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Interim Results of a Phase 1 Study of SGN-PDL1V (PF-08046054) in Patients with PDL1-Expressing Solid Tumors

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DECLARATION OF INTERESTS

Marc Oliva, MD, PhD

Leadership position: None

Consultant/Advisory role for: Merck, MSD, Beigene

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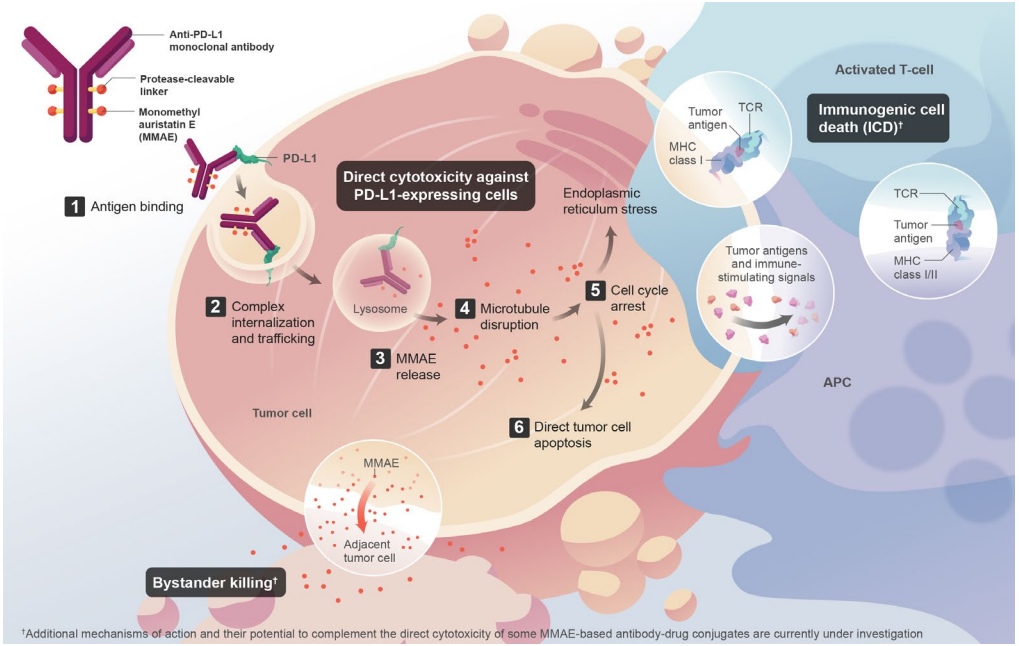
Patent/Royalty for: None

PDL1V* (PF-08046054), a Vedotin ADC Targeting PD-L1

Drives Antitumor Activity Through Direct Cytotoxicity, Bystander Killing & Immunogenic Cell Death[1]



PDL1V Unique Characteristics

- Antitumor activity in MMAE-sensitive xenograft models, across a broad range of PD-L1 expression[1]
- PK data suggest low likelihood of CPI activity by PDL1V
- Induction of ICD suggests potential for enhancement of T cell response by PD-1 checkpoint inhibition
- Minimal to no cytotoxicity to PD-L1+ T-cells or APCs in preclinical studies

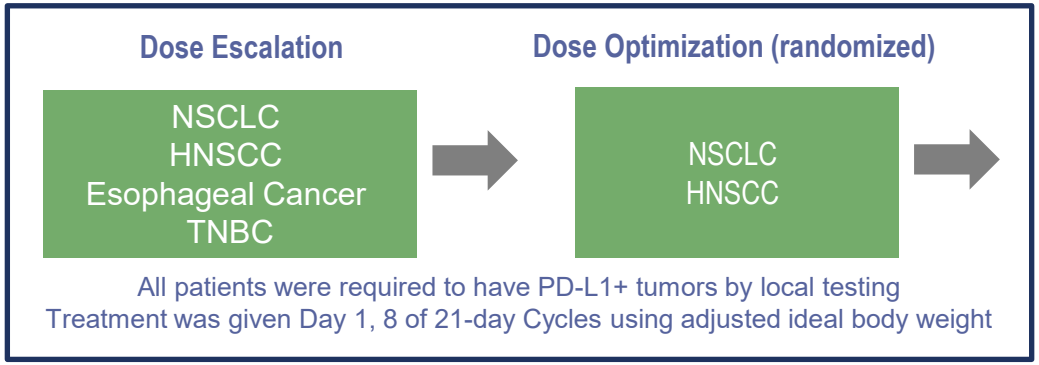
PDL1V is an investigational agent, and its safety and efficacy have not been established.

