

Supplemental Data

Inhaled dry powder alginate oligosaccharide (OligoG) in cystic fibrosis: A randomized, double-blind, placebo-controlled cross-over Phase 2b study.

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Fig S1.

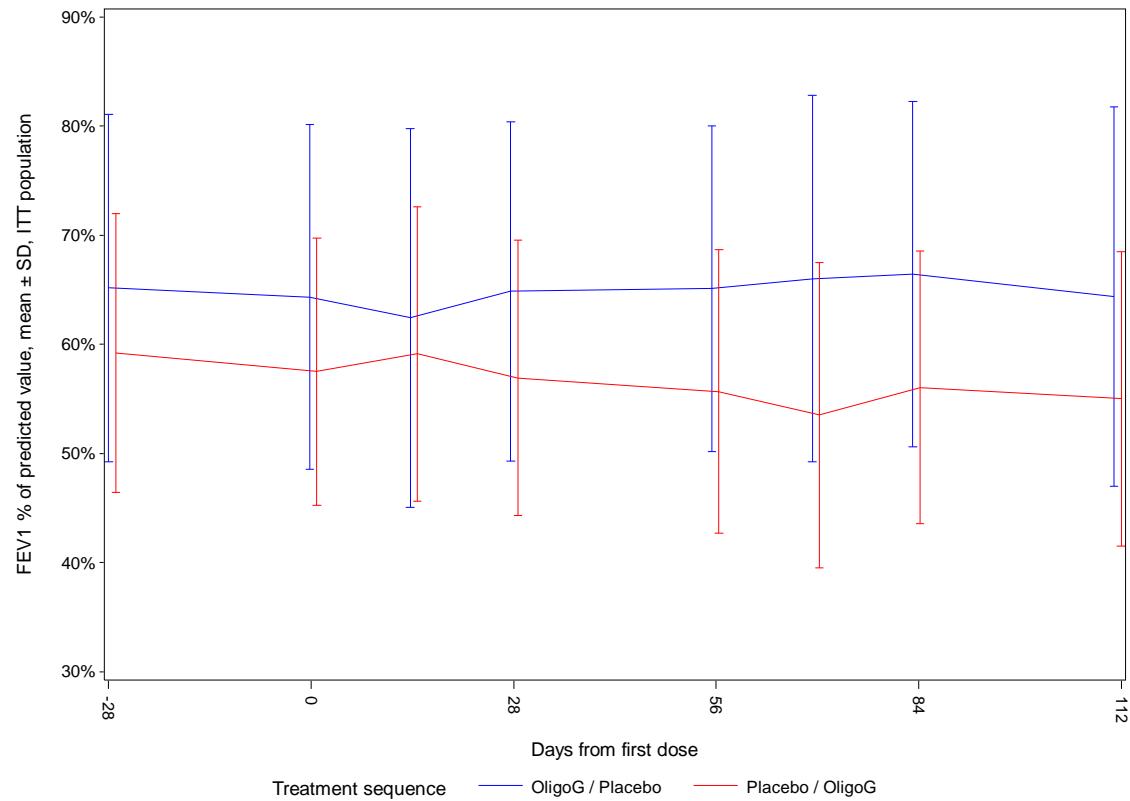


Table S1. Inclusion and exclusion criteria

Inclusion Criteria:

In order to participate in the study, the patient must have met all of the following inclusion criteria: The inclusion criteria were verified at the screening visit (Visit 1) and re-confirmed at the start of treatment/baseline visit (Visit 2):

