



Company Overview

May 2023

ADAGENE

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Our Story

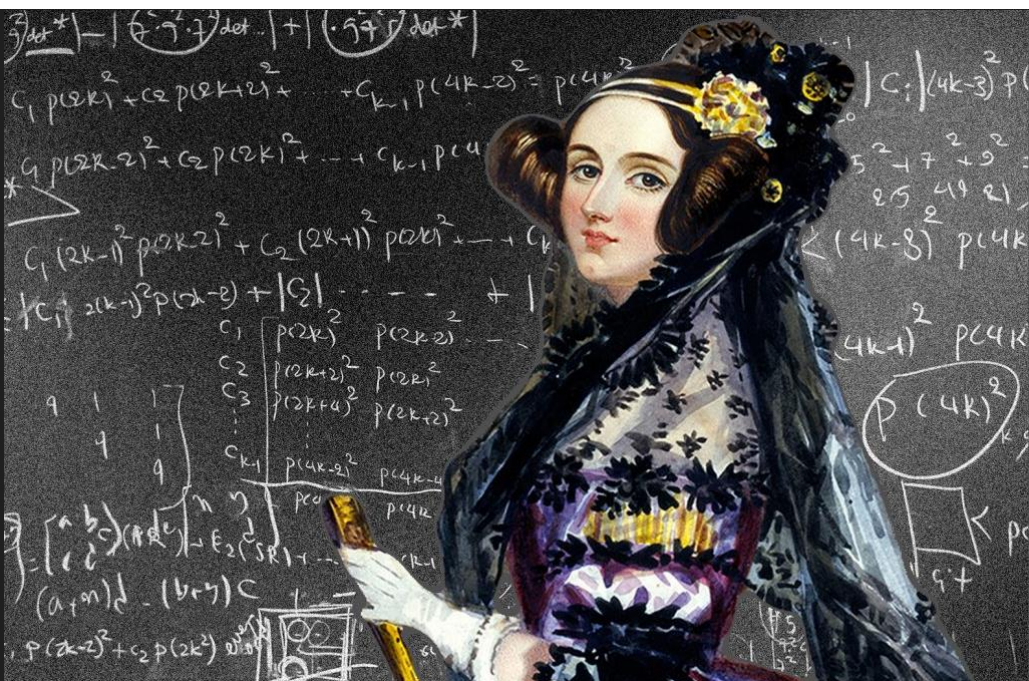
Ada

Mathematician who invented the first computational algorithm



Gene

Inherited through millions of years of evolution for survival



Leveraging AI and computational biology, we are pioneers in creating dynamic and precise antibodies with tailor-made safety and efficacy to transform cancer care

Highlights

Focus on anti-CTLA-4 franchise with validation by partners	<ul style="list-style-type: none">• One masked and one unmasked, targeting a unique epitope of CTLA-4• Roche sponsoring & conducting clinical trial of ADG126 in 1L liver cancer• Key readouts planned in 2023 for Ph 2 studies with anti-PD-1 (including pembrolizumab) in targeted tumor types, paving way for pivotal trial(s)• AACR data reinforce best-in-class profile of ADG126 in combination
Validation of SAFEbody[®] technology by partners	<ul style="list-style-type: none">• Sanofi and Exelixis technology licensing agreements for SAFEbody[®]
Additional pipeline candidates	<ul style="list-style-type: none">• Robust pipeline leveraging SAFEbody, with range of partner opportunities• Clinical candidates target CD137 (one masked, one unmasked)• Preclinical masked anti-CD47 and T-cell engagers (CD3, CD28)
Strong cash balance with runway into 2025	<ul style="list-style-type: none">• US\$143.8M as of December 31, 2022• Additional non-dilutive funding from collaborations• EXEL \$3M milestone achieved for 2nd target in 2023• Cash runway with streamlined operations into 2025

Experienced and Committed Management Team



Peter Luo, Ph.D.
Co-founder, Chairman & CEO



Dr. Peter Luo was Co-founder, President and CTO of Abmaxis which was acquired by Merck in 2006 for \$80M



Felix Du, Ph.D.
Chief Technology Officer



Qinghai Zhao, Ph.D.
Chief Manufacturing Officer



Jiping Zha, M.D., Ph.D.
EVP, Clinical Development



JC Xu, M.D., Ph.D.
Chief Scientific Officer



Raymond Tam, M.B.A
Chief Financial Officer



Yan Li, M.B.A
SVP,
Bioinformatics and IT



Ami Knoefler
VP,
IR and Corporate Communications

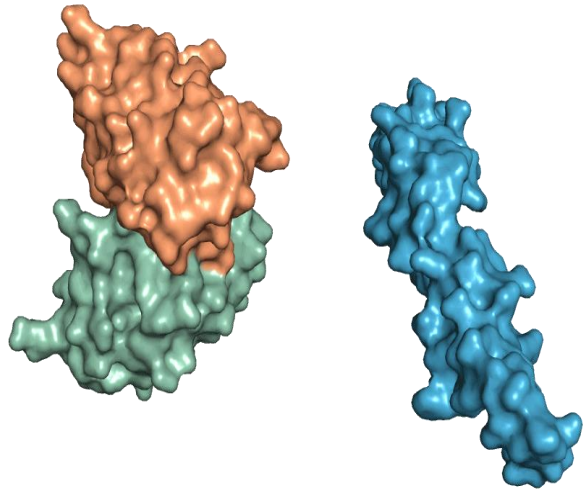


Alexander Goergen
VP,
Head of Business Development



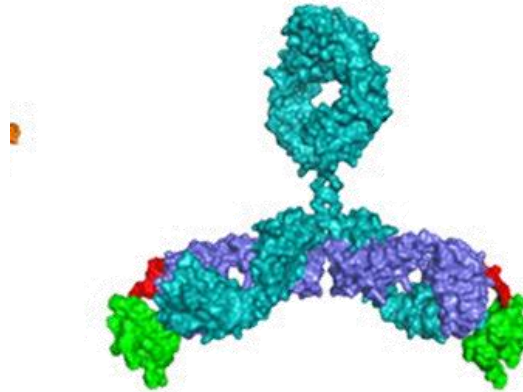
Disruptive Technologies For Tailor-Made Antibody Therapeutics

NEObody™



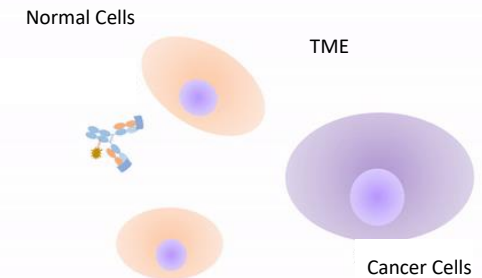
Dynamic engagement with novel epitope of a given target

SAFEbody®






Precision masking for antibody safety

POWERbody™



Empowered SAFEbody in different modalities

SAFEbody® Technology Licensing Collaborations: Provide Non-Dilutive Funding


Partner	Summary
	<ul style="list-style-type: none">• \$2.5B value for development of SAFEbody monoclonal & bispecific mAbs• \$17.5M upfront (initial 2 targets), plus royalties• Option for additional 2 targets
	<ul style="list-style-type: none">• Development of 2 SAFEbody antibody drug conjugates (ADCs)• \$11M upfront (2 targets), plus royalties• Achieved \$3M milestone for 1st target & \$1.1M upfront payment in 2022• Additional \$3M milestone for 2nd target achieved in 2023
	<ul style="list-style-type: none">• Development of SAFEbody ADCs• Licensing fee, up to \$166M milestones, plus royalties• Adagene retains certain rights in Greater China

**US \$21.6M received in 2022 from SAFEbody technology licensing collaborations,
plus additional \$3M milestone from EXEL in 2023**

Roche Collaboration: Validates SAFEbody with Clinical Trial of ADG126 in Combination for 1L HCC, Providing Path to Registration

- **Roche to sponsor & conduct phase 1b/2 clinical trial in 1L treatment of advanced hepatocellular carcinoma (HCC)**
 - Randomized trial, initially in 60 patients, paving way for registration
 - Adds ADG126 to atezolizumab and bevacizumab in triplet combination, vs. approved doublet
- **Further validates role of anti-CTLA-4 in HCC, leveraging Roche's expertise in liver cancer**
 - AstraZeneca's tremelimumab recently approved in single dose combo for 1L (HIMALAYA data)
 - Ipilimumab also approved for 2L HCC in combo
- **Roche sponsors multi-national trial**
 - Both companies provide their respective drugs
 - Adagene retains full commercial rights to ADG126 globally
 - Reduces Adagene R&D costs

A Robust, Transformative Pipeline of Wholly-Owned Assets

Program & Technology	Target	Development stage					Retained Rights
		Discovery	IND Enabling	Ph 1	Ph 2	Pivotal	
ADG116 NEObody	CTLA-4						Global
ADG126 SAFEbody							Global
ADG106 NEObody	CD137						Global
ADG206 POWERbody							Global
ADG153 SAFEbody	CD47						Global
ADG138 POWERbody	HER2xCD3						Global
ADG152 POWERbody	CD20xCD3						Global
POWERbody	Undisclosed						Global
NEObody, SAFEbody & POWERbody	Various (e.g., CD28)						Global

Two additional candidates derived from Adagene's AI-powered antibody platform are in development by other entities in China. These include ADG104, an anti-PD-L1 antibody in phase 2 development by Sanjin, and ADG125, an antibody targeting CSF-1R in phase 1 development by Dragon Boat BioPharmaceutical.

Why Next-Gen Anti-CTLA-4 Therapy?

