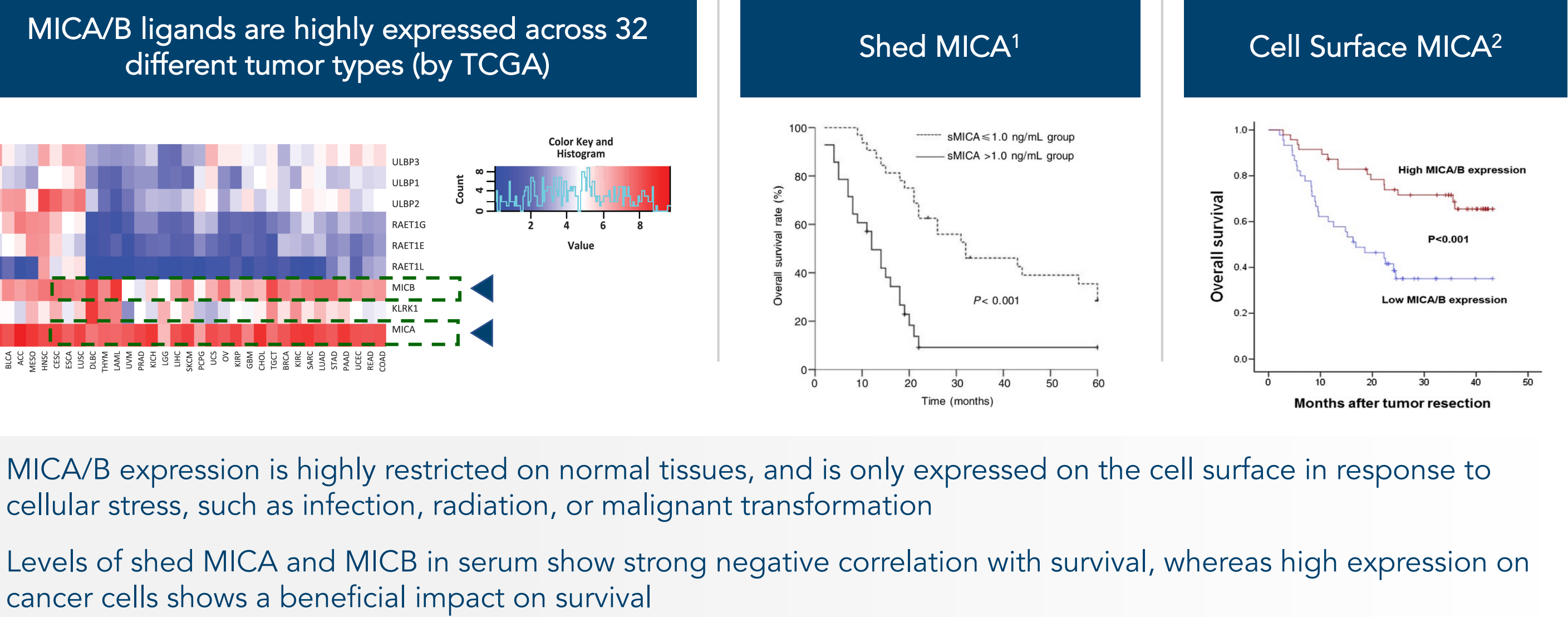


A Phase 1 Dose-Escalation Study to Investigate the Safety, Efficacy, Pharmacokinetics, and Pharmacodynamic Activity of CLN-619 (Anti-MICA/MICB Antibody) Alone and in Combination with Pembrolizumab in Patients with Advanced Solid Tumors

