ProQR®

QR-010

Study PQ-010-001
Multiple Ascending Dose

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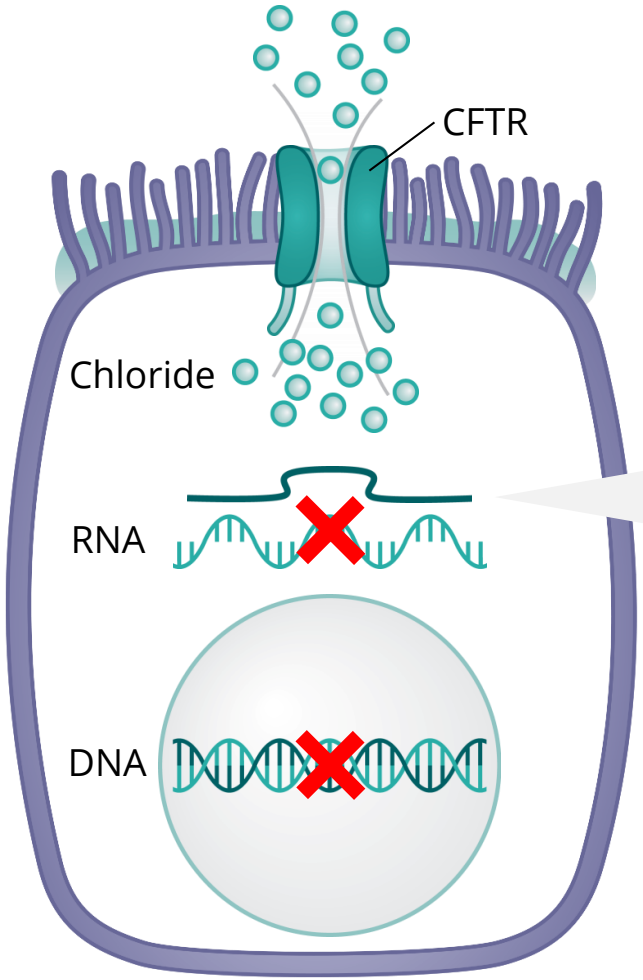
Disclosures

- Consultant/Advisor: Gilead Sciences, Novartis Pharmaceuticals Corporation; Vertex Pharmaceuticals; Gilead; Aptalis; Celtaxsys, ProAxis
- Speakers Bureau: Novartis Pharmaceuticals Corporation; Vertex Pharmaceuticals
- Research Grants: Gilead Sciences, Novartis Pharmaceuticals Corporation

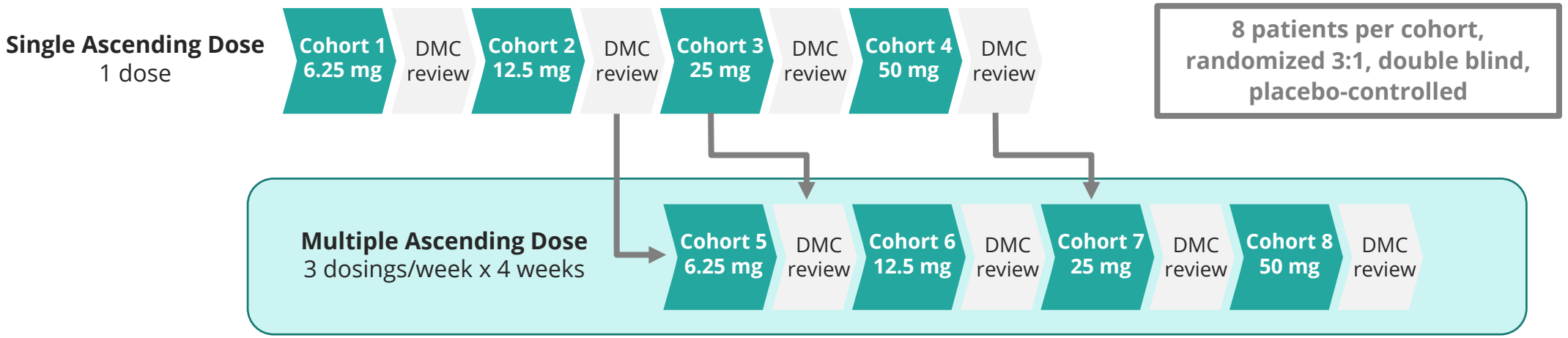
QR-010: A Novel Antisense RNA oligonucleotide



