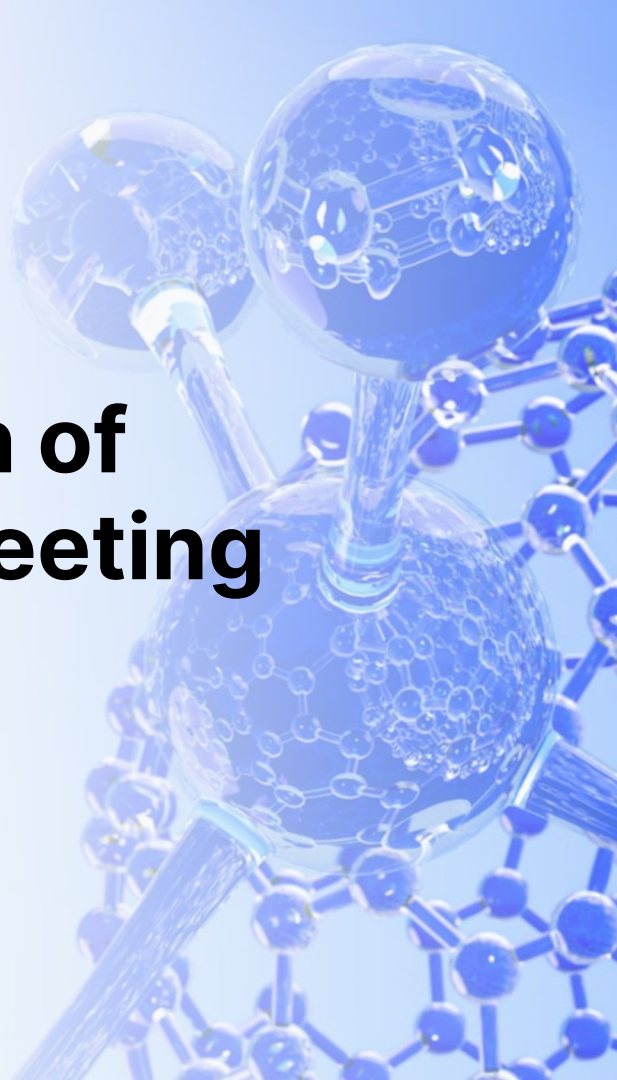
zymeworks

2023 American Association of Cancer Research Annual Meeting

Investor & Analyst Webcast and Conference Call

April 18, 2023



Legal Disclaimer

This presentation and the accompanying oral statements includes "forward-looking statements" or information within the meaning of the applicable securities legislation, including Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Forward-looking statements in this presentation and the accompanying oral statements include, but are not limited to, statements that relate to Zymeworks' preclinical pipeline; the potential therapeutic effects of zanidatamab and Zymeworks' other product candidates; the potential of Zymeworks' technology platforms to generate additional product candidates; Zymeworks' ability to achieve its strategic goals; Zymeworks' ability to enhance shareholder value through its Enterprise Value Framework; anticipated regulatory submissions and the timing thereof; Zymeworks' clinical development of its product candidates and enrollment in its clinical trials; anticipated preclinical and clinical data presentations; the ability to advance product candidates into later stages of development; anticipated initiation of additional preclinical and clinical studies and the timing of receipt of data; and other information that is not historical information. When used herein, words such as "plan", "believe", "expect", "may", "anticipate", "potential", "will", "continues", and similar expressions are intended to identify forward-looking statements. In addition, any statements or information that refer to expectations, beliefs, plans, projections, objectives, performance or other characterizations of future events or circumstances, including any underlying assumptions, are forward-looking. All forward-looking statements are based upon Zymeworks' current expectations and various assumptions. Zymeworks believes there is a reasonable basis for its expectations and beliefs, but they are inherently uncertain. Zymeworks may not realize its expectations, and its beliefs may not prove correct. Actual results could differ materially from those described or implied by such forward-looking statements as a result of various factors, including, without limitation: future clinical trials may not demonstrate safety and efficacy of any of Zymeworks' or its collaborators' product candidates; clinical trials may not demonstrate safety and efficacy of any of Zymeworks' or its collaborators' product candidates; despite promising results in preclinical animal models or trials, product candidates may exhibit unforeseen safety issues or inadequate efficacy, or could suffer setbacks in later clinical trials or studies; any of Zymeworks' or its partners' product candidates may fail in development, may not receive required regulatory approvals, or may be delayed to a point where they are not commercially viable; regulatory agencies may impose additional requirements or delay the initiation of clinical trials; the impact of the COVID-19 pandemic on Zymeworks' business, research and clinical development plans and timelines and results of operations, including impact on its clinical trial sites, collaborators, and contractors who act for or on Zymeworks' behalf, may be more severe and more prolonged than currently anticipated; the impact of new or changing laws and regulations; market conditions; inability to maintain or enter into new partnerships or strategic collaborations; and the factors described under "Risk Factors" in Zymeworks' quarterly and annual reports filed with the Securities and Exchange Commission, including its Annual Report on Form 10-K for its year ended December 31, 2022 (a copy of which may be obtained at www.sec.gov and www.sedar.com).

Although Zymeworks believes that such forward-looking statements are reasonable, there can be no assurance they will prove to be correct. Investors should not place undue reliance on forward-looking statements. The above assumptions, risks and uncertainties are not exhaustive. Forward-looking statements are made as of the date hereof and, except as may be required by law, Zymeworks undertakes no obligation to update, republish, or revise any forward-looking statements to reflect new information, future events or circumstances, or to reflect the occurrences of unanticipated events.

AACR Presentations Overview

Date	Time	Title	Abstract #	Session: Category, Title, Location & Poster Board #	Presenter
April 17	9:00 am – 12:30 pm ET	Revisiting the dogma of antibody drug conjugates (ADCs): Emerging data challenge the benefit of linker stability and the primacy of payload delivery	1538	Category: Experimental and Molecular Therapeutics Title: Antibody Drug Conjugates Location: Section 14 Poster Board: 18	Raffaele Colombo
		ZW220, a novel NaPi2b-targeting antibody drug conjugate bearing a topoisomerase 1 inhibitor payload	1533	Category: Experimental and Molecular Therapeutics Title: Antibody Drug Conjugates Location: Section 14 Poster Board: 13	Andrea Hernandez Rojas
	1:30 – 5:00 pm ET	ZW270, a conditionally masked IL-12 cytokine fusion protein displaying potent anti-tumor activity absent systemic toxicity	2935	Category: Immunology Title: Therapeutic Antibodies 2 Location: Section 23 Poster Board: 13	Nichole Escalante
		PROTECT™, a novel trispecific antibody masking platform with integrated immune modulation displays unique activity and differentiated modes of action	2926	Category: Immunology Title: Therapeutic Antibodies 2 Location: Section 23 Poster Board: 4	Anna von Rossum & Genevieve Desjardins
		TriTCE CPI, next generation trispecific T cell engagers with integrated checkpoint inhibition (CPI) for the treatment of solid tumors	2982	Category: Immunology Title: Therapeutic Antibodies 3 Location: Section 24 Poster Board: 29	Maya Poffenberger
		ZW171, a T cell-engaging, bispecific antibody for the treatment of mesothelin-expressing solid tumors	2942	Category: Immunology Title: Therapeutic Antibodies 2 Location: Section 23 Poster Board: 20	Nicole Afacan
		ZW191, a novel FRa-targeting antibody drug conjugate bearing a topoisomerase1 inhibitor payload	2641	Category: Experimental and Molecular Therapeutics Title: Antibody Technologies Location: Section 13 Poster Board: 9	Sam Lawn
		ZW251, a novel glypican-3-targeting antibody drug conjugate bearing a topoisomerase 1 inhibitor payload	2658	Category: Experimental and Molecular Therapeutics Title: Antibody Technologies Location: Section 13 Poster Board: 26	Laurence Madera
		Zanidatamab zovodotin (ZW49) induces hallmarks of immunogenic cell death and is active in patient-derived xenograft models of gastric cancer	2633	Category: Experimental and Molecular Therapeutics Title: Antibody Technologies Location: Section 13 Poster Board: 1	Stuart Barnscher
April 18	1:30 – 5:00 pm ET	TriTCE Co-stim, next generation costimulatory trispecific T cell engagers for the treatment of solid tumors	5121	Category: Immunology Title: Combination Immunotherapies 2 Location: Section 22 Poster Board: 24	Lisa Newhook
		RBB2 amplification detected in ctDNA as a surrogate for tumor tissue FISH analysis of HER2 status in a phase 1, study with zanidatamab for the treatment of locally advanced or metastatic HER2 expressing cancers	CT278	Session Title: Phase I Clinical Trials 2 Location: Section 47. Poster Board 18:	Diana Shpektor

Agenda

- **Introduction**: Overview of Zymeworks' research strategy and proprietary technology platforms
- **Antibody Drug Conjugates (ADC)**
  - ZW191: FRa-targeted TOPO1i ADC
  - ZW220: NaPi2B-targeted TOPO1i ADC
  - ZW251: GPC3-targeted TOPO1i ADC
- **Multispecific Antibody Therapeutics (MSAT)**
  - ZW171: 2+1 MSLN-targeted bispecific antibody
  - Trispecific antibody: T cell engager + co-stimulation (CD28)
  - Trispecific antibody: T cell engager + checkpoint inhibition (anti PD-L1)
  - Trispecific antibody with ProTECT: T cell engager with conditional masking
  - ZW270: Conditionally masked IL-12 cytokine fusion

Multifunctional Antibody Therapeutics for Oncology (and Beyond)

zymeworks

Integrated R&D Engine

Multispecific Antibody Therapeutics (MSAT)

Antibody Drug Conjugates (ADC)

Focus on indications with worst patient prognosis (e.g., lowest 5-year OS)

Desired Product Profile

First and Second-line

market opportunities

Accelerated Approval

regulatory pathway allows potential of early market entry

Pursue lead indications with global peak sales potential >$500MM per product

OS: overall survival

Corporate Value Framework – Elements of Enterprise Value

Our Strategy

Zymeworks is well positioned to build upon our key priorities and enhance shareholder value through focusing on our Enterprise value framework

Enterprise value framework focuses on delivering progress across all five key elements through 2023 and 2024

All elements of our framework are focused on our proven ability in ADC's and MSAT's

Goal of optimizing value as measured by per share returns for shareholders over the long-term

Jazz Pharmaceuticals

Zanidatamab Collaboration with Jazz Pharmaceuticals

BeiGene

Zanidatamab Collaboration with BeiGene (in APAC)

Zanidatamab Zovodotin

Research and Early Development Programs

Legacy Technology Licensing Portfolio

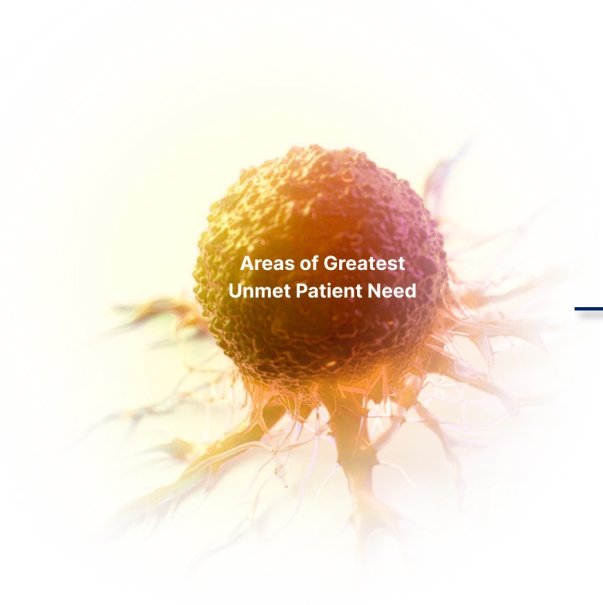
AACR 2023

Focused R&D Development

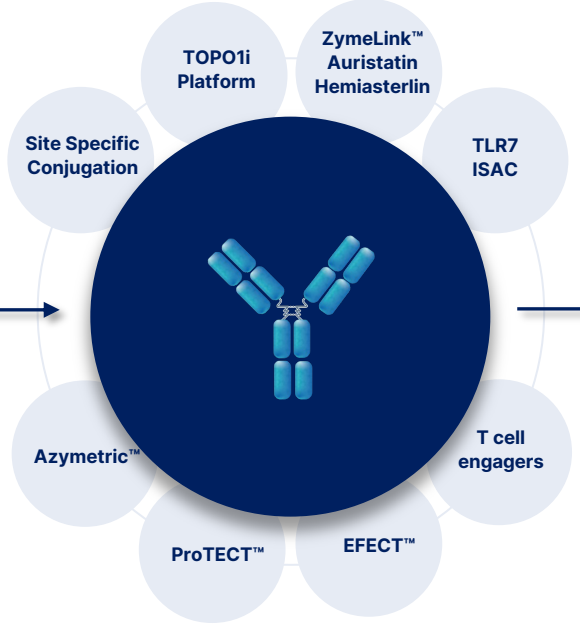
Paul Moore, Ph.D.
CHIEF SCIENTIFIC OFFICER

