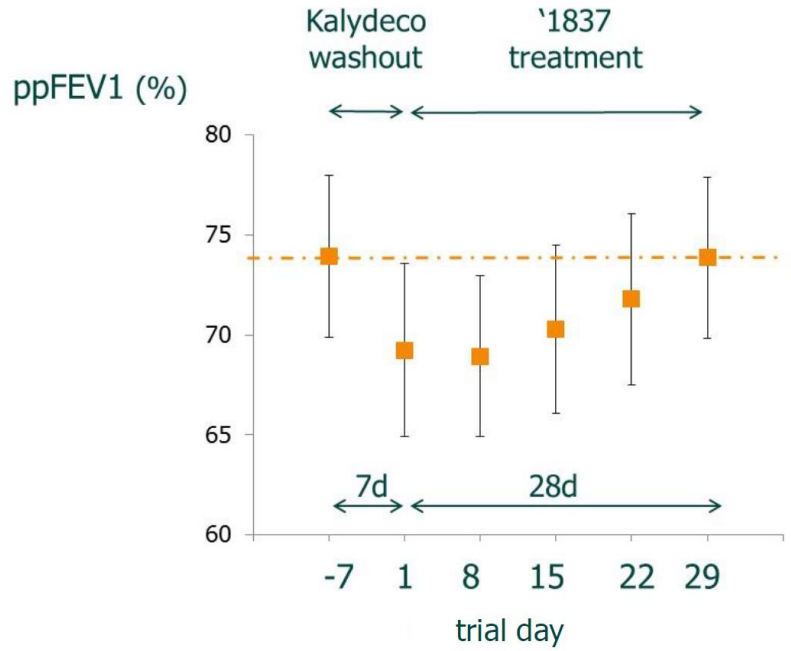
Pre-clinical assay outcomes at Vertex have proven to be reliable markers for *in vivo* results, we expect the same from Galapagos: Outcomes from the EVOLVE and EXPAND studies have set a new bar for clinical data, and the burden will be on Galapagos to prove they have competitive potentiators and correctors during 2H2017. We think that sentiment on the effort at Galapagos hinges on the results of a once daily potentiator, GLPG2451, as the twice daily dose of GLPG1837 has demonstrated comparable efficacy to ivacaftor but without a dosing advantage may have trouble differentiating. Furthermore, given that the SAPHIRA 1 study only evaluated Kalydeco responders post-washout, it is hard to make an efficacy comparison between GLPG1837 as a potentiator of G551d mutation CF patients relative to Kalydeco.

***The SAPHIRA 1 study demonstrated that GLPG1837 could return patients to 'on-treatment Kalydeco baseline' FEV1% function by Day 28 post an ivacaftor washout period* (Figure 51).**

Figure 51. GLPG1837 could return patients to Kalydeco baseline FEV1% function by Day 28



Source: SAPHIRA 1 Results (December 20th 2016), Ph2a open label trial of GLPG1837

GLPG2222 is expected to be the one of the corrector backbones (C1) of a once-daily triplet combo: Two Phase 2 studies of GLPG2222 are currently enrolling for patients with F508del/ Class III mutations and homozygous F508del mutations (Figure 52).

The ALBATROSS study was started during January 2017 and will evaluate the combination of GLPG2222 + Ivacaftor in the treatment of CF patients that have the F508del allele along with an impaired gating allele. The comparator arm will be placebo, but the more demonstrative analysis will be relative to patient baseline on FEV1 and CFQ-R, as all enrolled patients will be stable on ivacaftor heading into the study. Results of the ALBATROSS study will provide some insight into the potential additive effect of '2222 to Kalydeco, but the active treatment of only 4wks with 2wks of follow-up will prevent any analysis regarding the sustainable effects of the combination.

The FLAMINGO study was announced during the 1Q17 earnings call, and was initiated during March 2017. Importantly, the FLAMINGO study will be the first Cystic Fibrosis study that Galapagos/ AbbVie will be running at US sites. Given that US enrollment will be critical for pivotal studies in a triplet-combo, anecdotal information regarding US enrollment within the FLAMINGO study will be important. Beyond enrollment data, the FLAMINGO data set will provide a look at the stand-alone potential of GLPG2222 within the adult F508del homozygous population, which could provide some early data as to the relative effectiveness versus Orkambi.

