

1 SUPPLEMENTARY TABLES & FIGURE LEGENDS

2

3 **Supplementary table 1a. Bayesian linear mixed effects model estimates of ppFEV1.**

4 **Comparison of effects in participants with baseline FEV1pp <40%, between 40-90% and ≥90% (n=401, Years of observation=3844).**

	Unadjusted coefficient	95% CI	P-value	Adjusted coefficient#	95% CI	P-value
Intercept	67.46	65.91 – 69.00	<0.001	68.74	67.05 – 70.41	<0.001
ppFEV1 40-90%	Reference			Reference		
ppFEV1 <40%	-34.30	-37.87 – -30.75	<0.001*	-29.46	-32.74 – -26.19	<0.001*
ppFEV1 ≥90%	29.03	26.20 – 31.86	<0.001*	25.13	22.49 – 27.76	<0.001*
Time	-1.59	-1.82 – -1.36	<0.001*	-1.62	-1.84 – -1.41	<0.001*
Time : ppFEV1 40-90%	Reference			Reference		
Time : ppFEV1 <40%	-1.12	-2.50 – 0.26	0.112	-2.24	-3.58 – -0.90	0.001*
Time : ppFEV1 ≥90%	2.25	1.49 – 3.01	<0.001*	2.87	2.13 – 3.62	<0.001*
CFTR modulator	2.60	1.42 – 3.78	<0.001*	2.59	1.40 – 3.78	<0.001*
CFTR modulator : ppFEV1 40%-90%	Reference			Reference		
CFTR modulator : ppFEV1 <40%	-1.30	-4.30 – 1.69	0.395	-1.24	-4.25 – 1.78	0.420
CFTR modulator : ppFEV1 ≥90%	-4.12	-6.41 – -1.82	0.002*	-4.07	-6.36 – -1.77	<0.001*
Time : CFTR modulator	0.75	0.05 – 1.43	0.039*	0.81	0.11– 1.50	0.026*
Time : CFTR modulator : ppFEV1 40-90%	Reference			Reference		
Time : CFTR modulator : ppFEV1 <40%	1.50	0.10 – 2.92	0.035*	1.40	-0.0001 – 2.82	0.050*
Time : CFTR modulator : ppFEV1 ≥90%	-0.60	-1.97 – 0.7	0.389	-0.63	-2.01 – 0.76	0.368

5 Definitions and abbreviations: percent predicted forced expiratory volume in 1 s (ppFEV1), lumacaftor/ivacaftor (LUM/IVA), tezacaftor/ivacaftor (TEZ/IVA),

6 Cystic Fibrosis Transmembrane conductance Regulator (CFTR). Time in years. # Adjusted for sex, age at baseline and the interaction effect between age at

7 baseline with time. \* Significance level < 0.05.

8 **Supplementary table 1b. Bayesian linear mixed effects model estimates of ppFEV1.**

9 **Comparison of effects in participants who transitioned to TEZ/IVA and participants who continued LUM/IVA treatment (n=401, Years of**

10 **observation=3844).**

	<b>Unadjusted coefficient</b>	<b>95% CI</b>	<b>P-value</b>	<b>Adjusted coefficient#</b>	<b>95% CI</b>	<b>P-value</b>
Intercept	66.33	63.16 – 69.48	<0.001	70.20	67.25 – 73.14	<0.001
Continuation LUM/IVA	Reference			Reference		
Transition TEZ/IVA	5.22	0.98 – 9.48	0.017*	1.64	-1.95 – 5.21	0.365
Time	-1.22	-1.51 – -0.94	<0.001*	-1.28	-1.56 – -1.00	<0.001*
Time : continuation LUM/IVA	Reference			Reference		
Time : transition TEZ/IVA	-0.28	-0.74 – 0.18	0.234	-0.17	-0.63 – 0.29	0.462
CFTR modulator	1.81	0.41 – 3.21	0.011*	1.79	0.37 – 3.21	0.014*
CFTR modulator : continuation LUM/IVA	Reference			Reference		
CFTR modulator : transition TEZ/IVA	-0.56	-2.47 – 1.34	0.562	-0.52	-2.46 – 1.39	0.593
Time : CFTR Modulator	1.01	0.22 – 1.80	0.016*	1.03	0.22 – 1.83	0.013*
Time : CFTR modulator : continuation LUM/IVA	Reference			Reference		
Time : CFTR modulator : transition TEZ/IVA	-0.26	-1.30 – 0.79	0.629	-0.27	-1.34 – 0.80	0.612

11 # Adjusted for sex, age at baseline and the interaction effect between age at baseline and time. \* Significance level < 0.05.

