Cavosonstat Phase 2 Trial Results

November 28th, 2016

Agenda

Introduction

Mike Carruthers, Chief Financial Officer

Initial Remarks

Jon Congleton, President and CEO

Data Highlights

David Rodman, M.D., Chief Medical Officer

Joining for Q&A

Jan Troha, Chief Operating Officer

Steve Shoemaker, M.D., VP Medical/Clinical

Sherif Gabriel, PhD, VP Scientific Search

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Cavosonstat Added to Orkambi in F508del Homozygous Patients – SNO-6 Results

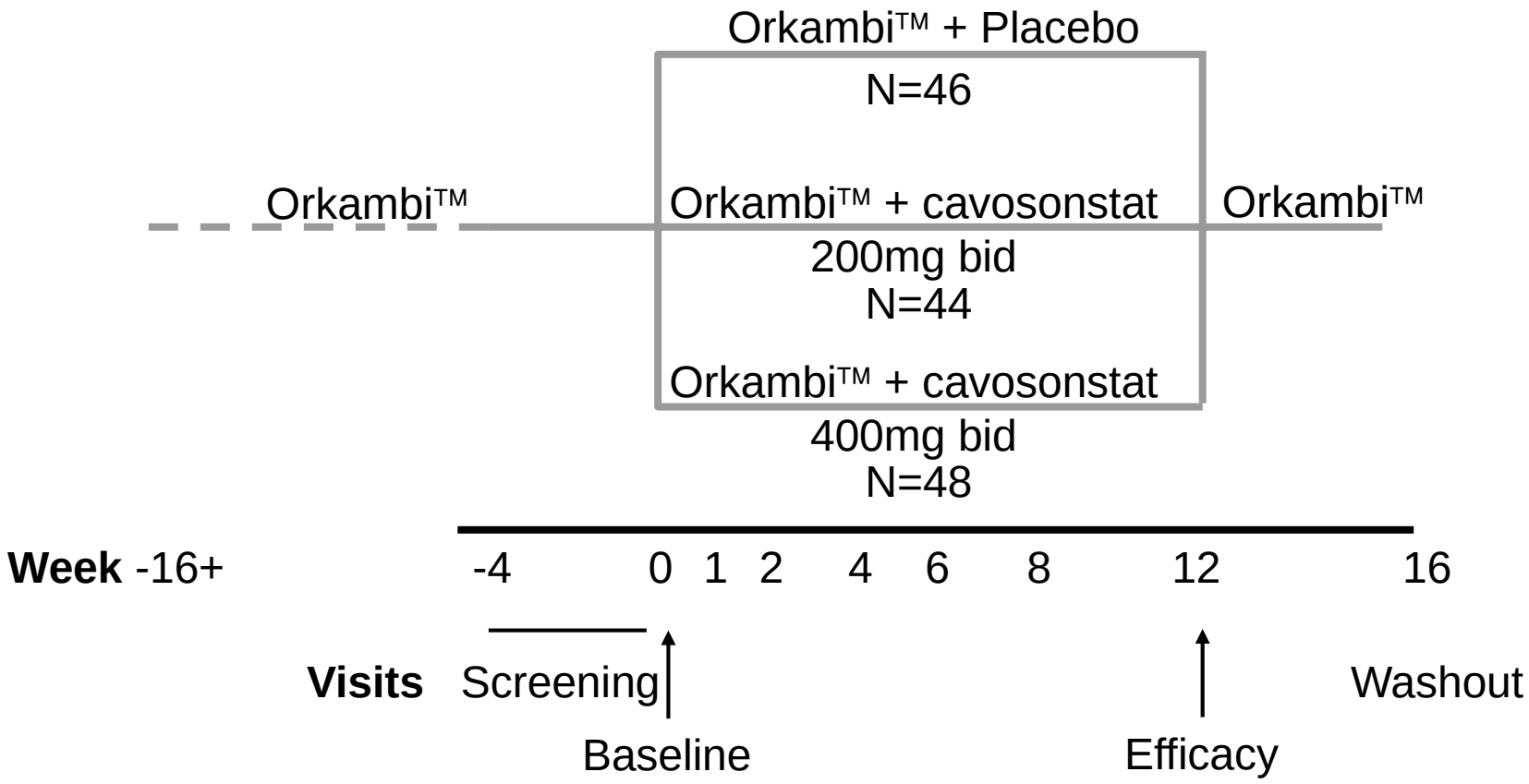
- Cavosonstat at doses up to 400mg bid was well tolerated with no unanticipated safety findings.
- Treatment did not result in improvement in lung function over the twelve week period of treatment in this patient population.
- Modest reduction in sweat chloride, consistent with CFTR modulation, was confirmed in the 200mg cohort but failed to produce durable or dose dependent effects.

