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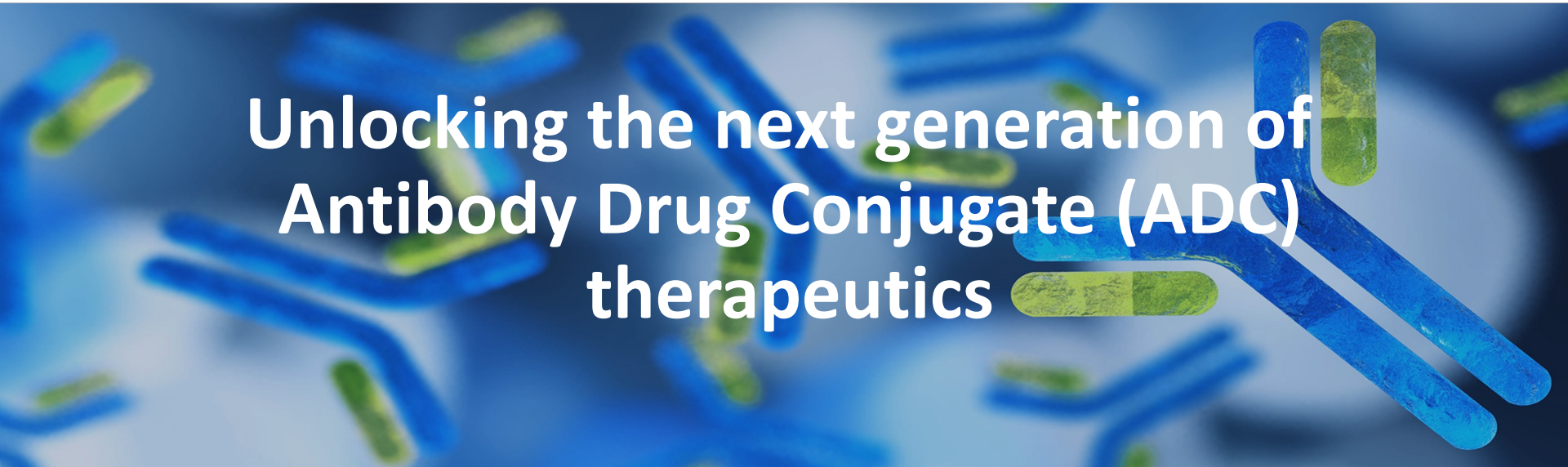
Linking targeted therapy to better patient outcomes

BioEquity 2023



Unlocking the next generation of Antibody Drug Conjugate (ADC) therapeutics

Summary

- **University of Cambridge** spin-out.
- **Strategy** to generate value via inhouse and partnered Antibody Drug Conjugates (**ADCs**) therapeutics. Three discovery stage in-house programmes
  - Targets selected and proprietary antibodies to Target 1 generated
- Patented linker technology ('hiDAR') enables **plug-and-play** payload flexibility at high Drug-to-Antibody Ratios (DAR) → "Any payload at any DAR"
- **Unique capability** to advance ADC field far beyond the limitations of a narrow range of cytotoxic payloads such as MMAE and Dxd (Enhertu)
- **Proven capability** to construct stable ADCs with a range of different payloads.
- Closed £2.6M seed financing in 2022. Series A raise to achieve clinical PoC scheduled for 2024

