

Subcutaneous administration of ADCs

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Disclosures



Co-founder: Recobia Tx, TherO2, TMAD

Shareholder: M&Wine, Recobia Tx, TherO2, L.E.A.F. Pharmaceuticals

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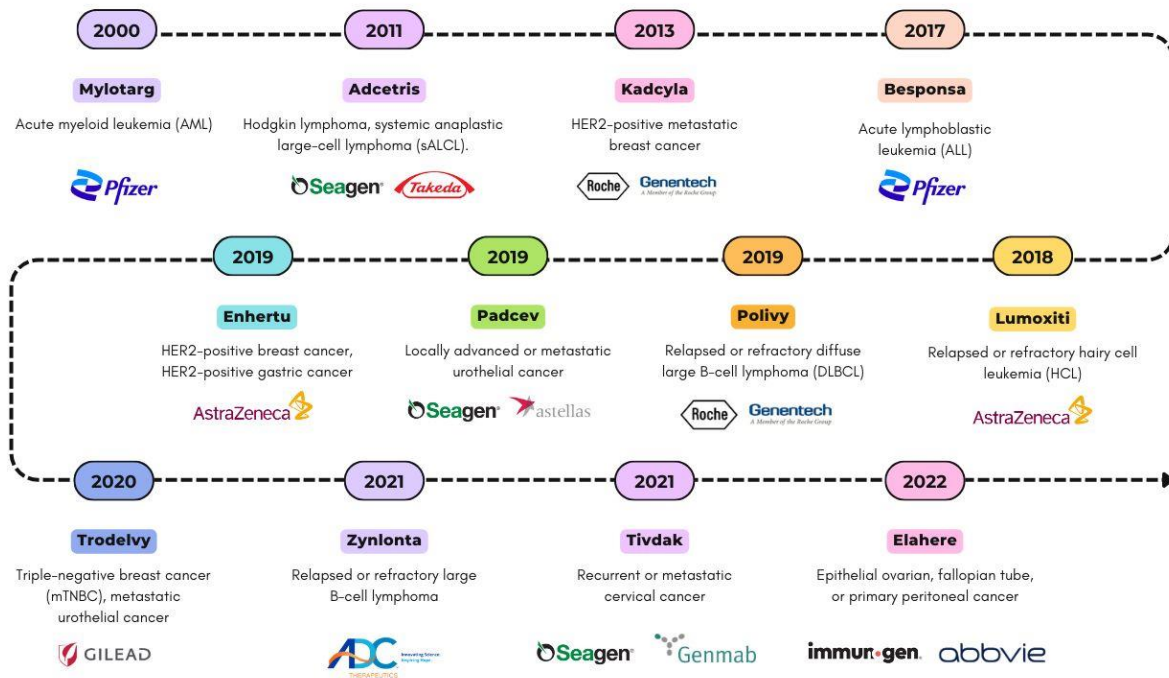
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**NEXT-GENERATION
DELIVERY INNOVATIONS**



Clinically approved ADCs

- 13 ADCs clinically approved
- 100+ in clinical trials
- All are developed for IV route



STEVE HARVEY • GENE MAKER • CAMENA BIOSCIENCE



Subcutaneous translation is a multi-benefit platform for every player in the value chain



