T-Body: A Novel Trispecific Antibody Platform to Accelerate and De-Risk Drug Discovery
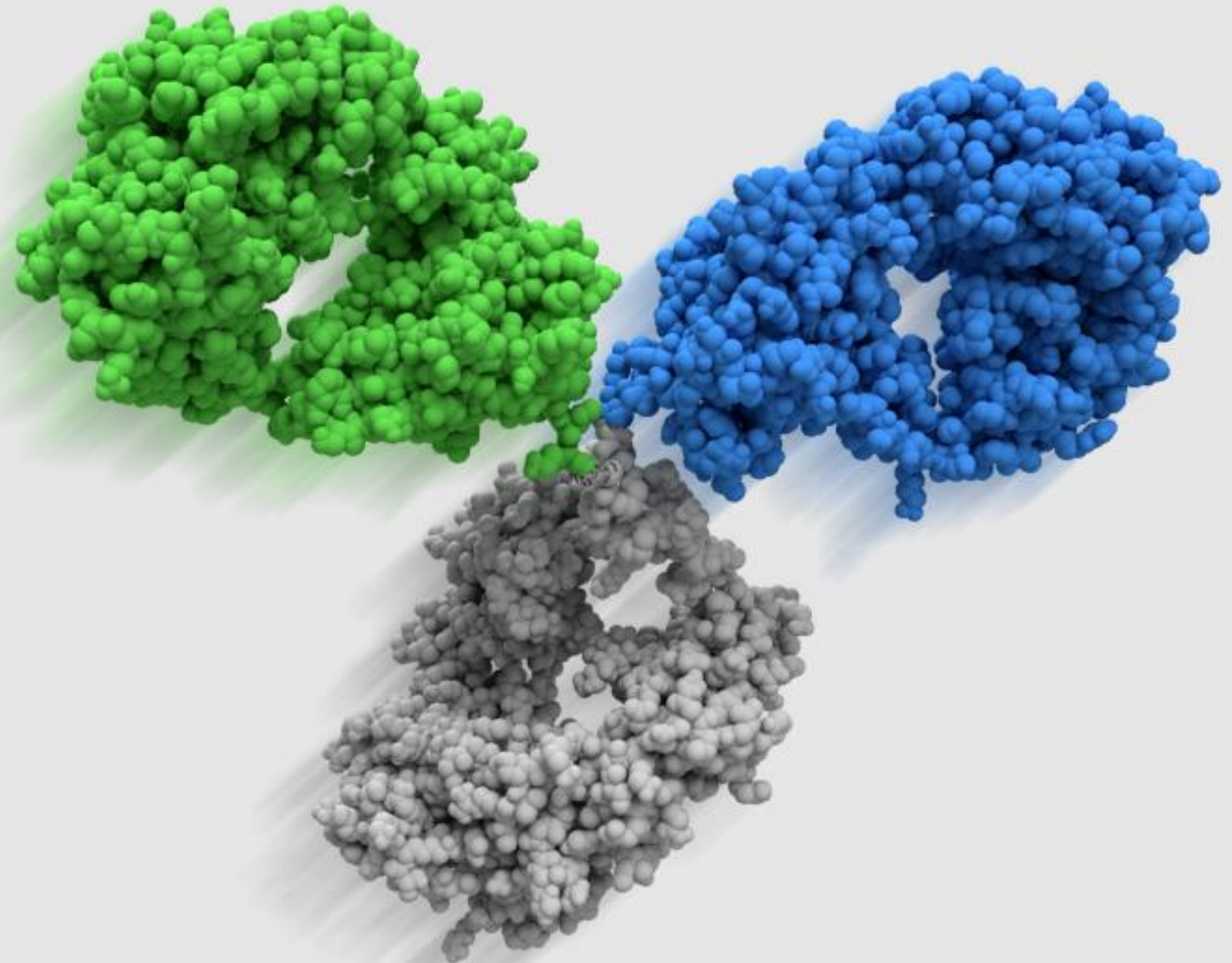
Antibody Engineering & Therapeutics

Dec. 16th, 2025

invenra

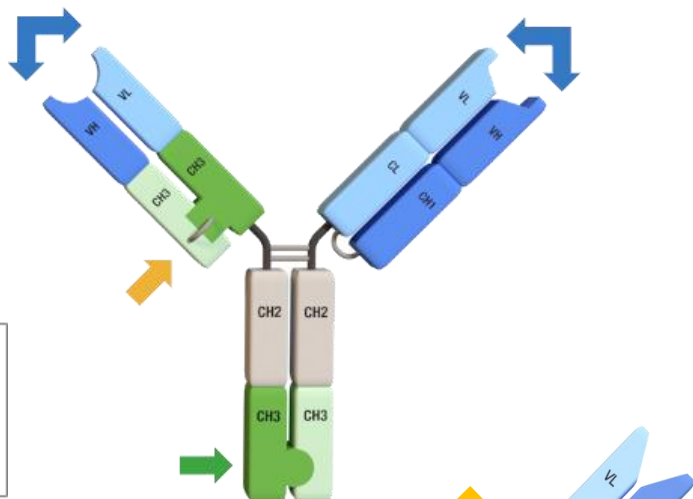# Invenra's Next-Generation Multispecific Antibody Platforms

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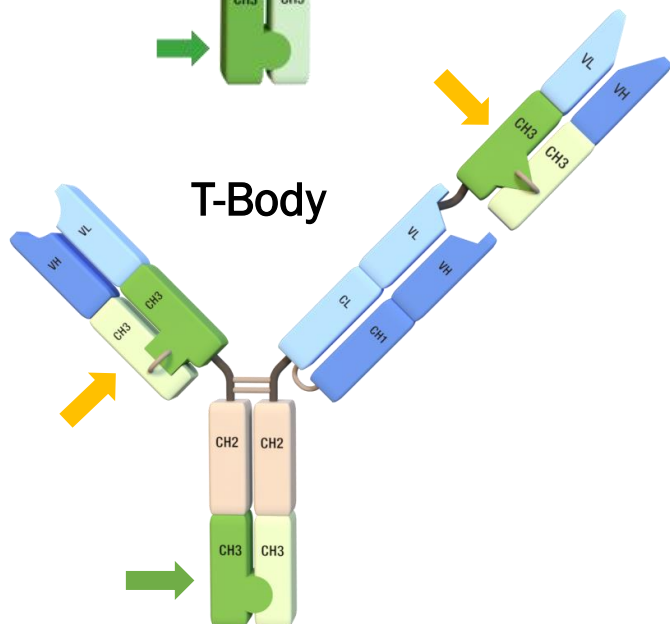
B-Body® Bispecific and T-Body™ Trispecific Platforms: Robust Solutions for Multispecific Antibody Development

B-Body

T-Body

Disulfides:

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
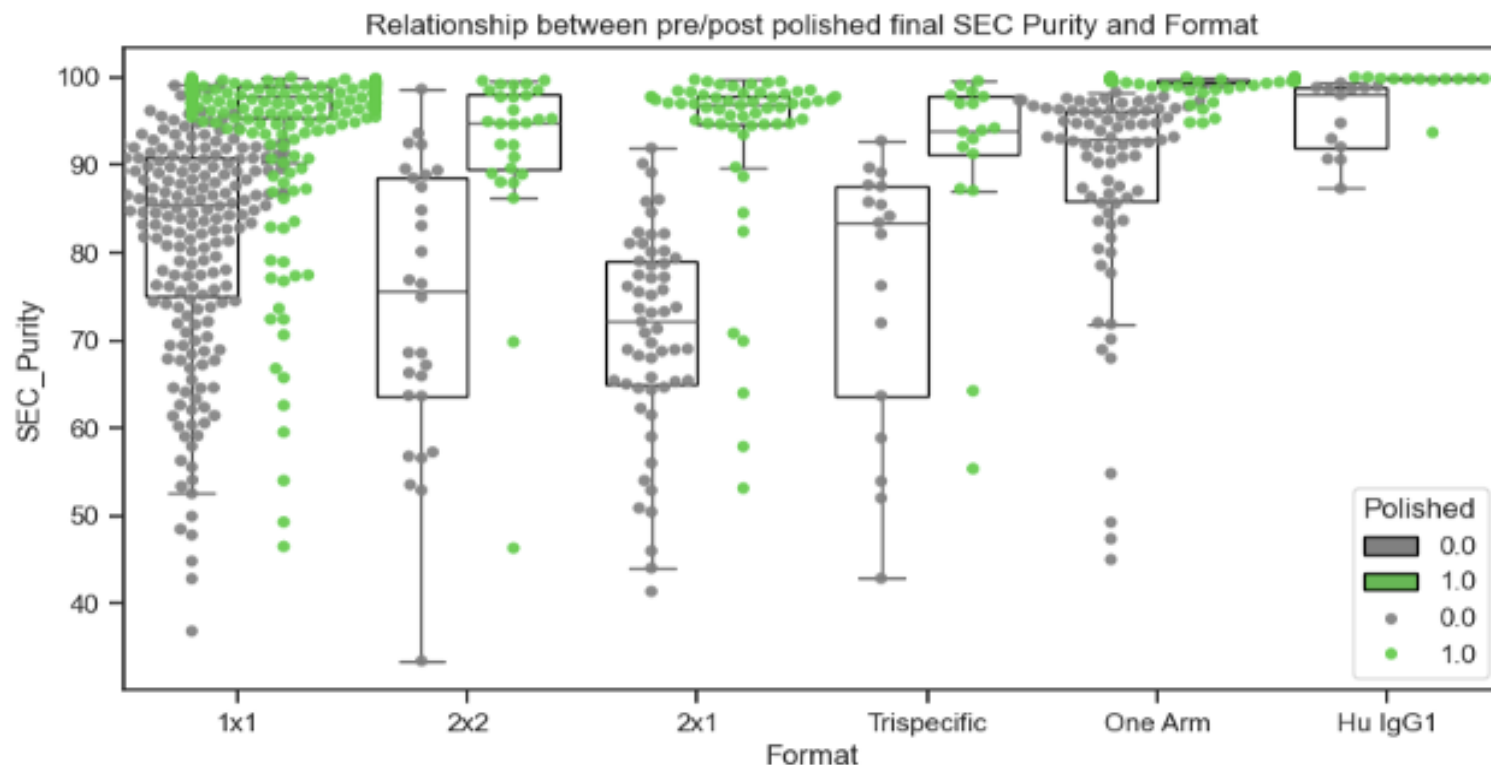- "Plug & Play" variable domains