1. Male or female with a confirmed diagnosis of cystic fibrosis defined by:
 - a. Clinical features consistent with the diagnosis of CF (Rosenstein BJ and Cutting GR 1998); and sweat chloride ≥ 60 mmol/L by pilocarpine iontophoresis; or
 - b. Genotypic confirmation of CFTR mutation
2. Aged 18 years or older
3. Diagnosed Pseudomonas aeruginosa (PA) infection within the subject medical history. For the study as a whole, at least 35 included subjects should be chronically infected with PA according to the following criterion:
Based on sputum or cough swabs over the last 12 months, subjects must have PA cultured on, a. ≥ 2 occasions; and b. $\geq 50\%$ of samples tested.
4. FEV1 must, at Screening (Visit 1), be between 40%-100% of the predicted normal value following adjustment for age, gender and height according to the GLI equation (66). For subjects to be included in the LCI assessment at selected sites, the FEV1 at Screening should be in the range of 60%-100%.
5. At Screening (Visit 1), no clinical or laboratory findings suggestive of significant pulmonary illness, other than CF, which in the opinion of the investigator would preclude participation in the study. In case lab values exceed 3x the upper limit, the subject will be excluded, as per exclusion criterion 14, below except in case of rise in Gamma-GT values, exceeding this threshold. These Gamma-GT cases will be carefully scrutinized alongside other clinical and laboratory data, and after discussion with the medical monitor and the DSMB clinical experts to exclude significant liver injury, the subject may be enrolled in the study.
6. Female subjects of child-bearing potential and male subjects participating in the study who are sexually active must use acceptable contraception. Female subjects documented as being of non-child-bearing potential (e.g. infertile or postmenopausal) are exempt from the contraceptive requirements. For the purpose of this study acceptable contraception is defined as:
 - a. oral, injected or implanted hormonal methods of contraception; or
 - b. placement of an intrauterine device (IUD) or intrauterine system (IUS); or
 - c. barrier methods of contraception: condom or occlusive cap (diaphragm or cervical/vault caps) with spermicidal foam/gel/film/cream/suppository
7. Provision of written informed consent.

Exclusion Criteria:

In order to participate in the study, the patient must not have met any of the following exclusion criteria: The exclusion criteria were verified at the screening visit (Visit 1) and re-confirmed at the start of treatment/baseline visit (Visit 2):

1. Changes in underlying therapy (e.g., chest physiotherapy, bronchodilators, NSAIDs, antibiotic agents, pancreatic enzyme preparations, nutritional supplements and DNase) within the 14 days prior to Day 0 (Visit 2). Subjects must be willing to remain on the same underlying stable therapy regimens for the duration of the study until the final follow-up visit at Day 112.
2. Changes in physiotherapy technique or schedule within 14 days prior to Day 0 (Visit 2).
3. Inhaled acetyl cysteine within 7 days prior to Day 0 (Visit 2) until Day 112 (Visit 8).
4. Concomitant use of inhaled mannitol or inhaled hypertonic saline within 7 days prior to Day 0 (Visit 2) and during the treatment periods. Inhaled mannitol or inhaled hypertonic saline can be re-started during the washout period, but have to be discontinued 7 days before the second treatment period starts.
5. Pulmonary exacerbation within 28 days of Screening (Visit 1).
6. Positive microbiological finding of Burkholderia sp. in expectorated sputum or cough swab documented within 12 months prior to Screening (Visit 1).
7. Lactose intolerance/milk allergy, A skin test for milk allergy will be performed for lactose intolerance unknowns at screening. Subjects who have previously received inhaled formulations containing lactose without any allergic or tolerance issues are allowed to proceed without a skin test. For subjects demonstrating a positive skin prick test for milk allergy but have no problems with eating milk and lactose products, the decision will be up to the investigator's discretion.
8. On-going acute illness. Subjects must not have needed an outpatient visit, hospitalization or required any change in therapy for other pulmonary disease between Screening (Visit 1) and Day 0 (Visit 2).
9. History of, or planned organ transplantation.
10. Allergic bronchopulmonary aspergillosis (ABPA) in the last 12 months prior to Screening (Visit 1), defined as having received pharmacological treatment for ABPA.
11. Requirement for continuous (24 hour/day) oxygen supplementation.
12. Diagnosed with the G551D-mutation, and currently on concomitant treatment with Ivacaftor (Kalydeco).
13. Initiation of cycled, inhaled tobramycin (TOBI), Colistin or Aztreonam (Cayston) less than 4 months OR less than 2 cycles of treatment prior to Screening (Visit 1). Cycled TOBI, Colistin and/or Aztreonam users are allowed to participate in this study, but subjects who have recently initiated cycled therapies should have at least 2 cycles in the preceding months before being enrolled in this study. Alternating TOBI and Colistin subjects should be starting an 'off-TOBI' period at Day 0 (Visit 2); alternating Colistin OR TOBI and Aztreonam should start an 'off-TOBI' alternatively an 'off-Colistin' period at Day 0 (Visit 2). Patients on cycled Aztreonam should preferably start concurrently with an 'on-Aztreonam'-cycle. Study treatment periods should in any case be phased in line with the antibiotic treatment.
14. Clinically significant abnormal findings or any value exceed 3x the upper limit of normal on haematology or clinical chemistry will exclude the subject from participating in the study except in case of rise in GGT values, exceeding this threshold. These Gamma-GT cases will be carefully scrutinized alongside other clinical and laboratory data, and after discussion with the medical monitor and the DSMB clinical experts to exclude significant liver injury, the subject may be enrolled in the study.

