



# Meaningfully Improving the Lives of Patients with Rare Cardiopulmonary Disease

Targeting the Hyperproliferative Cause  
of Pulmonary Arterial Hypertension

May 2024

Nasdaq: AVTE

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# Experienced Management Team

## Timothy Noyes

### Chief Executive Officer

- 30 years' commercial experience in pharma and biotech, including Merck, Genzyme, Proteon
- Extensive launch planning and commercial launch experience

## Ben Dake, PhD

### President & Founder

- Entrepreneur, Cancer Biologist and Investor
- Conceptualized AV-101 and secured up to \$79M in financing for Aerovate

## Hunter Gillies, MB ChB

### Chief Medical Officer

- Led AMBITION trial for Gilead that established current first-line PAH combination therapy
- Led successful Phase 2 and 3 trials for PAH product candidates at Pfizer and Gilead

## Donna Dea

### Head of Regulatory

- 35 years of pharmaceutical experience at AstraZeneca
- 20 years of global regulatory experience designing/ implementing strategies resulting in approval of treatments for asthma, COPD, rhinitis and others

## Susan Fischer

### EVP, Clinical Ops.

- 20 years' experience in clinical operations in both academic and the pharmaceutical industry.
- Previously built/led clinical ops teams at Syndax, EMD Serono, Acetylon

## George Eldridge

### Chief Financial Officer

- 25 years' experience in biotech, with both public and private companies, including Curis, Targanta, Proteon
- Extensive background raising capital in private, IPO and follow-on settings, investment banking and M&A

## Ralph Niven, PhD

### Chief Development Officer

- 25 years' broad expertise in translational medicine and inhalation dosage forms
- Managed experimental and clinical development at public and private companies, including Amgen, AIR and Novartis

## Timothy Pigot

### Chief Commercial Officer

- 25 years' experience in biotech and pharma working to launch and commercialize a range of products
- 10 years' experience in PAH overseeing the US launches of Revatio and Leairis while at Pfizer and Gilead Sciences, respectively

## Marco Verwijs

### Chief Technical Officer

- 15 years' experience developing drugs from clinical product development thru commercial launch
- Proven leader in drug product scale-up and validation.

# Aerovate: An Inventive Way Forward in PAH

## Demonstrated Clinical Benefit

The molecule in AV-101, imatinib, already has shown clinical benefit in a Phase 3 clinical trial conducted by Novartis of oral imatinib mesylate in PAH patients on top of two or more standard of care therapies.

Unfortunately, AEs with oral imatinib were common and development was discontinued

## Inventive Solution

Anti-proliferative targeted inhaled dry powder PAH product candidate AV-101 designed to provide robust clinical benefit of imatinib without systemic AEs observed with oral imatinib

## Significant Unmet Need

Despite three drug classes approved, 5-year survival for newly diagnosed PAH patients is 61%

## Efficient Execution

FDA and EMA orphan designation for AV-101 for the treatment of PAH

Phase 1 SAD/MAD in healthy volunteers complete

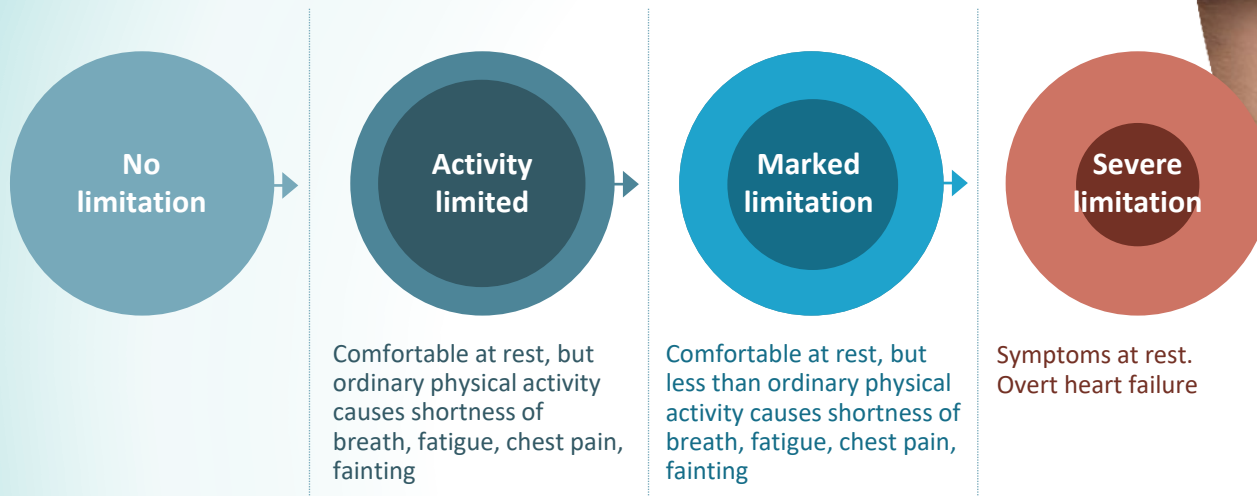
Phase 2b portion fully enrolled of seamless Ph2b/3 IMPAHCT trial and already enrolling in Phase 3 portion

