PRECISION BIOLOGICS

PB-223, A Novel Antibody Drug Conjugate Targeting Truncated Core-2 Glycans in Solid Tumors

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Festival of Biologics

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02
Platform Overview

Precision Biologics' Platform Overview

Clinically Validated Platform for Identifying Functional Tumor Specific Antigens and Generating Antibodies

Precision Biologics' Specialized Approach for Generating Clinically Relevant Antibodies

The Hollinshead Cancer Vaccine Platform

- The Hollinshead Cancer Vaccine Platform (the "Platform") is the only platform for identifying functional tumor specific antigens tested for immunogenicity and anti-tumor activity
- The Platform is rooted in human biology and contains tumor-associated antigens ("TAAs") derived from pooled specimens from 79 patients with colon cancer
- The TAAs were isolated from tumor membrane fractions derived from surgically resected specimens of each patient
  - Precision discovered that there were two synergistic TAAs with molecular weights of 72 kDa and 88 kDa that were defined to be biologically active and immunogenic in humans
- The Hollinshead Cancer Vaccine Platform was created by mixing the two purified TAAs with complete Freund's adjuvant and homogenizing the mixture
  - This vaccine was used in humans, and after five months of vaccination, most of the vaccinated subjects developed a sustained immunity against TAAs contained in the vaccine, suggesting that these TAAs were strongly immunogenic
  - Given the potent immunogenic activity, the Platform was used to immunize mice to generate different monoclonal antibodies against TAAs included in the vaccine platform
- Precision identified two antibodies with a strong affinity to these TAAs and discovered that the antibodies bind to O-glycans attached to glycoproteins expressed only by cancer cells

Key Differentiating Factors

Novel Approach
Ability to generate antibodies that trigger immune responses to the tumor-associated antigens in the Hollinshead Cancer Vaccine Platform, which Precision derived from tumor membrane fractions from surgically resected specimens from 79 patients with colon cancer

Robust Screening Capabilities
Utilized the Platform to generate monoclonal antibodies against targets expressed specifically on cancer cells and not on healthy tissue; subsequently screened thousands of antibody candidates to select antibodies with the highest binding affinity to tumor specific O-glycans (Core 1 or Core 2 O-glycans) attached to proteins of cancer cells

Rooted in Human Biology
Identified and generated antibodies that recognize tumor-associated antigens with proven immunogenicity and biological activity in humans, the most clinically relevant source for developing effective anticancer therapies, rather than utilizing predictive software, bioinformatics, AI or other structure-based drug design to determine clinical relevance

High Tumor Specificity
Focused on developing antibodies which bind to O-glycans attached to glycoproteins only expressed on cancer cells, which avoids the toxicity issues associated with targets that are not tumor specific and instead are overexpressed on both tumor cells and healthy cells

Compared to traditional methods using truncated glycans and newer bioinformatics and AI approaches, the Precision Biologics Platform generates clinically validated antibodies that induce an immune response and target O-glycans found on cancer cells but not on healthy tissues

Source: (Fantini et al., 2024).

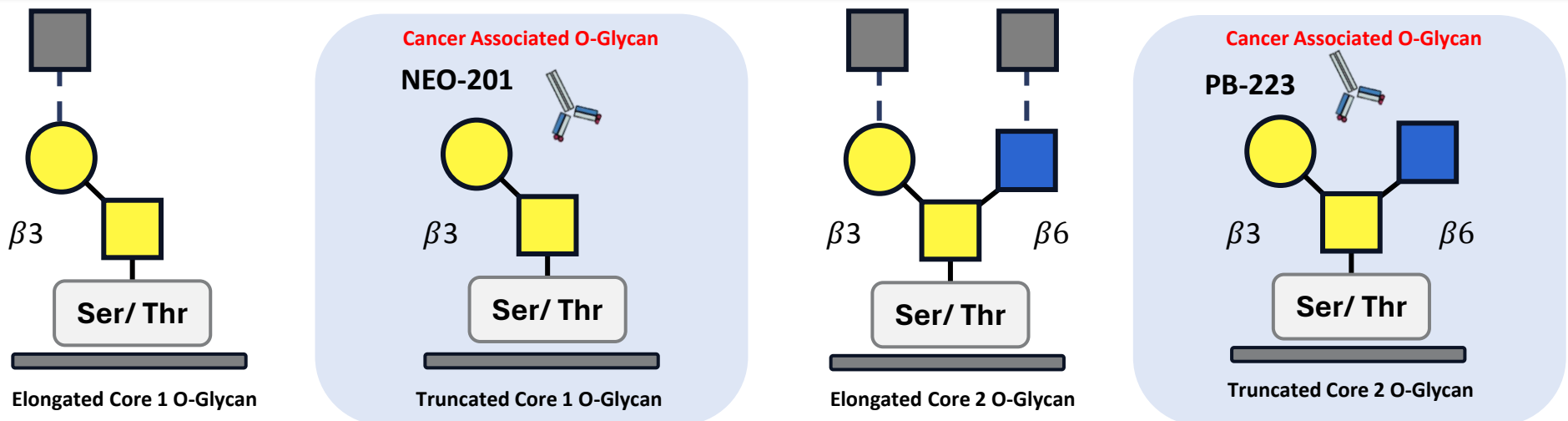
Precision Biologics Targets Tumor Specific O-glycans

O-glycans Are Optimal Targets for Treating Cancer

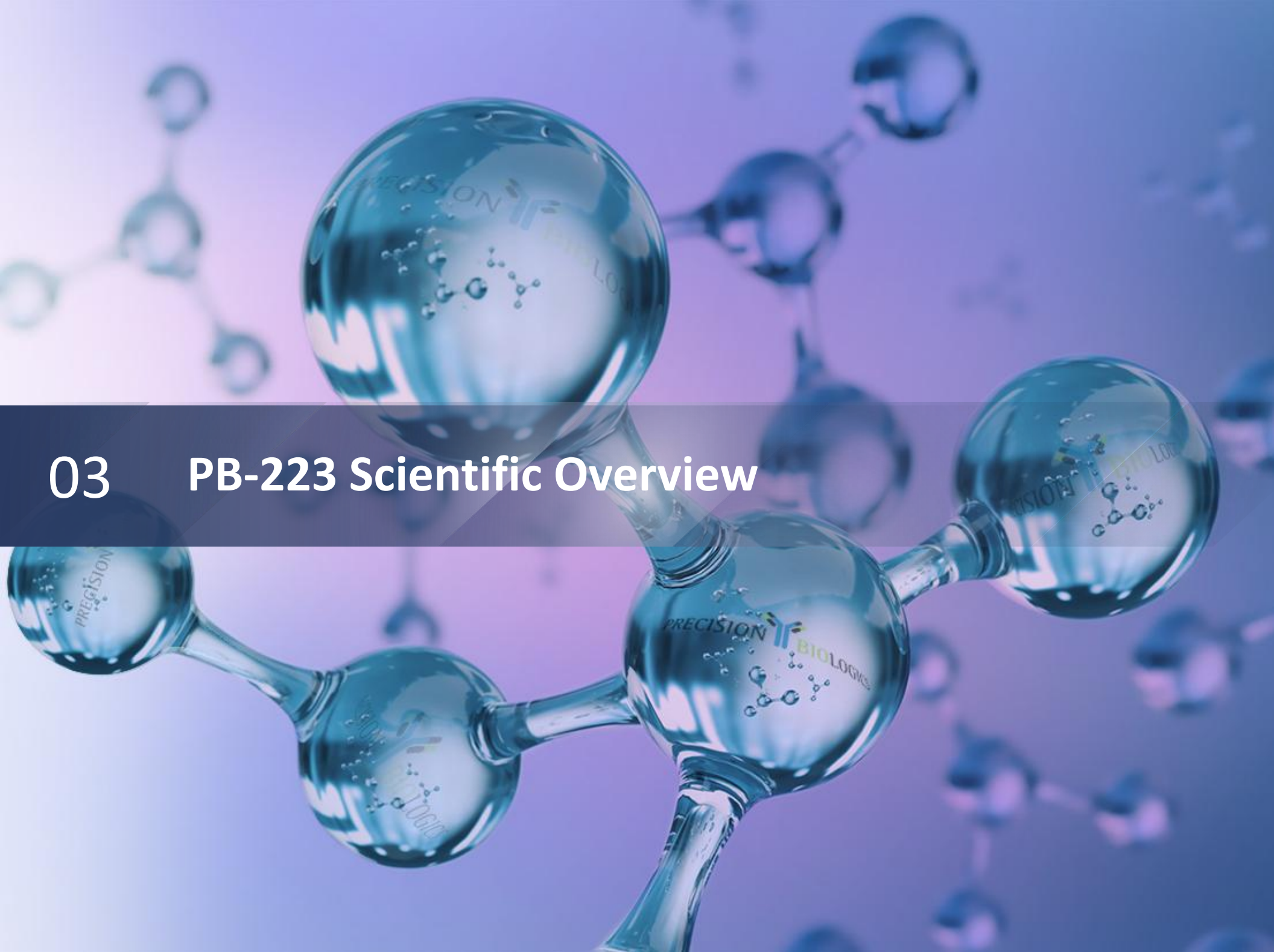
O-glycans Provide A Novel Avenue For Cancer Treatment