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, trispecific
- Compatible with diverse mAbs & standard functional mutations
- Validated for conjugation
- Strong IP protection

B-Body Bispecific and T-Body Trispecific Platforms: Delivery of High-Purity Multispecific Antibodies Across Many Formats

Across formats, polishing consistently yields ≥90–95% SEC purity

Relationship between pre/post polished final SEC Purity and Format

Grey - % main peak purity (HPLC-SEC), post anti-CH1 capture

Green - % main peak purity (HPLC-SEC), post polishing chromatography

- Purity data of >1000 B-Body bispecifics and T-Body trispecifics from transient CHO expression
- Variable domains are from diverse sources with format-specific single chain ratios
  - Lead molecules can be optimized for expression and purity
- Single chain ratio tested
- Fit-for-purpose expression and purification protocols
- >95% of 1x1s achieve SEC purity target

Fast and reliable multispecific antibodies from "off the shelf" variable domains

- Ideal for rapid generation of tool and proof-of-concept multispecific antibodies at low cost

Robust T-Body Expression and Purification

T-Body trispecific antibodies were expressed in transient CHO and purified using a 2-step workflow

Production Summary

Format	Trispecific
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)

NR   R

SEC—single-step, 84% Purity → *SEC—two-step , 96% Purity*

- Excellent in-culture assembly
- Low level product related impurities are easily removed
- High purity is delivered with fit-for-purpose methods
- Plug-and-play with human Fab variable domains from any source
  - No requirement for VHH or scFv domains
- No need to discover 3 common light chains
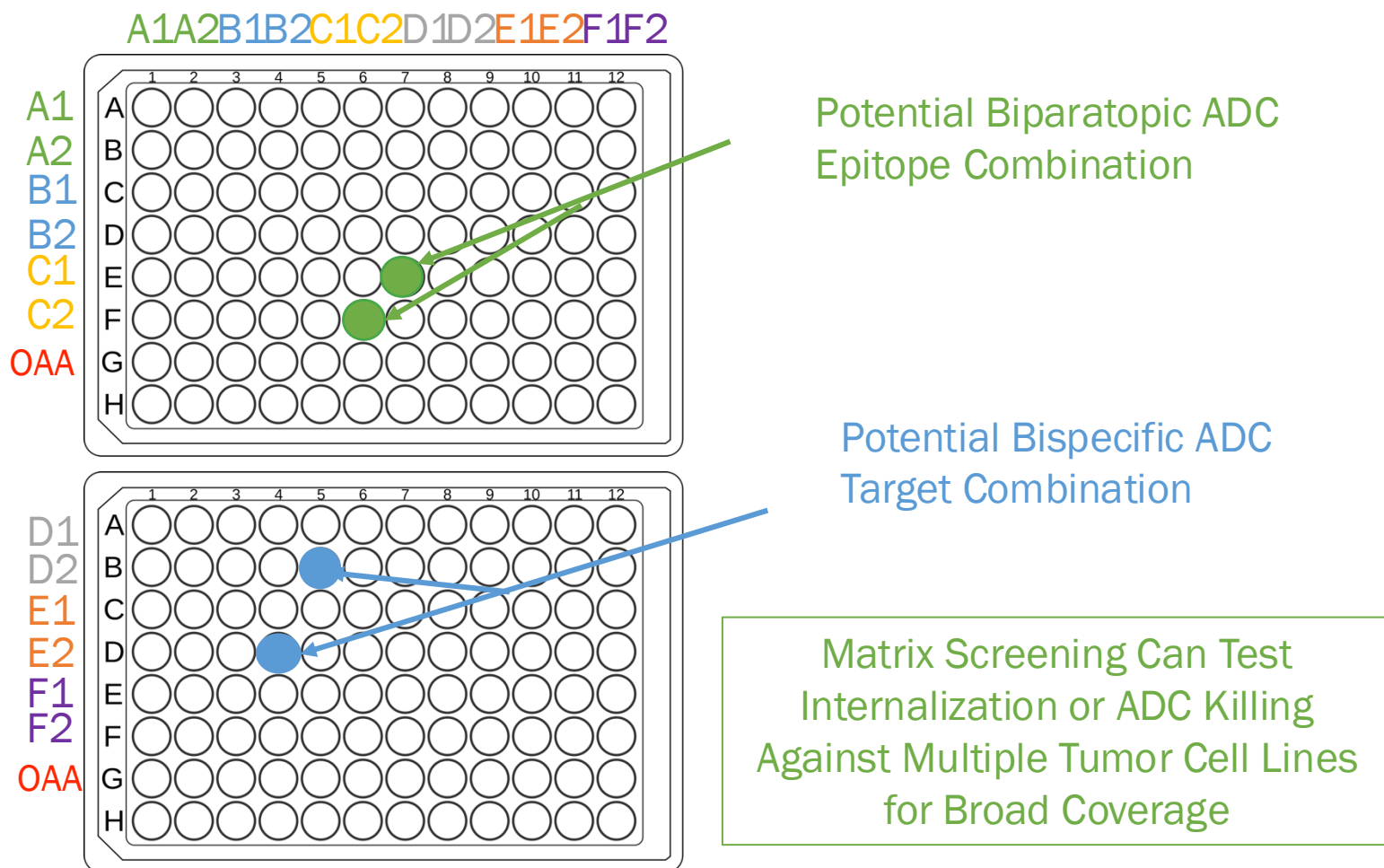- Potential for an "instant pipeline" using off-the-shelf Fab domains

T-Body Trispecific has IgG-Like PK in Rats
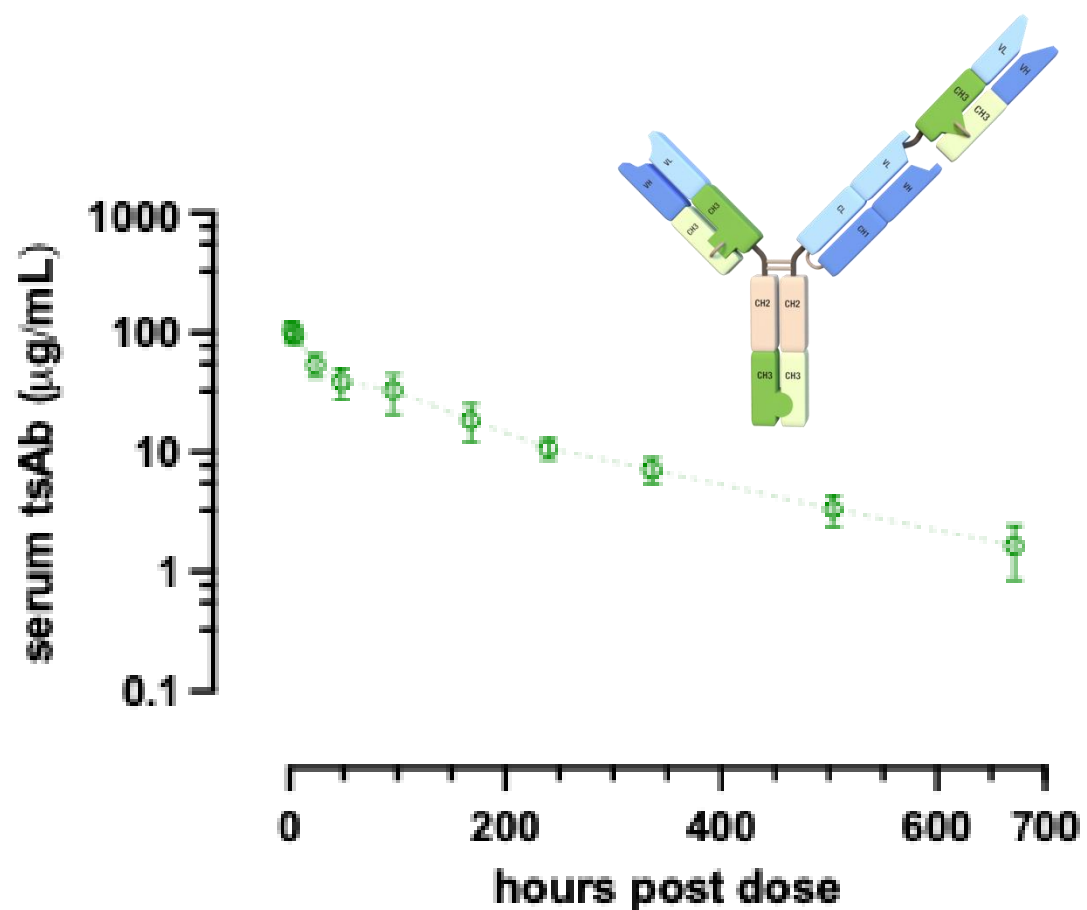
t1/2 (h)	158.83
Tmax (h)	2
Cmax (µg/ml)	104.84
AUC 0-t (ug/ml*h)	9651.04
Cl_obs (ml/h/kg)	0.499