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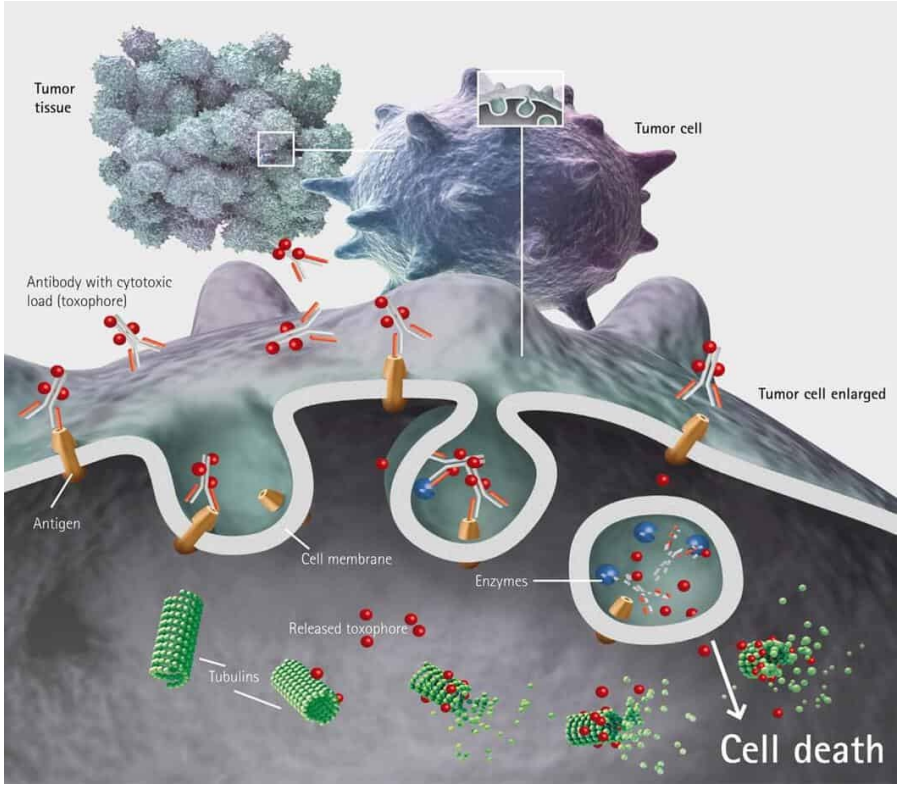
Antibody drug conjugates – an introduction (1)

- ADCs are a class of drugs designed as a targeted therapy for treating cancer
- ADCs combine the cell specificity of a monoclonal antibody with the cancer-killing capability of a cytotoxic drug
- ADCs discriminate between normal and cancer cells



ADCREVIEW

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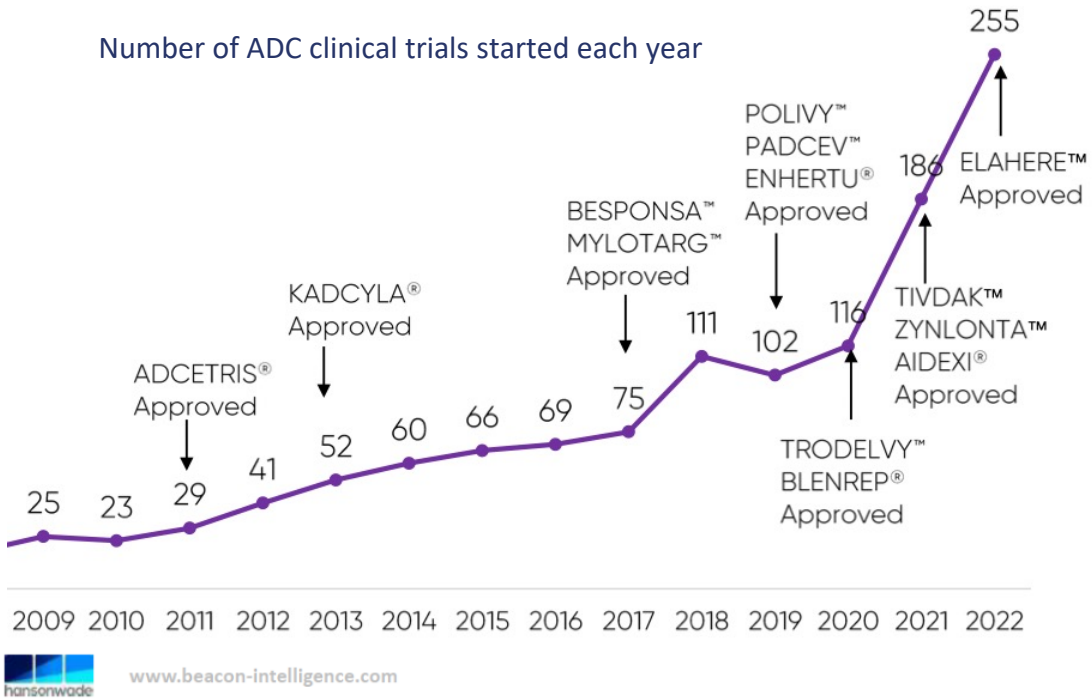
Antibody drug conjugates – an introduction (2)

