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CS2009 (PD-1/VEGF/CTLA-4 Trispecific Antibody) as the Next-Gen I/O Backbone

— 2026 ESMO Presentations & Post-ESMO Updates



October 2026
Stock Code: 2616. HK

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An Innovative Biopharma Driven by Globally Recognized R&D Capability

Proven track record for high-quality and efficient drug development worldwide

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Established in late 2015, CStone is an innovation-driven biopharmaceutical company focused on the research and development of therapies for oncology, immunology/inflammation, and other key disease areas

R&D Milestones

21 NDA Approvals

60+ Data Publications

60+ IND Approvals

10+ Discovery Projects Ongoing

Pipeline 2.0 Strength

13 Novel Assets

Potentially FIC/BIC **ADCs and Mono-/Multi-Specific Antibodies** in Oncology and Immunology/ Inflammation

Commercial Achievement

4 Products Commercialized*

9 Indications Approved

6 Territories Coverage

** The exclusive rights of ivosidenib has been transferred to Servier*

To drive business growth by maximizing commercial value of in-market products and advancing innovative Pipeline 2.0

Commercial-stage Programs

Sugemalimab
(PD-L1)

Pralsetinib
(RET)

Avapritinib
(KIT/PDGFRA)

Key Clinical Programs in Pipeline 2.0

CS2009
(PD-1/VEGF/CTLA-4 trispecific antibody)
Global first-in-class / best-in-class potential

CS5007
(EGFR/HER3 bsADC)

CS5001
(ROR1 ADC)

Innovative Early Programs in Pipeline 2.0

CS5006
(ITGB4 ADC)

CS5008
(SSTR2/DLL3 bsADC)

CS5009
(B7H3/PD-L1 dual-payload ADC)

CS5010
(HER2 biparatopic dual-payload ADC)

CS5012
(HER2 biparatopic novel-payload ADC)

CS1012
(GDF-15 mAb)

CS2013
(BAFF/APRIL bsAb)

CS2015
(OX40L/TSLP bsAb)

CS1016
(PD-1 agonist mAb)

CS2016
(TL1A/α4β7 bsAb)

More Exploratory Programs…

Recurring revenue to fuel pipeline advancement

Strong growth momentum in near term

Robust growth engine for the long run

bs: bispecific; Ab: antibody; mAb: monoclonal antibody

Oncology program | I&I program

Progress of Pipeline 2.0

	Right	Indication	Discovery	Preclinical Development	IND-Enabling	FIH	POC
Antibodies (Oncology)							
CS2009 (PD-1/VEGF/CTLA-4 trispecific antibody)	🌍	Solid tumors					
CS1012 (GDF-15 antibody)	🌍	Solid tumors					
ADCs (Oncology)							
CS5001[1] (ROR1 ADC)	🌍	Solid tumors; hematologic malignancies					
CS5007 (EGFR/HER3 bispecific ADC)	🌍	Solid tumors					
CS5006 (ITGB4 ADC)	🌍	Solid tumors					
CS5008 (SSTR2/DLL3 bispecific ADC)	🌍	Solid tumors					
CS5009 (B7H3/PD-L1 bispecific dual-payload ADC)	🌍	Solid tumors					
CS5010 (HER2 biparatopic dual-payload ADC)	🌍	Solid tumors					
CS5012 (HER2 biparatopic novel-payload ADC)	🌍	Solid tumors					
Antibodies (Immunology & Inflammation)							
CS2013 (BAFF/APRIL bispecific antibody)	🌍	Immunology & Inflammation					
CS2015 (OX40L/TSLP bispecific antibody)	🌍	Immunology & Inflammation					
CS1016 (PD-1 agonist antibody)	🌍	Immunology & Inflammation					
CS2016 (TL1A/α4β7 bispecific antibody)	🌍	Immunology & Inflammation					

🌍 Global Rights

Note: Assets status denotes progress in the region(s) noted in the column titled "Rights" ; FIH = First in Human, POC = Proof of Concept,
1. CStone obtains the exclusive global right from LigaChem Biosciences, Inc. (LCB) to lead development and commercialization of LCB71/CS5001 outside the Republic of Korea

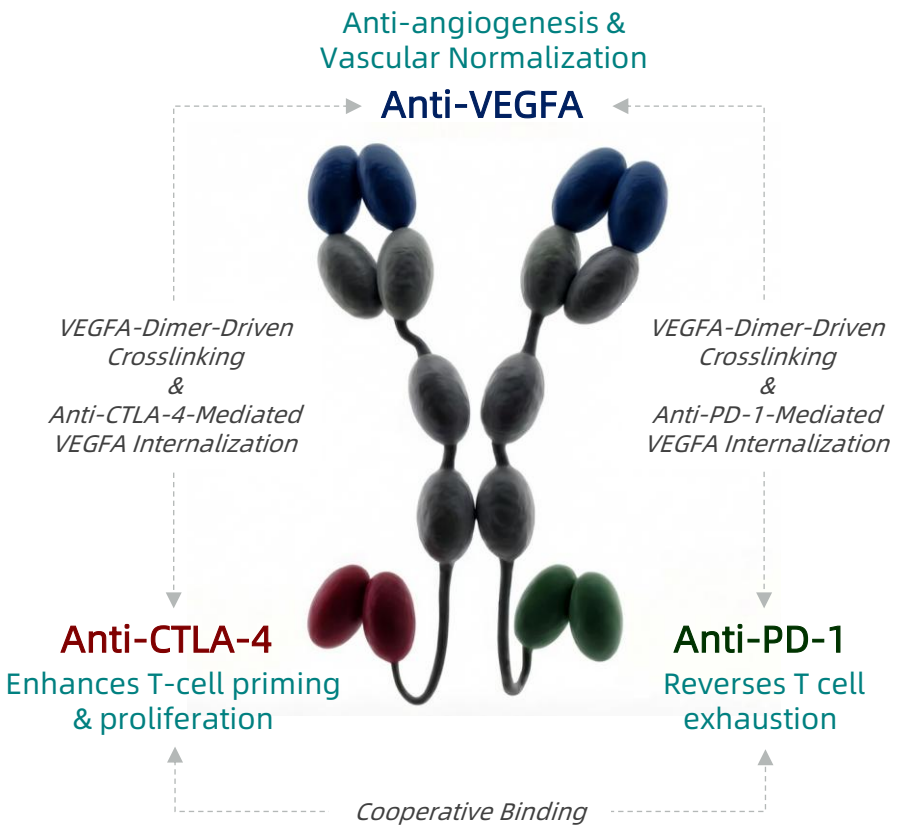


CS2009

- **Design, MoA, and Rationale**
- Phase 1/2 Clinical Data Update
  - Proof of Mechanism
  - Proof of Safety
  - Proof of Concept in Broad Cancer Types
    1. Non-small Cell Lung Cancer (NSCLC) Dataset
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    3. Preliminary Clinical Data for Other Tumor Types
- Regulatory and Clinical Plan for Global Phase 3 Trials

Molecular Design and MOA: Triple Synergy to Deliver Durable Survival Benefit with Minimized Toxicity

Potential First-in-Class / Best-in-Class Next-Generation Immuno-Oncology (I/O) Backbone



Triple synergy (PD-1/VEGF/CTLA-4)

- Simultaneously targets three pathways to restore T-cell function, remodel the tumor microenvironment, and enhance T-cell priming – driving deeper, more durable anti-tumor immunity.

Overcomes limitations of conventional immuno-combination therapies

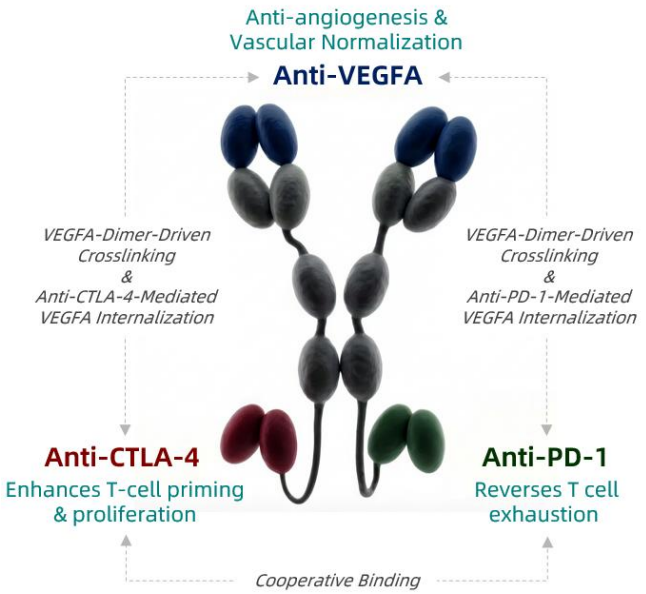
- Addresses high toxicity of conventional CTLA-4 antibodies (which restricts sustained dosing) and uncertain long-term OS benefit of PD-1/VEGF bispecifics or combination regimens
- Differentiated design reduces systemic immune-related and VEGF-related toxicities, enabling long-term continuous dosing

Expands immunotherapy scope for long-term survival

- Consistent clinical activity in traditionally "cold" tumors (e.g., pMMR/MSS colorectal cancer) and heavily pre-treated NSCLC, supported by a favorable safety profile
- Potential to benefit a broader patient population and deliver sustained long-term overall survival benefit

MoA: Mechanism of Action

Triple Synergy in the Tumor Microenvironment leads to enhanced anti-tumor activities



1 Anti-CTLA-4 Action in TME

➢ **Recruit and train T-cells inside TDLN/TME**

- Blocks CTLA-4 inhibitory checkpoint on T cells
- Drives T-cell priming and clonal expansion
- Expands tumor-reactive effector T-cell pool

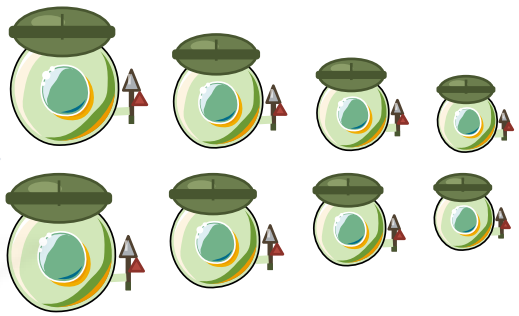


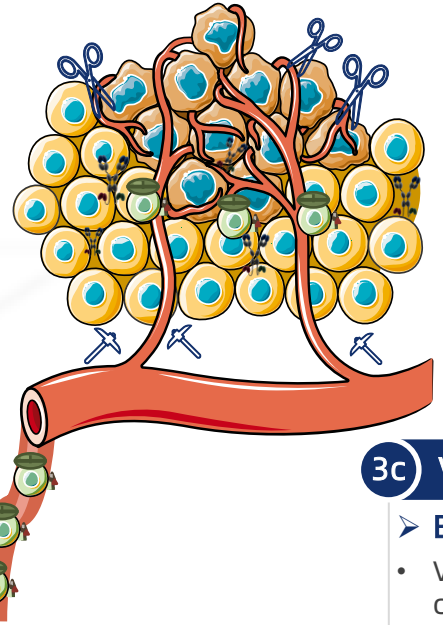
2 Anti-PD-1 Action in TME

➢ **Revive exhausted T-cells**

- Blocks PD-1 inhibitory checkpoint on T cells
- Reverses T-cell exhaustion
- Restores cytotoxic function







3a Anti-VEGFA Actions

➢ **Cut off blood supply**

- Blocks pathological angiogenesis
- Prunes immature & leaky tumor vessels
- Restricts tumor nutrient supply & growth

3b Anti-VEGFA Actions

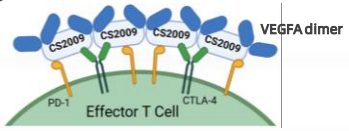
➢ **Clear pathways for T-cells**

- Induces tumor vascular normalization
- Improves vessel structure & perfusion
- Enhances T-cell trafficking into tumor

3c VEGFA-Crosslinking

➢ **Boost IO activities**

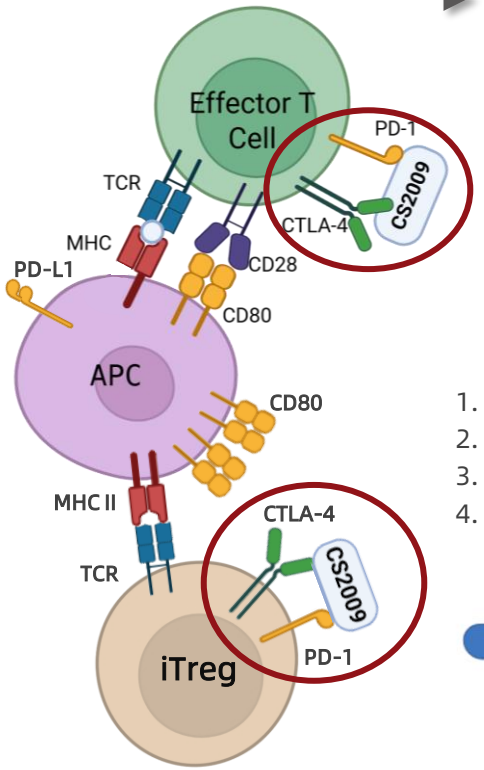
- VEGFA-dimer-driven CS2009 clustering boosts PD-1/CTLA-4^{+} T-cell binding and IO activities in TME



Note: Image adapted from Servier Medical Art, licensed under CC BY 4.0
TDLN: tumor-draining lymph node; TME: tumor microenvironment

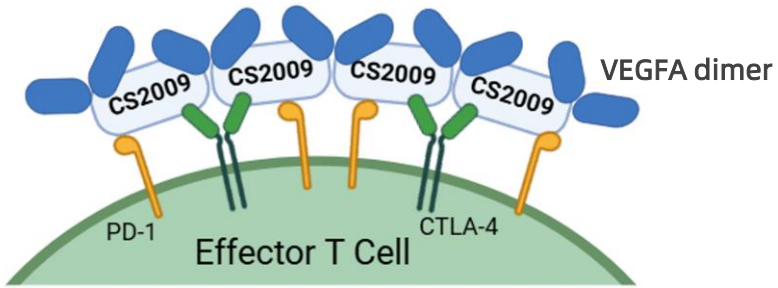
Multi-target engagement and synergistic interactions enhance CS2009's activities in TME while sparing peripheral CTLA-4+ T cells to widen its therapeutic window

TME and TDLN



Within the TME, CS2009's **monovalent PD-1 arm (K_D = 18.4 nM) can effectively block PD-1/PD-L1 interaction (K_D ~ 1 mM).** In addition, CS2009 **preferentially binds PD-1 and CTLA-4 on double-positive tumor-infiltrating lymphocytes (Teff and Treg)** via avidity-driven concurrent engagement of both checkpoints, enhancing its binding avidity (K_D ~ 1 nM) and checkpoint inhibitory (CPI) activity to reinvigorate Teff and block Treg activities, including:

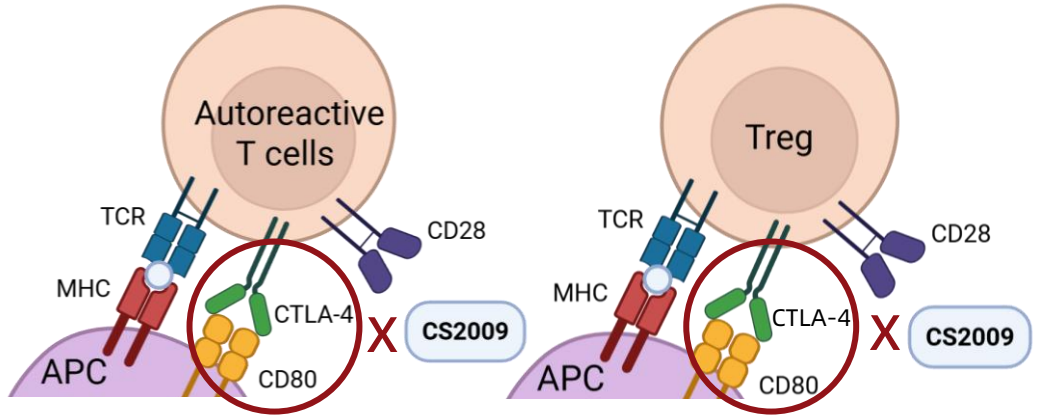
1. Blocking PD-1/PD-L1 interaction on **Teff**
2. Blocking CTLA-4/CD80 interaction on **Teff & Treg**
3. Inducing internalization of PD-1 & CTLA-4 on **Teff & Treg**
4. Blocking **Treg**-driven transcytosis of CD80 from APC surface



Within the TME, CS2009 forms clusters after crosslinking with VEGFA dimers, which **strengthens its binding affinity to PD-1/ CTLA-4-expressing T cells** and further amplifies its CPI activity

Peripheral

In the peripheral, In contract to high-affinity CTLA-4 mAbs/ bsAbs, CS2009's **monovalent CTLA-4 arm (K_D = 16.1 nM) is unable to block CTLA-4/CD80 interaction (avidity K_D 1-10 nM)** due to low affinity, thus preventing CTLA-4 single-positive T cells from over-activation, and reducing systemic autoimmune toxicity





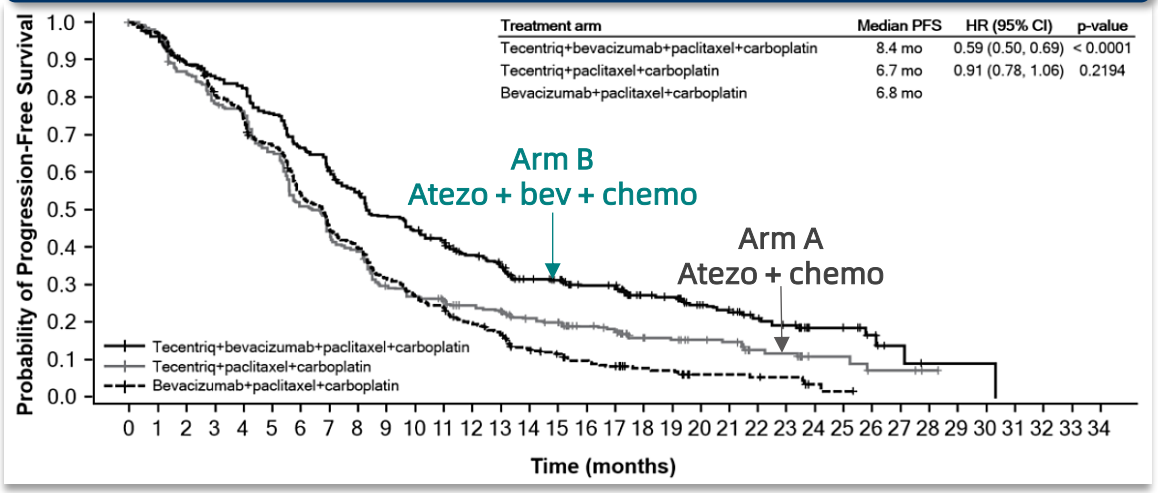
TME = tumor microenvironment (TME); TDLN = tumor-draining lymph node

No OS benefits from PD-(L)1 + VEGF combo therapy: Strong PFS but no OS benefit for PD-L1 mAb + VEGF mAb + Chemo vs. PD-L1 mAb + Chemo in 1L NSCLC in IMpower 150

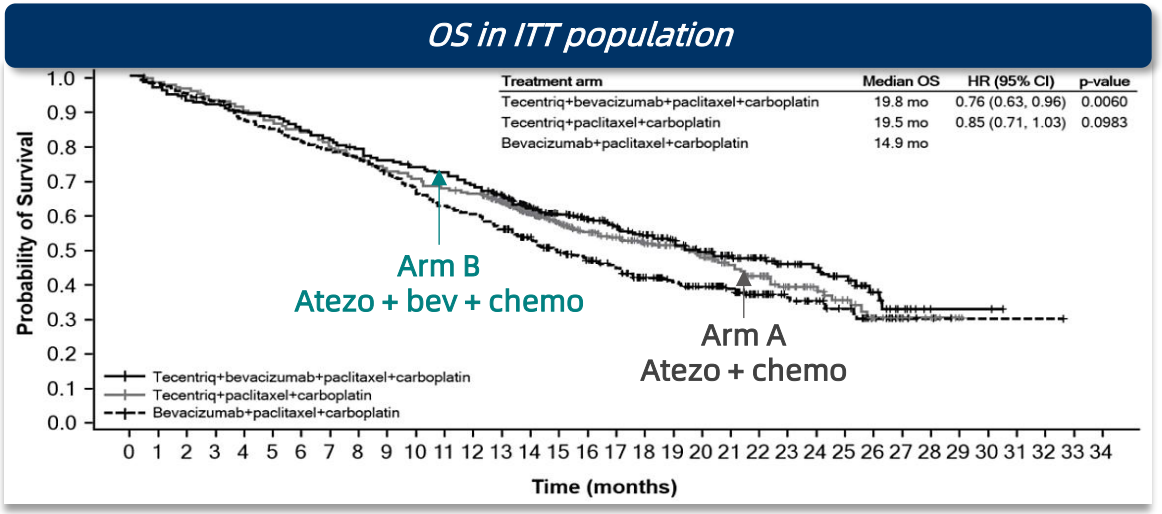
Efficacy endpoint	Arm A (Atezolizumab + Paclitaxel + Carboplatin)	Arm B (Atezolizumab + Bevacizumab + Paclitaxel + Carboplatin)
Investigator-assessed PFS (RECIST v1.1)*	n = 402	n = 400
No. of events (%)	330 (82.1%)	291 (72.8%)
Median duration of PFS (months)	6.7	8.4
95% CI	(5.7, 6.9)	(8.0, 9.9)
Stratified hazard ratio‡^ (95% CI)	0.67 (0.57, 0.79)	
p-value[1,2]	< 0.0001	
OS interim analysis*	n = 402	n = 400
No. of deaths (%)	206 (51.2%)	192 (48.0%)
Median time to events (months)	19.5	19.8
95% CI	(16.3, 21.3)	(17.4, 24.2)
Stratified hazard ratio‡^ (95% CI)	0.90 (0.74, 1.10)	
p-value[1,2]	0.3000	

- "PD-1/L1 + VEGF" combination significantly improved PFS in NSCLC vs. PD-1/L1 monotherapy, but did not show clear OS benefit, especially in PD-L1 low-expression subgroups.
- IMpower150 results showed that Arm B (PD-L1 + VEGF + chemo) improved PFS but not for OS vs. Arm A (PD-L1 + chemo). Additionally, Arm B (PD-L1 + VEGF + chemo) failed to demonstrate OS benefits in the subgroup with <1% PD-L1 expression compared to the control arm.

PFS in ITT population



OS in ITT population



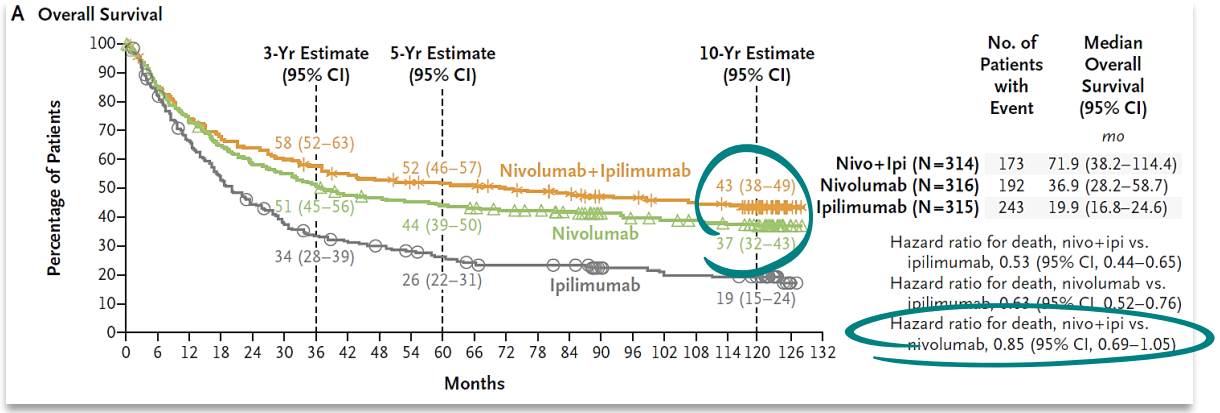
Source: Tecentriq label

Adding anti-CTLA-4 mAb (even for limited doses) to anti-PD-(L)1 mAb improves OS (HR ↓~0.1-0.2), validating CTLA-4's distinct contribution to survival benefit

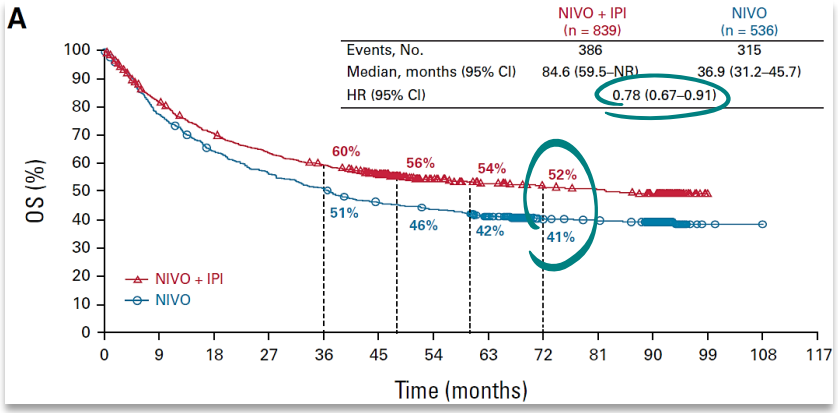
"PD-1/L1 + CTLA-4" combo shows significant PFS and OS benefits, particularly long-term OS improvement, e.g., Nivolumab (PD-1) + Ipilimumab (CTLA-4) in advanced melanoma

CheckMate 067: *10-Year Outcomes with Nivolumab plus Ipilimumab in Advanced Melanoma*

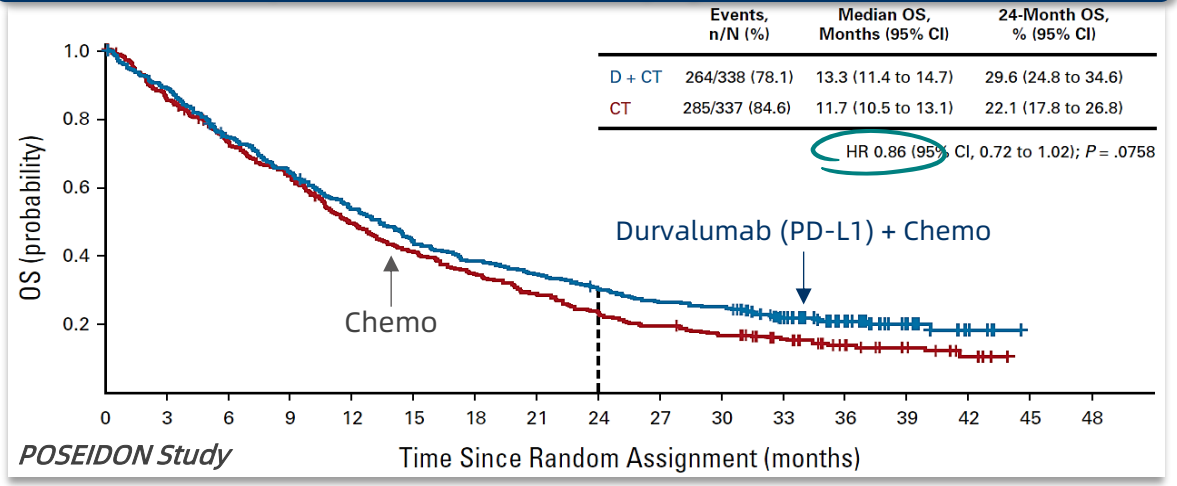
** **Note:** IPI (3 mg/kg Q3W) was administered for **4 doses max**.*



