# Conditionally Active Biologics: Transforming Cancer Therapy

**Corporate Presentation** 

November 2024



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# **BioAtla<sup>©</sup> Is A Clinical Stage Company Focused on Transforming Cancer Therapy**

with Conditionally Active Biologics (CABs)





#### **Leadership Team**



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Richard Waldron, M.B.A. Chief Financial Officer



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### Selective and Targeted CAB Technology Widens Therapeutic Window

Thus has the potential to enhance clinical outcomes in multiple tumor types



BioAtla discovered that acidic pH at the cancer cell surface unveils binding sites that are shielded at normal pH of healthy cells



BioAtla invented CAB technology, creating antibodies that bind **only** to these unveiled sites on cancer cells



CAB binding region is not masked or caged and thus different from prodrugs that require irreversible enzymatic cleavage to become activated



CAB antibodies have the potential for increased efficacy with improved safety relative to traditional antibodies



Chang, H.W., Frey, G., Liu, H., Xing, C., Steinman, L, Boyle, B.J., & Short, J.M. (2021) PNAS 118(9): 1-10, Suppl. 1-19.



#### Broad Applicability of BioAtla's CAB Platform Across Several Antibody Types

ADCs Targets: ROR2, AXL Widely expressed in a variety of tumor types, ROR2 and AXL overexpression correlates with poor prognosis, metastasis, and drug resistance to PD-1 and EGFR therapies



I/O Antibodies

Target: CTLA-4

CTLA-4 blockade activates effector T cells, thereby enhancing antitumor immunity



#### **Bispecific TCE**

Target: EpCAM & CD3

Bispecific antibodies bridge cancer cells and cytotoxic T lymphocytes, activating T cells and promoting cancer cell lysis





#### Focused Pipeline with Broad Applicability of Differentiated CAB Assets Designed to Deliver Near-term value

	CAB Program	Target	Indications	IND Enabling Pre-Clinical	Phase 1 Clinical	Phase 2 Clinical
CAR-ADCo	Mecbotamab Vedotin	AXL	NSCLC UPS			
CAD-ADCS	Ozuriftamab Vedotin	ROR2	SCCHN			
CAB-I/O	Evalstotug	CTLA-4	Melanoma			
CAB- Bispecific TCE	BA3182	EpCAM x CD3	Adenocarcinomas			
Next Gen CAB-ADC	BA3361	Nectin-4	Multiple tumor types			





Ozuriftamab Vedotin (CAB-ROR2-ADC): Squamous Cell Carcinoma of the Head and Neck (SCCHN)

#### **Potential Market Opportunity in SCCHN**



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<sup>1</sup>Clarivate, Disease Landscape and Forecast: SCCHN (2022). www.cancer.net; <sup>2</sup>Argiris A, et al.(2017) Evidence-Based Treatment Options in Recurrent and/or Metastatic Squamous Cell Carcinoma of the Head and Neck. *Front. Oncol.* 7:72; <sup>3</sup>Future Oncology, Jan. 2019. Vol. 15, No. 8; <sup>4</sup>Ketruda USPI accessed 2024; <sup>5</sup>Erbitux USPI accessed 2024.

SCCHN, squamous cell carcinoma of the head and neck; 1L, first line; 2L, second line; 2L+, second line or greater; ICIs – Immune checkpoint inhibitors.

# Phase 2 Ozuriftamab Vedotin in SCCHN: Demographics

#### Median of 3 prior lines of treatment

Patients with PD-1 treatment refractory SCCHN were treated with ozuriftamab vedotin 1.8 mg/kg 2Q3W or Q2W

	Q2W (N=12)	2Q3W (N=20)*	Total (N=32)*
Age, y, mean (range)	62.4 (47-84)	65.7 (54-79)	64.4 (47-84)
ECOG Status, n (%)			
0	5 (42%)	8 (40%)	13 (41%)
1	7 (58%)	12 (60%)	19 (59%)
# of prior systemic therapies, n (%)			
1	0	4 (20)	4 (13)
2	6 (50)	5 (25)	11 (34)
3	3 (25)	4 (20)	7 (22)
≥4	3 (25)	7 (35)	10 (31)