ADC and Multispecific Modalities Driving Our Pipeline

Select Difficult-to-Treat Cancers & Target



Design with Complementary Technology

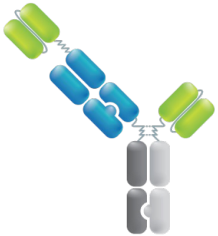


Optionality with Two Foundational Fit-for-Purpose Modalities

Antibody Drug Conjugates

Customization:

- Antibody properties
- Antibody format
- Payload
- DAR



Multispecifics

Customization:

- Multiple MOA in single molecule
- Synergistic biology
- Precision targeting through multivalency

DAR: drug to antibody ratio; ISAC: immune stimulating antibody conjugate; MOA: mechanism of action

A Growing Product Candidate Pipeline of Potential Best-in-Class Therapeutics

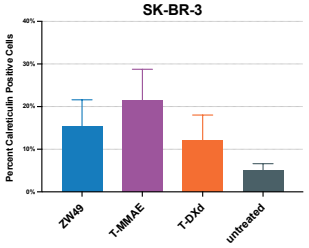
Reasearch and Early-Development Portfolio	Preclinical	Phase 1	Phase 2	Pivotal	Partner
Zanidatamab Zovodotin[1] HER2-Expressing Cancers Indications: NSCLC, mBC					BeiGene
ZW191 Folate Receptor-α Targeted Topoisomerase 1 Inhibitor Antibody Drug Conjugate Indications: OVCA, Gynecological, NSCLC, TNBC					
ZW171 2+1 MSLN x CD3 Bispecific Antibody Indications: Pancreatic, OVCA, CRC					
ZW251 Glypican-3 Targeted Topoisomerase 1 Inhibitor Antibody Drug Conjugate Indications: Hepatocellular carcinoma					
ZW220 NaPi2b Targeted Topoisomerase 1 Inhibitor Antibody Drug Conjugate Indication: OVCA, NSCLC, other solid tumors					

[1] Phase 2 studies anticipated to begin in 2023

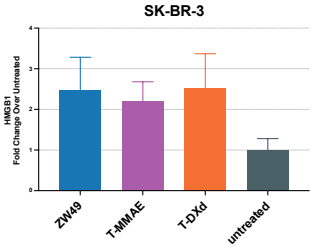
CRC: Colorectal cancer; GEA: gastroesophageal adenocarcinoma; mBC: metastatic breast cancer; NSCLC: non-small cell lung cancer; OVCA: ovarian cancer; TNBC: triple negative breast cancer

Mechanistic Rationale for Zanidatamab Zovodotin Combination with Anti-PD1

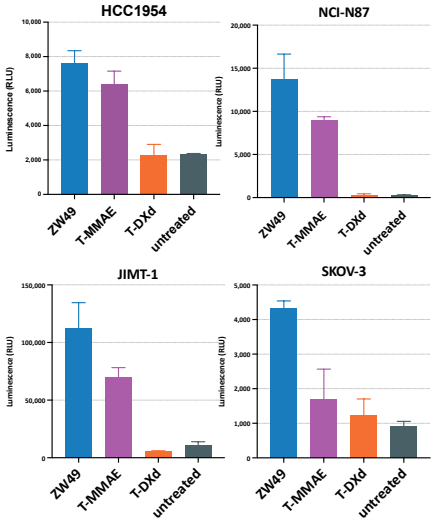
Calreticulin



HMGB1



Extracellular ATP



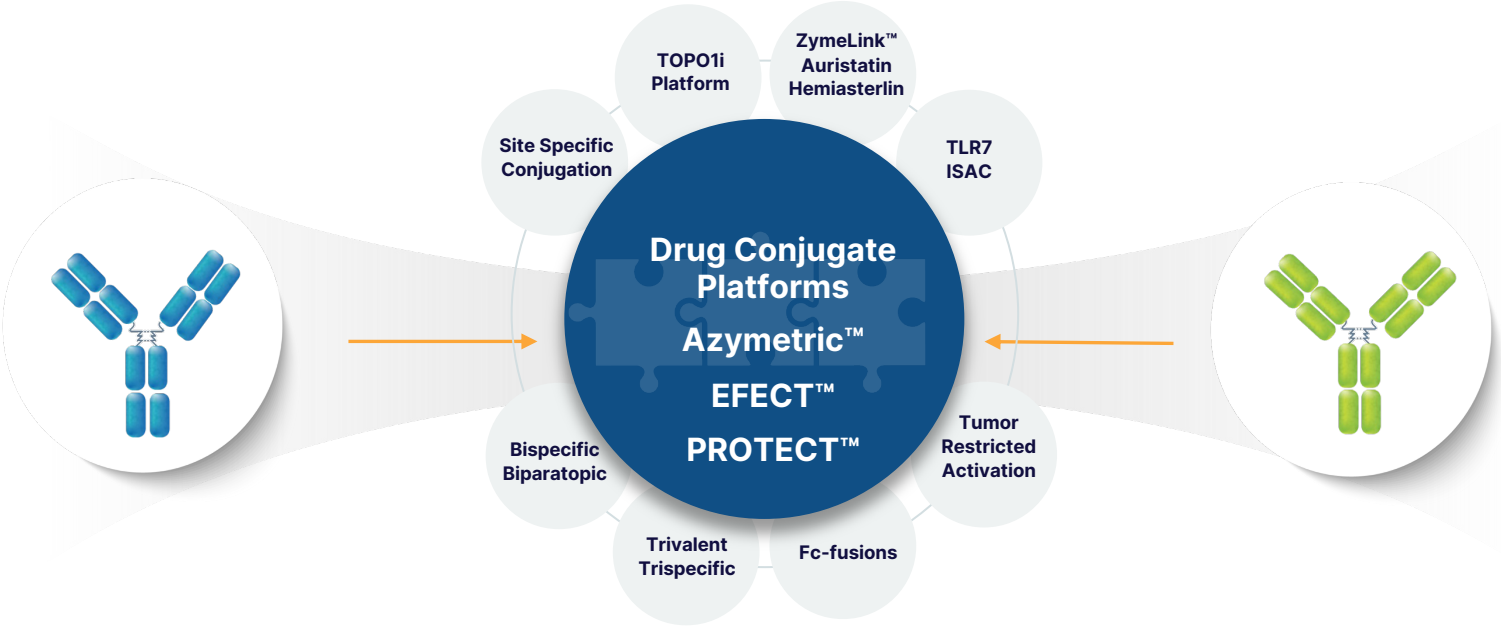
ADC	Antibody	Drug-linker (payload)	DAR
ZW49	zanidatamab (ZW25)	zovodotin (ZD02044)	2
T-MMAE	trastuzumab	vedotin (MMAE)	4
T-DXd	trastuzumab	deruxtecan (DXd)	8

- Zanidatamab zovodotin (zani zo) induces hallmarks of Immunogenic cell death (ICD) with preclinical evidence of enhanced activity compared to trastuzumab-based ADCs with either DXd or MMAE payloads
- ADCs that induce ICD may have a mechanistic advantage when combined with an anti-PD1
- Continued development of zani zo ongoing with planned Phase 2 studies in NSCLC and mBC anticipated to begin in 2023

DXd: deruxtecan; mBC: metastatic breast cancer; MMAE: Monomethyl auristatin E; NSCLC: non-small cell lung cancer

AACR 2023 Presentations Reflective of Power, Breadth, and Flexibility of our Protein Engineering Expertise and Platforms

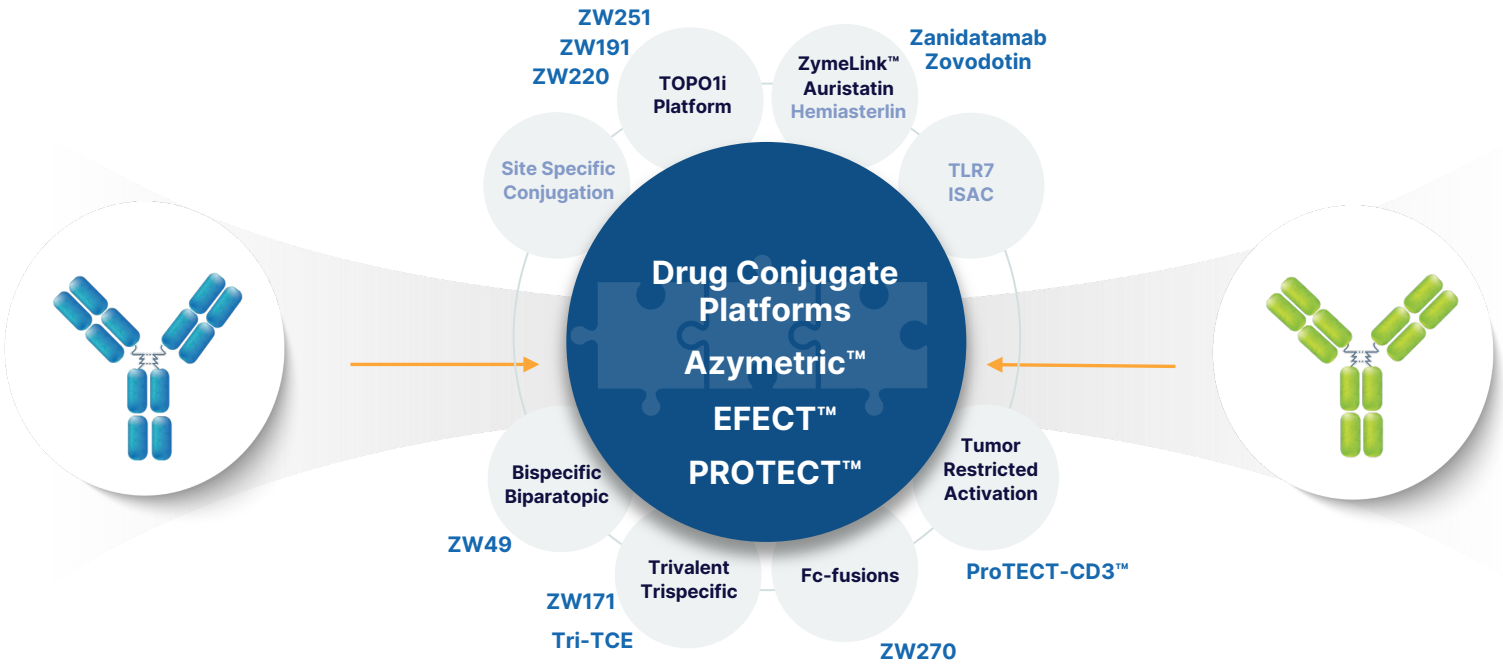
Proprietary Platform Technologies



ISAC: immune stimulating antibody conjugate

AACR 2023 Presentations Exhibit Growing and Differentiated Pipeline

Robust Pipeline

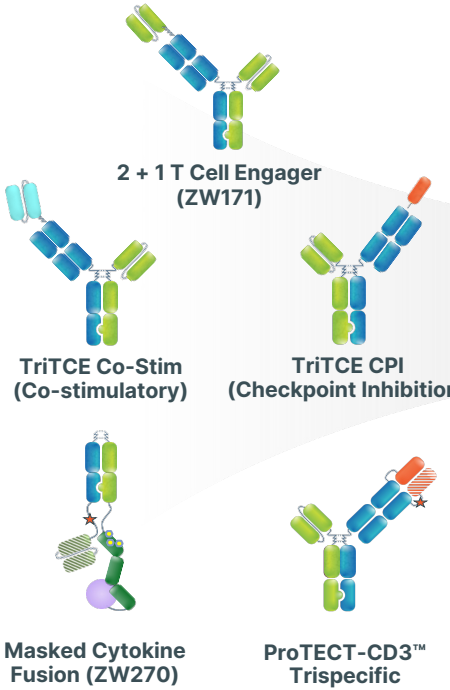


Proprietary Platform Technologies

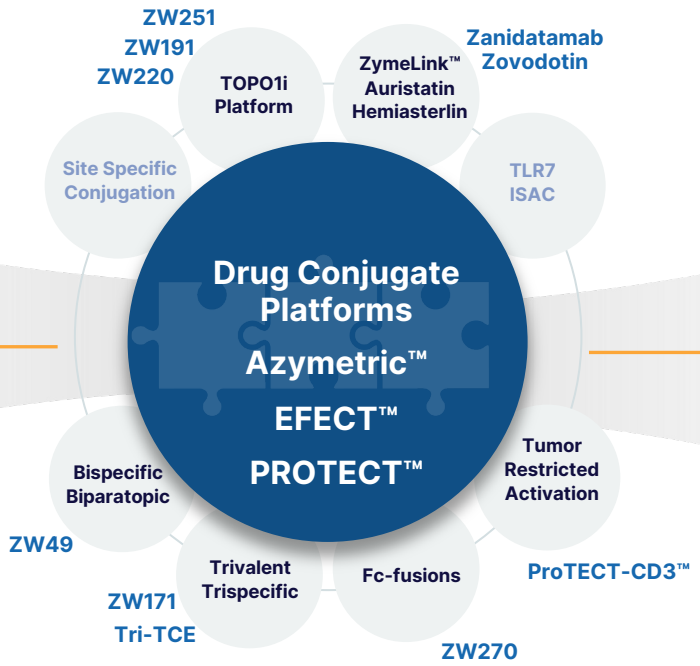
ISAC: immune stimulating antibody conjugate