- 15. Subjects unable to perform pulmonary function tests according to the ATS/ERS criteria.
 - 16. Pregnant or breast-feeding women. A negative urine pregnancy test must be demonstrated in females of child-bearing potential at Screening (Visit 1).
 - 17. Subjects who have participated in any clinical trial within the 28 days (or shorter than 5 half-lives of the investigational drug) prior to Screening (Visit 1).
 - 18. Subjects with documented or suspected, clinically significant, alcohol or drug abuse as per Investigator's discretion.
 - 19. Current malignant disease (with the exception of basal cell carcinoma and cervical neoplasia).
 - 20. Any serious or active illness incl. psychiatric diseases, which in the opinion of the Investigator, would interfere with subject treatment, assessment, or compliance with the protocol.
 - 21. Subjects not willing/able to follow the study instructions.
 - 22. DPI intolerance, active or placebo.
- For MCC sites only:
- 23. Smoking. A negative Cotinine test must be demonstrated at Screening (Visit 1)
 - 24. Subjects who have any non-removable metal objects such as metal plates, screws etc in their head, neck, chest or abdominal area except for Port-a-Cath®'s or other implantable ports.

Table S2a. FEV₁ percent of predicted measured values and changes from baseline, ITT population, summarized by treatment sequence, treatment, and visit.

			FEV1 (% of predicted)						Change from baseline					
			n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Sequence	Treatment	Visit												
OligoG / Placebo	Period 1: OligoG	V 1 (Screening)	32	65.2%	15.9%	40%	62%	100%	0
		V 2 (Day 0)	32	64.3%	15.8%	39%	61%	97%	0
		V 3 (Day 14)	30	62.4%	17.4%	32%	58%	96%	30	-2.2%	9.4%	-24%	-1%	20%
		V 4 (Day 28)	27	64.9%	15.5%	37%	60%	93%	27	-1.1%	8.9%	-31%	-2%	13%
	Period 2: Placebo	V 5 (Day 56)	28	65.1%	14.9%	38%	62%	91%	0
		V 6 (Day 70)	28	66.0%	16.8%	39%	66%	98%	28	0.9%	6.9%	-16%	1%	16%
		V 7 (Day 84)	26	66.4%	15.8%	43%	64%	104%	26	1.8%	7.2%	-16%	2%	14%
		V 8 (Day 112)	26	64.4%	17.4%	35%	63%	104%	26	-0.2%	7.4%	-18%	1%	12%
Placebo / OligoG	Period 1: Placebo	V 1 (Screening)	33	59.2%	12.8%	41%	58%	88%	0
		V 2 (Day 0)	33	57.5%	12.2%	39%	57%	84%	0
		V 3 (Day 14)	31	59.1%	13.5%	39%	61%	91%	31	1.3%	4.8%	-12%	2%	10%
		V 4 (Day 28)	31	56.9%	12.6%	38%	56%	88%	31	-0.6%	4.6%	-12%	-0%	10%
	Period 2: OligoG	V 5 (Day 56)	28	55.7%	13.0%	35%	56%	85%	0
		V 6 (Day 70)	28	53.5%	14.0%	33%	53%	88%	27	-2.2%	8.7%	-37%	-3%	14%
		V 7 (Day 84)	27	56.1%	12.5%	39%	56%	82%	26	-0.1%	5.8%	-8%	0%	21%
		V 8 (Day 112)	28	55.0%	13.5%	35%	53%	86%	27	-0.2%	5.7%	-15%	-1%	16%

Table S2b. FEV₁ (L) measured values and changes from baseline, ITT population, summarized by treatment sequence, treatment, and visit.

