INITIAL RESULTS OF DOSE ESCALATION OF ISB 1342, A NOVEL CD38XCD3 BISPECIFIC ANTIBODY, IN PATIENTS WITH RELAPSED / REFRACTORY MULTIPLE MYELOMA (RRMM)

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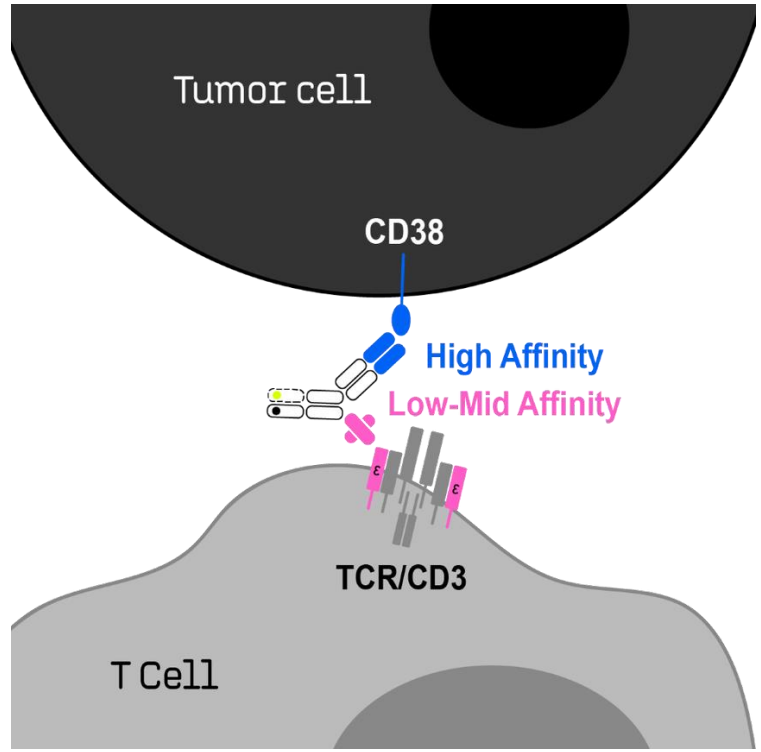
High Unmet Medical Need Remains in Patients with Relapsed / Refractory Multiple Myeloma, Despite Recent Advances in Treatment

- Significant unmet medical need exists in triple refractory patients that have progressed following treatment with proteasome inhibitors, IMiD and anti-CD38 monoclonal antibodies[1]
- BCMA targeted therapy, including CAR-T and T cell engagers, have demonstrated high overall response rates, however relapse continues to be observed[2]
- T cell engaging bispecific antibodies with alternative targets may offer an option that results in more complete and durable responses

[1] *Gandhi UH et al. Leukemia 2019; 33: 2266–75*
[2] *Watson, et al. Expert Rev Hematol. 2022 Jun;15(6):503-517*

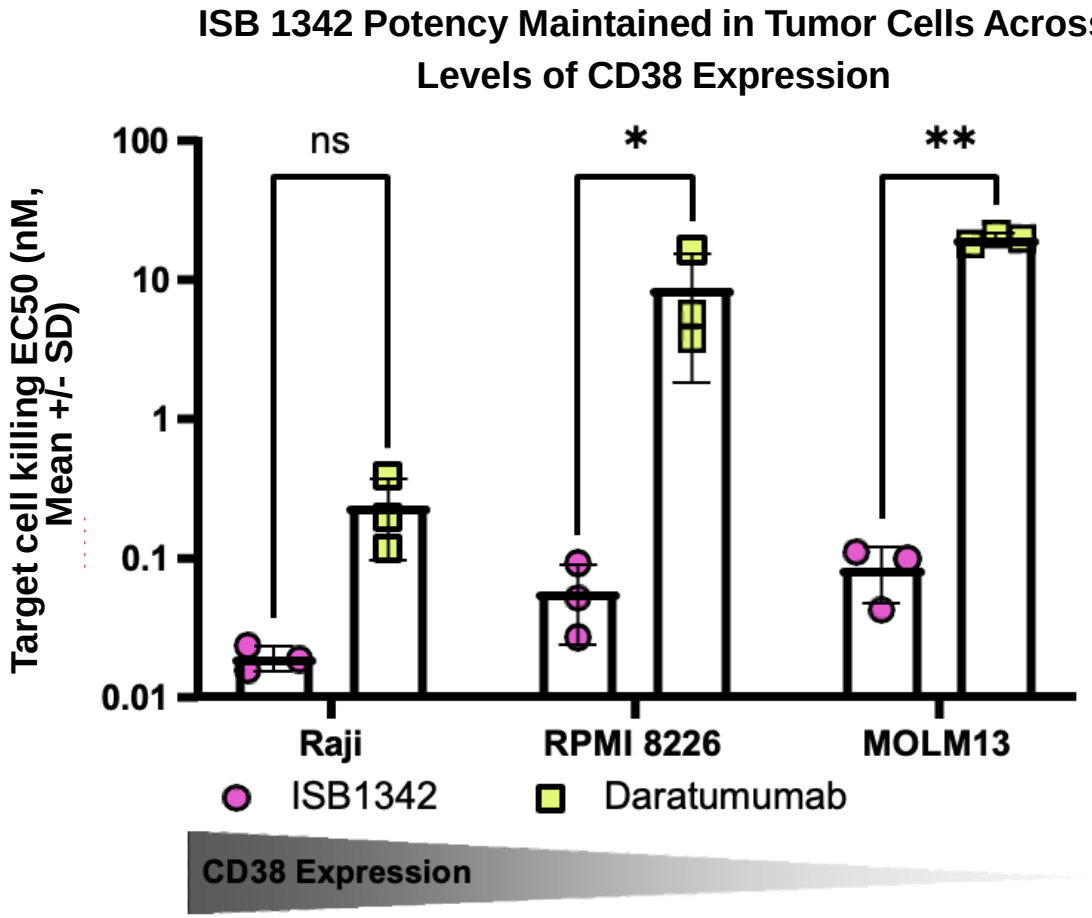
ISB 1342 (CD38 x CD3) Bispecific Antibody: Potential First-in-Class Therapy in Relapsed/Refractory Multiple Myeloma

