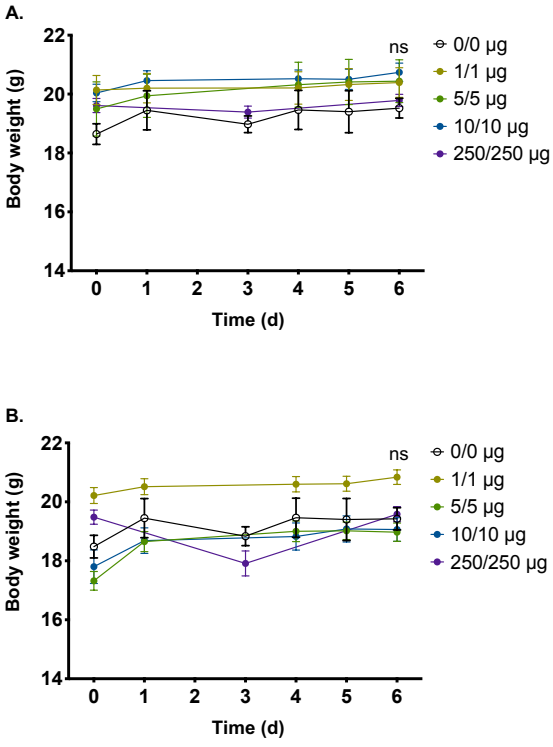

Fig S1. Intratracheal GH therapy is well tolerated by mice. Body weight of BALB/c mice following intratracheal administration of a single dose of (A) $PslG_h/PelA_h$ or (B) $PslG_h/Ega3_h$. ns indicates no significant difference in the change in body weight of mice treated with 250/250 µg combination GHs relative to buffer-treated mice as determined by two-way ANOVA with Dunnett's multiple-comparison test.

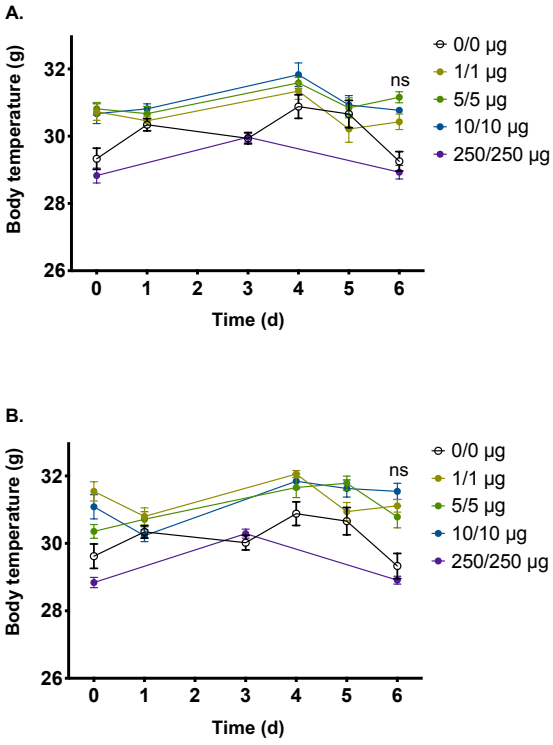

Fig S2. Intratracheal GH therapy is well tolerated by mice. Body temperature of BALB/c mice following administration of a single dose of (A) $PslG_h/PelA_h$ or (B) $PslG_h/Ega3_h$. ns indicates no significant difference in the change in body temperature of mice treated with 250/250 µg combination GHs relative to buffer-treated mice as determined by two-way ANOVA with Dunnett's multiple-comparison test.