- Treg is the key component of immune suppression
 - “Cold” tumors such as MSS-CRC, have a highly upregulated Treg in TME
- CTLA-4 expression is increased in Treg and is a validated target for mediating Treg depletion
 - Treg depletion can be achieved by intra-tumoral Ipi injection (very high local concentrations) in order to overcome the safety limit by the systemic delivery of Ipi (≤ 3 mg/kg) in combination with PD-1
- Our differentiated next generation anti-CTLA-4 candidates are designed to provide safe and potent immunotherapy
 - **ADG116:** Targeting a unique and cross-reactive epitope with strong ADCC-mediated Treg depletion
 - **ADG126:** Adds masking for conditional activation with better safety, which enables higher dose levels by systemic delivery to be used in both monotherapy (20 mg/kg) and (≥ 10 mg/kg) in combination with anti-PD-1 therapy

New Developments Rejuvenating Anti-CTLA-4 Therapy, yet Safety Remains a Core Challenge*

- **Two recent FDA approvals for tremelimumab**

FDA approves tremelimumab in combination with durvalumab for unresectable hepatocellular carcinoma

October 21, 2022

FDA approves tremelimumab in combination with durvalumab and platinum-based chemotherapy for metastatic non-small cell lung cancer

November 10, 2022

- **Treg depletion with next generation show efficacy in cold tumors (e.g., MSS CRC)**
 - **ORR is 23% but Grade 3 and higher TRAE is 43%**

ASCO[®] Gastrointestinal
Cancers Symposium

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Results from a phase 1a/1b study of botensilimab (BOT), a novel innate/adaptive immune activator, plus balstilimab (BAL; anti-PD-1 antibody) in metastatic heavily pretreated microsatellite stable colorectal cancer (MSS CRC)

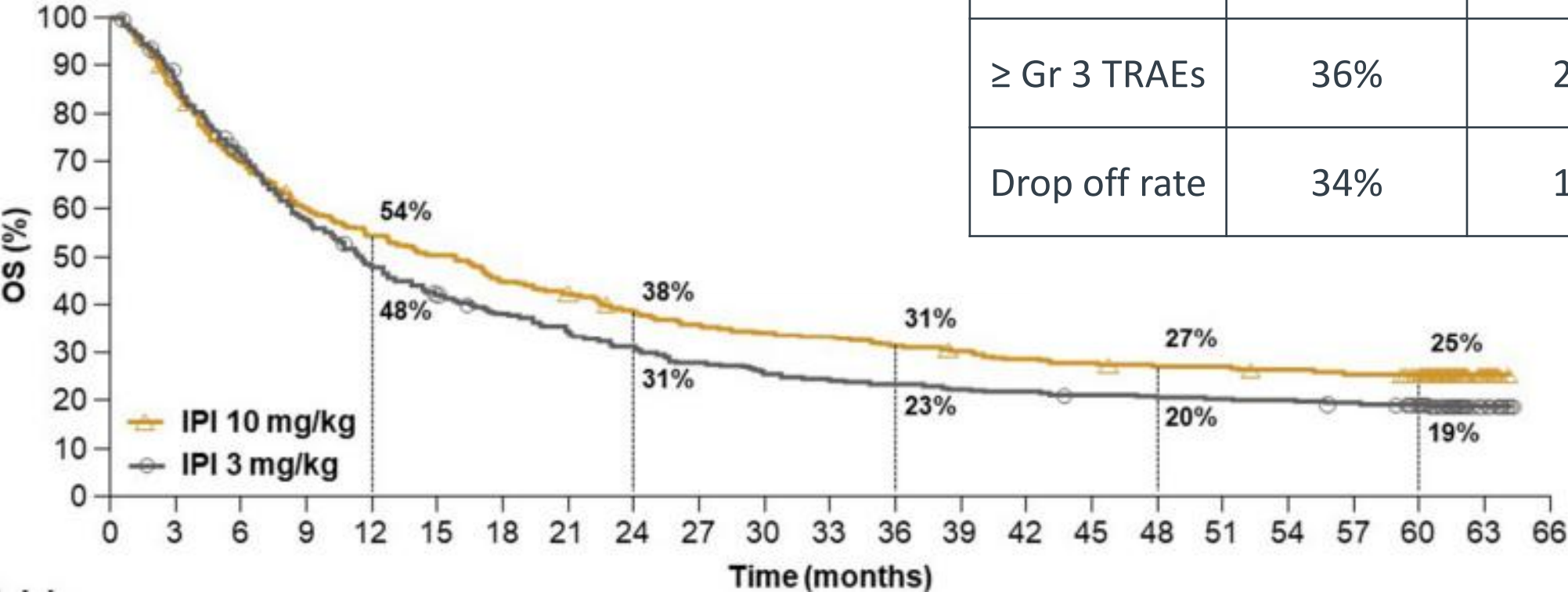
Botensilimab (Fc-enhanced anti-CTLA-4, balstilimab (anti-PD-1) and BMS-986249 (anti-CTLA-4 Probody[®]) are in clinical development and are not approved.

*References: [FDA.org](https://www.fda.org), [agenusbio.com](https://www.agenusbio.com), [ESMO 2022](https://www.esmo.org), SVB Leerink.

Ipilimumab: Approved Anti-CTLA-4, but Clinical Efficacy Is Limited by Dose-Dependent Toxicity (DDT)

Ipilimumab Monotherapy:
Long-Term Follow-up in Melanoma*

	10mg/kg	3mg/kg
OS @ 5 years	25%	19%
≥ Gr 3 TRAEs	36%	20%
Drop off rate	34%	19%



*Reference: Ascierto PA, et al. J Immunother Cancer 2020;8:e000391. doi:10.1136/jitc-2019-000391

Ipilimumab: Combination Data in HCC Highlight Dose-Dependent Challenge of Anti-CTLA-4 Therapy

Tumor Type	Ipilimumab Dosing Regimens	Overall Survival (OS)	TRAE \geq G3	AEs Lead to Discontinuation
HCC	1 mg/kg Q3W	12 months	29%	6%
HCC	3 mg/kg Q3W	23 months	53%	18%

Ipilimumab: Greater efficacy at higher doses associated with more side effects and discontinuations

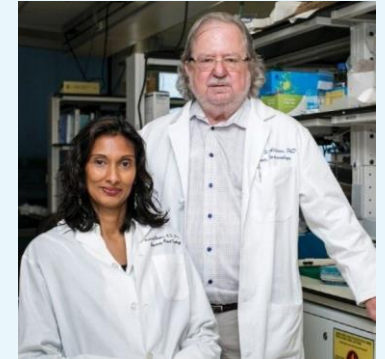
Nivo + 4 doses of Ipi; For HCC, approved dose level is Nivo 1mg/kg+ Ipi 3mg/kg; patient population is previously treated with sorafenib (2L); dosing regimens q3w for 4 doses. Reference on file.

Twin Story of anti-CTLA-4: Treg to Deplete or Not?

PRECISION MEDICINE AND IMAGING | AUTHOR CHOICE | FEBRUARY 15 2019

Anti-CTLA-4 Immunotherapy Does Not Deplete FOXP3⁺ Regulatory T Cells (Tregs) in Human Cancers ✓


Anu Sharma; Sumit K. Subudhi; Jorge Blando; Jorge Scutti; Luis Vence; Jennifer Wargo; James P. Allison ; Antoni Ribas; Padmanee Sharma 



**Padmanee Sharma,
M.D., Ph.D.**



**Aurélien Marabelle,
M.D., Ph.D.**


Society for Immunotherapy of Cancer

Intratumoral Anti-CTLA4: Checkpoint Blockade and/or Treg Depletion ?