			FEV1 (L)						Change from baseline					
			n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Sequence	Treatment	Visit												
OligoG / Placebo	Period 1: OligoG	V 1 (Screening)	32	2.478	0.821	1.42	2.310	4.30	0
		V 2 (Day 0)	32	2.437	0.789	1.42	2.260	4.33	0
		V 3 (Day 14)	30	2.392	0.793	1.13	2.305	4.00	30	-0.083	0.389	-1.25	-0.045	0.81
		V 4 (Day 28)	27	2.491	0.720	1.26	2.370	4.02	27	-0.053	0.401	-1.59	-0.060	0.52
	Period 2: Placebo	V 5 (Day 56)	28	2.528	0.745	1.39	2.460	4.10	0
		V 6 (Day 70)	28	2.558	0.786	1.43	2.415	4.05	28	0.030	0.250	-0.56	0.025	0.55
		V 7 (Day 84)	26	2.558	0.806	1.50	2.365	4.23	26	0.068	0.284	-0.52	0.085	0.63
		V 8 (Day 112)	26	2.473	0.825	1.35	2.355	4.11	26	-0.007	0.295	-0.79	0.040	0.56
Placebo / OligoG	Period 1: Placebo	V 1 (Screening)	33	2.167	0.577	1.25	2.080	3.77	0
		V 2 (Day 0)	33	2.106	0.558	1.20	2.060	3.51	0
		V 3 (Day 14)	31	2.195	0.627	1.14	2.170	3.70	31	0.056	0.175	-0.37	0.080	0.39
		V 4 (Day 28)	31	2.066	0.577	1.23	1.950	3.45	31	-0.019	0.166	-0.46	-0.020	0.39
	Period 2: OligoG	V 5 (Day 56)	28	2.023	0.593	1.08	1.870	3.46	0
		V 6 (Day 70)	28	1.962	0.625	1.10	1.850	3.27	27	-0.078	0.293	-1.22	-0.080	0.43
		V 7 (Day 84)	27	2.068	0.567	1.18	1.970	3.43	26	-0.006	0.196	-0.33	0.000	0.63
		V 8 (Day 112)	28	2.010	0.586	1.15	1.925	3.47	27	-0.011	0.203	-0.59	-0.040	0.49

The treatment difference OligoG - Placebo was found to be -0.054 L with a 95% confidence interval <-0.155, 0.048>, p = 0.29, the difference is not statistically significant. The sequence effect was found to be 0.05 L in favour of subjects randomised to the OligoG-Placebo sequence, with a 95% confidence interval <-0.054, 0.161>, p = 0.32. As the sequence effect was not statistically significant, no evidence of any carry-over effect

was found. The period effect was found to be -0.053 L for period 1 compared to period 2, with a 95% confidence interval <-0.155, 0.049>, p = 0.30. The coefficient for the baseline FEV1 covariate was found to be 0.92 with a 95% confidence interval <0.85, 1.00>, p <0.0001.

Table S3. Deposition patterns. Measured values and changes from baseline, ITT population.

Deposition patterns	Time	Treatment sequence	Treatment	Visit	Value						Change from baseline						
					n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max	
C/P	t=0	OligoG / Placebo	Period 1: OligoG	V 2 (Day 0)	7	2.347	0.800	1.450	2.372	3.680	0
				V 4 (Day 28)	7	1.784	0.632	1.250	1.400	2.687	7	-0.564	0.893	-2.430	-0.310	0.315	
			Period 2: Placebo	V 5 (Day 56)	7	2.391	0.615	1.790	2.240	3.400	0
				V 7 (Day 84)	7	2.084	0.761	1.380	1.620	3.490	7	-0.307	0.463	-1.250	-0.230	0.140	
		Placebo / OligoG	Period 1: Placebo	V 2 (Day 0)	7	2.349	1.263	1.240	1.960	4.750	0
				V 4 (Day 28)	5	2.814	1.576	1.721	1.990	5.460	5	0.334	0.379	-0.270	0.481	0.710	
	t=60	OligoG / Placebo	Period 2: OligoG	V 5 (Day 56)	5	2.372	1.700	1.418	1.620	5.400	0
				V 7 (Day 84)	5	2.264	1.139	1.270	1.530	3.590	5	-0.108	1.292	-1.810	-0.300	1.800	
			Period 1: Placebo	V 2 (Day 0)	7	1.750	0.297	1.310	1.770	2.149	0
				V 4 (Day 28)	7	1.539	0.420	1.070	1.500	2.070	7	-0.211	0.332	-0.670	-0.240	0.332	
		Placebo / OligoG	Period 1: OligoG	V 5 (Day 56)	7	1.740	0.389	1.304	1.590	2.350	0
				V 7 (Day 84)	7	1.563	0.307	1.140	1.430	2.010	7	-0.177	0.203	-0.480	-0.160	0.072	
Skew	t=90	OligoG / Placebo	Period 1: Placebo	V 2 (Day 0)	7	1.723	1.040	0.774	1.457	3.980	0
				V 4 (Day 28)	5	2.170	1.970	1.210	1.247	5.690	5	0.374	0.793	-0.202	0.050	1.710	
			Period 2: OligoG	V 5 (Day 56)	5	2.224	2.285	1.150	1.245	6.310	0
				V 7 (Day 84)	5	1.632	0.864	0.902	1.360	3.120	5	-0.592	1.478	-3.190	-0.006	0.390	
		Placebo / OligoG	Period 1: OligoG	V 2 (Day 0)	7	1.479	0.268	1.240	1.399	1.970	0
				V 4 (Day 28)	7	1.493	0.391	0.920	1.450	2.160	7	0.014	0.434	-0.520	-0.029	0.684	
	t=0	OligoG / Placebo	Period 2: Placebo	V 5 (Day 56)	7	1.720	0.632	1.050	1.542	2.970	0
				V 7 (Day 84)	7	1.469	0.244	1.080	1.420	1.890	7	-0.251	0.636	-1.550	-0.051	0.364	
		Placebo / OligoG	Period 1: Placebo	V 2 (Day 0)	7	1.763	1.329	0.809	1.320	4.700	0
				V 4 (Day 28)	5	2.040	1.897	0.869	1.330	5.400	5	0.118	0.483	-0.451	0.010	0.700	
		Placebo / OligoG	Period 2: OligoG	V 5 (Day 56)	5	2.044	2.319	0.750	1.105	6.180	0
				V 7 (Day 84)	5	1.667	0.836	0.979	1.400	3.120	5	-0.377	1.525	-3.060	0.170	0.750	