Ph2b data expected in June 2024

## Established Market

\$6B+ market, yet outcomes are poor

# Relentless Disease Progression Impairs Daily Life



Despite standard of care (SOC) most patients progress to overt heart failure

# Pulmonary Arterial Hypertension

**~ 70,000**

People with PAH  
in the US/EU

**~ 35,000**

People with PAH  
in the US

**\$6B+**

Global annual drug  
spending

**65-80%**

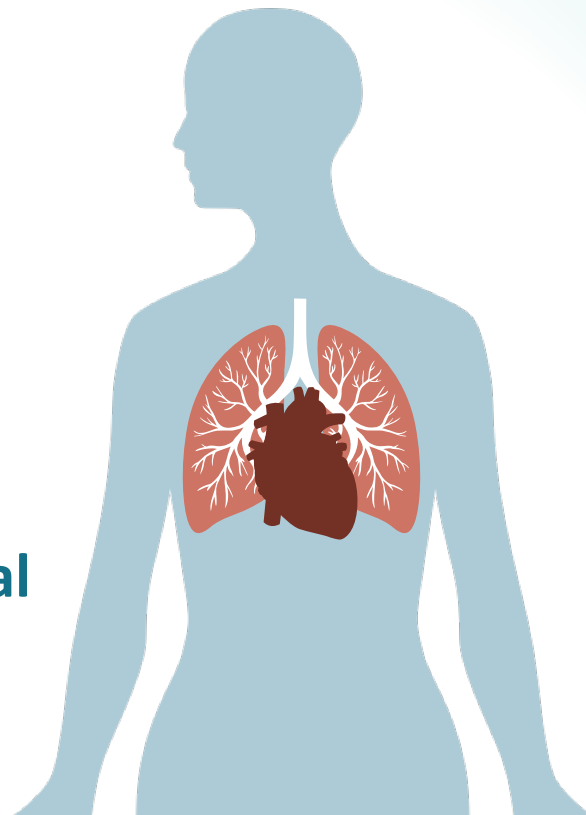
Female

**53 years**

Average age at  
diagnosis

**61-65%  
5-year survival**

Newly diagnosed and  
prevalent patients



# Patient Outcomes Are Poor Despite \$6B+ PAH Vasodilator Market

~65% patients take

**2-3 drugs**

5-year survival

**61-65%**

for newly diagnosed and  
prevalent patients

Prostanoids

**\$3.0B**

NO pathway

**\$0.7B**

SOC  
Vasodilators

ERAs

**\$2.4B**

No approved PAH therapy primarily addresses  
abnormal cellular proliferation



# Reinventing Imatinib From a Cancer Drug to a Potential PAH Therapy



# Phase 3 IMPRES Trial: Oral Imatinib Demonstrated Improvement on Top of Maximal Background

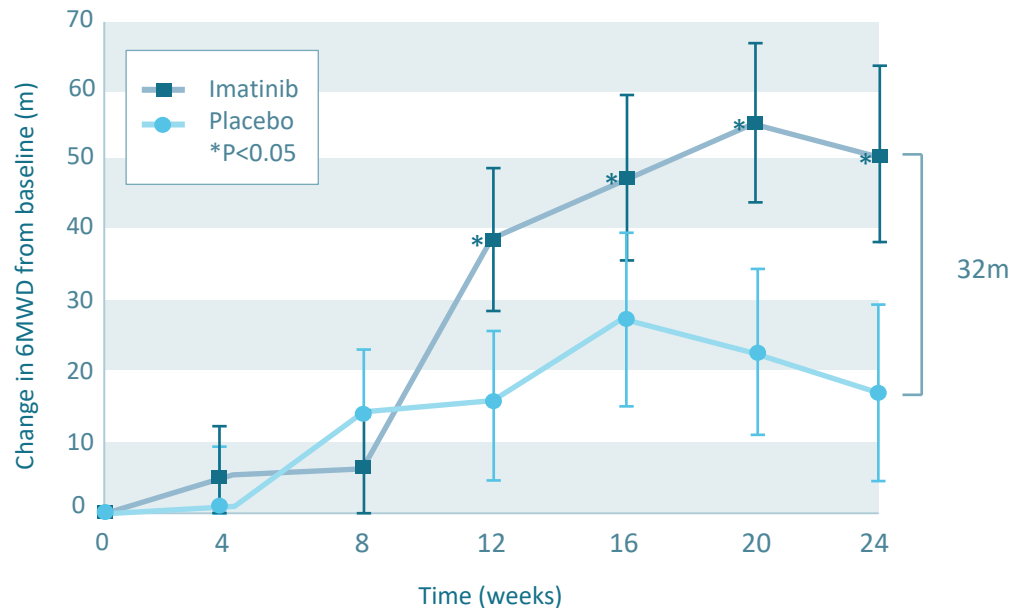
Novartis global Phase 3 trial  
(n=202) of oral imatinib

Required to be on at least 2 SOC  
PAH drugs

WHO functional class II- IV

Statistically significant and clinically  
meaningful benefit on primary  
endpoint 6MWD after 24 weeks

6MWD is an accepted endpoint for  
approval in PAH



(Adapted from Circulation. 2013;127:1128-1138.)

