

A stylized white line-art logo of a tree with a single trunk and many branching roots and leaves, positioned on the left side of the slide.

# VICORE PHARMA

Unlocking the potential of a new class of drugs – Angiotensin II type 2 receptor agonists (ATRAgS)

May 2023



# Forward looking statement

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This presentation may contain certain forward-looking statements and forecasts based on uncertainty, since they relate to events and depend on circumstances that will occur in the future and which, by their nature, will have an impact on Vicore Pharma's business, financial condition and results of operations. The terms "anticipates", "assumes", "believes", "can", "could", "estimates", "expects", "forecasts", "intends", "may", "might", "plans", "should", "projects", "will", "would" or, in each case, their negative, or other variations or comparable terminology are used to identify forward-looking statement.

There are a number of factors that could cause actual results and developments to differ materially from those expressed or implied in a forward-looking statement or affect the extent to which a particular projection is realized. Factors that could cause these differences include, but are not limited to, implementation of Vicore Pharma's strategy and its ability to further grow, risks associated with the development and/or approval of Vicore Pharma's products candidates, ongoing clinical trials and expected trial results, the ability to commercialize C21, technology changes and new products in Vicore Pharma's potential market and industry, the ability to develop new products and enhance existing products, the impact of competition, changes in general economy and industry conditions and legislative, regulatory and political factors.

No assurance can be given that such expectations will prove to have been correct. Vicore Pharma disclaims any obligation to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise.



# Vicore at a glance



**Unlocking the potential of a new drug class – ATRAGs**



**Unprecedented data in IPF phase 2a**



**Strong scientific rationale for disease modification in PAH**



**MoA with wide therapeutic implications**



**A clinical platform under development – capitalizing on lead**



# Company overview

## Background

The company was founded in the early 2000s, based on the synthesis of the first small molecule AT2 receptor agonist C21 by Professor Anders Hallberg's group at Uppsala University<sup>(1)</sup>

## Headquarters

Stockholm Sweden, with Clin Ops team in Copenhagen, Denmark

## Employees

~25 FTEs. Virtual setup

## Ticker

VICO, listed at Nasdaq Stockholm. Market Cap; 196 MUSD (May 19, 2023)

## Financials

Cash 18 MUSD (March 31, 2023)

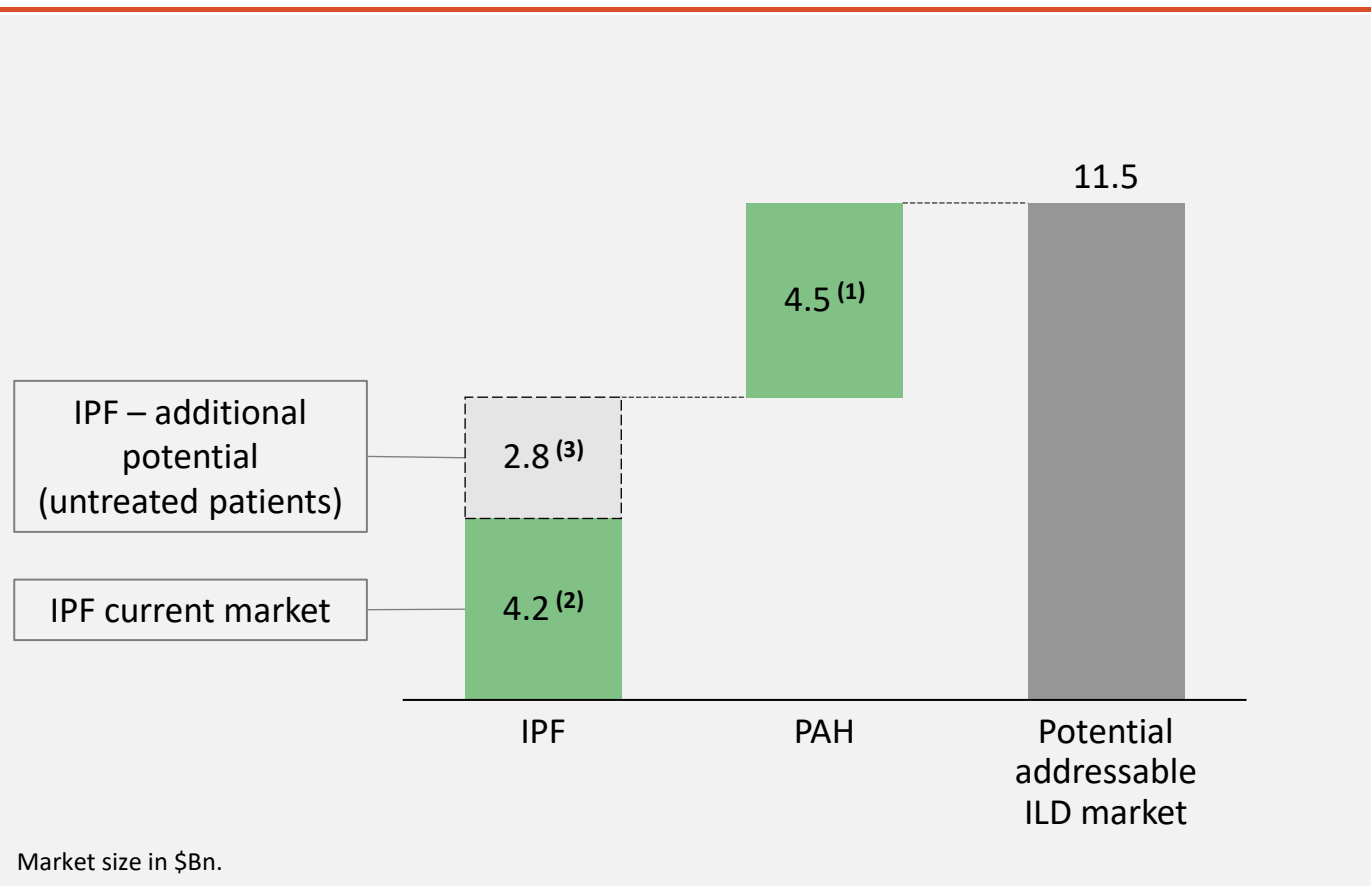
## Major shareholders

HealthCap, HBM Healthcare Investments and Fourth Swedish National Pension Fund



# Market leadership opportunity in rare lung diseases

## Possibility to expand the IPF market with more tolerable treatment



## Opportunity for market leadership

- Still huge unmet medical need in IPF and PAH
- C21 stabilizes disease in IPF with good safety and tolerability profile
- Potentially disease modifying in PAH





# Strong leadership team with extensive industry experience



**CARL-JOHAN DALSGAARD, MD, PhD**  
**CHIEF EXECUTIVE OFFICER**

Ex AstraZeneca R&D: Head of Therapy Area Pain Control, 10 years senior management. HealthCap: 19 years Venture Partner.



**ELIN ROSENDAHL, MSc Pharm**  
**VP CLINICAL DEVELOPMENT**

More than 20 years of global biopharmaceutical development at Pharmacia and SOBI. Solid experience of managing all clinical phases.



**ROHIT BATTÀ, MBBS, MRCGP, MFPM**  
**CHIEF MEDICAL OFFICER**

MD with extensive industry experience in Rare Diseases. Ex GSK: Led the global medical and clinical development of the world's first paediatric gene therapy.



**NINA CARLÉN**  
**CHIEF ADMINISTRATIVE OFFICER**

More than 20 years of marketing and communications experience. Responsible for HR and company administration.



**CAROLINE SPEARPOINT, PhD**  
**THERAPY AREA LEAD RARE LUNG DISEASES**

20 years industry experience from pharmaceutical, biotech and consulting, managing global cross-functional projects.



**HANS JEPSSON, PhD**  
**CHIEF FINANCIAL OFFICER**

Cross-disciplinary background in finance and medicine. Ex Danske Bank: Equity analyst.



**JOHANNA GRÄNS, PhD**  
**PROGRAM DIRECTOR, EARLY DEVELOPMENT**

Extensive experience in preclinical R&D. Project management and regulatory affairs. Research experience in drug metabolism.



**JOHAN RAUD, MD, PhD**  
**CHIEF SCIENTIFIC OFFICER**

Ex AstraZeneca: Director Inflammation research. 25 years of experience in drug development.



**JESSICA SHULL, PhD**  
**HEAD OF DIGITAL THERAPEUTICS**

More than 20 years of experience in the development and adoption of digital healthcare technologies.



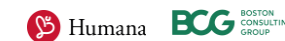
**STINE FURBO**  
**HEAD OF CMC**

More than 20 years of experience with pharmaceutical drug product development & product supply from early development to launch.



**MIKAEL NYGÅRD, PhD**  
**VP BUSINESS DEVELOPMENT**

Experienced healthcare Business Development executive, has led M&A and Corporate Development functions.



**ÅSA MAGNUSSON**  
**CHIEF COMMERCIAL OFFICER**

More than 20 years of experience as a commercial executive in the pharmaceutical industry with focus on securing market access and launching rare disease medicines.



## Board of Directors

### JACOB GUNTERBERG

Chairman. Experienced venture capitalist and life science sector financier.

