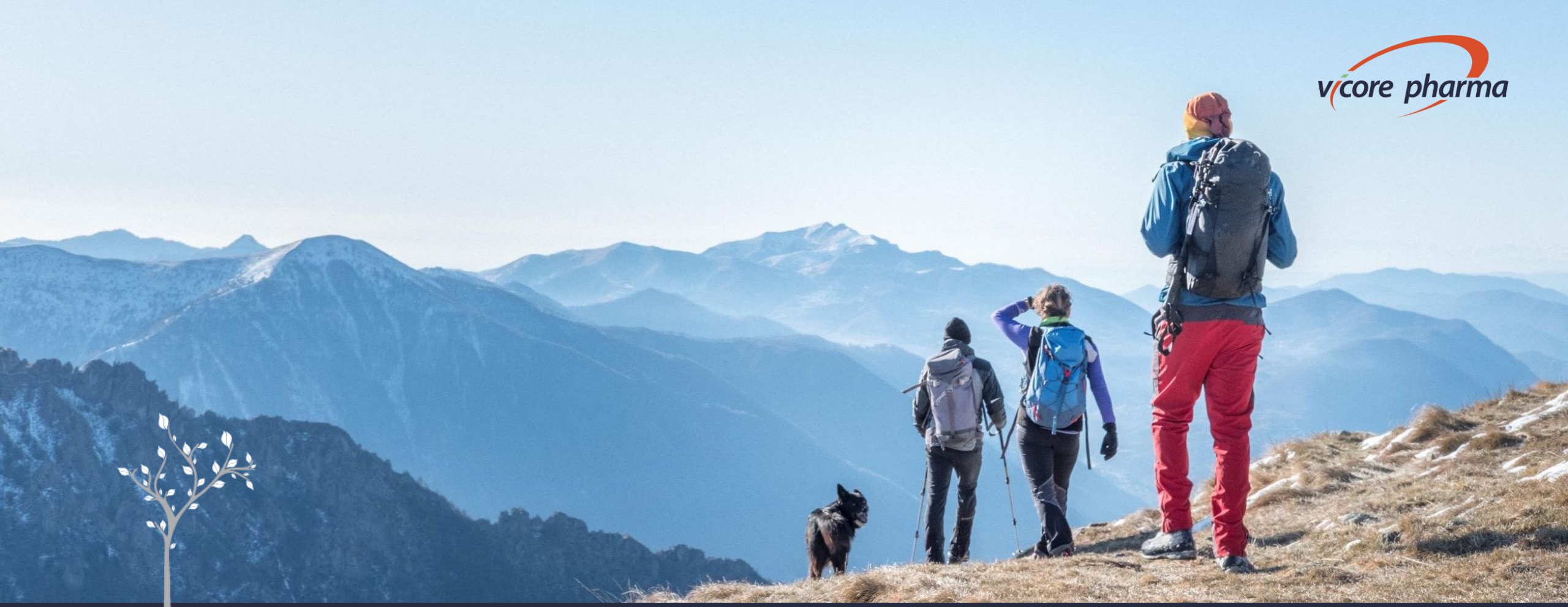


VICORE PHARMA

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

February 2023

Forward looking statement

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(1)

Headquarters

Stockholm Sweden, with Clin Ops team in Copenhagen, Denmark

Employees

~25 FTEs. Virtual setup

Ticker

VICO, listed at Nasdaq Stockholm. Market Cap; 140 MUSD (December 31, 2022)

Financials

Cash 25 MUSD (December 31, 2022)

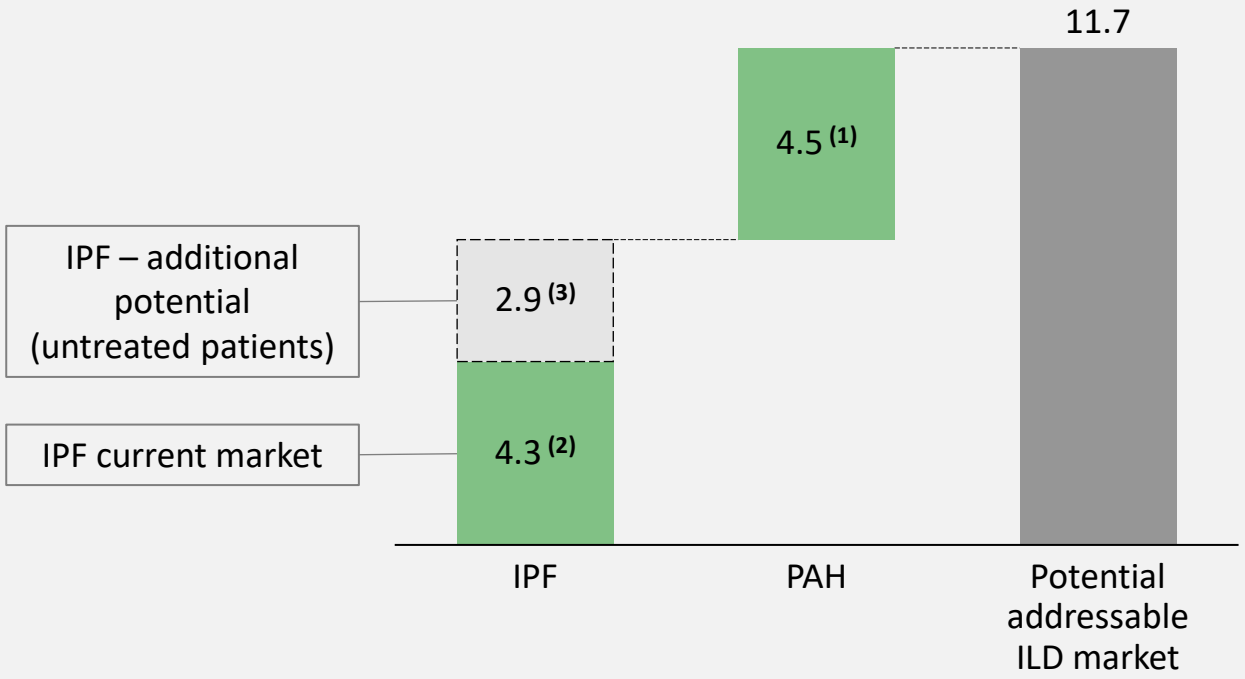
Major shareholders

HealthCap, HBM Healthcare Investments and Fourth Swedish National Pension Fund

(1) Wan Y, et al., J Med Chem. 2004 DOI: 10.1021/jm049715t

Market leadership opportunity in rare lung diseases

Possibility to expand the IPF market with more tolerable treatment



Market size in $Bn.

Opportunity for market leadership

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

(1) Market size in 7MM, source: Global Data (2) Combined sales of marketed drugs Ofev and Esbriet where Ofev sales since 2019 includes the indication SSc-ILD. Source: Evaluate Pharma
(3) Estimated based on ~40% of IPF patients currently not on treatment

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 BATTA, 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 CARLÈN
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 JEPPSSON, 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.