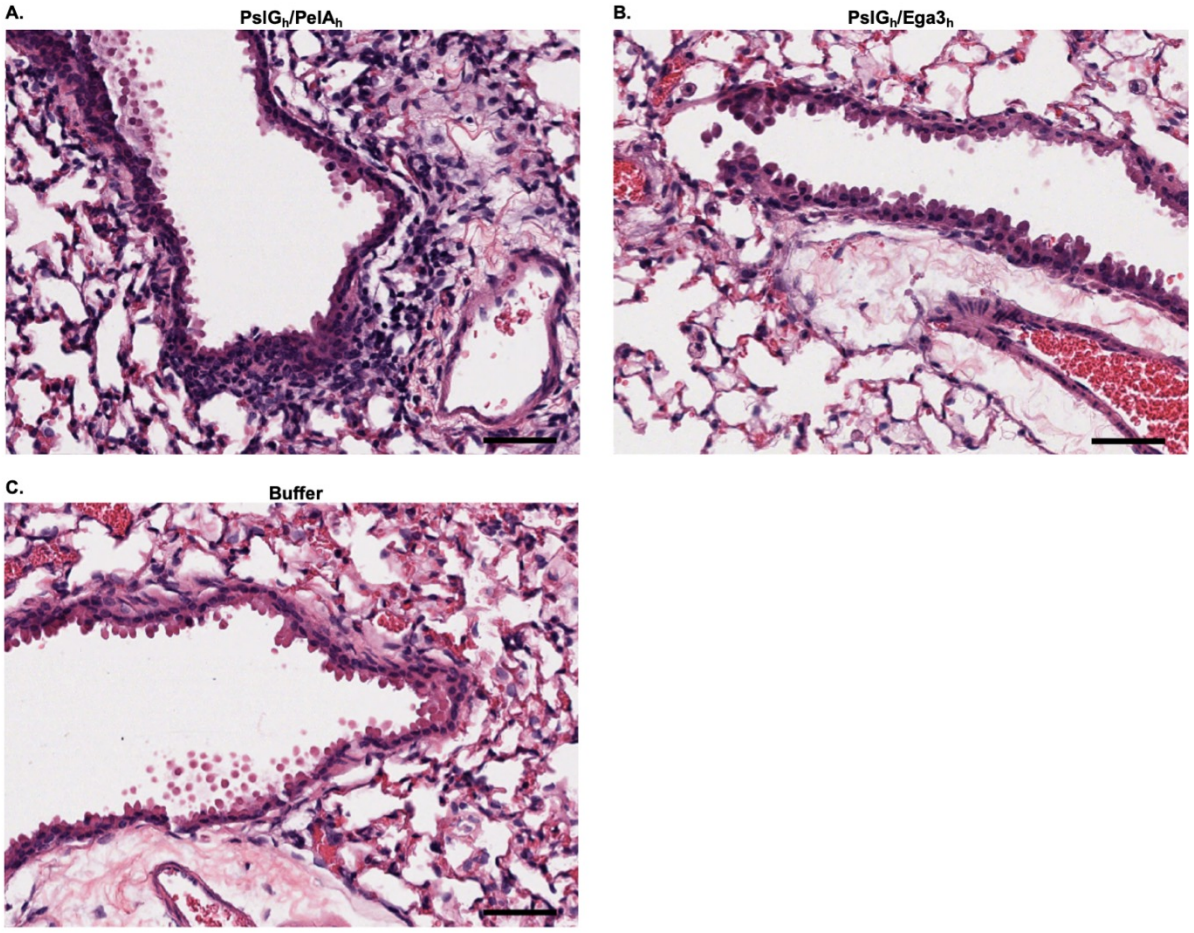

Fig S3. Intratracheal GH therapy is well tolerated by mice. Haematoxylin- and eosin-stained sections of lungs obtained from immunocompetent BALB/c mice 6 d after intratracheal administration of a single dose of 250/250 μg of (A) PslG$_h$/PelA$_h$, (B) PslG$_h$/Ega3$_h$ or (C) PBS. Representative images from groups of ≥2 mice imaged at 40X (scale bar, 50 μm).