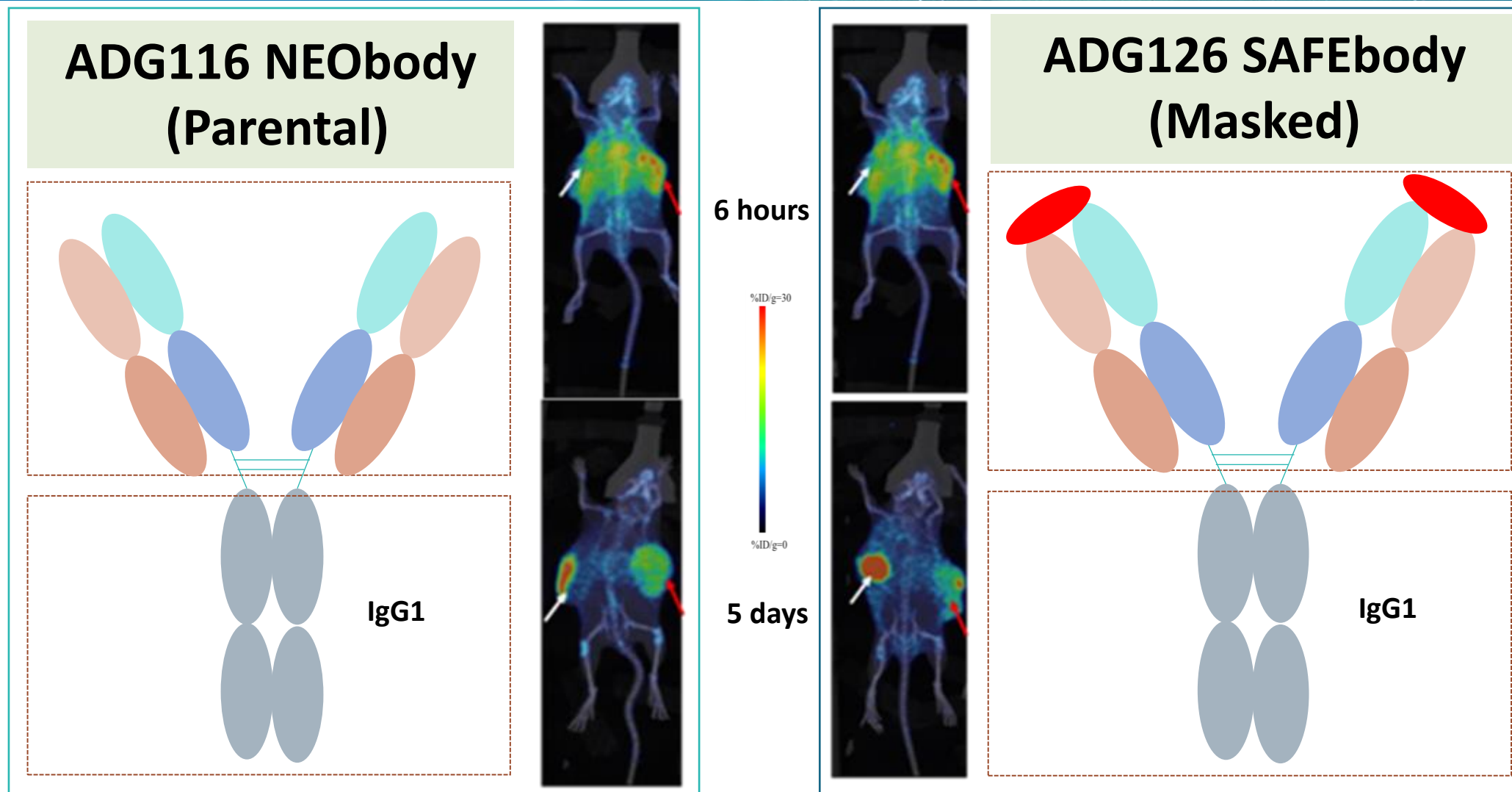
Prof. Aurélien Marabelle, MD, PhD
Drug Development Department
Clinical Investigation Center BIOTHERIS, INSERM 1428
Laboratory for Translational Immunotherapy, INSERM U1015
GUSTAVE ROUSSY Cancer Center & PARIS SACLAY University, France

Targets for Cancer Immunotherapy: A Deep Dive into Enhanced CTLA-4 Targeted Therapeutics
SITC Webinar, Oct 5th 2022

Safety is 'The Holy Grail' for Anti-CTLA-4 Therapy*

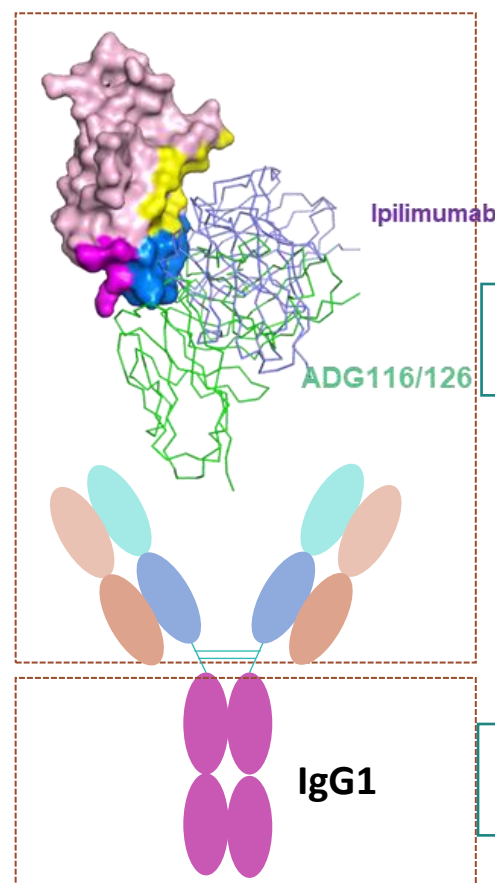
- **Safety** as monotherapy
- **Safety** in combination with PD-1
- **Safety** for late-onset AEs with repeat dosing

Enabling Anti-CTLA-4 Therapeutic Window for Immunotherapies



In vivo imaging of accumulation of SAFEbody ADG126 vs parental ADG116 in tumors

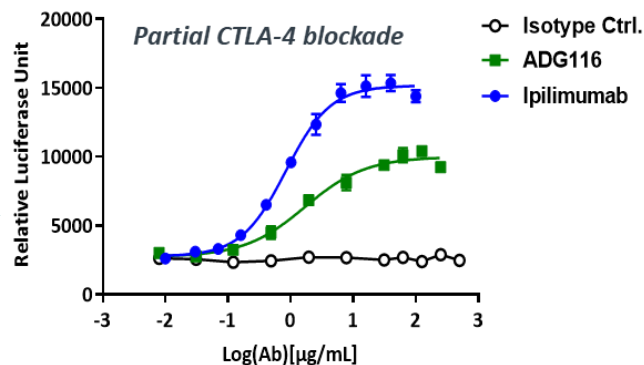
ADG116 & ADG126: Scientific Rationale Demonstrates Targeting a Distinct Epitope of CTLA-4 Matters



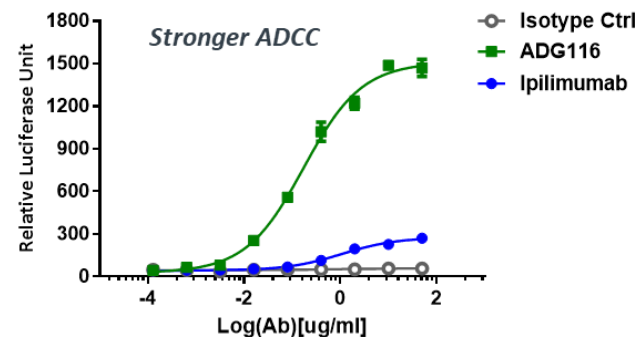
Partial CTLA-4 blockade

Stronger ADCC

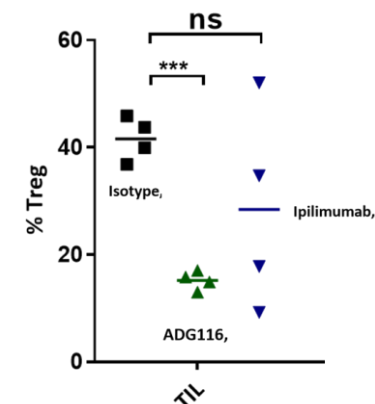
CD28 signaling reporter cell activity released by antibody mediated CTLA-4 functional blockade



ADCC signaling reporter cell activity triggered by anti-CTLA-4 antibodies

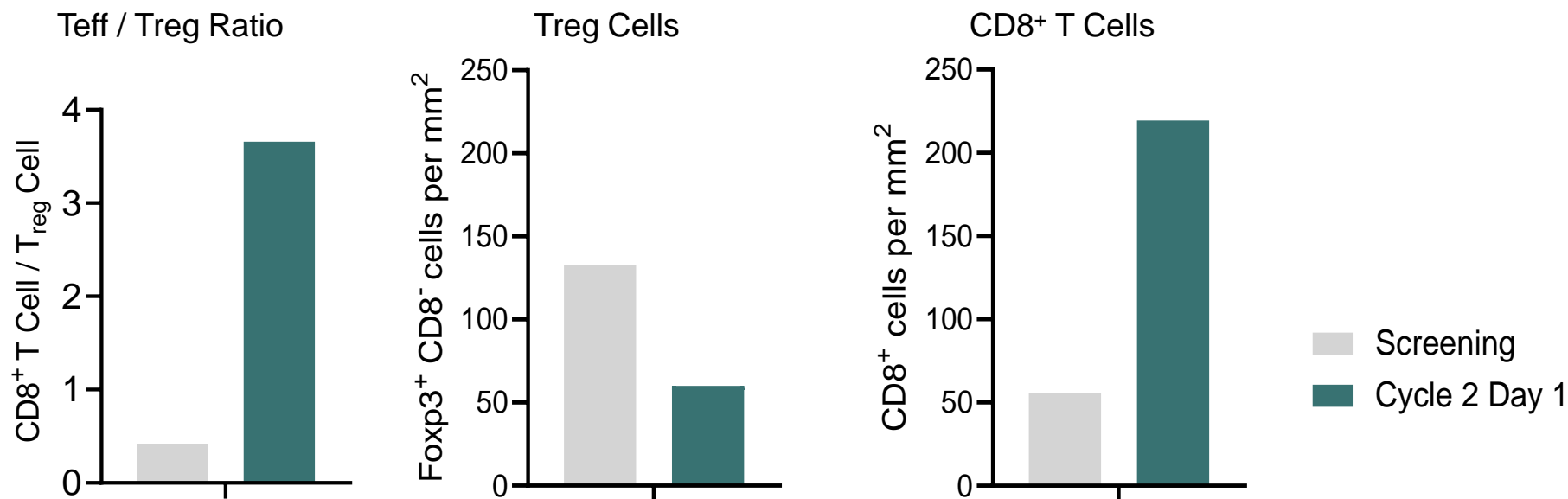


Strong ADCC for Treg Depletion in TME



Evolutionally conserved and distinct epitope of ADG116 from ipilimumab to enable partial CTLA-4 blockade and enhanced ADCC for Treg Depletion

ADG126 Mechanism Validated: Increased Teff/Treg Ratio in TME in HCC Monotherapy Patient who Progressed on IO Therapy*



- A 39-year-old male with stage IIIb HCC with ECOG PS 0
 - Ongoing ADG126 10 mg/kg Q3W treatment in C6 with control of tumor growth (stable disease)
- Previously progressed on anti-PD-L1 therapy
 - 1L: Atezolizumab + bevacizumab (Jul 2021 – Feb 2022, PD)
 - 2L: lenvatinib (Mar – Sep 2022, PD)
- Increased ratio of Teff / Treg, with Treg depletion and increased CD8⁺ T cells was observed in paired tumor biopsies

ADG126 & ADG116 Monotherapy Safety Profiles: Reduced Dose-Dependent Toxicity Suggests Clinical Improvement Over Historical Controls*

Masked	Dose	TRAE \geq Grade 3
ADG126* (SAFEbody)	10 and 20 mg/kg Q3W with repeat dosing (n=17)	0%
BMS 986249 (Ipi-Probody)	20 mg/kg** Q4W (n=10)	60%

Unmasked	Dose (Q3W)	TRAE \geq Grade 3
ADG116	\leq 6 mg/kg (n=24)	0%
	10 & 15 mg/kg (n=26)	13%
Ipilimumab⁺	3 mg/kg	20-27%
	10 mg/kg	36%

* This slide contains information from various clinical trials which are not head-to-head comparisons. Data on file.

