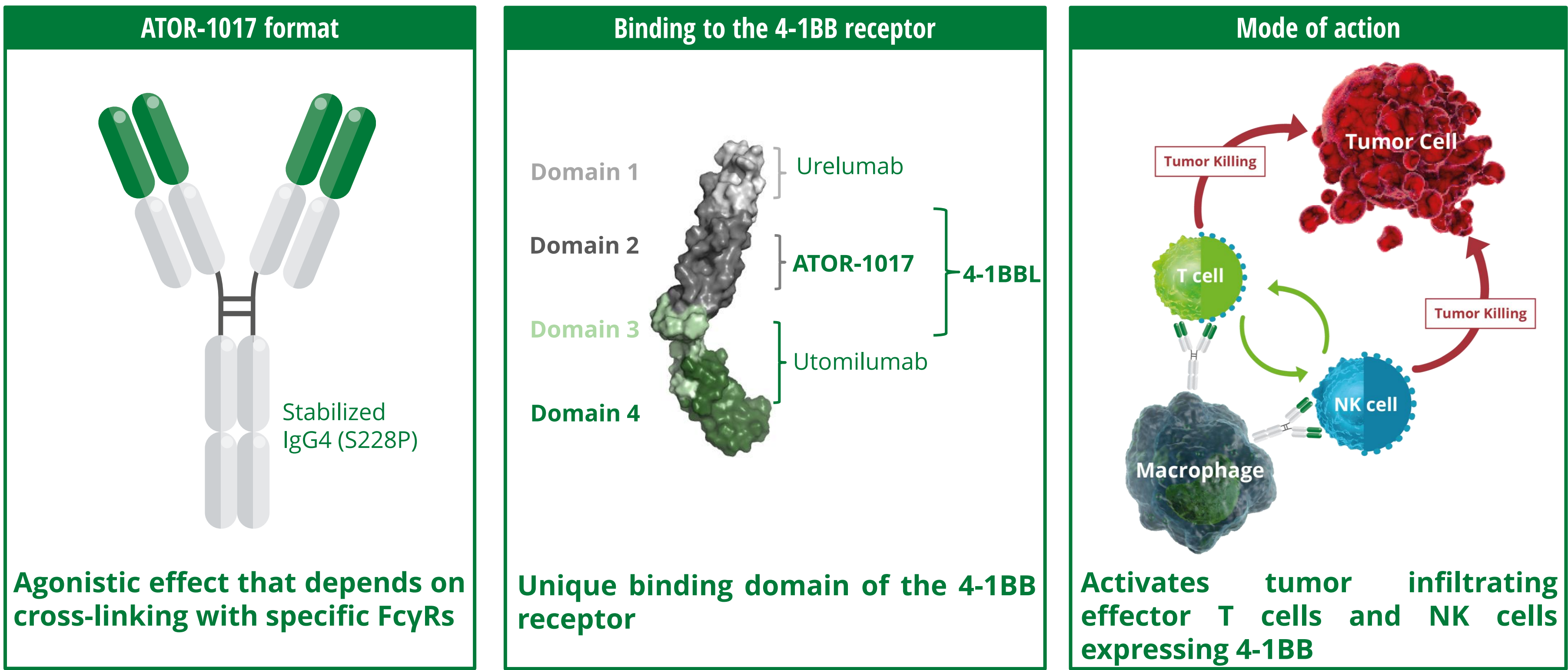




ATOR-1017, a tumor directed Fcy-receptor cross-linking dependent 4-1BB agonistic antibody