PATIENTS

Less painful, no infection, stronger treatment adherence



HEALTHCARE PROFESSIONALS

Time savings with less preparation, fewer risks



HOSPITALS / SPONSORS

Reduced medical resource utilization and treatment costs

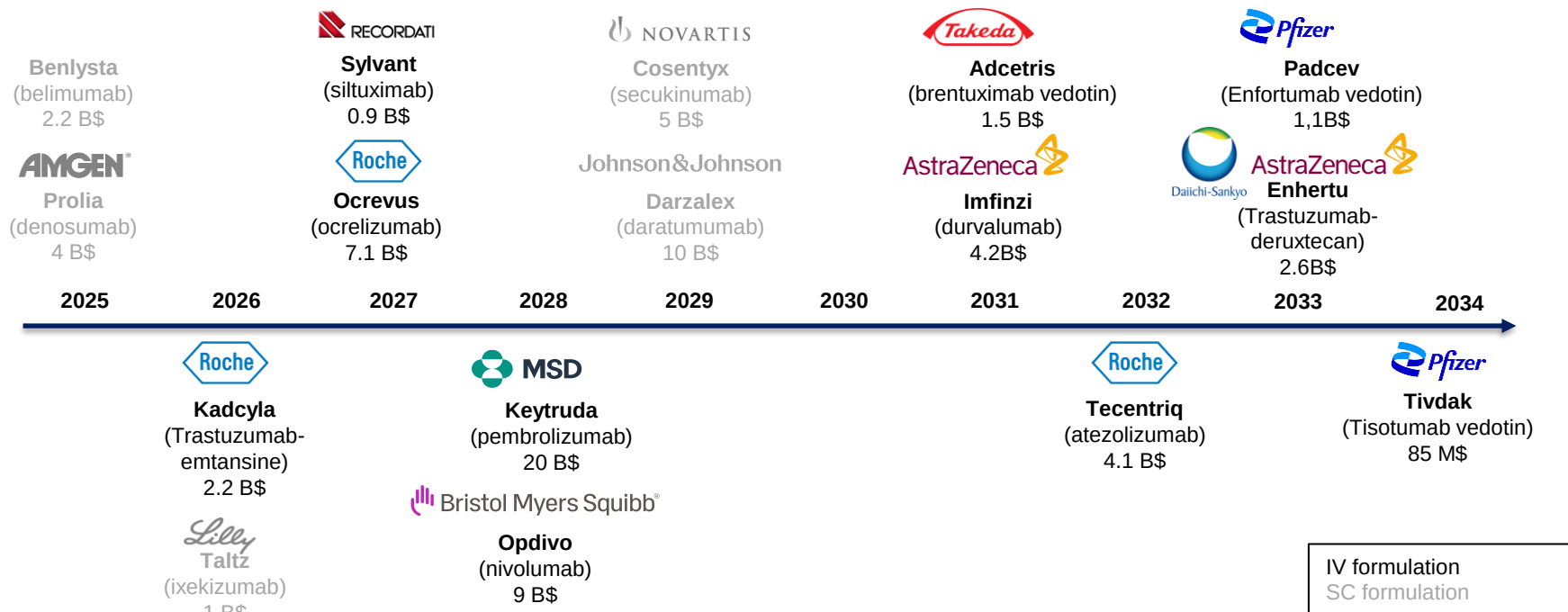


PHARMACEUTICAL INDUSTRY

Competitive advantage and life cycle management



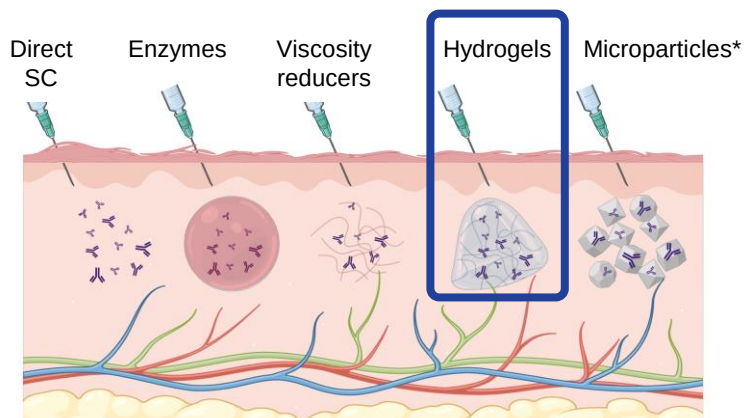
Patent cliffs for mAbs and ADCs over the next few years



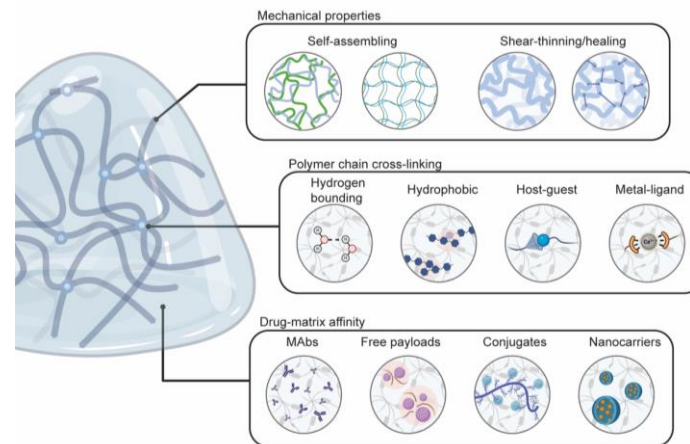
By reformulating the API from IV to SC, a new drug can be registered and launched