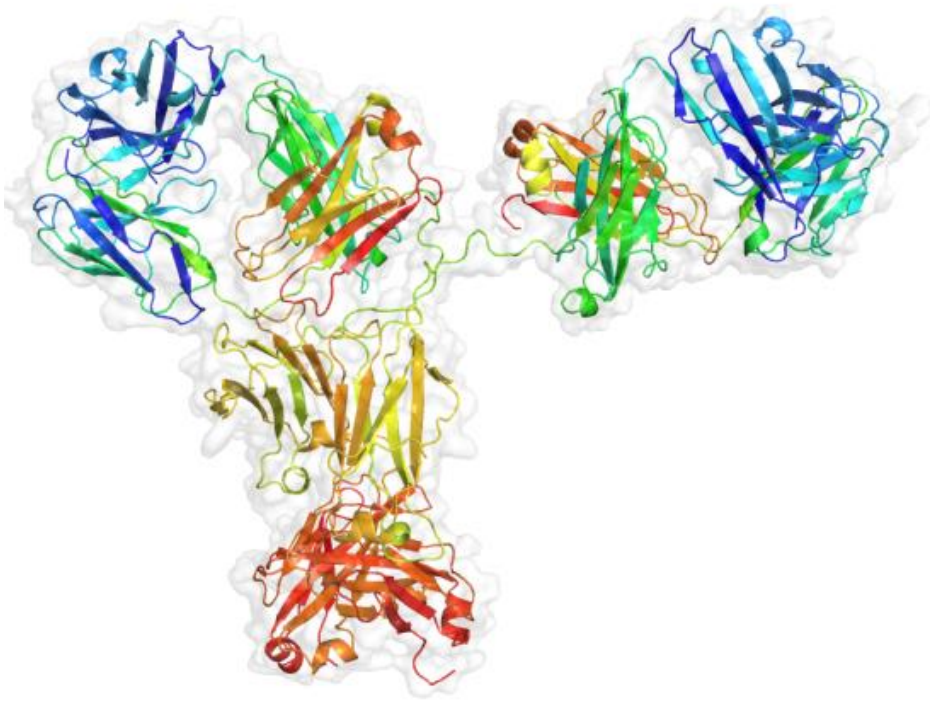
** Dosing of 10 & 20 mg/kg is calculated from 800 mg and 1600 mg, assuming 80kg body weight from ESMO 2022, 740P, NCT03369223

+ Data for Ipilimumab from trials in melanoma. Reference on file.

ADG116: Our NEObody Solution



ADG116 Clinical Results Show Differentiated Safety & Efficacy Profile in Heavily Pre-treated Patients with Difficult-to-treat Tumors*



ADG116 applies NEObody technology to target a unique, highly conserved epitope of CTLA-4.

- Comprehensive, differentiated monotherapy safety profile in >50 patients; low rate of TRAEs \geq Grade 3
- Demonstrated efficacy in heavily pre-treated patients, both as monotherapy & in combination with anti-PD-1
- Activity across warm and cold tumors, including 3 PRs (RCC, MSI-H endometrial & Kaposi's sarcoma) with ADG116 monotherapy, one CR in HNSCC & activity in MSS CRC with ADG116 + PD-1
- Manageable safety in combination with anti-PD-1; optimizing combination dosing

ADG116 Monotherapy: Comprehensive Safety Data Show Dose-Dependent Toxicity

- At 10 mg/kg dose level (n=23), rate of ≥ Grade 3 TRAEs is 13%*
- At ≤ 6 mg/kg dose level (n=24), rate of ≥ Grade 3 TRAEs is 0%*

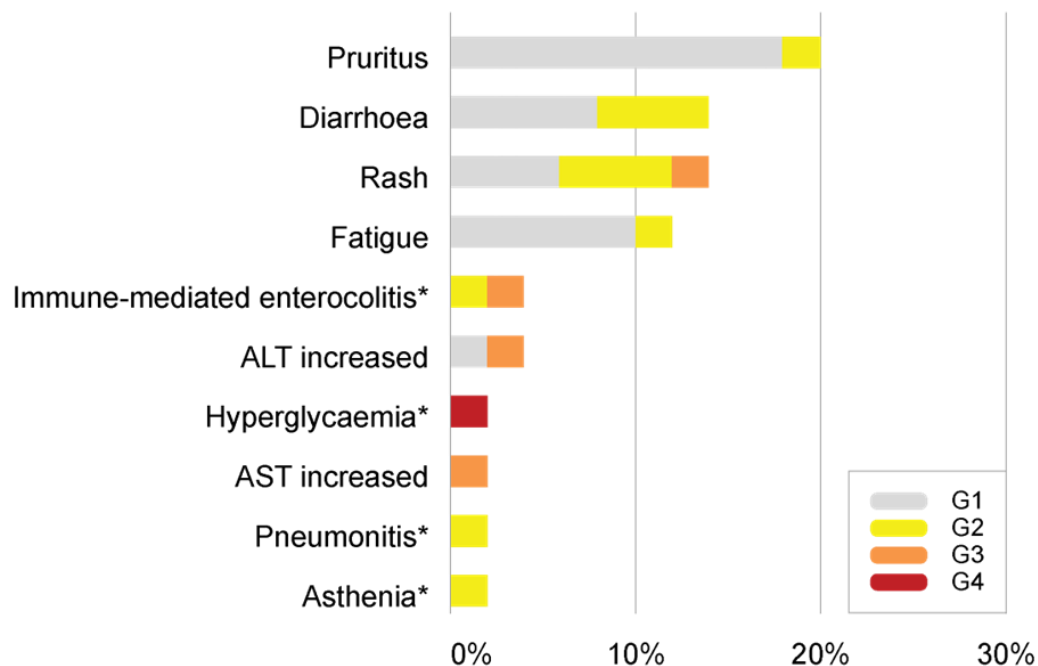


Table 2. TRAEs reported at any dose level of ADG116 monotherapy

Dose levels (mg/kg)	N	All G n (%)	G1 n (%)	G2 n (%)	G3 n (%)	G4 n (%)	G5 n (%)
All	50	31 (62)	17 (34)	11 (22)	2 (4)	1 (2)	0
≤ 0.3	11	3 (27)	3 (27)	0	0	0	0
1	3	2 (67)	2 (67)	0	0	0	0
3	4	3 (75)	1 (25)	2 (50)	0	0	0
6	6	5 (83)	3 (50)	2 (33)	0	0	0
10	23	15 (65)	8 (35)	4 (17)	2 (9)	1 (4)	0
15	3	3 (100)	0	3 (100)	0	0	0

Figure 2. TRAEs reported in > 10% of patients (any grade) or in ≥ 1 patient (grade 3/4 or treatment-related SAE) at any dose level of ADG116 monotherapy. *Treatment-related SAE included one G4 hyperglycemia, one G2 immune-related enterocolitis, one G2 pneumonitis and one G2 asthenia. AST=Aspartate aminotransferase; ALT=Alanine aminotransferase.

* TRAEs Grade 3 and higher for the approved anti-CTLA-4 therapy, ipilimumab, are ~36% at 10 mg/kg and 20% at 3 mg/kg in first-line monotherapy in melanoma patients. Source: Ascierto PA, et al.

ADG116 Monotherapy: Partial Response in Previously Treated Renal Cell Carcinoma Patient* Confirms Efficacy of Targeting Unique Epitope

- Male, 56 years old, with clear cell renal cell carcinoma
- Previously received sunitinib (1st line) followed by INCB86550 (Oral PD-L1 inhibitor)
- Dosed by ADG116 at 10mg/kg Q3W, with only G2 TRAEs

		Baseline	6 weeks	12 weeks*	21 weeks
Target Lesion	TL1- Lung RLL	15 mm	11 mm	11 mm	9 mm
	TL2 - Lung RML	16 mm	14 mm	14 mm	13 mm
	TL3 – LN	22 mm	14 mm	14 mm	14 mm
	TL-4- R kidney	47 mm	47 mm	30 mm	27 mm
	TL-5- LN	15 mm	10 mm	7 mm	5 mm
	Sum	115 mm	96 mm (-17%)	76 mm (-34%)	68 mm (-41%)
Non-Target Lesions	Multiple	Present	Present	Present	Present
New Lesion		N/A	No	No	No
Overall		N/A	SD	PR	PR

* Response on November 2, 2022 post data cutoff for SITC.