QR-010

- Single stranded 33-mer RNA oligonucleotide
- P=S and 2'Ome chemically modified for stability and uptake
- Designed to be complementary to mRNA region around F508-encoding deletion and to restore CFTR function
- Inhaled delivery by PARI eFlow nebulizer
- Improved CFTR activity has been demonstrated in F508del preclinical and animal models
- QR-010 improved CFTR chloride transport in F508del homozygous patients by nasal potential difference following local administration to the nasal epithelium

PQ-010-001 Study Design



Key Eligibility Criteria

- Male & female homozygous for F508del mutation
- >18 years old
- ppFEV1 > 70%
- CFTR modulators excluded

Study Objectives

- To evaluate the safety & tolerability of QR-010 via inhalation
- Characterise PK of QR-010 administered via inhalation
- Explore phamacodynamic effects of QR-010 for efficacy signals

Baseline Demographics

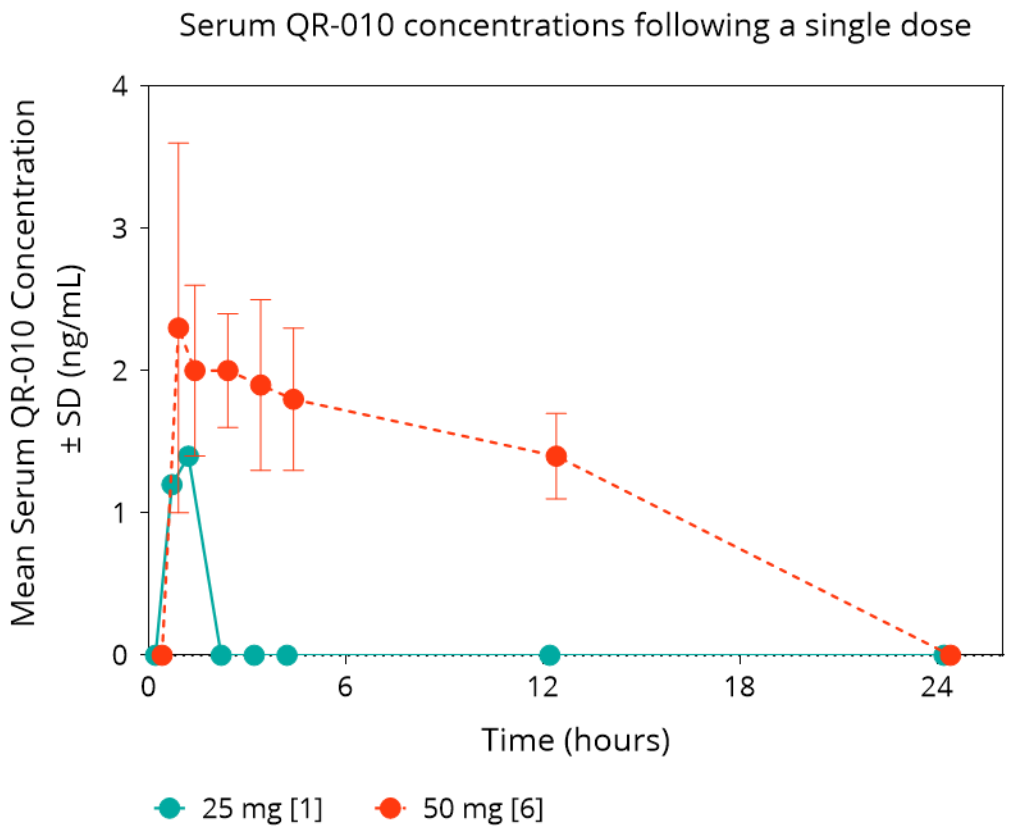
Characteristic		Placebo n=9	6.25 mg n=6	12.5 mg n=6	25 mg n=7	50 mg n=6	Total n=34
Age (years)	Mean Min, Max	26.3 [18, 38]	22.7 [19, 26]	27.7 [19, 41]	32.3 [21, 46]	23.3 [19, 30]	**26.6** **[18, 46]**
Sex, n (%)	Male Female	3 (33.3) 6 (66.7)	3 (50.0) 3 (50.0)	3 (50.0) 3 (50.0)	2 (28.6) 5 (71.4)	4 (66.7) 2 (33.3)	**15 (44.1)** **19 (55.9)**
Race, n (%)	White	9 (100.0)	6 (100.0)	6 (100.0)	7 (100.0)	6 (100.0)	**34 (100.0)**
pp FEV_1 (%)	Mean Min, Max	86.7 [70.7, 99.7]	90.7 [75.3, 115.6]	89.0 [74.4, 108.2]	79.9 [69.2, 94.9]	84.7 [73.7, 110.7]	**86.0** **[69.2, 115.6]**
Sweat Chloride (mmol/L)	Mean Min, Max	105.3 [93.0, 123.0]	101.1 [84.0, 126.0]	91.0 [61.0, 110.0]	99.7 [83.0, 109.0]	98.4 [91.0, 107.5]	**99.7** **[61.0, 126.0]**
BMI (kg/m^2)	Mean Min, Max	20.9 [19.2, 24.2]	23.5 [19.7, 26.7]	22.8 [19.1, 26.4]	23.6 [21.2, 25.6]	21.3 [18.1, 25.3]	**22.3** **[18.1, 26.7]**
CFQ-R RSS (points)	Mean Min, Max	77.8 [66.7, 88.9]	74.1 [61.1, 88.9]	72.2 [55.6, 94.4]	72.2 [61.1, 83.3]	78.7 [55.6, 88.9]	**75.2** **[55.6 94.4]**