AACR 2023 Presentations Exhibit Growing and Differentiated Pipeline

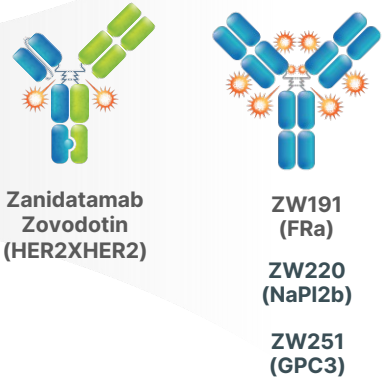
Azymetric™ → Multispecifics



Robust Pipeline



Antibody-Drug Conjugates



Proprietary Platform Technologies

ISAC: immune stimulating antibody conjugate

Antibody-Drug Conjugate (ADC) Program

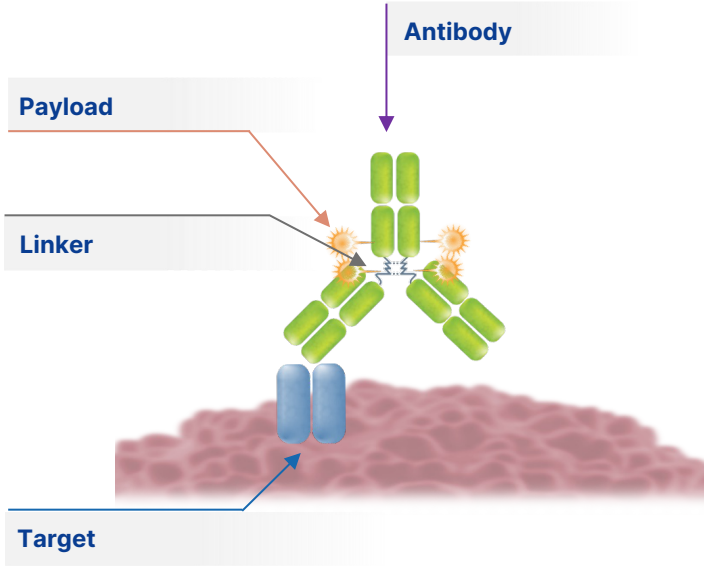
Building Next-Generation ADCs

Jamie Rich, Ph.D.
DIRECTOR, TECHNOLOGY, ADC THERAPEUTIC DEVELOPMENT

Stuart Barnscher
DIRECTOR, PRECLINICAL PROGRAMS, ADC THERAPEUTIC DEVELOPMENT

Building Next-Generation ADCs

Multiple Topoisomerase 1 inhibitor ADCs advancing towards the clinic with broad investment in ADC technologies to support future programs

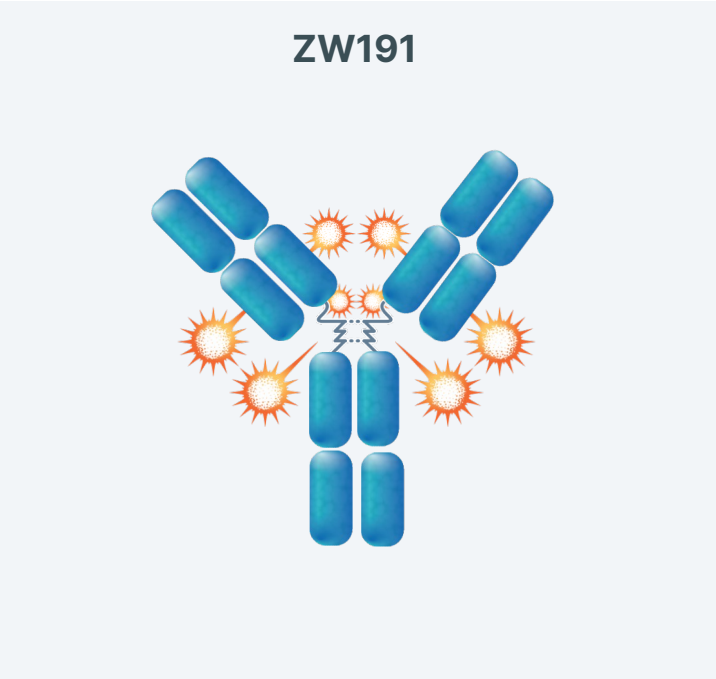


- Focusing on validated **targets** provides opportunity for benchmarking in preclinical development and expected clinical differentiation; novelty of targets anticipated to increase over time
- Exploiting our proprietary TOPO1i **payload** while exploring alternate mechanisms of action for longer-term development
- Leveraging validated peptide-cleavable **linkers** and stochastic **conjugation**. New chemistries under development to complement novel payloads
- Optimizing **antibody** properties for the ADC mechanism. Biparatopic and bispecific ADC formats may also provide future differentiated therapeutics

References:
1. Colombo R, Rich JR. The therapeutic window of antibody drug conjugates: A dogma in need of revision. *Cancer Cell* **2022**, 40, 1255-1263.
2. Colombo R, Barnscher SD, Rich, JR. Revisiting the dogma of antibody drug conjugates (ADCs): Emerging data challenge the benefit of linker stability and the primacy of payload delivery. *Cancer Res* **2023**, *83* (7) Abstr. 1538.
3. https://www.bioprocessonline.com/doc/focus-areas-to-expand-the-success-of-antibody-drug-conjugates-0001
4. https://www.clinicalleader.com/doc/the-clinical-landscape-of-adcs-in-diverse-technologies-narrow-target-0001

ZW191: Folate Receptor Alpha Topoisomerase-1 Inhibitor ADC

Lead ADC Preclinical Product Candidate



Target

Folate receptor alpha (FRα, FOLR1) is a clinically validated ADC target

FRα is over-expressed on the cell surface of ovarian cancer, other gynecological cancers, and additional high incidence solid tumors with unmet medical need (NSCLC, TNBC, etc.)

Antibody

Internally discovered, novel IgG1 monospecific antibody

Designed for optimal internalization, payload delivery, and tumor penetration

Drug Linker

Cysteine conjugated, DAR8, protease cleavable, traceless drug-linker

Novel bystander-active topoisomerase-1 inhibitor

Progress

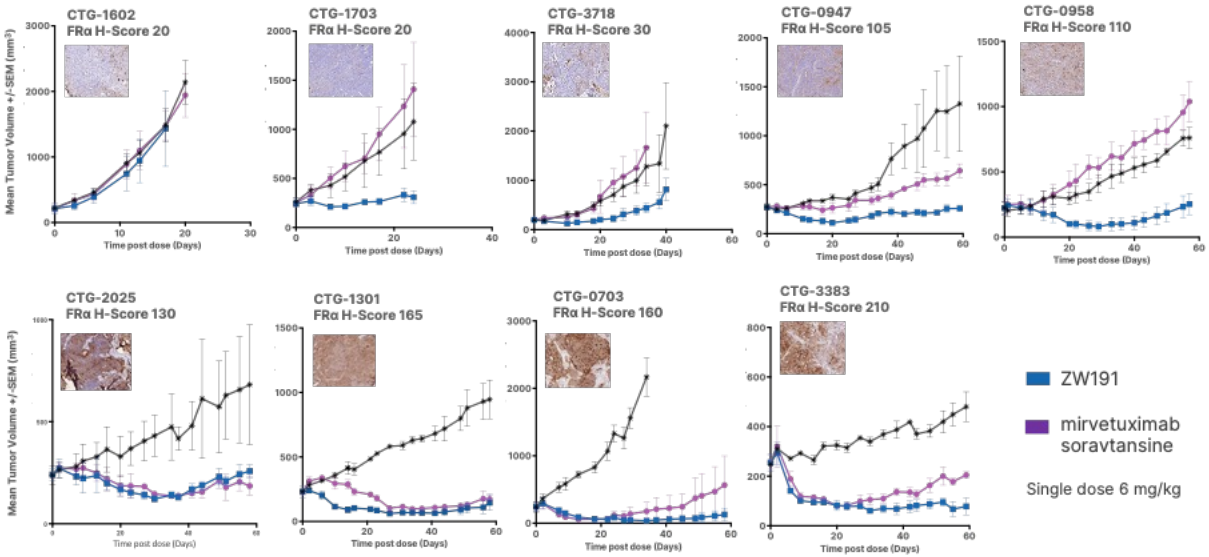
Robust anti-tumor activity in patient-derived xenograft models of ovarian cancer with low levels of FRα

On track for 2024 IND submission

ADC: antibody-drug conjugate; DAR: drug-to-antibody ratio; IND: investigational new drug; IgG1: immunoglobulin G1; NSCLC: non small cell lung cancer; TNBC: triple negative breast cancer

ZW191: Differentiated FRα-Targeting ADC Utilizing a Novel TOPO1i Payload

ZW191 Demonstrates Improved Anti-Tumor Activity Over Benchmark ADC Mirvetuximab Soravtansine in Ovarian Carcinoma PDX Models with Low FRα



	Incidence of Tumor Regression	
FRα Expression (H-Score)	ZW191	mirvetuximab soravtansine
>150	100% (3/3)	100% (3/3)
<150	83% (5/6)	33% (2/6)

- Improved activity in low FRα expressing ovarian cancer PDX models compared to the clinical benchmark
- Strong responses in FRα-low expressing PDX models set a precedent for potential activity in other indications with lower levels of FRα

PDX: patient derived xenograft

Lawn S et al. ZW191, a novel FRa-targeting antibody drug conjugate bearing a topoisomerase 1 inhibitor payload. Abstract # 2641 presented at American Association for Cancer Research annual meeting 2023.

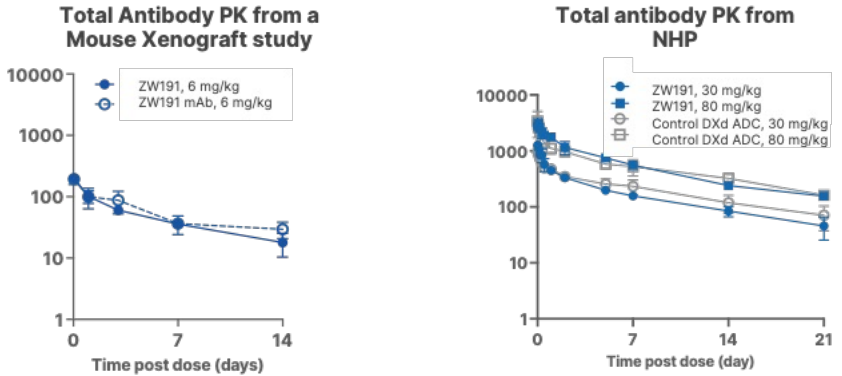
ZW191: Differentiated FRα-Targeting ADC Utilizing a Novel TOPO1i Payload

ZW191 Is Well-Tolerated in Non-Human Primate (NHP) at 30 mg/kg

Dose mg/kg q3w x2	Tolerated?	Histopathology; Clinical Chemistry; Hematology
30	Yes	Thymus, stomach; AST ↑; ABRETIC↓
80	No	Thymus, kidney, testis, and brain; AST ↑; BUN ↑; ABRETIC↓; ABLYMP↓

- MTD ≥ 30 mg/kg in a 2-dose non-GLP NHP toxicology study
- Histopathology findings at 30 mg/kg were considered as background/low severity and not adverse
- Clinical chemistry and hematology findings at 30 mg/kg were considered mild and/or non-dose responsive
- At 30 mg/kg, clinical observations were limited to fecal abnormalities, with no effect on body weight

ZW191 Has a Favorable Pharmacokinetic Profile



- ZW191 displays favorable PK and is well tolerated in NHP at exposure levels above those projected to be efficacious
- GMP process development is underway to support a 2024 IND

GMP: good manufacturing practices; IND: investigational new drug;; MTD: maximum tolerated dose; NHP: non-human primates; PK: pharmacokinetics

Lawn S et al. ZW191, a novel FRa-targeting antibody drug conjugate bearing a topoisomerase 1 inhibitor payload. Abstract # 2641 presented at American Association for Cancer Research annual meeting 2023

ZW251: Glypican-3 Topoisomerase-1 Inhibitor ADC

Target

Glypican-3 (GPC3) is a clinically validated target

GPC3 is expressed in 76% of hepatocellular carcinomas (HCC)[1] and exhibits limited expression in healthy tissues.