Current trend toward reformulating proteins for SC administration



*By dehydration technics, electrospray or spray-drying

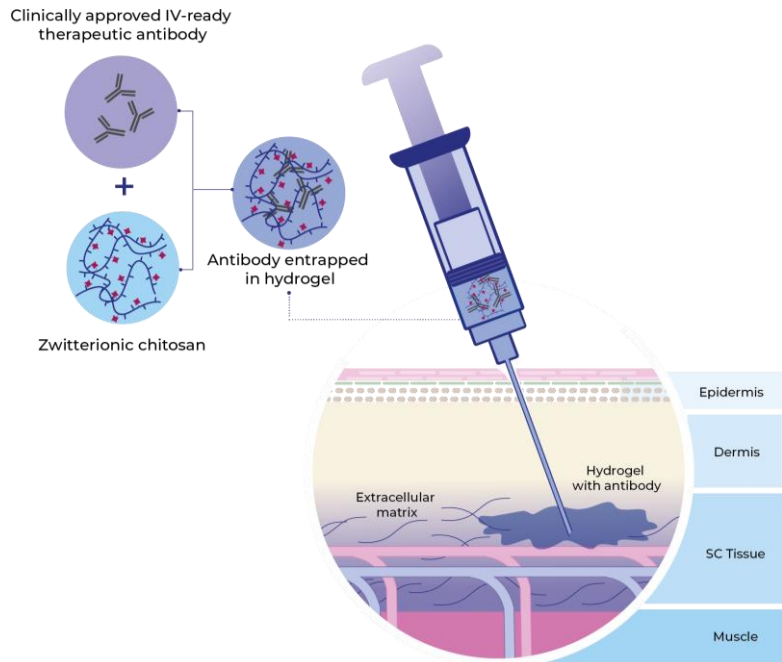


Jacquot et al. Adv Mater. 2024



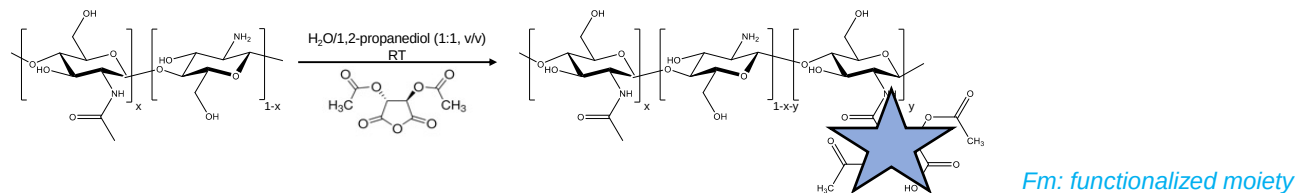
Our approach

- Mixture of a sterile polymeric solution and ready-to-use clinically approved antibodies (mAbs, ,bsAbs, ADCs, ...)
- Chitosan offers a wider range of functionalization option thanks to the reactivity of its amine and hydroxyl groups
- Easily injectable
- No cross-linking agent (potentially toxic and not suited to drug delivery approach)
- Fast gelation properties due to zwitterionic behavior

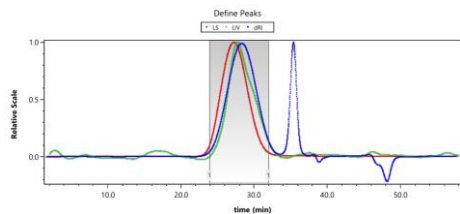




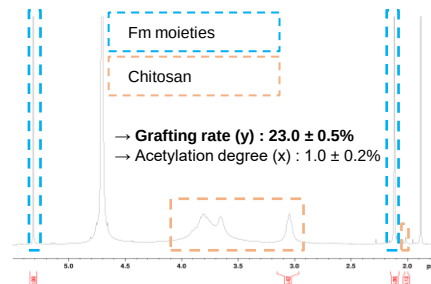
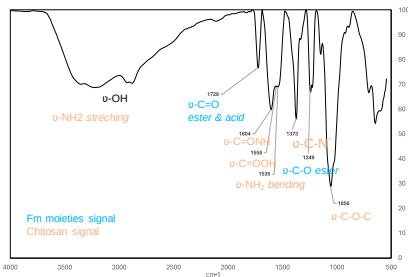
Characterization of the hydrogel platform



Polymer size by SEC-MALS



Structure identification by FTIR & NMR + quantification of grafting by ¹H NMR

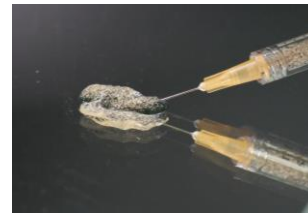
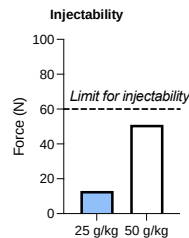
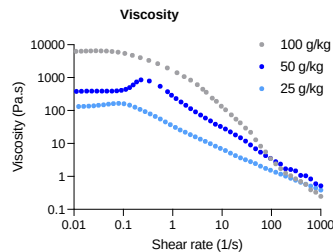
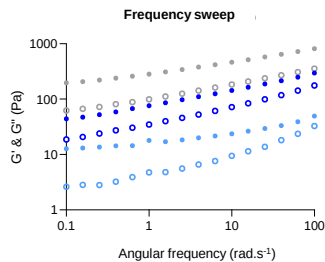


