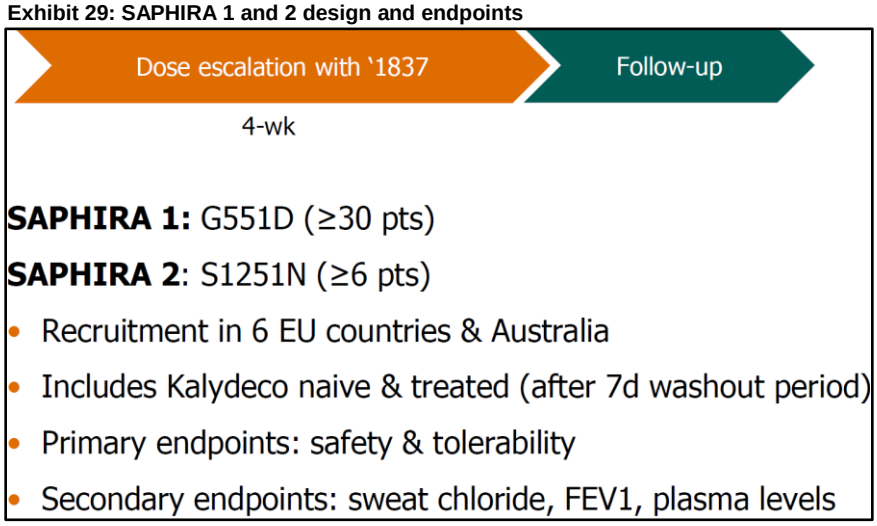
SAPHIRA 1 AND SAPHIRA 2 STUDIES UNDERWAY – COMPARISONS WITH KALYDECO

The primary endpoint in the two Kalydeco phase 3 studies was improvement in lung function (mean absolute change from baseline in percent predicted pre-dose FEV1, ppFEV1) through 24 weeks of treatment. The treatment difference between Kalydeco and placebo in ppFEV1 from baseline through week 24 was 10.6% ($p < 0.0001$) and 12.5% ($p< 0.0001$) in study one and two, respectively, and these changes persisted through 48 weeks. Other efficacy variables were all significantly in favor of Kalydeco and included:

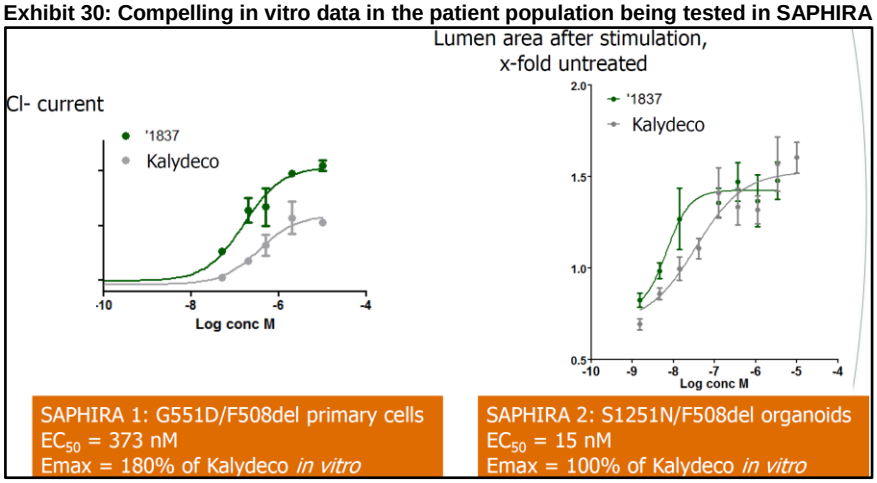
- Absolute change from baseline in sweat chloride (-48 in both study 1 and 2)
- Time to first pulmonary exacerbation (study 1 only)
- Absolute change from baseline in weight (2.8kg, and 2.7kg in studies 1 and 2, respectively), and
- Improvement from baseline in Cystic Fibrosis Questionnaire Revised (CFQ-R) respiratory domain score,

Exhibit 29: SAPHIRA 1 and 2 design and endpoints



Source: GLPG investor day June 2016

Exhibit 30: Compelling in vitro data in the patient population being tested in SAPHIRA



