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CStone Pharmaceuticals

基石藥業

(Incorporated in the Cayman Islands with limited liability)

(Stock Code: 2616)

INSIDE INFORMATION ANNOUNCEMENT LATEST BUSINESS UPDATE

This announcement is made by CStone Pharmaceuticals (the “**Company**” or “**CStone**”) pursuant to Rule 13.09 of the Rules Governing the Listing of Securities on The Stock Exchange of Hong Kong Limited (the “**Listing Rules**”) and the Inside Information Provisions (as defined in the Listing Rules) under Part XIVA of the Securities and Futures Ordinance (Chapter 571 of the Laws of Hong Kong).

The Company is pleased to announce that it will hold a conference on latest business update today. To ensure that all shareholders and potential investors of the Company have equal and timely access to material information pertaining to the Company and its operations, the Company has attached to this announcement selected pages from the presentation to be made at the conference that may contain material inside information of the Company. The presentation will also be available on the Company’s website (www.cstonepharma.com) under the section headed “Investor Relations”.

Key Highlights

- Preliminary results from the first-in-human (FIH) global multicenter study of CS5001 have been disclosed for the first time. As one of the two most advanced ROR1 ADCs in clinical stage globally, CS5001 has been evaluated at seven dose levels in its phase I clinical study, in which promising safety, stability and anti-tumor activity were observed in various hematological and solid malignancies. The evaluation at higher dose levels and longer follow-up is ongoing.
- The regulatory review on sugemalimab in major overseas markets such as the European Union (EU) and the United States (U.S.) is proceeding smoothly. The marketing authorization application (MAA) of sugemalimab as first-line treatment for metastatic non-small cell lung cancer (NSCLC) is under review by the European Medicines Agency (EMA) and the Medicines & Healthcare Products Regulatory Agency (MHRA) of the United Kingdom (U.K.). The EMA has already completed the inspection of one clinical site, and the remaining Good Clinical Practice (GCP) inspection is to be completed by early February of 2024 as scheduled. In addition, CStone and the U.S. Food and Drug

Administration (FDA) have reached an agreement in a Type B consultation regarding the registration pathway for relapsed or refractory extranodal NK/T-cell lymphoma (R/R ENKTL) indication.

- In order to further improve the commercialization efficiency, CStone has recently established commercial collaborations with two companies to leverage their strengths while enabling CStone to strategically focus on research and development. In addition, the Company currently has multiple assets at/near IND stage and intends to advance more innovative drugs into clinical development in the near future.
- Other businesses have also been progressing recently, anticipating multiple upcoming milestones.

Data Update on Safety and Effectiveness of ROR1 ADC

Preliminary results from the ongoing FIH global multicenter study of CS5001 have been disclosed for the first time. As one of the two most advanced ROR1 ADCs clinical stage globally, CS5001 has been evaluated at seven dose levels in its phase I clinical study, in which promising safety, stability and anti-tumor activity were observed in various hematological and solid malignancies.

- In this clinical study, dose level eight is currently being evaluated. The data from prior seven dose levels suggests that the drug is safe and well-tolerated; the majority of the adverse events observed were Grade 1 or 2; no dose limiting toxicity (DLT) was observed.
- CS5001 has exhibited anti-tumor activity in heavily pre-treated patients, with partial responses (PRs) observed in cancer types including advanced Hodgkin's lymphoma and pancreatic cancer. The evaluation at higher dose levels and continued follow-up is ongoing.
- CS5001 has demonstrated excellent human pharmacokinetics (PK) characteristics and linker stability as demonstrated by similar exposure level of ADC and total antibody in the blood.
- Updated phase I clinical data is expected to be presented at an international academic conference in the first half of next year.

Update on PD-L1 Overseas Progress

The Company is accelerating the regulatory review on sugemalimab in major global markets to further realize its asset value and is also actively engaging with potential partners worldwide. Currently, the overseas activities of sugemalimab in major markets such as the EU and the U.S. are progressing smoothly.

- The MAA of sugemalimab as first-line treatment for metastatic NSCLC is under review by the EMA and the MHRA of the U.K..The EMA has completed the inspection of one clinical site, and the remaining inspection will be completed by early February of 2024. It is expected that the regulatory decision by EMA for this indication will be received in the first half of next year.
- CStone and the FDA have reached an agreement in a Type B consultation regarding the registration pathway for R/R ENKTL indication.
- The Company will also discuss with the U.S. FDA regarding registration pathways for gastric /gastroesophageal junction (G/GEJ) adenocarcinoma and esophageal squamous cell carcinoma (ESCC) indications in the future.

Update on Commercialization Strategy

In order to further improve the commercialization efficiency, CStone has recently established commercial collaborations with two companies to leverage their strengths while enabling CStone to strategically focus on research and development going forward. In addition, the Company currently has multiple assets at/near IND stage and intends to advance more innovative drugs into clinical development in the near future.

- CStone has entered into a strategic collaboration for nofazinlimab (anti-PD-1 antibody) in Mainland China with 3SBio Inc. (“3SBio”) and granted 3SBio exclusive rights for the development, registration, manufacturing, and commercialization of nofazinlimab (anti-PD-1 antibody) in Mainland China. CStone will retain the rights to nofazinlimab outside of Mainland China. This partnership will combine the strengths of CStone and 3SBio in research and development, manufacturing, and commercialization, thus accelerating the clinical development and commercialization of nofazinlimab and benefitting more patients in mainland China.
- CStone has granted the exclusive commercial rights for GAVRETO[®] (pralsetinib), a selective rearranged during transfection (RET) inhibitor, to Allist Pharmaceuticals (“Allist”) in Mainland China.

About Other Recent Business Updates

CStone has made other business progresses recently and is expected to achieve multiple milestones in the near future:

- The supplemental biologics license application (sBLA) for sugemalimab in combination with fluorouracil and platinum-based chemotherapy as the first-line treatment for unresectable locally advanced, recurrent, or metastatic ESCC has been approved by the NMPA, making it the world’s first approved anti-PD-L1 monoclonal antibody for the first-line ESCC indication. As a result of the approval, the Company will receive a milestone payment from Pfizer for this indication. It is the fourth approved indication for sugemalimab in China following stage III and IV NSCLC and R/R ENKTL, and is also the thirteenth NDA approval received since the establishment of CStone.
- The sBLA for sugemalimab in combination with chemotherapy for the first-line treatment of locally unresectable advanced or metastatic G/GEJ adenocarcinoma has been accepted by the NMPA in China and is currently under review. It is expected to be approved in the first quarter of the next year, and upon achievement of this milestone, a regulatory milestone payment from the partner is expected.
- The global multi-regional phase III study of CS1003-305 of nofazinlimab in combination with lenvatinib versus placebo in combination with lenvatinib as the first-line treatment for patients with advanced hepatocellular carcinoma (HCC) has completed its prespecified patient enrollment and a topline readout is expected in the first quarter of 2024.

About CStone

CStone (HKEX: 2616) is a biopharmaceutical company focused on research, development, and commercialization of innovative immuno-oncology and precision medicines to address the unmet medical needs of cancer patients in China and worldwide. Established in 2015, CStone has assembled a management team with extensive experience in innovative drug development, clinical research, and commercialization. The company has built an oncology-focused pipeline of 14 drug candidates with a strategic emphasis on immuno-oncology combination therapies. Currently, CStone has received 13 NDA approvals for its four drugs. Multiple late-stage drug candidates are now under pivotal clinical trials or registration. CStone’s vision is to bring innovative oncology therapies to cancer patients worldwide.

For more information about CStone, please visit www.cstonepharma.com.

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Forward Looking Statements

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By Order of the Board
CStone Pharmaceuticals
Dr. Wei Li
Chairman

Suzhou, the People's Republic of China, December 20, 2023

As at the date of this announcement, the board of directors of the Company comprises Dr. Wei Li as Chairman and non-executive director, Dr. Jianxin Yang as executive director, Mr. Kenneth Walton Hitchner III, Mr. Xianghong Lin and Mr. Edward Hu as non-executive directors, and Dr. Paul Herbert Chew, Mr. Ting Yuk Anthony Wu and Mr. Hongbin Sun as independent non-executive directors.



基石药业

CSTONE
PHARMACEUTICALS

CStone Business Update

December 20th, 2023

Stock Code: 2616. HK

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- 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.

Agenda

- 1. ROR1 ADC Updates***
- 2. PD-L1 ex-China Progress***
- 3. Commercialization Strategy***
- 4. Expected Catalysts***

Agenda

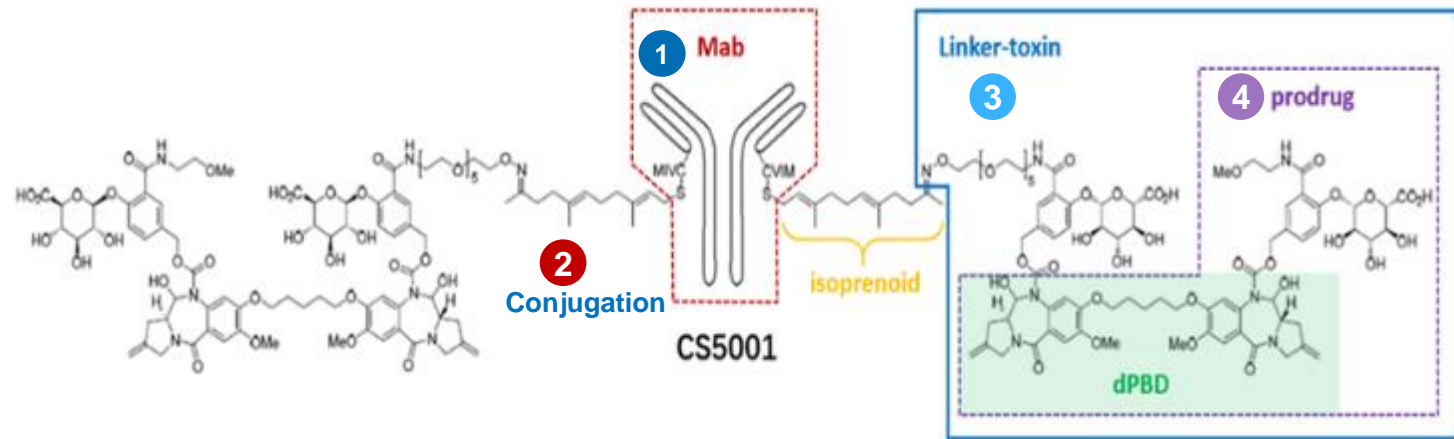
- 1. *ROR1 ADC Updates***
- 2. *PD-L1 ex-China Progress***
- 3. *Commercialization Strategy***
- 4. *Expected Catalysts***

CS5001 (ROR1 ADC) is a potential FIC/BIC ROR1 ADC globally with Ph1 study ongoing in US, Australia and China

An ADC target for both hematological malignancies and solid tumors

- Largely absent in normal blood lymphocytes and adult tissues ¹⁻³
- Embryonic protein over-expressed by various hematological malignancies, particularly B-cell lymphomas ^{4, 5}
- Widely expressed in solid tumors such as TNBC, ovarian cancer, and adenocarcinoma (NSCLC) ^{2,6-13}
- First-in-class molecule acquired by Merck for US\$2.75Bn in Nov 2020 at Ph1

4 key differentiators support best-in-class potential:



Potentially less immunogenicity

- 1** Fully human IgG1 mAb v.s. humanized mAb of other ROR1-ADCs

Controlled quality and production

- 2** Site-specific conjugation technology, ConjuAll, enables a **homogenous** drug to **antibody ratio of 2**