SNO-6 Trial
Top Line Results

David M. Rodman, MD

Chief Medical Officer

SNO-6 Trial Design



Baseline Demographics (138 Patients Enrolled)

	Placebo (N=46)	Cavosonstat 200 mg (N=44)	Cavosonstat 400 mg (N=48)
Males %	45.7%	65.9%	52.1%
Age (mean, years) (range)	31.5 (19-56)	30.6 (19-52)	31.6 (18-56)
Baseline FEV_1 (mean, % predicted) (range)	59.9% (29.8-86.4)	59.4% (38.7-83.9)	62.4% (38.3-83.9)
Baseline Sweat Chloride in (mean, mmol/L) (range)	78.0 (44-110)	80.0 (45-118)	78.5 (42-105)
Baseline BMI (kg/m^2) (range)	23.0 (17.3-32.8)	22.8 (18.8-30.2)	23.5 (16.6-31.2)

Safety and Disposition

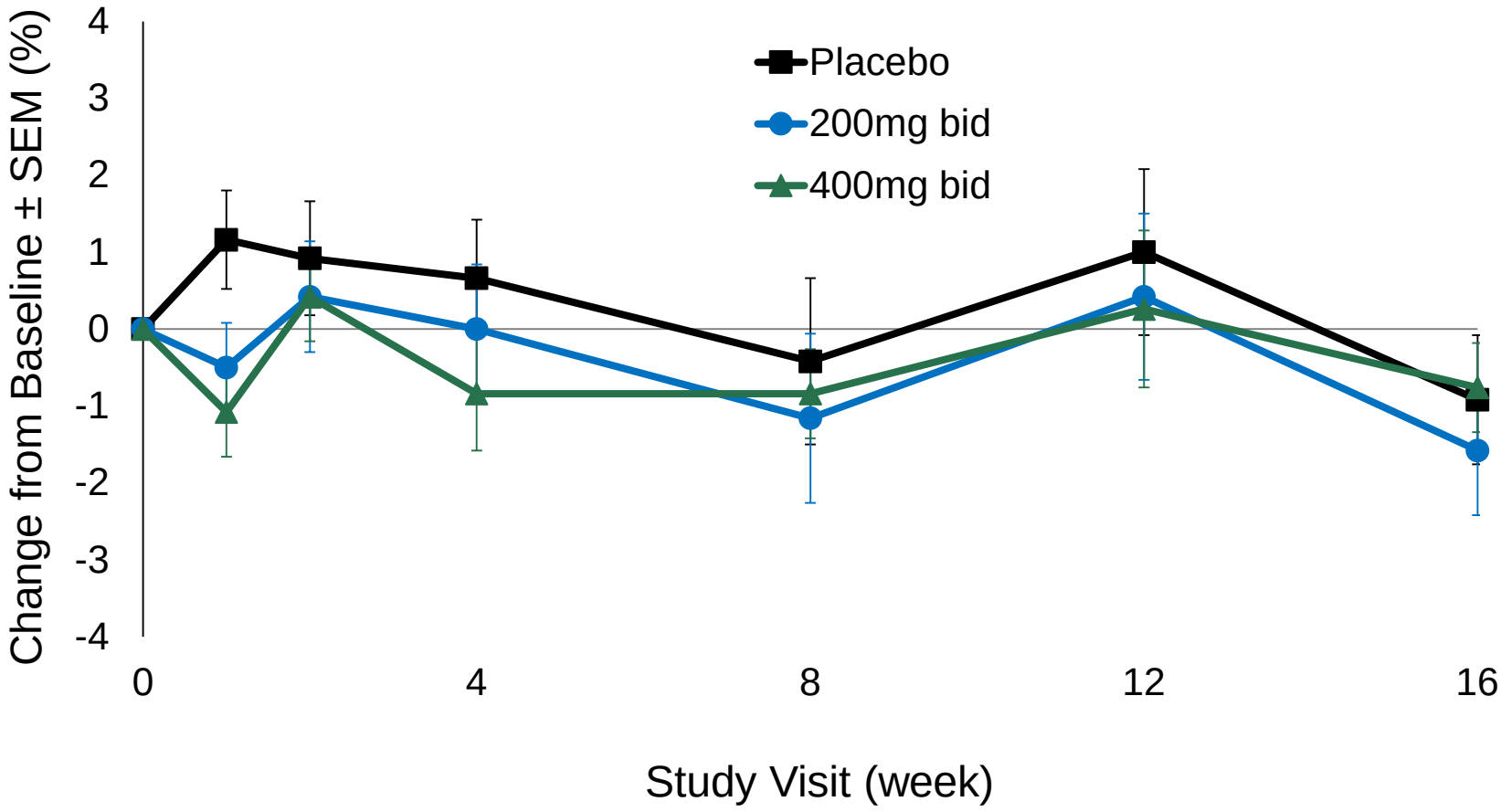
	Placebo (N=46)	Cavosonstat 200 mg BID (N=44)	Cavosonstat 400 mg BID (N=48)
Number of Patients who Experienced Any Adverse Event	42 (91.3%)	40 (90.9%)	40 (83.3%)
Number of Patients who Discontinued Treatment Due to Adverse Events	2 (4.3%)	3 (6.8%)	0 (0.0%)
Number of Patients who Experienced a Serious Adverse Event	8 (17.4%)	10 (22.7%)	7 (14.6%)
Most Common Adverse Events [number of patients (%)]			
- Cough	17 (37.0%)	24 (54.5%)	18 (37.5%)
- Infective Pulmonary Exacerbation	15 (32.6%)	17 (38.6%)	12 (25.0%)
- Sputum increased	11 (23.9%)	11 (25.0%)	12 (25.0%)
- Dyspnea	6 (13.0%)	6 (13.6%)	5 (10.4%)
- C-reactive protein increased	5 (10.9%)	5 (11.4%)	5 (10.4%)
- Fatigue	7 (15.2%)	8 (18.2%)	2 (4.2%)
- Oropharyngeal pain	5 (10.9%)	5 (11.4%)	5 (10.4%)