ADG116 + Anti-PD-1 Therapy is Tolerable up to 3 mg/kg for ADG116

ADG116 (3 mg/kg Q3W IV) + Pembrolizumab (200mg Q3W IV), n=6

- Manageable safety and tolerability profile with no dose-limiting toxicities
- Most frequent TRAEs observed: fatigue (4/6, 67%), pruritus (3/6, 50%) and nausea (3/6, 50%)
- Two patients had Grade 3 TRAEs: one Grade 3 dehydration (Cycle 3) and one Grade 3 rash (Cycle 1)

ADG116 (3 mg/kg Q3W IV) + Toripalimab (240mg Q3W IV), n=6

- G1/2 and G3 TRAEs were reported in 3 and 3 out of 6 patients, respectively
- No G4/5 TRAEs were reported. No patient discontinued due to TRAEs
- G3 TRAEs were observed in one patient in cycle 1 and two patients in \geq cycle 3
- Treatment-related SAEs were reported in 2 (33%) patients (G3 diarrhea & G3 nausea)
- DLTs were reported in 1 patient (G3 diarrhea)

ADG116 (6 mg/kg Q6W IV) + Toripalimab (240mg Q3W IV), n=3

- DLTs reported in 2 patients (G3 diarrhea and G3 immune-related myocarditis) and G3 TRAEs reported in 3 out of 3 patients
- Dose of ADG116 was de-escalated to 3 mg/kg Q3W

Case study: Durable Complete Response to ADG116 3mg/kg Q3W + Toripalimab 240mg Q3W in a Recurrent HNSCC Patient



Figure 6. Photos of external lesions (right mandibular and right submandibular) at C1D1, C2D1 and C4D2

Table 7. Tumor burden in a recurrent HNSCC patient administered ADG116 3 mg/kg Q3W + TORI 240 mg Q3W *

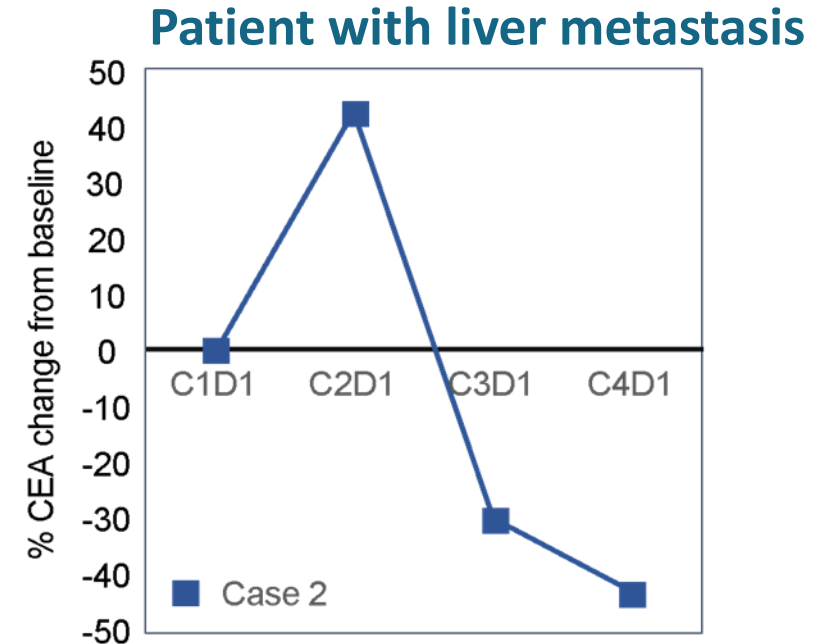
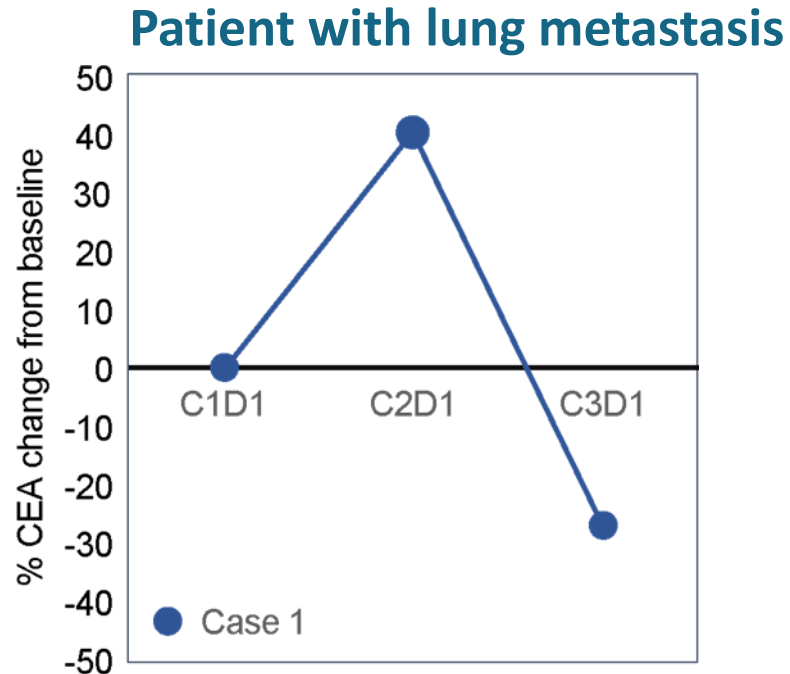
		Baseline	End of C2	End of C4	End of C6
Target Lesion	TL1 - Right mandibular	32 mm	Disappeared	Disappeared	Disappeared
	TL2 - Right submandibular	18 mm	Disappeared	Disappeared	Disappeared
	TL3 – Lymph node (left submandibular)	15 mm	8 mm	8 mm	5 mm
	Sum	65 mm	8 mm	8 mm	5 mm
Non-Target Lesions	3	Present	Disappeared	Disappeared	Disappeared
New Lesion		NA	No	No	No
Overall		NA	CR	CR	CR

- Male, 64 years, ECOG PS 1, HPV negative recurrent head and neck squamous cell carcinoma (HNSCC)
- Previously received
 - Locally advanced HNSCC initial therapy:
Right modified cervical lymph node dissection followed by adjuvant radiotherapy
 - Recurrent HNSCC therapy:
Concurrent chemoradiotherapy, including weekly cisplatin
- **Durable complete response sustained beyond week 54 with manageable safety profile****

* Data published in [poster presentation](#) at SITC 2022

** 20-F Filing on April 28, 2022

ADG116 in Combination with Pembrolizumab: Significant CEA Reduction in MSS CRC Patients

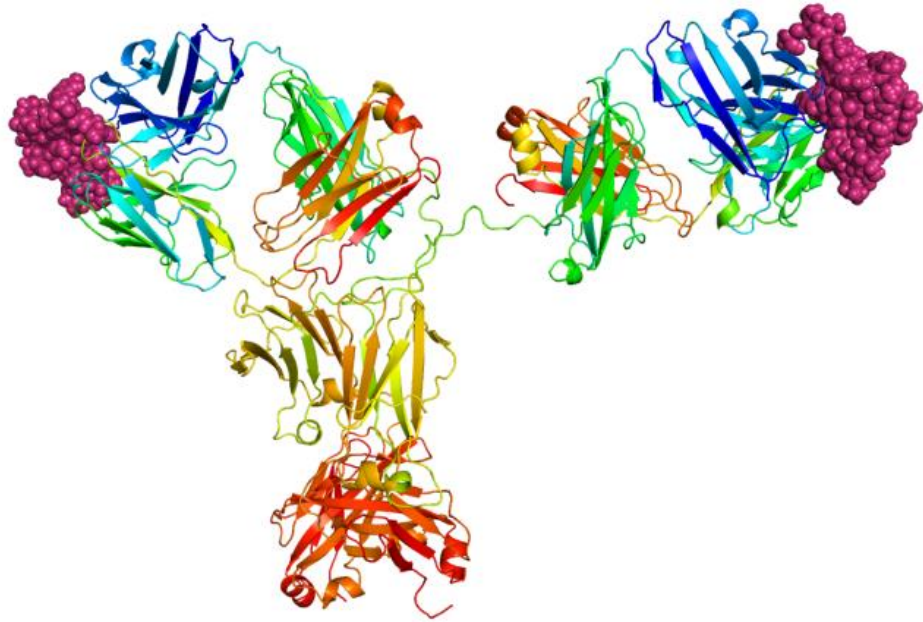


- Significant changes observed in a tumor-related biomarker in two patients with metastatic MSS CRC; a 43% and 27% reduction in (CEA) levels observed*
- Data support continued evaluation of ADG116 combo with pembrolizumab that may improve outcomes in certain patients with difficult-to-treat tumor types

ADG126: Our SAFEbody Solution



ADG126 Clinical Results Show Best-in-Class Safety & Differentiated Efficacy Profile in Heavily Pre-treated Patients *