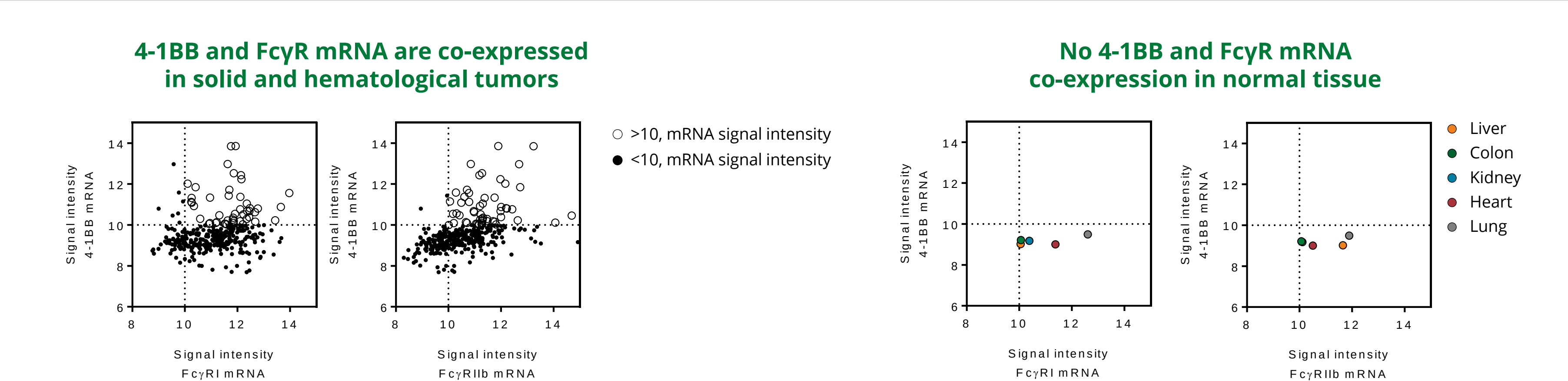
Karin Enell Smith*, Anna Rosén, Anna Dahlman, Karin Barchan, Ida Åberg, Doreen Werchau, Mia Thageson, Niina Veitonmäki, Christina Furebring, Peter Ellmark
Alligator Bioscience AB, Lund, Sweden *Presenting author