High expression is observed in ~55% of HCC[1]

Antibody

Novel IgG1 monospecific antibody

Strong binding and internalization in GPC3-expressing cells

Drug Linker

Cysteine conjugated, protease cleavable, traceless drug-linker

Novel bystander-active topoisomerase-1 inhibitor

Progress

Robust preclinical anti-tumor activity in HCC patient derived xenograft models including models with lower expression

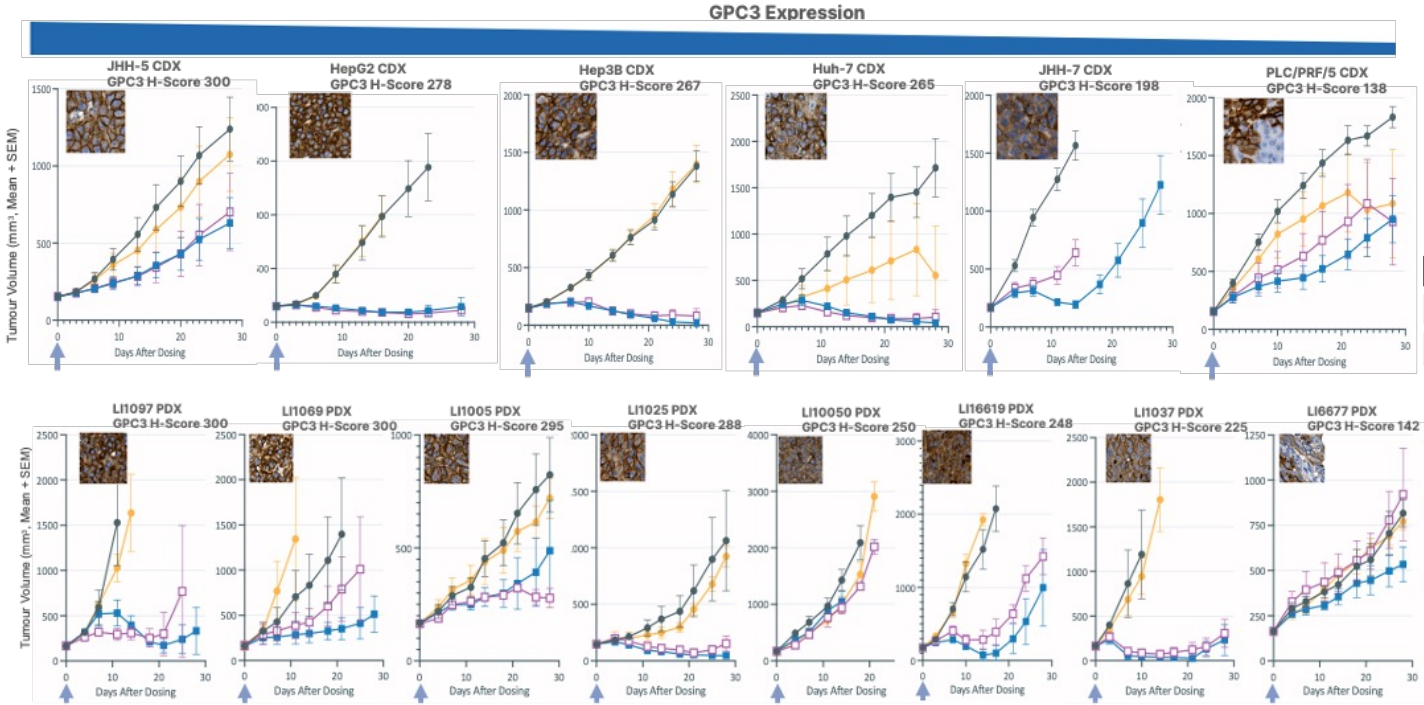
No mortalities at high doses in non-human primates

DAR4 and dAR8 still being considered
ADC: antibody-drug conjugate; DAR: drug-to-antibody ratio

1 Hanlin L. Wang, Florencia Anatelli, Qihui"Jim" Zhai, Brian Adley, Shang-Tian Chuang, Ximing J. Yang; Glypican-3 as a useful diagnostic marker that distinguishes hepatocellular carcinoma from benign hepatocellular mass lesions. Arch Pathol Lab Med. 2008, 132, 1723–1728.

ZW251: Novel Glypican 3-targeting ADC Utilizing a TOPO1i Payload

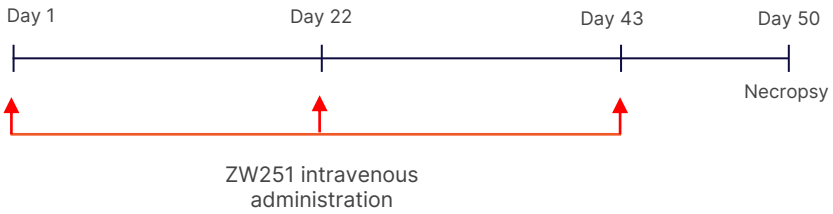
ZW251 Demonstrates Compelling Anti-Tumor Activity in a Broad Range of Liver Cancer Xenografts



	ZW251 Anti-Tumor Activity	
H-score	DAR 8	DAR 4
> 200	82% (9/11)	82% (9/11)
< 200	75% (3/4)	50% (2/4)

ZW251: Novel Glypican 3-targeting ADC Utilizing a TOPO1i Payload

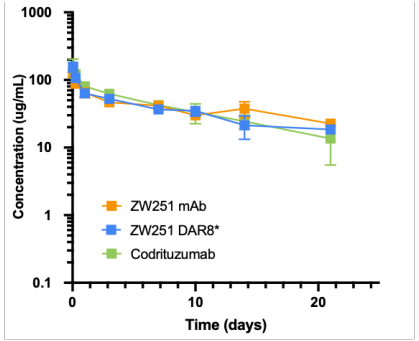
Three Dose Non-Human Primate (NHP) Toxicology Study



Test Article	Doses		
ZW251 DAR 8	10 mg/kg	30 mg/kg	60 mg/kg
ZW251 DAR 4	20 mg/kg	60 mg/kg	120 mg/kg

- Minimal changes in body weight, hematology parameters, and clinical chemistry parameters in all treatment groups
- **No mortality observed in any treatment group prior to necropsy**

Total IgG in Tg32 Mouse Serum



*Analog utilizes ZW251 mAb conjugated to a closely related linker-payload.

- ZW251 mAb exhibits comparable PK to a clinical-stage antibody comparator
- PK of ZW251 mAb unaffected by conjugation
- No mortality was observed in a repeat dose NHP toxicology study with doses up to 60 mg/kg (DAR 8) or 120 mg/kg (DAR 4)

DAR: drug-to-antibody ratio; NHP: non-human primate; mAB: monoclonal antibody; PK: pharmacokinetics

Madera L et al., ZW251, a novel glypican-3-targeting antibody drug conjugate bearing a topoisomerase 1 inhibitor payload. Abstract # 2658 presented at American Association for Cancer Research annual meeting 2023.

ZW220: NaPi2b Topoisomerase-1 Inhibitor ADC

Target

NaPi2b (SLC34A2) is a clinically validated ADC target highly expressed in 64% of serous ovarian cancer[1] and 68% of lung adenocarcinoma[2]

Antibody

Internally discovered, novel IgG1 monospecific antibody

Strong target binding and optimal internalization

Drug Linker

Stochastic, cysteine conjugated, protease cleavable, traceless drug-linker

Novel bystander-active topoisomerase-1 inhibitor

Progress

Robust preclinical anti-tumor activity in ovarian patient derived xenograft models including this with lower NaPi2b expression

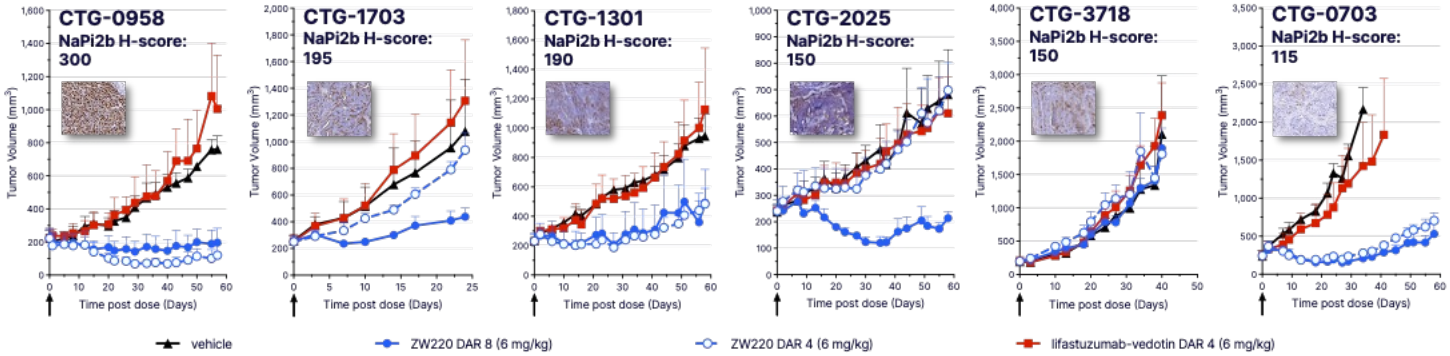
Tolerated at high doses in non-human primates

1 Richardson D, et al, Updated Results from the Phase 1 Expansion Study of Upifitamab Rilsodotin (UpRi; XMT-1536), a NaPi2b-directed Dolaflexin Antibody Drug Conjugate (ADC) in Ovarian Cancer. Annual Meeting on Womens' Cancer 2022, Abstract 076;
2 D'Arcangelo M, et al, Prevalence and Prognostic Significance of Sodium-Dependent Phosphate Transporter 2B (Napi2B) Protein Expression in Non-Small Cell Lung Cancer. 39th ESMO Congress 2014, Abstract 194P.

DAR4 and DAR8 still being considered
ADC: antibody-drug conjugate; DAR: drug-to-antibody ratio; IgG1: immunoglobulin G1

ZW220: a Novel NaPi2b-Targeting ADC Utilizing a TOPO1i Payload

ZW220 Demonstrates Improved Anti-Tumor Activity Over Benchmark ADC Lifastuzumab Vedotin in Ovarian Carcinoma Patient-Derived Xenograft Models



OvCa anti-tumor activity

(6 mg/kg single dose)

NaPi2b H-score	ZW220 DAR 8	ZW220 DAR 4	lifa-vedotin
>150	100% (3/3)	67% (2/3)	0% (0/3)
≤150	67% (2/3)	33% (1/3)	0% (0/3)
All	**83% (5/6)**	**50% (3/6)**	**0% (0/6)**

- Strong anti-tumor activity observed in models with low NaPi2b expression levels (H-score ≥ 115)
- Improved activity over benchmark in 5/6 models (83%)
- Responses to ZW220 at DAR 8 (5/6, 83%) and DAR 4 (3/6, 50%)

DAR: drug-to-antibody ratio; OvCa: ovarian cancer

Hernandez-Rojas A et al., ZW220, a novel NaPi2b-targeting antibody drug conjugate bearing a topoisomerase 1 inhibitor payload. Abstract # 1533 presented at American Association for Cancer Research annual meeting 2023.

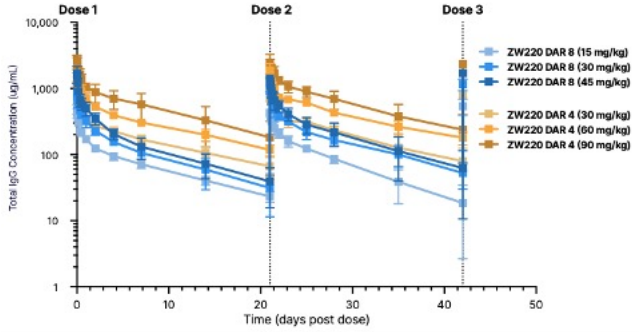
ZW220: a Novel NaPi2b-Targeting ADC Utilizing a TOPO1i Payload

ZW220 is Well-Tolerated in a Repeat Dose Non-human Primate (NHP) Toxicology Study

ZW220 3-dose non-GLP non-human primate (NHP) toxicology study, Q3Wx3

Test article	Dose	Mortality	Clinical Observations	Histo-pathology	Clinical Chemistry	Hema-tology	MTD	$T_{1/2}$ (days)
ZW220 DAR 8	15 mg/kg	None	None	None	None	None	45 mg/kg	8.7
	30 mg/kg	None	None	None	None	None		7.7
	45 mg/kg	None	Fecal abnormalities (soft/loose)	None	None	None		8.0
ZW220 DAR 4	30 mg/kg	None	None	None	None	None	90 mg/kg	10.3
	60 mg/kg	None	None	None	None	None		9.8
	90 mg/kg	None	Fecal abnormalities (soft/loose/watery)	None	None	None		8.0

Total IgG in Non-Human Primate Serum



ZW220 has a favorable toxicokinetic profile

- No mortality or adverse pathology findings at high doses
- MTD of DAR 8 is 45 mg/kg; MTD of DAR 4 is 90 mg/kg

Hernandez-Rojas A et al., ZW220, a novel NaPi2b-targeting antibody drug conjugate bearing a topoisomerase 1 inhibitor payload. Abstract # 1533 presented at American Association for Cancer Research annual meeting 2023.
DAR: drug-to-antibody ratio

ADC Therapeutic Development – Next Steps

Abstract #	Title	Next Steps
2641	ZW191, a novel FRa-targeting antibody drug conjugate bearing a topoisomerase 1 inhibitor payload	On-Track for IND anticipated in 2024
2658	ZW251, a novel glypican-3-targeting antibody drug conjugate bearing a topoisomerase 1 inhibitor payload	Candidate nomination
1533	ZW220, a novel NaPi2b-targeting antibody drug conjugate bearing a topoisomerase 1 inhibitor payload	Candidate nomination

Future Development Strategies

- Committed to advancing multiple topoisomerase 1 inhibitor ADCs into early clinical studies
- Actively pursuing payloads with alternative mechanisms of action and complementary linker chemistries
- Increasing focus on novel targets with biparatopic and bispecific ADC formats

IND: investigational new drug

Multispecific Antibody Therapeutic Development

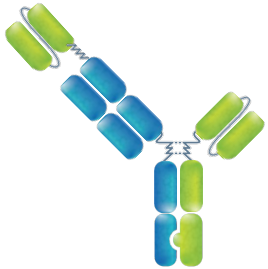
Differentiated Development of Multispecific Antibody-Based Therapeutics

Nina Weisser, Ph.D.
DIRECTOR, MULTISPECIFIC ANTIBODY RESEARCH

Thomas Spreter Von Kreudenstein, Ph.D.
DIRECTOR, PROTEIN ENGINEERING

Next-Generation Multispecific Antibody Therapeutics (MSAT) Development

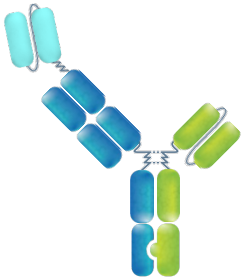
MSAT Technology Platforms



ZW171

T-cell engager (TCE) for MSLN-expressing cancers with enhanced therapeutic window.