12

13 **Supplementary table 1c. Bayesian linear mixed effects model estimates of ppFEV1.**

14 **Comparison of effects in females and males (n=401, Years of observation=3844).**

	Unadjusted coefficient	95% CI	P-value	Adjusted coefficient#	95% CI	P-value
Intercept	68.12	65.20 – 71.06	<0.001	70.89	68.39 – 73.38	<0.001
Male sex	Reference			Reference		
Female sex	2.30	-2.04 – 6.62	0.300	0.19	-3.37 – 3.75	0.918
Time	-1.35	-1.61 – -1.09	<0.001*	-1.38	-1.64 – -1.13	<0.001*
Time : male sex	Reference			Reference		
Time : female sex	0.01	-0.50 – 0.51	0.973	0.08	-0.42 – 0.58	0.762
CFTR modulator	1.43	0.15 – 2.70	0.028*	1.38	0.11 – 2.64	0.033*
CFTR modulator : male sex	Reference			Reference		
CFTR modulator : female sex	0.26	-1.67 – 2.19	0.797	0.32	-1.63 – 2.26	0.749
Time : CFTR Modulator	0.55	0.23 – 1.62	0.013*	0.97	0.27 – 1.65	0.011*
Time : CFTR modulator : male sex	Reference			Reference		
Time : CFTR modulator : female sex	-0.16	-1.24 – 0.91	0.767	-0.22	-1.29 – 0.86	0.685

15 # Adjusted for age at baseline and the interaction effect between age at baseline and time. \* Significance level < 0.05.

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17 **Supplementary table 1d. Bayesian linear mixed effects model estimates of ppFEV1.**

18 **Comparison of effects in adults >18 years and adolescents of 12-18 years (n=401, Years of observation=3844).**

	<b>Unadjusted coefficient</b>	<b>95% CI</b>	<b>P-value</b>	<b>Adjusted coefficient#</b>	<b>95% CI</b>	<b>P-value</b>
Intercept	86.22	82.66 – 89.77	<0.001	85.57	81.69 – 89.48	<0.001
Adolescents	Reference			Reference		
Adults	-24.08	-28.19 – -20.01	<0.001*	-24.01	-28.14 – -19.91	<0.001*
Time	-1.55	-1.91 – -1.18	<0.001*	-1.11	-1.91 – -1.18	<0.001*
Time : adolescents	Reference			Reference		
Time : adults	0.29	-0.18 – 0.75	0.215	0.29	-0.17 – 0.76	0.215
CFTR modulator	0.15	-1.60 – 1.91	0.881	0.14	-1.61 – 1.88	0.893
CFTR modulator : adolescents	Reference			Reference		
CFTR modulator : adults	1.95	-0.15 – 4.01	0.070	1.95	-0.14 – 4.04	0.067
Time : CFTR Modulator	0.48	-0.47 – 1.49	0.314	0.50	-0.46 – 1.45	0.289
Time : CFTR modulator : adolescents	Reference			Reference		
Time : CFTR modulator : adults	0.57	-0.59 – 1.72	0.334	0.55	-0.58 – 1.70	0.342

19 # Adjusted for sex. \* Significance level < 0.05.

20 **Supplementary table 2a. Bayesian linear mixed effects model estimates of BMI in adults  $\geq 19$  years.**

21 **Subgroup analysis in participants with baseline ppFEV1 40-90% (n=214, Years of observation=1564)**

	<b>Unadjusted coefficient</b>	<b>95% CI</b>	<b>P-value</b>	<b>Adjusted coefficient#</b>	<b>95% CI</b>	<b>P- value</b>
Intercept	21.35	21.03 – 21.66	<0.001	21.27	20.85 – 21.69	<0.001
Time	0.05	0.01 – 0.09	0.021*	0.06	0.02 – 0.11	0.008*
CFTR modulator	0.12	-0.05 – 0.30	0.175	0.14	-0.04 – 0.32	0.121
Time : CFTR Modulator	0.08	-0.04 – 0.20	0.212	0.13	-0.004 – 0.26	0.058

22 Definitions and abbreviations: body mass index (BMI) in kg/m<sup>2</sup>. # Adjusted for sex, age at baseline and the interaction effect between age at baseline and time

23 and between age at baseline, time and CFTR modulator treatment. \* Significance level < 0.05.

