmonary Hypertension [2] Estimated patient populations based on United Therapeutics internal market research [3] The World Health Organization [WHO] created a system of four functional classes [FC] for patients with PAH. Class I means fewer symptoms and less restriction of activity. Class I symptoms are considered the least severe, and Class IV symptoms the most severe. [4] ILD=Interstitial Lung Diseases. [5] COPD] Chronic Obstructive Pulmonary Disease


Thank You
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