* Previously SGN-PDL1V; **APC:** antigen-presenting cell; **CPI:** check point inhibitor; **ICD**: immunogenic cell death; **MHC:** major histocompatibility complex; **MMAE**: monomethyl auristatin E; **PD-1:** programmed cell death protein 1; **PD-L1**: programmed cell death ligand 1; **PK**: pharmacokinetic; **TCR:** T-cell receptor.

1. Kwan et al. *JITC* 2021;9(Supp 2):A818.

PDL1V Phase 1 Study Schema

NCT05208762



Primary Objectives

- Characterize safety profile and identify MTD / RP2D as monotherapy and in combination with pembrolizumab

Key Secondary Objectives

- Assess the antitumor activity as monotherapy and in combination with pembrolizumab
- Assess the PK and immunogenicity as monotherapy and in combination with pembrolizumab

Dose Expansion

- 2L HNSCC
- 2L/3L NSCLC
- 1L HNSCC (safety run-in-cohort included) Pembrolizumab combination*
- 1L NSCLC Pembrolizumab combination*

* PD-L1 ≥1 expression by historical testing required for cohort eligibility.

1L/2L/3L: first, second, or third line of treatment; **HNSCC:** head and neck squamous cell carcinoma; **MTD**: maximum tolerated dose; **NSCLC:** non-small cell lung cancer; **PD-L1:** programmed cell death ligand 1; **PK**: pharmacokinetic; **RP2D:** recommend phase 2 dose; **TNBC:** triple-negative breast cancer.

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Baseline Characteristics

Patients Were Heavily Pre-Treated Including Prior CPI (Median 3 Prior Lines of Systemic Therapy)

Characteristics	All Patients Enrolled in Dose Escalation/Optimization Dose Levels*						
	0.5 mg/kg (N=2)	0.75† mg/kg (N=4)	1.0 mg/kg (N=6)	1.25 mg/kg (N=33)	1.5 mg/kg (N=37)	1.75 mg/kg (N=12)	Total (N=94)
Age (years), median (min, max)	67.0 (66, 68)	50.0 (36, 57)	57.5 (39, 61)	63.0 (34, 72)	60.0 (24, 78)	56.5 (31, 70)	59.5 (24, 78)
Sex, n (%)							
Male	1 (50.0)	1 (25.0)	3 (50.0)	16 (48.5)	27 (73.0)	9 (75.0)	57 (60.6)
Female	1 (50.0)	3 (75.0)	3 (50.0)	17 (51.5)	10 (27.0)	3 (25.0)	37 (39.4)
ECOG performance status, n (%)							
0	0	1 (25.0)	2 (33.3)	7 (21.2)	10 (27.0)	4 (33.3)	24 (25.5)
1	2 (100)	3 (75.0)	4 (66.7)	26 (78.8)	27 (73.0)	8 (66.7)	70 (74.5)
Disease diagnosis, n (%)							
Head and Neck Squamous Cell Cancer	1 (50.0)	1 (25.0)	4 (66.7)	18 (54.5)	19 (51.4)	7 (58.3)	50 (53.2)
Non-Small Cell Lung Cancer	1 (50.0)	1 (25.0)	1 (16.7)	14 (42.4)	15 (40.5)	3 (25.0)	35 (37.2)
Triple Negative Breast Cancer	0	2 (50.0)	1 (16.7)	1 (3.0)	2 (5.4)	2 (16.7)	8 (8.5)
Esophageal Cancer	0	0	0	0	1 (2.7)	0	1 (1.1)
# prior lines of systemic treatment in recurrent or metastatic settings, median (min, max)	2.5 (2, 3)	1.0 (1, 4)	2.0 (1, 3)	3.0 (1, 6)	3.0 (1, 7)	3.0 (1, 6)	3.0 (1, 7)
Prior treatment in any setting							
CPIs, n (%)	2 (100)	2 (50.0)	4 (66.7)	32 (97.0)	33 (89.2)	11 (91.7)	84 (89.4)
Taxanes, n (%)	1 (50.0)	4 (100)	5 (83.3)	22 (66.7)	28 (75.7)	7 (58.3)	67 (71.3)