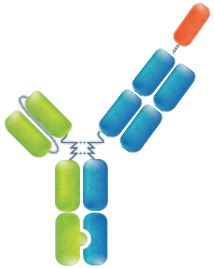
2+1 format with reduced T cell binding, to facilitate avidity-driven binding, enhanced anti-tumor activity and mitigate risk of CRS.



TriTCE Co-Stim

TCE incorporating co-stimulation for tumors with anergic and/or low T cell numbers.

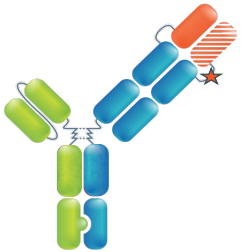
Increase tumor-dependent T cell fitness, activation and proliferation to improve depth and durability of anti-tumor responses.



TriTCE CPI

TCE incorporating checkpoint inhibition for tumors with immunosuppressive microenvironments.

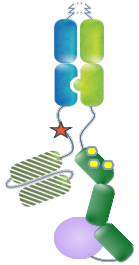
Increase T cells responses through avidity-driven binding and simultaneous checkpoint blockade.



TCE ProTECT™

TCE for tumor targets with normal tissue liability.

Conditional tumor activation with increased T cells responses through avidity-driven binding and simultaneous checkpoint blockade.



Masked Cytokine Fusion (ZW270)

To widen the therapeutic window of immune cell stimulating cytokines with PK and tolerability liabilities.

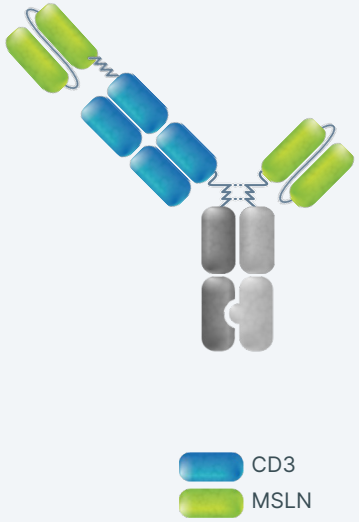
Potentiate anti-tumor immune cell cytotoxicity restricted to the tumor microenvironment.

CRS: cytokine release syndrome; PK: pharmacokinetics

ZW171: 2+1 Bispecific MSLN x CD3 T Cell Engaging Antibody

Lead MSAT Preclinical Product Candidate

ZW171



MSLN Targeted

Antibody targets mesothelin (MSLN), a glycoprotein that is elevated in many cancers including pancreatic, mesothelioma and ovarian cancer

Target is clinically validated, indications have high unmet clinical need

CD3 Targeted

Targeting CD3 receptor to redirect T cell cytotoxicity towards cancerous cells

Anti-CD3 antibody targeting novel epitope that mediates low T cell binding and cytokine release and potent tumor cell lysis

Format Engineering

Extensive assessment of different formats with different valences & geometries

2+1 dual scFv identified as avidity-driven format with optimal activity and safety profile

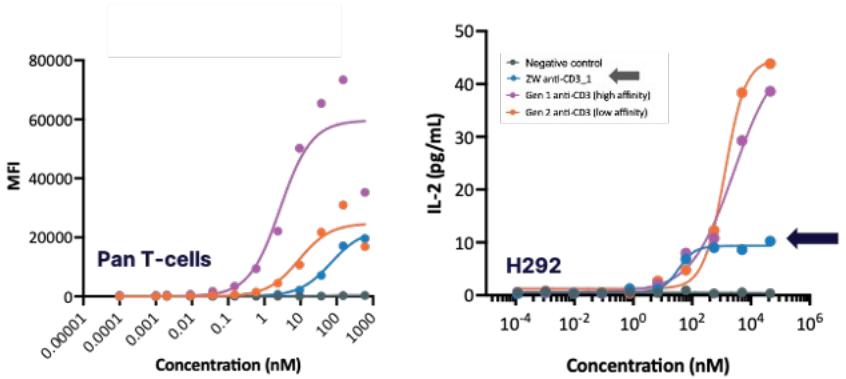
Progress

Pilot NHP toxicology and PK
On track for anticipated IND filing in 2024

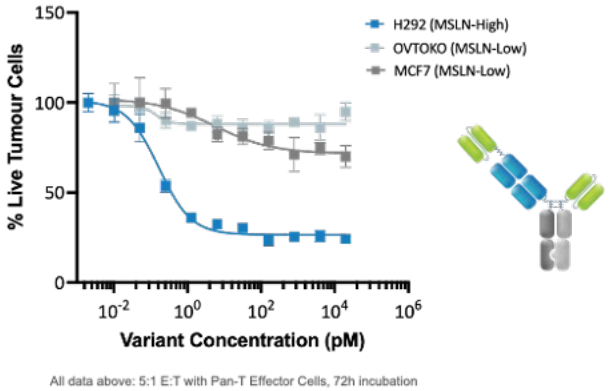
NHP: non-human primate; PK: pharmacokinetics; scFv: single-chain variable fragment

ZW171: T cell-Engaging, Bispecific Antibody Targeting MSLN-Expressing Solid Tumors

Reduced T cell Binding and Cytokine Release



Potent Tumor Cell Cytotoxicity in MSLN^{high} but not MSLN^{low} Tumor Cells



All data above: 5:1 E:T with Pan-T Effector Cells, 72h incubation

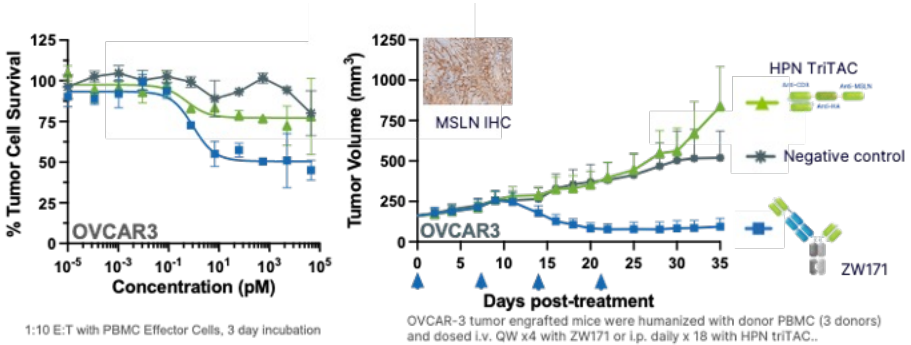
- ZW171 is engineered to widen the therapeutic window of TCE in solid tumors by reducing success limiting factors such as cytokine release syndrome and other off-target toxicities
- The 2+1 TCE format of ZW171 facilitates avidity-driven tumor cell binding and targets only cells with high levels of expression, limiting on-target off-tumor toxicities

TCE: t cell engager

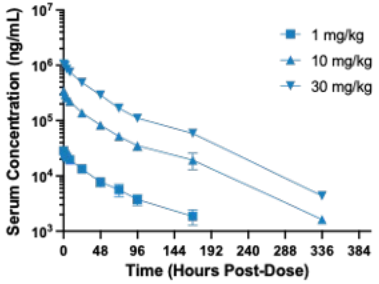
Afacan N et al., ZW171, a T cell-engaging, bispecific antibody for the treatment of mesothelin-expressing solid tumors. Abstract # 2942 presented at American Association for Cancer Research annual meeting 2023.

ZW171: T cell-Engaging, Bispecific Antibody Targeting MSLN-Expressing Solid Tumors

Superior In Vitro and In Vivo Anti-Tumor Activity Compared to Clinical Benchmark in Preclinical Studies



ZW171 Is Well-Tolerated in Non-Human Primate (NHP) at 30 mg/kg



- ZW171 compares favorably in vitro and in vivo when compared to currently available clinical benchmarks
- Pilot NHP toxicology data shows ZW171 is well-tolerated up to 30 mg/kg
- ZW171 shows prolonged half-life in NHP studies
- GLP toxicology study scheduled, and Good manufacturing practices (GMP) process established

Cynomolgus monkeys were given a single dose of 1, 10, or 30 mg/kg. Transient increases in IL-6 were observed. Histopathology was completed to assess microscopic changes to MSLN expressing. Hyperplasia/hypertrophy and inflammation in mesothelium of multiple tissues (stomach shown above) 1 week after dosing with ZW171.

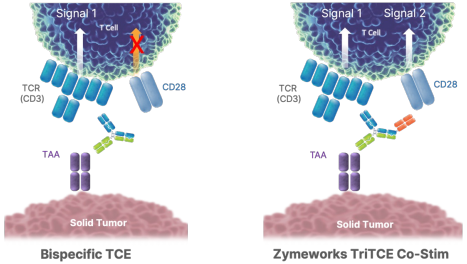
Afacan N et al., ZW171, a T cell-engaging, bispecific antibody for the treatment of mesothelin-expressing solid tumors. Abstract # 2942 presented at American Association for Cancer Research annual meeting 2023

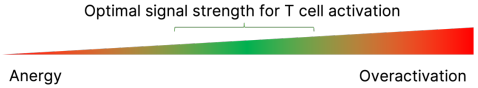
Multispecific Antibody Therapeutic Development

TriTCE Co-Stimulatory Therapeutic Program

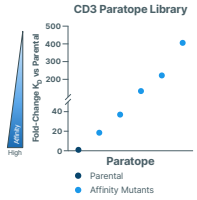
Novel Engineering and Screening Approach Identifies Costimulatory Trispecifics with Greater Anti-Tumor Activity and Target-dependent T cell Activation

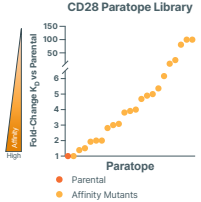
Co-stimulatory trispecific TCEs (TriTCE Co-Stim) have the potential to provide more durable responses and re-invigorate 'cold' tumors with lower T cell infiltration





Novel screening approach enables identification of optimal TriTCE format and paratope affinities for robust 'Signal 1' + 'Signal 2' T cell activation and synapse formation





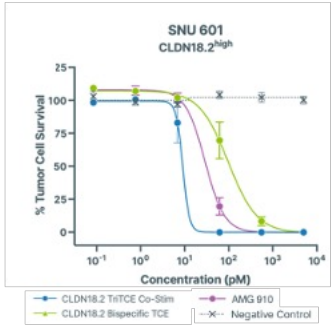
Antibody Format	1	2	3	4	5	6	7	8	9	10
IC50 (pM)										
TAA-Dependent?	✓	✓	✓	x	✓	✓	x	x	x	x

- Activity of bispecific T cell engagers (TCE) in solid tumors is limited by low numbers of intratumoral T cells and T cell anergy
- TriTCE Co-Stim have the potential to provide more durable responses and re-invigorate 'cold' tumors with lower T cell infiltration via tumor-dependent T cell activation (CD3) and co-stimulation (CD28)
- Engineering solutions employed to optimize signal strength for T cell activation and anti-tumor activity, including modifications paratope affinities and antibody format geometries
- In vitro screening identified TriTCE Co-stim molecules with enhanced TAA-dependent anti-tumor activity compared to a bispecific TCE, and transferability across TAA targets

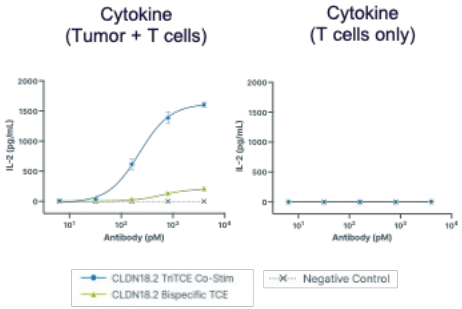
Newhook L et al., TriTCE Co-stim, next generation costimulatory trispecific T cell engagers for the treatment of solid tumors. Abstract #5121 presented at American Association for Cancer Research annual meeting 2023.