### HANS SCHIKAN

25 years management experience in global pharmaceuticals (e.g. CEO of Prosensa). Extensive board work in listed life science companies (e.g. Hansa Biopharma, SOBI and Pharvaris)

### HEIDI HUNTER

President Cardinal Health Specialty Solutions. 25 years in senior pharmaceutical development and commercialization positions.

### MAARTEN KRAAN

Extensive experience in biomedicine, managerial roles at AstraZeneca.

### ELISABETH BJÖRK

Broad drug development experience, currently leading global late-stage development activities in CVRM at AstraZeneca. Extensive board work experience in small and mid-size international life science companies.

### MICHAEL BUSCHLE

More than 25 years experience in basic research as well as biotech and pharma R&D. Extensive board work experience from US Nasdaq-listed biotech firms.

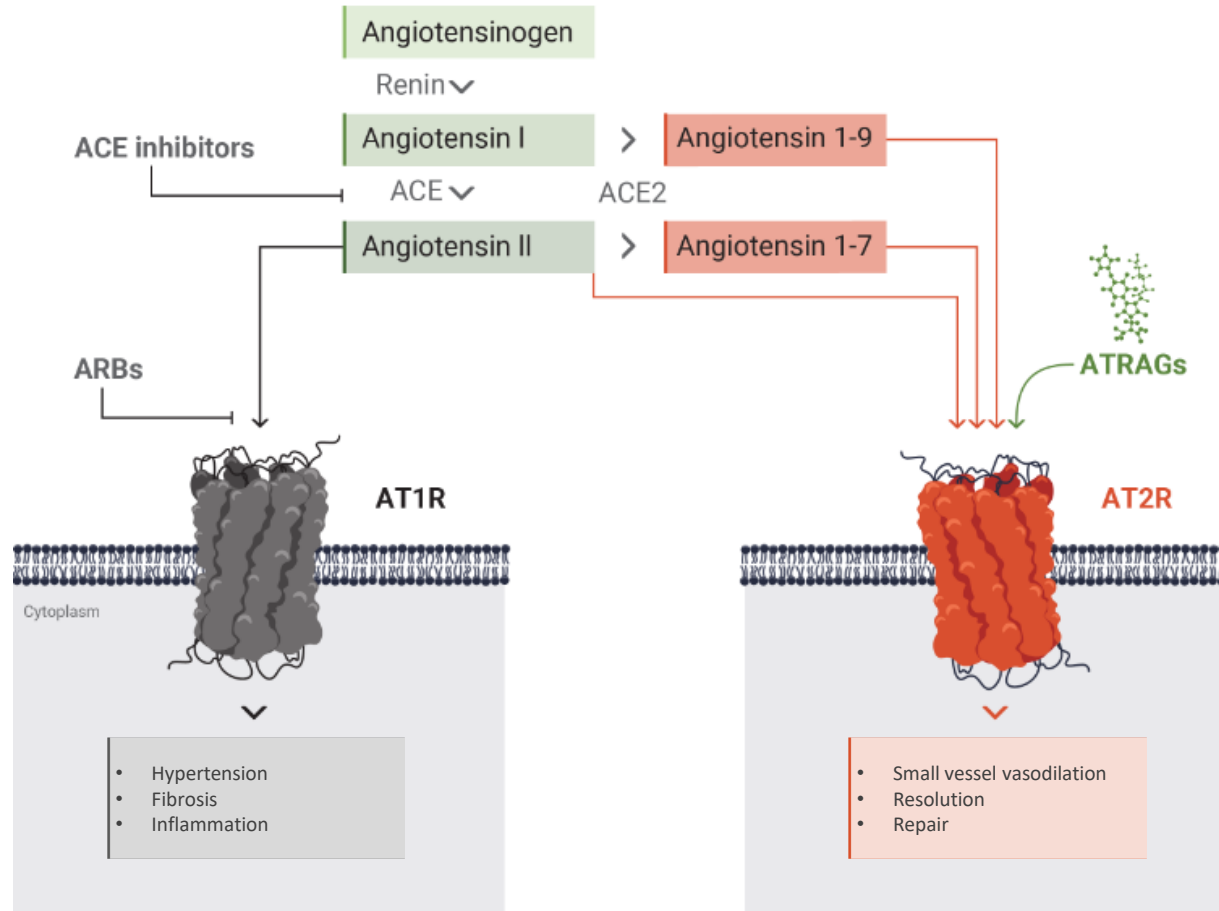


# Diversified pipeline with key readouts in the next year

Indication	Compound	Preclinical	Phase 1	Phase 2	Phase 3	Comments
IPF fibrosis	C21					Final data phase 2a, Q4 2023 Phase 2b trial preparations during 2023
PAH	C21					Proof-of principle study on endothelial function planned during 2023
Anxiety in pulmonary fibrosis	Almee™ DTx					Read-out pivotal study, Q4 2023
IPF cough	IMID					Preclinical formulation
Cardiorenal	C106					Phase 1 data, H1 2023
New indications	C103, C111, C112					Preclinical studies



# The Angiotensin II type 2 (AT2) receptor is an attractive drug target



## ATAGs (Angiotensin II type 2 receptor agonists) have a favorable pharmacological profile

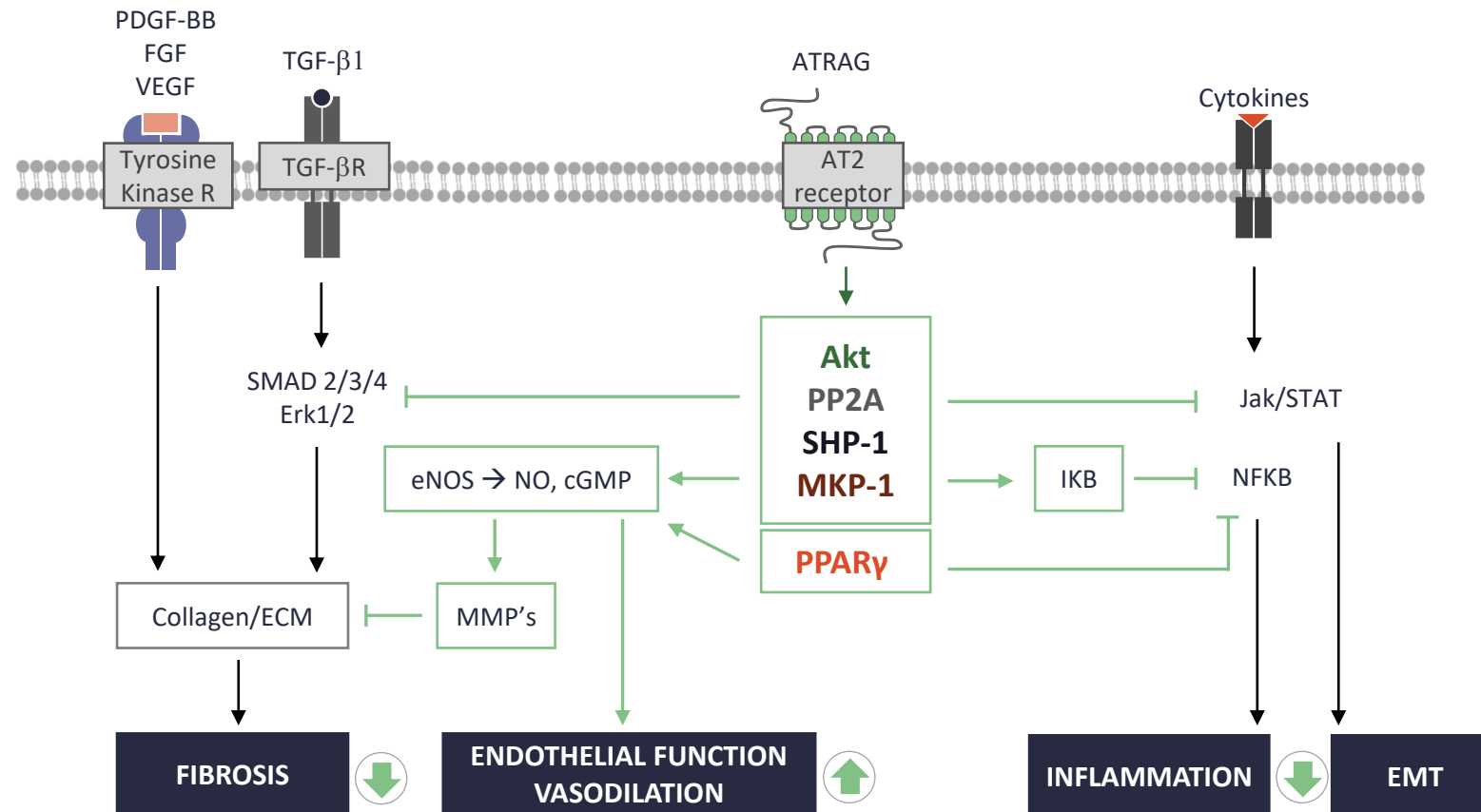
- Target is upregulated in diseased tissues
- Selective stimulation of an endogenous repair system
- Brief exposure is sufficient to elicit receptor response (“Hit and run”)