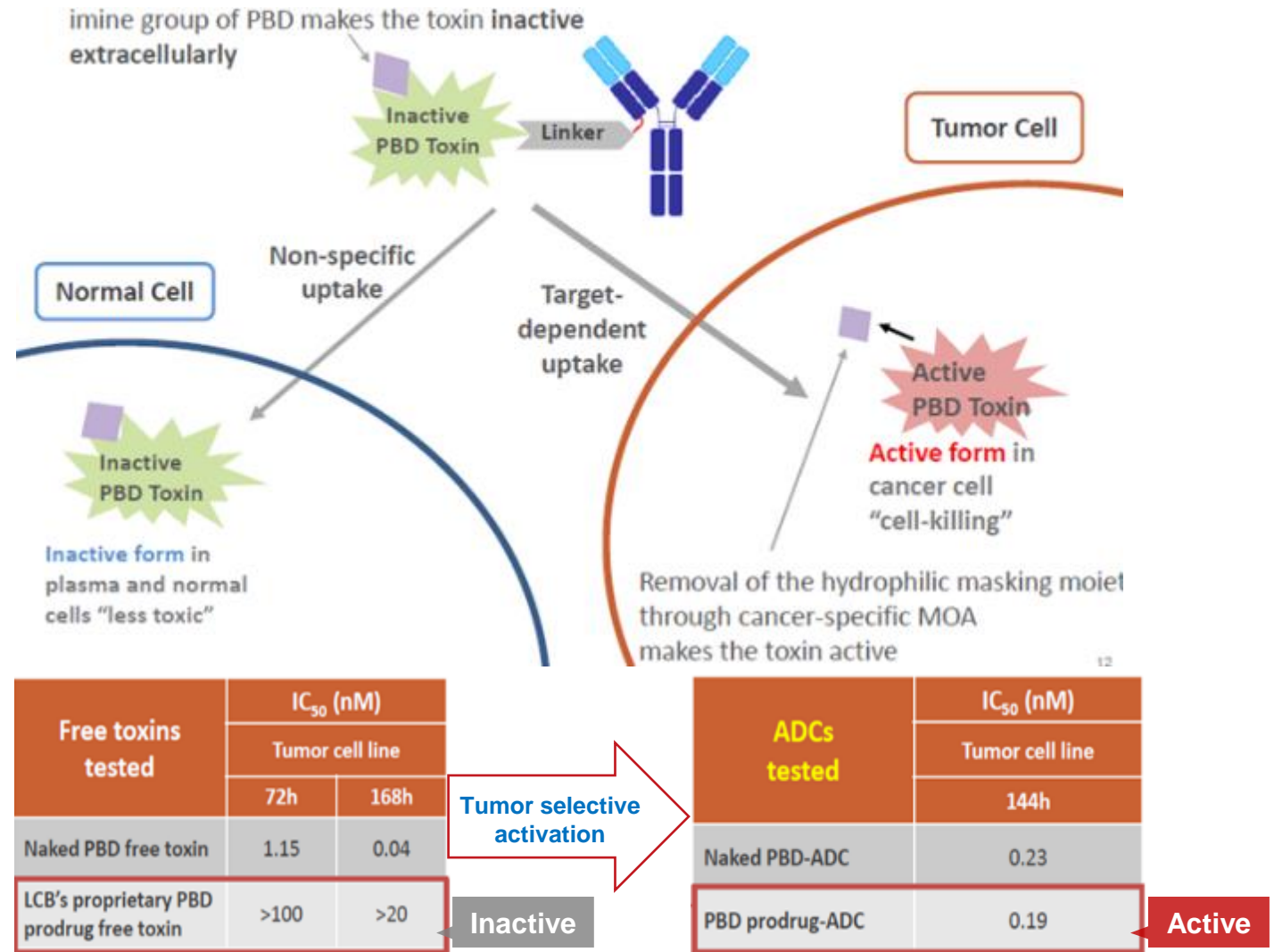
Potentially wider therapeutic window

- 3** Proprietary **tumor-selective cleavable linker** (cleaved by β -glucuronidase), shows exceptional stability in serum
- 4** Proprietary **tumor-activated PBD dimer toxin prodrug** (released by β -glucuronidase)

1. Baskar et al, *Clin Cancer Res* 2008, 14(2); 2. Balakrishnan et al, *Clin Cancer Res* 2017 23(12); 3. Uhrmacher et al, *Leukemia Research* 35 (2011) 1360; 4. Borchering et al, *Protein Cell* 2014, 5(7):496–502; 5. Daneshmanesh et al, *Leukemia & Lymphoma* 2013,54(4): 843–850; 6. Zhang et al, *PLoS ONE* 2012 7(3): e31127; 7. Chien et al, *Virchows Arch* 2016, 468(5):589-95; 8. Henry et al, *Transl Oncol.* 2017, 10(3):346-356; 9. Zhang et al, *Sci Rep.* 2014, 24(4):5811; 10. Zheng et al, *Sci Rep.* 2016, 10(6):36447; 11. Liu et al, *PLoS One.* 2015,10(5):e0127092; 12. Henry et al, *Gynecol Oncol.* 2018, 148(3):576-584; 13. Zhou et al, *Oncotarget* 2017, 8(20):32864-32872

Novel prodrug technology minimize systematic toxicity of conventional PBD

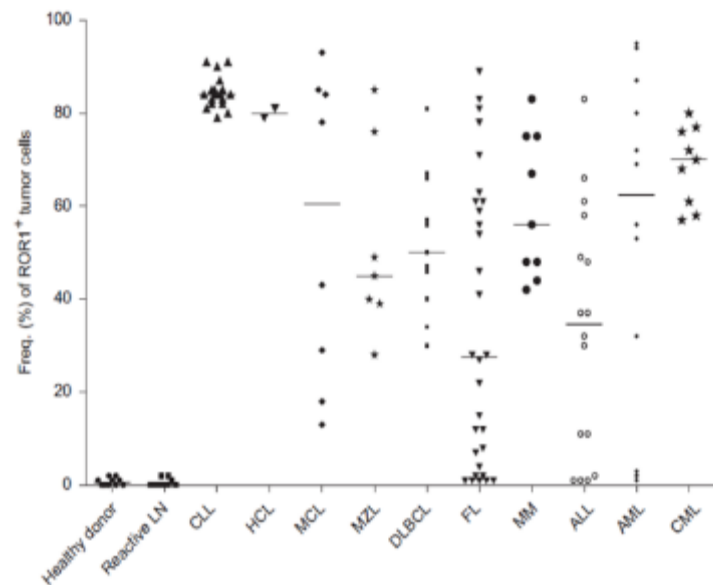
- PBD prodrug is inactive compared to naked PBD
- Prodrug, being in a highly polar form, cannot penetrate and kill normal cells
- Prodrug mitigates toxicity risk associated with systemic exposure of conventional PBD payloads
- Similar IC50 of naked PBD-bearing ADC and PBD prodrug-bearing ADC indicates no loss in payload activity and high efficiency of activating PBD prodrug in cancer cells



ROR1 is a promising target for the treatment of multiple tumor types

- Receptor tyrosine kinase-like orphan receptor 1 (ROR1) is a member of the receptor tyrosine kinase family
- Broad expression of ROR1 in both solid tumor and hematological malignancies (e.g., TNBC, lung cancer, ovarian cancer, pancreatic cancer, CLL, MCL, etc.)
- Predominantly absent from normal blood lymphocytes and adult tissues, indicating minimal off-target activity

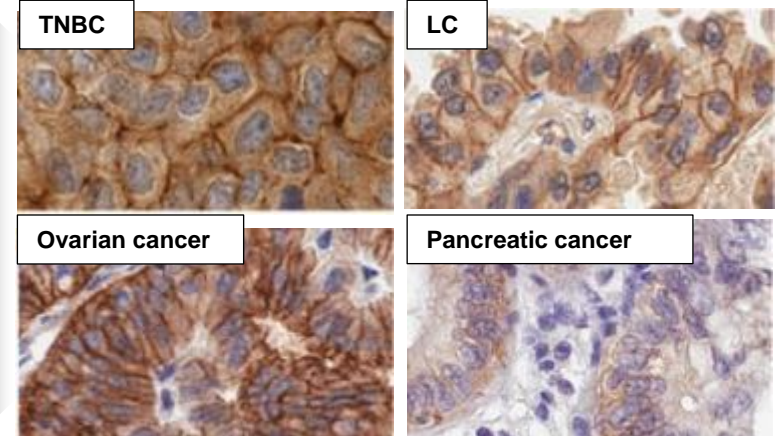
ROR1 expression in different hematological malignancies



Leuk Lymphoma. 2013 Apr;54(4):843-50

ROR1 expression in different solid tumor types

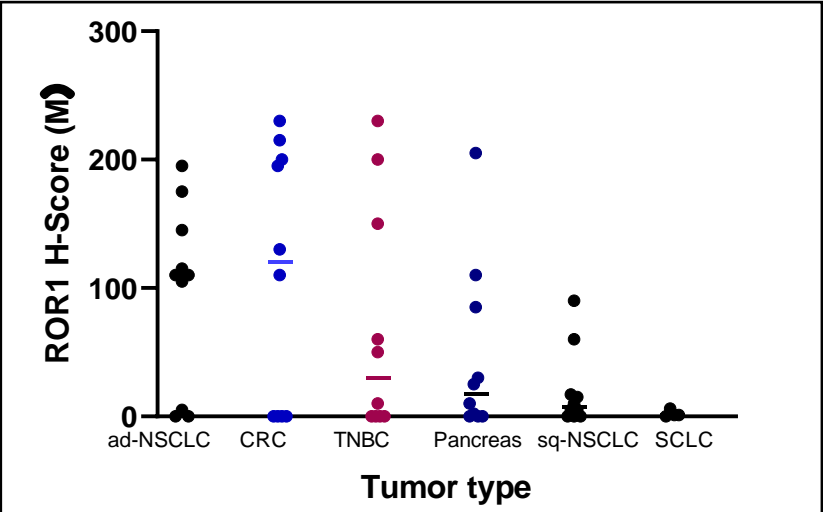
Tumor type	Positive rate
TNBC	56% (n=56)
Lung cancer	42% (n=137)
Ovarian cancer	50% (n=159)
Pancreatic cancer	15% (n=38)



