Supplemental Methods

Experimental Groups
An additional 28-day syngeneic group was treated with TRAM-34 with the same dosage to investigate the epithelial toxicity in a transplant setting. The same tracheal transplantation model was also performed from L2G to FVB mice to identify the origin of airway epithelium of graft 28 days after surgery.

Side Effect Screening
Complete necropsy of C57Bl/6J mice treated with TRAM-34 for 28 days (to investigate epithelial toxicity) was performed and the specimens were evaluated by an independent pathologist.

Histology

General Histology
The epithelium and the luciferase marker in L2G grafts were identified in immunofluorescent staining by antibodies against cytokeratin (Clone AE1/AE3, Dako) and firefly luciferase (Abcam, Cambridge, UK). Antigen retrieval was performed using heating-induced epitope retrieval method. After 1-hour incubation with primary antibody at 37°C, secondary antibody with desired fluorescent dyes was chosen according to the primary antibody host, and incubated also for 1-hour at 37°C. Nuclei were stained with DAPI. Confocal microscopy (PerkinElmer UltraVIEW VoX, PerkinElmer, Massachusetts, USA) was used to visualize the staining.
SDC, Figure S1: Co-localization of luciferase marker and cytokeratin identifies the donor-origin of the airway epithelium.

Syngeneic tracheal grafts transplanted from L2G to FVB mice were harvested on POD28. The close view of the Masson-Goldner stained section showed well-preserved airway epithelium, with the presence of pseudo-striated columnar structure, cilia, and goblet cells (A). Immunofluorescence staining of cytokeratin (clone AE1/AE3) visualized the epithelium (B). Positivity of luciferase (Luc) indicated the donor origin of the cells (C). Viewed by confocal microscopy, the co-localization of cytokeratin and luciferase proved the donor-origin of the epithelial cells along the lumen of tracheal grafts (D; red: cytokeratin; green: Luc; blue: DAPI).
SDC, Video S1: Co-localization of luciferase marker and cytokeratin identifies the donor-origin of the airway epithelium. 3D-reconstruction using confocal microscopy (PerkinElmer UltraVIEW VoX, PerkinElmer, Massachusetts, USA) showing the donor-origin of the airway epithelium.
**SDC, Figure S2:** No epithelial toxicity of TRAM-34 by histopathology.

Complete necropsy of mice treated with TRAM-34 for 28 days was done. The lung (A) and GI tract sections (B) stained with Masson-Goldner Trichrome (left) showed normal histology of respiratory and small intestinal epithelium, respectively. Immunofluorescence staining further demonstrated physiologic cytokeratin distribution (right). In syngeneic C57Bl/6J grafts of TRAM-34-treated C57Bl/6J recipients, the epithelium was also intact on POD 28 (C). Epithelial toxicity of TRAM-34 could not be demonstrated (green: cytokeratin; blue: DAPI).
SDC, Video S2: No epithelial toxicity of TRAM-34 by confocal microscopy (3D reconstruction).
**SDC, Figure S3:** KCa3.1 expression in human OAD.

A human lung allograft with OAD is stained with Masson-Goldner trichrome (A) and shows fibroproliferative airway narrowing. Confocal immunofluorescence staining demonstrates KCa3.1 channel expression in human OAD with a similar distribution as in murine OAD (B).