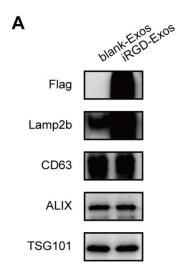
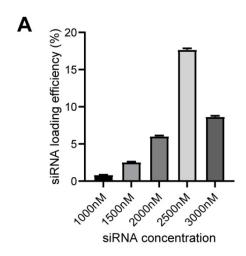
Supplementary Information (SI) for Nanoscale. This journal is © The Royal Society of Chemistry 2025

#### **Supplementary Figure S1**



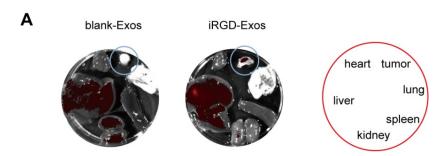
#### Supplementary Figure S1 Western blot analysis of iRGD-modified exosomes.

(A) Western blot showing the expression of iRGD-related proteins (Flag, Lamp2b) and exosomal markers (CD63, ALIX, TSG101) in blank-Exos and iRGD-Exos. CD63, ALIX, and TSG101 also served as internal reference proteins.



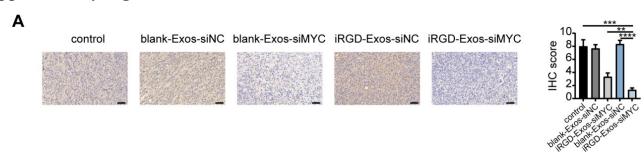
## Supplementary Figure S2 siRNA loading efficiency.

(A) siRNA loading efficiency of exosomes at different siRNA concentrations (1000–3000 nM) was determined by qRT-PCR.



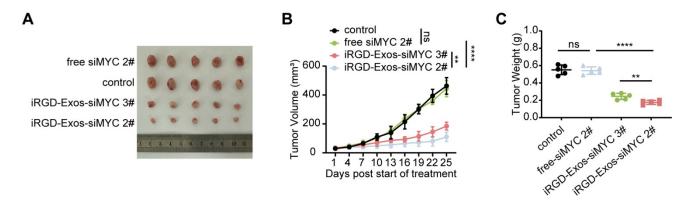
#### Supplementary Figure S3 Targeting of iRGD-Exos in vivo.

(A) Fluorescence imaging of tumors and major organs from Hs578T tumor-bearing nude mice 24 hours after tail vein injection of Dil-labeled blank-Exos/iRGD-Exos. The blue circle marks the tumor site.



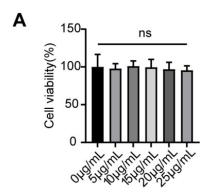
#### Supplementary Figure S4 IHC analysis of MYC expression in animal models.

(A) Representative images and quantification of MYC expression in the tumor by IHC. Scale bar: 50  $\mu$ m. Data are presented as mean  $\pm$  SD. \* P<0.05, \*\*P<0.01, \*\*\*P<0.001 and \*\*\*\*P<0.001. IHC, immunohistochemical.



Supplementary Figure S5 Comparison of tumor growth inhibition between free siMYC and iRGD-Exos-siMYC in TNBC xenograft mice.

(A) Representative images of excised tumors from each treatment group. (B) Tumor growth curves over time. (C) Final tumor weights at the end of treatment. Data are presented as mean  $\pm$  SD. \* P<0.05, \*\*P<0.01, \*\*\*P<0.001 and \*\*\*\*P<0.0001. ns, not significant; TNBC, triple-negative breast cancer.



## **Supplementary Figure S6 In vitro safety evaluation.**

(A) Viability of Hs578T cells treated with different concentrations of iRGD-Exos (0–25  $\mu g/mL$ ) for 48 h.