Anti-MUC16 Tumor Associated Epitope

Non-Shed Epitope Anti-MUC16 Antibody

MUC16 Potential for Ovarian and Other Cancers

Target Mechanism

Bind a membrane-proximal MUC16 epitope

Membrane-proximal binding avoids epitope elimination by tumors

Bind a non-glycosylated epitope to avoid altered glycosylation on tumors

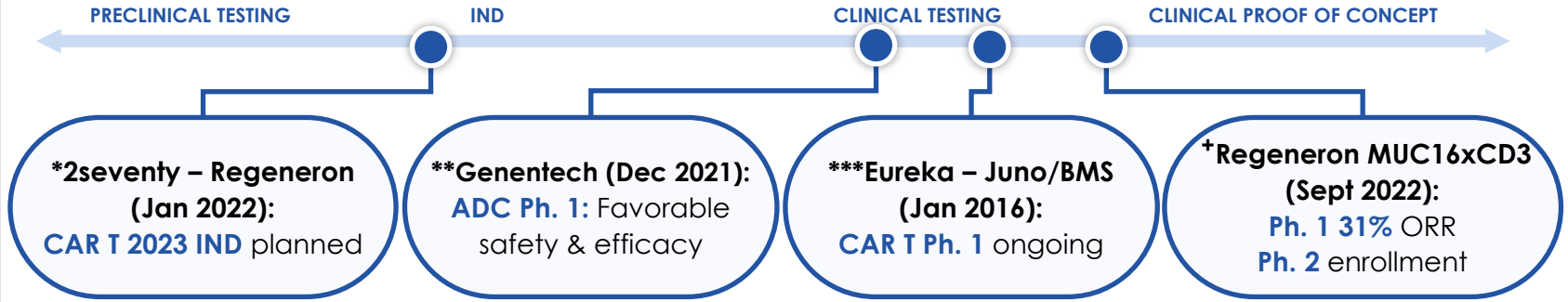
Potential Indications

- Ovarian
- Uterine
- Pancreatic

Differentiation / Opportunity

- MUC16 epitope avoids primary modes of tumor evasion
- Enabling modalities: T Cell engager, ADC, CAR-T

