



基石药业  
CSTONE  
PHARMACEUTICALS

# CS2009 First-in-Human ESMO 2025 Data Review

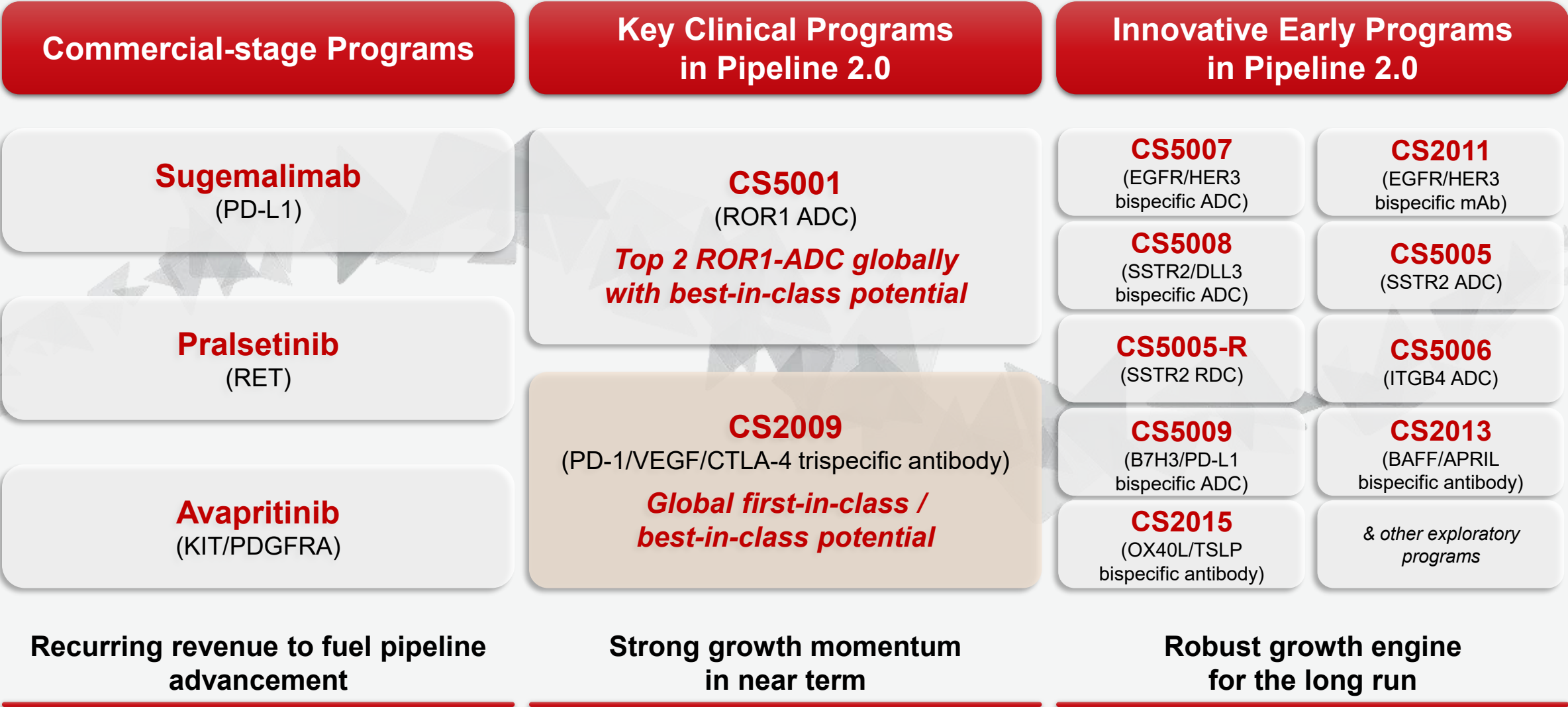
—*Novel PD-1/VEGF/CTLA-4 Trispecific Antibody*

October 2025  
Stock Code: 2616. HK

# Presentation Disclaimer

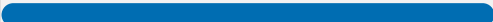
- By attending the meeting where this presentation is made, or by reading the presentation materials, you agree to be bound by the following:
- The information in this presentation has been prepared by representatives of CStone Pharmaceuticals (the "**Company**" and, together with its subsidiaries, the "**Group**") for use in presentations by the Group for information purpose. No part of this presentation will form the basis of, or be relied on in connection with, any contract or commitment or investment decision.
- Certain statements contained in this presentation and in the accompanying oral presentation, may constitute forward-looking statements. Examples of such forward-looking statements include those regarding investigational drug candidates and clinical trials and the status and related results thereto, as well as those regarding continuing and further development and commercialization efforts and transactions with third parties. Such statements, based as they are on the current analysis and expectations of management, inherently involve numerous risks and uncertainties, known and unknown, many of which are beyond the Company's control. Such risks include but are not limited to: the impact of general economic conditions, general conditions in the pharmaceutical industry, changes in the global and regional regulatory environment in the jurisdictions in which the Company's does business, market volatility, fluctuations in costs and changes to the competitive environment. Consequently, actual future results may differ materially from the anticipated results expressed in the forward-looking statements. In the case of forward-looking statements regarding investigational drug candidates and continuing further development efforts, specific risks which could cause actual results to differ materially from the Company's current analysis and expectations include: failure to demonstrate the safety, tolerability and efficacy of the Company's drug candidates, final and quality controlled verification of data and the related analyses, the expense and uncertainty of obtaining regulatory approval, the possibility of having to conduct additional clinical trials and the Company's reliance on third parties to conduct drug development, manufacturing and other services. Further, even if regulatory approval is obtained, pharmaceutical products are generally subject to stringent on-going governmental regulation, challenges in gaining market acceptance and competition. These statements are also subject to a number of material risks and uncertainties that are described in the Company's prospectus published onto the websites of the Company and The Stock Exchange of Hong Kong Limited and the announcements and other disclosures we make from time to time. The reader should not place undue reliance on any forward-looking statements included in this presentation or in the accompanying oral presentation. These statements speak only as of the date made, and the Company is under no obligation and disavows any obligation to update or revise such statements as a result of any event, circumstances or otherwise, unless required by applicable legislation or regulation.
- Forward-looking statements are sometimes identified by the use of forward-looking terminology such as "believe," "expects," "may," "will," "could," "should," "shall," "risk," "intends," "estimates," "plans," "predicts," "continues," "assumes," "positioned" or "anticipates" or the negative thereof, other variations thereon or comparable terminology or by discussions of strategy, plans, objectives, goals, future events or intentions.
- No representation or warranty, express or implied, is made as to, and no reliance should be placed on, the fairness, accuracy, completeness or correctness of the information, or opinions contained herein. The information set out herein may be subject to updating, revision, verification and amendment and such information may change materially.
- This presentation and the information contained herein is highly confidential and being furnished to you solely for your information and may not be reproduced or redistributed in any manner to any other person, in whole or in part. In particular, neither the information contained in this presentation, nor any copy hereof may be, directly or indirectly, taken or transmitted into or distributed in any jurisdiction which prohibits the same except in compliance with applicable securities laws. This presentation and the accompanying oral presentation contains data and information obtained from third-party studies and internal company analysis of such data and information. We have not independently verified the data and information obtained from these sources.
- By attending this presentation, you acknowledge that you will be solely responsible for your own assessment of the market and the market position of the Group and that you will conduct your own analysis and be solely responsible for forming your own view of the potential future performance of the business of the Group.

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



# Pipeline 2.0: an innovative portfolio with global rights

CS2009: leading position globally to target PD-1, VEGFA and CTLA-4

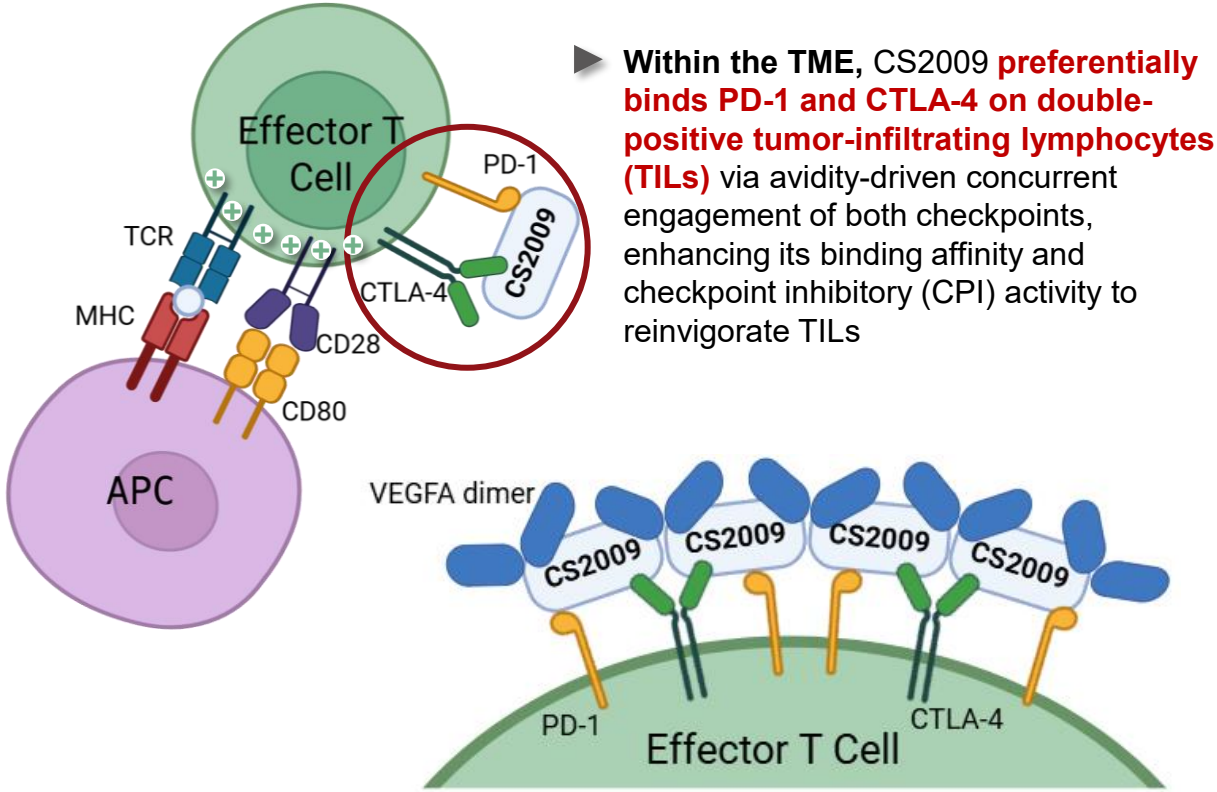
| Drug candidate                                 | Right                                                                               | Indication                               | Discovery                                                                             | Preclinical Development | IND-Enabling | FIH | POC |
|------------------------------------------------|-------------------------------------------------------------------------------------|------------------------------------------|---------------------------------------------------------------------------------------|-------------------------|--------------|-----|-----|
| CS5001 <sup>1</sup> (ROR1 ADC)                 |    | Solid tumors<br>hematologic malignancies |    |                         |              |     |     |
| CS2009 (PD-1/VEGF/CTLA-4 trispecific antibody) |    | Solid tumors                             |    |                         |              |     |     |
| CS5007 (EGFR/HER3 bispecific ADC)              |    | Solid tumors                             |    |                         |              |     |     |
| CS2011 (EGFR/HER3 bispecific antibody)         |    | Solid tumors                             |    |                         |              |     |     |
| CS5008 (SSTR2/DLL3 bispecific ADC)             |    | Solid tumors                             |    |                         |              |     |     |
| CS5005 (SSTR2 ADC)                             |    | Solid tumors                             |    |                         |              |     |     |
| CS5005-R (SSTR2 RDC)                           |    | Solid tumors                             |    |                         |              |     |     |
| CS5006 (ITGB4 ADC)                             |    | Solid tumors                             |    |                         |              |     |     |
| CS5009 (B7H3/PD-L1 bispecific ADC)             |  | Solid tumors                             |  |                         |              |     |     |
| CS2013 (BAFF/APRIL bispecific antibody)        |  | Autoimmune Diseases                      |  |                         |              |     |     |
| CS2015 (OX40L/TSLP bispecific antibody)        |  | Inflammatory Diseases                    |  |                         |              |     |     |

