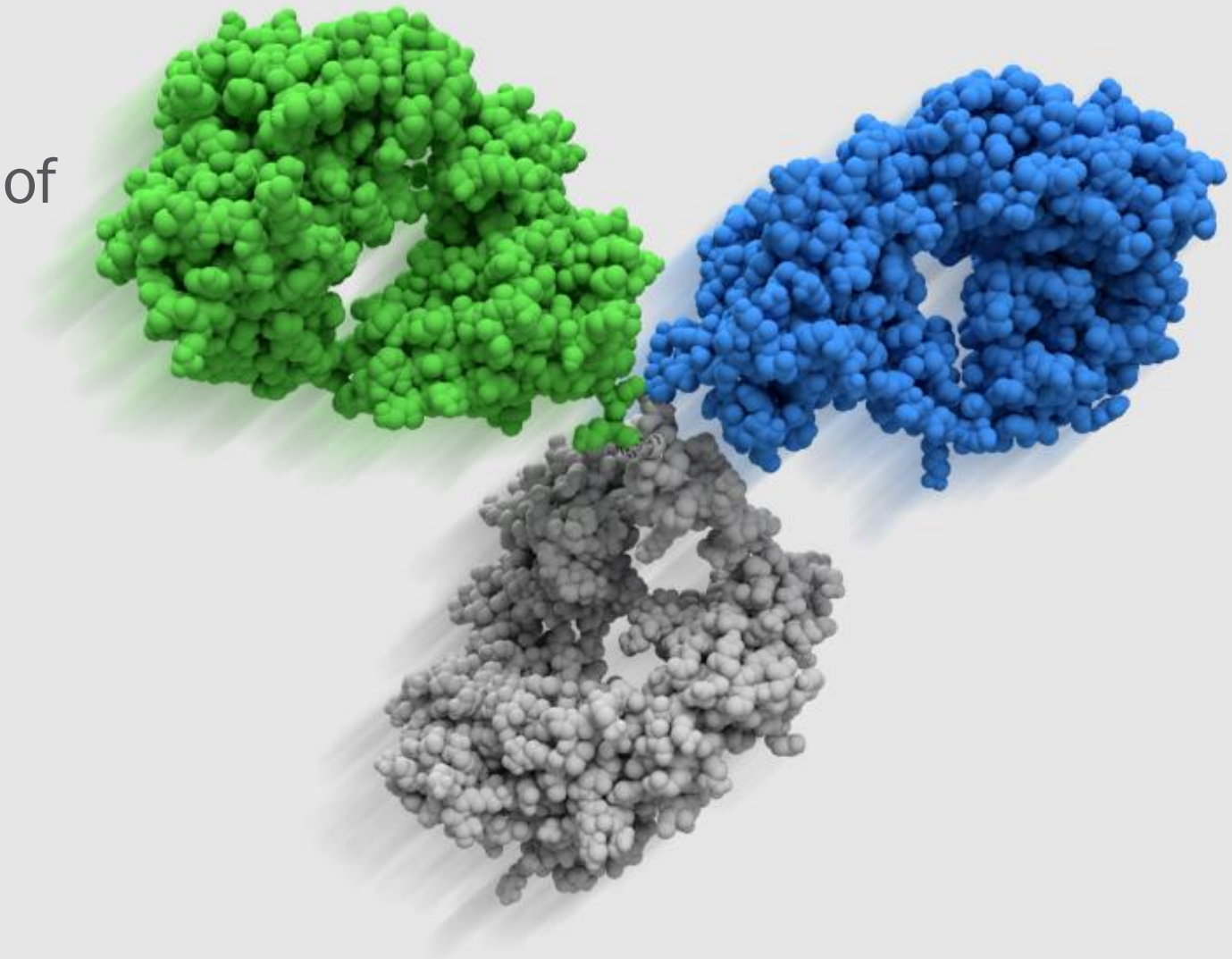
12x12 Matrix Screening with B-Body® and T-Body™ Platforms:

Comprehensive, Rapid Discovery of Multispecific Antibodies for ADCs Targeting Breast Cancer



16th Annual World ADC, San Diego

November 4, 2025

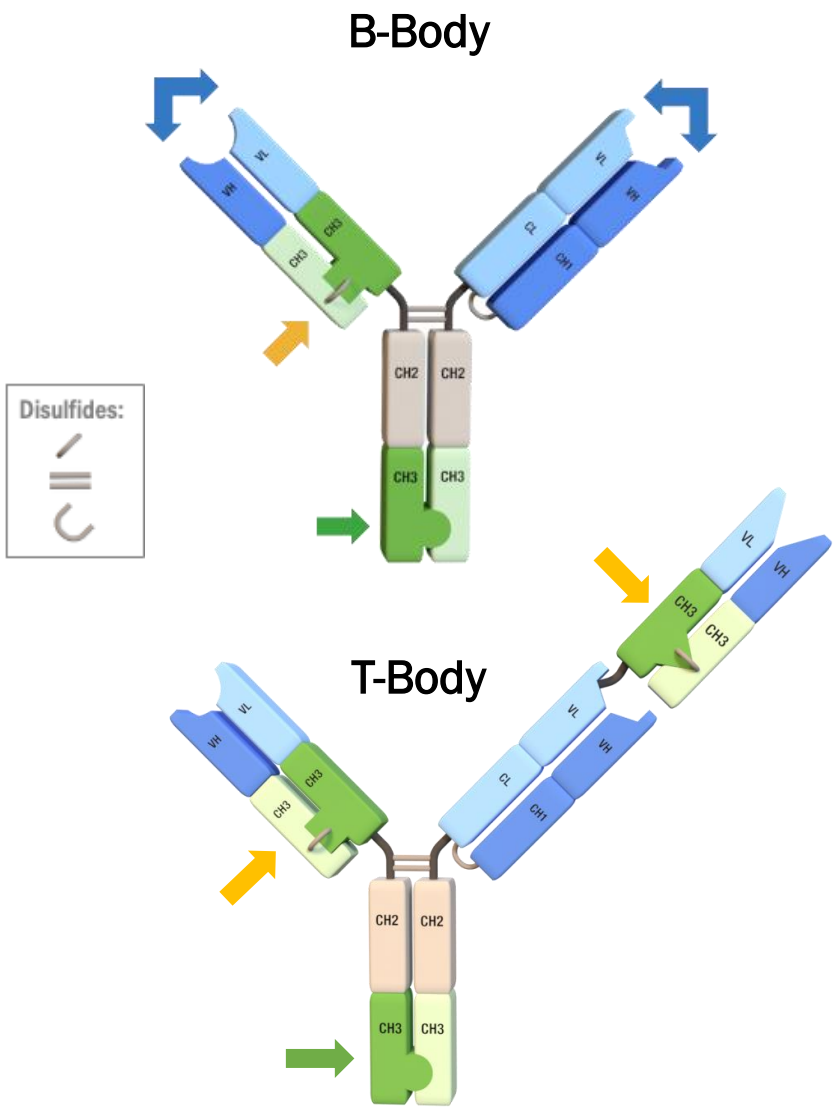
Overview

- Multispecific Antibody Platform Technologies for ADC Development
- 12x12 Matrix Screening Approach for Target Optimization
  - Systematic bispecific screening methodology
  - Trispecific construct evaluation and comparison
- Breast Cancer ADC Case Study: Platform Performance and Results
- Future Applications and Platform Scalability

Invenra's Next-Generation Multispecific Antibody Platforms

- 13+ years of specialized multispecific antibody engineering and discovery
- B-Body® bispecifics: Unprecedented expression yields and a clinical-stage bispecific in 2025
- T-Body™ trispecifics: Next-generation platform launched in 2025 for complex targeting
- Rapid timelines: Expression of bispecifics in 4 weeks or discovery of novel lead candidates in 4 months
- Manufacturing-ready formats: IgG-like PK/safety profiles, sub-Q compatible, up to 11g/L bispecific expression yields

The B-Body® Bispecific and T-Body™ Trispecific Platforms: Robust Solutions for Multispecific Antibody Development



Engineering

Fc Region: Clinically Validated Knobs-into-Holes

- Drive heavy chain heterodimerization
- Compatible with standard Fc substitutions

Fab Arms: Proprietary CH3 Domain Pairs

- Substitutes for CH1/CL in two Fab Arms
- Solves light chain mispairing issue
- Natural asymmetry in isoelectric point

Proprietary Symmetrical Heavy & Light Chain Inversions in Fab Arms

- Robust expression yields
- Efficient purification
- "Plug & Play" variable domains

Benefits

B-Body Bispecific and T-Body Trispecific Platforms provide a simple and accelerated path to Lead Candidates

- High stability, robust expression, mAb-like CMC
- Multiple formats: 1×1, 2×1, 2×2 bispecifics; trispecifics
- Compatible with diverse mAbs & standard functional mutations
- Validated for conjugation
- Strong IP protection

Breast Cancer Facts and Figures

- Breast cancer is the most common cancer diagnosed among women in the United States. 1 in 8 women in the US will develop breast cancer in their lifetime

- Breast cancer is the 2nd leading cause of death from cancer among women.
- Triple negative breast cancer accounts for 10-15% of all breast cancer diagnoses in the U.S.