24 **Supplementary table 2b Bayesian linear mixed effects model estimates of BMI in adults  $\geq 19$  years.**

25 **Comparison of effects in participants who transitioned to TEZ/IVA and participants who continued LUM/IVA treatment (n=312, Years of**

26 **observation=2317).**

	<b>Unadjusted coefficient</b>	<b>95% CI</b>	<b>P-value</b>	<b>Adjusted coefficient</b>	<b>95% CI</b>	<b>P-value</b>
Intercept	21.46	21.10 – 21.82	<0.001	21.40	21.00 – 21.81	<0.001
Continuation LUM/IVA	Reference			Reference		
Transition TEZ/IVA	-0.14	-0.66 – 0.38	0.604	-0.08	-0.60 – 0.44	0.765
Time	0.05	0.004 – 0.09	0.033*	0.07	0.02 – 0.11	0.005*
Time : continuation LUM/IVA	Reference			Reference		
Time : transition TEZ/IVA	0.03	-0.06 – 0.12	0.572	0.04	-0.05 – 0.13	0.350
CFTR modulator	0.28	0.01 – 0.44	0.038*	0.22	0.001 – 0.44	0.049*
CFTR modulator : continuation LUM/IVA	Reference			Reference		
CFTR modulator : transition TEZ/IVA	-0.20	-0.52 – 0.12	0.219	-0.20	-0.54 – 0.12	0.227
Time : CFTR Modulator	0.10	-0.04 – 0.25	0.147	0.14	-0.003 – 0.28	0.055
Time : CFTR modulator : continuation LUM/IVA	Reference			Reference		
Time : CFTR modulator : transition TEZ/IVA	-0.08	-0.28 – 0.12	0.434	-0.08	-0.27 – 0.10	0.387

27 # Adjusted for the main effects of sex, age at baseline, the interaction effect of age at baseline with time and the interaction effect of age at baseline with time and CFTR

28 modulator treatment. \* Significance level < 0.05.

29

30 **Supplementary table 2c Bayesian linear mixed effects model of BMI in adults  $\geq 19$  years.**

31 **Comparison of effect estimates in females and males (n=312, Years of observation=2317).**

	<b>Unadjusted coefficient</b>	<b>95% CI</b>	<b>P-value</b>	<b>Adjusted coefficient</b>	<b>95% CI</b>	<b>P-value</b>
Intercept	21.69	21.35 – 22.03	<0.001	21.32	20.95 – 21.69	<0.001
Male sex	Reference			Reference		
Female sex	-0.77	-1.29 – -0.25	0.004*	-0.71	-1.22 – -0.19	0.007*
Time	0.07	0.02 – 0.11	0.002*	0.09	0.05 – 0.14	<0.001*
Time : male sex	Reference			Reference		
Time : female sex	-0.04	-0.14 – 0.06	0.443	-0.04	-0.14 – 0.05	0.360
CFTR modulator	0.26	0.06 – 0.48	0.012*	0.26	0.05 – 0.48	0.016*
CFTR modulator : male sex	Reference			Reference		
CFTR modulator : female sex	-0.29	-0.62 – 0.03	0.078	-0.30	-0.63 – 0.03	0.078
Time : CFTR Modulator	0.03	-0.10 – 0.17	0.653	0.07	-0.07 – 0.20	0.330
Time : CFTR modulator : male sex	Reference			Reference		
Time : CFTR modulator : female sex	0.08	-0.12 – 0.29	0.432	0.08	-0.11 – 0.27	0.406

32 # Adjusted for the main effects of sex, age at baseline, the interaction effect of age at baseline with time and the interaction effect of age at baseline with time and CFTR

33 modulator treatment. \* Significance level < 0.05.