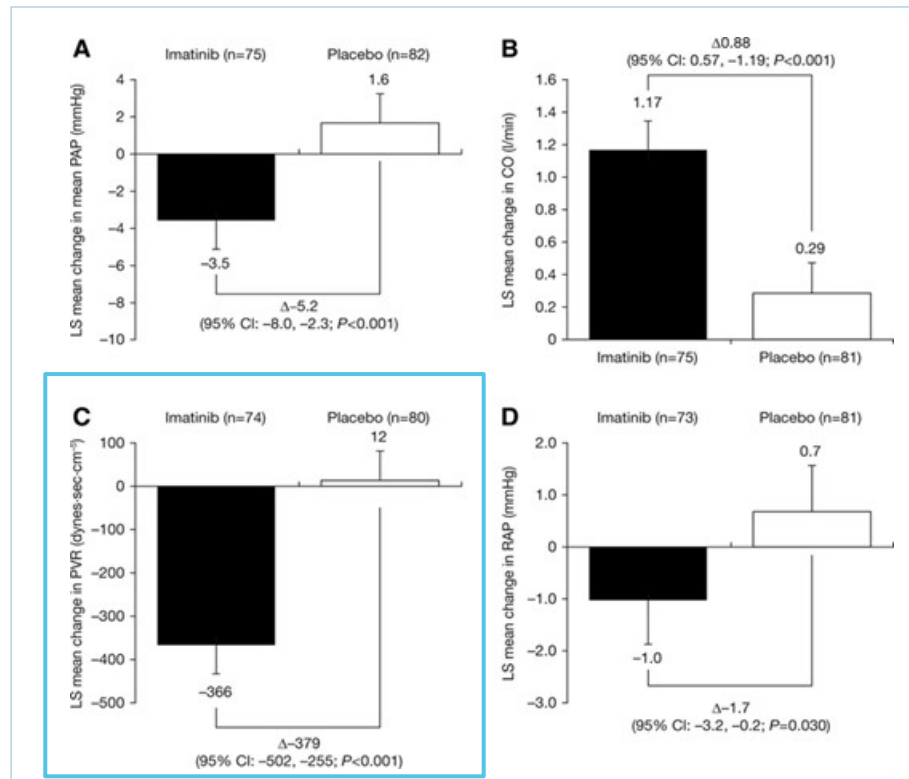
# Phase 3 IMPRES Trial: Benefit Consistent Across Secondary Endpoints

## Secondary Endpoints (24wk)

Demonstrated robust hemodynamic effect

- (A) Decreased mean pulmonary artery pressure
- (B) Increased cardiac output
- (C) Pulmonary vascular resistance (PVR) dropped 32% ( $P < 0.001$ ), a validated efficacy endpoint typically used for dose-finding
- (D) Right atrial pressure lowered

PVR is the primary endpoint for Aerovate's Phase 2b



(Circulation. 2013;127:1128-1138.)

# Oral Imatinib Caused Systemic Adverse Events

	Imatinib n=103 (%)	Placebo n=98 (%)
Adverse Event <sup>+</sup>	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)
Headache	25 (24)	22 (22)
Dyspnea	19 (18)	13 (13)
Nasopharyngitis	18 (18)	19 (19)
Hypokalemia	16 (16)	3 (3)
Anemia	14 (14)	3 (3)
Cough	11 (11)	15 (15)
Fatigue	11 (11)	7 (7)
Face edema	10 (10)	1 (1)
Muscle spasms	10 (10)	2 (2)

	Imatinib n=103 (%)	Placebo n=98 (%)
Serious Adverse Event <sup>+</sup>	45 (44)	29 (30)
Worsening of pulmonary hypertension	6 (6)	8 (8)
Anemia	7 (7)	1 (1)
Dyspnea	6 (6)	2 (2)
Peripheral edema	6 (6)	0
Presyncope	5 (5)	0
Diarrhea	3 (3)	2 (2)
Device-related infection	3 (3)	0
Syncope	1 (1)	5 (5)
Subdural hematoma <sup>*</sup>	2 (2)	0

<sup>\*</sup> In long-term extension portion of the trial, 6 additional patients experienced a subdural hematoma.

<sup>+</sup> Individual adverse events are shown if they occurred in >10% in the imatinib group. Individual serious adverse events are shown if they occurred in ≥3 patients in either group.

(Circulation. 2013;127:1128-1138.)

