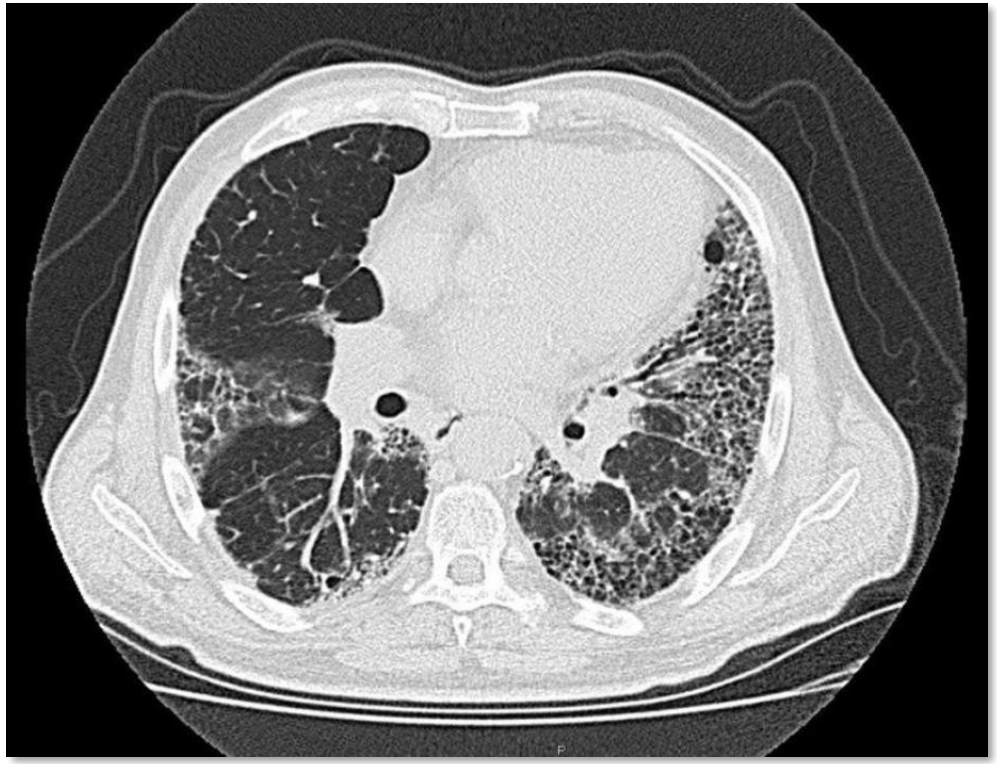
ziritaxestat

for idiopathic pulmonary fibrosis (IPF)

Progressive lung fibrosis leading to death

- 250k cases in US & EU
- 75k new cases every year
- median survival 2-5 years



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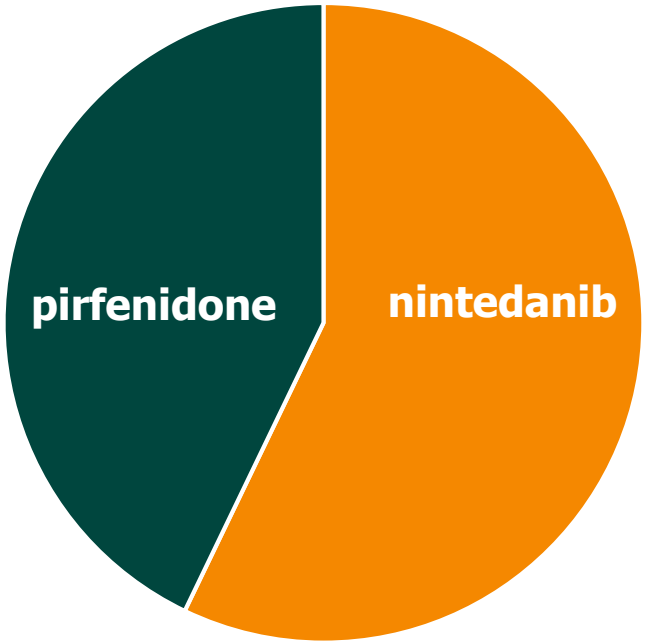
IPF $2.8B market with large unmet needs

