

Galápagos

Wells Fargo CF Seminar

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Agenda

- Galapagos at a glance
- About Cystic Fibrosis
- Kalydeco: first approved CF drug
 - experimental data with Kalydeco
 - can we improve on Kalydeco
- GLPG1837
- F508del mutation
 - experimental data with VX-809
 - can we improve on VX-809
- Conclusion



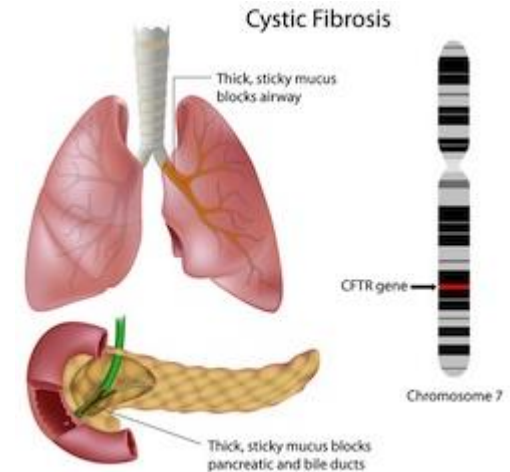
Galapagos at a glance

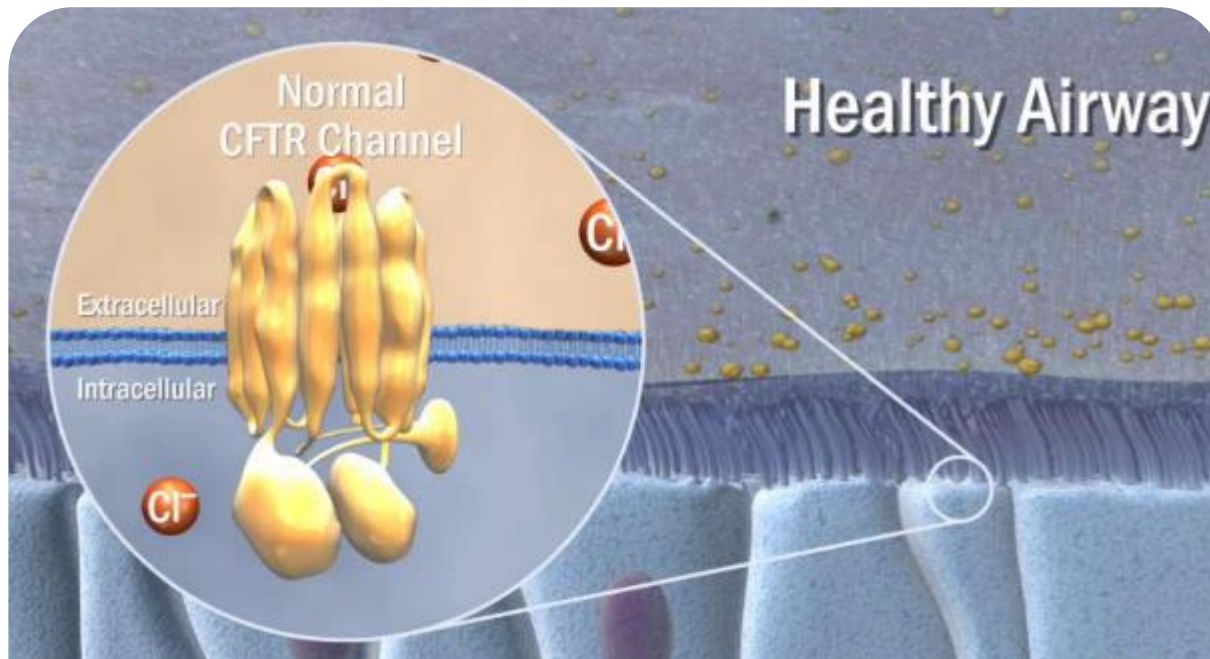
- Pipeline of novel mode of action medicines
 - five Phase 2 studies with JAK1 in five disease areas
 - two new modes of action in Phase 1 and 2, six candidates, 20 in discovery
- Major alliances with AbbVie, JnJ, GSK, Servier
- Leading fee-for-service provider with BioFocus & Argenta
- 800 staff, research sites in 5 countries, HQ in Belgium
- Market cap ~ \$690 M, 29.7 M shares