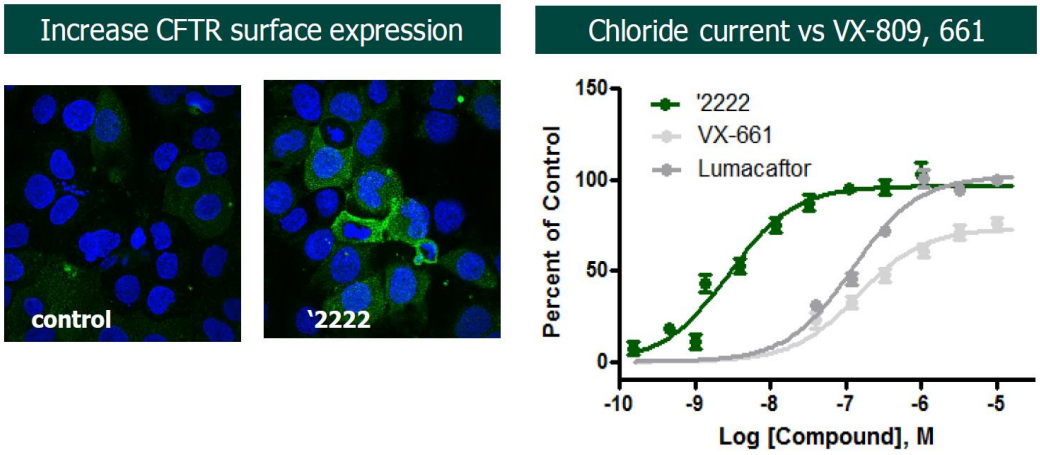
Figure 52. The FLAMINGO and ALBATROSS studies are currently enrolling patients with F508del mutations

Study Name	ALBATROSS	FLAMINGO
Patient Population	Adult F508del/ Class III	Adult F508del homozygous
Number of Patients	n=14 per Drug Arm	n=20 per Drug Arm
Drug	GLPG2222 + Ivacaftor	GLPG2222
Dose / Schedule	300mg QD / 150mg QD + IVA 150mg BID	A or B mg QD / C or D mg QD
Primary endpoints	Safety and Tolerability	Safety and Tolerability
Secondary endpoints	Sweat Chloride, FEV1, CFQ-R	Sweat Chloride, FEV1, CFQ-R and PK
Study Timeline		
Screening	4wks	4wks
Active	4wks	4wks
Follow-up	2wks	2wks
Expected Study Completion	2Q2017	3Q2017
Study Sites	27 sites: Australia, Belgium, Czech Rep, Germany, Ireland, UK	24 Sites: Belgium, Netherlands, Serbia, Spain, UK, US

Source: Company Reports, June 2017

Pre-clinical data from Galapagos has suggested that GLPG2222 is key to the upcoming triplet-regimen for severe forms of cystic fibrosis. CFTR surface expression assays and comparative chloride currents generated versus tezacaftor and lumacaftor, suggest that GLPG2222 may be a powerful corrector of F508del CFTR protein (Figure 53).

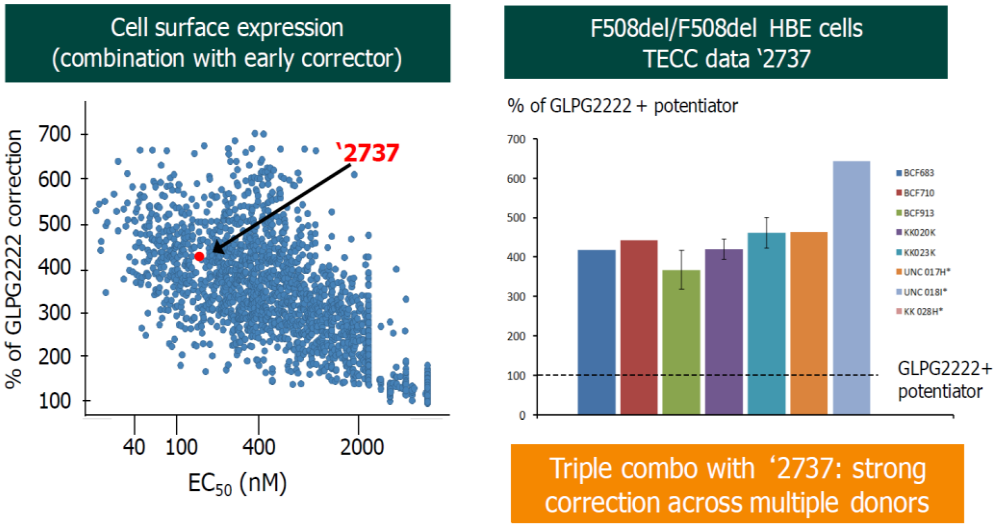
Figure 53. GLPG222 powerful F508del CFTR correction is the key to the triplet combo