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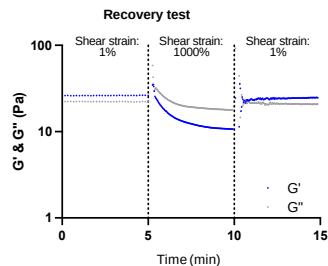
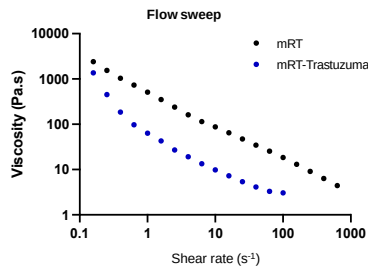
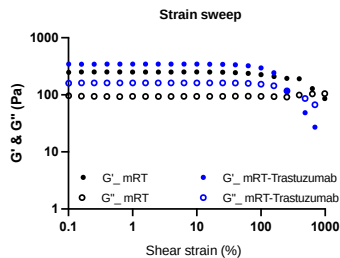
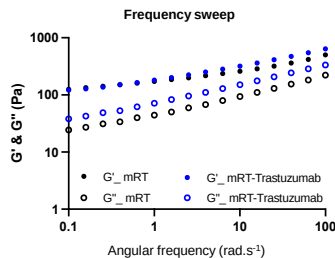


Characterization of the hydrogel platform with trastuzumab

Hydrogel only



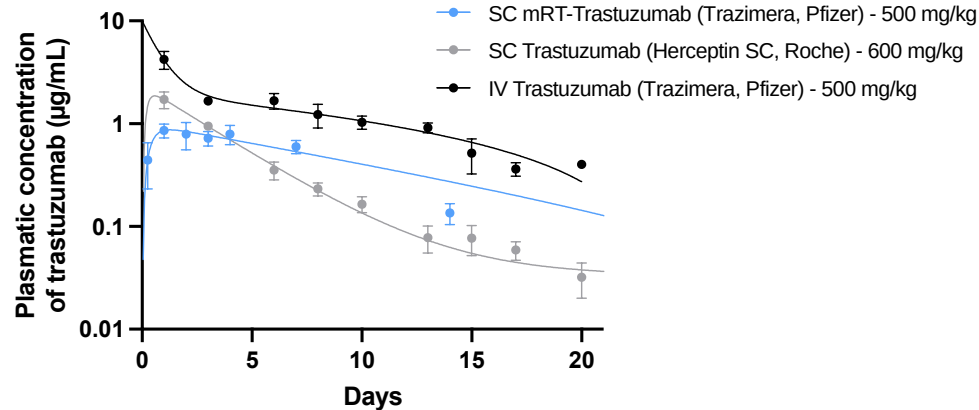
Hydrogel+
trastuzumab



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Pharmacokinetic profile comparison with Herceptin SC in balb/c mice

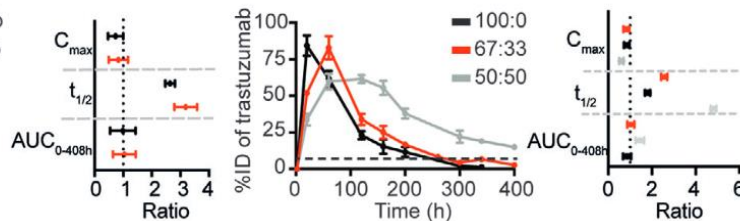
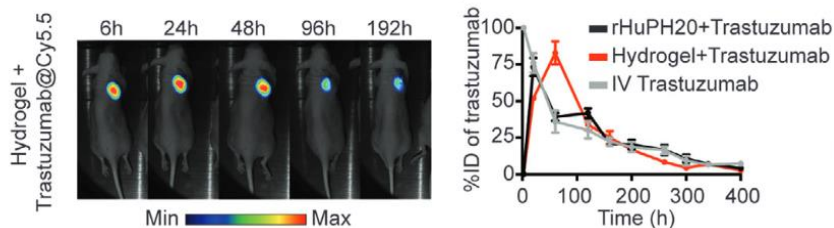


mRT with mAbs: PK in mice (n=15/groups)

Formulation	Dose (mg/kg)	AUC (mg.day/mL)	C _{max} (mg/mL)
IV Trastuzumab	500	28	4.22
Herceptin SC (rHuPH20)	600	7.9	1.72
mRT-Trastuzumab	500	9.5	0.86

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Playing with polymer concentration enables controlled release properties