Primary and Key Secondary Outcomes at Week 12*

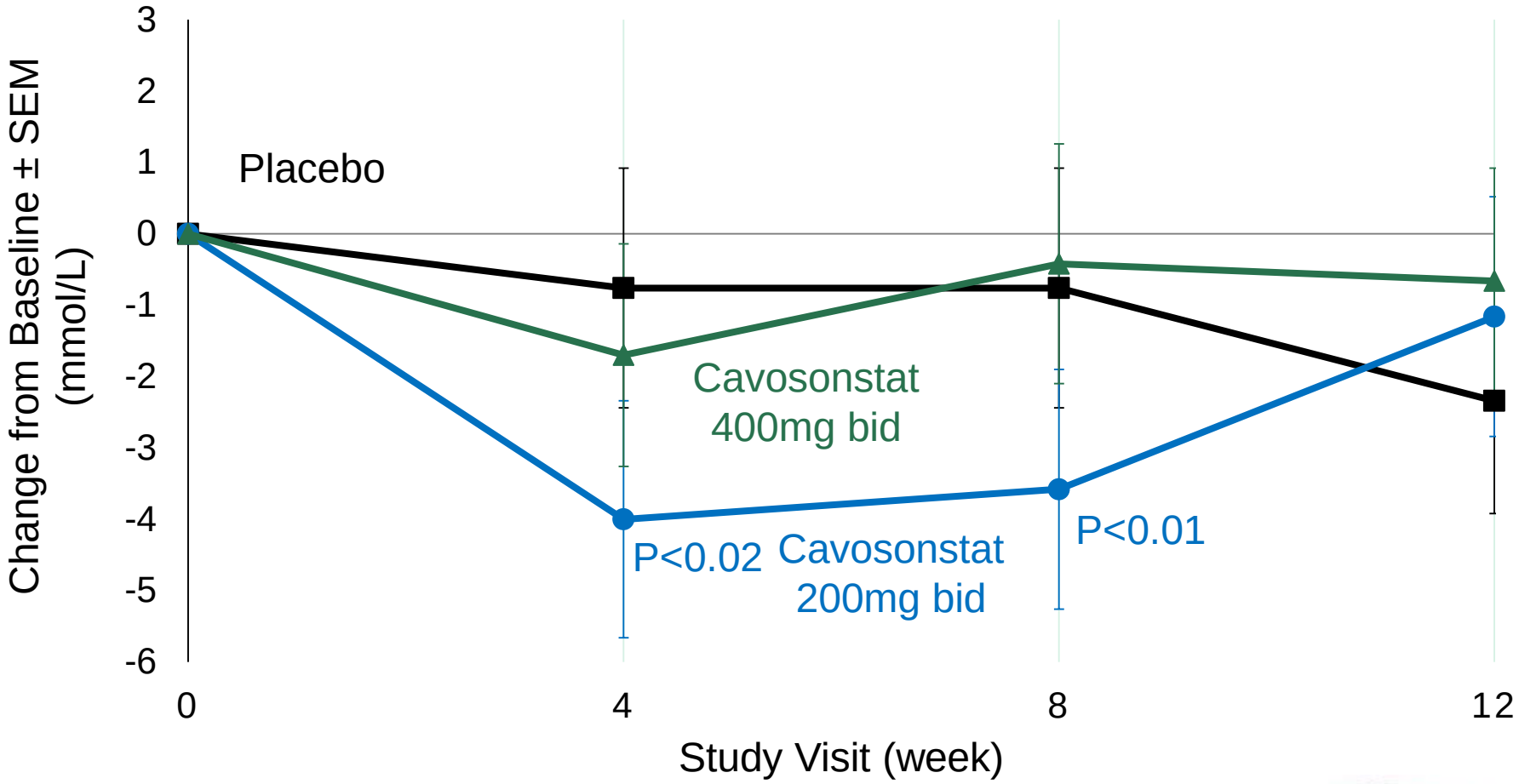
	Placebo (N=46)	200 mg BID (N=44)	400 mg BID (N=48)	Pooled Active (N=92)
Absolute Change in FEV1 (% predicted)	0.97	0.39	0.35	0.37
(Within group p-value)	(0.36)	(0.72)	(0.73)	(0.62)
Relative Change in FEV1 (% predicted)	1.87	0.66	1.11	0.91
(Within group p-value)	(0.31)	(0.72)	(0.53)	(0.48)
Absolute Change in Sweat Chloride (mmol/L)	-2.3	-1.2	-0.6	-0.8
(Within group p-value)	(0.16)	(0.46)	(0.69)	(0.44)
Absolute Change in CFQ-R respiratory domain	-3.03	-3.15	3.16	0.16
(Within group p-value)	(0.24)	(0.23)	(0.21)	(0.93)
Absolute change in BMI (kg/m^2)	-0.09	0.17	0.17	0.17
(Within group p-value)	(0.39)	(0.09)	(0.08)	(0.02)