Source: Company Reports, June 2017

Pre-clinical assays characterizing a potential triplet-combination of the early corrector '2222 + a late corrector '2737 + a potentiator, suggest a significant current amplification relative to combination therapy (Figure 54). Unfortunately, the baseline HCE cell TECC data is whatever the GLPG2222 + potentiator registers as a short circuit current on an ENaC assay. Although the absolute improvement is ambiguous, the +4x-fold improvement over the combo consistently across various HBE cell lines is important, given the research suggesting significant heterogeneity in response within the F508del homozygous population to lumacaftor (Amaral 2015)[24].

Figure 54. Triplet combo amplifies current relative to combination therapy

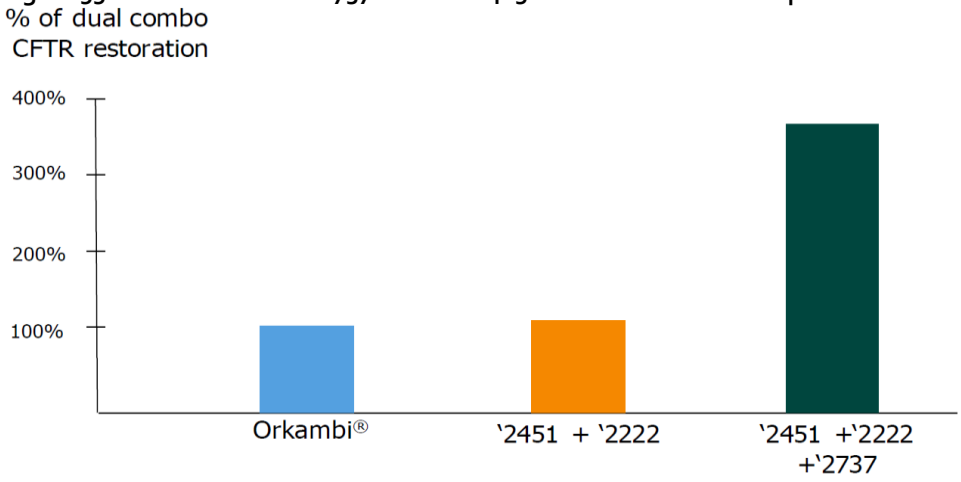


Source: Company Reports, June 2017

We hesitate to draw conclusions from pre-clinical assays that carry few details and context, but another example of CFTR restoration, seems to imply that GLPG2222 plus the once daily potentiator GLPG2451 performs inline with Orkambi, but is substantially amplified when combined with the second corrector GLPG2737 (Figure 55).

[24] *Measurements of Functional Responses in Human Primary Lung Cells as a Basis for Personalized Therapy for Cystic Fibrosis*; Awatade and Amaral et al.; *EbioMedicine* 2; 2015; 147 - 153

Figure 55. Addition of GLPG2737 to GLPG2415+GLPG2222 combo amplifies CFTR restoration



Source: Company Reports, June 2017

Galapagos efforts in Cystic Fibrosis date back 10 years to a collaboration with Cystic Fibrosis Foundation Therapeutics: Today's CFTR modulator program is a reboot of an effort announced during 2005 between Galapagos and the Cystic Fibrosis Foundation that resulted in ~19 molecules. However, the molecules that were identified were not CFTR modulators and ultimately did not warrant clinical development. The efforts with the Cystic Fibrosis Foundation failed to identify viable molecules for the treatment of CF, but the endeavor did help develop validated pre-clinical assays for modeling Cystic Fibrosis within Galapagos. **The company started the current programs for CFTR modulators during the 2011 – 2012 timeframe and officially announced a partnership agreement with AbbVie to co-develop drugs for the treatment of CF during 2013.**