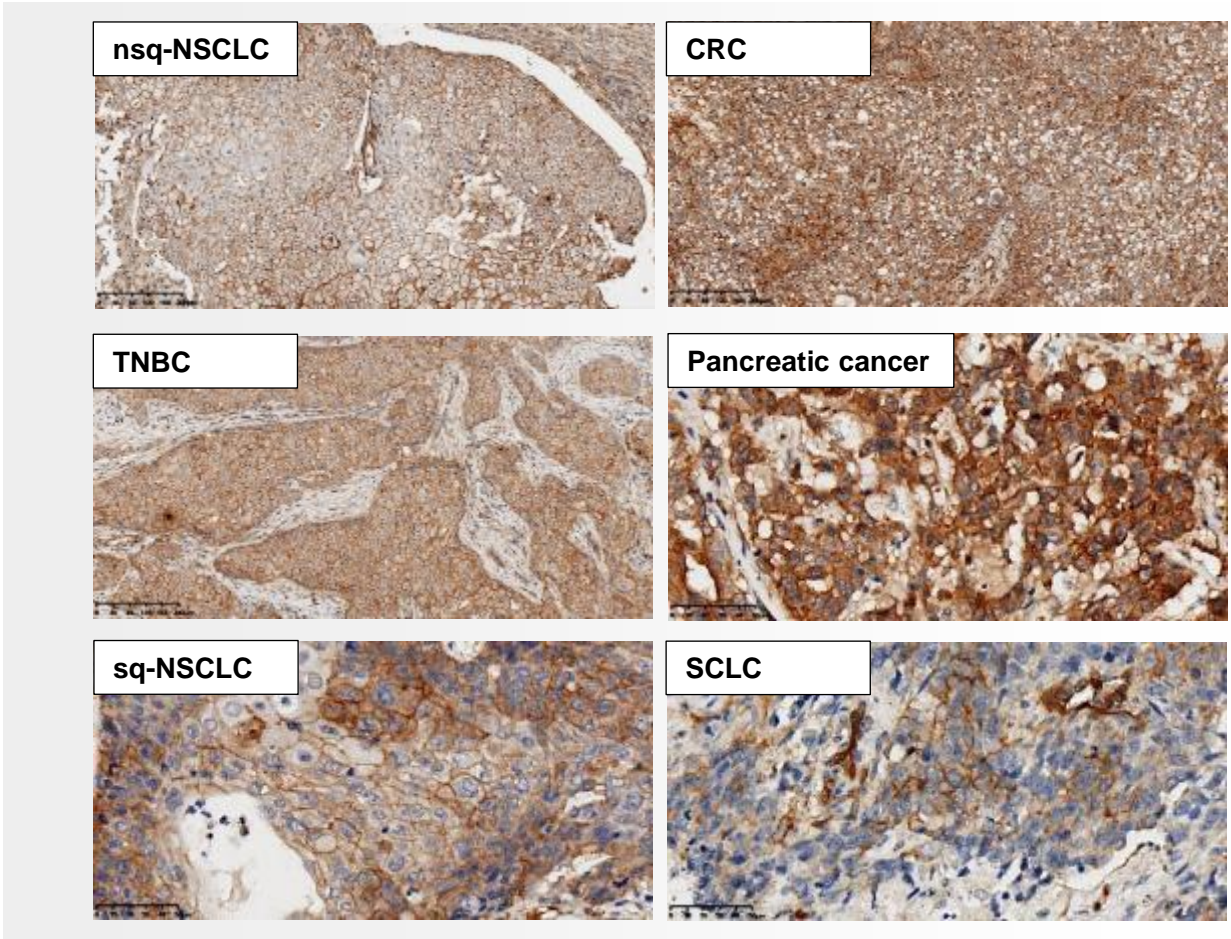
ROR1 expression is homogeneous, defined as definite membranous staining of over 50% of tumor cells

Clin Cancer Res. 2017 Jun 15;23(12):3061-3071

ROR1 expression in solid tumor has been validated by CStone proprietary mAb



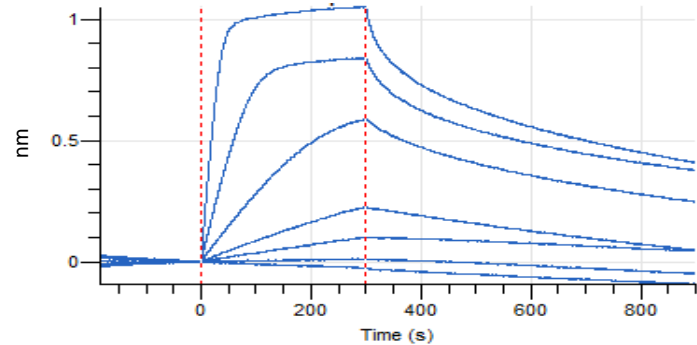
Tumor type	H-Score≥50
Nsq-NSCLC	70%
CRC	60%
TNBC	50%
Pancreatic cancer	30%
Sq-NSCLC	20%
SCLC	0



ROR1 expression in tumor membrane: $H\text{-Score (M)} = 1 \times (\% \text{ of } 1+ \text{ cells}) + 2 \times (\% \text{ of } 2+ \text{ cells}) + 3 \times (\% \text{ of } 3+ \text{ cells})$.

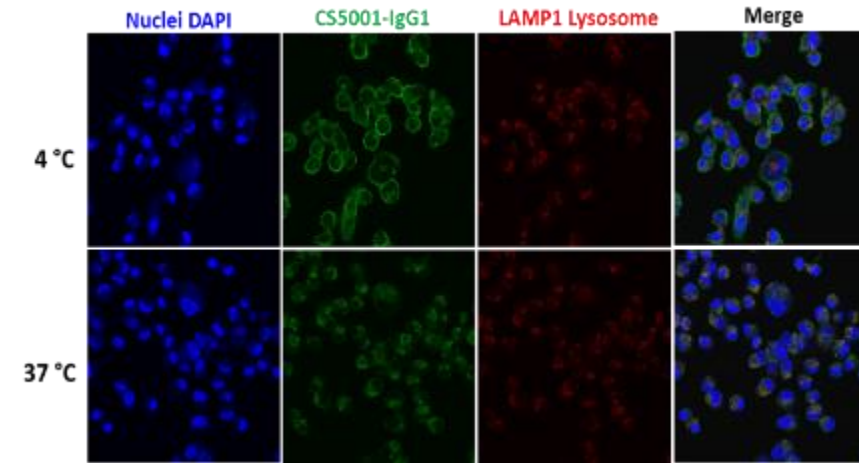
CS5001 selectively bound to human ROR1 with high affinity and triggered rapid and high internalization

CS5001 showed high affinity to human ROR1

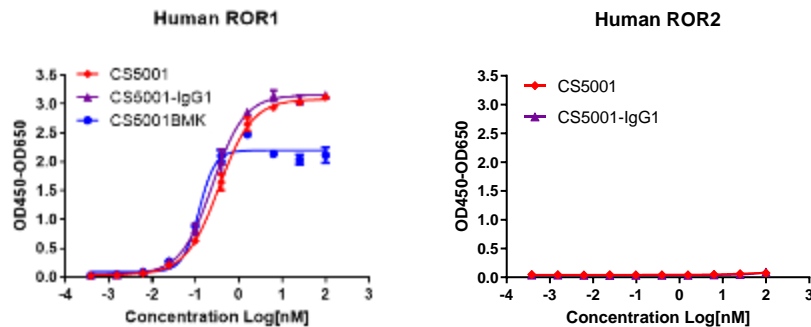


Sample	ka (1/Ms)	kd (1/s)	KD (M)
CS5001	1.59E+06	2.19E-03	1.38E-09

Internalization and intracellular trafficking of CS5001-IgG1

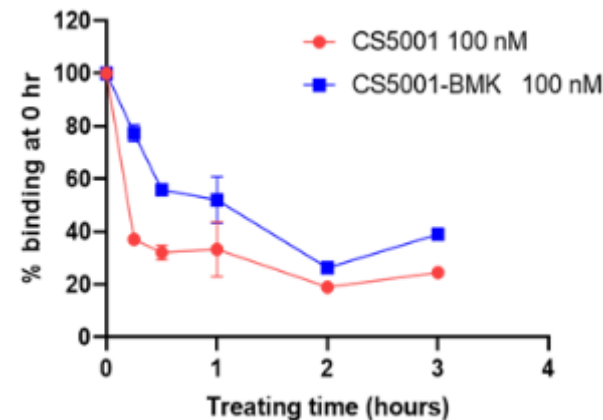


CS5001 was highly selectively binding to human ROR1



	Human ROR1	Human ROR2
CS5001 (EC ₅₀ , nM)	0.347	No binding
CS5001-IgG1 (EC ₅₀ , nM)	0.245	No binding
CS5001BMK (EC ₅₀ , nM)	0.119	-

Rapid internalization of CS5001(37° C)



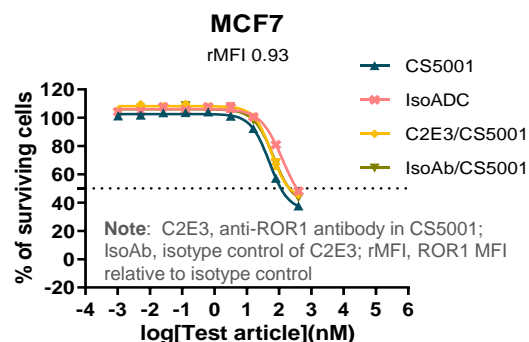
MDA-MB-231 cells were treated with ROR1 mAb or ADC at 4° C or 37° C and were examined using confocal microscope or flowcytometry

Note: CS5001-IgG1: mAb of CS5001. CS5001BMK: benchmark, an MMAE-based ROR1 ADC (same sequence, linker & toxin as VLS-101)

CS5001 demonstrated highly potent ROR1-dependent cytotoxicity in solid tumor and hematological malignancy cell lines

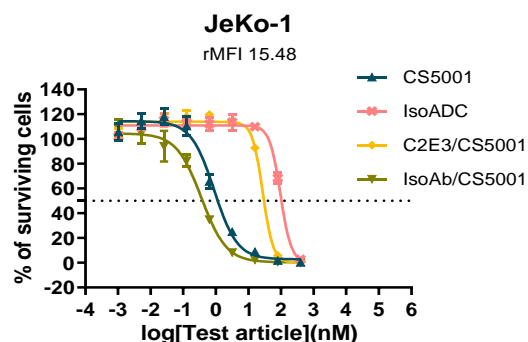
CS5001 killed tumor cells with potency and ROR1- dependency

ROR1 negative

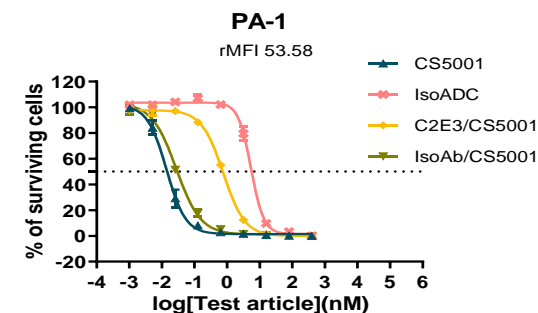


	CS5001	IsoADC	C2E3/CS5001	IsoAb/CS5001
IC ₅₀ (nM)	113.41	354.32	212.56	206.14
IC ₅₀ fold change	Ref.	3	1.9	1.8

ROR1 expressing



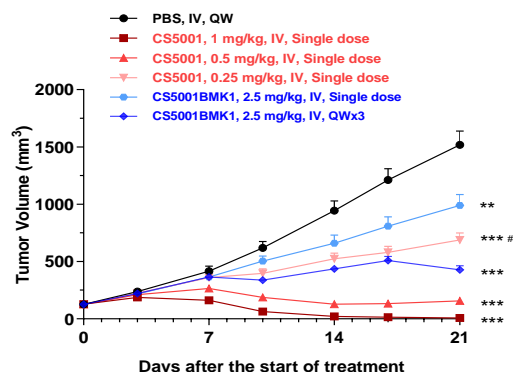
	CS5001	IsoADC	C2E3/CS5001	IsoAb/CS5001
IC ₅₀ (nM)	1.15	103.36	30.04	0.39
IC ₅₀ fold change	Ref.	90	26	0.4



	CS5001	IsoADC	C2E3/CS5001	IsoAb/CS5001
IC ₅₀ (nM)	0.02	5.68	0.74	0.03
IC ₅₀ fold change	Ref.	284	37	1.5

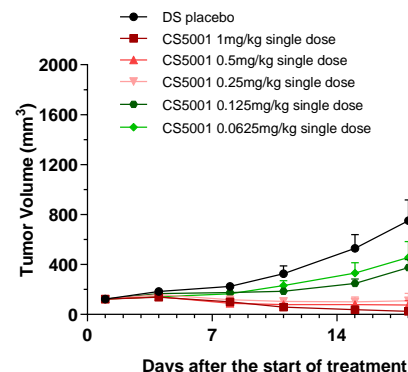
CS5001 remarkably killed tumor cells in CDX models

Jeko1 (Mantle cell lymphoma)



Treatment	TGI %	CR
CS5001, 1 mg/kg, Single dose	109	2/8
CS5001, 0.5 mg/kg, Single dose	98	0/8
CS5001, 0.25 mg/kg, Single dose	60	0/8
CS5001BMK1, 2.5 mg/kg, Single dose	38	0/8
CS5001BMK1, 2.5 mg/kg, QWx3	78	0/8

