



SELECTED OPPORTUNITY IN ONCOLOGY

ANTIBODIES HAVING SPECIFICITY TO NECTIN-4 (BIO15365 & 16330)

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Product factsheet

POC *in vivo*

▶ Target:

- ✦ Nectin-4, is a cell surface adhesion molecule expressed in tumors with adverse prognosis.
- ✦ As a Tumor Associated Antigen (TAA) Nectin-4 is found in 50%, 49% and 86% of breast, ovarian and lung carcinomas, respectively and not detected in corresponding normal tissues

▶ Product:

- ◆ Various proprietary chimeric anti-Nectine-4 antibodies (anti IgV domain) with different properties for various applications: treatment with naked (ADCC) or ADC and eligibility to treatment and follow-up

▶ Application:

- ◆ Treatment of breast, ovarian, lung, bladder cancers and carcinomas
- ◆ Treatment follow-up

▶ Rational / POC:

- ◆ In the serum of patients with these cancers, the detection of soluble forms of Nectin-4 is associated with a poor prognosis.
- ◆ Levels of serum Nectin-4 increase during metastatic progression and decrease after treatment
- ◆ Nectin-4 expression is associated with basal-like markers
- ◆ Nectin-4 overexpression activates cell migration and invasion *in vitro*; an anti-nectin-4 mAb reduces nectin-4 induced cell invasion *in vitro*
- ◆ Nectin-4 based ADC allows complete cure of a mouse model of cancer resistant to commercialized drugs (human triple negative breast tumor xenograft)
- ◆ Proprietary Ab display superior efficacy compared to Enfortumab (Ha-22 Ab) currently in clinical trial in various metastatic cancers

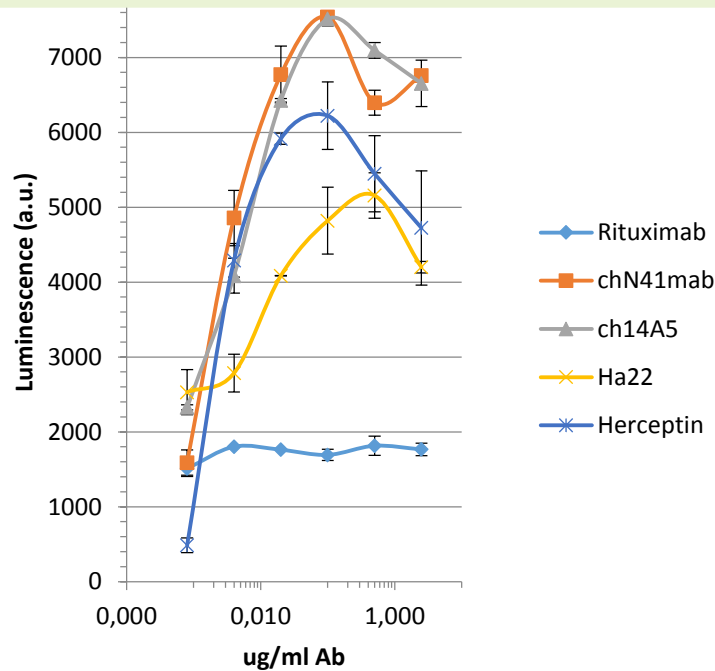
▶ Patent and publication:

- ◆ 2 antibodies N41 (WO2017042210A1) and 14A5 (PCT/EP2018/055109)) have been internationally patented
- ◆ Nectin-4: A New Prognostic Biomarker for Efficient Therapeutic Targeting of Primary and Metastatic Triple-Negative Breast Cancer M-Rabet M. et al. Ann Oncol. 2017 Apr 1;28(4):769-776. doi: 10.1093/annonc/mdw678.

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Proof of concept

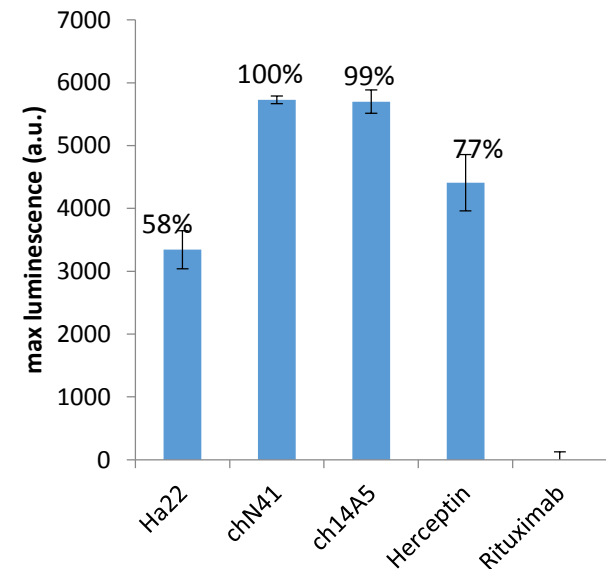
Antibody Dependent Cell mediated Cytotoxicity : N41 and 14A5 in vitro versus Ha22