2019 DRUG SALES: $2.8B

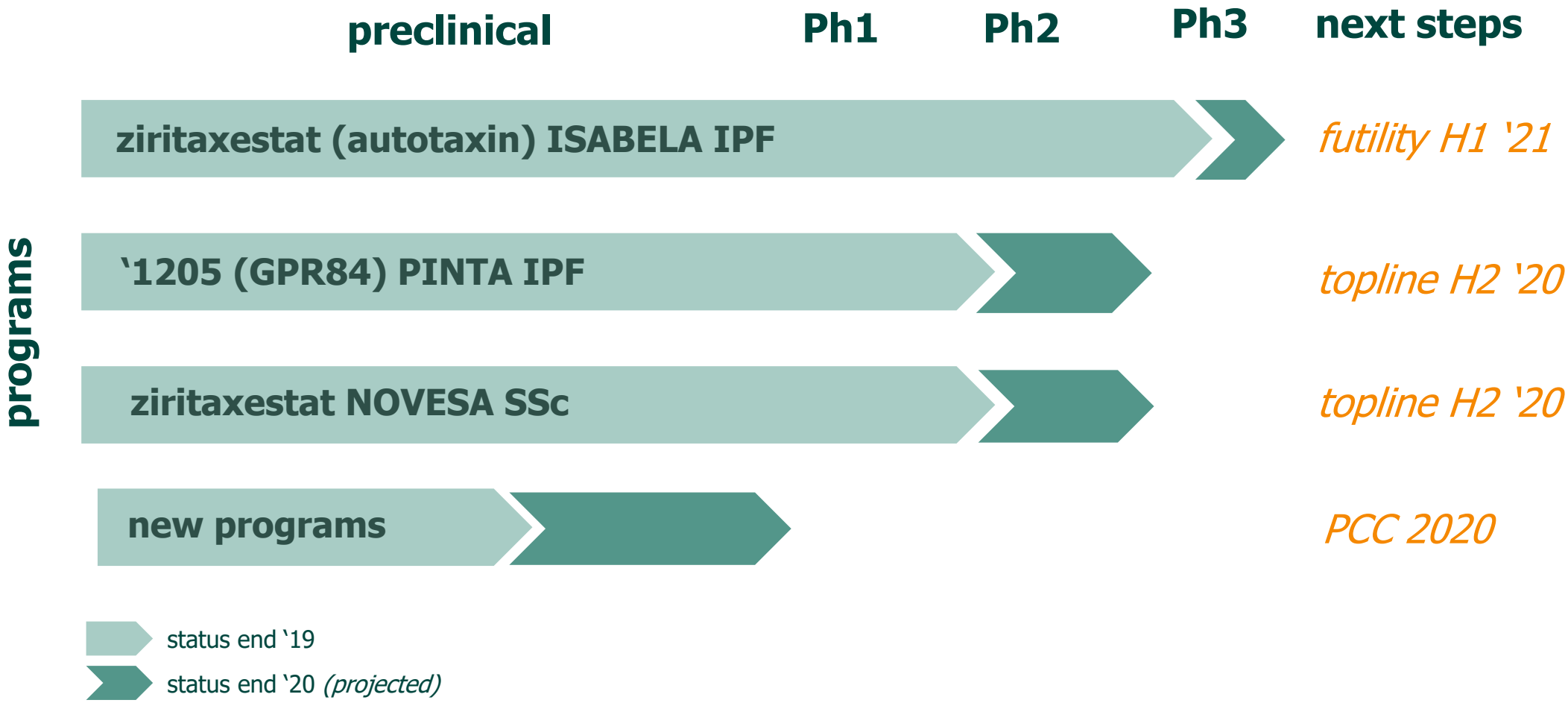


nintedanib & pirfenidone have limitations

- slow FVC decline
- poor tolerability for patients
- ~25% annual discontinuations

Sources: Global Data, Maher et al. BMC Pulmonary Medicine (2017) 17:124, sales figures from Roche (pirfenidone; Esbriet®) and Boehringer Ingelheim (nintedanib; Ofev®)
FVC: Forced vital capacity

IPF & fibrosis portfolio



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FLORA in *The Lancet Respir Med*

Articles

Safety, tolerability, pharmacokinetics, and pharmacodynamics of GLPG1690, a novel autotaxin inhibitor, to treat idiopathic pulmonary fibrosis (FLORA): a phase 2a randomised placebo-controlled trial

Toby M Maher, Ellen M van der Aar, Olivier Van de Steen, Lisa Allamassey, Julie Desrivot, Sonia Dupont, Liesbeth Fagard, Paul Ford, Ann Fieuw, Wim Wuyts

Summary

Background Idiopathic pulmonary fibrosis (IPF) causes irreversible loss of lung function. People with IPF have increased concentrations of autotaxin in lung tissue and lysophosphatidic acid (LPA) in bronchoalveolar lavage fluid and exhaled condensate. GLPG1690 (Galapagos, Mechelen, Belgium) is a novel, potent, selective autotaxin inhibitor with good oral exposure. We explored the effects of GLPG1690 in patients with IPF.