PA-1 (Ovarian cancer)

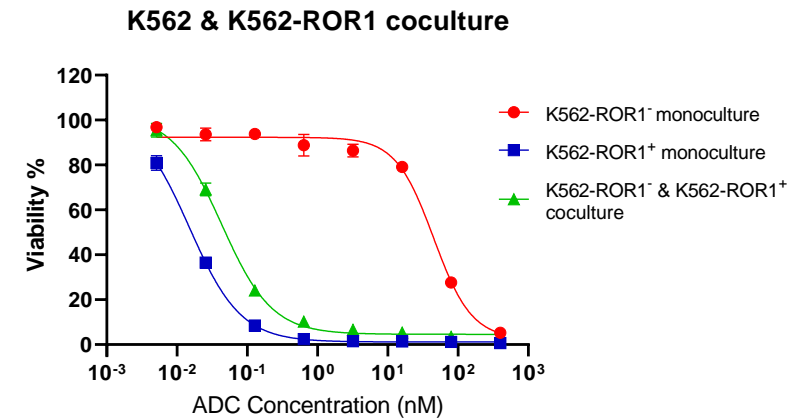
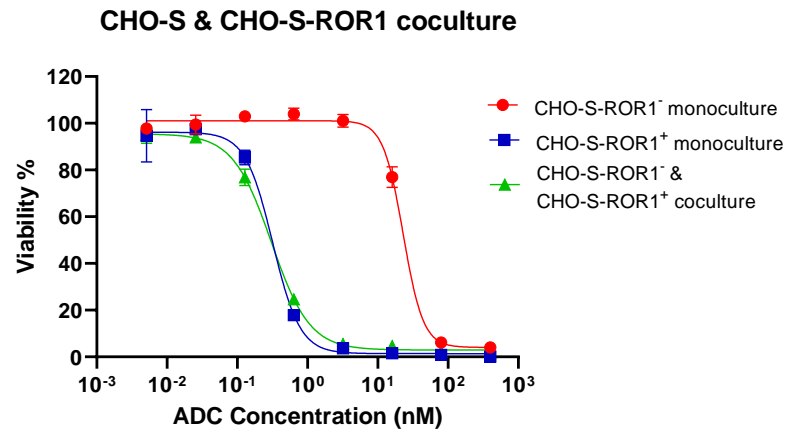


Treatment	TGI %	CR
CS5001, 1 mg/kg, Single dose	108	2/8
CS5001, 0.5 mg/kg, Single dose	98	1/8
CS5001, 0.25 mg/kg, Single dose	95	0/8
CS5001, 0.125 mg/kg, Single dose	57	0/8
CS5001, 0.0625 mg/kg, Single dose	53	0/8

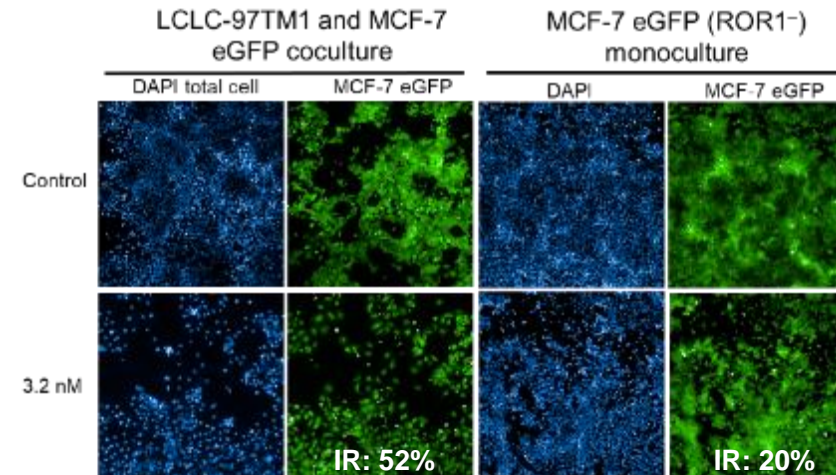
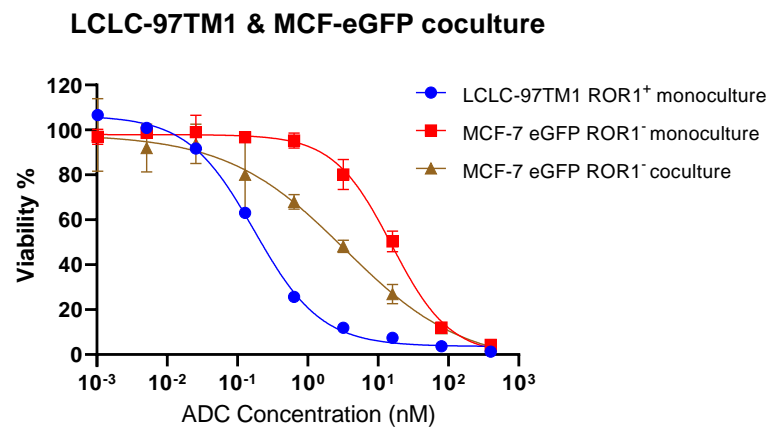
Note: $p < 0.01$, $***$, $p < 0.001$ vs PBS; #, $p < 0.05$, vs CS5001BMK1 single dose; TGI: tumor growth inhibition; CR: complete regression is defined as ≤ 13.5 mm³ for 3 consecutive measurements; CS5001BMK1: benchmark1, an MMAE-based ROR1 ADC (same sequence, linker & toxin as VLS-101)

CS5001 demonstrated robust bystander killing effect in co-culturing assays with ROR1+/- cells

ROR1- tumor cells co-cultured with the same cells but transfected with ROR1

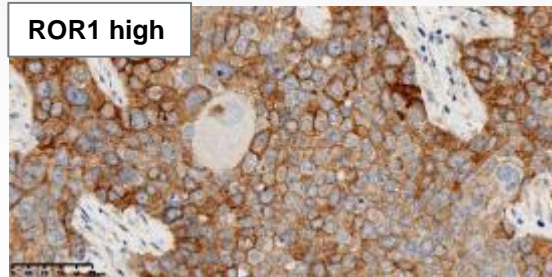
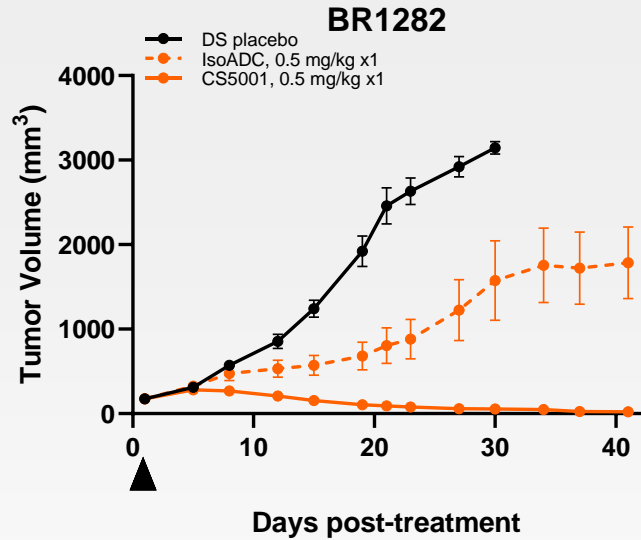


ROR1- tumor cells co-cultured with tumor cells endogenously expressing ROR1

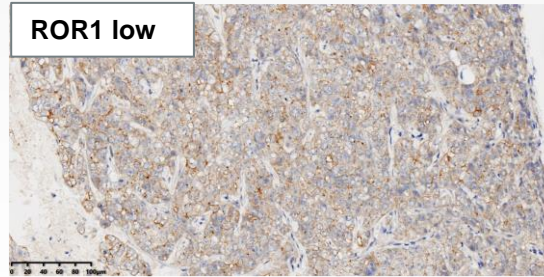
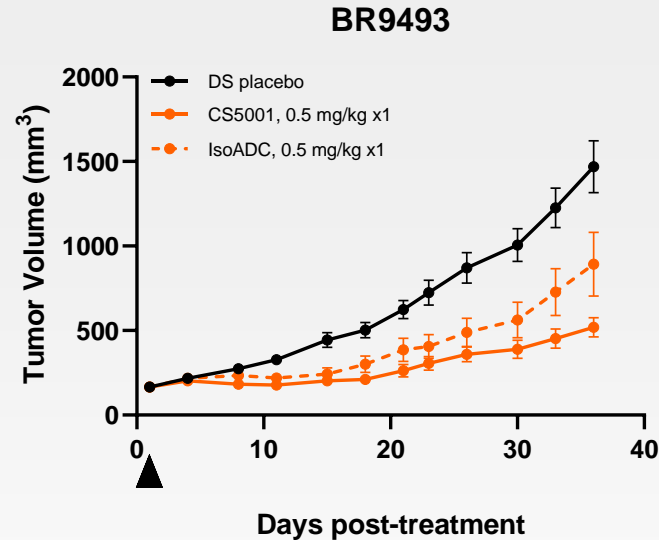


IR: inhibition rate

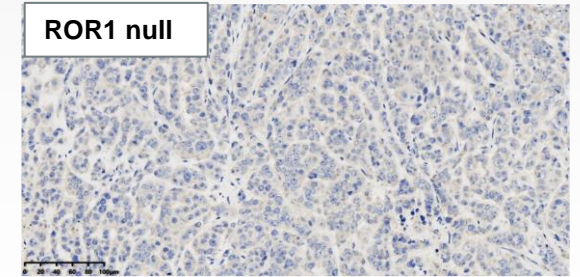
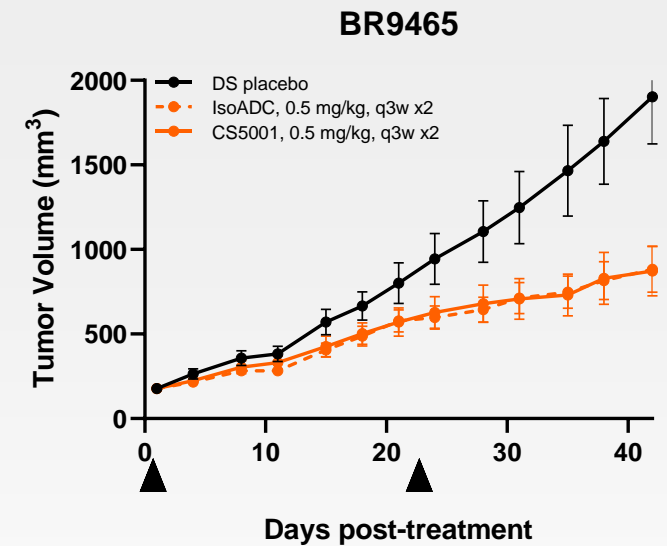
ROR1-dependent anti-tumor activity was demonstrated in solid tumor PDX models



Group	TGI(D30)
IsoADC	53%
CS5001	104%



Group	TGI(D30)
IsoADC	53%
CS5001	73%



Group	TGI(D30)
IsoADC	50%
CS5001	50%

Phase 1 Study Design: CS5001-101

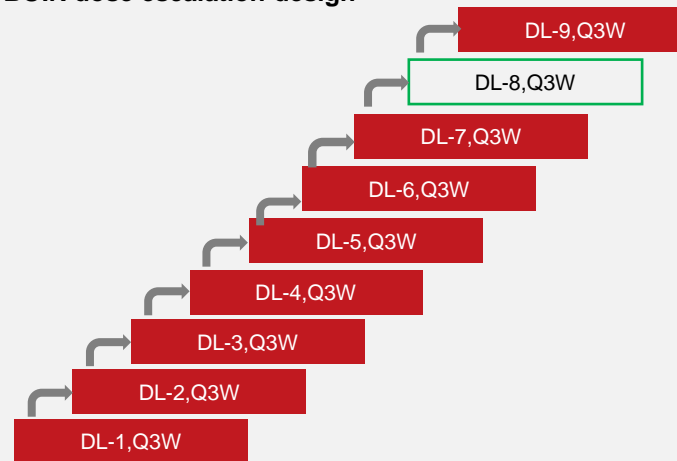
A Phase 1, Dose-Escalation and Dose-Expansion Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Antitumor Activities of CS5001, an Anti-ROR1 Antibody Drug Conjugate, in Patients with Advanced Solid Tumors and Lymphomas