\* One patient from Phase 1 not included



# Ozuriftamab Vedotin in SCCHN Continues to Demonstrate Clinical Responses and Median Overall Survival of ~9 months in a Heavily Pretreated Population

n=29 of 33\*\*; 1.8 mg/kg Q2W and 2Q3W; Median of 3 prior lines of tx



#### \*\*Evaluable patients defined as patients that had at least 1 scan after treatment with study drug

- Prior to first scan:
- 2 patients had clinical progression
- 2 patients withdrew consent



Data Cut Date: Live Database as of 15Oct

Confidential

### Ozuriftamab Vedotin Monotherapy Has Promising Clinical Profile in 2L+ SCCHN

Cross trial comparisons between 3 vs 1 – 2 median prior lines of therapy

	Ozuriftamab vedotin monotherapy (all PD-1 failures)	IC monotherapy (Checkmate-141) <sup>1,2</sup>	IC monotherapy (Keynote-040) <sup>3</sup>	Cetuximab monotherapy <sup>5,6</sup>
Median prior lines of therapy	3	2	1	1
ORR – confirmed (%)	21%*	5.8%	7.2%	13%
DCR	86%	41%	Not available	46%
Median PFS (mos)	2.7	2.3	2.3	2.3
Median OS (mos)	~8.8 (ongoing)	5.1	6.9	5.9

\*ORR = 38% (confirmed + unconfirmed responses)

#### 2L+ monotherapy market for ozuriftamab vedotin represents a peak \$1B+ worldwide revenue opportunity



<sup>1</sup>N Engl J Med 2016;375:1856-1867. <sup>2</sup> Journal of Clinical Oncology 2018; 36(15): 1551-1558. <sup>3</sup>Cohen E, et al. (2019) Lancet 393, 156–167. <sup>4</sup>British Journal of Cancer (2018) 119:153–159; https://doi.org/10.1038/s41416-018-0131-9. <sup>5</sup>2008 Jun 15;112(12):2710-9. doi: 10.1002/cncr.23442, <sup>6</sup>Erbitux USPI accessed 2024. IC = Investigators choice (Cetuximab, Methotrexate or Docetaxel)

The ability to interpret and draw conclusions from cross-study comparisons is limited.

#### Ph2 Ozuriftamab Vedotin: Overall Safety Summary of SCCHN patients

#### Median of 3 prior lines of Tx; Generally well-tolerated

	1.8 mg/kg Q2W (N=12)	1.8 mg/kg 2Q3W (N=20) <sup>3</sup>	Total (N=32) <sup>3</sup>
Any Adverse Events (AEs)	11 (92%)	20 (100%)	31 (97%)
Related AEs with CTCAE <sup>1</sup> Grade 3 or 4 <sup>2</sup>	1 (8%)	6 (30%)	7 (22%)
Any related serious AEs <sup>2</sup>	1 (8%)	3 (15%)	4 (13%)
Possibly Related AEs leading to death <sup>2</sup>	0	0	0
Related AEs leading to treatment discontinuation <sup>2</sup>	1 (8%)	1 (5%)	2 (6%)

<sup>1</sup>CTCAE: Common Terminology Criteria for Adverse Events. The NCI Common Terminology Criteria for Adverse Events is a descriptive terminology which is utilized for Adverse Event (AE) reporting. A grading (severity) scale is provided for each AE term. <sup>2</sup>As assessed by the investigator. Missing responses are counted as related.