- Glycosylation is a vital post-translational modification in mammalian cells, essential for proper function and cell signaling
- In cancer, O-glycosylation is frequently altered, leading to the expression of truncated O-glycans on cancer cell proteins and contributing to tumor progression and immune evasion
- Because O-glycans are selectively expressed on multiple proteins or lipids in tumors, including epithelial tumors and certain blood cancers, they are attractive for multiple therapeutic modalities like ADCs, radioimmunotherapy and cell therapy
  - 50–80% of cellular surface proteins are glycosylated
- Truncated O-glycans are ***only*** expressed on cancer cells and tumor tissue and are ***not*** expressed on healthy cells or tissue, offering a novel approach for treating solid and liquid tumors
- The employment of anti-cancer therapy with strong binding affinity for cancer cells carrying truncated O-glycans could represent a promising tool in treating both solid and liquid tumors
- Daiichi Sankyo's program DS-3939, a TA-MUC1-directed ADC, has demonstrated promising clinical activity in patients with solid tumors in a Phase 1/2 trial, which clinically validates glycoproteins as targets for cancer treatment

Precision Biologics' Antibodies Selectively Target Truncated O-glycans with High Binding Affinity



Source: (Rømer et al., 2021).



03 PB-223 Scientific Overview

Executive Summary of PB-223 and PB-223 ADC

PB-223 Is an Innovative mAb Developed through Affinity Maturation of Precision's Initial Development Program

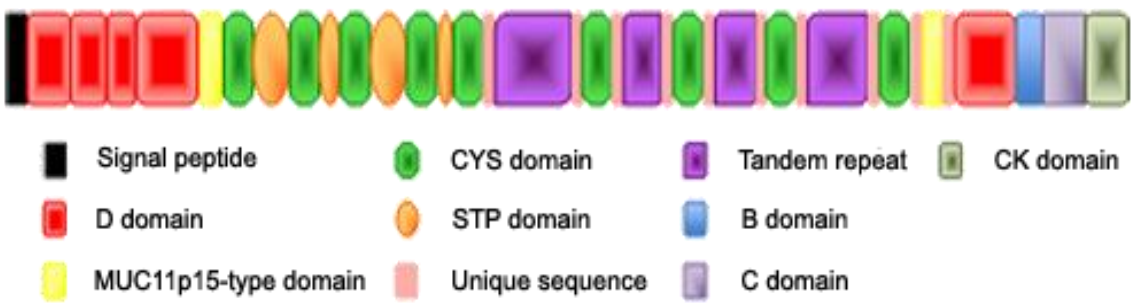
Target / MoA	▪ PB-223 targets truncated Core 2 O-glycans found on MUC-5AC, specifically expressed by cancer cells and not by healthy tissues ▪ PB-223 ADC was developed using monomethyl auristatin E ("MMAE"), a potent antimitotic agent that inhibits tubulin polymerization, as the cytotoxic payload; MMAE is linked through a protease-cleavable mc-vc-PABC linker and conjugated to PB-223 via a cysteine-based method
Preclinical Highlights	▪ PB-223 exhibited a binding affinity at least four times greater than predecessor antibody NEO-102, indicating enhanced tumor targeting ▪ Experiments show PB-223 does not bind to normal tissues and that it can be internalized into human cancer cell lines expressing its target ▪ Precision Biologics has completed key IND-enabling studies for PB-223 ADC, including preclinical safety, pharmacokinetics and toxicology assessments – PB-223 ADC has demonstrated promising binding, killing, safety and stability data in preclinical studies
Indication(s)	▪ Solid tumors (colorectal and pancreatic cancers, as well as triple-negative breast, ovarian, prostate, head and neck, NSCLC and bladder cancers)
Current Status	▪ PB-223 ADC has completed all preclinical work ▪ Remaining work prior to filing an IND includes GMP-related activities, GMP material studies and writing the FIH protocol
Differentiation	▪ Unlike other glycan platforms, the Precision Biologics Platform screened **patient derived** TAAs to generate clinically validated antibodies that induce an immune response and target O-glycans found on cancer cells but not on healthy tissues
Intellectual Property	▪ Patent application has been filed and is pending; upon issuance, will have protection to 2043

Homogeneity of the PB-223 Target and Epitope

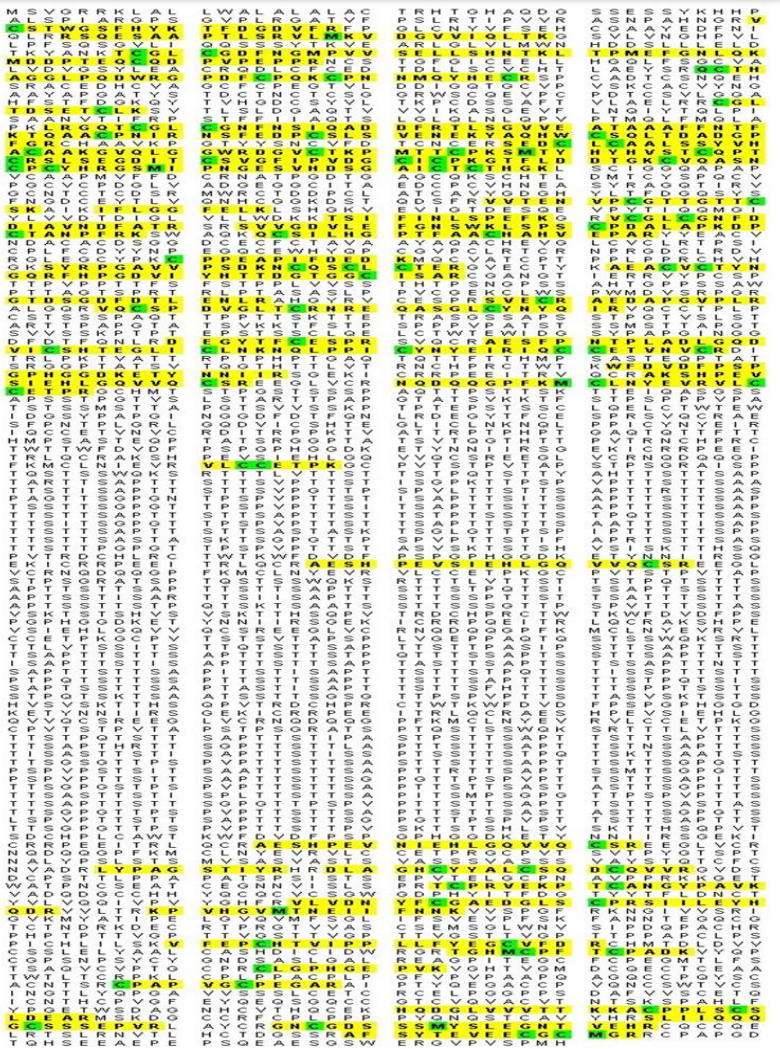
Leveraging Conserved Glycosylation Patterns for Tumor-Specific Targeting

MUC-5AC Glycoprotein Overview

- PB-223 targets MUC-5AC which is a secreted, gel-forming mucin with a high molecular weight of ~641 kDa
- Up to 80% of the total weight is due to the large number of O-glycosylated chains attached to Thr and Ser residues in the Tandem Repeat sequence
- MUC-5AC is normally produced by epithelial tissues and secreted into the lumen and can be aberrantly glycosylated in cancer cells
- Precision Biologics' technology selectively binds to this tumor-specific variant that is exclusively expressed on tumor cells
- The target antigen includes components of MUC-5AC, which Precision identified via a mass spectrometry ("MS") analysis of affinity-purified NPC1 antigen from CFPAC-1 cells
- A sandwich ELISA using an anti-MUC-5AC antibody revealed approximately 60% overlap with MUC-5AC in the pancreatic cancer cell line CFPAC-1 and about 40% overlap in the colon cancer cell line LS174T