In April 2016, AbbVie and Galapagos updated and expanded the collaboration agreement for Cystic Fibrosis, namely increasing the potential milestone payments to Galapagos from AbbVie to ~$600m, versus ~$350m under the original agreement (Figure 56). The increase in financial incentives for Galapagos was a result of successful Phase 1 and Phase 2 studies, and what seemed to be an expanded strategy to launch a successful triplet-combo. Galapagos will be responsible for development through Phase 2, and AbbVie will be responsible for Phase 3 development and commercial strategy, with Galapagos contributing financially to the efforts. **Galapagos management has staked confidence in AbbVie's ability to carry out the more complicated pivotal studies and commercial launch, based upon experience within the Hepatitis C drug market – the combo regimen Viekira Pak and more recently the combo of glecaprevir and pibrentasvir.**

Figure 56. Updated AbbVie agreement increased GLPG CF milestones to ~$600m vs ~$350m

AbbVie and Galapagos Cystic Fibrosis Collaboration Agreement

Original Agreement Announced during September 2013

- Goal to specifically target F508del and G551D mutations
- Timeline to initiate Phase 1 clinical studies at the end of 2014
- AbbVie made an initial upfront payment of $45m to Galapagos for rights related to the global alliance
- Potential developmental, regulatory milestones, and sales milestones of up to ~$360m
- Double-digit royalty payments on net sales
- Galapagos retains exclusive rights in China and South Korea and co-promotion rights in Belgium, the Netherlands, and Luxembourg

Updated Agreement Announced during April 2016

- Potential developmental, regulatory milestones, and sales milestones of up to ~$600m
- Increase payments based upon Phase 1 and Phase 2 achievements
- Tiered royalty payments on net sales, ranging from mid-teens to twenty percent
- Galapagos retains exclusive rights in China and South Korea and co-promotion rights in Belgium, the Netherlands, and Luxembourg

Source: Company Reports, June 2017

Other Clinical Candidates Being Development Could Provide an Additional Upside to Our Estimates

GLPG1690 (Autotaxin): Idiopathic Pulmonary Fibrosis

Galapagos has an ongoing Phase 2a study with GLPG1690 (anti-autotaxin) in Idiopathic Pulmonary Fibrosis (IPF). Idiopathic pulmonary fibrosis is a rare (<30 per 100,000 persons) progressive inflammatory condition characterized by persistent thickening, scarring, and ultimately stiffening of the lungs. The median survival of IPF is less than 3 years as IPF causes breathlessness that worsen leading to respiratory failure. Due to the idiopathic nature of the disease, many treatment options for IPF has failed, including corticosteroids, immunosuppressive, and anti-fibrotic agents commonly used for other inflammatory conditions. Marketed and clinical drug candidates currently under development are unable to reverse the scarring which characterizes IPF, therefore the goal of most therapies is to simply delay disease progression. To date, lung transplant remains the only viable treatment option offering long-term survival, with a 5-year survival rate of 45%, but cost and demands limitation associated with lung transplantation prevents it from being a viable option for many patients.[25]

GLPG1690 has been granted orphan designation by the European Commission (EC), but despite the small patient population there is significant opportunities for revenue potential. There are ~200K patients in U.S./E.U patients with ~60% being mild to-moderate IPH. Small molecule drugs Ofev and Esbriet were some of the first drugs approved for moderate to Severe IPH, and Esbriet generated up to $236 million in its first half year of sales at an estimated PPPY of $44,000. Newly approved, Ofev (nintedanib) and Esbriet (pirfenidone) both prevent further scarring and result in few exacerbations and maintenance of lung function, but neither drugs shown significant decreases in mortality. Gilead's simtuzumab (a lysyl oxidase-like-2 inhibitor), attained following the acquisition of Arresto for $225 million was also terminated as has a few other compounds causing a significant gap in the market. Of note, Actelion's (ATLN, Not Rated) small molecule drug approved for PAH, Opsumit (macitenan), also did not meet its primary endpoint in IPH and was discontinued, leaving Exbriet and Ofev as the only approved drugs for this indication.

