TRIgnite-1 Study: Phase 1, First-in-Human, Dose-Escalation Study of ISB 2001, a BCMA × CD38 × CD3 Targeting Trispecific Antibody in Patients with Relapsed/Refractory Multiple Myeloma (RRMM)

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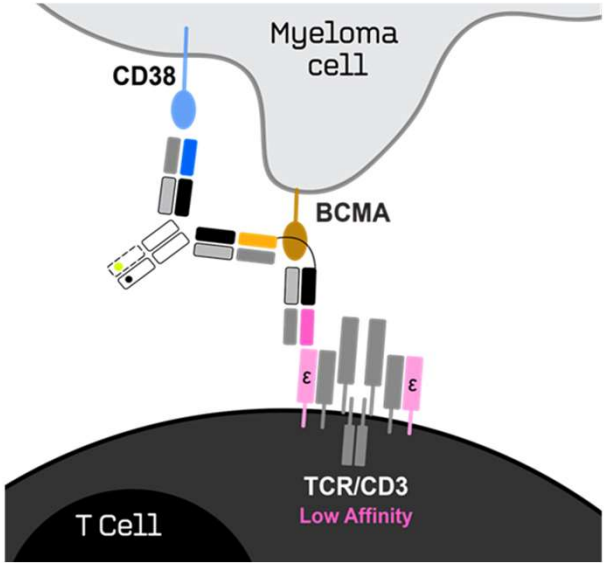
ISB 2001 BCMA x CD38 x CD3 Trispecific
TRIgnite-1 Dose Escalation Study – Key Takeaways

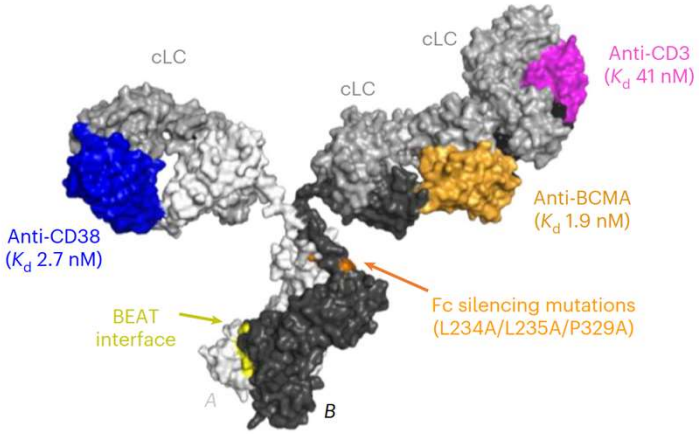
- **Dose escalation completed with no DLTs** observed up to 2700 µg/kg
- **35 heavily pretreated RRMM patients** with ≥1-month follow-up analyzed
- **Favorable safety profile for a T-cell engager:**
  - Mild CRS, a single Grade 1 ICANS, well manageable neutropenias and infections, enabling continuation of study treatment
- **Deep and durable responses** at active doses (≥ 50 µg/kg):
  - ORR 79%, ≥CR 30%, ≥VGPR 64%, MRD negativity rate* 75% with most responders still on treatment (median DOR not reached)
- **Robust activity** across key subgroups
  - Effective regardless of prior CAR-T, TCEs, BCMA therapies, CD38-refractoriness, extramedullary disease, or high-risk cytogenetics

* MRD in evaluable CR patients at 10^{-5} sensitivity

DLT: Dose Limiting Toxicity, RRMM: relapsed/refractory multiple myeloma, CRS: Cytokine Release Syndrome, ICANS: Immune Effector Cell-Associated Neurotoxicity Syndrome, ORR: overall response rate, CR: complete response, VGPR: very good partial response, MRD: minimal residual disease, DOR: duration of response, TCE: T-cell engager

ISB 2001 (BCMA × CD38 × CD3): First TREAT ™ Trispecific Antibody for Relapsed/Refractory Multiple Myeloma