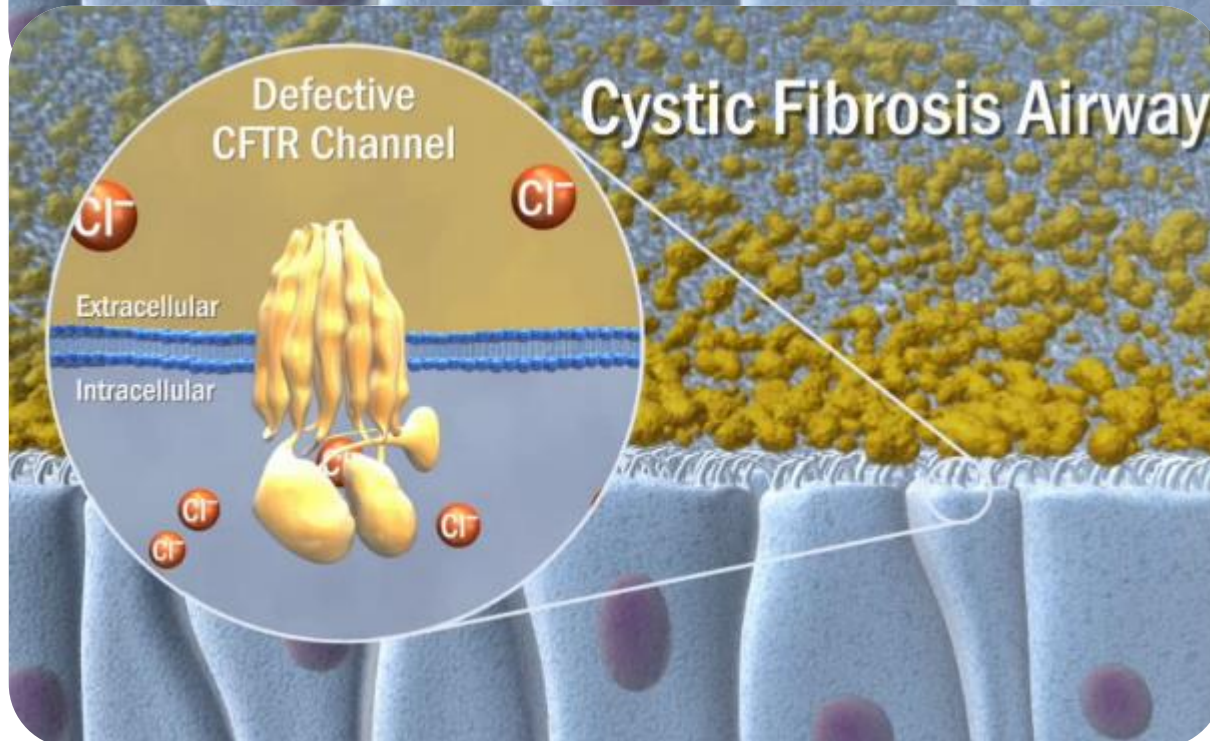
About Cystic Fibrosis

- Fatal inherited disease of the lungs & digestive system
- Debilitating disease, impairs quality of life
- Life expectancy: 37 years
- 70,000 patients worldwide, 30,000 in the US
- Patients carry a defective gene/protein (CFTR)
 - CFTR channel transports chloride across cell membrane
 - 1600 mutations identified grouped into 5 different classes