34

35 **Supplementary table 3a. Bayesian linear mixed effects model estimates of BMI Z-score in children < 19 years.**

36 **Subgroup analysis in participants with baseline ppFEV1 40-90% (n=147, Years of observation=941)**

	<b>Unadjusted coefficient</b>	<b>95% CI</b>	<b>P-value</b>	<b>Adjusted coefficient#</b>	<b>95% CI</b>	<b>P- value</b>
Intercept	-0.71	-0.87 – -0.55	<0.001	-0.82	-1.09 – -0.54	<0.001
Time	-0.07	-0.10 – -0.05	<0.001*	-0.08	-0.12 – -0.05	<0.001*
CFTR modulator	-0.07	-0.28 – 0.14	0.502	0.01	-0.21 – 0.22	0.924
Time : CFTR Modulator	0.08	-0.04 – 0.19	0.181	0.09	-0.02 – 0.20	0.113

37 Definitions and abbreviations: BMI Z-score was normalized for age and sex and according to the WHO growth reference standard. # Adjusted for the main

38 effects of sex, age at baseline, the interaction effect of sex with time and the interaction effect of age at baseline with time. \* Significance level p<0.05.



39 **Supplementary table 3b Bayesian linear mixed effects model estimates of BMI Z-score in children < 19 years.**

40 **Comparison of effects in participants who transitioned to TEZ/IVA and participants who continued LUM/IVA treatment (n=225, Years of**

41 **observation=1552).**

	<b>Unadjusted coefficient</b>	<b>95% CI</b>	<b>P-value</b>	<b>Adjusted coefficient</b>	<b>95% CI</b>	<b>P-value</b>
Intercept	-0.71	-0.89 – -0.53	<0.001	-0.87	-1.11 – -0.64	<0.001
Continuation LUM/IVA	Reference			Reference		
Transition TEZ/IVA	0.19	-0.001 – 0.38	0.051	0.12	-0.09 – 0.32	0.253
Time	-0.05	-0.08 – -0.01	0.011*	-0.07	-0.10 – -0.03	<0.001*
Time : continuation LUM/IVA	Reference			Reference		
Time : transition TEZ/IVA	-0.04	-0.08 – 0.005	0.083	-0.02	-0.07 – 0.02	0.283
CFTR modulator	0.16	-0.11 – 0.44	0.242	0.14	-0.17 – 0.44	0.375
CFTR modulator : continuation LUM/IVA	Reference			Reference		
CFTR modulator : transition TEZ/IVA	-0.17	-0.47 – 0.13	0.271	-0.11	-0.45 – 0.24	0.520
Time : CFTR Modulator	0.02	-0.21 – 0.26	0.862	0.11	-0.07 – 0.30	0.228
Time : CFTR modulator : continuation LUM/IVA	Reference			Reference		
Time : CFTR modulator : transition TEZ/IVA	0.11	-0.15 – 0.37	0.398	0.03	-0.18 – 0.23	0.786

42 # Adjusted for the main effects of sex, age at baseline, the interaction effect of sex with time and the interaction effect of age at baseline with time. \*

43 Significance level p<0.05.

44

45 **Supplementary table 3c Bayesian linear mixed effects model estimates of BMI Z-score in children < 19 years.**

46 **Comparison of effects in females and males (n=225, Years of observation=1552).**

	<b>Unadjusted coefficient</b>	<b>95% CI</b>	<b>P-value</b>	<b>Adjusted coefficient</b>	<b>95% CI</b>	<b>P-value</b>
Intercept	-0.58	-0.73 – -0.42	<0.001	-0.83	-1.05 – -0.60	<0.001
Male sex	Reference			Reference		
Female sex	-0.05	-0.24 – 0.15	0.639	-0.05	-0.24 – 0.14	0.594
Time	-0.07	-0.10 – -0.04	<0.001*	-0.07	-0.09 – -0.04	<0.001*
Time : male sex	Reference			Reference		
Time : female sex	0.002	-0.04 – 0.05	0.919	0.004	-0.04 – 0.05	0.853
CFTR modulator	-0.14	-0.29 – 0.02	0.086	-0.11	-0.29 – 0.08	0.270
CFTR modulator : male sex	Reference			Reference		
CFTR modulator : female sex	0.33	0.09 – 0.56	0.007*	0.33	0.06 – 0.61	0.018*
Time : CFTR Modulator	0.10	-0.04 – 0.23	0.161	0.12	0.02 – 0.23	0.023*
Time : CFTR modulator : male sex	Reference			Reference		
Time : CFTR modulator : female sex	0.01	-0.19 – 0.21	0.898	0.03	-0.13 – 0.19	0.717