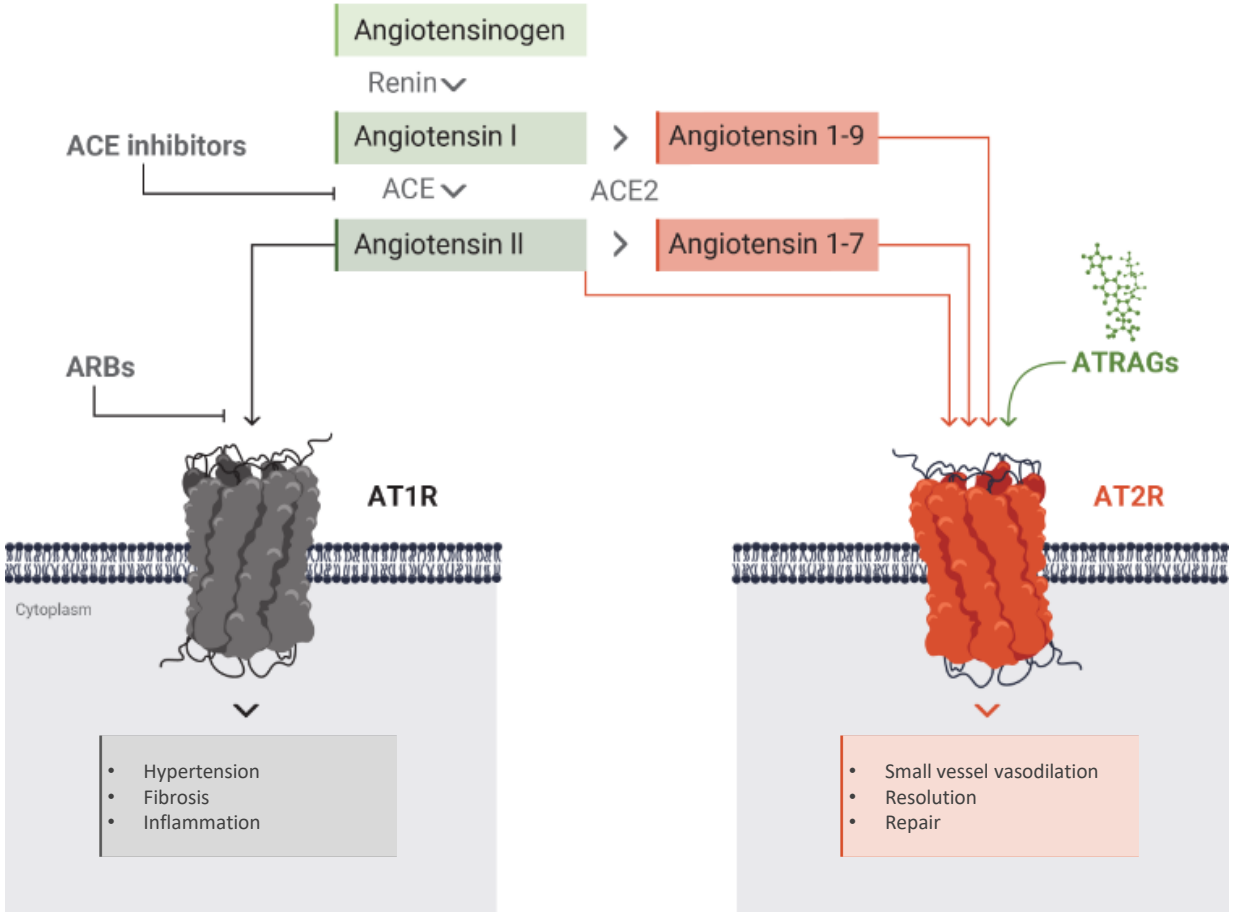
SARA MALCUS
10 years experience in operational management and board work at AstraZeneca and GU Ventures.

MAARTEN KRAAN
Extensive experience in biomedicine, managerial roles at AstraZeneca.

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

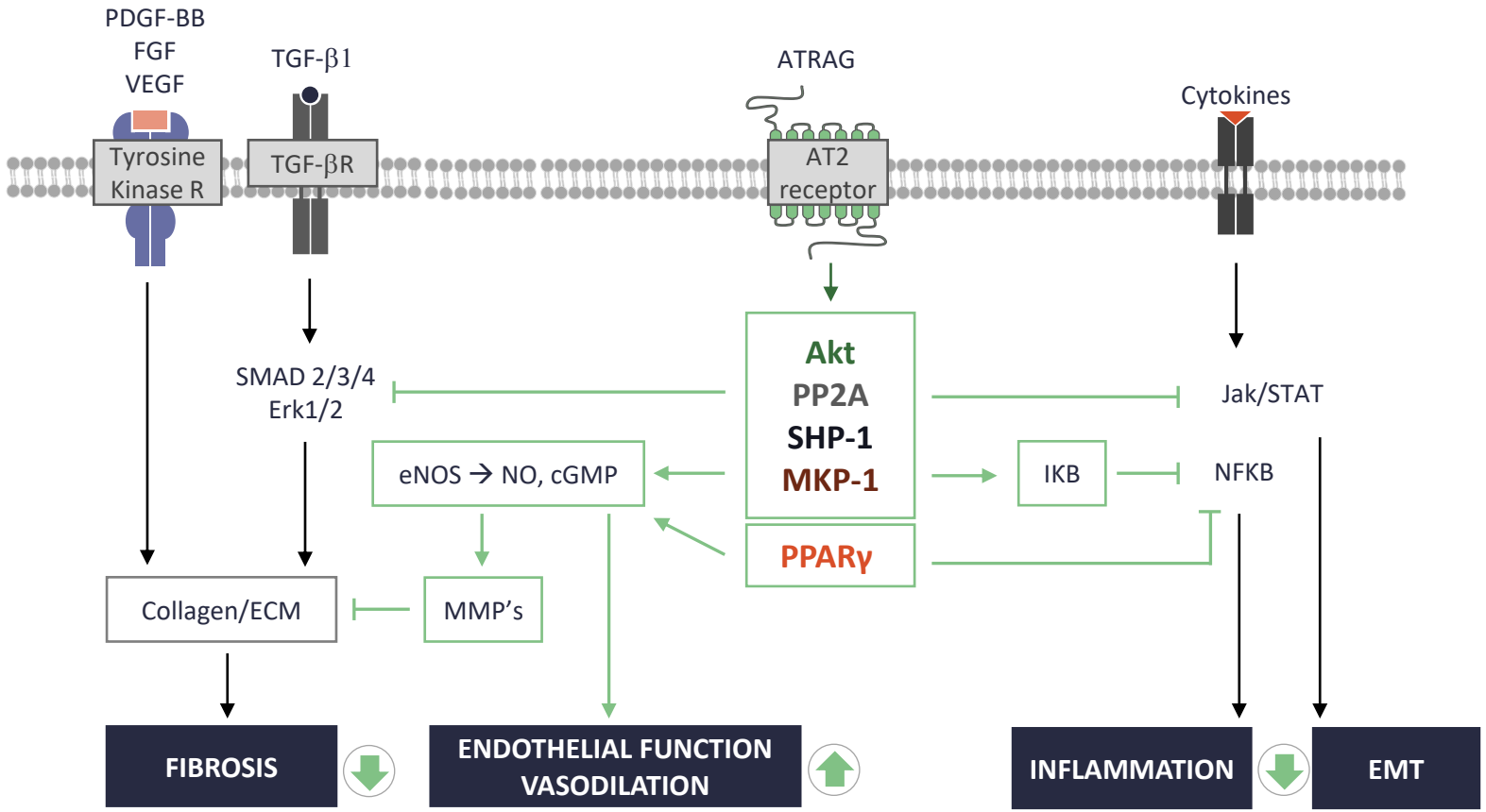


ATRAGs (Angiotensin II type 2 receptor agonists) have a favorable pharmacological profile

