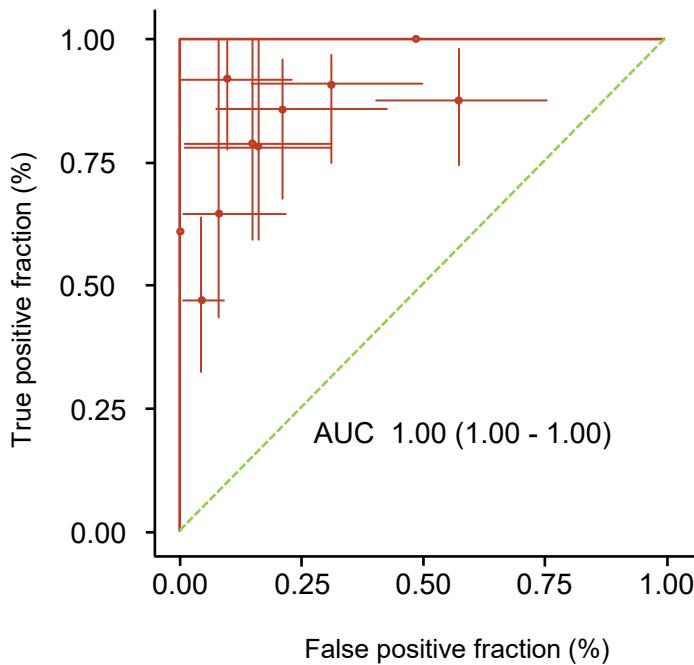
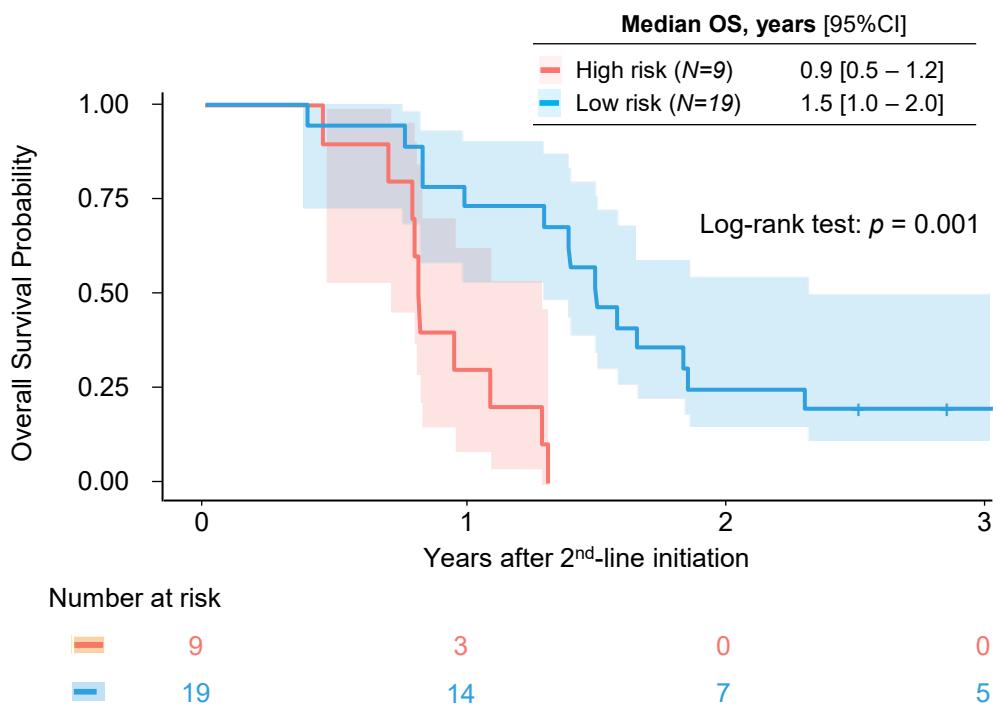


**Supplementary Figure S1: Study design for the identification and validation of the circulating exosomal miRNAs panel for differentiating patients with responder and non-responder to second-line treatment in gastric cancer.**