Lancet Respir Med 2018
Published Online
May 20, 2018
http://dx.doi.org/10.1016/
S2213-2600(18)30181-4

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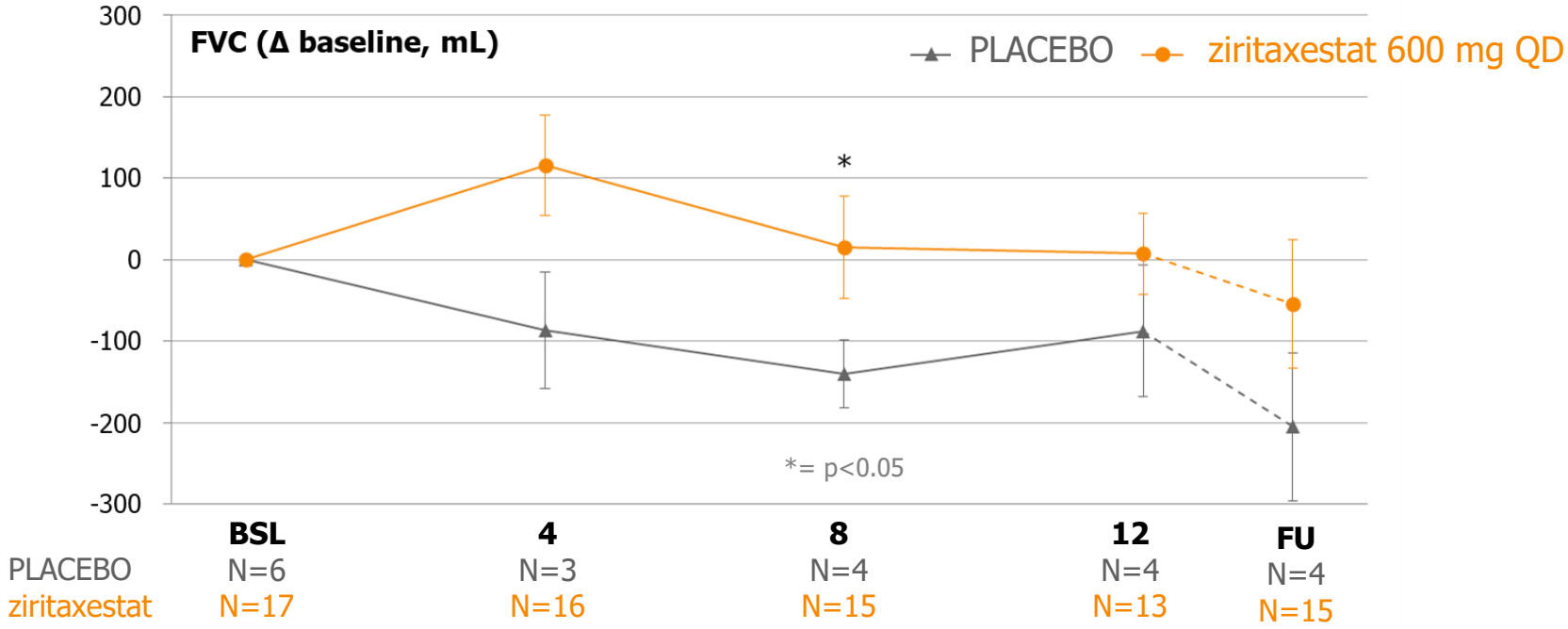
Positive ziritexestat data in patients



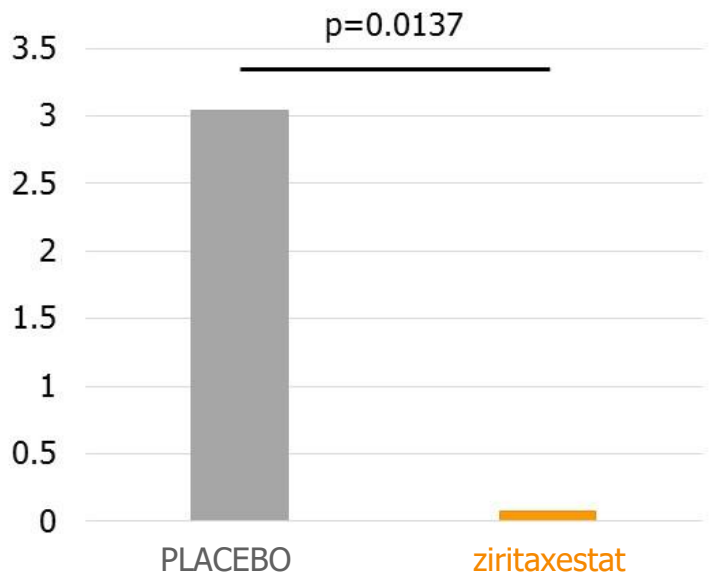
	Wk4		Wk8		Wk12		Follow-up	
	Placebo	'1690	Placebo	'1690	Placebo	'1690	Placebo	'1690
FVC (Δ baseline, mL)	-87	+116	-140	+15	**-87**	**+8**	-205	-55

