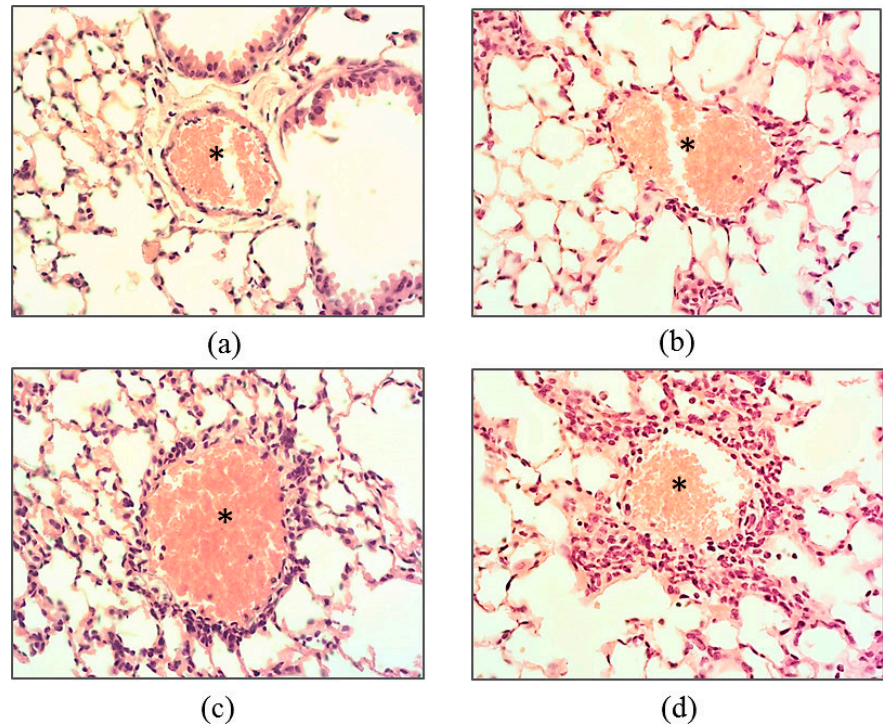


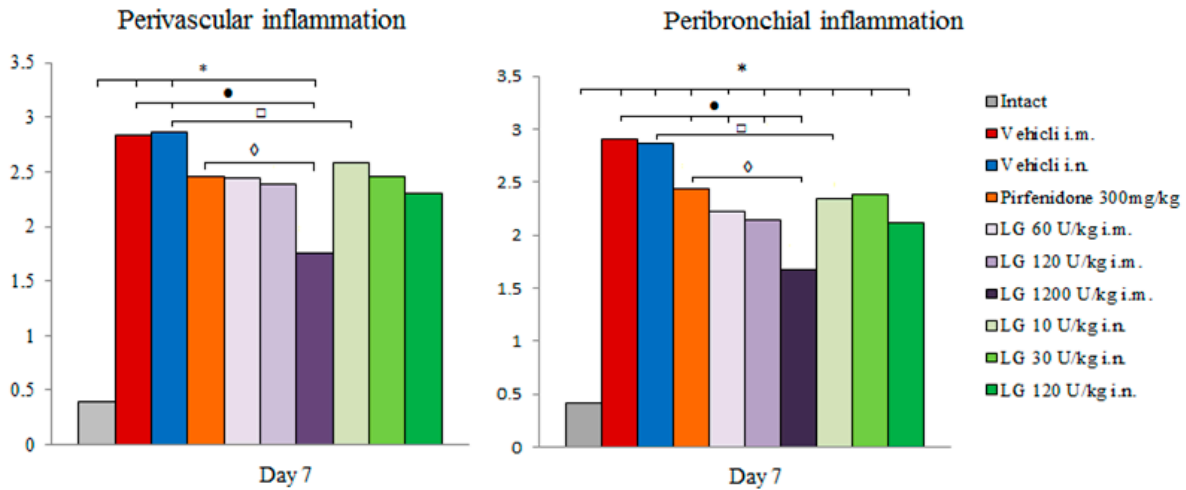
**Table S1.** Study Design and Experimental Groups.

