## THE RACE FOR THE SUPERIOR CORRECTOR – AN AGGRESSIVE TRIPLE COMBO STRATEGY

Vertex – TRAFFIC AND TRANSPORT studies leave room from improved outcomes in patients. Key gaps include:

- Modest clinical benefit The difference between active treatment and placebo with respect to the mean absolute improvement in the percentage of predicted FEV1 ranged from 2.6 to 4.0% points (P<0.001), which corresponded to a mean relative treatment difference of 4.3 to 6.7% (P<0.001).
- Orkambi's limited clinical benefit is limited to homozygous patients Implies at least 40% of the commercial opportunity is currently untapped
- Dropout rates (between 30% to 15%) and compliance (between 80% to 70%) on Orkambi suggests room for improved safety profile

The challenge here is all the drugs need to bind to the same target without interacting and increasing the possibility of adverse events. Logically, one can either fix each dose on its own, in a sequence. However, since triple combo is the play here, the Galapagos program is in trouble if the third component affects the binding of the first two.

Galapagos has two correctors in development, which include:

- C1- 2222, its and backup;
- And C2 2737

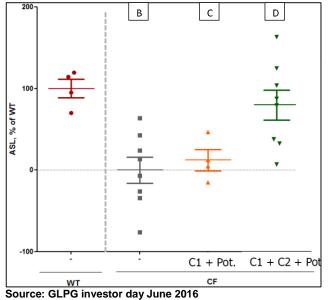
Note, C1- 2222 healthy volunteer study is complete and a PK study in CF patients will be initiated later this year.

Importantly, 2222 was well-tolerated in healthy volunteers. Key take-aways from the randomized, double blind, placebo-controlled healthy volunteer study:

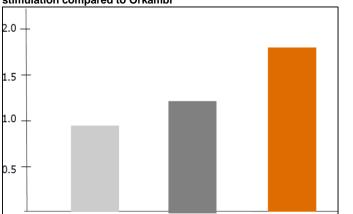
- SAD doses ranged from 50 800 mg
- MAD doses ranged from 150 600 mg qd. for 14 days
- PK supports once daily dosing regimens for future development
- Favorable & rapid absorption in patients was noted
- Phase 1 in combination with potentiator to start after the SAPHIRA 1 and 2 read out

Also note, healthy volunteer phase 1 with C2 – 2737 is likely to commence during 4Q16. As a note of caution highlighting the risks (unfavorable drug-drug interactions) of aggressively developing multiple programs targeting the same target, a previous corrector 2665 has been discontinued in favor of 2737. C2 -2737 selection was likely based on lung penetration and 2665 had a negative impact on the competitive binding to the CFTR protein when combined with P+C1). -2737 is currently in preclinical toxicological studies, which is rate limiting in the race for a triple combo *vs.* VRTX.

Exhibit 33: *In vitro* data: (A) Control cell line – healthy (100%); (B) Untreated delta F508 homozygous cell line; (C) Corrector + potentiator; and (D) Triple therapy, C1+C2+potentiator drives recovery close to normal cells.



While Kalydeco provides significant clinical benefit for 10% of the CF patients, and Orkambi provides a modest clinical benefit for ~45% of the 508del homozygous patients, ~40% of the market (heterozygous patients) remains underserved. In vitro data suggests potential benefit for the heterozygous patients might be within the scope with the emerging focus on triple combo. As highlighted in the assay on organoids, the Galapagos triple combo appears to provide a benefit over Orkambi. However, these are in vitro assays, and will need to be translated into the clinic.



Orkambi

Exhibit 34: Triple combo in heterozygous G542X/F508del organoids - Lumen area after stimulation compared to Orkambi



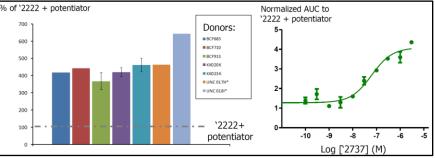
Untreated

Note, Galapagos has had to make some changes to its original development strategy, dropping a previous corrector in favor of new and potentially better one, highlighting the risks of an aggressive development strategy. C2 – 2737 was selected because it has a higher lung penetration (compared to 2665), and it has the least impact on binding of potentiator and C1. C2 – 2737 delivers between 400% to 600% increase of ion currents over the membrane compared to dual therapy (left panel, exhibit 25). Additionally, C2 – 2737 has nanomolar EC50, implying less drug.