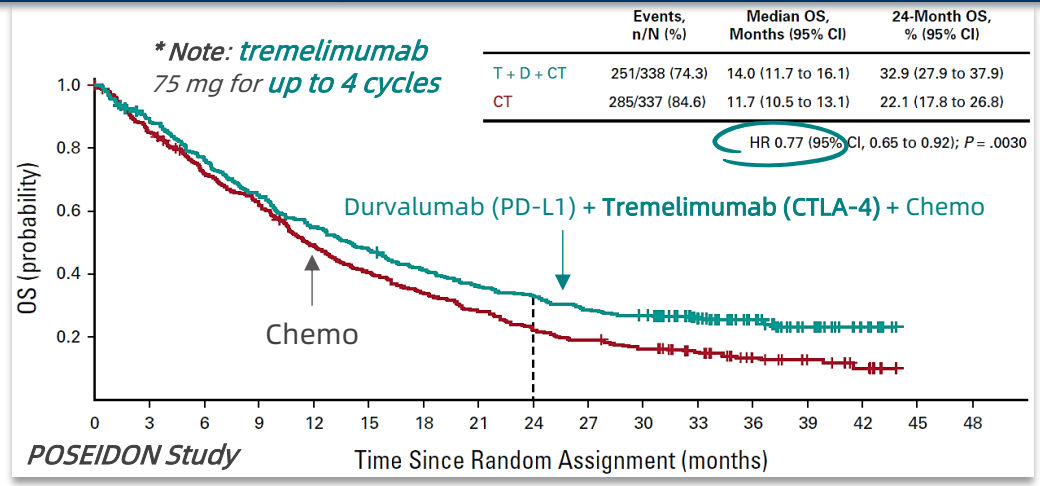
** **Note:** Data pooled from six **CheckMate studies** in treatment-naive melanoma patients receiving NIVO + **4 doses of IPI** (NIVO 1 mg/kg + IPI 3 mg/kg or NIVO 3 mg/kg + IPI 1 mg/kg), Q3W, or NIVO mono (3 mg/kg), Q2W.*



In NSCLC, Durvalumab (PD-L1) + Chemo vs. Chemo Alone: Improved PFS but No Statistically Significant OS Benefit



Durvalumab (PD-L1) + Tremelimumab (CTLA-4) + Chemo vs. Chemo Alone: Significant Improvement in Both PFS and OS

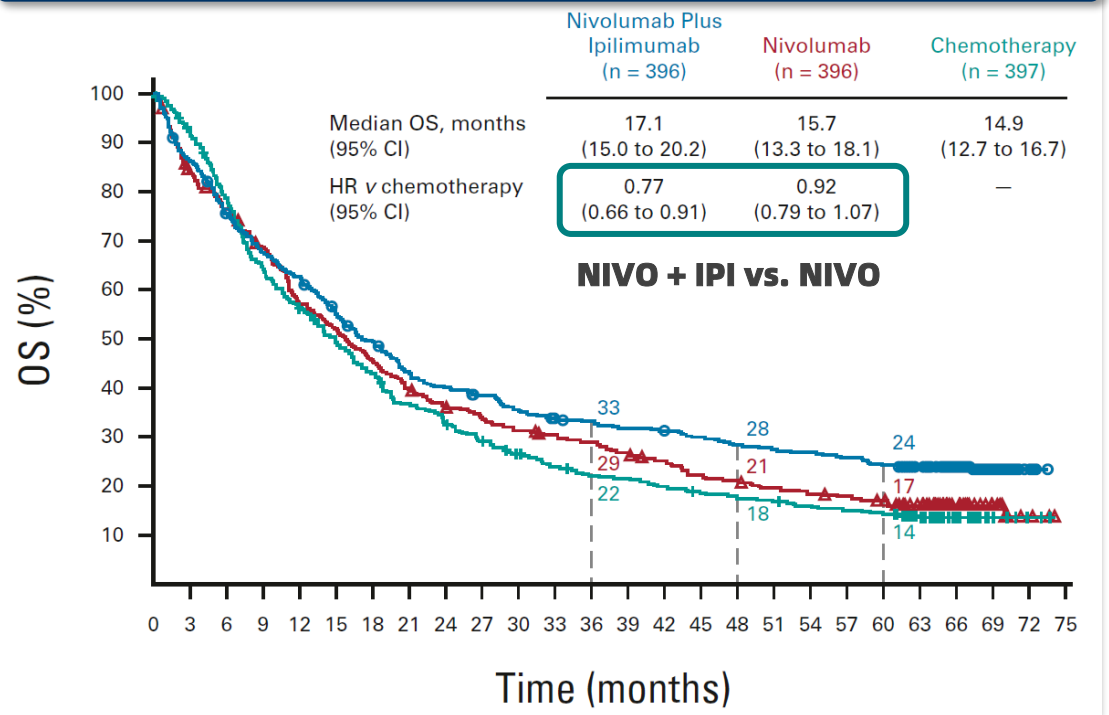


Continuous CTLA-4 Exposure Drives Long-Term OS Benefit: Checkmate-227 5-yr Validation

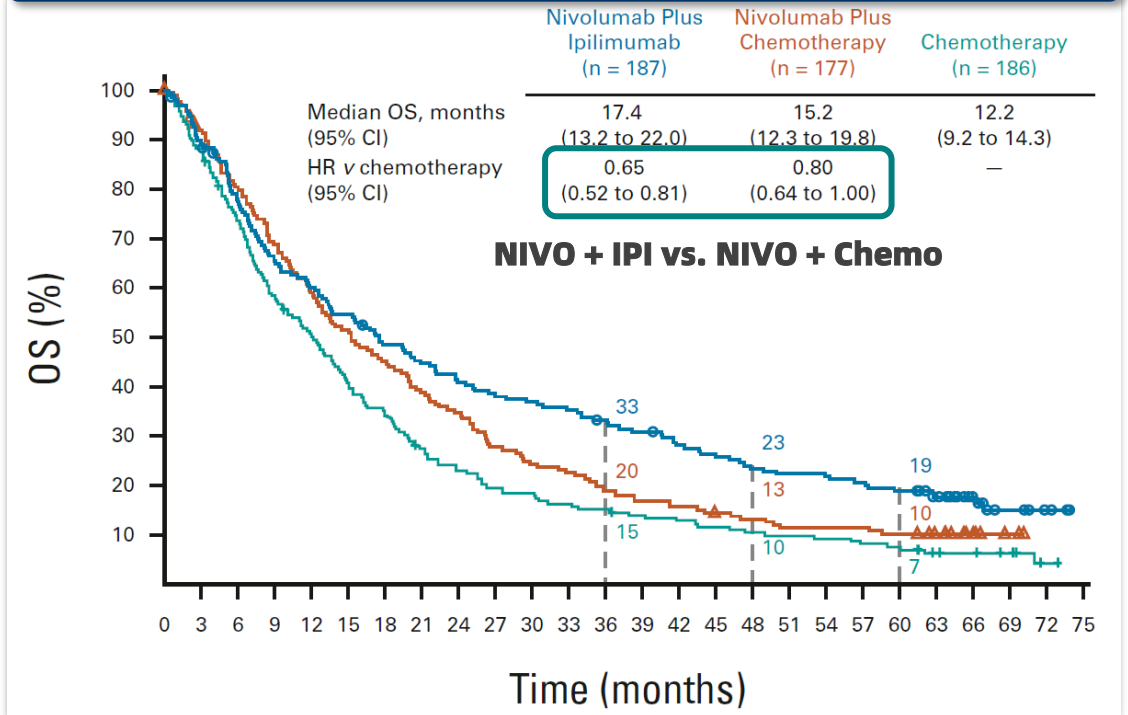
Enhanced survival (OS HR ↓~0.15) with PD-1 + CTLA-4 (continuous IPI at 1 mg/kg, Q6W) vs. PD-1 + chemo in 1L NSCLC

CheckMate 227 led by Dr. Julie R. Brahmer (Johns Hopkins): As the Leading PI of CheckMate 227 and recent discussant for AK112's HARMONi-6 at ASCO 2026, Dr. Brahmer's deep mechanistic understanding of IO combinations underscores a critical consensus in the field: true long-term survival "tails" require the unique, complementary T-cell priming that CTLA-4 provides

OS in first-line NSCLC patients with PD-L1≥1%



OS in first-line NSCLC patients with PD-L1 < 1%



Note: In CheckMate 227, the **overall median duration of treatment (DOT) for the Nivo+Ipi arm was ~4 months**, implying actual Ipi exposure was ≤4 months due to early discontinuations primarily driven by Ipi-related toxicities (irAEs). Conversely, **5-year survivors** received a substantially higher median number of **Ipi doses (10 for PD-L1 ≥1%; 6 for PD-L1 <1%), equating to an estimated Ipi DOT of 8–14 months.** This suggests that while early Ipi withdrawal is largely toxicity-driven, prolonged Ipi tolerance enables deeper CTLA-4–mediated immune priming, serving as a critical driver for long-term survival

Source: Checkmate-227 5-yr follow-up (Brahmer et al., JCO 2023)

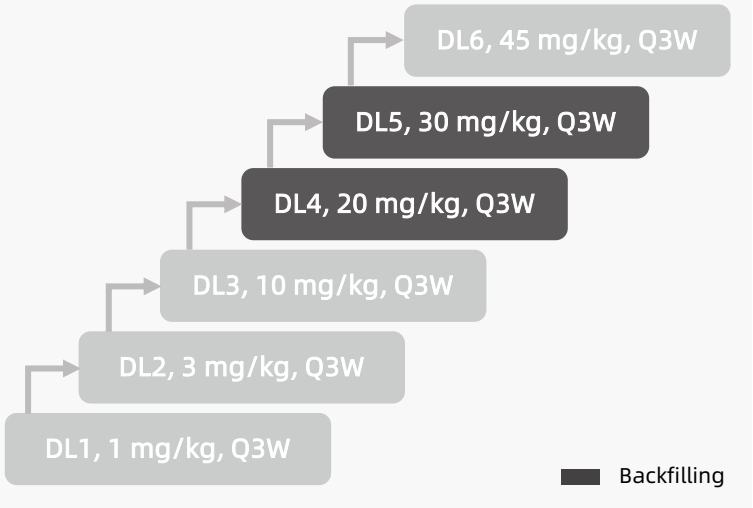


CS2009

- Design, MoA, and Rationale
- **Phase 1/2 Clinical Data Update**
  - Proof of Mechanism
  - Proof of Safety
  - Proof of Concept in Broad Cancer Types
    1. Non-small Cell Lung Cancer (NSCLC) Dataset
    2. Colorectal Cancer (CRC) Dataset
    3. Preliminary Clinical Data for Other Tumor Types
- Regulatory and Clinical Plan for Global Phase 3 Trials

CS2009 Clinical Development Plan: Efficient and Clearly Defined Global Development Path Forward

Phase I – Mono Dose Escalation (Completed) + Backfilling



Phase II – Dose Expansion

Lung

- 1L NSQ-NSCLC, AGA(-), plus PEM + CPT
- 1L SQ-NSCLC, AGA(-), plus PTX + CPT
- Treated NSCLC–[2L] Mono, [2/3L] plus docetaxel
- 1L NSCLC, AGA(-), PD-L1 TPS ≥1%, Mono
- 1L ES-SCLC, plus ETO + CPT

Gastrointestinal

- 1L pMMR/MSS CRC / pancreatic cancer, plus chemo
- 1L gastric cancer, plus CAPOX
- 1L ESCC, plus TP/FP
- HCC–[1L] Mono; [2/3L] Mono

Breast

- 1L TNBC, plus nab-PTX
- 2/3L TNBC, Mono

Gynecologic

- 1L cervical cancer, plus PTX + Pt
- PROC–[1/2L] plus PTX; [2/3L] Mono

Kidney & Others

- 1L RCC, Mono
- 1L MSI-H/dMMR solid tumors, Mono

Prioritized Phase III MRCT Trials

- **1L metastatic NSQ-NSCLC, AGA(-),** CS2009 + PEM + CPT vs. pembrolizumab + PEM + CPT
- **1L metastatic SQ-NSCLC, AGA(-),** CS2009 + PTX + CPT vs. pembrolizumab + PTX + CPT
- **2/3L metastatic NSCLC, AGA(-),** CS2009 + docetaxel vs. docetaxel
- **1L metastatic NSCLC, AGA(-), PD-L1 TPS ≥50%,** CS2009 vs. pembrolizumab
- **Stage III NSCLC, post-CRT consolidation** CS2009 vs. durvalumab
- **1L ES-SCLC,** CS2009 + ETO + CPT vs. atezolizumab + ETO + CPT
- **1L MSS CRC,** CS2009 + FOLFOX vs. bevacizumab + FOLFOX
- **1L TNBC,** CS2009 combination TBD, contingent on regulatory feedback
- **1L Clear-cell RCC,** CS2009 +/- axitinib vs. pembrolizumab + axitinib
- **1L HCC,** CS2009 vs. atezolizumab + bevacizumab
- **1L MSI-H Solid Tumors,** Selected tumor types

AGA: actionable oncogenic alterations; CAPOX: Capecitabine + Oxaliplatin; CPT: Carboplatin; CRC: colorectal cancer; DL: dose level; ES-SCLC: extensive-stage small cell lung cancer; ESCC: esophageal squamous cell carcinoma; ETO: Etoposide; FOLFOX: folinic acid, fluorouracil and oxaliplatin; *FP: 5-fluorouracil + Cisplatin; HCC: hepatocellular carcinoma; NSCLC: non-small cell lung cancer; NSQ: non-squamous; PEM: Pemetrexed; PROC: platinum-resistant ovarian cancer; PTX: Paclitaxel; Pt: platinum; pMMR/MSS: proficient mismatch repair or microsatellite stable; Q3W: once every 3 weeks; RCC: renal cell carcinoma; SQ: squamous; TNBC: triple-negative breast cancer; TP: Paclitaxel + Cisplatin; TPS: tumor proportion score*

R&D Milestones & Upcoming Catalysts

- **Mar. 2025** – First patient dosed in global phase I trial
- **Sept. 2025** – First patient dosed in global phase II trial
- **Q4 2025** – Phase I data debut at ESMO
- **Feb 2026** – US IND
- **Q2 2026** – Phase I data and preliminary Phase II data presented at ASCO
- **Q4 2026** – Two oral presentations at ESMO
- **Q4 2026** – Initiating Phase III registrational trial

Three Important Key Clinical Validations Achieved from over 300 Patient Data

2026 ESMO **Oct. 2026**

Phase I/II key updates **Aug. 2026**

2026 ASCO **May 2026**

Preliminary 1L NSCLC mono and Phase I data **Apr. 2026**

2025 ESMO *Presented Phase I data from 72 patients* **Oct. 2025**

Phase II *First patient in* **Sept. 2025**

Phase I *First patient in* **Mar. 2025**

➢ Proof of Mechanism

- Dose-dependent **ICOS upregulation on CD4+ T cells**: PD biomarker specific to CTLA-4 blockade
- Linear **PK** with half-life of ~6-9 days; low incidence of ADA positivity
- Sustained **PD-1/CTLA-4 receptor occupancy** at doses ≥20 mg/kg
- **Serum-free VEGFA** reduced deeply and rapidly; effect sustained throughout dose intervals

➢ Proof of Safety

- **Grade ≥3 irAEs 12.7%**; CTLA-4-related tox markedly reduced from CTLA-4 mAb monotherapy or in combination with PD-1/L1, including **extremely rare colitis,** due to **preserved CTLA-4 signaling** in peripheral Tregs & autoreactive T cells
- **Grade ≥3 VEGF-related tox 5.1%;** likely mediated by PD-1/CTLA-4-driven VEGFA immune complex internalization by T cells in TME as indicated by the data

➢ Proof of Concept in Broad Cancer Types

- Robust mono & chemo-combo efficacy in **1L and late-line NSCLC**
- Robust mono & chemo-combo efficacy in **1L and late-line pMMR/MSS mCRC**
- Promising antitumor activity in other "**cold tumors**" including STS and nccRCC, and other solid tumors including SCLC, OC, HCC, GC, EC, mCRPC, TNBC, etc.

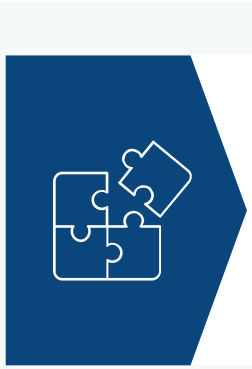
TME: tumor microenvironment; ICOS: inducible T-Cell Co-stimulator; NSCLC: non-small cell lung cancer; STS: soft tissue sarcoma; nccRCC: non-clear-cell renal cell carcinoma; pMMR/MSS: proficient mismatch repair / microsatellite stable; mCRC: metastatic colorectal cancer; SCLC: small-cell lung cancer; mCRPC: metastatic Castration-Resistant Prostate Cancer; OC: ovarian cancer; TNBC: triple-negative breast cancer; GC: gastric cancer; EC: esophageal cancer



CS2009

- Design, MoA, and Rationale
- **Phase 1/2 Clinical Data Update**
  - **Proof of Mechanism**
  - Proof of Safety
  - Proof of Concept in Broad Cancer Types
    1. Non-small Cell Lung Cancer (NSCLC) Dataset
    2. Colorectal Cancer (CRC) Dataset
    3. Preliminary Clinical Data for Other Tumor Types
- Regulatory and Clinical Plan for Global Phase 3 Trials

Three Important Key Clinical Validations Achieved from over 300 Patient Data



2026 ESMO **Oct. 2026**

Phase I/II key updates **Aug. 2026**

2026 ASCO **May 2026**

Preliminary 1L NSCLC mono and Phase I data **Apr. 2026**

2025 ESMO *Presented Phase I data from 72 patients* **Oct. 2025**

Phase II *First patient in* **Sept. 2025**

Phase I *First patient in* **Mar. 2025**

➢ Proof of Mechanism

- Dose-dependent **ICOS upregulation on CD4+ T cells**: PD biomarker specific to CTLA-4 blockade
- Linear **PK** with half-life of ~6-9 days; low incidence of ADA positivity
- Sustained **PD-1/CTLA-4 receptor occupancy** at doses ≥20 mg/kg
- **Serum-free VEGFA** reduced deeply and rapidly; effect sustained throughout dose intervals

➢ Proof of Safety

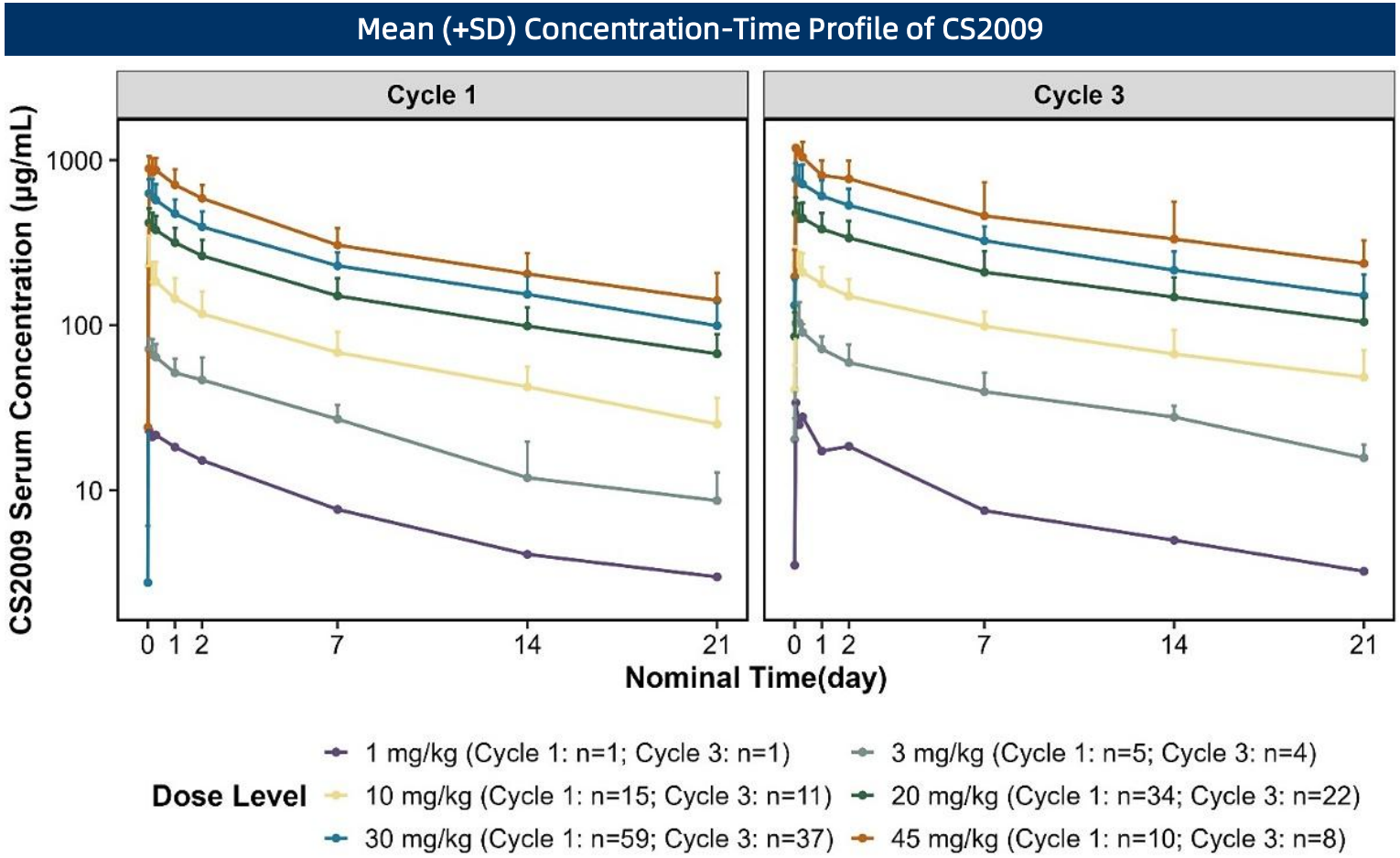
- Grade ≥3 irAEs 12.7%; CTLA-4-related tox markedly reduced from CTLA-4 mAb monotherapy or in combination with PD-1/L1, including extremely rare colitis, due to preserved CTLA-4 signaling in peripheral Tregs & autoreactive T cells
- Grade ≥3 VEGF-related tox 5.1%; likely mediated by PD-1/CTLA-4-driven VEGFA immune complex internalization by T cells in TME as indicated by the data

➢ Proof of Concept in Broad Cancer Types

- Robust mono & chemo-combo efficacy in **1L and late-line NSCLC**
- Robust mono & chemo-combo efficacy in **1L and late-line pMMR/MSS mCRC**
- Promising antitumor activity in other "**cold tumors**" including STS and nccRCC, and other solid tumors including SCLC, OC, HCC, GC, EC, mCRPC, TNBC, etc.