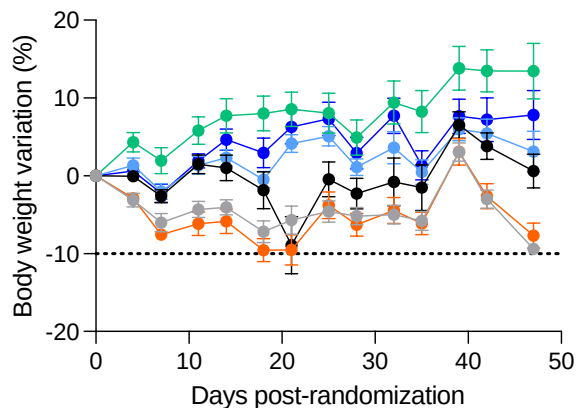


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Therapeutic study with repeated administration in xenograft BT474 mice

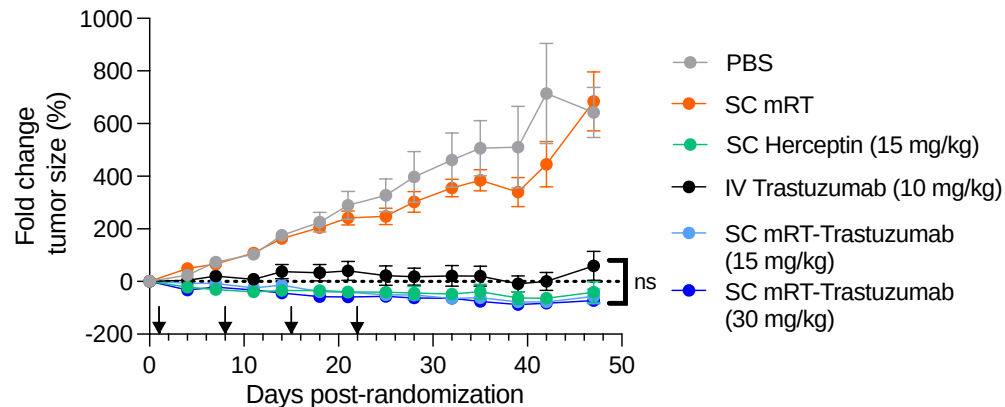


Bodyweight change (%) (n=8/group)



Mean ($\pm$ SEM) tumor fold change (n=8/group)

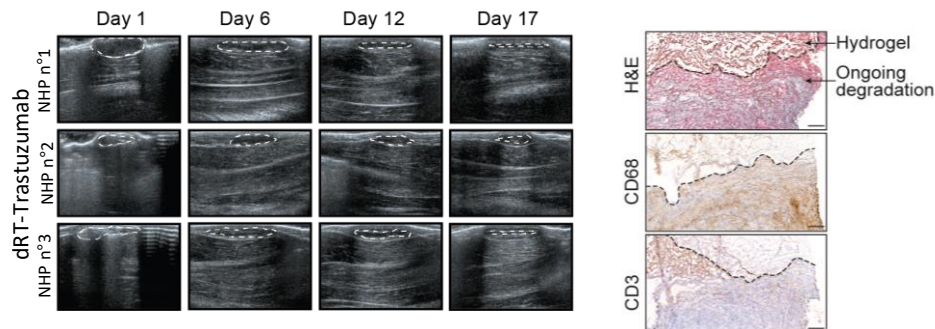
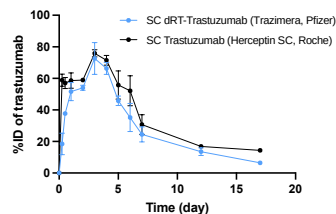
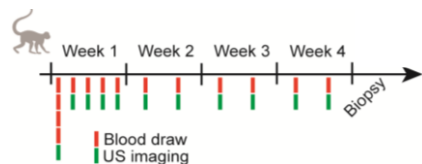
Arrows indicate treatment administration.



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Modifying the hydrogel formulation enables controlled release profile



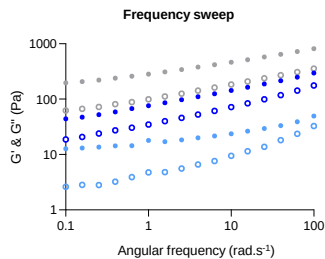
- In nonhuman primates, dRT formulation provides similar pharmacokinetic profiles than the clinically-approved formulation
- Biodegradability is observed by ultrasound imaging upon 1 mL hydrogel SC administered at 100 mg/mL trastuzumab concentration

Grea et al. Adv Mater 2023

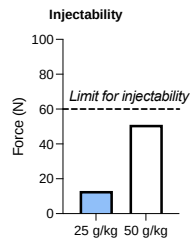
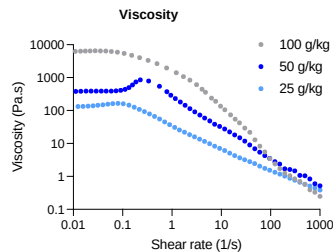


