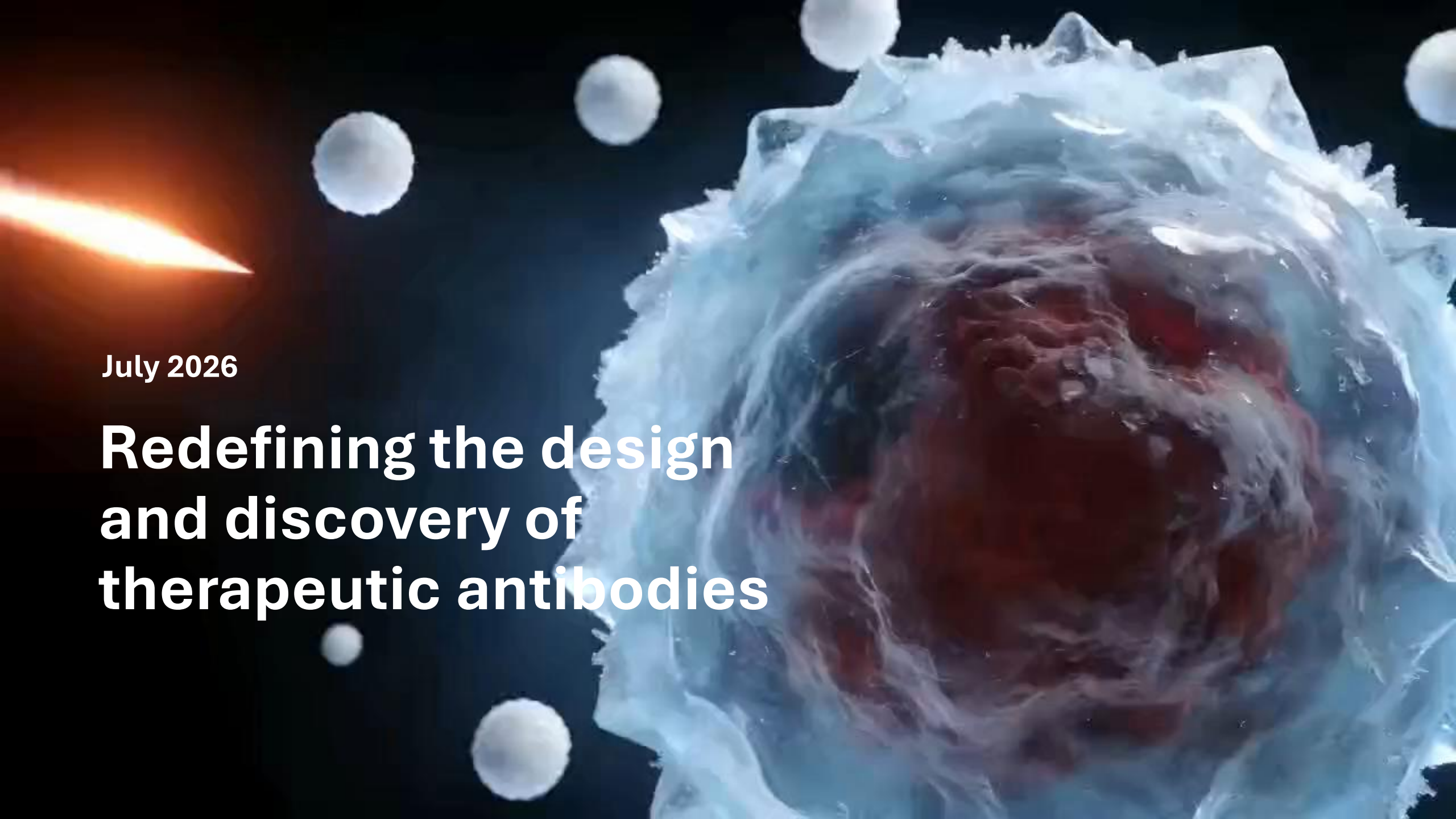

July 2026

Redefining the design and discovery of therapeutic antibodies

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Adagene has filed a shelf registration statement on Form F-3 (including a base prospectus, Registration No. 333-287161) and will file a prospectus supplement with the SEC for the offering to which this presentation relates. This presentation has been prepared solely for use by prospective investors in connection with a proposed offering of our equity securities and contains a summary of selected information to be included in a prospectus supplement to be filed with the SEC, and the accompanying prospectus. Before you invest in the offering to which this communication relates, you should read the base preliminary prospectus in that registration statement, the prospectus supplement related to the offering (when available) and the other documents Adagene has filed and will file with the SEC for more complete information about Adagene and the offering. You may get these documents for free by visiting EDGAR on the SEC website at www.sec.gov. Alternatively, Adagene , any underwriter or any dealer participating in the offering will arrange to send you the prospectus supplement, when available, by request at Leerink Partners LLC, Attention: Syndicate Department, 53 State Street, 40th Floor, Boston, Massachusetts 02109, by telephone at (800) 808-7525, ext. 6105, or by email at syndicate@leerink.com; or LifeSci Capital LLC, 1700 Broadway, 5th Floor, New York, New York 10019, or by email at legalnotices@lifescicapital.com.

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This presentation concerns product candidates that are or have been under clinical investigation and which have not yet been approved for marketing by the U.S. Food and Drug Administration, European Medicines Agency, The China National Medical Products Administration, or other foreign regulatory authorities. These product candidates are currently limited by U.S. Federal law to investigational use, and no representations are made as to their safety or effectiveness for the purposes for which they are being investigated.

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Company Highlights

Potential best-in-class anti-CTLA-4 with blockbuster opportunity

- ADG126 (Muzastotug): is a novel anti-CTLA-4 leveraging our proprietary masking technology, with FDA Fast Track Designation
- Positive interim efficacy results with minimal discontinuations in late-stage MSS colorectal cancer (CRC) without liver metastases
- Initial global addressable market for ADG126 in 3L+ CRC to exceed USD1Bn

SAFEbody® technology validated by strategic collaborations

- Existing technology licensing agreements with Sanofi, Exelixis and Third Arc
- Equity investment of up to USD25m from Sanofi
- Novel clinical collaboration with Incyte and Sanofi
- Adagene is eligible to receive milestone payment and royalties

Pipeline candidates showcase platform versatility

- ADG138 is a double-masked HER2xCD3 T cell engager
- Multiple masked T-cell engagers in discovery

Strong cash balance

- Consolidated unaudited cash balance: ~USD128m as of June 30, 2026
- Cash runway until late 2028

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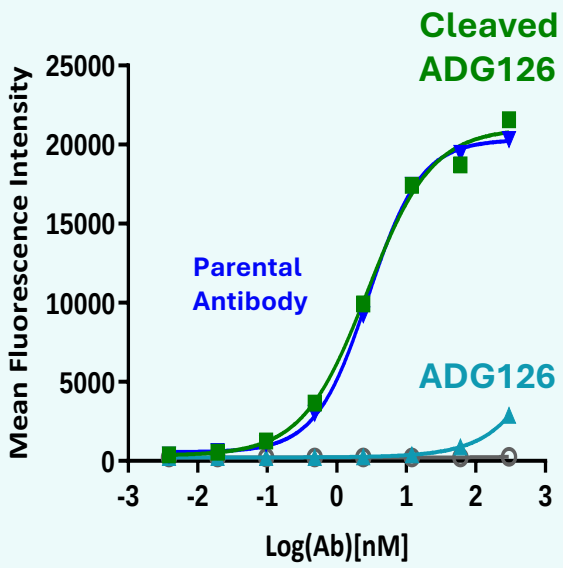
Adagene Pipeline – Overcoming Complex Target Challenges, Featuring Masked Anti-CTLA-4 as Lead Program

Program & Technology	Target	Development stage				
		Discovery	IND Enabling	Ph 1	Ph 2	Pivotal
ADG-126 (muzastotug) Masked antibody	**CTLA-4**					
ADG-138 Masked T-cell engager	HER2xCD3					
ADG-152 Masked T-cell engager	CD20xCD3					

ADG126(Muzastotug): A Novel Anti-CTLA-4 with Epitope-Enhanced ADCC Incorporating a Protease-Cleavable Mask

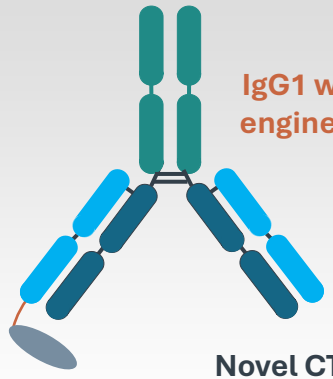
Protease cleavable mask enabling tumor-specific activation

Binding to CTLA-4-Expressing Cells



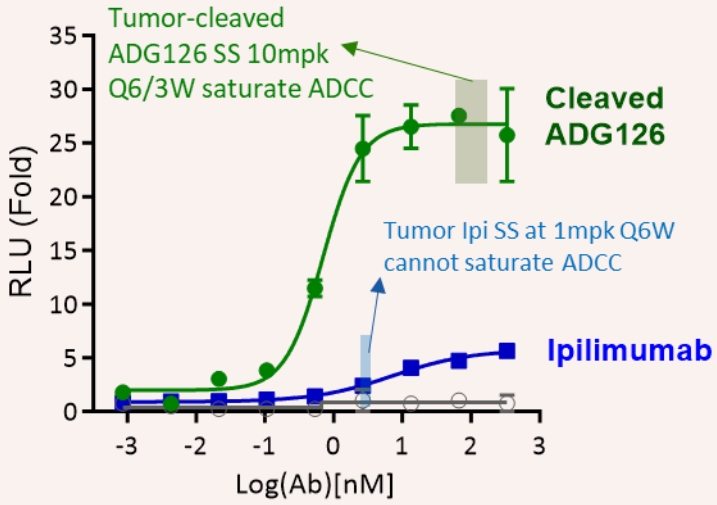
- Masking enables 20X higher dosing level over ipilimumab, consistent with our GLP-tox data