 Antibody  ADC  RDC  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

Multi-target engagement and synergistic interactions among anti-PD-1, CTLA-4 and VEGFA arms enhance CS2009's activities in TME, while sparing peripheral CTLA4-single-positive T cells, potentially leading to significant improvement of its therapeutic window

Tumor Microenvironment (TME)

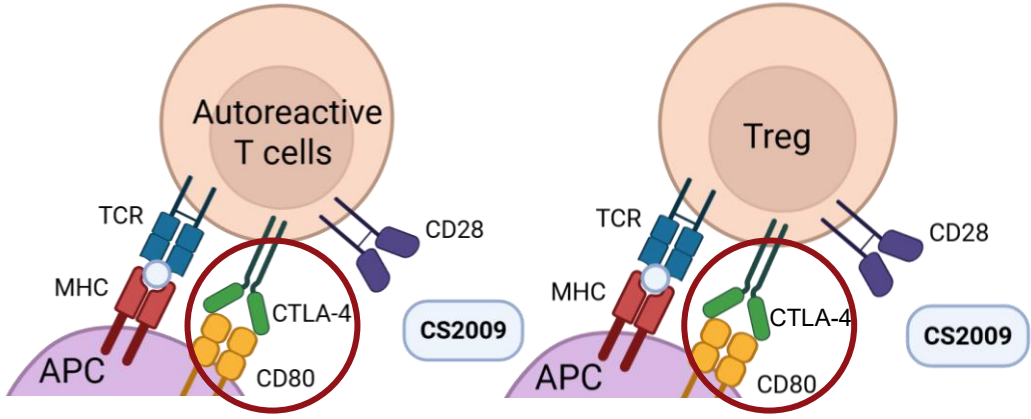


Within the TME, CS2009 preferentially binds PD-1 and CTLA-4 on double-positive tumor-infiltrating lymphocytes (TILs) via avidity-driven concurrent engagement of both checkpoints, enhancing its binding affinity and checkpoint inhibitory (CPI) activity to reinvigorate TILs

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, CS2009's CTLA-4 arm is unable to block CTLA-4/CD80 interactions due to low affinity, thereby sparing CTLA-4 single-positive T cells from over-activation, thus reducing systemic autoimmune toxicity

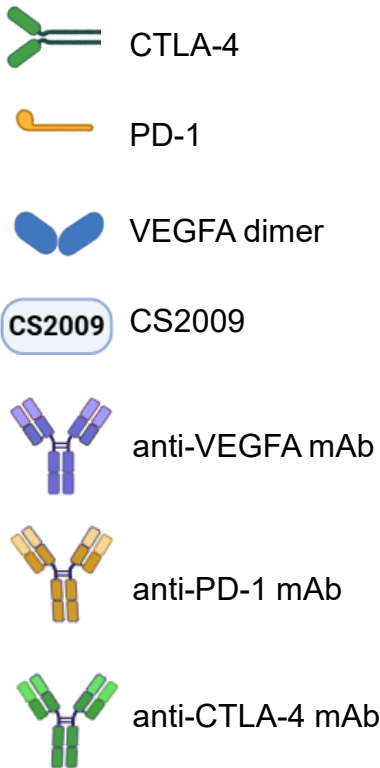
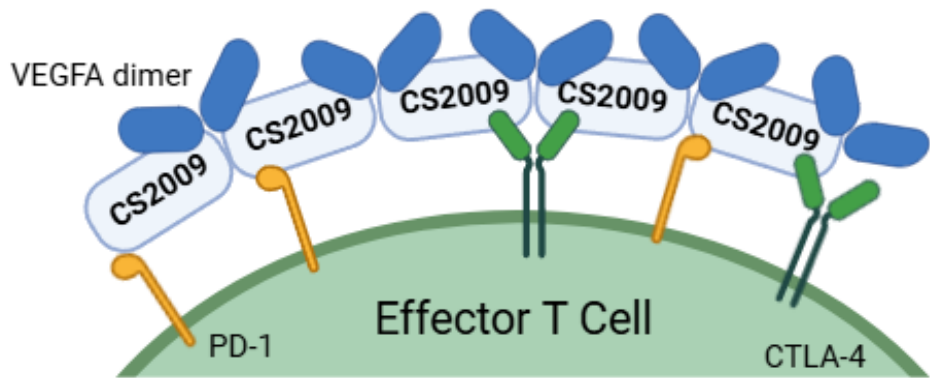


- |                                                                                       |        |                                                                                       |             |
|---------------------------------------------------------------------------------------|--------|---------------------------------------------------------------------------------------|-------------|
|  | TCR    |  | MHC         |
|  | CD28   |  | CD80        |
|  | CTLA-4 |  | VEGFA dimer |
|  | PD-1   |  | CS2009      |

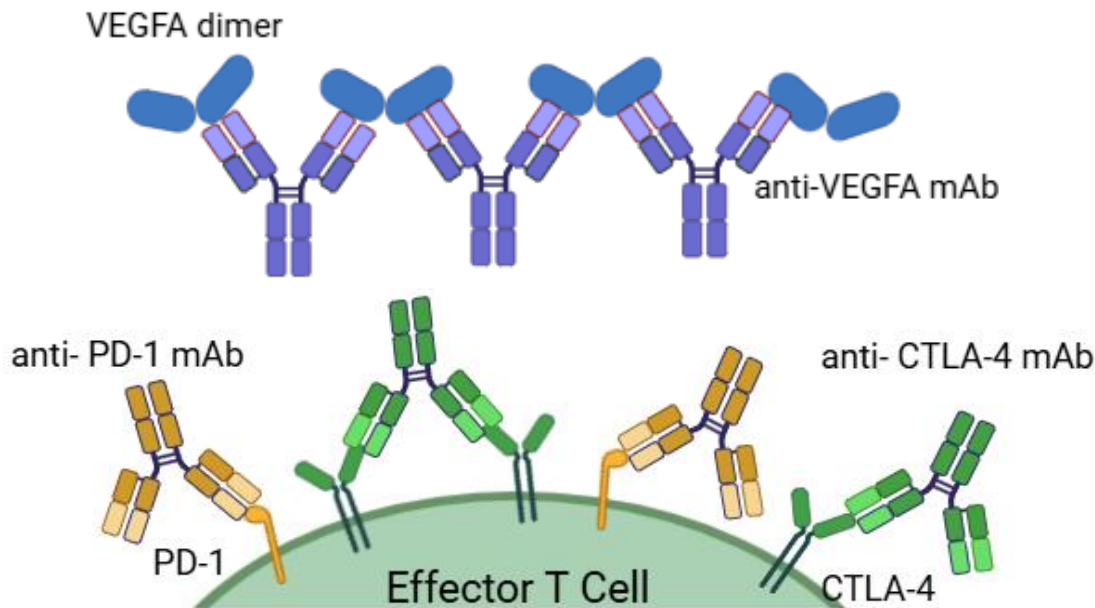


# CS2009 clustering with VEGFA dimers leads to significant increase of its binding affinities to PD-1 and CTLA-4 on T cells in the TME

The crosslinking between VEGFA dimers and CS2009 leads to over 20-fold increase of the blocking activities against PD-1 and PD-1/CTLA4 in cell-based assay, due to synergistic binding

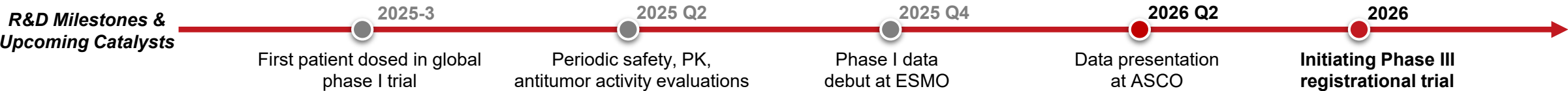
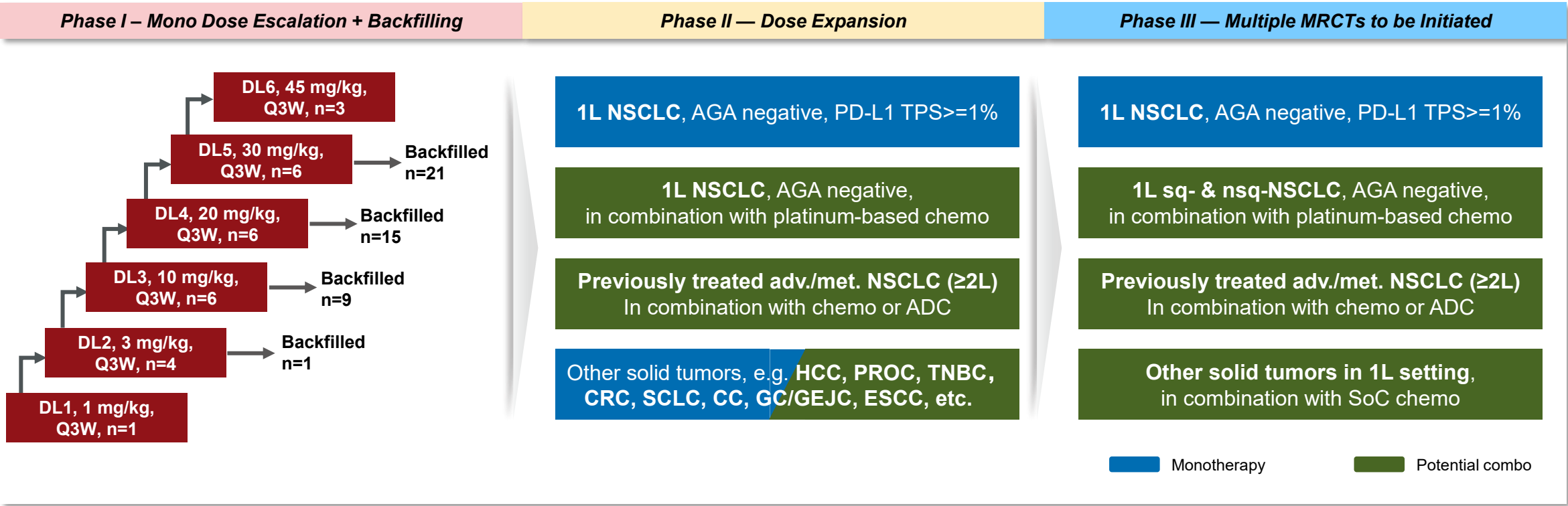