Key Attributes

- Generated using IGI's proprietary BEAT® protein platform
- Enhanced avidity-based binding to myeloma cells with both BCMA and CD38 Fab domains
- CD38 Fab domain targets non-overlapping epitopes with Daratumumab
- Tuned BCMA>CD38>CD3 binding affinity and distal positioning of the CD38 vs CD3 binders drive potent tumor killing while minimizing CD38-related off-tumor adverse events

TRIgnite-1 (ISB 2001): Dose-Expansion Phase Started

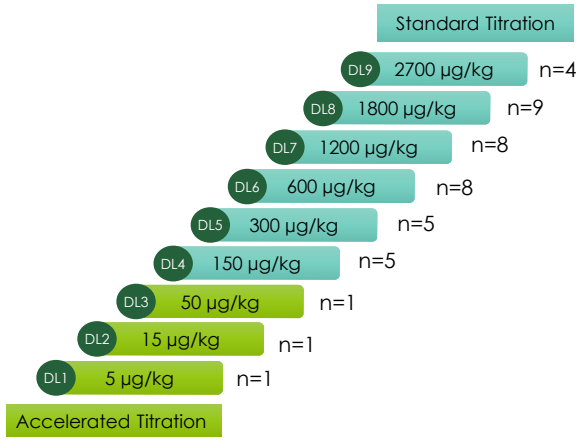
Key Eligibility :

- RRMM, after CD38 antibody, PIs, IMiDs
- Failed 3 or more prior lines
- Prior CARTs and/or bispecifics allowed

Dosing :

- ISB 2001 administered SC, weekly
- Preceded by 2 step-up doses on Day 1 and Day 4

Part 1 : Dose Escalation (n = 42)



Part 2 : Dose Expansion (n ≈ 80)
(FDA Project Optimus)

Randomization 1:1:1

Stratification: 1:1 prior TCE/CART vs. no prior TCE /CART

Cohort A:
Low Dose / q1w→2w→4w

Cohort B:
Medium Dose / q1w→2w→4w

Cohort C:
High Dose / Monthly

Primary Objectives :

- Safety and tolerability
- Determine MTD/RP2D

Secondary Objectives :

- PK, Immunogenicity
- Clinical activity by IMWG

We present data from Dose Escalation (Part 1) of the study on 35 patients with ≥ 1 month of follow-up
Median follow up was 6.3 months (1-16)

RRMM, Relapse or refractory multiple myeloma; PI, Proteasome inhibitor; IMID, immunomodulatory drug; BCMA, B-cell maturation antigen; CAR, Chimeric antigen receptor; MTD, Maximum tolerated dose; RP2D, recommended phase 2 dose; IMWG, International Myeloma Working Group; PK, pharmacokinetics; DL dose level. As of 08-May-2025 data extract, 42 patients dosed in Australia and US in DL1 to DL9, including backfills. Dose expansion has started.

TRIgnite-1 (ISB 2001): Heavily Pretreated RRMM Patients

Characteristic	Total (N=35)
Gender	
Female, n (%)	12 (35)
Median age, range (years)	65 (47; 82)
Race, n (%)	
Black or African American	2 (6)
White	27 (77)
Other	6 (17)
Ethnicity, n (%)	
Not Hispanic or Latino	34 (97)
ECOG performance status, n (%)	
0	26 (74)
1	8 (23)
Lytic Bone Disease, n (%)	25 (71)
Extramedullary disease at screening, n (%)	12 (34)
Revised ISS at screening, n (%)	
I	11 (31)
II	13 (37)
III	5 (14)
Cytogenetics available, n (%)	25 (71)
High risk cytogenetics	10 (40)
Bone marrow plasma cells ≥ 30%, n (%)	6 (17)

Characteristic	Total (N=35)
Median number of lines of previous therapy (range)	6 (3-11)
Previous therapy exposure, n (%)	
Triple class-exposed / refractory	35 (100) / 17 (49)
Penta drug-exposed / refractory	25 (71) / 5 (14)
Refractory to last line of therapy	25 (71)
Refractory to CD38	25 (71)
ASCT	30 (86)
Prior BCMA therapies	16 (46)
Prior T-cell directed therapies	15 (43)
Bispecifics	15 (43)
BCMA	7 (20)
FcRH5	7 (20)
GPRC5D	4 (11)
Anti-BCMA CAR-T	4 (11)
Anti-BCMA ADC	7 (20)