* MMRM LS Means

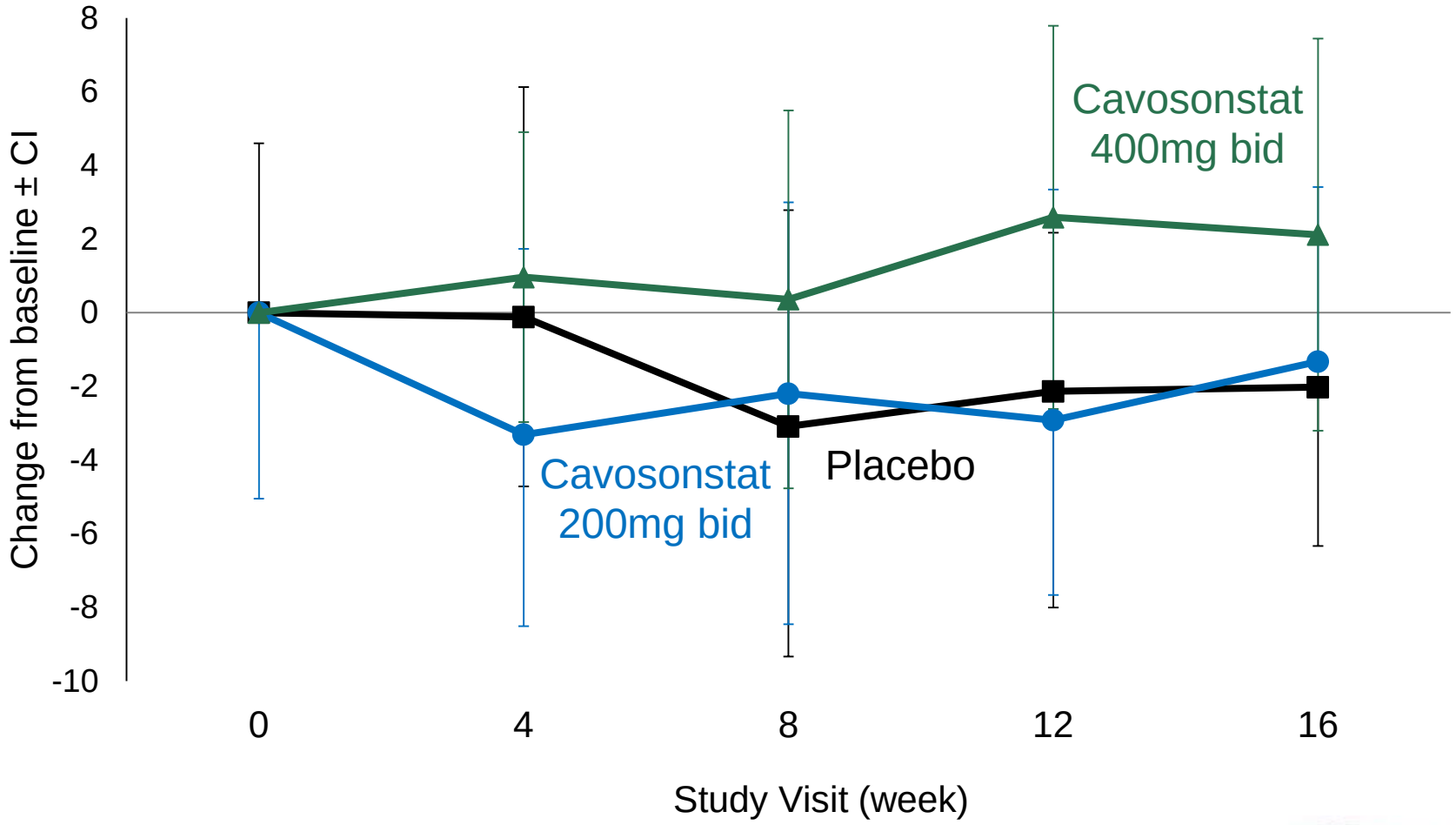
FEV_1 (Absolute % Predicted) Change from Baseline