<sup>3</sup>One patient from Phase 1 not included



#### Phase 2 Ozuriftamab Vedotin Safety Data

#### Most frequent treatment-emergent adverse events irrespective of causality (>15%)

	1.8 mg/kg Q2W (N=12)		1.8 mg/kg 2Q3W (N=20)^		Total (N=32)^	
Preferred Term	All Grades n (%)	Grade 3-4 n (%)	All Grades n (%)	Grade 3-4 n (%)	All Grades n (%)	Grade 3-4 n (%)
Number of subjects with at least one TEAE	11 (92)	8 (67)	20 (100)	14 (70)	31 (97)	22 (69)
Fatigue	8 (67)	0 (0)	11 (55)	1 (5)	19 (59)	1 (3)
Anaemia	6 (50)	2 (16)	5 (25)	1 (5)	11 (34)	3 (9)
Nausea	4 (33)	1 (8)	7 (35)	0 (0)	11 (34)	1 (3)
Constipation	4 (33)	0 (0)	5 (25)	0 (0)	9 (28)	0 (0)
Hyponatraemia	2 (17)	0 (0)	7 (35)	4 (20)	9 (28)	4 (13)
Decreased appetite	2 (17)	0 (0)	6 (30)	1 (5)	8 (25)	1 (3)
Diarrhoea	1 (8)	0 (0)	7 (35)	2 (10)	8 (25)	2 (6)
Blood lactate dehydrogenase increased	3 (25)	0 (0)	4 (20)	0 (0)	7 (22)	0 (0)
Lymphocyte count decreased	1 (8)	0 (0)	6 (30)	4 (20)	7 (22)	4 (13)
Neutropenia*	1 (8)	0 (0)	6 (30)	2 (10)	7 (22)	2 (6)
Neuropathy <sup>¥</sup>	3 (25)	0 (0)	3 (15)	1 (5)	6 (19)	1 (3)
Hypercalcaemia	2 (17)	0 (0)	4 (20)	1 (5)	6 (19)	1 (3)
Weight decreased	2 (17)	0 (0)	4 (20)	1 (5)	6 (19)	1 (3)
White blood cell count decreased	2 (17)	0 (0)	4 (20)	0 (0)	6 (19)	0 (0)

^ One patient from Phase 1 not included

\* Derived from neutropenia, and neutrophil count decreased

<sup>¥</sup> Derived from neuropathy peripheral, peripheral motor neuropathy, and peripheral sensory neuropathy



# FDA Actionable Guidance Received on Pivotal Trial in Second-Line Plus SCCHN

**Ozuriftamab vedotin has Fast Track Designation** 

- Supportive of:
  - At the current dose of 1.8 mg/kg of ozuriftamab vedotin, limited randomized evaluation of the Q2W and 2Q3W dosing schedules
  - Proposed pivotal randomized, controlled trial of ozuriftamab vedotin monotherapy vs investigator's choice (cetuximab, docetaxel, or methotrexate)
  - Dual primary endpoints
    - Overall Response Rate (potential for accelerated approval with DOR)
    - Overall Survival (supports full approval)
  - Patient population: recurrent or metastatic SCCHN with disease progression on or after platinum-based chemotherapy and PD-1 antibody therapy (2L and 3L)



# Phase 3 Study of Ozuriftamab Vedotin in Patients with Previously-treated SCCHN

Ozuriftamab vedotin vs investigator's choice



- Patient population: Previously treated advanced SCCHN (2L and 3L)
- **Prior therapies**: PD-1 inhibitor and platinum chemotherapy
- **N** = ~570 patients (full approval based on OS)
- N = -300 350 (accelerated approval based on ORR)
- **Opportunity:** 1L in combination with PD1



#### **Strategic Paths to Registration**



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\*Interim analysis based on ORR may potentially support accelerated approval and OS results from the same study could potentially verify its clinical benefit to support regular approval. Timelines BioAtla | Overview 18 subject to change based on FDA feedback.



Mecbotamab Vedotin (CAB-AXL-ADC) in Non-Small Cell Lung Cancer (NSCLC)

#### Potential Market Opportunity In Metastatic NSCLC with mKRAS Variants



<sup>1</sup>https://www.lung.org/lung-health-diseases/lung-disease-lookup/lung-cancer/resource-library/lung-cancer-fact-sheet <sup>2</sup>https://www.cancer.net/cancer-types/lung-cancer-non-small-cell/statistics, <sup>3</sup>3Cancer Genetics Volume 209, Issue 5, May 2016, Pages 195-198, <sup>4</sup>Nat. Rev. Cancer, 19 (2019), pp. 495-509, <sup>5</sup>Clin Cancer Res. 2021 April 15; 27(8): 2209–2215;



#### **Co-expression of mutant KRAS and AXL is Significant and Functionally Linked**

- In lung cancer cells, AXL over-expression is involved in resistance to chemotherapy and targeted therapies and drives epithelial to mesenchymal transition
- Prevalence of AXL expression in KRAS mutant NSCLC is significant, the majority of these tumors exhibit high levels of AXL
  - Upregulation is associated with aggressive tumor characteristics, resistance to therapies, and poor patient outcomes.
- AXL signaling mediates the adaptive resistance to mKRAS inhibitors adagrasib and sotorasib (G12C) in lung cancer (85% AXL positive) (Morimoto et al., Cancer Letters 587 (2024) 216692)
- Potential significant opportunity for mecbotamab vedotin to improve outcomes in the mKRAS population across mKRAS variants