Mature oncology drugs, with 12 ADCs approved by the FDA



Companies with approved ADCs

ADC resurgence resulting from incremental technology improvements and the success of Daiichi's Enhertu (Dxd payload)

Pfizer acquires Seagen for $43B

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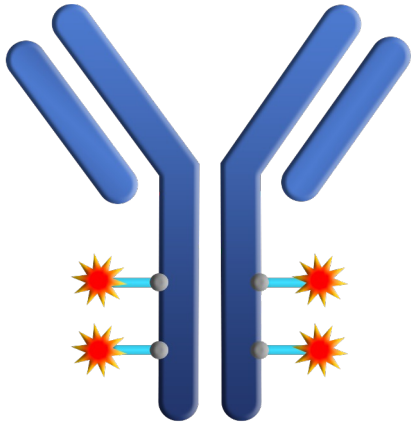
Problem – payload hydrophobicity and poor therapeutic indexes

The number of cancer killing payloads conjugated to the targeting antibody is limited:

Payload hydrophobicity (aggregation and fast clearance) limits the DAR → High potency payloads & no flexibility → High ADC drug toxicity → **LOWER** dosing



Drug-Antibody Ratio
DAR = 4

REDUCED
Therapeutic index → **LOWER**
Clinical success

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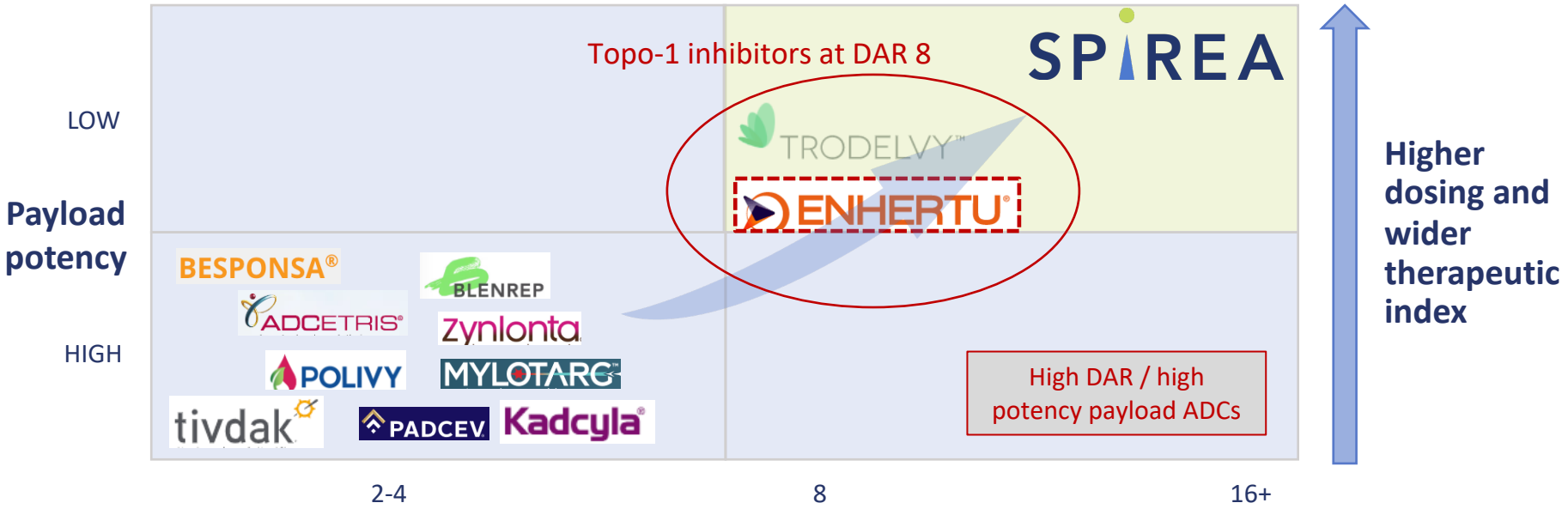
Problem - limited developments in payloads and DAR

The success of Enhertu has reinvigorated ADCs but the even the newer ADCs are restricted to one family of payloads (Topo-1 inhibitors) at DAR 8.