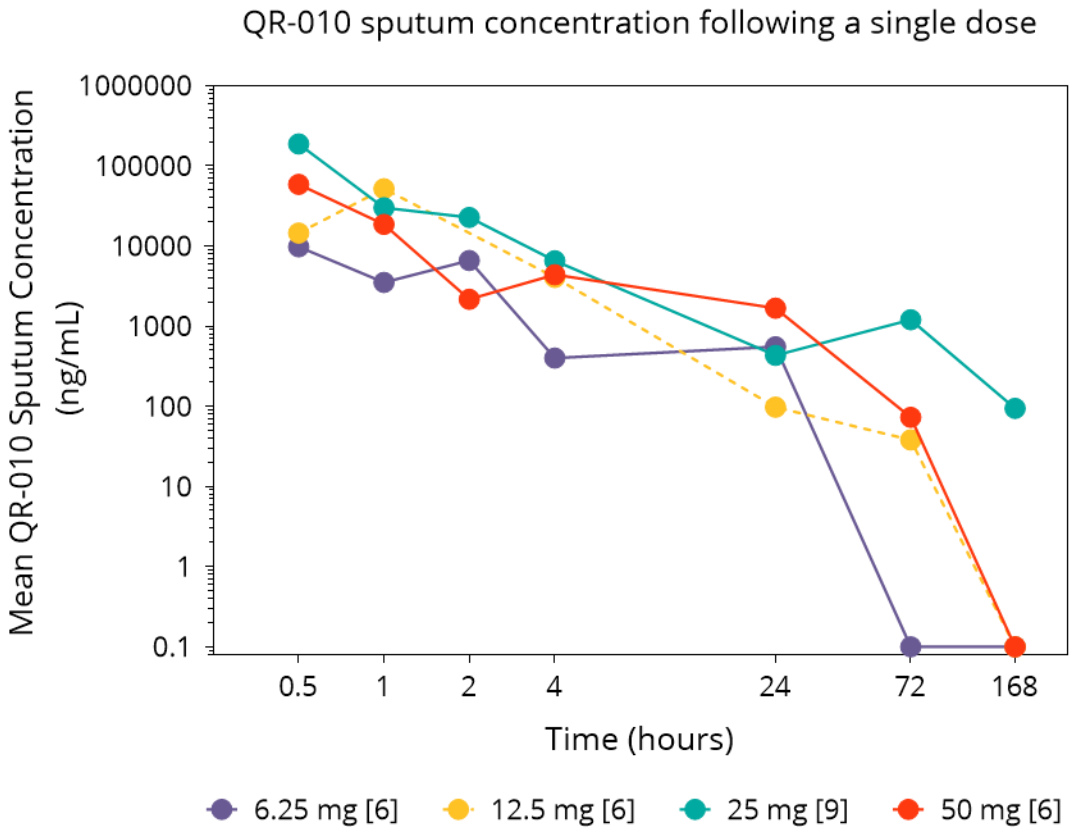
QR-010 is Safe and Well-tolerated

Most Frequent Treatment-Emergent Adverse Events

Preferred term	Placebo n=9 n (%)	6.25 mg n=6 n (%)	12.5 mg n=6 n (%)	25 mg n=7 n (%)	50 mg n=6 n (%)	QR-010 total n=25 n (%)
Cough	2 (22.2)	3 (50.0)	1 (16.7)	0	2 (33.3)	6 (24.0)
Sputum Increased	3 (33.3)	2 (33.3)	1 (16.7)	1 (14.3)	0	4 (16.0)
Fatigue	0	2 (33.3)	1 (16.7)	1 (14.3)	0	4 (16.0)
Nasal Congestion	1 (11.1)	2 (33.3)	0	0	1 (16.7)	3 (12.0)
Wheezing	0	3 (50.0)	0	0	0	3 (12.0)
Pyrexia	1 (11.1)	0	1 (16.7)	2 (28.6)	0	3 (12.0)