Background and Mode of Action

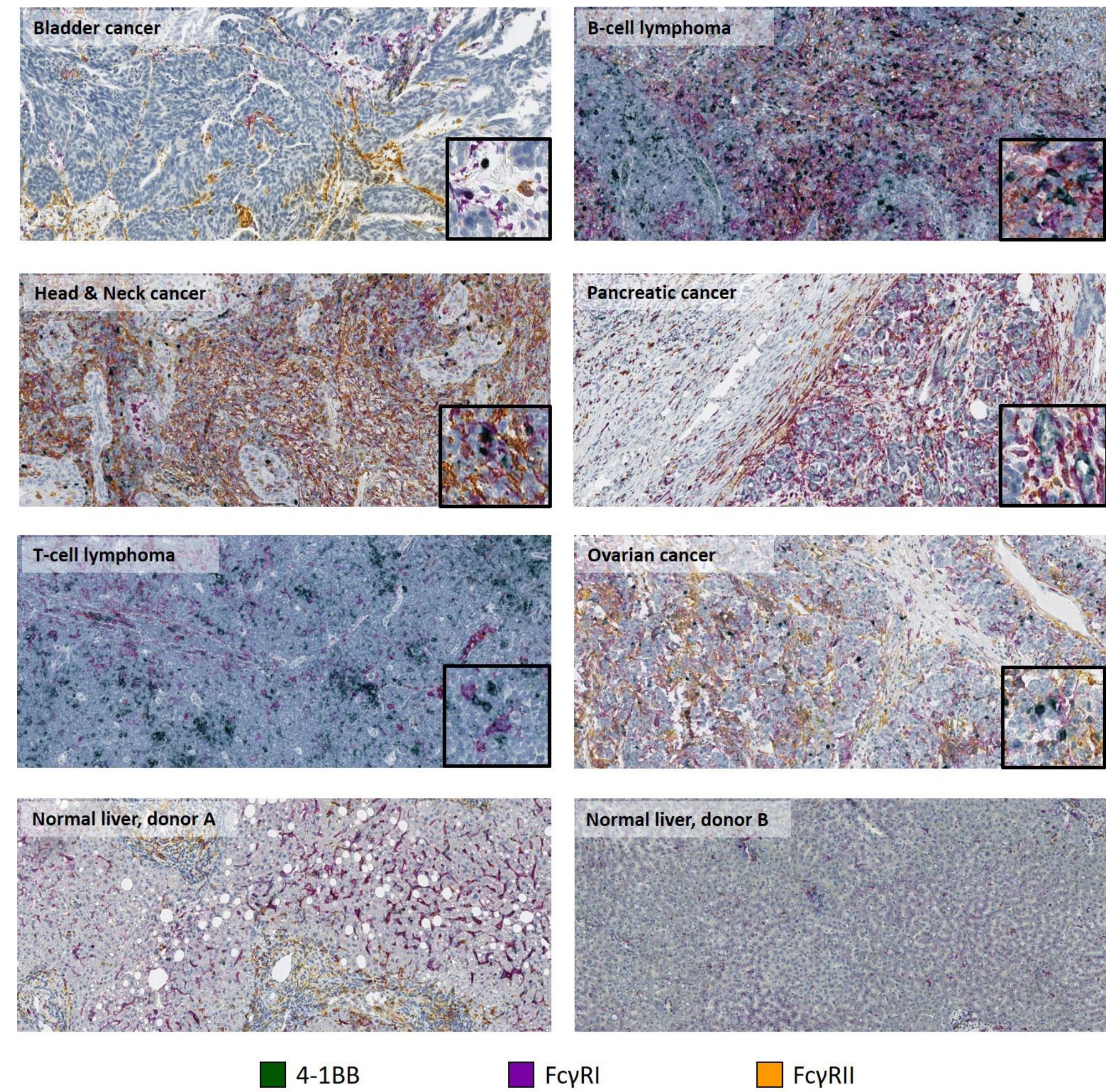


- ATOR-1017 is designed for an optimal efficacy and improved safety, by combining the IgG4-format that mediates a potent FcγR cross-linking with a unique binding epitope on 4-1BB
- ATOR-1017 generates a strong tumor directed immune response in patients with tumors infiltrated with 4-1BB expressing T cells and NK cells and cells expressing specific FcγRs

4-1BB and specific FcγRs are co-expressed and co-localized in tumors



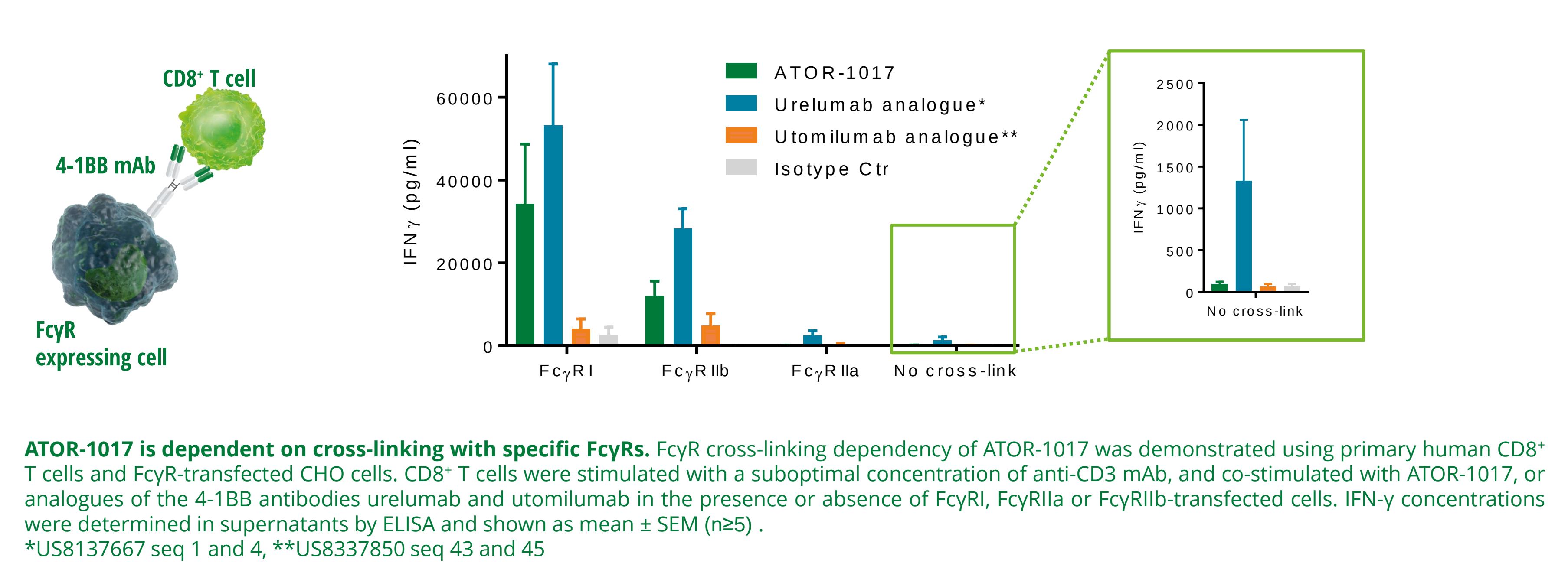
4-1BB and FcγRI or FcγRIIb mRNA are co-expressed in in tumor tissue. mRNA expression values were obtained from the public Affymetrix microarray platform. mRNA expression signal intensity range is between 5-19 on a log2 scale. Tumors with high level of co-expression (>10) include renal, breast, ovarian tumor and lung cancer as well as T and B cell lymphomas. No 4-1BB and FcγRI or FcγRIIb mRNA co-expression was observed in normal tissues such as liver, colon, kidney, heart and lung.