10x ADCC via Epitope-Enhanced FcgR Affinity



Enhanced ADCC due to a differentiated epitope

ADCC Signaling Reporter Cell Activity Triggered by anti-CTLA-4 Antibodies



- 10X higher ADCC of cleaved ADG-126 over ipilimumab without Fc engineering

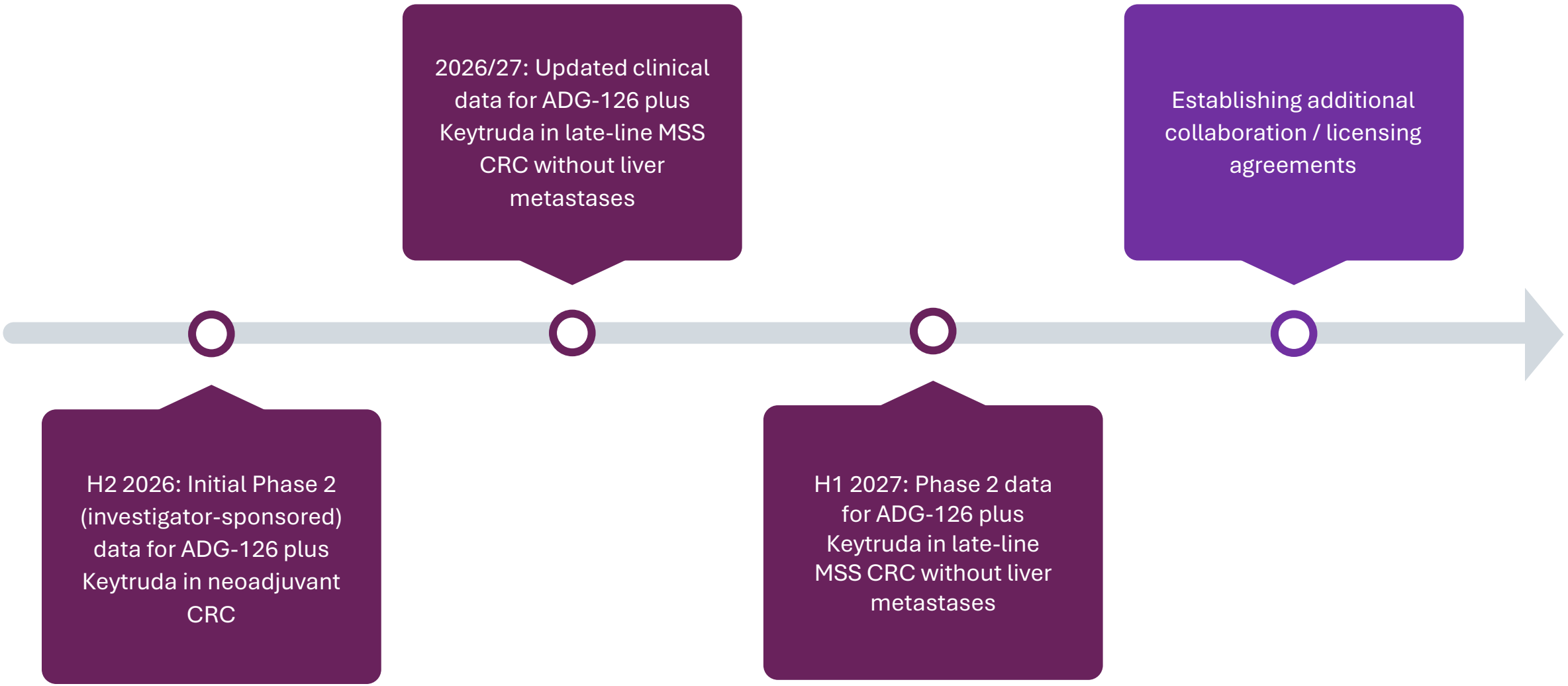
Clinical Collaboration with Incyte to Evaluate ADG126 in Combination with Incyte's TGFßR2xPD-1 Bispecific in Patients with MSS CRC

- Phase 1 study of INCA33890 and ADG126 expected to begin in 2026 in 3L MSS CRC patients with and without liver metastases. The study will be sponsored and conducted by Incyte; Adagene will provide clinical supply of ADG126
- As a monotherapy, INCA33890 demonstrated promising clinical efficacy and safety results in immune checkpoint sensitive and insensitive cancers, including MSS CRC (ORR: 15%, including 12% in patients with liver mets and 23% in those without)
- The complementary mechanisms may help enhance anti-tumor immune responses particularly for patients with liver metastases, who have an especially poor prognosis and limited treatment options

Strategic Investment and Clinical Collaboration from Sanofi in 2025

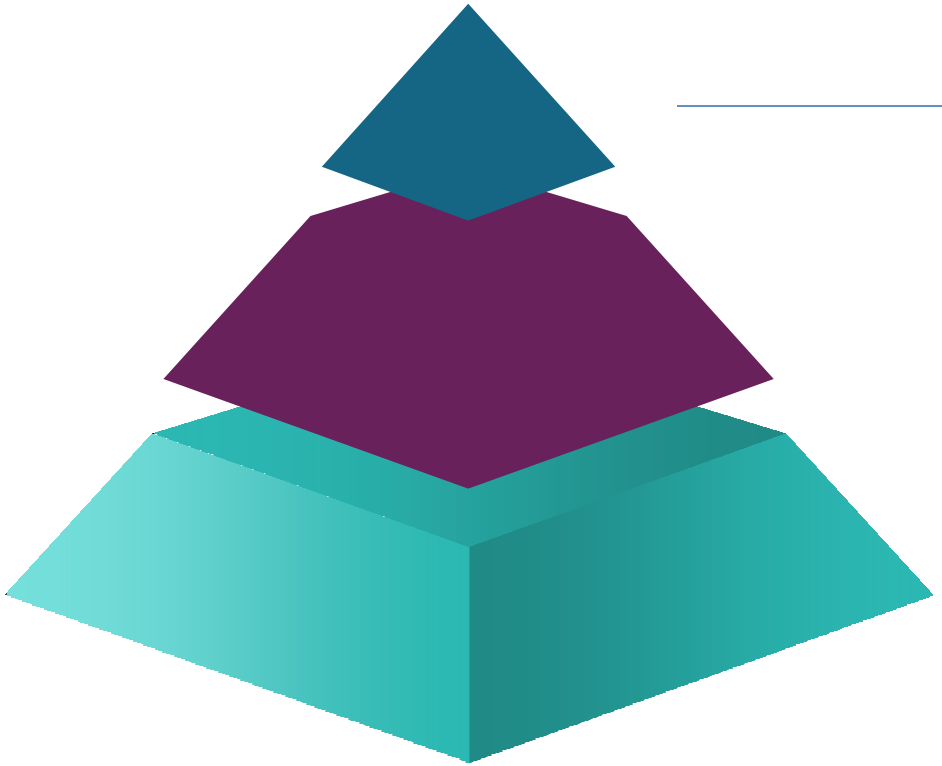
- Sanofi to invest up to USD25m to support Adagene's R&D, including a randomized phase 2 trial of ADG126 with pembrolizumab in advanced MSS CRC without liver metastases.
- Clinical Collaboration: Adagene to supply ADG126 for a Sanofi-sponsored phase 1/2 trial in combination with SAR445877 (PD-1 x IL-15 fusion protein) on adults with advanced solid tumors, enrolling 100+ patients.
- Option on Third SAFEbody: Sanofi exercised option on third SAFEbody discovery program, triggering an option exercise fee, as well as potential milestone and royalty payments.

2026/2027 Objectives



Updated Phase 1b/2 Results of ADG126/Pembrolizumab in advanced MSS CRC without liver metastases

3L+ MSS CRC Without Liver Metastases is a Substantial Initial Opportunity for ADG-126



Initial Opportunity
3L+ NLM MSS CRC
~10-13k patients*

1L MSS CRC
~120k patients*

Neoadjuvant (Stage II-III) MSS/MSI-H CRC
~140k patients*

- Patients without liver metastases (NLM) represent up to **25-35% of all MSS CRC** patients
- **Regulatory precedents** for Phase 3 trials in MSS CRC without liver metastases
- Thanks to its safety data, ADG-126 plus pembrolizumab could potentially be added to the current 3L+ standard of care
- Future cohorts to evaluate the potential of **novel combinations** in 3L+ patients **with and without liver metastases**

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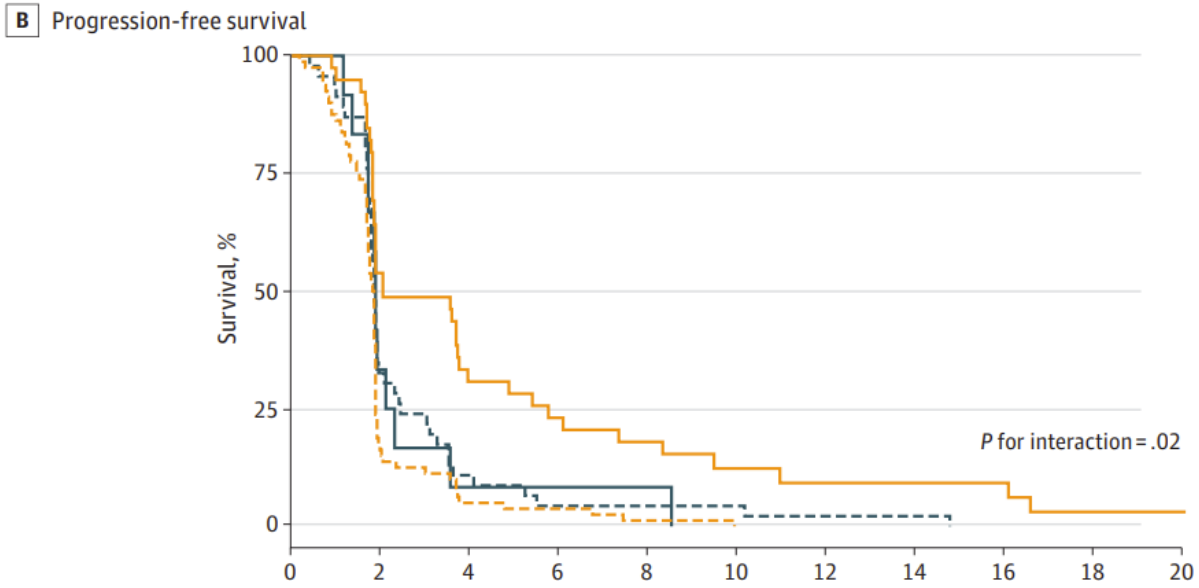
Source: Cerner/Envisa 2022 Drug Treated Patients and CancerMpact Treatment Architecture
* US/EU5 patients treated annually

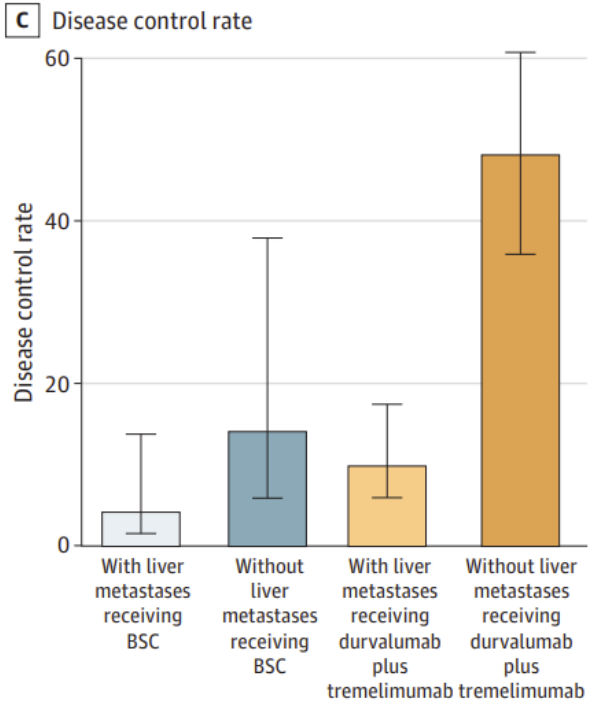
The Standard of Care Treatments for Late-Line MSS CRC Remain Minimally Effective, Including in Patients Without Liver Mets

Compounds	Sunlight regimen TAS102 plus Avastin	Fruquintinib	
		w/o Liver mets	with Liver mets
ORR (%)	6.1	4.3	4.9
≥ Grade 3 TRAEs	72%	36-46%	
Discontinuation Rate	13%	15-20%	

Source: Josep Tabernero et al. 2023 ASCO Gastrointestinal; Gerald W. Prager et al. N Engl J Med 2023 May 04;388(18); Shukui Qin et al. 2019 CSCO; Jin Li et al. JAMA. 2018;319(24):2486-2496;

The First Generation of Anti-CTLA-4 Failed To Show A Significant Benefit in Late-Line MSS CRC Without Liver Mets…



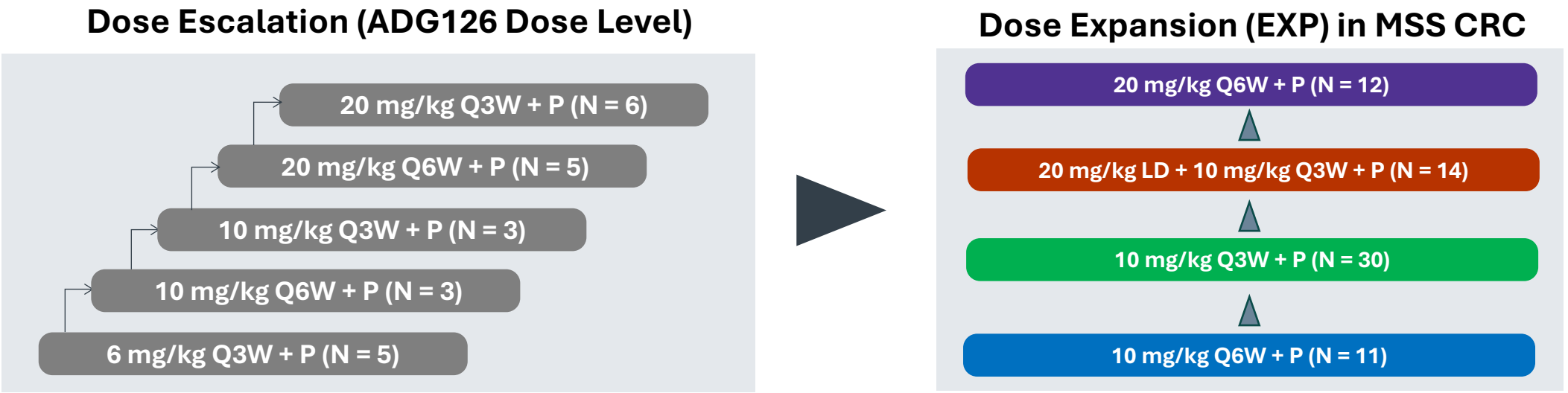


- Assuming that the sole response occurred in patients without liver metastases, AstraZeneca's durvalumab/tremelimumab (anti-PD-L1 plus anti-CTLA-4) generated an **ORR of 2.5%** in that subgroup.