ECOG, Eastern Cooperative Oncology Group; ISS, International Staging System; ASCT, Autologous stem cell transplantation; FcRH5, Fc receptor-like protein 5; GPRC5D, G-protein coupled receptor family C group 5 member D; ADC, antibody-drug conjugate

TRIgnite-1 (ISB 2001): Manageable Hematologic Aes Enabling Continuation of Study Treatment

Hematologic TEAE	Total N=35			
	All		Related	
	Any Grade n (%)	Grade ≥ 3 n (%)	Any Grade n (%)	Grade ≥ 3 n (%)
Any Hematologic TEAEs	24 (69)	21 (60)	20 (57)	17 (49)
Neutropenia	18 (51)	15 (43)	12 (34)	10 (29)
Thrombocytopenia	17 (49)	8 (23)	13 (37)	5 (14)
Anaemia	7 (20)	5 (14)	2 (6)	2 (6)
Lymphopenia	4 (11)	3 (9)	4 (11)	3 (9)

TRIgnite-1 (ISB 2001): Manageable Non-Hematologic Aes Enabling Continuation of Study Treatment

Non-Hematologic TEAEs (≥ 15%, N=35)				
	All		Related	
AEs, n (%)	Any Grade	Grade ≥ 3	Any Grade	Grade ≥ 3
Any Non-Hem TEAEs	35 (100)	20 (57)	32 (91)	7 (20)
Infections	26 (74)	10 (29)	12 (34)	4 (11)
Cytokine release syndrome	24 (69)	0	24 (69)	0
Injection site reaction	19 (54)	0	19 (54)	0
Nausea	11 (31)	0	4 (11)	0
Back pain	8 (23)	0	1 (3)	0
Headache	7 (20)	0	4 (11)	0
ALT increase	6 (17)	0	5 (14)	0
AST increase	6 (17)	2 (6)	5 (14)	1 (3)
Diarrhea	6 (17)	2 (6)	0	0
Fatigue	6 (17)	0	4 (11)	0

No DLT observed across full dose escalation

CRS events were low grade (G1: 57%, G2: 11%)

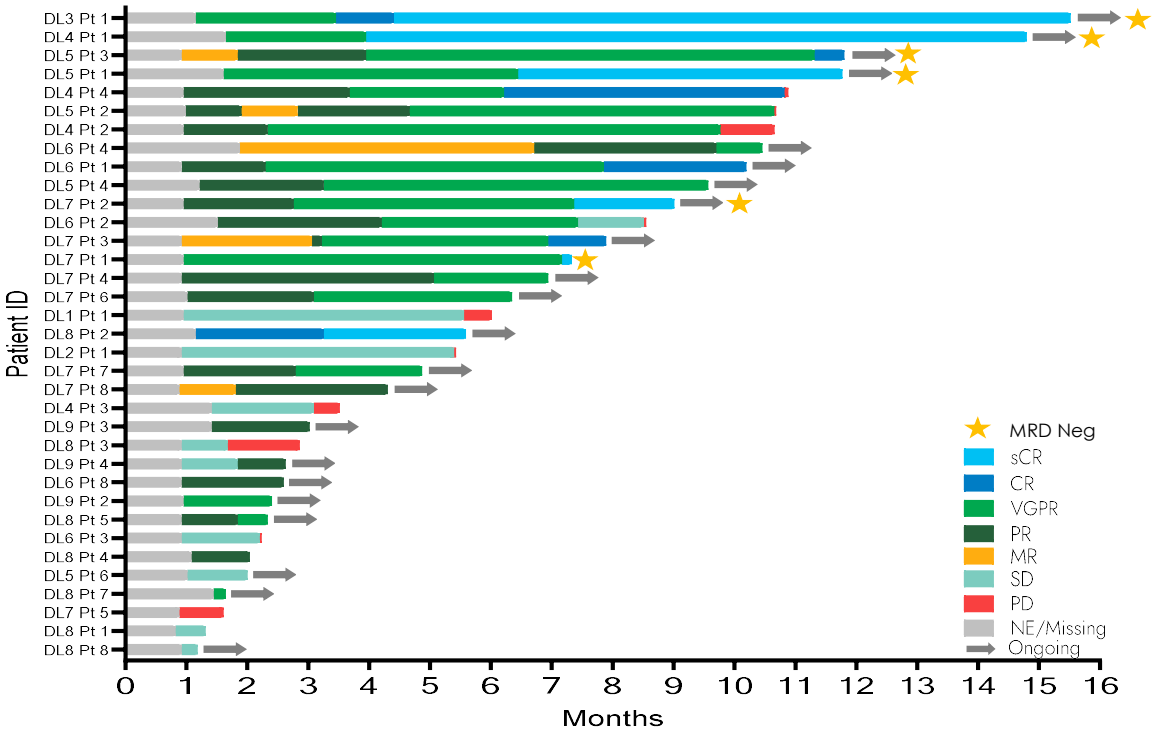
- Mostly after first step-up dose only (50%)
- Median time to CRS: 2 (1-118) days
- Median duration of CRS: 2 (1-8) days
- No prophylactic use of tocilizumab
- 13 patients received Tocilizumab: 4 pts for G2 per protocol, 9 pts for G1 as per local guidelines