* Day 1, 8 of 21-day Cycles using adjusted ideal body weight.
† Two patients at 0.75 mg/kg switched to 1.5 mg/kg from Cycle 5 onwards in dose escalation cohorts.
CPI: check point inhibitor; **ECOG:** Eastern Cooperative Oncology Group; **max:** maximum; **min**: minimum; **PD-L1:** programmed death ligand 1.

Data cutoff: 01JUL2024. Data snapshot: 26JUL2024.

PDL1V Has a Manageable Safety Profile

Adverse Events	Dose Levels*						
	0.5 mg/kg N=2	0.75† mg/kg N=4	1.0 mg/kg N=6	1.25 mg/kg N=33	1.5 mg/kg N=37	1.75 mg/kg N=12	Total N=94
TEAEs, n (%)	2 (100)	4 (100)	6 (100)	33 (100)	**37 (100)**	12 (100)	94 (100)
Treatment-related TEAEs, n (%)	2 (100)	2 (50.0)	4 (66.7)	20 (60.6)	**29 (78.4)**	10 (83.3)	67 (71.3)
≥Grade 3 treatment-related TEAEs, n (%)	1 (50.0)	1 (25.0)	0	2 (6.1)	**12 (32.4)**	6 (50.0)	22 (23.4)
Serious treatment-related TEAEs, n (%)	1 (50.0)	0	1 (16.7)	3 (9.1)	**4 (10.8)**	4 (33.3)	13 (13.8)
Treatment discontinue due to treatment-related TEAEs, n (%)	0	0	0	1 (3.0)	**3 (8.1)**	2 (16.7)	6 (6.4)
TEAEs resulting in dose modification^ n (%)	2 (100)	2 (50.0)	1 (16.7)	17 (51.5)	**23 (62.2)**	7 (58.3)	52 (55.3)
Dose reduction	0	2 (50.0)	0	2 (6.1)	**9 (24.3)**	6 (50.0)	19 (20.2)
Dose delay	1 (50.0)	2 (50.0)	0	8 (24.2)	**14 (37.8)**	7 (58.3)	32 (34.0)
Dose elimination	1 (50.0)	1 (25.0)	0	7 (21.2)	**11 (29.7)**	1 (8.3)	21 (22.3)

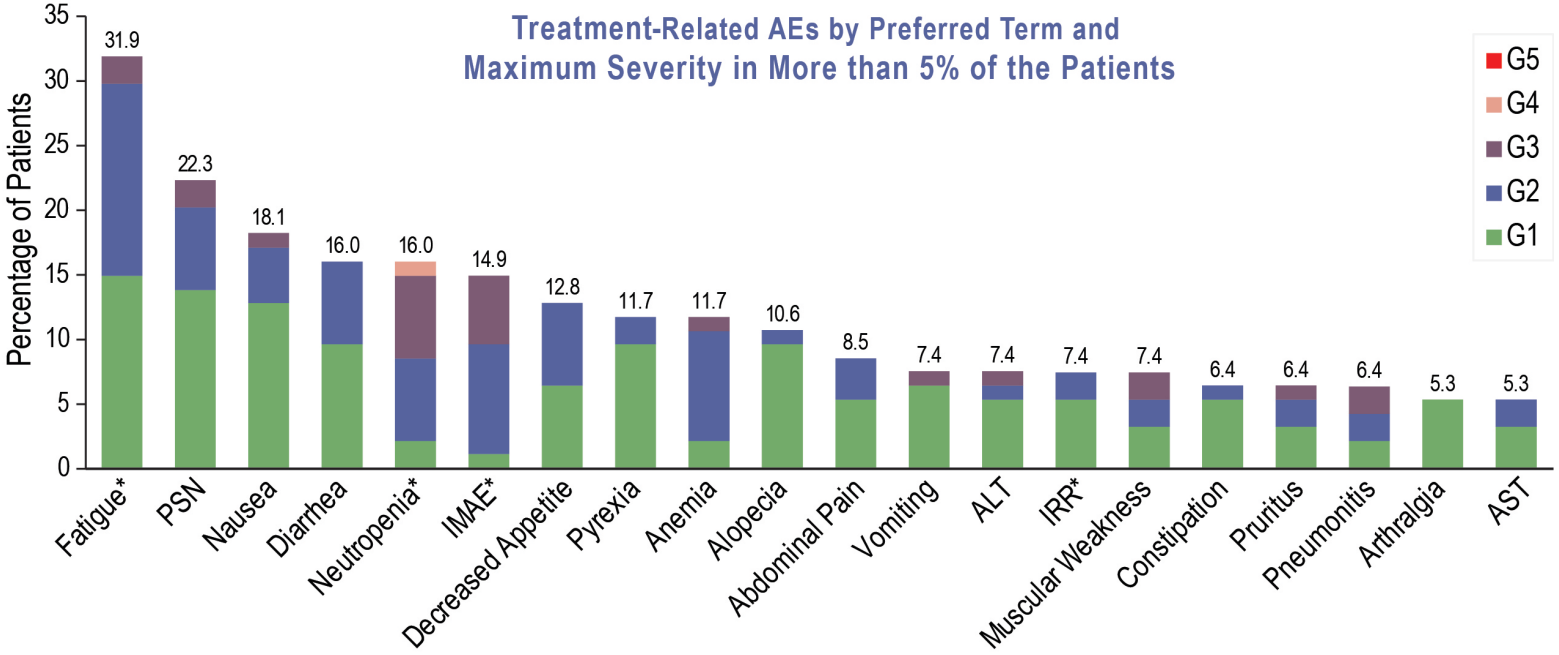
No DLTs or treatment-related deaths were observed