Phase 1a Dose Escalation (BOIN Design) + Backfill

Key eligibility criteria

- Age 18 years or older
- Solid tumor: pathologically confirmed, unresectable advanced solid tumor ($\geq 2L$)
- Lymphoma: pathologically confirmed B-cell lymphoma ($\geq 3L$)
- r/r CHL must have received brentuximab vedotin and checkpoint inhibitor.
- r/r CLL/SLL must have received BTKi
- ≥ 1 evaluable lesion
- Adequate organ function
- Available tumor samples for biomarker analysis

MRCT phase 1 trial is ongoing in the USA, AUS and China BOIN dose escalation design



Phase 1b Dose Expansion/pivotal Extension

- A** B cell lymphoma 1 ($\geq 3L$); N = up to 80
- B** B cell lymphoma 2 ($\geq 3L$); N = up to 124
- C** Solid tumor 1 ($\geq 2L$); N = up to 82
- D** ROR1-positive solid tumors (including TNBC, endometrial cancer, ovarian cancer, NSCLC, gastric cancer and pancreatic cancer) ($\geq 3L$); N = up to 30

Tentative RP2D

Primary objective:

- Characterize CS5001 safety and tolerability, and determine MTD/tentative RP2D

Secondary objective:

- PK profile of CS5001 (ADC), total antibody, prodrug and the free cytotoxin SG2057
- Preliminary anti-tumor activity of CS5001

Exploratory objective:

- The predictive value of ROR1 expression on treatment response to CS5001

Primary objective:

- To evaluate the efficacy of CS5001 in patients with selected advanced malignancies

Secondary objective:

- To further evaluate the efficacy of CS5001 in patients with selected advanced malignancies
- To further assess the safety and tolerability of CS5001 in patients with selected advanced malignancies
- To further characterize the PK profile of CS5001 (ADC), total antibody, prodrug and the free cytotoxin SG2057

Exploratory objective:

- The predictive value of ROR1 expression on treatment response to CS5001

The enrollment of dose escalation portion of this MRCT phase 1 trial is ongoing in the USA, AUS and China

CS5001 is a well tolerated and stable ADC and has demonstrated preliminary anti-tumor activities

A Escalated to Dose Level 8 (DL8) with no DLT events

- DLT evaluation completed at prior 7 dose levels, DL8 currently under evaluation
- DLT not observed, suggesting the drug being safe and well-tolerated
- Adverse events observed to date mostly Grade 1 or 2

B Anti-tumor activity observed in both lymphoma and solid tumor

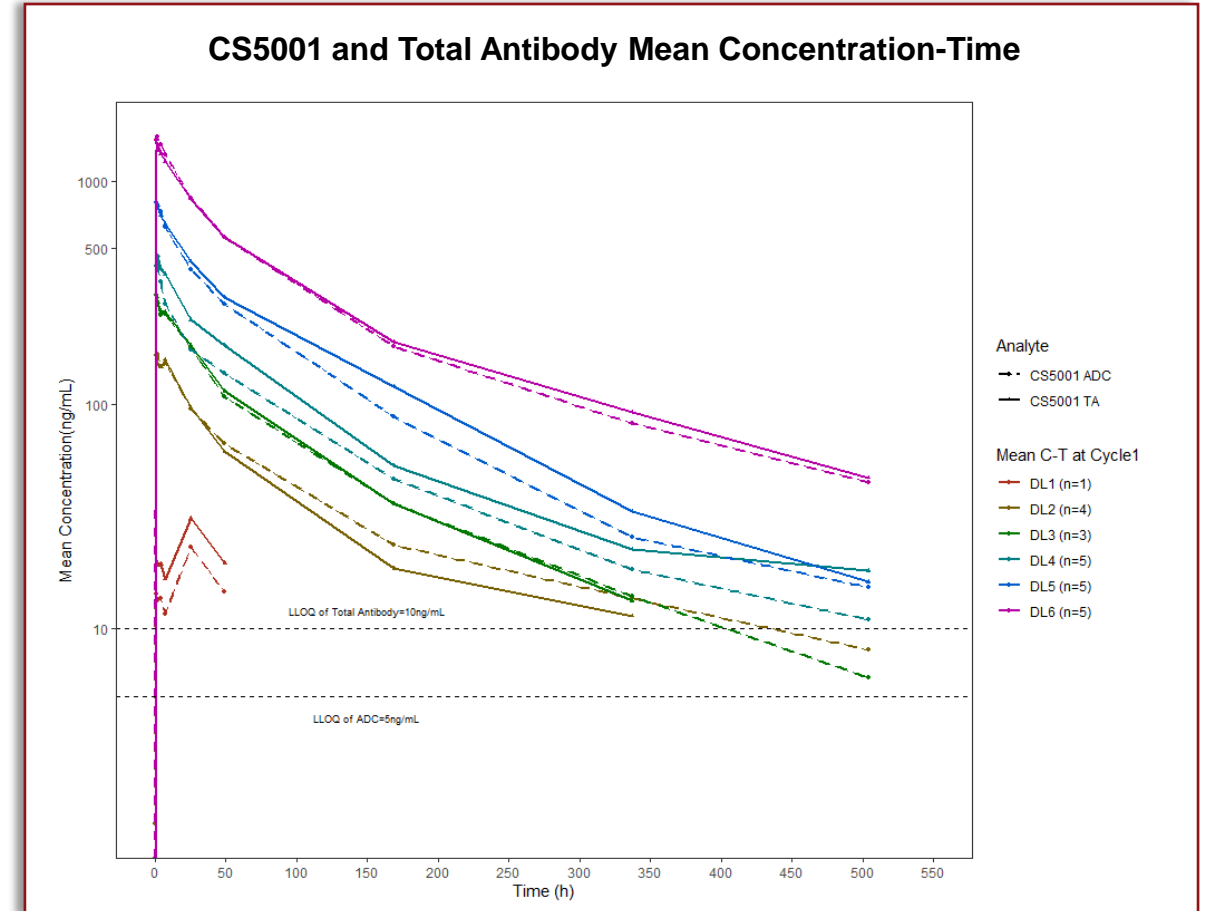
- Two PRs out of the five Hodgkin Lymphoma patients from DL3, DL5 and DL6
- One PR out of the two pancreatic adenocarcinoma patients from DL2 and DL7
- Efficacy at higher dose levels being evaluated

C Clinical pharmacokinetics profile as expected

- PK data suggested a dose proportional exposure of CS5001
- Excellent linker stability—ADC and total antibody demonstrate similar exposure

Human pharmacokinetics profile as expected

- PK data suggested a dose proportional exposure of CS5001 following *i.v.* administration
- Immunoconjugate exhibited excellent linker stability, with close similarity observed between ADC and total antibody PK profiles
- The levels of toxin and prodrug in plasma are below the limit of quantification
- No anti-drug antibody formation has been detected



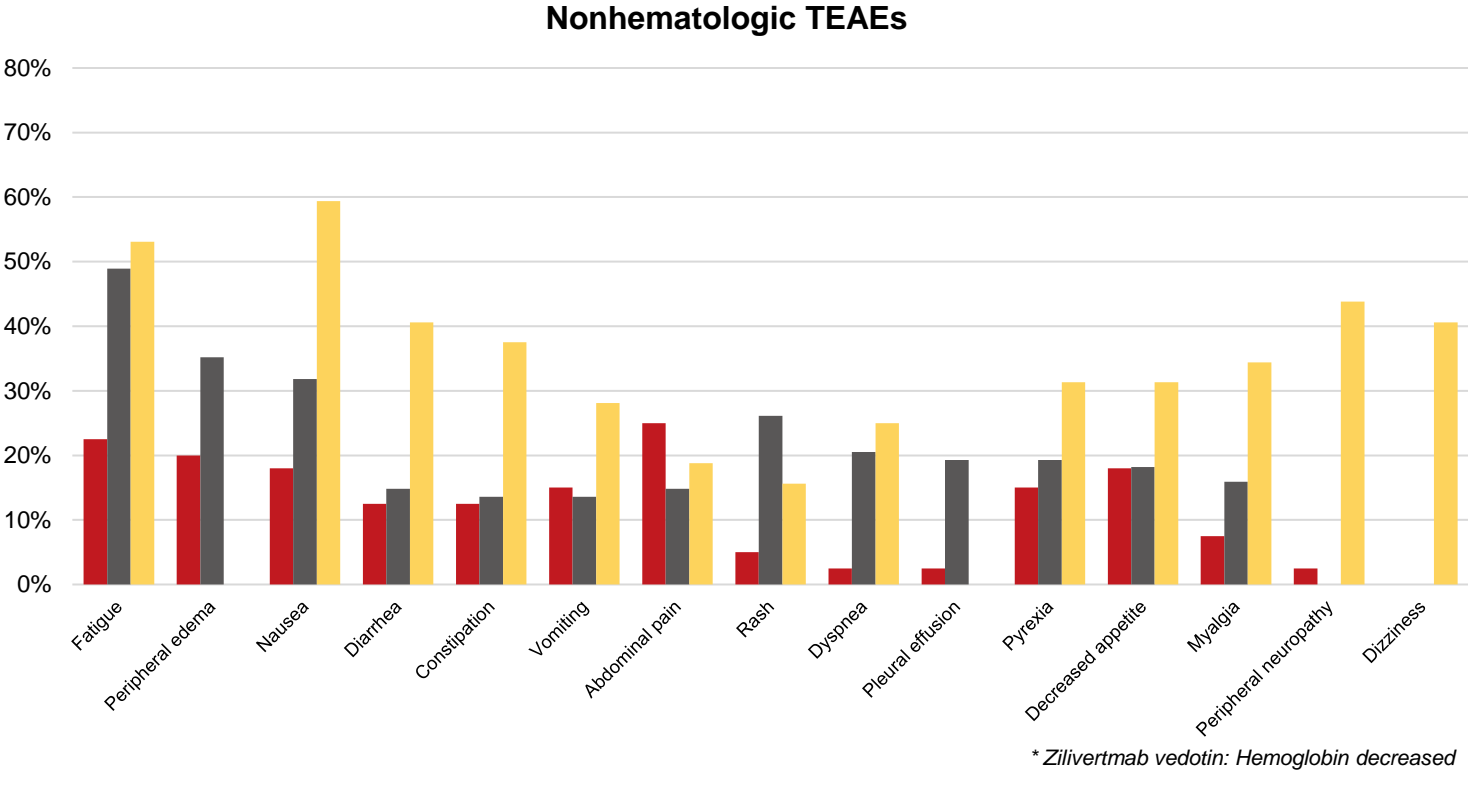
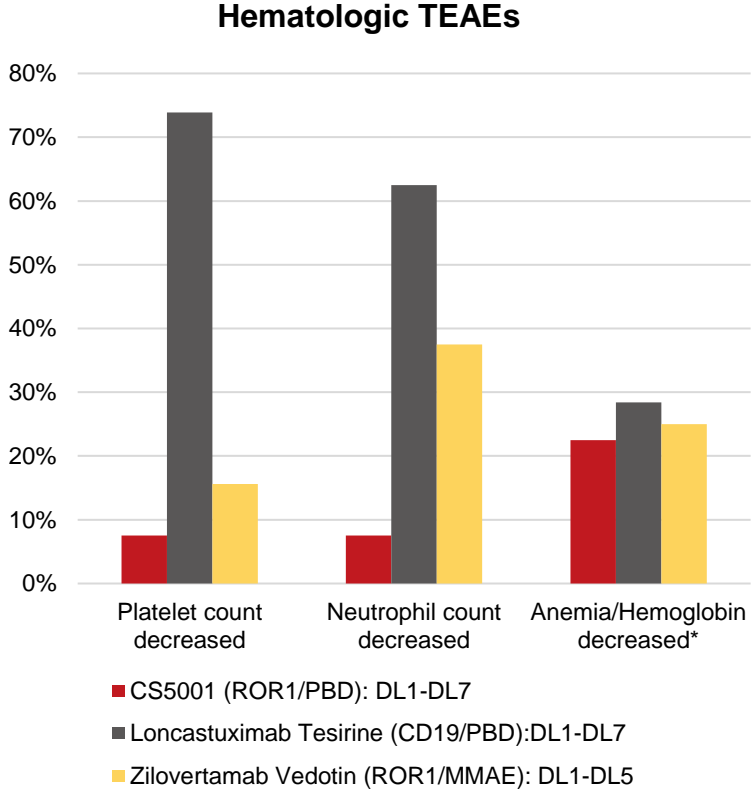
Background information of three relevant ADCs for safety comparisons