Sweat Chloride Change from Baseline



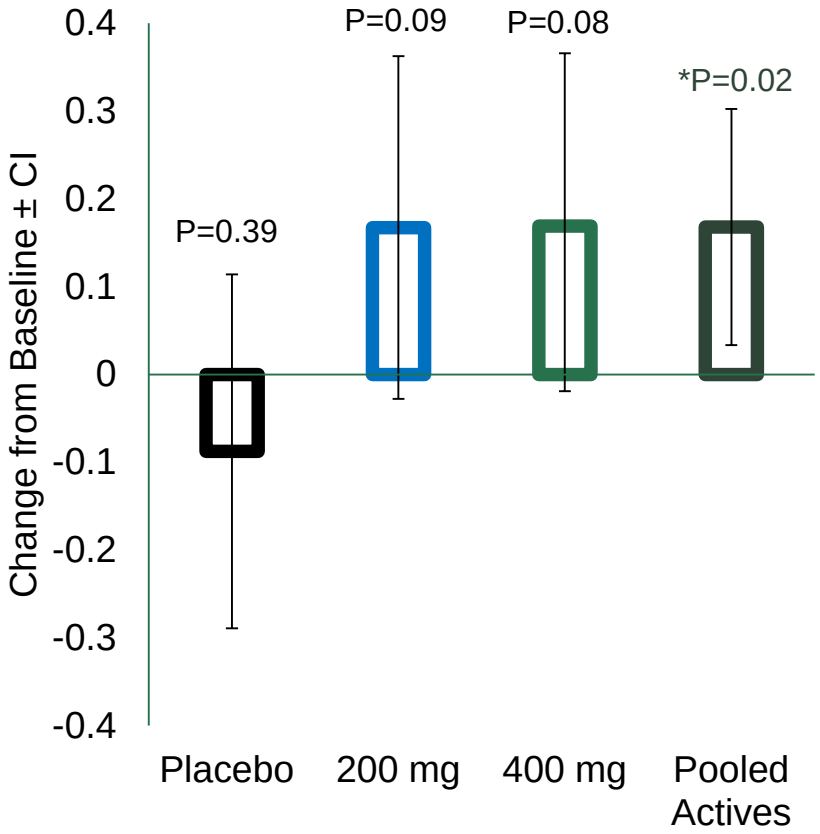
CFQ-R Respiratory Domain Change from Baseline*