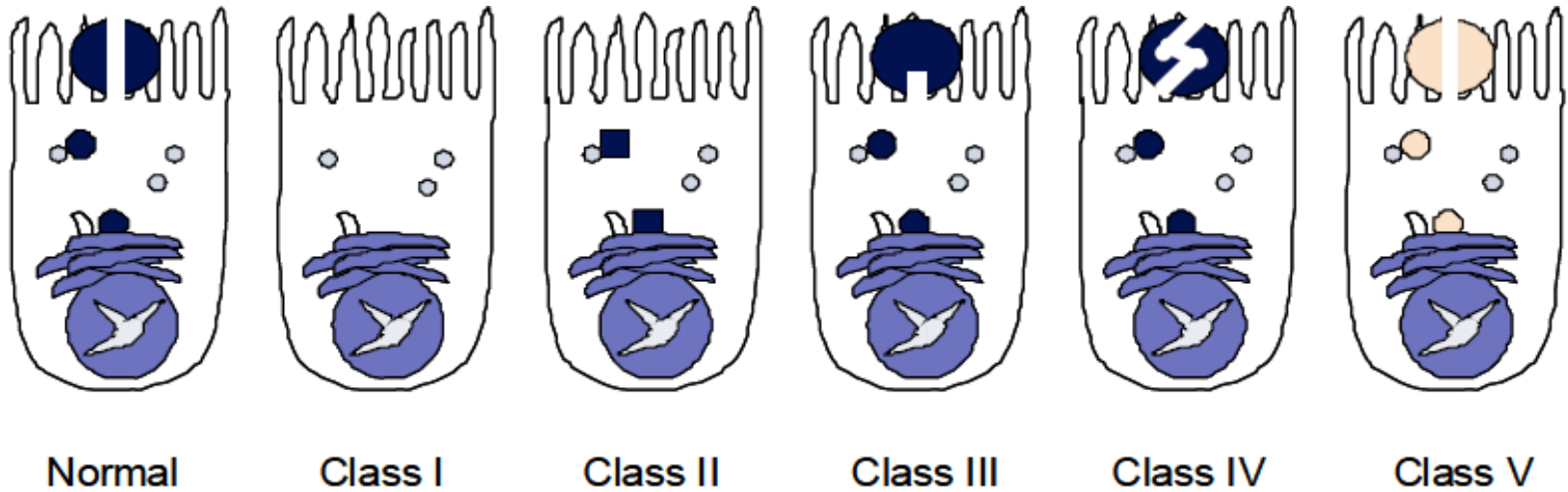
Surface liquid allows cilia to efficiently clear mucus, particles and pathogens to maintain airway health



1. Dehydration of airway surface liquid
2. Mucus builds up on cilia, particles and pathogens become trapped
3. Lung infection

Most CF patients are Class II (F508del)

We target the main mutation



Source: Adapted from Proesmans *et al.*, 2008

DATAMONITOR

Representative genotype	W1282X	F508del	G551D	R117H D1152H	3849+10kb C→T
Allele frequency	~6%	~70%	~3%	<2%	<1%
Approved drugs			Kalydeco®		
Drugs in development	PTC124	VX-809+Kalydeco® VX-661+Kalydeco®		Kalydeco®	



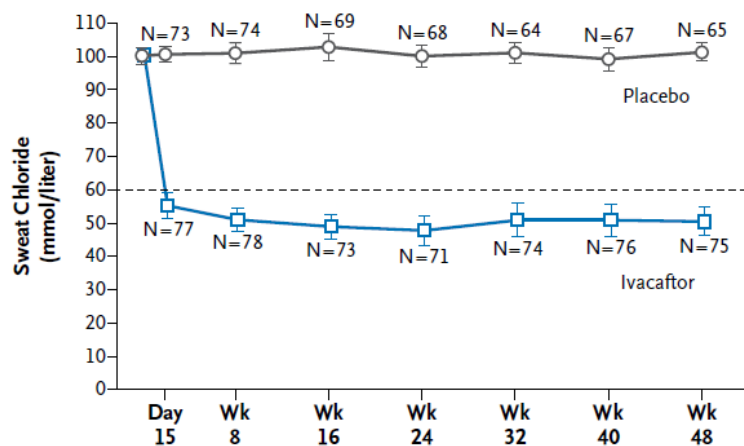
Kalydeco: first approved CFTR-drug

- Synonyms: VX-770, ivacaftor
- Approved as monotherapy for G551D patients (class III)
 - 75% of patients showed >5% FEV1 improvement
 - >10% of mean absolute change in % predicted FEV1
 - Positive effect on weight gain
 - effect on CF symptoms, pulmonary exacerbations and hospitalizations
 - approved for patients 6 years and older
- Recent Phase 3 data in class IV patients
 - Ok for adult patients with impaired FEV1
 - no effect in children with almost normal FEV1

