

# N-Myristoyltransferase (NMT) inhibitors are completely novel payloads for Antibody Drug Conjugates that deliver extensive tumor regression at well tolerated doses

MyricxBio

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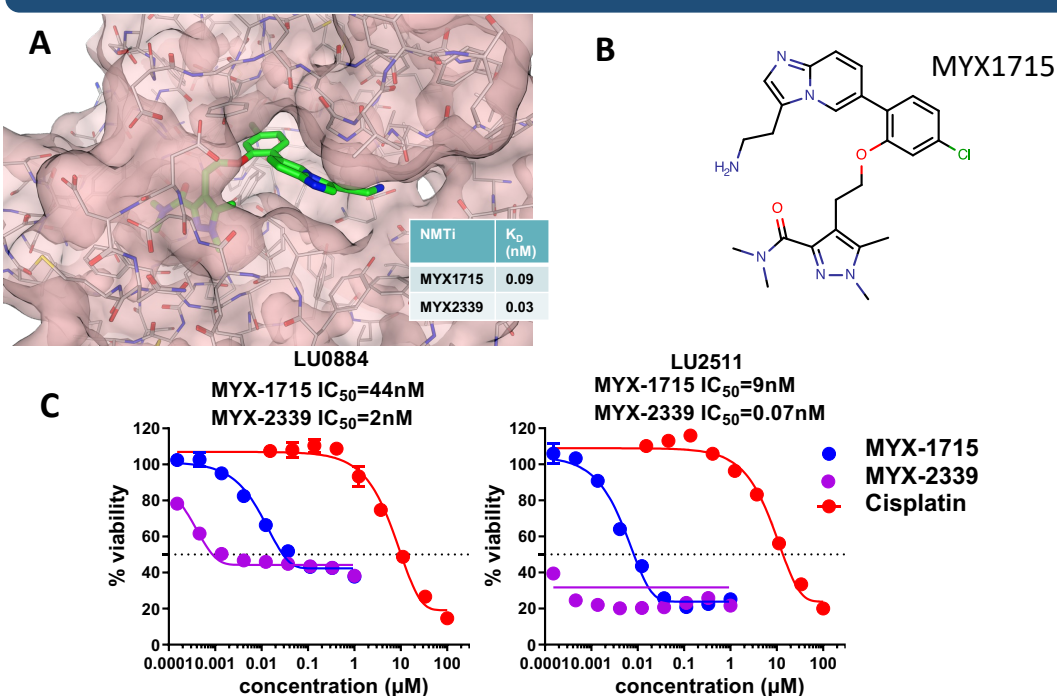
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## Introduction