		CS5001 (ROR1/PBD prodrug)	Zilovetamab Vedotin (ROR1/MMAE)	Loncastuximab Tesirine (CD19/naked PBD)
Molecule property	Antibody	Fully human ROR1 mAb	Humanized ROR1 mAb	Humanized CD19 mAb
	Linker	Isoprenoid- β -glucuronide	Mc-vc-PAB	cathepsin-cleavable valine-alanine
	Payload	Prodrug of PBD dimer	MMAE	Naked PBD dimer
	Cleavage mechanism of linker	Cleavable by β -glucuronidase (tumor selective)	Cleavable by proteases	Cleavable by proteases
	Conjugation	Site specific and homogeneous	Randomized	Randomized
	DAR	2	Avg. 4 (0-8)	2.3 (0-6)
Clinical	Indications	Both heme & solid tumor (Ph I)	Heme (Ph I) ; Solid tumor (Ph II); DLBCL (Ph II and Ph II/III combo)	Heme DLBCL (Launched)
	Regions	Ongoing trial in US, AUS, CN	Ongoing trial in US, CN	Marketed in US, EU
	PK T _{1/2}	~5 days	3.8 days	7.2-12.5 days

Note: mc-vc-PAB linker: maleimidocaproyl-valine-citrulline-para-aminobenzoate; Gly5-EDA (Glycine)5-ethylene diamine

Favorable phase 1 safety profile of CS5001 vs. two other relevant ADCs

Lower frequency of hematologic and nonhematologic AEs observed for CS5001 up to Dose Level 7

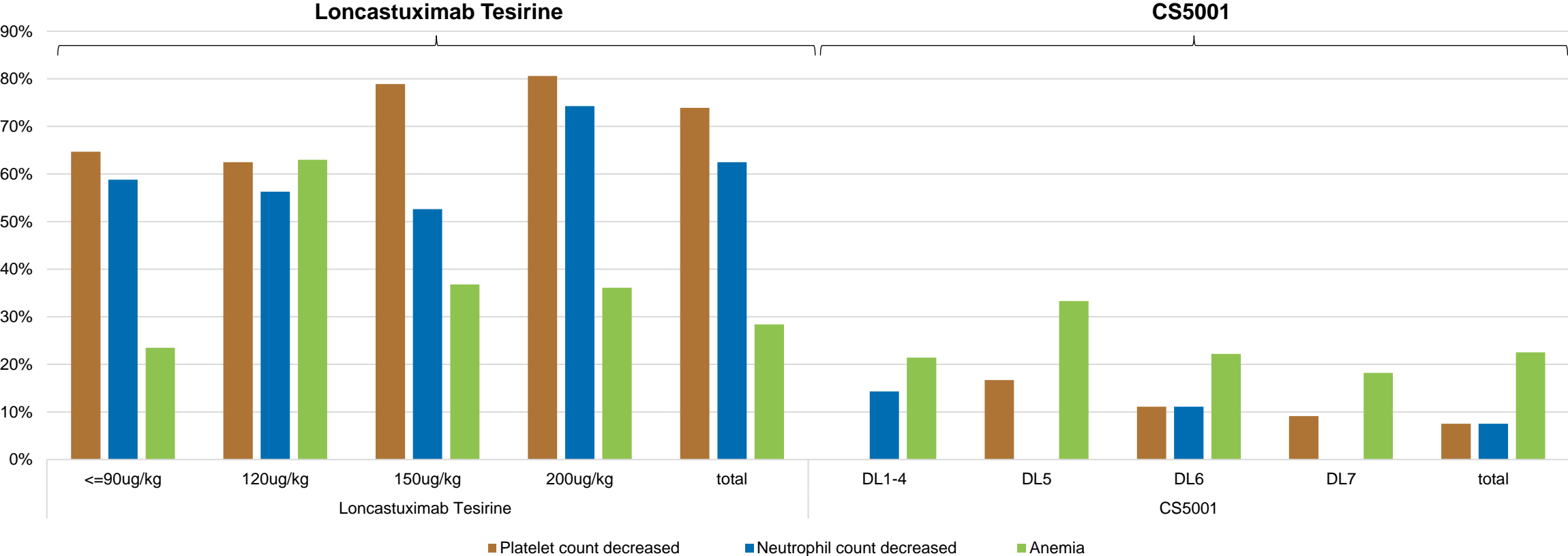


* Zilovertmab vedotin: Hemoglobin decreased

TEAE ≥ 25%

Comparing to other PBD-based ADC, CS5001 exhibited lower hematologic toxicity across different dose levels

Hematologic TEAEs by Dose Levels-Loncastuximab Tesirine vs. CS5001

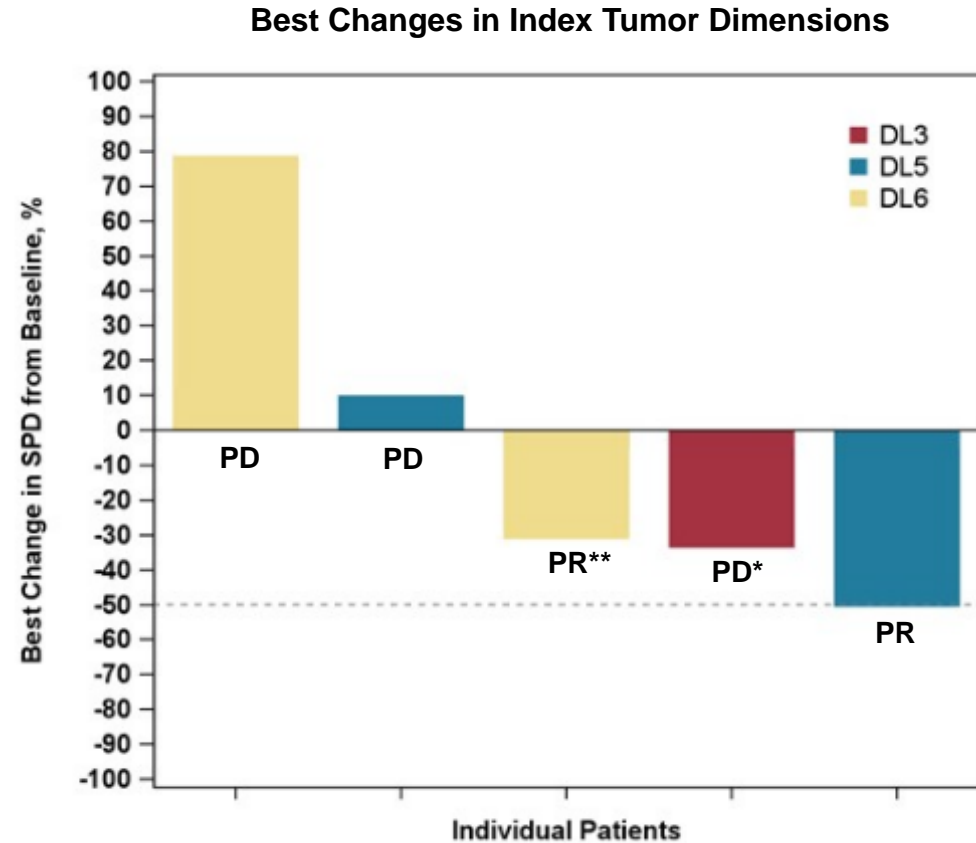


Wang ML, et al. NEJM Evidence. DOI: 10.1056/EVIDoa2100001; Brad S Kahl 1, Clin Cancer Res. doi: 10.1158/1078-0432.CCR-19-0711.

Preliminary efficacy observed in Hodgkin Lymphoma during dose escalation

Two partial responses and one mixed response observed in Hodgkin Lymphoma patients

- **Five Hodgkin Lymphoma patients from DL3, DL5 and DL6 had at least one post-baseline tumor assessment**
 - Male/female: 3/2
 - Median age: 36 (33-54) years
 - Four (80%) patients received ≥ 3 prior lines of anti-tumor treatment
- **Two PRs per Lugano 2014 and one mixed response* observed among the five Hodgkin Lymphoma patients**

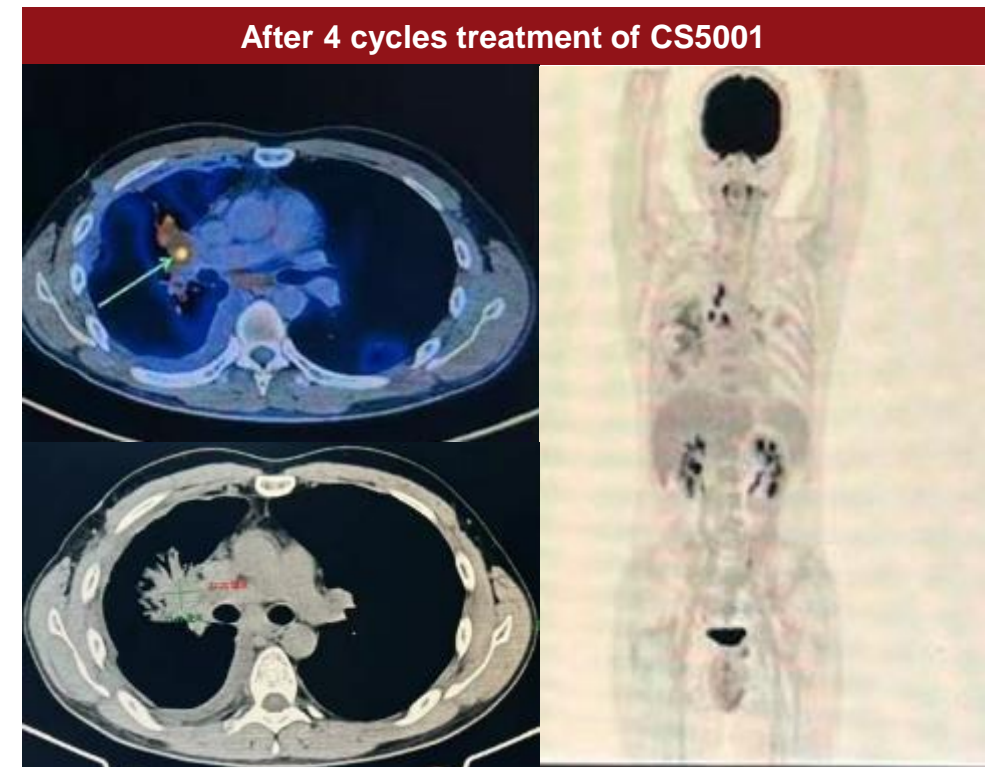
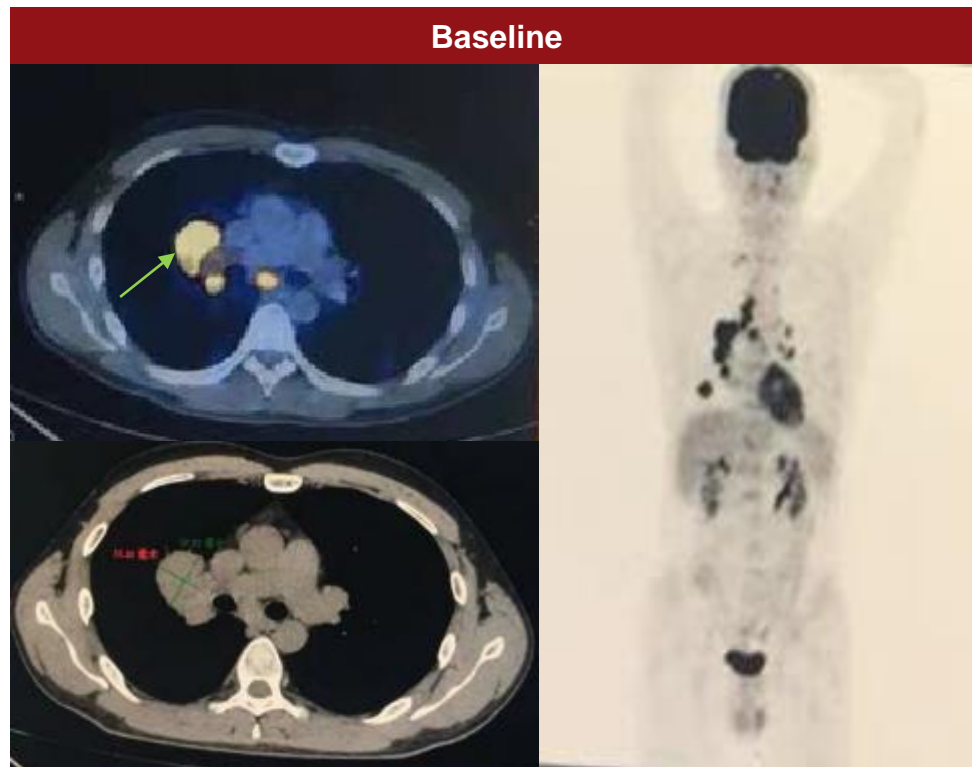


