Galápagos

Novel targets, better treatments

Investor Presentation | Nov 2017

Disclaimer

This presentation contains forward-looking statements, including (without limitation) statements concerning the progress of our clinical pipeline, the slides captioned "Our strategy" "R&D delivery" "Filgotinib" "Clinical pipeline" "Filgotinib in RA & Crohn's" "'1690 in FLORA" "Strategy to a triple combo in CF" "Deep CF Portfolio" "CF triple combinations" "6 CF patient studies" "Clinical news flow" and "Outlook", statements regarding the development of the triple combination therapy CF program, statements regarding the expected timing, design and readouts of ongoing and planned clinical trials (i) with filgotinib in RA, IBD, and other potential indications (ii) in the CF program, (iii) with GLPG1690 in IPF, (iv) with GLPG1972 in OA, (v) with MOR106 in atopic dermatitis, and expectations regarding the commercial potential of our product candidates. When used in this presentation, the words "anticipate," "believe," "can," "could," "estimate," "expect," "intend," "is designed to," "may," "might," "will," "plan," "potential," "possible," "predict," "objective," "should," and similar expressions are intended to identify forward-looking statements.

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Selapagos at a glance

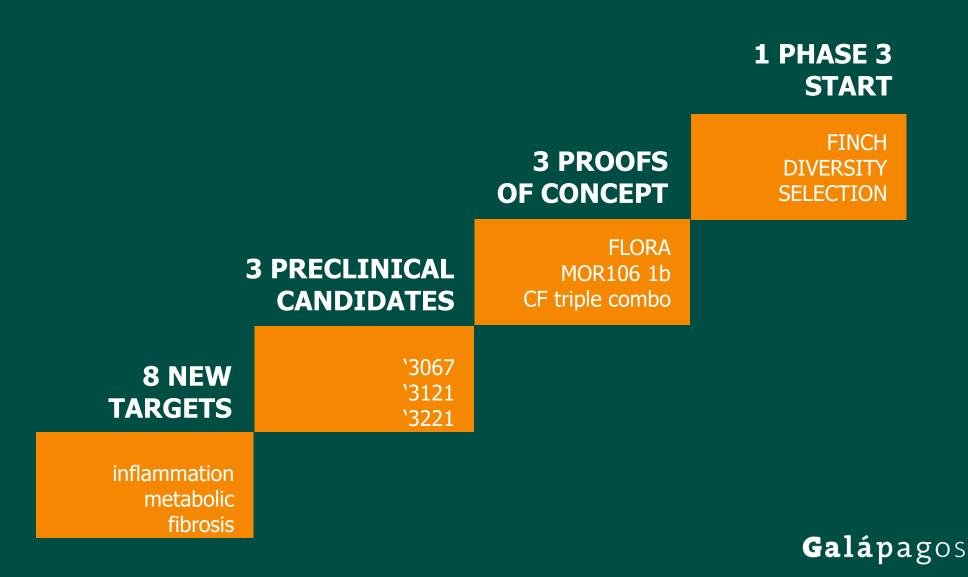
- Listed Euronext & NASDAQ: GLPG
- Novel mode of action drugs
- Proven platform:
 - Filgotinib in Ph3 in RA & IBD
 - `1690 FLORA Ph2a data in IPF
 - MOR106 in Ph1a in AtopicD
- Partners: GILD, ABBV, Servier, MOR
- Sept `17 cash €1.2b
- 580 employees at 6 sites







Since June 2016...





Area	Preclinical	Ph 1	Ph 2	Ph 3
RA				
UC				
CD				
Small bowel CD				
Fistulizing CD				
Sjögren's				
Ank. spon.				
Pso. arthritis				
Cutaneous lupus				
Lupus nephropathy				
Uveitis				

More PoC studies planned

Solution Clinical pipeline Promising pipeline next to filgotinib

Area	Pre-clinical	Ph 1	Ph 2	Ph 3
IPF	`3499	autotaxin	`1690	
Undisclosed	`2384	GPR84 `1205		
CF	1 st triple			
CF	2 nd triple			
CF	3 rd triple			
OA	ADAMTS-5	`1972		
Atopic derm	`2534 I	-17C MOR106		
Inflammation	`3121 `3312			
Pain	`3535			





Two key partnerships GLPG retains significant rights in both deals

Filgotinib	🚺 GILEAD	CF	abbvie
JAK1 in autoimmune		Triple combo for 90%	of patients
GLPG co-develops, contributes 20% of cost		GLPG responsible to en contributes to Ph3	nd Ph2,
Upfront \$725m, milestones \$1.35b		Milestones \$600m, incl. \$250m increase fo	or Ph1 & 2
Profit split in co-promote t EU big 5 + Benelux	territory:	Profit split in co-promo Benelux, GLPG retains	· · · · · · · · · · · · · · · · · · ·
Royalties 20% - 30%		Royalties mid-teens to	20%

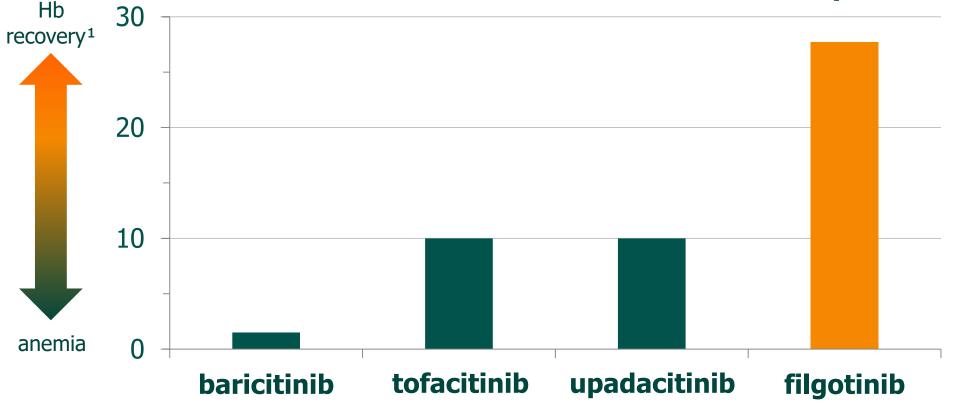
Filgotinib in RA and Crohn's >1900 patient years' experience

- Shown high, sustained activity in Phase 2 studies
- Once daily oral
- Improvement of lipid profile, haemoglobin, platelets
- No impact on NK cells



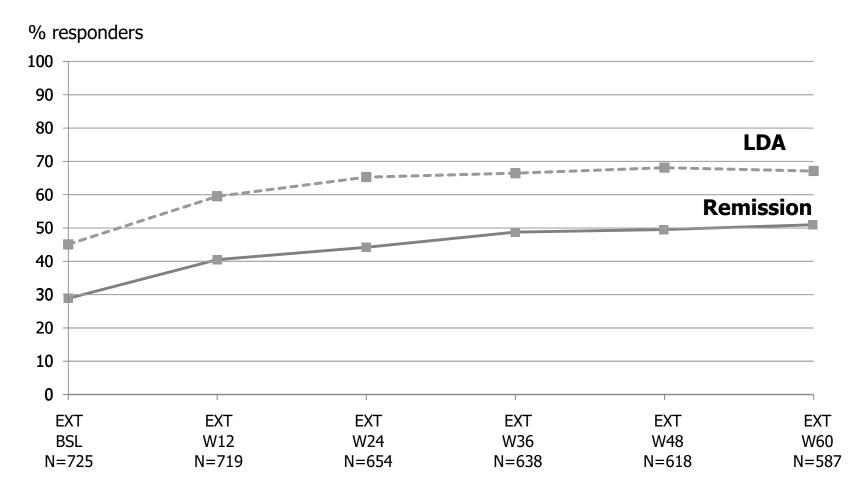
Selectivity matters Filgotinib is a highly selective JAK1 inhibitor

Ratio JAK1/JAK2 in human whole blood assay



Note: 1 - A Pardanani, et al, Leukemia (2013) 27, 1322–1327

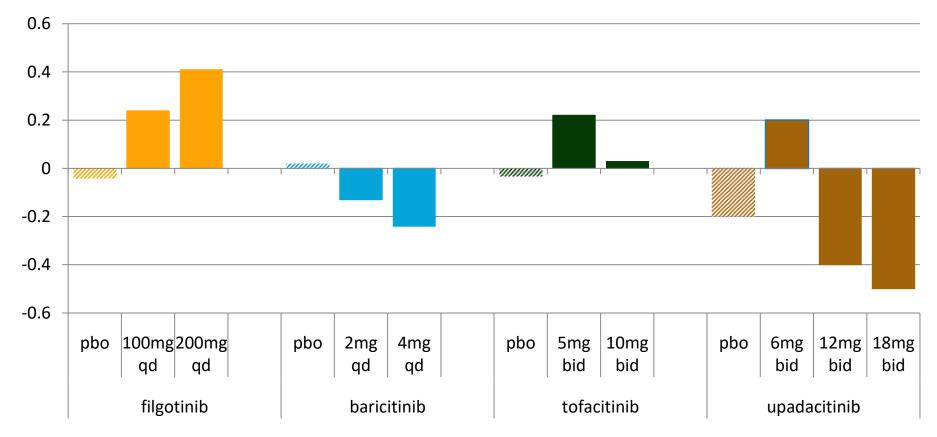
Efficacy maintained DARWIN 3, week 60 observed case



----Overall total



Hb mean CFB (g/dL), W12

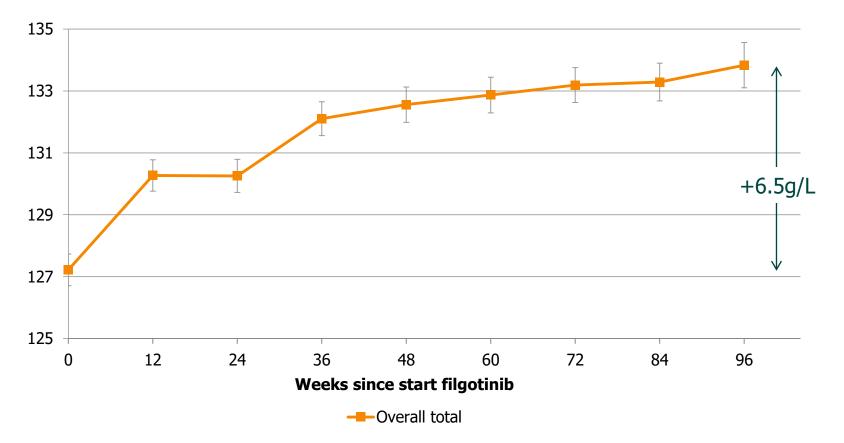


Note: data from separate RA studies not conducted by the Company.

filgotinib – Westhovens et al, and Kavanaugh et al, ARD 2016; baricitinib – Dougados et al, Annrheumdis 2016, RA-BUILD; tofacitinib – FDA AdComm briefing document May 2012; upadacitinib – Genovese et al A&R 2016 BALANCE 2.