Sources: Breast Cancer Facts & Figure 2024-2025, American Cancer Society
National Breast Cancer Foundation, Inc.

Challenges and Opportunities for the Treatment of Breast Cancer

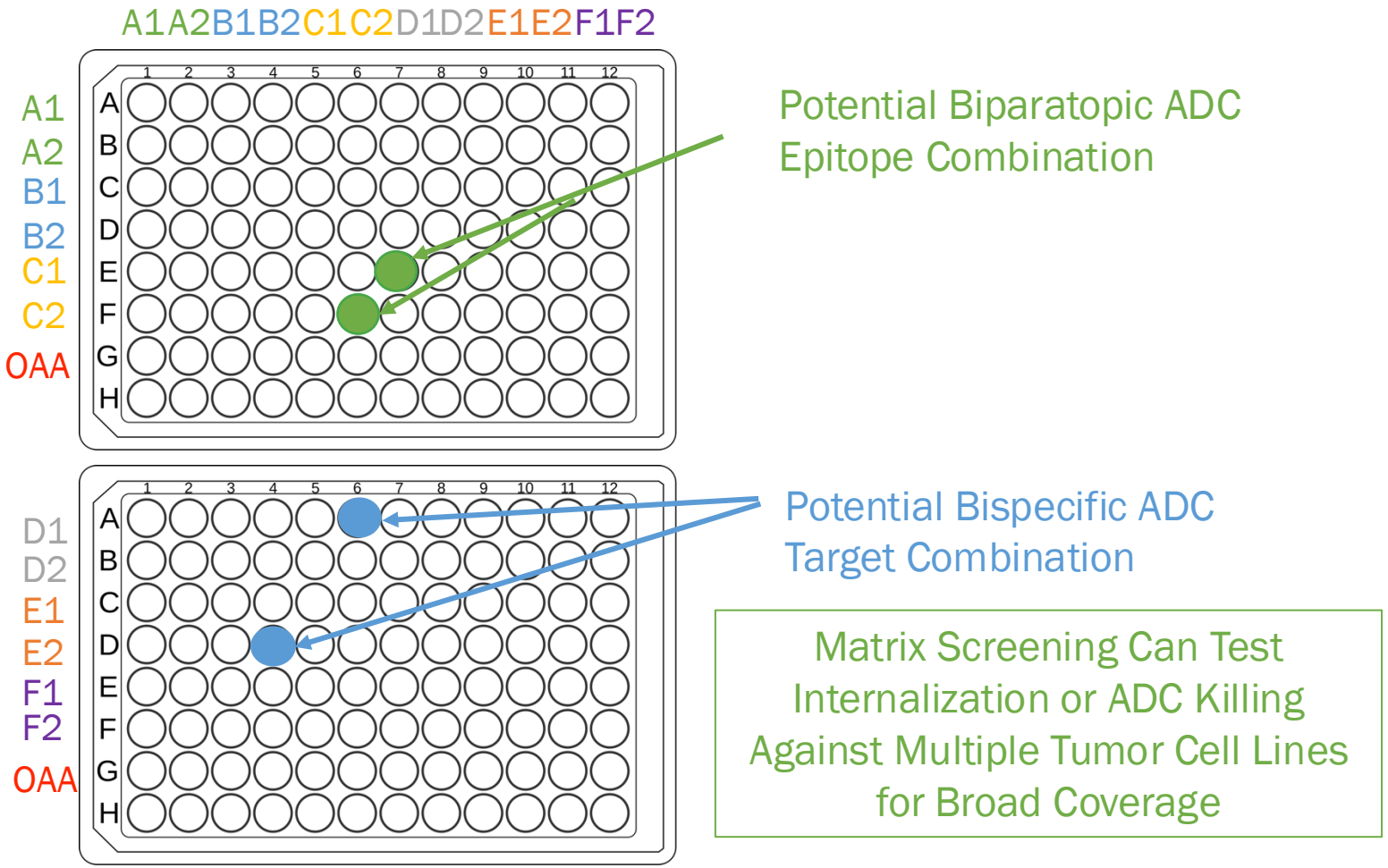
Challenges

- Suboptimal efficacy & safety profile of many monospecific ADCs
- Tumors are heterogeneous
- Many tumors develop resistance leading to relapse
- Difficult to treat subtypes such as TNBC

Opportunities for Multispecifics

- Enhance tumor-targeting and overcome tumor resistance, improving efficacy & safety
- Allow targeting of complementary pathways in cancer signaling and progression
- Allow targeting of molecules involved in immune modulation—potential added antitumor activity beyond just cytotoxic drug delivery

Case Study: Using the B-Body Bispecific Platform for Multispecific ADC Discovery (12x12 Matrix)



Matrix Screening Can Test Internalization or ADC Killing Against Multiple Tumor Cell Lines for Broad Coverage

Matrix Screening of Antibodies to Multiple Target Epitopes

Unique Targets (ABCDEF) & Unique Epitopes (1-2)

Key Questions for Multispecific ADCs:

1. How does target expression influence the selection of target combination?
2. How might target combinations perform against heterogeneous or relapsed/refractory tumors?
3. Can we target a variety of cancer subtypes?

Multiple Breast Cancer Cell Lines Used in 12x12 B-Body Bispecific Matrix Screen

Target Cell Surface Expression Determined in Multiple Cell Lines

Cell Line	Target A	Target B	Target C	Target D	Target E	Target F
TNBC						
Her2 High						
Her2 Low						

Expression
High
Medium
Low

Selected cell lines show diverse phenotypes and expression of targets

Heat Maps of Cytotoxicity Across Three Distinct Breast Cancer Cell Lines for B-Body Bispecific Matrix in Piggyback ADC (MMAE)

% Cytotoxicity at 4 nM

HER 2 Low

11	3	37	-5	3	-10	50	-10	-14	43	59	53	-13
8	2	46	-4	-8	-10	52	-7	43	54	66	56	-18
32	15	0	-4	14	2	49	-7	45	39	56	47	-5
2	0	-3	-2	6	1	23	-6	13	10	38	9	-12
-5	-5	-2	-5	-6	-7	8	-2	45	7	65	42	-17
0	-4	-5	-1	-3	-4	17	-5	37	-1	52	4	-9
53	44	-8	18	36	24	52	-11	57	64	63	67	27
53	53	0	27	44	18	56	-3	60	60	62	63	-8
54	41	45	19	54	30	62	-3	33	57	58	57	4
58	46	13	27	39	11	65	8	50	33	55	48	2
69	55	51	49	58	56	65	1	60	54	47	53	46
56	44	16	29	31	8	67	7	54	50	50	40	4
5	-1	5	-3	0	-7	35	1	9	-12	37	-14	