C21 is a first-in-class, highly selective, orally available ATAG



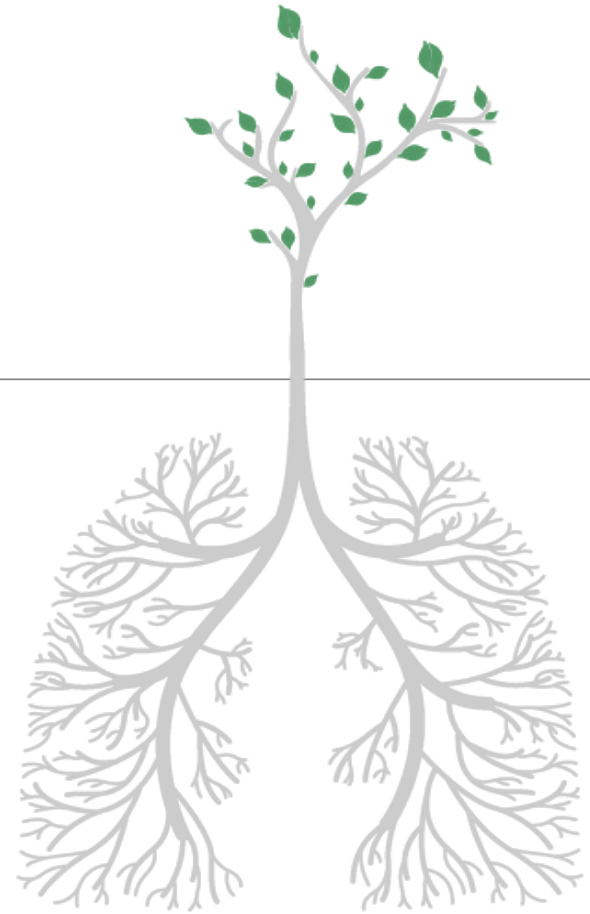


# Multimodal action of AT2 receptor activation with broad therapeutic potential



AT2 receptor targets fibrosis and inflammation and promotes endothelial functions

## Rare lung disease – IPF and PAH

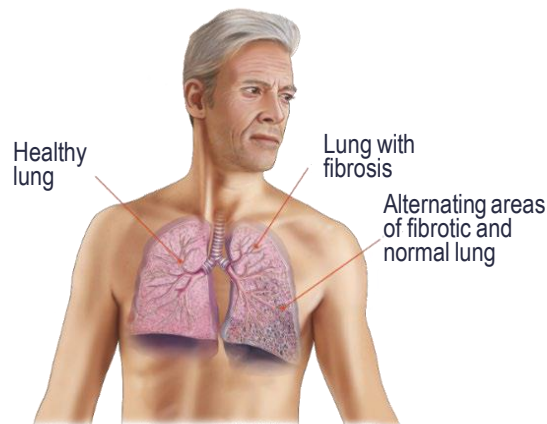




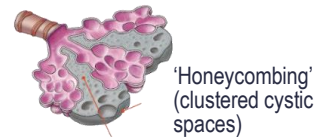
# Idiopathic Pulmonary Fibrosis (IPF) – a significant unmet need

## A devastating interstitial lung disease...

- ~250 000 patients in the US and Europe
- Life expectancy 3-5 years



Alveolus in fibrosis



Fibrosis between alveoli decreases gas exchange so that less oxygen is transferred to the bloodstream

Healthy alveolus



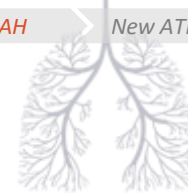
## ...with limited therapeutic options...

- Only 2 approved IPF therapeutics to date with limited efficacy
- Significant GI and other side-effects
- Therapies rarely improve disease or quality of life<sup>(1,2)</sup>

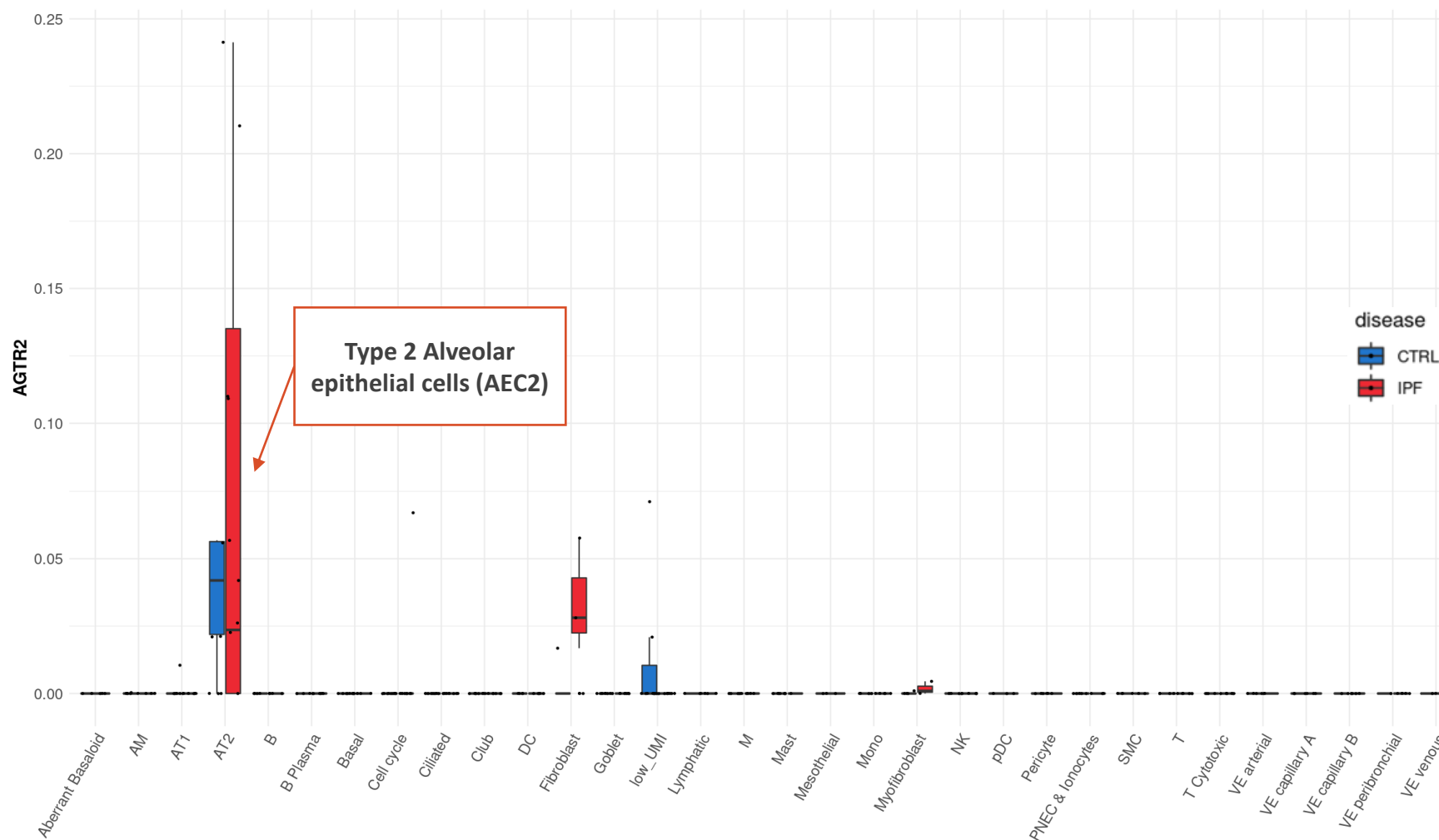
## ...and low compliance

- Only 26.5% of all patients in the US started on drugs
- 43% discontinue, main reasons are side effects and costs
- Patients are on drug on average for 10 months<sup>(3)</sup>