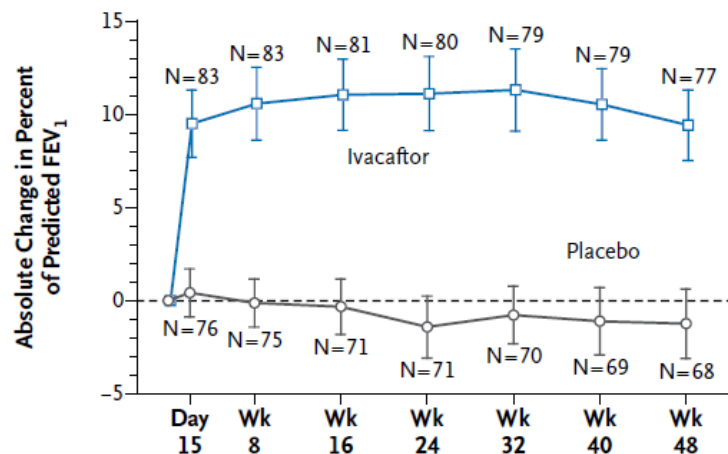
Phase 3 data with Kalydeco monotherapy

Clear read-outs in G551D patients

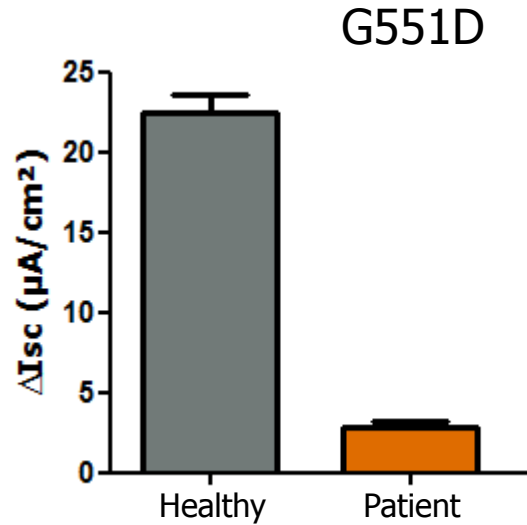
Effect on chloride transport



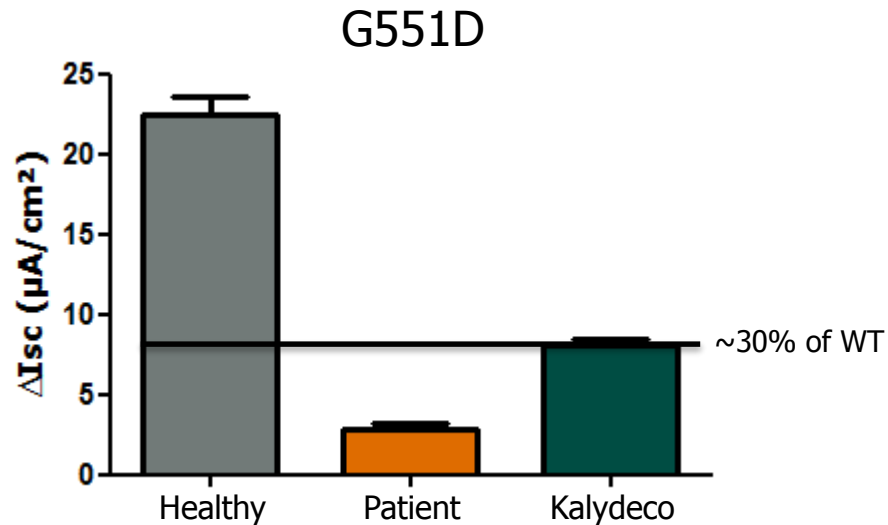
Effect on clinical endpoint



Experimental data with Kalydeco



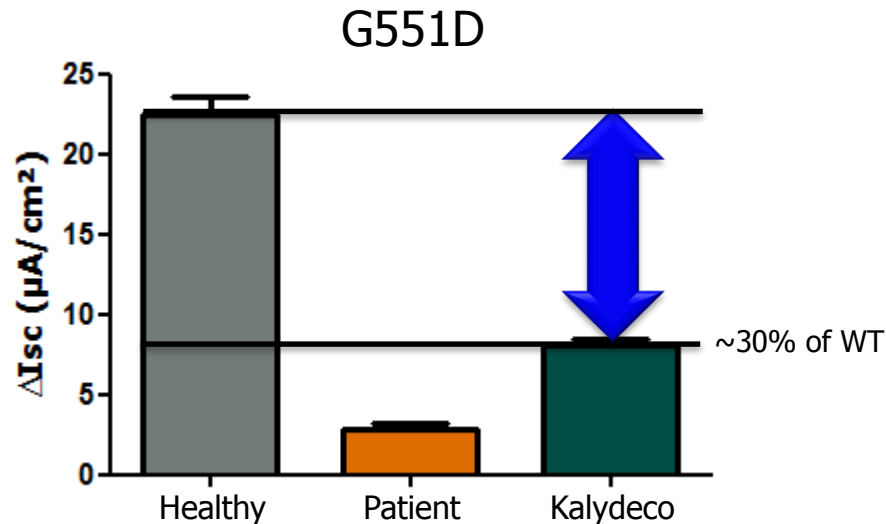
Experimental data with Kalydeco



Translation to the clinic
75% responders ($FEV_1 \geq 5\%$) on G551D/F508del

Can we improve on Kalydeco?