Groups	Introduction of bleomycin (day)	Estimation of body weight of animals (day)	Drugs	Euthanasia and sampling
1 – intact control (Intact)	-	d0 d7 d14 d21	-	d7 d21
2 – pulmonary fibrosis + NaCl (Vehicle i.m.*)	d0	d0 d7 d14 d21	NaCl intramuscularly	d7 d21
3 –pulmonary fibrosis + NaCl (Vehicle i.n.*)	d0	d0 d7 d14 d21	NaCl intranasally	d7 d21
4 – pulmonary fibrosis + Pirfenidone	d0	d0 d7 d14 d21	Pirfenidone at a dose 300 mg/kg p.o.*	d7 d21
5 – pulmonary fibrosis + LG 60 U/kg i.m.	d0	d0 d7 d14 d21	Longidaze intramuscularly at a dose of 60 U/kg	d7 d21
6 – pulmonary fibrosis + LG 120 U/kg i.m.	d0	d0 d7 d14 d21	Longidaze intramuscularly at a dose of 120 U/kg	d7 d21
7 – pulmonary fibrosis + LG 1200 U/kg i.m.	d0	d0 d7 d14 d21	Longidaze intramuscularly at a dose of 1200 U/kg	d7 d21
8 – pulmonary fibrosis + LG 10 U/kg i.n.	d0	d0 d7 d14 d21	Longidaze intranasally at a dose of 10 U/kg	d7 d21
9 – pulmonary fibrosis + LG 30 U/kg i.n.	d0	d0 d7 d14 d21	Longidaze intranasally at a dose of 30 U/kg	d7 d21
10 – pulmonary fibrosis + LG 120 U/kg i.n.	d0	d0 d7 d14 d21	Longidaze intranasally at a dose of 120 U/kg	d7 d21

\* i.m. – intramuscularly; i.n. – intranasally; p.o. – per os.

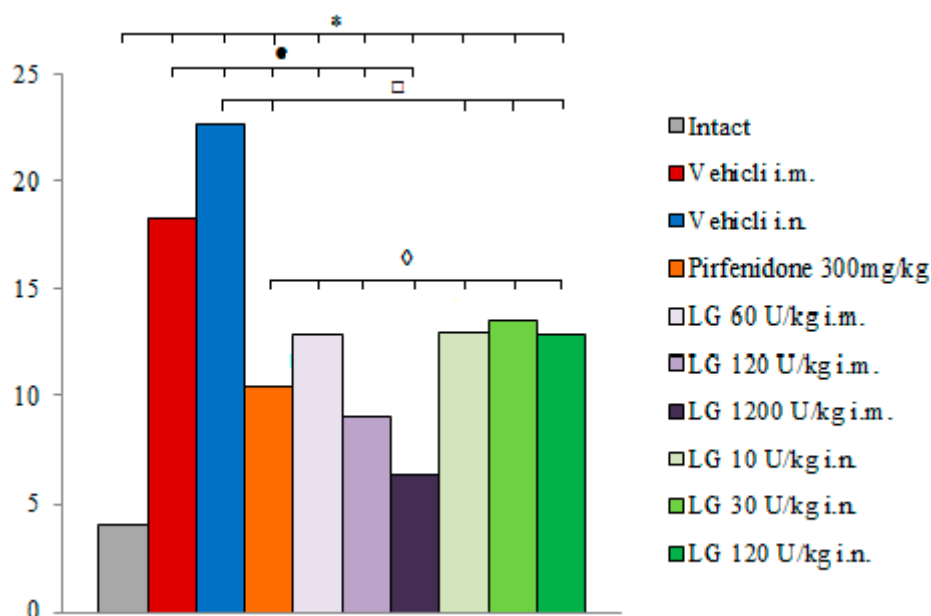


**Figure S1.** Histology analyses of H&E stained sections: Lung sections graded as (a) normal, (b) Grade I, (c) Grade II and (d) Grade III. \* Lumen of an artery. Original magnification:  $\times 20$