Serum and Sputum Concentrations after Single Dose Administration

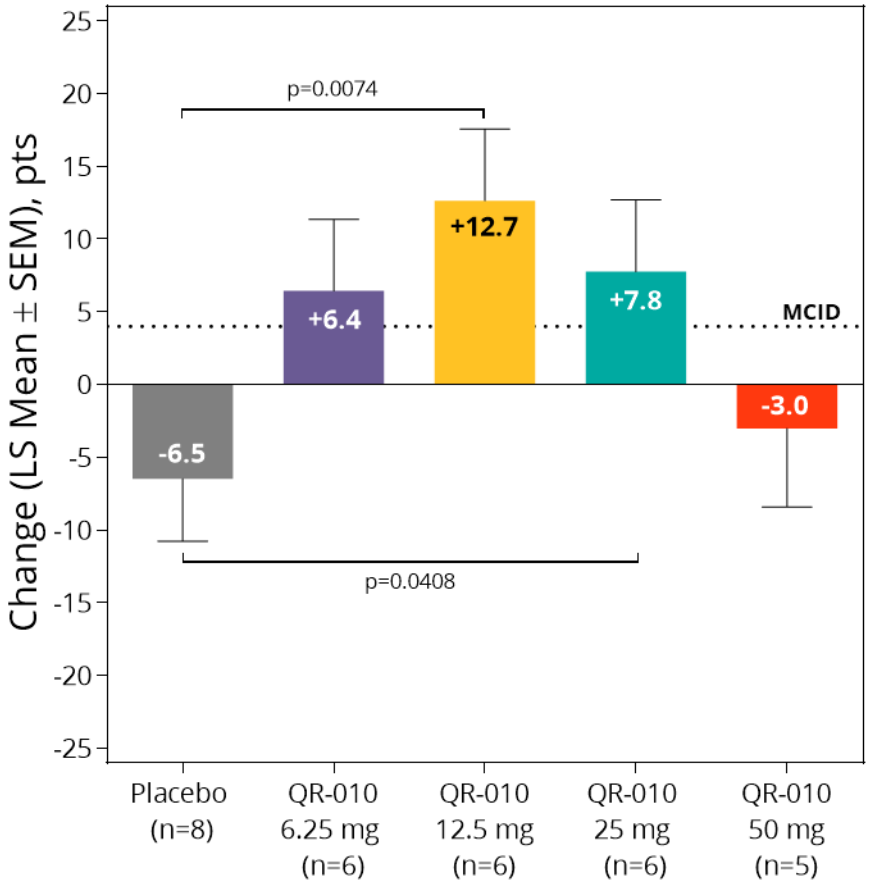




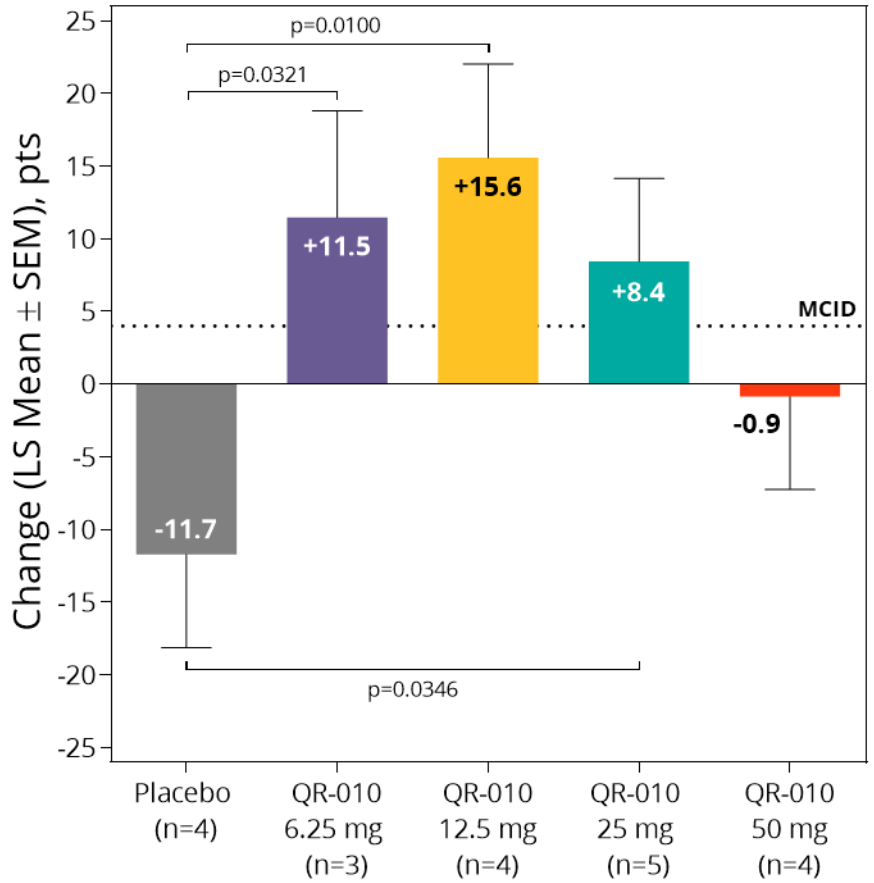
Exploratory Efficacy Endpoints

Improvement of CFQ-R RSS at EoT

Per protocol population
baseline 69-116 $ppFEV_1$ (n=31)