		<i>Placebo / OligoG</i>	<i>Period 1: Placebo</i>	V 2 (Day 0)	7	1.952	0.908	0.668	1.776	3.654	0
				V 4 (Day 28)	5	2.480	0.955	1.370	2.946	3.519	5	0.424	0.732	-0.490	0.560	1.293
			<i>Period 2: OligoG</i>	V 5 (Day 56)	5	2.198	0.837	1.360	2.179	3.367	0
				V 7 (Day 84)	5	1.545	1.232	0.569	0.730	2.998	5	-0.653	0.686	-1.534	-0.630	0.370
<i>t=60</i>		<i>OligoG / Placebo</i>	<i>Period 1: OligoG</i>	V 2 (Day 0)	7	1.240	0.270	0.916	1.183	1.611	0
				V 4 (Day 28)	7	1.022	0.196	0.803	1.063	1.288	7	-0.218	0.091	-0.335	-0.239	-0.113
			<i>Period 2: Placebo</i>	V 5 (Day 56)	7	1.167	0.422	0.728	1.117	1.799	0
				V 7 (Day 84)	7	1.020	0.362	0.422	1.008	1.535	7	-0.147	0.191	-0.473	-0.109	0.098
<i>t=-90</i>		<i>Placebo / OligoG</i>	<i>Period 1: Placebo</i>	V 2 (Day 0)	7	1.215	1.130	-0.083	0.799	3.352	0
				V 4 (Day 28)	5	1.150	0.913	0.342	0.615	2.483	5	-0.241	0.482	-0.869	-0.313	0.425
			<i>Period 2: OligoG</i>	V 5 (Day 56)	5	1.278	0.744	0.684	1.038	2.487	0
				V 7 (Day 84)	5	1.256	1.022	0.226	0.865	2.806	5	-0.023	0.331	-0.495	-0.019	0.319
	<i>OligoG / Placebo</i>		<i>Period 1: OligoG</i>	V 2 (Day 0)	7	1.172	0.266	0.841	1.163	1.572	0
				V 4 (Day 28)	7	1.079	0.261	0.775	1.149	1.380	7	-0.092	0.123	-0.197	-0.162	0.128
			<i>Period 2: Placebo</i>	V 5 (Day 56)	7	1.162	0.346	0.719	1.212	1.800	0
				V 7 (Day 84)	7	0.960	0.377	0.564	0.815	1.603	7	-0.201	0.217	-0.585	-0.146	0.028
		<i>Placebo / OligoG</i>	<i>Period 1: Placebo</i>	V 2 (Day 0)	7	1.091	1.057	0.159	0.677	3.297	0
				V 4 (Day 28)	5	1.219	0.967	0.485	0.691	2.670	5	-0.018	0.383	-0.627	0.126	0.333
			<i>Period 2: OligoG</i>	V 5 (Day 56)	5	1.264	0.968	0.464	0.899	2.884	0
				V 7 (Day 84)	5	1.356	1.548	0.174	0.660	3.967	5	0.092	0.604	-0.467	-0.025	1.083

Table S4. Lung clearance index (LCI). Within-patient treatment differences for **A:** ITT population, and **B:** PP population.