Large share of untreated patients provides medical and commercial opportunity

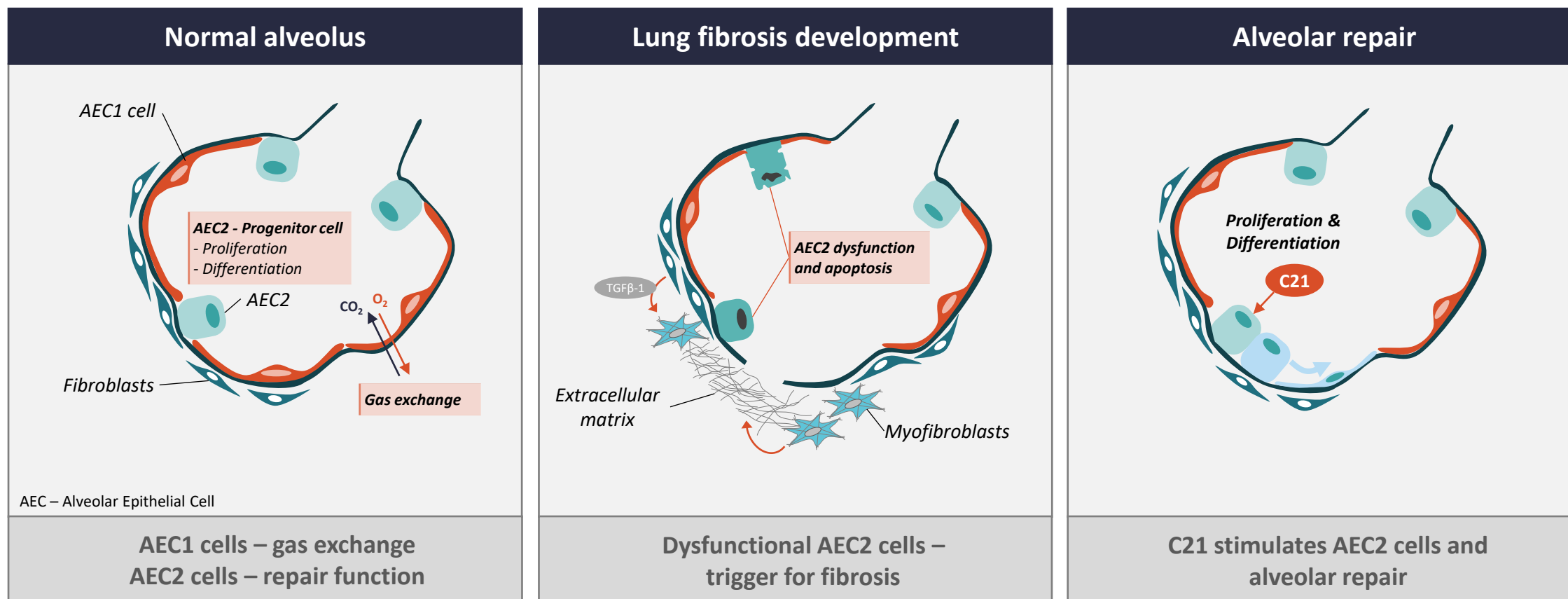


# The AT2 receptor is highly expressed in lung AEC2 cells





# AEC2 cell dysfunction is a key trigger for development of fibrosis in IPF



AT2 receptor activation triggers protective signaling pathways, promoting alveolar repair and maintenance of alveolar integrity



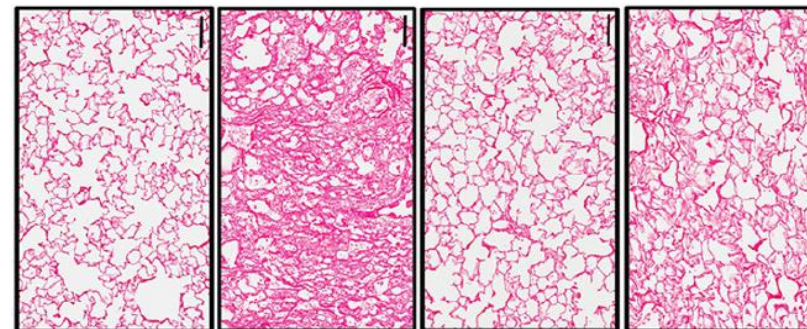
# Strong preclinical in-vivo data demonstrate multimodal effects of C21

## Significant and consistent effects of C21 treatment across animal fibrosis models

↓ Lung fibrosis	<ul style="list-style-type: none"> <li>Collagen content (Picro-sirius staining, Hydroxyproline, Collagen gene expression)</li> </ul>
↓ Remodeling of pulmonary vessels	<ul style="list-style-type: none"> <li>H&amp;E staining, Ashcroft scoring</li> <li><math>\alpha</math>-SMA staining</li> <li>Vessel wall thickness, luminal opening and vascular lesions</li> </ul>
↓ Cardiac remodeling	<ul style="list-style-type: none"> <li>Right ventricular hypertrophy (RVH)</li> </ul>
↓ Pulmonary hypertension	<ul style="list-style-type: none"> <li>Right ventricular systolic pressure (RVSP)</li> <li>Right ventricular end diastolic pressure (RVEDP)</li> <li>Stroke volume</li> </ul>
↑ Cardiac output	<ul style="list-style-type: none"> <li>mL/min</li> </ul>

### Bleomycin rat model

#### Collagen staining

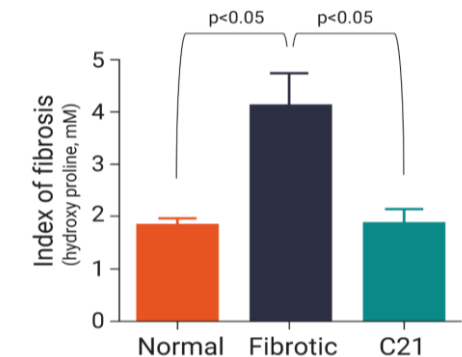


Control

Bleomycin

C21 Prevention  
protocolC21 Therapeutic  
protocol\*

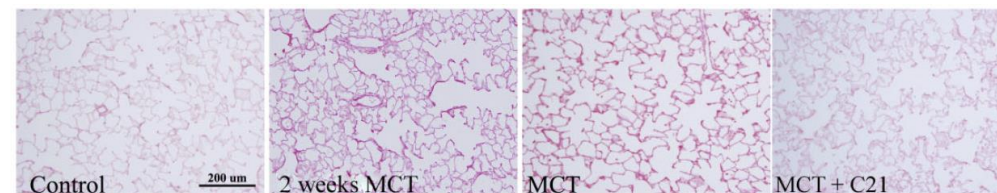
\*Low dose C21 i.p. once daily for 2 weeks



Adapted from Rathinasabapathy 2018

### Monocrotaline rat model

#### Collagen staining



Control

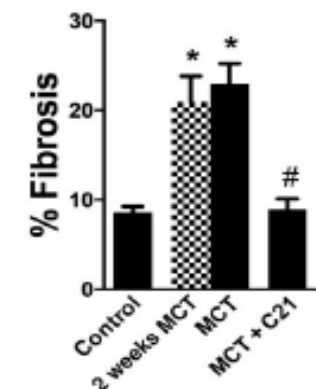
200 µm

2 weeks MCT

MCT

MCT + C21

Low dose C21 i.p. once daily for 2 weeks

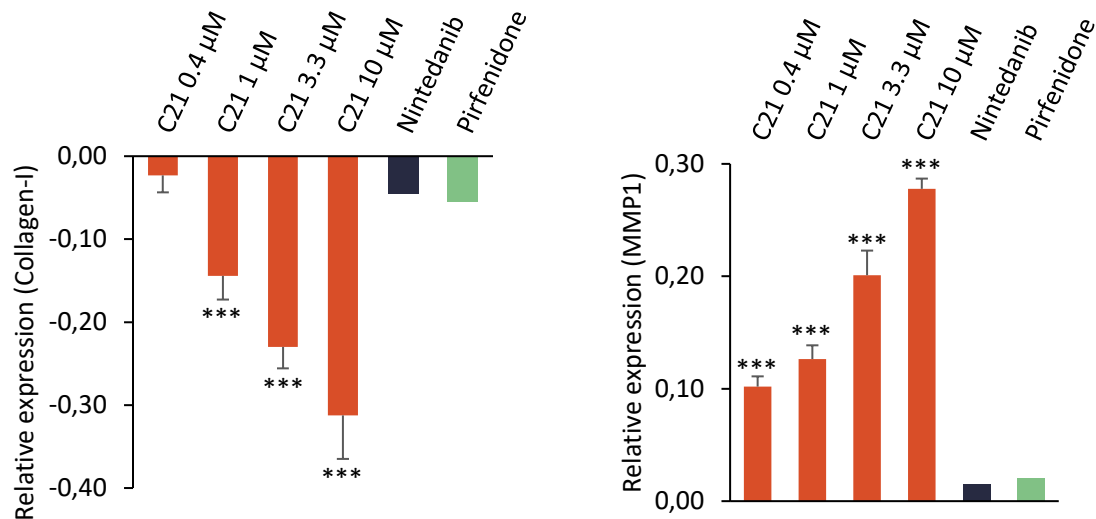


Adapted from Bruce 2015



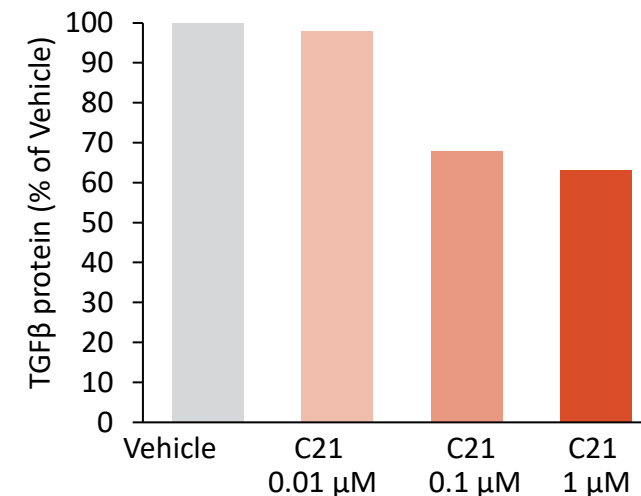
# C21 modulates gene expression in human lung tissue slices and primary cells

## Inhibition of profibrotic Collagen-1 and induction of anti-fibrotic MMP1 in primary lung cells



- Human primary small airway epithelial cells + Lung fibroblast co-culture (SAEMyoF) stimulated with TGFβ1 and TNF to resemble fibrotic lung disease.
- Protein expression analyzed with BioMAP fibrosis biomarker panel. Effects of reference substances (Nintedanib 1,1μM, Pirfenidone 1700 μM) shown as benchmark.