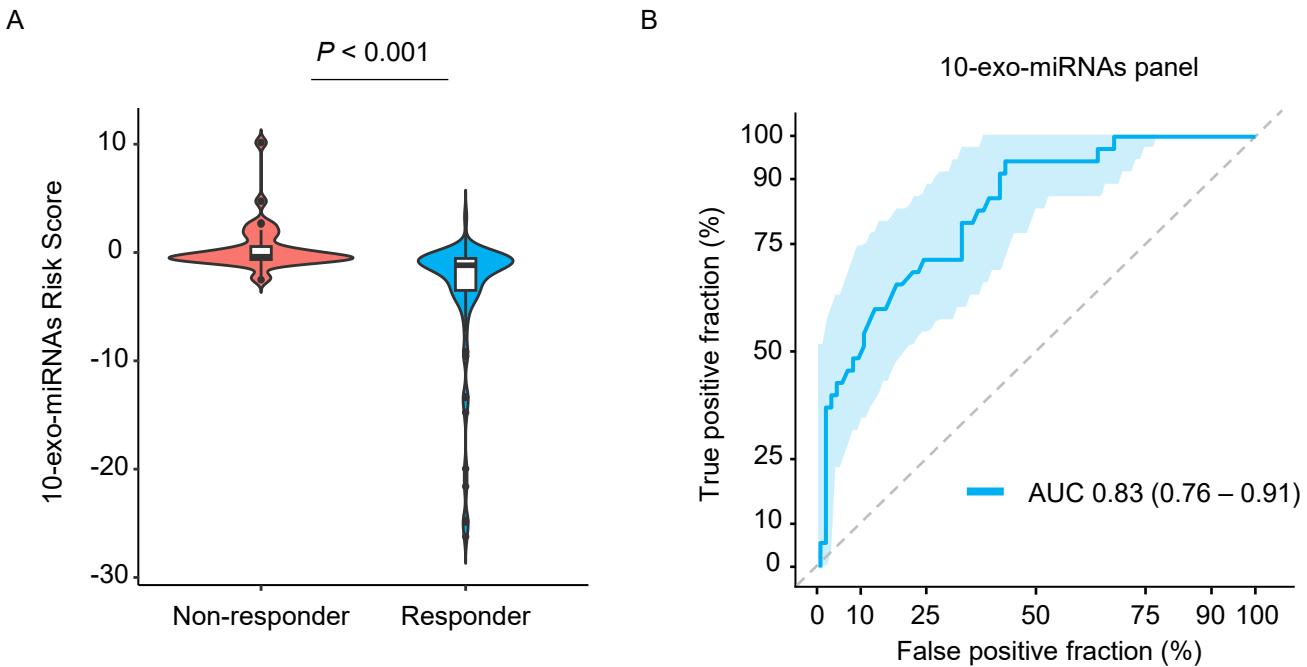
**Supplementary Figure S2: Genome-wide discovery of circulating exosomal miRNA candidates for predicting response to RAM plus PTX chemotherapy in gastric cancer patients in the small RNA sequencing assay.** ROC curve analysis shows the performance of the 10-exo-miRNAs panel. Red lines indicate the specificity and sensitivity with 95% CIs for each exo-miRNA under the best threshold; red points show the optimal threshold for specificity and sensitivity.

RAM, ramucirumab; PTX, paclitaxel; ROC, receiver operating characteristics; AUC, area under the curve; CI, confidence interval.



**Supplementary Figure S3: Prognostic potential of candidate exo-miRNAs in discovery cohort.** Kaplan-Meier survival plot showing overall survival in patients with gastric cancer stratified by expression levels of candidate exo-miRNAs. Kaplan-Meier curves are shown with 95%.