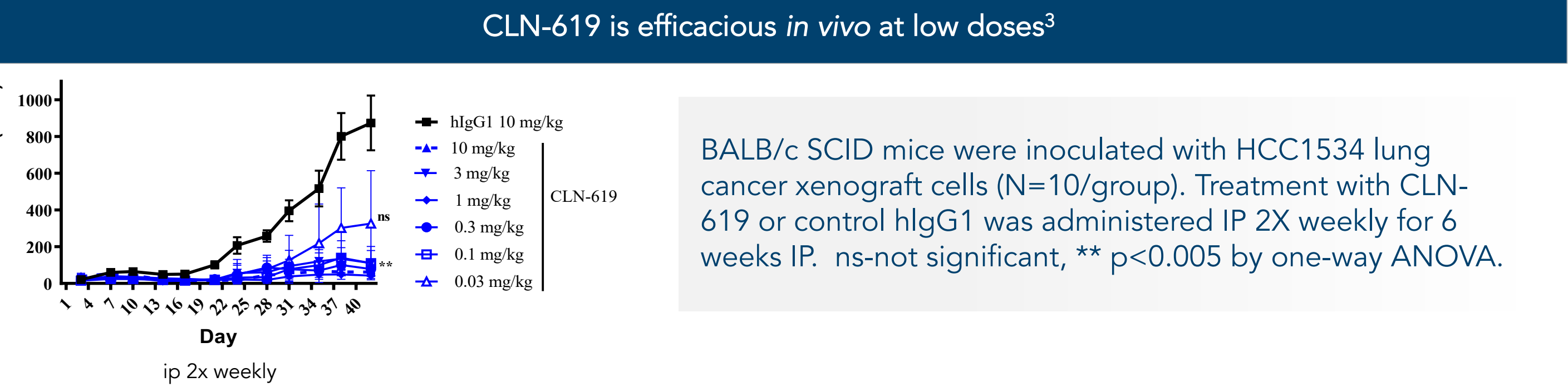