CLDN18.2 TriTCE Co-Stimulatory Molecules Mediate Enhanced in vitro and in vivo Anti-Tumor Activity Compared to Bispecific TCE

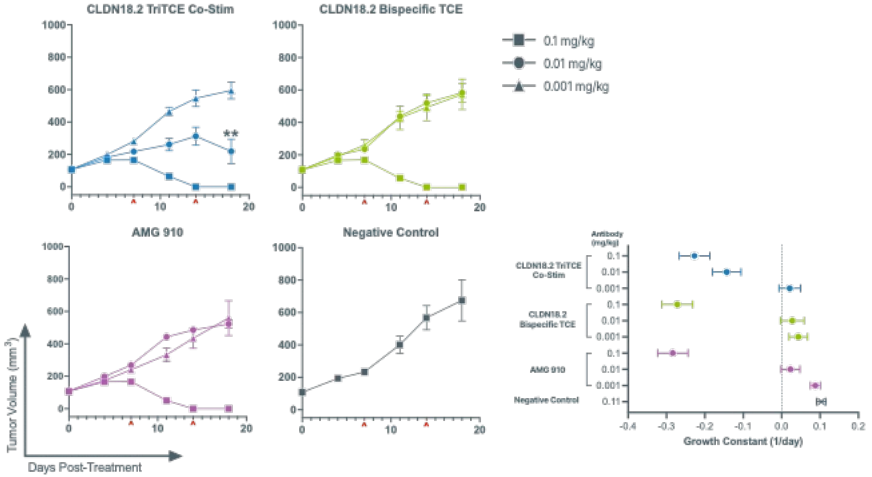
Enhanced Cytotoxicity at Low E:T



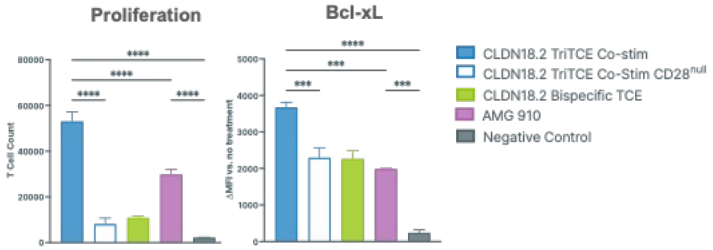
TAA-Dependent Cytokine Release



Superior in vivo Anti-Tumor Activity



Improved T cell Proliferation and Survival



TriTCE Co-Stim may provide more durable responses in solid tumors

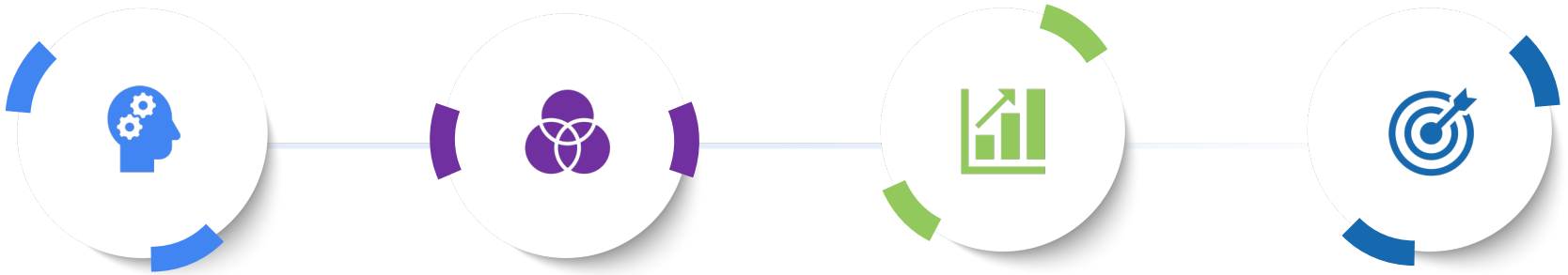
- CLDN18.2 TriTCE molecules show enhanced TAA-dependent anti-tumor activity and T cell functionality compared to bispecifc TCE
- Additional mechanistic assessment and TAA target evaluations underway

TAA: tumor-associated antigen; TCE: t cell engager

Newhook L et al., TriTCE Co-stim, next generation costimulatory trispecific T cell engagers for the treatment of solid tumors. Abstract #5121 presented at American Association for Cancer Research annual meeting 2023.

TriTCE Co-Stimulatory Therapeutic Technology

Addressing lack of activity of bispecific TCEs in solid tumors with low T cell infiltration



Therapeutic Rationale

Activity of bispecific T cell engagers in solid tumors is limited by **low numbers of intratumoral T cells and T cell anergy**

Next Gen TriTCE Co-Stim can provide increased T cell fitness, activation and proliferation via tumor-dependent T cell co-stimulation

Product Differentiation

Novel approach of **affinity and modular geometry screening** of trispecifics to optimize T cell activation by Signal 1 and Signal 2

TriTCE Co-Stim molecules show **superior *in vitro* activity** to bispecific benchmarks at **low effector to target ratios**

TriTCE Co-Stim molecule show no activation of T cells without presence of tumor cells

Opportunity

TriTCE Co-Stim may provide more durable responses in solid tumors and show superior activity in cold tumors with low T cell counts

Currently targeting **CLDN18.2**, a clinically validated target, for benchmarking purposes. Additional TAA evaluation ongoing

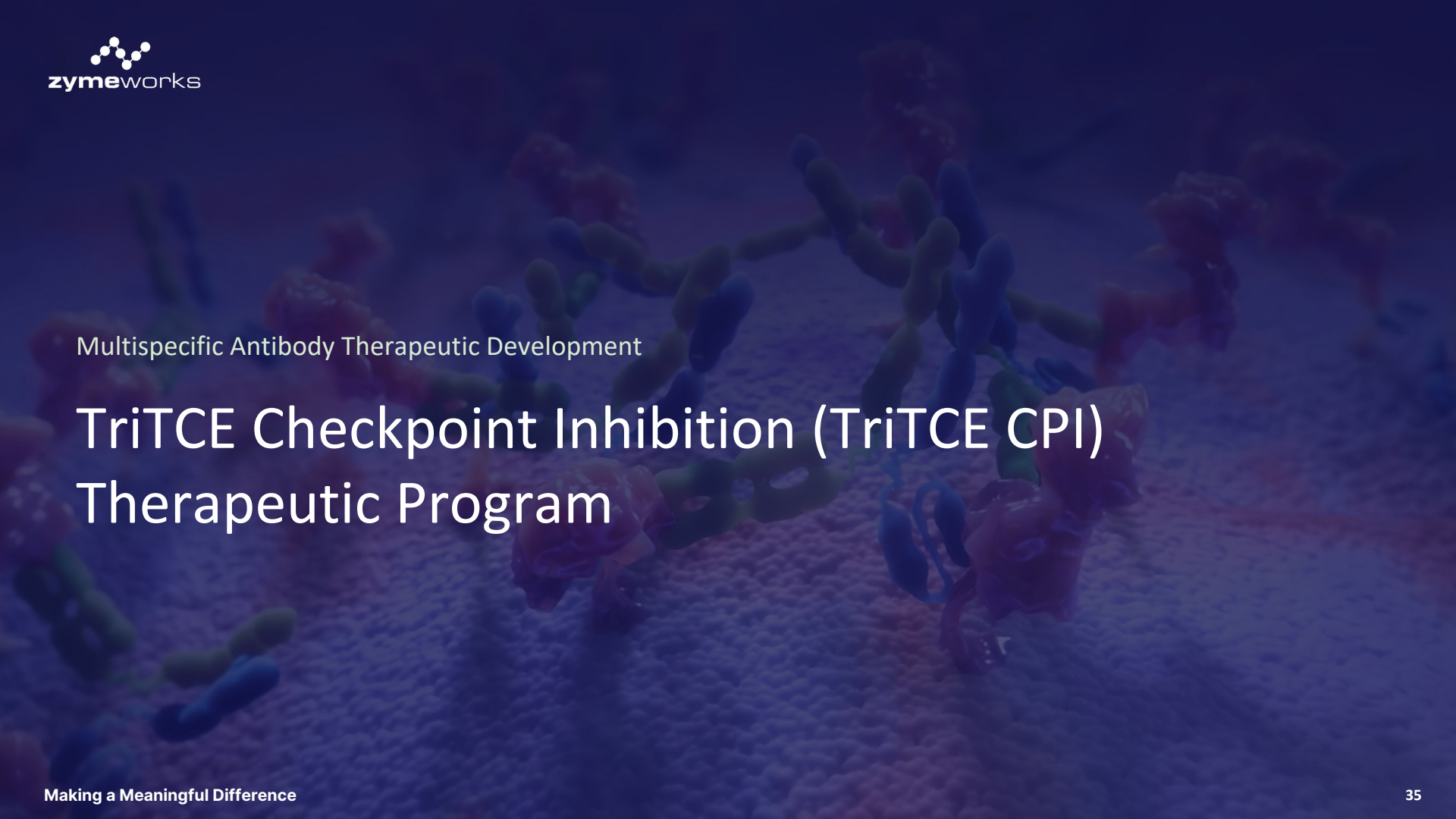
TriTCE Co-Stim approach provides novel approach to targeting CLDN18.2

Progress

Unique screening approach evaluating multiple parameters to identify lead with desired target criteria

Demonstrated enhanced TAA-dependent anti-tumor activity and T cell functionality in low E:T settings across multiple TAA targets, including CLDN18.2

TAA: tumor-associated antigen; TCE: t cell engager

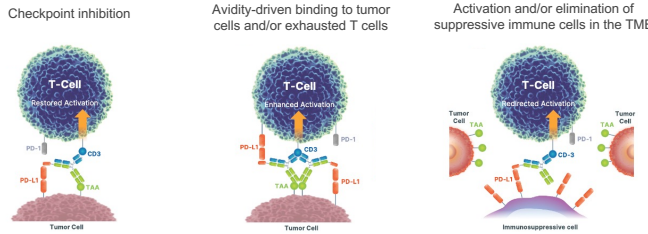


Multispecific Antibody Therapeutic Development

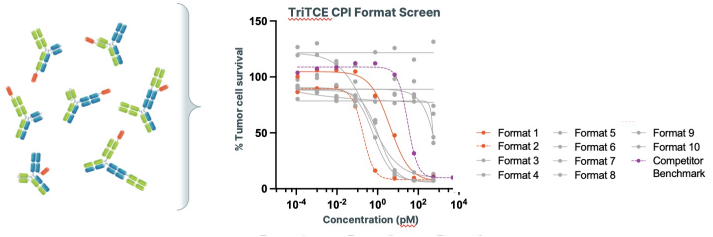
TriTCE Checkpoint Inhibition (TriTCE CPI) Therapeutic Program

TriTCE CPI: Next Generation Trispecific T Cell Engagers (TriTCE) with Integrated Checkpoint Inhibition (CPI) for the Treatment of Solid Tumors

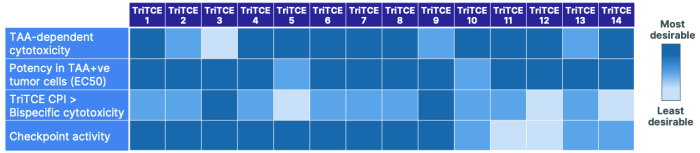
Proposed mechanisms of action for TriTCE CPI therapeutics



Different TriTCE CPI geometries and PD-L1 affinities were screened for increased T cell-dependent cytotoxicity



Lead TriTCE CPI formats were identified by TAA-dependent cytotoxicity and PD-1/PD-L1 checkpoint blockade activity

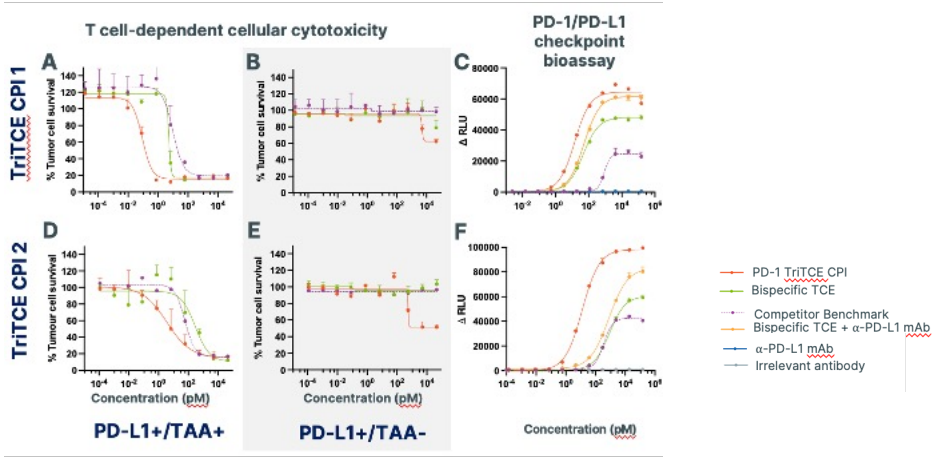


- CD3-bispecific T cell engager (TCE) treatment of solid tumors is hindered by immunosuppressed microenvironments due to the expression of inhibitory immune checkpoints, such as PD-1 on exhausted T cells and PD-L1 on tumor cells
- TriTCE CPI have the potential to improve T cell responses and anti-tumor activity in immunosuppressed solid tumors via concurrent T cell activation and checkpoint inhibition
- Engineering solutions employed to optimize TAA-dependent cytotoxicity and checkpoint inhibition, including modifications PD1 domain affinities and antibody format geometries
- In vitro screening identified TriTCE CPI molecules with enhanced TAA-dependent anti-tumor activity and CPI compared to a bispecific TCE

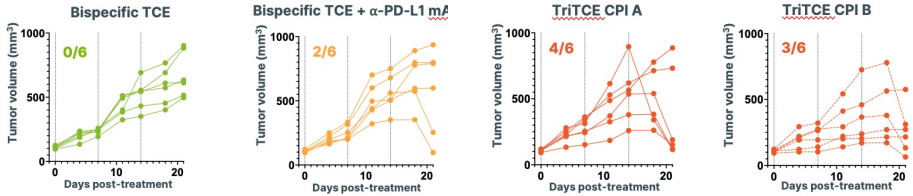
Pffenberger MC et al., TriTCE CPI, next generation trispecific T cell engagers with integrated checkpoint inhibition (CPI) for the treatment of solid tumors. Abstract #2982 presented at American Association for Cancer Research annual meeting 2023.