- 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 ATRAG

Multimodal action of AT2 receptor activation with broad therapeutic potential

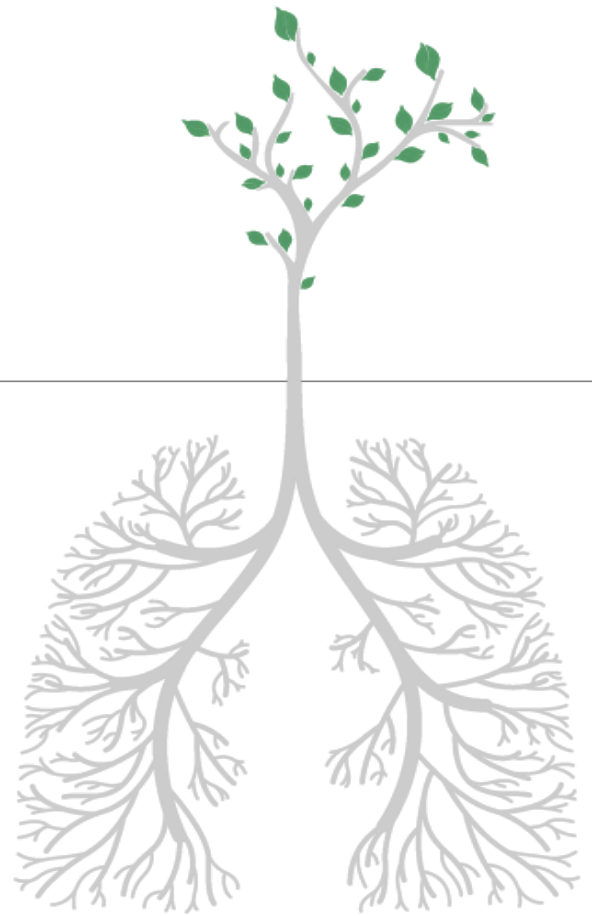


AT2 receptor targets fibrosis and inflammation and promotes endothelial functions

Reviewed in Steckelings et al. Pharmacological Reviews 2022. DOI: 10.1124/pharmrev.120.000281

Green arrows and boxes indicate key AT2 receptor signaling pathways. Green bold arrows indicate effects of AT2 receptor stimulation. PP2A (serine-threonine protein phosphatase-2A), MKP-1 (MAPK phosphatase 1), SHP-1 (Src homology region 2 domain-containing phosphatase-1), Akt (protein kinase B), PPARγ (peroxisome proliferator-activated receptor- γ), EMT (Epithelial mesenchymal transition), ECM (extracellular matrix)

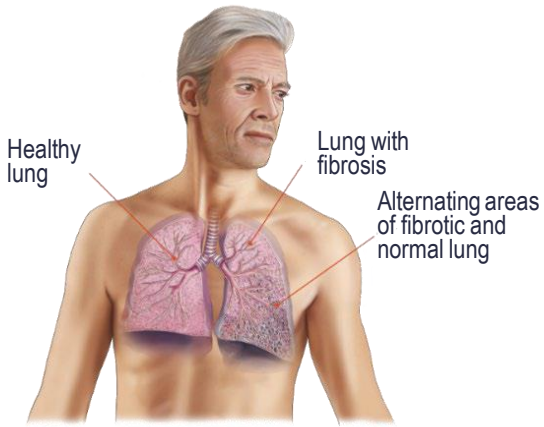
Rare lung disease – IPF and PAH

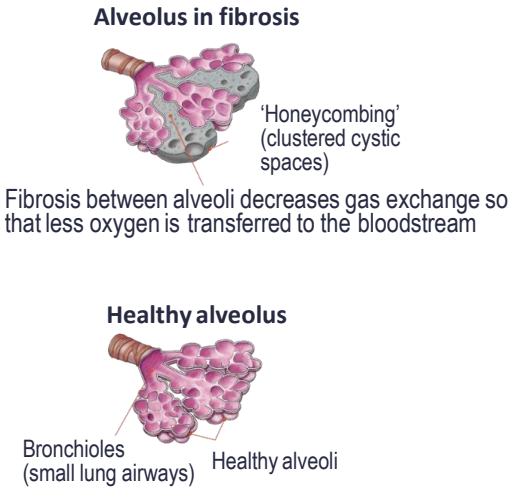


Idiopathic Pulmonary Fibrosis (IPF) – a significant unmet need

A devastating interstitial lung disease…

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





…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[1,2]