Half-life = 6.6 days

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

A1A2B1B2C1C2D1D2E1E2F1F2

Potential Biparatopic ADC Epitope Combination

Potential Bispecific ADC Target Combination

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

Key Questions:

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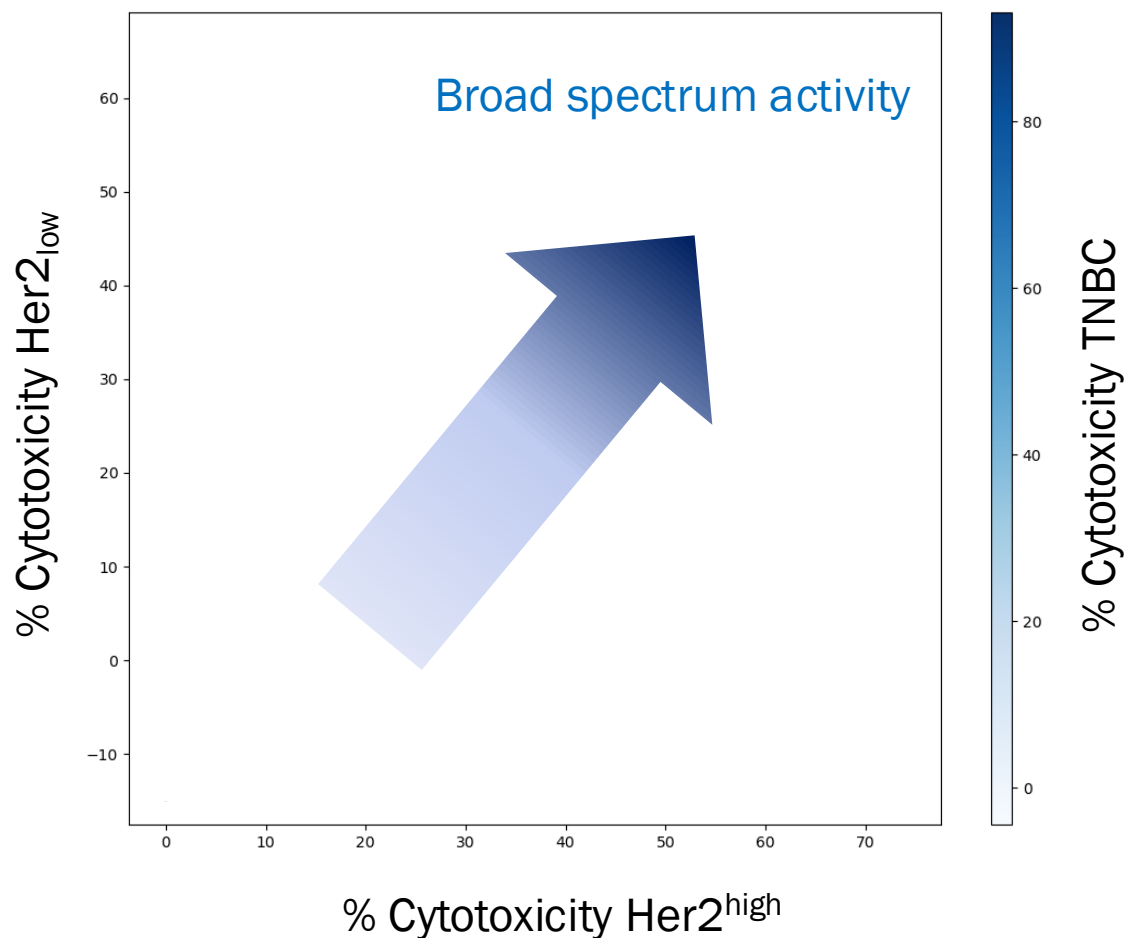3. Can we target a variety of cancer subtypes?

Matrix Screening of Antibodies to Multiple Target Epitopes
Unique Targets (ABCDEF) & Unique Epitopes (1-2)

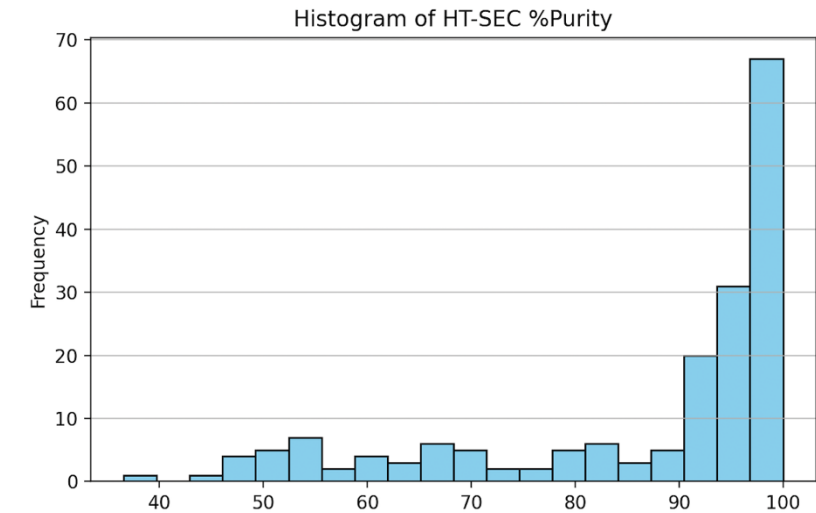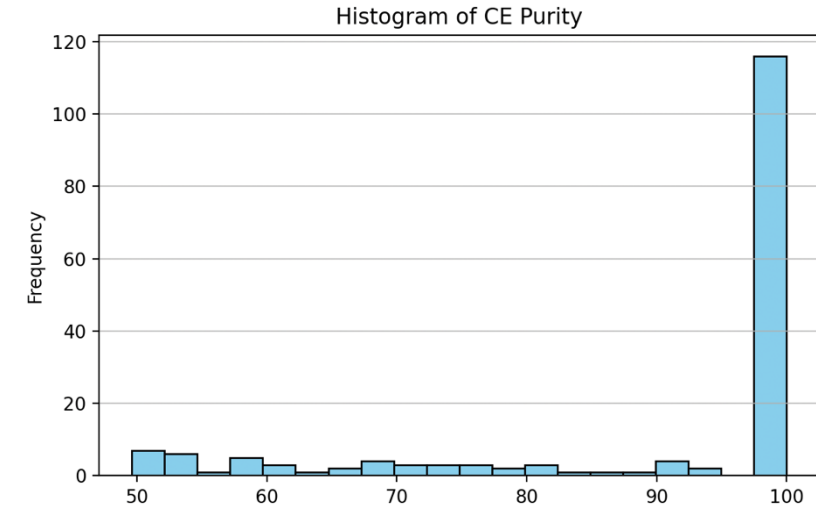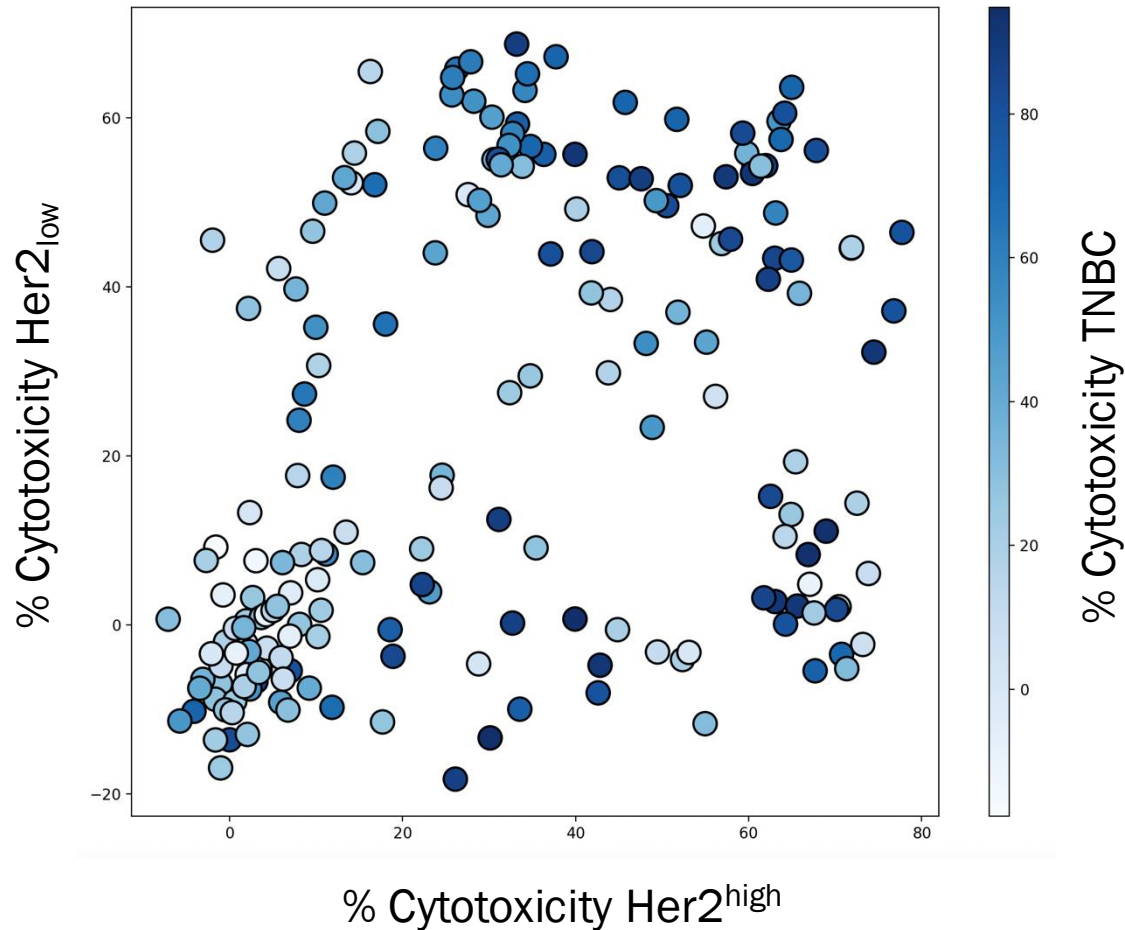# Identification of Multispecifics for ADCs with Broad Cytotoxic Activity