TriTCE CPI: Next Generation Trispecific T Cell Engagers (TriTCE) with Integrated Checkpoint Inhibition (CPI) for the Treatment of Solid Tumors

TriTCE CPIs induce TAA-dependent T cell cytotoxicity and PD-1/PD-L1 checkpoint blockade



TriTCE CPIs promote strong in vivo anti-tumor responses

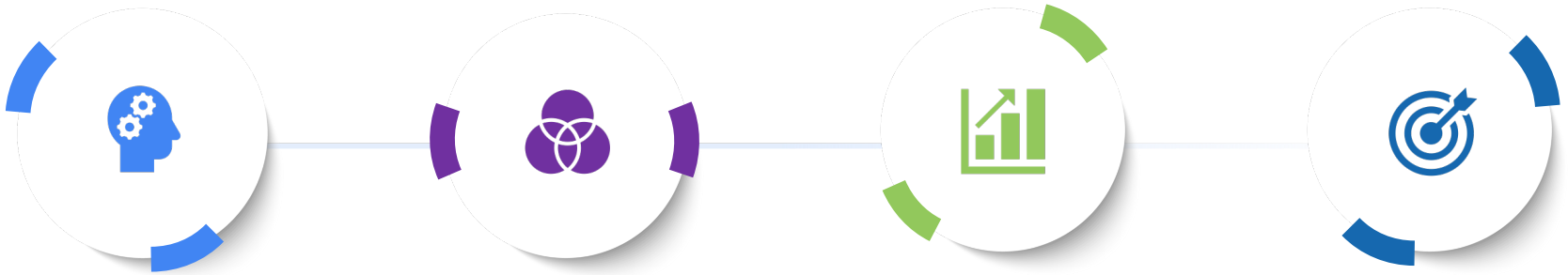


- TriTCE CPIs induce TAA-dependent T cell cytotoxicity and PD-1/PD-L1 checkpoint blockade
- TriTCE CPIs show enhanced cytotoxicity compared bispecific TCE and enhanced checkpoint inhibition compared to bispecific TCE and anti-PD-L1 combination treatment
- TriTCE CPI therapeutics display superior in vivo anti-tumor activity compared to bispecific TCE
- Additional mechanistic assessment and TAA target evaluations underway

Pffenberger MC et al., TriTCE CPI, next generation trispecific T cell engagers with integrated checkpoint inhibition (CPI) for the treatment of solid tumors. Abstract #2982 presented at American Association for Cancer Research annual meeting 2023.

Next Gen Trispecific T Cell Engagers with Checkpoint Inhibition (TriTCE CPI)

Addressing lack of activity of bispecific TCEs in suppressive tumor microenvironment



Therapeutic Rationale

PD-1/PD-L1 upregulation in solid tumors and **suppressive tumor microenvironment** are resistance mechanism to bispecific T cell engager treatment

Next Gen trispecific T Cell engager (TriTCE CPI) combining redirected T cell killing with immune checkpoint modulation to enhance activity and therapeutic applications for T cell engagers in solid tumors

Product Differentiation

Novel trispecific T cell engager with **dual MOA** of both checkpoint inhibition (CPI) and avidity driven tumor cell binding and T cell activation

Demonstrated potent and **differentiated activity** *in vitro* and *in vivo* and **high activity in exhausted T cells**

Superior activity of trispecifics **to combination therapy** of bispecific with checkpoint inhibitor *in vivo*

Opportunity

Potential for **TriTCE CPI** to be **active** in **suppressive tumor** microenvironments

TriTCE CPI potentially less susceptible to PD-1/PD-L1 mediated secondary resistance providing **more durable responses**

TriTCE CPI modified with **ProTECT™ functional masking** to mitigate potential on-target toxicities associated with tumor targets that have normal tissue expression

Progress

Unique screening approach evaluating multiple parameters to identify lead with desired target criteria

Identified lead geometries with *superior in vitro* and *in vivo* activity and strict TAA dependent activity

Potential novel MOA of engaging DCs to enhance T cell activation and proliferation

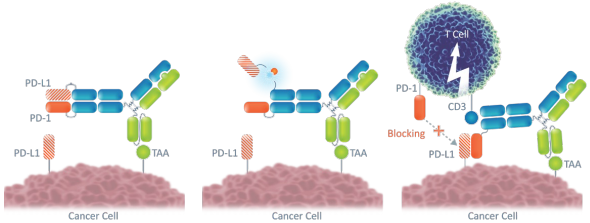
Continued TAA Evaluation

Multispecific Antibody Therapeutic Development

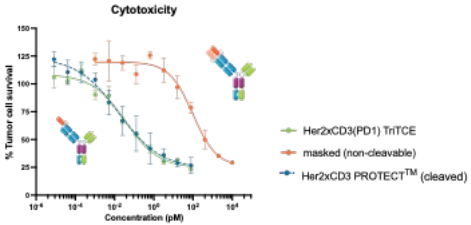
Conditional Masking for Trispecific T cell Engagers (ProTECT™ TriTCE)

ProTECT™: Applying Novel Masking Platform to Enhance the Therapeutic Window of TCEs

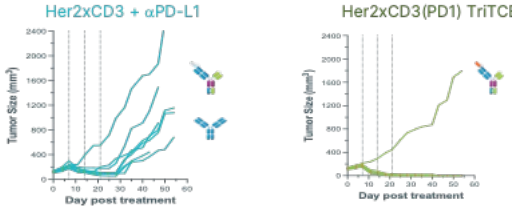
Proposed mechanism for ProTECT T cell engager



Masked ProTECT mediates >1000x reduced cytotoxicity *in vitro* while protease activated PROTECT recovers cytotoxicity



ProTECT induces durable tumor response *in vivo*



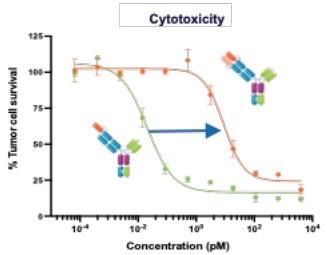
- Masked, protease activated T Cell Engagers (TCEs) are a potentially promising new modality for more targeted TCEs with reduced on-target off-tumor toxicities
- ProTECT platform combines masking and linker technology with TriTCE CPI immune modulation to enhance the therapeutic window of TCEs
- ProTECT provides solutions for two main limitations of TCEs in the clinic:
  - a protease cleavable masking approach to reduce toxicity in the periphery
  - additional immunomodulatory properties to overcome lack of efficacy in solid tumors
- ProTECT is a transferable 'plug and play' TCE masking platform with >500x masking window and efficient unmasking *in vitro*
- In vitro and *in vivo* data suggest superior activity to combination of TCE and checkpoint inhibitor

von Rossum A et al., PROTECT™, a novel trispecific antibody masking platform with integrated immune modulation displays unique activity and differentiated modes of action. Abstract # 2926 presented at American Association for Cancer Research annual meeting 2023.

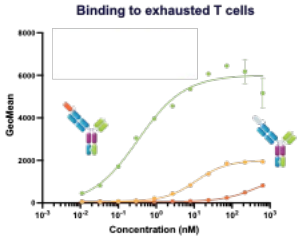
ProTECT™: Applying Novel Masking Platform to Enhance the Therapeutic Window of TCEs

Differentiated TAA x CD3 ProTECT™ T cell engager activity mediated by multiple mechanism of action

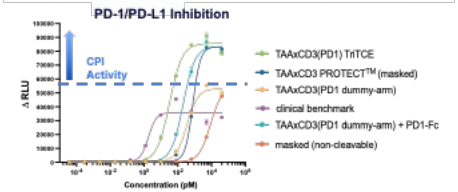
Masking to reduce toxicity



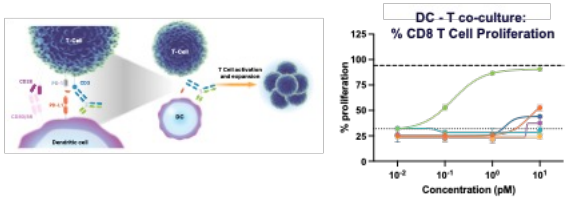
PD-L1 driven avidity and potential activity in suppressive TME



PD1/PD-L1 checkpoint inhibition



DC - T cell mediated enhanced T cell proliferation

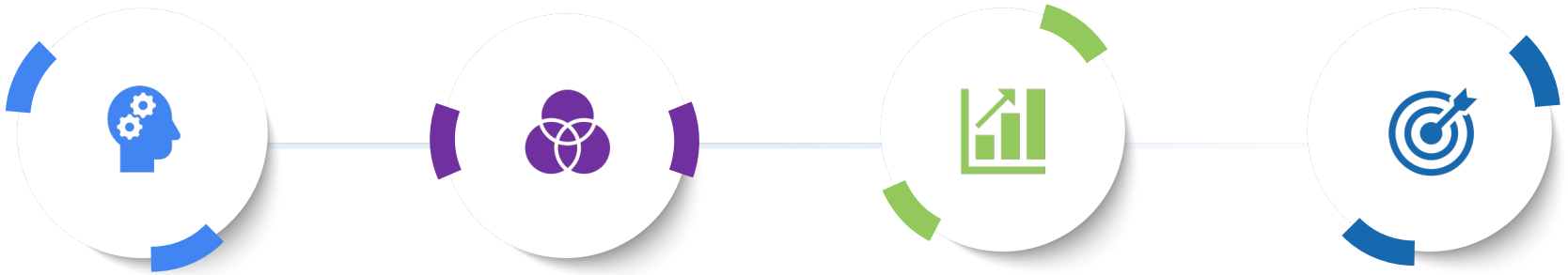


- ProTECT incorporates several engineering solutions to improve tolerability: anti-CD3 masking, low affinity CD3 binding, increased binding to tumor cells, and enhanced selectivity for PD-L1+ tumor microenvironment
- Protease activated ProTECT displays the unique mechanisms of action of the TriTCE CPI to increase efficacy including increased avidity and checkpoint inhibition
- ProTECT has been shown to crosslink PD-L1 positive dendritic cells (DC) and T cells and may have the ability to induce and potentiate T cell activation via PD-L1 on APCs in the tumor microenvironment
- ProTECT therapeutic program offers multiple mechanisms of action that cannot be achieved through combination therapy

von Rossum A et al., PROTECT™, a novel trispecific antibody masking platform with integrated immune modulation displays unique activity and differentiated modes of action. Abstract # 2926 presented at American Association for Cancer Research annual meeting 2023.