ADCC	Ha22	N41	14A5	Herceptin	Rituximab
IC50 (ng/ml)	24	4	5.8	2.8	>2500

ADCC IC50 of ch14A5: $\approx$ 4 fold better than Ha22

lysis efficiency



Efficiency	Ha22	N41	14A5	Herceptin	Rituximab
max lysis	5156	7540	7513	6222	1814

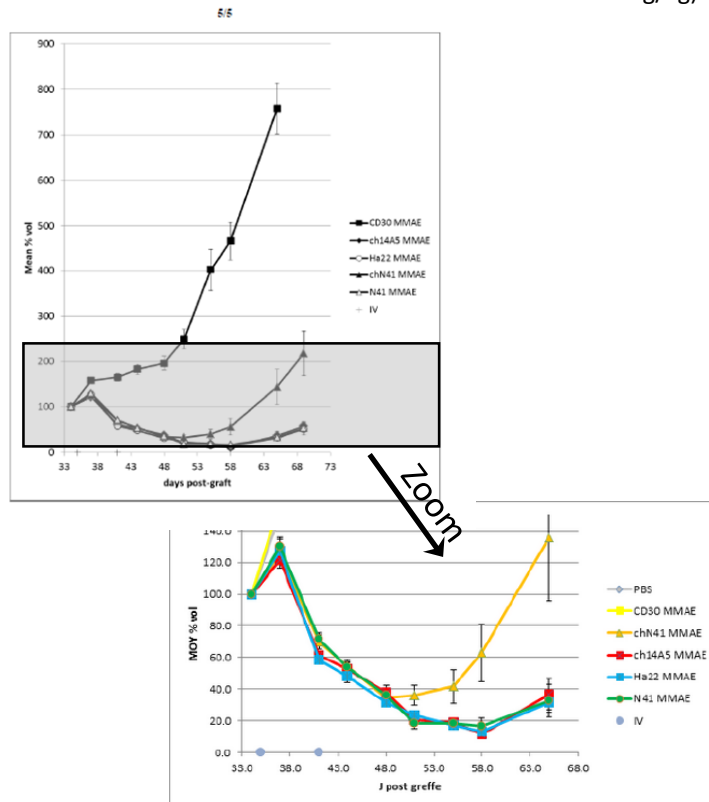
ADCC killing efficiency of Ha22 is $\sim$ half of ch14A5 and chN41

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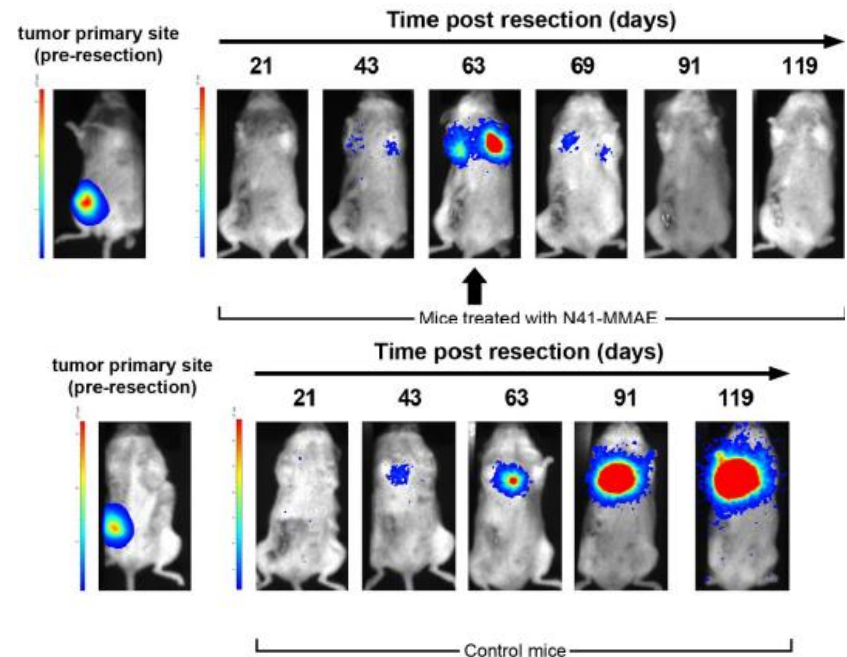
Proof of concept

a rapid and long-lasting tumor regression. N41mab-MMAE

Comparison of tumor cell growth in vivo after treatment with the different ADC (in vivo test: SUM190 xenografted NSG mice: 2 x 2.5mg/kg)



PDX 317



N41mab-vcMMAE treatment of PDX317 and PDX400 mice impacts spontaneous metastasis progression.