In contrast, combination treatment using three independent monoclonal antibodies unlikely to have synergistic enhancement of neutralizing/blocking activities within the TME



# CS2009 global phase I/II trial ongoing in Australia and China; US IND in preparation

Phase II first-patient-enrollment initiated in Australia



AGA: actionable oncogenic alterations; TPS: tumor proportion score; IO: immuno-oncology therapy; NSCLC: non-small cell lung cancer; HCC: hepatocellular carcinoma; PROC: platinum-resistant ovarian cancer; TNBC: triple-negative breast cancer; CRC: colorectal cancer; SCLC: small cell lung cancer; CC: cervical cancer; GC/GEJC: gastric/gastroesophageal junction cancer; ESCC: esophageal squamous cell carcinoma; sq: squamous; nsq: non-squamous; SoC: standard of care

## 72 heavily pretreated patients with advanced solid tumors; >50% IO-treated; median follow-up of 1.9 months only

| Characteristics             | Total<br>(N=72) | Characteristics                               | Total<br>(N=72) |
|-----------------------------|-----------------|-----------------------------------------------|-----------------|
| <b>Age, years</b>           |                 | <b>Prior IO therapy, n (%)</b>                | 37 (51.4)       |
| Median (range)              | 60.5 (19-80)    | <b>Prior anti-angiogenic therapy, n (%)</b>   | 30 (41.7)       |
| <b>Sex, n (%)</b>           |                 | <b>Tumor type, n (%)</b>                      |                 |
| Female                      | 36 (50.0)       | Non-small cell lung cancer (NSCLC)            | 33 (45.8)       |
| Male                        | 36 (50.0)       | Ovarian carcinoma (OC)                        | 10 (13.9)       |
| <b>Race, n (%)</b>          |                 | Soft tissue sarcoma (STS)                     | 9 (12.5)        |
| Black or African American   | 1 (1.4)         | Renal cell carcinoma (RCC)                    | 4 (5.6)         |
| Asian                       | 31 (43.1)       | Triple negative breast carcinoma (TNBC)       | 4 (5.6)         |
| White                       | 39 (54.2)       | Adrenocortical carcinoma (AC)                 | 2 (2.8)         |
| Other                       | 1 (1.4)         | Cervical carcinoma (CC)                       | 2 (2.8)         |
| <b>ECOG PS, n (%)</b>       |                 | Gastric carcinoma (GC)                        | 2 (2.8)         |
| 0                           | 32 (44.4)       | Prostate carcinoma (PC)                       | 2 (2.8)         |
| 1                           | 40 (55.6)       | Biliary tract carcinoma (BTC)                 | 1 (1.4)         |
| <b>Prior therapy, n (%)</b> |                 | Bladder mucinous adenocarcinoma               | 1 (1.4)         |
| 1                           | 24 (33.3)       | Hepatocellular carcinoma (HCC)                | 1 (1.4)         |
| 2                           | 17 (23.6)       | Head and neck squamous cell carcinoma (HNSCC) | 1 (1.4)         |
| ≥3                          | 27 (37.5)       |                                               |                 |

**Median follow-up:  
1.9 (0.1-6.7) months**

**Median treatment duration:  
1.4 (0.1-6.7) months**

**Median treatment cycle:  
2.0 (1-10) cycles**



# Favorable Safety Profile: Grade $\geq 3$ TRAEs: 13.9%; Grade $\geq 3$ irAEs: 4.2%; No Grade 4/5 TRAEs

CS2009 Safety Overview

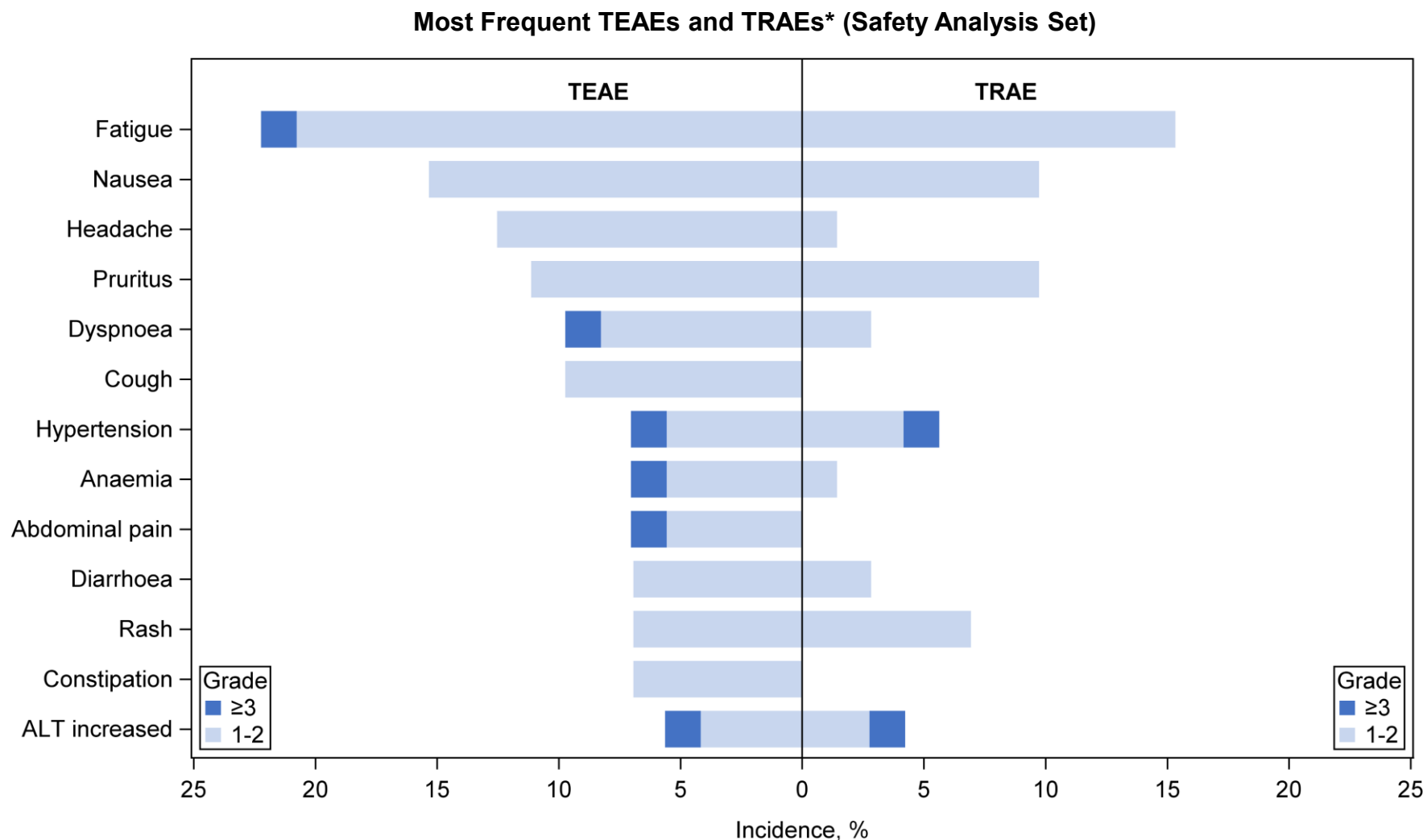
| n (%)                                                | DL1-3<br>1-10 mg/kg, Q3W*<br>(N=21) | DL4<br>20 mg/kg, Q3W<br>(N=21) | DL5<br>30 mg/kg, Q3W<br>(N=27) | DL6<br>45 mg/kg, Q3W<br>(N=3) | All DLs<br>(N=72) |
|------------------------------------------------------|-------------------------------------|--------------------------------|--------------------------------|-------------------------------|-------------------|
| No. of patients with $\geq 1$ following event        |                                     |                                |                                |                               |                   |
| Treatment-emergent adverse event (TEAE)              | 21 (100.0)                          | 19 (90.5)                      | 13 (48.1)                      | 3 (100.0)                     | 56 (77.8)         |
| Grade $\geq 3$ TEAE                                  | 8 (38.1)                            | 6 (28.6)                       | 6 (22.2)                       | 1 (33.3)                      | 21 (29.2)         |
| Treatment-related TEAE (TRAE)                        | 18 (85.7)                           | 16 (76.2)                      | 8 (29.6)                       | 3 (100.0)                     | 45 (62.5)         |
| <b>Grade <math>\geq 3</math> TRAE</b>                | <b>5 (23.8)</b>                     | <b>2 (9.5)</b>                 | <b>2 (7.4)</b>                 | <b>1 (33.3)</b>               | <b>10 (13.9)</b>  |
| Serious TEAE                                         | 7 (33.3)                            | 6 (28.6)                       | 4 (14.8)                       | 0                             | 17 (23.6)         |
| Treatment-related serious TEAE                       | 2 (9.5)                             | 4 (19.0)                       | 0                              | 0                             | 6 (8.3)           |
| Immune-related TEAE                                  | 8 (38.1)                            | 2 (9.5)                        | 2 (7.4)                        | 0                             | 12 (16.7)         |
| <b>Grade <math>\geq 3</math> immune-related TEAE</b> | <b>2 (9.5)</b>                      | <b>1 (4.8)</b>                 | <b>0</b>                       | <b>0</b>                      | <b>3 (4.2)</b>    |
| Infusion-related reaction                            | 0                                   | 1 (4.8)                        | 0                              | 1 (33.3)                      | 2 (2.8)           |
| TEAE leading to drug permanent discontinuation       | 0                                   | 1 (4.8)                        | 0                              | 0                             | 1 (1.4)           |

\* Patients at DL1-3 (1-10 mg/kg) were permitted for intra-escalation to DL4, 20mg/kg based on investigator assessment of tolerability and potential benefit.