HER 2 High

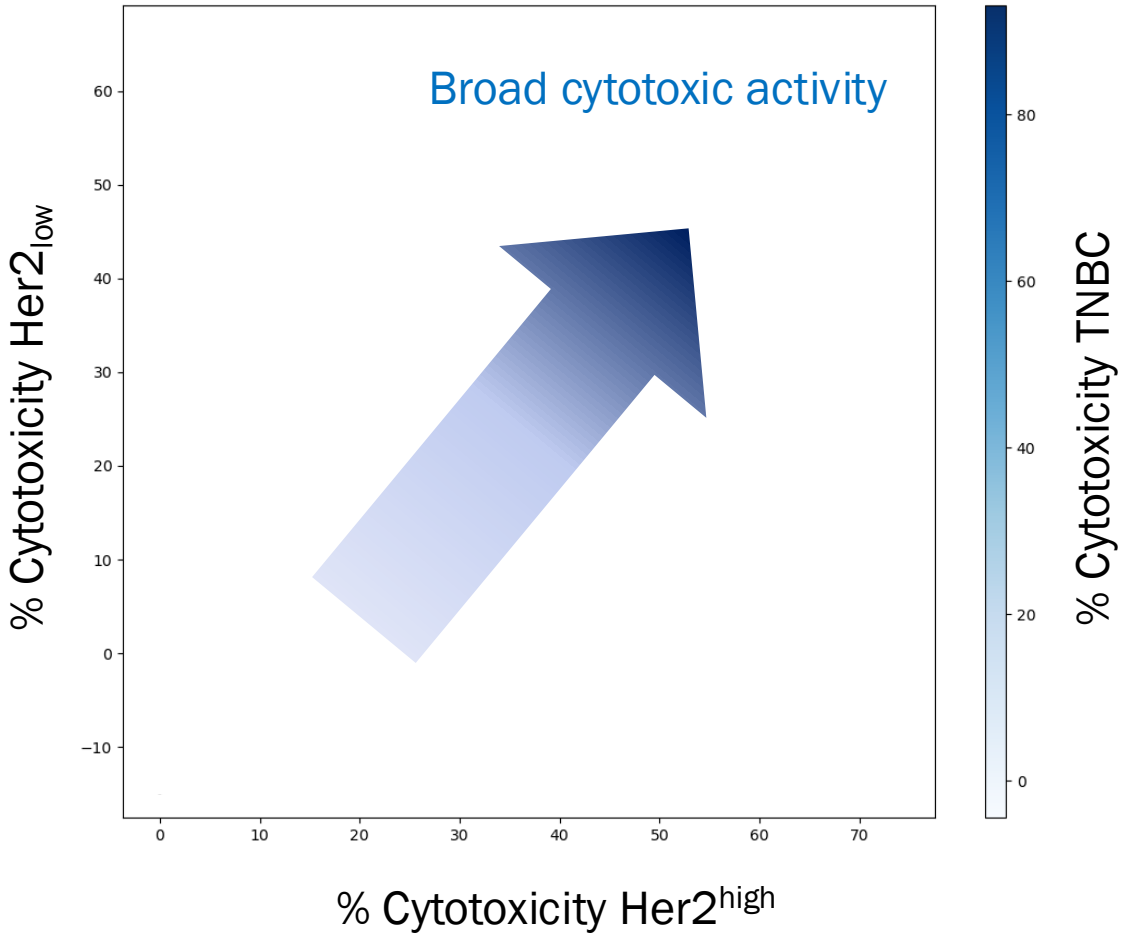
69	63	77	68	62	34	51	-4	0	63	33	45	30
67	66	78	71	43	12	52	3	65	61	26	36	26
74	63	8	52	73	70	63	-1	72	66	60	55	71
70	64	49	73	74	68	49	-3	65	64	44	35	55
43	7	2	29	2	2	11	0	57	15	16	6	-1
33	19	4	45	4	6	12	-1	52	10	14	7	-2
48	42	9	25	18	8	17	-6	35	65	34	38	9
60	57	2	32	24	8	24	-2	52	64	28	26	-3
62	62	72	65	61	44	46	2	48	64	33	32	23
59	58	2	56	42	13	34	-3	49	55	31	30	11
33	31	28	40	17	14	26	4	30	34	10	13	-2
40	37	24	35	10	8	28	6	31	29	11	8	-1
22	19	67	53	1	2	10	-7	22	18	2	-2	

Triple Negative

93	91	80	74	85	74	83	72	82	85	74	81	94
94	91	80	70	80	68	80	86	77	81	64	74	87
91	83	27	20	20	15	59	28	27	35	36	-6	32
84	79	11	7	9	23	50	36	26	14	17	28	31
91	80	2	2	-4	2	58	19	25	31	16	9	25
88	84	17	20	8	11	60	10	36	22	-2	-4	28
88	85	40	35	66	60	68	50	71	71	57	71	64
92	90	25	24	44	15	59	0	71	50	52	54	40
88	87	19	19	30	18	71	41	54	70	59	52	47
83	84	2	5	28	9	67	21	50	43	40	43	24
88	80	-1	20	29	19	61	29	46	31	27	42	18
91	81	10	26	18	19	62	33	41	46	42	35	-7
86	74	-10	0	9	19	53	31	24	27	29	22	

Identification of Multispecifics for ADCs with Broad Cytotoxic Activity

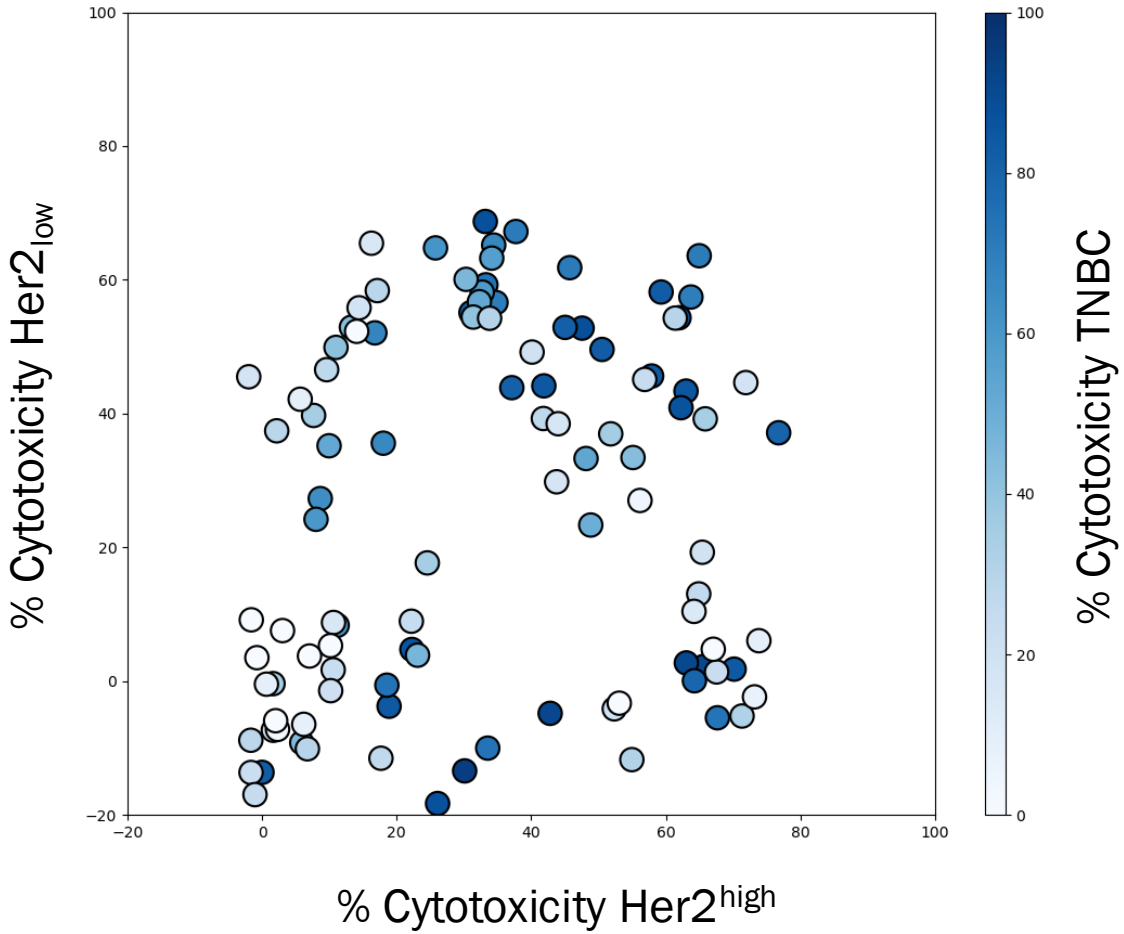
Comparison of Cell Killing Against 3 Tumor Cell Lines