GLPG

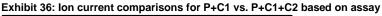
triple combo

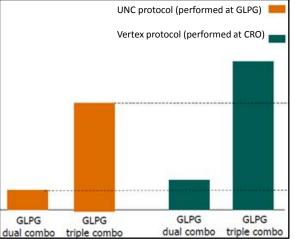
Exhibit 35: Triple combo delivers robust correction across multiple patient F508del/F508del donor cells: C2 – 2737, is the most advanced corrector



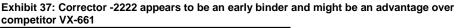


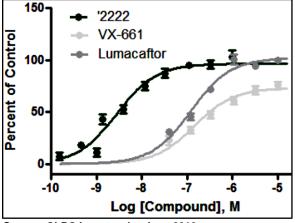
-2222, it's an early binder like Kalydeco and VX-661 and appears to be more potent and hence, dosing and potentially lower SAE 's could be an advantage. Also, the maximal efficacy (Emax) with -2222 appears to be similar to that of Kalydeco (both of which are consistently higher than -661) and if this holds up in the clinic then -2222 could well be a superior corrector than VX-661.





Source: GLPG investor day June 2016





Source: GLPG investor day June 2016

P+C1 combination studies in healthy volunteers will be initiated only after SAPHIRA and phase 1 data from 2451 becomes available. Current timelines imply a 1H17 P+C1 combo study initiation in healthy volunteers.