TME: tumor microenvironment; ICOS: inducible T-Cell Co-stimulator; NSCLC: non-small cell lung cancer; STS: soft tissue sarcoma; nccRCC: non-clear-cell renal cell carcinoma; pMMR/MSS: proficient mismatch repair / microsatellite stable; mCRC: metastatic colorectal cancer; SCLC: small-cell lung cancer; mCRPC: metastatic Castration-Resistant Prostate Cancer; OC: ovarian cancer; TNBC: triple-negative breast cancer; GC: gastric cancer; EC: esophageal cancer

CS2009 PK Profile: Dose-proportional exposure; terminal half-life of ~6-9 days; no significant accumulation after repeated doses



- **Dose-proportional exposure**
- **Terminal half-life:** Approximately 6-9 days
- **No significant accumulation** observed following repeated dosing

ADA: anti-drug antibody
Data cutoff date: Aug 26, 2026

Immunogenicity (ADA): Low incidence of treatment-emergent ADA positivity was observed (0.43%, 1/234 ADA-evaluable patients from Phase I/II)

	Patient Number (%)
ADA-evaluable	234
ADA Prevalence	11/234 (4.7%)
Treatment-emergent ADA-positivity	1/234 (0.43%)
• Treatment-induced positivity	1/234 (0.43%)
• Treatment-enhanced positivity	0
• Baseline ADA missing & post-baseline positive	0

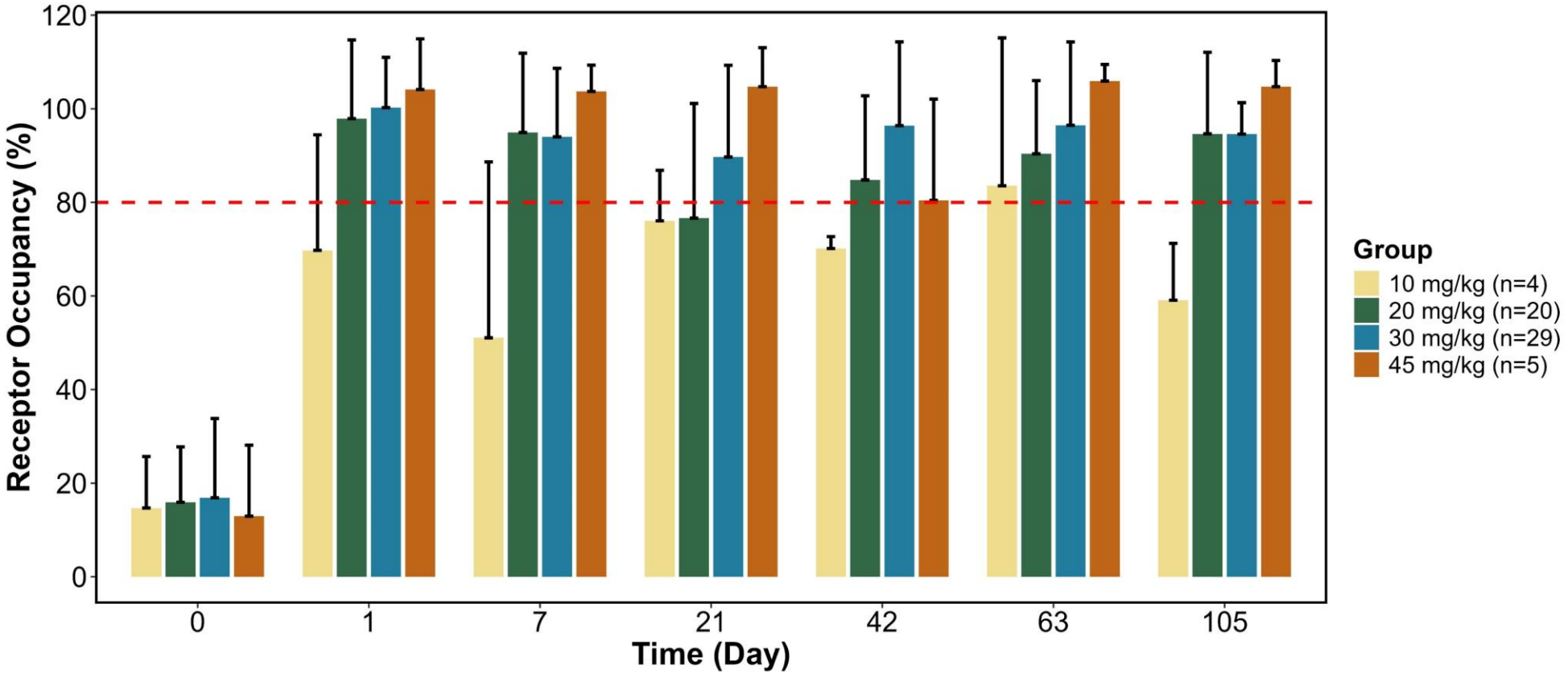
- **ADA-evaluable**: Treated and with ≥1 post-baseline ADA assessment
- ADA positive at any time point, i.e., at baseline or during treatment
- **Treatment-induced**: ADA-negative at baseline → positive post-dose
- **Treatment-enhanced**: ADA-positive at baseline → ≥4-fold titer increase

ADA Sampling Schedule:

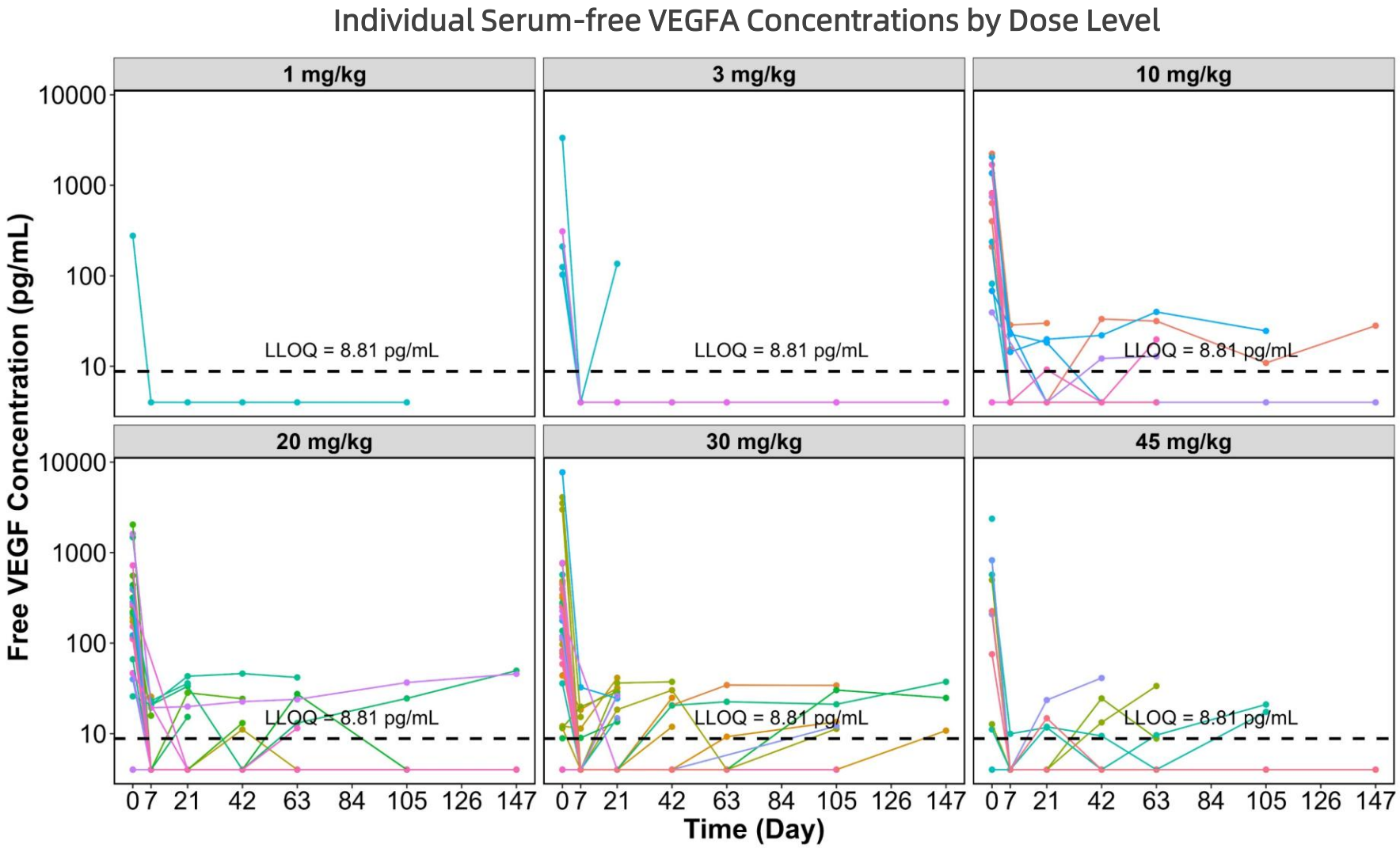
- Pre-dose at baseline; Cycles 2, 3, 4, 6, 8, 12; then every 4 cycles
- Post-baseline data availability: Up to Cycle 16 (Day 315)
- Median last post-baseline assessment: Cycle 4 (Day 63)

ADA=anti-drug antibody
Data cutoff date: Aug 26, 2026

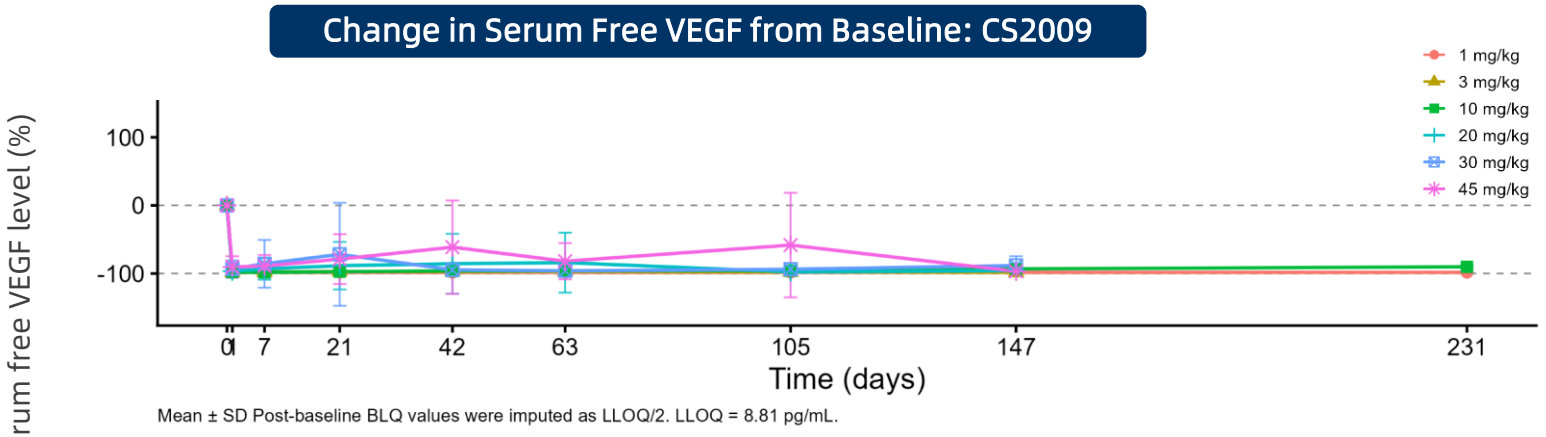
Receptor Occupancy of PD-1/CTLA-4 on peripheral T cells reached saturation throughout dosing interval at ≥20 mg/kg



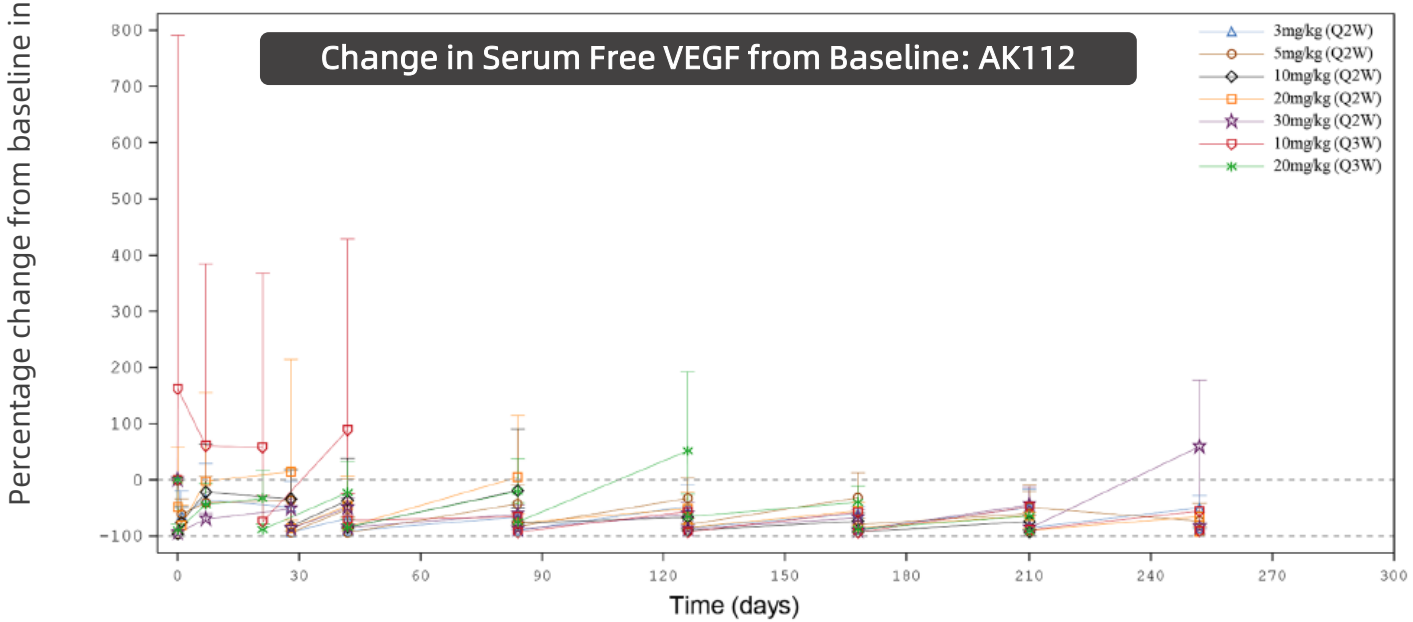
VEGF neutralization: Serum-free VEGFA reduced deeply and rapidly across all doses, and the effect sustained throughout dose interval



Serum Free VEGF Suppression: CS2009 vs. AK112



Mean ± SD Post-baseline BLQ values were imputed as LLOQ/2. LLOQ = 8.81 pg/mL.



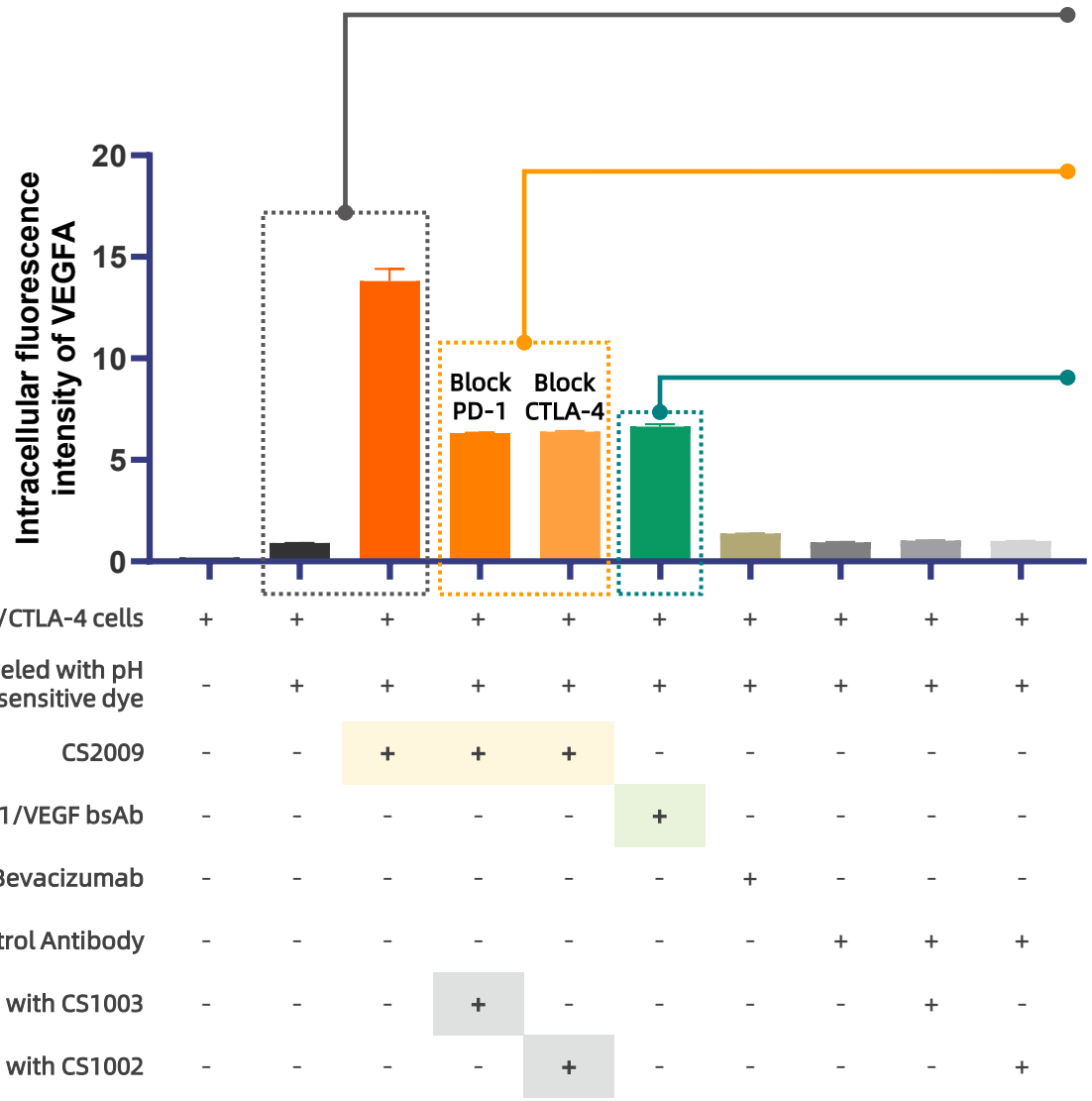
- CS2009 maintains **sustained suppression of serum free VEGF** levels over time, with **minimal to no rebound** observed across all dose cohorts

- Published **AK112** Phase Ib data* show **inconsistent VEGF suppression**, with **rebounds** observed at multiple time points

***Note**: Cross-trial comparison only; differences in assay methodologies and sampling schedules may impact data interpretation*

** Source: Cancer Medicine, 2025; 14:e70653*

VEGFA Internalization Assay: CS2009 mediates VEGFA internalization by T cells via dual PD-1 and CTLA-4 pathways



** CS1003 is the parental antibody of CS2009's PD-1 arm*
 # CS1002 is the parental antibody of CS2009's CTLA-4 arm

CS2009 Mediates Robust VEGFA Internalization by Jurkat T Cells Expressing PD-1 and CTLA-4

CS2009 (orange bar) vs. control (black bar)

CS2009 Mediates VEGFA Internalization via Dual PD-1/CTLA-4 Pathways

Blockade of either PD-1 or CTLA-4 attenuates CS2009-mediated VEGFA internalization, indicating that both pathways contribute synergistically to VEGFA clearance by T cells

CS2009 Induces Greater VEGFA Internalization than a PD-1/VEGF bispecific antibody

PD-1/VEGF bsAb mediates substantially less VEGFA internalization (green bar vs. 1st orange bar from the left) via PD-1 pathway alone

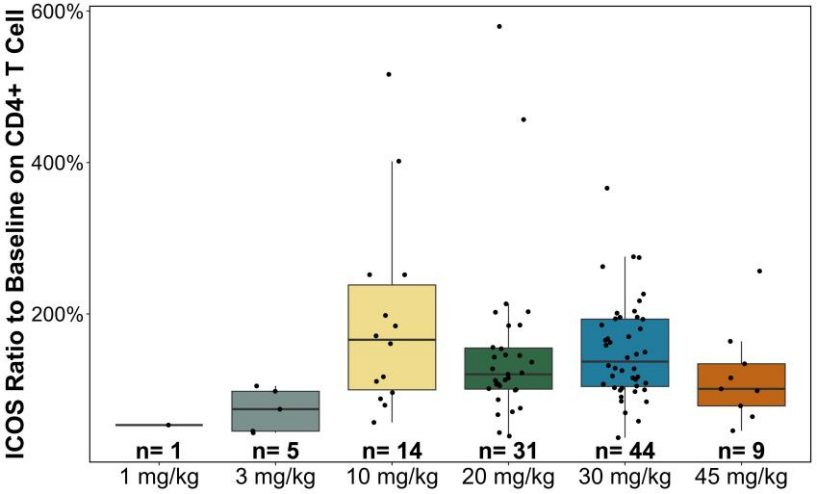
Multiple Mechanisms of Action:

"VEGF Signaling Blockade" + "Active Directional VEGF Clearance" + "Checkpoint Downregulation"

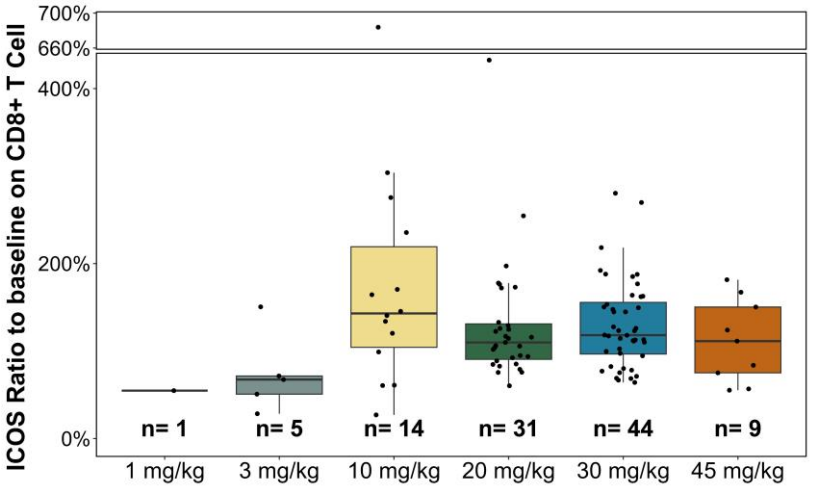
- Clearance of VEGFA and its immune-complexes in the TME may limit their redistribution to the periphery and thereby attenuate common VEGF-related toxicities - including hypertension, proteinuria, and hemorrhage - conferring a differentiated safety profile for CS2009
- Although not the primary objective of this assay, the data indicate that CS2009 also induce efficient internalization of cell-surface PD-1 and CTLA-4. Beyond its checkpoint blockade activity, this enhanced checkpoint downregulation on T cells may further augment the immuno-oncologic activity of CS2009

Robust T cell activation (ICOS and Ki67 up-regulation with plateau at doses ≥10 mg/kg)

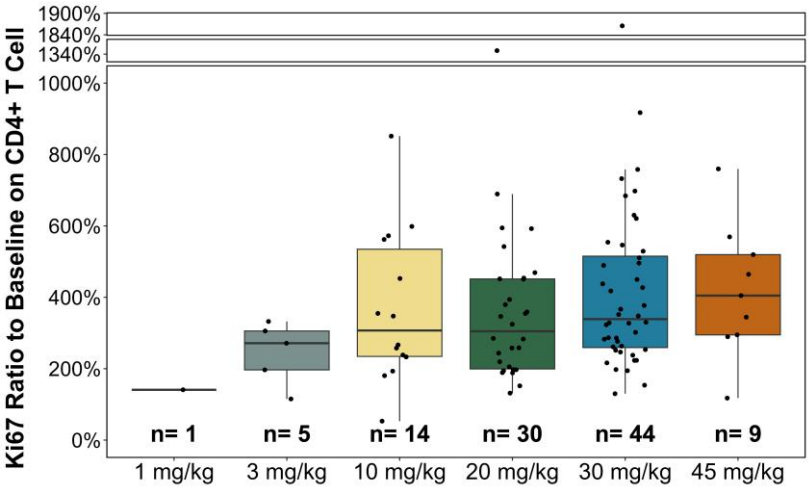
ICOS expression on CD4+ T cells



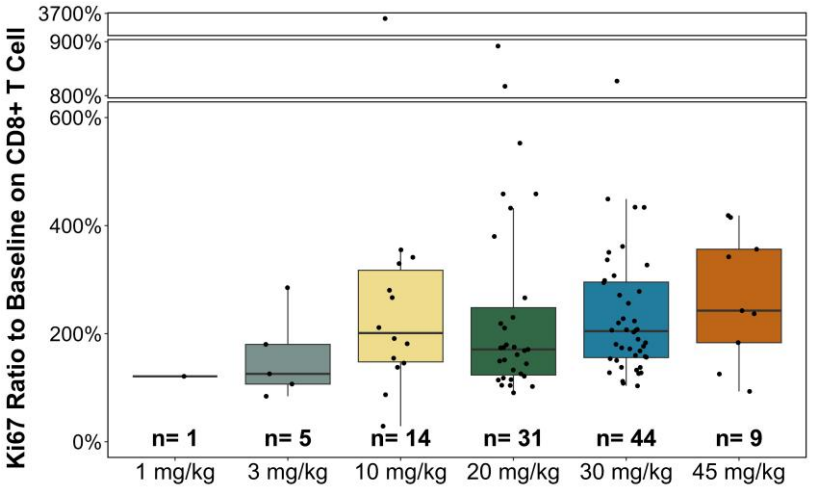
ICOS expression on CD8+ T cells



Ki67 expression on CD4+ T cells



Ki67 expression on CD8+ T cells



- **ICOS upregulation on CD4 T cells** provides specific evidence of CTLA-4 signaling blockade driven by CS2009's anti-CTLA-4 arm.

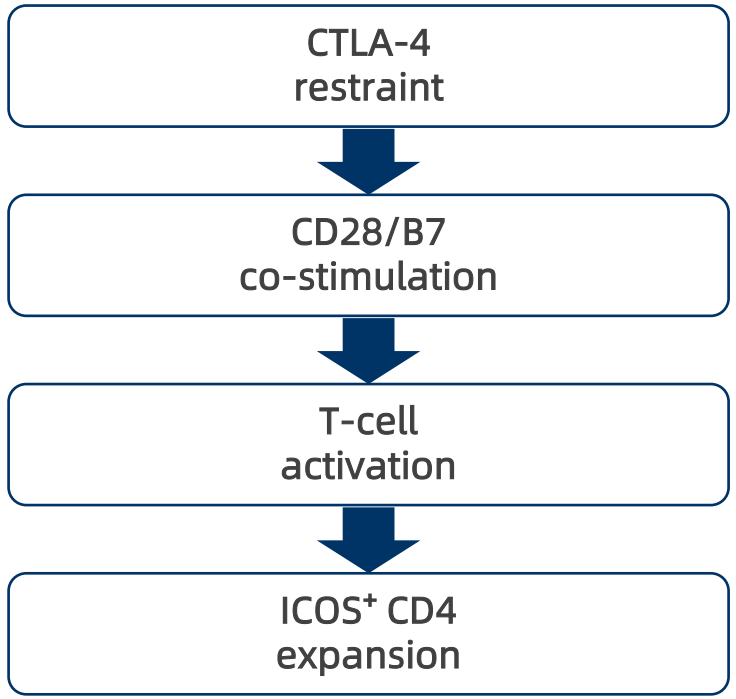
- **T-cell proliferation & activation:** On Cycle 1 Day 8, CS2009 induced notable, dose-dependent upregulation of **Ki67** (proliferation) and **ICOS** (activation) expression on both **CD4+** and **CD8+ T cells**, collectively demonstrating effective PD-1 and CTLA-4 inhibition

CD4 or CD8_ICOS_ratio = CD4 or CD8_ICOS+% (day8 / baseline)
CD4 or CD8_ICOS+%= (CD45+CD3+%) × (CD3+CD4 or CD8+%) × (CD3+CD4 or CD8+ICOS%)

CD4 or CD8_Ki67_ratio = CD4 or CD8_Ki67+% (day8 / baseline)
CD4 or CD8_Ki67+%= (CD45+CD3+%) × (CD3+CD4 or CD8+%) × (CD3+CD4 or CD8+Ki67%)

Background: CD4 ICOS upregulation reflects CTLA-4 pathway blockade

ICOS is an activation-induced co-stimulatory receptor expressed on activated T cells and supports T-cell expansion and effector function.[1,2]

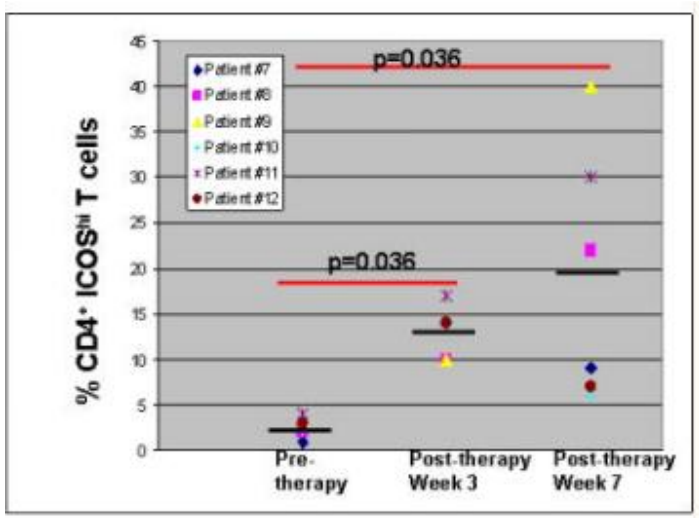


- CTLA-4 and CD28 compete for the B7 ligands CD80/CD86; CTLA-4 restrains CD28-mediated co-stimulation during T-cell priming.[1]
- CTLA-4 blockade releases this inhibitory constraint, enhancing CD28-dependent T-cell activation and expansion.[1]
- Systemic CTLA-4 blockade reproducibly expands activated $ICOS^{hi}$ CD4 T cells, making peripheral CD4 ICOS a well-established CTLA-4 PD signature.[1]

Notes: 1. Carthon BC et al. Preoperative CTLA-4 Blockade: Tolerability and Immune Monitoring in the Setting of a Presurgical Clinical Trial. Clin Cancer Res. 2010;16:2861–2871. 2. Wei SC et al. Distinct Cellular Mechanisms Underlie Anti-CTLA-4 and Anti-PD-1 Checkpoint Blockade. Cell. 2017;170:1120–1133.e17.