In the lab...



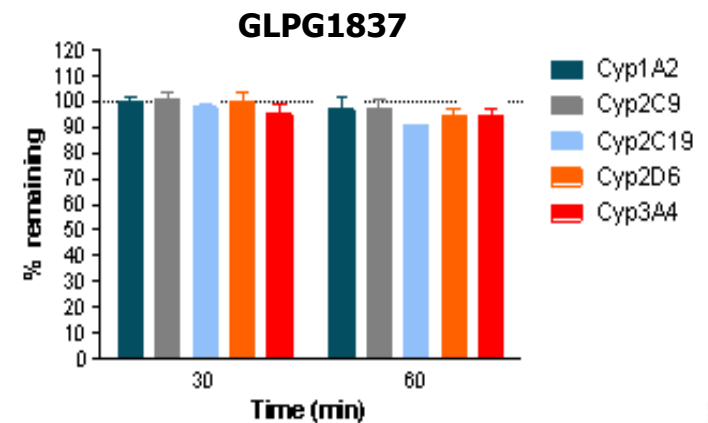
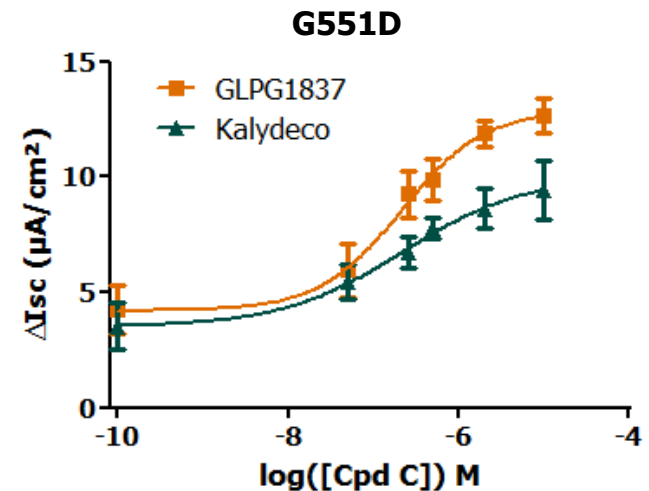
In the clinic

- Increase absolute change in FEV1 of 10%?
- Increase number of patients with 5% improvement?

GLPG1837

Positioning a potentiator for clinical development

- Improved efficacy in primary cells
- Favorable metabolic profile
 - reduced DDI liabilities
- Favorable PK profile across species
 - acceptable human PK projections (BID)
- Targeting initiation of FIH by the end of the year





F508del patients require combo treatment

- Biggest of all CF-populations (class II)
 - 40% of all CF-patients is homozygote for F508del
 - 40% of all CF-patients is heterozygote for F508del
- Combination of potentiator and corrector is required
- Phase 2 data of 2 different Kalydeco combo's are available
 - Kalydeco + VX-809: 200-600 mg QD, 4+4 week design
 - Kalydeco + VX-661: 10-150 mg QD, 4 week design