#### AXL Plays a Crucial Role in the Survival of KRAS G12C mutant NSCLC Cells Treated with KRAS G12C Inhibitors

#### **AXL driving resistance to KRAS inhibitors**



p = Phosorylated form of protein



- KRAS inhibition leads to upregulation and activation of AXL expression
  - Autocrine/paracrine of increased GAS6 expression
- AXL inhibition alone does not lead to tumor killing, but potentiates antitumor effects of KRAS inhibition
- These results indicated pivotal roles for the YAP-GAS6-AXL axis and its inhibition in the intrinsic resistance to KRAS G12C inhibitors
- AXL-ADC improves outcomes via tumor killing



Morimoto et al. Cancer Letters 587 (April 2024)

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# **Emerging Opportunity for Mecbotamab Vedotin in Patients with Mutated KRAS** (mKRAS) Variants

mKRAS constitutes 30% of all NSCLC patients

mutant KRAS; all NSCLC (SQ+NSQ); median of approximately 3 prior lines of tx for both mKRAS and wtKRAS

	Total (N=78)
Age, y, mean (range)	67 (46-82)
KRAS Status, n (%)	
WtKRAS	50 (64)
mKRAS	24 (31)
Unknown KRAS status	4 (5)*

\* Two responders with no additional biopsy sample for KRAS mutation assessment



### Confirmed Responses with Mecobotamab Vedotin Across mKRAS Variants -Ongoing

N=21 of 24\*\*; 1.8 mg/kg Q2W, 2Q3W, and Q2W+nivo



# Complete Response as defined by disappearance of all pathologic lymph nodes

^ Patient was previously treated with Sotorasib

\*Confirmed responses

est % Change in TL	
--------------------	--

Median of 3 prior lines of tx	mKRAS N=21
BOR all	5 (24%)
BOR confirmed	4 (19%)
DCR	76%
DOR	4.8 months
PFS	4.6 months
OS	12.6 months

\*\*Evaluable patients defined as patients that had at least 1 scan after treatment with study drug Prior to first scan:

Two patient withdrew consent One patient DC due to AE



#### Improved Overall Survival with Mecbotamab Vedotin among NSCLC Patients with Tumors Expressing mutant KRAS Variants Compared to KRAS Wildtype

#### Median of 3 prior lines of tx





# Ph2 Mecbotamab Vedotin: Overall Safety Summary of NSCLC patients

#### Generally well-tolerated

	1.8 mg/kg Q2W (N=26)	1.8 mg/kg 2Q3W (N=33)	1.8 mg/kg Q2W + Nivo (N=19)	Total (N=78)
Any Adverse Events (AEs)	26 (100)	33 (100)	19 (100)	78 (100)
Related AEs with CTCAE <sup>1</sup> Grade 3 or $4^2$	10 (39)	12 (36)	4 (21)	28 (33)
Any Related Serious AEs <sup>2</sup>	4 (15)	3 (9)	1 (5)	8 (9)
Possibly Related AEs leading to death <sup>2</sup>	0	0	0	0
Related AEs leading to treatment discontinuation <sup>2</sup>	1 (4)	4 (12)	1 (5)	6 (7)

<sup>1</sup>CTCAE: Common Terminology Criteria for Adverse Events. The NCI Common Terminology Criteria for Adverse Events is a descriptive terminology which is utilized for Adverse Event (AE) reporting. A grading (severity) scale is provided for each AE term.

<sup>2</sup>As assessed by the investigator. Missing responses are counted as related.



#### Mecbotamab Vedotin: Phase 2 Safety Data of NSCLC patients

Most frequent treatment-emergent adverse events irrespective of causality (≥15%)