MS Analysis Demonstrated Uniformity to MUC-5AC



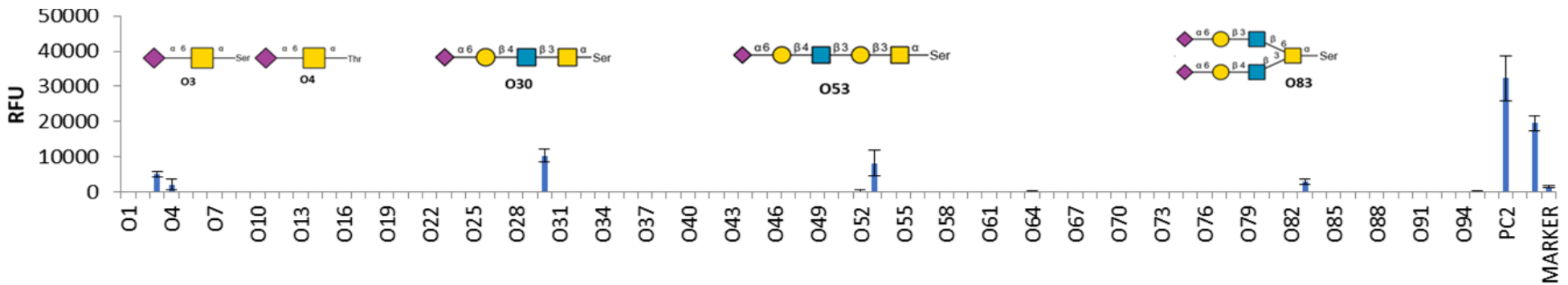
Identified Peptides

Repetitive Regions Consisting of the Most O- and N-glycosylation

PB-223 Binding Data

PB-223 Has Demonstrated Strong Binding to Cancer Cell Lines Expressing Core 2 O-glycans

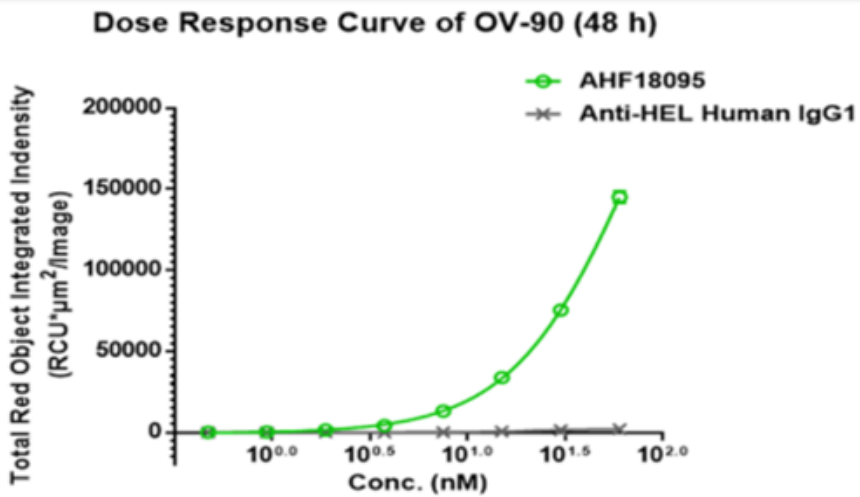
PB-223 Binds to Core 2 O-glycans



Flow Cytometry Analysis

Cell Line	Tumor Type	% PB-223 Positive Cells (MFI)	% Core 2 O-glycan expression
LoVo	Colorectal adenocarcinoma	1.01% (254)	053 (0.29%)
SW-403	Colorectal adenocarcinoma	51.23% **(102)**	N.T.
COLO-205	Colorectal adenocarcinoma	41.05% **(78)**	N.T.
HCC1937	Triple negative breast cancer	42.08% **(134)**	053 (6.32%)
OV90	Ovarian adenocarcinoma	43.12% **(469)**	053 (6.76%)

PB-223 Internalizes Into OV-90



PB-223 binds specifically to Core 2 O-glycans expressed only on cancer cells and not on healthy tissues

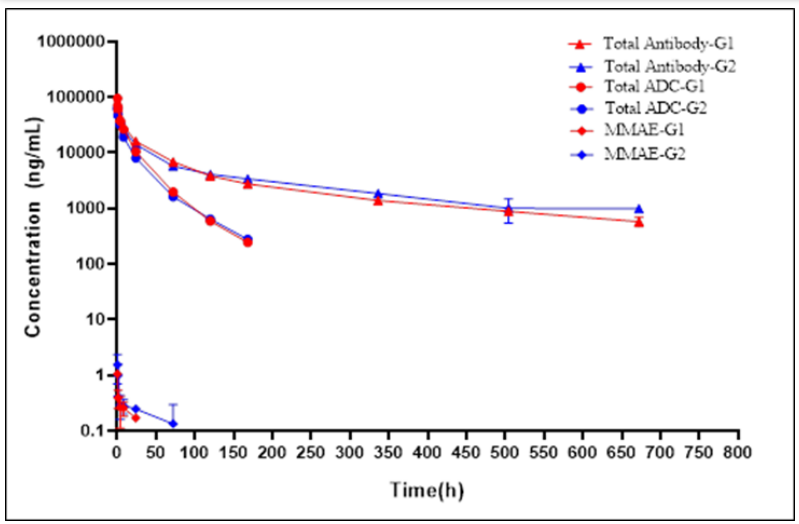
PB-223 and PB-223 ADC Pharmacokinetics in Rats

PB-223 and PB-223 ADC Exhibited an Extended Half-Life in Pharmacokinetic ("PK") Studies

Dosing and Sampling Strategy

- PB-223 ADC was administered intravenously at a dose of 3 mg/kg as a single dose to male ("G1") and female ("G2") rats
- Blood samples for PK analysis were collected at 15 minutes, 1 hour, 4 hours, 8 hours and on days 1, 3, 5, 7, 14, 21 and 28 post-administration

Extended Half-Life Observed



The half-life of the total antibody and ADC were ~200 hours and ~35 hours, respectively, and there were no significant differences observed between the G1 and G2 groups

Total PB-223 ADC[1]

Group	T 1/2	Cmax	AUClast	VZobs	CLobs	MRTlast
	H	μg/mL	h × μg/mL	mL/kg	mL/h/kg	h
G1	31.95 ± 0.55	94.88 ± 4.83	1,038.67 ± 116.31	132.96 ± 16.62	2.88 ± 0.31	21.08 ± 0.77
G2	37.67 ± 1.78	64.4 ± 4.92	804.26 ± 79.02	199.82 ± 13.36	3.69 ± 0.39	23.24 ± 0.64

Total PB-223 Antibody[1]

Group	T 1/2	Cmax	AUClast	VZobs	CLobs	MRTlast
	H	μg/mL	h × μg/mL	mL/kg	mL/h/kg	h
G1	268.15 ± 37.84	84.88 ± 5.35	2,375.04 ± 102.87	445.78 ± 16.62	1.15 ± 0.04	124.63 ± 9.59
G2	224.12 ± 87.96	68.44 ± 4.65	2,343.98 ± 248.63	362.05 ± 110.81	1.16 ± 0.19	142.03 ± 31.04

(1) Values displayed as Mean ± SD.

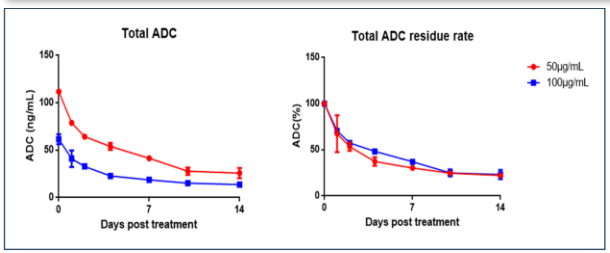
PB-223 ADC Preclinical Data Overview

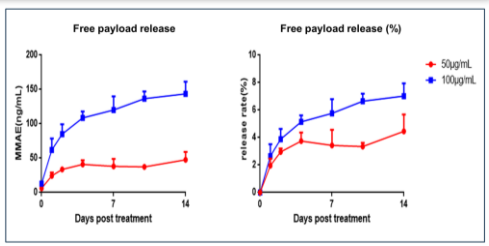
PB-223 ADC Has Generated Promising Preclinical Data To Date, With Additional In Vivo Preclinical Studies Ongoing

PB-223 ADC Drug-to-Antibody Ratio ("DAR")

ADC Clone	Conc. (mg/ml)	Purity SEC-HLPC%	DAR	Endotoxin (EU/mg)
PB-vcMMAE-2	1.421	95.11	3.72	<3
PB-vcMMAE-5	1.482	99.48	3.92	<3
PB-vcMMAE-6	1.428	99.50	4.15	<3

PB-223 ADC Is Stable In Human Plasma

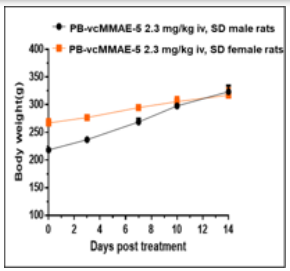


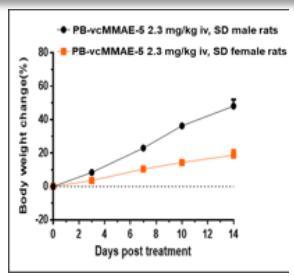


After 14 days, the mean residual rate of PB-vcMMAE-5 ADC in human plasma was 23% for ADC at 100 µg/mL and 22% for ADC at 50 µg/mL

After 14 days, the mean free payload release rate of PB-vcMMAE-5 ADC in human plasma was 7.02% for ADC at 100 µg/mL and 4.46% for ADC at 50 µg/mL