- CD38 is expressed on the surface of multiple myeloma cells and is a validated target
- ISB 1342 is a bispecific antibody that redirects T lymphocytes to kill CD38-expressing tumor cells in MHC-antigen-independent manner
- ISB 1342 binds with high-affinity to a proprietary anti-CD38 epitope, which is different from that of daratumumab or isatuximab
- ISB 1342 is designed to overcome:
  - + Daratumumab resistance by killing low CD38-expressing tumor cells
  - + Resistance to CDC and ADCC mediated by daratumumab



MHC: Major Histocompatibility Complex
CDC: Complement-Dependent Cytotoxicity
ADCC: Antibody-Dependent Cell-mediated Cytotoxicity

ISB 1342 Demonstrates Superior Potency to Daratumumab in Both CD38 High- and Low-Expressing Cells



*Multiple modes of action killing assay combines Antibody-Dependent Cell-mediated Cytotoxicity (ADCC), Complement-Dependent Cytotoxicity (CDC) and re-directed cell lysis. ISB 1342 induced a statistically significantly better killing than daratumumab. ns: p ≥ 0.05; * p <0.01; ** p <0.0001*

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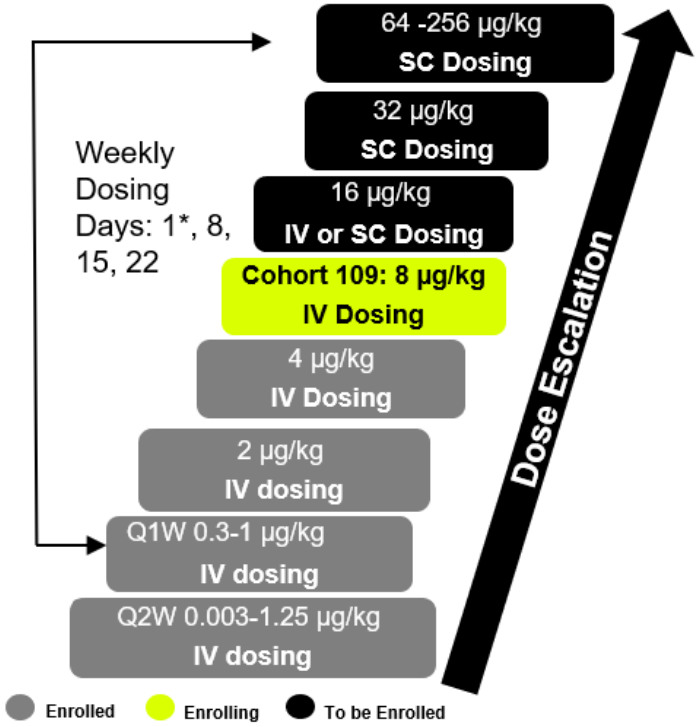
ISB 1342 Phase 1 Escalation Cohort Summary

3 + 3 Design



Patients

- 29 patients were enrolled in bi-weekly dosing cohorts
- **30** patients have been enrolled in weekly dosing cohorts

Eligibility:

- Adults (>18 yo) with RRMM
- Triple class refractory
- Anti-CD38 Rx 2-month washout
- Measurable disease

Phase I Objectives

- **Primary:** Determine MTD and/or recommended Phase 2 dose
- **Secondary:** Assess safety and tolerability, PK &PD, immunogenicity, antimyeloma activity

**Priming dose administered on Cycle 1 Day 1 followed by maintenance dose onwards (as shown). Data cutoff as of Oct 25, 2022 (including 3 ongoing patients in cohort 109 who received 1, 3, and 3 doses of ISB 1342).*

Baseline Characteristics

Baseline Characteristics	ISB 1342-101 Q1W cohort
Median age	68 (54-76)
ISS stage at BL (n=21)	
Stage 1	30%
Stage 2	30%
Stage 3	30%
Median prior regimens	6.0 (2-11)
Triple refractory	90%
Penta-refractory	73%
Median time from last CD38-directed therapy	16.6 months (3-50)
Prior anti-BCMA	30%
Prior T-cell-based treatment	10%

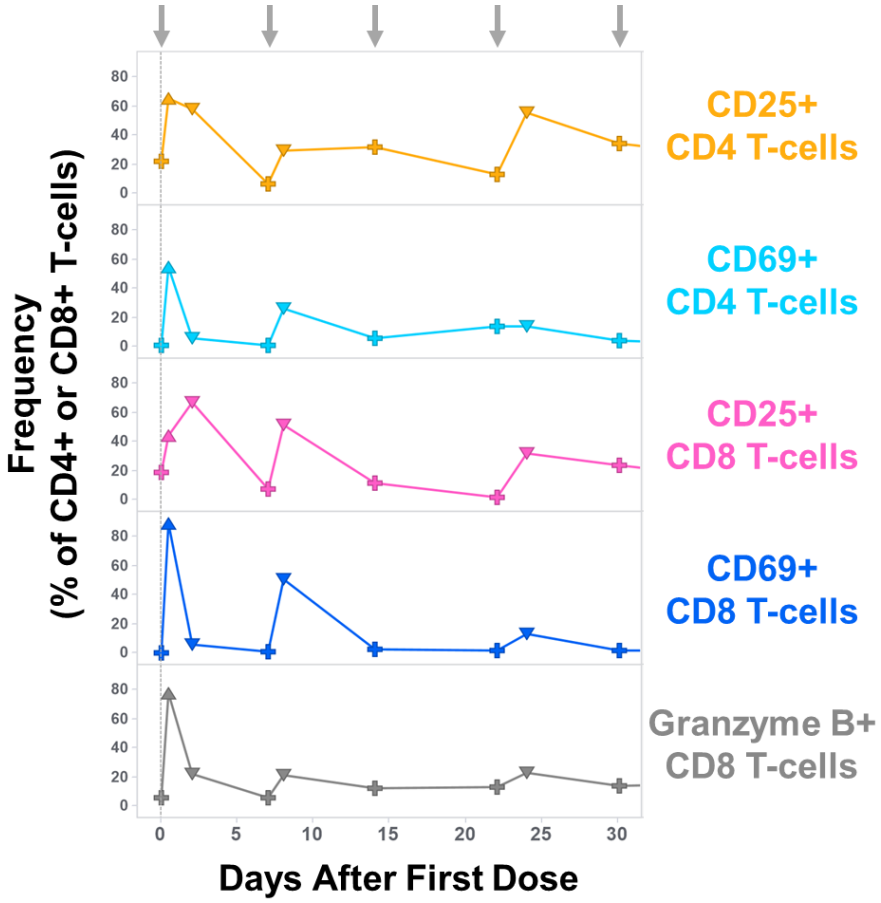
TEAEs Observed in >10% of Patients in Q1W