	BA301 (N=	1 Q2W 26)	BA301 (N=	1 2Q3W :33)	BA3011 Q (N=	2W + Nivo 19)	T07 (N=	ГАL 78)
Preferred Term	All Grades	Grade 3-4	All Grades	Grade 3-4	All Grades	Grade 3-4	All Grades	Grade 3-4
Number of Subjects with at Least One TEAE	26 (100)	17 (65)	33 (100)	18 (55)	19 (100)	9 (47)	78 (100)	44 (56)
Fatigue	12 (46)	1 (4)	8 (24)	2 (6)	8 (42)	0	28 (36)	3 (4)
Diarrhoea	8 (31)	1 (4)	12 (36)	2 (6)	6 (32)	0	26 (33)	3 (4)
Decreased Appetite	6 (23)	1 (4)	13 (39)	0	6 (32)	0	25 (32)	1 (1)
Neuropathy <sup>¥</sup>	8 (31)	1 (4)	12 (36)	0	4 (21)	0	24 (31)	1 (1)
Nausea	6 (23)	0	9 (27)	0	8 (42)	0	23 (29)	0 (0)
Neutropenia*	9 (35)	3 (12)	8 (24)	7 (21)	1 (5)	0	18 (23)	10 (13)
Constipation	8 (31)	0	9 (27)	1 (3)	5 (26)	0	22 (28)	1 (1)
Anaemia	3 (12)	1 (4)	5 (15)	1 (3)	6 (32)	2 (11)	14 (18)	4 (5)
Aspartate Aminotransferase Increased	5 (19)	2 (8)	5 (15)	0	4 (21)	1 (5)	14 (18)	3 (4)
Alanine Aminotransferase Increased	5 (19)	2 (8)	5 (15)	0	3 (16)	1 (5)	13 (17)	3 (4)
Arthralgia	3 (12)	0	7 (21)	0	3 (16)	0	13 (17)	0 (0)
Back Pain	4 (15)	0	7 (21)	0	3 (16)	1 (5)	14 (18)	1 (1)

\* Derived from neutropenia, and neutrophil count decreased

<sup>¥</sup> Derived from neuropathy peripheral, peripheral motor neuropathy, and peripheral sensory neuropathy



### **Mecbotamab Vedotin NSCLC Summary**

#### Median of 3 prior lines of tx

- Promising anti-tumor activity among patients whose tumors express KRAS mutations
  - mKRAS represents 30% of all NSCLC patients and is associated with increased AXL expression
  - Improved overall survival observed among treated patients with tumors expressing mutated KRAS variants (12.6 months) compared to KRAS wildtype (8.7 months)
  - Anti-tumor activity across nine different KRAS mutation variants
    - Partial response observed in a patient who had experienced prior failure of sotorasib
    - Patient treated with mecbotamab vedotin + anti-PD-1 antibody remains in complete response for >2 years
- Potential for a pan mKRAS strategy in NSCLC; currently determining the most efficient path forward for a future pivotal trial





### Evalstotug (CAB-CTLA-4)

#### **Evalustotug Is a Next Generation Adaptation of Ipilimumab**

CAB-CTLA4 selectively active in tumor microenvironment, thereby reducing immune related adverse events (irAEs)



#### pH-dependent binding of CAB-anti-CTLA-4

### **Evalstotug Effectively Reduces Clinically Relevant GI Toxicity in NHP**

Evalstotug significantly reduces GI toxicity relative to ipilimumab analog in combination with nivo



Nivo: 20mg/kg QW (~14.6mg/kg human dose) + Ipi or evalstotug: 15mg/kg QW (~11mg/kg human dose) Once weekly for four weeks exposure to Nivo + Ipi or BA3071 NHP – Nonhuman primates



#### Multicenter, Open-Label, Evalstotug Ph1 Dose Escalation and Ph2 Monotherapy



At 350 mg, evalstotug was administered with nivolumab either sequentially (starting in cycle 2) or concurrently (starting in cycle 1). At 700 mg, evalstotug was administered either with nivolumab sequentially (starting in cycle 2) or as monotherapy.

Treatment continued until confirmed disease progression per RECIST v1.1 or unacceptable toxicity. aResponse assessment was performed Q6W for 24 weeks, then Q12W until progression



### **Evalstotug Phase 1: Demographics – Tumor Types**

Median of 3 prior lines; all patients experienced failure of prior PD-1 treatment

	Total (N=23)		Total (N=23)	Prior # of treatments
Age, y, mean (SD)	62 (11)	Tumor type, n (%)		
Sex, n (%)		Melanoma	6 (26)	1-4
Female	8 (35)	Gastric	5 (21)	2-6
Male	15 (65)	Renal cell	4 (17)	1-6
White race, n (%)	20 (87)	Cervical	3 (13)	1–3
ECOG, n (%)		NSCLC	2 (8)	3-7
0	13 (56)	Urothelial	1 (4)	4
1	10 (44)	SCLC	1 (4)	3
Prior Anti-PD-1 Therapy, n (%)	22 (96)	Parathyroid Cancer	1 (4)	0