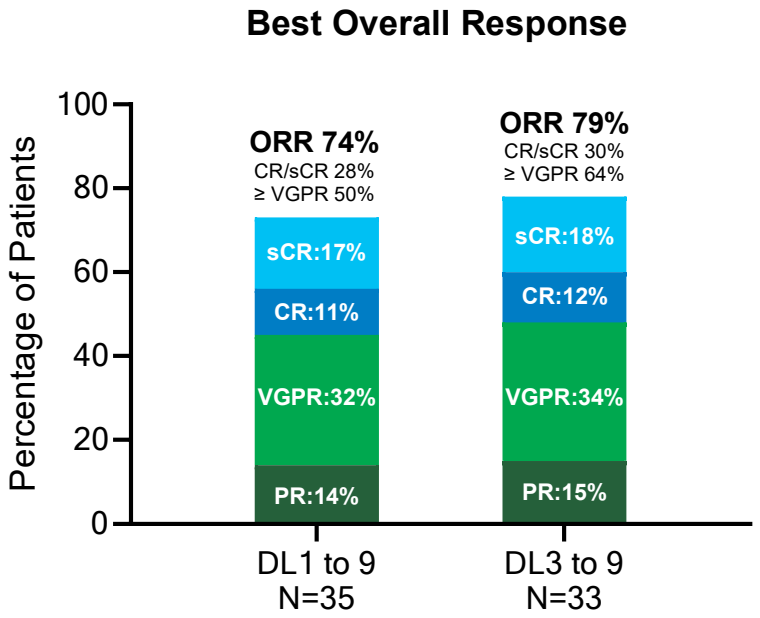
1 patient with G1 ICANS. No other drug related neurologic AEs

1 G5 cardiac arrest unrelated to study treatment in a pt with significant cardiovascular medical history

1 treatment discontinuation due to G2 sinusitis and bronchitis

TRIgnite-1 (ISB 2001): Deep and Durable Responses at ≥ 50 µg/kg





First objective response observed at 50 µg/kg DL3 (sCR, MRD negative at 10^{-5} sensitivity)