Jarwin 1, 2, and 3 over time

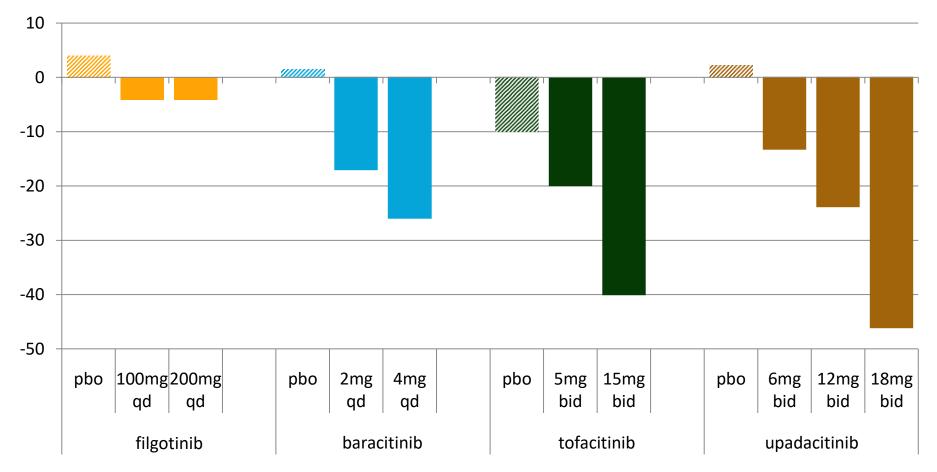
Hb mean (g/L)



CTCAE grade 3-4: 0.4% of patients



NK cells, mean CFB (%), W12

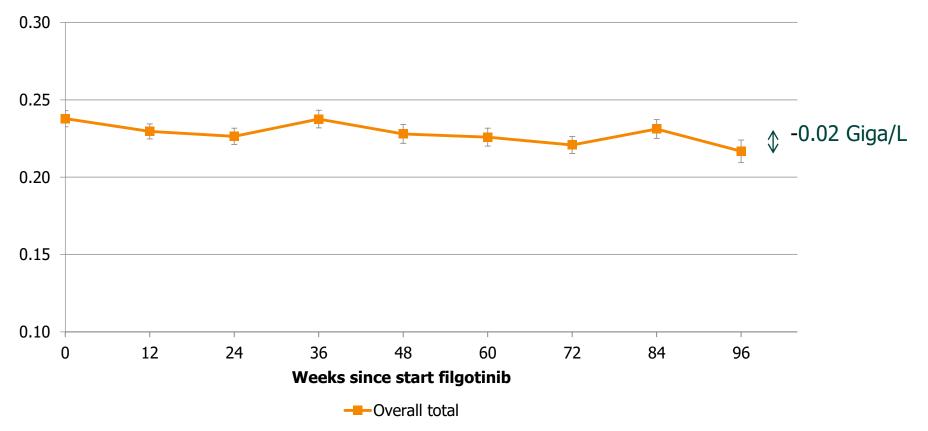


Note: data from separate RA studies not conducted by the Company.

filgotinib – Westhovens et al, and Kavanaugh et al, ARD 2016; baricitinib – Dougados et al, Annrheumdis 2016, RA-BUILD and Tanaka EULAR 2016 abstract RA-BEAM; tofacitinib – Van Vollenhoven abstract 2013, median CFB at W6; upadacitinib – Genovese et al A&R 2016 BALANCE 2. 14

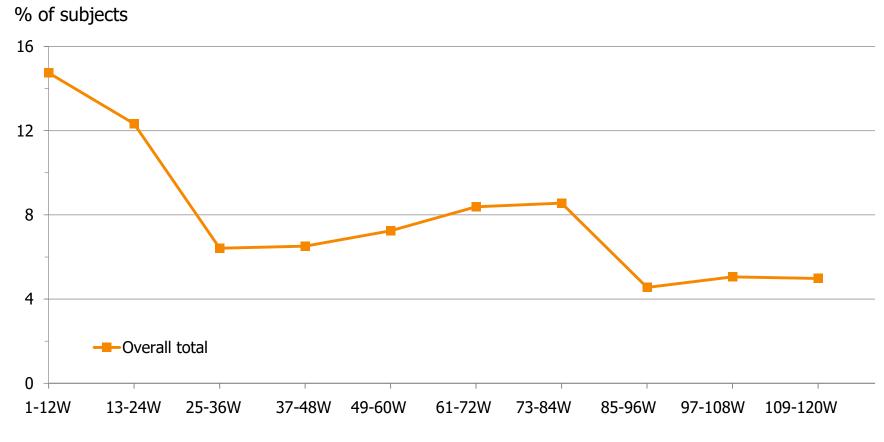
Stable natural killer cells DARWIN 1, 2, and 3 over time

NK cells, mean (giga/L)



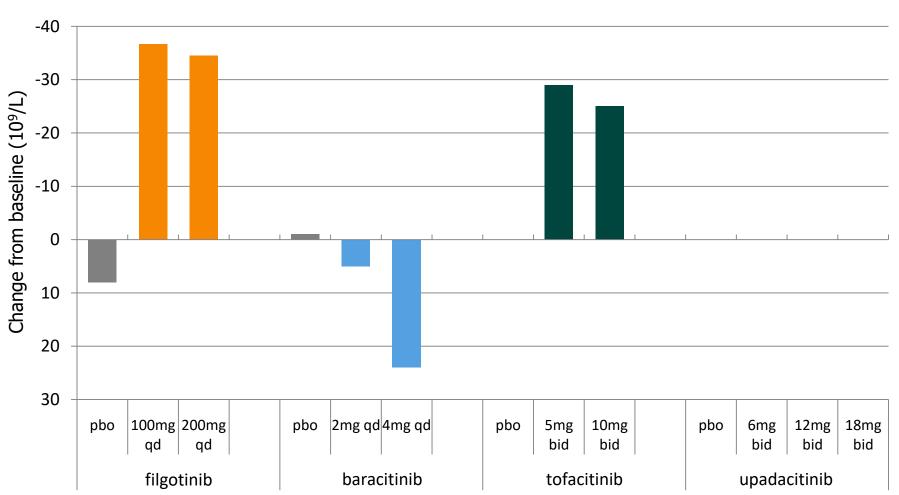
CTCAE grade 3-4: 1.6 % of patients

DARWIN 1, 2, and 3 over time



Weeks since start filgotinib



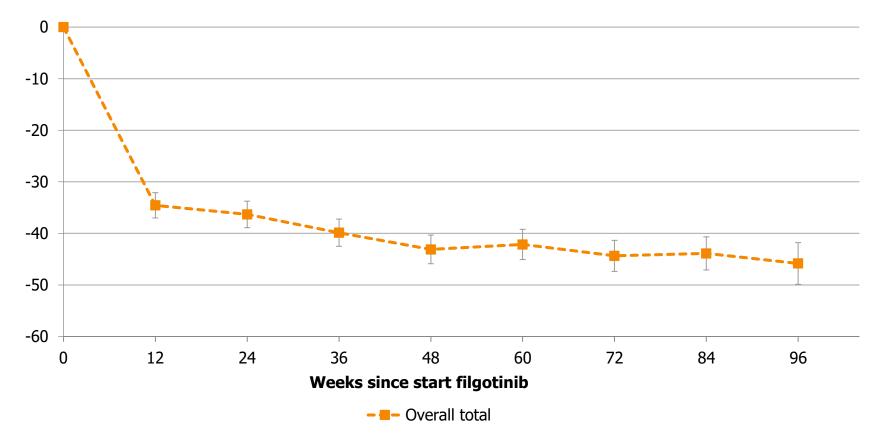


platelets, mean CFB (giga/L), W12

Note: filgotinib – DARWIN 1 W12 results; baracitinib – Dougados et al, Annrheumdis 2016; tofacitinib – FDA AdComm briefing document May 2012

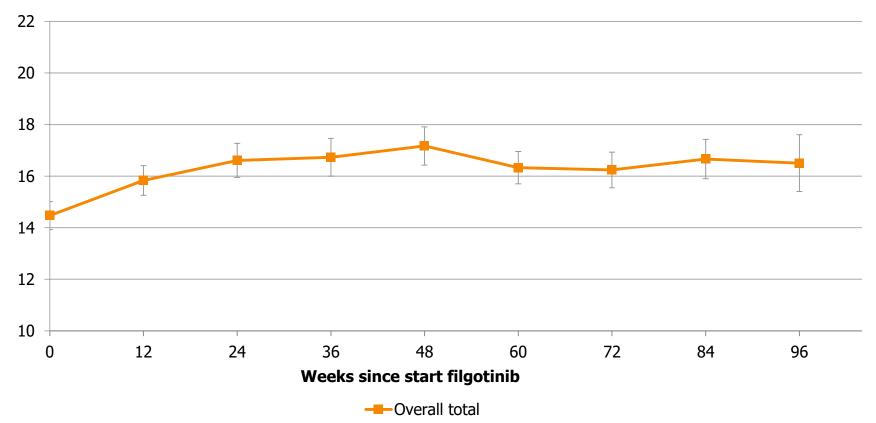


platelets mean CFB (giga/L), W12



Stable testosterone DARWIN 1, 2 and 3, measured in males

total testosterone, mean (nmol/L)



Solution Filgotinib: favorable safety profile

Event Per 100 PYE	filgotinib (50-)200mg daily	upadacitinib	baricitinib 2mg and 4mg QD	tofacitinib 5mg bid	tocilizumab (4 or 8 mg/kg)	adalimumab
	DARWIN 3 Wk 84	BALANCE-EXTENT	Genovese et al, ACR 2017	FDA, Medical review, 2012	Genovese et al, ACR 2012	Burmeester et al, 2011
Patient year exposure	1708	725	6637	901	14994	23943
Deaths	0.3	0.3	0.33	0.55	0.57	0.8
Malignancies, excl NMSC	0.5	0.8	0.8	0.55	0.86	0.9 (excl also lymphomas)
MACE	NAV	0.4*	0.5	0.44	0.25 (MI) - 0.31 (stroke)	NR
Serious infection	1.5	2.3	2.9	3.2	4.5	4.6
Herpes Zoster	1.2	3.7	3.2	4.4	NR	NR