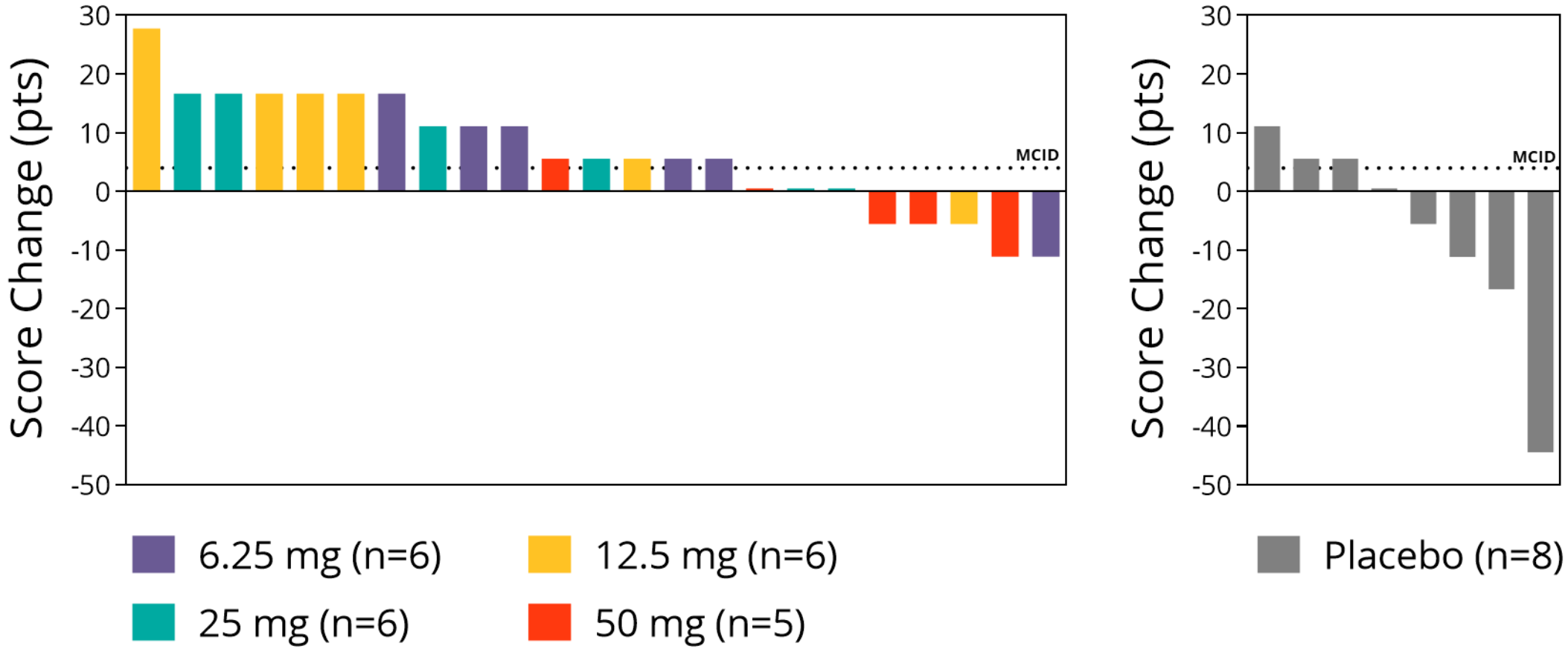


Baseline $ppFEV_1$ 70-90
predefined subgroup (n=20)