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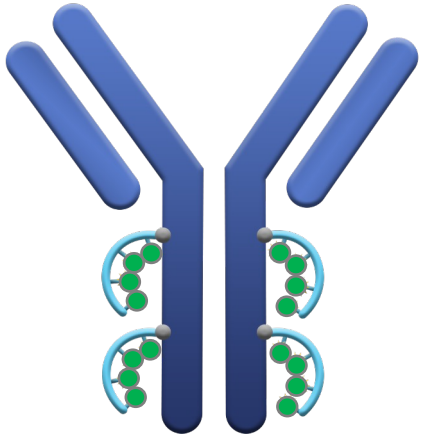
Spirea's hiDAR linker technology increases payload options

hiDAR enables very high DARs by **preventing ADC aggregation** and fast clearance → Lower potency payloads & payload flexibility → Lower ADC toxicity → **HIGHER** Dosing



DAR > 16

INCREASED Therapeutic index → **HIGHER** Clinical success

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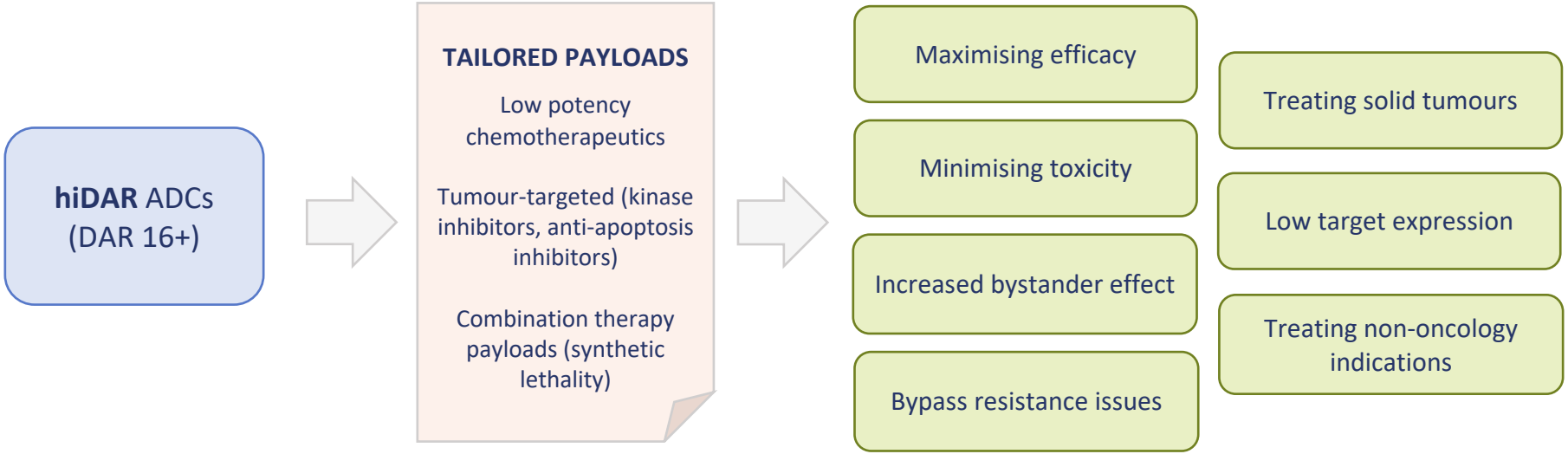
Payload flexibility with hiDAR will be transformational

Spirea's hiDAR linker technology offers plug-and-play capability to change the payload to address a particular clinical need



Profound effect on drivers of efficacy & safety → better patient outcomes

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Business strategy and partnering

R&D STRATEGY

- Proprietary pipeline
- Oncology - solid tumours
- Clinically-validated targets
- Tailored payloads

PARTNERING

- Product collaborations
  - Novel targets
  - Novel small molecule payloads
  - Radioimmunoconjugates
  - Oncology/non-oncology
  - Programme rescue
- Product specific licensing

Currently in talks with a high profile global pharmaceutical company

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Highly versatile and developable high DAR ADCs

Model hiDAR ADCs (DAR 16+) with 3 different payloads have been generated

Antibody	Payload	Linker	Payload release	Avg. DAR
Trastuzumab	MMAE	**hiDAR**	Peptide	**18**
Trastuzumab	SN38	**hiDAR**	pH	**18**
Trastuzumab	Payload 3*	**hiDAR**	Peptide	**16**

