

## Supplemental Figures

**Supplemental Figure S1. Dose-Response Curve of BMDM and validation of *in vitro* BMDM polarization assay.** A. SPR (Surface Plasmon Resonance) dose response for the binding of CD206 receptor by different concentrations (0 $\mu$ M - 100 $\mu$ M) of RP-832c. B. Validation of *in vitro* BMDM polarization assay using C57BL/6 mice-derived macrophages. Bone marrow-derived macrophages polarized to M1 macrophages with 20ng/ml of M-CSF & 20ng/ml of INF- $\gamma$  showed increased CD86 expression, while those polarized to an M2 phenotype using 20ng/ml of M-CSF & 20ng/ml of IL4 stimulation showed increased CD206 expression.

**Supplemental Figure S2. RP-832c shows no cytotoxicity against lung fibroblasts.** RP-832c (1 $\mu$ M - 100 $\mu$ M) did not show cytotoxicity against lung fibroblast cell lines MRC5 and IMR91. All data presented are the means of three independent experiments, performed in triplicate  $\pm$  S. E. \*\*\*P < 0.0001, and \*\* P<0.001 and \*P<.05 is significant.

**Supplemental Figure S3. Analysis of publicly available data sets showed that CD206 expression is increased by BLM treatment.** A. Secondary analysis of the GSE48455 data set (n=72) showed upregulation of CD206 expression in the BLM-treated mice compared to normal saline-treated mice. B. Secondary analysis of the GSE40151 data set (n=111) treated with BLM or normal saline for 35 days showed upregulation of CD206 gene expression with time. C. 10x and 40x IHC images representing anti-CD206 staining of lung tissues of BLM-treated mice compared to naïve mice lung tissues. D. Quantification of the IHC staining of CD206 of the lung tissues of BLM-challenged mice compared to lung tissues of naïve mice. n=3 mice \*\*\*P < 0.0001, and \*\* P<0.001 and \*P<.05 is significant.

**Supplemental Figure S4. Intranasal administration of RP-832c peptide shows similar activity to subcutaneous administration.** A. RP-832c peptide was administered intranasally at 25 $\mu$ g/mouse QD through day 24. Images are 10x representative images of Masson's Trichrome staining of each of the treatment groups. B. Lung-to-body weight ratio of lung tissues of mice from the different treatment groups. C. Modified Ashcroft score of lung tissues from the different treatment groups. \*\*\*P < 0.0001, and \*\* P<0.001 and \*P<.05 is significant.

**Supplemental Figure S5. RP-832c peptide decreased fibrosis to a greater extent compared to Nintedanib in an established late model of BLM-induced lung fibrosis model.** A. A schematic of the animal study in which on day 0 mice were challenged with 2.5U/kg body weight dose of BLM; starting 14 days post-BLM challenge, mice were treated daily with 10mg/kg of RP-832c (QD), 30mg/kg Nintedanib (Q3D), or a combination of both for an additional 21 days. B. Representative 10x images of Masson's Trichrome staining show a significant reduction of collagen deposition in the lungs of RP-832c treated mice compared to the other treatment groups. C. Lung weights of mice from the different treatment groups were measured at the end of the study. D. Modified Ashcroft scoring of lung tissue sections from the different treatment groups. n=6 per treatment group. S. E. \*\*\*P < 0.0001, and \*\* P<0.001 and \*P<.05 is significant.

**Supplemental Figure S6. RP-832c peptide lacks toxicity.** A. Animal toxicity study conducted using CD1 mice showed that 50mg/kg RP-832c treatment did not have any significant effect on body weight compared to the vehicle-treated mice. B. Bar graph showing that 50 mg/kg of RP-832c treatment lacks any significant effect on the weight of various organs when compared to the vehicle-treated mice. C. Complete Blood Cell count shows that 50 mg/kg of RP-832c does not significantly affect the complete blood cell count compared to vehicle-treated mice.