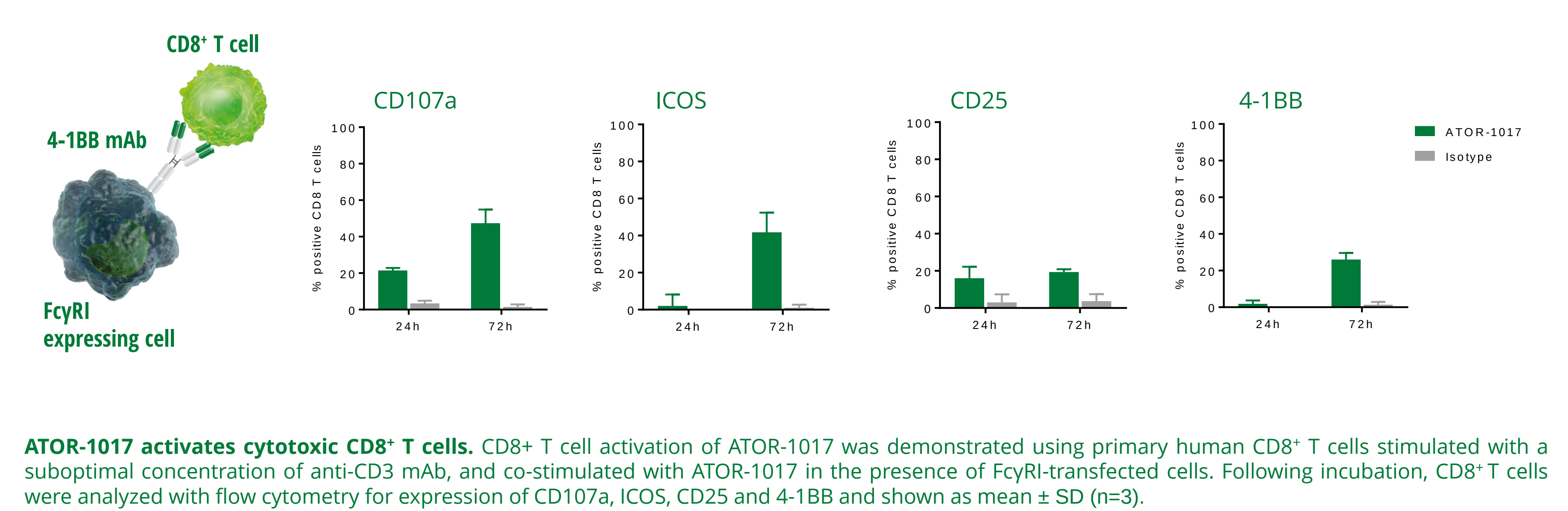
Indication	4-1BB co-localized w. FcγRs on immune cells	Highest freq. on immune cells	4-1BB co-localized w. FcγRs in intra-tumoral stroma	Highest freq. in intra-tumoral stroma
Bladder cancer	3/3	FcγRI or FcγRII	3/3	FcγRI or FcγRII
Lung cancer	1/2	FcγRII	2/2	FcγRII or 4-1BB
Head and neck cancer	2/2	FcγRI	2/2	FcγRI
Ovarian cancer	2/3	FcγRI or FcγRII	2/3	FcγRI or FcγRII
Pancreatic cancer	3/3	FcγRI	3/3	FcγRI
B cell lymphoma	3/3	4-1BB (2/3)	2/3	FcγRI or FcγRII
T cell lymphoma	1/3	4-1BB (2/3)	1/3	4-1BB (2/3)

4-1BB and FcγRI or FcγRII protein are co-expressed in tumor tissue but not in normal human liver. A multiplex immunohistochemical (IHC) staining method was developed and employed to assess the expression of FcγRI, FcγRII and 4-1BB in whole sections of formalin-fixed paraffin embedded (FFPE) tumors from different indications (n=2-3 donors per indication). 4-1BB (clone BBK-2, ThermoFisher) is visualized in green; FcγRI (clone OT13D3, Abcam) in purple; and FcγRII (clone EPR6658, Abcam) in orange.