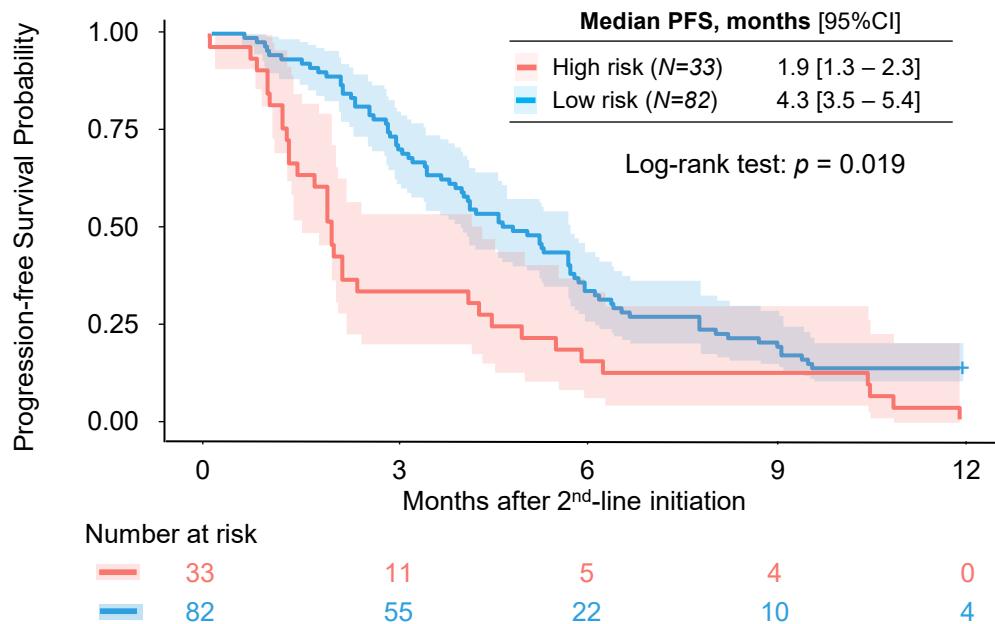
Exo-miRNA, exosomal microRNA; CI. RAM, ramucirumab; PTX, paclitaxel; CI, confidence interval; OS overall survival.



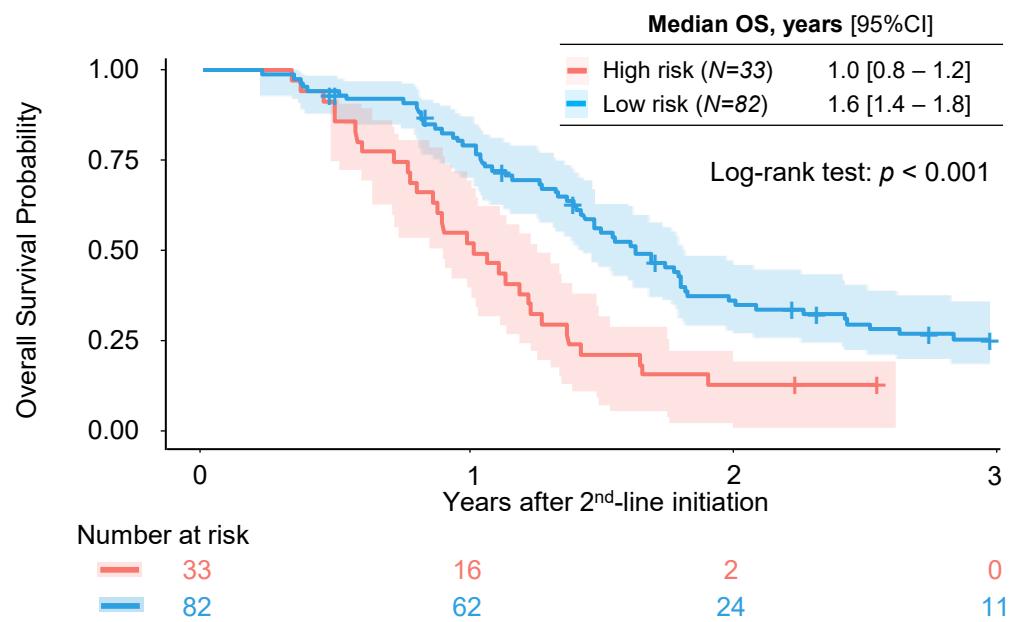
**Supplementary Figure S4: Evaluation of predictive potential of the candidate 10-exo-miRNA biomarker panel to identify gastric cancer patients with response and non-response to RAM plus PTX treatment.** Risk score analysis based on risk prediction formula in patients with response and non-response to RAM plus PTX treatment in IVY study cohort. (A) Violin plots for the 10-exo-miRNAs panel scores in patients with response and non-response. (B) ROC curve analysis to identify patients with response and non-response with AUC of 0.83 (95% CI 0.76 – 0.91)

ROC, receiver operating characteristics; AUC, area under the curve; CI, confidence interval.