Comparison of Cell Killing Against 3 Tumor Cell Lines

Broad spectrum activity

% Cytotoxicity Her2$_{low}$ (y-axis)

% Cytotoxicity TNBC (color bar)

% Cytotoxicity Her2^{high} (x-axis)

- 12x12 matrix of bispecifics produced
  - 6 targets, 2 arms per target
  - Biparatopics included
  - One-armed controls included
  - **All binding domains were human Fab domains that were previously discovered or publicly available**
- 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
- Timeline – Start to finish in about 7 weeks

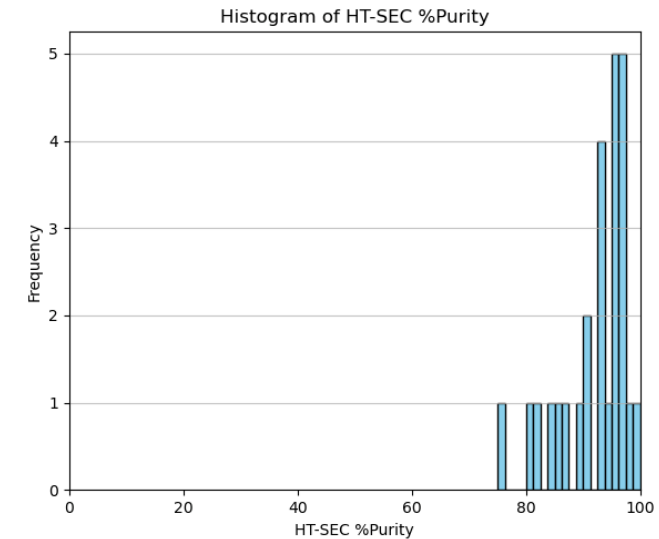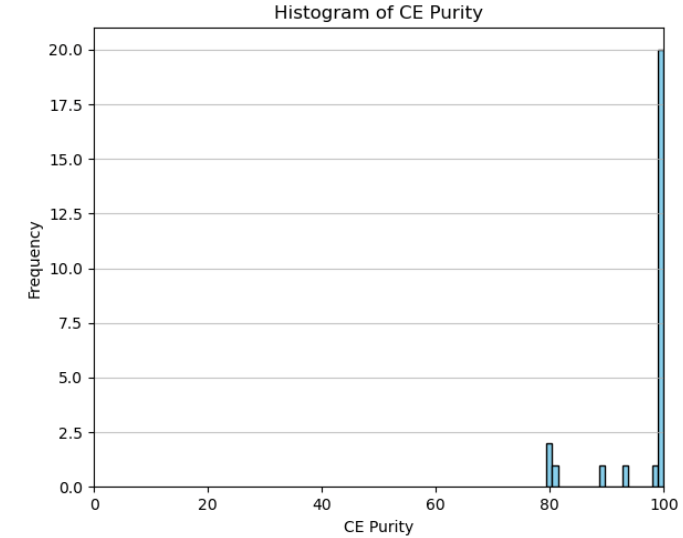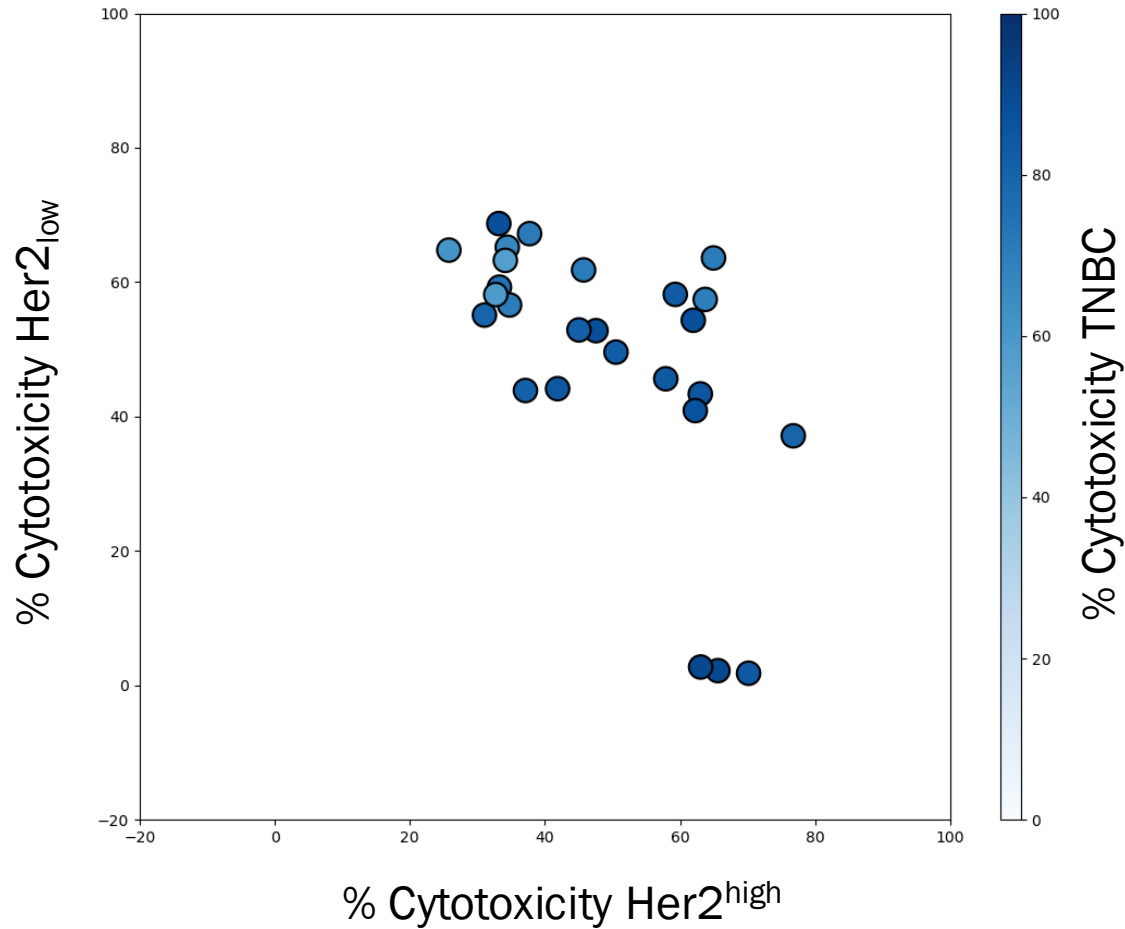# Identification of Multispecifics for ADCs with Broad Cytotoxic Activity