Source: Chen et al., Liver Metastases and Immune Checkpoint Inhibitor Efficacy in Patients With Refractory Metastatic Colorectal Cancer, JAMA Network Open, December 5, 2023

Methods and Study Design Schema: ADG126-P001 Study

- This is a Phase 1b/2, open-label, multicenter dose escalation and expansion combination study of ADG126 + pembrolizumab (200 mg, Q3W) in advanced solid tumors. The study design schema for the dose escalation (DE) and dose expansion (EXP) MSS CRC cohorts is shown below:



MSS CRC Patients' Characteristics

- As of Jan 24, 2026, 102 Pts have been treated in ADG126-P001: 22 Pts in DE (all comers) and 80 Pts in EXP (primarily MSS CRC).

- 67 Pts from EXP are metastatic MSS CRC.

Baseline Characteristics of MSS CRC Patients

Characteristics	N=67
Median Age (Years), (range)	58 (26-77)
Female, n(%)	36 (54)
Race, n(%)	
Asian, (n%)	45 (67)
White, n(%)	22 (33)
ECOG 0/1, n(%)	26 (39)/41 (61)
Prior line of therapy ≥ 3, n(%)	21 (31)
Prior immunotherapy, n(%)	0
Demographics	
US, n	26 (39)
SK, n	39 (58)
CHN/HK, n	2 (HK=2) (3)
Without Liver Metastasis (NLM), n(%)	67 (100)
Peritoneal involvement, n(%)	15 (22)

ADG126/Pembrolizumab Has Demonstrated Robust Dose-Dependent Efficacy Data

ADG126 Dose Level + Pembro 200mg Q3W	10 mg/kg			20 mg/kg		
Subpopulation (N)	Combined (N=39)	Q6W (10)	Q3W (29)	Combined (N=26)	Q6W (12)	20 mg/kg x1 +10 mg/kg Q3W (14)
ORR, % (95% CI)	13 (4-27)	0[a] (0-31)	17[b] (6-36)	31 (14-52)	25 (5-57)	36 (13-65)
BoR, N (%)						
CR	0	0	0	1 (4)	1 (8)	0
PR	5 (13)	0	5[b] (17)	7 (27)	2 (17)	5 (36)
SD	24 (62)	7 (70)	17 (59)	14 (54)	7 (58)	7 (50)
DCR (CR+PR+SD), %, (95% CI)	74 (58-87)	70 (35-93)	76 (56-90)	85 (65-96)	83 (52-98)	86 (57-98)
6-month CBR, %, (95% CI)	31 (17-48)	20 (3-56)	34 (18-54)	38 (20-59)	33 (10-65)	43 (18-71)
Median PFS, months (95%CI)	4.8 (2.6-6.7)	4.5 (1.4-7.1)	4.8 (2.6-6.7)	6.7 (2.7-NA)	4.9 (1.2-NA)	15.4 (2.6-NA)
6-month PFS, %, (95% CI)	39.6 (24.3-54.6)	40 (12.3-67)	39.6 (21.9-56.8)	50.4 (29.5-68.1)	45.5 (16.7-70.7)	54.5 (25.4-76.5)

Efficacy evaluable set (participants who received ≥1 post-baseline scheduled imaging scan) – Data cutoff date: 20260124

a. One patient with target lesion assessed as "PR", overall assessment as "PD" due to new lesion.

b. Including one unconfirmed PR (10 mg/kg Q3W)

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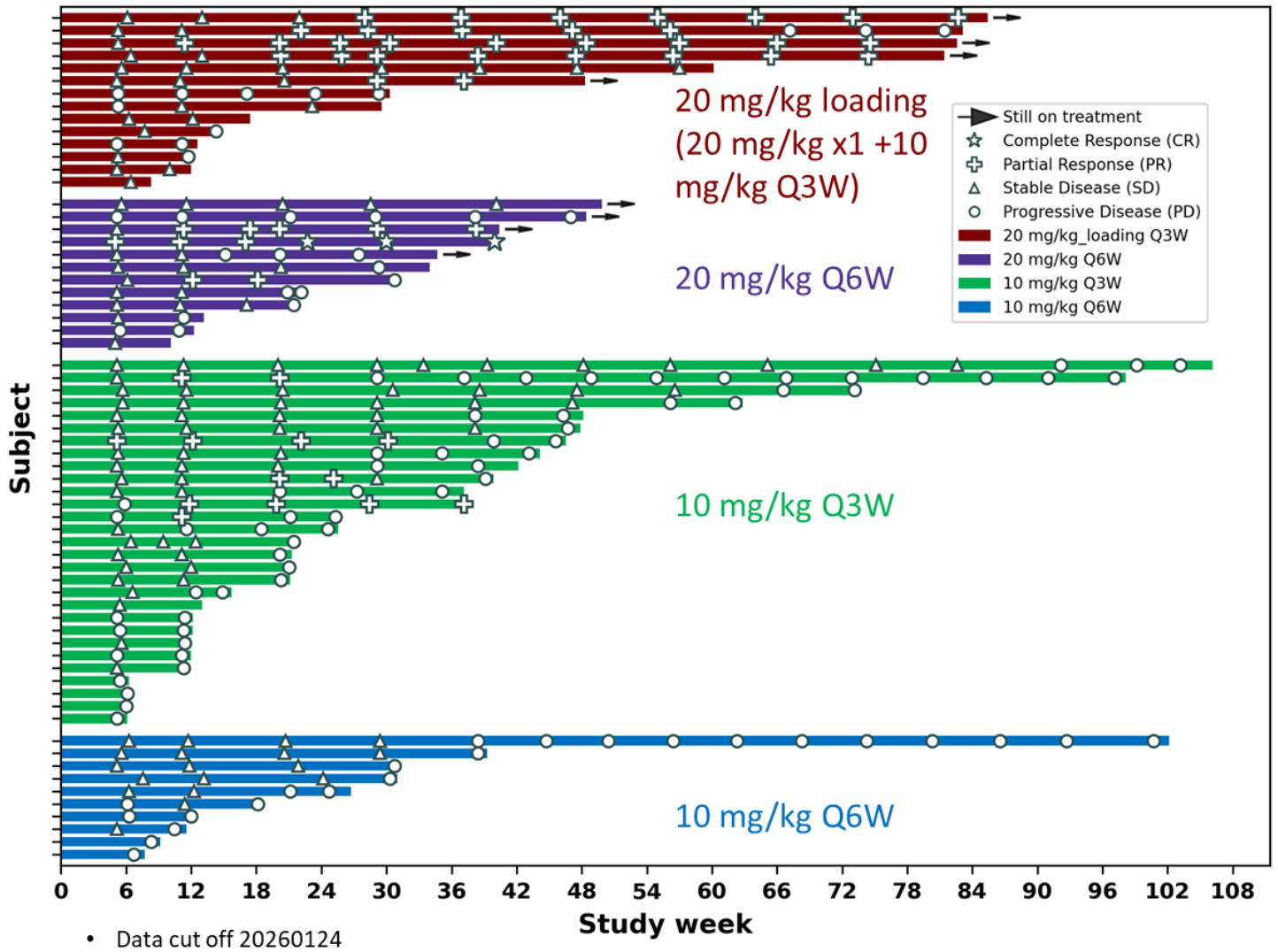
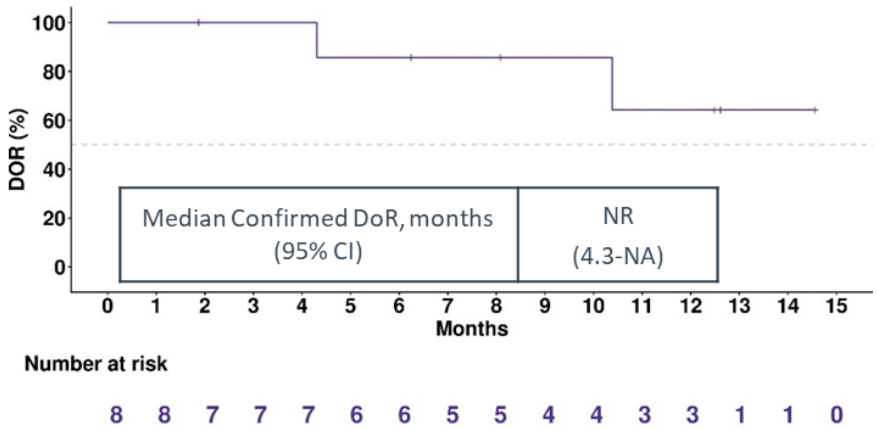
Clinical Efficacy: Longer DOR for the 20 mpk Dose Cohorts