A

	Difference OligoG - Placebo						Baseline adjusted difference OligoG - Placebo					
	n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Visits												
Visit 5 - Visit 2	5	0.266	1.306	-0.90	-0.320	1.74	0
Visit 6 - Visit 3	8	0.095	1.564	-2.23	0.350	1.79	4	1.280	1.298	0.14	1.220	2.54
Visit 7 - Visit 4	7	0.707	1.682	-1.45	-0.240	2.60	4	1.340	1.156	0.56	0.870	3.06

B

	Difference OligoG - Placebo						Baseline adjusted difference OligoG - Placebo					
	n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Visits												
Visit 5 - Visit 2	3	0.850	1.430	-0.80	1.610	1.74	0
Visit 6 - Visit 3	6	-0.117	1.696	-2.23	-0.210	1.79	2	1.220	1.471	0.18	1.220	2.26
Visit 7 - Visit 4	5	1.132	1.859	-1.45	2.260	2.60	3	1.600	1.264	0.86	0.880	3.06

Table S5. Quality of life (QoL). CFQ-R summary score within-patient treatment differences, ITT population.

			Difference OligoG - Placebo						Baseline adjusted difference OligoG - Placebo					
			n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Physical	Total	Visit 5 - Visit 2	58	2.5	12.9	-25	0	33	0
		Visit 6 - Visit 3	57	-2.6	13.1	-33	0	38	57	-5.3	15.4	-50	0	21
		Visit 7 - Visit 4	56	-2.7	13.6	-29	0	29	56	-5.7	16.8	-63	-4.2	33
Role	Total	Visit 5 - Visit 2	58	0	14.7	-50	0	25	0
		Visit 6 - Visit 3	57	-1.9	14.5	-50	0	42	57	-2.3	15.7	-42	0	50
		Visit 7 - Visit 4	56	0.3	13	-33	0	42	56	-0.1	19.4	-42	0	58
Vitality	Total	Visit 5 - Visit 2	58	2.3	16.1	-25	0	42	0
		Visit 6 - Visit 3	57	-3.2	18.7	-50	0	33	57	-5.1	21.7	-58	-8.3	50
		Visit 7 - Visit 4	56	-3.7	18.5	-50	0	42	56	-5.8	24.4	-67	0	58
Emotion	Total	Visit 5 - Visit 2	58	0.5	11.9	-33	0	27	0
		Visit 6 - Visit 3	57	-1.9	12.6	-33	0	27	57	-2.3	11.5	-33	0	20
		Visit 7 - Visit 4	56	-2.3	11	-27	0	27	56	-2.7	14.5	-40	0	47
Social	Total	Visit 5 - Visit 2	58	0.9	11.5	-22	0	33	0
		Visit 6 - Visit 3	57	-1.5	10.3	-28	0	28	57	-2.5	14.9	-33	-5.6	39
		Visit 7 - Visit 4	56	-1.4	11.5	-39	0	22	56	-2.5	16.1	-44	0	33
Body	Total	Visit 5 - Visit 2	58	-1.5	13.2	-44	0	33	0
		Visit 6 - Visit 3	57	-4.1	12.4	-33	0	22	57	-2.5	16.3	-33	0	33
		Visit 7 - Visit 4	56	-0.4	11.6	-22	0	33	56	-1	16.7	-33	0	33
Eat	Total	Visit 5 - Visit 2	58	1.9	18.6	-33	0	89	0
		Visit 6 - Visit 3	57	-1.9	13	-33	0	22	57	-3.9	20	-78	0	44
		Visit 7 - Visit 4	56	-3.6	11.6	-33	0	22	56	-5.4	21.5	-89	0	33
Treat	Total	Visit 5 - Visit 2	58	-1.1	12.9	-33	0	22	0
		Visit 6 - Visit 3	57	-2.1	11.6	-44	0	22	57	-1	15.2	-33	0	22
		Visit 7 - Visit 4	56	-1.1	12.9	-33	0	22	56	-1	15.2	-33	0	22