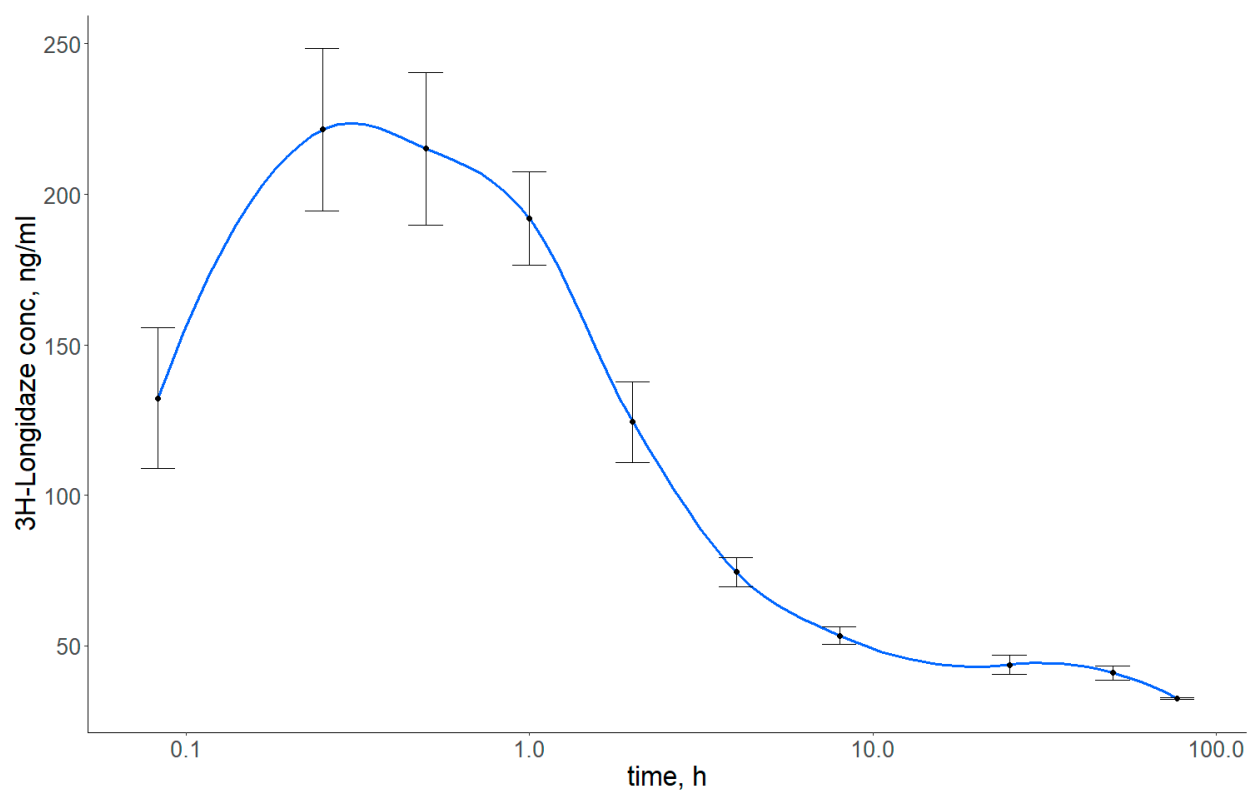
**Figure S2.** Effect of Longidaze on perivascular and peribronchial inflammation in the lungs of C57BL/6 mice on d7. Groups: Intact - mice of intact control (group 1); Vehicle i.m. and Vehicle i.n. - mice treated with bleomycin (groups 2 and 3); Pirfenidone 300 mg/kg p.o. - pulmonary fibrosis + pirfenidone (group 4); LG 60 U/kg i. m. - pulmonary fibrosis + Longidaze intramuscularly at a dose of 60 U/kg (group 5); LG 120 U/kg i.m. - pulmonary fibrosis + Longidaze intramuscularly at a dose of 120 U/kg (group 6); LG 1200 U/kg i. m. - pulmonary fibrosis + Longidaze intramuscularly at a dose of 1200 U/kg (group 7); LG 10 U/kg i.n. - pulmonary fibrosis + Longidaze intranasally at a dose of 10 U/kg (group 8); LG 30 U/kg i. n. - pulmonary fibrosis + Longidaze intranasal at a dose of 30 U/kg (group 9); LG 120 U/kg i.n. - pulmonary fibrosis + Longidaze intranasal at a dose of 120 U/kg (group 10). P.o. - per os, i.m. - intramuscular, i.n. - intranasal. \*  $p < 0.05$  significance of difference compared with the Intact (Mann-Whitney test); •  $p < 0.05$  significance of difference compared with the Vehicle i.m. (negative control for i.m. groups) (Mann-Whitney test); ◊  $p < 0.05$  significance of difference compared with the Vehicle i.n. (negative control for inhalation groups) (Mann-

Whitney test);  $\diamond$   $p < 0.05$  significance of difference compared with the Pirfenidone (Mann–Whitney test).



**Figure S3.** Content of the connective tissue in the lungs of C57BL/6 mice on d21. Groups: Intact - mice of intact control (group 1); Vehicle i.m. and Vehicle i.n. - mice treated with bleomycin (groups 2 and 3); Pirfenidone 300 mg/kg p.o. - pulmonary fibrosis+ pirfenidone (group 4); LG 60 U/kg i. m. - pulmonary fibrosis + Longidaze intramuscularly at a dose of 60 U/kg (group 5); LG 120 U/kg i. m. - pulmonary fibrosis + Longidaze intramuscularly at a dose of 120 U/kg (group 6); LG 1200 U/kg i. m. - pulmonary fibrosis + Longidaze intramuscularly at a dose of 1200 U/kg (group 7); LG 10 U/kg i. n. - pulmonary fibrosis + Longidaze intranasally at a dose of 10 U/kg (group 8); LG 30 U/kg i. n. - pulmonary fibrosis + Longidaze intranasal at a dose of 30 U/kg (group 9); LG 120 U/kg i.n. - pulmonary fibrosis + Longidaze intranasal at a dose of 120 U/kg (group 10). P.o. - per os, i.m. - intramuscular, i.n. - intranasal.

\*  $p < 0.05$  significance of difference compared with the Intact (Mann–Whitney test); •  $p < 0.05$  significance of difference compared with the Vehicle i.m. (negative control for i.m. groups) (Mann–Whitney test); □  $p < 0.05$  significance of difference compared with the Vehicle i.n. (negative control for inhalation groups) (Mann–Whitney test);  $\diamond$   $p < 0.05$  significance of difference compared with the Pirfenidone (Mann–Whitney test).



**Figure S4.** Graph of the Longidaze concentration (ng/ml) versus time after intramuscular injection.