Clinical Evidence: Ipilimumab induces robust CD4+ ICOS+ T cell expansion

Increased frequency of $CD4^{+}ICOS^{hi}$ T cells in the peripheral blood of bladder cancer patients after ipilimumab treatment[1]



N=6; 10 mg/kg/dose
Fold change to baseline: *at Week 3:* ***4-5 X***

Increased frequency of $CD4^{+}ICOS+$T cells in the peripheral blood of bladder and melanoma patients after ipilimumab treatment[2]

Cohort	Baseline	After dose 1 (W3)	After dose 2 (W7)	Fold vs baseline
Bladder N=12	2.36 ± 1.18%	**13.33** ± 4.14%	16.27 ± 10.29%	**5.65×** → 6.89×
Melanoma N=24	2.08 ± 1.67%	**6.13** ± 5.27%	7.46 ± 6.18%	**2.95×** → 3.59×

Notes: 1. Carthon BC et al. Clin Cancer Res. 2010;16:2861-2871. 2. Tang DN et al. Increased Frequency of ICOS+ CD4 T Cells as a Pharmacodynamic Biomarker for Anti-CTLA-4 Therapy. Cancer Immunol Res. 2013;1:229-234.

Volrustomig a novel PD-1/CTLA-4 bispecific antibody leads to robust increase in peripheral and intra-tumoral pharmacodynamic biomarkers in solid tumors from FTiH study

Ikbel Achour[1], Michael Kuziora[1], Florian Song[1], Steven Eck[2], Lina Meinecke[1], Jorge Blando[1], Jennifer Pearson[2], Megha Saraiya[1], Christian Eisen[1], Felix Segerer[1], Markus Schick[1], Nicolas Triltsch[1], Michael Surace[1], Gisele Silva Boos[1], Harald Hessel[1], Mai Bui[1], Katrin Pratsch[1], Alma Andoni[1], Shelby Gainer[1], Dan Freeman[1], Deepa Subramaniam[1] and Ben Tran[3]

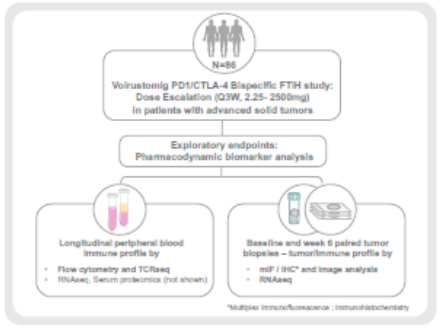
[1]R&D Early Oncology AstraZeneca USA, [2]R&D Biopharmaceutical AstraZeneca USA, [3]Peter MacCallum Cancer Centre, Melbourne, Australia

Abstract 3627

Background

Volrustomig (MEDI5752) is designed to fully inhibit PD-1 while preferentially inhibiting CTLA-4 on activated PD-1+ T cells. In a FTiH trial, volrustomig demonstrated meaningful clinical activity in patients with advanced solid tumors (including 1L RCC and NSCLC), acceptable safety profile, sustained PD-1 receptor occupancy, and T cell proliferation at levels greater than seen with clinically tolerable doses of CTLA-4 inhibitors with co-administration of anti-PD(L)-1[1-4]. We sought to further characterize volrustomig pharmacodynamic effect in the periphery and tumor to demonstrate its biological activity and inform dose optimization.

Methods

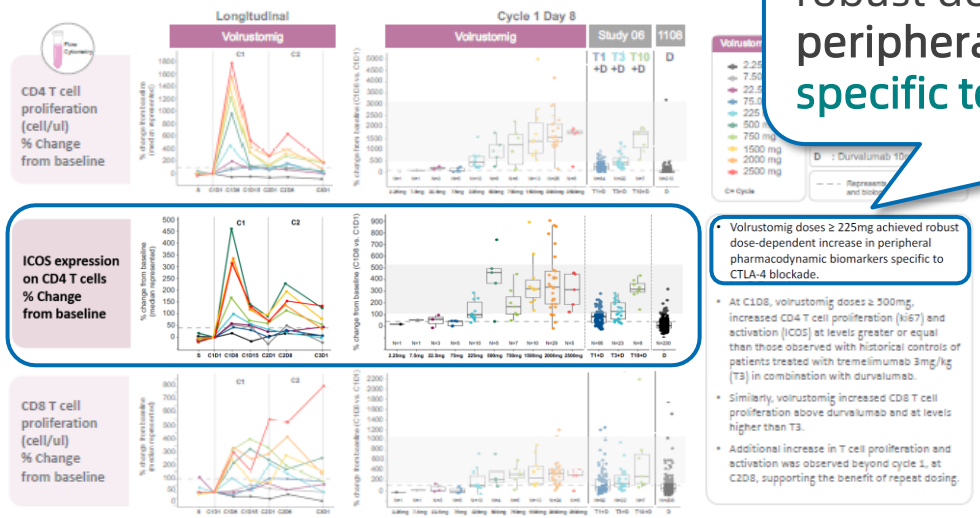


Patient Demographics in ITT and BEP	ITT Total N=86	Pharmacodynamic BEP			
		Peripheral Blood longitudinal		Tumor paired biopsies baseline/week6	
		Flow Cytometry** N=72	TCRseq*** N=71	RNAseq N=12	mIF/IHC N=17
Median age (range), years	60.5 (23–82)	59.5 (23–78)	60.0 (23–82)	56.0 (45.0–62.0)	60.0 (40.0-62.0)
Sex, n (%)					
Male	65 (75.6)	54 (75.0)	52 (73.2)	8 (66.7)	12 (70.6)
Female	21 (24.4)	18 (25.0)	19 (26.8)	4 (33.3)	5 (29.4)
ECOG PS, n (%)					
0	42 (48.8)	35 (48.6)	38 (53.5)	3 (25.0)	4 (23.5)
1	44 (51.2)	37 (51.4)	33 (46.5)	9 (75.0)	13 (76.5)
Cancer types*, n (%)					
Renal cell carcinoma	19 (22.1)	15 (20.8)	16 (22.5)	2 (16.7)	4 (23.5)
Non-small cell lung cancer	14 (16.3)	9 (12.5)	9 (12.7)	1 (8.3)	4 (23.5)
Others	43 (51.6)	40 (55.7)	46 (64.8)	7 (58.3)	9 (47.1)
PD-L1 TC expression, n (%)					
≥1%	16 (18.6)	14 (19.4)	16 (22.5)	3 (12.0)	1 (5.9)
<1%	53 (61.6)	43 (59.7)	40 (56.3)	16 (64.0)	13 (76.5)
Not evaluable	17 (19.8)	15 (20.8)	15 (21.1)	6 (24.0)	3 (17.6)
IO-naïve, n (%)	78 (90.7)	65 (90.3)	64 (90.1)	12 (100)	17 (100)
Prior lines of therapies, n (%)					
0	13 (15.1)	11 (15.3)	11 (15.5)	1 (8.3)	1 (5.9)
1	35 (40.7)	32 (44.4)	30 (42.3)	3 (25.0)	8 (47.1)
≥2	38 (44.2)	29 (40.3)	30 (42.3)	8 (66.7)	8 (47.1)

*25 cancer types ; **Sample size based on CD4 T cell proliferation readout up to C2D1; ***sample size based on TCRseq data available up to C2D1. ITT: intend to treat population ; BEP: Biomarker evaluable population ; TC: tumor cells

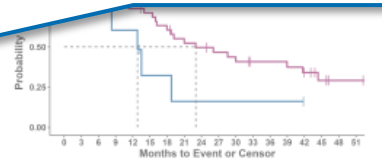
Results

Figure 1 Volrustomig doses ≥ 225mg achieved dose dependent increase in pha… biomarker specific to CTLA-4 blockade at levels ≥ tremelimumab 3mg/kg in comb…



- Volrustomig doses ≥ 225mg achieved robust dose-dependent increase in peripheral pharmacodynamic biomarkers specific to CTLA-4 blockade.
- At C1D8, volrustomig doses ≥ 500mg, increased CD4 T cell proliferation (ki67) and activation (ICOS) at levels greater or equal than those observed with historical controls of patients treated with tremelimumab 3mg/kg (T3) in combination with durvalumab.
- Similarly, volrustomig increased CD8 T cell proliferation above durvalumab and at levels higher than T3.
- Additional increase in T cell proliferation and activation was observed beyond cycle 1, at C2D8, supporting the benefit of repeat dosing.

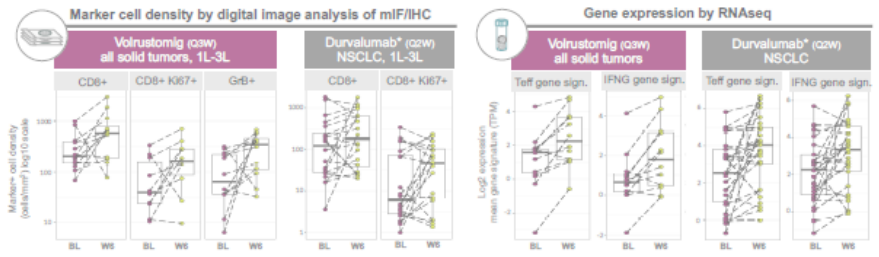
Volrustomig doses ≥225 mg achieved robust dose-dependent increases in **peripheral pharmacodynamic biomarkers** specific to CTLA-4 blockade.



median number of total expanded T cell clones (TCRseq)	% patient by subgroup	mOS (95% CI)	OS HR (95% CI)
≥32	81.7%	23.0 (16- 41.7)	0.43 (0.19 -1.01)
<32	18.3%	12.8 (5-18.8)	

*Cutoff=32: represents median number of total expanded T cell clones in durvalumab monotherapy arm in study 23[4]. ≥ 32 expanded T cell clones was associated with CTLA-4 blockade.
BEP represents ITT ; OS: Overall survival ; HR: Hazard Ratio ; CI: Confidence of Interval
Volrustomig clinical data based on DCO August 25, 2023

Figure 3 Volrustomig leads to greater increase in intra-tumoral T cell proliferation and cytotoxic activity than durvalumab alone



Effect size:								
#pts (%) with biomarker ≥ 2-fold increase w6 vs. BL	6/12 (50%)	7/10 (70%)	6/12 (50%)	7/20 (35%)	10/20 (50%)	6/12 (50%)	6/12 (50%)	12/29 (41.4%)	13/29 (31%)
Cohort level: biomarker median fold increase w6 vs. BL ; *p-value Wilcoxon test*	2.3 *p=0.04*	2.14 *p=0.04*	2.2 ; *p=0.01*	1.62 *p = 0.165*	1.62 *p= 0.475*	2.2 *p=0.002*	2.5 *p=0.005*	1.7 *p=0.0002*	1.4 *p=0.008*

BL: Baseline ; W6: Week 6 following 2 doses of volrustomig or 3 doses of durvalumab; GrB: Granzyme B ; *Durvalumab 1108 study[4] ; For 1108 study, GrB was not performed due to the lack of available materials ; T effector (Teff) and interferon gamma (IFNG) gene signatures[5,6]

Conclusion

Volrustomig demonstrated robust peripheral and intra-tumoral T cell activation and proliferation, broadening the pool of antigen experienced T cells, at levels greater than seen with dual checkpoint blockade currently used in the clinic.

References

1. Tran B et al. AACR 2022; Cancer Research, 2022
2. Albiges L et al. ASCO 2022; Journal of Clinical Oncology, 2022
3. Ahn, M-J et al. ESMO 2022; Annals of Oncology, 2023
4. Voss M et al. ESMO 2023 ; Annals of Oncology, 2023
5. Antonia S, et al Lancet Oncol 2016;17(3):299-308
6. Antonia S. et al. Journal of thoracic Oncology 2019
7. Higgs BW, et al. Clinical Cancer Research 2018
8. Achour I et al. SITC 2018; Journal of Immunotherapy cancer 2018
9. McCoon P, et al. Journal of Clinical Oncology 2021

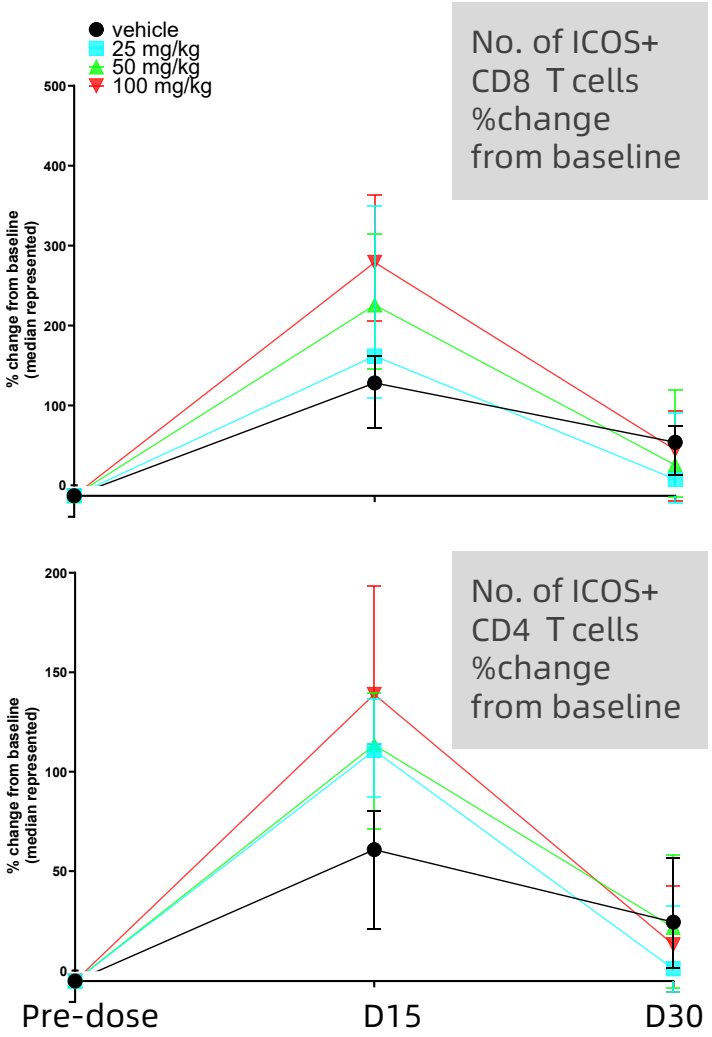
Acknowledgements

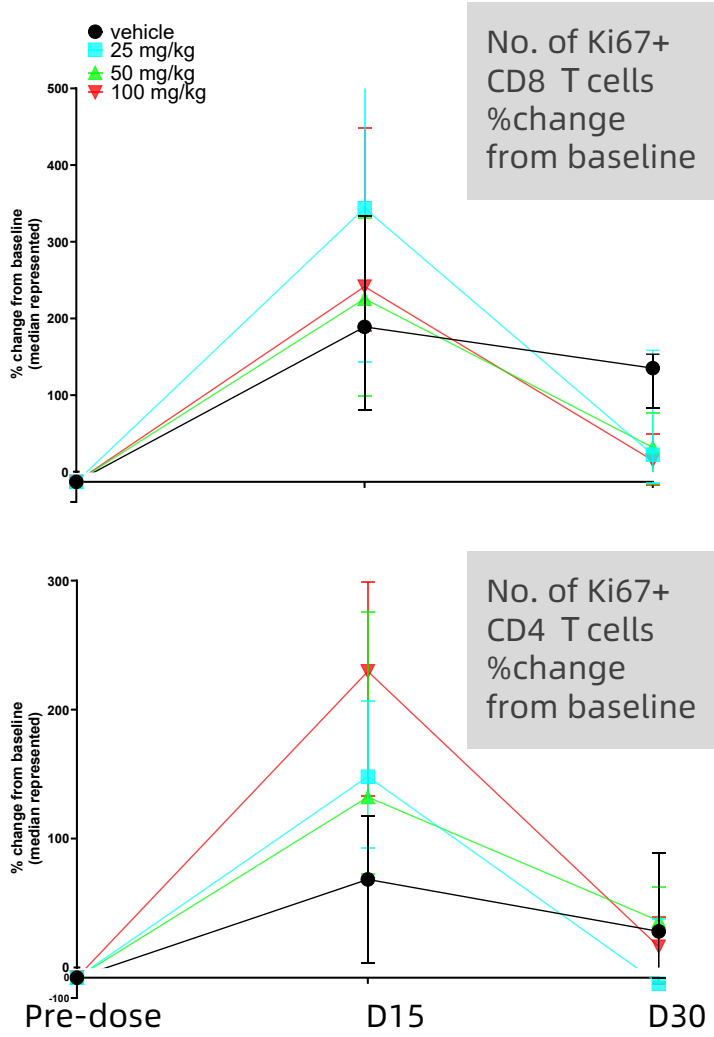
On behalf of the study team, the authors thank the patients and their families and caregivers for their participation in this study. This study was sponsored by MedImmune/Astrazeneca (Gaithersburg, MD, USA). Copies of this poster are for personal use only and may not be reproduced without written permission of the authors.

Contact Email: ikbel.achour@astrazeneca.com

CS2009 activated Cyno T Cells during GLP-toxicity study with dose dependency

Cyno study PD biomarker analysis





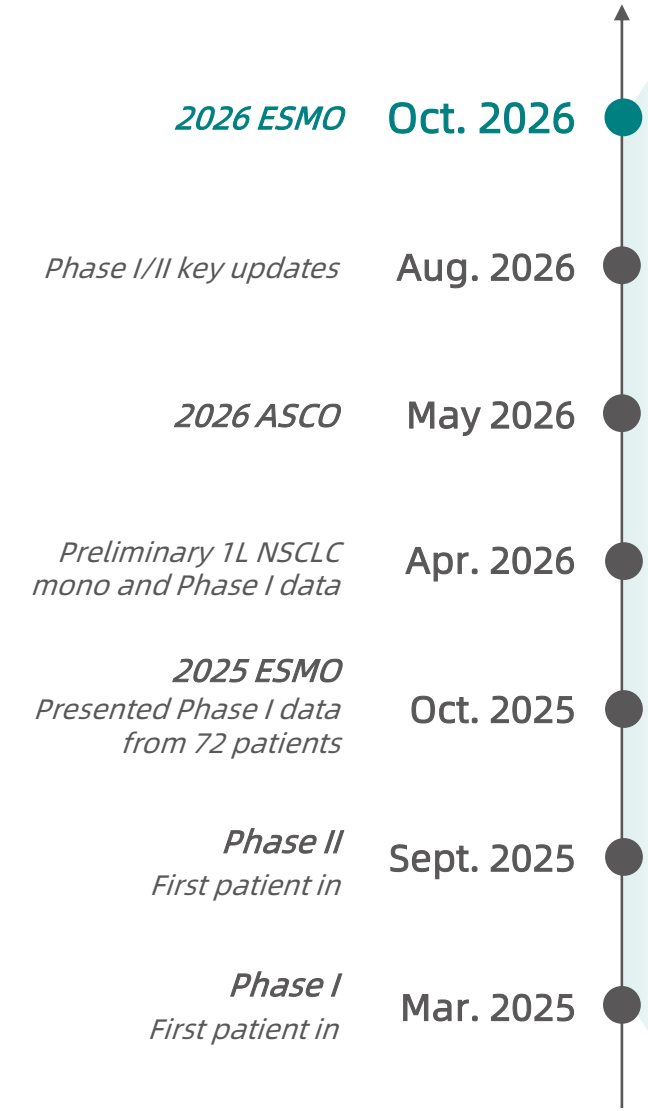
- CS2009 remarkably induced proliferation (Ki67) and activation (ICOS) biomarkers on CD4 and CD8 T cells
- The increase of these activities were dose-dependent, except for Ki67 on CD8 T cells, which reached plateau at a lower dose



CS2009

- Design, MoA, and Rationale
- **Phase 1/2 Clinical Data Update**
  - Proof of Mechanism
  - **Proof of Safety**
  - Proof of Concept in Broad Cancer Types
    1. Non-small Cell Lung Cancer (NSCLC) Dataset
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    3. Preliminary Clinical Data for Other Tumor Types
- Regulatory and Clinical Plan for Global Phase 3 Trials

Three Important Key Clinical Validations Achieved from over 300 Patient Data



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- Dose-dependent **ICOS upregulation on CD4+ T cells**: PD biomarker specific to CTLA-4 blockade
- Linear **PK** with half-life of ~6-9 days; low incidence of ADA positivity
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➢ Proof of Safety

- **Grade ≥3 irAEs 12.7%**; CTLA-4-related tox markedly reduced from CTLA-4 mAb monotherapy or in combination with PD-1/L1, including **extremely rare colitis,** due to **preserved CTLA-4 signaling** in peripheral Tregs & autoreactive T cells
- **Grade ≥3 VEGF-related tox 5.1%;** likely mediated by PD-1/CTLA-4-driven VEGFA immune complex internalization by T cells in TME as indicated by the data

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- Robust mono & chemo-combo efficacy in **1L and late-line pMMR/MSS mCRC**
- Promising antitumor activity in other "**cold tumors**" including STS and nccRCC, and other solid tumors including SCLC, OC, HCC, GC, EC, mCRPC, TNBC, etc.

TME: tumor microenvironment; ICOS: inducible T-Cell Co-stimulator; NSCLC: non-small cell lung cancer; STS: soft tissue sarcoma; nccRCC: non-clear-cell renal cell carcinoma; pMMR/MSS: proficient mismatch repair / microsatellite stable; mCRC: metastatic colorectal cancer; SCLC: small-cell lung cancer; mCRPC: metastatic Castration-Resistant Prostate Cancer; OC: ovarian cancer; TNBC: triple-negative breast cancer; GC: gastric cancer; EC: esophageal cancer

Phase I Safety: Phase I Data Demonstrate Compelling Safety Profile

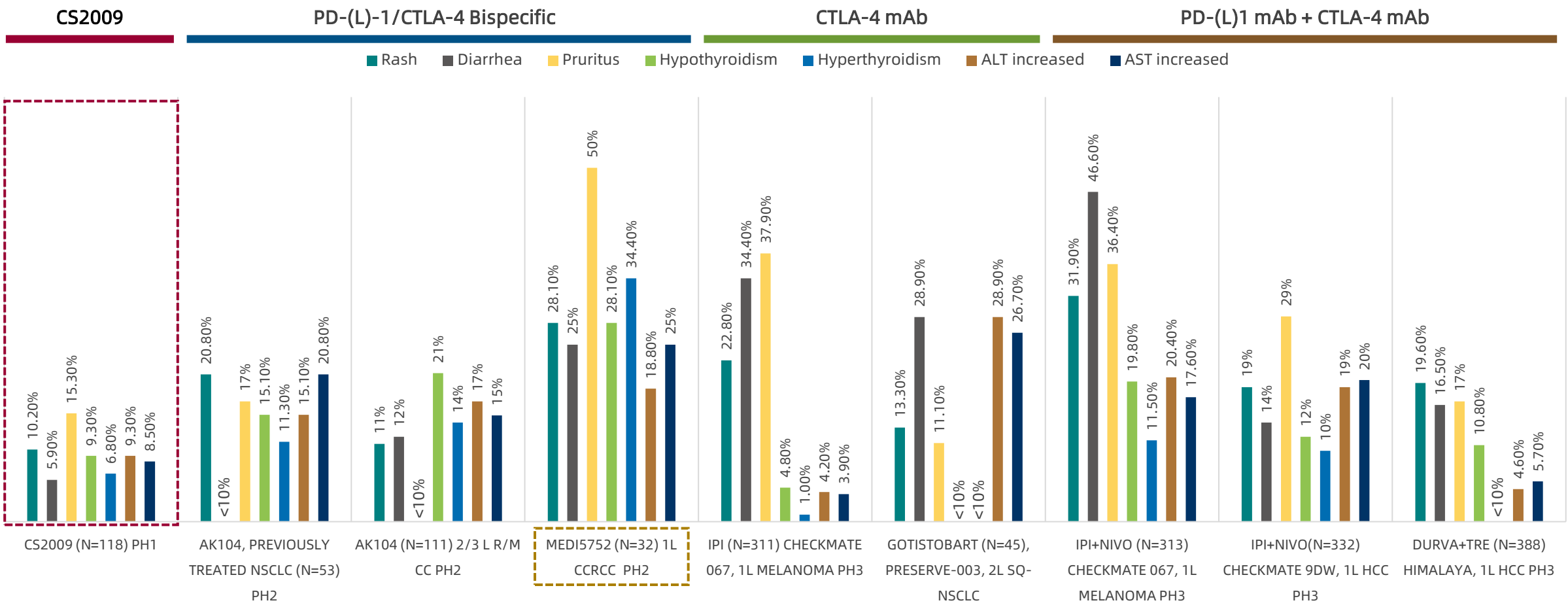
- Dose escalation completed; no DLT; MTD not reached
- Without excessive toxicities that typically occurred in CTLA-4- and PD-(L)1-containing combination therapies; low ≥G3 VEGF-related AEs
- **Up to date, no new safety signals identified; CS2009's safety profile remained consistent with that presented at 2026 ASCO**

n (%)	1-10 mg/kg (n=21)	20 mg/kg (n=33)	30 mg/kg (n=54)	45 mg/kg (n=10)	All DLs (N=118)
TEAE	21 (100)	31 (93.9)	45 (83.3)	10 (100)	107 (90.7)
Grade ≥3 TEAE	10 (47.6)	15 (45.5)	20 (37.0)	5 (50.0)	50 (42.4)
Treatment-related TEAE (TRAE)	18 (85.7)	27 (81.8)	39 (72.2)	10 (100)	94 (79.7)
• Grade ≥3 TRAE	6 (28.6)	7 (21.2)	13 (24.1)	3 (30.0)	**29 (24.6)**
Immune-related TEAE (irAE)	9 (42.9)	18 (54.5)	16 (29.6)	3 (30.0)	46 (39.0)
• Grade ≥3 irAE	3 (14.3)	6 (18.2)	5 (9.3)	1 (10.0)	**15 (12.7)**
Infusion-related reaction	1 (4.8)	1 (3.0)	1 (1.9)	2 (20.0)	5 (4.2)
TRAE possibly related to anti-VEGF	5 (23.8)	11 (33.3)	9 (16.7)	2 (20.0)	27 (22.9)
• Grade ≥3 TRAE possibly related to anti-VEGF	2 (9.5)	1 (3.0)	3 (5.6)	0	**6 (5.1)**
TRAE leading to drug discontinuation	1 (4.8)	3 (9.1)	5 (9.3)	0	9 (7.6)

- Most frequent (≥5%) any-grade **irAE:** hypothyroidism (6.8%), rash / AST increased / ALT increased (5.1% each)
- Most frequent (≥5%) any-grade **TRAE possibly related to anti-VEGF therapy:** proteinuria (11.9%), hypertension (8.5%)

TEAE: treatment-emergent adverse event; AST: aspartate aminotransferase; ALT: alanine aminotransferase
Data source: 2026 ASCO

Safety Comparison: Much lower incidence of frequent any-grade treatment-related and suspected irAE* vs. PD-(L)1/CTLA-4 bispecific or combination regimens