Recent Transactions & Milestones



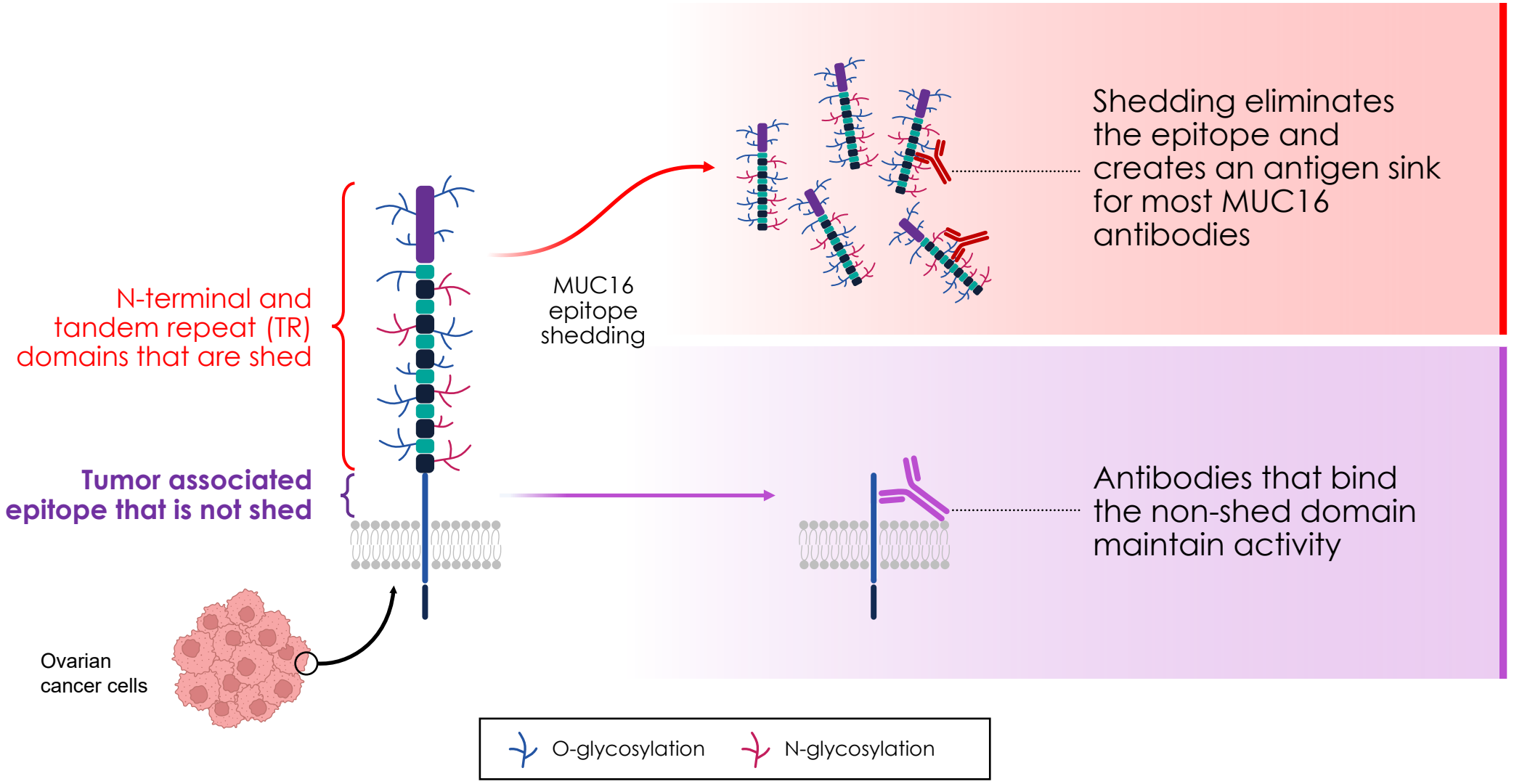
*Regeneron, 2seventy name the target of their first solid tumor CAR-T, aim for 2023 IND

** Liu et al., An open-label phase I dose-escalation study of the safety and pharmacokinetics of DMUC4064A in patients with platinum-resistant ovarian cancer

***Eureka Therapeutics Announces Exclusive License Agreement between Memorial Sloan Kettering Cancer Center and Juno Therapeutics for Use of a Novel, Fully-Human MUC16 Binder in CAR T Cell Immunotherapy

+Novel Regeneron Bispecific Antibodies Show Encouraging Anti-Tumor Activity in Two Advanced Solid Tumors

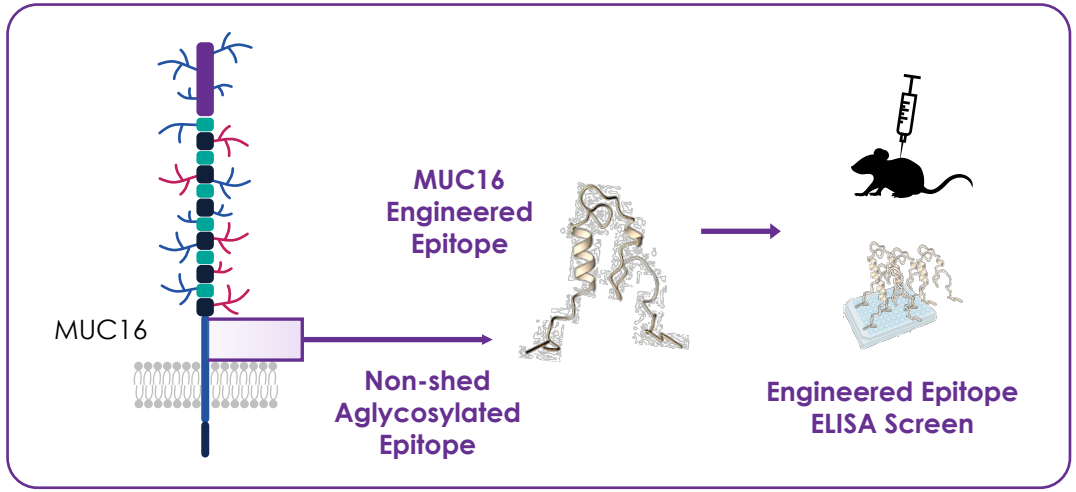
MUC16 Is Overexpressed and Shed by Tumor Cells