# AV-101

Potential Targeted Treatment for PAH



# AV-101

AV-101 is a combination product comprised of a proprietary dry powder imatinib formulation in a capsule delivered by a dry powder inhaler designed to:

- Deliver drug to the lungs
- Limit systemic exposure
- Be easily administered

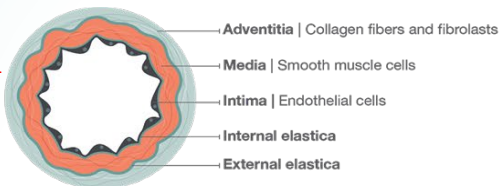
Imatinib molecular structure unmodified



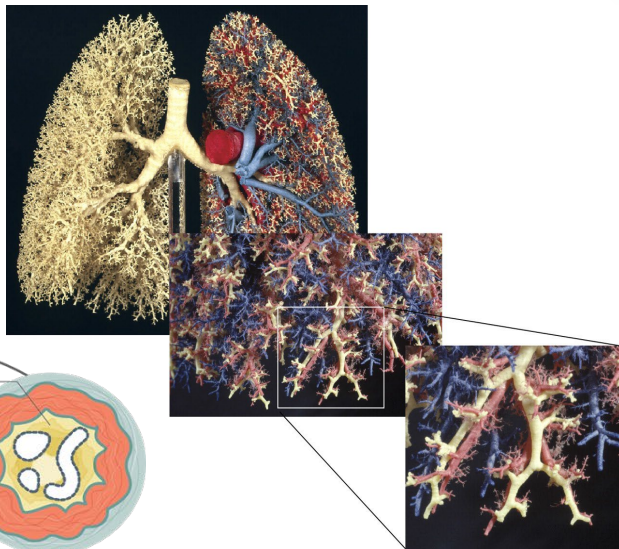
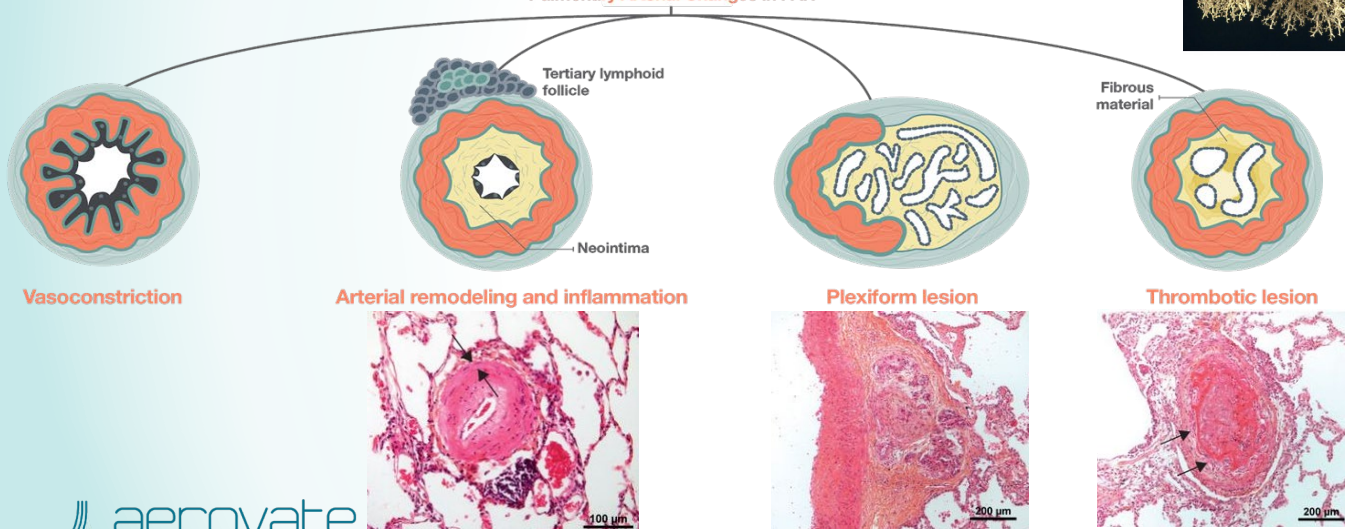
# PAH is a Disease of All Layers of the Pulmonary Arteries

## Normal Pulmonary Artery<sup>1</sup>

Thin media and monolayer of endothelial cells on top of wavy elastica



## Pulmonary Arterial Changes in PAH



Latex cast of human airway (white), arterial tree (red), and venous tree (blue)<sup>3</sup>