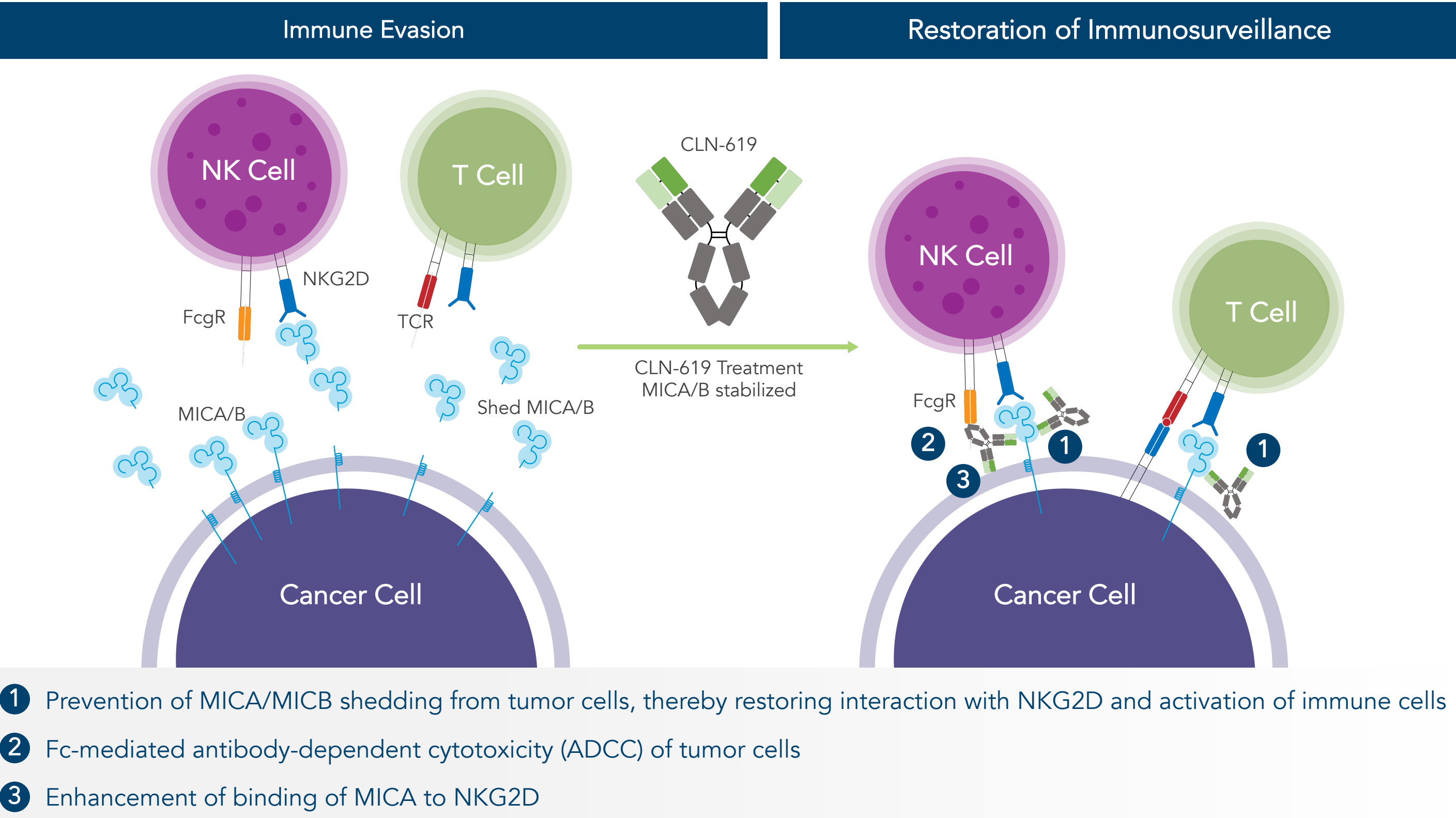