1.75 mg/kg AiBW 2Q3W* dose was associated with higher incidence of dose delays and reductions

* Day 1, 8 of 21-day Cycles using adjusted ideal body weight.
† Two patients at 0.75 mg/kg switched to 1.5 mg/kg from Cycle 5 onwards in dose escalation cohorts.
^ Dose interruption and treatment discontinuation not shown.
2Q3W: day 1 and day 8 of a 21-day cycle; **AE**: adverse event; **AiBW**: adjusted ideal body weight; **DLT**: dose-limiting toxicity; **TEAE**: treatment-emergent adverse event.

Data cutoff: 01JUL2024. Data snapshot: 26JUL2024.

Majority of Treatment-Related AEs Were Low-Grade Across All Dose Levels



All-grade treatment-emergent AEs by preferred term in more than 20% of patients included fatigue* (46.8%), diarrhea (27.7%), nausea (27.7%), PSN (25.5%), anemia (24.5%) and decreased appetite (23.4%).

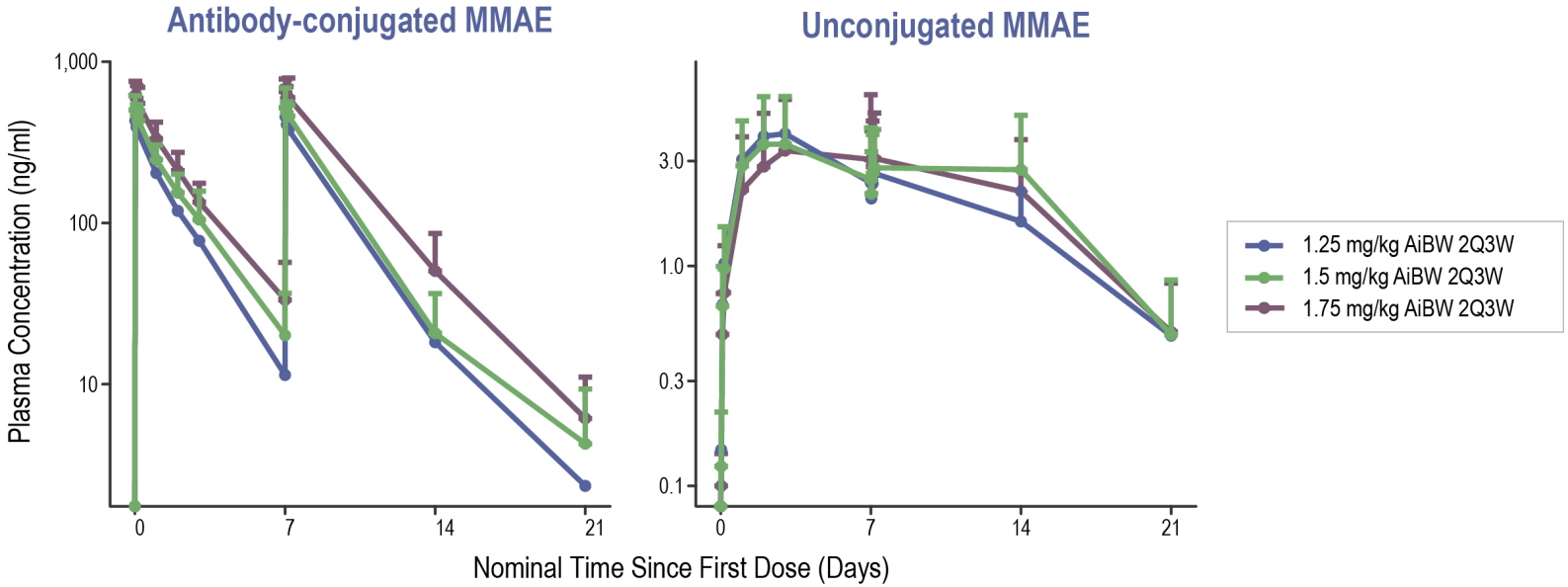
Treatment-related G3 IMAEs were muscular weakness (2.1%), peripheral motor neuropathy, pneumonitis, pruritus, and hyponatremia (1.1% each).

Data cutoff: 01JUL2024. Data snapshot: 26JUL2024.

* Composite of related preferred terms; IMAE includes some of the IRR and pneumonitis events that are also separately reported in the bar graph above.

AE: adverse event; **ALT:** alanine aminotransferase increase; **AST:** aspartate aminotransferase increase; **G:** grade per CTCAE v5.0; **IMAE:** immune mediated adverse events (investigator-assessed); **IRR:** infusion related reaction; **PSN:** peripheral sensory neuropathy.

Linear PK at Clinically Active Dose Levels with Concentrations Comparable to Other Vedotin ADCs