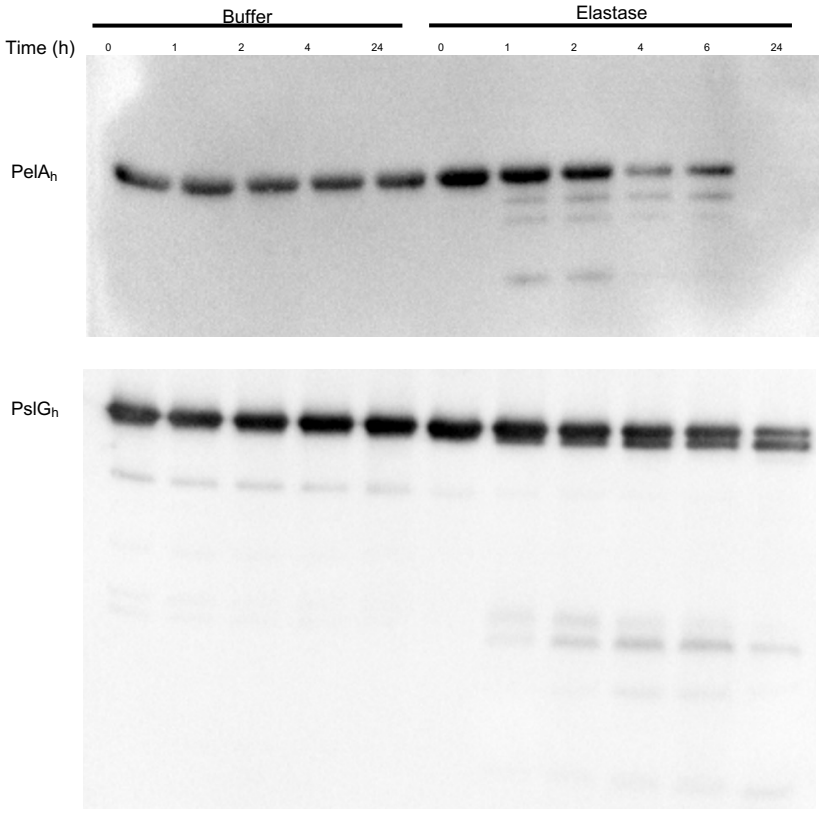

Fig S4. GHs are susceptible to degradation by elastase. 10 μg PelAh or PslGh was treated with 100 μg/mL neutrophil elastase in vitro for the indicated time intervals, and the integrity of the protein analyzed by Western blot.