* IR of 1/100PYE exposure (7 cases) was reported in the abstract Note: data shown are from separate studies

FINCH Ph3 design for RA 100 and 200 mg

			₽ ₽
FINCH 1: MTX - IR	1,650	52 weeks	ACR20 at W12 MTX add-on adalimumab control radiographic assessment
FINCH 2: biologic - IR	423	24 weeks	ACR20 at W12 cDMARD add-on
FINCH 3: MTX naive	1,200	52 weeks	ACR20 at W24 monotherapy, +MTX arms radiographic assessment

DIVERSITY & SELECTION in IBD 100 and 200 mg



DIVERSITY 2	Long term extension study				
SELECTION 1	UC Ph2/3 1,300 pts	58 weeks	Mayo score components Induction & maintenance		

SELECTION 2 Long term extension study

RA & IBD: \$28b market today

RA

2016 market size ~ \$19b 2016 market size ~ \$8b ~0.5m patients (US+EU) ~1.5m patients (US+EU) 100% 80% 60% 40% 20% 0% 1st line **3**rd 3rd 2nd 1st line 2nd

IBD

JAK

TNF

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non-TNF

Sources: IMS Health Autoimmune Data Platform, IPSOS Healthcare, IMS Health Analytics, GlobalData 2016, Nature Drug Discovery Review May 2016 IBD includes Crohn's disease and ulcerative colitis

JPF unmet need

- 200,000 prevalent cases in EU/USA, mainly elderly
- Half of patients die within 2-5 years after diagnosis
- Approved drugs only slow down decline in lung function



We developed `1690 for IPF

- In-house from target identification to candidate drug
- Our second new mode of action with PoC in patients
- Fully proprietary
- Orphan drug designation in EU & US
- Lead program in IPF franchise



Solution FLORA study design





- Main inclusion/exclusion criteria were:
 - > IPF patients diagnosed by HRCT/biopsy, centrally confirmed
 - > FVC \geq 50% predicted of normal, DLCO \geq 30% predicted of normal, FEV1/FVC \geq 0.7
 - no pirfenidone/nintedanib 4 weeks prior to screening
 - > no exacerbations 6 weeks before screening & during screening period
- 17 sites in UK, Italy & Ukraine

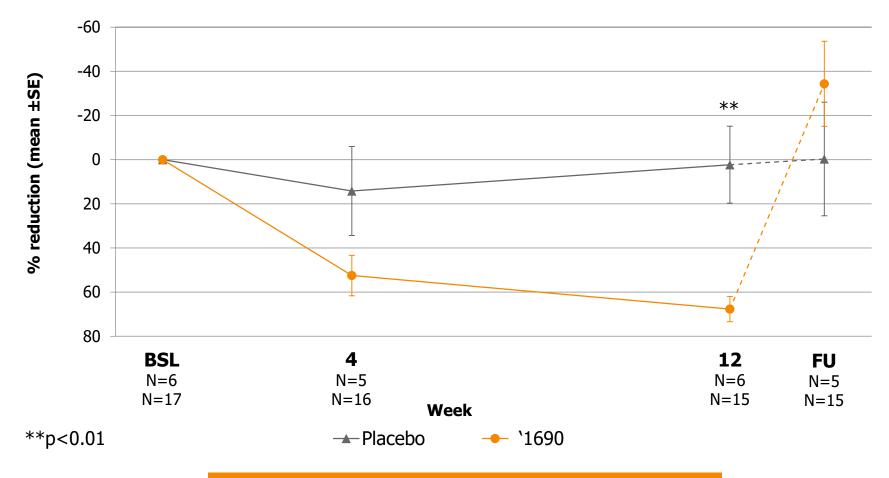
FLORA vs other studies Baseline characteristics aligned

	TOMORROW (nintedanib)	INPULSIS (nintedanib)	ASCEND (pirfenidone)	`1690
age (y)	65	67	68	66
male sex (%)	75	80	79	65
% predicted FVC	78	80	68	74
FVC (L)	2.7	2.7		2.8
DLCO (%)		47	44	39
duration of IPF (y)	1.3	1.6	1.7	1.7





Plasma LPA18:2 drops in '1690 arm

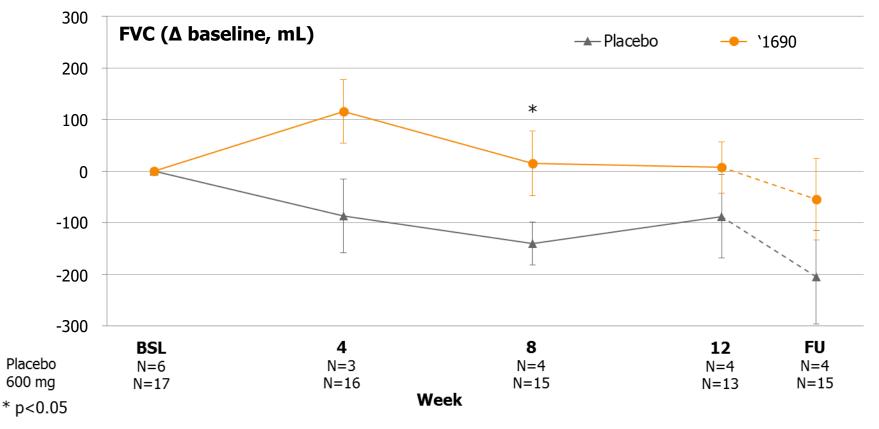


Shows '1690 target engagement

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Flora

FVC: stabilization with `1690



	W	k4	W	k8	Wk	:12	Follo	w-up
	Placebo	'1690	Placebo	'1690	Placebo	'1690	Placebo	'1690
FVC (Δ baseline, mL)	-87	+116	-140	+15 <	-87	+8	> -205	-55

LOCF basis reinforces observed case conclusions

Flora

Solution FRI changes in IPF patients

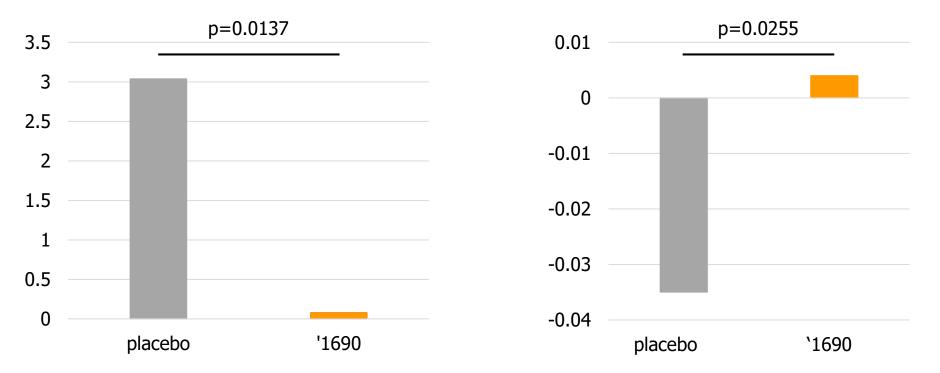
- Compared to healthy, IPF patients have:
 - smaller lung lobes
 - > larger airway dimensions
 - > smaller airway resistance
- Disease more pronounced in lower lobes
- Structural deformations caused by fibrotic traction & fibrotic tissue stiffening
- FRI shows signal before FVC



🕁 FRI: airway volume & resistance Flora 🄅

Significant difference between '1690 & placebo

Specific airway volume (Δ baseline, mL/L)



FRI's more sensitive endpoints confirm early FVC findings

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Specific airway resistance (Δ baseline, kPa/sec)



Balanced safety endpoints

Between '1690 & placebo

Overview safety endpoints	Placebo (N=6)	`1690 (N=17)
Treatment Emergent Adverse Event	67% (4)	65% (11)
Serious TE AE	33% (2)	6% (1)
Mild TE AE	0% (0)	24% (4)
Moderate TE AE	50% (3)	35% (6)
Severe TE AE	17% (1)	6% (1)
Related TE AE	0% (0)	12% (2)
Temporarily stopped treatment	0% (0)	12% (2)
Permanently stopped treatment	17% (1)	6% (1)

 Related TEAEs: headache (mild intensity, no change in treatment) & peripheral swelling of shin (moderate intensity, treatment temporarily stopped)

 Discontinuations: 1 placebo SAE, 2 GLPG1690: withdrawal of consent and SAE

 All AEs reported in subjects with ≥ 1 reported AE

 32



`1690 in FLORA Conclusions

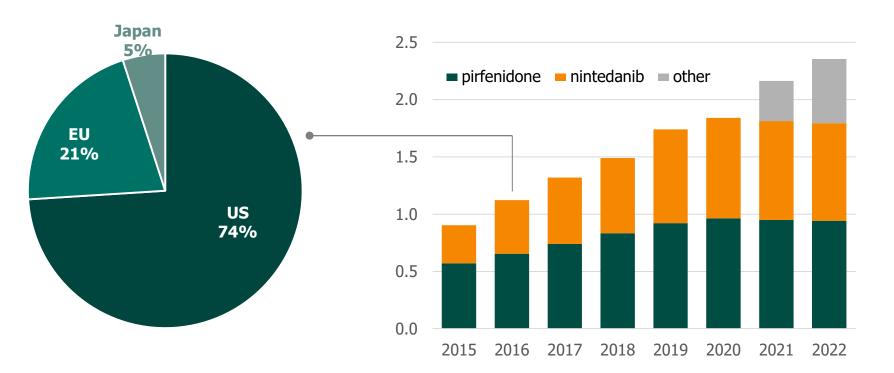
- First autotaxin inhibitor to show effect in IPF patient trial
- Monotherapy shows stabilization of lung function over 12week period as measured by FVC
- Functional respiratory imaging (FRI) confirms FVC data with statistical significance
- Generally well tolerated
- Results support rapid move to late stage trial



IPF: \$2.4b market by 2022 200,000 cases in US & EU

Drug sales, region

Sales of approved IPF drugs, \$b



Strategy to a triple combo in CF

- Aim for triple combination therapy for 90% of CF patients
- Create portfolio of potentiators & correctors
- Gain additional patient experience off the critical path
- Follow up with multiple triple combinations