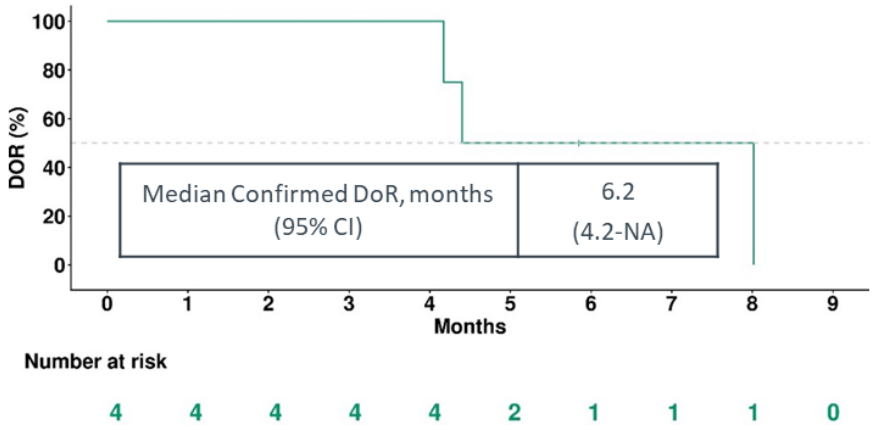


- Data cut off 20260124

20 mg/kg DoR K-M Curve



10 mg/kg DoR K-M Curve

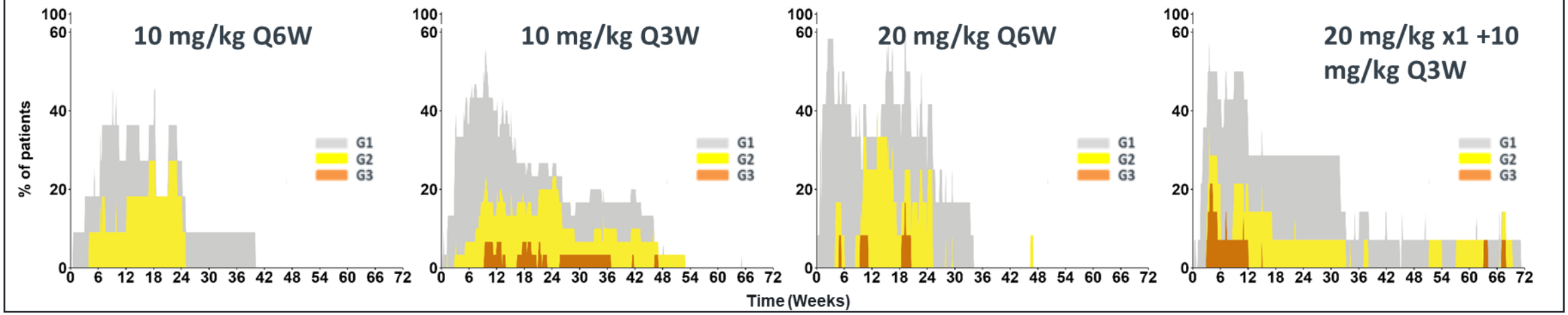


TRAEs across Dose Levels of ADG126 + Pembrolizumab

Dose levels (mg/kg)	N	All G n (%)	G1 n (%)	G2 n (%)	G3 n (%)	Discont. Rate (%)
All	**67**	**57 (85)**	**15 (22)**	**26 (39)**	**16 (24)**	**3 (4)**
10 mg/kg Cohorts	**41**	**34 (83)**	**10 (24)**	**18 (44)**	**6 (15)**	**3 (7)**
10 mg/kg Q6W	11	8 (73)	2 (18)	6 (55)	0	0
10 mg/kg Q3W	30	26 (87)	8 (27)	12 (40)	6 (20)	3 (10%)
20 mg/kg Cohorts	**26**	**23 (88)**	**5 (19)**	**8 (31)**	**10 (38)**	**0**
20 mg/kg Q6W	12	11 (92)	2 (17)	6 (50)	3 (25)	0
20 mg/kg x1 +10 mg/kg Q3W	14	12 (86)	3 (21)	2 (14)	7 (50)	0

- **Overall:** No dose-limiting toxicities (DLT) or G4/5 TRAEs; low discontinuation rate (4%).
- **10 mg/kg Q3W:** Average follow-up time of 16.1 months; manageable AE profile consistent with previous reports.
- **20 mg/kg Q6W:** Lower G3 TRAE% than that from 20 mg/kg x1 +10 mg/kg Q3W cohort.
- **20 mg/kg x1 +10 mg/kg Q3W:** Manageable AE profile with prompt dose modification. Infrequent use of infliximab.

Safety kinetics data



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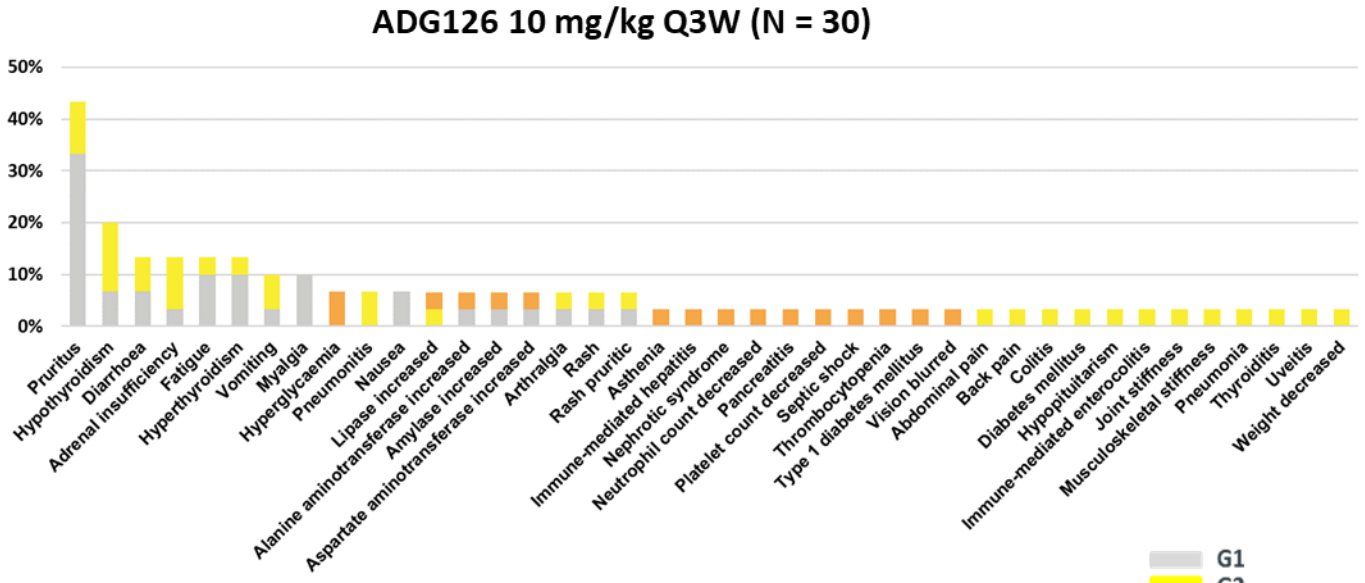
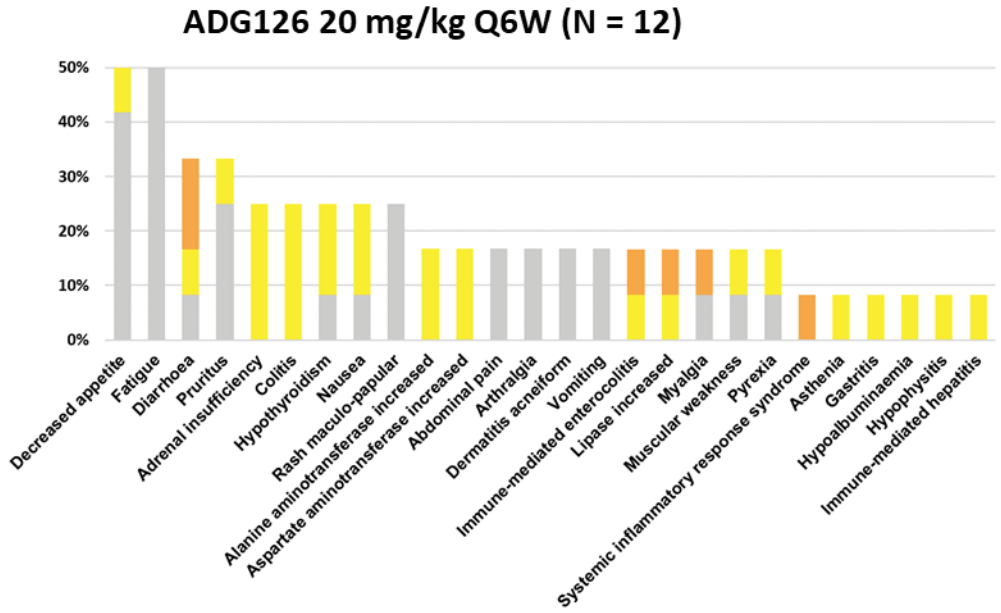
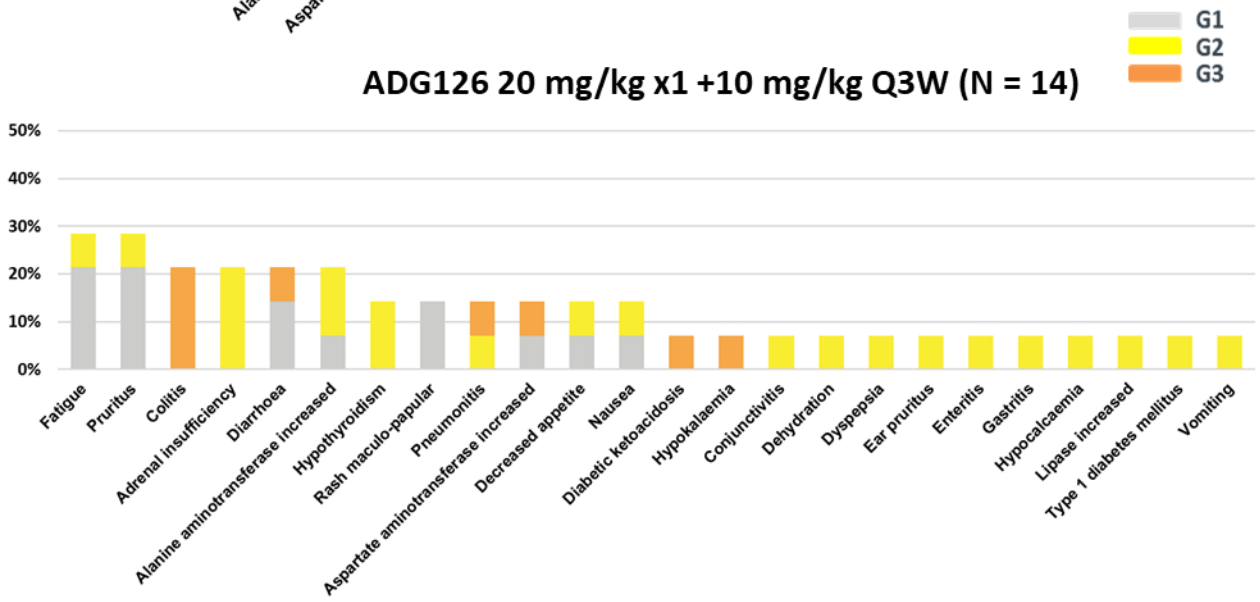
Clinical Safety Summary







Excluding Preferred Term with G1 TRAE that occurred only once.