		Visit 7 - Visit 4	56	-1.6	14.6	-33	0	22	56	-0.6	19.7	-56	0	44
Health	Total		58	1.1	14.2	-33	0	44	0
		Visit 5 - Visit 2	58	1.1	14.2	-33	0	44	0
		Visit 6 - Visit 3	57	0.4	13.4	-22	0	33	57	-0.6	18.8	-67	0	44
		Visit 7 - Visit 4	56	-1.4	13.4	-33	0	22	56	-2.6	20	-56	0	44
Weight	Total	Visits	58	2.3	27.1	-67	0	100	0
		Visit 5 - Visit 2	58	2.3	27.1	-67	0	100	0
		Visit 6 - Visit 3	57	-1.8	25.5	-100	0	67	57	-4.7	32.4	-100	0	67
		Visit 7 - Visit 4	56	-4.2	26.3	-67	0	100	56	-7.7	41.7	-133	0	167
Resp	Total	Visits	58	3.1	13	-28	2.8	33	0
		Visit 5 - Visit 2	58	3.1	13	-28	2.8	33	0
		Visit 6 - Visit 3	57	-3.6	15.8	-50	0	44	57	-7.1	18.5	-61	-5.6	44
		Visit 7 - Visit 4	56	-4.2	15.8	-39	-5.6	44	56	-7.6	20.4	-50	-11.1	67
Digest	Total		58	0.6	16.4	-56	0	33	0
		Visit 5 - Visit 2	58	0.6	16.4	-56	0	33	0
		Visit 6 - Visit 3	57	0.6	12.3	-33	0	22	57	-0.2	18.2	-33	0	56
		Visit 7 - Visit 4	56	1	12.9	-33	0	33	56	0.4	20	-44	0	56

Table S6. Sputum rheology Phase angle values, changes from baseline for ITT population for (A) 0.1Hz, (B) 1.0Hz and (C) 10Hz.

A

Sequence	Treatment	Visit	Phase angle (0.1 Hz)						Change from baseline					
			n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
OligoG / Placebo	Period 1: OligoG	V 1 (Screening)	31	21.788	19.992	13.49	17.377	127.96	0
		V 2 (Day 0)	30	17.883	4.295	3.08	17.794	27.49	0
		V 3 (Day 14)	28	17.436	4.416	2.24	16.199	24.46	28	-0.176	3.842	-7.12	-0.528	7.41
		V 4 (Day 28)	26	19.900	5.804	13.66	17.484	37.21	25	1.831	6.666	-7.30	0.494	19.50
	Period 2: Placebo	V 5 (Day 56)	26	21.314	7.120	12.75	20.852	47.85	0
		V 6 (Day 70)	25	18.090	4.104	13.02	17.653	32.53	25	-2.978	7.874	-30.67	-2.230	9.00
		V 7 (Day 84)	23	22.538	9.473	13.18	20.022	60.33	23	1.683	11.869	-31.94	0.880	38.82
		V 8 (Day 112)	22	19.507	4.518	13.77	18.976	29.97	22	-0.122	5.697	-17.24	1.756	10.92
Placebo / OligoG	Period 1: Placebo	V 1 (Screening)	30	18.360	6.766	-7.52	18.241	29.86	0
		V 2 (Day 0)	31	20.152	4.886	13.84	19.426	40.27	0
		V 3 (Day 14)	31	19.441	4.915	13.65	18.534	37.94	31	-0.886	4.977	-10.19	-1.772	15.65
		V 4 (Day 28)	27	18.739	8.826	-19.3	18.790	30.13	27	-1.418	8.952	-38.80	0.492	12.85
	Period 2: OligoG	V 5 (Day 56)	25	21.360	7.236	14.71	20.425	51.08	0
		V 6 (Day 70)	27	20.725	4.888	14.01	19.448	32.58	24	-0.461	7.702	-25.44	0.792	11.15
		V 7 (Day 84)	25	20.848	5.884	13.66	19.102	37.78	24	-0.477	8.941	-30.89	-0.487	17.24
		V 8 (Day 112)	23	21.812	7.463	9.79	20.794	43.65	22	2.112	8.134	-9.91	1.685	25.19