47 # Adjusted for the main effects of sex, age at baseline, the interaction effect of sex with time and the interaction effect of age at baseline with time. \*

48 Significance level p<0.05.

49 **Supplementary table 4a Negative binomial mixed effects model estimates of the duration of IV antibiotic treatment.**

50 **Comparison of effects in participants with baseline FEV1pp <40%, between 40-90% and >=90% (n=361, Years of observation=2827).**

	<b>Unadjusted coefficient</b>	<b>IRR</b>	<b>95% CI (IRR)</b>	<b>P-value</b>	<b>Adjusted coefficient</b>	<b>IRR</b>	<b>95% CI (IRR)</b>	<b>P-value</b>
Intercept	2.01	7.49	4.82 – 11.63	<0.001	1.81	6.16	3.81 – 9.97	<0.001
ppFEV1 40-90%	Reference	Reference			Reference	Reference		
ppFEV1 <40%	1.08	2.96	1.04 – 8.44	0.043*	1.10	3.02	1.04 – 8.77	0.042*
ppFEV1 >=90%	-1.48	0.23	0.09 – 0.55	0.001*	-1.51	0.22		<0.001*
Time	0.09	1.09	0.99 – 1.20	0.080	0.09	1.09	0.99 – 1.20	0.079
Time : ppFEV1 40-90%	Reference	Reference			Reference	Reference		
Time : ppFEV1 <40%	0.02	1.02	0.78 – 1.34	0.879	0.03	1.03	0.78 – 1.35	0.851
Time : ppFEV1 >=90%	0.31	1.36	1.11 – 1.66	0.003*	0.31	1.36	1.11 – 1.66	0.003*
CFTR modulator	-1.19	0.30	0.19 – 0.48	<0.001*	-1.20	0.30	0.19 – 0.47	<0.001*
CFTR modulator : ppFEV1 40%-90%	Reference	Reference			Reference	Reference		
CFTR modulator : ppFEV1 <40%	0.01	1.01	0.34 – 3.01	0.990	0.03	1.03	0.34 – 3.14	0.954
CFTR modulator : ppFEV1 >=90%	-0.08	0.92	0.36 – 2.34	0.866	-0.07	0.93	0.36 – 2.39	0.881
Time : CFTR modulator	0.25	1.29	0.97 – 1.70	0.077	0.26	1.30	0.98 – 1.72	0.071
Time : CFTR modulator : ppFEV1 40-90%	Reference	Reference			Reference	Reference		
Time : CFTR modulator : ppFEV1 <40%	0.12	1.12	0.58 – 2.18	0.730	0.10	1.10	0.56 – 2.16	0.774
Time : CFTR modulator : ppFEV1 >=90%	-1.04	0.35	0.17 – 0.73	0.005*	-1.03	0.36	0.17 – 0.75	0.006*

51 Definitions and abbreviations: intravenous (IV). Coefficients are on the log-scale. Incidence rate ratios (IRR) are transformed back to the original scale. #

52 Adjusted for age at baseline and sex. \* Significance level < 0.05.

53

54 **Supplementary table 4b Negative binomial mixed effects model estimates of the duration of IV antibiotic treatment.**

55 **Comparison of effects in participants who transitioned to TEZ/IVA and participants who continued LUM/IVA treatment (n=364, Years of**