Characterization of the hydrogel platform with T-DM1

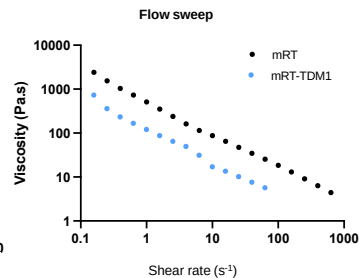
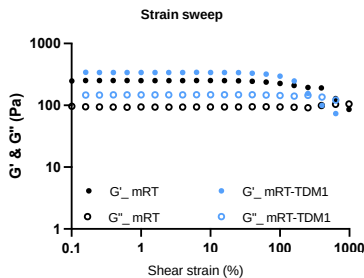
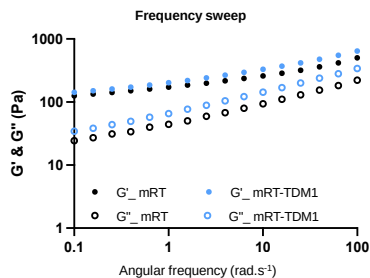
Hydrogel only



• G' - 100 g/kg
• G'' - 100 g/kg
• G' - 50 g/kg
• G'' - 50 g/kg
• G' - 25g/kg
• G'' - 25g/kg

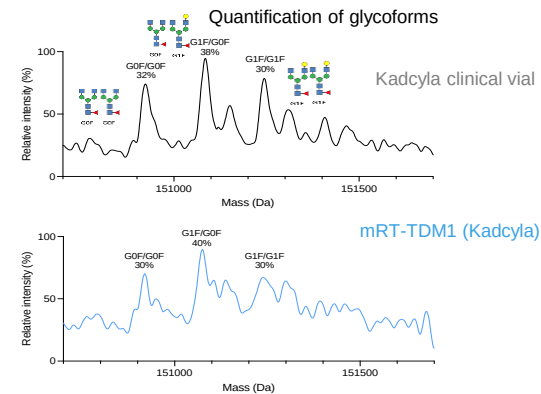
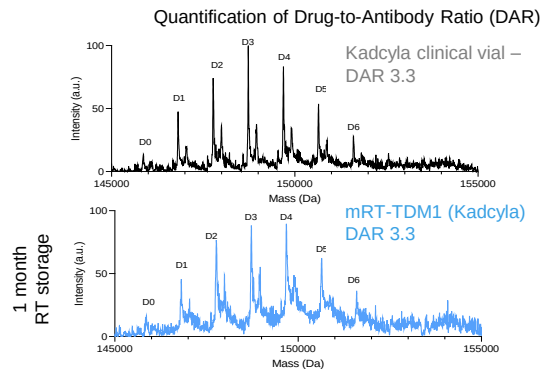
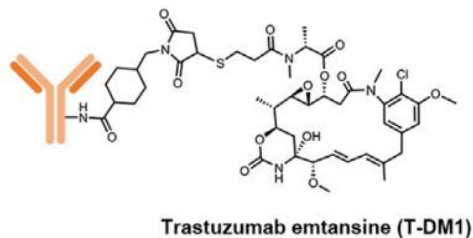


Hydrogel+TDM1



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T-DM1 remains stable up to 1 month at room temperature

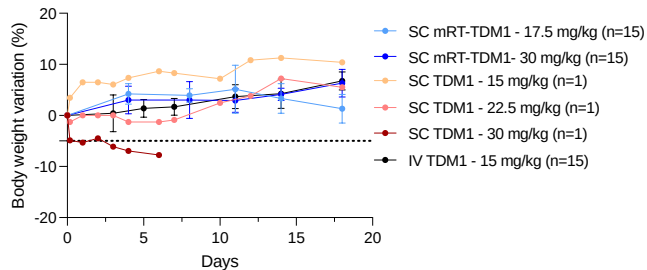
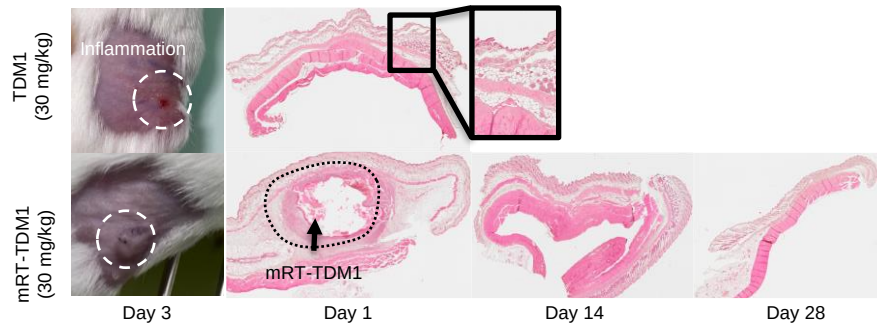