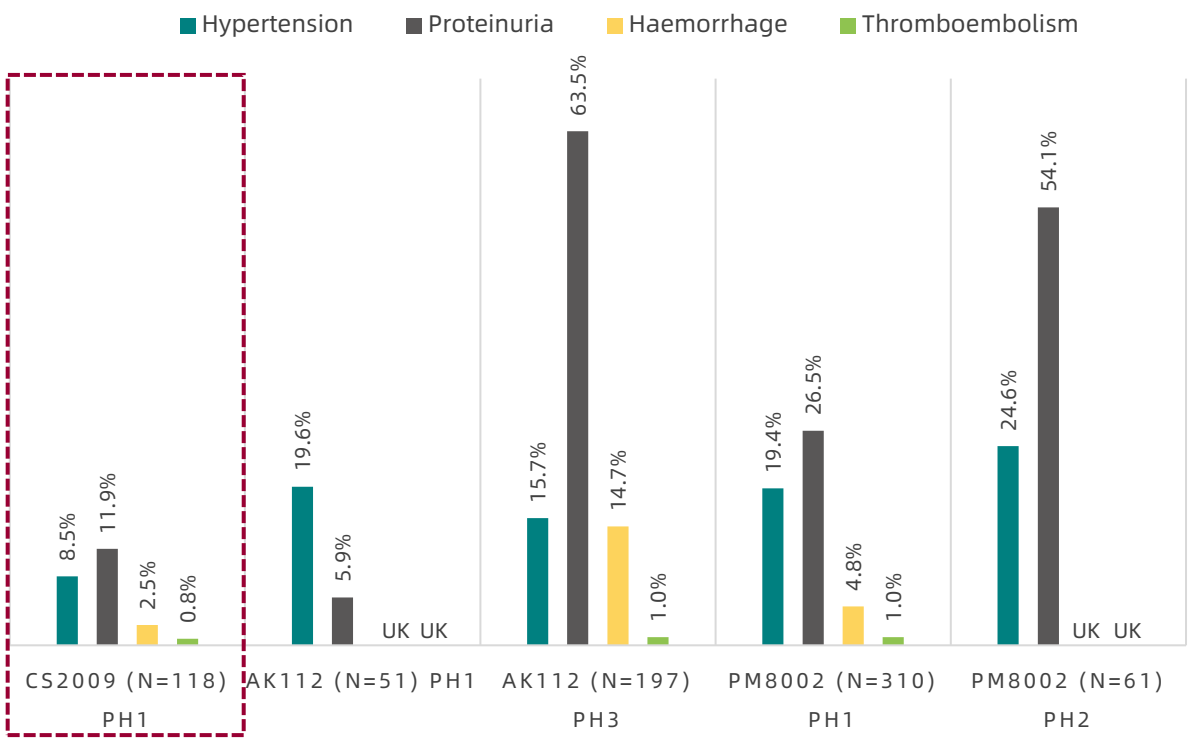
** Data show incidence of treatment-related adverse events (TRAEs) using preferred terms for immune-related adverse events (irAEs). TRAEs are presented instead of irAEs due to inconsistent reporting, varying definitions and assessment methods across comparator trials*

Note: AE of <10% incidence not shown

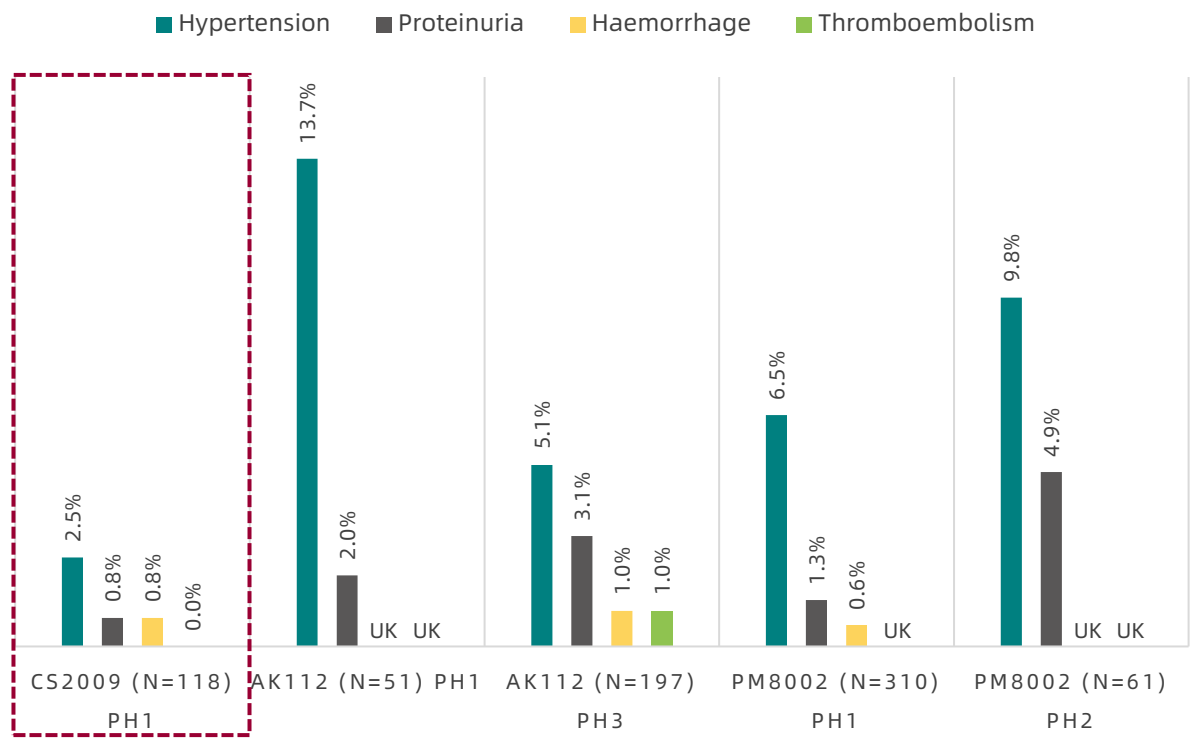
Source: Lung Cancer 184 (2023) 107355; Lancet Oncol 2023; 24: 1134-46; 2023 ESMO; April 16, 2018, at NEJM.org; N Engl J Med. 2025 January 02; 392(1): 11-22; Lancet 2025; 405: 1851-64; June 6, 2022 NEJM Evid 2022; 1 (8); Nat Med. 2026 Mar 27

Safety Comparison: Markedly lower incidence of any-grade or Grade ≥3 TRAE possibly related to anti-VEGF vs. PD-(L)1/VEGF bispecifics

Any-grade TRAE possibly related to anti-VEGF



Grade ≥3 TRAE possibly related to anti-VEGF



TRAE: treatment-emergent adverse event; UK: unknown
Source: 2026 ASCO; J Immunother Cancer. 2024 Apr 19;12(4):e008037; Lancet 2025; 405: 839-49; 2023 ASCO, #414802; 2024 ASCO, #8533



CS2009

- Design, MoA, and Rationale
- **Phase 1/2 Clinical Data Update**
  - Proof of Mechanism
  - Proof of Safety
  - **Proof of Concept in Broad Cancer Types**
    1. Non-small Cell Lung Cancer (NSCLC) Dataset
    2. Colorectal Cancer (CRC) Dataset
    3. Preliminary Clinical Data for Other Tumor Types
- Regulatory and Clinical Plan for Global Phase 3 Trials

Three Important Key Clinical Validations Achieved from over 300 Patient Data

2026 ESMO **Oct. 2026**

Phase I/II key updates **Aug. 2026**

2026 ASCO **May 2026**

Preliminary 1L NSCLC mono and Phase I data **Apr. 2026**

2025 ESMO *Presented Phase I data from 72 patients* **Oct. 2025**

Phase II *First patient in* **Sept. 2025**

Phase I *First patient in* **Mar. 2025**

➢ Proof of Mechanism

- Dose-dependent **ICOS upregulation on CD4+ T cells**: PD biomarker specific to CTLA-4 blockade
- Linear **PK** with half-life of ~6-9 days; low incidence of ADA positivity
- Sustained **PD-1/CTLA-4 receptor occupancy** at doses ≥20 mg/kg
- **Serum-free VEGFA** reduced deeply and rapidly; effect sustained throughout dose intervals

➢ Proof of Safety

- **Grade ≥3 irAEs 12.7%**; CTLA-4-related tox markedly reduced from CTLA-4 mAb monotherapy or in combination with PD-1/L1, including **extremely rare colitis,** due to **preserved CTLA-4 signaling** in peripheral Tregs & autoreactive T cells
- **Grade ≥3 VEGF-related tox 5.1%;** likely mediated by PD-1/CTLA-4-driven VEGFA immune complex internalization by T cells in TME as indicated by the data

➢ Proof of Concept in Broad Cancer Types

- Robust mono & chemo-combo efficacy in **1L and late-line NSCLC**
- Robust mono & chemo-combo efficacy in **1L and late-line pMMR/MSS mCRC**
- Promising antitumor activity in other **"cold tumors"** including STS and nccRCC, and other solid tumors including SCLC, OC, HCC, GC, EC, mCRPC, TNBC, etc.

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*ESMO 2026 Baseline Characteristics in NSCLC Cohorts

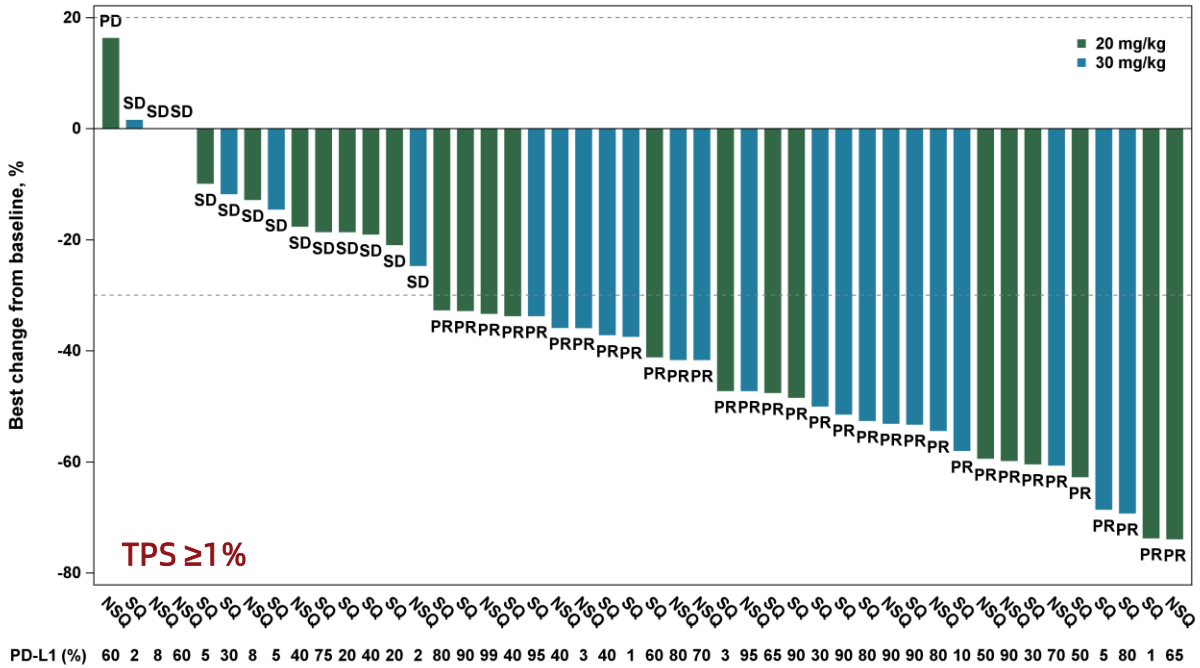
Characteristics	≥2L NSCLC monotherapy (n=57)	2/3L NSCLC combination (n=18)	1L NSCLC monotherapy (n=55)	1L SQ NSCLC combination (n=27)	1L NSQ NSCLC combination (n=18)
Age, median (range), years	67.0 (37–78)	64.0 (44–74)	66.0 (40–82)	67.0 (38–74)	63.0 (52–75)
Male, n (%)	43 (75.4)	13 (72.2)	46 (83.6)	22 (81.5)	11 (61.1)
Race, n (%)					
Asian	42 (73.7)	16 (88.9)	55 (100)	27 (100)	17 (94.4)
White	14 (24.6)	2 (11.1)	0	0	1 (5.6)
Other	1 (1.8)	0	0	0	0
ECOG performance status, n (%)					
0	13 (22.8)	3 (16.7)	7 (12.7)	11 (40.7)	3 (16.7)
1	44 (77.2)	15 (83.3)	48 (87.3)	16 (59.3)	15 (83.3)
Histology type, n (%)					
Squamous	25 (43.9)	11 (61.1)	31 (56.4)	27 (100)	0
Non-squamous	32 (56.1)	7 (38.9)	24 (43.6)	0	18 (100)
PD-L1 TPS, n (%)					
<1%	10 (17.5)	8 (44.4)	0	8 (29.6)	11 (61.1)
1%-49%	22 (38.6)	5 (27.8)	25 (45.5)	15 (55.6)	7 (38.9)
≥50%	15 (26.3)	0	30 (54.5)	2 (7.4)	0
Unknown	10 (17.5)	5 (27.8)	0	2 (7.4)	0
Prior lines of therapy, n (%)					
1 line	36 (63.2)	17 (94,4)	–	–	–
2 lines	11 (19.3)	1 (5.6)	–	–	–
≥3 lines	10 (17.5)	0	–	–	–
Prior immunotherapy, n (%)	48 (84.2)	18 (100)	–	–	–

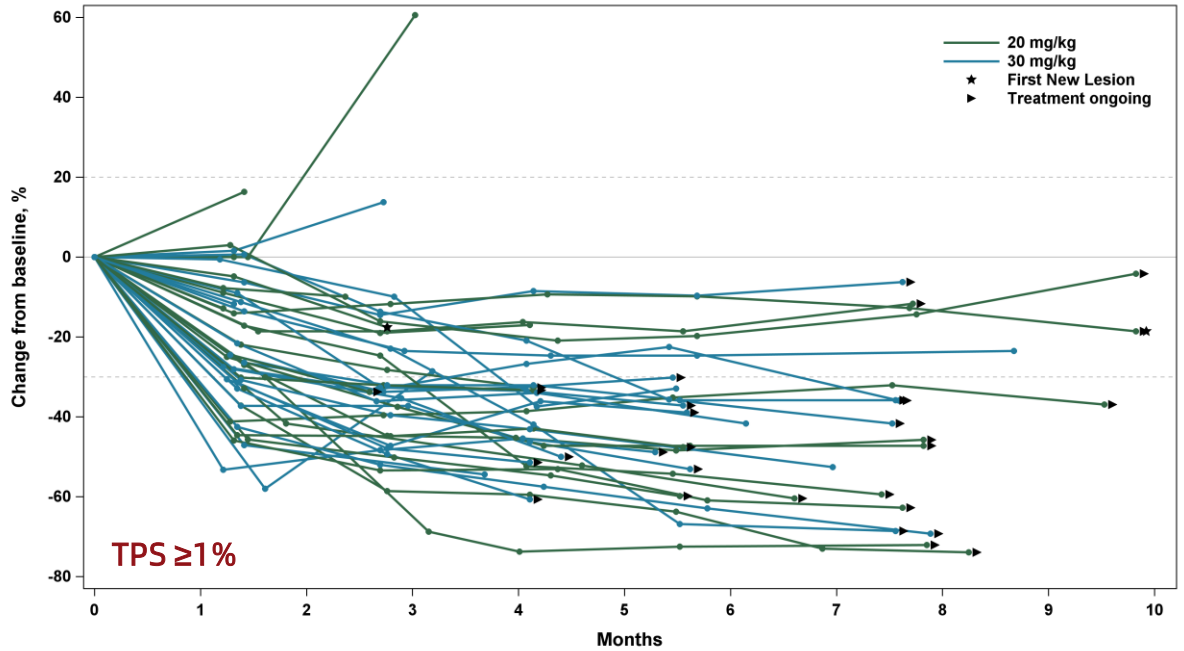
NSCLC: non-small cell lung cancer; PD-L1: programmed death-ligand 1; TPS: tumor proportion score

*Post-ESMO 1L NSCLC mono: CS2009 monotherapy demonstrated compelling clinical efficacy in first-line NSCLC (PD-L1 TPS ≥1%)

Monotherapy at 20 or 30 mg/kg, Q3W; enrollment completed; ORRs for TPS 1-49% and 20 mg/kg cohorts expected to increase with longer follow-up — early SDs often convert to PRs as treatment continues; **median PFS / DoR not reached due to limited follow-up**

		All Evaluable Patients	20 mg/kg	30 mg/kg	Squamous	Non-squamous
TPS ≥50%	ORR, % (n)	87.5% (21/24)	76.9% (10/13)	**100% (11/11)**	91.7% (11/12)	83.3% (10/12)
	DCR, % (n)	95.8% (23/24)	92.3% (12/13)	100% (11/11)	100% (12/12)	91.7% (11/12)
TPS ≥1%	ORR, % (n)	66.7% (32/48)	58.3% (14/24)	**75.0% (18/24)**	69.0% (20/29)	63.2% (12/19)
	DCR, % (n)	93.8% (45/48)	95.8% (23/24)	91.7% (22/24)	96.6% (28/29)	89.5% (17/19)





NSCLC: non-small cell lung cancer; TPS: tumor proportion score; SQ: squamous; NSQ: non-squamous; ORR: objective response rate; cORR: confirmed ORR; DCR: disease control rate; DoR: duration of response; PFS: progress-free survival
Data source: 2026 ESMO oral presentation and in-house Oct-2026 waterfall & spider plots

Higher ORR with CS2009 Monotherapy vs. IO Monotherapy and IO-Based Combo across TPS Subgroups in 1L PD-L1+ NSCLC

	CS2009 [1] (PD-1/VEGF/CTLA-4)		AK112 [2] (PD-1/VEGF)		Pembrolizumab [3] (anti-PD-1)		Nivolumab +/- Ipilimumab [4,5] (anti-PD-1 +/- anti-CTLA-4)		
Stage of data cited	Phase 2 CS2009-101		Phase 3 HARMONi-2		Phase 3 KEYNOTE-042		Phase 3 CheckMate 227		
Treatment	20 mg/kg, Q3W	30 mg/kg, Q3W	AK112 20mg/kg, Q3W	Pembro. 200mg, Q3W	Pembro. 200mg, Q3W	Platinum-based chemo	NIVO (3 mg/kg, Q2W) + IPI (1 mg/kg, Q6W)	NIVO (240mg, Q2W)	Platinum-based chemo
ORR, % (n) PD-L1 TPS ≥50%	76.9% (10/13)	100% (11/11)	60.2% (50/83)	48.2% (41/85)	39.5% (118/299)	32.0% (96/300)	45.4% (93/205)	36.9% (89/214)	35.4% (68/192)
ORR, % (n) PD-L1 TPS ≥1%	58.3% (14/24)	75.0% (18/24)	50.0% (99/198)	39.0% (78/200)	27.3% (174/637)	26.5% (169/637)	36.4% (144/396)	27.5% (109/396)	29.7% (118/397)

Note: The ORR of **pembrolizumab + chemo** for 1L NSCLC (PD-L1 TPS ≥50%) was **61.4%** (non-squamous, KEYNOTE-189) or **60.3%** (squamous, KEYNOTE-407), **lower than the monotherapy ORR with CS2009** (**83.3%** for non-squamous; **91.7%** for squamous)

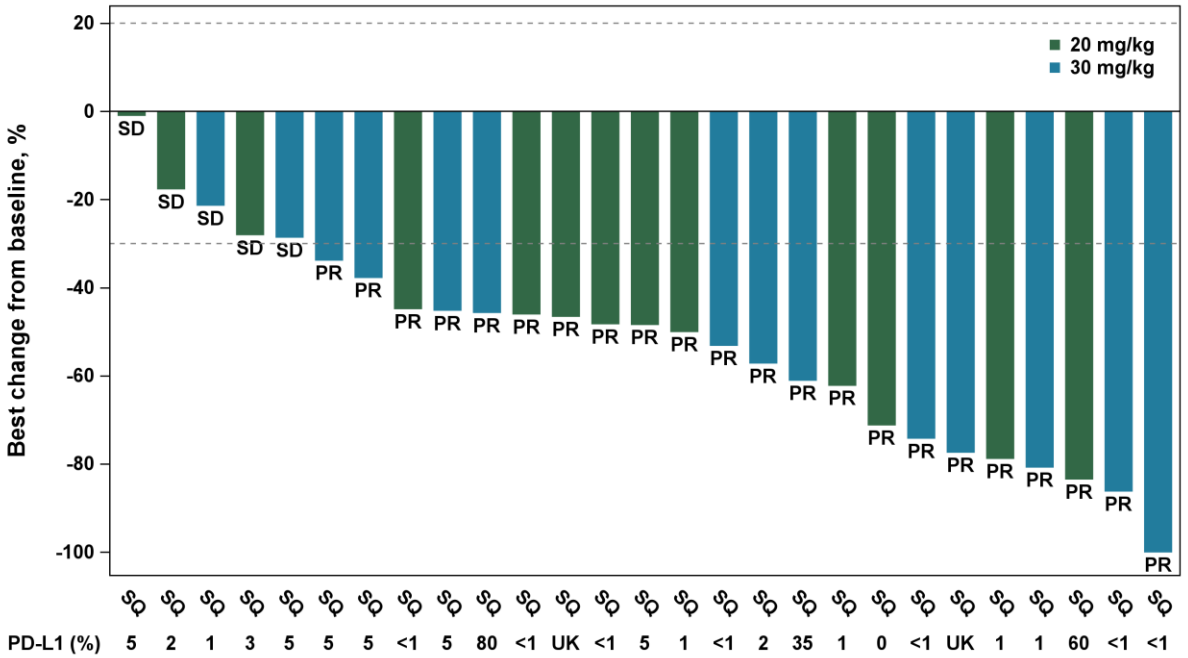
NSCLC: non-small cell lung cancer; TPS: tumor proportion score; ORR: objective response rate; Q3W: once every 3 weeks
Date source: 1. ESMO 2026; 2. WCLC 2025; 3. Lancet 2019; 4. JCO 2022; 5. JTO 2021

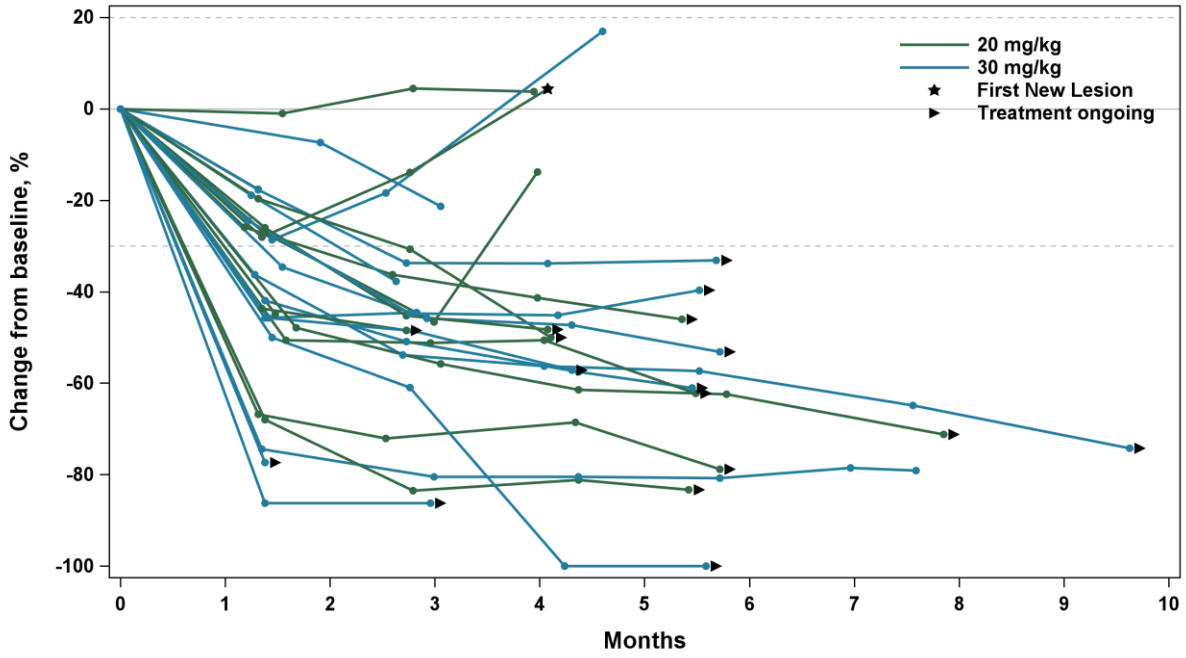
*Post-ESMO 1L squamous NSCLC combo: CS2009 + paclitaxel/carboplatin demonstrated compelling clinical efficacy in first-line squamous NSCLC

Most patients with PD-L1 TPS ≤5%. Patients received CS2009 at 20 or 30 mg/kg, plus paclitaxel and carboplatin for up to 4 cycles, followed by maintenance therapy of CS2009. **Enrollment ongoing**; ORR expected to increase with longer follow-up—early SDs often convert to PRs as treatment continues, as observed in more mature NSCLC cohorts. **Median PFS / DoR not reached due to limited follow-up**

	All Evaluable Patients	20 mg/kg	30 mg/kg	PD-L1 TPS <1%	PD-L1 TPS 1-49% *Note: 14/15 had TPS ≤5%*	PD-L1 TPS ≥50%
ORR, % (n)	81.5% (22/27)	76.9% (10/13)	85.7% (12/14)	**100% (8/8)**	66.7% (10/15)	100% (2/2)
DCR, % (n)	100% (27/27)	100% (13/13)	100% (14/14)	**100% (8/8)**	100% (15/15)	100% (2/2)