* Mixed response (coexistence of responding and non-responding lesions) was observed for this patient in the first tumor assessment. The patient continued to receive CS5001 after disease progression as a potential clinical benefit was derived. This patient had two intra-subject dose escalations with DL6 as the highest dose.

** The reduction of SPD based CT didn't reach 50%, however, PET based response was PMR for this patient, resulting in the overall response of PR

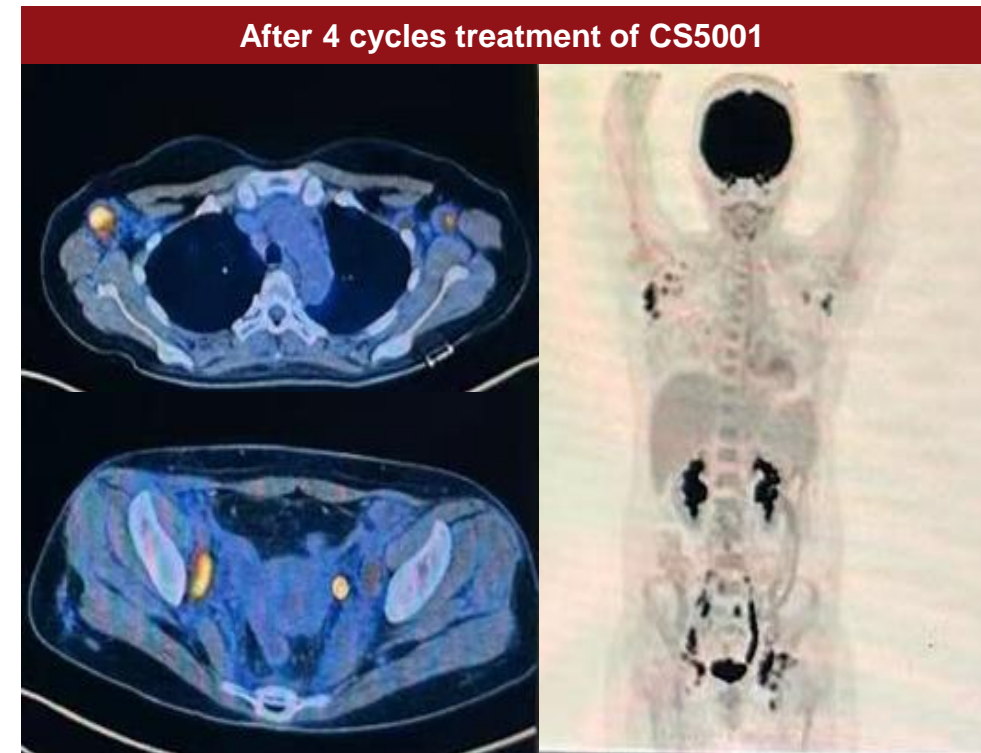
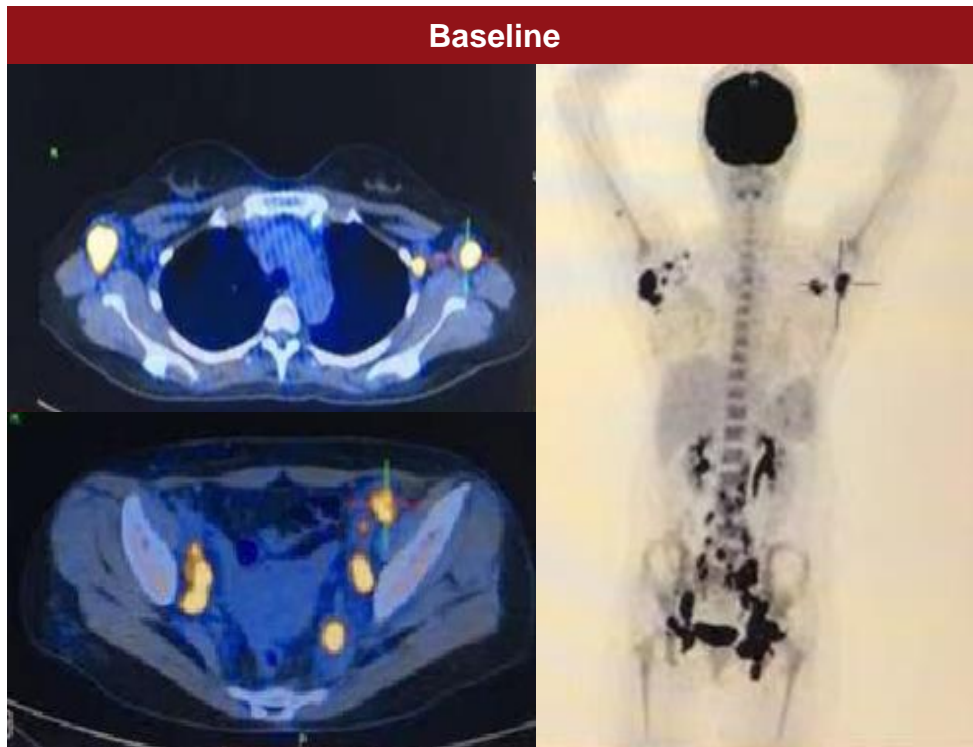
Patient 0104003: 33-year-old (y/o) male, Stage IV Hodgkin Lymphoma

- ✓ The patient's disease relapsed following two prior lines of chemotherapies, which included ABVD and RCHOP.
- ✓ After receiving 4 cycles of CS5001 treatment, a **partial response** was observed per Lugano 2014.



Patient 0104002: 34 y/o female, Stage IV Hodgkin Lymphoma

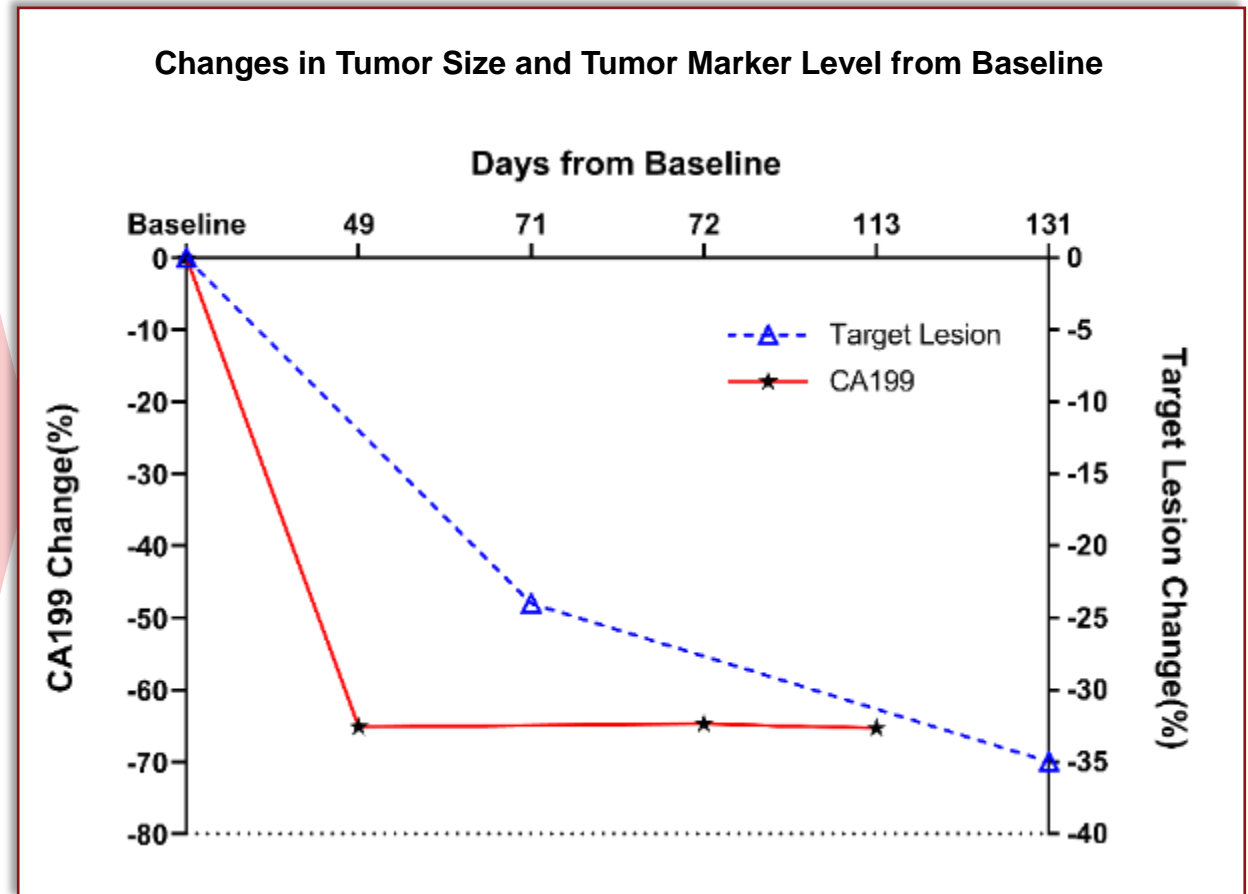
- ✓ The patient had a refractory disease following five prior lines of therapies, which included ABVD, GVD, Sintilimab+Decitabine, ICE+Sintilimab, and IBI-322.
- ✓ Following 4 cycles of CS5001 treatment, a **partial response** was observed per Lugano 2014