## Inhibition of TGFβ1 in human IPF lung tissue slices



- Precision-cut human lung slices from IPF patient lung transplants, incubated with clinically relevant concentrations of C21.
- Downregulation of TGFβ1 (master regulator of fibrosis formation in IPF) indicates strong antifibrotic effects.

**Strong antifibrotic properties compared to SoC in human lung models**



# AIR Phase 2a trial in treatment-naïve IPF patients

- **Primary aim:** To evaluate safety of C21 in patients with IPF
- **Secondary aim:** To evaluate efficacy of C21 in IPF as measured by FVC change

## Trial Design

- N=60 treatment naïve IPF patients
  - Open label single arm
  - Centrally read HRCT
  - Gold standard FVC measurement
- 6-month treatment duration with a possible 3-month extension

Open label phase 2a trial to demonstrate safety and efficacy of C21 alone



# AIR baseline characteristics in line with other IPF trials

AIR interim analysis May 2023

## Key characteristics

		AIR (N=51)	INPULSIS 1&2 (N=1,061) <sup>1</sup>
Age (years) - Mean (SD)		<b>68 (9)</b>	67 (8)
Gender	Males	<b>77%</b>	80%
	Females	<b>23%</b>	20%
Ethnicity	White	<b>28%</b>	57%
	Asian	<b>72%</b>	30%
BMI (kg/m <sup>2</sup> ) – Mean (SD)		<b>24.5 (4.1)</b>	28 (4.6)
HRCT pattern	Probable UIP	<b>39%</b>	32%
	Typical UIP	<b>57%</b>	68%
FVC % predicted - Mean (SD)		<b>75.3 (14)</b>	79.7 (17)
% SoC	Pirfenidone	<b>0%</b>	0%
	Nintedanib	<b>0%</b>	0%

In line with other trials

Proportion of Asian (Indian) patients is higher than other trials.  
Indian patients progress equally to any global study population

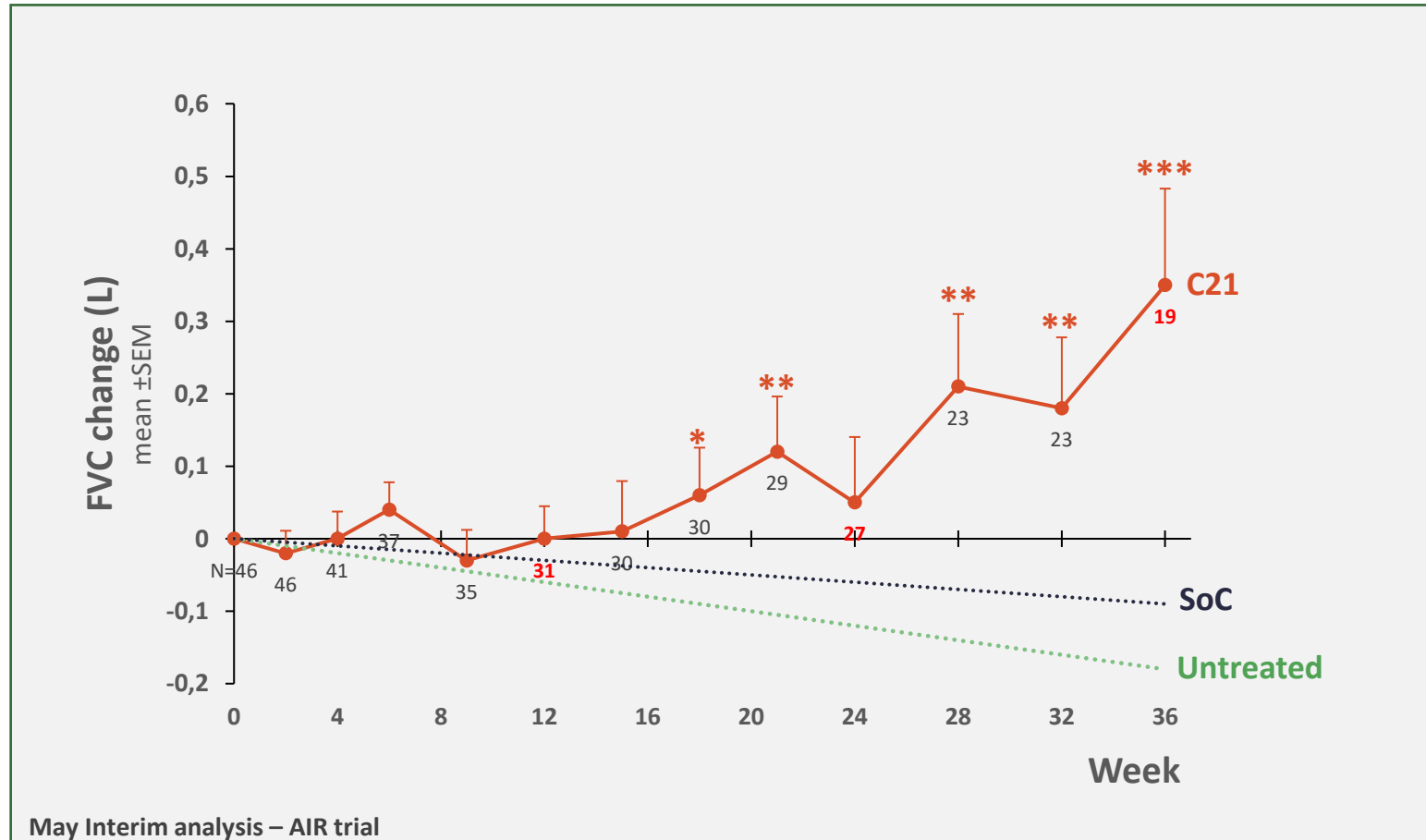
In line with other trials

AIR is in treatment naïve patients



# Consistent FVC stabilization

AIR interim analysis May 2023



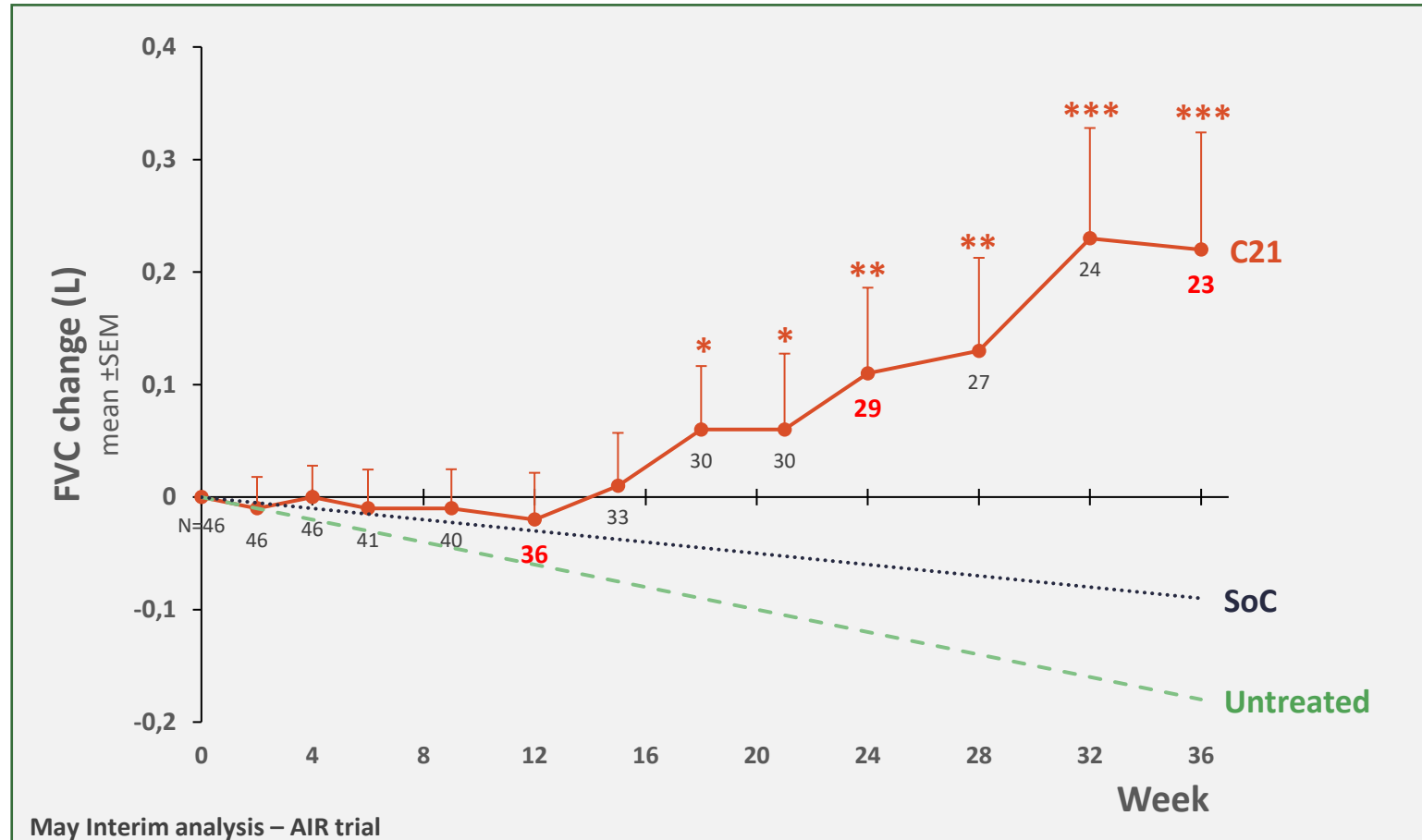
- Observed values
- N = all patients at time of analysis
- No imputation