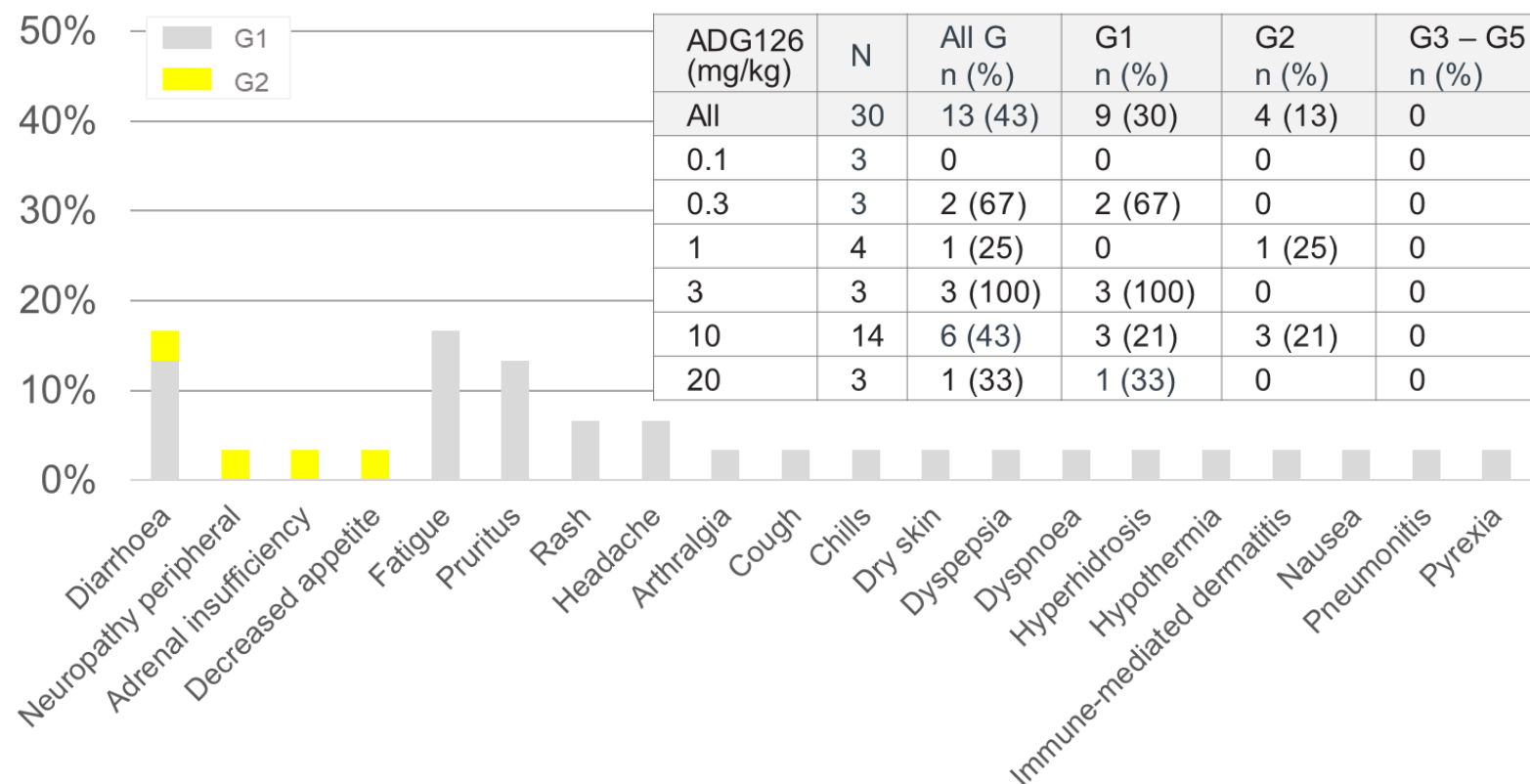
ADG126 applies SAFEbody precision masking technology to ADG116 for a best-in-class safety profile and enhanced efficacy.

- No G3 TRAEs as monotherapy up to 20mg/kg Q3W, with early efficacy signals in heavily pre-treated patients
- Best-in-class safety profile with anti-PD-1 in comparison with other anti-CTLA-4 molecules at similar doses / schedules
- Differentiated combination efficacy at 10 mg/kg dose level with 4 PRs reported in dose escalation with anti-PD-1:
 - Includes an IO-experienced patient with PD-1 resistance; only G2 TRAEs
 - PRs include tumor types where PD-1 monotherapy or its combination with CTLA-4 therapy not approved
 - 2 cases of significant tumor shrinkage (20% reduction and higher in target lesions) in MSS CRC patients with liver metastasis
- Results pave way for improved clinical benefit at higher doses

ADG126 Monotherapy: No DLT up to 20 mg/kg Q3W with repeat dosing

- Well tolerated with no dose limiting toxicities at doses up to 20 mg/kg Q3W with repeat dosing
- No > G2 treatment-related adverse events (TRAEs) and no treatment-related serious adverse events (SAEs)
- No patient discontinued study treatment due to TRAE

Figure 2 and Table 2. TRAEs reported at any dose level of ADG126 monotherapy



Better Monotherapy Safety Translates into Better Combination Safety with Anti-PD-1 at Higher Doses with Repeat Dosing

Masked	ADG126 Dosing Regimens	DLT	TRAE \geq Grade 3	AEs Lead to Discontinuation
ADG126 (SAFEbody)	6 mg/kg Q3W 10 mg/kg Q3W/Q6W (N=20)	No	25% [§]	5%
BMS 986249* (Ipi-Proboddy)	3 mg/kg Q4W**	No	33%	8%
	10 mg/kg Q4W**	Yes	45%	36%
Ipilimumab*	3 mg/kg Q3W**	Yes	>50%	>30%
	1 mg/kg Q6W**	Yes	>30%	>10%

[§] Data is from tori combination ADG126-1001 study (data cutoff: Mar 14, 2022). Data published in [poster presentation](#) at AACR 2023.

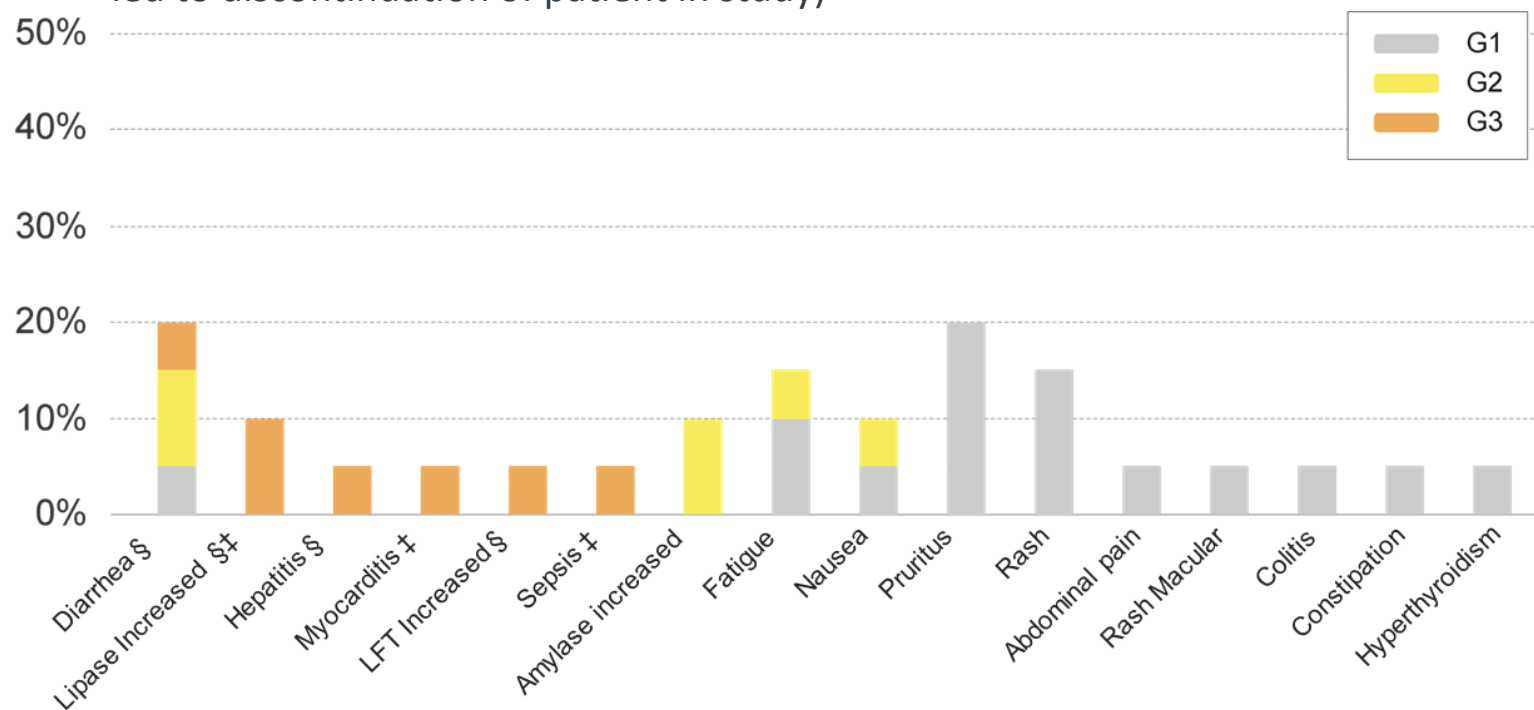
* This slide contains information from various clinical trials which are not head-to-head comparisons. Data on file.