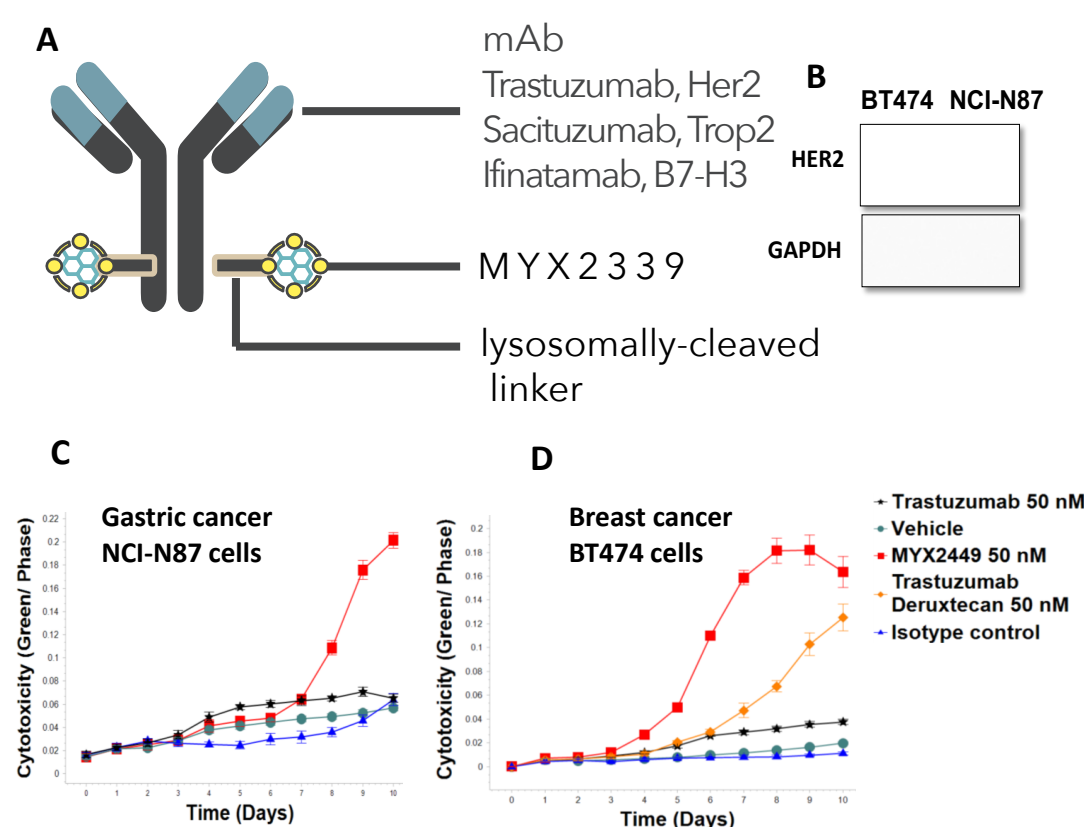
N-myristoylation is the N-terminal modification of proteins with myristic acid, a 14-carbon fatty acid. Catalysed by two enzymes, N-myristoyltransferase (NMT1, NMT2), this modification can be co- or post-translational [1]. NMT inhibitors (NMTi) have been shown to inhibit viability and growth of cancers [2]. Here, we have developed novel highly potent and selective NMTi which are cytotoxic in multiple cell lines and exhibit tumour regression in *in vivo* models. To explore targeted delivery of NMTi, we tethered a selective NMTi to trastuzumab (HER2+ mAb), Sacituzumab (Trop2+ mAb) and Ifinatamab (B7-H3+ mAb) to produce antibody drug conjugates (ADC) each of which display excellent *in vivo* efficacy in solid cancer xenograft models at well tolerated doses.