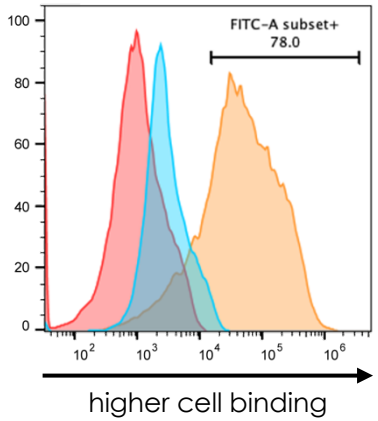
Immunizations Were Steered to a MUC16 Epitope that Avoids Epitope Shedding

AI Discovery Engine

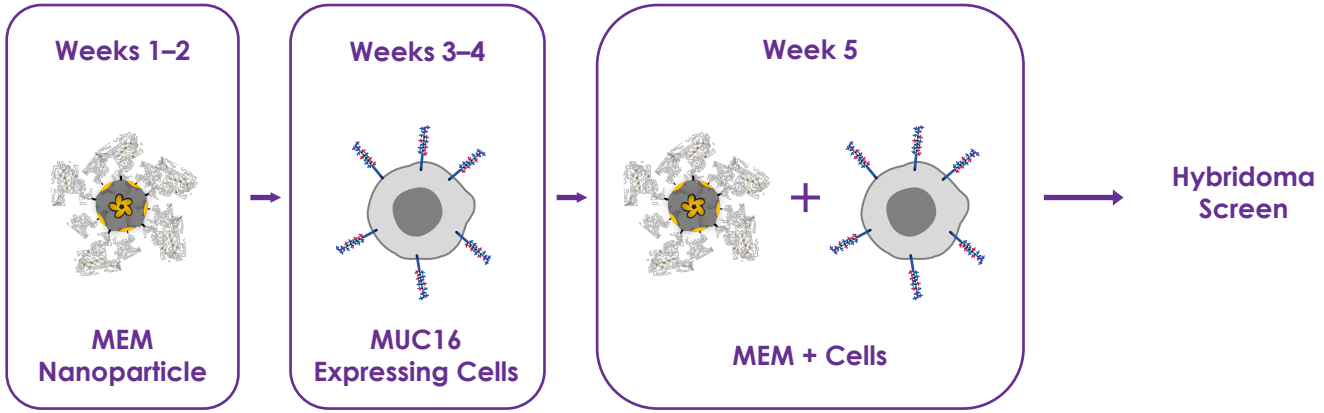
Structural-epitope Immunization & Screening



OVCAR-3 MUC16$_{high}$ Cell Binding Screen

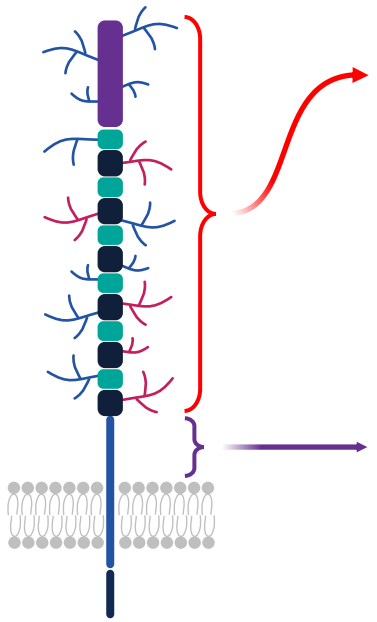


Engineered Epitope Prime + MUC16 Cell Boost



Top Three Hit Clones Bind the Non-Glycosylated MUC16 Epitope Closest to the Membrane