FVC stabilization over 12-week period

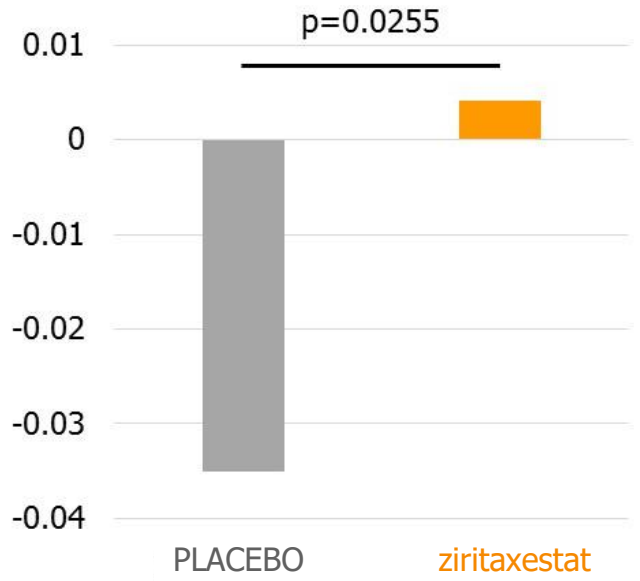
FRI indicates disease stabilization

Flora

SPECIFIC AIRWAY VOLUME (Δ baseline, mL/L)



SPECIFIC AIRWAY RESISTANCE (Δ baseline, kPa/sec)



Functional respiratory imaging tracks ahead of FVC

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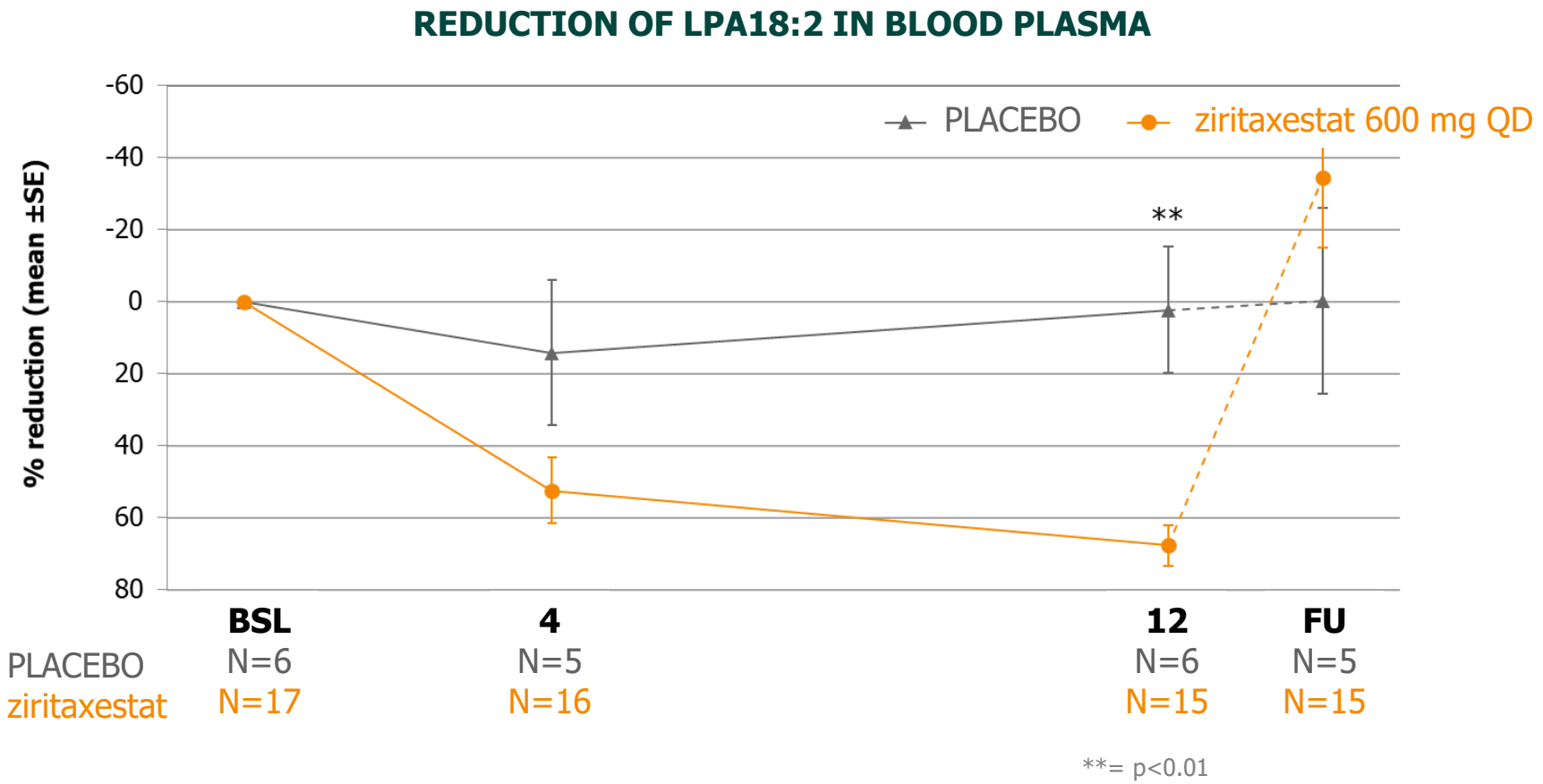
Strong biomarker reduction