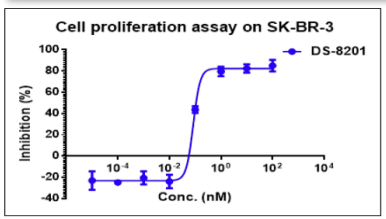
Positive Safety Data *In Vivo*

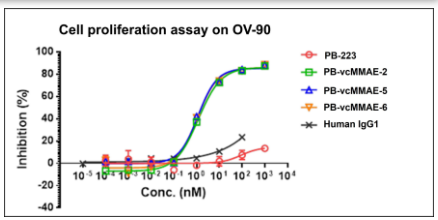




PB-223 ADC was well tolerated in rats with no signs of distress or loss of body weight observed after administration

Killing Assay: PB-223 ADCs Kill OV-90 Cells





- **All three PB-223 ADCs effectively killed OV-90 cells**
  - At a concentration of 333nM, the percentage of cell killing for PB-vcMMAE-2, PBvcMMAE-5 and PB-vcMMAE-6 was 82.91%, 84.04% and 83.16%, respectively
  - In contrast, both human IgG1 and naked PB-223 mAb showed no killing of OV-90 cells
- **PB-223 ADC compares favorably to Trastuzumab deruxtecan**
  - At a concentration of 10nM, DS-8201 inhibited cell proliferation by 82.39%

PB-223 and PB-223 ADC Preclinical Efficacy

PB-223 Shows High Tumor Specificity, and PB-223 ADC Demonstrated Significant Cancer Cell Killing In Vitro

PB-223 Binding to Human Cancer Tissue by IHC

Cancer Type	% Tissue Reactive With PB-223	H-score
Colorectal Cancer	100%	300
Lung Adenocarcinoma Cancer	100%	300
Breast Cancer	100%	300
Ovarian Cancer	90%	180
Prostate Cancer	60%	120
Squamous Cell Carcinoma Lung Cancer	60%	120
Pancreatic Cancer	50%	50
Normal Tissue and Normal Adjacent Tissue to the Tumor	None	0

PB-223 ADC *In Vitro* Efficacy

Cancer Type	PB-223 ADC (1000 nM) % killing
MDA-MB-231 (TNBC)	89.87%
LnCAP (Prostate)	89.58%
OV-90 (Ovarian)	88.88%
NCI-H226 (Lung)	82.00%
BT-474 (Breast)	80.12%
SW403 (Colorectal)	78.71%
PC-3 (Prostate)	78.66%
CFPAC-1 (Pancreas)	68.73%
HCC1937 (TNBC)	51.14%

PB-223 mAb is highly expressed across multiple tumor types, demonstrates strong tumor specificity, and does not bind to normal tissue or adjacent non-tumor tissue

PB-223 ADC demonstrated significant tumor cell killing *in vitro* across a range of cancer types

Denotes selected human cancer and cell line for in vivo subcutaneous mouse tumor model study.

PB-223 Binding Comparison

PB-223 Has Demonstrated Superior Binding to Cancer Tissue Than NEO-102

Cancer Tissue

Human Cancer	TNM Status and Stage of Cancer	% Tissue Reactive with NEO-102 IHC-Score	% Tissue Reactive with PB-223 IHC-Score
Colorectal Adenocarcinoma	Patient 1: T3N0M0, Stage IIA	**100% IHC Score: 3**	**100% IHC Score: 3**
	Patient 2: T3N0M0, Stage IIA	**0% IHC Score: 0**	**50% IHC Score: 1**
Pancreatic Cancer	(Adenocarcinoma) Patient 1: T2N1M0, Stage IIB	**100% IHC Score: 3**	**100% IHC Score: 3**
	(Neuroendocrine Carcinoma) Patient 2: T2N0M0, Stage IB	**0% IHC Score: 0**	**80% IHC Score: 1**
Lung Adenocarcinoma	Patient 1: T2N0M0, Stage IB	**80% IHC Score: 3**	**100% IHC Score: 3**
	Patient 2: T2aN1M0, Stage IIA	**80% IHC Score: 3**	**100% IHC Score: 3**
Squamous Cell Carcinoma of the Lung	T2N1M0, Stage IIB	**30% IHC Score: 1**	**60% IHC Score: 2**
Breast Cancer	Patient 1: T1cN3M0, Stage IIIC	**70% IHC Score: 2**	**90% IHC Score: 2**
	Patient 2: T2N0M0, Stage IIA	**90% IHC Score: 3**	**100% IHC Score: 3**
Prostate Adenocarcinoma	Patient 1: T3N0M0, Stage III	**0% IHC Score: 0**	**30% IHC Score: 1**
	Patient 2: T3N0M0, Stage III	**20% IHC Score: 1**	**60% IHC Score: 2**
Ovarian High Grade Serous Carcinoma	Patient 1: T1aN0M0, Stage IA	**20% IHC Score: 2**	**25% IHC Score: 2**
	Patient 2: T2N0M0, Stage II	**10% IHC Score: 2**	**20% IHC Score: 2**

Normal Tissue or Normal Adjacent Tissue to the Tumor

Normal Human Tissue	% Tissue Reactive with NEO-102 IHC-Score	% Tissue Reactive with PB-223 IHC-Score
Adjacent Normal Tissue to Colorectal Adenocarcinoma	20% IHC Score: 3 (Positive in Goblet Cells)	70% IHC Score: 3 (Positive in Goblet Cells)
Adjacent Normal Tissue to Pancreatic Cancer	0% IHC Score: 0	0% IHC Score: 0
Adjacent Normal Tissue to Lung Cancer	0% IHC Score: 0	0% IHC Score: 0
Adjacent Normal Tissue to Breast Cancer	0% IHC Score: 0	0% IHC Score: 0
Adjacent Normal Tissue to Prostate Cancer	0% IHC Score: 0	0% IHC Score: 0
Adjacent Normal Tissue to Ovarian Cancer	0% IHC Score: 0	0% IHC Score: 0

PB-223 Binding Comparison (Cont.)

PB-223 Demonstrated High Tumor Specificity and Superior Binding to Cancer Tissue Than NEO-102

Cancer Tissue		
Human Cancer	**Tissue Reactive with NEO-102**	**Tissue Reactive with PB-223**
Colorectal Adenocarcinoma	Positive	Positive
Stomach Cancer	ND	Positive
Esophagus Cancer	ND	Positive
Hepatocellular Carcinoma	Negative	Positive
Pancreatic Cancer	ND	Positive
Ovarian Cancer	ND	Positive
Endometrioid adenocarcinoma	ND	Positive
Cervical Cancer	Positive	Positive
Lung Papillary Adenocarcinoma	ND	Positive
Thyroid Cancer	ND	Positive
Head and Neck Cancer	Negative	Positive
Kidney Cancer	Negative	Positive
Bladder Cancer	Negative	Positive
Prostate Cancer	Positive	Positive
Testis Cancer	ND	Positive
Breast Cancer	ND	Positive
Triple Negative Breast Cancer	Negative	Positive
Skin Cancer	ND	Negative
Thyroid Cancer	ND	Negative

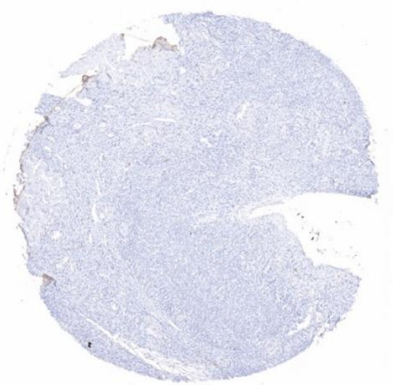
Normal Tissue or Normal Adjacent Tissue to the Tumor	
Normal Human Tissue	**Tissue Reactive with PB-223**
Brain	Negative
Liver	Negative
Lung	Negative
Colon	Negative
Lymph node	Negative

Note: "ND" denotes "Not Done".