#### **Evalstotug Phase 1: Grade 3+ Adverse Events of Special Interest**

Cleared all dose levels up to and including 1 gram (14.2 mg/kg)

Most related AEs were low grade; no related grade 4 or 5 events

#### <u>All Grade 3 related events (N=4 pts):</u>

- CRS-like events:
  - New onset atrial fibrillation (only AE to meet DLT criteria)
  - Readily reversible hypertension
- Immune Mediated:
  - Endocrine: Hyperglycemia/DKA
  - GI Lipase increase and Gastritis/Diarrhea

Only 2/21 pts discontinued due to an adverse event (atrial fibrillation and gastritis)

NUMBER OF PATIENTS	All	AE	Related		
WITH ANY, n (%)	All grades	Grade 3-4	All grades	Grade 3-4	
All (n=21)	23 (100)	12 (52)	20 (87)	5 (22)	
Fatigue	11 (48)	2 (9)	4 (17)	0	
Chills	9 (39)	0	9 (39)	0	
Nausea	8 (35)	0	4 (17)	0	
Vomiting	8 (35)	0	3 (13)	0	
CRS	7 (30)	0	7 (30)	0	
Abdominal pain	6 (26)	2 (9)	1 (4)	0	
Diarrhea	6 (26)	1 (4)	2 (9)	0	
Arthralgia	5 (22)	0	3 (13)	0	
Back pain	5 (22)	0	0	0	
Decreased appetite	4 (17)	0	1 (4)	0	
Headache	4 (17)	0	1 (4)	0	
Pyrexia	4 (17)	0	4 (17)	0	



#### Phase 1 Evalstotug: 3 of 8 Responders in the 350mg + Nivolumab Cohort

**Durable antitumor activity across multiple solid tumor types** 



Mehmi I, Selfridge JE, Mangla A, et al. Poster presented at: Society for Immunotherapy of Cancer Annual Meeting; November 8–10, 2024; Houston, TX.

### Phase 2 Multicenter, Open-Label, Evalstotug in Combination with PD-1

**Evaluate the efficacy and safety of evalstotug in combination** 



\*Coded by MedDRA and graded according to NCI CTCAE v5

Abbreviations: ORR: overall response rate; AEs: adverse events; DOR: duration of response; PFS: progression-free survival; BOR: best overall response; DCR: disease control rate; TTR: time to response; OS: overall survival



🛛 Mehmi I, Selfridge JE, Mangla A, et al. Poster presented at: Society for Immunotherapy of Cancer Annual Meeting; November 8–10, 2024; Houston, TX.

#### All 8 First-Line Unresectable and/or Metastatic Cutaneous Melanoma Patients Treated with Evalstotug plus PD-1 Antibody Achieved Tumor Reduction

Four of 8 achieved objective responses (including 3 partial responses and 1 complete response)

Evalstotug dose (mg)	Age (yrs)	Sex	ECOG	Prior Treatment	Best change in target lesion (%)	Response to evalstotug	Grade 3 imAE
350	34	Μ	0	None	-54%	cPR	None
350	54	F	0	Adjuvant anti-PD-1 for 3mos	-83%	cCR	None
350	63	М	0	Adjuvant anti-LAG- 3/anti-PD-1 for 11mos	-9%	SD	Colitis (resolved within 3wks)*
350	59	F	0	Adjuvant anti-PD-1 for 12mos	-6%	SD	None
700	73	Μ	0	Adjuvant anti-PD-1 for 7mos	-38%	PR (confirming)	None
700	57	F	1	Neo-adjuvant anti-PD-1 for 12mos	-8%	SD	Pneumonitis & pancreatitis (resolved within 1mo)*
70 ≽210 ≽350	75	F	1	Adjuvant anti-PD-1 for 11mos	-46%	cPR	None
700 > 1000	57	Μ	0	Adjuvant anti-LAG- 3/anti-PD-1 for 3mos	-14%	SD	None

All patients were Caucasian; The patient with -54% tumor reduction initially experienced tumor growth with new lesions and Investigator continued treatment per protocol resulting in confirmed partial response.





IO – immuno-oncology; imAE – immune-mediated adverse events

Mehmi I, Selfridge JE, Mangla A, et al. Poster presented at: Society for Immunotherapy of Cancer Annual Meeting; November 8–10, 2024; Houston, TX.