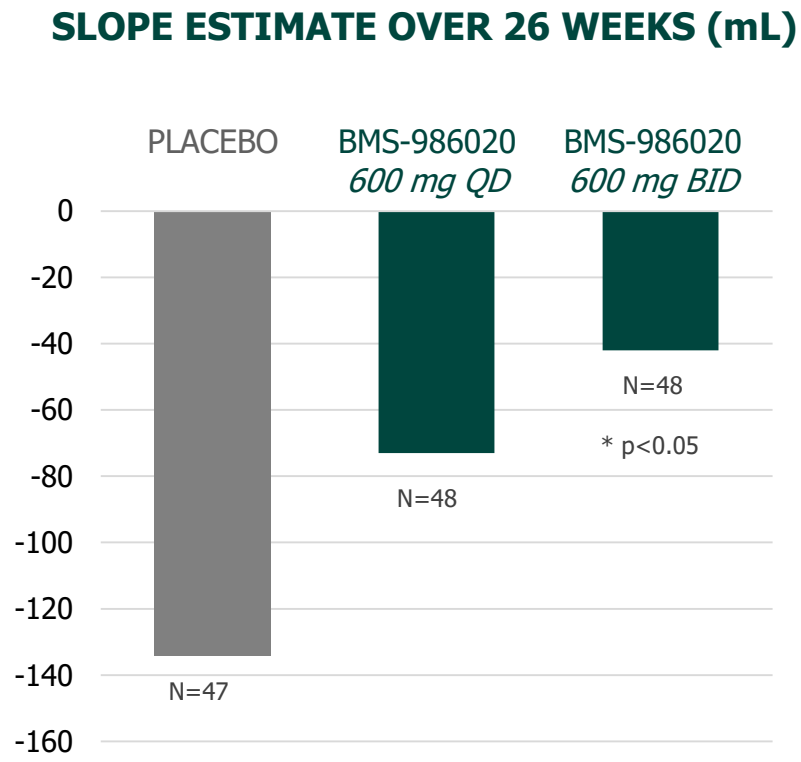


Biomarker reduction = target engagement

ziritaxestat pathway clinically validated

LPA1 inhibition has impact

- BMS-986020 reduced FVC decline
- Trial stopped due to off-target cholecystitis
- BMS-986020 inhibits LPA1
- ‘1690, an autotaxin inhibitor, markedly reduces LPA1 levels