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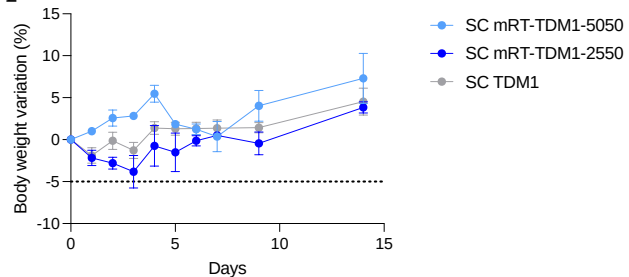
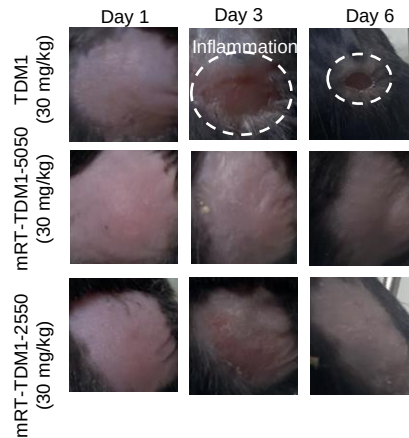


Hydrogel improves biocompatibility of SC TDM1 in mice

► Balb/c mice (immunodeficient)



► C57BL/6 mice (immunocompetent)

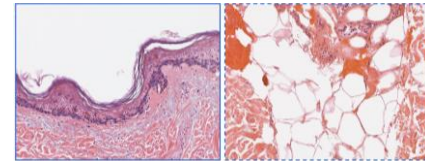
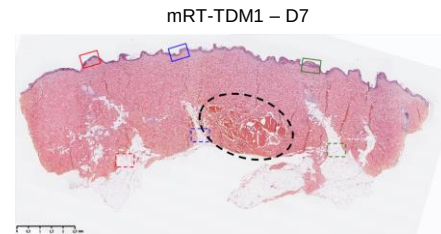
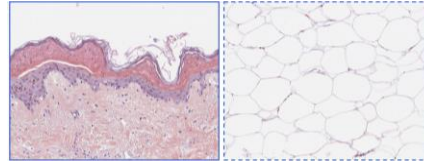
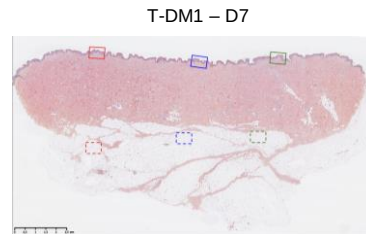
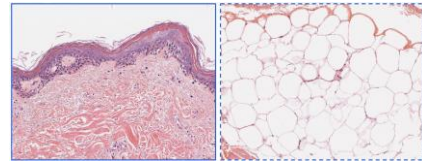
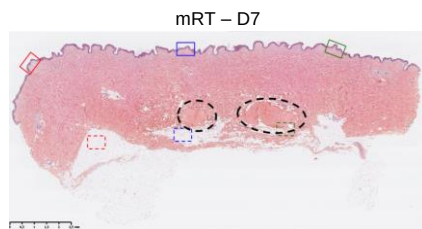
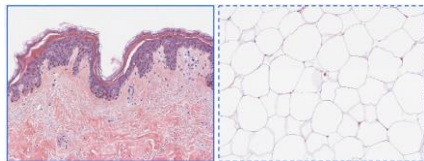
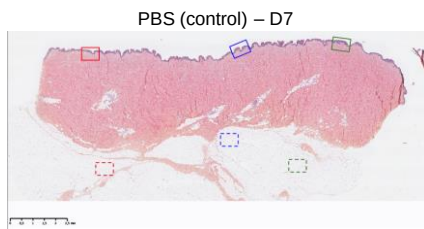
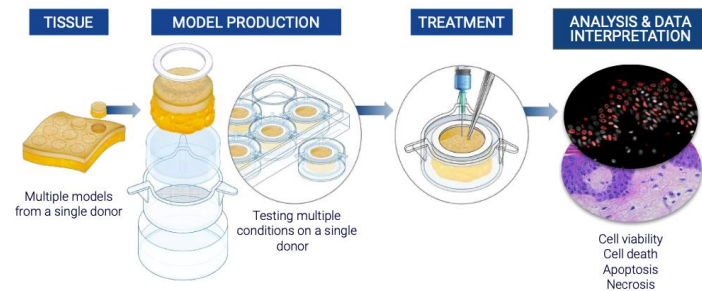