N-terminal and tandem repeat (TR) domains that are shed



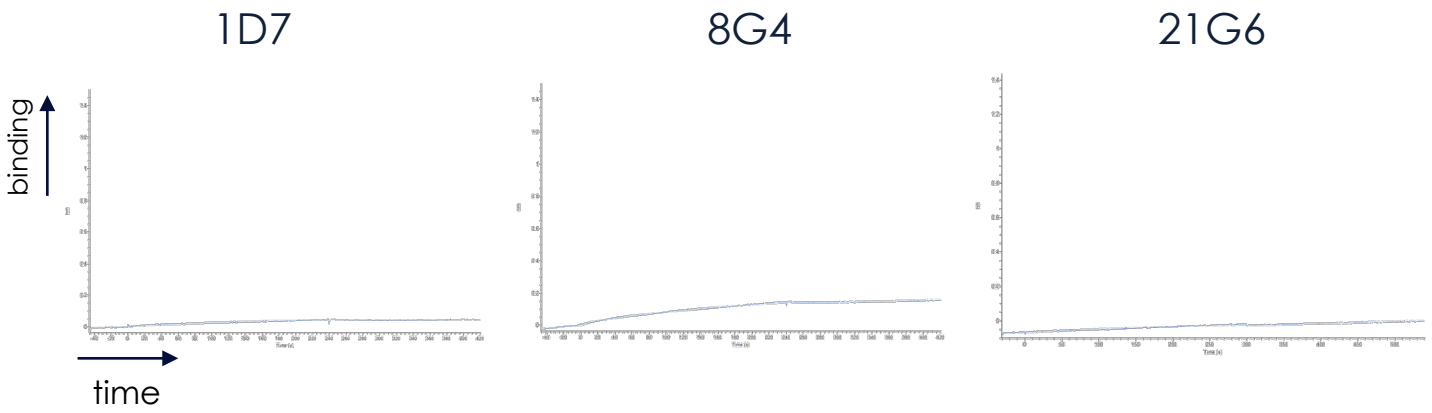
Epitope

Shed 230-mer

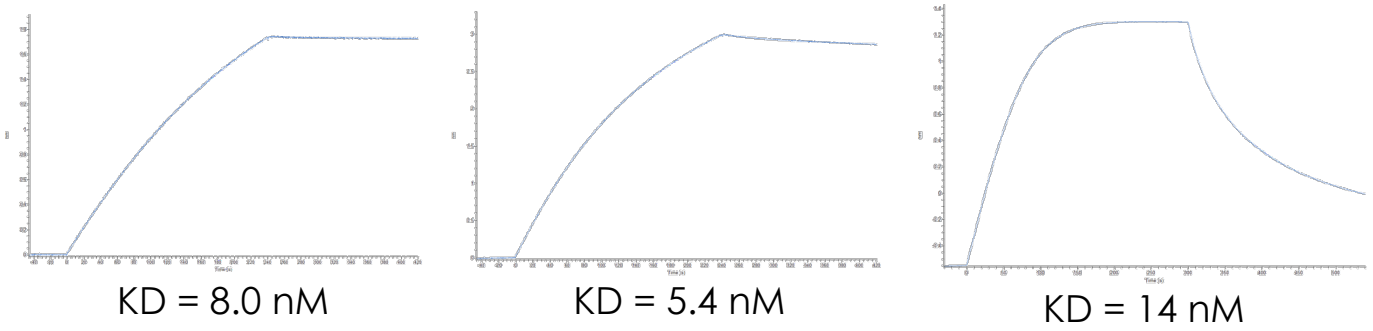
Aglycosylated non-shed 29-mer

O-glycosylation N-glycosylation

Hits do not bind shed 230-mer



Hits bind non-glycosylated non-shed 29-mer



KD = 8.0 nM

KD = 5.4 nM

KD = 14 nM

Top MUC16 Clone 8G4 Binds OVCAR-3 Cells Comparable to Regeneron Benchmark

Clone ID:

