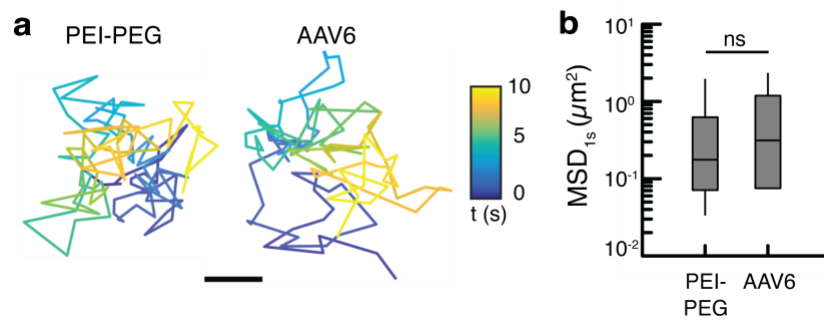**Supplemental Information**

An Adeno-Associated Viral Vector Capable

**of Penetrating the Mucus Barrier to Inhaled**

Gene Therapy

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Supplementary Table 1. Patient Demographics for Figure 1

Number of Patients	10
Age (yr, mean ± SD)	31 ± 6
Forced expiratory volume after 1 second, FEV_1 (% predicted value, mean ± SD)	63 ± 25
Gender (number)	
Male	3
Female	7
CFTR genotype (number)	
F508del homozygous	6
F508del heterozygous	3
Other	1

Supplementary Figure 1. *Synthetic and viral gene vector diffusion in spontaneously expectorated CF sputum.* **(a)** Representative trajectories of synthetic mucus-penetrating gene delivery nanoparticles based on polyethylene glycol-conjugated polyethylenimine (PEI-PEG)[19] and AAV6 in CF sputum. Trajectories show ~10 seconds of gene vector motions. Color bar indicates the time (t) of the trajectory in seconds. Scale bar = 1 μm. **(b)** Box-and-whisker plots of MSD_{1s} of PEI-PEG and AAV6 in sputum samples collected from 3 individual CF patients. Maximum whisker length is 1.5 times the interquartile range; outliers are not shown. A Mann-Whitney test was used to compare MSD_{1s} and there was no significant difference ($p > 0.05$).
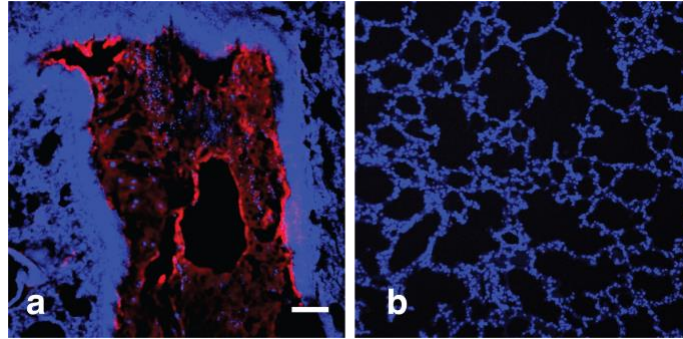
Supplementary Figure 2. *Mucus in the lungs of Scnn1b-Tg mice.* Representative confocal images of mucus in the airways **(a)** versus the airspace **(b)**. Cell nuclei and DNA are stained with DAPI (blue) and mucins are stained with anti-MUC5B/5AC Ab (red).