Supplementary Figure Legends

Supplementary Figure 1. Analysis of LunX expression. (**A**) Analysis of the correlation between LunX expression and KRAS or p53 mutations in NSCLC. (**B**) Kaplan-Meier curves of the 5-year postoperative survival were generated according to the LunX staining grade in samples from 74 NSCLC patients. Survival analyses were performed with the log-rank test. (**C**) Immunohistochemical assessment of LunX expression in pneumonia and tuberculosis samples and other organs or cancers (colon, liver and breast). Scale bar, 200 μm. (**D**) RT-PCR analysis of the expression of the human LunX family of proteins in NSCLC.

Supplementary Figure 2. Analysis of lung cancer cell migration and proliferation. (**A**) Transwell assays to assess the NCI-H292, PG, A549, H460, SK-MES-1 and SK-lu-1 cell migration. (**B**) Wound-healing assays to assess A549 cell migration after LunX knockdown. A549 cell proliferation based on cell clone formation after LunX knockdown. (**C**) IF for Ki67 in A549 cells after LunX knockdown. Scale bar, 100 μm.

Supplementary Figure 3. LunX-interacting proteins and the pathways regulated by LunX. (**A**) Immunoassay of the A549 cells by IP with anti-LunX, and Western blot analysis with anti-14-3-3. (**B**) Immunoblotting analysis of 14-3-3 phosphorylation in A549 cells after LunX siRNA silencing. Native gel electrophoresis and immunoblotting analysis of dimeric and monomeric 14-3-3 in A549 cells after LunX

siRNA silencing. (**C**) Western blot analysis of 14-3-3 θ or ζ levels in NCI-H292 cells transfected with 14-3-3 θ siRNA, 14-3-3 ζ siRNA or mock siRNA. (**D, E**) Western blot analysis of the protein expression in A549 cells following LunX siRNA silencing. Transwell assays and cytometry to assess the A549 cell migration and proliferation after knockdown with 14-3-3 θ siRNA, 14-3-3 ζ siRNA or mock siRNA and to assess the migration and proliferation of the LunX-overexpressing or mock-transfected A549 cells after knockdown with 14-3-3 θ siRNA and 14-3-3 ζ siRNA (***$p<0.001$; ns, $p>0.05$). The data are expressed as the mean±SD. (**F, G**) Western blot analysis of the protein expression and phosphorylation in NCI-H292 cells following LunX siRNA silencing. (**H**) Transwell analysis of the migration in A549 cells treated with SP600125 (inhibitor of JNK phosphorylation) or DMSO (***$p<0.001$). Cytometry analysis of the proliferation in A549 cells treated with SP600125 (inhibitor of JNK phosphorylation) or DMSO. The data are presented as the mean±SD. (**I**) Assessment of apoptosis by flow cytometry in NCI-H292 cells following LunX knockdown or overexpression.

Supplementary Figure 4. LunX-targeted small interfering RNA suppresses lung cancer growth and metastasis. (**A**) Pathological analysis of tissue sections from mice bearing an orthotopic xenograft. Scale bar, 200 μm. (**B, C**) Stable LunX-knockdown (sh-LunX^1 and sh-LunX^2) or LunX-overexpressing A549 cells were injected subcutaneously (s.c.) into nude mice. Tumor weight (C) and immunohistochemical staining for Ki-67 in tumors (B) are presented (***$p<0.001$).

Scale bar, 200 μm. The data are expressed as the mean±SD.

Supplementary Figure 5. Characterization of the LunX therapeutic antibody (S-35-8). (**A**) The effect of S-35-8 and 251512 (LunX antibody, R&D) on LunX expression in NCI-H292 cells. (**B, C**) Transwell analysis and cytometry analysis of NCI-H1299 and NCI-H358 cell migration and proliferation after treatment with or without IgG (160 μg/ml) or S-35-8 (80 or 160 μg/ml; 48 h; ***p<0.001, **p<0.01). The data are presented as the mean±SD. (**D**) Analysis of apoptosis by flow cytometry in A549 and NCI-H292 cells treated without or with S-35-8. (**E**) Immunofluorescence analysis of the antibody endocytosis in A549 cells treated with S-35-8-Rho (160 μg/ml; 0, 6, 24 or 48 h). S-35-8-Rho, S-35-8 LunX antibody labeled with rhodamine. Scale bar, 5 μm.

Supplementary Figure 6. The LunX antibody (S-35-8) treats lung cancer. (**A**) IF staining for Ki67 in the A549 xenograft tumors treated with or without S-35-8. Scale bar, 100 μm. (**B**) A549 cells were injected into nude mice lung parenchyma. Mice were treated with S-35-8-FITC at 10 mg/kg body weight. IF was used to assess the distribution of S-35-8-FITC in the normal lung tissue and tumor tissue 12 h after treatment. Scale bar, 50 μm. (**C**) LunX antibody (30 mg/kg body weight) or PBS vehicle was injected i.v. twice weekly, and 4 weeks later, the mice were evaluated by body weight. Lung sections were stained with eosin and hematoxylin. Scale bar, 200 μm. The data are expressed as the mean±SD.

Supplementary Table Legends

Table S1. Clinical characteristics of the cancer patients in this study.

Table S2. LunX levels in 150 cases of non-small-cell lung cancer (75 lung adenocarcinoma, 75 squamous cell lung carcinoma).

Table S3. The 4-year survival rate in 102 cases of non-small-cell lung cancer (NSCLC).