Exhibit 38: CF U.S revenue build and rNPV

			2036	2017	2018	2019	2020	2023	2022	2023	2024	2025	2026	2027	2028
Mutetion	464														
FS08del Homozygous Growth rate	12+		8,500	8,602	8,705	8,810	0,915	9,022	9,133	9,240	9,751	9,463 1.2W	9,577	9,692	9,000 1,7 N
GLPG adoption			1.2%	1.09	12%	12%	7.0%	2.0 1	12.78	11.78	16.0%	17.2%	11.19	22.6W	200
Growth rote GIP G							7.0%	40.0%	30.0%	15.0%	10.0%	7.0%	3.0%	3.0%	10%
Growth /Dat GOrg Chronizator			80.0W	80.0%	80.0W	80.0%	80.0%	40.0%	30.0%	15.0%	10.0%	2.0%	3.0%	3.0%	10%
Drag out			15.0W	25.0N	15.0W	15.0%	25.0%	15.0N	15.0W	25.0N	15.0W	15.0W	25.0%	15.0 N	25.0%
GLPG pet ients			10.0%	1208	12.0%	1100	624	004	1163	1354	25.07	16 32	1774	1007	2047
GJP G Price per potient							375,000.00	797,750.00	413,437.50	474,109,30	455,034.04	470,605.59	502,575.87	527,662.66	55 4,045,79
Aur u rrice per posent Price increase				24	5%	5%	375,000.00 SN	750,750.00 SN	410,417.50	55,105,0	455,834,84	476,605.59	502,525.87	522,892.69	104045.73
GLPG revenue		_		399	198	576	197,223,961	278,521,110	304,743,491	470.152.699	549,542,604	624820,140	697,130,574	762,994,077	818,845,081
Mutetion	A	A					207,223,401	140,021,110	301,713,101	470,152,055	543,542,604	62 9020, 240	637,151,574	762,539,077	100,000,001
	Age 6 to 11	Pepuli	abon 2,460	2,490		2,558	2,50.0	2.611	2.643	2.674	2,706	2,739	2,772	2.005	2,039
FS08del Homozygous Growth rate	6 10 11		2,460	2,490	2,529	2,550	2,500	2,611	2,643	2,674	2,706	2,739	2,772	2,005	2,039
GLPG adoption			1.2%	120	1230	123	5.0%	6.5%	7.8%	8.6%	8.29	9.6W	9.99	20.256	30.84
Growth rate GIP G							60.0%	30.0%	20.0%	20.0%	2.0%	5.0W	1.0%	3.0%	10%
Omplance			80.0W	20.0%	80.0W	80.0%	20.054	20.0%	20.0%	20.0%	80.0%	30.0%	80.0%	80.0%	80.0%
Drop out			15.0W	25.0%	25.0W	15.0%	25.0%	15.0 %	15.0W	25.0%	15.0%	15.0%	25.0%	15.0%	25.0N
GLPG pet lents			15.0%	12.000	12.0%	12.0%	129	170	204	229	240	264	225	20.7	293
GLFG petients GLFG Price per potient							375,000.00	393,750.00	413,437.50	434,109,39	240 455,834,84	470,605.59	502,535.87	207	293 55 4,045,79
Gur u Price per posent Price increase				76	5%	5%	375,000.00	393,750.00 5%	433,437.50	434,109.30	400,014.84	426,605.59	502,53587	522,892.66	204,045.79
are increase are increase		_		599	5%	5%	30,703,337	53.464.016	68.173.036	73.604.725	90.600.130	101.005.260	110.635.584	121,088,223	119.955.030
Mutation	Age	Popula					30,703,337	52,969,016	60,173,036	73,464,735	90,000,130	101,065,240	230,435,594	121,088,223	119,955,030
F508del Homozygous	0 to 5	repos	2,050	2.075	2,099	2,125	2,150	2,176	2,272	2.229	2,255	2.29.2	2,710	2,337	2,365
Follodel Homozygous Growth rate	U to S		2,050	2,0 %	2,099	12%	2,150	2,176	2,202	2,229	2,255	2,262	2,310	2,557	2,95
GLPG adoption			1.2%	120	12%	129	25.0 %	17.5%	15.0%	20.38	2179	22.8%	23.5%	24.25	24.4%
ucre adoption					41.2%	42.0%	42.5%	43.0%	67.0%	43.76	43.9%	94.2N	44.256	44.3%	61.5%
Growth roter GUP G					43.2%	42.0%	42.8%	43.0% 15.0N	43.4% 30.0%	43.74 7.0%	43.9%	44.2% 5.0%	3.0%	3.0%	10%