Abbr: DL, dose level

Source: ESMO 2025 poster

# CS2009 was well tolerated; most frequent TRAEs were manageable

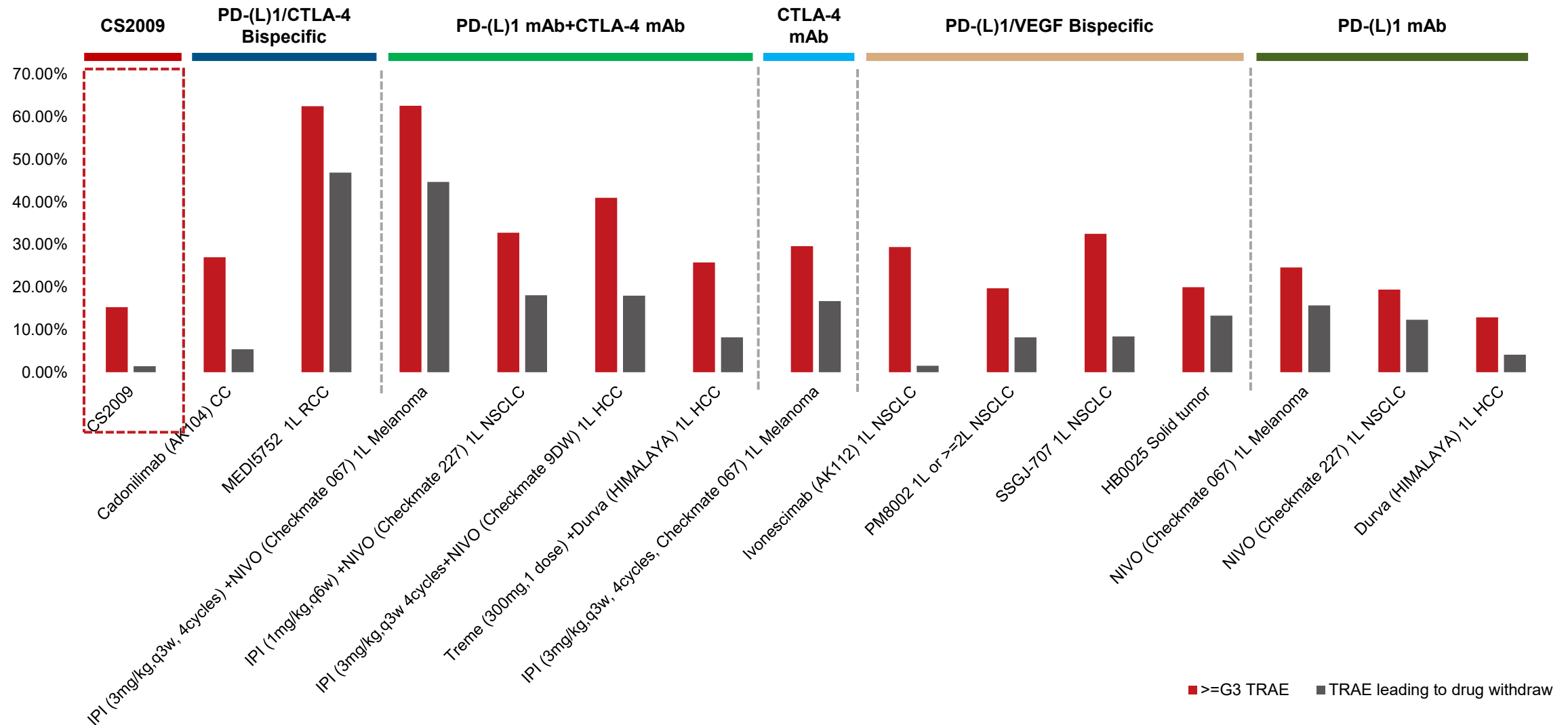


\*TEAEs with incidence rate  $\geq 5\%$  and the corresponding TRAEs. AEs were graded according to National Cancer Institute Common Terminology Criteria for AE (NCI-CTCAE) v5.0.

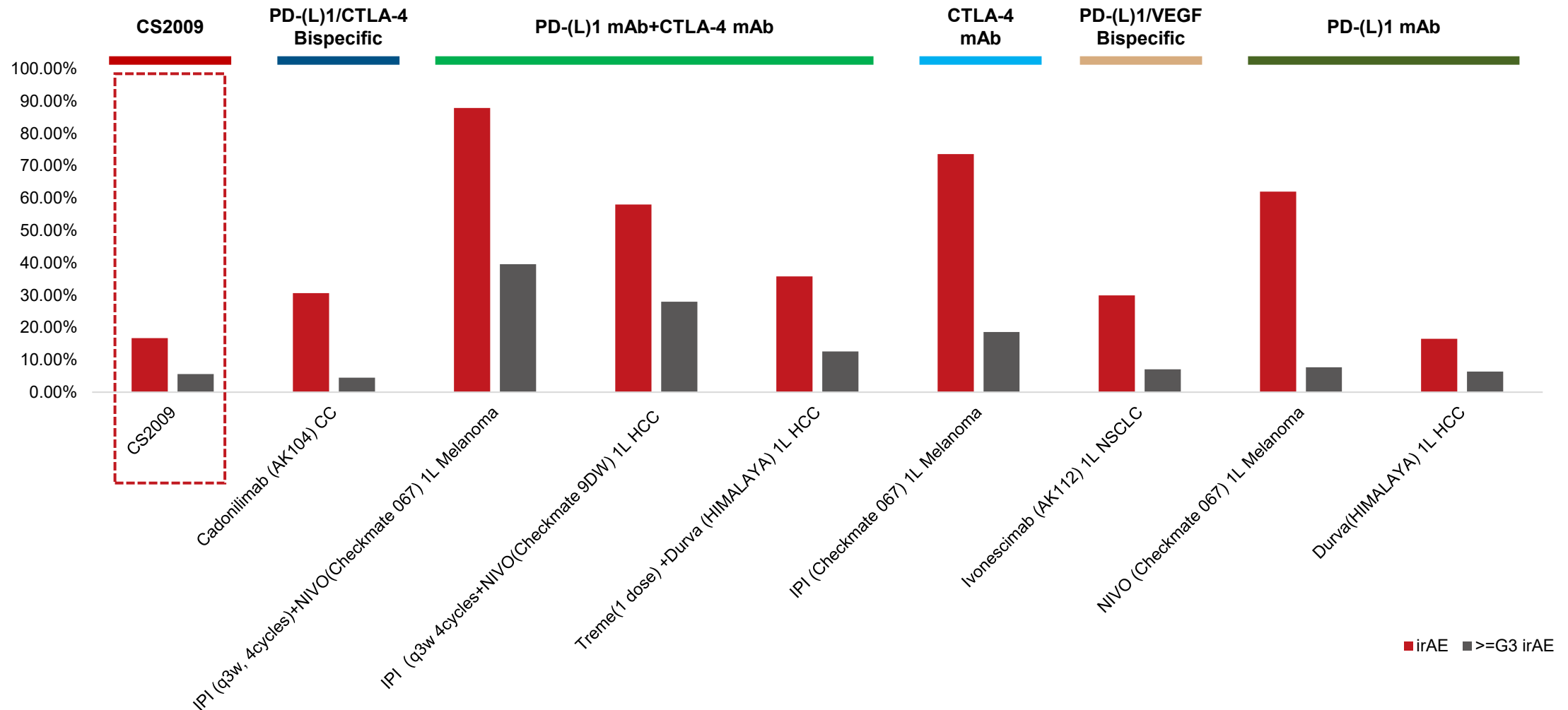
ALT=alanine aminotransferase; TEAE=treatment-emergent adverse event; TRAE=treatment-related adverse event.

Source: ESMO 2025 poster

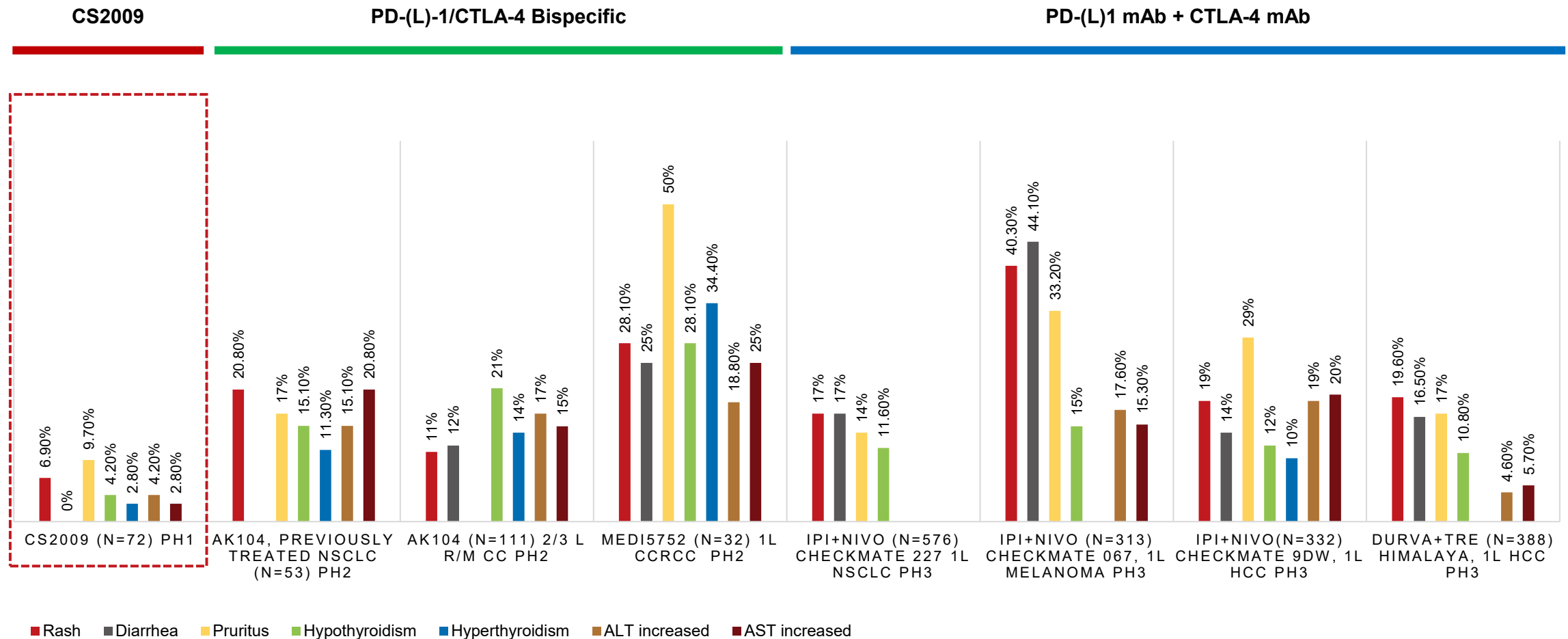
## Safety Comparison (1/4): Much lower incidence of grade $\geq 3$ TRAE and TRAE leading to treatment discontinuation vs. IO bispecific or combination regimens, with the caveat of shorter follow-up



## Safety Comparison (2/4): Much lower incidence of any-grade and grade $\geq 3$ irAE vs. IO bispecific or combination regimens, with the caveat of shorter follow-up