Source: GLPG investor day June 2016

The big question: Will the superior Emax compared to Kalydeco translate into superior FEV1 in patients? The wait isn't very long with topline data during 2H16. Note, along with phase 2 data from -1837, investors will also get PK data in CF patients from -2451. Although, 1837 may turn out to be the lead potentiator, 2451 is dosed once daily and

hence, has advantages in the chronic dosing for combination therapy. However, the formal choice will have to wait the outcome of the SAPHIRA 1 and 2 studies, which are being evaluated independently in different patient subsets. Assuming the advantage over Kalydeco holds up in the clinical studies, the worst-case scenario could be a launch targeting ~10% of the addressable market.

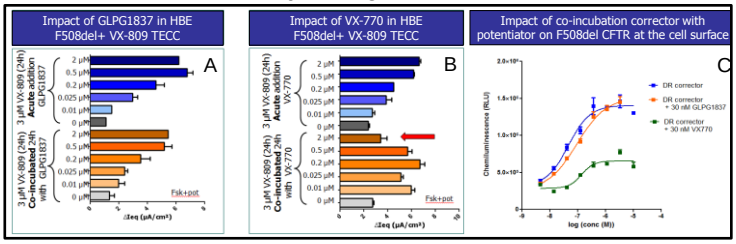
IS THERE ROOM FOR A NEW POTENTIATOR DESPITE THE SUCCESS OF KALYDECO

In the Vertex sponsored TRAFFIC and TRANSPORT phase 3 studies, the chronic co-administration of Orkambi and Kalydeco resulted in a small, but significant improvement in lung function (ΔFEV1% predicted = 2.6 to 4.0%), improved disease stability (pulmonary exacerbations fell by 30 to 39%) and reduced modestly sweat Cl–concentration (~–10 mmol/l). Paradoxically, emerging data suggests that chronic co-administration of Kalydeco with Orkambi reduces, rather than enhances, functional rescue of F508del-CFTR. This implies efficacy of the current Vertex correctors may be self-limiting when administered with Kalydeco.

Data suggests chronic treatment with Kalydeco abrogates pharmacological correction of F508del-CFTR by Orkambi and also by corrector VX-661 (currently in phase 3 studies). Note, one of the VX-661 phase 3 studies in heterozygous F508del patients was stopped due to futility. Significantly, chronic Kalydeco treatment also reduced UTP-stimulated trans-epithelial Cl^- secretion, suggesting potential off-target effects.

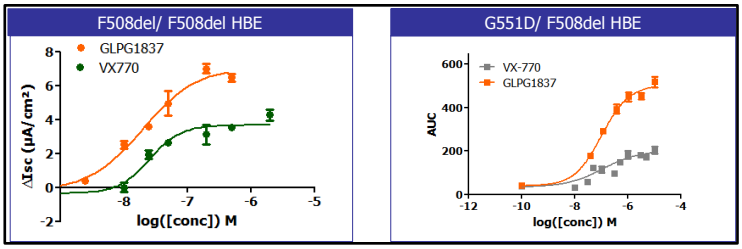
Hence, there appears to be a need for a superior potentiator. Galapagos' potentiator GLPG1837 rescue F508del/F508del 'corrected' & G551D/F508del patient cells. Importantly, chronic GLPG1837 treatment does not negatively impact drug-induced F508del-CFTR correction, both functionally and structurally (Exhibits 23 and 24). In vitro patient cell data appear to be promising and could justify the novel potentiators being developed by Galapagos either as a stand-alone therapy and perhaps more importantly, in triple-combo.

Exhibit 31: Chronic treatment of 2uM VX-770 negatively influenced VX-809 correction (B, red arrow) and chronic treatment GLPG1837 up to 2uM did not (A). Chronic treatment with VX-770 reduced cell surface stability of drug-corrected HRP-F508del, but not with GLPG1837 (C).



Source: Cholon et al.,2014 Veit et al, 2014

Exhibit 32: Potentiation of the channel by GLPG1837 (red), compared to VX-770 (blue) in Transepithelial Clamp Circuit assays on primary HBE cells from homozygote F508del (left panel) or G551D/F508del (right panel). 1837 improved function ~2x compared to the VX-770



Source: GLPG 2015 NACFC poster