Improvement of CFQ-R RSS at EoT

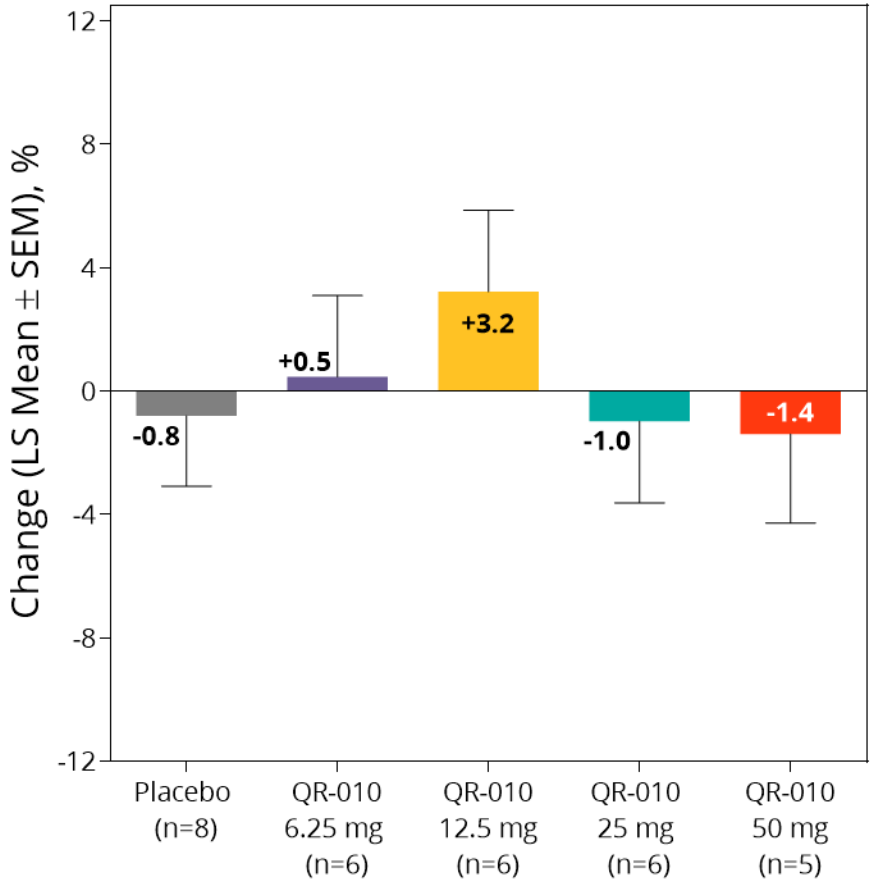
65% of patients improved above MCID (4 pts)