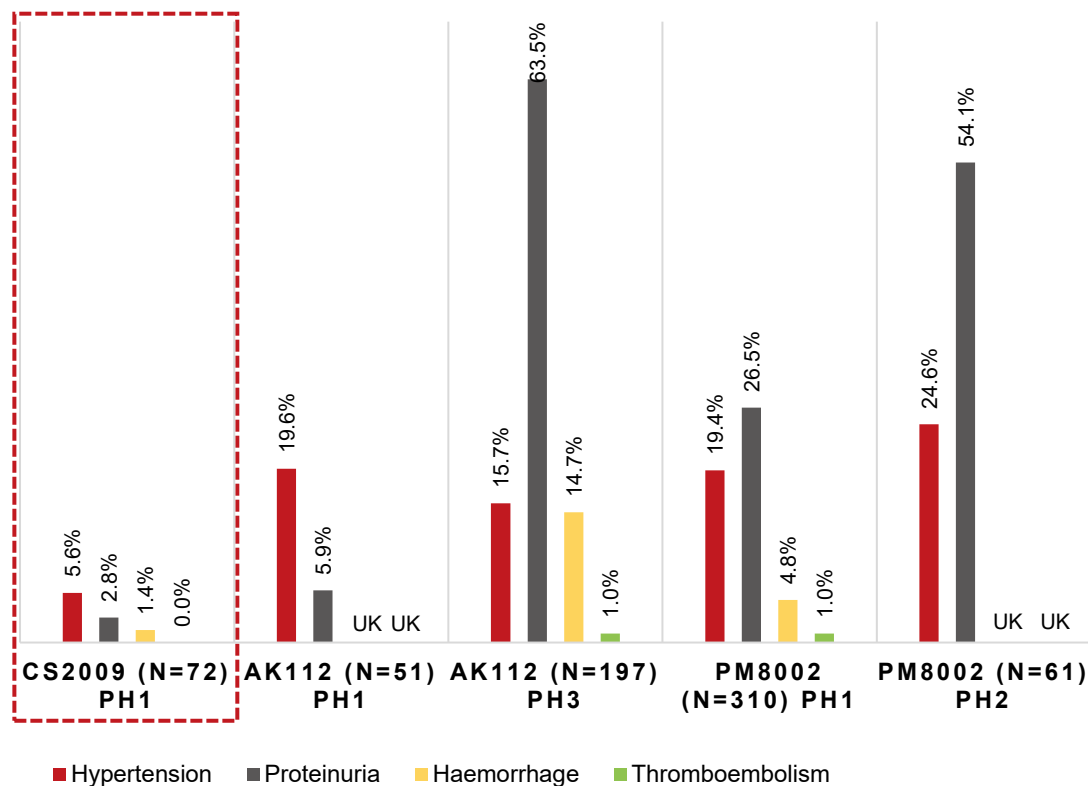
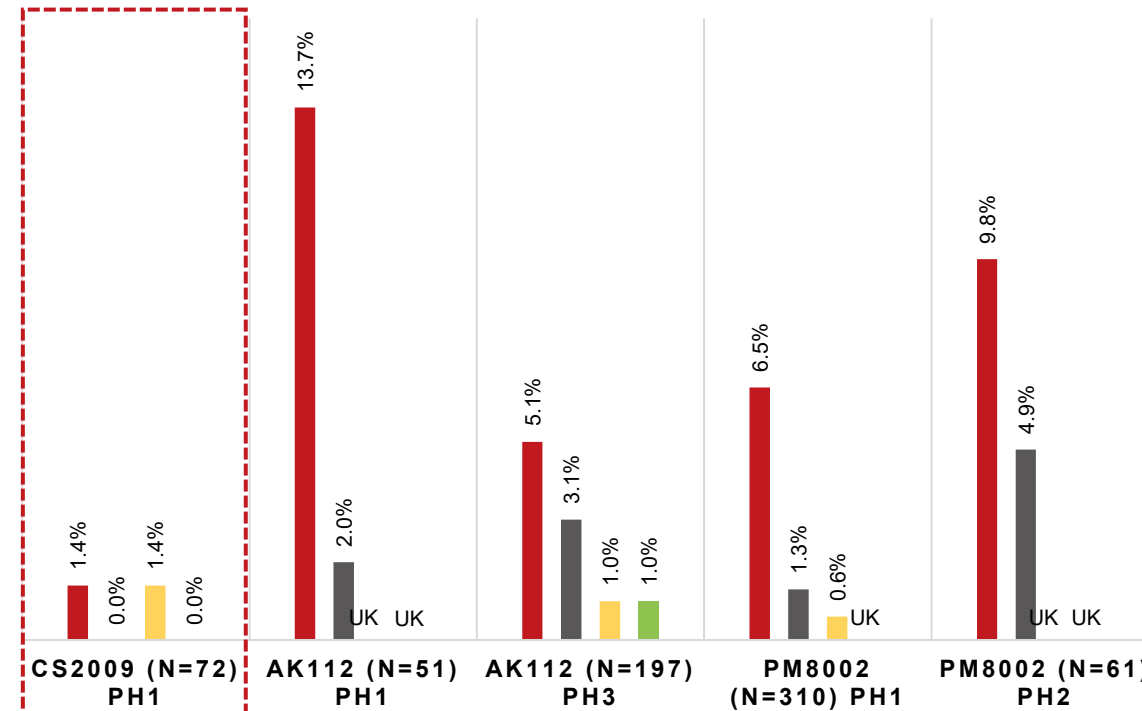


# Safety Comparison (3/4): Much lower incidence of frequent any-grade irAE vs. PD-(L)1/CTLA-4 bispecific or combination regimens, with the caveat of shorter follow-up



## Safety Comparison (4/4): Much lower incidence of any-grade and grade $\geq 3$ VEGF-related TRAE vs. PD-(L)1/VEGF bispecific, with the caveat of shorter follow-up

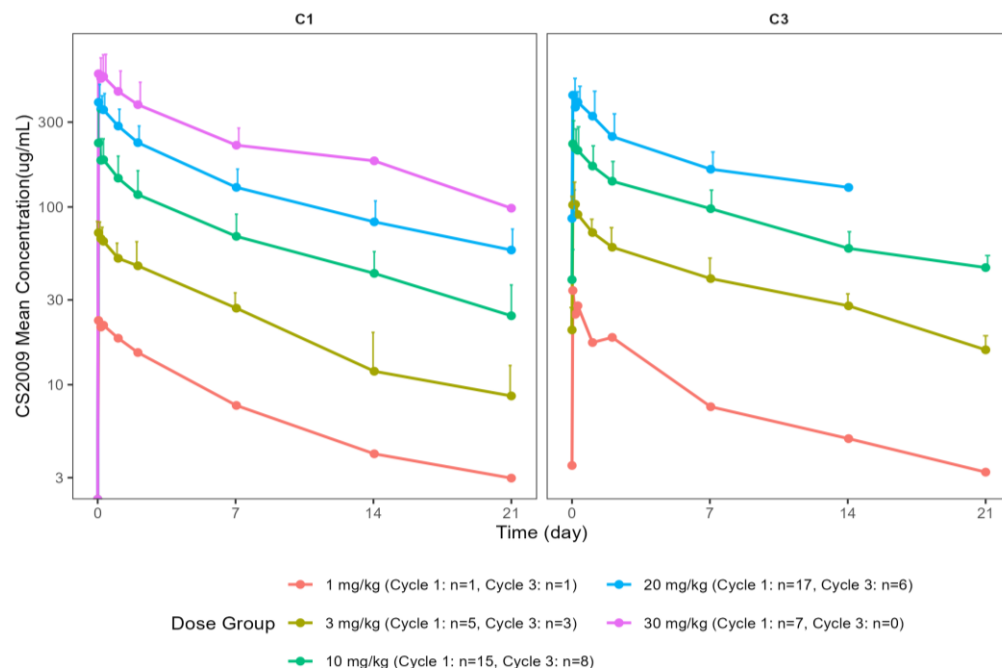
Any-grade VEGF-related TRAE

Grade  $\geq 3$  VEGF-related TRAE



# CS2009 PK Profile: Dose-proportional exposure; terminal half-life of ~6-8 days; no significant accumulation after repeated doses; very low ADA-positivity incidence

Mean (+SD) Concentration-Time Profile



CS2009 PK Parameters after First Dose

| Parameter               | 1 mg/kg<br>n=1 | 3 mg/kg<br>n=5 | 10 mg/kg<br>n=15 | 20 mg/kg<br>n=17 | 30 mg/kg<br>n=7 |
|-------------------------|----------------|----------------|------------------|------------------|-----------------|
| $C_{max}$ (ug/mL)       | 23 (-)         | 71 (16.1)      | 215 (41.5)       | 386 (24.3)       | 580 (23.5)      |
| half-life (h)           | 175 (-)        | 151 (68.4)     | 189 (33.3)       | 191 (24.5)       | - (-)           |
| $AUC_{0-504}$ (ug/mL*h) | 3720 (-)       | 10900 (37.5)   | 31630 (34.8)     | 61450 (27.3)     | (-)             |
| $AUC_{0-inf}$ (ug/mL*h) | 3790 (-)       | 12670 (48.9)   | 37590 (44.8)     | 76630 (37.3)     | - (-)           |

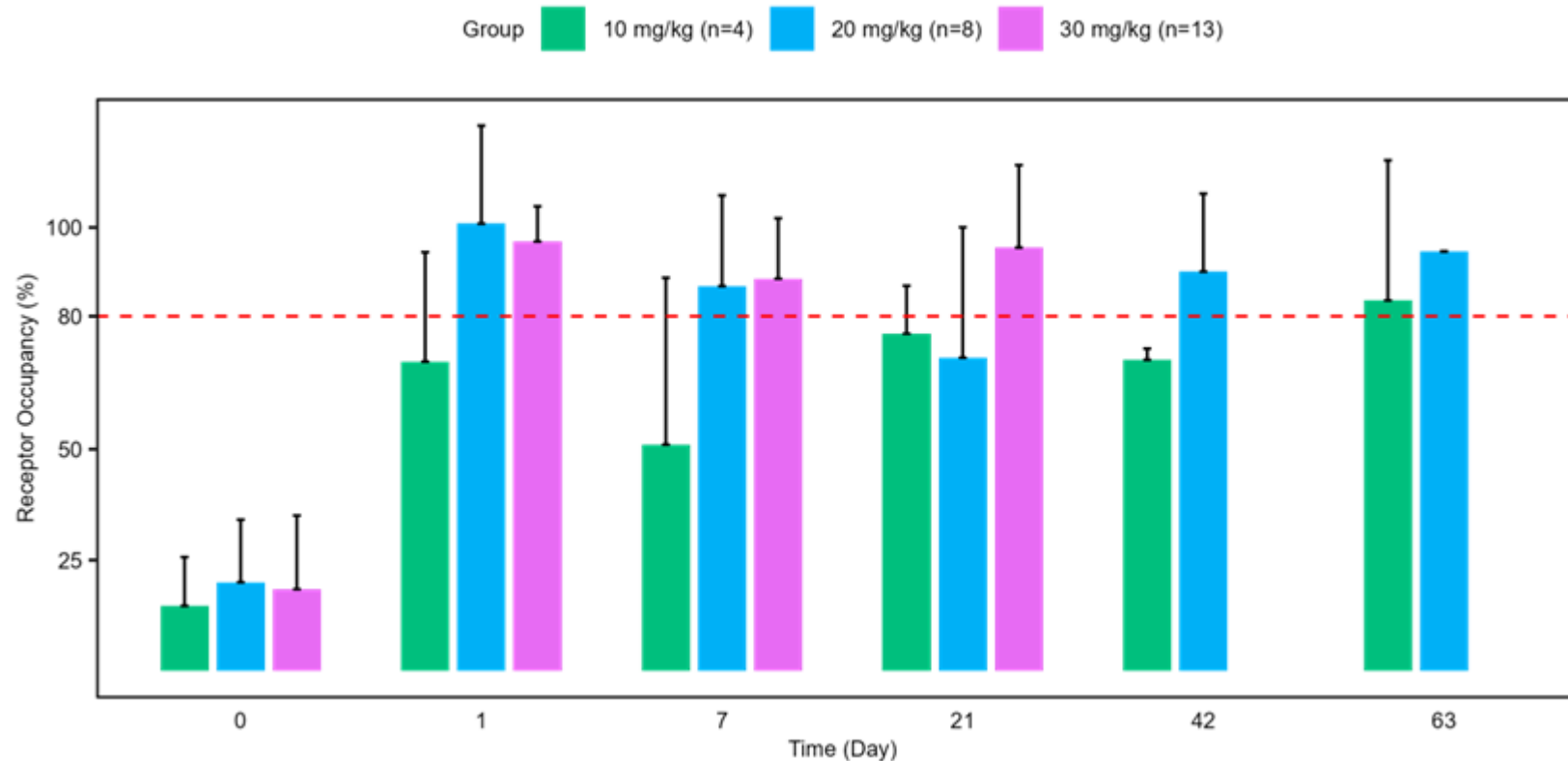
CS2009 PK Parameters after Third Dose

|                         | n=1      | n=3          | n=8          | n=6         |  |
|-------------------------|----------|--------------|--------------|-------------|--|
| $C_{max}$ (ug/mL)       | 33.9 (-) | 111 (23.5)   | 232 (32.1)   | 417 (26.3)  |  |
| $AUC_{0-504}$ (ug/mL*h) | 4350 (-) | 18290 (17.3) | 45450 (21.8) | 96200 (-)   |  |
| Rac, $C_{max}$          | 1.47 (-) | 1.5 (8.0)    | 0.92 (68.4)  | 1.15 (10.4) |  |
| Rac, AUC                | 1.17 (-) | 1.31 (6.6)   | 1.18 (7.5)   | 1.5 (-)     |  |