- 12x12 matrix of bispecifics produced
  - 6 targets, 2 arms per target
  - Biparatopics included
  - One-armed controls included
- ADC killing and developability metrics scored from plate data
  - Bispecifics screened for ADC killing activity across 3 tumor cell lines
  - Cytotoxicity measured using a piggyback ADC assay (MMAE toxin)
- Pairs identified for synergistic activity
  - Optimal pairs explored as T-Body trispecifics

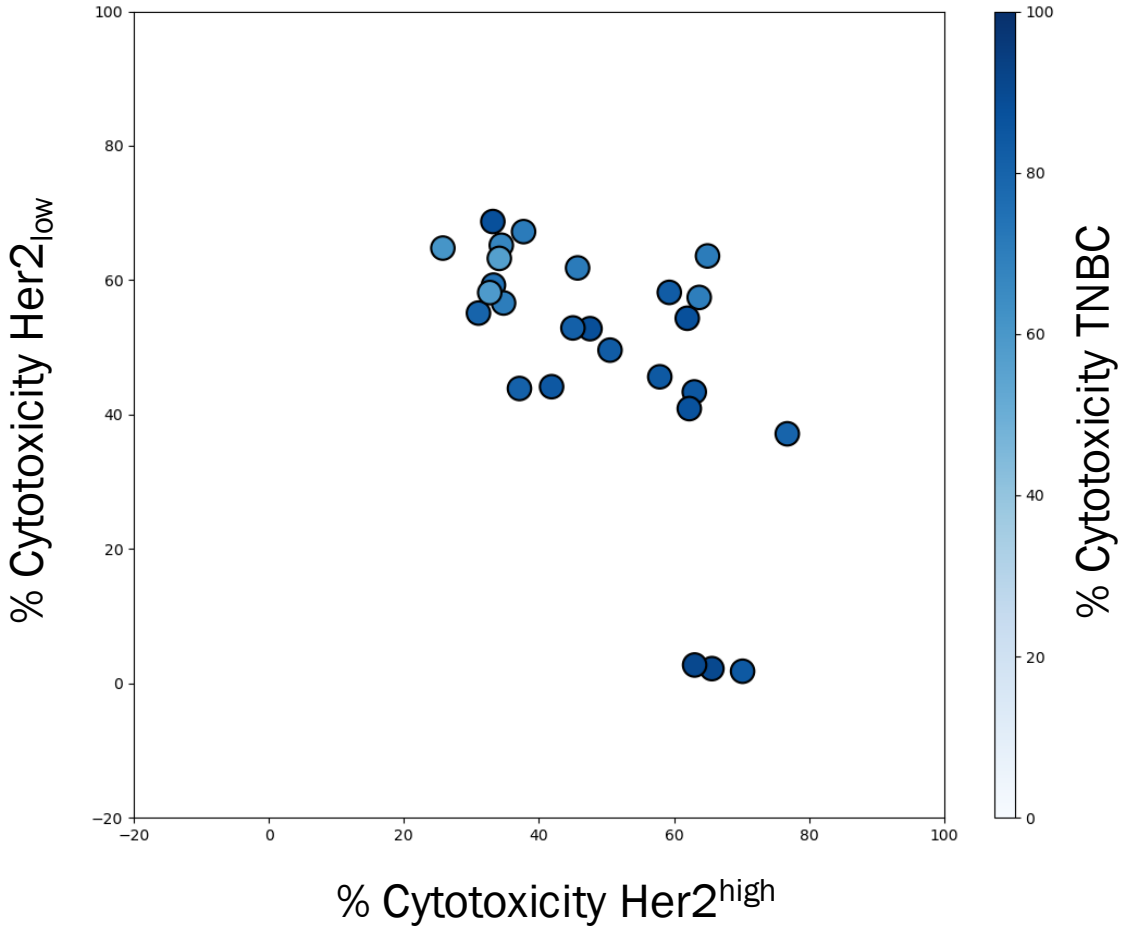
Identification of Multispecifics for ADCs with Broad Cytotoxic Activity

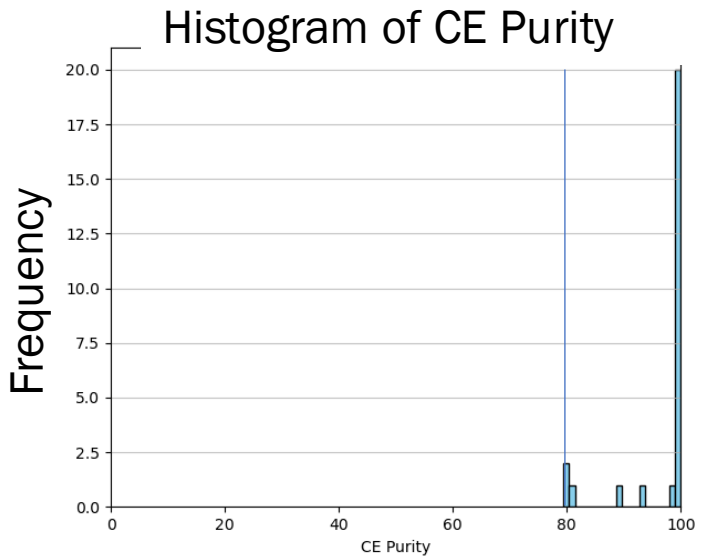
Comparison of Cell Killing Against 3 Tumor Cell Lines