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Background: MICA/MICB are Pan-Cancer Targets

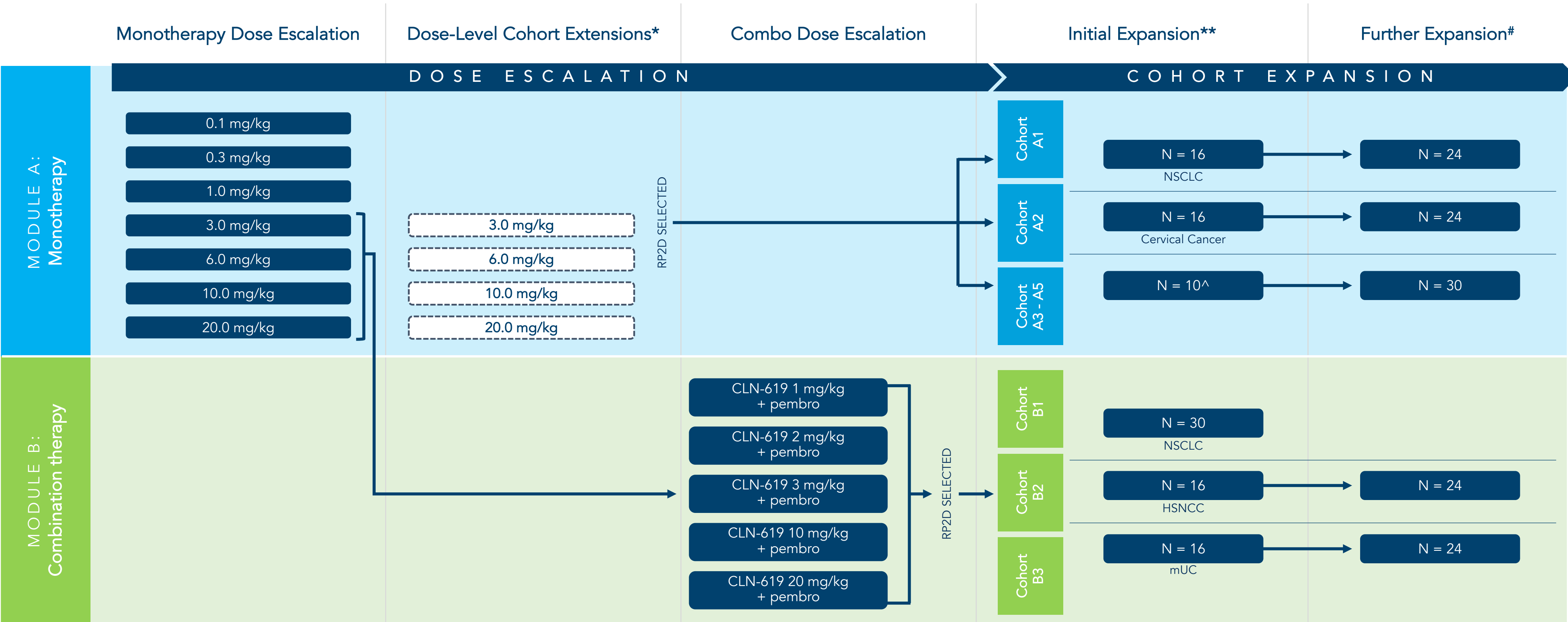


Background: CLN-619 Proposed Modes of Action



CLN-619-001 Study Schema

This is an open label, first-in-human, multicenter, dose escalation and dose expansion study of CLN-619 administered alone (Module A) or in combination with pembrolizumab (Module B) in patients with advanced solid tumors.



*Enrollment may be up to N = 10 per dose level that have been cleared for safety; **Dose escalation cohort initial expansion N = up to 16 per dose level; #Further expansion dependent on signal or emerging data; ^Inclusive of patients with the identified tumor type dosed during Module A dose escalation; NSCLC = non-small cell lung cancer; HNSCC = head and neck squamous cell carcinoma; mUC = metastatic urothelial carcinoma

Key Eligibility Criteria

Inclusion Criteria	Exclusion Criteria
- Age $\geq$ 18 years - ECOG 0 or 1 - Estimated life expectancy $\geq$ 12 weeks - Adequate liver and kidney function and hematological parameters - Histologically or cytologically-confirmed metastatic or locally advanced, unresectable solid tumors - Patients should have received any other available standard therapy (except cohort B1) - Measurable disease based on RECIST v1.1	- Investigational drug within 28 days (or 5 half-lives) of dosing on C1D1 - Active autoimmune disease or history of known/suspected autoimmune disease, or history of a syndrome that requires systemic corticosteroids or immunosuppressive medications - Serious, uncontrolled medical disorder that would impair the ability of the patient to receive protocol therapy or whose control may be jeopardized by the complications of this therapy - Treatment with systemic antimicrobial agent for acute infection within $\leq$ 7 days of dosing on C1D1 - History of grade $\geq$ 3 immunological adverse event or liver dysfunction satisfying Hy's Law in conjunction with prior checkpoint inhibitor immunotherapy - Prior allogeneic organ or hematopoietic transplantation - Active CNS metastases and/or carcinomatous meningitis - Module B2 & B3 cohorts only: refractory disease defined as progressive disease at 16 weeks after at least 3 doses of PD-1 therapy