			80.0%	82.0%	80.0W	80.0%	80.0%	15.0%	30.0%	20%	2.0%	3.0%	3.0%	0.0%	10%
Ompliance Drop out			15.0W	15.0%	15.0W	15.0%	15.0%	15.0N	15.0N	15.0%	15.0%	20.0%	25.0%	15.0%	25.0N
			15.0%	13.0%	12.08	13.0%	13.0%	375	418	452	490	521	543	566	578
GLPG pat ionts															
GLP G Price per potient				5%	5%	5%	375,000.00	393,750.00	413,437.50	434,109.38	455,814.84	478,605.59	502,535.87	527,662.66	55 9,045.79
Price Increase GP 9 revenue				598	578	5%	5%	5% 118.237.728	138.203.351	5% 157.134.722	5% 178.659.351	5N 193.335.598	238.168.426	5% 238.780.543	256.265.487
OLP ID REVENUE		_						110,237,720	130,203,351	257,139,722	170,053,351	199,000,090	230,100,420	230,700,543	250,205,407
			2015	2017	2019	265.9	2020	2023	20.22	2023	2024	20.25	2026	2027	2029
Mutation		Peed		2017	2108	212.9	2020	2021	2022	20.23	2024	20.25	2026	2027	2028
05510.2117H.etc		rapus	4000	4048	409.0	4113	4146	4179	4213	42.46	4280	4314	4349	4394	4419
			1.2%	1.76	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Growth rate GLFG Adoption			1.26	1.24	0.0%	0.0%	25%	16%	2,9%	2.0%	276	2.96	25%	25%	25%
							25.96	27%	276	279	276	246	2576	2016	2016
GPLG growth rate Comiliance							92%	97%	20%	10%	80%	906	576	976	07%
							15%	15%	156	156	196	15%	25%	15%	15%
Drop out OPLC petients							25% 529	15%	19%	15%	15% 822	15%	25% 521	15%	15%
OPLC price per patient							375000.00	386250.00	397037.53	409772.63	422055.80	434727.78	447769.61	461202.70	475030.70
DFLG price per patient Price increase				24	2%	25	375000.00	304250.00	397037.53	405772.63	422055.00	404727.70	447765.51	46 12 0 2.70	475030.70
		_		74	29	29									74
GLP G revenue							158,581,872	175,622,445	218,805,897	249,890,338	277,607,375	302,634,235	339,917,317	352,809,355	369,963,793
GLPG gross revenue		5	- 5	- 5	- 5	- 5	384,538,670.70 3		009,925,775.95 S				1,355,851,910.20 5	1,475,672,190.20 5	3,575,049,390.33
GLPG royalty rate							25%	17%	20%	1976	20%	20%	276	27%	20%
Netreverser				0		0	61,523,307	106,293,701	245, 70 6, 640	30 3,0 07,0 74	219,203,904	245,575,047	271,170,302	295,334,440	315,009,070
						1 m m m m *									
R&Dexpenditure			(35,000,000)	(35,000,000)	(30,000,000)	(30,000,000)	(15,000,000)								
Affestore				250,000,000	150,000,000	50,000,000	50,000,000	50,000,000	50,000,000						
Net revenue		\$	(35,000,000.00) \$			20,000,000.00 \$		5 156,393,701.02 5		181,803,874,04 5		245,575,046.53 \$	271,170,382.16 \$	295,134,439.64 \$	315,009,878.07
Probabb lity of success			85%	75%	50%	30%	20%	20%	20%	20%	20%	20%	20%	20%	20%
Probability adjusted revenue		5	(29,750,000.00) \$	161,250,000.00 5	60,000,000.00 \$	6,000,000.00 5	19,334,277.46 3	5 31,270,740.20 5	39,157,327.93 \$	36,360,774.01 5	43,056,300.77 \$	49,115,009.31 5	54,234,076.43 \$	59,026,007.93 \$	63,001,975.61
Discount rate	7	56													
rNPV	5333,367,374.2														
FDEO rNFShare	39,076,000.0 S 8.0														