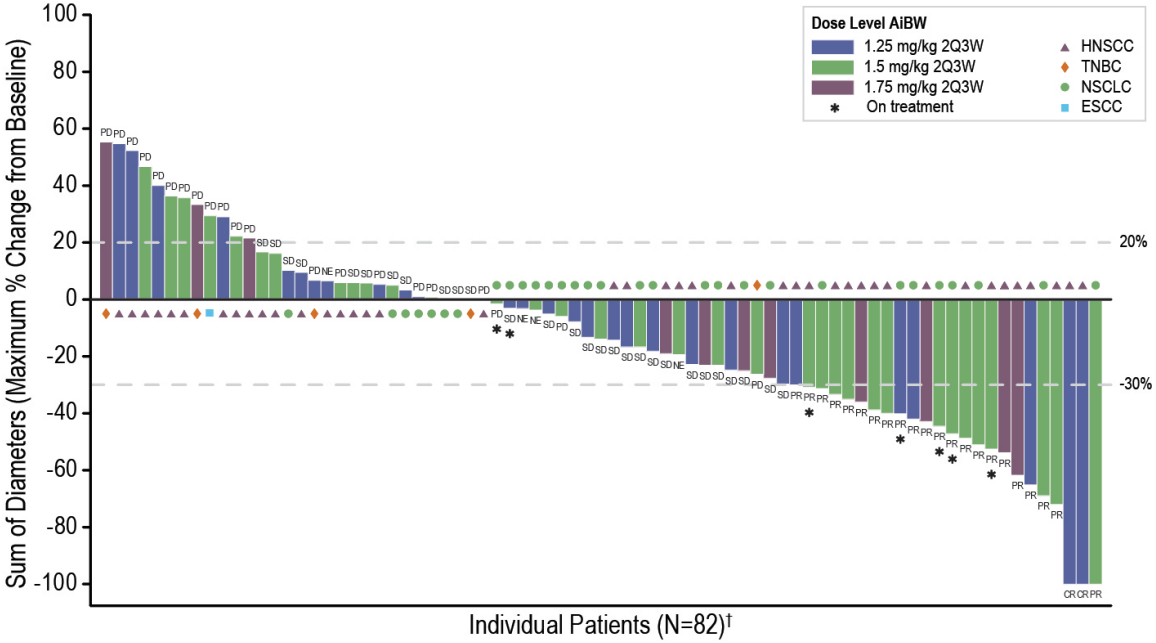


The half-life of PDL1V (active analyte: acMMAE) was approximately 3.8 days with negligible accumulation following 2Q3W regimen
Plasma concentrations of antibody-conjugated MMAE and unconjugated MMAE were approximately dose proportional at active dose levels

Data shown are average concentrations with one-sided standard deviations.

2Q3W: day 1 and day 8 of a 21-day cycle; **acMMAE:** antibody-conjugated monomethyl auristatin E; **ADC:** antibody-drug conjugate; **AiBW:** adjusted ideal body weight; **MMAE:** monomethyl auristatin E; **PD-L1:** programmed death ligand 1; **PK**: pharmacokinetics.