#### Intrapatient Evalstotug Dose Escalation Re-achieved Disease Control

3 of 3 patients experienced tumor volume reduction following continued exposure and dose escalations





Phase 2 data are from a live data cut as of October 22, 2024 and are subject to change.

Mehmi I, Selfridge JE, Mangla A, et al. Poster presented at: Society for Immunotherapy of Cancer Annual Meeting; November 8–10, 2024; Houston, TX.

# 57-Year-old Male Achieved Tumor Volume Reduction Following Dose Escalation of Evalstotug in Combination with PD-1 Antibody (still ongoing)

Prior adjuvant therapy with investigational anti-PD-1 and anti-LAG-3 combination



# FDA Guidance Regarding Evalstotug Pivotal Trial in 1L Unresectable and / or Metastatic Melanoma

- Centrally reviewed PFS acceptable as primary endpoint
- General agreement with proposed study population and sample size
- Additional guidance received on ongoing dose optimization and control arm:
  - IO-based combination regimen should be included in the control arm
  - Project Optimus should guide determination of Phase 3 evalstotug dose
- Anticipated to enable study initiation in 2025





### BA3182 (CAB-EpCAM x CAB-CD3 Bispecific T-Cell Engager): Adenocarcinoma

# CAB-EpCAM x CAB-CD3 Bispecific T-Cell Engager (BA3182)

Significant opportunity for safe and effective EpCAM x CD3 bispecific

- EpCAM is an attractive, but challenging therapeutic target because it's expressed in most solid tumors, as well as in normal epithelial tissues
- BA3182 exhibits efficient tumor shrinkage with encouraging safety profile in vitro and in vivo<sup>1</sup>
- In non-GLP and GLP tox studies in NHP, dual selection results in high selectivity with 100-fold therapeutic index (TI) increase<sup>1</sup>
- Phase 1 dose escalation ongoing
  - Observed multiple patients with tumor reduction, including one colorectal cancer patient with stable disease for one year (ongoing)
  - Maximally tolerated dose has not yet been reached
  - Implemented priming dose to modulate cytokine release syndrome that is commonly observed with Tcell engagers and can also occur in patients with heavy tumor volume
- Given encouraging continued ongoing dose escalation with increasing antitumor activity, we now anticipate data readout of Phase 1 study around mid-2025



<sup>1</sup>Gerhard Frey, Ana Paula G. Cugnetti, Haizhen Liu, Charles Xing, Christina Wheeler, Hwai Wen Chang, William J. Boyle & Jay M. Short (2024) A novel conditional active biologic anti-EpCAM x anti-CD3 bispecific antibody with synergistic tumor selectivity for cancer immunotherapy, mAbs, 16:1, 2322562, DOI: 10.1080/19420862.2024.2322562

#### **Key Milestones And Catalysts Throughout 2024**

2024							
1H	2Н						
<ul> <li>Evalstotug:         <ul> <li>Dose escalation:                 <ul> <li>Cleared 10mg/kg</li> <li>Evaluate safety and efficacy at 14.2mg/kg dose level</li> <li>Initial readout Phase 2 in treatment-refractory solid tumors (~20 pts)</li> <li>Demonstrate supportive data as mono- and combo- therapy</li> </ul> </li> <li>Mecbotamab Vedotin:                     <ul> <li>Evaluate clinical benefit in target-agnostic NSCLC patients (~30 pts)</li> <li>Update UPS status</li> <li>Ozuriftamab Vedotin: Readout final data sets in melanoma (n = ~25 pts) and SCCHN (n = ~30 pts)</li> <li>BA3361: IND clearance</li></ul></li></ul></li></ul>	<ul> <li>Evalstotug:         <ul> <li>Readout additional Phase 2 data in treatment-refractory solid tumors</li> <li>Define pivotal path in treatment-refractory indications</li> </ul> </li> <li>Ozuriftamab Vedotin: FDA actionable guidance received on pivotal trial in second-line plus SCCHN</li> <li>BA3182: Given encouraging continued ongoing dose escalation with increasing antitumor activity, we now anticipate data readout of Phase 1 study around mid-2025</li> <li>Establish strategic collaboration for evalstotug and/or one CAB-ADC         <ul> <li>Completed out-licensing deal for preclinical TCE asset</li> </ul> </li> </ul>						



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with Conditionally Active Biologics (CABs)