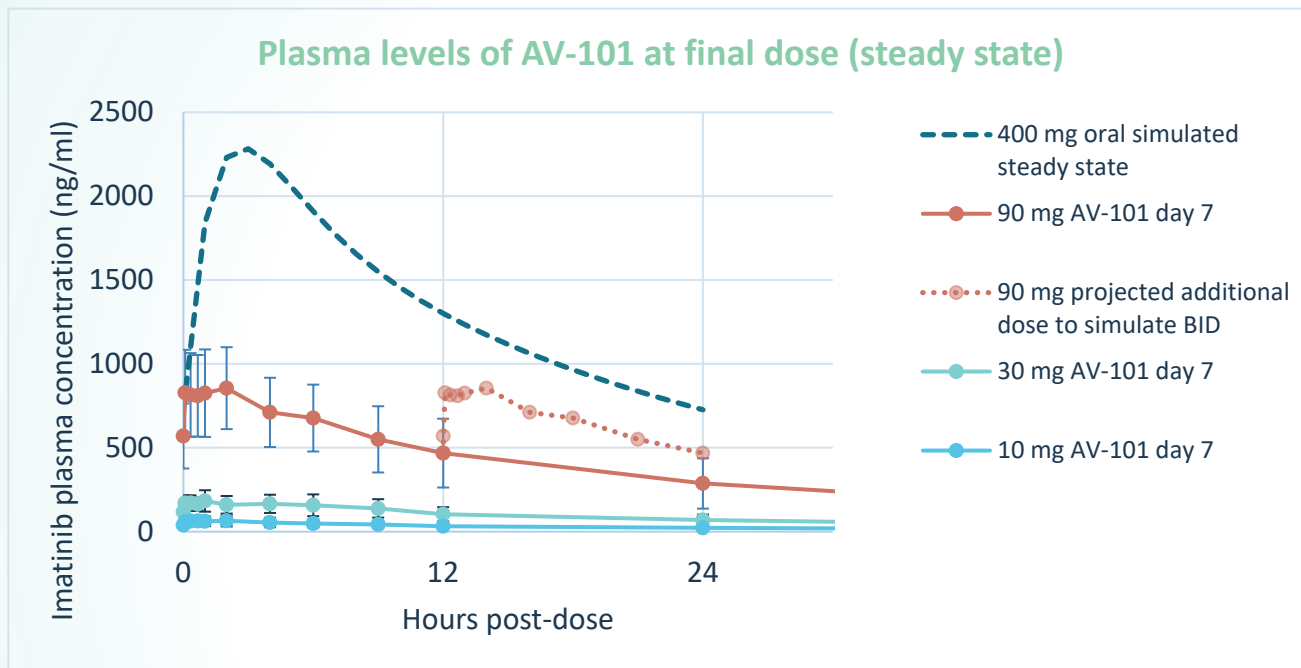
# AV-101 Phase 1 Trial

A single and multiple ascending dose Phase 1 study (n=82) in healthy volunteers to determine safety and tolerability

SAD	MAD	STUDY ASSESSMENTS
Five AV-101 cohorts from 1 mg to 90 mg n=6 Active / 2 Placebo	Seven days of BID dosing	Vital Signs
400 mg imatinib tablet for systemic exposure comparison n=8	Low dose 10 mg	Pulmonary Function Testing (FEV1 and FVC)
	Med dose 30 mg	Oxygen Saturations
	High dose 90 mg	QTc
n=8 per cohort	n=12 per cohort; 9 Active / 3 Placebo	Adverse Events



# AV-101 Phase 1 Trial: Lower Systemic Exposures Observed



Systemic exposures for all doses of AV-101 observed to be lower than simulated steady-state exposure of 400 mg of oral imatinib

# AV-101 Phase 1 Tolerability Profile

## AV-101 was generally well tolerated

- No serious adverse events were reported
- No change in pulmonary function, oxygen saturation, and QTc interval
- Most AEs mild to moderate
- One discontinuation due to vomiting on Day 1 in the MAD 90 mg Cohort
- Most common AE, cough, was at max dose and limited to within 30 minutes of dosing

Adverse Event n(%)	10 mg (n=8)	30 mg (n=9)	90 mg* (n=9)
Cough	1 (13)	1 (11)	5 (56)
Persistent cough	-	-	-
Headache	-	-	4 (44)
Nausea	-	-	2 (22)
Chest discomfort	-	-	2 (22)
Throat irritation	-	1 (11)	1 (11)
Musculoskeletal pain	-	-	2 (22)

Single incidence AEs: Vomiting (discontinued), Dysgeusia, Musculoskeletal chest pain, Nasal congestion, Oropharyngeal pain, Back pain, Abdominal pain, Covid-19, Presyncope, Alanine aminotransferase increased

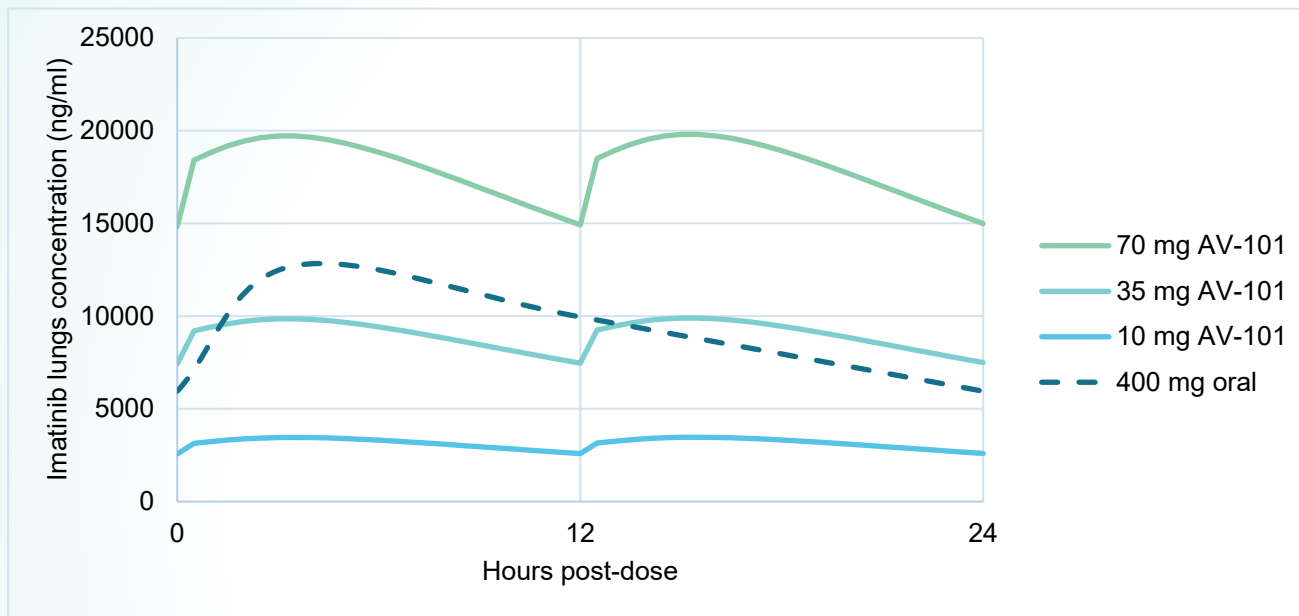
\*90mg dose was administered as 9 x 10mg capsules