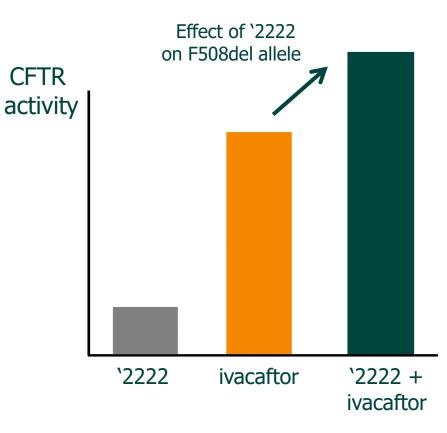




Preclinical	Ph1	Ph2
Potentiator `2451		
Potentiator `3067		
C1 corrector `2222		
C1 corrector `2851		
C2 corrector `2737		
C2 corrector '3221		



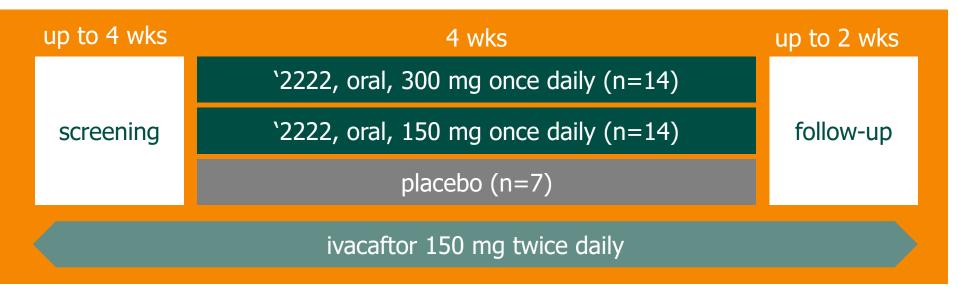
Albatross Albatross HBE assay: '2222 + ivacaftor in F508del/Class III cells





ALBATROSS

`2222 in ivacaftor-treated Class III patients



- Adult CF patients with F508del/Class III mutation
- Patients remain on stable dose of ivacaftor
- 27 sites: Australia, Belgium, Czech Rep, Germany, Ireland, UK
- Primary endpoints: safety & tolerability
- Secondary endpoints: sweat chloride, FEV1, CFQ-R

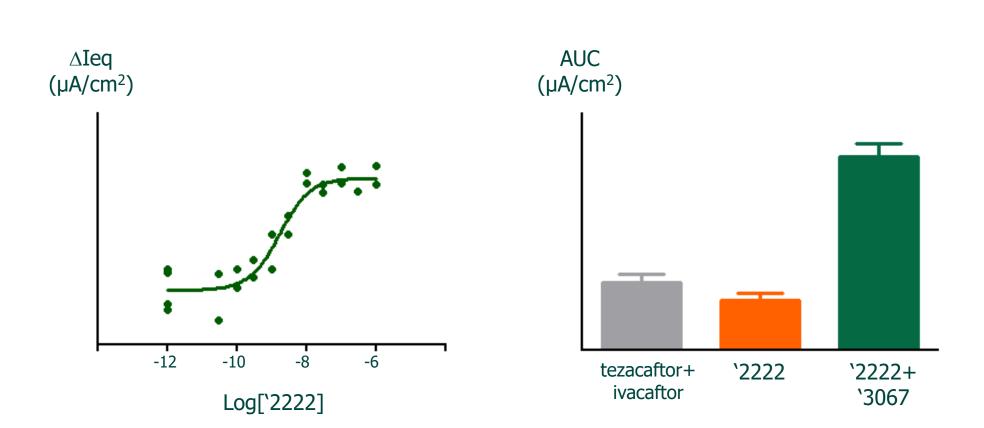
Study recruited in 5 months



Albatros



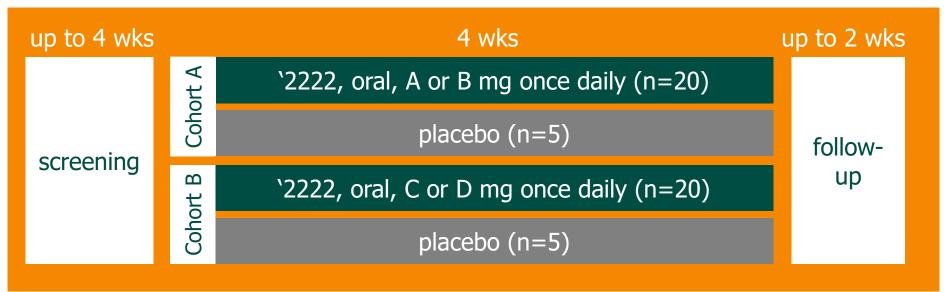
Potent corrector `2222 HBE assay with homozygous F508del patient cells



FLAMINGO



`2222 monotherapy in homozygous F508del patients

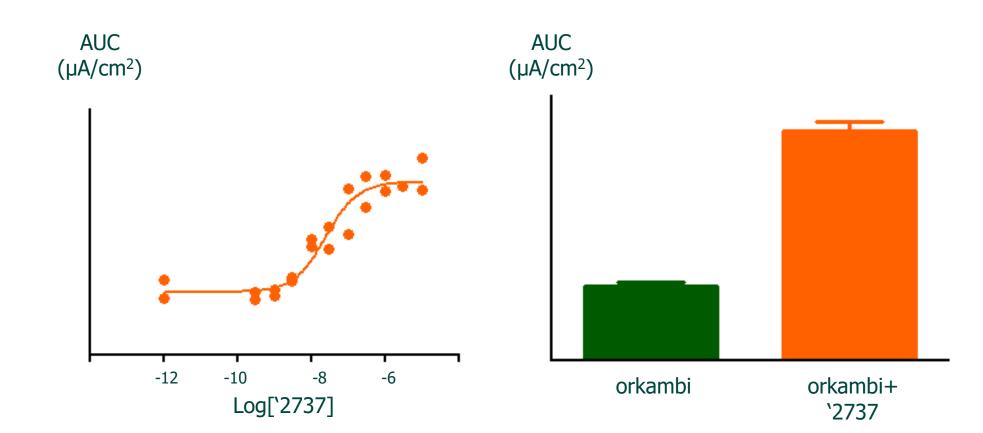


- Adult CF patients with homozygous F508del mutation
- 24 sites: US, UK, Belgium, Netherlands, Serbia, Spain
- Primary endpoints: safety and tolerability
- Secondary endpoints: sweat chloride, FEV1, CFQ-R and PK

Study recruited in 4 months

Add on orkambi F508del HBE data

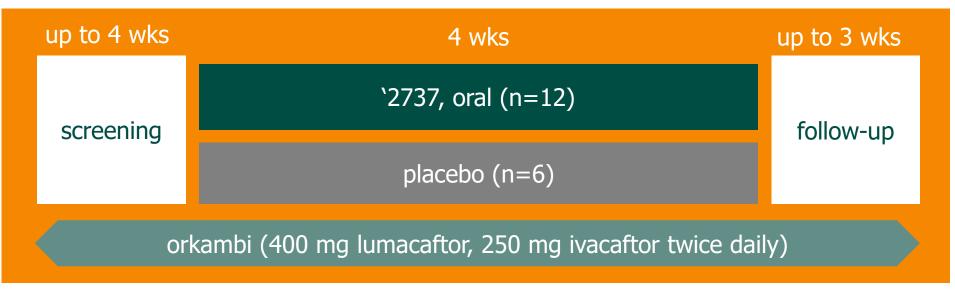








`2737 in orkambi-treated F508del/F508del patients

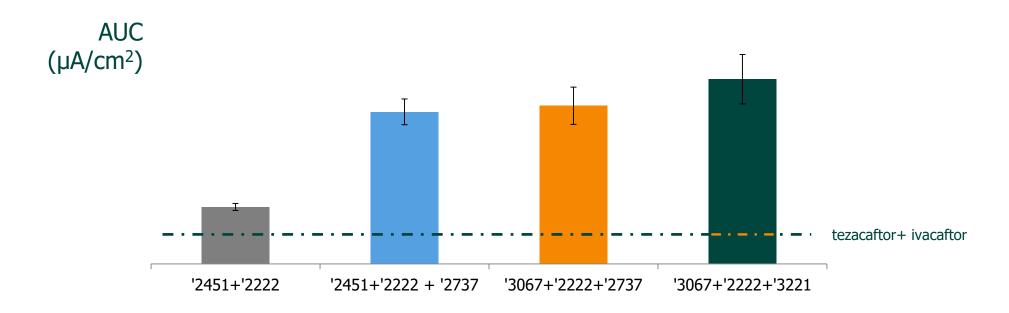


- Adult CF patients homozygous for F508del mutation
- Patients remain on stable dose of orkambi
- 10 sites in Germany
- Primary endpoints: safety & tolerability
- Secondary endpoints: sweat chloride, FEV1, CFQ-R

Study underway

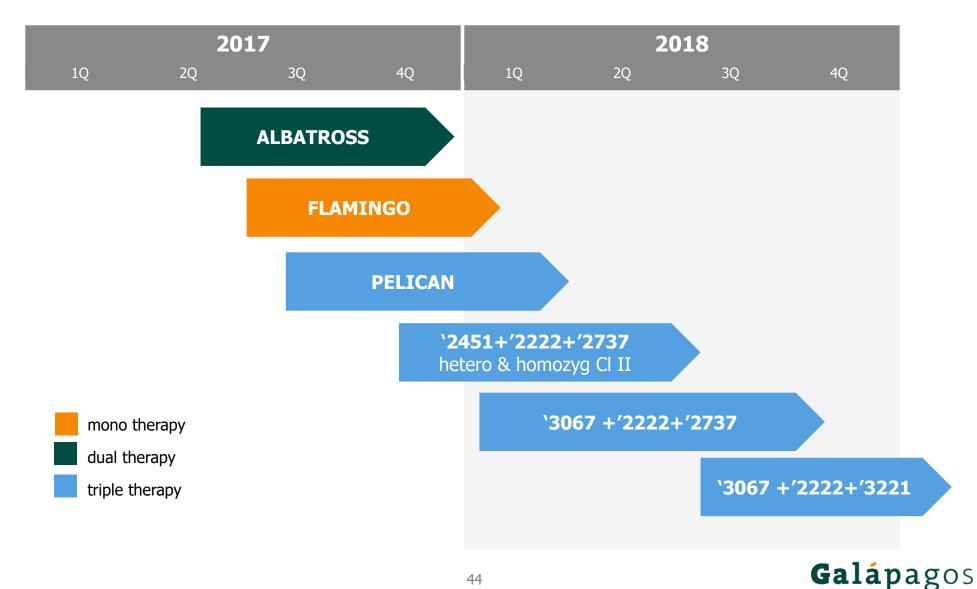


CF triple combinations HBE assay with homozygous F508del cells

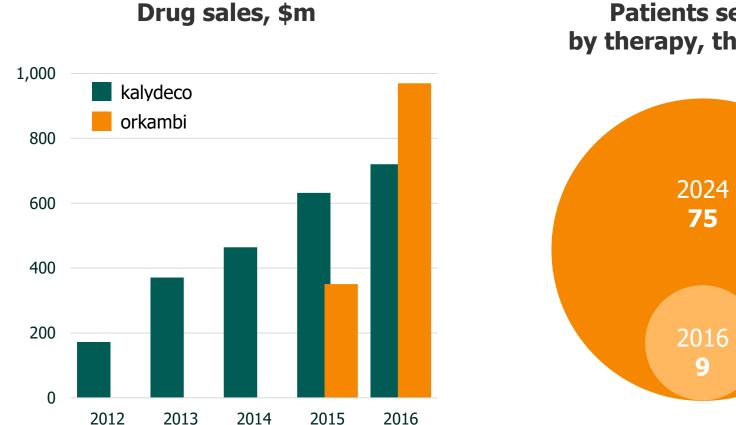




6 CF patient studies







Patients served by therapy, thousands



Source: Vertex Pharmaceuticals



OA: breakdown of joint cartilage 118 M patients in US, Europe & Japan No disease-modifying drugs approved today