Histology Across Tumor Types

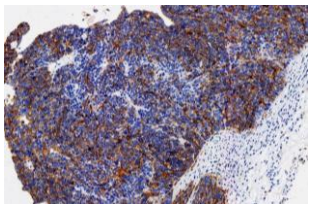
Ovarian Cancer

Adjacent Normal Tissue

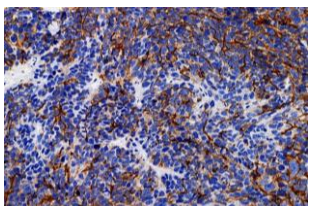


IHC Score: N/A

Tumor Tissue



100x

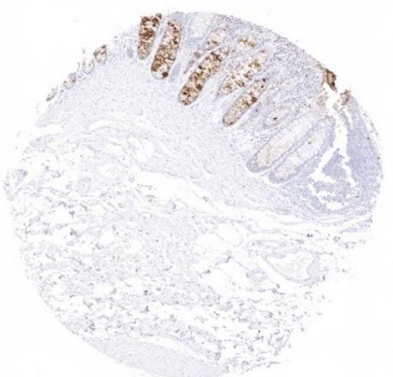


200x

IHC Score: 2
% Positive: 90%
H-score: 180

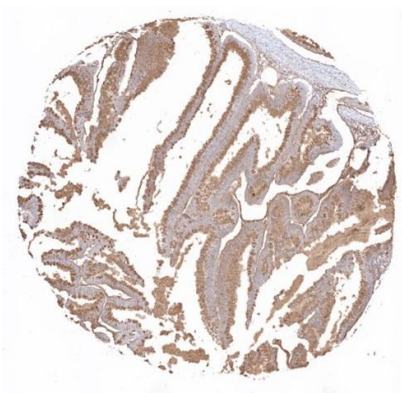
Colorectal Cancer

Adjacent Normal Tissue



IHC Score: N/A

Tumor Tissue

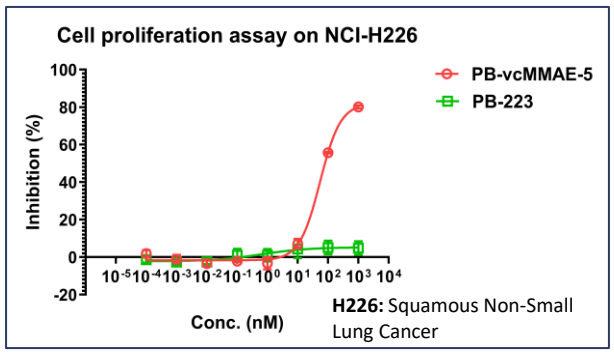


IHC Score: 3
% Positive: 100%
H-score: 300

In Vitro Efficacy of PB-223 ADC

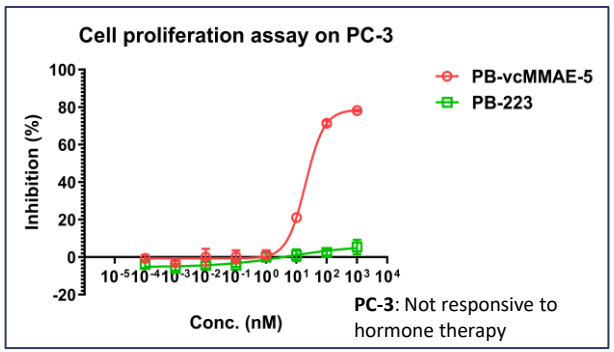
Human Lung, Prostate, Triple Negative Breast, Ovarian, Colon and Pancreatic Cancer Cell Lines

Lung Cancer Cell Lines



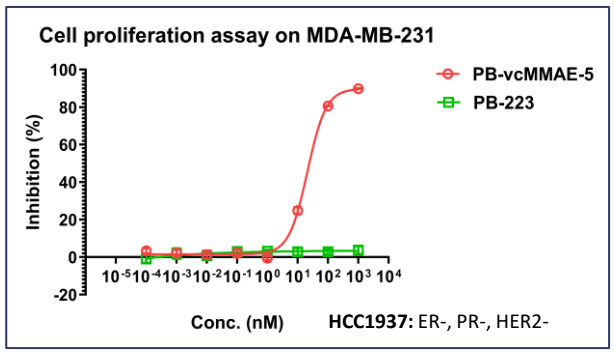
H226: Squamous Non-Small Lung Cancer

Prostate Cancer Cells Lines



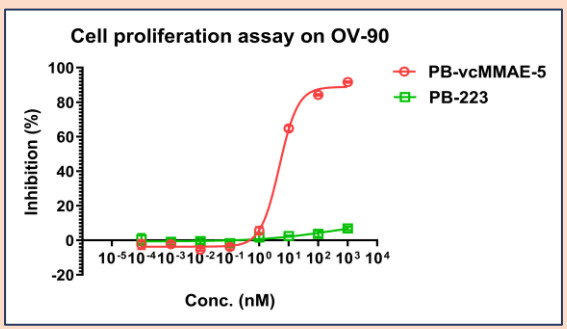
PC-3: Not responsive to hormone therapy

Triple Negative Breast Cancer Cell Lines

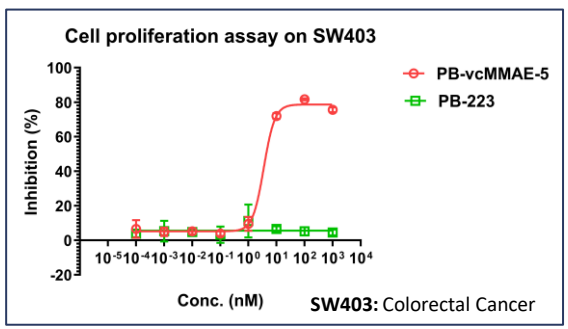


HCC1937: ER-, PR-, HER2-

Ovarian Cancer Cell Lines

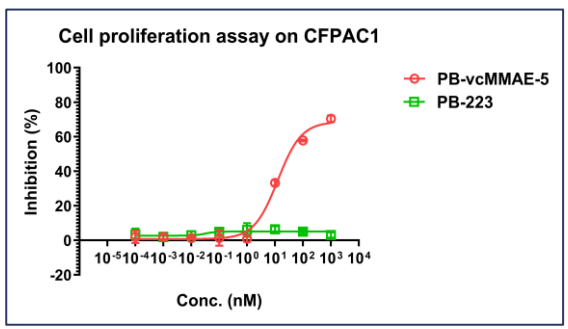


Colon Cancer Cell Lines



SW403: Colorectal Cancer

Pancreatic Cancer Cell Lines



CFPAC-1: Pancreatic Cancer

The PB-223 ADC has demonstrated significant *in vitro* efficacy across a broad spectrum of human cancer cell lines, including prostate, breast, lung, ovarian, colon and pancreatic cancers

Denotes selected cell line for in vivo subcutaneous mouse tumor model study.

In Vivo Study Design of PB-223 ADC

Preclinical OV90 Tumor Model Overview, Study Groups and Dosing Information

Preclinical Mouse Tumor Model Overview

- The efficacy of PB-223 ADC ("U566-vcMMAE-5-5") was assessed in an OV-90 ovarian human cancer cell line
- PB-223 ADC was administered intravenously at doses 1 mg/kg and 3 mg/kg, 6 mg/kg and 9 mg/kg, once per week for seven weeks to evaluate the therapeutic effect of different doses of the test substance against the control free payload
- This experiment indicates the animal's tolerance to the test substance through body weight changes
  - There was no significant weight loss or death of any of the mice, demonstrating good tolerance to the test object at the experimental dose
- Group 4, 5 and 6 showed significant tumor inhibition effects while the average tumor volumes of the other groups had no significant differences compared with the Vehicle group
- These results indicate that PB-223 ADC at doses of 3 mg/kg, 6 mg/kg, and 9 mg/kg demonstrate strong antitumor efficacy, which could support movement of the candidate into clinical trials

Study Groups and Dosing Information

Group	N(1)	Treatment	Dose (mg/kg)	Dose Volume (mL/kg)	Dose Route	Schedule
1	6	Vehicle	0.00	10	*IV*	QW*5
2	6	MMAE	0.15	10	*IV*	QW*5
3	6	U566-vcMMAE-5-5	1.00	10	*IV*	QW*5
4	6	U566-vcMMAE-5-5	3.00	10	*IV*	QW*5
5	6	U566-vcMMAE-5-5	6.00	10	*IV*	QW*5(2)
6	6	U566-vcMMAE-5-5	9.00	10	*IV*	QW*5(2)

Note: "IV" denotes "intravenous injection".

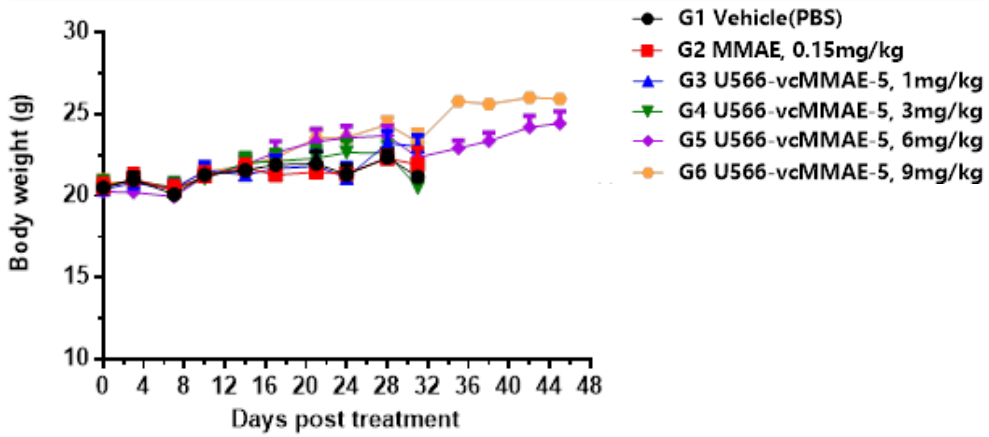
(1) Number of animals per group.