ProTECT™ Platform Combines Masking and Linker Technology with TriTCE CPI Immune Modulation to Enhance the Therapeutic Window of TCEs

Addressing lack of activity of bispecific TCEs due to narrow therapeutic index and suppressive tumor microenvironment



Therapeutic Rationale

Masked, protease activated T Cell Engagers (TCEs) are a potentially promising new modality for more targeted TCEs with reduced on-target off-tumor toxicities

ProTECT technology provides potential solutions for the main two causes for TCE failure in the clinic, peripheral toxicity and lack of efficacy in solid tumors

Product Differentiation

ProTECT is a transferable TCE masking platform with >500x masking window *in vitro*

Demonstrated potential to enable better tolerated and more potent next-generation CD3-engaging multispecifics *in vitro* and *in vivo*

In vitro and in *vivo* data suggest superior activity to combination of TCE and checkpoint inhibitor

Opportunity

Unique and highly differentiated approach, potential first-in-class opportunity

ProTECT therapeutic program offers multiple mechanisms of action that cannot be achieved through combination therapy

Progress

Demonstrated 'plug-and-play' of platform with efficient masking and un-masking for different TCE targets

In vitro and *in vivo* efficacy suggests superior activity of combination of TCE and checkpoint

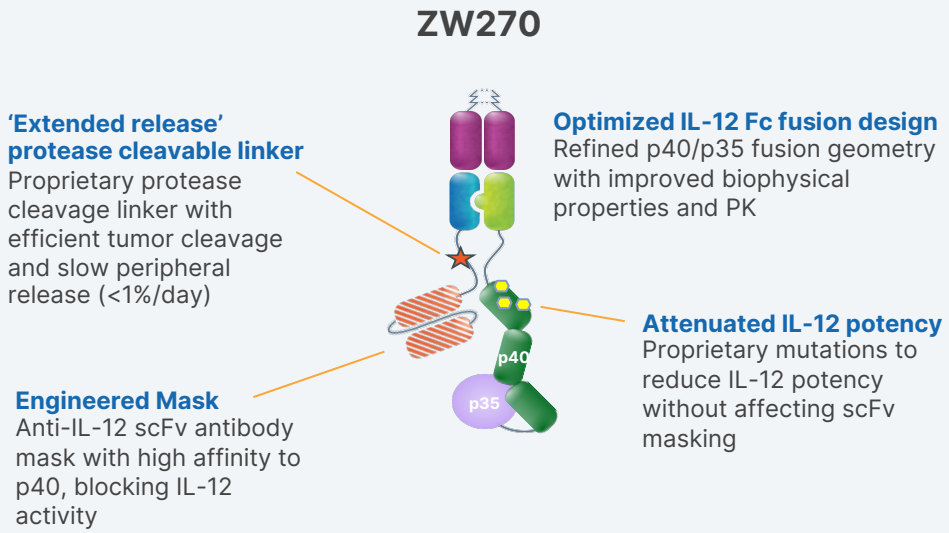
Unique ability of ProTECT to crosslink DCs and T cells in the tumor microenvironment to potentially enhance T cell activation and proliferation

Multispecific Antibody Therapeutic Development

IL-12 Cytokine Fusion Program

ZW270: Conditionally Masked IL-12 Cytokine Fusion Protein Displaying Potent Anti-tumor Activity Absent Systemic Toxicity

ZW270 – a masked, extended-release protease activated IL-12 Fc with attenuated IL-12 potency



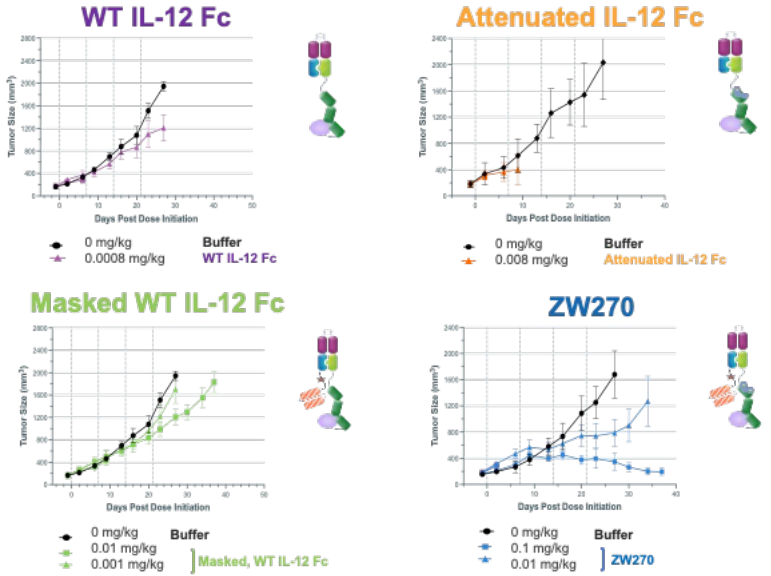
- IL-12 significantly reduces tumor growth in multiple mouse models, but efficacy has been limited by toxicity in clinical trials[1,2]
- Protease dependent activation of therapeutics with high on-target, off-tumor toxicities may be used to localize activity to the tumor micro-environment but achieving sufficient exposure of activated therapeutic in the tumor micro-environment remains a challenge[2,3]
- To widen the therapeutic index of this highly active cytokine, we have engineered a masked, potency attenuated IL-12 that is activated via extended-release gradual protease cleavage
- ZW270 employs a proprietary cleavable linker technology that is the same as in ProTECT™
- We hypothesize that combining these engineering strategies of potency attenuation plus masking with an 'extended release' protease cleavage, has the potential to widen the therapeutic index of IL-12 therapeutics and be superior to comparator IL-12 engineering strategies

[1] Elia D. Tait Wonjo et al. Immunity 2019; 50:851-870.
[2] Khue G. Nguyen et al. Frontiers In Immunology 2020; 11:575597.
[3] Duffy, M. J. Clinical Cancer Research 1996; 2, 613–618.

ZW270 displays potent and superior anti-tumor activity absent of systemic toxicity

ZW270 reduces tumor growth in a humanized mouse model and is superior to IL-12 Fc comparators

	WT IL-12 Fc	Attenuated IL-12 Fc	Masked WT IL-12 Fc	ZW270
Tumor growth inhibition at highest tolerated dose	✗	✗	✗	✓
Highest tolerated dose*	< 0.0008 mg/kg	< 0.008 mg/kg	> 0.01 mg/kg	> 0.1 mg/kg



A single dose of ZW270 at 10 mg/kg or 31.8 mg/kg is well tolerated in cynomolgus monkeys

	Dose	Mortality	Clinical signs	Body weight loss
WT IL-12 Fc	0.2 mg/kg	Yes	Several	**-39.28%**
ZW270	31.8 mg/kg	No	Loose feces	-7.58%

- ZW270 has potent and superior anti-tumor activity to IL-12 Fc and masked IL-12 Fc comparators at tolerated dose levels in a humanized mouse model
- ZW270 is well tolerated in non-human primates to >30 mg/kg single dose
- Additional QSP modelling using experimental and literature data showed that ZW270 enhanced projected TI is mediated by Fc half-life extension, IL-12 attenuation, and 'extended release' gradual protease unmasking
- ZW270 utilizes a novel, differentiated engineering approach and our data suggests ZW270 might have the potential to overcome current limitations of IL-12 therapies
- In addition, the unique geometry of ZW270 allows design of targeted IL-12 Fc as next Generation therapy

Escalante N et al., ZW270, a conditionally masked IL-12 cytokine fusion protein displaying potent anti-tumor activity absent systemic toxicity. Abstract #2935 presented at American Association for Cancer Research annual meeting 2023.

ZW270: masked, ‘extended release’ protease activated IL-12 Fc with attenuated IL-12 potency

Addressing lack of therapeutic index of current IL-12 Fc fusions

Therapeutic Rationale

IL-12 is a cytokine that significantly reduces tumor growth in multiple mouse models, but efficacy has been limited by toxicity in clinical trials [1, 2]

Protease dependent activation may be a useful tool to localize activities and reduce off-tumor toxicities

Product Differentiation

ZW270 uses a masked, ‘extended-release’ protease-activated IL-12 Fc with attenuated IL-12 potency to potentially address shortcomings of previous IL-12 Fc fusions[3]

Combining antibody masking technology with ‘extended release’ gradual unmasking and IL-12 attenuation potentially yields a superior masking window and a widened therapeutic index of IL-12[3]

Opportunity

IL-12 remains a very attractive therapeutic cytokine due to its unique ability to potentiate innate and adaptive anti-cancer immunity and potentially remodel non-inflamed tumor microenvironments

ZW270 utilizes a novel, differentiated engineering approach and has the potential to overcome current limitations of IL-12 therapies

The unique geometry of ZW270 allows design of targeted IL-12 Fc as next Gen

Progress

Targeting potential partnership to advance program

[1] Elia D. Tait Wonjo et al. Immunity 2019; 50:851-870.
[2] Khue G. Nguyen et al. Frontiers In Immunology 2020; 11:575597.
[3] Escalante N et al., ZW270, a conditionally masked IL-12 cytokine fusion protein displaying potent anti-tumor activity absent systemic toxicity. Abstract #2935 presented at American Association for Cancer Research annual meeting 2023.

Multispecific Antibody Therapeutics Abstracts at AACR 2023

Abstract #	Title	Next Steps
2942	ZW171, a T cell-engaging, bispecific antibody for the treatment of mesothelin-expressing solid tumors	• Anticipating IND 2024
5121	TriTCE Co-stim, next generation costimulatory trispecific T cell engagers for the treatment of solid tumors	• Lead format selection • Pilot toxicology studies
2982	TriTCE CPI, next generation trispecific T cell engagers with integrated checkpoint inhibition (CPI) for the treatment of solid tumors	• Lead format selection • Pilot toxicology studies
2926	PROTECT™, a novel trispecific antibody masking platform with integrated immune modulation displays unique activity and differentiated modes of action	• Lead format selection
2935	ZW270, a conditionally masked IL-12 cytokine fusion protein displaying potent anti-tumor activity absent systemic toxicity	• Targeting potential partnership • Evaluating opportunities for next-gen molecule

Future Development Strategies

- Actively pursuing next-generation T cell engaging antibodies to help overcome historical challenges in solid tumors
- Next-gen MSAT platforms able to address multiple shortfalls with previous generation T cell engagers
- Continue applying technology to additional tumor associated antigens

Summary

Focused R&D Strategy

Zymeworks Moving Forward “5 by 5”

Goal of 5 new product candidates planned for IND filing by 2027

2017-2022

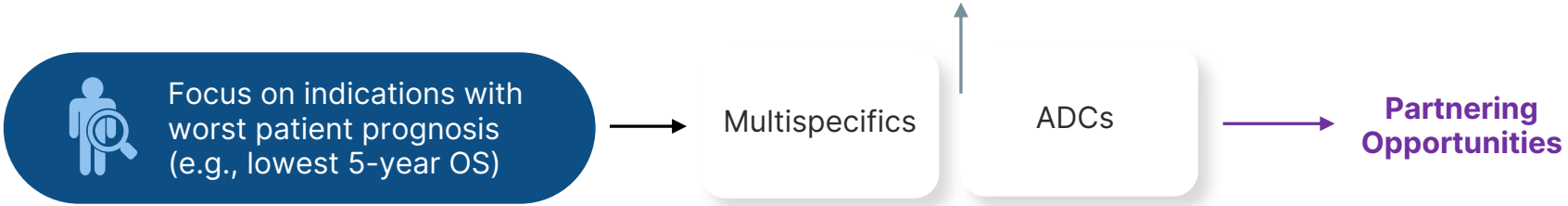
- Select Product Pipeline
- Platform Technologies & Tools

2022-2027

- **Accelerate Product Pipeline**
- **5 New Molecules in Clinic in 5 Years**
- **Select Product Partnerships**

Integrated Platforms Help Drive Growing Product Candidate Pipeline

Research and Early-Development Portfolio	Target	Late-Discovery	IND-Enabling	Phase 1	Milestone
ZW191 TOPO1i ADC Program	**FRα**	OVCA, Gynecological, NSCLC			**Expected IND 2024**
ZW171 2+1 CD3-Engager Program	**MSLN**	Pancreatic, OVCA, CRC			**Expected IND 2024**
ZW251 TOPO1i ADC Program	**GPC3**	Hepatocellular carcinoma			
ZW220 TOPO1i ADC Program	**NaPi2b**	OVCA, NSCLC			
Tri-TCE (CPI, Co-Stim, ProTECT) Trispecific T Cell Engagers	**Solid Tumors**	TAA Selection Ongoing			



Integrated R&D Engine Fuels Clinical Pipeline

ADC: antibody drug conjugate; IND: investigational new drug; OS: overall survival

Focused R&D Strategy

- Build a **diversified pipeline** of both best-in-class ADC's and MSAT's with 5 x 5 goals by 2027
- **Accelerate speed of early clinical development** through global diversification of early clinical studies ex-US from our hubs in Dublin and Singapore
- Ongoing efforts to **reduce time period** from preclinical development candidate selection through IND filing
- Supplement internal product portfolio with **advancement of additional product candidates** through collaboration and partnerships
- Retention of US commercial rights wherever feasible with **ex-US partnering strategy prior to registration studies**
- **Selected expansion of R&D efforts** in adjacent areas for **continued innovation** in ADC's and MSAT's with expansion of core capabilities where appropriate to ensure long-term competitiveness
- Expected cash flows from zanidatamab commercialization by JAZZ and BGNE to provide **non-dilutive funding for development** of diversified, clinical-stage oncology pipeline of ADC's and MSAT's

ADC: antibody drug conjugate; MSAT: multispecific antibody therapeutic

Key Anticipated Events & Milestones Opportunities Throughout Product Pipeline

2023

- **Phase 2 1L GEA Follow-Up (presented January 19 at ASCO GI)** zanidatamab + chemotherapy
- **Additional publications** on preclinical development candidates **(presented at AACR)**
- **HERIZON-BTC-01 (1H23)** Full data presentation
- **Present additional Phase 1 data** for zanidatamab zovodotin **(2H23)**
- **Expand zanidatamab zovodotin into Phase 2** studies in key expansion areas: non-small cell lung cancer, and breast cancer
- **Earn additional milestone payments** for expansion or extension of existing legacy platform agreements
- **Nomination of next product candidate** for Preclinical Development **(2H23)** with target IND filing in 2025

2024

- **Submit 2 IND Applications** for ZW171 and ZW191
- **HERIZON-GEA-01** Anticipate Top-Line Data
- **Continue leveraging platforms** to generate preclinical product candidates and partnerships
- **Earn additional milestone payments** for expansion or extension of existing legacy platform agreements
- **Nominate additional potential product candidate** for preclinical development with target IND filing in 2026

IND: investigational new drug

Company Contacts

Investor Relations

Jack Spinks
Director, Investor Relations
ir@zymeworks.com
(604) 678-1388

Media Relations

Diana Papove
Director, Corporate Communications
media@zymeworks.com
(604) 678-1388