PDL1V Demonstrates Antitumor Activity in PD-L1+ Tumors



	Dose Levels*		
	1.25 mg/kg N=33	1.5 mg/kg N=37	1.75 mg/kg N=12
Confirmed Response per RECIST v.1.1 Assessed by Investigator (%)			
ORR	**12.1**	**18.9**	**25.0**
DCR	63.6	62.2	66.7
Best Overall Response per RECIST v.1.1 Assessed by Investigator (%)			
CR	6.1	0	0
PR	6.1	18.9	25.0
SD	51.5	43.2	41.7
PD	21.2	27.0	33.3
NE/NA	15.2	10.8	0

* Day 1, 8 of 21-day Cycles using adjusted ideal body weight

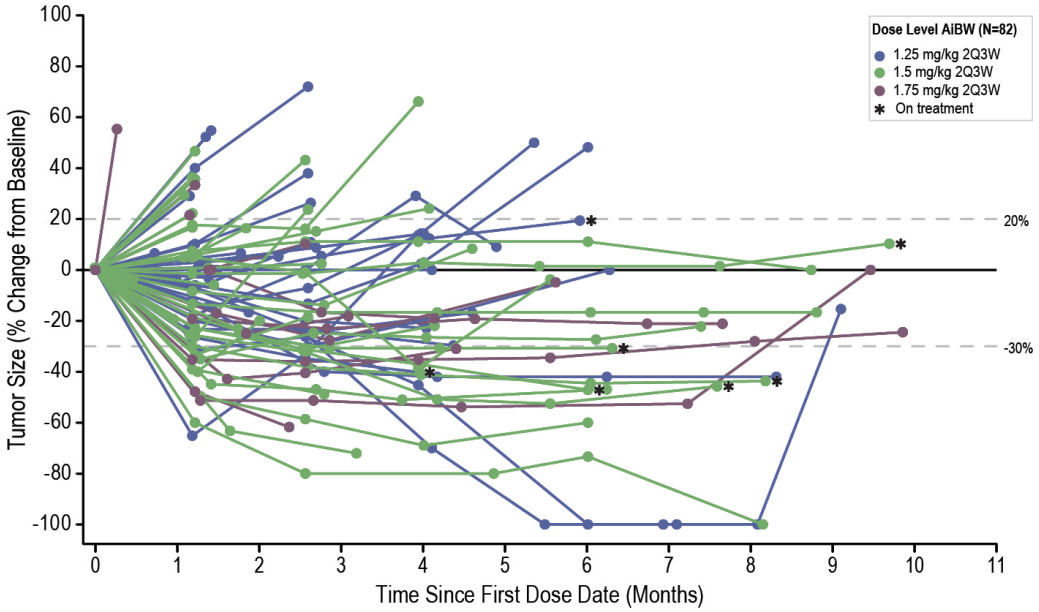
† 5 patients are not displayed due to lack of tumor assessment data

Data cutoff: 01JUL2024. Data snapshot: 26JUL2024.