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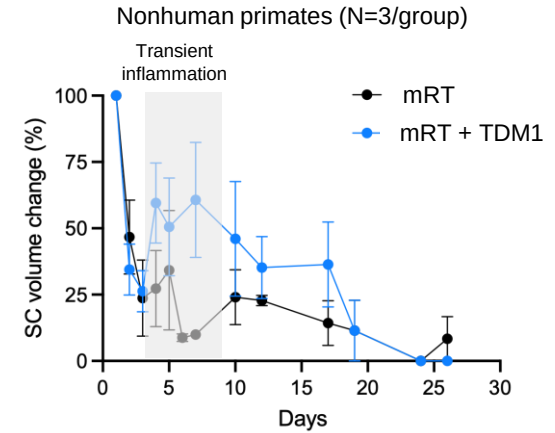
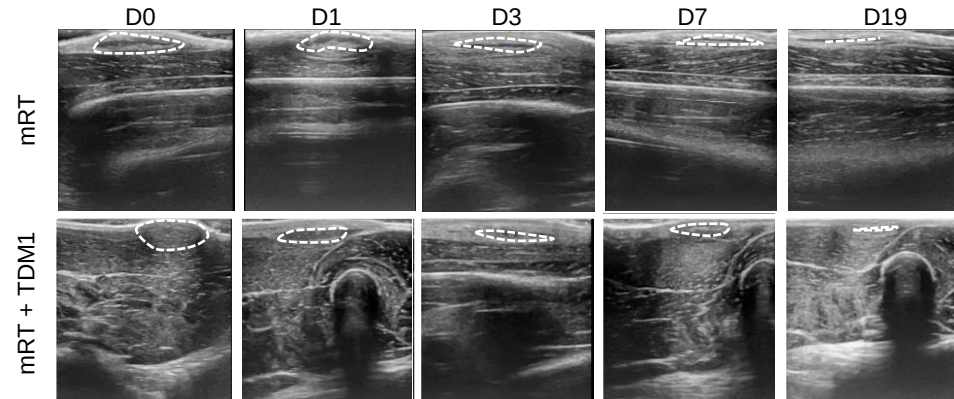


Hydrogel improves biocompatibility of SC TDM1 in human skin

- mRT is well-tolerated: no adverse effects observed
- mRT protects T-DM1 and limits skin alteration due to T-DM1 alone



Biodegradability is observed on nonhuman primates

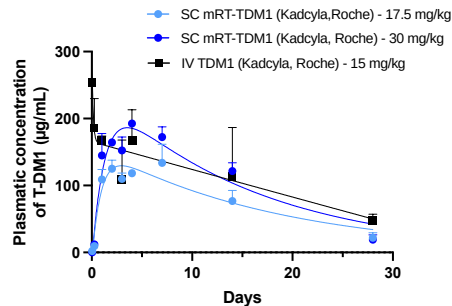


► Complete biodegradation is observed after 25 days post-SC administration



Mono-administration study

► Pharmacokinetic study in healthy balb/c

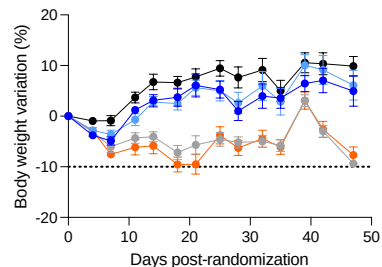


mRT with ADC: PK in mice (n=15/group)
(Titration of trastuzumab antibody)

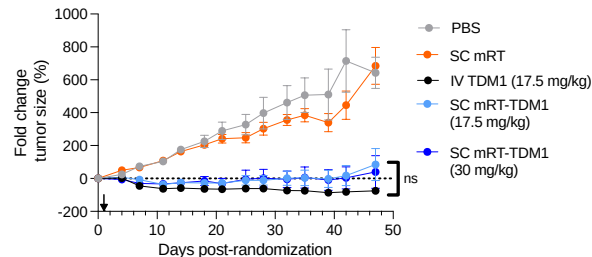
Formulation	Dose (mg/kg)	AUC (µg.day/mL)	C _{max} (µg/mL)	Bioavailability
IV TDM1	15	3753	196	100%
mRT-TDM1	17.5	2428	132	55%
mRT-TDM1	30	3283	193	44%

► Therapeutic efficacy study in BT-474

Bodyweight change (%) (n=8/group)



Mean (± SEM) tumor fold change (n=8/group)
Arrow indicates treatment administration.





- ▶ Successful translation of chitosan-based hydrogel for SC mAbs delivery
- ▶ Improved stability at room temperature of ADCs
- ▶ Biocompatibility of SC administration of hydrogel-TDM1
- ▶ Non-inferior therapeutic outcome in comparison to IV TDM1

Remaining tasks: Therapeutic study with multi-administrations, versatility study with additional ADCs



Acknowledgements

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