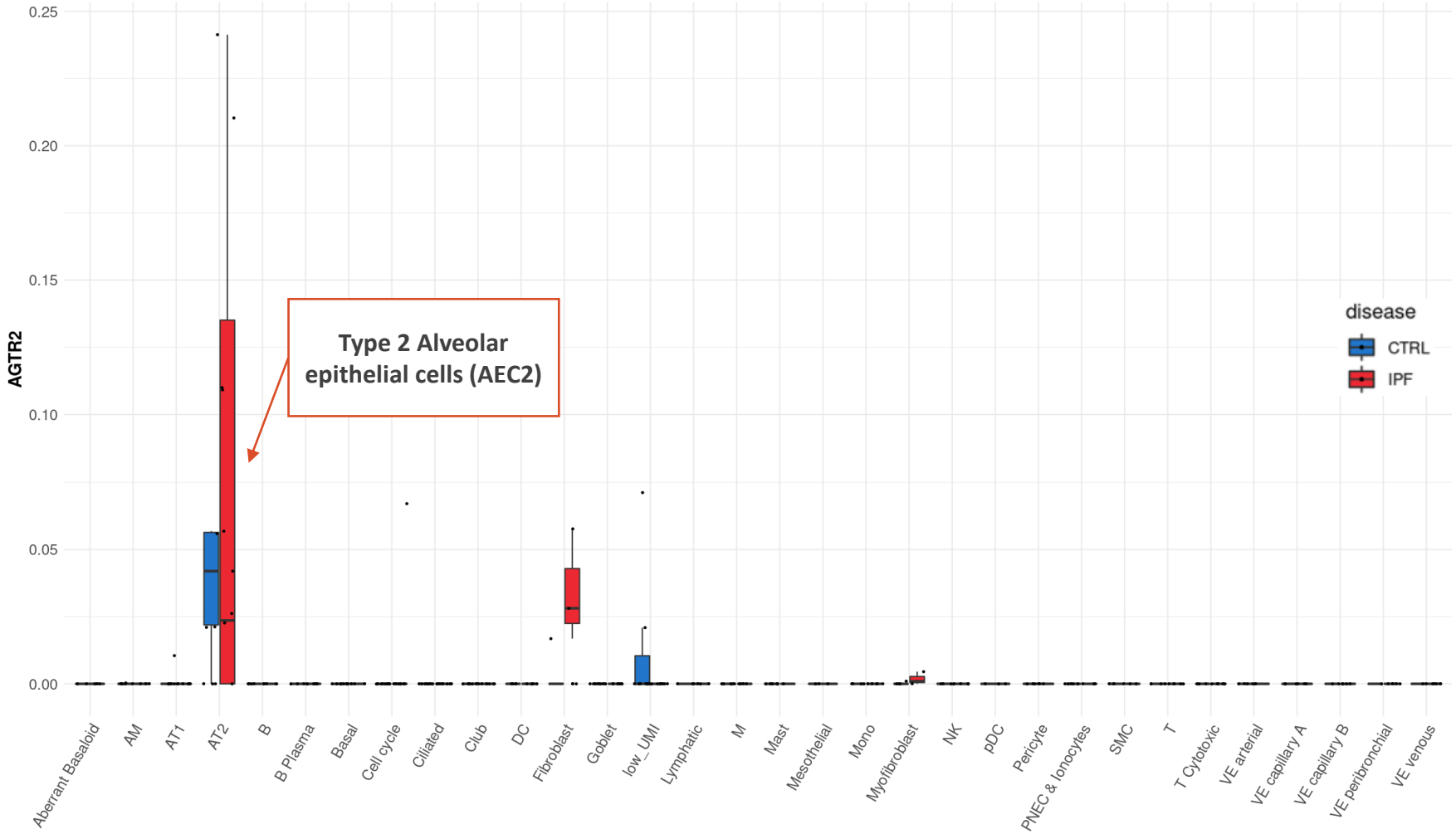
…and low compliance

- 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[3]

Large share of untreated patients provides medical and commercial opportunity

Source: (1) iHealthcareAnalyst (2) Pulmonary Fibrosis Foundation, Resp Res. 21, Article no: 48 (2020) (3) Dempsey et al. Ann Am Thorac Soc Vol 18, No 7, pp 1121–1128, Jul 2021. DOI: 10.1513/AnnalsATS.202007-901OC

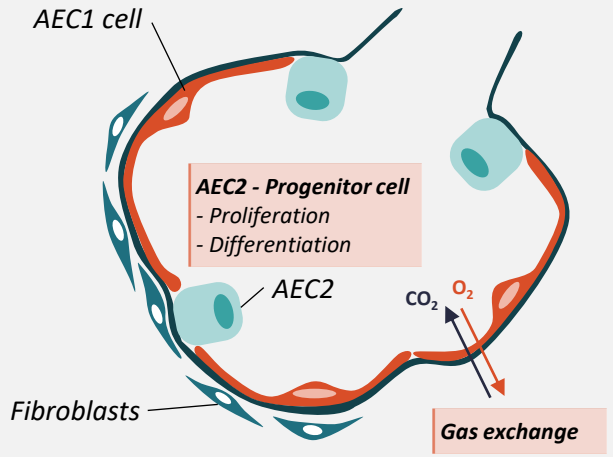
The AT2 receptor is highly expressed in lung AEC2 cells



Source: IPF cell atlas. Note: Single-cell RNA-sequencing (scRNA-seq) of single-cell suspensions generated from non-fibrotic control and PF lungs. N=30

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

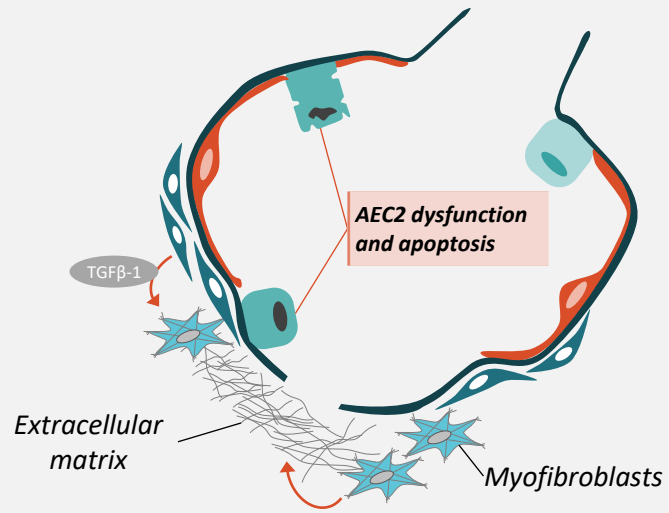
Normal alveolus



AEC – Alveolar Epithelial Cell

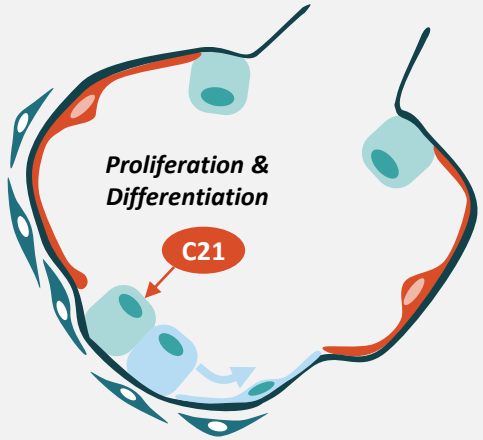
AEC1 cells – gas exchange
AEC2 cells – repair function

Lung fibrosis development



Dysfunctional AEC2 cells – trigger for fibrosis

Alveolar repair



C21 stimulates AEC2 cells and alveolar repair

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

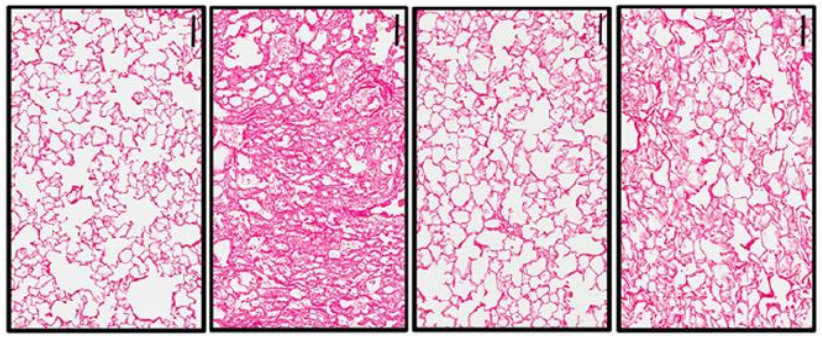
Strong preclinical in-vivo data demonstrate multimodal effects of C21