Targets ADAMTS-5



Phase 1: target engagement, favorable safety and PK Half-life ~10 hours, steady state after 2 days



Inhibits cartilage breakdown in healthy volunteers

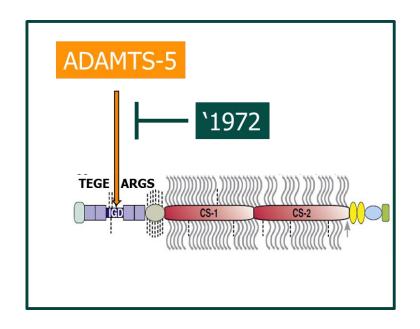


GLPG has full US rights, Servier licensed ex-US rights GLPG recruited Ph1b 30-patient study in US Ph2 plans being prepared



>>> `1972 targets ADAMTS-5 in OA

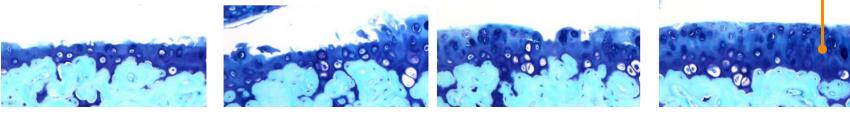
- `1972 is a potent and selective chondroprotective ADAMTS5 inhibitor
- ADAMTS-5 plays a key role in aggrecan degradation in OA
- Strong literature evidence for ADAMTS-5:
 - validated in animal models^{2,3}
 - validated in human samples¹
 - ARGS levels increased in human knee synovial fluid in OA⁴



Source: ¹ Song, 2007; ² Glasson, 2005 & Malfait, 2010; ³ Miller, 2016; ⁴ Larsson, 2009

1972 protects cartilage Histopathology in mouse model

cartilage



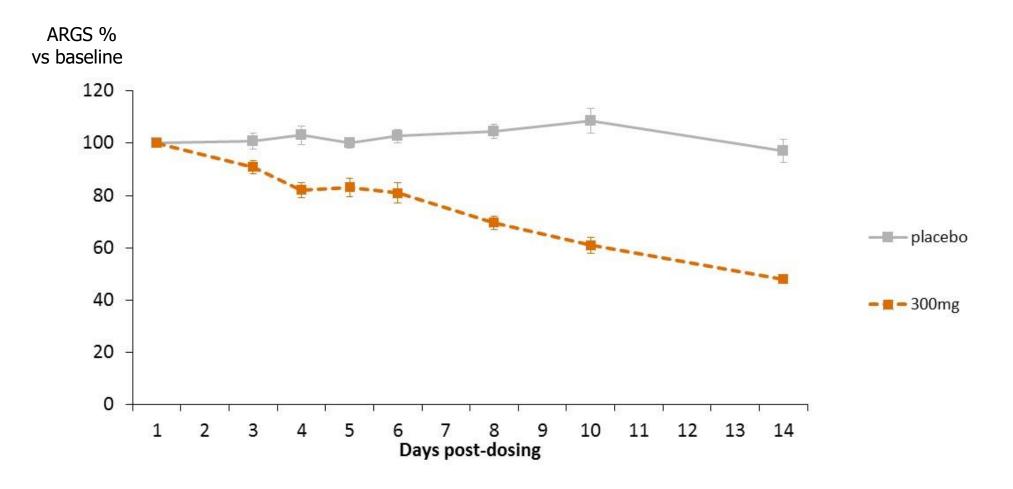
vehicle

`1972 low dose

`1972 medium dose `1972 high dose



Solution Increasing target engagement Biomarker reduction with `1972 in FiH





up to 4 wks	to 4 wks 4 weeks	
screening	GLPG1972, dose escalation, 3 doses (n=8/cohort)	follow.up
	placebo (n=2/cohort)	follow-up

- Patients with hip and/or knee osteoarthritis
 - > stratified for age
- Primary objectives: safety/tolerability and PK
- Secondary objective: serum neoepitope ARGS
- Exploratory objective: Western Ontario & McMaster Universities osteoarthritis index
- Topline data early 2018

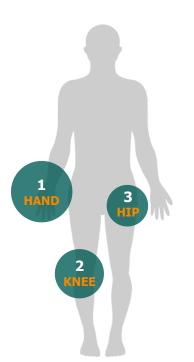
Servier and Galapagos preparing global Ph2 program



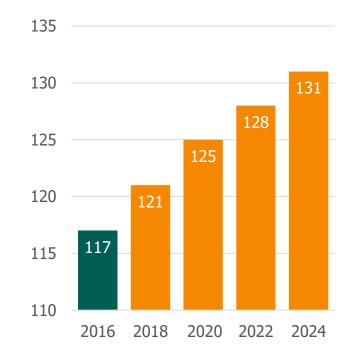
• Osteoarthritis: unmet need is large

'1972 a disease-modifying drug in OA

Localization



Prevalence US & EU, million cases



Source: Global Data



MOR106 for atopic dermatitis

2	2

AtD: inflammatory disease causing very dry skin, severe itching 35M patients in US, Europe & Japan, ~7M moderate-to-severe



First-in-class human MAb Novel mechanism: IL-17C target discovered by Galapagos



Ph1 (SAD): favorable safety & PK in healthy volunteers Ph1 (MAD): dosing of 24 moderate to severe AtD patients

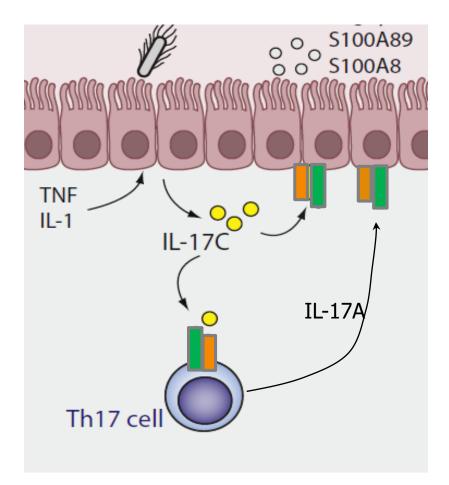


Intravenous infusion

50/50 collaboration with Morphosys Topline Ph1b results reported Sept `17



Dual mode of action



- IL-17C target of MOR106
- Dual action described
- Local amplifier of inflammation
- First-in-class

Source: Haines & Cua, Immunity 2011



illorphosys

MOR106 Ph1 in atopic dermatitis

single ascending dose	healthy males, 7 cohorts, i.v. infusion $(n=42)$	7 week	
	placebo (n=14)	follow up	

	4 weeks		
multiple ascending	patients, 3 cohorts, weekly i.v. infusion $(n=18)$	10 week	
dose	placebo (n=6)	follow up	

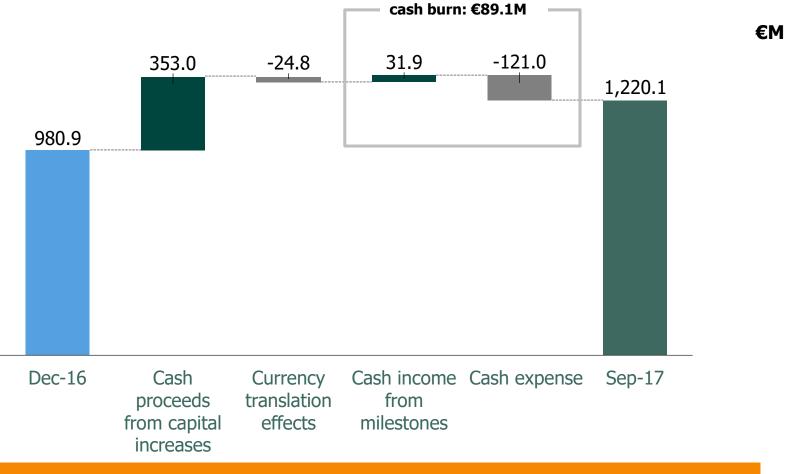
- Primary & secondary objectives: safety/tolerability and PK
- Exploratory objectives on efficacy
 - > Eczema Area & Severity Index, Scoring Atopic Dermatitis, Investigator Global Assessment
 - Dermatology Quality of Life Index
 - effect on Thymus & Activation-Regulated Chemokine (TARC)

MOR106 Ph1b topline

- Generally well tolerated with no safety concerns
- Favorable PK properties: dose dependent exposure and half life in line with healthy volunteers
- Promising initial results in skin efficacy parameters
 - rapid onset with >80% of patients showing a 50% improvement in AD symptoms (EASI-50) by week 4 at highest dose level
 - response maintained after stopping treatment (> 2 months)
- Subcutaneous administration in evaluation

Supports move into Phase 2

Cash, equivalents & restricted cash



YTD cash burn of €89M, cash of ≈€1.2B end of Sep

Notes:

includes restricted cash of €7.7M in Dec'16 and €1.2M in Sep '17

excluding tax receivable from Belgian & French governments of €76.2M in Sep `17

Clinical news flow

Disease area	Program	H2 '17
IPF	`1690	preparation pivotal study
Cystic fibrosis	multiple	ALBATROSS topline 1 st triple combo in patients additional study starts
Osteoarthritis	`1972	Ph1b fully recruited
Atopic dermatitis	MOR106	preparation Ph2