## PK Summary

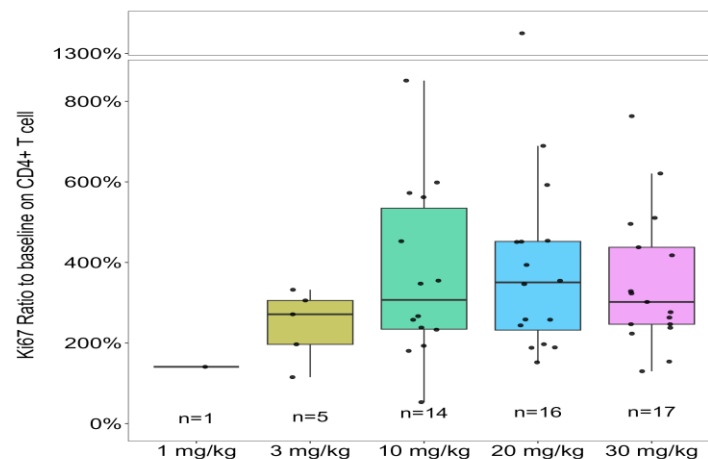
- $C_{max}$  and AUC increased approximately proportionally with dose across the five cohorts evaluated so far.
- The terminal half-life is approximately **6~8 days**.
- No significant accumulation observed at Cycle 3 (accumulation index: 0.9–1.5).

## Receptor Occupancy (RO): PD-1/CTLA-4 receptor occupancy on peripheral T cells reached saturation throughout dosing interval at $\geq 20$ mg/kg

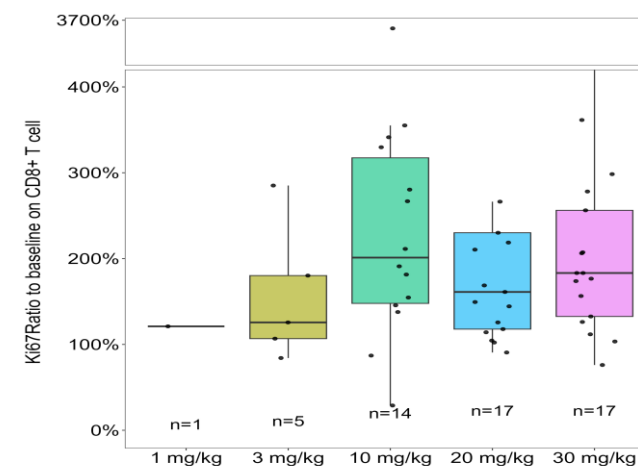


## T-cell Proliferation & Activation: CS2009 induced notable, dose-dependent upregulation of Ki67 (proliferation due to PD-1 and CTLA-4 blockade) and ICOS (activation due to CTLA-4 blockade) on both CD4+ and CD8+ T cells

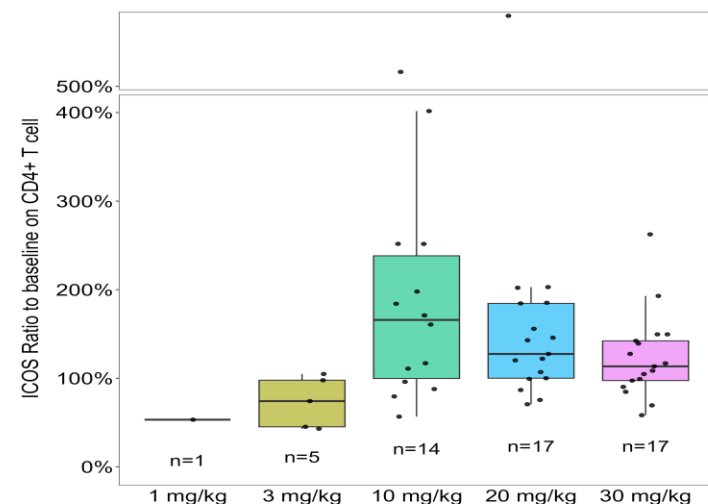
### Ki67 expression on CD4+ T cells



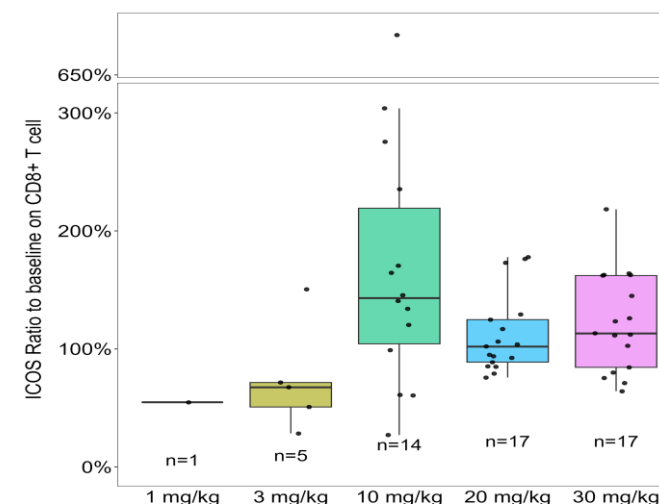
### Ki67 expression on CD8+ T cells



### ICOS expression on CD4+ T cells

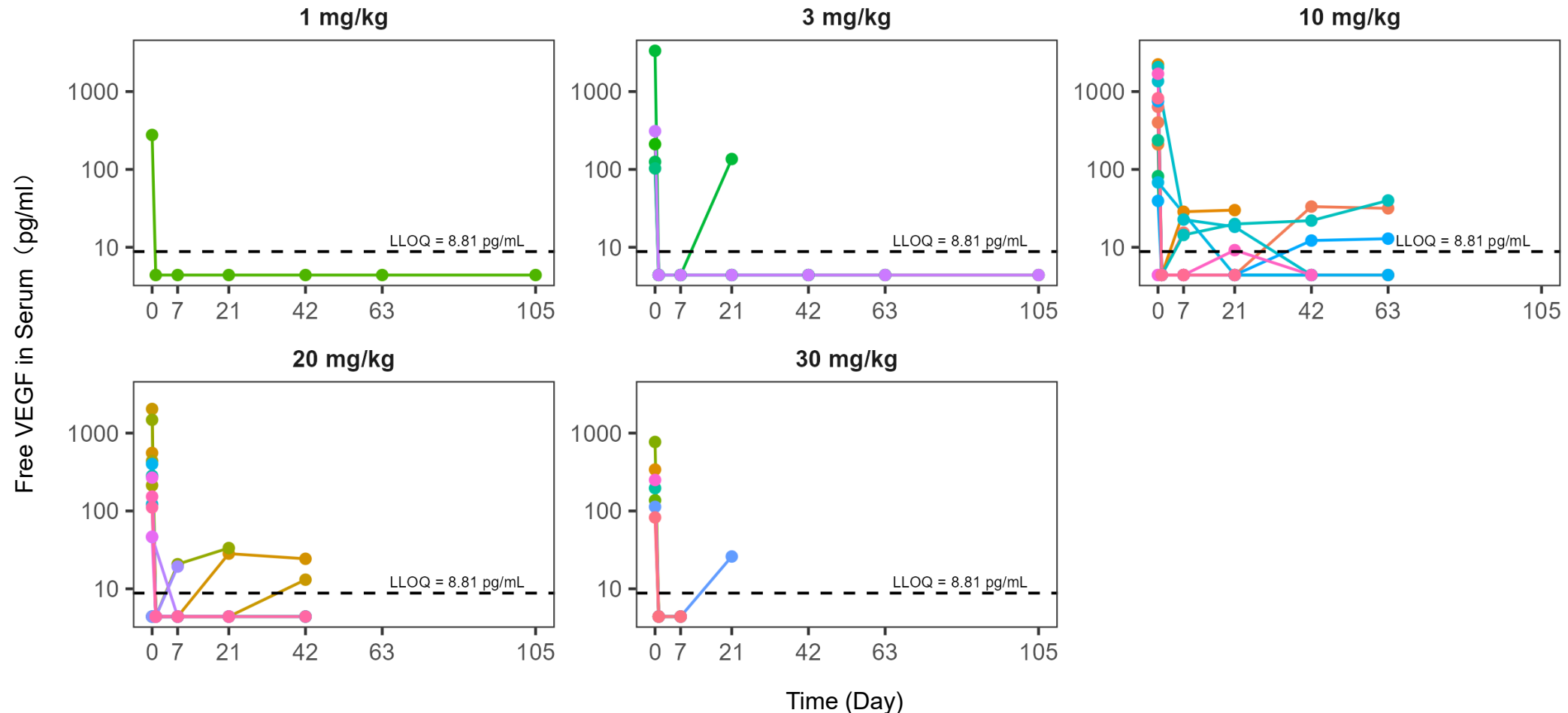


### ICOS expression on CD8+ T cells



# VEGF Neutralization: Serum-free VEGFA reduced deeply and rapidly across all doses, and the effect sustained throughout dose intervals

Serum-free VEGFA Concentrations by Dose Level



Note: Concentrations below the lower limit of quantification (LLOQ, 8.81 pg/mL) were imputed as one-half of the LLOQ.