## Cytotoxic effects of NMTi in cancer cell lines

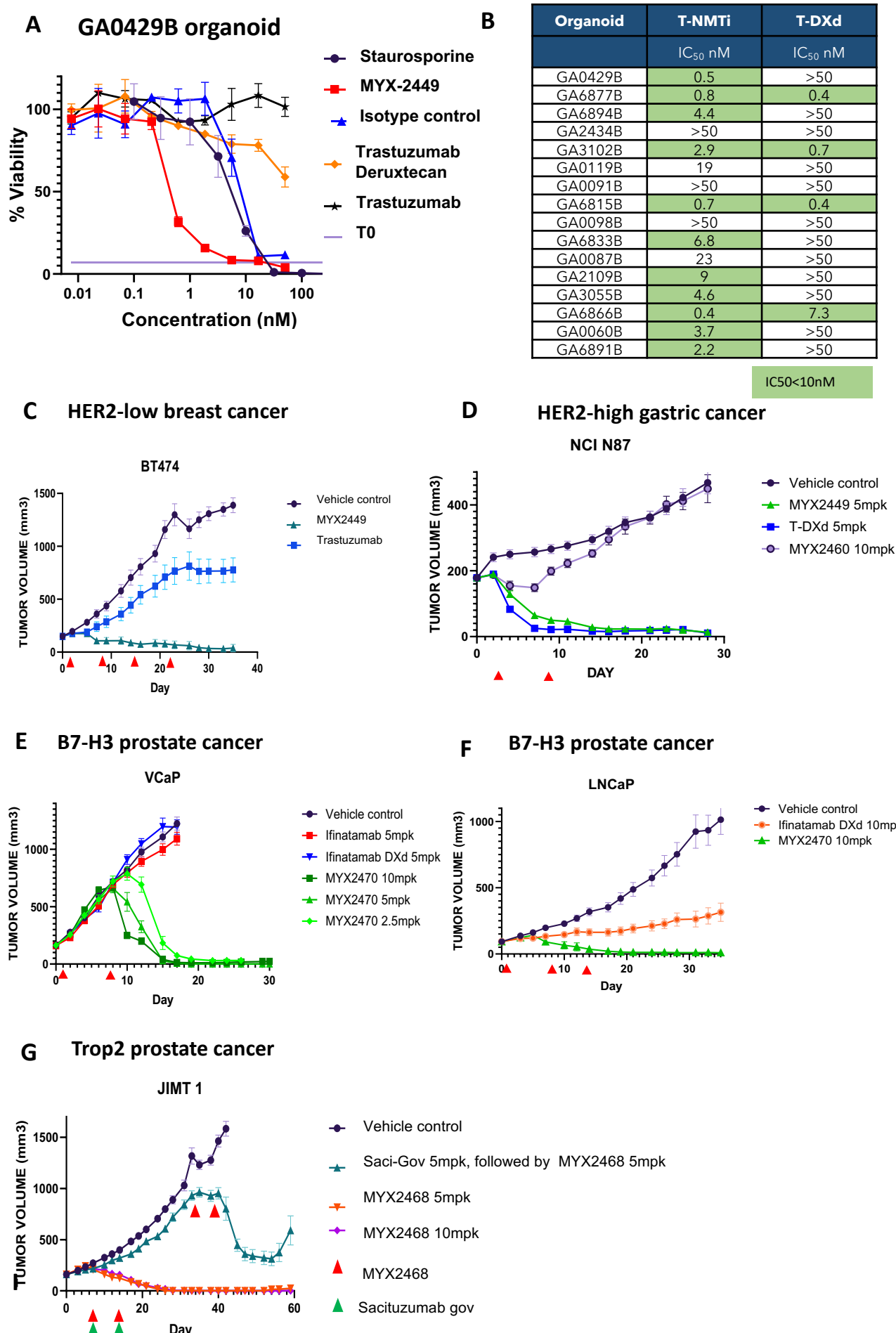


**Figure 1:** Structure (A) and dissociation constant (K<sub>d</sub>) of NMTi (B) Structure of MYX1715. (C) IC<sub>50</sub> of MYX1715 and MYX2339 in NSCLC PDXs

## Antitumour efficacy of NMTi - ADCs

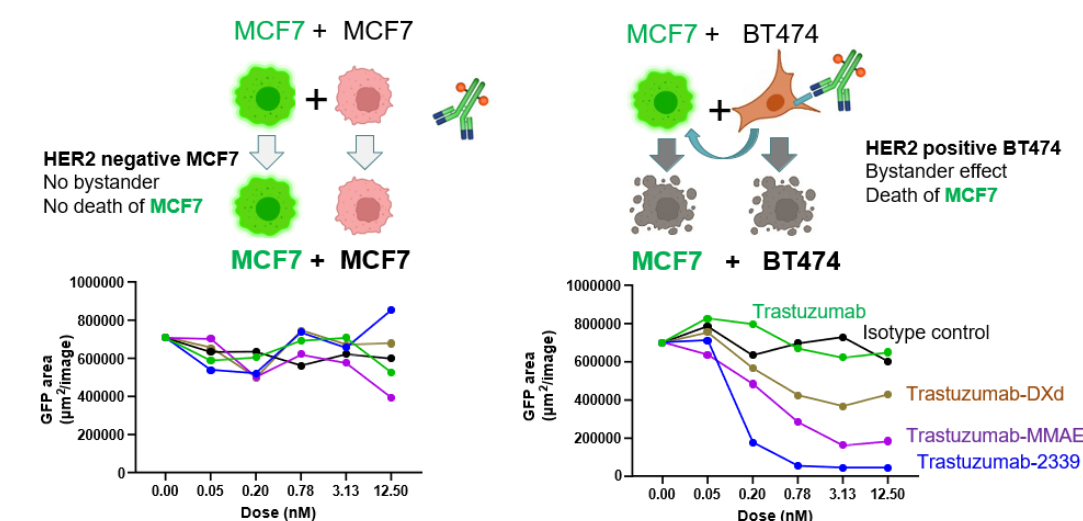


**Figure 2:** Cartoon of NMTi- ADCs, Her2-NMTi (MYX2449), Trop2-NMTi (MYX2468) and B7-H3-NMTi (MYX2470) (A). Expression of HER2 in breast (BT474) and gastric (NCI-N87) cancer cell lines (B). Anti tumor effects of MYX2449 in gastric (C) and breast cancer (D) cell lines