→ No aggregation. Good PK profile. Good tolerability. Good anti-tumour activity

→ Versatility and Developability demonstrated

* Undisclosed

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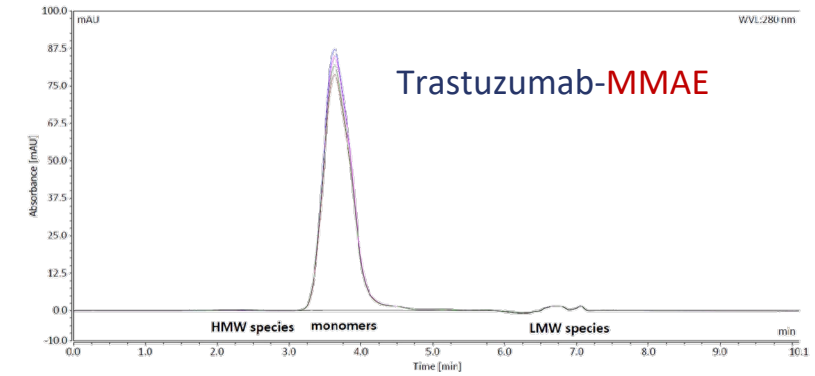
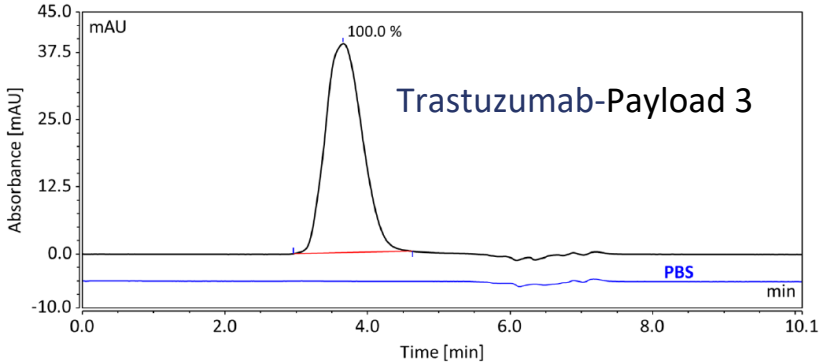
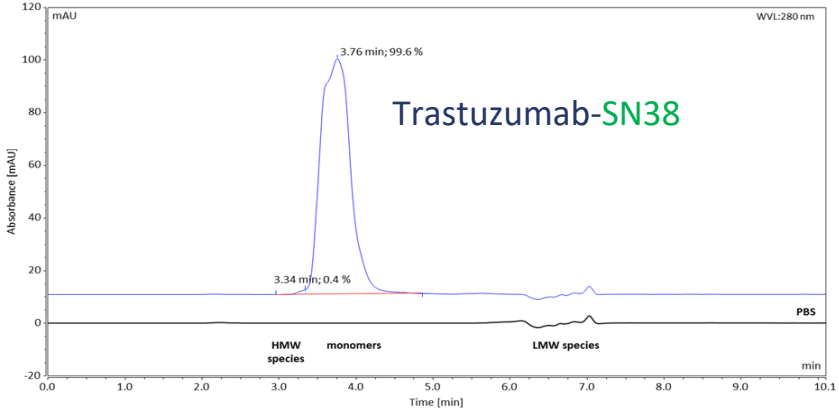
Unmatched capability to generate DAR 16 ADCs without aggregation

Spirea DAR 16 ADCs show no evidence of aggregation (>95% monomeric by SEC)