Comparison of Cell Killing Against 3 Tumor Cell Lines

Well-assembled bispecifics

Identification of Multispecifics for ADCs with Broad-Spectrum Activity

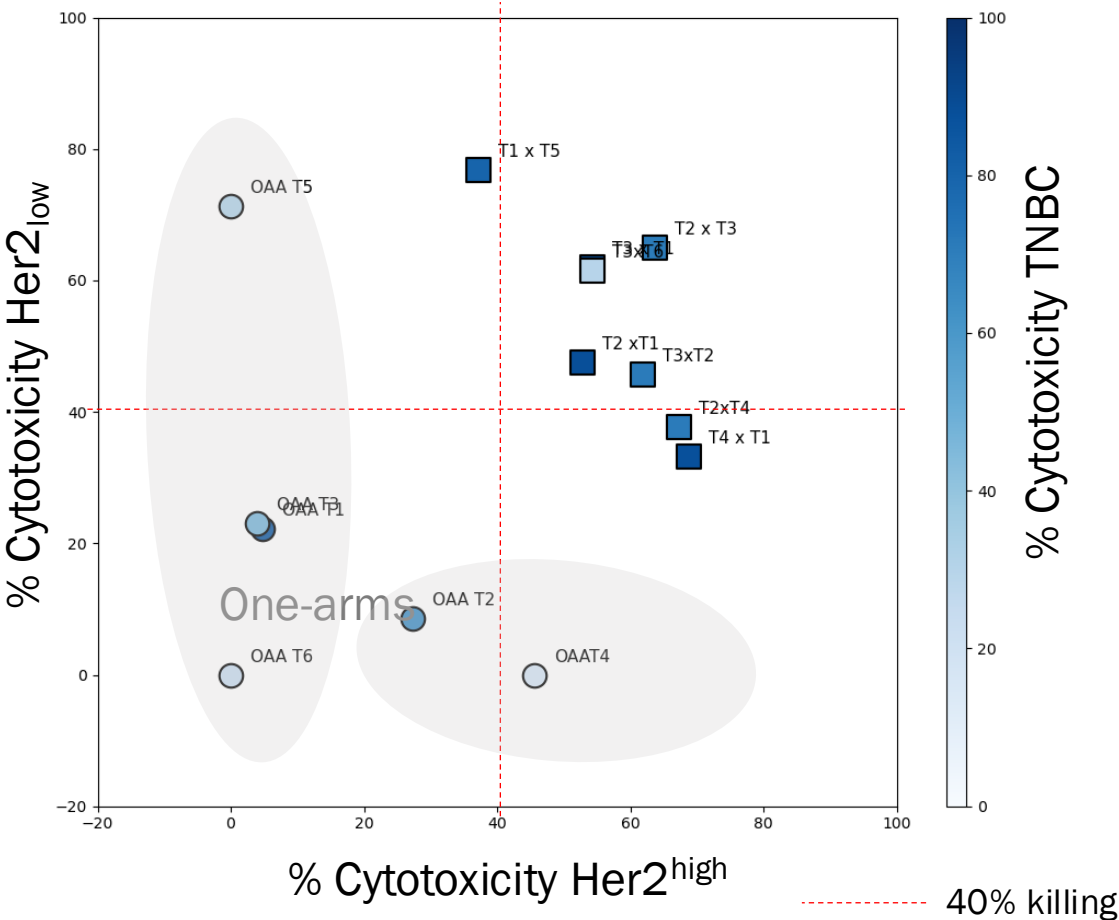Top 25% Cell Killing Against 3 Tumor Cell Lines

Well-assembled bispecifics

Identification of Top Target Combinations for ADCs

Combinations were prioritized for reformatting into T-Body trispecifics

% Cytotoxicity Her2^{low} vs % Cytotoxicity Her2^{high}

One-arms

------- 40% killing

	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

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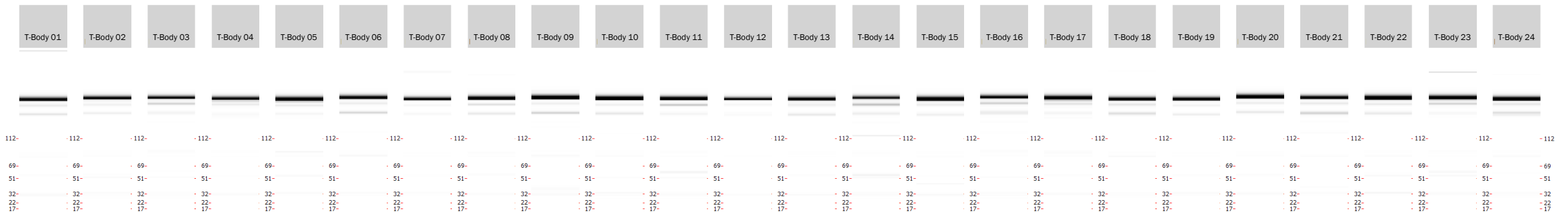

T-Body Trispecific Expression Results

- 5 Chain transient transfection into CHO cells

- Expression followed by CH1 purification showed yields ranging from 70 to 340 mg/L

- Non-reducing CE-SDS of proteins post CH1 purification showed purities ranging from 75 to 95%.

Identification of Top Multispecific Antibodies for ADCs

Top Multispecifics for ADC Cell Killing of 3 Tumor Cell Lines
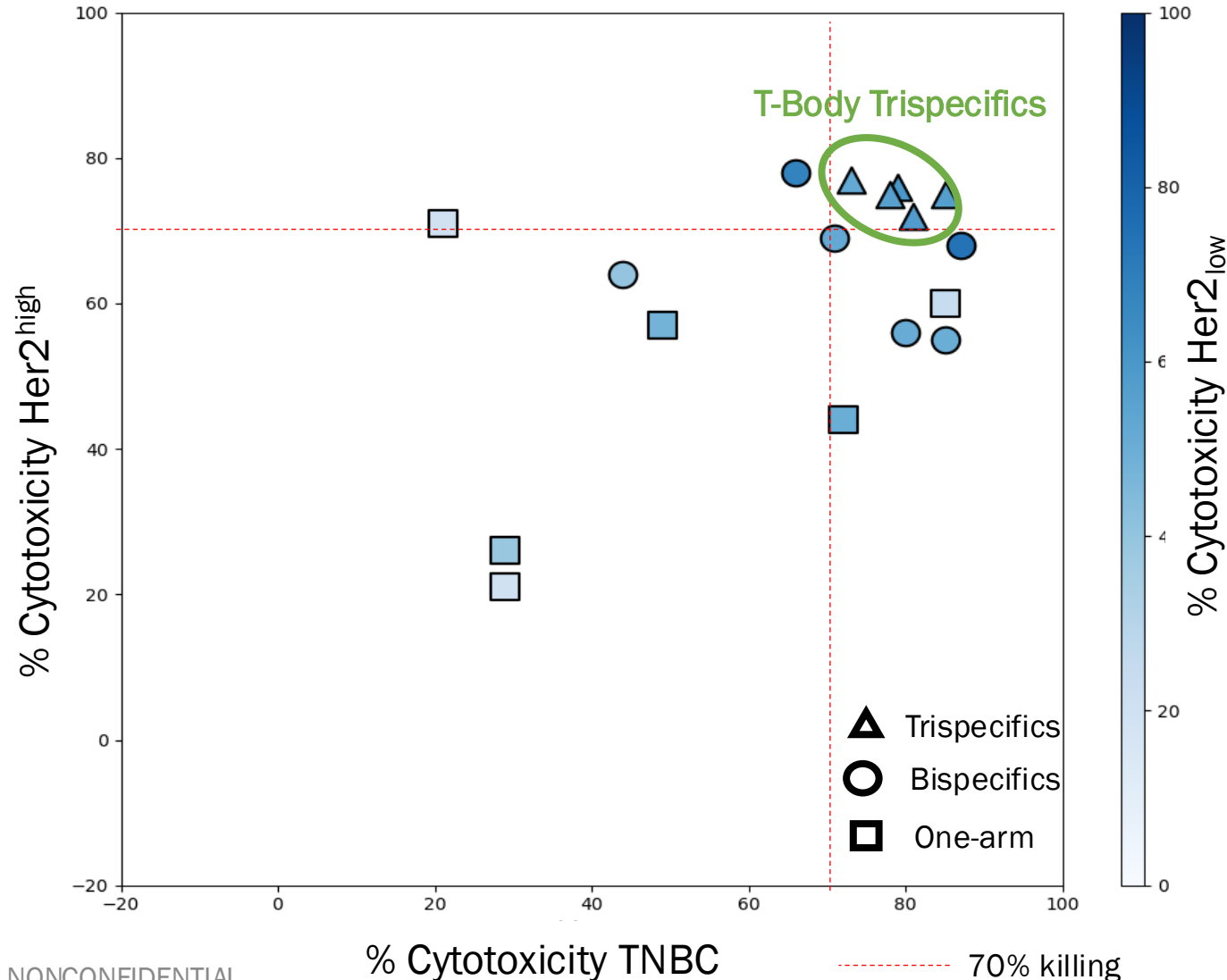
- Invenra's B-Body bispecific and T-Body trispecific platforms enable direct comparison of multispecific formats to identify lead candidates

- Trispecifics exhibited broader and more potent ADC killing activity than bispecifics

- Trispecific ADCs are hypothesized to be more effective in heterogeneous tumors

- Parental mAb combinations can be screened in matrix format, enabling selection and generation of T-Body trispecifics in 7 weeks, format-ready for cell line development