Note: Two additional patients with unknown PD-L1 status achieved PR





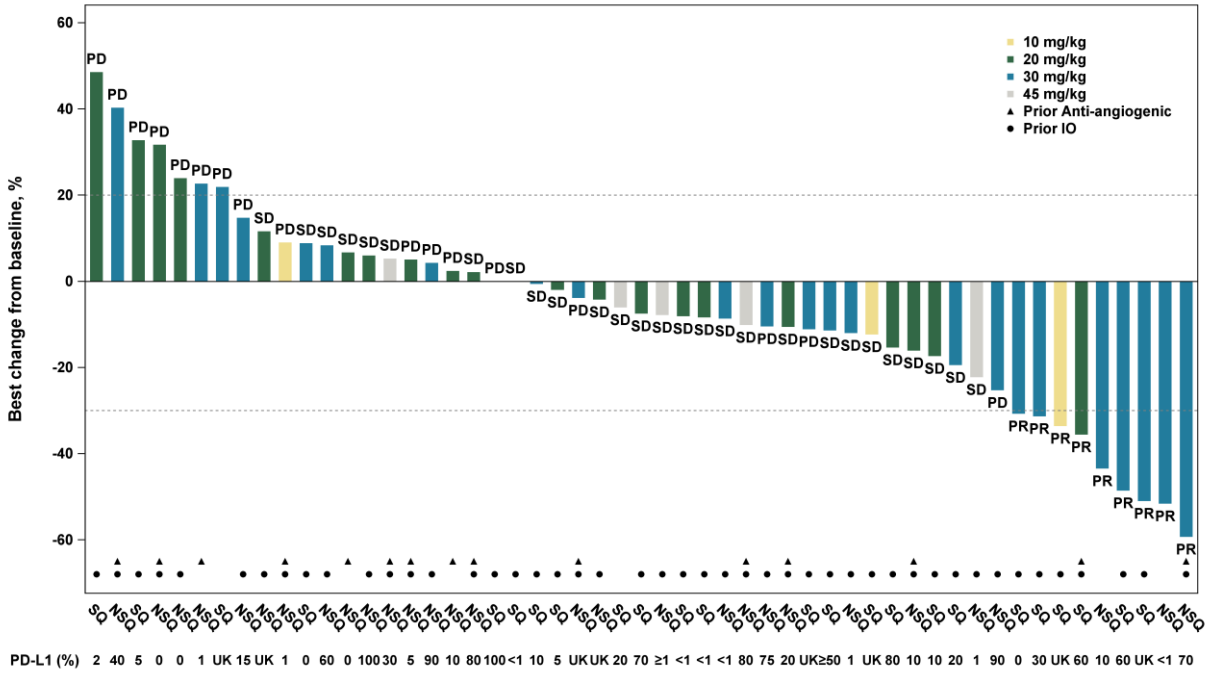
NSCLC: non-small cell lung cancer; combo: combination; chemo: chemotherapy; TPS: tumor proportion score; ORR: objective response rate; DCR: disease control rate; DoR: duration of response; PFS: progress-free survival
Data source: In-house Oct-2026 update

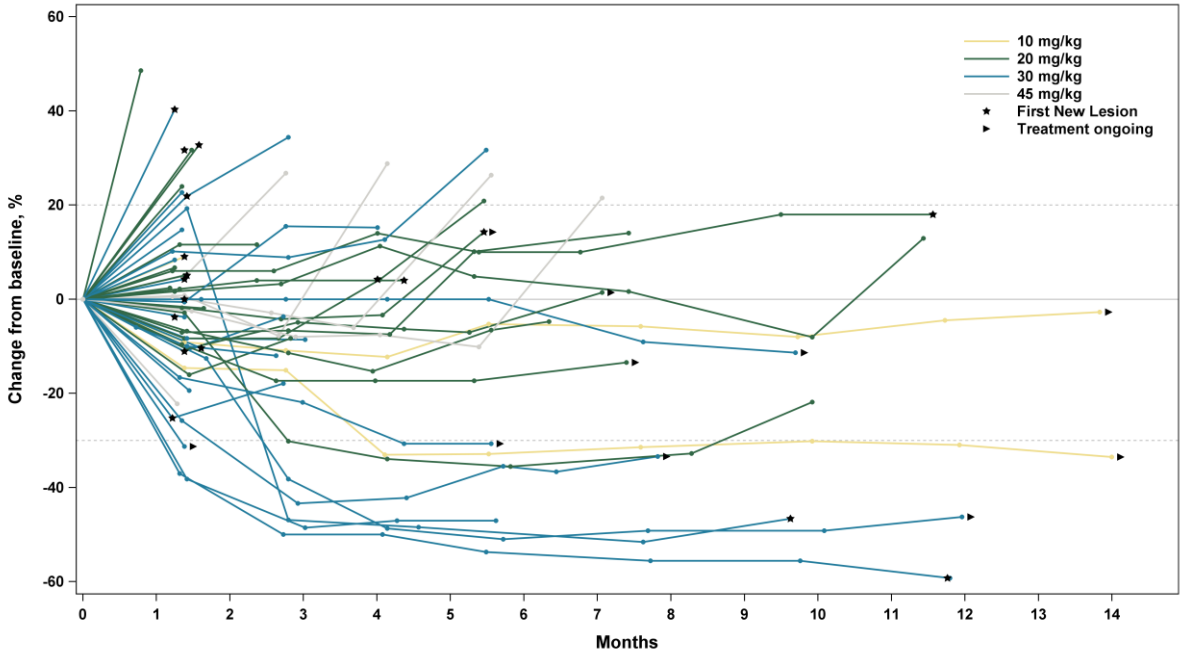
*ESMO 2026 ≥2L NSCLC mono: CS2009 monotherapy demonstrated promising clinical efficacy in heavily pre-treated, mostly post-IO NSCLC

Monotherapy at 10/20/30/45 mg/kg, Q3W. CS2009 is well tolerated with treatment duration exceeding 12 months at 10, 20 & 30 mg/kg

	All Evaluable Patients *(87.0% post-IO)*	30 mg/kg *(84.0% post-IO)*	Squamous, 30 mg/kg	Non-squamous, 30 mg/kg
ORR, % (n)	16.7% (9/54)	**28.0%* (7/25)**	33.3% (4/12)	23.1% (3/13)
DCR, % (n)	68.5% (37/54)	**60.0%* (15/25)**	75.0% (9/12)	46.2% (6/13)
mDoR, month	10.5	**10.5**	-	-

* For later-line, post-IO patients (n=21), ORR and DCR were 23.8% (5/21) and 61.9% (13/21)
For 2L only, post-IO patients (n=13, all treated with I/O plus chemo), ORR and DCR were 38.5% (5/13) and 84.6% (11/13)





Note: One patient is not shown in the waterfall and spider plots due to absence of measurable target lesion at baseline.
NSCLC: non-small cell lung cancer; mono: monotherapy; L: line; Q3W: every 3 weeks; ORR: objective response rate; DCR: disease control rate; DoR: duration of response
Data source: 2026 ESMO oral presentation

Higher Monotherapy ORR with CS2009 vs. bsAbs in Heavily Pre-treated and Mostly Post-IO NSCLC Patients, Reflecting CTLA-4 Arm's Activity

	CS2009[1] (PD-1/VEGF/CTLA-4)	AK104+AK109[2] (PD-1/CTLA-4+VEGF)	AK104+anlotinib[3] (PD-1/CTLA-4+TKI)	AK104[4] (PD-1/CTLA-4)	AK104[5] (PD-1/CTLA-4)	AK112[6] (PD-1/VEGF)	BNT327/PM8002[7] (PD-L1/VEGF)
Stage of data cited	Phase 1/2 In ≥2L AGA(-) NSCLC **30 mg/kg**	Phase 1b/2 in 2L NSCLC	Phase 1b/2	Phase 1 dose escalation	Phase 1b/2	Phase 1 dose escalation	Phase 1b/2a
Evaluable patients, n	25	47^	6	6	23†	2	8^
ORR, % (n)	**28.0%*** (7/25)	12.8% (6/47)	16.7% (1/6)	0%	0%	0%	12.5% (1/8)
ORR, %: SQ vs. NSQ	33.3% vs. 23.1%	11.5% vs. 14.3%	n/a	0%	0%	0%	n/a
DCR, % (n)	60.0%* (15/25)	95.7% (45/47)	100% (6/6)	33.3% (2/6)	30.4% (7/23)	50% (1/2)	62.5% (5/8)

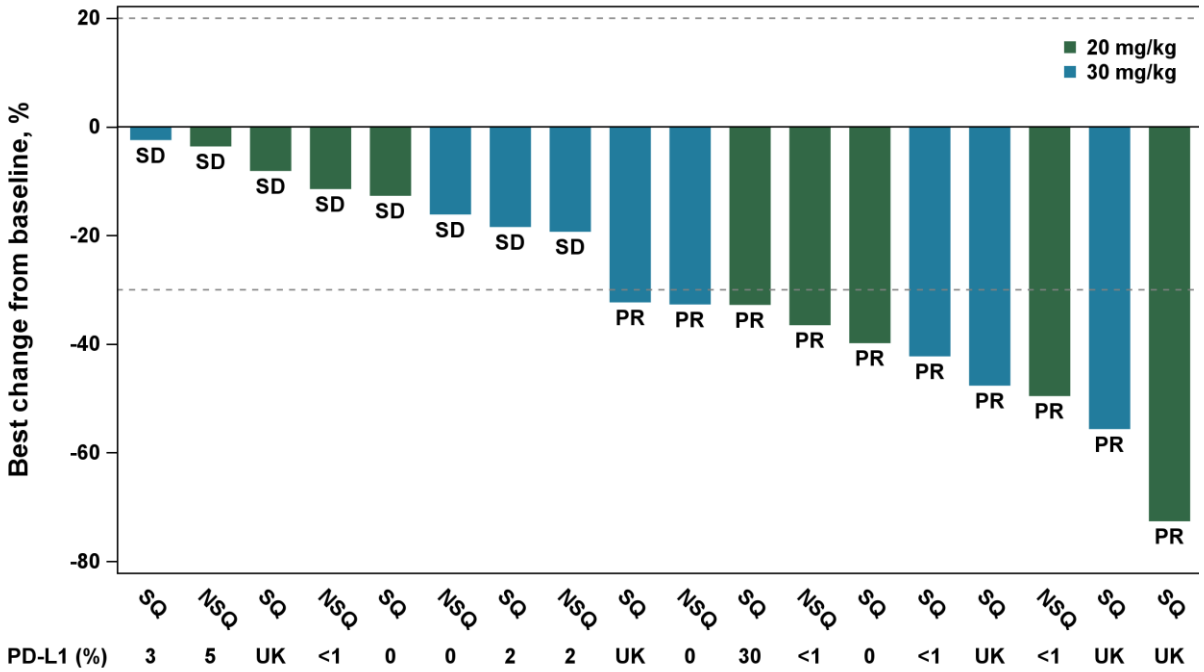
* For 2L only, post-IO patients (n=13, all treated with I/O plus chemo), ORR and DCR were 38.5% (5/13) and 84.6% (11/13)
For 2L and above, post-IO patients (n=21), ORR and DCR were 23.8% (5/21) and 61.9% (13/21)
^ All patients are AGA-negative and 2L post-IO NSCLC
† All patients are AGA-negative/unknown and ≥2L post-IO NSCLC

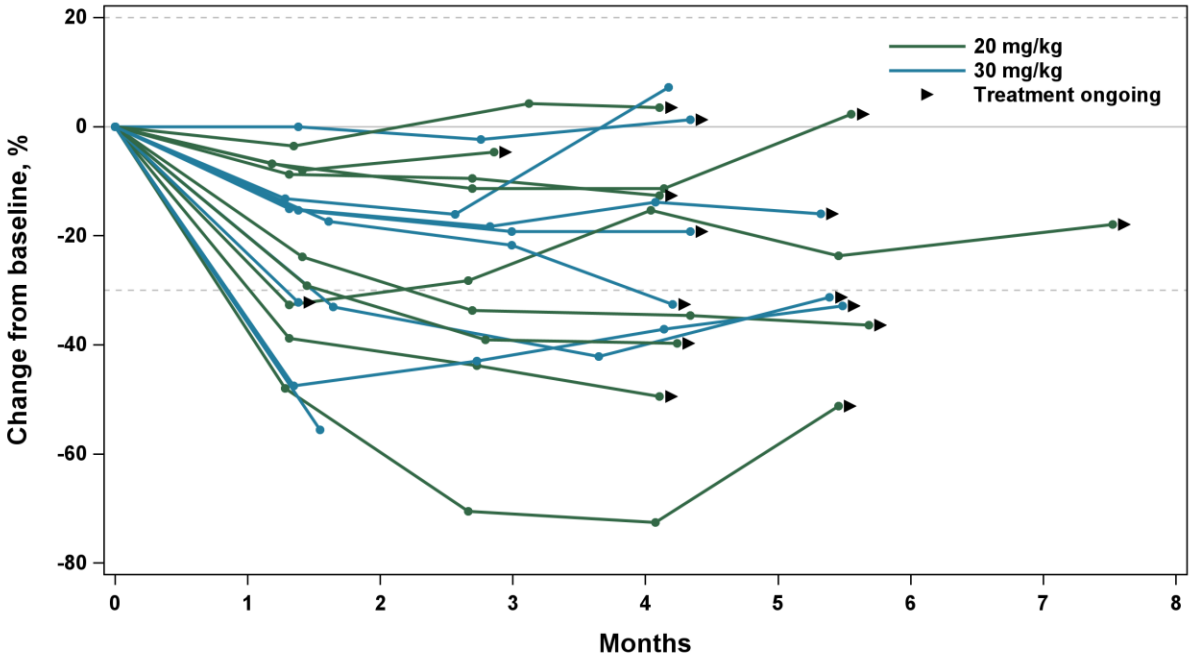
≥2L: second-/later-line; NSCLC: non-small cell lung cancer; AGA: actionable oncogenic alterations; ORR: objective response rate; DCR: disease control rate; I/O: immuno-oncology
Data source: 1. ESMO 2026; 2. WCLC 2025 (2L NSCLC); 3. ESMO 2021; 4. Cell Reports Medicine 2023; 5. Lung Cancer 2023; 6. JITC 2024; 7. ASCO 2024

*ESMO 2026 2/3L NSCLC combo: CS2009 + docetaxel demonstrated promising clinical efficacy in I/O- & chemo-treated NSCLC

CS2009 at 20 or 30 mg/kg, Q3W, plus docetaxel. **Enrollment ongoing**; ORR expected to increase with longer follow-up — early SDs often convert to PRs as treatment continues, as observed in more mature NSCLC cohorts. **Median PFS / DoR not reached due to limited follow-up**

	All Evaluable Patients	20 mg/kg	30 mg/kg
ORR, % (n)	55.6% (10/18)	55.6% (5/9)	55.6% (5/9)
DCR, % (n)	100% (18/18)	100% (9/9)	100% (9/9)





NSCLC: non-small cell lung cancer; I/O: immuno-oncology; chemo: chemotherapy; Q3W: every 3 weeks; ORR: objective response rate; DCR: disease control rate; DoR: duration of response; PFS: progress-free survival
Data source: 2026 ESMO oral presentation

*ESMO 2026 Safety in NSCLC Cohorts

CS2009 monotherapy and in combination with chemotherapy demonstrated a favorable safety profile in advanced NSCLC

- CS2009 combined with standard chemotherapy showed no additive immune or VEGF toxicity
- CS2009 showed no excessive CTLA-4-related toxicities typically observed with conventional PD-(L)1 + CTLA-4 antibody combinations; incidence of Grade ≥3 VEGF-related toxicity was much lower than that reported for PD-(L)1/VEGF bispecific antibodies
- No new safety signals were identified; **CS2009's safety profile remains consistent with that presented at 2026 ASCO and 2025 ESMO**

n (%)	CS2009 Monotherapy (n=112)	CS2009 + Chemotherapy (n=63)
TEAE	106 (94.6)	58 (92.1)
Grade ≥3 TEAE	45 (40.2)	37 (58.7)
Treatment-related TEAE (TRAE)	96 (85.7)	57 (90.5)*
Grade ≥3 TRAE	**29 (25.9)**	**33 (52.4)***
Immune-related TEAE (irAE)	51 (45.5)	23 (36.5)
Grade ≥3 irAE	**13 (11.6)**	**8 (12.7)**
Possible anti-VEGF-related TRAE	35 (31.3)	11 (17.5)
Grade ≥3 possible anti-VEGF-related TRAE	**6 (5.4)**	**3 (4.8)**
TRAE leading to CS2009 discontinuation	9 (8.0)	3 (4.8)

CTLA-4: cytotoxic T-lymphocyte-associated protein 4; NSCLC: non-small cell lung cancer; PD-1: programmed cell death protein 1; PD-L1: programmed death-ligand 1; TEAE: treatment-emergent adverse event; VEGF: vascular endothelial growth factor
Data source: 2026 ESMO oral presentation



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*ESMO 2026 Baseline Characteristics in CRC Cohorts

Characteristics	Later-line mCRC CS2009 monotherapy (N=23)	First-line mCRC CS2009 + XELOX (N=23)
Age, years		
median (range)	60.0 (40, 74)	59.0 (35, 75)
Male, n (%)	13 (56.5)	16 (69.6)
Race, n (%)		
Asian	20 (87.0)	22 (95.7)
White	3 (13.0)	1 (4.3)
ECOG PS, n (%)		
0	7 (30.4)	2 (8.7)
1	16 (69.6)	21 (91.3)
Location, n (%)		
Left colon or rectum	19 (82.6)	19 (82.6)
Right colon	4 (17.4)	4 (17.4)
MSI/MMR status, n (%)		
pMMR/MSS	22 (95.7)	22 (95.7)
Unknown	1 (4.3)	1 (4.3)

Characteristics	Later-line mCRC CS2009 monotherapy (N=23)	First-line mCRC CS2009 + XELOX (N=23)
Liver metastases, n (%)	15 (65.2)	16 (69.6)
Prior systemic anti-cancer therapy, n (%)		
1 line	11 (47.8)	0
2 lines	7 (30.4)	0
≥3 lines	5 (21.7)	0
Prior anti-angiogenic therapy, n (%)		
Yes	18 (78.3)	0
No	5 (21.7)	23 (100)
RAS mutation status*, n (%)		
Mutated	5 (21.7)	10 (43.5)
Wild type	7 (30.4)	6 (26.1)
BRAF mutation status*, n (%)		
Mutated	3 (13.0)	2 (8.7)
Wild type	8 (34.8)	15 (65.2)

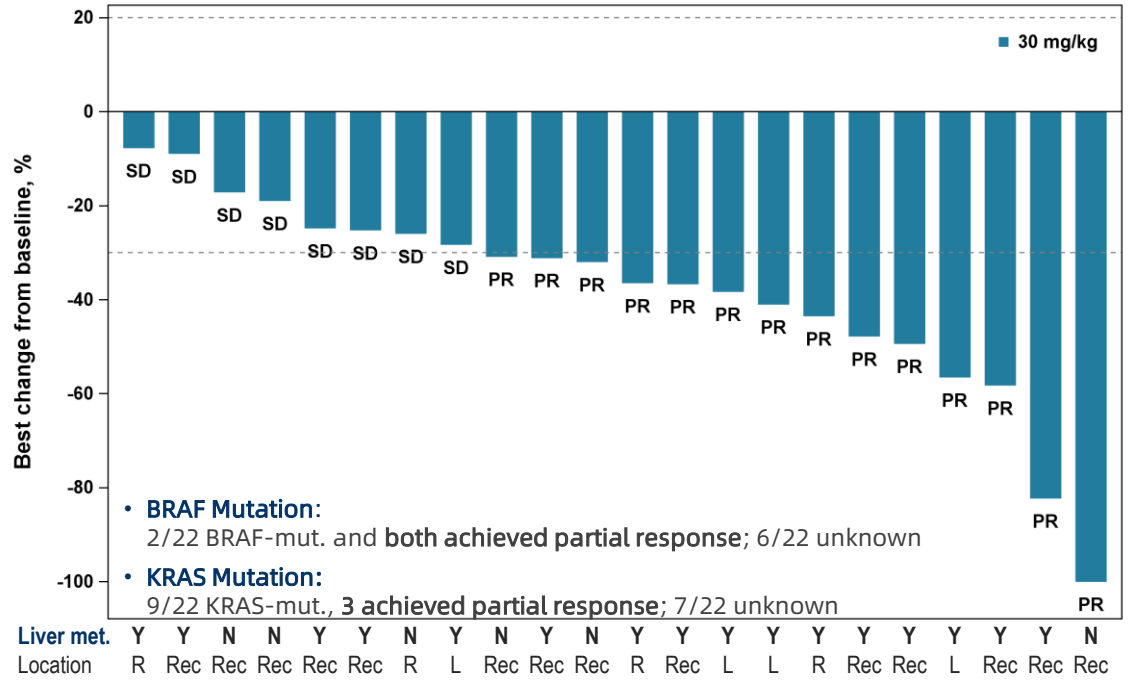
*Patients with unknown status were not shown.
ECOG PS: Eastern Cooperative Oncology Group performance status; mCRC: metastatic colorectal cancer; MSI/MMR: microsatellite instability/mismatch repair; pMMR/MSS: proficient mismatch repair/microsatellite stable; XELOX: capecitabine + oxaliplatin.

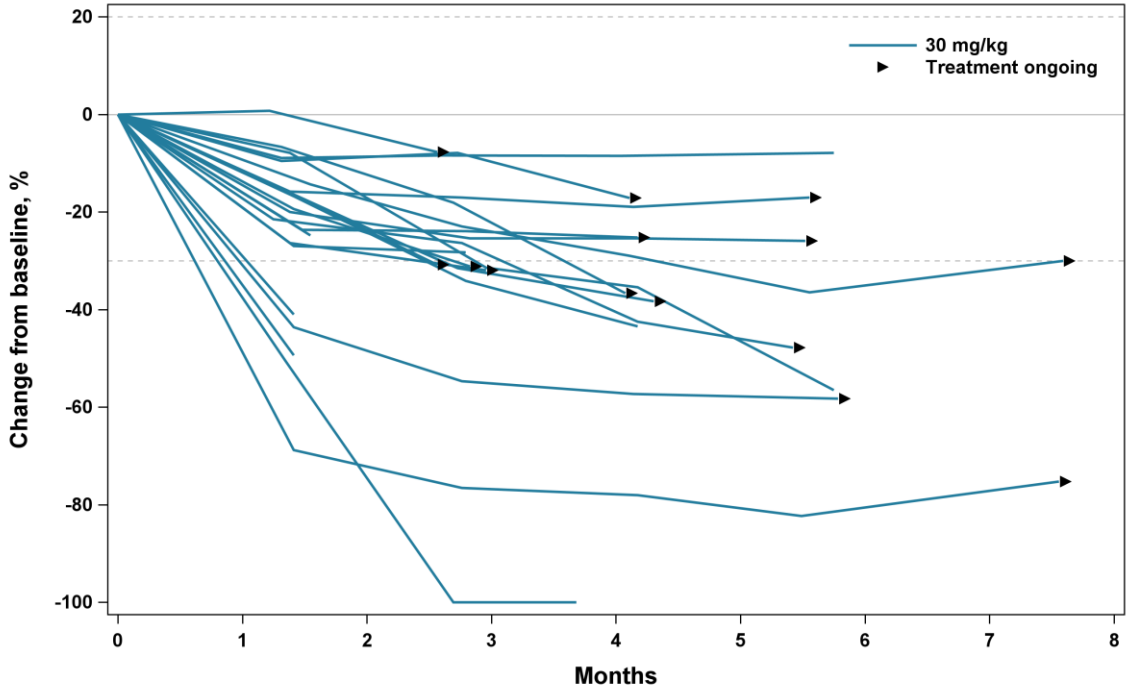
*ESMO 2026 1L mCRC combo: CS2009 + XELOX demonstrated promising preliminary clinical efficacy in first-line metastatic CRC, especially in patients with liver metastases

CS2009 (**30 mg/kg, Q3W**) + XELOX (oxaliplatin + capecitabine) for 8 cycles, followed by CS2009 + capecitabine maintenance. ORR expected to increase with longer follow-up—early SDs often convert to PRs as treatment continues. **Median PFS / DoR not reached due to limited follow-up**

	All evaluable patients	Patients with liver metastases	Patients with baseline target lesion SLD >100mm
ORR, % (n)	63.6% (14/22)	**68.8% (11/16)**	85.7% (6/7)
DCR, % (n)	100% (22/22)	**100% (16/16)**	100% (7/7)
Early tumor shrinkage ≥10% at 1st tumor assessment*, % (n)	77.3% (17/22)	**75% (12/16)**	85.7% (6/7)

** Defined as the proportion of patients with ≥10% decrease in the pretreatment sum of diameters at first post-treatment tumor scan in target lesions*



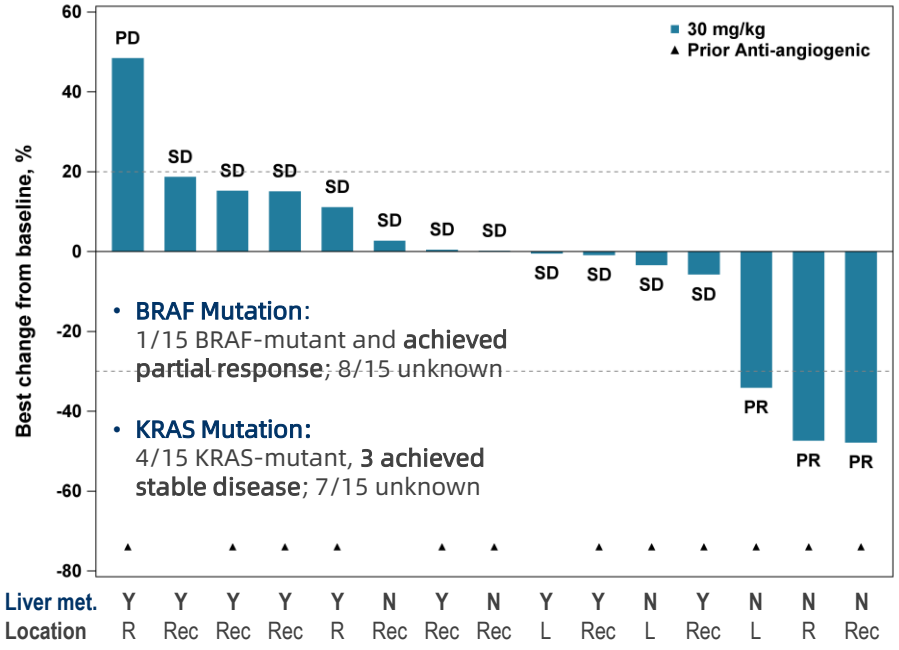


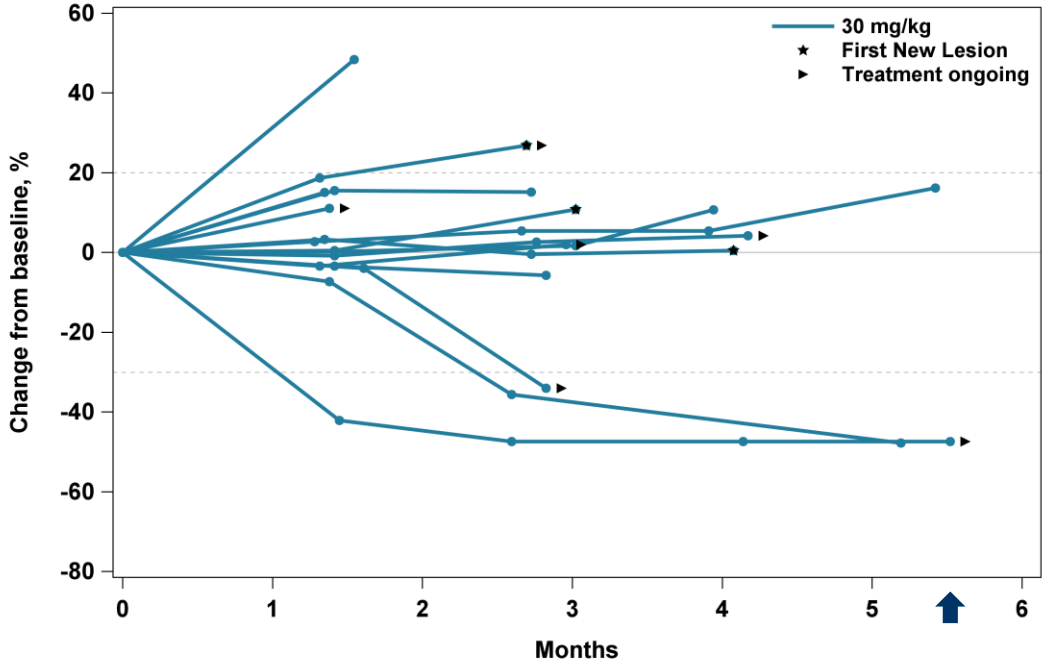
DCR: disease control rate; L=Left colon; met.=metastases; mut.=mutation; N=No; ORR: objective response rate; R=Right colon; Rec.=Rectum; SLD: sum of the longest diameters; UK=Unknown; Y=Yes.
Data source: 2026 ESMO oral presentation