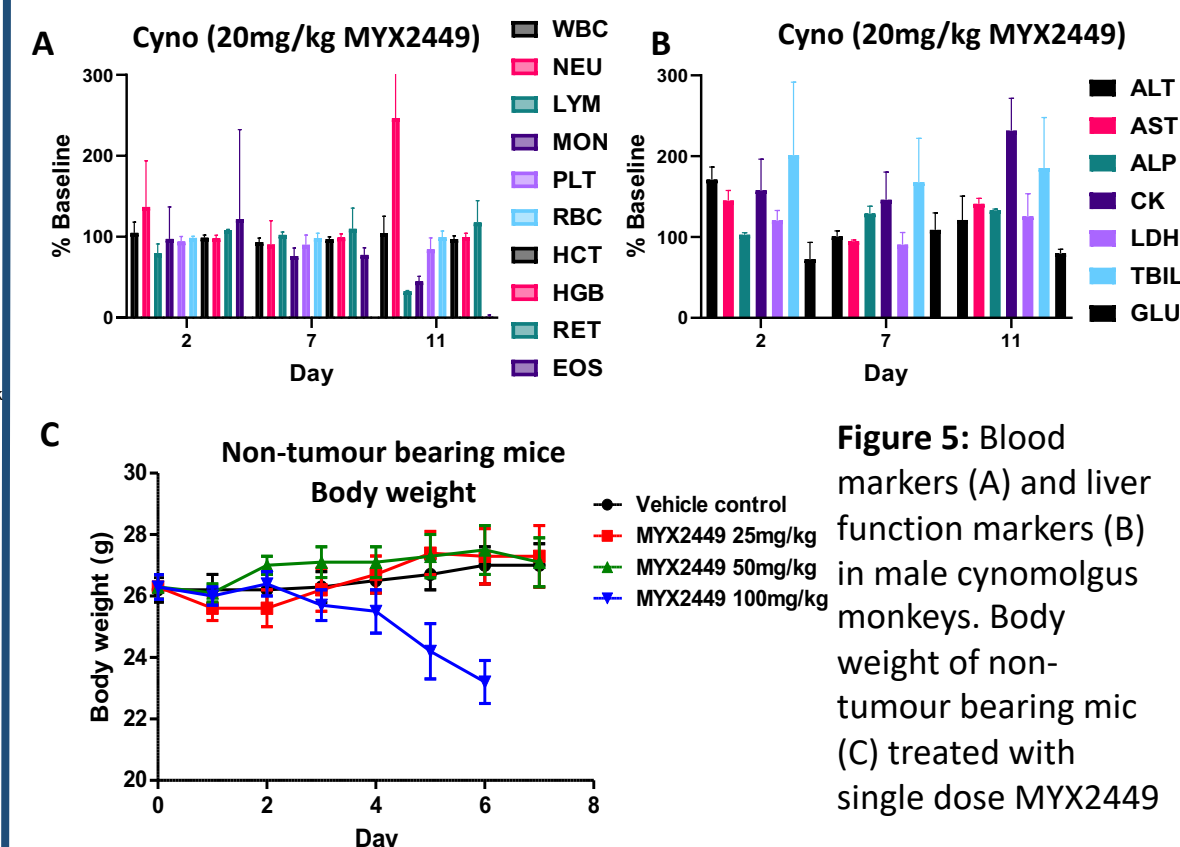
**Figure 3:** Antitumour effects of MYX2449 in gastric cancer (GC) PDX organoids (A,B). Antitumour effects of MYX2449 in HER2 breast cancer (C) and HER2 gastric cancer (D), MYX2470 in B7-H3 prostate cancers (E,F) and MYX2468 in Trop2 breast cancer (G) xenograft models.

## MYX2449 exhibits good bystander effect in cell lines



**Figure 4:** Bystander effect of MYX2449.

## In vivo tolerability of MYX2449



**Figure 5:** Blood markers (A) and liver function markers (B) in male cynomolgus monkeys. Body weight of non-tumour bearing mice (C) treated with single dose MYX2449

## Conclusion

NMTi-ADCs MYX2449 (Her2), MYX2468 (Trop2) and MYX2470 (B7-H3) each demonstrate extensive tumor regression in a range of solid cancer models at well tolerated doses with superior or equal efficacy to comparator Topo1-ADCs. MYX2449 was shown to be well tolerated in mice (50mpk) and Cyno (20mpk). MYX2468 and MYX2470 are currently in Cyno repeat dose tox studies. NMTi has the potential to deliver a completely novel and highly differentiated class of ADC payload.

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