** Dosing of BMS-986249 at 3 & 10 mg/kg is calculated from 240 mg and 800 mg, assuming 80kg body weight from ESMO 2022, 740P, NCT03369223

Safety Profile of ADG126 + Toripalimab (Anti-PD-1)

ADG126 (6 mg/kg Q3W and 10 mg/kg Q3W or Q6W) + Toripalimab (240 mg Q3W) Dose Escalation

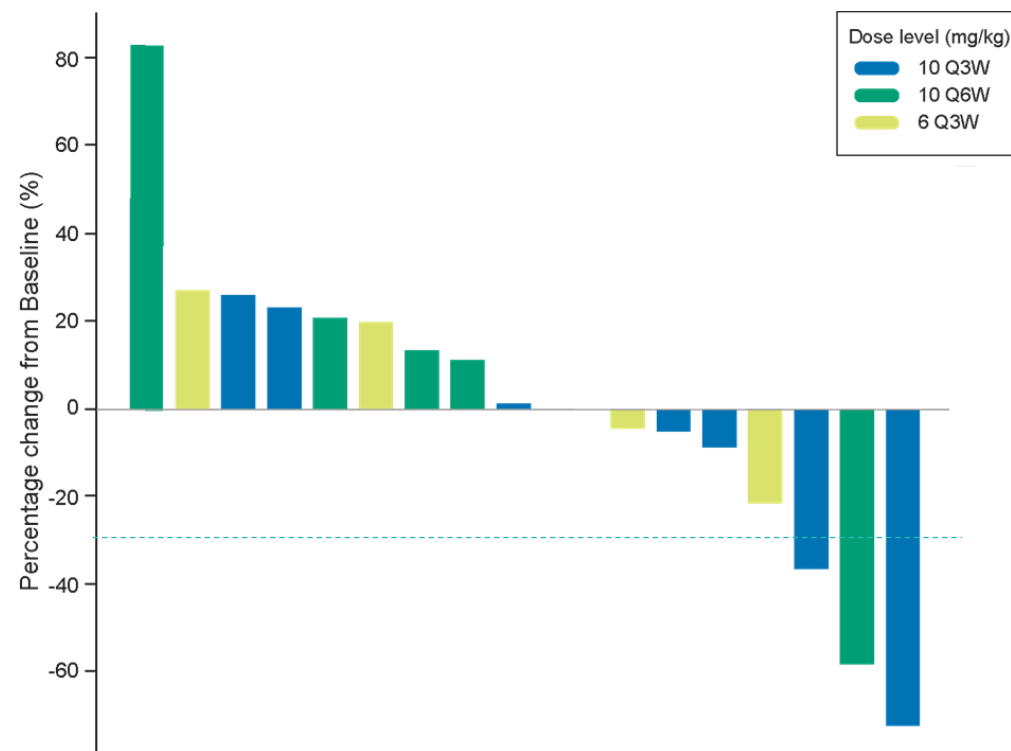
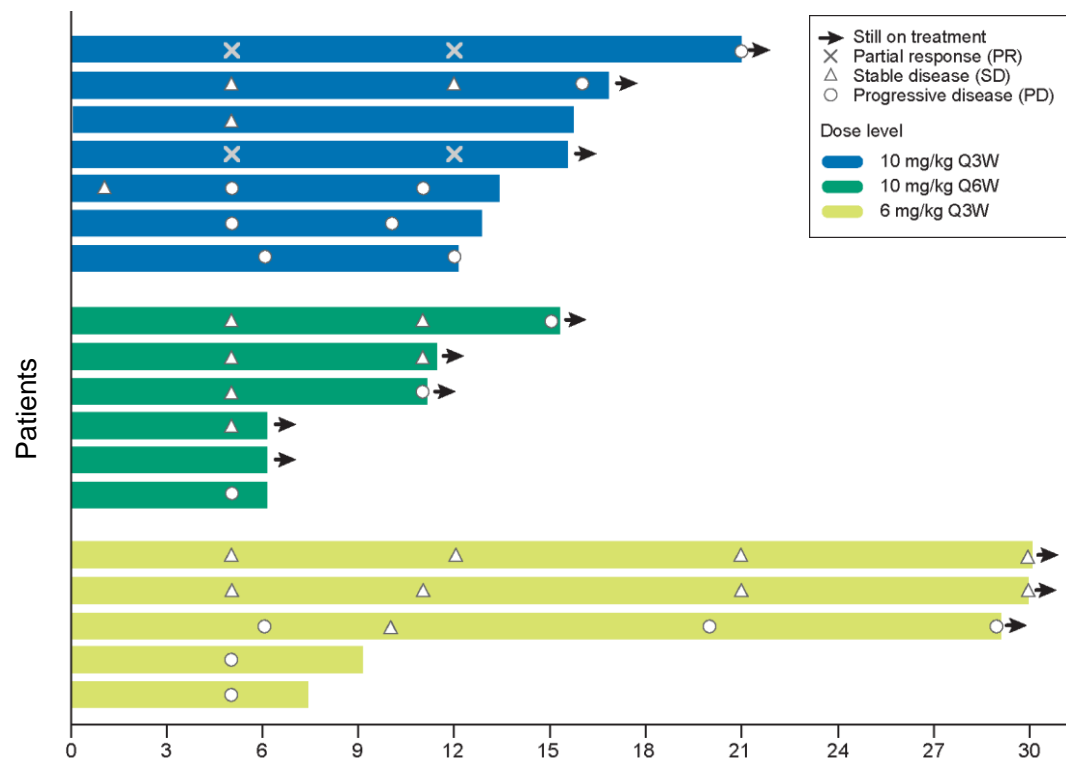
- No significant differences in safety across the three dose escalation cohorts
- No DLT or >G3 TRAE has been reported
- Five patients (25%) experienced G3 TRAEs: Most of G3 TRAEs occurred no earlier than Cycle 4
 - Three patients experienced treatment-related SAE: one G3 hepatitis[§], one G3 sepsis[‡] and one G3 myocarditis[‡] (this led to discontinuation of patient in study)



TRAEs in 20 patients of three dose escalation cohorts who received ADG126 (6 mg/kg Q3W and 10 mg/kg Q3W or Q6W) + TORI (240mg Q3W). LFT = Liver function test; § G3 TRAE observed at ADG126 6 mg/kg Q3W + TORI 240 mg Q3W; ‡ G3 TRAE observed at ADG126 10 mg/kg Q3W or Q6W + TORI 240 mg Q3W

Two Confirmed PRs with ADG126 + Toripalimab in Dose Escalation

- Among the 18 evaluable patients* in the three dose escalation cohorts, overall ORR = 11% and DCR = 56%
 - ORR = 28% and DCR = 57% among the 7 evaluable patients* who received ADG126 10 mg/kg Q3W + TORI 240 mg Q3W
 - Confirmed PR in two patients with penile SCC (-72%) and anal SCC (-36%) previously treated with chemotherapy



* Data published in [poster presentation](#) at AACR 2023. Data cutoff March 14, 2023. Evaluable patients with at least 1 valid post-treatment tumor assessment. For the swimmer plot, bars end at the study day of EOT, last dose date, or the last tumor assessment, whichever is latest.

Prolonged Stable Disease and Reduced Target Lesions in “Cold” Gastrointestinal Adenocarcinoma



- A **58%** and **21%** reduction in the sum of target lesions were observed in two MSS CRC patients with liver metastasis at baseline, respectively
- Prolonged SD in a PDAC patient with ongoing treatment in C11 and a **5%** reduction in the sum of target lesions

Response to ADG126 + TORI in gastrointestinal epithelial “cold tumors” including MSS CRC and PDAC

Case Study #1 in MSS CRC Patient with Liver Mets: 58% Reduction of Target Lesions

- Male, 53 years old, ECOG PS 0
- MSS CRC rectosigmoid adenocarcinoma with liver metastasis at baseline
- Previously received surgery and 3 lines of prior therapies
- Mixed response with a 58% reduction in the sum of target lesions was observed at week 17; treatment is ongoing (ADG126 10 mg/kg ADG126 Q6W + 240 mg TORI Q3W)

		Baseline	Week 7	Week 13	Week 17
Target Lesion	TL1 – Lung	15 mm	14 mm	13 mm	16 mm
	TL2 – Lymph Node	22 mm	12 mm	12 mm	Disappeared
	TL3 – Lymph Node	18 mm	10 mm	6 mm	Disappeared
	TL4 – Lymph Node	19 mm	14 mm	15 mm	Disappeared
	TL5 – Liver	17 mm	20 mm	22 mm	22 mm
	Sum	91 mm	70 mm (-23%)	68 mm (-25%)	38 mm (-58%)
Non-Target Lesion	NTL1 – Lung	Present	Present	Present	Disappeared
	NTL2 – Bone	Present	Present	Present	Present
New Lesion		NA	No	No	Yes
Overall Response		NA	SD	SD	PD (iuPD)

* Data published in [poster presentation](#) at AACR 2023. Data cutoff March 14, 2023.

Case Study #2 in MSS CRC Patient with Liver Mets: 21% Reduction of Target Lesions

- Male, 74 years old, ECOG PS 1
- MSS colorectal adenocarcinoma with liver metastasis at baseline
- Prior therapies: XELOX + bevacizumab; irinotecan + cetuximab; irinotecan + panitumumab
- A 21% reduction in the sum of target lesions was observed; treatment is ongoing (ADG126 6 mg/kg Q3W + TORI 240 mg Q3W)

		Baseline	Week 8	Week 14	Week 24	Week 33
Target Lesion	TL1 - Liver	55 mm	52 mm	44 mm	40 mm	38 mm
	TL2 - Liver	48 mm	48 mm	44 mm	44 mm	43 mm
	Sum	103 mm	100 mm (-3%)	88 mm (-15%)	84 mm (-18%)	81 mm (-21%)
Non-Target Lesion		Present	Present	Present	Present	Present
New Lesion		NA	No	No	No	No
Overall Response		NA	SD	SD	SD	SD

* Data published in [poster presentation](#) at AACR 2023. Data cutoff March 14, 2023.