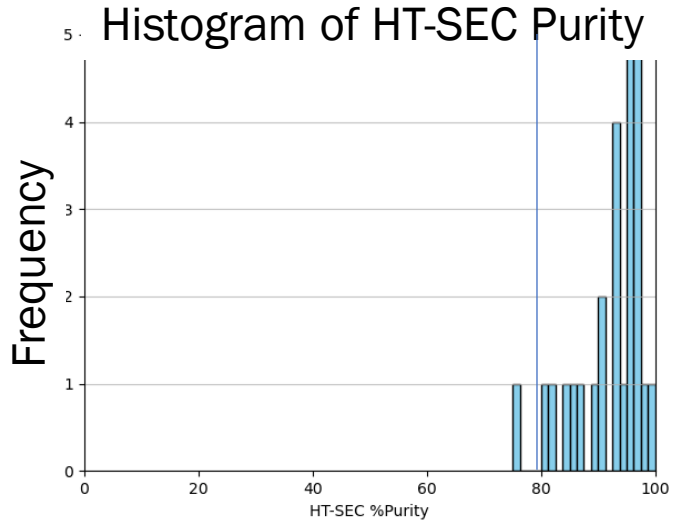


Identification of Multispecifics for ADCs with Broad Cytotoxic Activity

Top 25% Cell Killing Against 3 Tumor Cell Lines



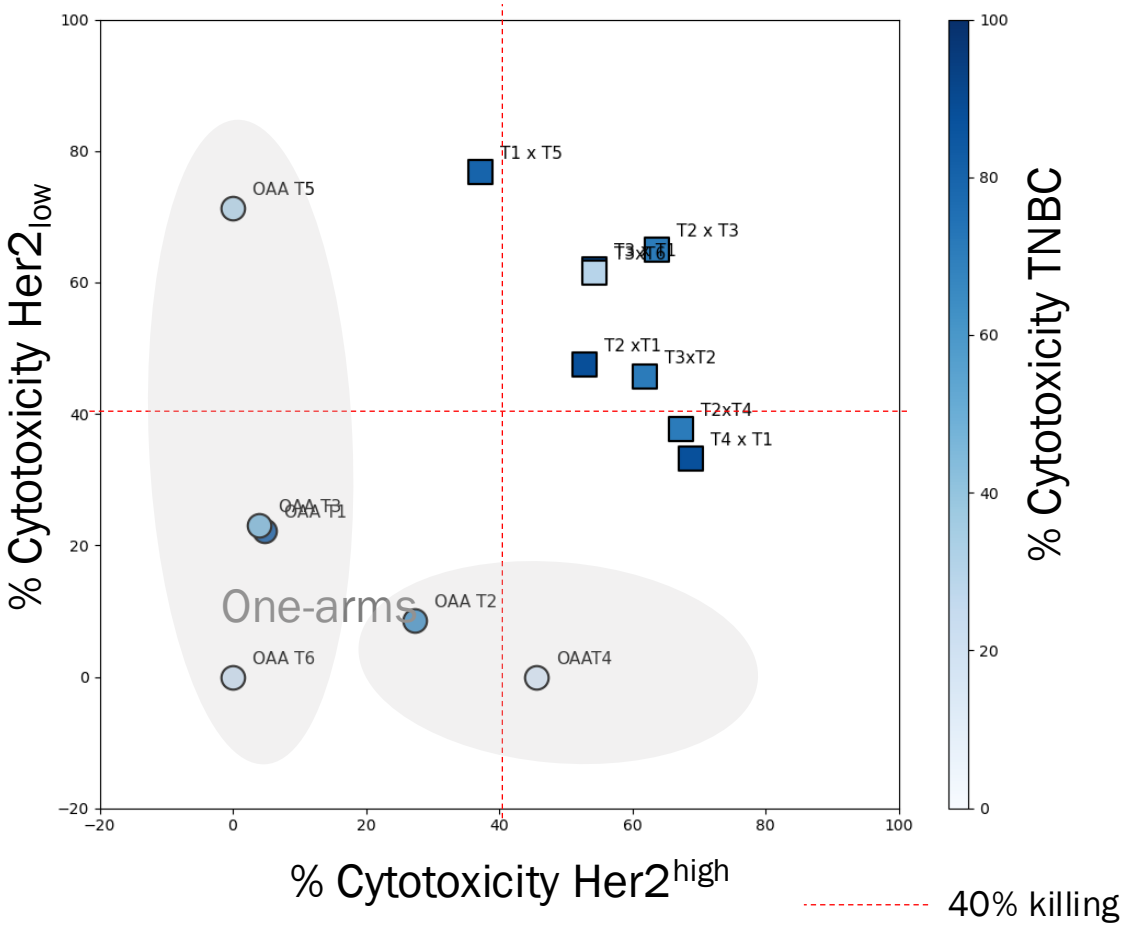




Well-assembled bispecifics

Identification of Top Target Combinations for ADCs

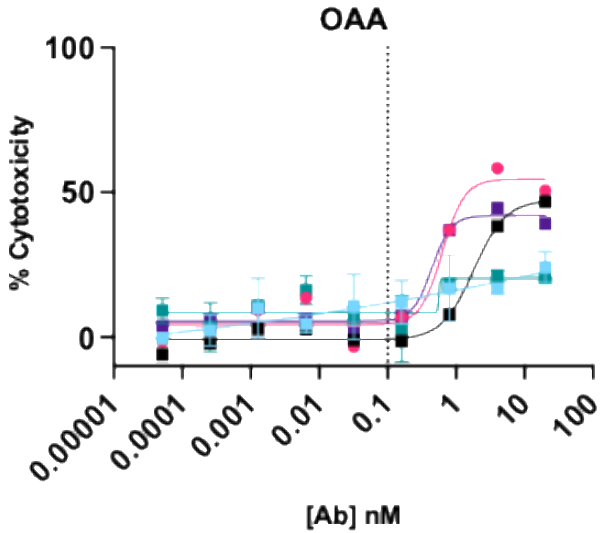
Combinations were prioritized for reformatting into T-Body trispecifics

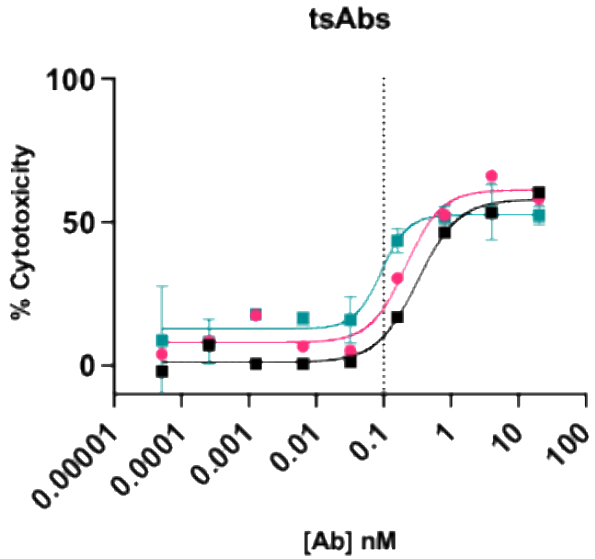


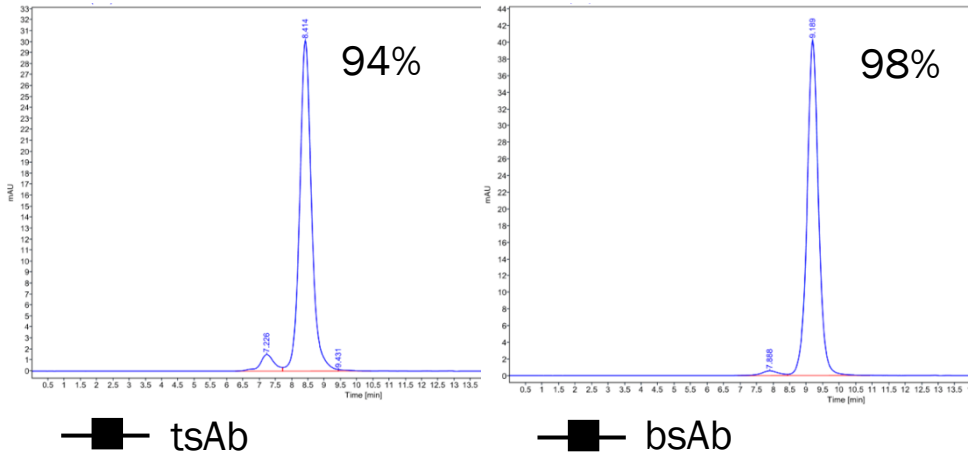
	HER2 High	HER2 Low	TNBC
OAA T1	22.27	4.75	85.81
OAA T2	8.65	27.3	63.81
OAA T3	23.11	3.89	47.23
OAA T4	0	45.51	17.88
OAA T5	71.34	-5.2	31.97
OAA T6	0	0	24.73
T3 x T1	61.97	54.33	87.89
T2 x T3	64.97	63.6	70.84
T1 x T5	76.78	37.14	79.72
T4 x T1	33.18	68.72	87.84
T2 x T1	47.57	52.78	87.92
T3 x T2	45.73	61.82	71.23
T2 x T4	37.73	67.22	71.37
T3 x T6	61.43	54.28	29.93

Data used to select targets for trispecific ADCs

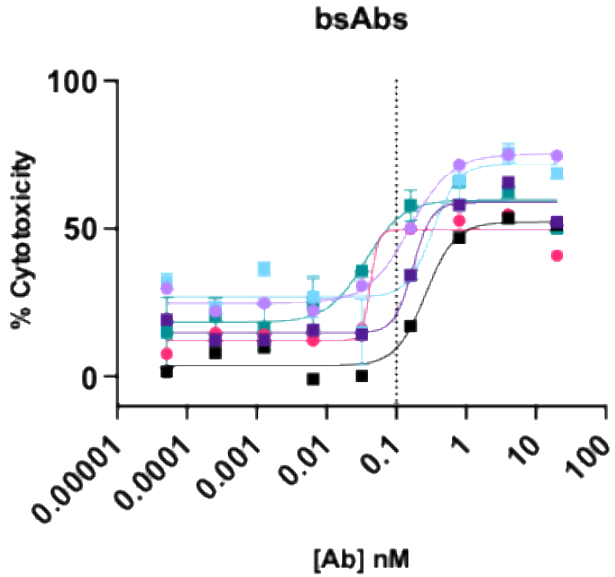
Production & Validation of Trispecifics for ADCs