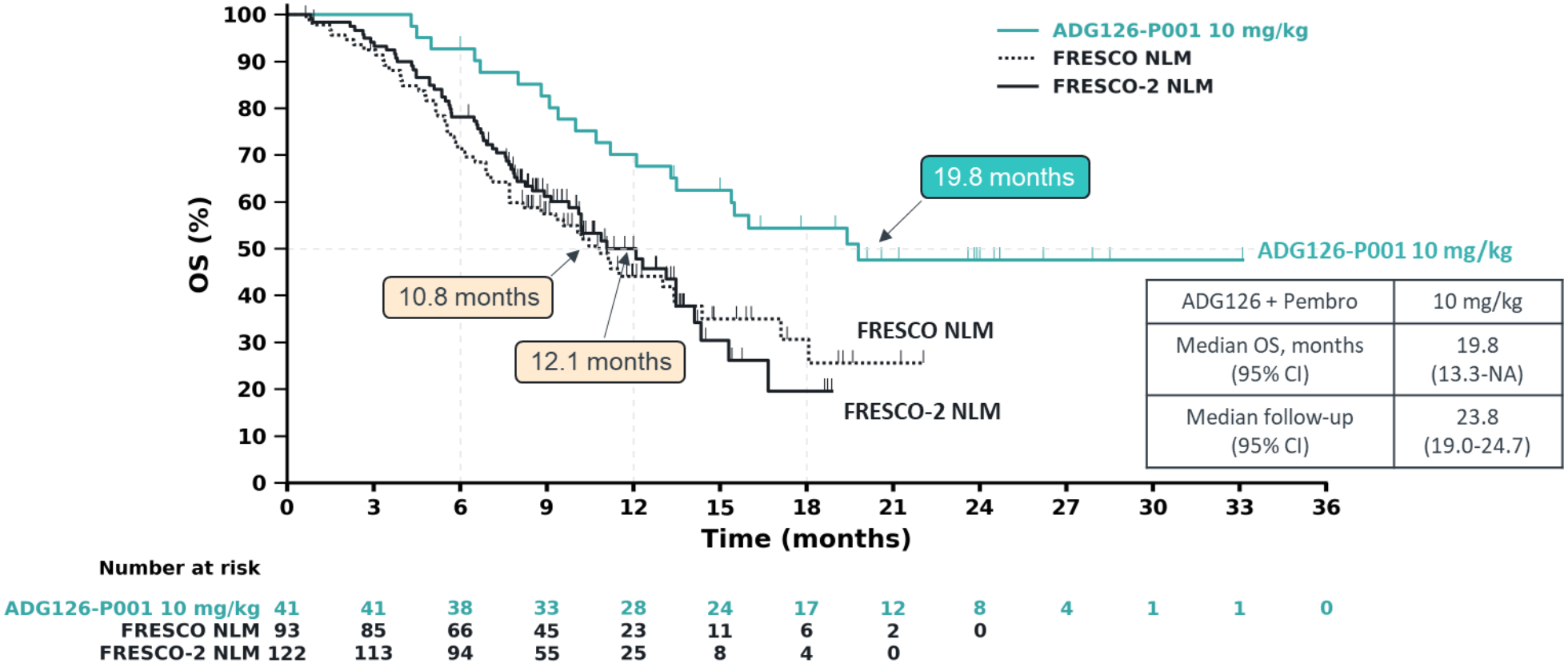
- Data cut off 20260124

Summary of Key TRAEs

Group	Dose levels (mg/kg)	Safety (TRAEs), N (%)										
		Patients Dosed	Diarrhea/Colitis/ Immune-mediated enterocolitis			Pneumonitis			Hepatitis (Hepatitis/LFT/AST/ALT)			Discontinuation Rate (%)
			G1 n (%)	G2 n (%)	G3 n (%)	G1 n (%)	G2 n (%)	G3 n (%)	G1 n (%)	G2 n (%)	G3 n (%)	
ADG126/ Pembrolizumab	All	67	1 (1)	7 (10)	6 (9)	1 (1)	3 (4)	1 (1)	1 (1)	4 (6)	3 (4)	3 (4)
	10 mg/kg Q6W	11	0	1 (9)	0	1 (9)	0	0	0	0	0	0
	10 mg/kg Q3W	30	1 (3)	4 (13)	0	0	2 (7)	0	0	0	2 (7)	3 (10)
	20 mg/kg Q6W	12	0	2 (17)	2 (17)	0	0	0	0	3 (25)	0	0
	20 mg/kg x1 +10 mg/kg Q3W	14	0	0	4 (29)	0	1 (7)	1 (7)	1 (7)	1 (7)	1 (7)	0

Data cut off 20260124

Overall Survival Across Dose Cohorts of ADG126 + Pembro vs Fruquintinib Historical Controls



ADG126 + Pembro	10 mg/kg
Median OS, months (95% CI)	19.8 (13.3-NA)
Median follow-up (95% CI)	23.8 (19.0-24.7)

Data cut off 20260124

The data presented above were derived from separate clinical trials and not from a head-to-head trial. Cross-trial comparisons should be interpreted with caution, as differences in trial design, patient populations, endpoints, inclusion and exclusion criteria, and other methodological factors may significantly affect observed results. Accordingly, no direct comparison of efficacy or safety between therapies should be inferred from the data presented.

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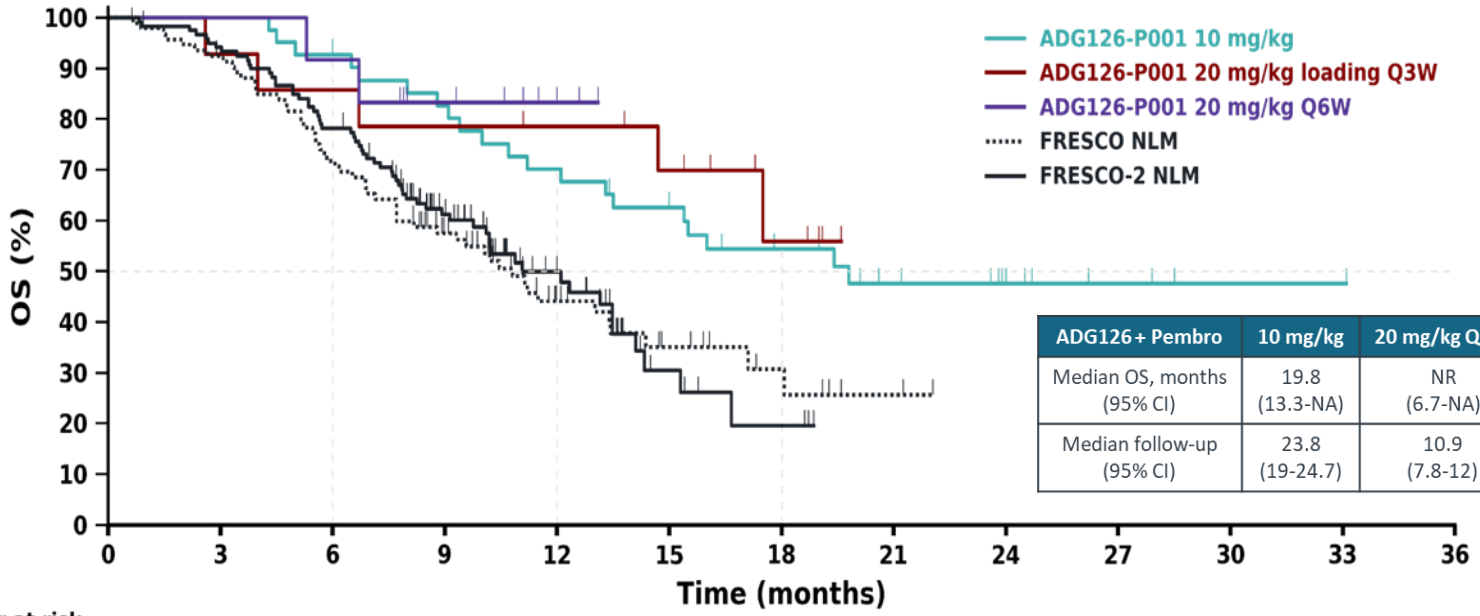
Sources: FRESCO: Li J.et al. JAMA. 2018;319(24):2486–2496; FRESCO-2: Garcia-Carbonero, R. et al .Annals of Oncology, Volume 35, S439. Fruq: fruquintinib. BSC: Best Standard of Care (used in trial)

Overall Survival Across Dose Cohorts of ADG126 + Pembro vs Fruquintinib Historical Controls



ADG126+ Pembro	10 mg/kg	20 mg/kg Q6W	20 mg/kg LD
Median OS, months (95% CI)	19.8 (13.3-NA)	NR (6.7-NA)	NR (6.7-NA)
Median follow-up (95% CI)	23.8 (19-24.7)	10.9 (7.8-12)	18.7 (13.8-19.1)

Number at risk

ADG126-P001 10 mg/kg	41	41	38	33	28	24	17	12	8	4	1	0
ADG126-P001 20 mg/kg loading Q3W	14	13	12	11	10	8	4	0				
ADG126-P001 20 mg/kg Q6W	12	12	11	7	3	0						
FRESCO NLM	93	85	66	45	23	11	6	2	0			
FRESCO-2 NLM	122	113	94	55	25	8	4	0				

The data presented above were derived from separate clinical trials and not from a head-to-head trial. Cross-trial comparisons should be interpreted with caution, as differences in trial design, patient populations, endpoints, inclusion and exclusion criteria, and other methodological factors may significantly affect observed results. Accordingly, no direct comparison of efficacy or safety between therapies should be inferred from the data presented.

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Landmark OS: ADG126-P001 vs FRESCO and Agenus in NLM Patients

ADG126 Dose Level + Pembro 200mg Q3W	10 mg/kg	20 mg/kg	Fresco NLM		Agenus (bot+bal) NLM		
Subpopulation (N)	Combined Q3W & Q6W (N=41)	20 mg/kg x1 +10 mg/kg Q3W (N=14)	Fresco (N=93)	Fresco-2 (N=122)	2024 report NLM (N=77)	2025 report NLM 3L+ (N=123)	2025 report NLM 4L+ (N=37)
12-month OS, %, (95% CI)	70.1 (53.4-81.8)	78.6 (47.2-92.5)	*44.1**	*50.0**	**69**	*64.5**	*54.2**
24-month OS, %, (95% CI)	47.6 (30.8-62.6)	NA	*NA*	*NA*	*45.9**	**42**	**43**
Median follow-up (95% CI)	23.8 (19.0-24.7)	18.7 (13.8-19.1)	*13.3#*	*11.3#*	13.0	25.8 (19.4–31.2)	19.4 (18.5–28.8)

** OS rates for Agenus study were estimated from their published OS curves.*
 # Median follow-up for ITT population.

The data presented above were derived from separate clinical trials and not from a head-to-head trial. Cross-trial comparisons should be interpreted with caution, as differences in trial design, patient populations, endpoints, inclusion and exclusion criteria, and other methodological factors may significantly affect observed results. Accordingly, no direct comparison of efficacy or safety between therapies should be inferred from the data presented.

Fresco:
Qin S, Xu RH, Shen L, Et Al. Subgroup Analysis By Liver Metastasis In The FRESCO Trial Comparing Fruquintinib Versus Placebo Plus Best Supportive Care In Chinese Patients WithMetastatic Colorectal Cancer. Onco Targets Ther. 2021;14:4439
Garcia-Carbonero R, Dasari NA, Eng C, et al. 520P Efficacy and safety of fruquintinib in patients with refractory metastatic colorectal cancer with and without liver metastasis: A subgroup analysis of the phase III FRESCO-2 trial. Ann Onc 2024;35:S439
Agenus:
Bullock AJ, Schlechter BL, Fakih MG, Et Al. Botensilimab Plus Balstilimab In Relapsed/Refractory Microsatellite Stable Metastatic Colorectal Cancer: A Phase 1 Trial. Nat Med. 2024;30:2558-67
Botensilimab plus balstilimab in an expanded cohort of 123 patients with metastatic microsatellite stable colorectal cancer and no active liver metastases

AACR 2026

Roche Morpheus Collaboration on 1L HCC - Patient characteristics

Table 1. Baseline Characteristics

	Atezo+Bev (N=40)	Muza 6 mg/kg Q6W Atezo+Bev (N=6)
Median Age (Years), (range)	66.5 (42-86)	65 (54-82)
Female, n(%)	5(12.5)	1(16.7)
Race, n(%)		
Other, n(%)	14(35)	2(33.3)
Asian, n(%)	16(40)	2(33.3)
White, n(%)	10(25)	2(33.3)
ECOG 0/1, n(%)	31(77.5)/9(22.5)	5(83.3)/1(16.7)
Child-Pugh Class A5/A6/B7, n(%)	28(70)/11(27.5)/1(2.5)	5(83.3)/1(16.7)/0
Metastatic disease, n(%)	17(42.5)	1(16.7)
BCLC Stage at study entry		
A1	1(2.5)	0
A4	1(2.5)	0
B	9(22.5)	1(20)
C	28(70)	4(80)
D	1(2.5)	0