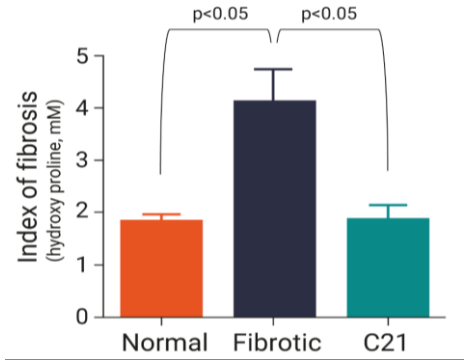
Significant and consistent effects of C21 treatment across animal fibrosis models

↓ Lung fibrosis	• Collagen content (Picro-sirius staining, Hydroxyproline, Collagen gene expression)
↓ Remodeling of pulmonary vessels	• H&E staining, Ashcroft scoring • α-SMA staining • Vessel wall thickness, luminal opening and vascular lesions
↓ Cardiac remodeling	• Right ventricular hypertrophy (RVH)
↓ Pulmonary hypertension	• Right ventricular systolic pressure (RVSP) • Right ventricular end diastolic pressure (RVEDP) • Stroke volume
↑ Cardiac output	• mL/min

Bleomycin rat model

Collagen staining



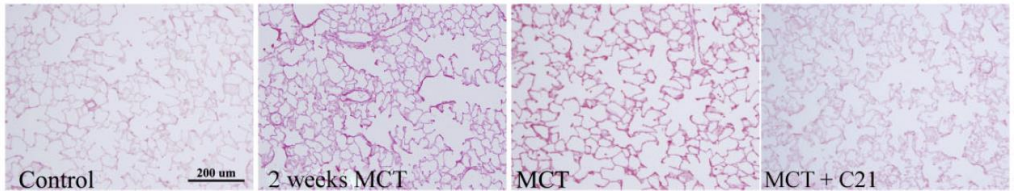


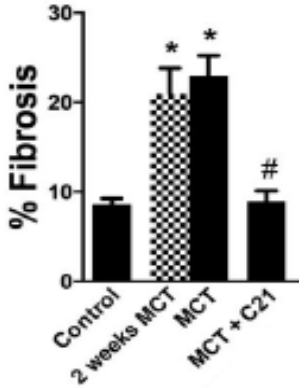
**Low dose C21 i.p. once daily for 2 weeks*

Adapted from Rathinasabapathy 2018

Monocrotaline rat model

Collagen staining





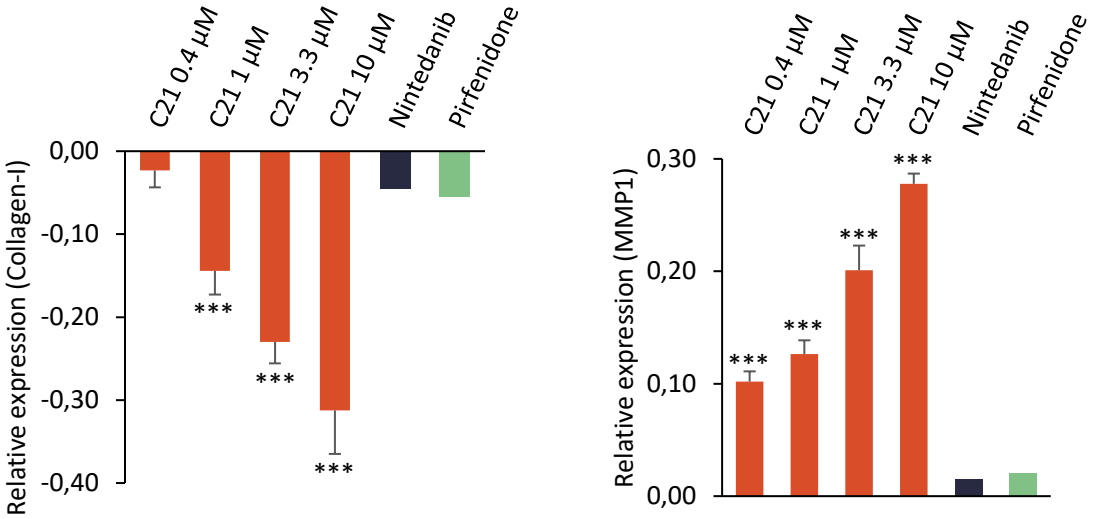
Low dose C21 i.p. once daily for 2 weeks

Adapted from Bruce 2015

Sources: Bruce et al. Br J Pharmacol. 2015. DOI: 10.1111/bph.13044, Rathinasabapathy et al. Front Physiol. 2018 DOI: 10.3389/fphys.2018.00180

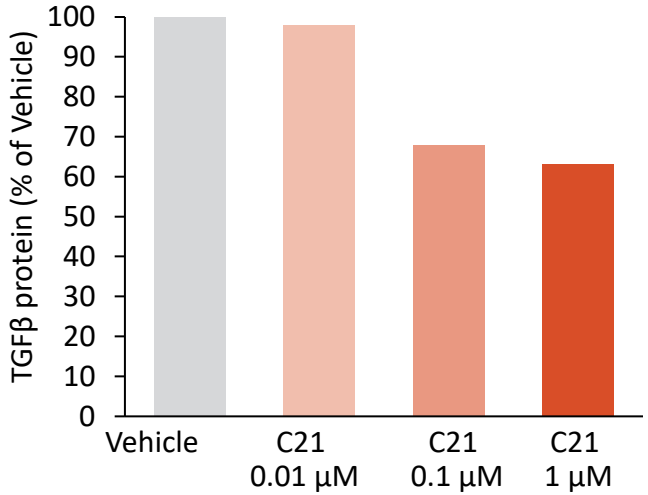
C21 modulates gene expression in human lung tissue slices and primary cells

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

Source: Vicore data on file

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 IPF Phase 2a data – Demography and baseline characteristics

Interim analysis October 2022

Patient characteristics

		All enrolled (N=45)
Age (years) - Mean (SD)		67.0 (9.1)
Gender	Males Females	33 (73.3%) 12 (26.7%)
Weight (kg) – Mean (SD)		63.4 (12.6)
BMI (kg/m^2) – Mean (SD)		24.2 (3.9)
Smoking status	Former smoker Never smoker	8 (17.8%) 37 (82.2%)
Duration of diagnosis (years) – Mean (SD)		0.6 (1.0)
HRCT pattern	Probable UIP Typical UIP Missing	18 (40.0%) 24 (53.3%) 3 (6.7%)