17 of 19 patients have an FVC change above the expected mean of an untreated population at 36 weeks



# Consistent FVC stabilization

AIR interim analysis May 2023



3-visit rolling average

N = all patients at time of analysis

No imputation

The FVC stabilization and improvement is seen across subgroups (region, gender, HRCT pattern)



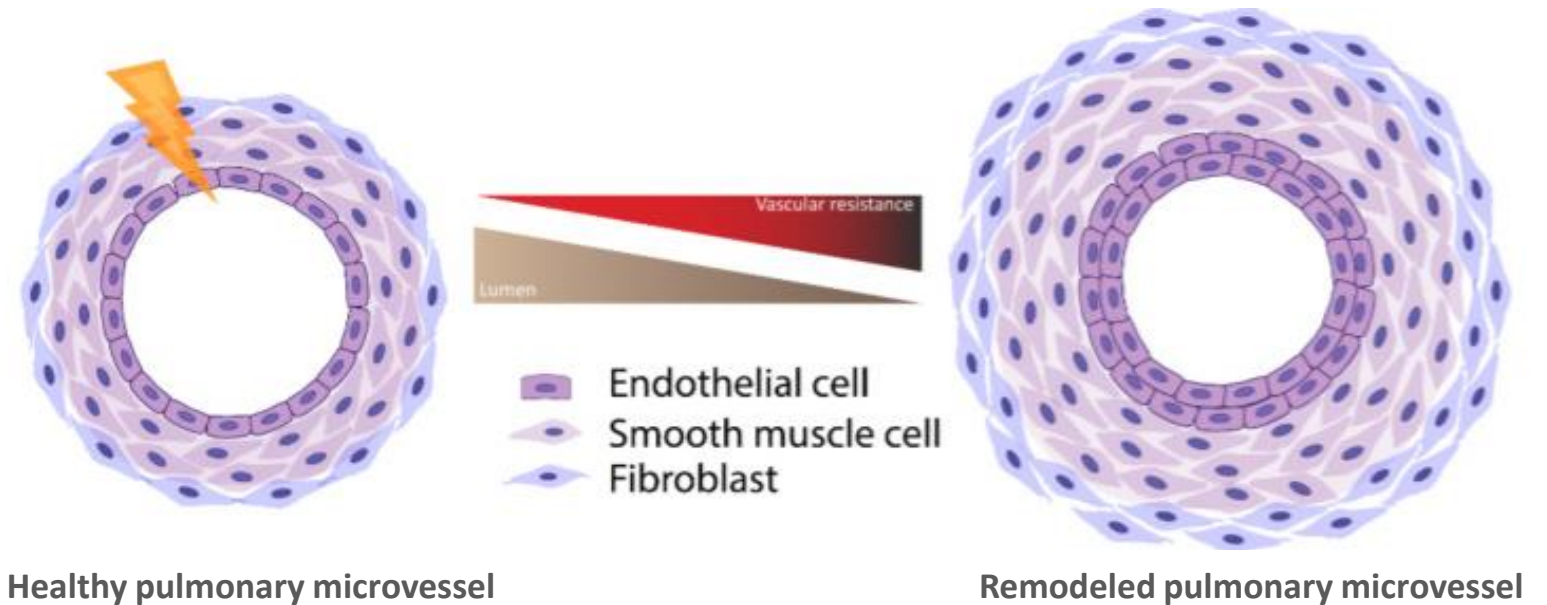
# PAH – a microvascular rare disease with poor prognosis

## PAH is a rare, fatal disease...

- Orphan disease with ~67 000 patients in US and Europe<sup>(1)</sup>
- Approved PAH drugs mainly act as vasodilators – but no disease-modifying treatment
- 5-year survival rate is ~50%

## ...triggered by endothelial dysfunction

- Endothelial dysfunction and vascular remodeling leads to pulmonary arterial obstruction
- Progressing disease leads to elevated resting mean pulmonary artery pressure (PAP), reduced cardiac output, right heart failure, and ultimately, death



Need for disease-modifying treatment addressing endothelial function and vascular remodeling





# Strong preclinical data with C21 in disease-relevant animal model

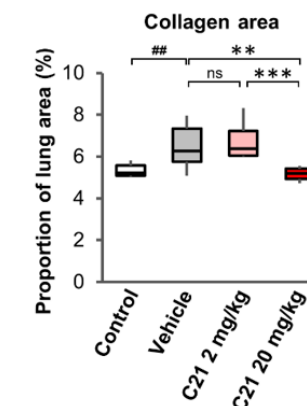
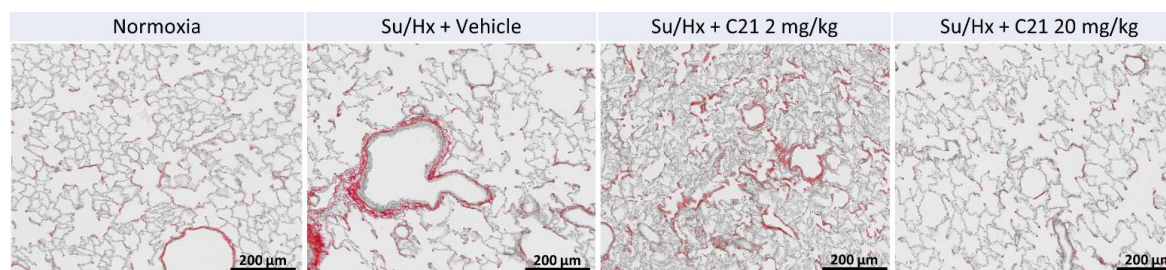
## Effects of C21 treatment:

- ↓ Lung fibrosis
- ↓ Remodeling of pulmonary vessels
- ↓ Cardiac remodeling
- ↓ Pulmonary hypertension
- ↑ Cardiac output

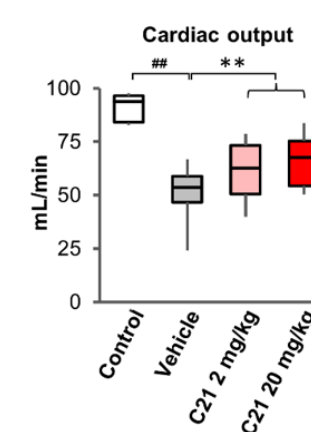
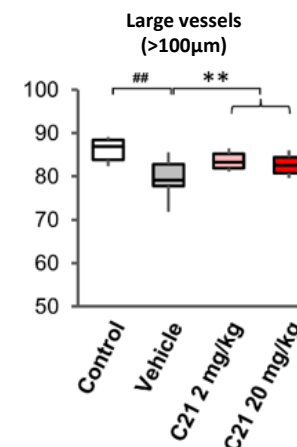
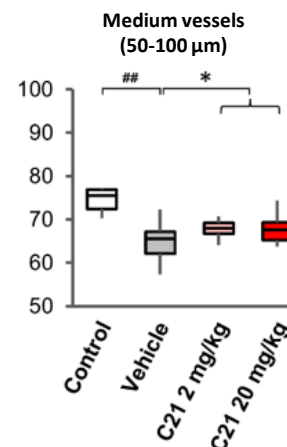
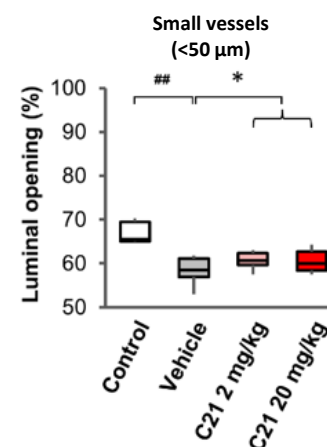
Protocol: C21 p.o. for 34 days, initiated 21 days after Sugén-Hypoxia period. N=10-11 per treatment group