	Atezo+Bev (N=40)	Muza 6 mg/kg Q6W Atezo+Bev (N=6)
Prior cancer surgery	7(17.5)	2(33.3)
Prior cancer radiotherapy	6(15)	0
MVI and/or EHS at study entry	20(50)	2(33.3)
Varices at enrollment	10(25)	2(33.3)
Varices treated	4(23.5)	1(100)
Disease caused by Hepatitis B	9(22.5)	5(83.3)
Disease caused by Hepatitis C	12(30)	1(16.7)
Disease caused by Alcohol	8(20)	2(33.3)
Disease caused by Non-viral Etiology	19(47.5)	0
Baseline Alpha Fetoprotein <400µg/L	20(50)	6(100)

Phase 1b of ADG126 (Muza) with Atezolizumab and Bevacizumab in 1L HCC – Clinical Efficacy Data

RECIST v1.1

	Atezo+Bev (c) (N=40)	Muza 6 mg/kg Q6W Atezo+Bev (N=6)
ORR, % (95% CI)	17.5 (7.3-32.8)	50.0 (11.8-88.2)
BoR, N (%)		
CR	1 (2.5)	0
PR	6 (15.0)	3 (50.0)
SD*	19 (47.5)	2 (33.3)
DCR# %, (95% CI)	52.5 (36.1-68.5)	83.3 (35.9-99.6)
Median DoR, months (95%CI)	NR (NA-NA)	NR (>16 months) (4.2-NA)
Median PFS, months (95%CI)	4.3 (2.8-11.4)	8.2 (5.6-NA)
Median OS, months (95%CI)	17.5 (13.0-27.1)	NR (>22 months) (7.7-NA)
Median duration of follow-up (months)	17.2	18.8

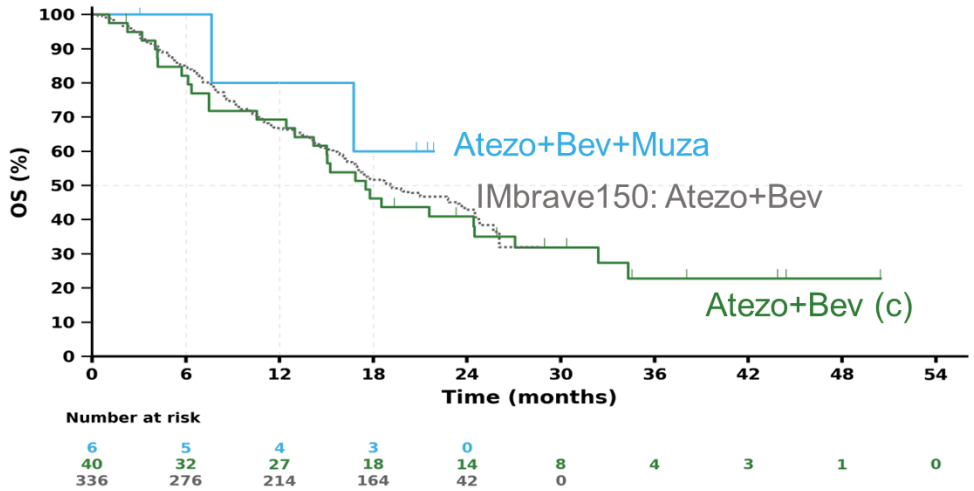
HCC-specified modified RECIST v1.1

	Atezo+Bev (c) (N=40)	Muza 6 mg/kg Q6W Atezo+Bev (N=6)
ORR, % (95% CI)	32.5 (18.6-49.1)	66.7 (22.3-95.7)
BoR, N (%)		
CR	5 (12.5)	0
PR	8 (20.0)	4 (66.7)
SD*	15 (37.5)	1 (16.7)
DCR# %, (95% CI)	57.5 (40.9-73.0)	83.3 (35.9-99.6)
Median DoR, months (95%CI)	14.4 (4.2-NA)	NR (>16 months) (2.7-NA)
Median PFS, months (95%CI)	5.5 (4.2-11.4)	8.2 (5.6-NA)
Median OS, months (95%CI)	17.5 (13.0-27.1)	NR (>22 months) (7.7-NA)
Median duration of follow-up (months)	17.2	18.8

Criteria for disease control is either response and/or stable disease or better for at least 12 weeks.

* Patients were classified as "Stable Disease" if assessment was at least 6 weeks from randomization.

	Median OS, months (95% CI)
Muza 6 mg/kg Q6W + Atezo+Bev (n=6)	NR (7.66-NA)
Atez+Bev (c) (n=40)	17.51 (12.98-27.07)
IMbrave150: Atezo+Beva (n=336)	19.2 (17.0-23.7)



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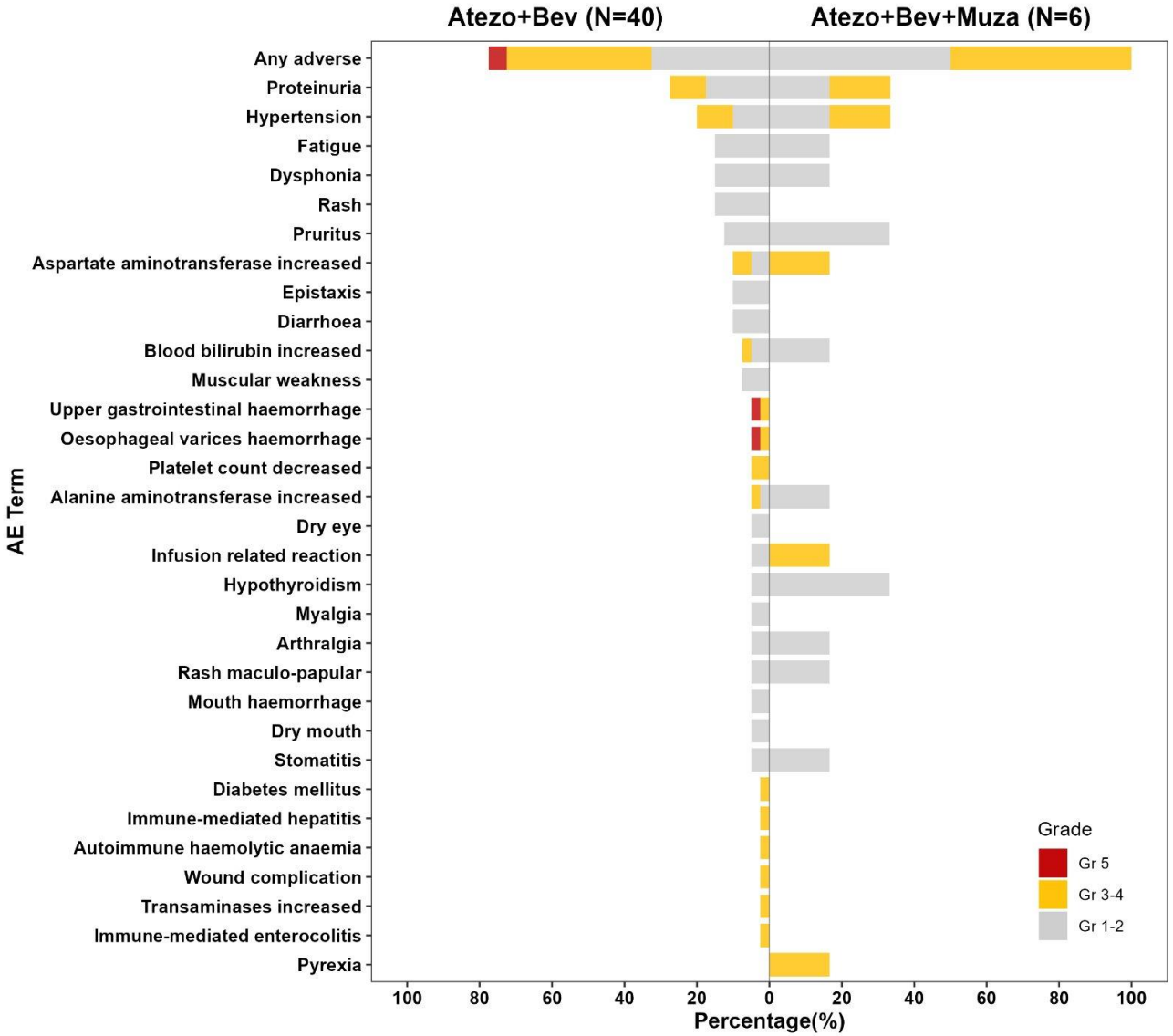
Phase 1b of ADG126 (Muza) with Atezolizumab and Bevacizumab in 1L HCC – Safety Data

Safety Summary	Atezo + Bev (n=40)	Muza + Atez + Bev (n=6)
TEAEs (all grades)	40 (100)	6 (100)
Grade≥3	28 (70)	4 (67)
Serious AEs	22 (55)	2 (33)
TRAEs (all grades)	31 (78)	6 (100)
TR Grade≥3	18 (45)	3 (50)
TR Serious AEs	9 (23)	2 (33)
TEAE leading to bev discontinuation	3 (8)	2 (33)
TEAE leading to atezo +bev discontinuation	4 (10)	0
TEAE leading to ADG126 discontinuation	/	0
Drug discont, rate n(%)	7 (18)	2 (33)



- In the triplet cohort, Bev was discontinued for 2 patients without impacting Muza + Atezo treatment, illustrating treatment flexibility for the triple combo
- Muza safety allows for continuous dosing without impacting Atezo + Bev

Phase 1b of ADG126 (Muza) with Pembrolizumab and Fruquintinib in advanced MSS CRC without liver mets – Clinical Safety Data

Characteristics	N=9
Median Age, years(range)	48 (29-78)
Female, n(%)	2 (22)
Race, n(%)	
Other, n(%)	2 (22)
White, n(%)	7 (78)
ECOG 0/1, n(%)	7 (78)/2 (22)
Prior line of therapy ≥ 3, n(%)	5 (56)

Characteristics	N=9
Prior immunotherapy, n(%)	0
Demographics	
US (n%)	9 (100)
With Liver Metastasis (NLM), n(%)	0
Peritoneal involvement, n(%)	1 (11)
Prior fruquintinib treatment, n(%)	0

Treatment Emergent Adverse Events

Dose levels (Muza mg/kg)	N	All G: N (%)	G1: N (%)	G2: N (%)	G3: N(%)	Discont. Rate (%)
All	9	9 (100)	0	4 (44)	5 (56)	0
10 mg/kg Q6W	4	4 (100)	0	2 (50)	2 (50)	0
15 mg/kg Q6W	5	5 (100)	0	2 (40)	3 (60)	0

Treatment Related Adverse Events

Dose levels (Muza mg/kg)	N	All G: N (%)	G1: N (%)	G2: N (%)	G3: N(%)	Discont. Rate (%)
All	9	9 (100)	0	5 (56)	4 (44)	0
10 mg/kg Q6W	4	4 (100)	0	3 (75)	1 (25)	0
15 mg/kg Q6W	5	5 (100)	0	2 (40)	3 (60)	0

- Discontinuation Rate: 0% for the combination regimen, compared to 15–20% historical discontinuation rate for Fruq monotherapy (FRESCO/FRESCO-2).
- Overall Profile: Manageable and transient, demonstrating safety comparable to Fruq monotherapy (historical Gr3+ TEAEs of 61–63%; Gr3+ TRAEs of 36–46%) despite the addition of dual immunotherapy.