Invenra's Multispecific Antibody Platform Technologies

Platform Innovation: Proprietary B-Body® bispecific and T-Body™ trispecific 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
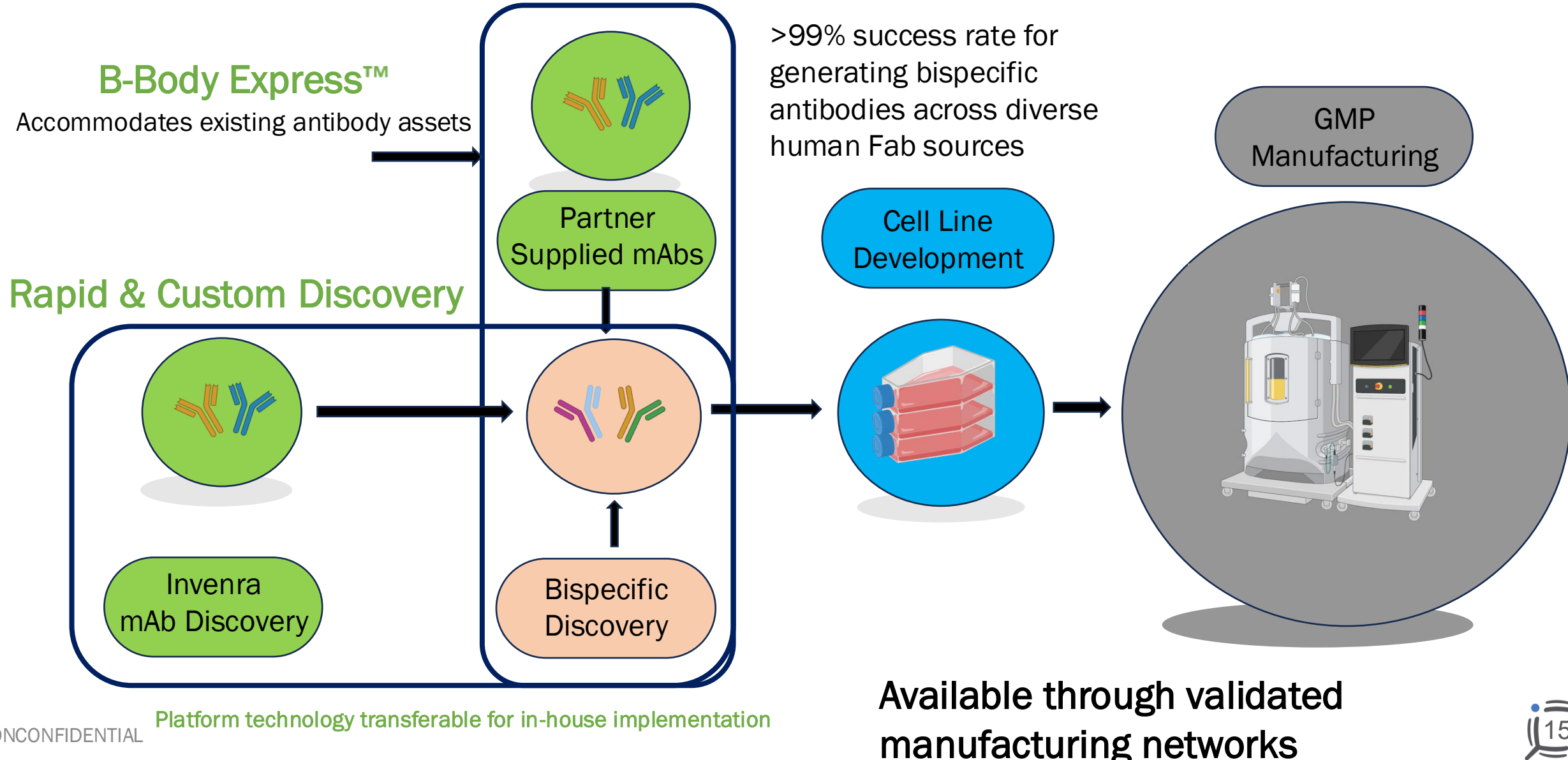
Development Timeline: Accelerated discovery timelines with bispecific leads generated in 4 months, B-Body bispecific constructs from existing mAb sequences in 4 weeks via B-Body Express™

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
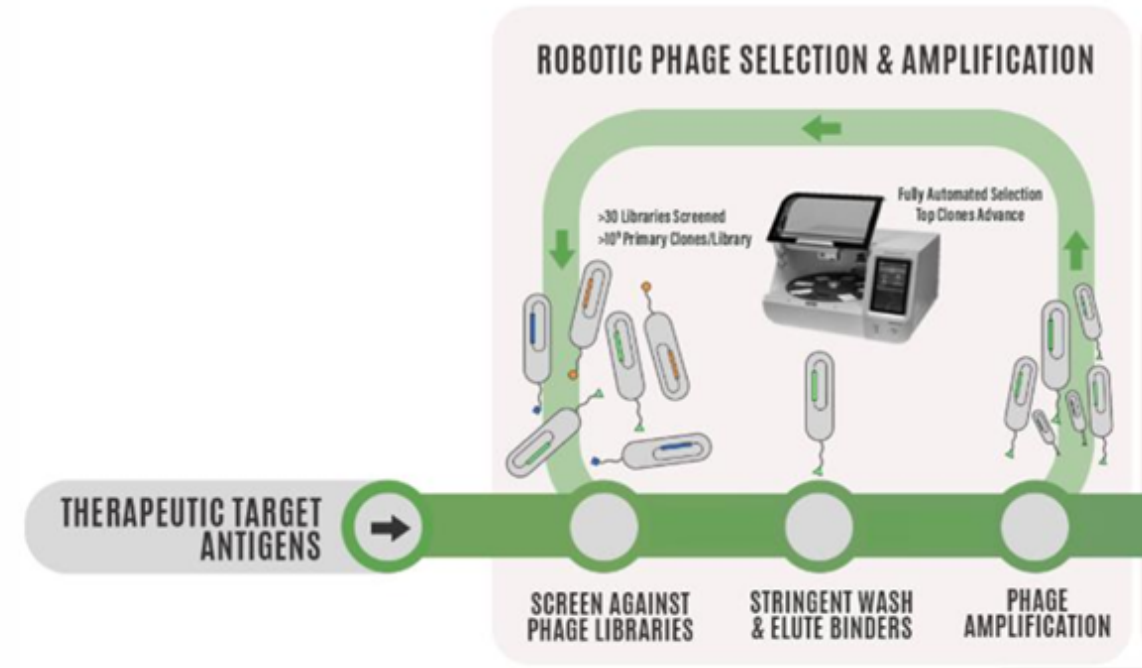

B-Body Express™
Accommodates existing antibody assets

Partner Supplied mAbs

>99% success rate for generating bispecific antibodies across diverse human Fab sources

GMP Manufacturing

Rapid & Custom Discovery

Cell Line Development

Invenra mAb Discovery

Bispecific Discovery

Platform technology transferable for in-house implementation

Available through validated manufacturing networks

Rapid Discovery Step 1: Automated Antibody Discovery

Next Generation Libraries Empowering Discovery

- Founded on Data Science Biology

- Represents diverse array of human germlines

- Natural CDR diversity and pairings with minimal liabilities

- Germline frameworks for clinical success

- >30 proprietary phage libraries with >10^9 primary clones/library.

Robotic Phage Selection and Amplification

- >30 libraries screen with up to 3 different conditions for >90 unique screens run in parallel to identify mAb candidates

- Wide range of affinities (KDs) and epitope diversity possible

- Optimized for high developability and human-likeness

ROBOTIC PHAGE SELECTION & AMPLIFICATION

>30 Libraries Screened
>10⁹ Primary Clones/Library

Fully Automated Selection
Top Clones Advance

THERAPEUTIC TARGET ANTIGENS

SCREEN AGAINST PHAGE LIBRARIES

STRINGENT WASH & ELUTE BINDERS

PHAGE AMPLIFICATION

Rapid Discovery Step 2: Clonal mAb Characterization

Standard Assays
- Full binding kinetics for human and cynomolgus antigen on up to four 96 well plates

Example Available Add-On Assays
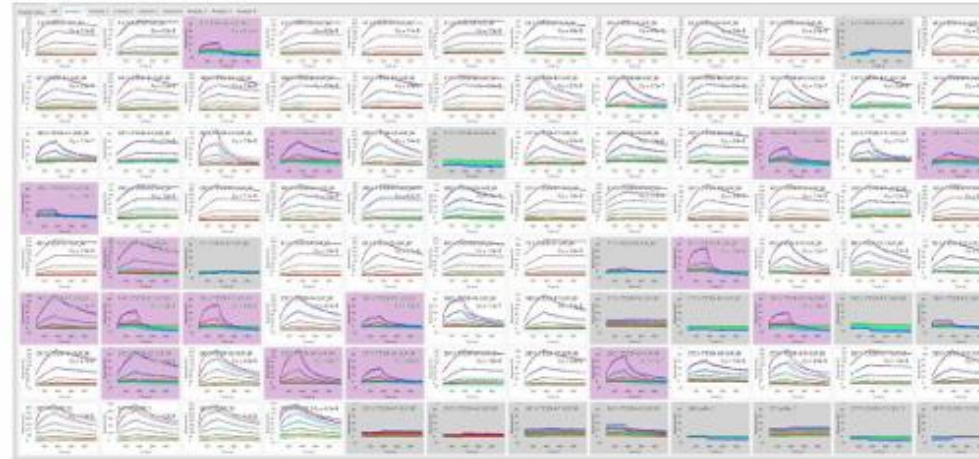- All by All Binning for up one 96 well plate
- Ligand blocking assay