2Q3W: day 1 and day 8 of a 21-day cycle; **AiBW:** adjusted ideal body weight; **CR**: complete response; **DCR**: disease control rate; **ESCC**: esophageal squamous cell carcinoma; **HNSCC:** head and neck squamous cell carcinoma; **NE/NA**: not evaluable/not available; **NSCLC:** non-small cell lung cancer; **ORR**: objective response rate; **PD:** progressive disease; **PD-L1:** programmed cell death ligand 1; **PR:** partial response; **RECIST:** Response Evaluation Criteria in Solid Tumours; **SD:** stable disease; **TNBC:** triple-negative breast cancer

Durable Clinical Responses with a mDOR of 7.9 Months (95% CI: 4.8, 8.2)*

Responses Seen Across PD-L1 Expression Levels



Number of Patients with Confirmed Response by PD-L1 Expression Per Local Testing			
NSCLC (TPS)	**1 to 49 (N=14)**	**≥50 (N=17)**	**Unknown (N=1)**
PRs	3	3	1
HNSCC (CPS)	**1 to 19 (N=18)**	**≥20 (N=21)**	**Unknown (N=5)**
CRs/PRs	3	2	2

Data cutoff: 01JUL2024. Data snapshot: 26JUL2024.

* At 1.25 mg/kg and higher dose levels; Day 1, 8 of 21-day Cycles using adjusted ideal body weight; median follow-up for overall survival (OS) was 9.4 months (95% CI: 8.1, 10.2).

2Q3W: day 1 and day 8 of a 21-day cycle; **AiBW:** adjusted ideal body weight; **CI**: confidence interval; **CPS**: combined positive score; **CR:** complete response; **HNSCC:** head and neck squamous cell carcinoma; **mDOR:** median duration of confirmed response; **NSCLC:** non-small cell lung cancer; **PD-L1:** programmed cell death ligand 1; **PR:** partial response; **TPS**: tumor proportion score.

PDL1V Antitumor Activity in NSCLC and HNSCC

At 1.25 mg/kg and Higher Dose Levels*

	Dose Levels*					
	NSCLC			HNSCC		
	1.25 mg/kg N=14	1.5 mg/kg N=15	1.75 mg/kg N=3	1.25 mg/kg N=18	1.5 mg/kg N=19	1.75 mg/kg N=7
Confirmed Response per RECIST v.1.1 Assessed by Investigator (%)						
ORR	**14.3**	**33.3**	**0**	**11.1**	**10.5**	**42.9**
DCR	78.6	66.7	100	55.6	63.2	71.4
Best Overall Response per RECIST v.1.1 Assessed by Investigator (%)						
CR	0	0	0	11.1	0	0
PR	14.3	33.3	0	0	10.5	42.9
SD	64.3	33.3	100	44.4	52.6	28.6
PD	7.1	20.0	0	27.8	26.3	28.6
NE/NA	14.3	13.3	0	16.7	10.5	0

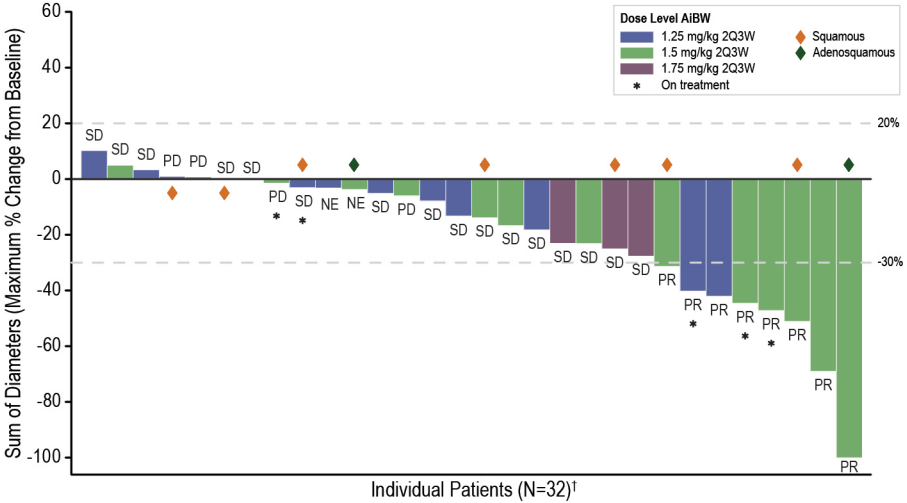
Data cutoff: 01JUL2024. Data snapshot: 26JUL2024.