Source: Janney Montgomery Scott LLC estimates

		2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028
Mutation	Age	Population												
F508del Homozygous	12+	12,000	12,144	12,290	12,437	12,586	12,737	12,890	13,045	13,202	13,360	13,520	13,683	13,847
Growth rate		1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%
GLPG adoption						7.0%	9.8%	12.7%	14.7%	16.1%	17.2%	18.1%	18.6%	18.8%
Growth rate GLPG							40.0%	30.0%	15.0%	10.0%	7.0%	5.0%	3.0%	1.0%
Compliance		80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%
Drop out		15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%
GLPG patients						881	1248	1642	1911	2128	2304	2448	2552	2608
GLPG Price per patient						112,500.00	115.312.50	118.195.31	121.150.20	124.178.95	127.283.42	130,465,51	133,727,15	137.070.33
Price increase			2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%
GLPG revenue						79.294.643	115,153,266	155.283.027	185.236.347	211,360,229	234,591,043	255,508,353	272,989,979	286.004.231
	Age	Population				10,001,010								
	6 to 11	3.540	3.582	3.625	3.669	3.713	3.758	3.803	3.848	3.894	3.941	3.988	4.036	4.085
Growth rate		1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%
GLPG adoption						5.0%	6.5%	7.8%	8.6%	9.2%	9.6%	9.9%	10.2%	10.3%
Growth rate GLPG							30.0%	20.0%	10.0%	7.0%	5.0%	3.0%	3.0%	1.0%
Compliance		80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%
Drop out		15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%
GLPG patients						186	244	297	330	358	380	396	413	422
GLPG Price per patient						112,500.00	115.312.50	118.195.31	121.150.20	124.178.95	127.283.42	130.465.51	133.727.15	137.070.33
Price increase			2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%
GLPG revenue			- 10	1.1/4	4.374	16 708 514	22 531 264	28.046.016	32 001 346	35 518 646	38 685 666	41 332 500	44 160 429	46 265 689
Mutation	Age	Population				10,700,714		20,040,010	34,004,340	33,310,040	30,003,000	44,334,300	44,200,423	40,203,003
	0 to 5	2,950	2.985	3.021	3.057	3,094	3,131	3,169	3,207	3.245	3,284	3.324	3.364	3,404
Growth rate	0105	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%
GLPG adoption						15.0%	17.3%	19.0%	20.3%	21.7%	22.8%	23.5%	24.2%	24.4%
Growth rate GLPG						13.070	15.0%	10.0%	7.0%	7.0%	5.0%	3.0%	3.0%	1.0%
Compliance		80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0N	80.0%	80.0%	80.0%	80.0%
Drap out		15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%
GLPG patients		15.0%	13.0%	13.0%	15.0%	464	540	601	651	705	749	781	814	832
GLPG Price per patient						112,500.00	115.312.50	118.195.31	121.150.20	124.178.95	127.283.42	130.465.51	133.727.15	137.070.33
Price increase			3%	3%	3%	3%	3%	110,195.51	121,150.20	124,178.95	127,265.42	130,405.51	155,727.15	137,070.33
SLPG revenue			34	374	3/4	41.771.285	49.828.757	56.856.106	63.105.218	70.041.176	76.285.397	81,505,836	87.082.384	91.233.862
Mutation		Population				44,774,403	47,040,131	30,030,200	03,203,220	10,044,410	10,400,331	01,000,030	01,004,304	34,433,004
G551D. 2117H. etc		5000	5060	5121	5182	5244	5307	5371	5435	5501	5567	5633	5701	5769
Growth rate		1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%
GLPG Adoption		1.1.1	1.1.14	1.1.1	1.1.7	20%	26%	31%	34%	37%	39%	40%	42%	42%
GPLG growth rate						20%	30%	20%	10%	3/%	5%	40%	42%	42%
Comliance						80%	80%	80%	80%	80%	80%	80%	80%	80%
Drop out						15%	15%	15%	15%	15%	15%	15%	15%	15%
GPLG patients						892	1173	1424	15%	1717	13%	1939	2021	2065
GPLG price per patient/month						112500.00	115312.50	118195.31	121150.20	124178.95	127283.42	130465.51	133727.15	137070.33
Price increase		3%	3%	3%	3%	3%	3%	3%	3%	3%	3%	3%	3%	3%
SLPG revenue		3%	34	374	3/4	80.238.626	108.200.985	134.684.258	153.678.779	170,569,768	185.778.621	202.343.572	216.187.717	226,494,034
of oneverse						00,230,020	100,200,303	137,007,230	133,010,113	110,303,100	103,770,041	AVA, 373, 31 A	****,****,***	****
GPLG product sale		0	0	0	0	218.013.067.72	295.714.271.89	374,869,408,38	434.021.690.08	487,489,817,94	535.341.726.86	580.690.261.52	620.420.508.53	649.997.815.43
royalty		0	0	0	0	16%	295,714,271.89	374,009,408.38	+3+,021,050.08	487,489,817.94	20%	20%	20%	649,997,815.43
Net revenue						34.882.090.84	50.271.426.22	67.476.493.51	82.464.121.12	97,497,963,59	107.068.345.37	116.138.052.30	124.084.101.71	129,999,563.09
Probabbility of success		85%	75%	50%	30%	25%	25%	25%	25%	25%	25%	25%	25%	25%
		85%	/5%	50%	30%	8.720.522.71	12.567.856.56	16.869.123.38	20.616.030.28	25%	25%	25%	31.021.025.43	32,499,890,77
Probability adjjusted revenue Discount rate	9%	0	0	0	0	6,720,522.71	12,007,856.56	10,009,123.38	20,010,030.28	24,374,490.90	20,707,086.34	29,034,513.08	31,021,025.43	32,499,890.77
rNPV	\$88.147.071.25													
FDSO	\$88,147,071.25 39.076.000.00													
	\$ 2.00													
rNP/share	> 2.00													

Source: Janney Montgomery Scott LLC estimates