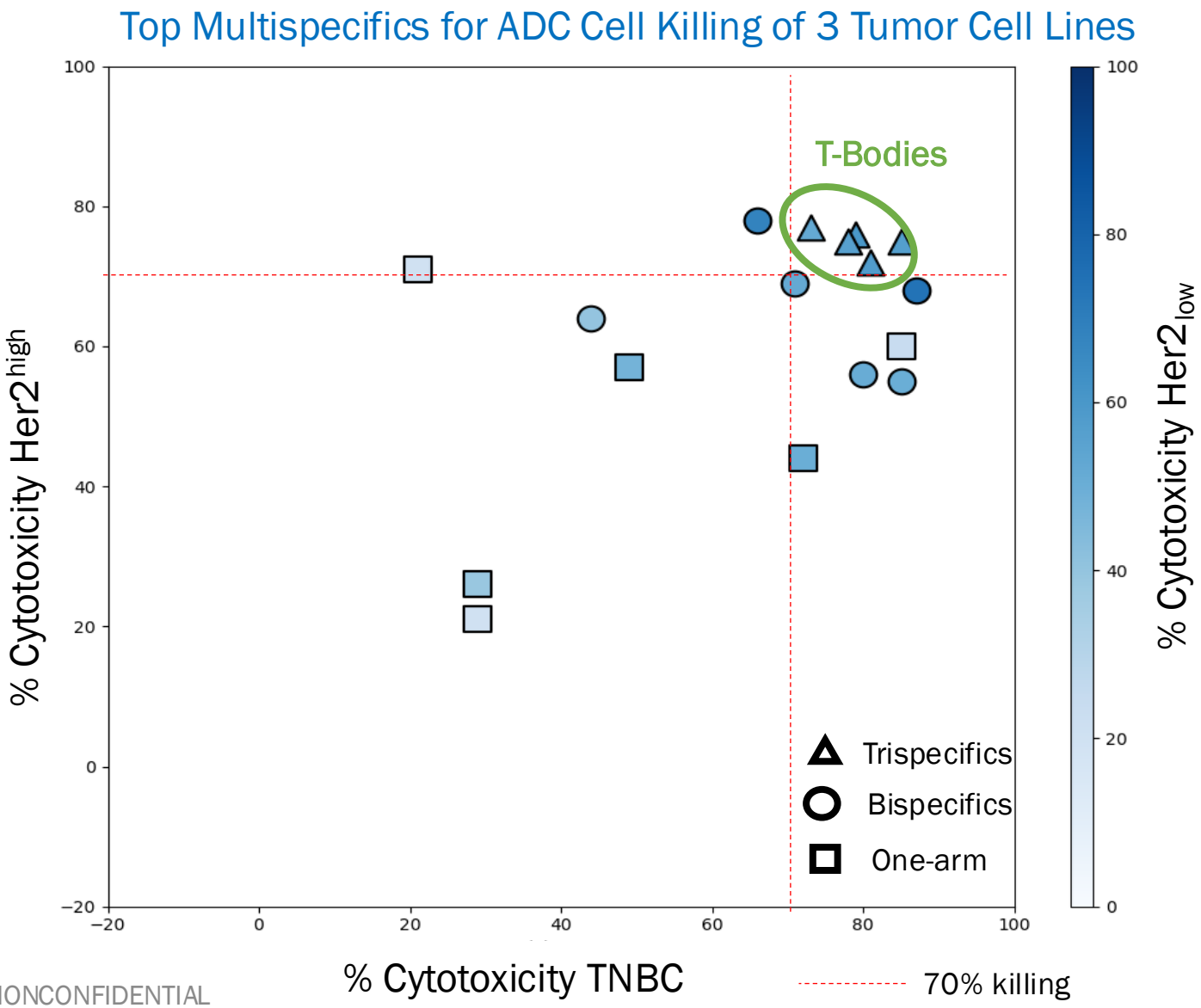


2-step purified



- T-Body trispecifics produced and screened against cell lines for killing
- Multispecific formats address problems of target heterogeneity and target loss in tumor environment

Identification of Top Multispecifics for ADCs

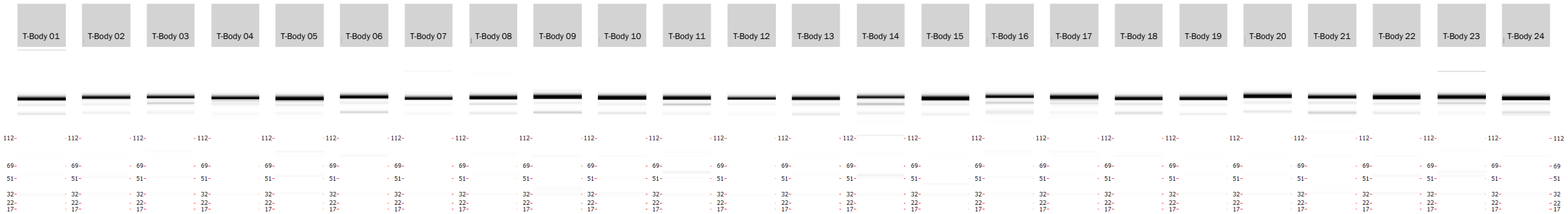


Invenra's B-Body bispecific and T-Body trispecific platforms enable direct comparison of multispecific formats to identify lead candidates

Trispecifics exhibited broader and more potent ADC killing activity than bispecifics

Trispecific ADCs are hypothesized to be more effective in heterogeneous tumors

T-Body Trispecific Platform Enables Exploration of Target Combinations from a Bispecific Matrix



T-Body Matrix Expression Results

- 5 Chain transient transfection into CHO cells
- Expression followed by CH1 purification yields range from 70-340 mg/L
- Non-reducing CE-SDS of proteins post CH1 purification showed purities ranging from 75 to 95%.

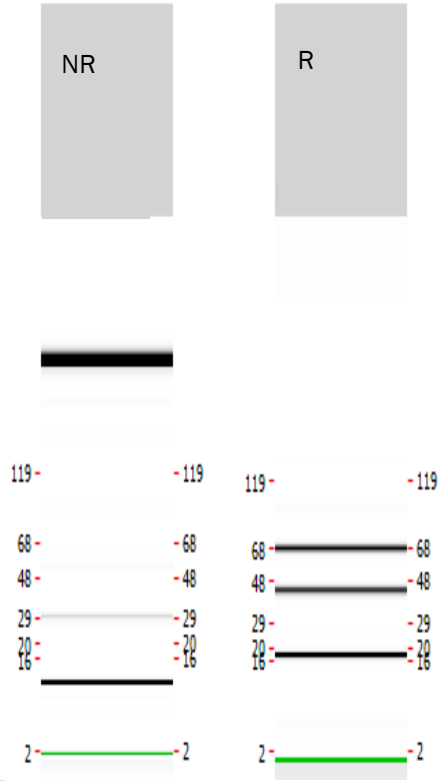
Robust T-Body Trispecific Production Enables Generation of ADCs

T-Body trispecific antibodies were produced from transient CHO and 2-step purified

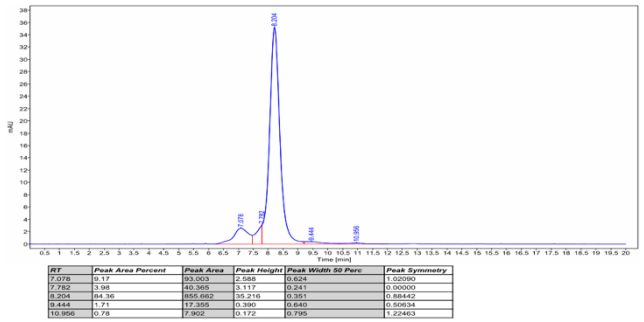
Production Summary	
Format	Trispecific
Expression System	ExpiCHO
Expression Yield (ug/mL)	306.44
Predicted MW (Da)	197997