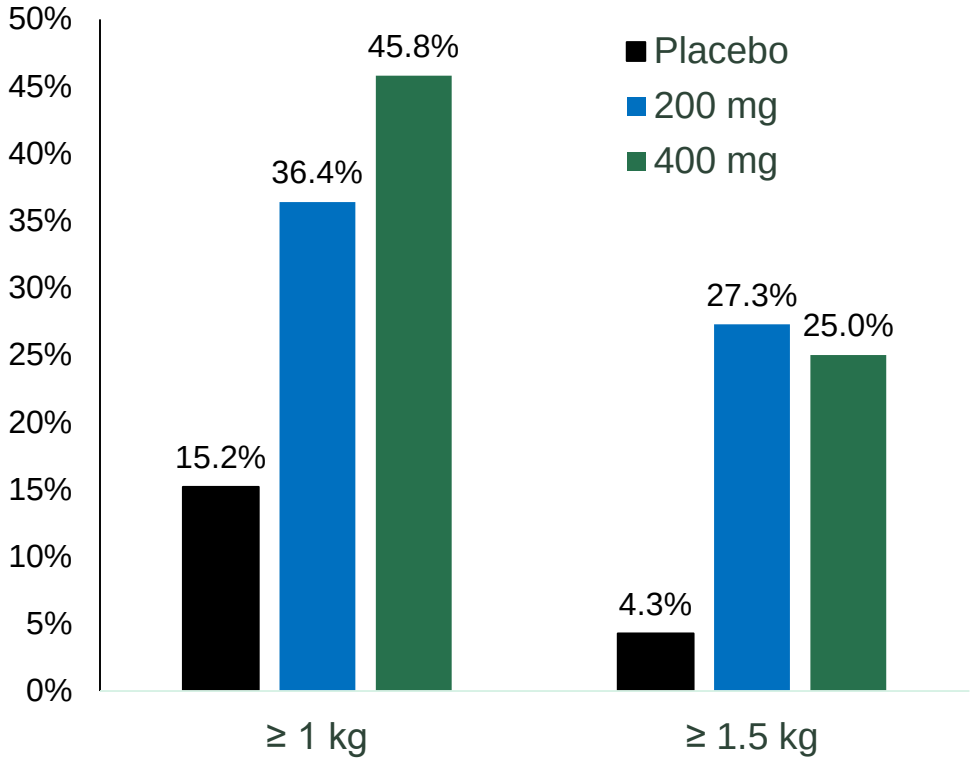
* Arithmetic Means

Change in BMI and Body Weight

BMI Change from Baseline at Week 12



Weight Change from Baseline at Week 12
1 kg and 1.5 kg Responders



Summary of SNO-6 Trial

- Cavosonstat at doses up to 400mg bid was well tolerated with no unanticipated safety findings.
- Treatment did not result in improvement in lung function over the twelve week period of treatment in this patient population.
- Modest reduction in sweat chloride, consistent with CFTR modulation, was confirmed in the 200mg cohort but failed to produce durable or dose dependent effects.
- Increase in weight and body mass index was observed in both treatment groups, which may indicate potential therapeutic benefit to CF-related gastrointestinal and/or metabolic disease.

Forward Plans

- We do not envision moving forward with cavosonstat for treatment of CF-related lung disease in F508del homozygous patients.
- We await results of the SNO-7 trial in Kalydeco-treated patients heterozygous for F508del and a CFTR gating mutation.
- The observation of improved weight and BMI in an adult CF population is interesting and we plan further evaluation of the data and consultation with CF GI/Nutrition experts in the near future.
- We plan to investigate the therapeutic potential of cavosonstat and our S-nitrosoglutathione reductase (GSNOR) inhibitor portfolio and determine next steps.