# Phase 2b Dose-Ranging Trial

- Placebo controlled dose-ranging study
  - 10 mg, 35 mg and 70 mg AV-101 BID for 24 weeks
  - Targeting 200 patients across 4 dose groups
- Multicenter international trial
- Two or more background PAH therapies
- Functional class II - IV
- Primary endpoint: change in pulmonary vascular resistance (PVR) at 24 weeks
  - Statistically significant improvement on PVR already demonstrated with oral imatinib in multiple third-party clinical trials
  - Validated endpoint
  - Powered to detect statistically significant change
- Key secondary endpoints: Change in 6MWD, NTproBNP, QoL



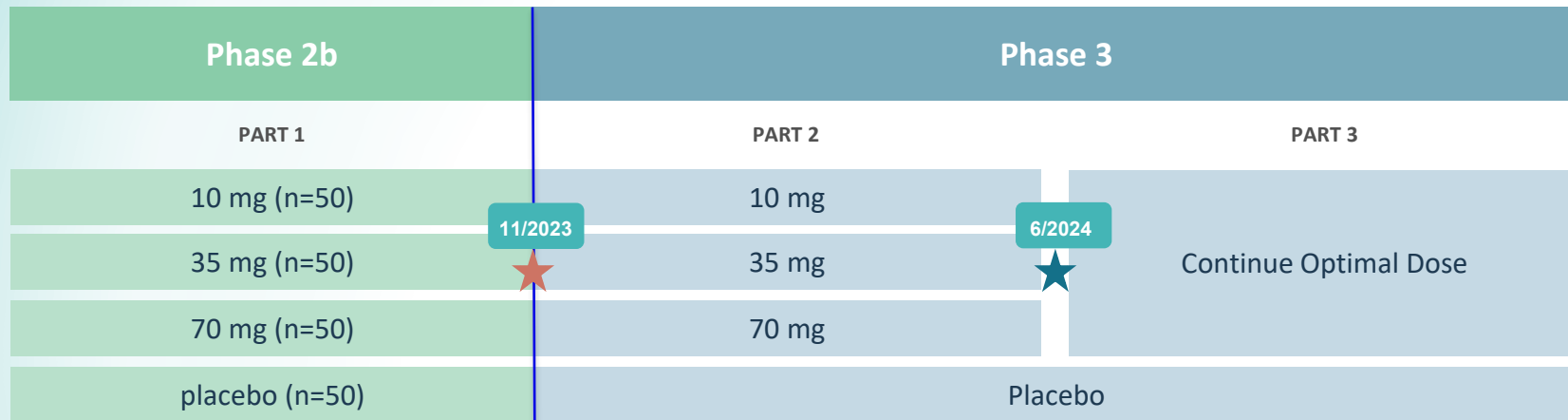
# Expected AV-101 Lung Exposures of IMPAHCT Doses, Extrapolated based on Phase 1 Results



Predicted lung concentrations of Phase 2b doses of AV-101 in IMPAHCT trial overlap or surpass 400 mg oral imatinib dose

Predicted lung concentrations extrapolation based on a published PK model using plasma levels observed in Phase 1 trial

# IMPAHCT Phase 2b/3 Seamless Trial of AV-101



- All patients are treated for 24 weeks
- 6MWD is primary endpoint in Phase 3

★ Phase 3 enrollment began immediately upon completion of Phase 2b enrollment

★ Phase 3 dose selected based on Phase 2b data after 24 weeks of follow up

# Key Baseline Characteristics Among Recent PAH Clinical Trials

Baseline characteristics with first 147 patients from IMPAHCT Ph2b compared with select PAH trials