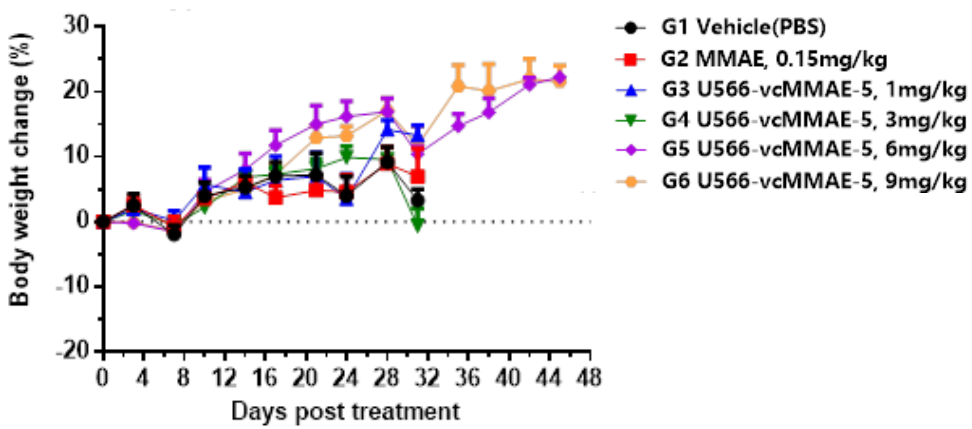
(2) In G5 and G6, 3 mice were randomly selected from each group, and the observation was extended for two weeks.

In Vivo Safety of PB-223 ADC: Ovarian Cancer Model

PB-223 ADC Exhibited Promising Safety and Tolerability in the Preclinical Mouse Model

Body Weight by Days Post Treatment





Body Weight as a Safety Indicator

- Animal body weight was monitored twice weekly as an indirect indicator of toxicity
- No abnormal behaviors such as weight loss were observed in either the treatment or control groups, suggesting that all tested compounds were well tolerated by the mice

Body Weight Before and 31-Days After Treatment

		Body Weight (g)[1]	
Treatment	Dose (mg/kg)	Day 0	Day 31
Vehicle	0.00	20.50 ± 0.35	21.16 ± 0.32
MMAE	0.15	20.51 ± 0.56	21.93 ± 1.00
U566-vcMMAE-5	1.00	20.39 ± 0.38	23.03 ± 0.69
U566-vcMMAE-5	3.00	20.62 ± 0.58	20.51 ± 0.87
U566-vcMMAE-5	6.00	20.26 ± 0.36	22.36 ± 0.27
U566-vcMMAE-5	9.00	20.84 ± 0.42	23.29 ± 0.76

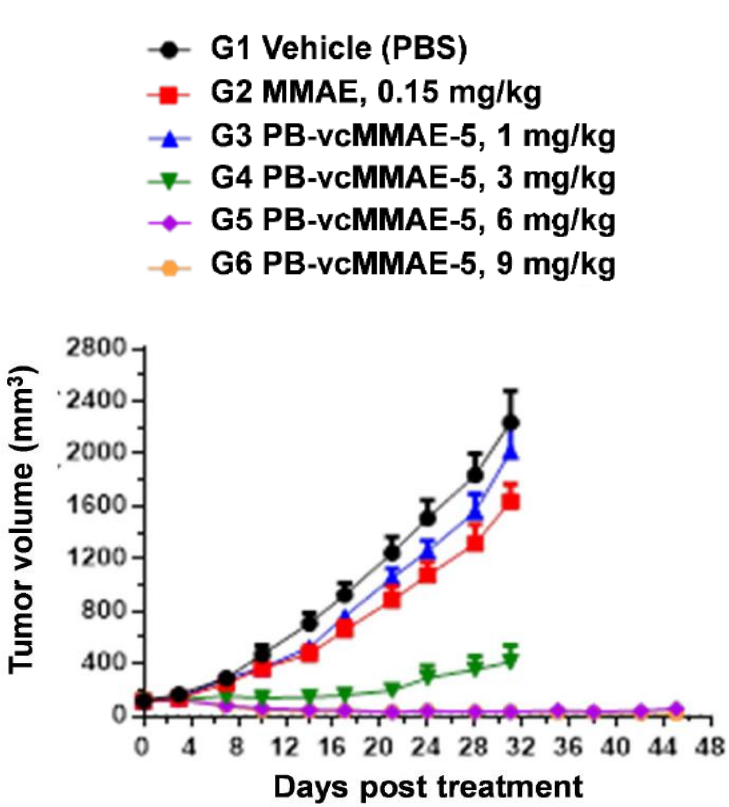
PB-223 ADC was well tolerated in NOD-SCID mice, with no signs of distress or body weight loss observed following each dose across all test groups

(1) Values displayed as Mean ± SE.

In Vivo Efficacy of PB-223 ADC: Ovarian Cancer Model

PB-223 Demonstrated Meaningful Anti-Tumor Activity

PB-223 ADC Exhibits Dose Dependent Anti-Tumor Activity



Tumor Growth Inhibition Analysis

Treatment	Dose (mg/kg)	Tumor Volume (mm^3)[1] Day 0	Tumor Volume (mm^3)[1] Day 31	Tumor Weight (g)[1] Day 31	T/C(%)[2]	TGI(%)[3]	P Value[4]
Vehicle	NA	116.89 ± 7.17	2239.36 ± 241.54	2.29 ± 0.30	-	-	-
MMAE	0.15	116.59 ± 6.70	1637.01 ± 131.11	1.72 ± 0.14	74.05	28.37	0.0254
U566-vcMMAE-5	1.00	116.59 ± 4.57	2018.27 ± 209.99	1.91 ± 0.26	93.15	10.40	0.7515
U566-vcMMAE-5	3.00	116.28 ± 5.07	414.04 ± 123.98	0.40 ± 0.13	17.94	85.97	< 0.0001
U566-vcMMAE-5	6.00	116.53 ± 7.98	33.81 ± 3.63	0.04 ± 0.01	1.51	103.90	< 0.0001
U566-vcMMAE-5	9.00	116.53 ± 6.54	36.55 ± 3.06	0.03 ± 0.00	1.63	103.77	< 0.0001

PB-223 ADC demonstrated strong dose-dependent antitumor activity in the OV90 xenograft model, with 3–9 mg/kg showing significant tumor inhibition

(1) Values displayed as Mean ± SE.
(2) T/C (%) = TRTV /CRTV × 100 %.
(3) TGI (%) = 100% × (1-(Tt-T0)/(Vt-V0)).
(4) P Value (one-way ANOVA) is calculated based on tumor volume and compared with group Vehicle .

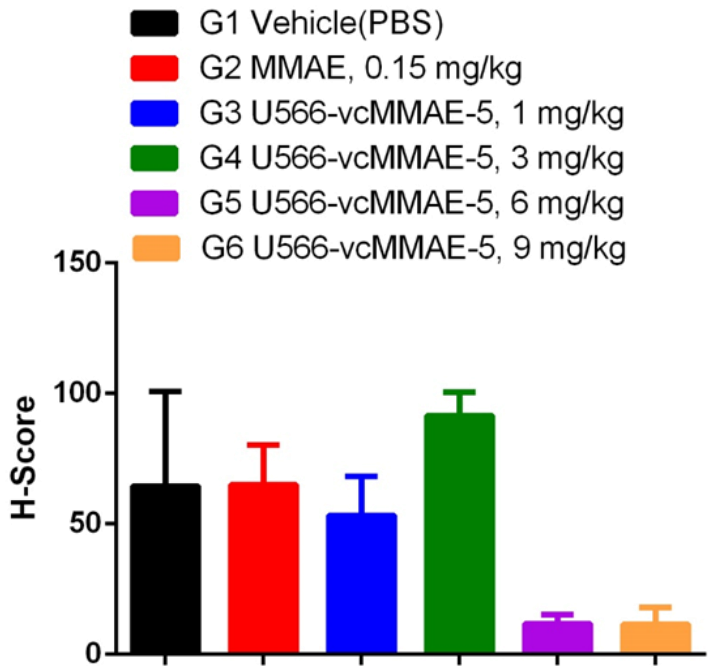
In Vivo Efficacy of PB-223 ADC: Ovarian Cancer Model (Cont.)