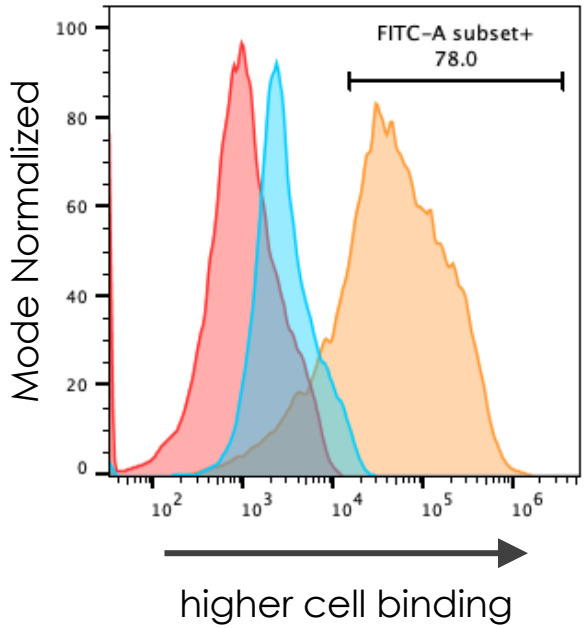
8G4
top clone

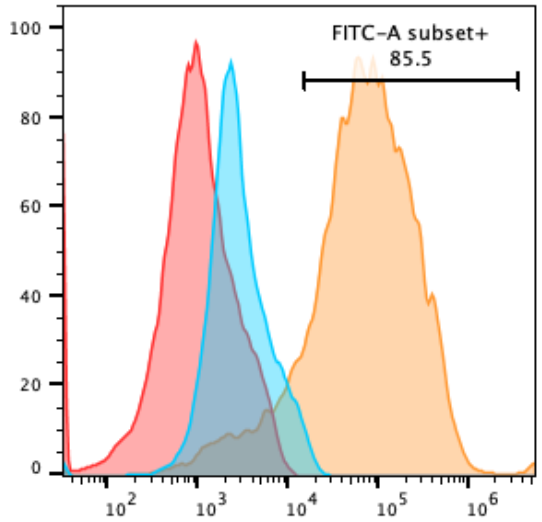
Regeneron
benchmark

Unstained

Secondary Only

OVCAR-3 Cells

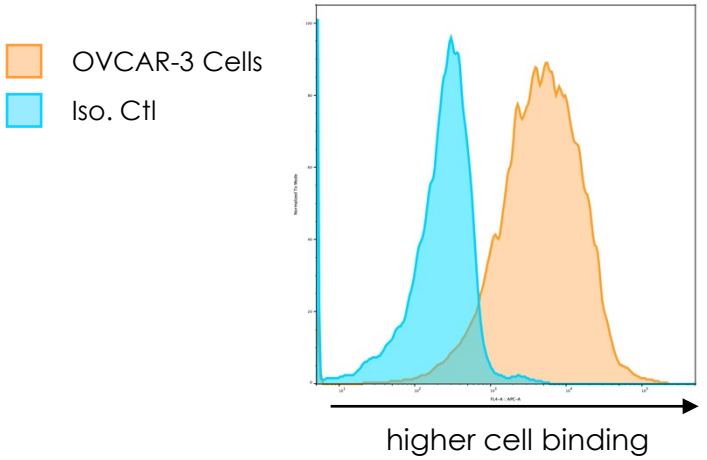




8G4 Clone Maintains OVCAR-3 Cell and MUC16 Epitope Binding in a Fully Human Framework

8G4 with fully human framework reduces immunogenicity risk

Cell binding



Glycosylated MUC16 membrane-proximal epitope SPR:

KD = 5.1 nM

Epitope binding