Biophysical	
PDI	0.01
Z-Ave D (nm)	13.19
Tm (°C)	64
Tagg 266 (°C)	65.28
Tagg 473 (°C)	65.28

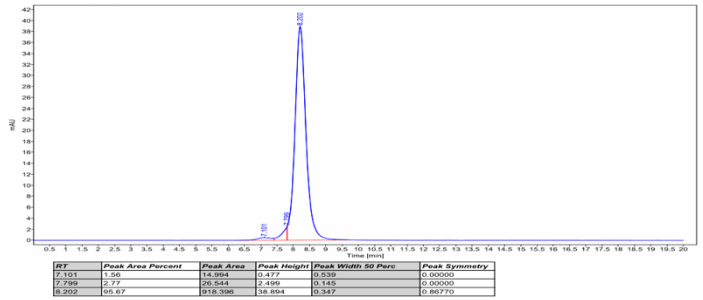
Capillary Electrophoresis (CE)



SEC—Single Step 84% Purity → *SEC—2 step 96% Purity*

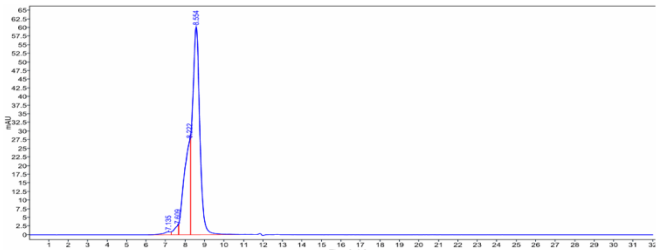


RT	Peak Area Percent	Peak Area	Peak Height	Peak Width 50 Perc	Peak Symmetry
7.078	9.17	93.003	2.588	0.624	1.02090
7.782	3.98	40.365	3.117	0.241	0.00000
8.204	84.36	855.662	35.216	0.351	0.88442
8.444	1.71	17.355	0.390	0.640	0.50634
10.956	0.78	7.902	0.172	0.795	1.22463



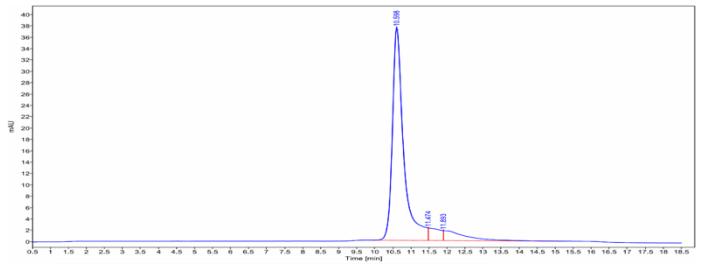
RT	Peak Area Percent	Peak Area	Peak Height	Peak Width 50 Perc	Peak Symmetry
7.101	1.56	14.994	0.477	0.539	0.00000
7.799	2.77	26.544	2.499	0.145	0.00000
8.202	95.67	918.396	38.894	0.347	0.66770

SMAC



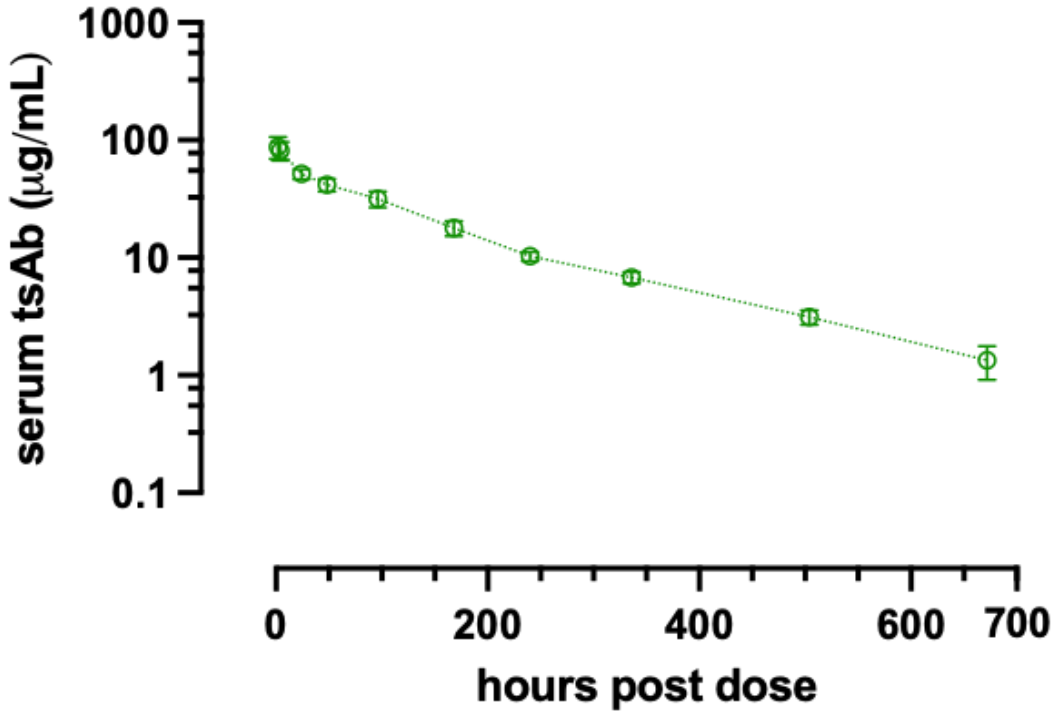
RT	Area	Peak Area Percent	Height	Peak Width 50 Perc	Peak Symmetry
7.135	24.6521	1.10	0.8758	0.376	0.00000
7.609	41.4078	1.84	2.6905	0.208	0.00000
8.222	631.7177	28.13	27.5027	0.379	0.00000
8.554	1548.2014	68.93	60.2228	0.455	0.87916

HIC



RT	Peak Area Percent	Peak Area	Peak Height	Peak Width 50 Perc	Peak Symmetry
10.598	86.57	812.061	37.452	0.289	0.60764
11.474	5.33	49.967	2.201	0.420	0.00000
11.893	8.11	76.044	1.735	0.562	0.00000

T-Body Trispecific has IgG-Like PK in Rats
(5 mg/kg dosing)



t1/2 (h)	158.83
Tmax (h)	2
Cmax (µg/ml)	104.84
AUC 0-t (ug/ml*h)	9651.04
Cl_obs (ml/h/kg)	0.499

Half-life = 6.6 days

Summary and Next Steps

Summary

- B-Body bispecific and T-Body trispecific antibodies exhibited good killing in piggyback ADC assays across a diverse set of breast cancer cell lines and had better activity than one-armed antibodies.
- B-Body bispecific and T-Body trispecific antibodies have the potential to more effectively address heterogeneous tumors and/or tumors that have become refractory to single-agent treatments.

Next Steps

- Explore applicability of top identified bispecifics and trispecifics in additional cancers beyond breast cancer
- Explore linkers/payloads for direct conjugation to top identified bispecifics and trispecifics to assess performance
- Explore in *in vivo* efficacy and toxicity models

Invenra's Multispecific Antibody Platform Technologies

Platform Innovation: Proprietary B-Body® and T-Body™ platforms enable rapid generation of highly developable multispecific constructs

Technical Performance: Industry-leading expression yields (up to 11 g/L for bispecifics) with CMC-ready formats and sub-Q compatibility

Development Timeline: Accelerated discovery timelines - bispecific leads generated in 4 months, B-Body bispecific constructs from existing mAb sequences in 4 weeks

Discovery & Development Programs: Portfolio includes 30+ active programs with 2 antibody constructs advancing to clinical development through partner programs

Manufacturability: Standard downstream processing compatibility with robust chain pairing and assembly for complex multispecific formats

Multispecific Antibody Development Pathways via B-Body Bispecific & T-Body Trispecific Platforms