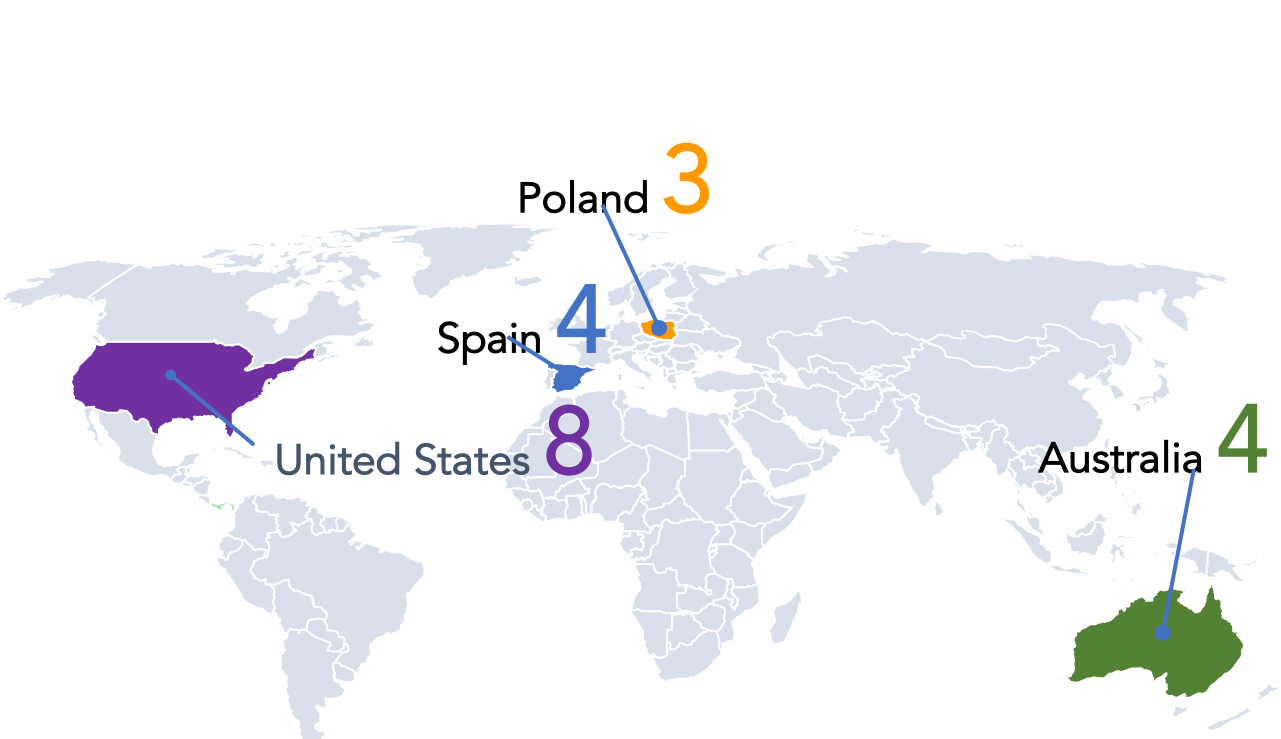
Study Objectives

Primary Objectives:
To characterize the safety, tolerability, and preliminary anti-tumor activity of CLN-619 administered alone (Module A) or in combination with pembrolizumab (Module B) in patients with advanced solid tumors

Secondary Objectives:
To assess the PK profile and immunogenicity of CLN-619 administered alone or in combination with pembrolizumab in patients with advanced solid tumors

Exploratory Objectives:
To explore various pharmacodynamic and predictive biomarkers and their relationship to measures of clinical anti-tumor activity including overall response rate (ORR), duration of response (DOR), progression-free (PFS) and overall survival (OS) in patients treated with CLN-619 alone or in combination with pembrolizumab

Global Site Footprint



Exploratory Biomarker Plan

Pharmacodynamic and Predictive Biomarker Analysis in the tumor and at the periphery		
Pharmacodynamic (PD) Biomarkers/ Mechanism of Action (MoA)	Exploratory Predictive Biomarkers*	
Peripheral PD/MoA ELISA (sMICA) Flow Cytometry (Immunophenotyping) Luminex (46 cyto-/chemokine panel) ctDNA** (Targeted NGS panel)	Intra-tumoral PD/MoA IHC (MICA/B/ & NKG2D) Multiplex IF (NK- and T-cell infiltration) WES/RNASeq (immune gene expression) Paired tumor biopsy analysis for PD; Baseline (archival/fresh) for predictive analysis	Predictive/Genotyping NGS typing (MICA/B alleles) Real-time PCR (NKG2D haplotype, FcγRIIIa SNP (ADCC)) Whole blood at baseline

Study Information

- Protocol Number: CLN-619-001
- Status: Monotherapy (Module A) and combination (Module B) dose escalation are ongoing
- ClinicalTrials.gov Identifier: NCT05117476
- Contact: Timna Serino clinops@cullinanoncology.com

References

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- Whalen KA, Mehta NK, Yalcin S, Meetze K, Gibson NW, Michaelson JS, Baeuerle PA. CLN-619, a clinical-stage MICA/MICB-specific IgG1 antibody, restores the MICA/MICB-NKG2D axis to promote NK-mediated tumor cell lysis. AACR 2022 Abstract #3506.