PB-223 ADC Demonstrated Significant Tumor Weight and H-Score Reductions

Tumor Weight Analysis

Treatment	Dose (mg/kg)	Tumor Weight (g)[1] At Day 31	T/C_{weight}(%)[2]	P Value[3]
Vehicle	0.00	2.29 ± 0.30	-	-
MMAE	0.15	1.72 ± 0.14	75.11	0.1259
U566-vcMMAE-5	1.00	1.91 ± 0.26	83.46	0.4515
U566-vcMMAE-5	3.00	0.40 ± 0.13	17.64	< 0.0001
U566-vcMMAE-5	6.00	0.04 ± 0.01	1.88	< 0.0001
U566-vcMMAE-5	9.00	0.03 ± 0.00	1.11	< 0.0001

Tumor Tissue Analysis



- The H-scores for groups G1, G2, and G3 remained relatively stable
- Group G4 exhibited a moderate increase in H-score compared to G1–G3, while groups G5 and G6 showed a significant decrease relative to G1–G4

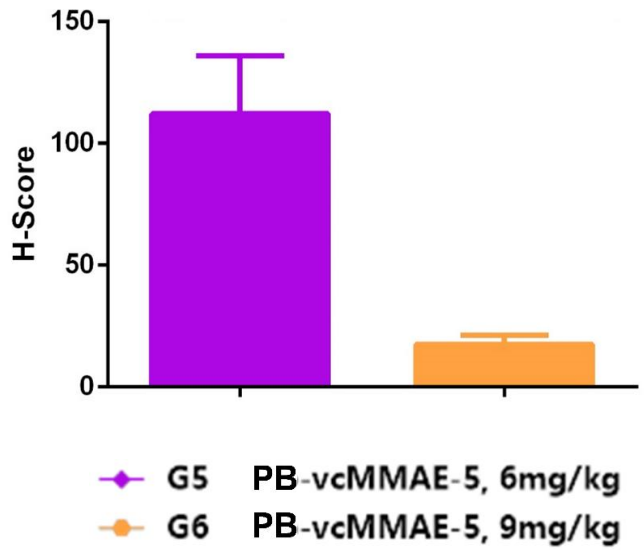
Higher doses of PB-223 ADC (6–9 mg/kg) led to a significant reductions in tumor weight and H-scores

(1) Values displayed as Mean ± SE.
(2) T/C (%) = TRTV /CRTV × 100 %.
(3) p value (one-way ANOVA) is calculated based on tumor volume and compared with group Vehicle

In Vivo Efficacy of PB-223 ADC: Ovarian Cancer Model (Cont.)

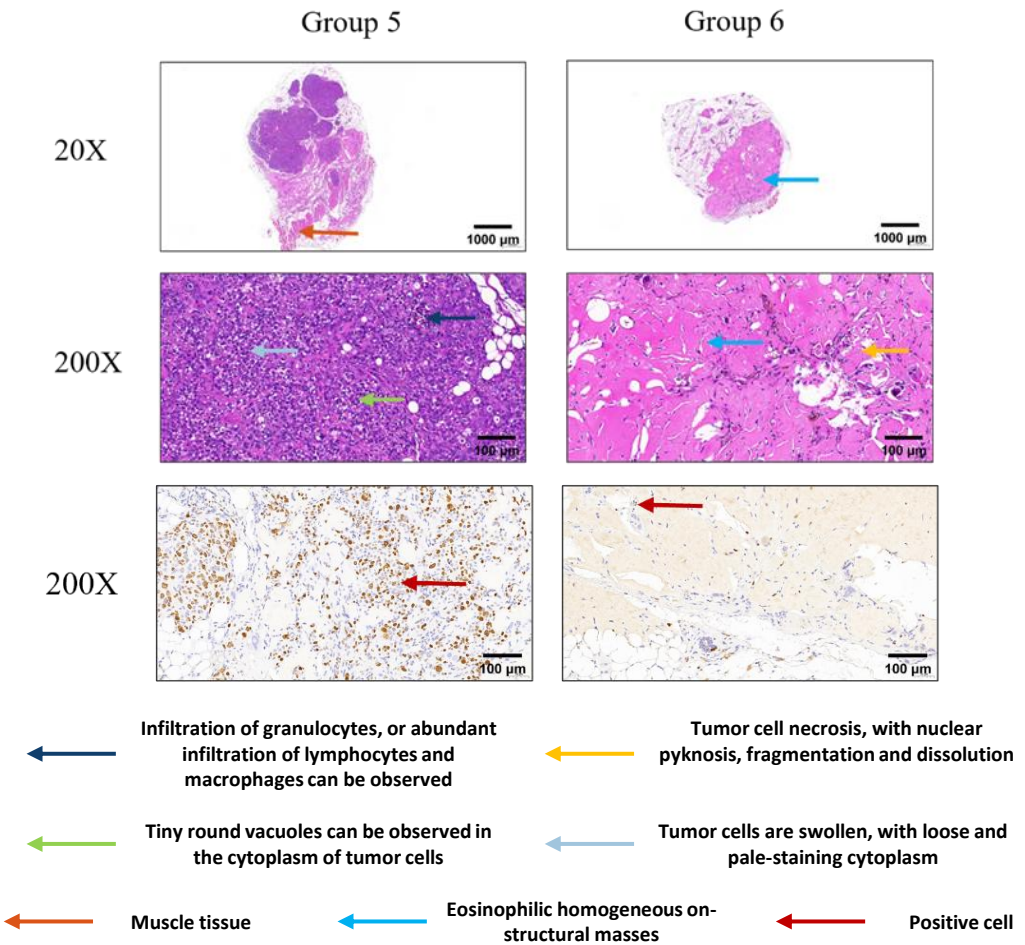
While PB-223 ADC Reduced Tumor Growth at the 6 mg/kg Dose, it Killed All Tumor Tissue at the 9 mg/kg Dose

Ki-67 H-score in Excised Tumors at Day 45



- Group 5 exhibited relapse of tumor growth at day 45, with residual viable tumor cells detected by immunohistochemistry and Ki-67 staining
- Group 6 tumors showed complete necrosis with no viable cells, as confirmed by IHC and Ki-67 staining, along with immune cell infiltration (macrophages, lymphocytes, granulocytes), indicating full tumor tissue eradication at the 9 mg/kg dose

IHC Staining in Excised Tumors at Day 45



PB-223 ADC completely eradicated tumor tissue at the 9 mg/kg dose, leaving behind no viable tumor cells

In Vivo PDX Model of PB-223 ADC

Anti-tumor Activity in a Moderate Expressing PDX Model (H Score = 180)

Ovarian PDX Model Summary

- Precision Biologics conducted additional *in vivo* studies in a Patient-Derived Xenograft ("PDX") ovarian cancer model to evaluate the anti-tumor efficacy and of PB-223 ADC
- The ovarian PDX model testing was conducted in mice where the target was moderately expressed on the tumor (H-score=180)
- PB-223 ADC demonstrated statistically significant anti-tumor activity at both the 9 mg/kg and 3 mg/kg dose levels versus the control group
- The data strongly supports:
  - Deep and durable tumor regression where the target is highly expressed, including near-complete tumor killing at the highest dose levels
  - Target-specific activity
  - A clean safety profile
- PB-223 ADC maintained a favorable safety and tolerability profile, with no significant body weight loss observed in any of the treatment groups after dosing, indicating that the tumor-bearing mice tolerated the therapeutic doses of PB-223 ADC well
- Additional PDX model data across five other tissue types, including pancreatic cancer and colorectal cancer, will be available in Summer 2026

Key Takeaways

High Potency & Efficacy

PB-223 ADC demonstrated robust, durable anti-tumor activity, with near-complete responses and no recurrence at the 9 mg/kg dose, confirming strong target-mediated efficacy

Dose-Dependent Response

While PB-223 ADC showed statistically significant anti-tumor activity at the 3 mg/kg dose, the 9 mg/kg dose demonstrated near-complete tumor killing, showing that the anti-tumor effect was correlated to the PB-223 ADC dose

Clean Safety Profile

All mice tolerated PB-223 ADC, with no meaningful reductions in body weight across the dosing groups

PB-223 ADC demonstrated strong dose-dependent efficacy in the ovarian PDX model, with exceptional anti-tumor activity in tumors where the target is present, and a clean safety profile across dosing groups

PB-223 ADC demonstrated significant dose-dependent anti-tumor activity in the ovarian PDX model while maintaining a favorable safety and tolerability profile

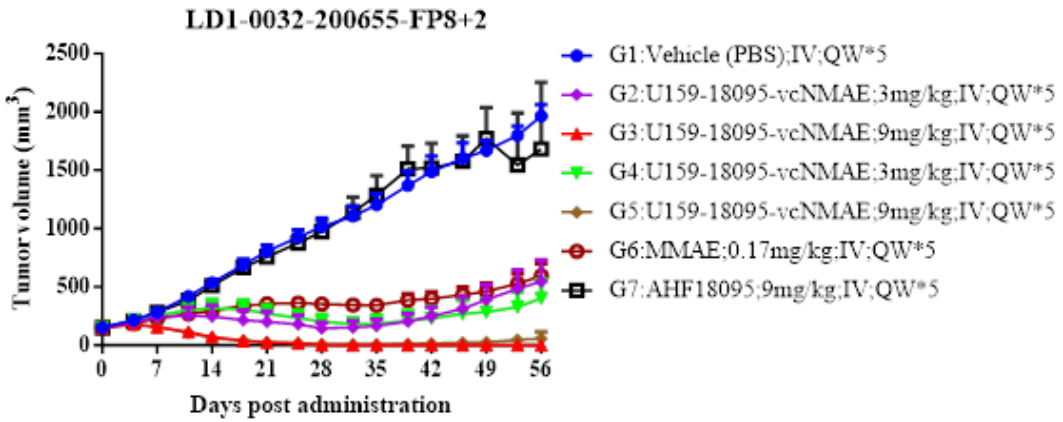
In Vivo Efficacy of PB-223 ADC: Ovarian PDX Model