Measure	IMPAHCT N=147	PULSAR N=106	STELLAR N=323	TORREY N=86
PVR, dynes.sec.cm <sup>-5</sup> , mean	790	779	764	669
6MWD, m, mean	394	397	401	408
WHO FC II/III	49%; 51%	53%; 47%	49%; 51%	68%; 32%
NTproBNP, pg/mL, mean	754	908	1121	628
Age, years, mean	47	48	48	49
Gender	F82% ; M18%	F87%; M13%	F 79%; M21%	F91%; M9%
IPAH or HPAH	71%	74%	77%	66%
Non-IPAH or HPAH	29%	26%	23%	34%
Mono/Double/triple background	0%; 40%; 59%	9%; 35%; 56%	4%; 35%; 61%	3%; 40%; 57%
Mean PA pressure, mmHg	50.9	52.4	52.6	Not reported
Cardiac index, L/min/m <sup>2</sup>	2.7	2.6	2.7	Not reported

The data in the chart above are based on a cross-trial comparison and not a head-to-head clinical trial. Such data may not be directly comparable due to differences in trial design, study protocols, conditions and patient populations.

# Phase 2 Trials for Non-Vasodilator Therapies

	Oral Imatinib	Merck/Acceleron Sotatercept (activin trap)		Gossamer Seralutinib (TKI)
	Phase 2	PULSAR (Ph2)		TORREY (Ph2)
		Low dose	High dose	
PVR	-26.0%	-18.5%	-31.8%	-14.3%
6MWD	+21.7 m P=0.21	+29.4 m P=0.02	+21.4 m P=0.08	+6.5m P=0.597

The data in the chart above are based on a cross-trial comparison and not a head-to-head clinical trial. Such data may not be directly comparable due to differences in trial design, study protocols, conditions and patient populations. The percent reduction in PVR for the Oral Imatinib Phase 2 study is calculated using the placebo corrected arithmetic means. The STELLAR and TORREY study percent reduction in PVR are calculated using least square means (LSM) corrected for placebo.



# AV-101: Potential to Be An Ideal Add-On Agent

- At Launch, AV-101 has the potential to be an ideal add on agent\*
  - Compelling clinical profile in combination with current therapies
  - Simplicity and ease-of-use
  - Potential to be part of the future standard of care
- Potential positioning within target populations\*
  - In front of inhaled and oral prostacyclin therapy
  - In front of sotatercept for patients who prefer inhalation vs injection and for sotatercept ineligible patients
  - Patients who remain at moderate to high risk of poor outcomes despite sotatercept and prostacyclin therapy
  - Patients who do not tolerate sotatercept and prostacyclin therapy



# AVTE's Perspective on Current And Future PAH Landscape Informed by Extensive Experience, Stakeholder Engagement, and Market Research

- Global Advisory Boards with PAH Experts and PAH Patients
- Interactions with Investigators, KOL's, PAH Treaters, Nurses, Patients, Advocacy Associations\*
- Robust Market Research
  - 100+ U.S. Physician Market Landscape Research (Oct 2021)
  - 100+ European Physician Market Landscape Research (June 2022)
  - 150+ U.S. Physician Conjoint Demand Study post Sotatercept Data (Aug 2023)



Prof. Vizza MD investigator discussion

\*Individual interactions focus solely on treatment landscape unless seeking bona-fide advice with an appropriate consulting agreement

# PAH Treatment Pathways Have Not Changed Since 2005 and Outcomes Remain Poor

## Significant Efforts to Optimize Traditional Pathways

### Multiple Agents Within Pathways

Prostacyclin Pathway  
Epoprostenol → Treprostinil

Endothelin Pathway  
Bosentan → Ambrisentan

Nitric Oxide Pathway  
Sildenafil → Tadalafil

### More Convenient Prostacyclin Pathway Routes of Administration

Infusion → Inhalation → Oral

### More Aggressive Treatment Approaches

Initial Monotherapy → Upfront Combination Therapy → Treat to Low Risk

**61%-65% 5 Year Survival among Newly Diagnosed and Prevalent Patients**

# Urmets Need Beyond Sotatercept

The STELLAR trial represents significant progress in therapy for PAH however...

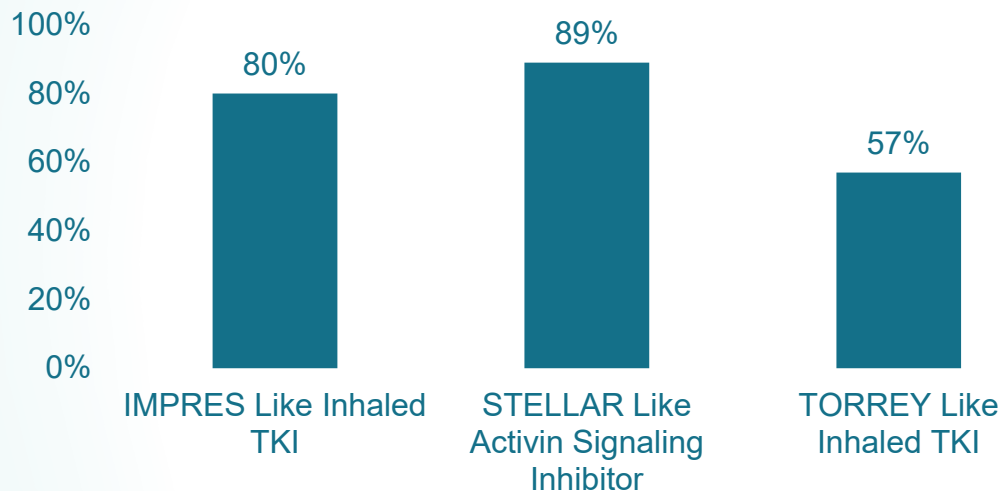


- 60% of patients did not meet multi-component improvement measure
- 60% of patients did not achieve low risk on the simplified French risk model
- 70% of patients did not improve functional class
- Long term effects not fully established