Source: Chest. 2018 Sep 7. pii: S0012-3692(18)32411-5

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Phase 3 program ISABELA 1&2

- 1500 IPF patients total in two identical Phase 3 studies
- Patients remain on standard of care throughout
- Global program with US & EU component
- Primary endpoint: FVC decline at 52 weeks
- Secondary: hospitalizations, mortality, quality of life, safety/tolerability

ziritaxestat has orphan status in IPF in US and EC

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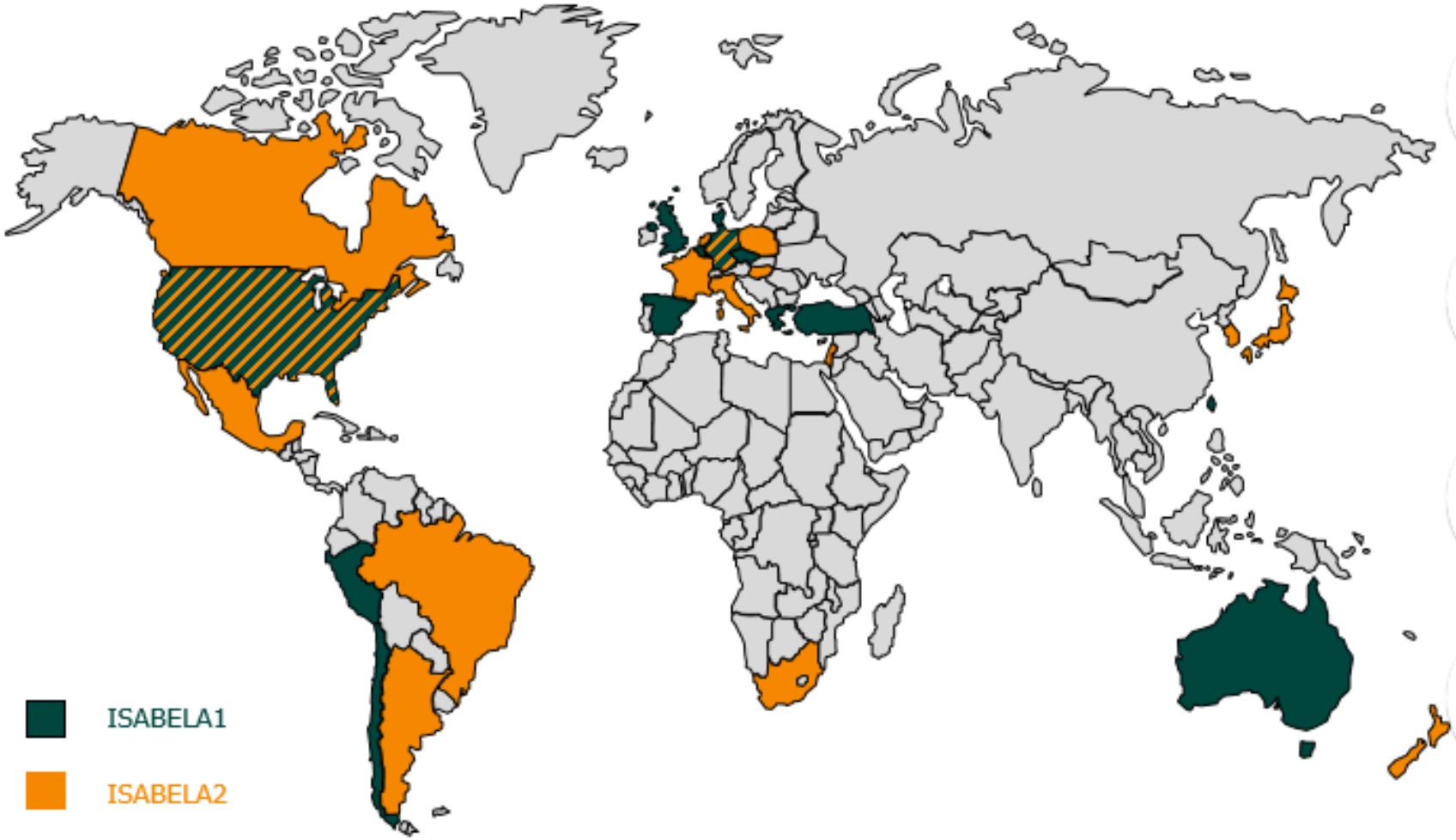
ISABELA participating countries



APAC

ISABELA1: Australia, Taiwan
ISABELA2: Japan, New Zealand, South Korea

EMEA

ISABELA1: Belgium, Czech Republic, Denmark, Germany, Greece, Spain, Turkey, UK
ISABELA2: France, Germany, Hungary, Israel, Italy, Netherlands, Poland, South Africa

LATAM

ISABELA1: Chile, Peru
ISABELA2: Argentina, Brazil, Mexico

North America

ISABELA1: USA
ISABELA2: Canada, USA

** As of Nov 8, 2019*

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ISABELA, innovative program in IPF