*ESMO 2026 Later-line mCRC mono: CS2009 monotherapy demonstrated promising efficacy in later-line metastatic CRC, mostly pMMR/MSS – a "cold tumor" not sensitive to PD-(L)1 mAb, reflecting CTLA-4 arm's activity

Monotherapy at 30 mg/kg, Q3W

	Aug-2026 Cutoff	2026-ASCO Cutoff
Evaluable patients, n	15	8
ORR, % (n)	20.0% (3/15)	25.0% (2/8)
DCR, % (n)	93.3% (14/15)	87.5% (7/8)





L=Left colon; met=metastases; mut=mutation; N=No; R=Right colon; Rec.=Rectum; UK=Unknown; Y=Yes; pMMR/MSS: proficient mismatch repair / microsatellite stable; mCRC: metastatic colorectal cancer; ORR: objective response rate; DCR: disease control rate
Data source: 2026 ESMO oral presentation

*ESMO 2026 Safety in CRC Cohorts

CS2009 monotherapy and in combination with Chemo demonstrated a favorable safety profile in mCRC

n (%)	Group 1: Later-line mCRC CS2009 Monotherapy (n=23)		Group 2: First-line mCRC CS2009 + XELOX (n=23)	
	Any-grade*	Grade ≥3	Any-grade*	Grade ≥3
Immune-related adverse event (irAE)				
Total	6 (26.1)	3 (13.0)	9 (39.1)	5 (21.7)
Adrenal insufficiency	2 (8.7)	0	0	0
Alanine aminotransferase increased	1 (4.3)	1 (4.3)	3 (13.0)	1 (4.3)
Amylase increased	1 (4.3)	1 (4.3)	3 (13.0)	0
Aspartate aminotransferase increased	1 (4.3)	1 (4.3)	3 (13.0)	1 (4.3)
Hyperthyroidism	1 (4.3)	1 (4.3)	2 (8.7)	0
Hypothyroidism	1 (4.3)	0	2 (8.7)	0
Lipase increased	0	0	4 (17.4)	1 (4.3)
Possible anti-VEGF-related TRAE				
Total	7 (30.4)	2 (8.7)	4 (17.4)	1 (4.3)
Proteinuria	4 (17.4)	0	2 (8.7)	1 (4.3)
Epistaxis	2 (8.7)	0	0	0
Urinary occult blood positive	2 (8.7)	0	1 (4.3)	0

**Any-grade irAEs and possible anti-VEGF-related TRAEs reported in ≥2 patients*
irAE: immune-related adverse event; mCRC: metastatic colorectal cancer; TEAE: treatment-emergent adverse event; VEGF: vascular endothelial growth factor; XELOX: capecitabine + oxaliplatin.
Data source: 2026 ESMO oral presentation



CS2009

- Design, MoA, and Rationale
- **Phase 1/2 Clinical Data Update**
  - Proof of Mechanism
  - Proof of Safety
  - **Proof of Concept in Broad Cancer Types**
    1. Non-small Cell Lung Cancer (NSCLC) Dataset
    2. Colorectal Cancer (CRC) Dataset
    3. **Preliminary Clinical Data for Other Tumor Types**
- Regulatory and Clinical Plan for Global Phase 3 Trials

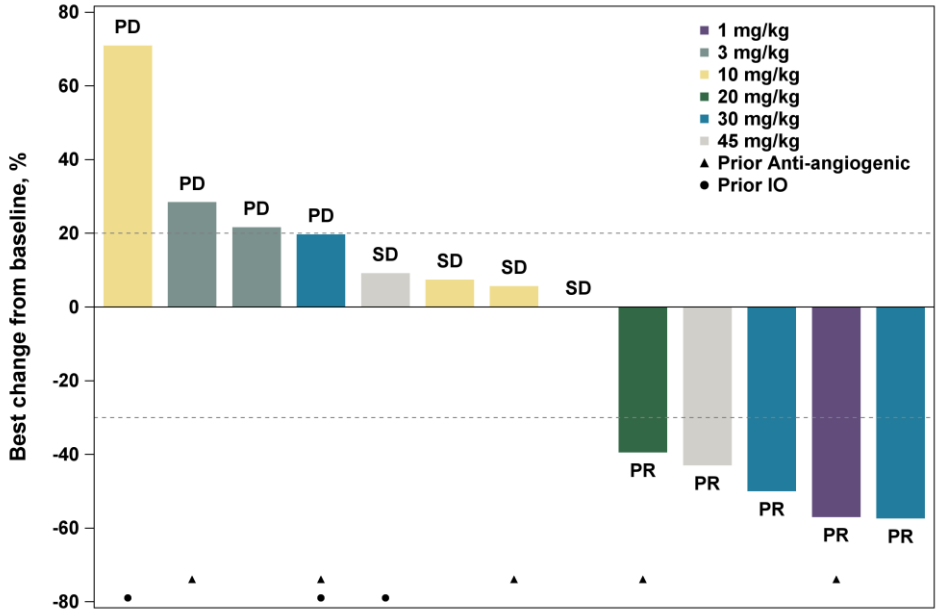
Later-line STS mono: CS2009 monotherapy demonstrated promising clinical efficacy in later-line soft tissue sarcoma (STS) – a "cold tumor" not sensitive to PD-(L)1 mAb, reflecting CTLA-4 arm's activity

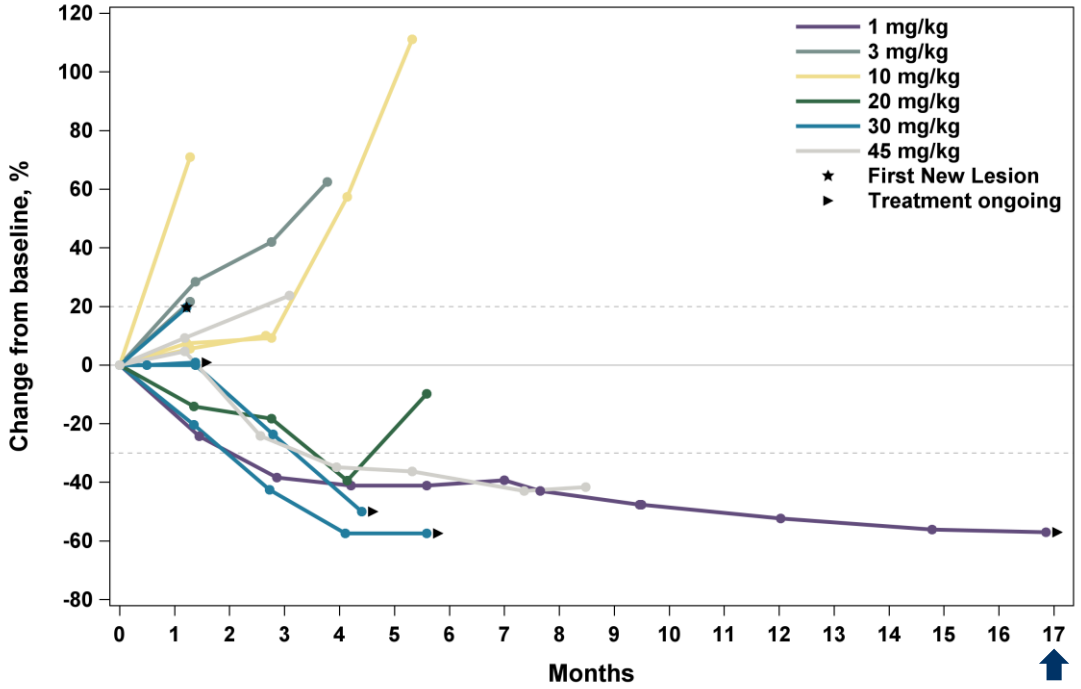
Monotherapy at 1, 3, 10, 20, 30, 45 mg/kg, Q3W

	Aug-2026 Cutoff	2026-ASCO Cutoff
Evaluable patients, n	13	12
ORR, % (n)	38.5% (5/13)	33.3% (4/12)
DCR, % (n)	69.2% (9/13)	66.7% (8/12)

CLINICAL CONTEXT

Treatment options in clinic for STS are mainly TKIs, of which ORR is typically ~20% and ~6% in the first-line and later-line setting, respectively





ORR: objective response rate; DCR: disease control rate; TKI: tyrosine Kinase Inhibitor: IO: immuno-oncology
Data source: CStone 2026 Interim Results presentation

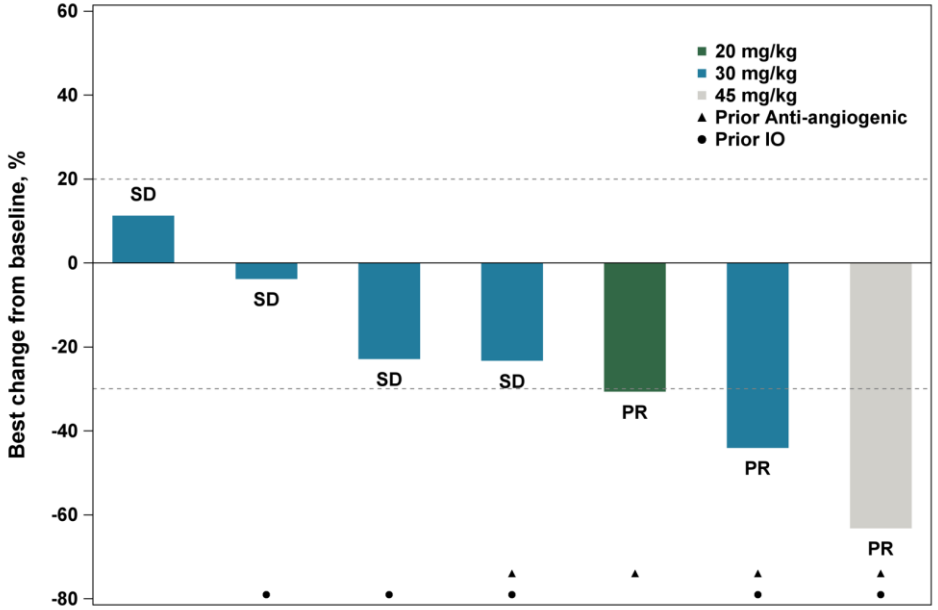
Later-line nccRCC: CS2009 monotherapy showed promising efficacy in later-line non-clear-cell renal cell carcinoma (nccRCC) – a "cold tumor" not sensitive to PD-(L)1 mAb, reflecting CTLA-4 arm's activity

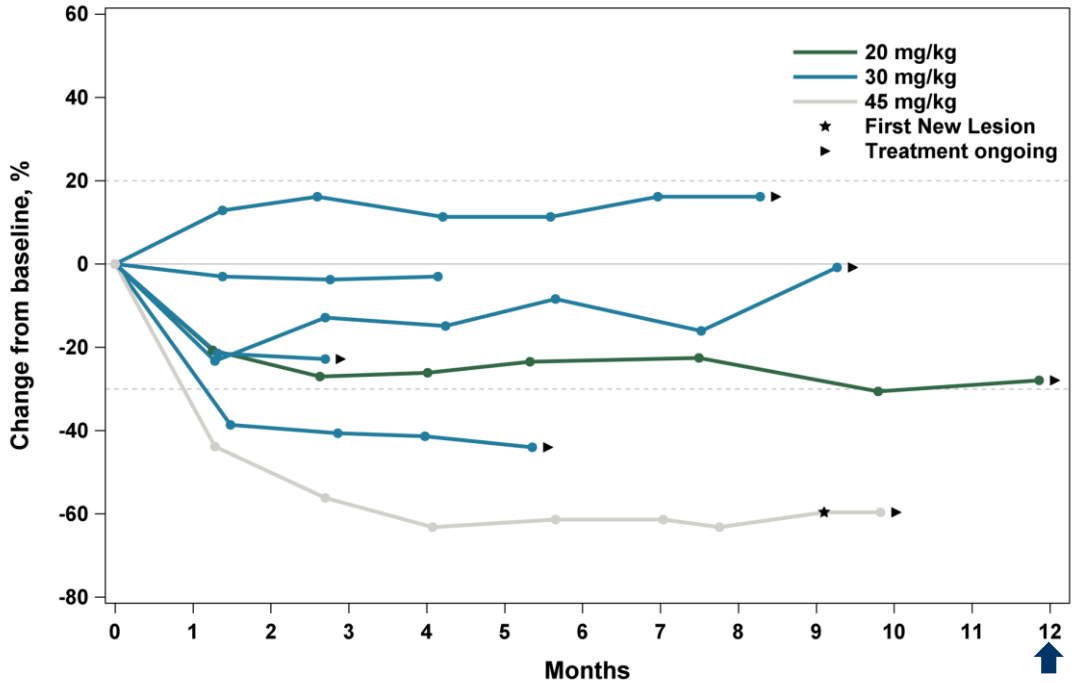
Monotherapy at 20, 30, 45 mg/kg, Q3W

	Aug-2026 Cutoff	2026-ASCO Cutoff
Evaluable patients, n	7	6
ORR, % (n)	42.9% (3/7)	33.3% (2/6)
DCR, % (n)	100% (7/7)	100% (6/6)

CLINICAL CONTEXT

1st-tier recommendation for these patients is clinical trial; Current investigator's choice for later-line nccRCC typically results in ORR ~14%



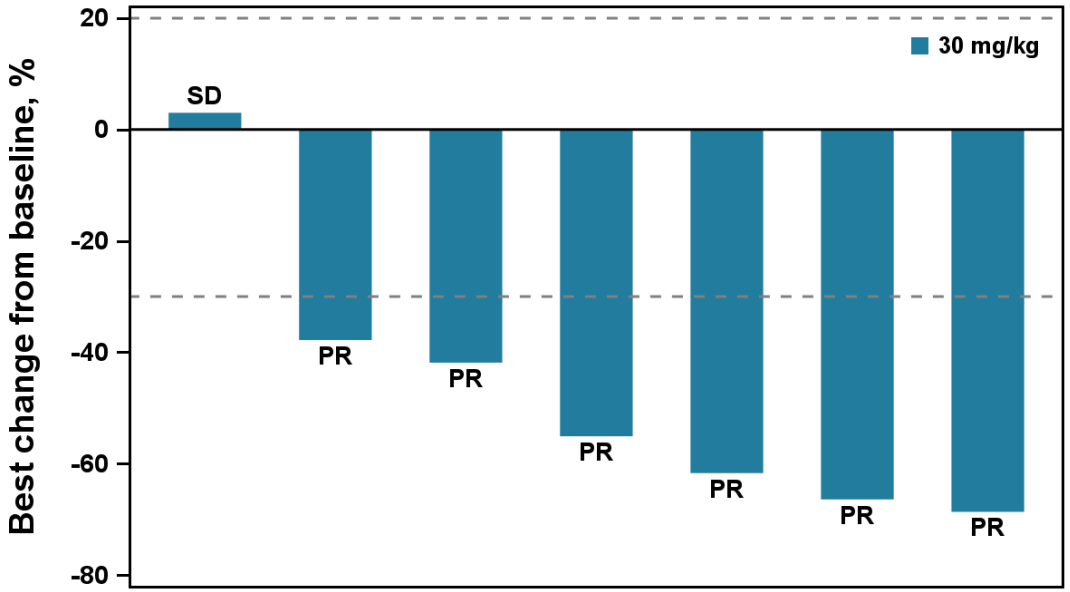


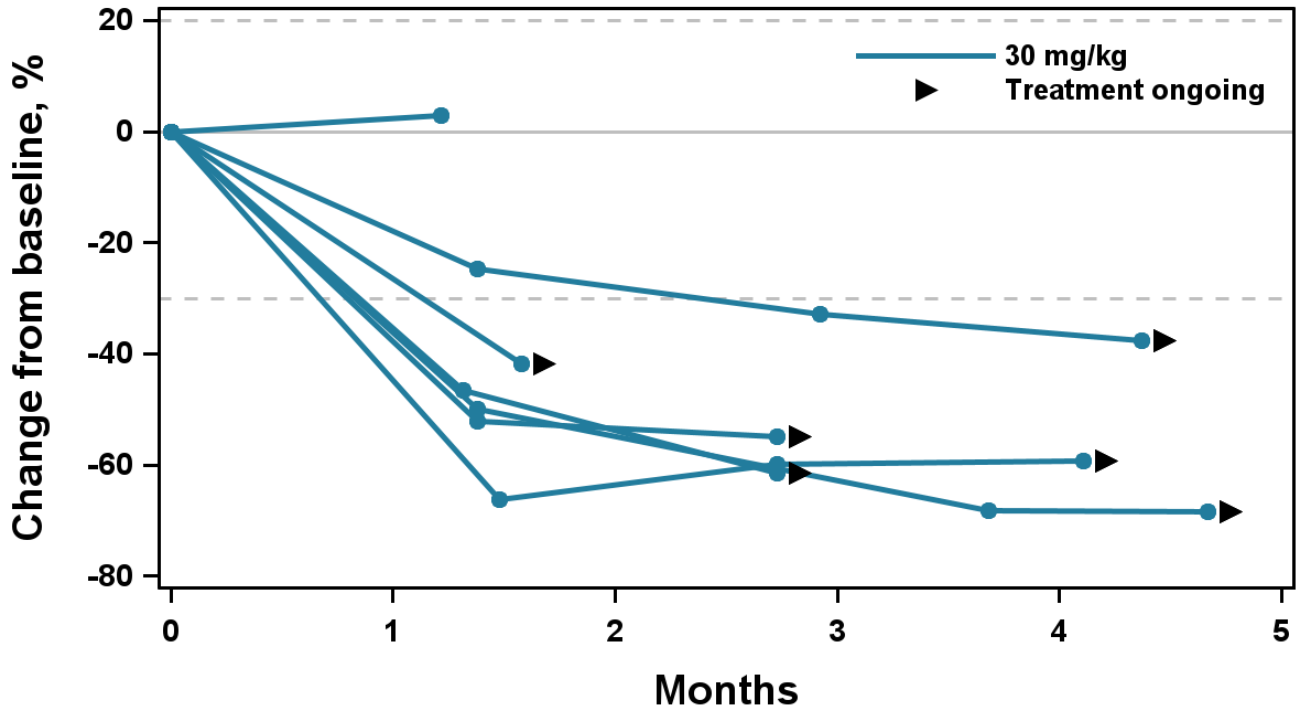
ORR: objective response rate; DCR: disease control rate; IO: immuno-oncology
Data source: CStone 2026 Interim Results presentation

*Post-ESMO Other Solid Tumors from Phase 2 Cohorts: CS2009 in combination with SoC demonstrated promising preliminary clinical efficacy in first-line ES-SCLC

CS2009 (30 mg/kg, Q3W) + etoposide/carboplatin

ORR 85.7% (6/7), DCR 100% (7/7)

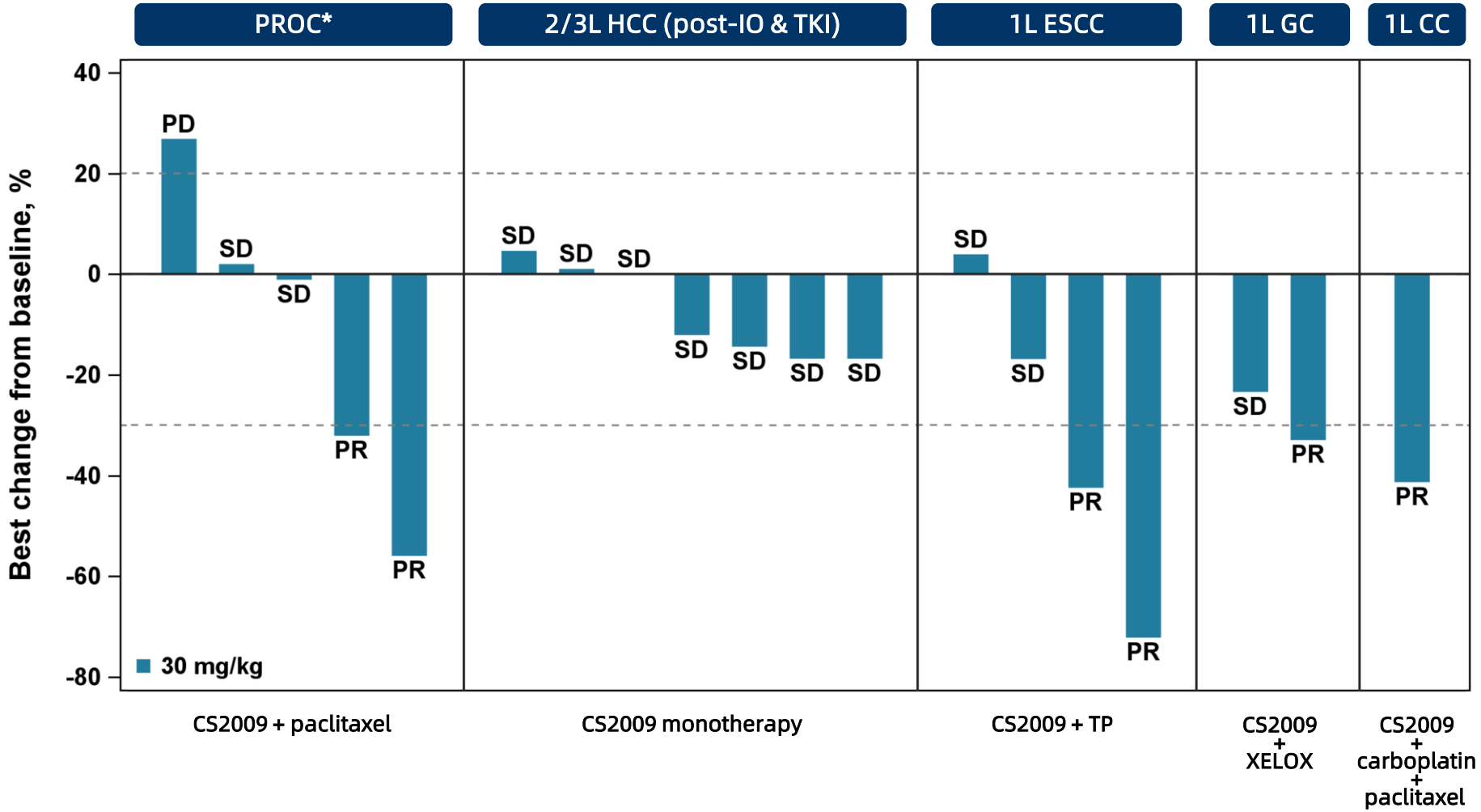




ES-SCLC: extensive-stage small cell lung cancer; ORR: objective response rate; DCR: disease control rate
Data source: In-house Oct-2026 data; not publicly disclosed in the ESMO presentations.

*Post-ESMO Other Solid Tumors: CS2009 monotherapy/in combination with SoC demonstrated promising preliminary clinical efficacy in first-/later-line solid tumors

CS2009 (30 mg/kg, Q3W) monotherapy or plus SoC



*PROC: platinum-resistant ovarian cancer (progressed within 6 months of at least one systemic platinum-based therapy);
CC: cervical cancer; ESCC: esophageal squamous cell carcinoma; GC: gastric cancer; HCC: hepatocellular carcinoma; TP: Paclitaxel + Cisplatin; XELOX: oxaliplatin + capecitabine
Data source: In-house Oct-2026 data; not publicly disclosed in the ESMO presentations.

Summary: Three Key Clinical Validations Achieved from over 300 Patient Data

➢ Proof of Mechanism

- Dose-dependent **ICOS upregulation on CD4+ T cells**: PD biomarker specific to CTLA-4 blockade
- Linear **PK** with half-life of ~6-9 days; low incidence of ADA positivity
- Sustained **PD-1/CTLA-4 receptor occupancy** at doses ≥20 mg/kg
- **Serum-free VEGFA** reduced deeply and rapidly; effect sustained throughout dose intervals

➢ Proof of Safety

- **Grade ≥3 irAEs 12.7%;** CTLA-4-related tox markedly reduced from CTLA-4 mAb monotherapy or in combination with PD-1/L1, including **extremely rare colitis**, due to **preserved CTLA-4 signaling** in peripheral Tregs & autoreactive T cells
- **Grade ≥3 VEGF-related tox 5.1%;** likely mediated by PD-1/CTLA-4-driven VEGFA immune complex internalization by T cells in TME as indicated by the data

➢ Proof of Concept in Broad Cancer Types

- Robust mono & chemo-combo efficacy in **1L and late-line NSCLC:**
  - CS2009 monotherapy in 1L NSCLC (PD-L1 TPS≥50%): ORR 87.5% (100% at 30 mg/kg), DCR 95.8% (100% at 30 mg/kg)
  - CS2009 monotherapy in 1L NSCLC (PD-L1 TPS≥1%): ORR 66.7% (75.0% at 30 mg/kg), DCR 93.8% (91.7% at 30 mg/kg)
  - CS2009 monotherapy (30 mg/kg) in ≥2L NSCLC: ORR 28.0%, DCR 60.0%; mDoR 10.5 months
  - CS2009 (30 mg/kg) + paclitaxel/carboplatin in 1L squamous NSCLC: ORR 85.7%, DCR 100%
  - CS2009 (20/30 mg/kg) + docetaxel in 2/3L, I/O- & chemo-treated NSCLC: ORR 55.6%, DCR 100%
- Promising mono & chemo-combo efficacy in **1L and late-line pMMR/MSS mCRC**
  - CS2009 monotherapy (30 mg/kg) in later-line mCRC: ORR 20.0%, DCR 93.3%
  - CS2009 (30 mg/kg) + XELOX in 1L mCRC: ORR 63.6%, DCR 100%
- Robust activity in **other IO-unresponsive "cold tumors** " in addition to later-line pMMR/MSS mCRC:
  - CS2009 monotherapy in later-line STS: ORR 38.5%, DCR 69.2%
  - CS2009 monotherapy in later-line nccRCC: ORR 42.9%, DCR 100%
- Promising mono activity also observed in **other solid tumors** including SCLC, OC, HCC, GC, EC, mCRPC, TNBC, etc.