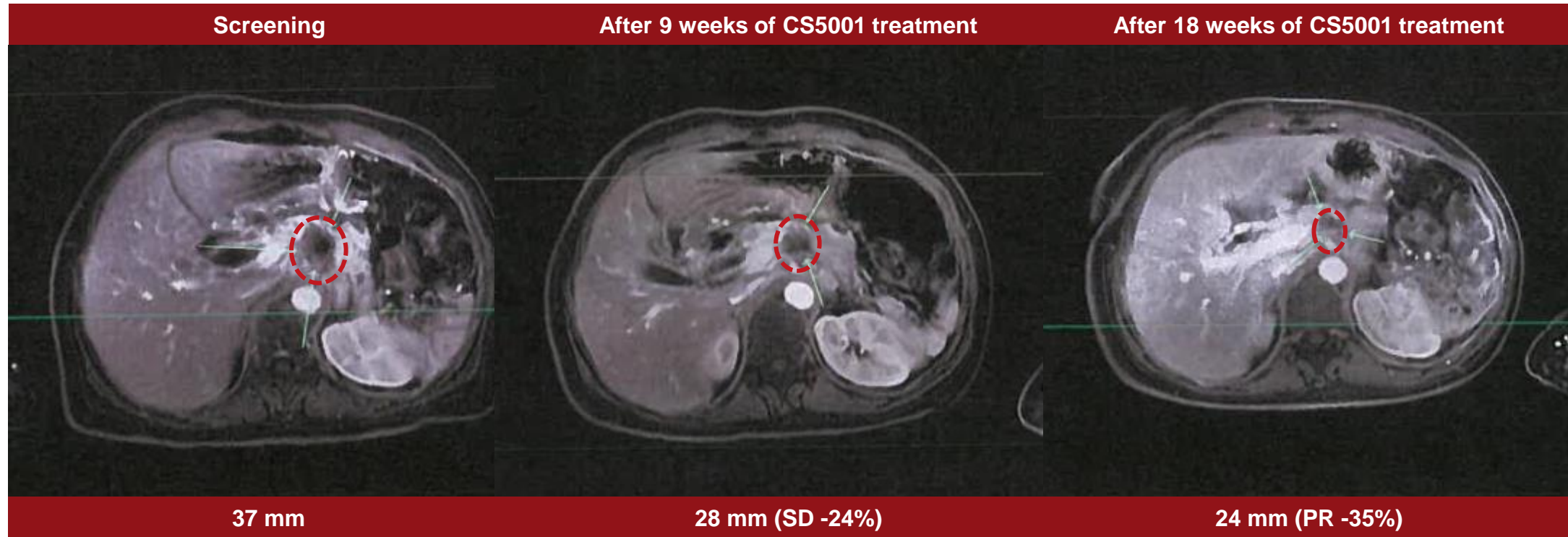
Preliminary efficacy observed in Pancreatic Adenocarcinoma during dose escalation

One partial response observed in pancreatic adenocarcinoma

- 52 y/o Jordanian female with advanced pancreas adenocarcinoma treated at Scientia Clinical Research, Australia
- **Prior Therapies:** Two NTRK inhibitors with the best response being stable disease
- **Tumor Biomarker:** At Week 6, tumor biomarker CA199 decreased by 65%, and maintained at a low level thereafter.
- **Treatment Response:** At Week 18, a partial response was observed per RECIST v1.1



Patient 0201010: 52 y/o female with advanced pancreatic adenocarcinoma



- ✓ 52 y/o female with advanced pancreatic adenocarcinoma
- ✓ Baseline MRI: target lesion pancreatic surgical bed soft tissue mass with a longest diameter of 37 mm
- ✓ After 9 weeks of CS5001 treatment, the longest diameter of target lesion reduced to 28 mm (24% reduction), the overall response is SD
- ✓ After 18 weeks of CS5001 treatment, the longest diameter of target lesion reduced to 24 mm (35% reduction), the overall response is PR

Summary

1

CS5001, a novel ROR1–directed PBD-ADC, appears well tolerated and safe in the first-in-human phase 1 study

- *No DLT was observed and MTD was not reached*
- *Lower toxicities were observed comparing to other relevant ADCs*

2

CS5001 demonstrated preliminary antitumor activities in both solid tumor and lymphoma

3

PK data suggested a dose-proportional exposure and excellent stability of the linker

4

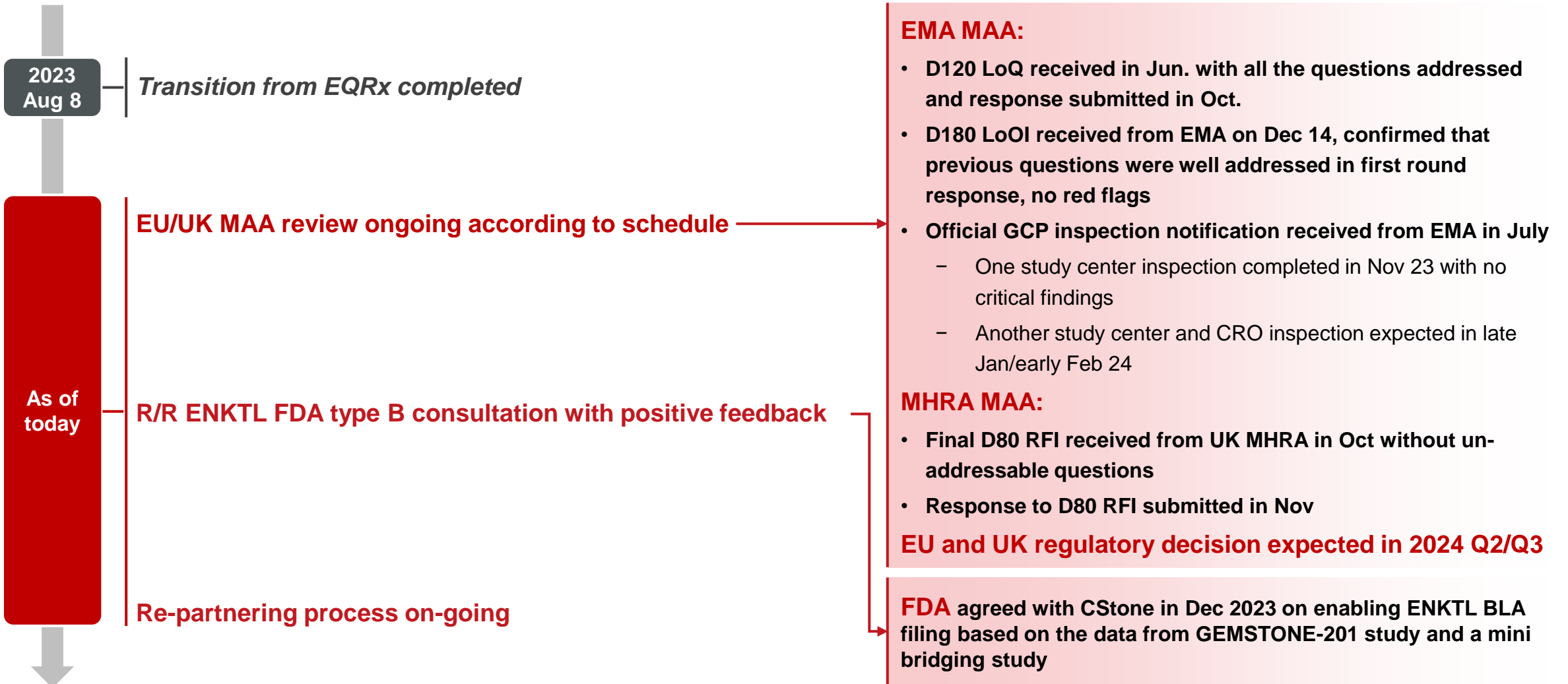
Enrolment in the dose escalation portion is ongoing, with continued evaluation of tolerability and efficacy in both solid tumors and lymphomas

Agenda

1. *ROR1 ADC Updates*
2. ***PD-L1 ex-China Progress***
3. *Commercialization Strategy*
4. *Expected Catalysts*

Sugemalimab – Ex-China Progress

EU/UK MAA regulatory review proceeding as expected; positive feedback from FDA type B consultation



Agenda

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Commercialization Strategy

Leverage the strength of partners in commercialization to maximize the value of commercial / late-stage pipeline

📅 Nov. 1st, 2023

Partner with:
 三生制药
3SBIO INC.

Strategic partnership and exclusive licensing

Nofazinlimab
Anti-PD-1 antibody

- RMB60 million upfront
- Regulatory and sales-based milestones and tiered sales royalties
- CStone retains the rights to nofazinlimab outside mainland China and is actively looking for partners

📅 Nov. 8th, 2023

Partner with:
 艾力斯

Exclusive commercial promotion right

Pralsetinib
RET inhibitor

- Sizable upfront
- CStone to book revenue and Allist to charge service fee
- CStone retains the rights besides commercial promotion in mainland China

Benefits for CStone

1 The right partner with commercial synergy and efficiency

2 Improved profit margin with commercial cost savings from 2024

3 Replenish cash position to fuel further R&D

Internally-developed multiple pipeline assets for future growth

Tri-specific antibody

CS2009

(PD-1 x VEGF x another IO target)

 Expect IND in 2024

- ✓ Potential FIC next-generation IO backbone to replace current PD-(L)1 based SOC
- ✓ Target 3 critical immune-suppressive pathways in the tumor microenvironment
- ✓ May deepen response of a PD(L)1-based therapy in large tumor types including NSCLC and HCC

ADCs

CS5005

 Expect IND in 2024/25

- ✓ Potential FIC ADC for multiple solid tumors
- ✓ Lead ADC candidate molecule shows better therapeutic window compared to control drug (a peptide-coupled drug)

CS5006

 Expect IND in 2024/25

- ✓ Global FIC, machine learning multi-omics algorithm discovered novel tumor-associated antigens, express in multiple tumor types
- ✓ Novel clinical PoC topoisomerase I inhibitor toxin, stable hydrophilic linker (DAR8)

Other programs

 Under exploration

Bi/tri-specific antibodies and bi-specific ADCs

 Current status or progress

Abbr.: FIC = first in class; BIC = best in class; IO = immune-oncology; PCC = preclinical candidate compounds; PoC = proof of concept; IND = investigational new drug

Agenda

1. *ROR1 ADC Updates*
2. *PD-L1 ex-China Progress*
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4. ***Expected Catalysts***

Expected Catalysts for the Next 12 Months

Assets	Catalysts	Date
Sugemalimab (PD-L1) Marketed	★ Regulatory decision for 1L stage IV NSCLC in EU and ex-China partnership exploration	1H 2024
	★ Regulatory decision for 1L stage IV NSCLC in UK	2H 2024
	NDA approval for 1L GC/GEJ in mainland China	Q1 2024
Lorlatinib (ROS1) In pivotal trial	Topline readout and supplemental NDA filing for ROS1-positive NSCLC in mainland China	2024
Nofazinlimab (PD-1) In pivotal trial	★ Topline readout in 1L HCC (in combination with lenvatinib) and ex-China partnership exploration	Q1 2024
CS5001(ROR1 ADC) In Ph1 trial	Update on clinical safety and efficacy	By the end of 2023
	★ Conference presentation on Ph1 data and partnership exploration	1H 2024
	★ Initiation of Ph1b/2 trial with registration potential	2024

Other potential catalysts

Ex-China partnerships for other assets with global rights

IND of pre-clinical assets with BIC / FIC potential

★ Key value driver

Abbr.: NDA = new drug application; ENKTL = Extranodal Natural KILLER/T Cell Lymphoma; NSCLC = non-small cell lung cancer; MAA = marketing authorization application; GC/GEJ = gastric adenocarcinoma/gastroesophageal junction adenocarcinoma; ESCC = esophageal squamous cell carcinoma; HCC = hepatocellular carcinoma

C1



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Thanks



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Q&A





END