# 80% of Physicians Would Prescribe an “IMPRES” Like Inhaled TKI if it Were Available Alongside Sotatercept

**Market Research with >150 U.S. PAH Treating Physicians Conducted Post STELLAR Data\***

**% Who Would Prescribe Each Hypothetical Agent to Their Patients**



# AV-101: Unmet Need, Blockbuster Potential

## Positioning

Added to two agents  
before prostacyclin

Added to three agents  
before parenteral  
prostacyclin



**~65%**  
**(~22,750)**

We estimate to be  
taking 2-3 drugs

# Positive Regulatory Interactions and Feedback

## Regulatory Interactions Completed

- FDA Pre-IND meeting in January 2020
- FDA and EMA Orphan Designation granted for AV-101 for the treatment of PAH
- Received EMA Scientific Advice in March 2021
- End-of-Phase-1 Meeting with FDA in April 2021

## Feedback from FDA and EMA on Clinical Development

- A single Phase 2b/3 trial could support NDA
- Aligned on Phase 2b/3 endpoints for potential NDA/MAA submission



# Intellectual Property Protection for AV-101 to 2040+

## **Multiple issued US patents covering AV-101 drug product and methods of use**

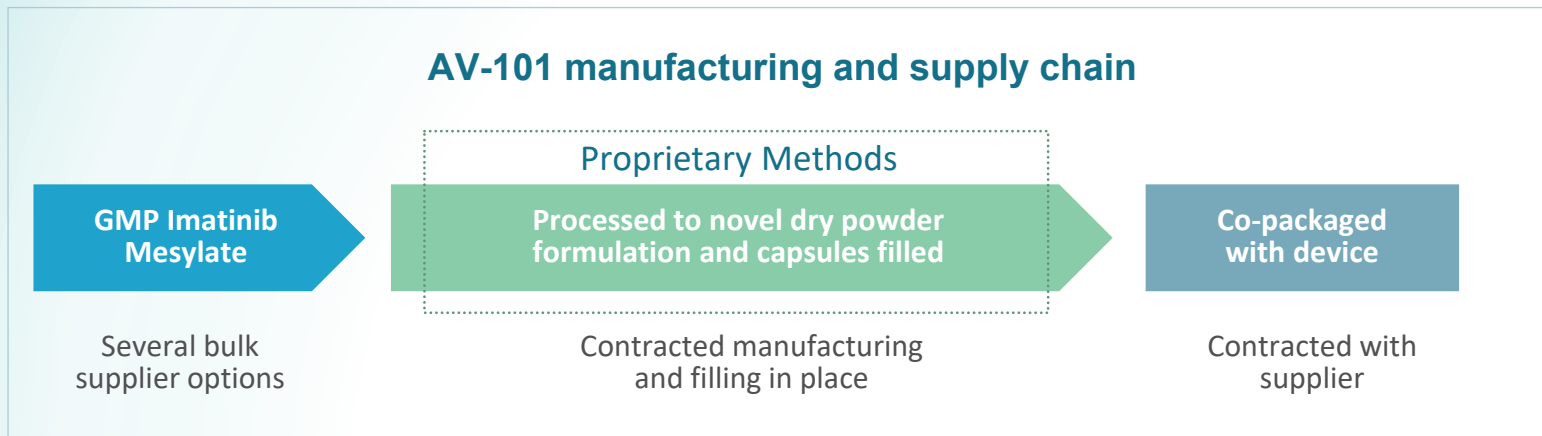
- Patent coverage extends at least until 2040
- Current US patents being extended worldwide

## **Multiple additional pending applications pursuing**

- Methods of manufacture
- Filing on other aerosol compositions
- Filing on mechanism of action (composition agnostic)

**Regular reviews enacted to extend or file new IP based on discoveries in research, clinical trials and CMC**

# Chemistry, Manufacturing and Controls



## Stability of AV-101

- Release and stability testing supports
  - API stability of at least 36 months
  - Drug product stability of at least 30 months
- Filled product stability testing ongoing

# AV-101 Device and Delivery Performance

## AV-101 Device

- Off-the-shelf commercial scale dry powder inhaler
  - No batteries, compressors or cords
  - No sterile vials containing solutions or suspensions
  - CE mark in EU and Device Master File registered with FDA
- Designed for ease of use and convenience
- Intended dosing of 2 capsules twice a day
- Device replaced weekly

## AV-101 Delivery Performance

- Consistently high delivered and fine particle dose
- Ideal size and size distribution for lung penetration

**NOTE:** Device in IMPAHCT was not used in Phase 1 trial, but delivery performance was assessed.

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