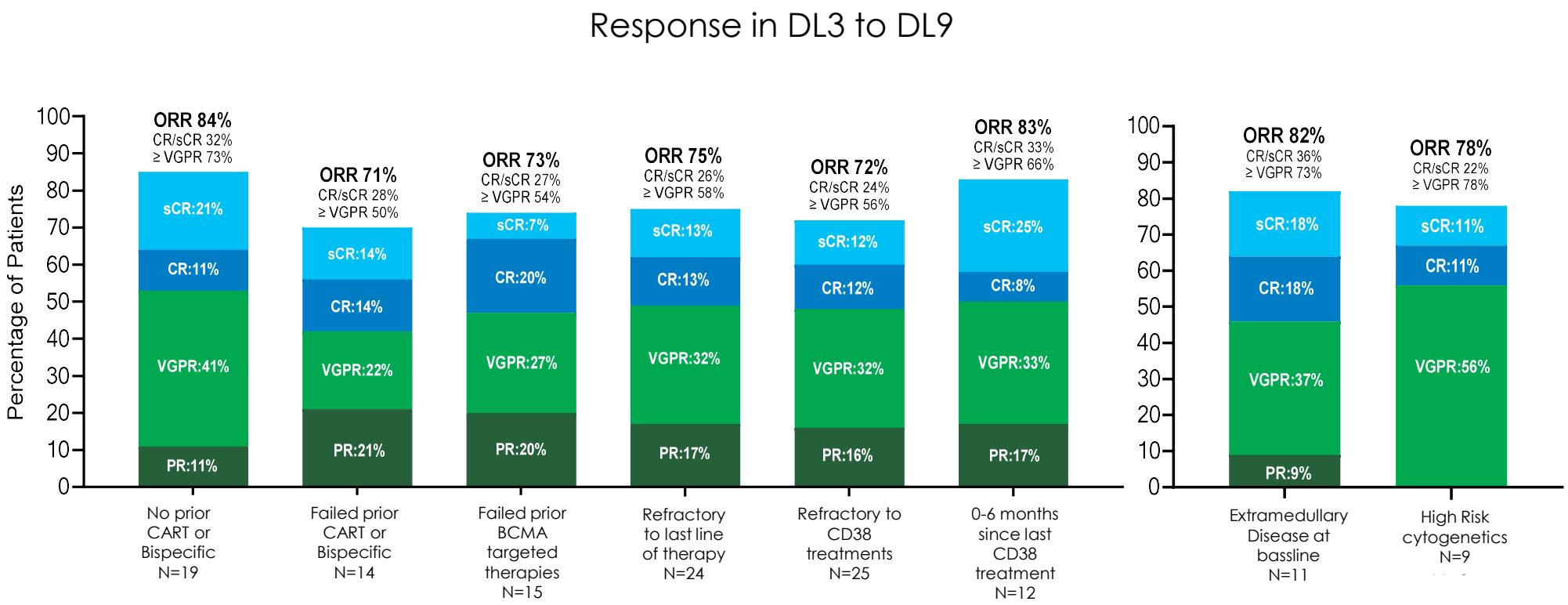
Median time to first response was 35 days (range: 29-205)

8 out of 10 patients with ≥CR were MRD evaluable. 75% (6/8) were MRD negative by clonoSEQ® or flow cytometry at 10^{-5} sensitivity

	N=35 ORR: n=26
Median DOR, months (95% CI)	NR (7–NR)
6-months DOR Estimate, % (95% CI)	90 (NR–NR)

NR: Not Reached

TRIgnite-1 (ISB 2001): High Response Rates in Difficult to Treat Patient Subgroups



Clinical Results from Dose-Escalation of TRIgnite-1 Study with ISB 2001, a Novel TREAT™ Trispecific Antibody

Dose escalation :

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- **35 heavily pretreated RRMM patients** with ≥1-month follow-up included
- **Favorable safety profile** for a T-cell engager: Mild CRS, a single Grade 1 ICANS, well manageable neutropenias and infections enabling continuation of study treatment
- **Deep and durable responses at active doses (≥ 50 µg/kg)**: ORR 79%, ≥CR 30%, ≥VGPR 64%, MRD negativity rate 75% with most responders still on treatment (median DOR not reached)
- **Robust activity across key subgroups**: Effective regardless of prior CAR-T, TCEs, BCMA therapies, CD38-refractoriness, extramedullary disease, or high-risk cytogenetics
- Pharmacokinetics: Dose-proportional PK with a **median half-life of 17 days** supports less-frequent dosing.

Next Steps:

- Dose-expansion Part 2 is ongoing to establish RP2D and best dosing schedule for further development

Acknowledgment

- **Participating patients and their families**

- **Investigators and dedicated site staff:**
- Hang Quach
- Bradley Augustson
- Hanlon Sia
- Nishi Shah
- David Levitz
- Eben Lichtman
- Michaela Liedtke
- Nicole Wong Doo
- Amit Khot

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