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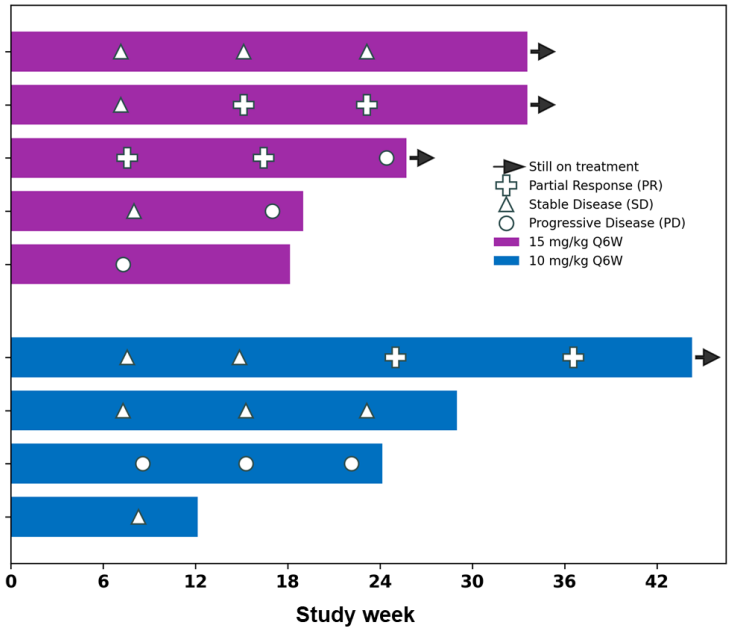
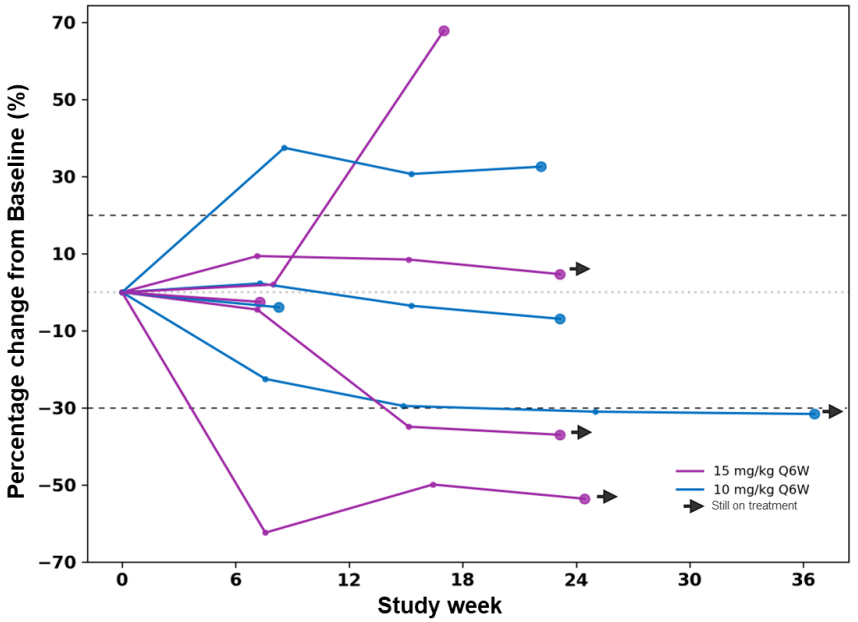
Phase 1b of ADG126 (Muza) with Pembrolizumab and Fruquintinib in advanced MSS CRC without liver mets – Clinical Efficacy Data

Muza Dose Level + Pembro + Fruq	10 mg/kg Q6W (4)	15 mg/kg Q6W (5)
ORR, % (95% CI)	25 (1-81)	40 (5-85)
BoR, N (%)		
PR	1 (25)	2 (40)
SD	2 (50)	2 (40)
CBR (CR, PR, or SD ≥6 months)	25 (1-81)	40 (5-85)
DCR (CR+PR+SD), % (95% CI)	75 (19-99)	80 (28-99)
Median PFS, months (95% CI)	NR (2-NA)	5.6 (1.7-NA)
Median follow-up, months (95% CI)	6.7 (5.6-NA)	5.9 (4.2-NA)





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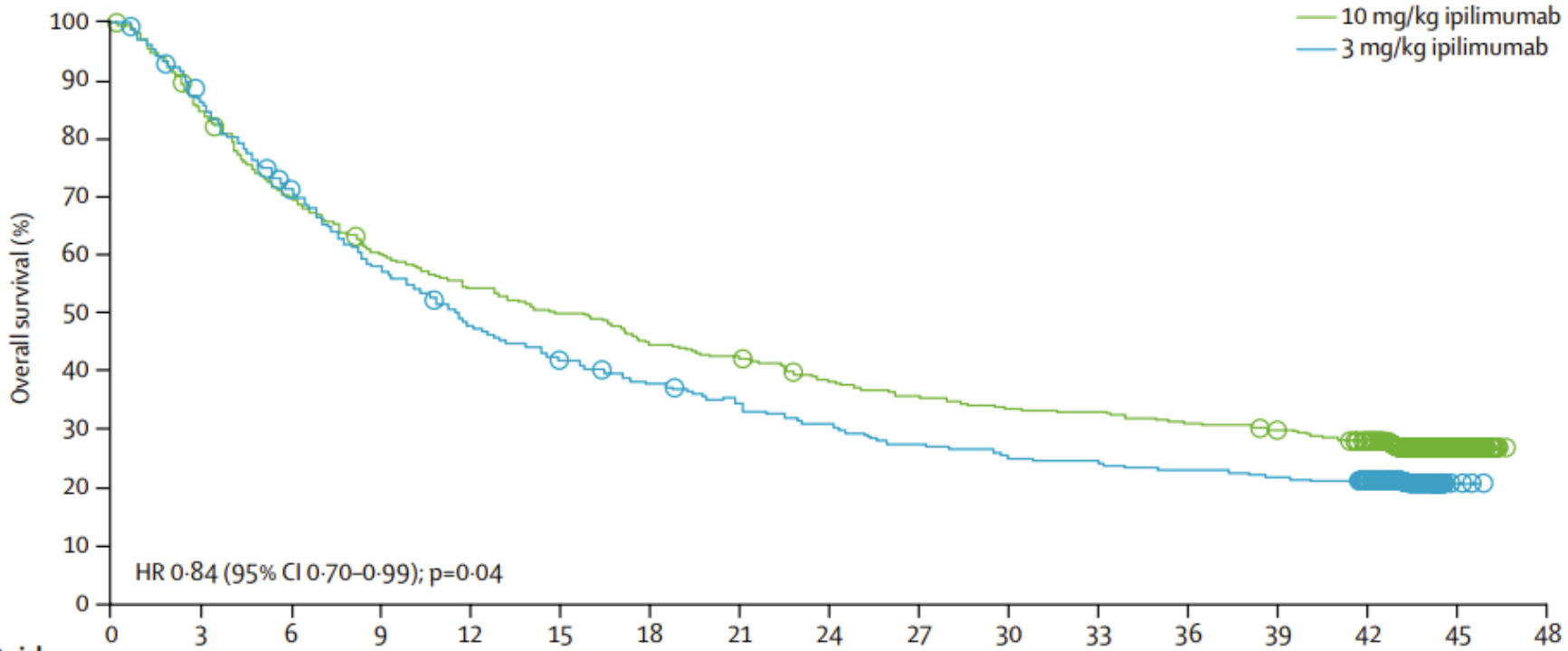
Appendix

First-generation Anti-CTLA-4 Agents Have Shown Dose-dependent Efficacy as Monotherapy—Higher Doses Resulted in Greater Therapeutic Benefit



Number at risk (number censored)																
10 mg/kg ipilimumab	365 (0)	306 (1)	253 (2)	217 (3)	196 (3)	181 (3)	161 (3)	151 (4)	137 (5)	126 (5)	120 (5)	118 (5)	111 (5)	105 (7)	94 (12)	16 (87)	0 (103)
3 mg/kg ipilimumab	362 (0)	310 (3)	253 (6)	205 (6)	168 (7)	146 (9)	131 (10)	118 (10)	107 (10)	95 (10)	87 (10)	83 (10)	80 (10)	76 (10)	71 (13)	8 (75)	0 (83)

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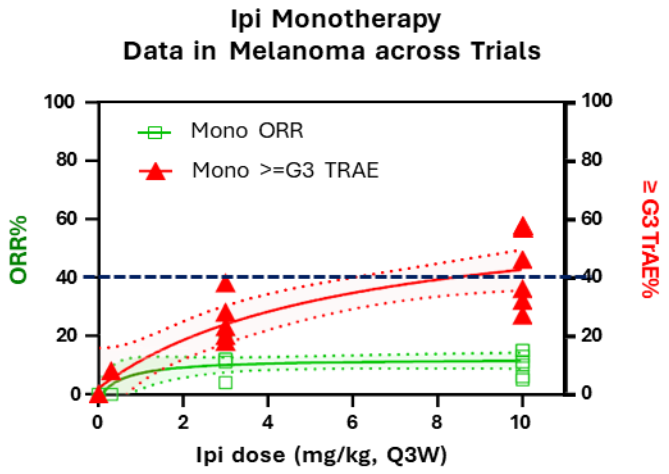
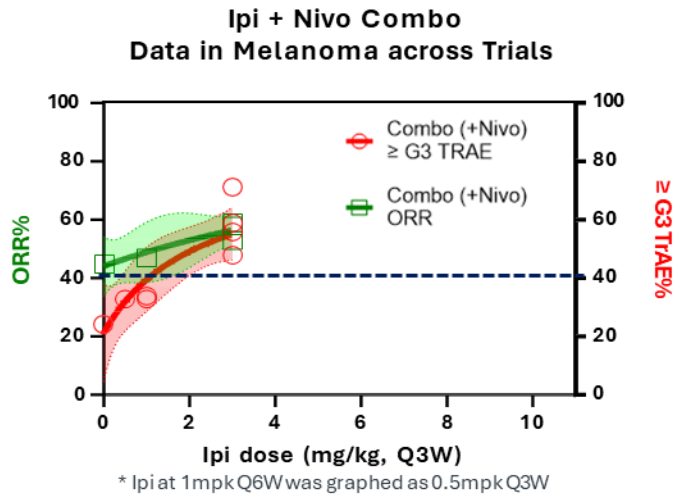
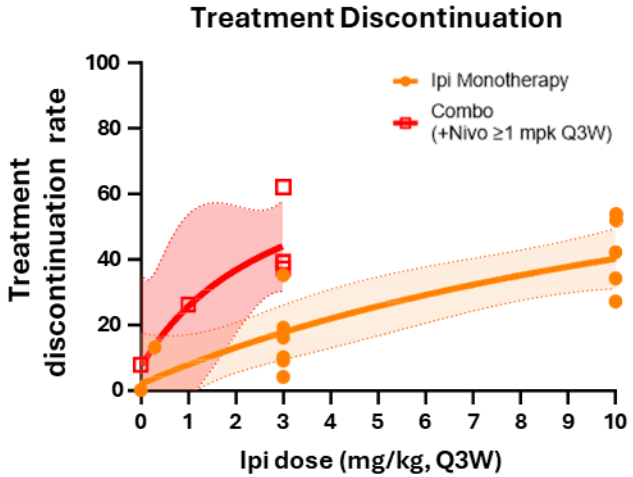
Source: Ascierto, Paolo A et al., Ipilimumab 10 mg/kg versus ipilimumab 3 mg/kg in patients with unresectable or metastatic melanoma: a randomised, double-blind, multicentre, phase 3 trial, The Lancet Oncology, Volume 18, Issue 5, 611 - 622

However, Combining Anti-CTLA-4 with Anti-PD-1 Led to a Disproportionate Increase in Toxicity, Thereby Limiting the Feasible Dose of Anti-CTLA-4