## Sugén-Hypoxia rat model

### Collagen



### Vascular remodeling and cardiac output



Positive effects on vascular remodeling, fibrosis and cardiac function

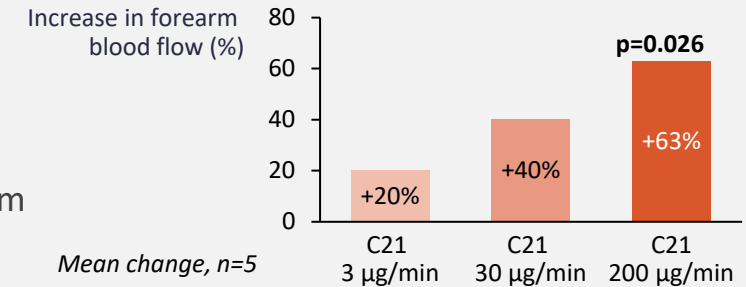


# Investigating effects on endothelial dysfunction in PAH

## C21 increases local blood flow

### Forearm blood flow in healthy volunteers

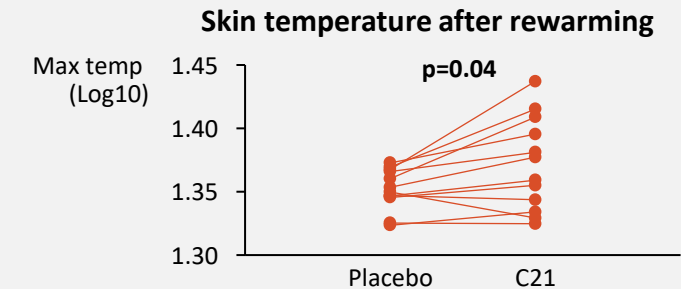
- Increase in blood flow (63%,  $p=0.026$ ) at clinically relevant doses
- No systemic blood pressure effects or other side effects
- Vasodilation is mediated by nitric oxide (NO) released from the endothelium



## C21 improves blood flow also in diseased tissue

### Forearm blood flow in Systemic Sclerosis patients with Raynaud's phenomenon

- Randomized DB cross-over study ( $n=12$ )
- SSc patients with severe vasculopathy (19 years disease history)
- Temperature after 15 minutes higher with C21 than placebo ( $p=0.04$ )



## Evaluation of endothelial dysfunction in PAH as a next step

### Peripheral endothelial function and efficacy of C21 in PAH

- PAH is a microvascular disease with endothelial dysfunction and impaired NO release as drivers of pathology
- Peripheral vascular changes are correlated to disease severity and a treatment effect on peripheral vascular function will serve as a strong indicator of effects on pulmonary microvasculature
- As a first step a PoP trial with PAH patients will be performed to assess effects of C21 on peripheral endothelial function by a non-invasive plethysmograph (EndoPAT)



# Almee™ – Digital Therapy for Anxiety in Pulmonary Fibrosis

- Treat symptoms of anxiety and improve quality of life in adults with pulmonary fibrosis
- Reduce costs for overburdened hospital systems (nurse/psychologist resources, hospitalizations, ER visits)

**250 000 Pulmonary  
Fibrosis patients in  
the US**

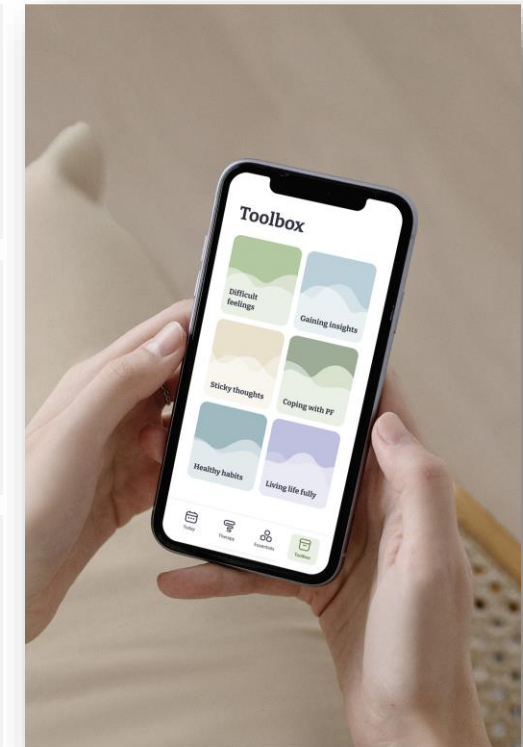
- Huge unmet need: 63% of patients with treatable levels of anxiety<sup>1</sup>
- Current pharmacological treatments do not improve patients' quality of life
- Health care resource utilization two-fold versus controls

**Almee™ – CBT-based  
digital therapy**

- CBT has strong evidence base in anxiety
- Pilot study showed reduction of GAD-score by 49% after 4 weeks treatment

**COMPANION –  
decentralized study**

- US based RCT planned for 250 patients
- FPI December 2022
- Treatment period 9 weeks





# Inhaled thalidomide – targeted approach to address IPF cough

## Background

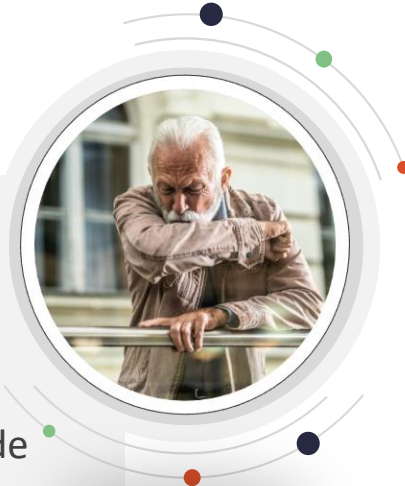
- Unlike other types of chronic cough, IPF cough does not respond to placebo treatment
- No approved therapies today
- In a double-blind cross-over study, oral thalidomide significantly improved cough frequency
- Oral treatment not in use due to side effect profile

## Vicore development program – inhaled thalidomide

- Inhaled drug delivery directly to the lung
- Reduces the risk of adverse effects and is expected to reduce systemic exposure by ~50-85%

## Milestones

- Formulation development ongoing

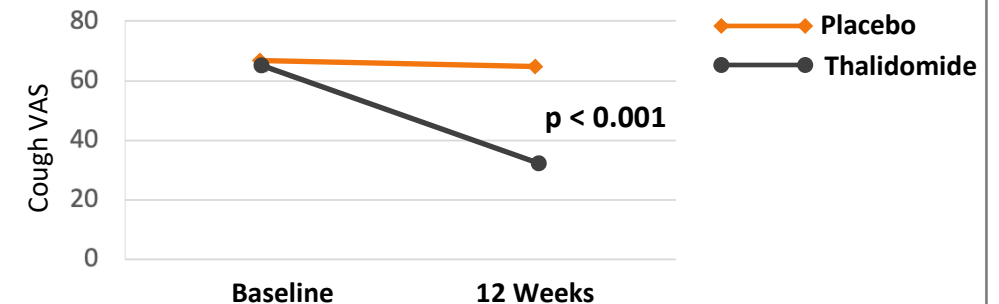


## Annals of Internal Medicine®

### Thalidomide for the Treatment of Cough in Idiopathic Pulmonary Fibrosis

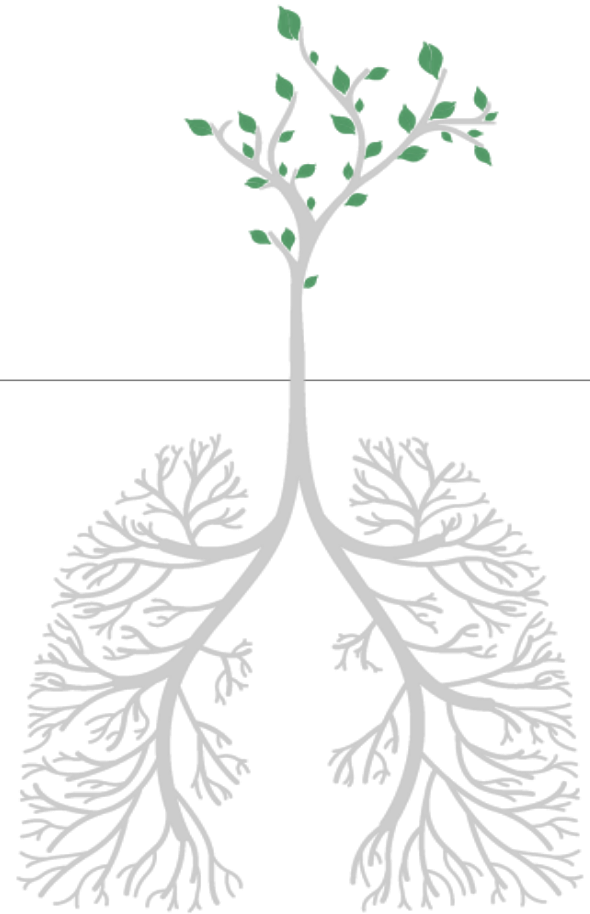
#### A Randomized Trial

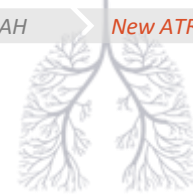
Maureen R. Horton, MD, Victoria Santopietro, Leena Mathew, BS, Karen M. Horton, MD, Albert J. Polito, MD,



Relevant patient group: 78% men, mean age 67.6 years, mean FVC 70.4%

## New ATRAGs





# Vicore has a platform of proprietary ATRAGs

## C21 – first in class – rare lung diseases

- NCE patent expires 2024
- Market exclusivity (NCE) – US 5 years, Europe 10 years
- Orphan drug status in IPF granted – US 7y, EU 10 years
- Several pending patents (formulation, manufacturing, use) specifically covering C21, projected expiry 2040 and beyond