Source: ESMO 2025 poster

Promising Antitumor Activity: Response observed across all dose levels, with dose-dependent uptrend, including 70+% DCR overall and 25% ORR at ≥30 mg/kg (median follow-up ~2 months only)

Best Overall Response in All Evaluable Patients (Efficacy Analysis Set)  
(Patients who had at least one post-baseline tumor-assessment)

| All Evaluable Patients, n (%) | DL1-3<br>1-10 mg/kg, Q3W<br>(N=20) | DL4<br>20 mg/kg, Q3W<br>(N=17) | DL5<br>30 mg/kg, Q3W<br>(N=9) | DL6<br>45 mg/kg, Q3W<br>(N=3) | All DLs<br>(N=49) |
|-------------------------------|------------------------------------|--------------------------------|-------------------------------|-------------------------------|-------------------|
| Overall Response Rate (ORR)   | 2 (10.0)                           | 1 (5.9)                        | 2 (22.2)                      | 1 (33.3)                      | 6 (12.2)          |
| Partial Response (PR)         | 2 (10.0)                           | 1 (5.9)                        | 2 (22.2)                      | 1 (33.3)                      | 6 (12.2)          |
| Stable Disease (SD)           | 11 (55.0)                          | 12 (70.6)                      | 4 (44.4)                      | 2 (66.7)                      | 29 (59.2)         |
| Progressive Disease (PD)      | 7 (35.0)                           | 4 (23.5)                       | 3 (33.3)                      | 0                             | 14 (28.6)         |
| Disease Control Rate (DCR)    | 13 (65.0)                          | 13 (76.5)                      | 6 (66.7)                      | 3 (100.0)                     | 35 (71.4)         |

Median follow-up: 1.9 months

## Post-ESMO Update: One NSCLC patient with stable disease converted to partial response

**Best Overall Response in All Evaluable Patients (Efficacy Analysis Set)**  
(Patients who had at least one post-baseline tumor-assessment)

| All Evaluable Patients, n (%) | DL1-3<br>1-10 mg/kg, Q3W<br>(N=20) | DL4<br>20 mg/kg, Q3W<br>(N=17) | DL5<br>30 mg/kg, Q3W<br>(N=9) | DL6<br>45 mg/kg, Q3W<br>(N=3) | All DLs<br>(N=49) |
|-------------------------------|------------------------------------|--------------------------------|-------------------------------|-------------------------------|-------------------|
| Overall Response Rate (ORR)   | 2 (10.0)                           | 2 (11.8) ↑                     | 2 (22.2)                      | 1 (33.3)                      | 7 (14.3) ↑        |
| Partial Response (PR)         | 2 (10.0)                           | 2 (11.8) ↑                     | 2 (22.2)                      | 1 (33.3)                      | 7 (14.3) ↑        |
| Stable Disease (SD)           | 11 (55.0)                          | 11 (64.7)                      | 4 (44.4)                      | 2 (66.7)                      | 28 (57.1)         |
| Progressive Disease (PD)      | 7 (35.0)                           | 4 (23.5)                       | 3 (33.3)                      | 0                             | 14 (28.6)         |
| Disease Control Rate (DCR)    | 13 (65.0)                          | 13 (76.5)                      | 6 (66.7)                      | 3 (100.0)                     | 35 (71.4)         |

Median follow-up: ~ 2 months

## Efficacy observed across tumor types despite limited follow-up

### Best Overall Response in Specific Tumor Types (Efficacy Analysis Set)

(Patients who had at least one post-baseline tumor-assessment)

| Tumor Type, n (%)                                                                                      | NSCLC*<br>(N=17)  | Ovarian Cancer<br>(N=6) | TNBC<br>(N=4)   | nccRCC<br>(N=3)  | STS<br>(N=9)    |
|--------------------------------------------------------------------------------------------------------|-------------------|-------------------------|-----------------|------------------|-----------------|
| Prior IO Therapy                                                                                       | 17 (100.0)        | 1 (16.7)                | 2 (50.0)        | 2 (66.7)         | 2 (22.2)        |
| Prior Anti-VEGF Therapy                                                                                | 7 (41.2)          | 4 (66.7)                | 1 (25.0)        | 3 (100.0)        | 4 (44.4)        |
| <b>Overall Response Rate (ORR)</b>                                                                     | <b>3 (17.6*)</b>  | <b>1 (16.7)</b>         | <b>1 (25.0)</b> | <b>1 (33.3)</b>  | <b>1 (11.1)</b> |
| Partial Response (PR)                                                                                  | 3 (17.6)          | 1 (16.7)                | 1 (25.0)        | 1 (33.3)         | 1 (11.1)        |
| Stable Disease (SD)                                                                                    | 11 (64.7)         | 3 (50.0)                | 2 (50.0)        | 2 (66.7)         | 5 (55.6)        |
| Progressive Disease (PD)                                                                               | 3 (17.6)          | 2 (33.3)                | 1 (25.0)        | 0                | 3 (33.3)        |
| <b>Disease Control Rate (DCR)</b>                                                                      | <b>14 (82.4*)</b> | <b>4 (66.7)</b>         | <b>3 (75.0)</b> | <b>3 (100.0)</b> | <b>6 (66.7)</b> |
| # For NSCLC, 10 mg/kg (n=5), 20 mg/kg (n=8), 30 mg/kg (n=4), one responder was observed in each cohort |                   |                         |                 |                  |                 |

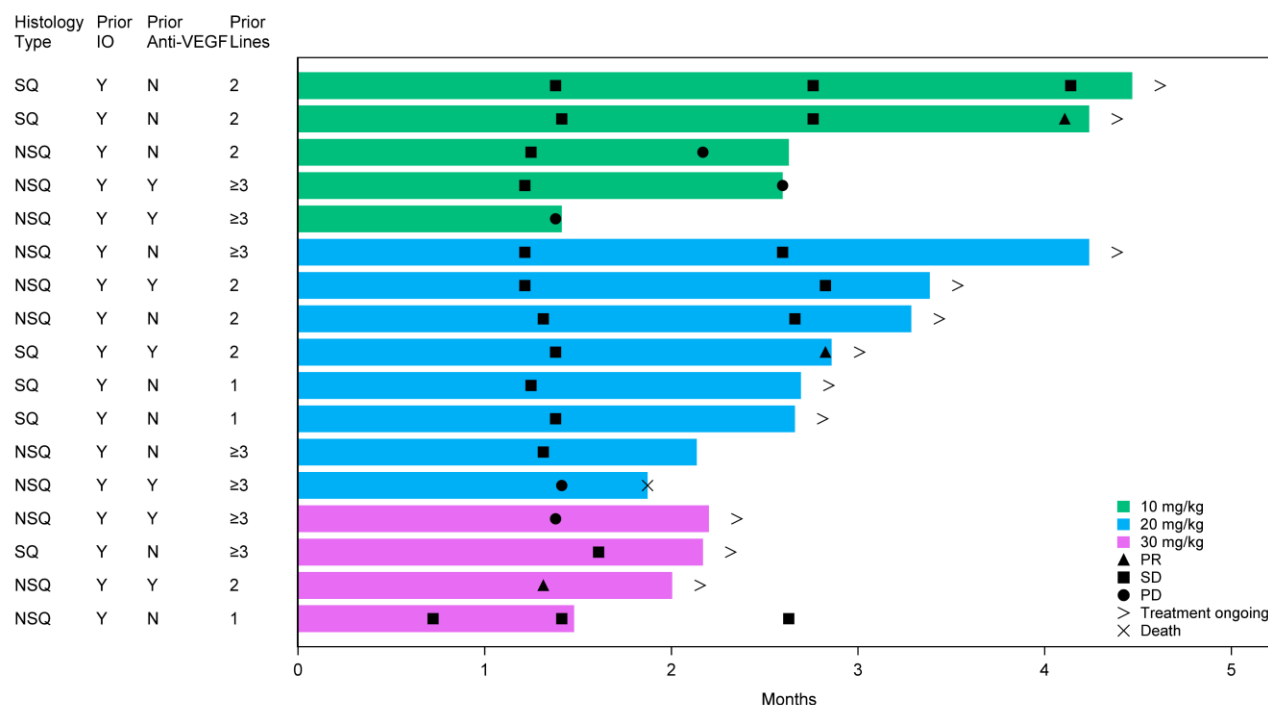
\* In AGA-negative post-IO NSCLC subgroup , ORR reached **25%** (3/12), DCR reached **83.3%** (10/12)