Baseline pulmonary function tests

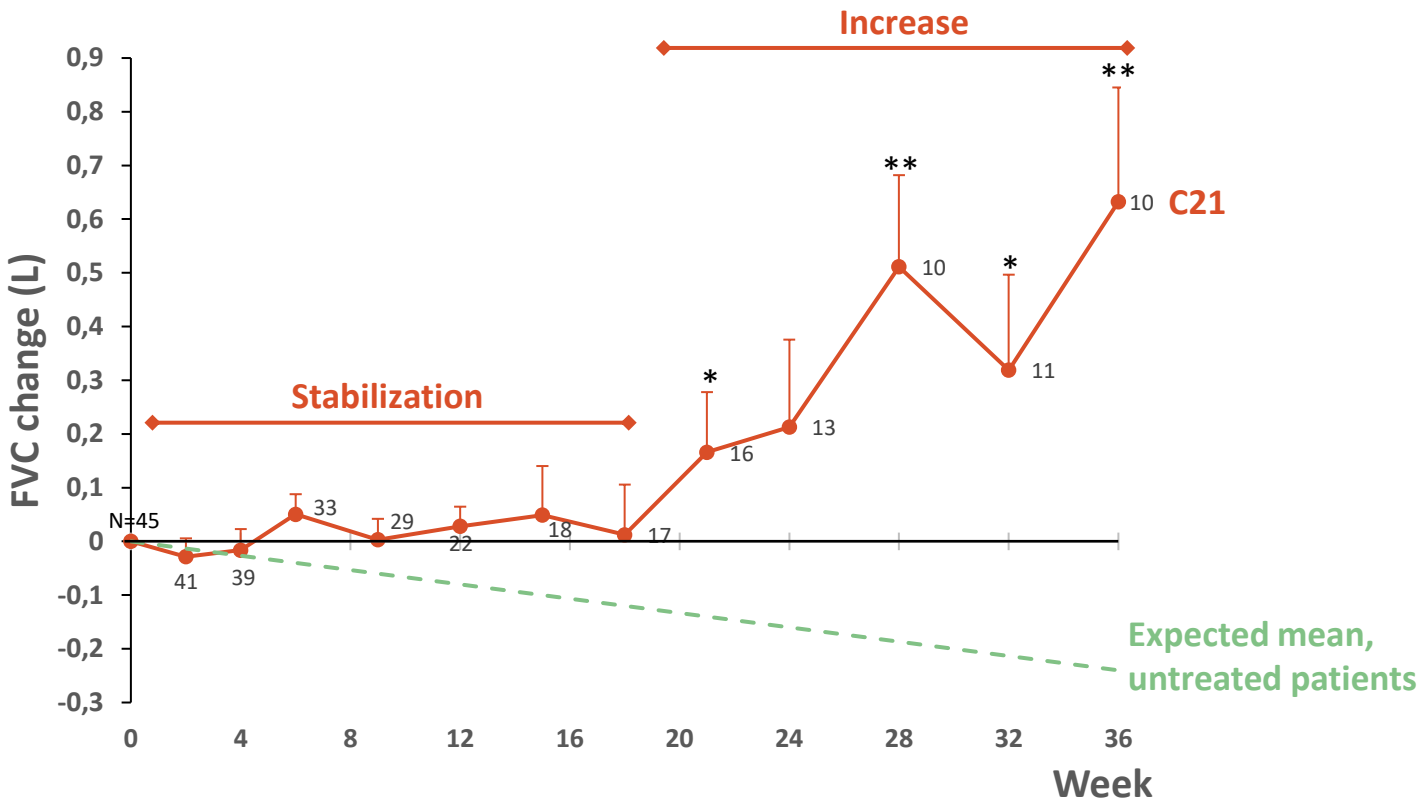
	All enrolled (N=45)
FVC (L) - Mean (SD)	2.41 (0.69)
FVC (% predicted) - Mean (SD)	76.8 (16.0)
FEV_1/FVC - Mean (SD)	0.80 (0.07)
SpO_2 - Mean (SD)	95.5 (2.4)

Baseline data in line with previous IPF trials

AIR interim analysis shows disease stabilization with later increase in FVC

Interim analysis October 2022

Mean change (±SEM) from baseline in FVC over time, observed values



- **Stabilizes disease over 36 weeks**
- **Increased FVC in high responders**
- **Safe and well tolerated – no GI signals**
- **Encouraging patient testimonies**

A placebo-controlled dose confirmatory trial (2b) will be the next step

Note: Expected mean untreated patients based on placebo data from previous clinical trials. Slope values at 21, 28, 32 and 36 weeks are statistically significant (*p<0.05 and **p<0.01) vs. the expected mean for untreated patients.

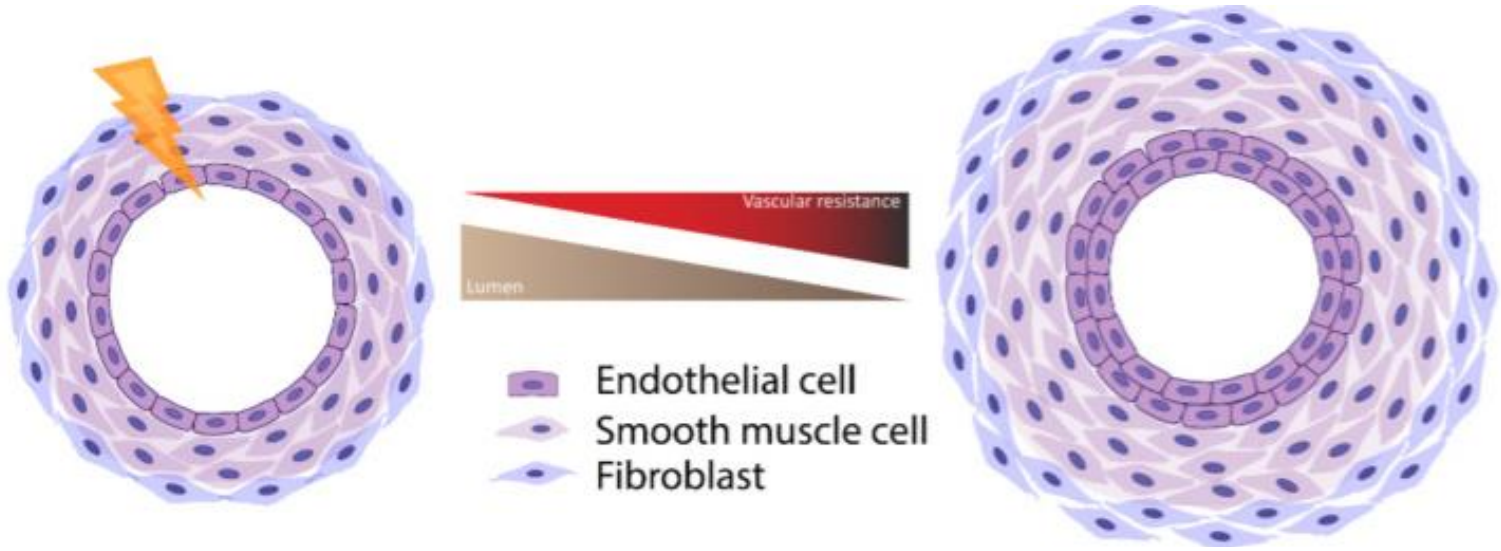
PAH – a microvascular rare disease with poor prognosis

PAH is a rare, fatal disease…

- Orphan disease with ~67 000 patients in US and Europe(1)
- 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