B-Body Express™

Accommodates existing antibody assets

Any starting mAbs

Rapid & Custom Discovery

Invenra mAb Discovery

Bispecific Discovery

Cell Line Development

GMP Manufacturing

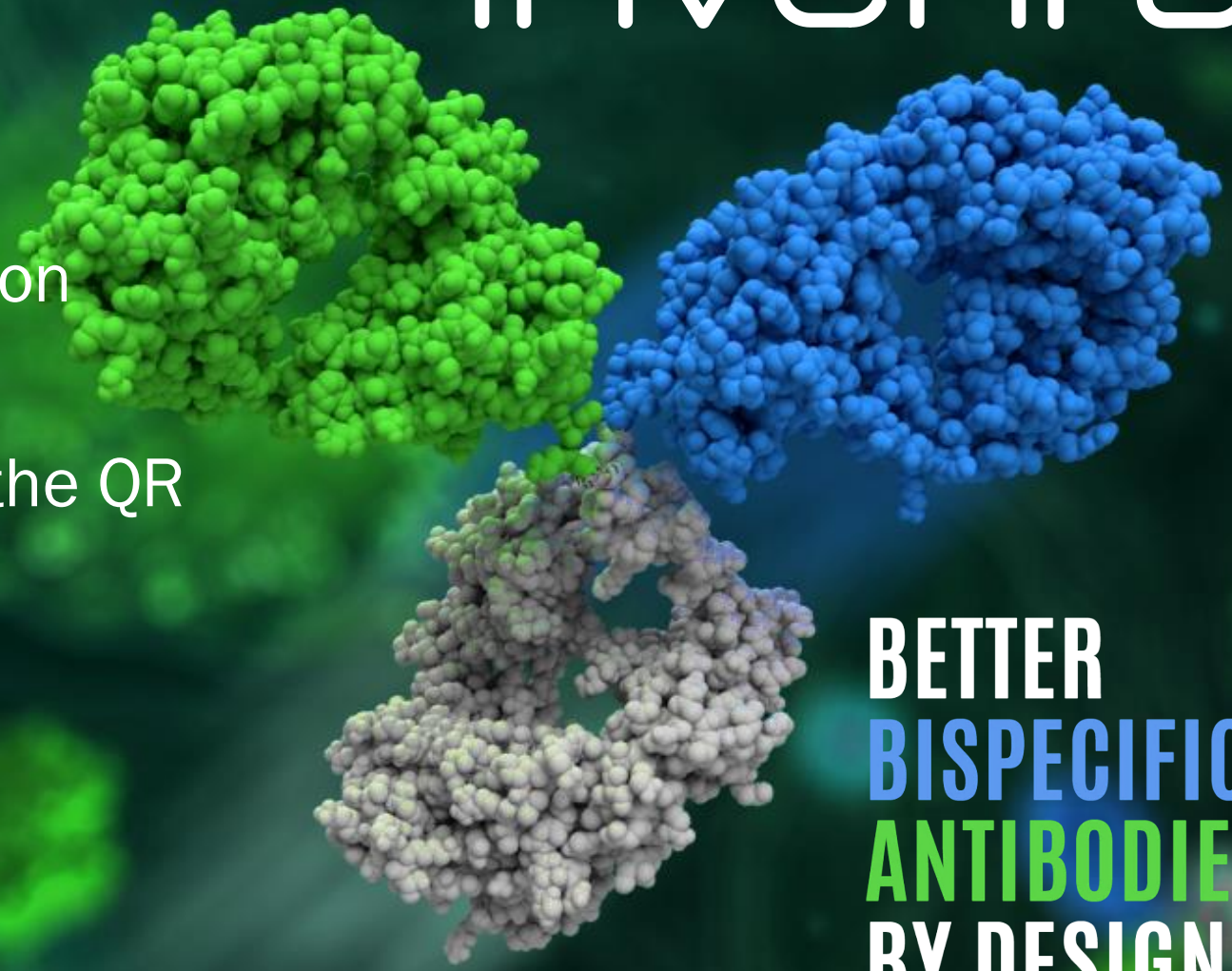
Platform technology transferable for in-house implementation

Available through validated manufacturing networks

Acknowledgments

- Our Invenra research team
- Our partners and collaborators
- All of you for your time and attention

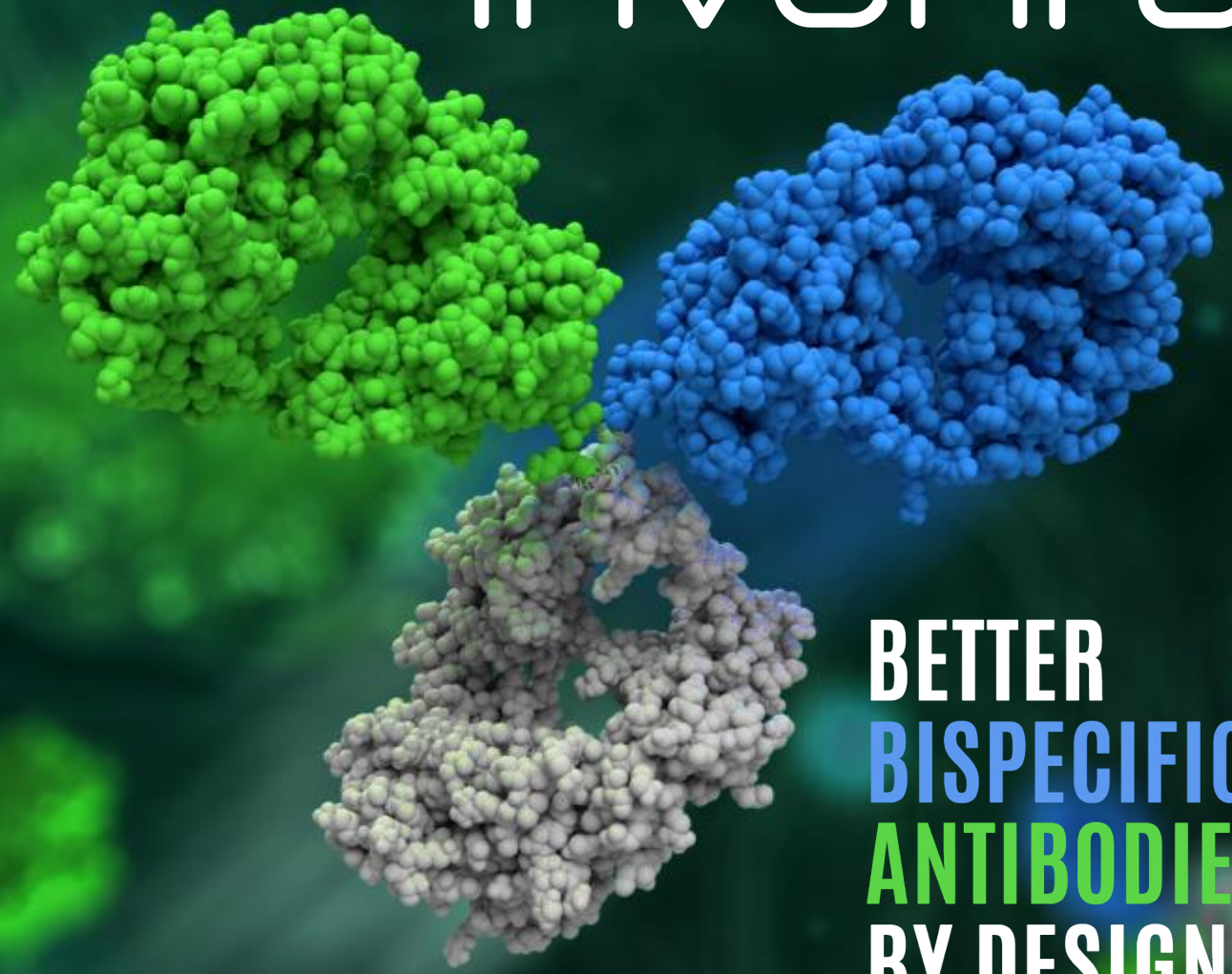
Visit us at our booth (#14) or scan the QR code to learn more



BETTER BISPECIFIC ANTIBODIES BY DESIGN

invenra

Thank you!



BETTER
BISPECIFIC
ANTIBODIES
BY DESIGN