Se Outlook

- Programs on track and delivering
 - > filgotinib in Ph3, more Ph2 studies
 - > CF triple combo in patients
 - > '1690 in late stage IPF program
 - > MOR106 in Ph2 in atopic derm
 - `1972 in Ph2 in OA
- More proprietary clinical programs
- Building commercial organization
- Solid balance sheet







Solution Service Service Antipation Service Service Antipation Servic

	Hb	NK cells	platelets	lipids	ALT	H. zoster
filgotinib						
upadacitinib						
baricitinib						
tofacitinib						

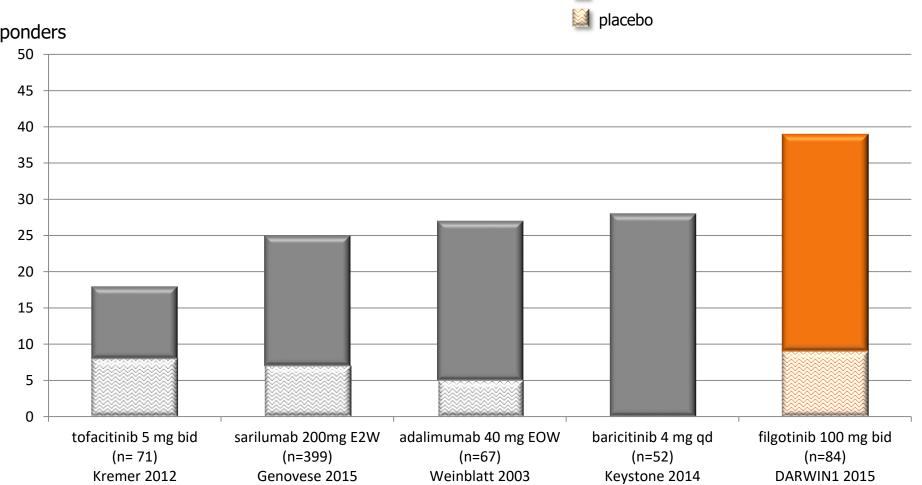
Best profile

Not/less favorable profile

Unknown







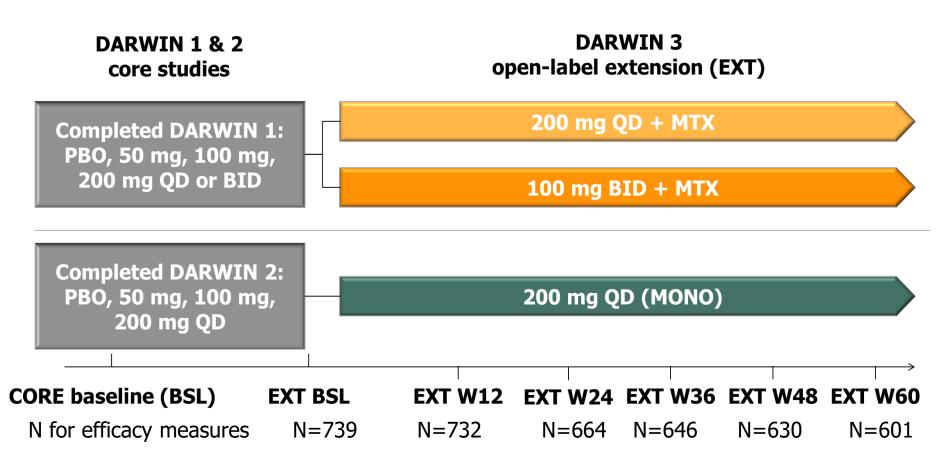
active treatment

% responders

Note: data reported in listed publications, not resulting from head-to-head studies. Ph3/marketed dose (competitors) vs best Ph2 dose (filgotinib)

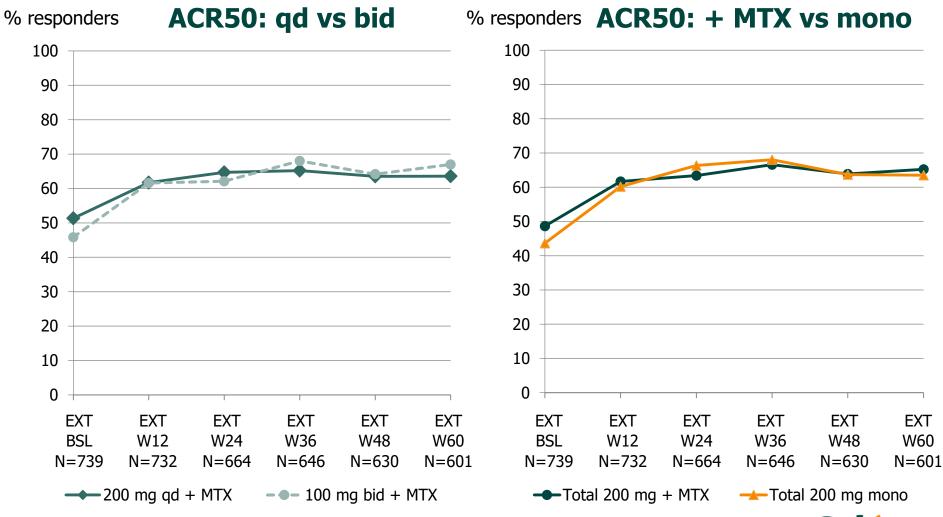


Filgotinib long term extension study design

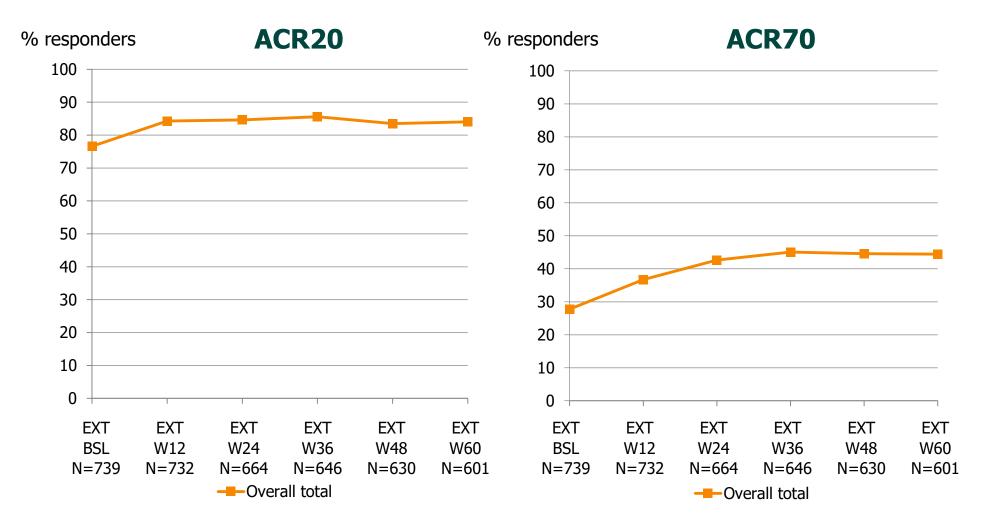


This Darwin 3 interim analysis cut off date was when last subject completed 60 weeks of therapy; efficacy results include all data from subjects up to week 60 whereas the safety results include all data available by the cut off date. The 100mg QD groups were not analyzed separately. All male subjects were US males and were added to 200 mg QD groups.

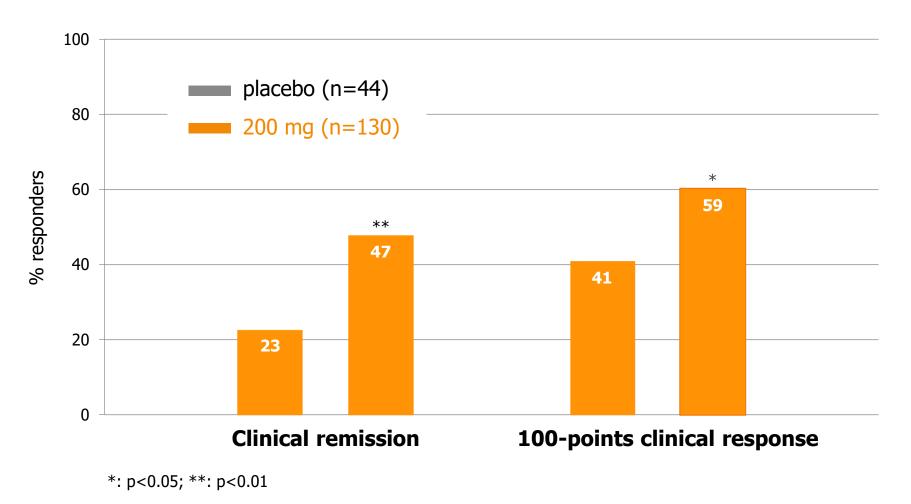
Similar qd vs bid, +MTX vs mono DARWIN 3, week 60 observed case



Efficacy maintained DARWIN 3, week 60 observed case



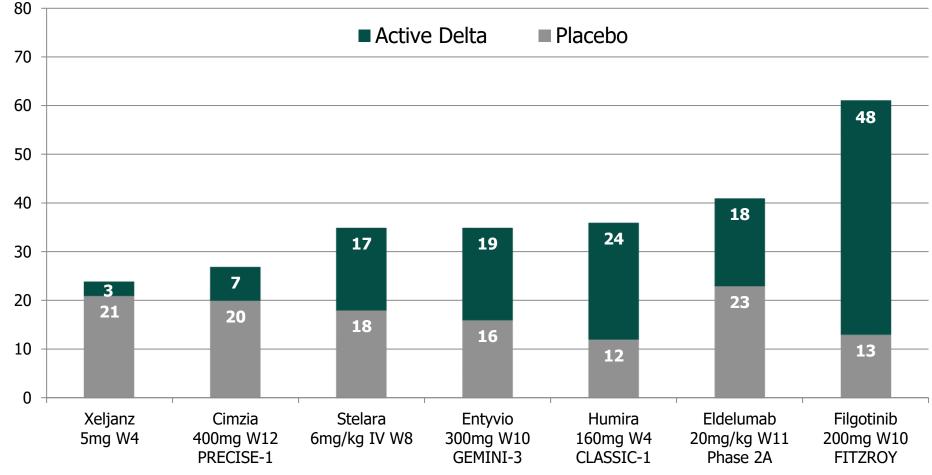
Crohn's: primary endpoint achieved FITZROY study CDAI responses, ITT-NRI, Week 10