B

Sequence	Treatment	Visit	Phase angle (1 Hz)						Change from baseline					
			n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
OligoG / Placebo	Period 1: OligoG	V 1 (Screening)	31	21.941	29.940	12.48	15.708	182.25	0
		V 2 (Day 0)	30	16.080	3.558	6.05	15.873	24.54	0
		V 3 (Day 14)	28	16.032	6.691	7.21	14.467	46.43	28	0.054	6.169	-6.26	-1.072	28.42
		V 4 (Day 28)	26	17.599	6.607	12.38	16.545	47.14	25	1.467	7.352	-6.47	0.382	31.66
	Period 2: Placebo	V 5 (Day 56)	26	19.594	8.012	11.16	17.703	43.03	0
		V 6 (Day 70)	25	15.573	3.730	10.98	14.924	26.31	25	-3.624	8.822	-30.59	-1.991	8.99
		V 7 (Day 84)	23	20.698	14.197	11.61	17.333	81.44	23	1.290	16.344	-30.42	0.273	60.72
		V 8 (Day 112)	22	16.877	3.303	12.21	15.747	25.52	22	-1.494	6.977	-28.60	-0.334	5.96
Placebo / OligoG	Period 1: Placebo	V 1 (Screening)	30	18.602	8.299	10.31	16.088	54.49	0
		V 2 (Day 0)	31	17.680	4.854	12.56	17.255	39.55	0
		V 3 (Day 14)	31	16.780	3.572	10.90	17.057	27.18	31	-1.128	4.082	-12.37	-1.669	7.02
		V 4 (Day 28)	27	17.399	3.704	12.86	16.644	25.41	27	-0.372	5.522	-21.09	-0.024	10.34
	Period 2: OligoG	V 5 (Day 56)	25	18.462	4.233	12.42	18.490	27.11	0
		V 6 (Day 70)	27	18.437	4.411	12.93	17.492	29.69	24	-0.074	4.736	-12.20	0.254	12.31
		V 7 (Day 84)	25	18.873	6.539	10.97	15.740	37.70	24	0.420	7.413	-11.82	-0.630	18.69
		V 8 (Day 112)	23	19.710	7.100	11.85	16.841	39.74	22	1.815	7.819	-9.54	1.784	23.94

C

Sequence	Treatment	Visit	Phase angle (10 Hz)						Change from baseline					
			n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
OligoG / Placebo	Period 1: OligoG	V 1 (Screening)	31	40.169	35.195	5.85	25.397	127.58	0
		V 2 (Day 0)	30	34.475	33.638	7.82	22.013	150.69	0
		V 3 (Day 14)	28	38.218	36.037	8.37	23.455	160.71	28	3.226	31.727	-68.67	2.433	89.83
		V 4 (Day 28)	26	52.074	45.721	5.89	34.930	196.98	25	21.452	53.579	-110.4	15.635	160.10
	Period 2: Placebo	V 5 (Day 56)	26	61.108	51.048	4.32	42.041	163.49	0
		V 6 (Day 70)	25	32.003	23.021	1.36	24.764	100.26	25	-26.33	46.828	-148.0	-3.917	28.80
		V 7 (Day 84)	23	46.233	50.048	13.34	26.061	210.09	23	-7.602	70.737	-140.2	-2.827	199.54
		V 8 (Day 112)	22	44.668	48.993	9.36	23.269	169.82	22	-4.778	32.817	-88.24	-1.177	75.18
Placebo / OligoG	Period 1: Placebo	V 1 (Screening)	30	53.577	42.304	2.24	35.495	156.95	0
		V 2 (Day 0)	31	39.396	35.613	9.83	23.865	136.12	0
		V 3 (Day 14)	31	39.455	33.011	-0.46	24.052	134.19	31	-0.318	48.642	-120.3	-1.954	124.37
		V 4 (Day 28)	27	45.071	33.840	12.95	35.324	134.21	27	11.234	38.879	-88.20	11.299	96.32
	Period 2: OligoG	V 5 (Day 56)	25	57.277	50.983	0.52	29.935	174.07	0
		V 6 (Day 70)	27	49.324	41.158	14.07	34.409	156.99	24	-14.47	60.413	-145.9	-2.338	103.89
		V 7 (Day 84)	25	56.539	42.244	7.50	41.835	158.59	24	-1.795	56.482	-131.1	7.958	85.64
		V 8 (Day 112)	23	50.013	45.567	5.52	28.242	202.58	22	-7.032	49.034	-141.0	3.945	55.00