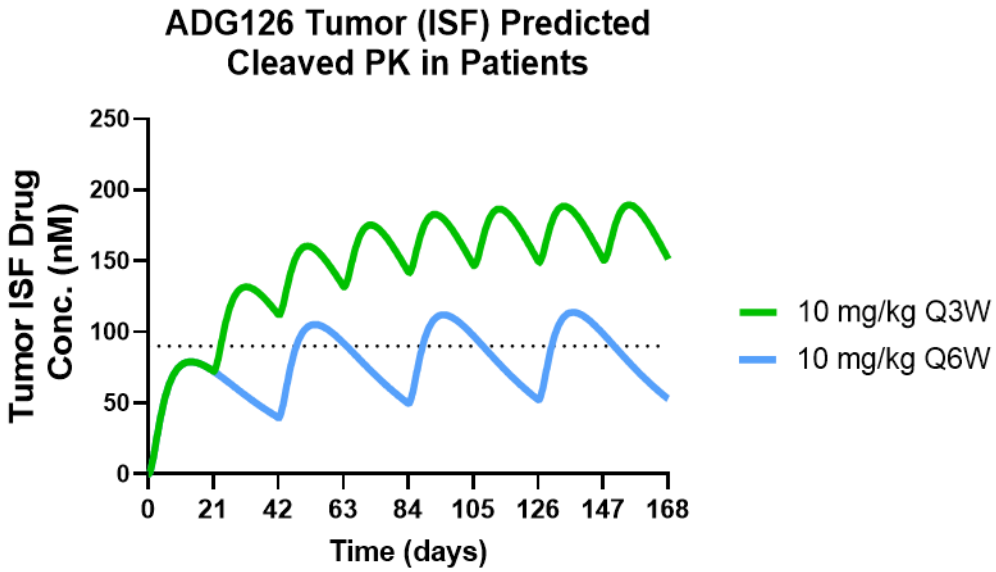
* Ipi at 1mpk Q6W was graphed as 0.5mpk Q3W

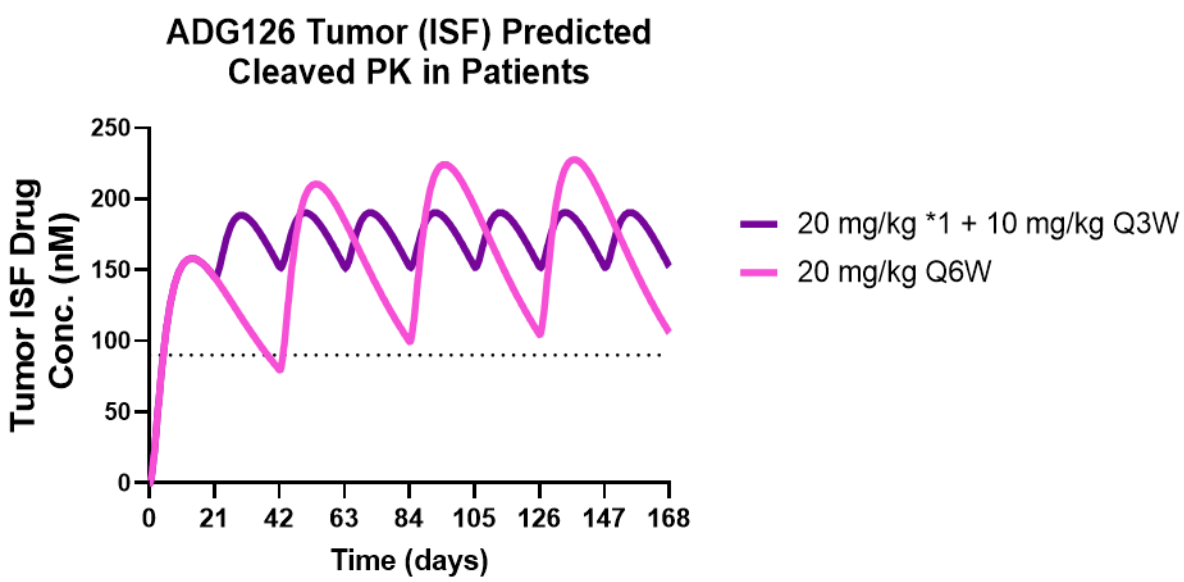


- Efficacy outcomes with ipilimumab (anti-CTLA-4) were improved when combined with anti-PD-1 (nivolumab in this instance).
- However, the incidence of severe adverse events leading to discontinuations was undesirable, even with a strong reduction in the dose of ipilimumab compared to monotherapy regimen.

Literature data were digitized; each symbol represent one data point from each study; the shaded area represent 90% confidence interval for nonlinear regression of the data (when applicable)

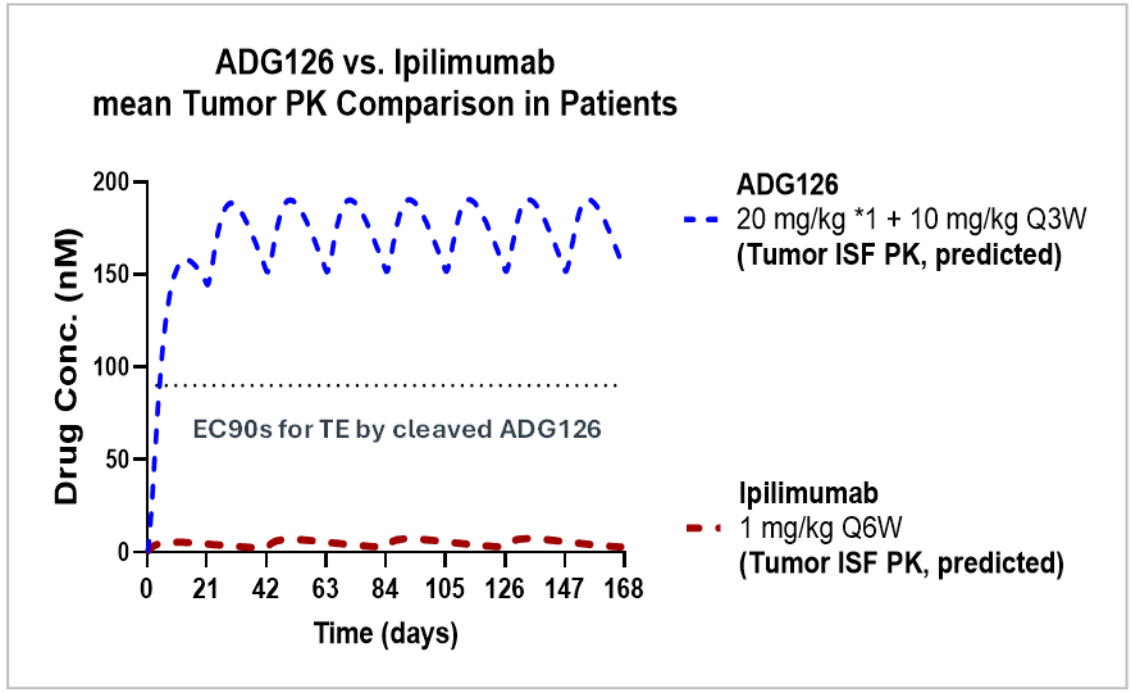
Our Pharmacokinetic Model Indicated That The 20mg Cohorts Should Reach Optimal Tumor Concentrations of Active ADG-126 More Rapidly in the TME

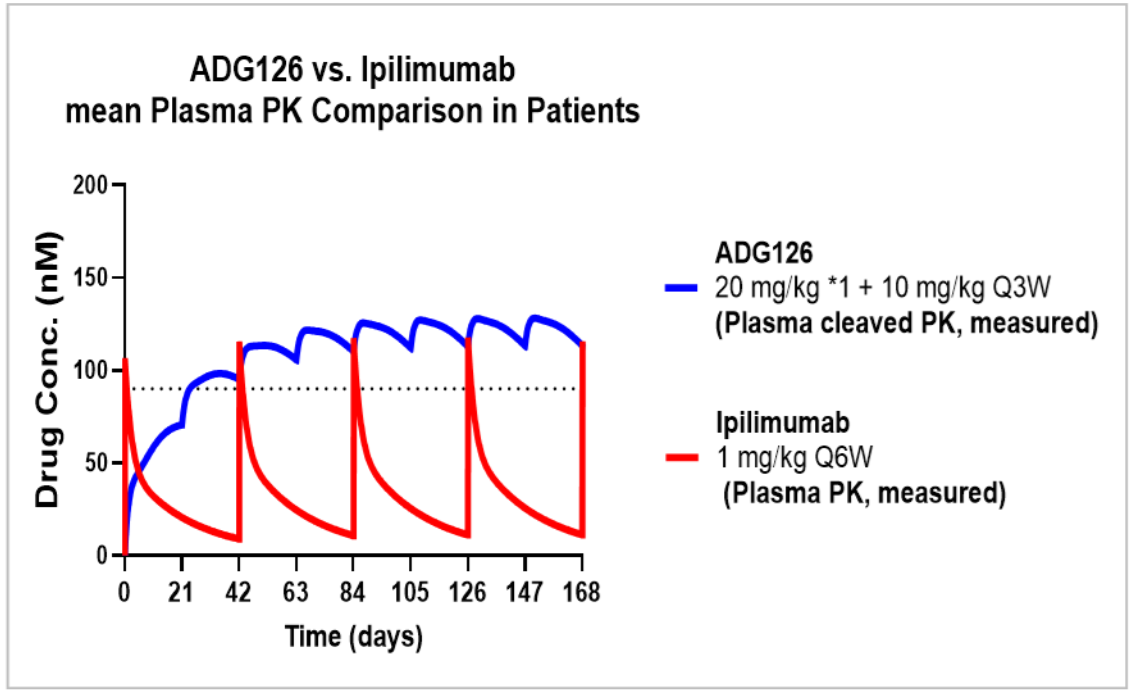




Black dashed line = Upper bound of in vitro human T cell binding EC_{90s} by cleaved ADG126 (e.g., target efficacious concentration within TME)

ADG-126's Enhanced Therapeutic Index Is Derived from an Increased Concentration in the TME vs Periphery





- With the 20 mpk followed by 10 mpk Q3W regimen of ADG126, the predicted average tumor active drug concentration is 25+ times higher than Ipilimumab at 1 mpk Q6W (range: 26-70X).

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Session PO.ET01.01 - Engineering the Next Wave of Antibody-Based Cancer Therapeutics

1760 / 5 - Preclinical characterization of XB404, a masked anti-ROR1/2 antibody-drug conjugate

Abstract

Background: Receptor tyrosine kinase-like orphan receptors (ROR) 1 and 2 are single-pass transmembrane proteins that are part of the ROR family that mediates Wnt signaling. ROR1 and ROR2 are aberrantly expressed in various cancers, including lung, breast, ovarian, and endometrial cancers, and their expression can be associated with poor disease outcomes. XB404, a masked anti-ROR1/2 antibody-drug conjugate (ADC) developed using the Adagene masking platform and the SMARTag® ADC platform, is designed to deliver a cytotoxic payload to ROR1/2-expressing tumors while minimizing on-target, off-tumor side effects. XB404 is composed of a tandem-cleavage topoisomerase 1 inhibitor-based linker-payload conjugated to a masked monoclonal antibody that binds to both ROR1 and ROR2 with high affinity. Here, we describe the preclinical characterization of XB404, including its in vitro cytotoxicity and internalization and in vivo efficacy in cell line-derived xenograft (CDX) and patient-derived xenograft (PDX) models.

Conclusions

XB404 demonstrated in vitro cytotoxicity and internalization, in vivo stability, and in vivo efficacy across multiple CDX and PDX models. Taken together, these preclinical results support further development of XB404. Investigational New Drug-enabling studies are ongoing.

Results

Unmasked XB404 displayed potent in vitro cytotoxic activity, and unmasked XB404 antibody demonstrated internalization properties. XB404 demonstrated improved clearance and half-life compared with the non-masked ROR1/2 ADC in rats. In addition, overlapping total antibody and total ADC curves for XB404 indicated good in vivo stability. In vivo antitumor activity was observed in the Jeko-1 and MDA-MB-231 xenograft models. XB404 demonstrated dose-related tumor growth inhibition and improved survival in both NSCLC and TNBC PDX models. Tumor regression was observed in both PDX models and complete responses were observed in the TNBC PDX model.