56 **observation=2848).**

	<b>Unadjusted coefficient</b>	<b>IRR</b>	<b>95% CI (IRR)</b>	<b>P-value</b>	<b>Adjusted coefficient#</b>	<b>IRR</b>	<b>95% CI (IRR)</b>	<b>P-value</b>
Intercept	1.81	6.13	3.43 – 10.97	<0.001	1.54	4.64	2.53 – 8.54	<0.001
Continuation LUM/IVA	Reference	Reference			Reference	Reference		
Transition TEZ/IVA	-0.04	0.96	0.45 – 2.03	0.914	-0.03	0.97	0.46 – 2.07	0.944
Time	0.21	1.23	1.08 – 1.41	0.002*	0.21	1.23	1.08 – 1.41	0.002*
Time : continuation LUM/IVA	Reference	Reference			Reference	Reference		
Time : transition TEZ/IVA	-0.09	0.91	0.77 – 1.08	0.284	-0.09	0.91	0.77 – 1.08	0.277
CFTR modulator	-1.47	0.23	0.13 – 0.41	<0.001*	-1.49	0.23	0.13 – 0.40	<0.001*
CFTR modulator : continuation LUM/IVA	Reference	Reference			Reference	Reference		
CFTR modulator : transition TEZ/IVA	0.31	1.37	0.64 – 2.90	0.415	0.34	1.40	0.66 – 2.97	0.375
Time : CFTR Modulator	0.16	1.18	0.81 – 1.71	0.391	0.17	1.19	0.82 – 1.73	0.361
Time : CFTR modulator : continuation LUM/IVA	Reference	Reference			Reference	Reference		
Time : CFTR modulator : transition TEZ/IVA	-0.01	0.99	0.61 – 1.60	0.969	-0.02	0.98	0.61 – 1.58	0.937

57 # Adjusted for age at baseline and sex. \* Significance level < 0.05.

58

59 **Supplementary table 4c Negative binomial mixed effects model estimates of the duration of IV antibiotic treatment.**

60 **Comparison of effects in females and males (n=364, Years of observation=2848).**

	<b>Unadjusted coefficient</b>	<b>IRR</b>	<b>95% CI (IRR)</b>	<b>P- value</b>	<b>Adjusted coefficient</b>	<b>IRR</b>	<b>95% CI (IRR)</b>	<b>P- value</b>
Intercept	1.57	4.81	2.85 – 8.12	<0.001	1.51	4.53	2.68 – 7.66	<0.001
Male sex	Reference	Reference			Reference	Reference		
Female sex	0.46	1.58	0.75 – 3.31	0.226	0.50	1.65	0.79 – 3.45	0.186
Time	0.15	1.16	1.03 – 1.30	0.014*	0.15	1.16	1.03 – 1.30	0.015*
Time : male sex	Reference	Reference			Reference	Reference		
Time : female sex	0.001	1.00	0.85 – 1.78	0.984	0.002	1.00	0.85 – 1.78	0.977
CFTR modulator	-1.46	0.23	0.14 – 0.39	<0.001*	-1.45	0.23	0.14 – 0.39	<0.001*
CFTR modulator : male sex	Reference	Reference			Reference	Reference		
CFTR modulator : female sex	0.38	1.47	0.70 – 3.08	0.312	0.37	1.45	0.69 – 3.05	0.325
Time : CFTR Modulator	0.28	1.32	0.96 – 1.80	0.084	0.28	1.32	0.97 – 1.81	0.081
Time : CFTR modulator : male sex	Reference	Reference			Reference	Reference		
Time : CFTR modulator : female sex	-0.24	0.78	0.49 – 1.26	0.313	-0.25	0.78	0.49 – 1.25	0.297

61 # Adjusted for age at baseline. \* Significance level < 0.05.

62

63 **Supplementary table 4d Negative binomial mixed effects model estimates of the duration of IV antibiotic treatment.**

64 **Comparison of effects in adults >18 years and adolescents of 12-18 years (n=364, Years of observation=2848).**

	<b>Unadjusted coefficient</b>	<b>IRR</b>	<b>95% CI (IRR)</b>	<b>P-value</b>	<b>Adjusted coefficient#</b>	<b>IRR</b>	<b>95% CI (IRR)</b>	<b>P-value</b>
Intercept	1.49	4.45	2.21 – 8.95	<0.001	2.25	9.49	4.91 – 18.33	<0.001
Adolescents	Reference	Reference			Reference	Reference		
Adults	0.38	1.46	0.65 – 3.30	0.361	0.36	1.44	0.68 – 3.03	0.341
Time	0.24	1.28	1.10 – 1.48	0.001*	0.22	1.25	1.07 – 1.45	0.005*
Time : adolescents	Reference	Reference			Reference	Reference		
Time : adults	-0.14	0.87	0.73 – 1.04	0.122	-0.10	0.90	0.75 – 1.09	0.284
CFTR modulator	-1.61	0.20	0.10 – 0.40	<0.001*	-1.08	0.34	0.16 – 0.71	0.004*
CFTR modulator : adolescents	Reference	Reference			Reference	Reference		
CFTR modulator : adults	0.48	1.62	0.71 – 3.71	0.252	-0.03	0.97	0.40 – 2.35	0.948
Time : CFTR Modulator	0.04	1.04	0.66 – 1.64	0.855	0.10	1.11	0.68 – 1.79	0.685
Time : CFTR modulator : adolescents	Reference	Reference			Reference	Reference		
Time : CFTR modulator : adults	0.17	1.19	0.70 – 2.02	0.516	0.16	1.17	0.67 – 2.06	0.583

65 # Adjusted for sex. \* Significance level < 0.05.