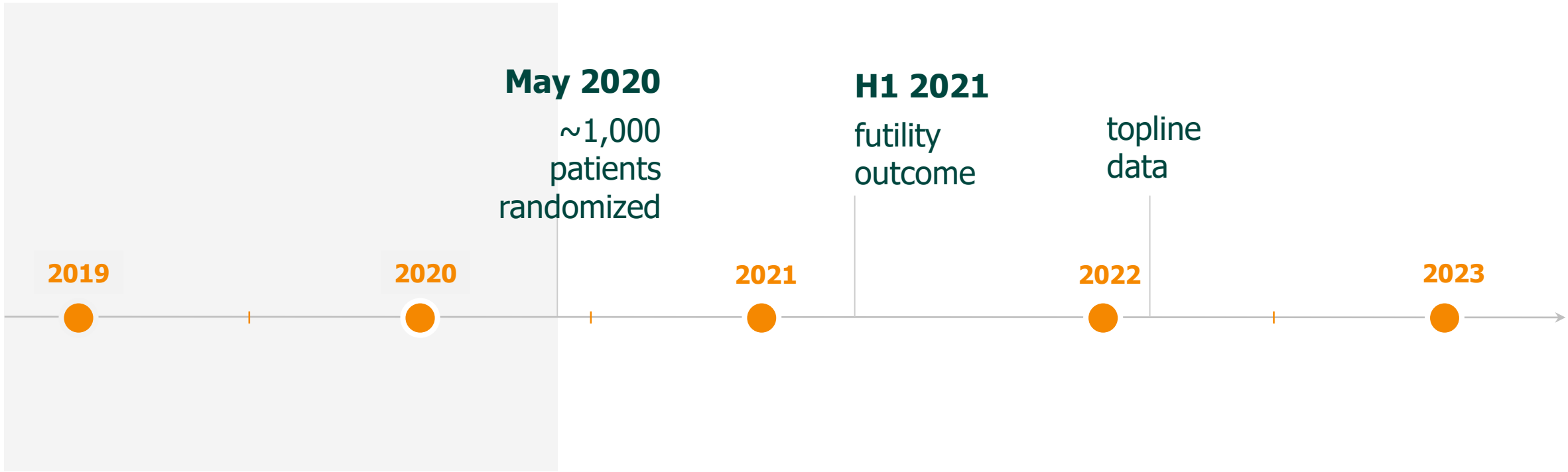
Largest IPF program thus far

Assesses efficacy & safety in **real-world setting**

Controlled data on **medically-relevant, hard endpoints** like changes in FVC, mortality rates, respiratory-related hospitalizations and PROs

Large safety dataset in 1,500 patients over 52 weeks or longer

ISABELA
timeline



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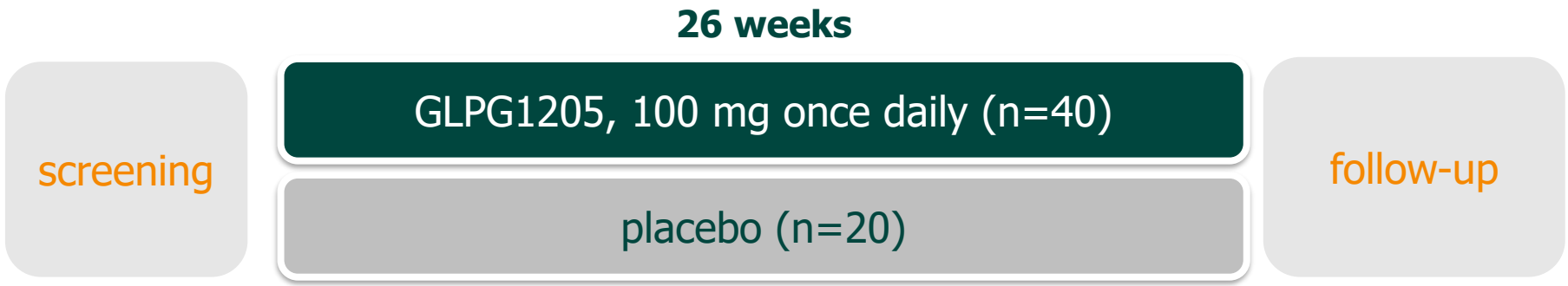
PINTA Phase 2 in IPF



- 60 IPF patients on local standard of care
- Primary endpoint: forced vital capacity (FVC) at 26 weeks
- Secondary: safety, tolerability, broad range of measurements, incl. functional respiratory imaging (FRI)
- Recruitment in 9 countries in Europe, North Africa, & Middle East