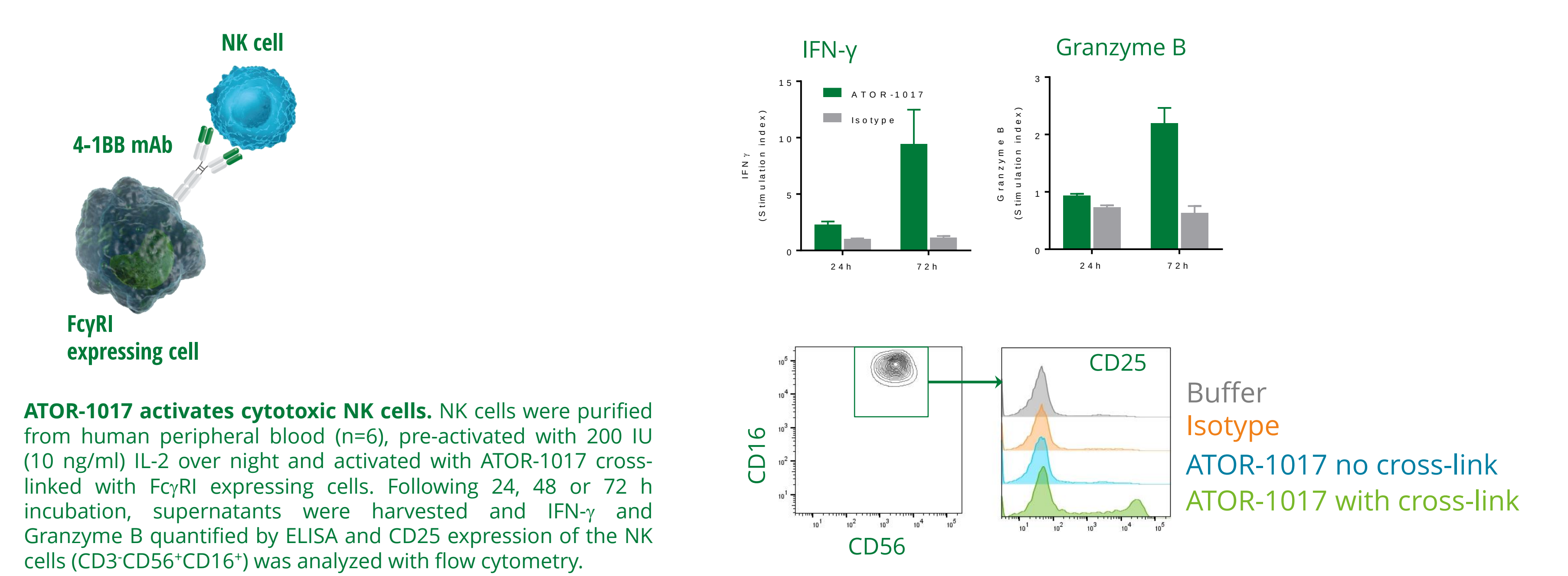
The agonistic effect of ATOR-1017 depends on cross-linking with FcγRs



ATOR-1017 activates cytotoxic CD8⁺ T cells



ATOR-1017 activates cytotoxic NK cells



Summary and Conclusions

- ATOR-1017 is an agonistic 4-1BB antibody activating cytotoxic CD8⁺ T cells and NK cells
- The agonistic function of ATOR-1017 is dependent on cross-linking with FcγRI and FcγRIIb
- 4-1BB is co-expressed and co-localized with FcγRI and FcγRII in several tumors
- The immune activation will be directed to tumors co-expressing both specific FcγRs and 4-1BB, which are potential biomarkers for patients and tumor indication selection
- ATOR-1017 is in pre-clinical development with initiation of phase I in 2019