

**Supplementary Table 1. Prevalence of physical frailty (Fried’s phenotype) in treated and control mice at the 3<sup>rd</sup> month (before treatment) and at the 7<sup>th</sup> month (after treatment) from the inclusion in the study\*.**

Age of mice at the beginning of the study	Status	Month 3 (Before treatment)		Month 7 (Post treatment)	
		Control	LAV-BPIFB4	Control	LAV-BPIFB4
		<b>Adult mice</b>	Frail	2 (8.3%)	1 (4.5%)
	Non-frail	22 (91.7%)	21 (95.5%)	19 (90.5%)	20 (95.2%)
<b>Old mice</b>	Frail	4 (15.4%)	3 (10.7%)	8 (44.4%)	5 (20%)
	Non-frail	22 (84.6%)	25 (89.3%)	10 (55.6%)	20 (80%)

\*Data are reported as number of mice (%). At month 3: p = 0.741 by Fisher’s exact test; At month 7: p = 0.170 by Fisher’s exact test; The reduced number of mice at month 7 is due to death events occurring during the study.

**Supplementary Table 3. Measurement performed to define Physical Frailty phenotype\*.**

Criterion	Shrinking	Weakness	Endurance	Slowness	Activity
Measurement 1	Current weight	Grip strength meter	Treadmill distance	Highest speed interval that the mouse traveled for at least 3 s in an open field test (5 min)	% the mice walked or run in a 5-min open field test
Measurement 2	Weight loss in 1 month	Dynamometer force	Mean time at Rotarod test	Mean stride length	Total distance run by the mouse in a 5-min open field test
Measurement 3	Weight loss in 2 month	Increasing weights lift test	Increasing weights lift test	Max speed at rotarod test	-

\*For each criterion a composite Z-score was derived as the mean of the Z-scores from each measurement. Mice that fell in the bottom 20% of our cohort for the composite score computed for each criterion (Shrinking, Weakness, Endurance, Slowness and Activity), were assigned one point. The mice were considered as frail when they reached 3 or more points on a maximum of 5.