66

67 **Supplementary figure 1. Comparison of longitudinal ppFEV1 trends before and after CFTR modulator initiation in subgroups with baseline ppFEV1**  
68 **<40%, between 40-90% and ≥90%.**

69 Time ranges from -7 years before to +3 years after CFTR modulator initiation, with time=0 (baseline) defined by the start date of CFTR modulator treatment.

70 Dashed lines represent 95% confidence intervals, which are also shown between square brackets. **Panel 1a:** The impact of CFTR modulator use in the  
71 subgroup with baseline ppFEV1 40-90% was demonstrated by an acute change from baseline ppFEV1 of 2.59% (95% CI: 1.40 – 3.78%, p<0.001) in addition to  
72 an improvement in ppFEV1 decline of 0.81% per year, 95% CI: 0.11 – 1.50%, p=0.026; Supplementary table 1a) that was comparable to the main analysis.

73 **Panel 1b:** Compared to the group with baseline ppFEV1 40-90% (black lines), the average estimated change in ppFEV1 decline after CFTR modulator  
74 initiation was on average even 1.40% per year higher (95% CI -0.0001 - 2.82%, p=0.050; Supplementary table 1a) in the group with baseline ppFEV1 <40% (grey  
75 lines). In the group with baseline ppFEV1 ≥90% (dark blue lines), a longitudinal decline in ppFEV1 was not observed.

76

77 **Supplementary figure 2. Comparison of longitudinal BMI and BMI Z-score trends before and after CFTR modulator initiation in subgroup with baseline**  
78 **ppFEV1 between 40-90%.**

79 Time ranges from -7 years before to +3 years after CFTR modulator initiation, with time=0 (baseline) defined by the start date of CFTR modulator treatment.

80 Dashed lines represent 95% confidence intervals, which are also reported between square brackets. **Panel 2a:** In adults ≥19 years, BMI trend before and after  
81 CFTR modulator initiation in this subgroup was comparable to the observed overall trends, with a change in annual BMI of 0.13 (95% CI: -0.04 – 0.32, p=0.058)  
82 after CFTR modulator initiation (Supplementary table 2a). **Panel 2b:** Trends of BMI Z-score in children <19 years were similar to the entire population,

83 although the longitudinal change after CFTR modulator initiation was slightly smaller compared to the entire cohort (change: 0.09 per year, 95% CI: -0.02 –  
84 0.20, p=0.113; Supplementary table 3a).

85

86 **Supplementary figure 3. Comparison of longitudinal trends in IV antibiotic treatment duration before and after CFTR modulator initiation in subgroups**  
87 **with baseline ppFEV1 <40%, between 40-90% and ≥90%.**

88 Time ranges from -7 years before to +3 years after CFTR modulator initiation, with time=0 (baseline) defined by the start date of CFTR-modulator treatment.

89 Dashed lines represent 95% confidence intervals, which are also reported between square brackets. **Panel 3a:** trends in the average annual duration of IV  
90 antibiotic treatment (in days) were comparable to the overall population, although the average duration of received IV antibiotics in the last year preceding  
91 CFTR modulator initiation was slightly higher (6.16 days, 95% CI: 5.32 – 15.38 days; Supplementary table 4a). **Panel 3b:** Compared to the group with baseline  
92 ppFEV1 40-90% (black lines), average trends of participants with a baseline ppFEV1 <40% (grey lines) were comparable to participants with baseline ppFEV1  
93 40-90%, but the average IV antibiotic treatment duration in participants with a baseline ppFEV1 ≥90% (dark blue lines) was considerably lower and did not  
94 increase after CFTR modulator initiation (Supplementary table 4a).