Comparison of early efficacy data

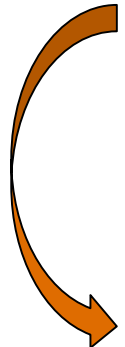
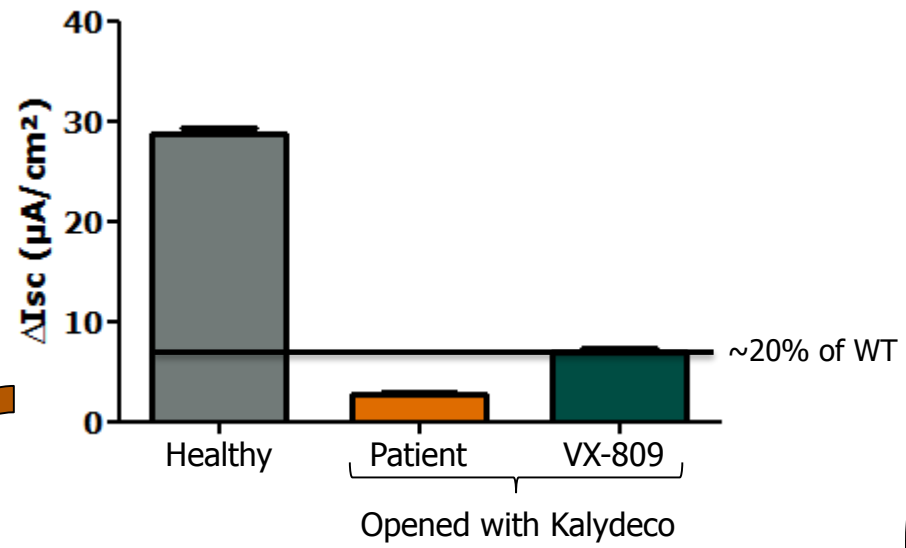
4-8 week clinical results

Therapy	Mutation	Change Sweat Cl-	Mean absolute change FEV1%
Kalydeco® (150 mg)	G551D	-60	8.7
Kalydeco® + VX-809	F508del		
200 mg		-5	1.9
400 mg		-9	0.6
600 mg		-10.1	3.4
Kalydeco® + VX-661	F508del		
10 mg		-4	2.3
30 mg		-6	3.4
100 mg		-6	4.8
150 mg		-4	4.5



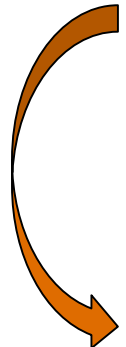
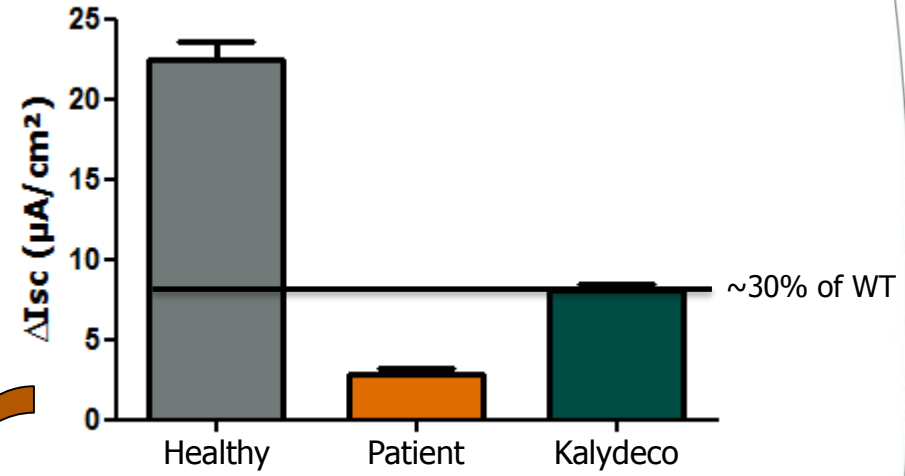
From the clinic to the lab...

F508del



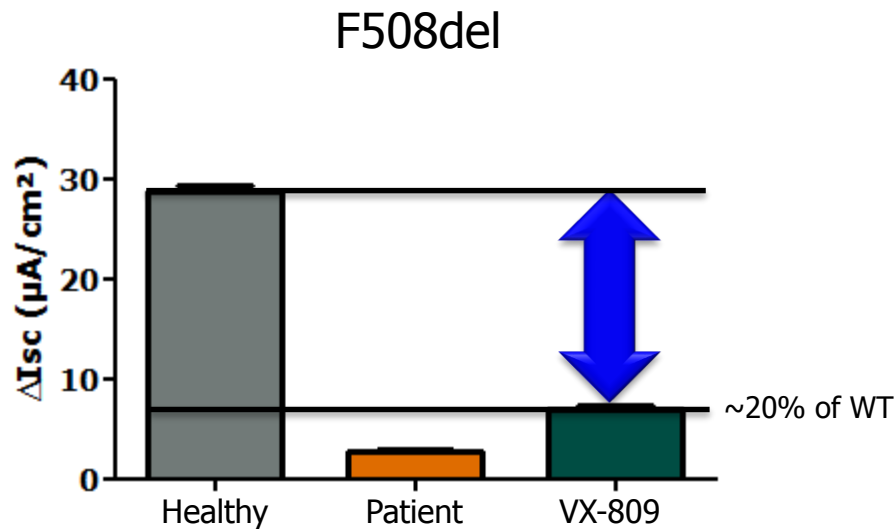
Translation to the clinic
55% responders ($FEV_1 \geq 5\%$) on F508del/F508del