$ppFEV_1$ Absolute Change at EoT

Dose-response similar to CFQ-R RSS

Per protocol population
baseline 69-116 $ppFEV_1$ (n=31)



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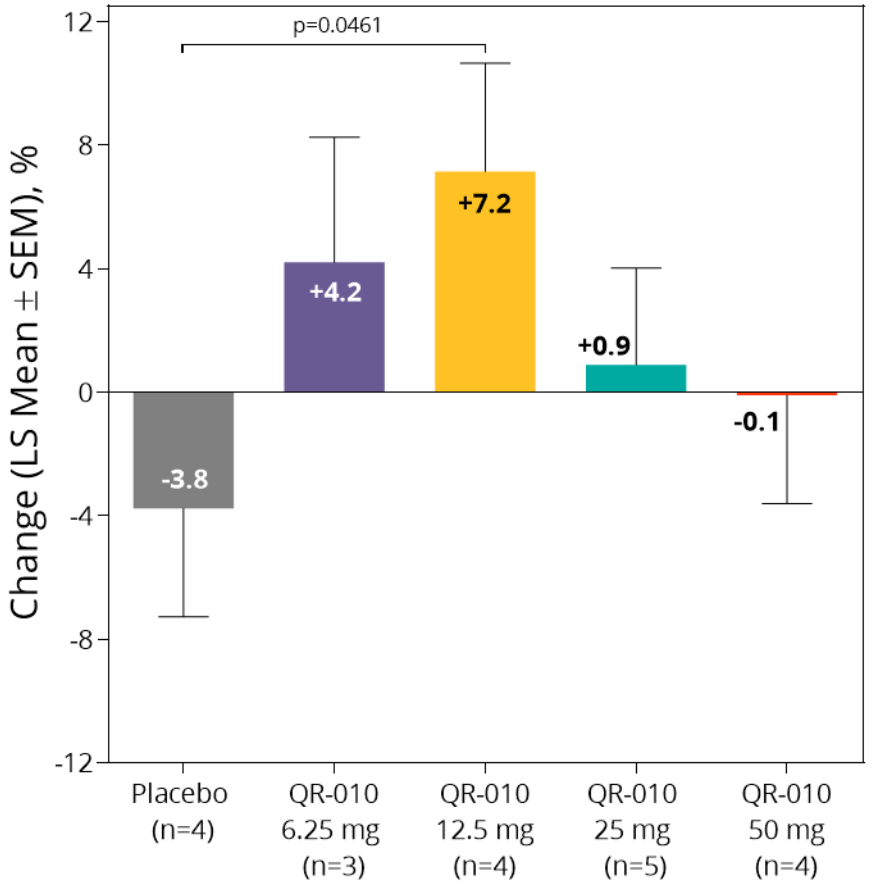

Conclusions

- QR-010 is safe and well-tolerated over 4 weeks of treatment
- There were no safety signals on lab parameters, vitals signs, markers of inflammation, or other assessments
- QR-010 demonstrated a convincing signal of clinical benefit in CF patients, as measured by CFQ-R RSS
- This trial validates the therapeutic potential of inhaled oligonucleotides targeting the basic defect of CF

Acknowledgements

- Thank you to the PQ-010-001 Investigators and researchers and especially to the CF community for their participation, resulting in the successful completion and analysis of this multiple ascending dose study
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CYSTIC FIBROSIS FOUNDATION

European Commission | Horizon 2020 European Union funding for Research & Innovation