Case Study #3 in a PDAC Patient: Prolonged Control of Tumor Growth

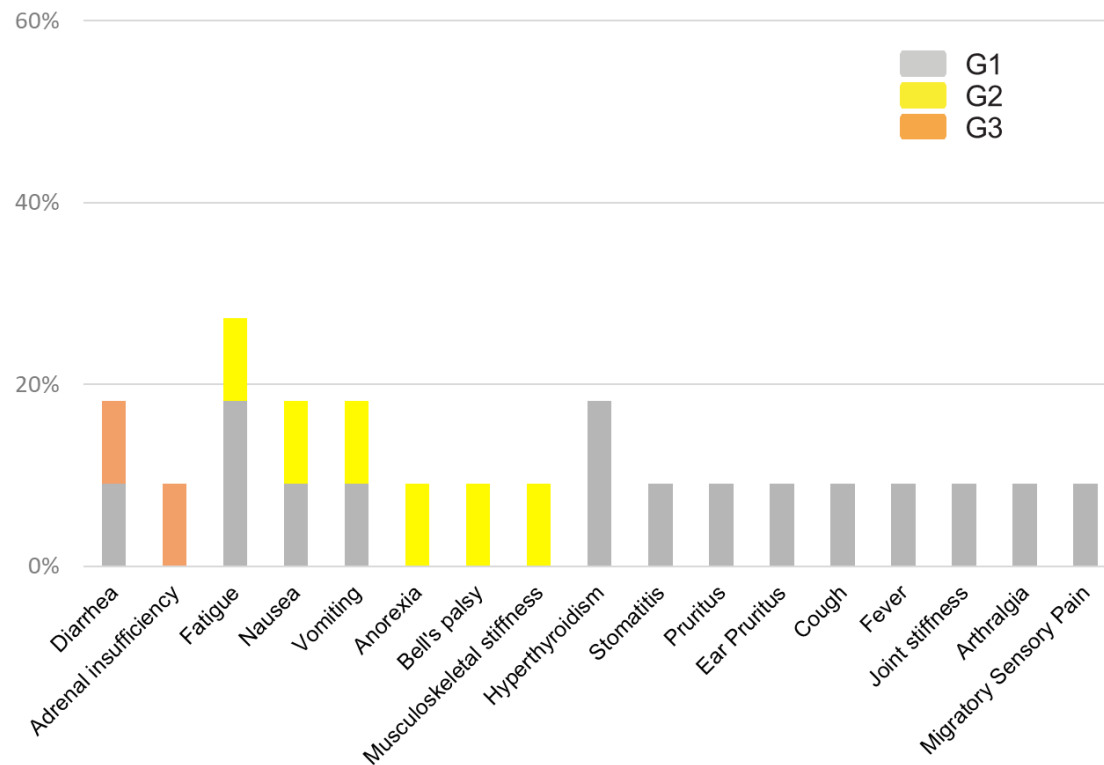
- Female, 56 years old, ECOG PS 0
- Pancreatic ductal adenocarcinoma
- Previously received curative surgery and 4 lines of therapies: gemcitabine / nab-paclitaxel; FOLFIRINOX; oxaliplatin, raltitrexed, irinotecan and leucovorin; gemcitabine / capecitabine
- Prolonged control of tumor growth (SD) with a 5% reduction in the sum of target lesions; treatment is ongoing (ADG126 6 mg/kg Q3W + TORI 240 mg Q3W)

		Baseline	Week 8	Week 15	Week 23	Week 31
Target Lesion	TL1 - Liver	23 mm	22 mm	23 mm	23 mm	17 mm
	TL2 - Liver	21 mm	21 mm	20 mm	19 mm	25 mm
	Sum	44 mm	43 mm (-2%)	43 mm (-2%)	42 mm (-5%)	42 mm (-5%)
Non-Target Lesion		Present	Present	Present	Present	Present
New Lesion		NA	No	No	No	No
Overall Response		NA	SD	SD	SD	SD

* Data published in [poster presentation](#) at AACR 2023. Data cutoff March 14, 2023.

ADG126 + Pembro Dose Escalation: Favorable Safety Profile in Heavily Pre-Treated Patients

TRAE by Cohort	Cohort N	G1 (%)	G2 (%)	G3 (%)	G4/5
ADG126 6mg/kg Q3W	5	0	2 (40%)	1 (20%)	0
ADG126 10mg/kg Q3W or Q6W	6	3 (50%)	2 (33%)	1 (17%)	0

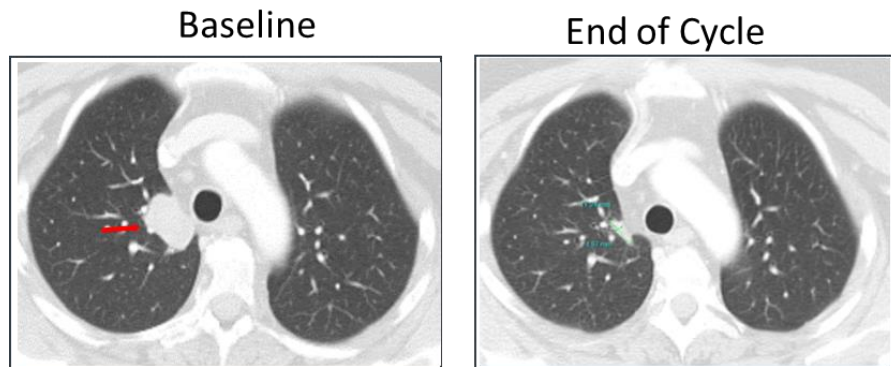


ADG126 (6mg/kg Q3W, 10mg/kg Q3W and Q6W) + pembrolizumab 200 mg Q3W

- No DLTs; most frequent TRAEs: fatigue (3), diarrhea (2), nausea (2) and vomiting (2)
- Most TRAEs were G1 and G2
- Two Pts (18%) had G3 TRAEs: one G3 diarrhea as late onset toxicity (C8 in 6 mg/kg Q3W cohort) and one G3 adrenal insufficiency (C3 in 10 mg/kg Q6W cohort); no G4/5 events
- Safety profile comparable to pembrolizumab monotherapy

ADG126 + Pembro Dose Escalation: PR in a Patient with Metastatic Endometrial Cancer

- Advanced adenocarcinoma of endometrium (MSI-H) with lung metastasis
- Previously received carboplatin + paclitaxel × 6 cycles followed with anastrozole as a maintenance therapy until new lung metastasis lesion developed
- ADG126 10mg/kg Q3W + pembro 200mg Q3W
- PR with a 33% and a 37% target lesion reduction at the end of C2 and C4, respectively



Courtesy of Tammy Lamb, M.D. Florida Cancer Specialists

	Lesion #	Location	Baseline	End of C2	End of C4
Target lesion	TL#1	Lung, Right	27 mm	18 mm	17mm
	Sum		27 mm	18 mm	17mm
Non-target lesion		N/A	N/A	N/A	N/A
New lesion				No	No
Overall response				PR (-33%)	PR (-37%)

ADG126 + Pembro Dose Escalation: PR in IO-experienced patient with Cervical Cancer Patient

- Advanced cervical cancer (stage IV squamous carcinoma) with mediastinal lymph node metastasis
- PD-L1 CPS score = 1, TMB high: 24 Muts/Mb
- Previously received 2 lines of therapies:
 - Carboplatin/paclitaxel/bevacizumab x 6 cycles
 - Pembrolizumab monotherapy x 9 cycles
- ADG126 10 mg/kg Q3W + Pembro 200 mg Q3W

	Lesion #	Location	Baseline	End of C2	End of C4	End of C6	End of C8
Target lesion	TL#1	Lymph node (Subcarinal)	25 mm	25 mm	21 mm	17 mm	13 mm
	TL#2	Lymph node (Pre-carinal)	29 mm	29 mm	30 mm	30 mm	25 mm
	Sum		54 mm	54 mm	51 mm	47 mm	38 mm
Non target lesion		Lymph node (Right Supra-clavicular)	Present	Present	Present	Present	Present
New lesion				No	No	No	No
Overall response				SD (+0%)	SD (-5.6%)	SD (-13%)	PR (-30%)*

* PR reported on April 28, after publication of AACR 2023 poster with data cutoff of March 14, 2023.

MSS CRC: Multi-Billion Market Opportunity Reflects Serious Global Unmet Need

US\$ 18.6B

CAGR of 3.3%
from 2022 to 2028

US\$ 24.1 B

95% of metastatic CRC patients are microsatellite stable (MSS) CRC

20% of patients with CRC have metastases at the time of diagnosis, and up to **50%** of patients with initially localized disease will develop metastases

1.9 million new CRC cases and 0.9 million deaths worldwide (2020)

Conclusion

- Both ADG116 (NEObody) & ADG126 (SAFEbody) have demonstrated compelling safety and differentiated efficacy profiles with repeat doses, both as monotherapy & in combo with PD-1
- The clinical activity of ADG116 (unmasked) demonstrates efficacy of targeting a unique epitope of CTLA-4 with strong ADCC and Treg depletion, while ADG126 (adds precision masking) provides evidence of improved clinical benefit by achieving much higher doses than first generation molecules
- Dose expansion cohorts are ongoing in MSS CRC with multiple dosing regimens being evaluated, including 10 mg/kg at Q3W and Q6W
- Potential in PD-1 resistant and first-line therapy for warm tumors, such as HCC collaboration with Roche evaluating ADG126 in 1L HCC with atezolizumab and bevacizumab
- Both candidates are designed to overcome the safety challenges of anti-CTLA-4 therapy, unlocking its full potential as a cornerstone of cancer care

2023 Milestones

- Establish registration path and strategy (e.g., recommended phase 2 dose, indication and design) for phase 2/3 pivotal trial of anti-CTLA-4 in combination with anti-PD-1 therapy in targeted tumors
 - ADG126 phase 2 proof-of-concept data from combination dose expansion cohorts
 - Advance ADG116 phase 2 combination dose expansion cohorts
- Providing path to registration for triple combination with Roche's atezolizumab/bevacizumab, advance ADG126 randomized phase 1b/2 trial in 1L HCC conducted by Roche; provide update on trial status
- Advance ADG206 phase 1 and IND-enabling programs, as resources allow
- Additional collaborations and/or technology licensing agreements