TME: tumor microenvironment; ICOS: inducible T-Cell Co-stimulator; NSCLC: non-small cell lung cancer; STS: soft tissue sarcoma; nccRCC: non-clear-cell renal cell carcinoma; pMMR/MSS: proficient mismatch repair / microsatellite stable; CRC: metastatic colorectal cancer; mCRPC: metastatic Castration-Resistant Prostate Cancer; OC: ovarian cancer; TNBC: triple-negative breast cancer; GC: gastric cancer; EC: esophageal cancer

Conclusion: With an innovative design for triple synergy and conditional CTLA-4 activation, CS2009 exhibits superior antitumor activities with a favorable safety profile *vs* PD-1/VEGF and PD-1/CTLA-4 bsAbs, with the potential for more durable OS benefit

Favorable safety and post-IO activity enable broad combination potential, including with ADCs and RLT, across first and later lines

	Differentiated Molecular Design	Significantly Reduced Toxicity	Stronger Monotherapy Anti-tumor Activity
CS2009 *vs* PD-(L)1/VEGF bsAbs ▶	• **CTLA-4 arm** drives T-cell priming – key OS driver • Dual PD-1/CTLA-4 blockade + Deeper VEGFA clearance in TME • Sustained VEGF suppression; no rebound (vs AK112)	• Lower any-grade & Grade ≥3 anti-VEGF TRAEs • Grade ≥3 anti-VEGF TRAEs: 5.1% (Phase I, N=118) • No DLT; MTD not reached	• 1L NSCLC TPS ≥50% (30 mg/kg): ORR 100% (vs AK112: 60.2%) • 1L NSCLC TPS ≥1% (30 mg/kg): ORR 75.0% (vs AK112: 50.0%) • IO-pretreated 2L NSCLC (30 mg/kg): ORR 38.5% (vs AK104+VEGF: 12.8%, BNT327: 12.5%) • IO-pretreated 2L+ NSCLC (30 mg/kg): ORR 23.8% (vs AK112/AK104: 0%, AK104+TKI: 16.7%) • Higher ORR in late-line "cold" tumors (mCRC, STS, nccRCC) vs SOC – rarely demonstrated by bsAbs
CS2009 *vs* PD-(L)1/CTLA-4 bsAbs ▶	• **VEGF arm** remodels TME and clears local VEGF • TME-selective avidity binding to double-positive TILs • Monovalent low-affinity CTLA-4 arm spares peripheral T cells (vs high-affinity MEDI-5752)	• Lower any-grade irAEs vs PD-(L)1/CTLA-4 bsAbs and combos • Very low colitis incidence • No DLT / unreached MTD supports continuous CTLA-4 dosing	

Source: 2026-ASCO presentation & in-house data and Aug-2026 in-house update; WCLC 2025



CS2009

- Design, MoA, and Rationale
- Phase 1/2 Clinical Data Update
  - Proof of Mechanism
  - Proof of Safety
  - Proof of Concept in Broad Cancer Types
    1. Non-small Cell Lung Cancer (NSCLC) Dataset
    2. Colorectal Cancer (CRC) Dataset
    3. Preliminary Clinical Data for Other Tumor Types
- **Regulatory and Clinical Plan for Global Phase 3 Trials**

Clinical Data and CMC Readiness for FDA Meetings and Phase III Initiation

Clinical Safety & Efficacy Dataset for NSCLC Meetings ▶

- Phase 1 All solid tumors (n≈130)
- Phase 2 1L NSCLC mono (n≈48)
- Phase 1/2 Later-line NSCLC mono (n≈57)
- Phase 2 1L NSCLC combo (n≈60)
- Phase 2 2L NSCLC combo (n≈40)

FDA Meetings Planned

CMC Meeting
120,000 vials planned for Year 2027, covering >1000 patients in Phase III clinical trials
Q3 2026
Concluded with positive feedback from FDA

1L AGA(-) NSCLC
(SQ & NSQ)
CS2009 + chemo vs. pembrolizumab + chemo
Q4 2026

1L AGA(-) NSCLC
(SQ & NSQ, TPS ≥50%)
CS2009 vs. pembrolizumab
Q4 2026

2L AGA(-) NSCLC
(SQ & NSQ)
CS2009 + docetaxel vs. docetaxel
Q1 2027

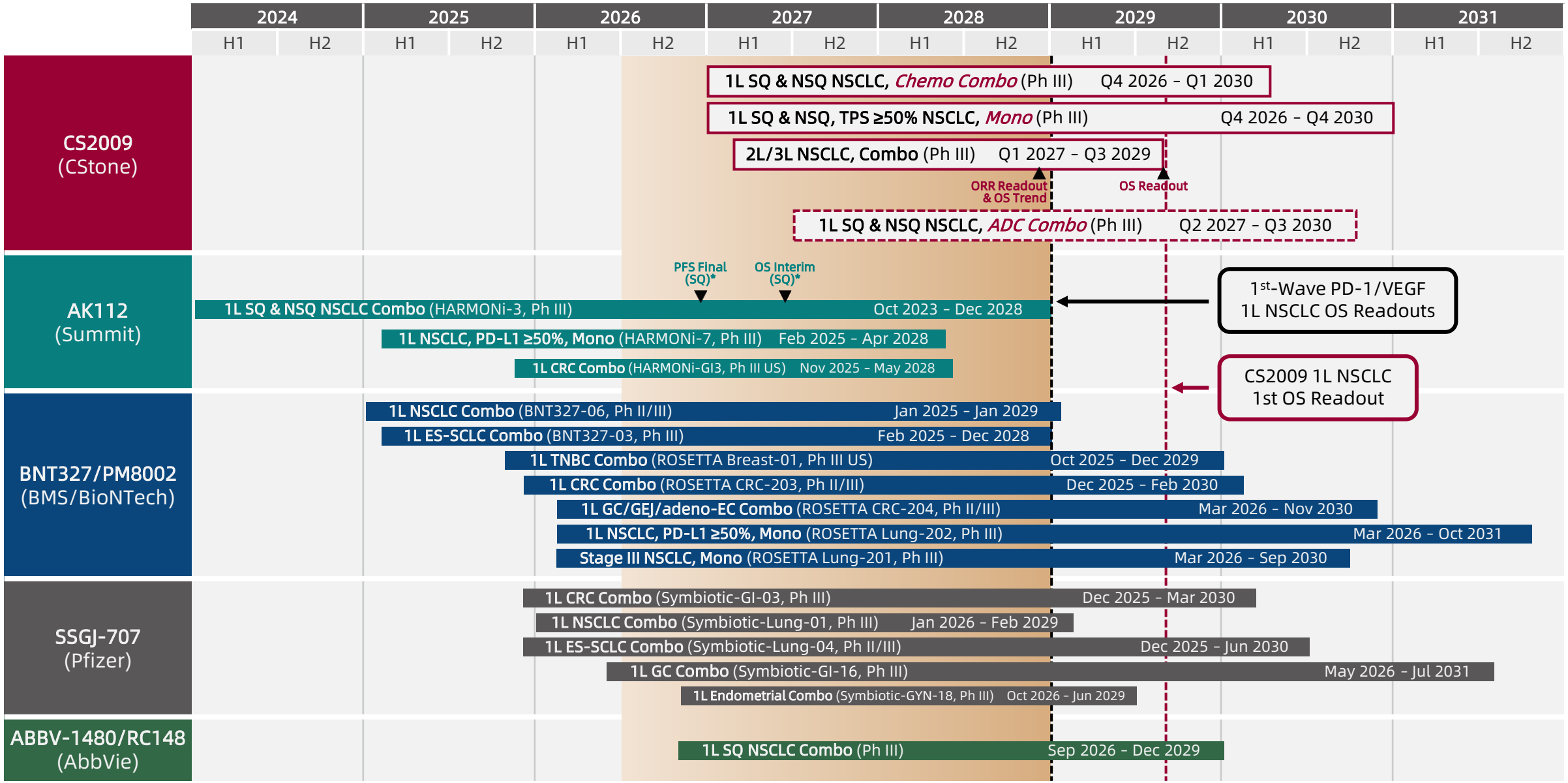
1L mCRC
CS2009 + chemo vs. bevacizumab + chemo
Q1 2027

Clinical Safety & Efficacy Dataset for CRC Meeting ▶

- Phase 1 All solid tumors (n≈130)
- Phase 1 Later-line CRC mono (n≈20)
- Phase 2 1L CRC combo (n≈40)

AGA: actionable oncogenic alterations; NSCLC: non-small cell lung cancer; SQ: squamous; NSQ: non-squamous; mCRC: metastatic colorectal cancer; chemo: chemotherapy

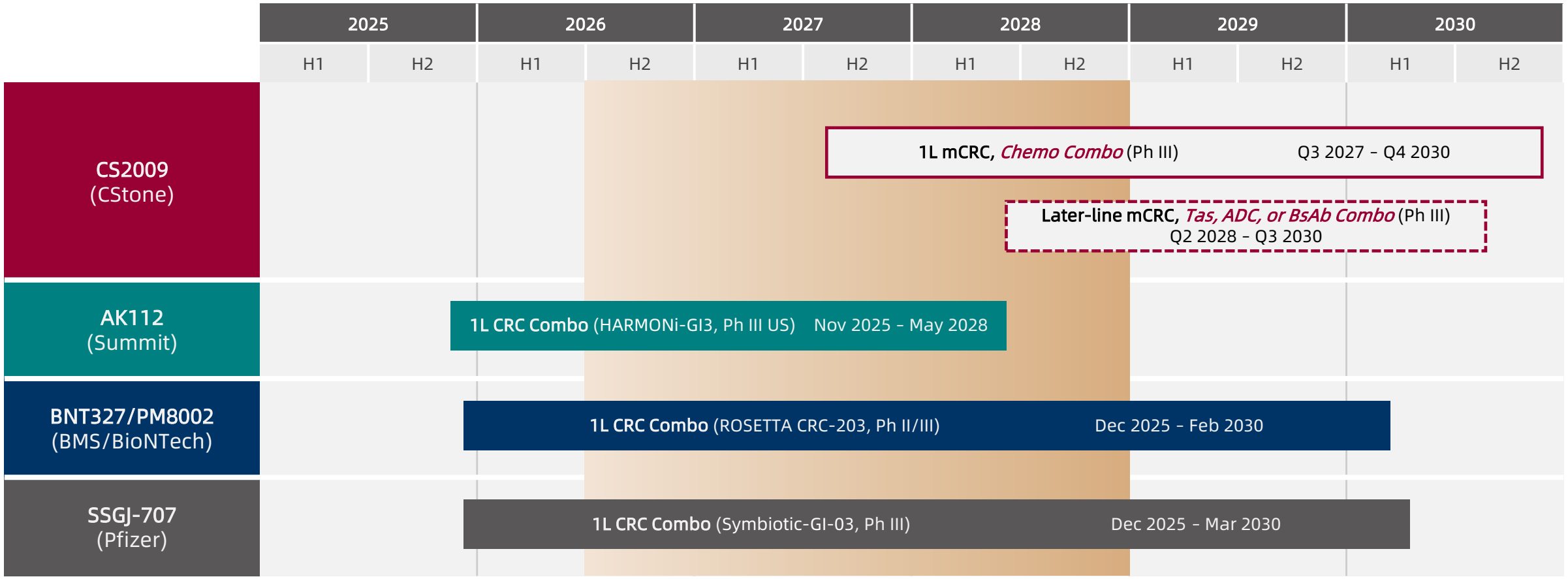
Global Development and Regulatory Window Wide Open for CS2009 Phase III Trials (NSCLC)



AGA: actionable oncogenic alterations; CRC: colorectal cancer; EC: esophageal carcinoma; ES-SCLC: extensive-stage small cell lung cancer; GC/GEJ: Gastric Cancer/Gastroesophageal Junction; NSQ: non-squamous; NSCLC: non-small cell lung cancer; OS: overall survival; PFS: progression-free survival; pMMR/MSS: proficient mismatch repair or microsatellite stable; TNBC: triple-negative breast cancer; SQ: Squamous

** Source: Summit Therapeutics Inc. (SMMT) Q2 2026 Earnings Call July 23, 2026*

Global Development and Regulatory Window Wide Open for CS2009 Phase III Trials (MSS CRC)



mCRC: metastatic colorectal cancer; MSS: microsatellite stable

CS2009: Broad Tumor Indication Coverage as a Potential Next-Generation I/O Backbone

Replacing & Expanding beyond Current PD-1/L1 Standard of Care (SOC)

PD-1/L1 Fully Established SOC in Key Indications

- **1L metastatic NSCLC:** Pembrolizumab + Platinum-based Chemo
- **Locally advanced NSCLC, post-CRT:** Durvalumab consolidation
- **Resectable NSCLC (Neoadjuvant/Adjuvant):** Nivolumab + Platinum-based Chemo
- **ES-SCLC:** Atezolizumab + Etoposide + Carboplatin
- **LS-SCLC:** Durvalumab consolidation
- **1L HCC:** Atezolizumab + Bevacizumab
- **1L HNSCC:** Pembrolizumab + Chemo
- **1L Advanced ccRCC:** Pembrolizumab + Axitinib
- **Unresectable/Metastatic Melanoma:** Pembrolizumab

PD-1/L1 Partially Established SOC (CPS-Dependent)

- **1L TNBC:** **CPS ≥10**: Pembrolizumab + Chemo; **CPS <10**: Chemo
- **1L GC/GEJ:** **CPS ≥1**: Pembrolizumab + Chemo; **CPS <1**: Chemo
- **1L ESCC:** **CPS ≥1**: Nivolumab + Chemo; **CPS <1**: Chemo
- **2L/3L PROC:** **CPS ≥1**: Pembrolizumab + Paclitaxel +/- Bevacizumab
- **1L Cervical Cancer (recurrent/metastatic):** **CPS ≥1**: Pembrolizumab + Bevacizumab; **CPS <1**: Chemo + Bevacizumab

PD-1/L1 Ineligible (I/O Not Yet Approved as SOC)

- **2L/3L Metastatic NSCLC (AGA-):** Docetaxel
- **1L pMMR/MSS CRC:** Bevacizumab + FOLFOX/CAPEOX/FOLFIRI
- **Non-clear-cell RCC:** TKI
- **mCRPC:** Chemo

→ **CS2009 Replacing PD-1/L1 in Chemo Combo**

→ **CS2009 Expanding into IO-Ineligible with Chemo/ADC**

AGA: actionable oncogenic alterations; CAPEOX: Capecitabine + Oxaliplatin; ccRCC: clear cell renal cell carcinoma; CPS: combined positive score; CRC: colorectal cancer; CRT: chemoradiotherapy; ES-SCLC: extensive-stage small cell lung cancer; ESCC: esophageal squamous cell carcinoma; HCC: hepatocellular carcinoma; HNSCC: head and neck squamous cell carcinoma; LS-SCLC: limited-stage small cell lung cancer; mCRPC: metastatic Castration-Resistant Prostate Cancer; NSCLC: non-small cell lung cancer; PROC: platinum-resistant ovarian cancer; pMMR/MSS: proficient mismatch repair or microsatellite stable; TNBC: triple-negative breast cancer

PD-1/VEGF/CTLA-4 Trispecific Ab: Substantial Clinical and Commercial Potential with Anticipated Durable PFS and OS Benefits

Prolonged PFS and expanded indications boost CS2009's commercial upside if approved as a next-gen I/O backbone therapy

Approved indications for 3 targets

- Lung cancer ►
- Hepatocellular carcinoma ►
- Renal cell carcinoma ►
- Colorectal cancer ►

Approved indications for PD-(L)1 & VEGF

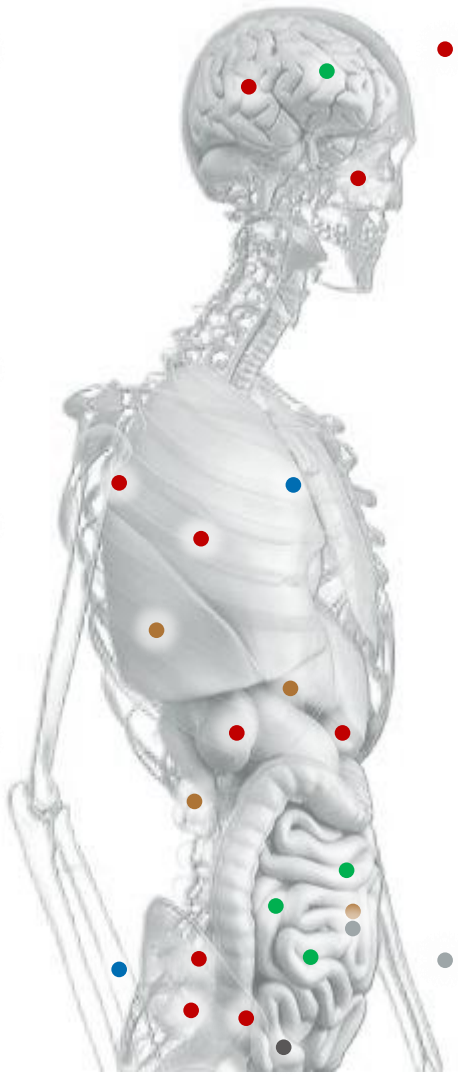
- Cervical cancer ►

Approved indications for PD-(L)1 & CTLA-4

- Esophageal cancer ►
- Melanoma ►

Approved indications for VEGF

- Glioblastoma ►
- Peritoneal cancer ►
- Ovarian cancer ►
- Fallopian tube carcinoma ►



Approved indications for PD-(L)1

- ◄ Head and neck squamous cell carcinoma
- ◄ Nasopharyngeal carcinoma
- ◄ Hodgkin lymphoma
- ◄ Triple negative breast cancer
- ◄ Biliary tract cancer
- ◄ Gastric cancer
- ◄ Urothelial carcinoma
- ◄ Bladder cancer
- ◄ Endometrial cancer

Potential new indications

- ◄ MSS/pMMR CRC, etc.

Broad indications with substantial commercial potential

60+ Approved indications targeting PD-(L)1, VEGF, CTLA-4 (mono or multi-targeting)

Remarkable value to exceed current market potential for CPI

$32bn	Keytruda 2025 global sales revenue
$59bn	PD-(L)1 inhibitors 2025 global sales revenue
$99bn	PD-(L)1 global sales revenue by 2029 (IQVIA forecast)
$90bn	Current CPI market potential (Summit's projection)

Note: The indications listed above are not exhaustive of all approved indications for the three targets
CPI, checkpoint inhibitor ; pMMR/MSS: proficient mismatch repair / microsatellite stable; CRC: colorectal cancer

CS2009 Upcoming Catalysts

- All pivotal registrational studies are multi-regional clinical trials (MRCTs) using global standard-of-care as control
- Trial design and timeline are not impacted by data readouts from other bispecific/trispecific competitors, giving CS2009 an independent development space and rhythm
- **In-depth discussions with Global MNCs for partnership**

Q4 2026

FDA consultation on Phase III MRCT study design for first-line NSCLC (+ chemo)

2026 Year-end

First MRCT registrational study initiated

FDA consultation on Phase III MRCT study design for first-line TPS ≥50% NSCLC (monotherapy)

Q4 2026



Appendix

Well-balanced portfolio of 16 innovative assets (1/2)

- Commercial/Late-stage Programs

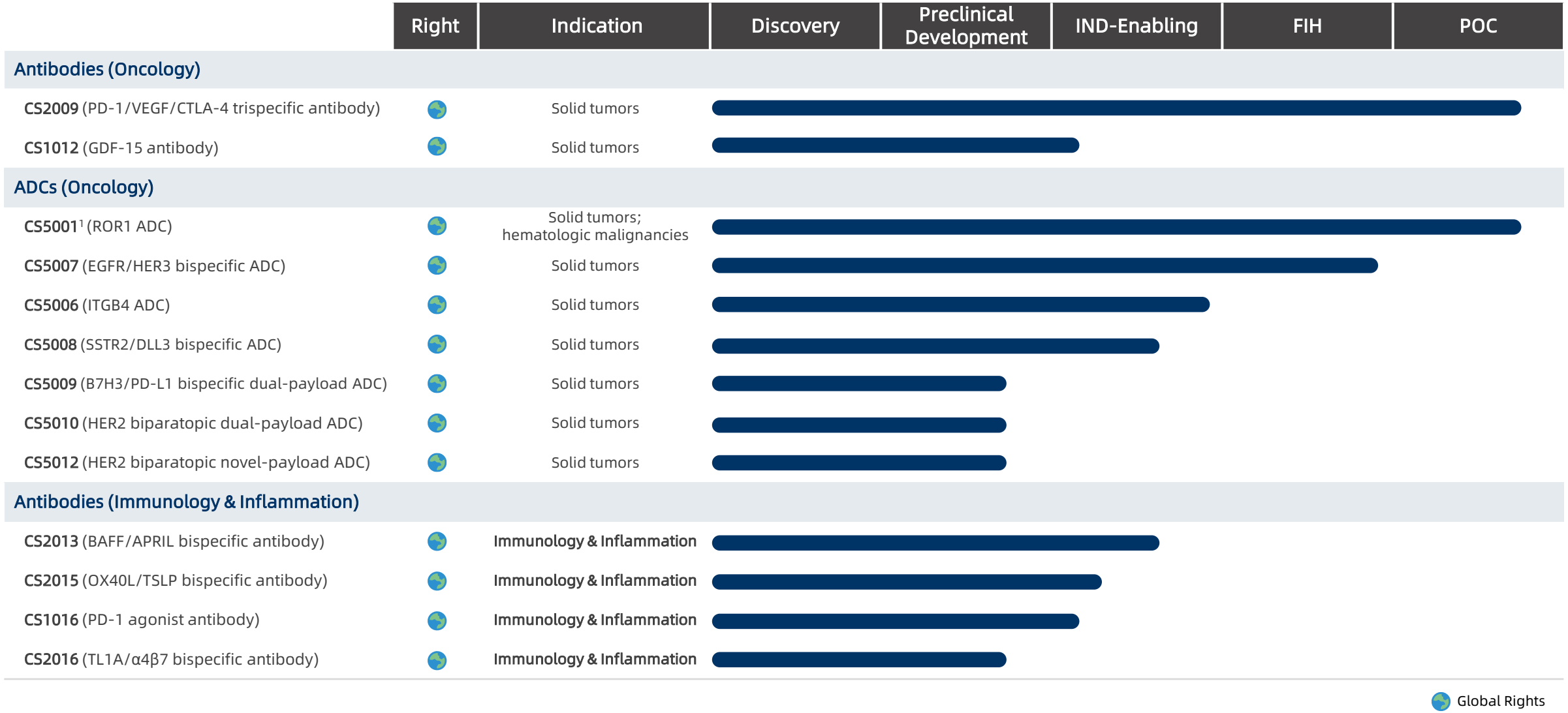
Asset	Indication	POC	Pivotal	NDA	Marketed	Approval						Partners	Partnering Regions
						CN	TW	HK	US	EU	UK		
Pralsetinib (RET)	1L NSCLC	■	■	■	■	✓	✓	✓				blueprint MEDICINES a sanofi company	◀ Mainland China
	2L NSCLC	■	■	■	■	✓	✓	✓					
	NSCLC	■	■	■	■				✓			rigel	
	TC	■	■	■	■				✓				
	Multiple tumors	■											
Avapritinib (KIT/PDGFRA)	PDGFRA exon 18 GIST	■	■	■	■	✓	✓	✓	✓			blueprint MEDICINES a sanofi company	◀ Mainland China
	PDGFRA D842V GIST	■	■	■	■					✓			
	ISM[1]	■	■	■	■				✓	✓			
	Advanced SM[1]	■	■	■	■				✓	✓	✓		
Sugemalimab (PD-L1)	1L Stage IV NSCLC	■	■	■	■	✓				✓	✓	Pfizer	◀ Mainland China
	Stage III NSCLC	■	■	■	■	✓				✓	✓	ewo pharma	◀ Switzerland and CEE
	1L G/GEJ	■	■	■	■	✓						PHARMALINK	◀ Middle East and Africa
	1L ESCC	■	■	■	■	✓						STEINCARES	◀ Latin America
	R/R ENKTL	■	■	■	■	✓						GENTILI	◀ West Europe and the UK
												arrotex PHARMACEUTICALS	◀ Australia & New Zealand
CS1002 (CTLA-4)	Solid tumors	■	■										◀ Greater China

CN = Mainland China, TW = Taiwan, China, HK = Hong Kong SAR, China, US = United States, EU = European Union, UK = United Kingdom, POC = Proof of Concept, NDA = New Drug Application, NSCLC = Non-small Cell Lung Cancer, TC = Thyroid Cancer, GIST = Gastrointestinal Stromal Tumor, ISM = Indolent Systemic Mastocytosis, Advanced SM = Advanced Systemic Mastocytosis, G/GEJ = gastric/gastroesophageal junction adenocarcinoma, ESCC = Esophageal Squamous Cell Carcinoma, R/R = Relapsed or Refractory, ENKTL = Extranodal NK/T Cell Lymphoma, CEE=Central & Eastern Europe

1. POC study was conducted in North American and Europe. No clinical trials have been conducted in China while IND application is under preparation

Well-balanced portfolio of 16 innovative assets (2/2)

– Pipeline 2.0



Note: Assets status denotes progress in the region(s) noted in the column titled "Rights" ; FIH = First in Human, POC = Proof of Concept,
1. CStone obtains the exclusive global right from LigaChem Biosciences, Inc. (LCB) to lead development and commercialization of LCB71/CS5001 outside the Republic of Korea

Trusted Global Partner — Proven Track Record Across Continents

基石药业 CSTONE PHARMACEUTICALS

Sugemalimab (PD-L1)	Pralsetinib (RET)	Avapritinib (KIT/PDGFRA)	Ivosidenib (IDH1)
Pfizer	blueprint MEDICINES a sanofi company; rigel	blueprint MEDICINES a sanofi company	agios
ewo pharma since 1959	ALLIST	HENGRUI	SERVIER moved by you
PHARMALINK			
STEINCARES			
GENTILI			
arrotex PHARMACEUTICALS			

CS5001 (ROR1)	Nofazinlimab (PD-1)	CS1002 (CTLA-4)
LigaChemBio	三生制药 3SBIO INC.	HENGRUI

Regorafenib Co-D	CS2006 (PD-L1/4-1BB/HSA)	Discovery Collaboration
BAYER	NUMAB	DotBio

CStone has built a strong track record of successful partnerships with leading multinational corporations and biotech companies worldwide.

CStone's Leadership Depth and Expertise Translates Science into Patient Value



Jason Yang, MD, PhD
Chief Executive Officer & President of R&D

Pfizer · AMGEN · COVANCE · BeiGene



Michael Choi, MBA
Chief Business & Strategy Officer

sparc · Pfizer · IQVIA · life technologies



Qingmei Shi, MD, PhD
Chief Medical Officer

COVANCE · parexel



Yujuan La, PhD
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Ye Shi, MS
Head of Quality

AsymBio · CMAB · 齐鲁制药 QILU PHARMACEUTICAL



Weicong (Nicky) Ni, MBA, CFA
Chief Financial Officer & Company Secretary

Deutsche Bank · Harvard Business School



Yinghua Zhang, MS
Chief Operating Officer

先声药业 Simcere · 先声默沙东 SMSD



Qinzhou Qi, PhD
Head of R&D Management & Chief of Staff

BeiGene · Northern Illinois University