G551D



Translation to the clinic
75% responders ($FEV_1 \geq 5\%$) on G551D/F508del

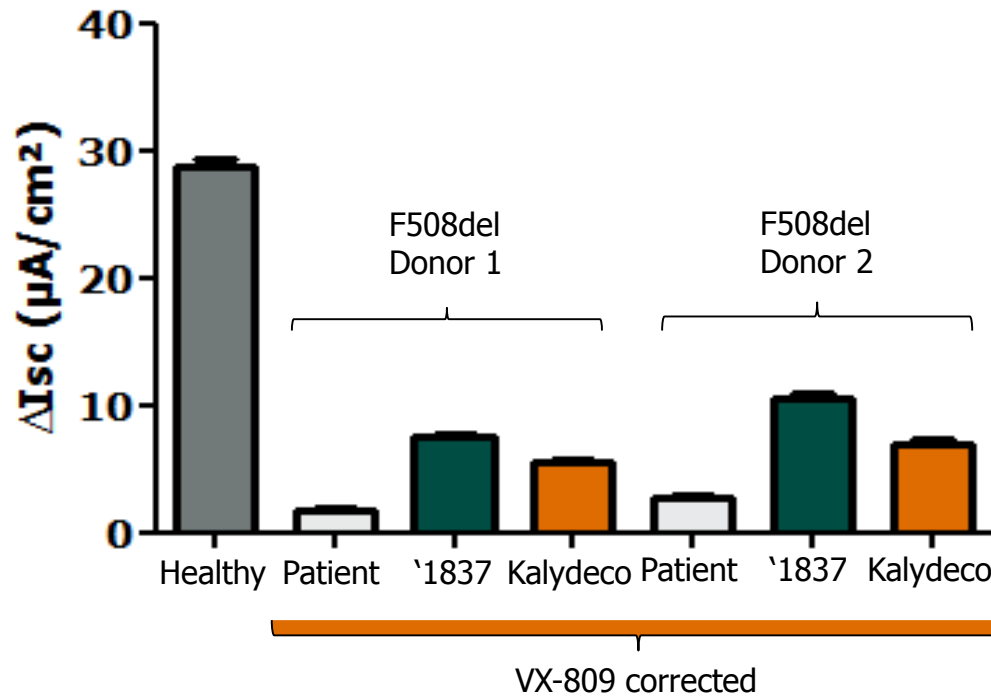
Can we improve on VX-809?



Plenty of room to improve:

- Superior potentiator
- Superior corrector
- Combination of correctors
- Combo of superior correctors

Example of superior potentiator



Primary HBE and F508del-CFTR homozygous primary cells (from 2 different donors) grown for 21 days on ALI cultures were corrected with 3 μM VX-809 for 48 h. Current measured after addition of 10 μM Fsk and 500 nM GLPG1837 or 500 nM of Kalydeco in TECC.



Bring superior treatment to the patient

- Objective: superior combination of potentiator & corrector
- Collaboration with AbbVie
 - contribute key technologies and funding
 - develop novel therapies for main mutations
- Testing cascade in place with state-of-the-art & gold standard technologies
- Learning from Vertex: Ussing chamber predicts clinical outcome
- Potentiator in preclinical development, corrector PCC expected end 2014