Standard Assays
- Y/N cell binding to one cell line on up to four 96 well plates
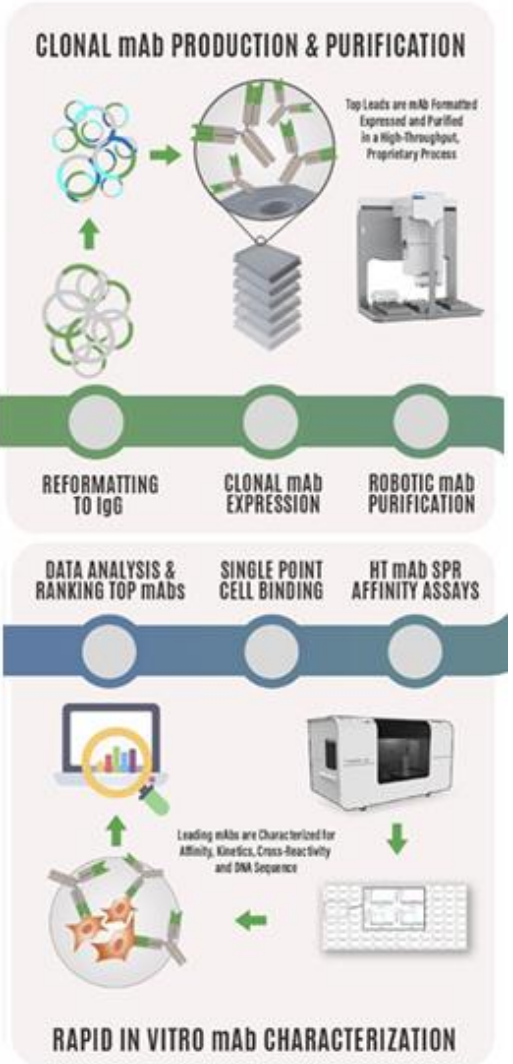
Example Available Add-Ons Assays
- Single concentration reporter gene assay for up to one 96 well plate

Binding (SPR) Data Collected on Carterra

Cell Binding ELISA

% Signal of Benchmark	1	2	3	4	5	6	7	8	9	10	11	12
A	50	17	154	35	7	1	24	93	43	61	20	1
B	34	32	24	1	4	8	49	35	47	24	25	164
C	25	55	0	36	97	96	121	47	67	112	15	3
D	27	4	55	45	17	0	107	28	42	144	195	68
E	3	102	156	1	26	52	46	1	26	0	15	3
F	117	0	60	105	4	0	-1	9	30	19	80	99
G	1	23	75	23	26	58	81	52	122	4	0	93
H	0	0	0	0	107	99	105	95	0	0	0	0

Benchmark Average: 142135

CLONAL mAb PRODUCTION & PURIFICATION

Top Leads are mAb Formatted Expressed and Purified in a High-Throughput, Proprietary Process

REFORMATTING TO IgG — CLONAL mAb EXPRESSION — ROBOTIC mAb PURIFICATION

DATA ANALYSIS & RANKING TOP mAbs — SINGLE POINT CELL BINDING — HT mAb SPR AFFINITY ASSAYS

Leading mAbs are Characterized for Affinity, Kinetics, Cross-Reactivity and DNA Sequence

RAPID IN VITRO mAb CHARACTERIZATION

Rapid Discovery Step 3:
High-Throughput Bispecific Antibody Production

Entry point for pre-discovered or public-domain Fabs

Standard Assays

- Expression of 12x12 B-body Matrix in 2 Orientations
- Single Step CH1 Affinity Purification
- Y/N Cell Binding
- Single Concentration Functional Assay
- Capillary electrophoresis
- Size exclusion chromatography (SEC)
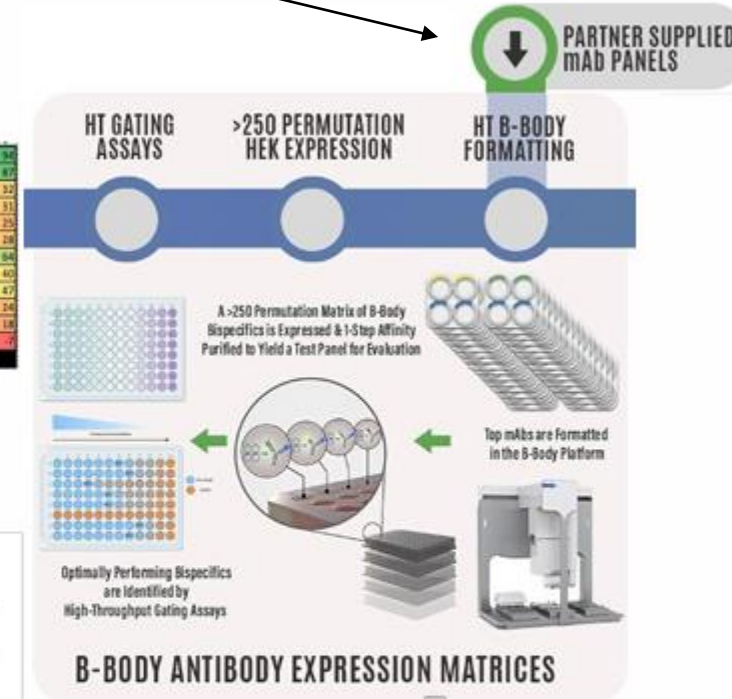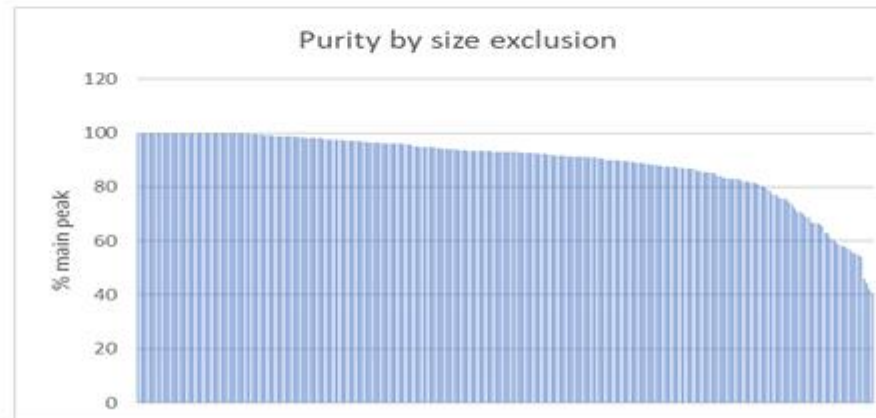- Polyreactivity
- AC-SINS

Example Available Add-On Assays

- Additional functional assays at single concentration for 12x12x2 Matrix
- 3 concentration functional assay for up to one 96 well plate

Example ADC Piggyback Functional Data

Example SEC Data 12x12x2 Matrix

Purity by size exclusion

PARTNER SUPPLIED mAb PANELS

HT GATING ASSAYS — >250 PERMUTATION HEK EXPRESSION — HT B-BODY FORMATTING

A >250 Permutation Matrix of B-Body Bispecifics is Expressed & 1-Step Affinity Purified to Yield a Test Panel for Evaluation

Top mAbs are Formatted in the B-Body Platform

Optimally Performing Bispecifics are Identified by High-Throughput Gating Assays

B-BODY ANTIBODY EXPRESSION MATRICES

Rapid Discovery Step 4: Functional Characterization

Expression and CH1 Purification

Target A Fabs

Target B Fabs

1x1
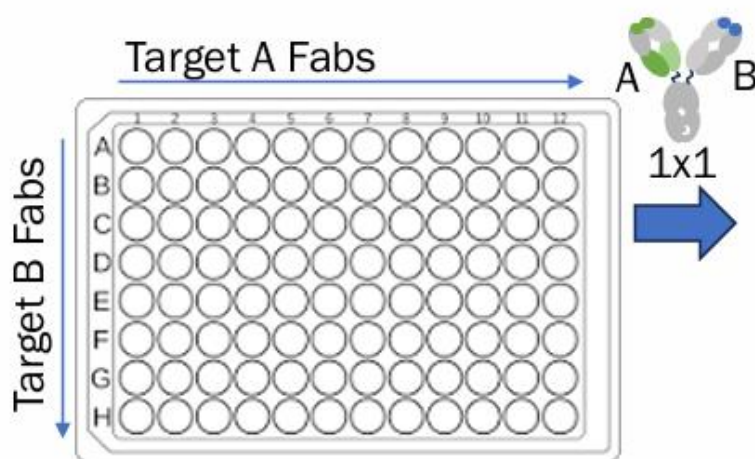
Cell Reporter/Viability Assays

% Killing Scale

Select Wells with Biggest Activity Differential from One-Armed Antibodies

Follow Up Dose Response

Top B-Body Candidates

- A x B
- A x C
- A x D
- A x E
- B x D
- C x D
- D x E
- B x E
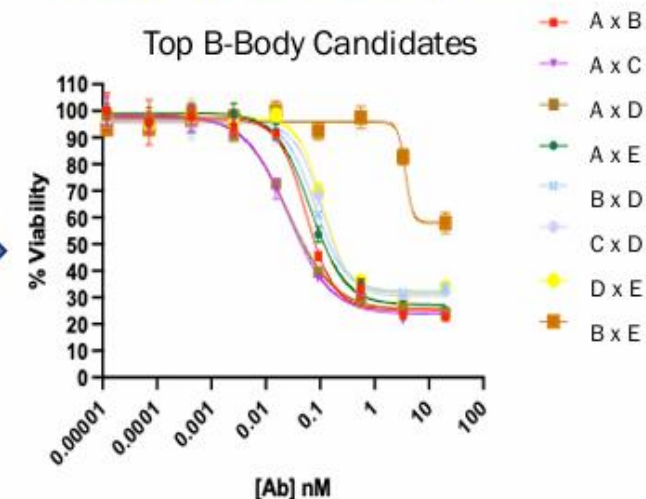
- Diverse off-the-shelf assay offerings
- Experienced team with deep expertise in executing kit-based assays
- Capability to on-board and run custom assays