Robust Antitumor Activity Observed Across PB-223 ADC Treatment Groups in the Ovarian PDX Model

Results Summary & Discussion

- Strong efficacy observed for PB-223 ADC ("U159-18095-vcNMAE") at both dose levels (3 mg/kg and 9 mg/kg), with substantial tumor suppression (T/C ≤ ~28%), versus the control group which exhibited signification tumor growth over the testing period
- Statistically significant antitumor activity demonstrated for all 3 mg/kg and 9 mg/kg dose groups versus control
- Near-complete tumor killing achieved at the 9 mg/kg dose, with RTV and T/C approaching zero
- Clear dose-dependent response observed for PB-223 ADC, with higher doses driving greater antitumor effect as measured by tumor volume and tumor weight

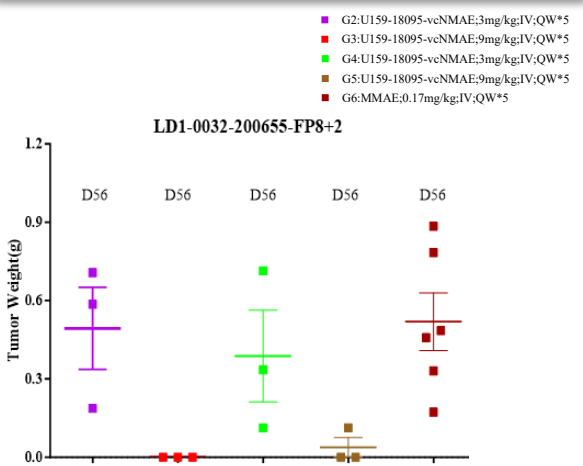
Tumor Growth by Treatment Group



Summary of Efficacy Endpoints

Group	Treatment	Mean Tumor volume (mm³)(1) (Day 0)	Mean Tumor volume (mm³)(1) (Day 39)	RTV (Day 39)	T/C (%) (Day 39)	TGI (%) (Day 39)
1	Vehicle	151.21±8.65	1369.34±118.98	9.06	-	-
2	U159-18095-vcNMAE (3 mg/kg)	151.64±6.11	203.08±69.09	1.34	14.79	95.78
3	U159-18095-vcNMAE (9 mg/kg)	151.38±5.90	0.00±0.00	0.00	0.00	200.00
4	U159-18095-vcNMAE (3 mg/kg)	151.37±13.22	210.43±89.47	1.39	15.35	95.15
5	U159-18095-vcNMAE (9 mg/kg)	150.97±12.22	10.67±10.67	0.07	0.78	192.93
6	MMAE	151.45±7.73	385.80±57.52	2.55	28.13	80.76
7	AHF18095 (Ab Control)	150.70±5.45	1511.97±195.21	10.03	110.79	-11.75

The Tumor Weight by Treatment Group



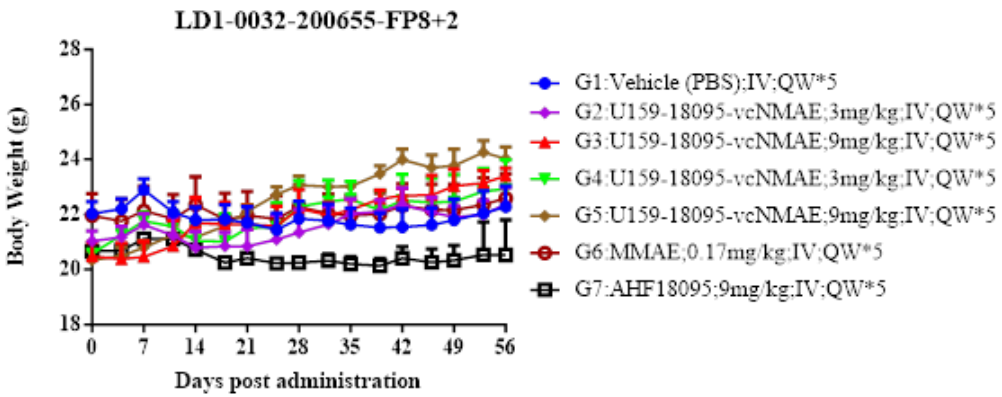
PB-223 ADC demonstrated dose-dependent tumor volume and weight reductions in the ovarian PDX model

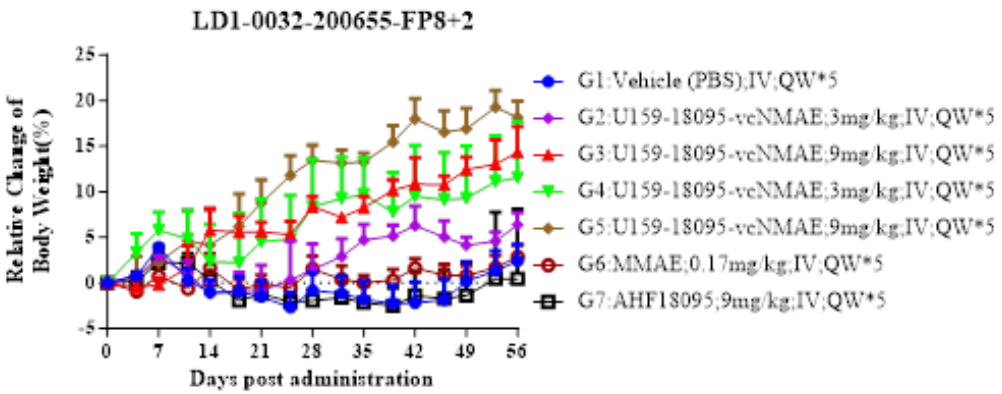
(1) Values displayed as Mean ± SE. Note: "AHF18095" denotes "Unconjugated Antibody Control".

In Vivo Safety of PB-223 ADC: Ovarian PDX Model

Clean Safety and Tolerability Profile in the Ovarian PDX Model

Ovarian Model – Body Weight and Body Weight Change Across Treatment Groups





	Body Weight (g)[1]		
Treatment Group	**Day 0**	**Day 39**	**Average Body Weight Change (%) (Day 29)**
Vehicle	22.03±0.44	21.53±0.53	-2.24±1.95
U159-18095-vcNMAE (3 mg/kg)	21.03±0.38	22.11±0.43	5.16±1.18
U159-18095-vcNMAE (9 mg/kg)	20.49±0.50	22.57±0.32	10.19±1.12
U159-18095-vcNMAE (3 mg/kg)	20.58±0.19	22.16±0.72	7.75±4.39
U159-18095-vcNMAE (9 mg/kg)	20.34±0.34	23.48±0.30	15.46±1.77
MMAE	21.97±0.80	22.02±0.76	0.30±1.19
AHF18095 (Ab Control)	20.66±0.16	20.14±0.26	-2.47±1.93

PB-223 ADC demonstrated a clean safety profile with no observable systemic toxicity in the ovarian PDX model, with minimal body weight reductions across all treatment groups and dose levels

(1) Values displayed as Mean ± SE. Note: "AHF18095" denotes "Unconjugated Antibody Control".

Summary of PB-223 and PB-223 ADC

PB-223-ADC Has Demonstrated Exceptional Anti-tumor Efficacy and Non-toxicity in Both PDX and CDX Testing

Key Takeaways	▪ PB-223 ADC selectively **targets** cancer cells while **sparing** healthy tissue, delivering strong anticancer activity when the target is present with minimal off-target binding ▪ PB-223 has demonstrates robust antitumor efficacy in moderate and high expressing models ▪ Underlying its success are important distinctions that PB-223 ADC has from other ADCs: **1. Antibody Source** – The antibody for PB-223-ADC was developed from human cancer tissue directly removed from patients during surgery – The lead antibody was selected for its specificity to the tumor antigen and immunogencity in patients as compared to cell lines **2. Greater Tumor Target Relevance** – Antigen proteins on the surface of cancer cell lines growing in an incubator may alter from the original proteins expressed on human cancers growing in the body – The difference in the tumor microenvironment allows antibodies developed from actual tumor tissue to have greater relevance in targeting human cancers growing in patients and higher confidence in delivering clinical outcomes – The truncated glycosylation that PB-223 ADC targets is found only on epithelial cancer not healthy tissues
Preclinical Results	**1. Better Safety Profile** – Increase in body weight following dosing of therapy – No change in hematology markers or observed hematological toxicities – No binding observed in healthy organs or adjacent healthy tissue **2. Improved Potency** – High tumor specificity allows the antibody to effectively deliver the payload into the tumor, and avoid non-tumor targeted delivery