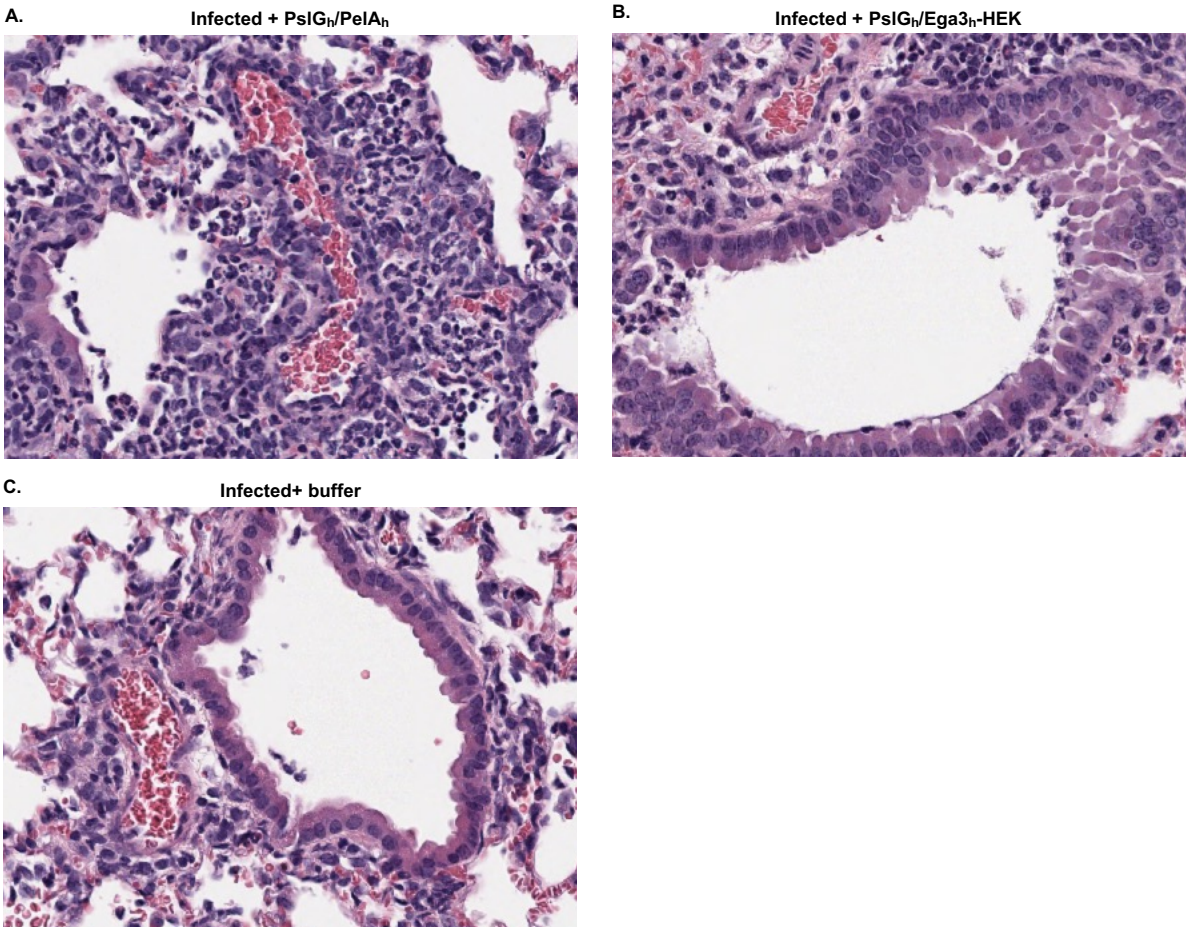

Fig S5. Pulmonary histopathology of mice infected with *P. aeruginosa* and treated with GH enzymes. Haematoxylin- and eosin-stained sections of lungs obtained from immunocompetent BALB/c mice 24 h after intratracheal infection with 3 x 10^7 *P. aeruginosa* and co-administration of a single dose of 250/250 μg of (A) PslG$_h$/PelA$_h$, (B) PslG$_h$/Ega3$_h$-HEK or (C) PBS. Representative images from groups of ≥2 mice imaged at 40X (scale bar, 50 μm).

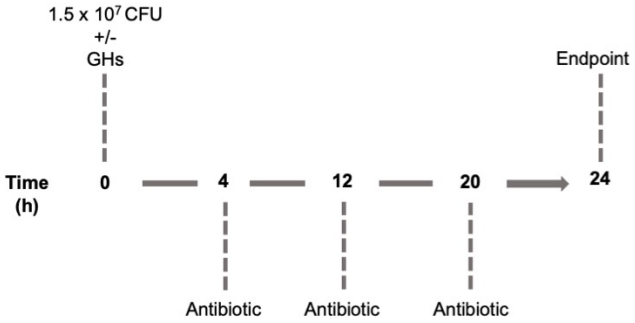

Fig S6. Experimental design of combination GH-antibiotic evaluation in a mouse model of acute *P. aeruginosa* pulmonary infection. Mice were intratracheally infected with 1.5 x 10^7 *P. aeruginosa* CFU and co-administered with or without a single dose of 250/250 μg $PslG_h$/$PelA_h$ or $PslG_h$/$Ega3_h$-HEK then treated by intraperitoneal injection with 10 mg/mL ciprofloxacin or subcutaneous injection with 25 mg/mL ceftazidime beginning at 4 h every 8 h. Pulmonary and blood bacterial burden was measured 24 h after prophylaxis.