Competition TNF naives

Clinical remission: induction

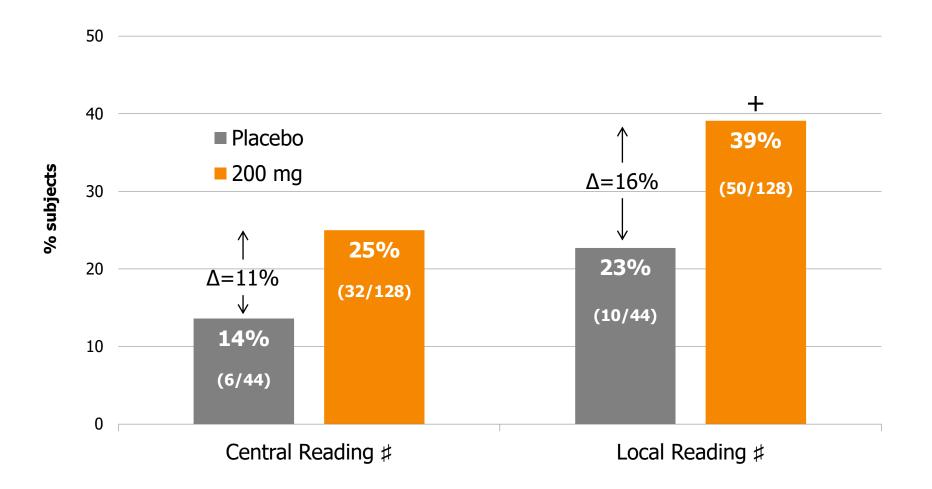
% responders



Note: data not from head-to-head studies

FITZROY: SES-CD endoscopy

Improvement of at least 50%, ITT-NRI, Week 10

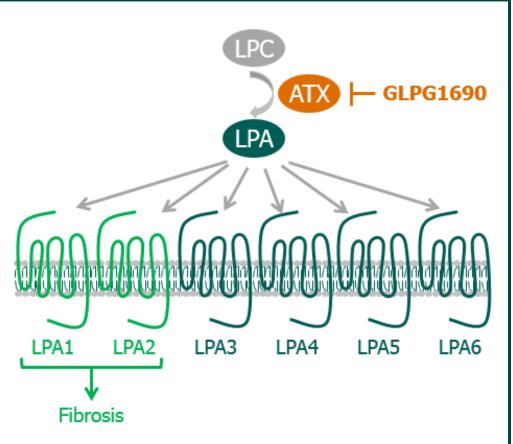


Notes: +: p<0.10; #: Only using segments explored at both baseline and week 10 (matching segments) Vermeire et al., The Lancet, 2016



At the heart of fibrotic pathways

Autotaxin biology



- ATX main source of LPA in blood
- LPA controls activities like migration, contraction & survival
- Conditional genetic deletion of ATX in bronchial epithelial cells or macrophages attenuates disease severity in IPF models



•

How efficacy was assessed



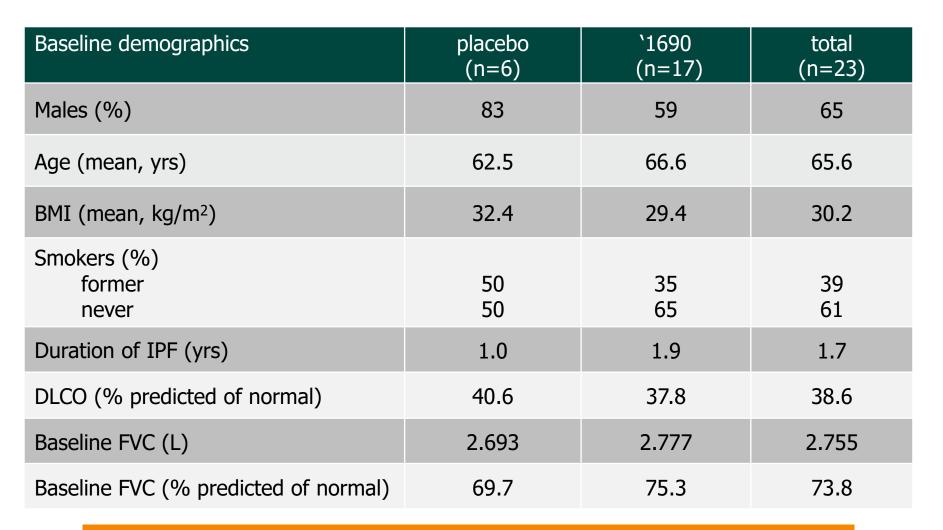
Pulmonary function by spirometry & FRI

• Spirometry:

- active measurement of lung function
- key parameter is forced vital capacity (FVC)
- Functional respiratory imaging (FRI):
 - > combines CT-scans with dynamic flow simulations
 - > measures specific & regional parameters



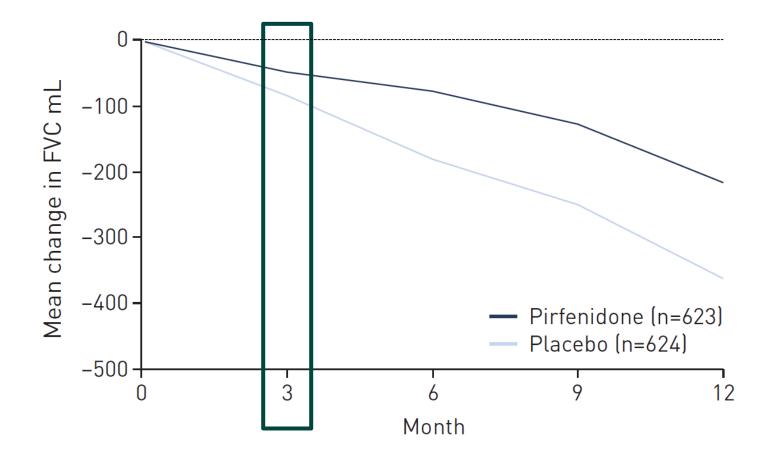
Balanced patient demographics Flora



In line with previous studies of marketed therapies

FVC: pirfenidone results at wk12

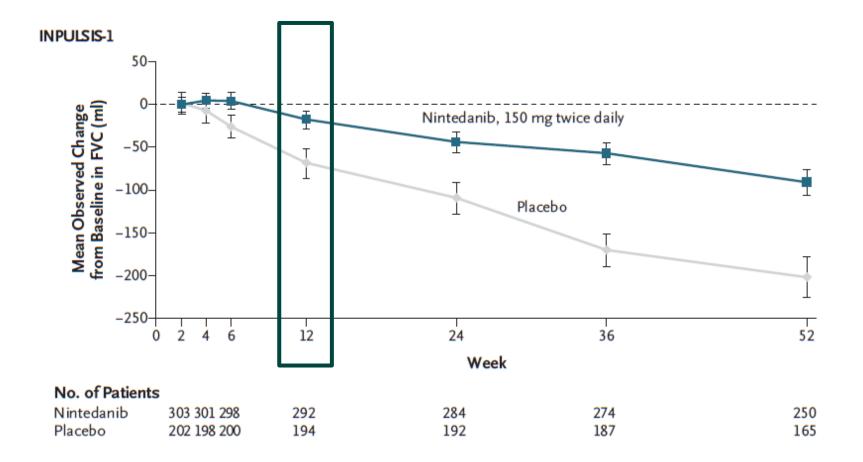
From ASCEND and CAPACITY Ph3 trials



Source: Noble et al. Eur Respir J 2016

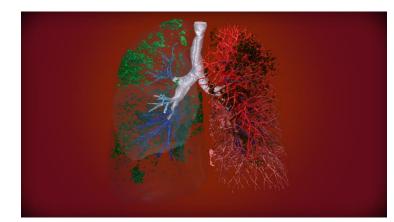
FVC: nintedanib results at wk12

From INPULSIS Ph3 trials

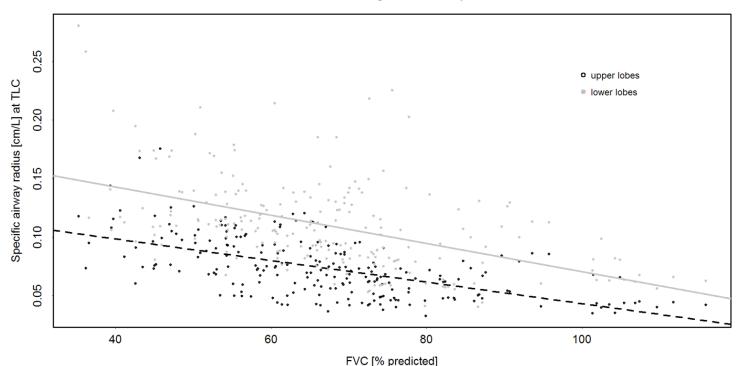


Source: Richeldi et al. NEJM 2014

Sunctional Respiratory Imaging



Upper Lobes: Marginal $R^2 = 0.31$, p < 0.001 Lower Lobes: Marginal $R^2 = 0.28$, p < 0.001

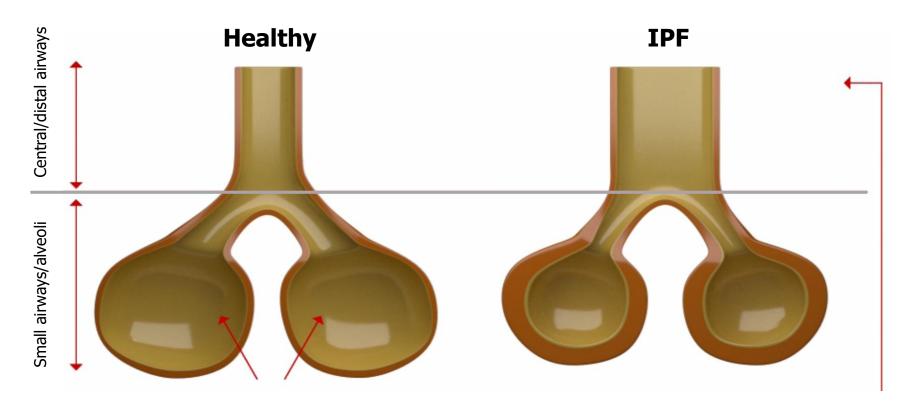






FRI changes in IPF patients

Airway volume increases, airway resistance decreases



Intrathoracic pressure expands small airways & alveoli

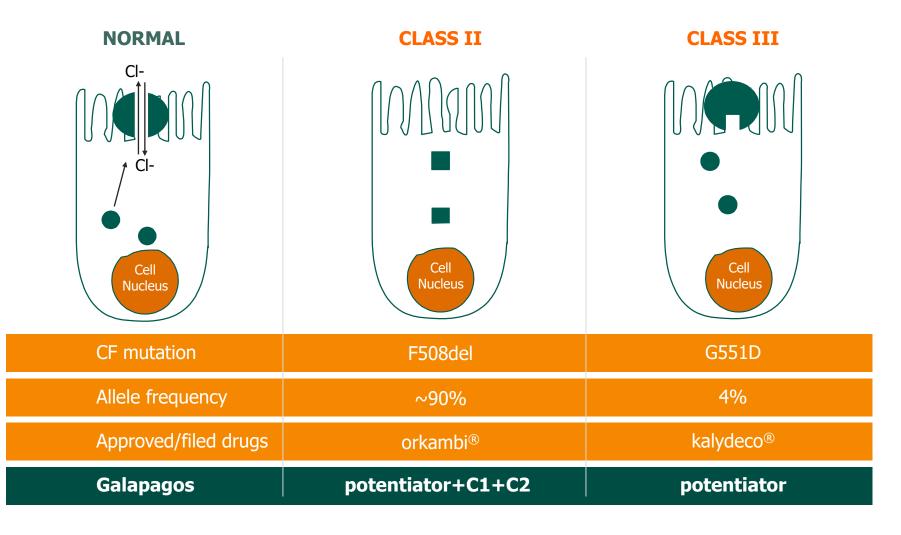
Increased stiffness of small airways alveoli, intrathoracic pressure causes increase of central & distal airways