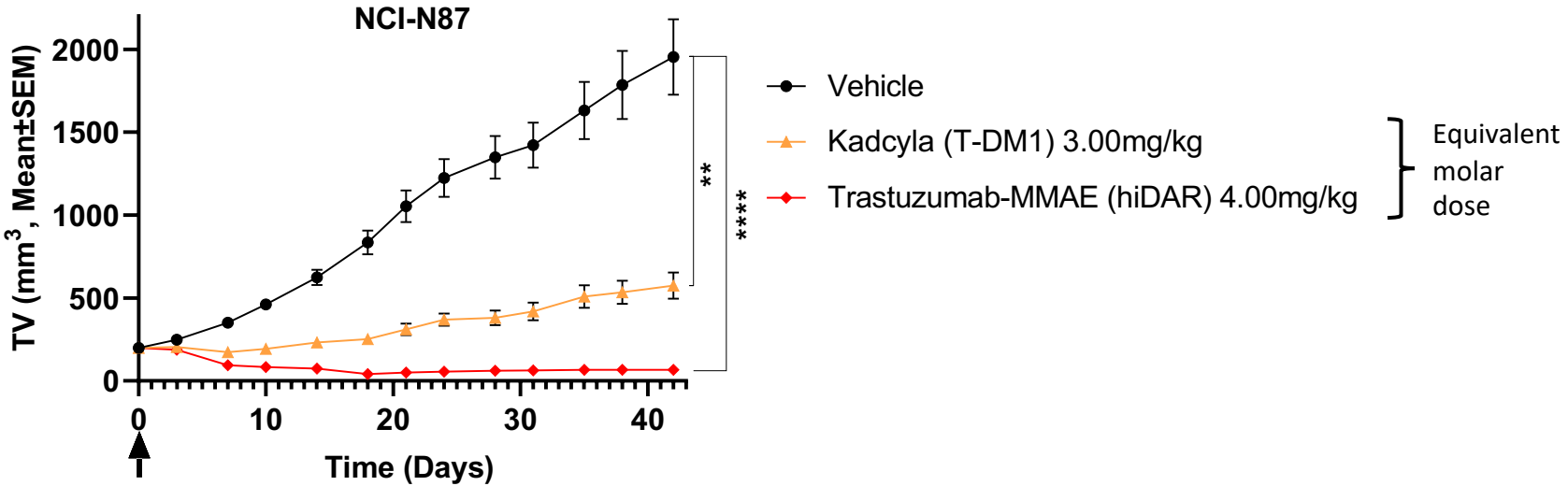




Superior and highly reproducible manufacturing with a range of payloads compared to other high DAR platforms

Tumour cell killing in vivo with hiDAR MMAE ADC

Tumour regression and complete inhibition of tumour growth observed at 4mg/kg over 6 weeks



DAR 18 MMAE ADC shows better tumor growth inhibition than Kadcyla at equivalent molar dose

NCI-N87 human gastric cancer xenograft model

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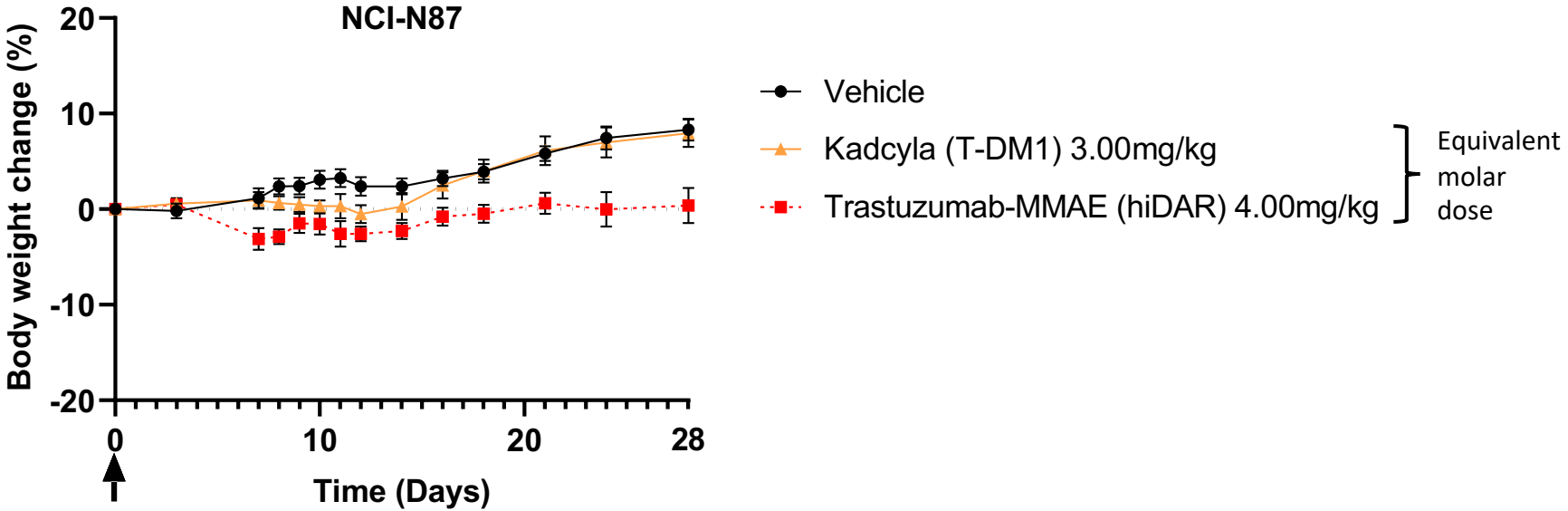
hiDAR MMAE ADC very well tolerated