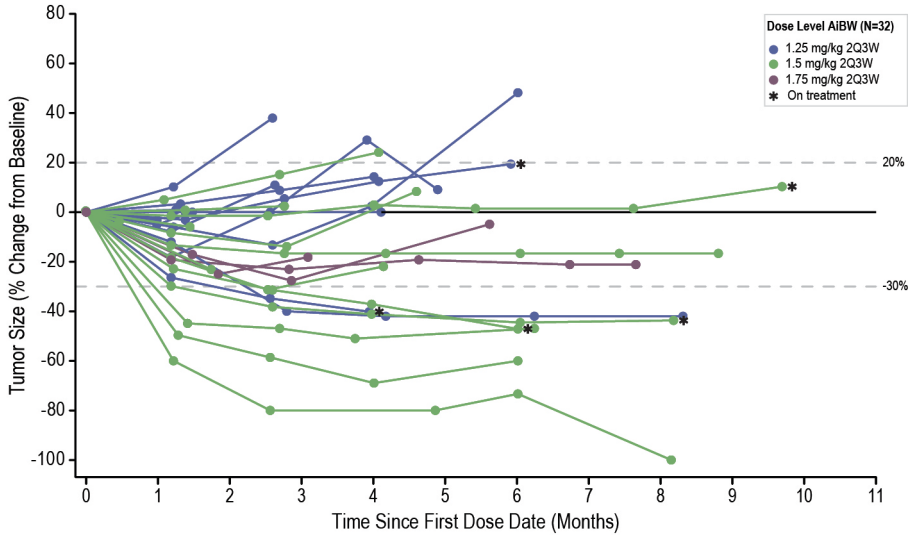
* Day 1, 8 of 21-day Cycles using adjusted ideal body weight.

CR: complete response; **DCR:** disease control rate; **HNSCC**: head and neck squamous cell carcinoma; **NE/NA**: not evaluable/not available; **NSCLC**: non-small cell lung cancer; **ORR:** objective response rate; **PD:** progressive disease; **PR**: partial response; **RECIST:** Response Evaluation Criteria in Solid Tumours; **SD:** stable disease.

Encouraging PDL1V Antitumor Activity in PD-L1+ NSCLC

Including Squamous and Non-Squamous Histologies*





cORR, Active Dose Levels^ (N= 32)	21.9%
Patients in 1.25 mg/kg (N=14)	14.3%
Patients in 1.5 mg/kg (N=15)	**33.3%**
mDOR months (95% CI)	5.6 (4.8, -)

Recommended Dose for Expansion

Data cutoff: 01JUL2024. Data snapshot: 26JUL2024.

* Subtypes: 68.6% adenocarcinomas, 20% squamous, 5.7% adenosquamous, 5.7% others.
† 2 subjects are not displayed due to lack of tumor assessment data.
^ Day 1, 8 of 21-day cycles using adjusted ideal body weight.
2Q3W: day 1 and day 8 of a 21-day cycle; **AiBW:** adjusted ideal body weight; **CI**: confidence interval; **cORR**: confirmed objective response rate; **CR**: complete response; **mDOR**: median duration of confirmed response; **mPFS**: median progression-free survival, **NSCLC**: non-small cell lung cancer; **NE**: not evaluable; **PD**: progressive disease; **PD-L1**: programmed cell death ligand 1; **PR:** partial response; **SD**: stable disease.

Marc Oliva, MD, PhD

Conclusions

Safety

- PDL1V was well-tolerated with a manageable safety profile
- No DLTs, unexpected adverse events or treatment-related deaths were observed

Efficacy

- Encouraging PDL1V antitumor activity was seen in PD-L1 positive tumors with high unmet need
- Clinically meaningful and durable responses observed in patients with heavily pretreated NSCLC and HNSCC

Next steps

- Based on favorable safety profile and antitumor activity, PDL1V monotherapy and pembrolizumab combination cohorts in NSCLC and HNSCC are actively enrolling

DLT: dose-limiting toxicity; **HNSCC**: head and neck squamous cell carcinoma; **NSCLC**: non-small cell lung cancer; **PD-L1**: programmed cell death ligand 1.

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Oral Presentation Slides

Plain Language Summary

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