Use of potentiators and correctors





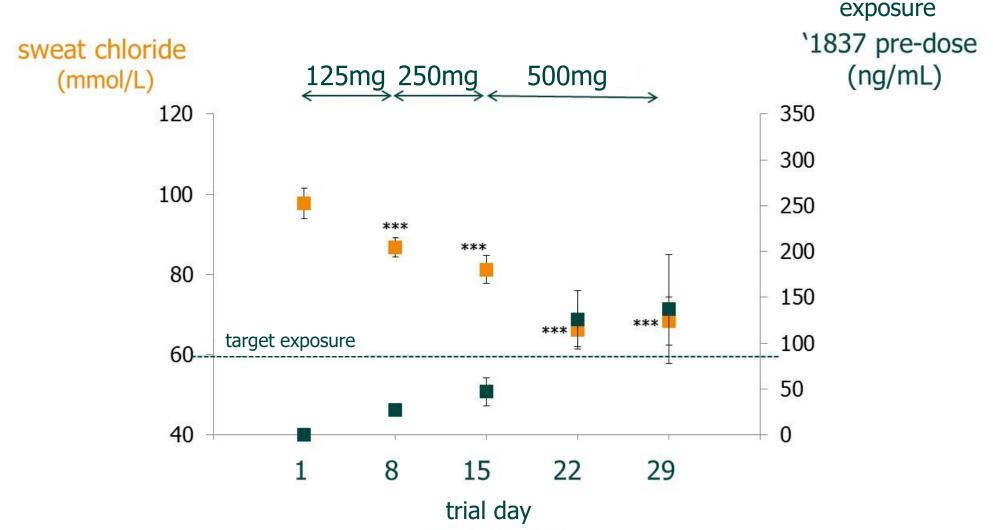
	7 days	7 days	7 days	14 days	4 days
screen on kalydeco / naïve	washout	125 mg b.i.d.	250 mg b.i.d.	500 mg b.i.d.	washout

26 patients harboring a G551D mutation

- 25 kalydeco treated & 1 naive patient
- Recruited at 16 centers in 6 EU countries & Australia
- Study executed within 1 year
- Primary endpoints: safety & tolerability
- Secondary endpoints: sweat chloride, FEV1, plasma levels

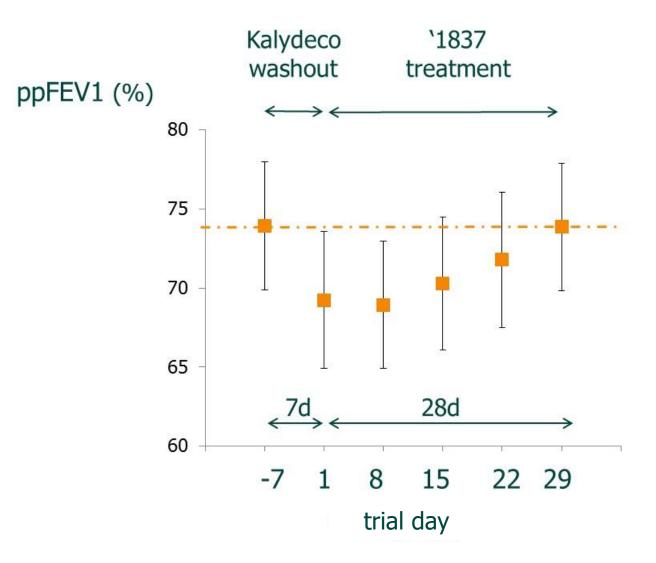


SAPHIRA 1 SAPHIRA 1



Notes: *** p<0.001; All '1837 exposure measurements are taken pre-dose escalation, except for days 22 and 29 in which there is no escalation. Here '1837 concentration measurements are taken prior intake of first daily dosis.

Effect on FEV1 in SAPHIRA 1



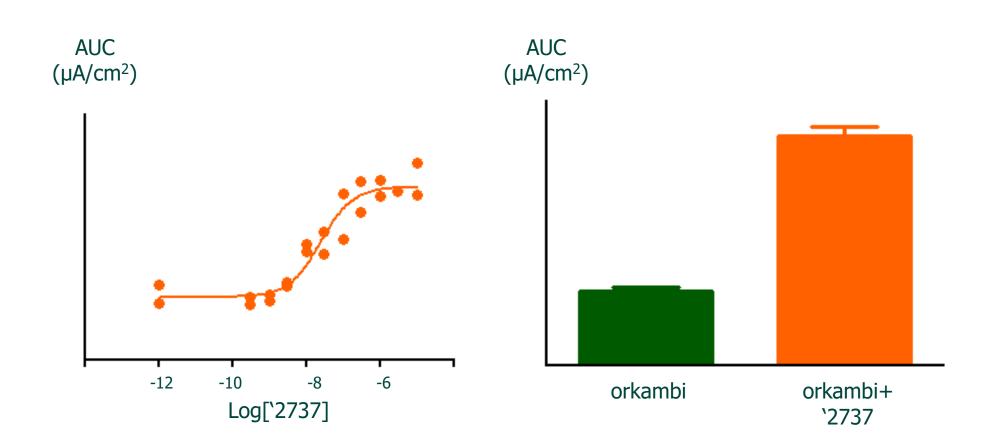


SAPHIRA 1 topline

Conclusions on '1837

- First potentiator after kalydeco to show positive results in G551D
- Appears safe & well tolerated
- Statistically significant decreases in sweat chloride
- Full restoration of FEV1 % loss from kalydeco washout
- Supports our predictive *in vitro* assays
- Strengthening of our dosing modelling for triple combination

Add on orkambi F508del HBE data



>>> `2737: well tolerated in Ph1

- Randomized, double blind, placebo-controlled healthy volunteer study
 - > SAD completed
 - > MAD for 14 days completed
 - > single dose in patients: ongoing
- Well tolerated over dose range studied in healthy volunteers
- PK supports once daily dosing regimens for future development
- Favorable & rapid absorption
- Next step: start Ph2 study add-on to orkambi



>>> '2451: well tolerated in Ph1

- Randomized, double blind, placebo-controlled healthy volunteer study
 - > SAD completed
 - > MAD doses up to 14 days: completed
 - > dual with `2222, up to 14 days: completed
- Well tolerated over dose range studied in healthy volunteers
- PK supports once daily dosing regimens for future development
- Active metabolite with half-life of ~approx. 1 month detected
 - extended period of follow-up included
- Next steps:
 - > regulatory meeting for triple in Q3, followed by filing in Q4
 - > triple in Class II homozygote & heterozygote patients

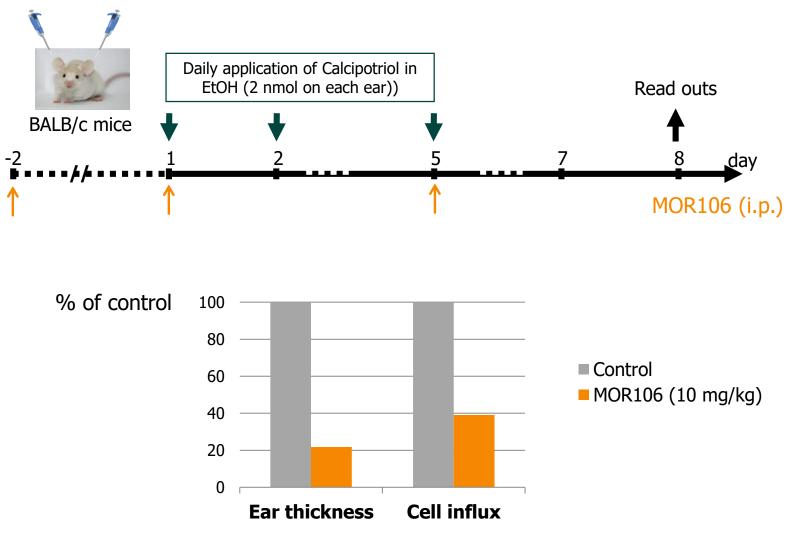
3067 Ph1 ongoing

- Ph1 healthy volunteers
 - > SAD: completed
 - MAD: ongoing
 - dual: + `2222 planned in Q3 `17
 - triple: + '2222 + '2737 planned in Q4 '17
- Patient studies
 - bioavailability Q3 `17
 - dual study: + `2222 planned for Q4 `17
 - triple: + '2222 + '2737 planned in Q1 '18

Solution Triple patient studies

- Phase 1b: 1 month studies
- `2737 add-on to orkambi
 - submission in July `17
 - start Q4 2017 data H1 `18
- `2451 + `2222 + `2737
 - > start of regulatory process in July `17
 - start Q4 `17 data mid `18
- `3067 + `2222 + `2737
 - start early `18 data H2 '18
- `3067 + `2222 + `3221
 - start mid '18 data early `19

MOR106 reduces inflammation Calcipotriol-induced atopic dermatitis mouse model



Results dupilumab Ph2a 4 weeks, mono

	Different doses	Placebo
EASI-50 (%)	59	19
EASI-75 (%)	29	6
Change in EASI score (%)	-57,7	-25,4
% patients with IGA 0 or 1 (%)	12	6
Change in IGA score (% points)	-34,8	-16