A



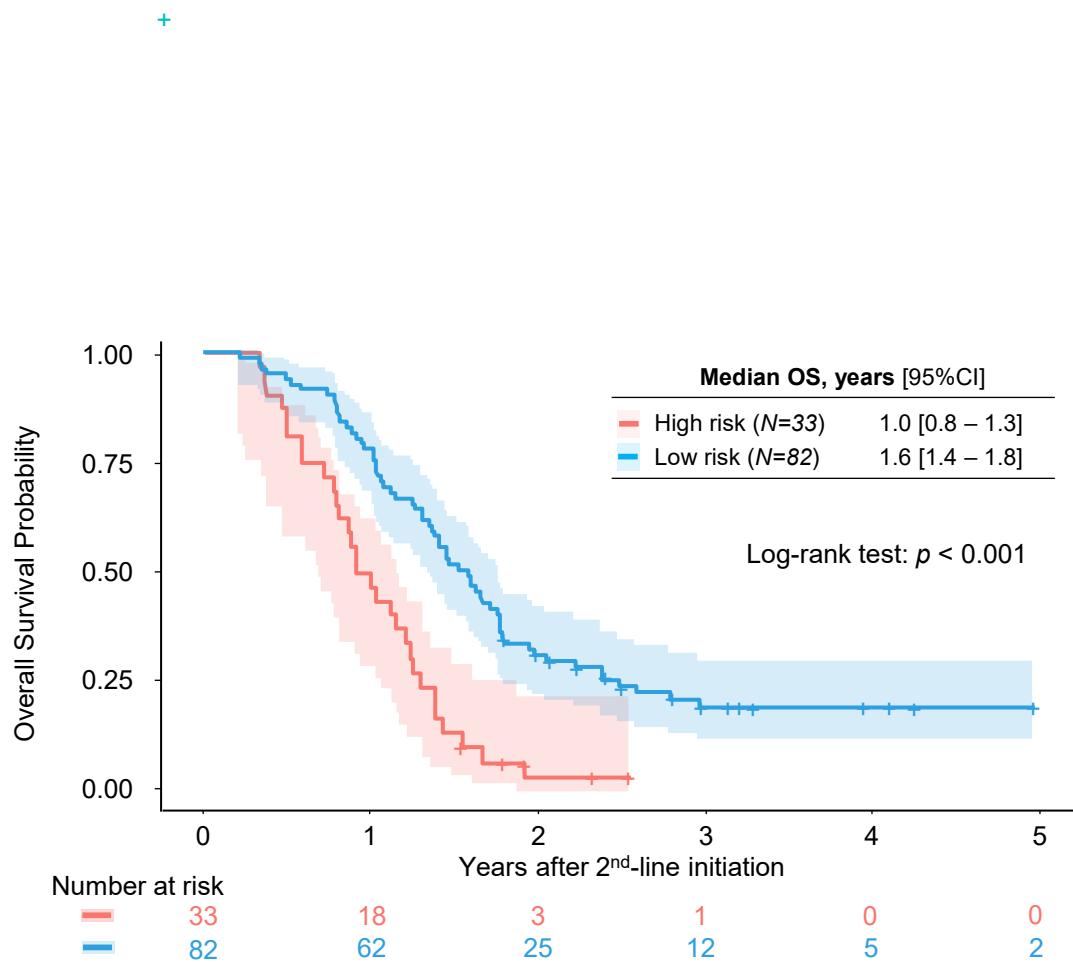
B



**Supplementary Figure S5: Prognostic potential of the candidate 10-exo-miRNA biomarker panel in gastric cancer patients undergoing RAM plus PTX therapy.**

(A) Kaplan-Meier curves of the progression-free survival for patients with high or low-risk scores in the 10-exo-miRNAs panel. (B) Overall survival for patients with high or low-risk scores in the 10-exo-miRNAs panel. ROC curves and Kaplan-Meier curves are shown with 95% CI.

PFS, progression-free survival; OS overall survival; CI, confidence interval.



**Supplementary Figure S6: Prognostic potential of the established 5-exo-miRNAs panel in gastric cancer patients undergoing RAM plus PTX therapy.**  
 Kaplan-Meier analysis of the risk panel for overall survival. Kaplan-Meier curves are shown with 95% CI.

OS overall survival; CI, confidence interval.