GLPG1690 is a potent small molecule selective inhibitor of the enzyme autotaxin (ATX) that plays a role in the production of lipid lysophosphatidic acid (LPA) through the breakdown of lysophospholipids. LPA, has been considered a key factor in multiple indications including cancer, cardiovascular and CNS disorders. LPA increases endothelin-1 expression and mediates the production of matrix metalloprotease 2 which is a fundamental regulator of extracellular matrix remodelling required for endothelial cell migration during angiogenesis. In a preclinical model heterozygous for the null autotaxin allele, there was reduced level of circulating LPA, with no major changes in phenotype, which could suggest limited impacted on normal physiology.[26] However, there are very few drugs targeting autotaxin, since there remains some uncertainty

[25] Huang H. et al. Idiopathic pulmonary fibrosis: The current status of its epidemiology, diagnosis, and treatment in China. Intractable Rare Dis Res. 2013 Aug; 2(3): 88–93.
[26] Federico L. Therapeutic Potential of Autotaxin/Lysophospholipase D Inhibitors. Curr Drug Targets. 2008 Aug; 9(8): 698–708.

regarding its in LPA metabolism and signalling so Galapagos was the first to really show efficacy of an ATX in preclinical modes for IPF. A phase 1 study (NCT03143712) in healthy adults confirmed a good safety profile, and continuous reduction of LPA by >60% was observed from 0 to 24 hours, supporting initiation of the ongoing phase 2a study (FLORA; NCT02738801) of GLPG1690 in ~24 IPF patients in April 2016. The primary completion date is June 2017, so we would expect data by YE2017.

GLPG1972 (ADAMTS-5): Osteoarthritis

Galapagos is also developing GLPG1972 (ADAMTS-5), a phase 1b drug candidate for Osteoarthritis, in collaboration with Servier. Osteoarthritis is one of the most common joint conditions affecting millions of Americans and over 100 million people worldwide, particularly the aging population (~33% of OA patients > age 65).[27] OA is considered a chronic and progressive disease resulting from inflammatory response to the loss of cartilage in the joints, which typically absorb forces from the impact occurring during joint mobility. The number of patients with OA in the United States is ~30 million with 80% of OA patients having movement limitations, 20% being unable to perform some major daily activities, and 11% needing personal care.[28] There are several approved drugs for OA including non-steroidal anti-inflammatories. However, NSAIDS carry increased risk of gastrointestinal bleeding, renal dysfunction, and elevated blood pressure associated with NSAIDs, and many patients continue to experience inadequate pain relief (IPR) and experience significant functional loss, and an overall lower quality of life.

GLPG1690 is a potent and selective small inhibitor of the enzyme ADAMTS-5, with the potential to address the underlying cause of the disease, as ADAMTS-5 can protect the cartilage from degradation. ADAMTS-5 is a disintegrin and metalloproteinase with thrombospondin motifs, a family of extracellular matrix proteases that have been implicated in multiple connective tissue diseases. ADAMTS-4 and ADAMTS-5 are the more characterized ADAMTS, and have been shown to be specially associated with cartilage degradation. Early studies from GSK also showed the potential for anti-ADAMTS-4 and ADAMTS-5 antibodies to inhibit cartilage degradations as measured by a reduction in the breakdown of Alanine-Arginine-Glycine-Serine (ARGs) in the synovium.[29] ARGS are the building blocks of aggrecan, the main proteogyclan of the cartilage matrix and ARGS are directly associated with the Osteoarthritis Outcomes Score.[30] The ADAMTS targets are no longer being explored by GSK, and there are no marketed inhibitors of ADAMTS.

Galapagos phase 1 study (NCT03143712) of GLPG1690 in healthy adults showed (at the 2017 OARSI meeting) an excellent safety profile, and up to 60% reduction of serum ARGS-neoepitope following 2 weeks of treatment. Galapagos has also initiated a phase 1b study (NCT03143725) to evaluate bioavailability of different formulations of GLPG1972, and that data is expected before YE2017, which could potentially support initiation of a phase 2a study.

[27] Bhatia D. et al. Current interventions in the management of knee osteoarthritis. J Pharm Bioallied Sci. 2013 Jan-Mar; 5(1): 30–38.
[28] Neogi T. et al. The Epidemiology and Impact of Pain in Osteoarthritis. Osteoarthritis Cartilage. 2013 Sep; 21(9): 1145–1153.
[29] Larkin J. et al. Translational development of an ADAMTS-5 antibody for osteoarthritis disease modification. Osteoarthritis Cartilage. 2015 Aug;23(8):1254-66.
[30] Wasilko SM. Et al. Relationship between synovial fluid biomarkers of articular cartilage metabolism and the patient's perspective of outcome depends on the severity of articular cartilage damage following ACL trauma. J Orthop Res. 2016 May;34(5):820-7.