Healthy pulmonary microvessel

Remodeled pulmonary microvessel

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

Source: (1) Orphanet. PAH - Pulmonary Arterial Hypertension

Strong preclinical data with C21 in disease-relevant animal model

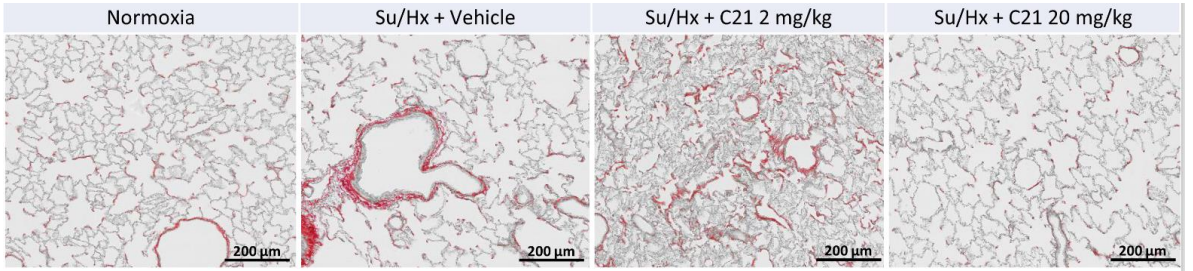
Sugen-Hypoxia rat model

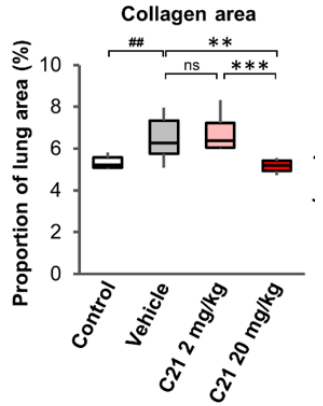
Effects of C21 treatment:

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

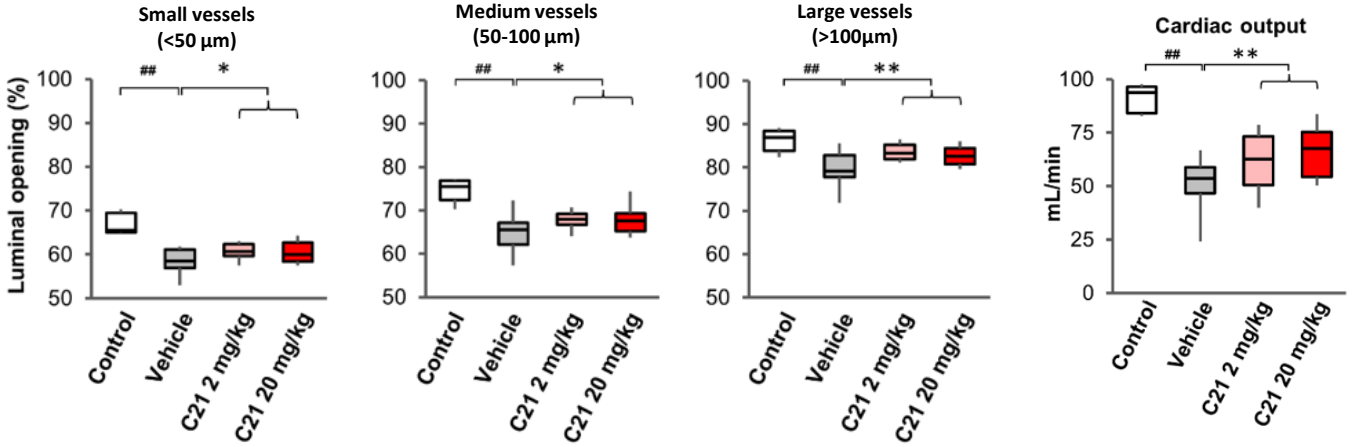
Protocol: C21 p.o. for 34 days, initiated 21 days after Sugen-Hypoxia period. N=10-11 per treatment group

Collagen





Vascular remodeling and cardiac output



Positive effects on vascular remodeling, fibrosis and cardiac function

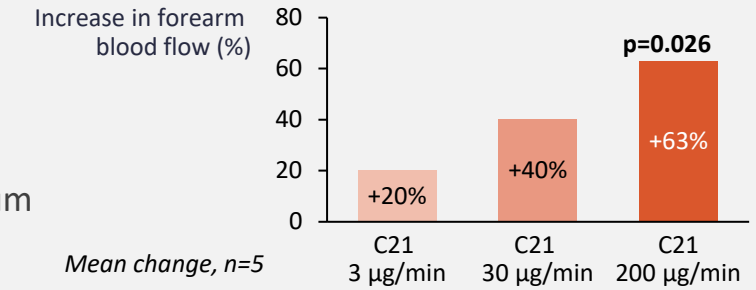
Source: Vicore data on file (submitted manuscript).

Investigating effects on endothelial dysfunction in PAH

C21 increases local blood flow

Forearm blood flow in healthy volunteers

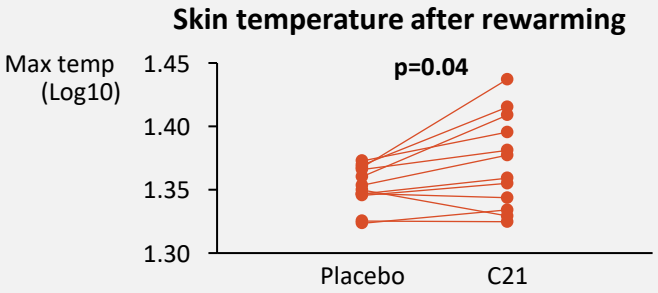
- Increase in blood flow (63%, p=0.026) at clinically relevant doses
- No systemic blood pressure effects or other side effects
- Vasodilation is mediated by nitric oxide (NO) released from the endothelium



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)

Source: Vicore data on file

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

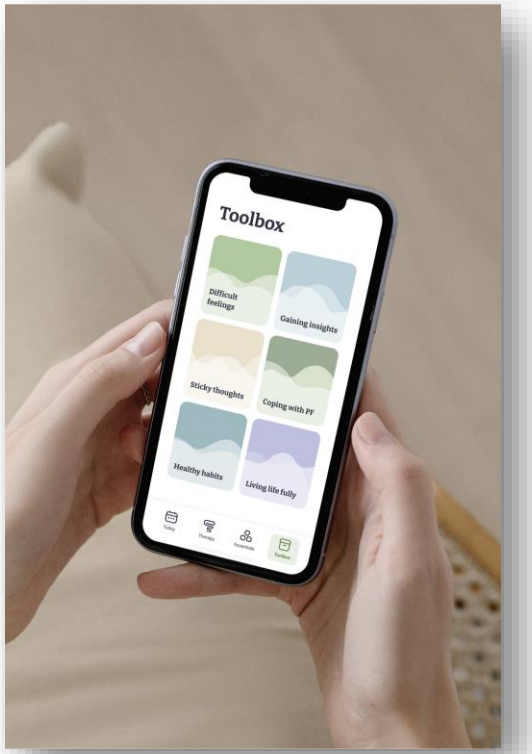
- Huge unmet need: 63% of patients with treatable levels of anxiety[1]
- Current pharmacological treatments do not improve patients' quality of life
- Health care resource utilization two-fold versus controls