Median follow-up: ~ 2 months

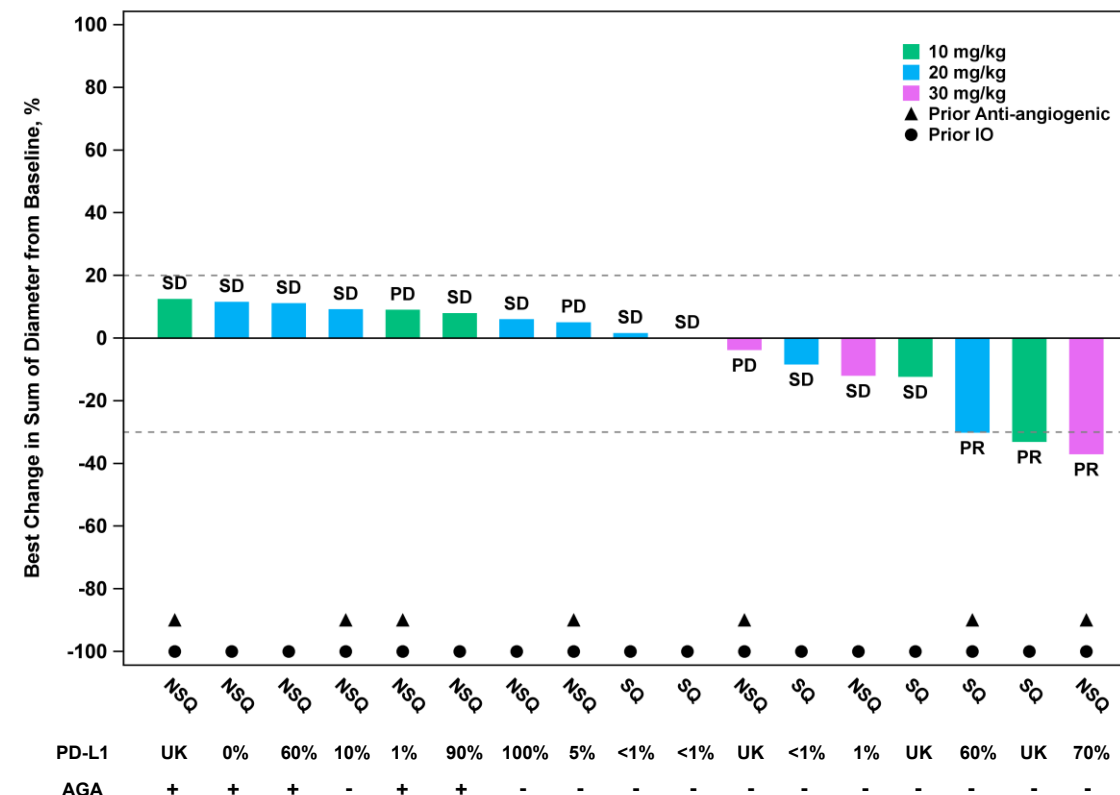


# CS2009 demonstrated promising ORR and impressive DCR in post-IO NSCLC

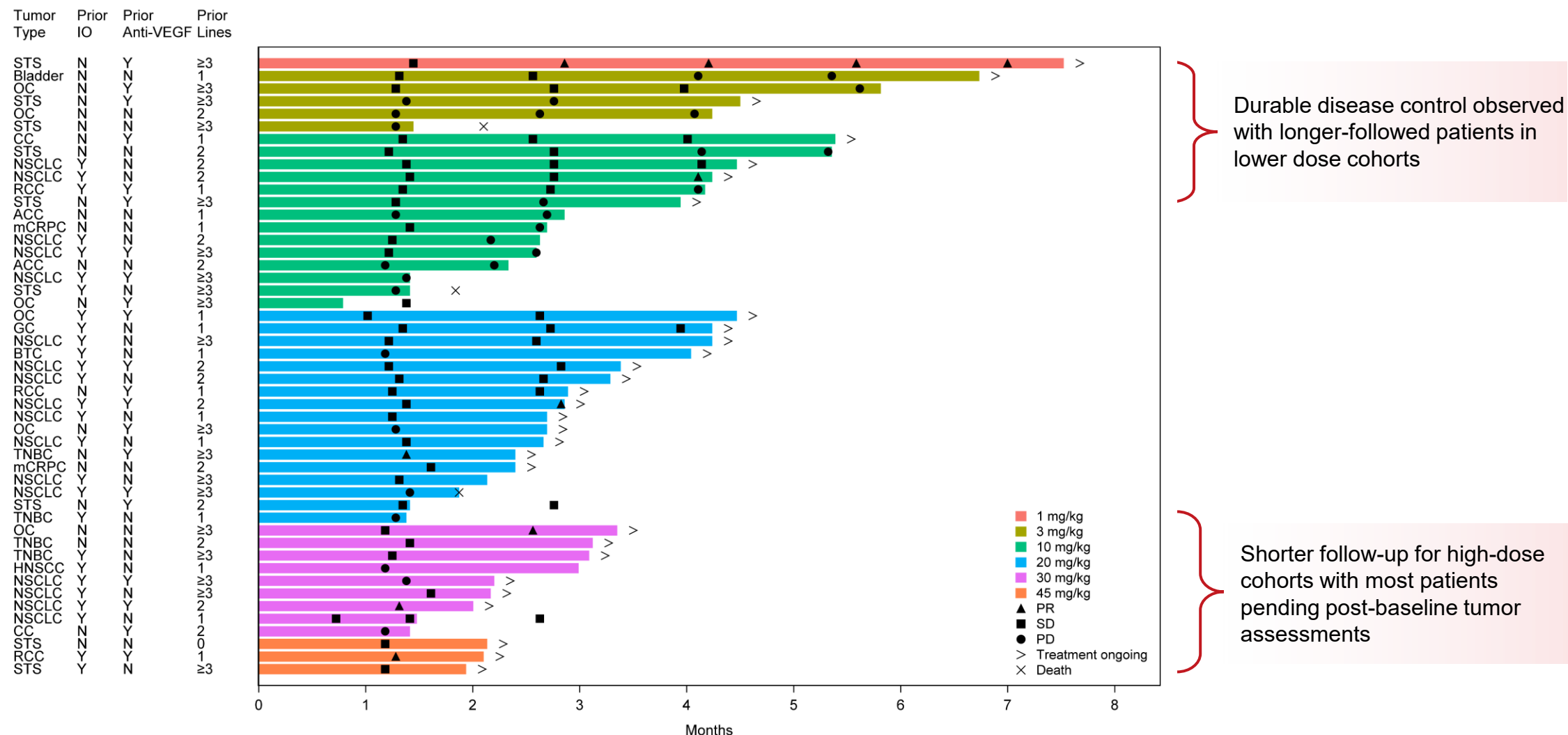
Given short follow-up, only **17 of 33** enrolled NSCLC patients underwent at least one post-baseline tumor assessment



In AGA-negative, post-IO NSCLC subgroup, ORR reached **25%** (3/12)  
DCR reached **83.3%** (10/12)



# Persistent disease control with majority of patients remaining on treatment despite limited follow-up (especially high-dose cohorts)



**Antitumor Activity in Phase I Trials:** CS2009 demonstrated promising ORR and strong DCR (71%) vs. bispecific antibodies, even with much shorter follow-up (median ~2 months) and higher prior-IO exposure (>50%)

Comparative Analysis: CS2009 vs. Lead Bispecific Antibodies in Phase I Trials of Advanced Solid Tumor

|                                   | CS2009 <sup>1</sup><br>PD-1/VEGF/CTLA-4 | AK112 <sup>2</sup><br>PD-1/VEGF | AK104 <sup>3</sup><br>PD-1/CTLA-4 | SSGJ-707 <sup>4</sup><br>PD-1/VEGF | KN046 <sup>5</sup><br>PD-L1/CTLA-4 | IMM2510 <sup>6</sup><br>PD-L1/VEGF | SI-B003 <sup>7</sup><br>PD-1/CTLA-4 |
|-----------------------------------|-----------------------------------------|---------------------------------|-----------------------------------|------------------------------------|------------------------------------|------------------------------------|-------------------------------------|
| Evaluable patients, n             | 49                                      | 47                              | 119                               | 85                                 | 88                                 | 19                                 | 56                                  |
| Age<br>Median (range)             | 60.5 (19-80)                            | 63 (30, 76)                     | 61 (20, 85)                       | NA                                 | 51.5 (21, 73)                      | 55.5 (36, 68)                      | 55.5                                |
| Prior IO therapy                  | 51.4%                                   | 29.4%                           | 16.8%                             | NA                                 | 35.0%                              | NA                                 | NA                                  |
| Follow-up Duration,<br>median, mo | ~ 2.0                                   | 12.8                            | NA                                | NA                                 | 23.2                               | NA                                 | NA                                  |
| ORR                               | 14.3%                                   | 25.5%                           | 13.4%                             | 14.0%                              | 12.5%                              | 12.0%                              | 16.1%                               |
| DCR                               | 71.4%                                   | 63.8%                           | NA                                | 59.6%                              | 35.2%                              | 40.0%                              | 50.0%                               |

Note: PM8002 (PD-L1/VEGF, BioNTech), MEDI5752 (PD-1/CTLA-4, AstraZeneca), and HB0025 (PD-L1/VEGF, Huabo Biopharma) excluded from comparative analysis - Phase Ia multi-tumor efficacy data either unpublished or limited to single tumor types per public disclosures

Source: 1. ESMO 2025+post-ESMO analysis; 2. JTC 2024; 3. Cell Reports Medicine 2023; 4. JPM 2025; 5. JTC 2023; 6. ASCO 2024; 7. ASCO 2023

## Antitumor Activity in NSCLC in Early-phase Trials: Promising ORR and DCR observed for CS2009 in comparison with lead bispecific antibodies in post-IO NSCLC

|                                | CS2009 <sup>1</sup><br>(PD-1/VEGF/CTLA-4) | AK104+AK109 <sup>2</sup><br>(PD-1/CTLA-4+VEGF) | AK104+anlotinib <sup>3</sup><br>(PD-1/CTLA-4+TKI) | AK104 <sup>4</sup><br>(PD-1/CTLA-4) | AK104 <sup>5</sup><br>(PD-1/CTLA-4) | AK112 <sup>6</sup><br>(PD-1/VEGF) | PM8002 <sup>7</sup><br>(PD-L1/VEGF) |
|--------------------------------|-------------------------------------------|------------------------------------------------|---------------------------------------------------|-------------------------------------|-------------------------------------|-----------------------------------|-------------------------------------|
| Stage of data cited            | Phase 1 dose escalation                   | Phase 1b/2                                     | Phase 1b/2                                        | Phase 1 dose escalation             | Phase 1b/2                          | Phase 1 dose escalation           | Phase 1b/2a                         |
| Evaluable patients, n          | 17 <sup>*</sup>                           | 47 <sup>^</sup>                                | 6                                                 | 6                                   | 23 <sup>†</sup>                     | 2                                 | 8 <sup>^</sup>                      |
| Follow-up Duration, median, mo | ~ 2.0                                     | 16.7                                           | NA                                                | 25                                  | NA                                  | 12.8                              | 5.8                                 |
| ORR                            | 3/17 (17.6%)                              | 6/47 (12.8%)                                   | 1/6 (16.7%)                                       | 0/6 (0%)                            | 0/23 (0%)                           | 0/2 (0%)                          | 1/8 (12.5%)                         |
| DCR                            | 14/17 (82.4%)                             | 45/47 (95.7%)                                  | 6/6 (100%)                                        | 2/6 (33.3%)                         | 7/23 (30.4%)                        | 1/2 (50%)                         | 5/8 (62.5%)                         |

\* In AGA-negative, ≥2L post-IO NSCLC subgroup, ORR reached 25% (3/12) and DCR reached 83.3% (10/12)

<sup>^</sup> All patients are AGA-negative and 2L post-IO NSCLC

<sup>†</sup> All patients are AGA-negative/unknown and ≥2L post-IO NSCLC

# Lead bispecific antibodies generated impressive efficacy in 1L NSCLC despite low ORR observed in post-IO NSCLC in early-phase trials

—CS2009 phase II trial in 1L NSCLC started, with global pivotal trials in preparation

| Monotherapy                     | AK112 <sup>1</sup><br>(PD-1/VEGF)          |                                        | SSGJ-707 <sup>2</sup><br>(PD-1/VEGF)              |                                    |                                     |
|---------------------------------|--------------------------------------------|----------------------------------------|---------------------------------------------------|------------------------------------|-------------------------------------|
| Stage of data cited             | Phase 3<br>(vs. pembrolizumab monotherapy) |                                        | Phase 2                                           |                                    |                                     |
| ORR                             | ITT: 50.0% vs 38.5%                        |                                        | ITT: 67.6%<br>PD-L1 ≥50%: 77%<br>PD-L1 1-49%: 62% |                                    |                                     |
| DCR                             | ITT: 89.9% vs 70.5%                        |                                        | ITT: 97%<br>PD-L1 ≥50%: 100%<br>PD-L1 1-49%: 95%  |                                    |                                     |
| Combination therapy<br>(+PT-CT) | AK112 <sup>3</sup><br>(PD-1/VEGF)          | MEDI5752 <sup>4</sup><br>(PD-1/CTLA-4) | SSGJ-707 <sup>5</sup><br>(PD-1/VEGF)              | HB0025 <sup>6</sup><br>(PD-1/VEGF) | IMM2510 <sup>7</sup><br>(PD-1/VEGF) |
| Stage of data cited             | Phase 2                                    | Phase 1b                               | Phase 2                                           | Phase 2                            | Phase 2                             |
| ORR                             | Nsq 52.0%<br>Sq 77.8%                      | Nsq 43.7%<br>Sq 65.0%                  | Nsq 58.3%<br>Sq 81.3%                             | Nsq 62.3%<br>Sq 82.8%              | Nsq 46%<br>Sq 80%                   |

# Key Takeaways

## 1 Safety & Tolerability

- **CS2009 is well tolerated** in heavily pretreated patients with advanced solid tumor across dose levels of 1 to 45mg/kg, Q3W
- **No Grade 4 or 5 TRAE** observed
- **No DLTs** observed, **MTD not reached**
- Low incidence of infusion-related reactions

## 3 Anti-tumor Activity

- CS2009 demonstrates **promising anti-tumor activities** across tumor types; data remains immature due to **limited follow-up time** as of the cutoff date
- **Promising phase I ORR: 14.3%** (7/49); strong **DCR: 71.4%** (35/49); **higher ORR** at tentative RP2D (30 mg/kg) and above: **25.0%** (3/12)
- **Post-IO NSCLC**: Promising **ORR** of **17.6%** (3/17) and strong **DCR** of **82.4%** (14/17); **higher ORR** of **25%** (3/12) and **DCR** of **83.3%** (10/12) in AGA-negative subgroup

## 2 Pharmacokinetics (PK)/Pharmacodynamics Profile

- Linear PK with **half life of 6-8 days**, low incidence of ADA positivity
- **Sustained PD-1/CTLA-4 receptor occupancy** at doses  $\geq 20$  mg/kg
- Robust, dose-dependent increase of pharmacodynamic biomarkers (Ki67 and ICOS) confirming **effective PD-1 and CTLA4 blockade**
- **Serum-free VEGFA reduced deeply and rapidly** across all doses, and the effect **sustained** throughout dose intervals

## 4 Future Development Plan

- Phase 2 dose expansion in **1L patients** started in selected tumor types for dose optimization and to generate data supporting **registration trials in 1L NSCLC and other tumors** as monotherapy or in combinations



**Thanks for Listening!**