B-Body Express: A Low Barrier Entry Point to Invenra's Multispecific Antibody Platforms

Step 1
- Partner provides variable domain sequences of interest to Invenra

Step 2
- Invenra concatenates the variable domain sequences into B-Body bispecific constructs and orders plasmid DNA

Step 3
- Invenra expresses and purifies the desired molecules using format-dependent, fit-for-purpose expression and purification methods

Step 4
- Invenra performs quality assessment and delivers the product to the partner, or retains material for downstream assay support

Excellent for rapid proof-of-concept studies when Fab domains are already available

B-Body Bispecifics:
Superior Manufacturability and Developability

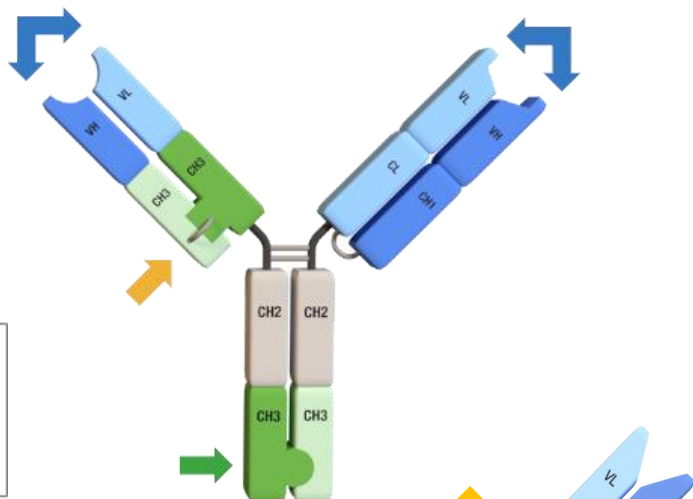| Metric	B-Body Platform	Industry Standard
Discovery Throughput	High: 250+ bispecifics screened in final format per project	Low: Limited capacity, often requires reformatting
Lead Screening Speed	Full lead panels delivered in 4 months	6–12 months, with additional time for reformatting
Yield (CHO Stable Clone)	6-11 g/L	1-3 g/L
Purification	Protein A + Ion Exchange	Multi-step Custom Process
Sub-Q Concentration	Up to 200 mg/mL	Limited

DEVELOPABAILITY REPORT CARD

B-Body Platform

	Expression & Purity	A
	Thermal Stability	A
	Self-Association	A
	Aggregation	A
	Solubility	A
	Immunogenicity Risk	A
	Viscosity	A
	TOTAL GRADE	A

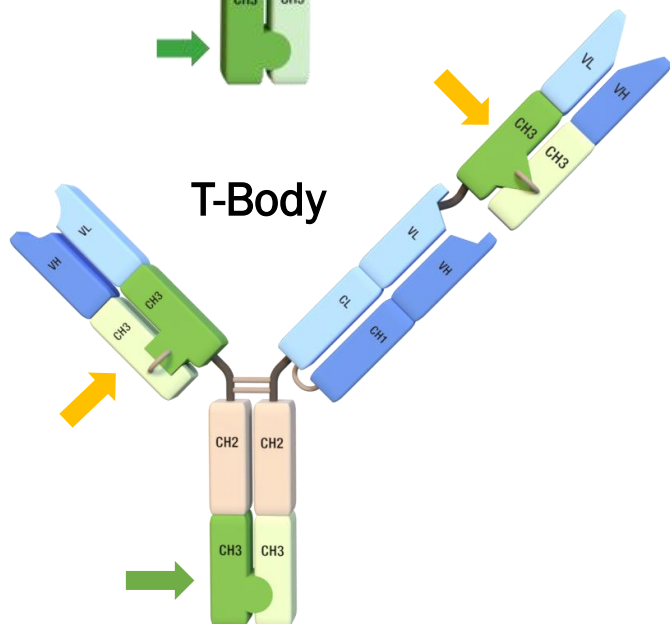## Superior Yields. Seamless Purification. Unmatched Developability

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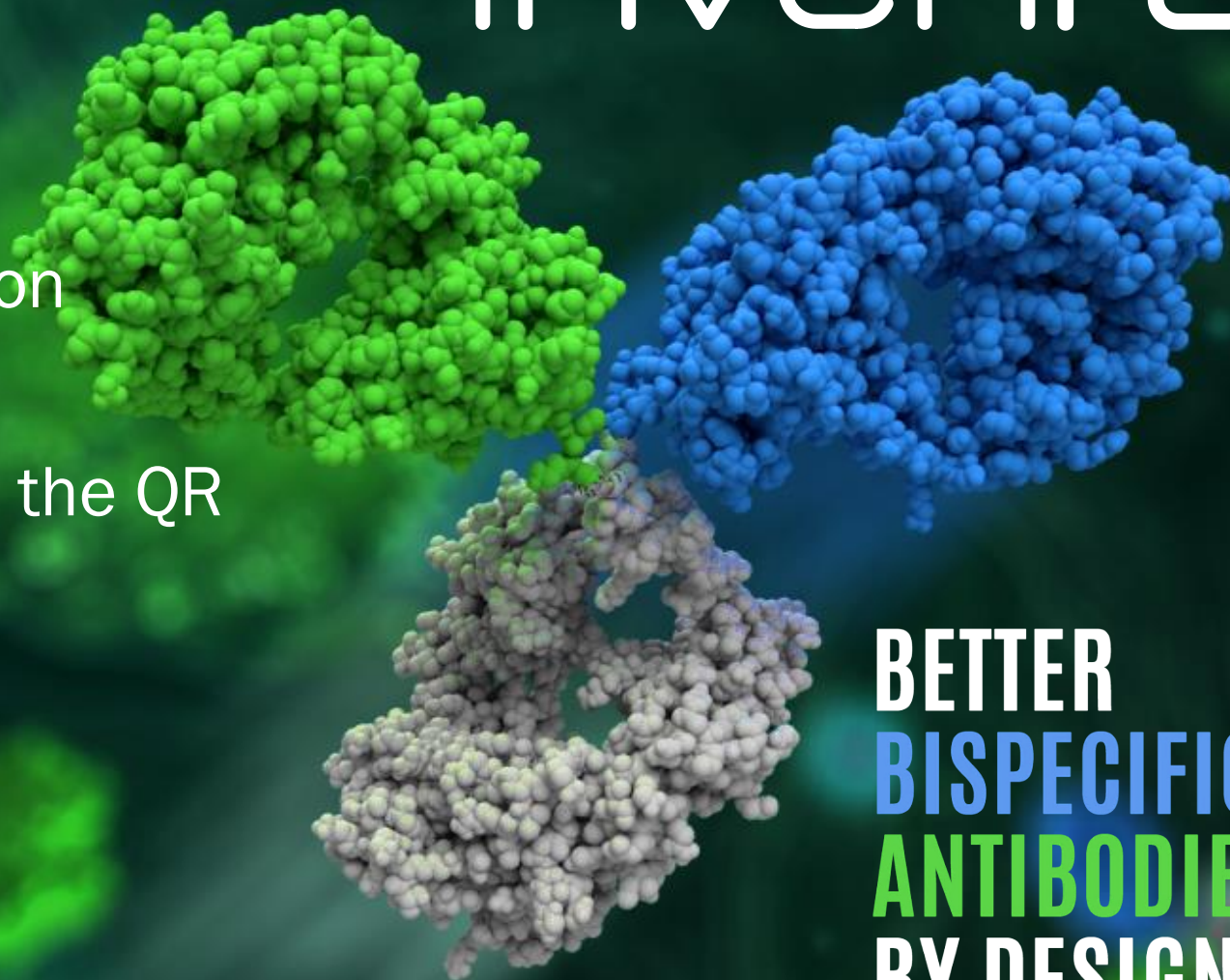- Strong IP protection

Acknowledgments

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

Visit us at our booth (#108) or scan the QR code to learn more

Thank you!

invenra

BETTER
BISPECIFIC
ANTIBODIES
BY DESIGN