Fully recruited, topline data expected in H2

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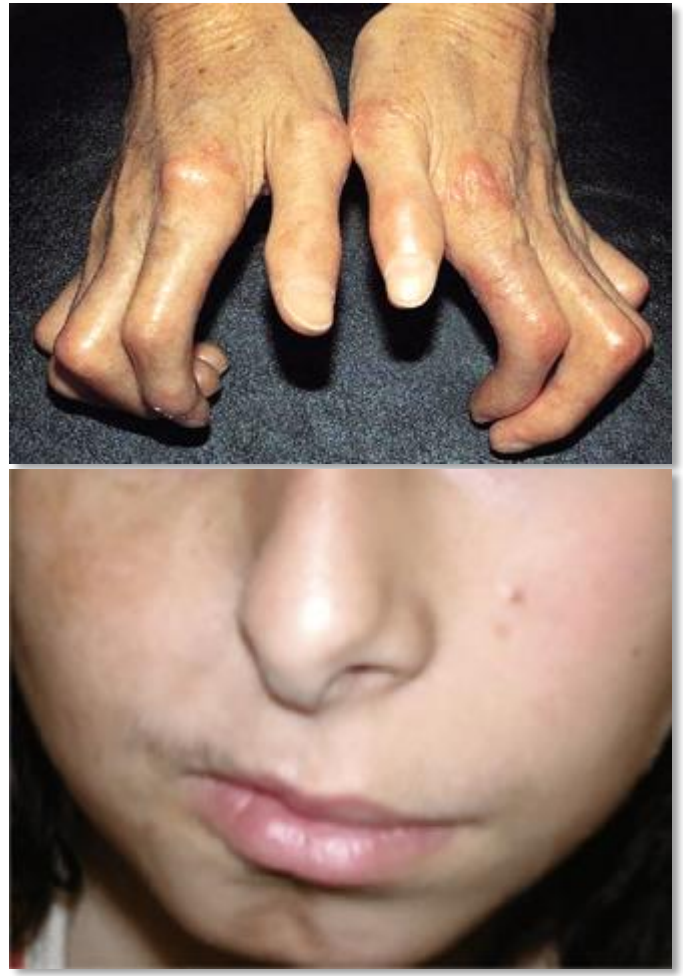
Systemic sclerosis (SSc)

- Multi-organ ("systemic") fibrosis
- Rare disease: ~95k patients[1]
- Among the highest mortality of all autoimmune/rheumatic diseases[2]
- No approved anti-fibrotic drugs[3]



[1] Global Data 2014; [2] Nikpour et al Curr Opin Rheumatol. 2014; [3] Denton et al Lancet 2017

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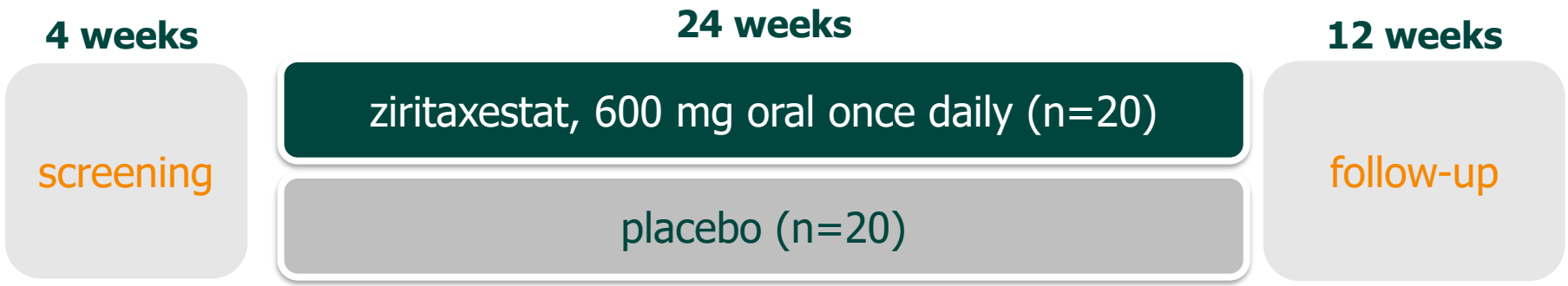
NOVESA Phase 2 in SSc



- 30 patients with progressive diffuse (multi-organ) SSc
- Recruitment in US & 5 EU countries
- Primary endpoint: mRSS at 24 weeks
- Secondary & exploratory endpoints: safety, tolerability, broad range of measures (FVC, quality of life, CRISS)

Fully recruited, topline data expected in H2, orphan status in SSc in US and EC

CRISS: Composite Response Index in Systemic Sclerosis; FVC: forced vital capacity; mRSS: modified Rodnan Skin Score

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