DAR 18 MMAE ADC very well tolerated in mice

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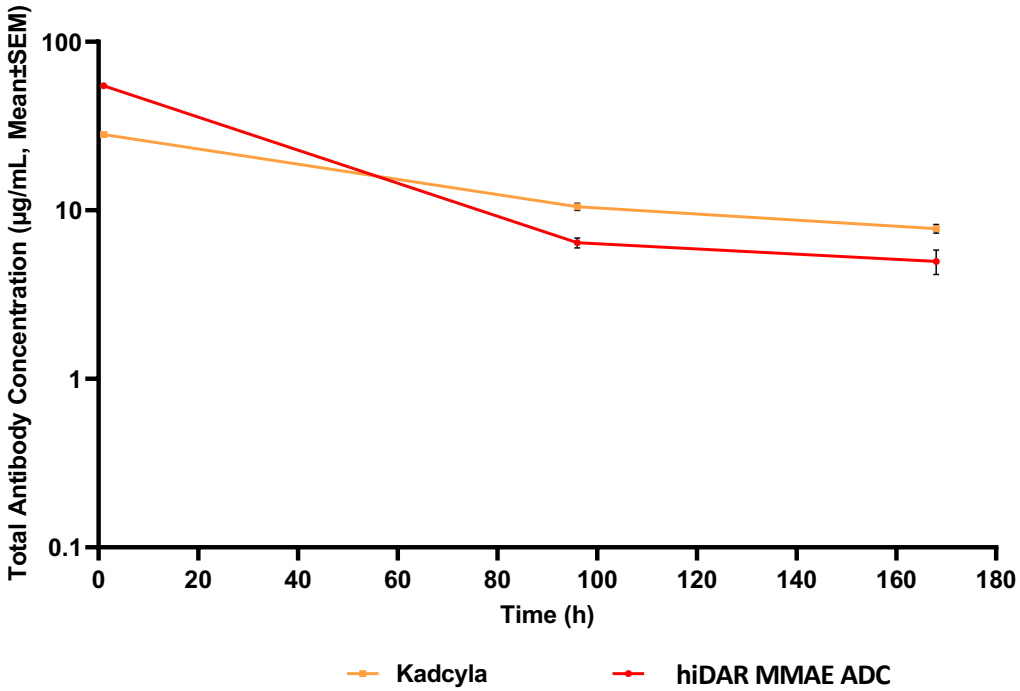
hiDAR MMAE ADC - Good PK profile at high DAR

hiDAR MMAE (DAR 16) ADC demonstrates comparable profile to Kadcyla (approved DAR 3.5 DM1 ADC)



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Team

MANAGEMENT

Dr Myriam Ouberai
Chief Executive Officer

Dr Adam Collier
Chief Business Officer

BOARD

- **Jane Dancer**, Chair
- **Gaynor Fryers**
- **Christine Martin**
- **Barbara Domayne Hayman**
- **Mike Murphy**

WORLD CLASS ADVISORS

- **Anthony Tolcher, MD**
- **Prof John Hartley**
- **Dr Paul Varley**
- **Dr Rakesh Dixit**

Key goals for Series A

- Progress programmes to value inflection points, at least **one programme to clinical PoC**
  - Tailor choice of payload mode-of-action to match target-indication
  - Screen targets against clinical comparators utilising hiDAR plug-and-play capability
  - Fast go/no-go decisions based on efficacy → select best preclinical candidates
- Establish significant partnerships with pharma
- Expansion of the management and scientific team

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