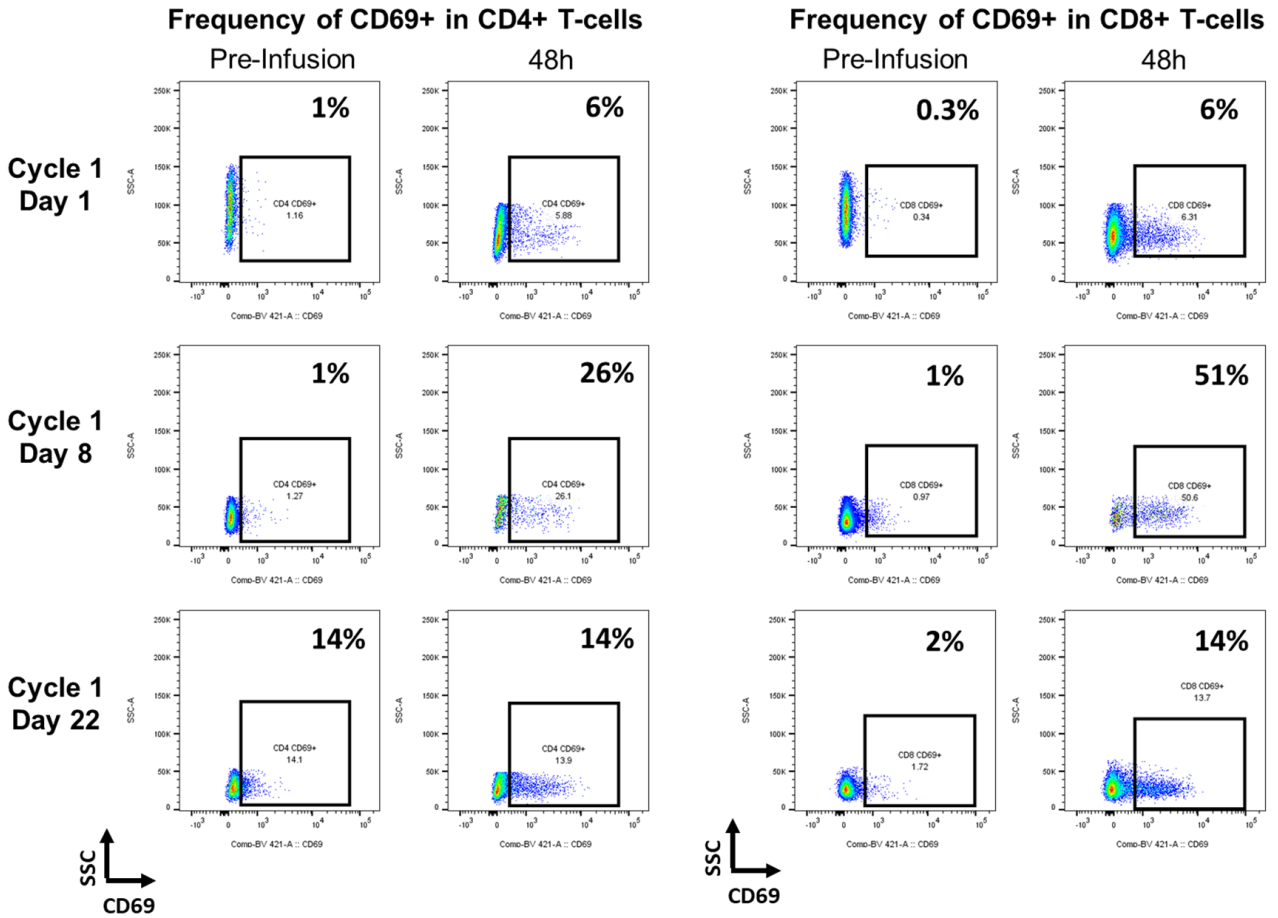
TEAE[#] (>10% Q1W cohort)	All Grade n (%)	Grade ≥3 n (%)
Any TEAE	30 (100.0)	25 (83.3)
Infusion related reaction	13 (43.3)	5 (16.7)
Anemia	10 (33.3)	7 (23.3)
Thrombocytopenia	9 (30.0)	3 (10.0)
Blood creatinine increased	6 (20.0)	1 (3.3)
Cytokine release syndrome*	6 (20.0)	0
Hypoalbuminemia	5 (16.7)	0
Hypokalemia	5 (16.7)	0
Hyponatremia	4 (13.3)	0
Leukopenia	4 (13.3)	1 (3.3)
Lymphopenia	4 (13.3)	2 (6.7)

Data in this table include all treated patients in the Q1W IV cohort as of Oct 25, 2022. At the data cutoff, cohort 109 testing a priming dose of 2 µg/kg followed by a weekly dose of 8 µg/kg is open, and 3 patients have received 1, 3, and 3 doses of ISB 1342.
*Tocilizumab was given to 1 patient

- A single DLT (Grade 3 delirium) was observed in a 73-year-old patient treated in cohort 104 (0.3/0.55 µg/kg) after the third dose of ISB 1342. This event was not a CRS event.

Evidence of T-Cell Activation Following Treatment with ISB 1342 (Cohort 108, 1 µg/kg priming and 4 µg/kg targeted dose)





Plots from one patient in cohort 108

Conclusions

- Treatment with ISB 1342 was well tolerated at the evaluated Q1W dose levels up to cohort 109 (2µg/kg priming, 8µg/kg targeted dose)
- The observed CRS events were moderate and manageable with supportive care
- No increased risk of infection has been observed
- Dose escalation continues with participants enrolling in additional cohorts