## New compounds – new indications – long patent life

- 7 novel proprietary classes developed with NCE patent protection to 2040 and beyond expected
- Improved physicochemical and metabolic properties
- 1<sup>st</sup> compound, C106 in phase 1



Behind C21 there are 4 new compounds in development



# ATRAGs in development have confirmed potency, selectivity and efficacy

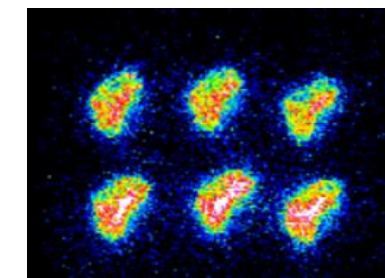
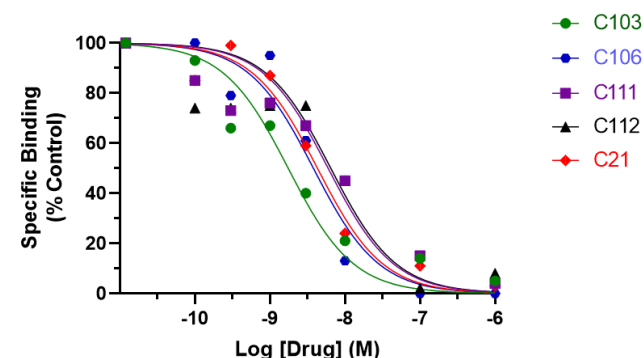
## New ATRAGs compound characteristics

- Small molecules
- High AT2 receptor affinity and selectivity
- Patent protection to 2040+
- Developed targeting different indications

## Target engagement - autoradiography with human lung tissue

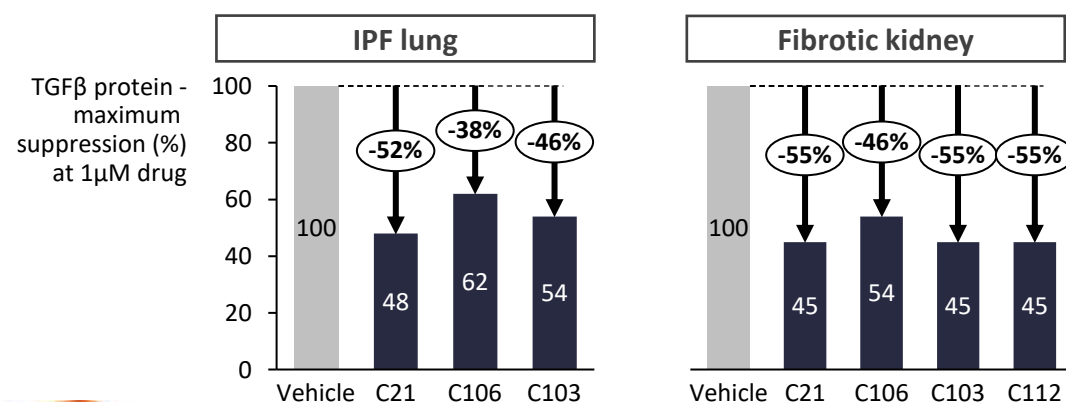
- Displacement with cold ATRAGs at clinically relevant concentrations

[<sup>125</sup>I]Angiotensin II Binding in Human Lung Tissue



## Efficacy in human ex-vivo lung and kidney tissue

- Strong TGF-β1 suppression



## Pharmacological safety profile

- A safe and well tolerated drug class

- C21 now exposed to more than 300 individuals
- No safety concerns in clinical trials
- 24 h Holter ECG confirm CV safety
- No apparent pharmacological side effects



# ATRAG – a new class of drugs

Based on the extensive preclinical documentation, the localization of the receptor in man as well as accumulating clinical data, stimulating AT2 receptor may be beneficial in a wide range of diseases

## ATRAG indications

### IPF

- **IPF** - Ph2 ongoing
- **Digital therapeutic (DTx)** and...
- **IPF Cough** programs to build strong presence in IPF

### PAH

- **Pulmonary arterial hypertension (PAH)** – strong preclinical in vivo data, planning for PoC trial

### Cardiorenal

- Several preclinical studies supporting rationale in **Diabetic Nephropathy** and **Cardiovascular disease (HFpEF)**

### Women's Health

- Intriguing preclinical data supporting rationale in **Preeclampsia**

### Other areas

- Several different areas to be explored. Strong preclinical data in **Stroke/Cognitive disorders**

Vicore has deep AT2 receptor expertise and is well positioned to pursue these opportunities



## Vicore at a glance



**Unlocking the potential of a new drug class – ATRAGs**



**Unprecedented data in IPF phase 2a**



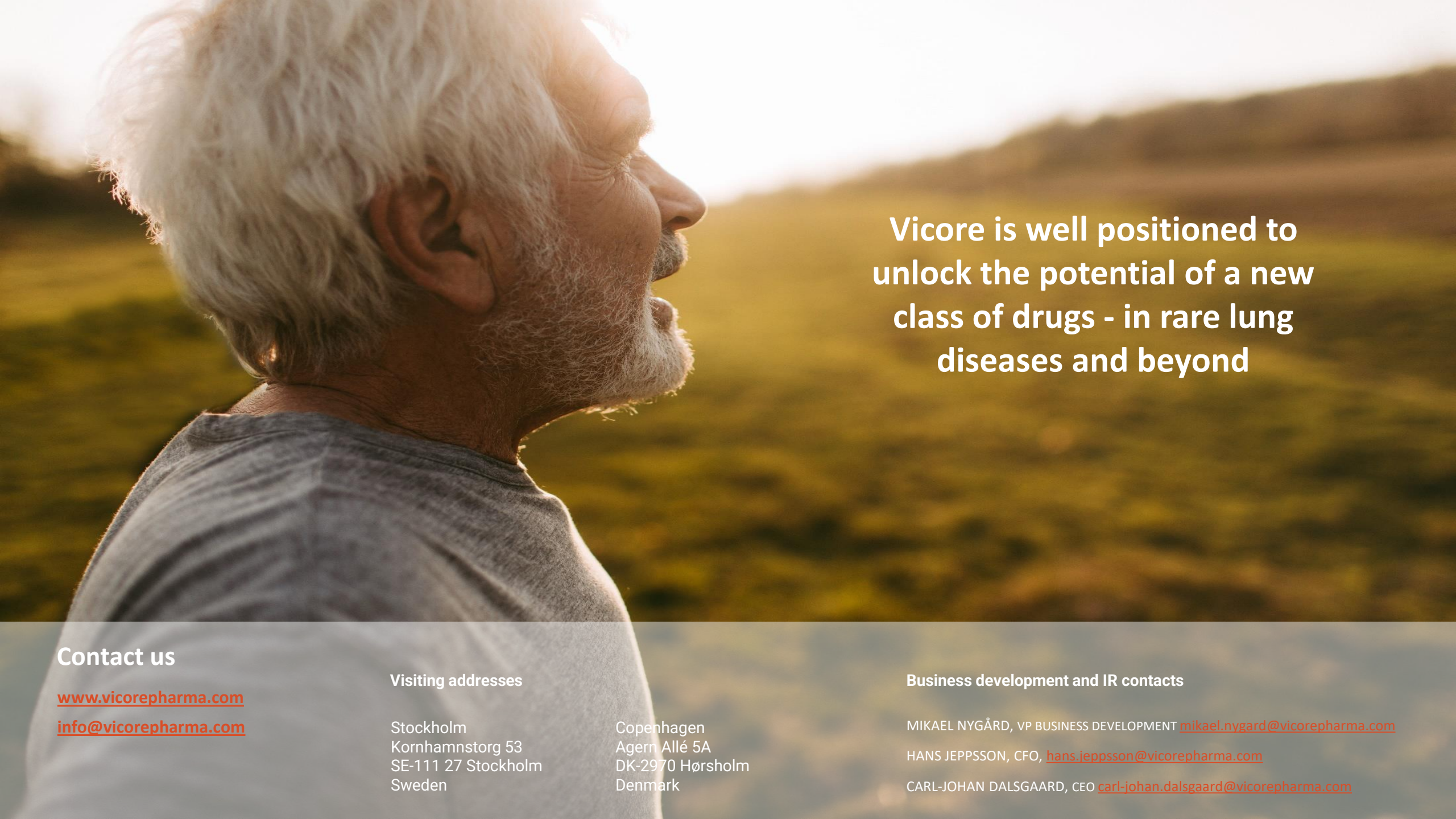
**Strong scientific rationale for disease modification in PAH**



**MoA with wide therapeutic implications**



**A clinical platform under development – capitalizing on lead**

A man with white hair and a beard is shown in profile, looking out over a vast, hilly landscape at sunset. The sun is low on the horizon, creating a warm, golden glow. The man is wearing a grey t-shirt.

**Vicore is well positioned to  
unlock the potential of a new  
class of drugs - in rare lung  
diseases and beyond**

## Contact us

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