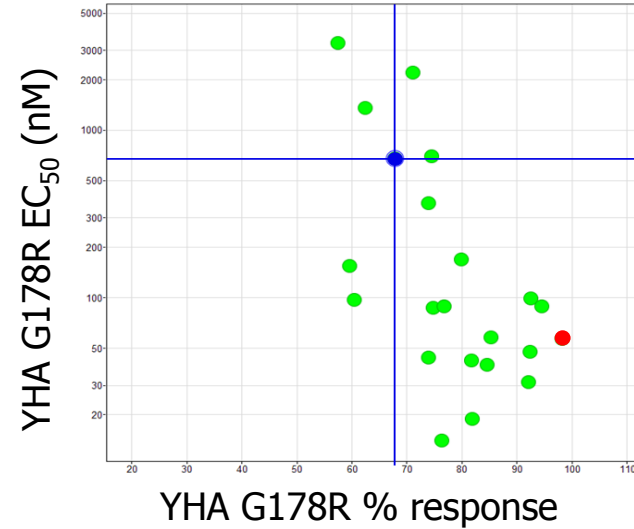
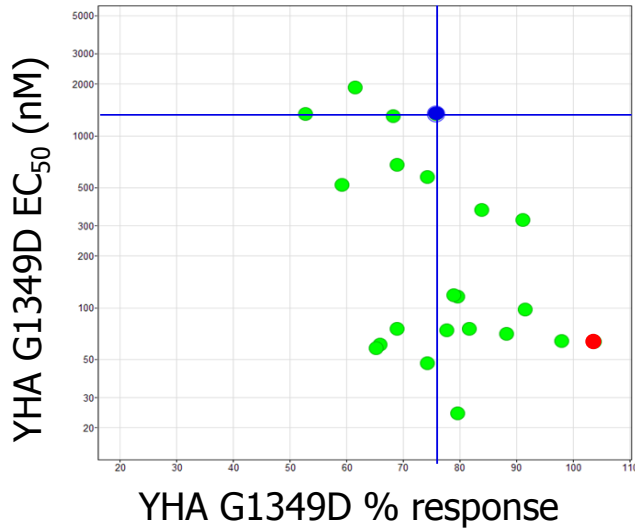
CF potentiator program on track to deliver FIH by end 2014

Galápagos

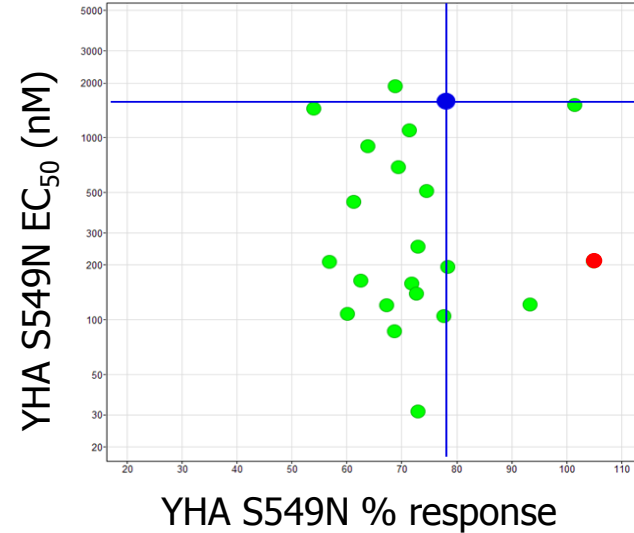
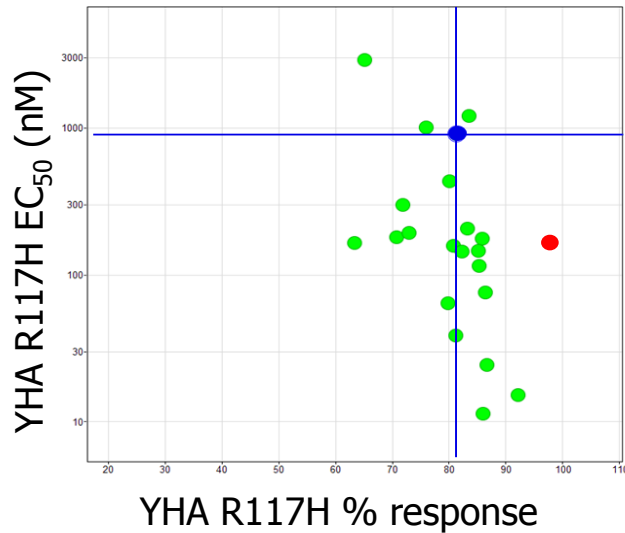
Back-up



Superior activity confirmed on mutants



- VX-770
- GLPG1837





Kalydeco Phase 3 for class IV patients

Clinical results

Mutation	Exposure	Change in sweat Cl-	Mean absolute change FEV1%
G551D (class III)	48w		10.5
R117H (class IV)	24w		
>6 years old		/	2.6
>18 years old		/	4.5