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

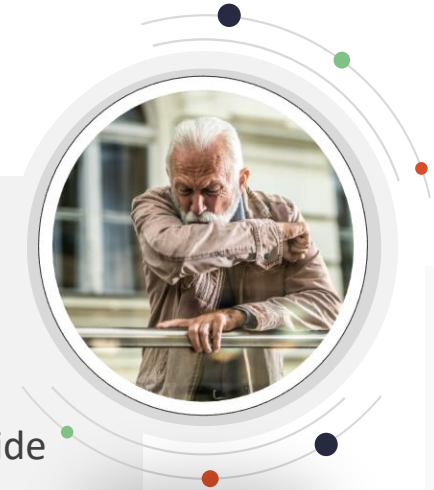
COMPANION – decentralized study

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



(1) Share of patients with self-reported score 5 or higher on the GAD7 scale. Source: Shull & Walmar, poster presentation, Respiratory Effectiveness Group Summit, March 2022

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

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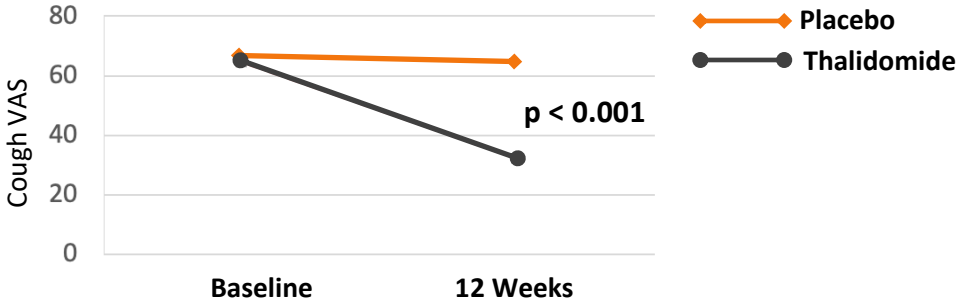
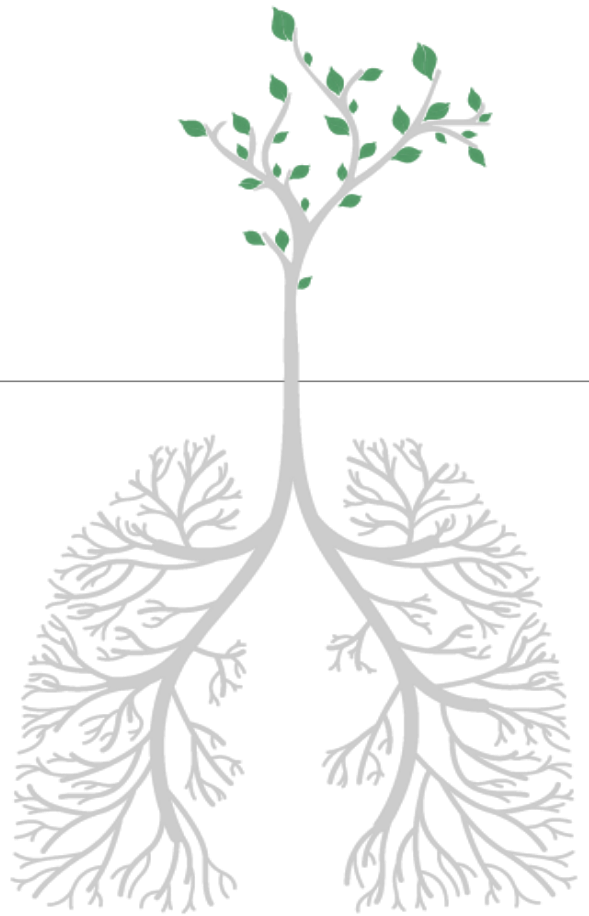


Relevant patient group: 78% men, mean age 67.6 years, mean FVC 70.4%

Source: Horton et al. Ann Intern Med. 2012. DOI: 10.7326/0003-4819-157-6-201209180-00003

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
- 1st compound, C106 in phase 1

Behind C21 there are 4 new compounds in development

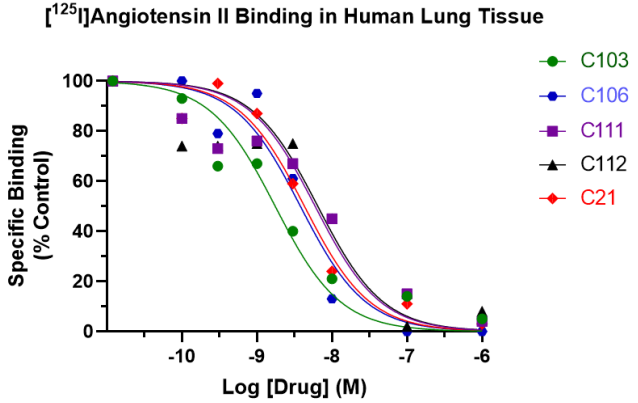
ATRAGs in development have confirmed potency, selectivity and efficacy

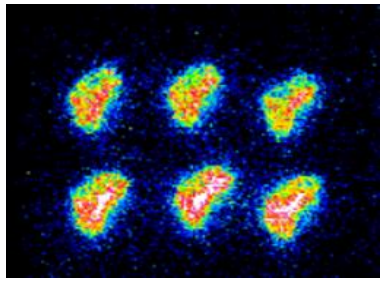
New ATRAGs compound characteristics

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

Target engagement - autoradiography with human lung tissue

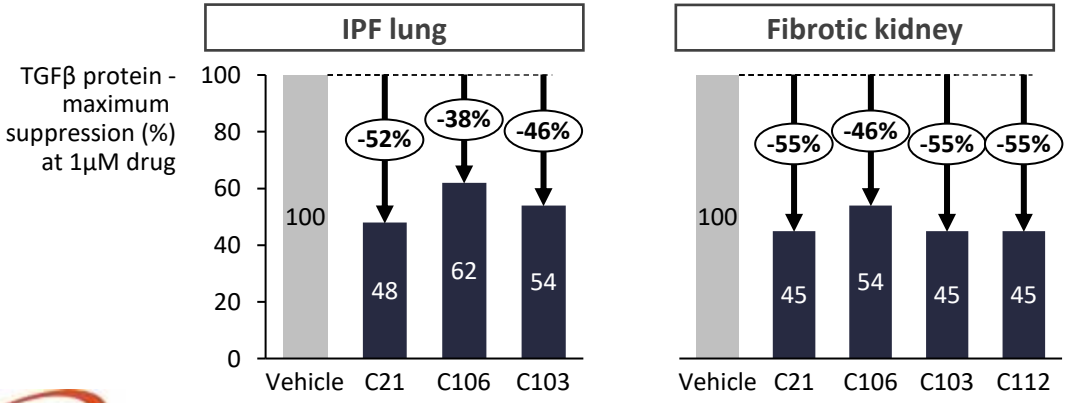
- Displacement with cold ATRAGs at clinically relevant concentrations





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**

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

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