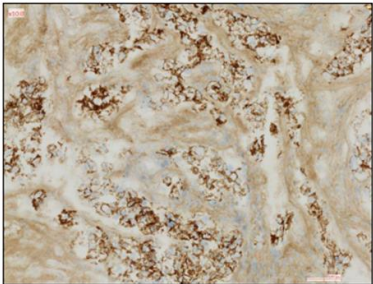
After surgical resection of primary mammary tumors, spontaneous metastasis occurrence was followed by bioluminescence imaging. Metastatic mice were treated with N41mabvc-MMAE (left) or vehicle (right) by caudal i.v. injection. Quantification of total bioluminescence signal was measured.

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Proof of concept

Overview & Next steps

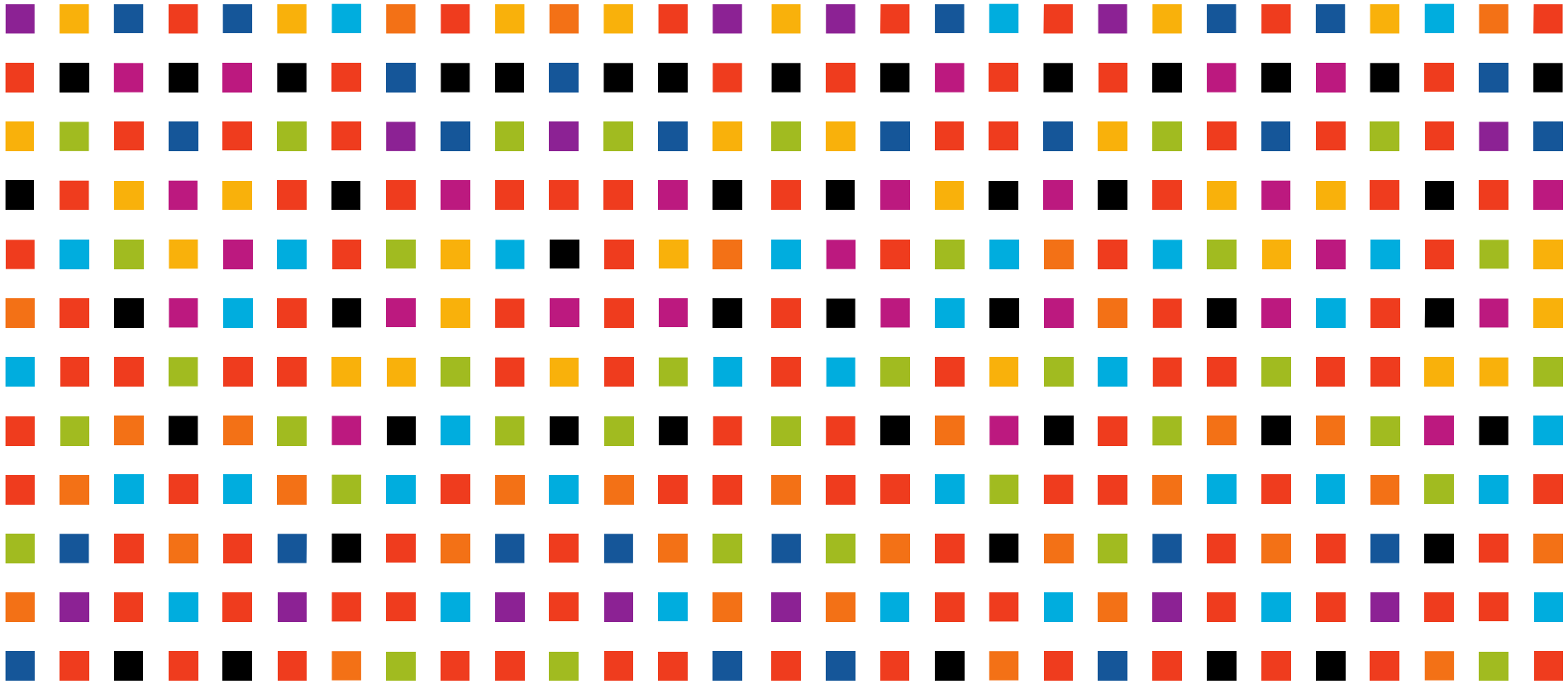
	Epitope	Migration/invasion	ADC	ADCC	IHC frozen
N41	Different from Ha22 Overlapping with 14A5	Block	++	+++	+++
14A5	Different from Ha22 Overlapping with N41	Ongoing	+++	+++	?
Ha22 SG	Different from N41 & 14A5	Ongoing	+++	++	+++



Frozen section
N4.61: 0.5ug/ml

Next steps

Ongoing generation of multispecific antibodies for diverse application including imaging



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