Phase 1 Study of SGN-BB228, an Investigational CD228 x 4-1BB Costimulatory Antibody Anticalin Bispecific, in Patients with Advanced Melanoma and Other Solid Tumors (SGNBB228-001: Trial in Progress)

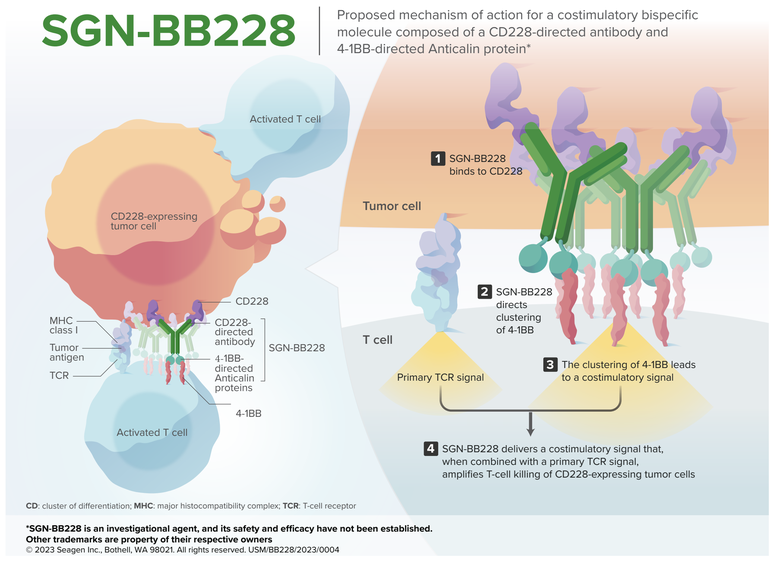
Jason T. Henry,[1] Janice M. Mehnert,[2] Erika Rudnicki,[3] Juan Pinelli,[3] Adil Daud[4]

[1]Sarah Cannon Research Institute at HealthONE, Denver, CO, USA; [2]New York University Langone Health, New York, NY, USA; [3]Seagen Inc., Bothell, WA, USA; [4]University of California San Francisco, San Francisco, CA, USA

Background

- CD228 is a tumor-associated antigen selectively expressed by multiple tumor types including melanoma, mesothelioma, and pancreatic, colorectal, and lung cancers[1]
- 4-1BB is an inducible costimulatory receptor expressed on activated T cells and other immune cell populations[2]
- The clinical development of 4-1BB agonist antibodies has been hampered by limited efficacy and/or poor tolerability at active doses[3,4]
- SGN-BB228 is an investigational costimulatory antibody Anticalin (Mabcalin) bispecific molecule directed to CD228 and 4-1BB that delivers a potent costimulatory bridge between tumor-specific T cells and tumor cells, potentially localizing antitumor activity to the tumor microenvironment and expanding the therapeutic window for 4-1BB agonism
- In vitro, SGN-BB228 shows potent CD228-conditional 4-1BB stimulation and cytotoxic T cell activation[5]
- SGNBB228-001 (NCT05571839) is a phase 1, open-label study to evaluate SGN-BB228 in patients with advanced melanoma and other solid tumors

SGN-BB228 Proposed Mechanism of Action



Eligibility

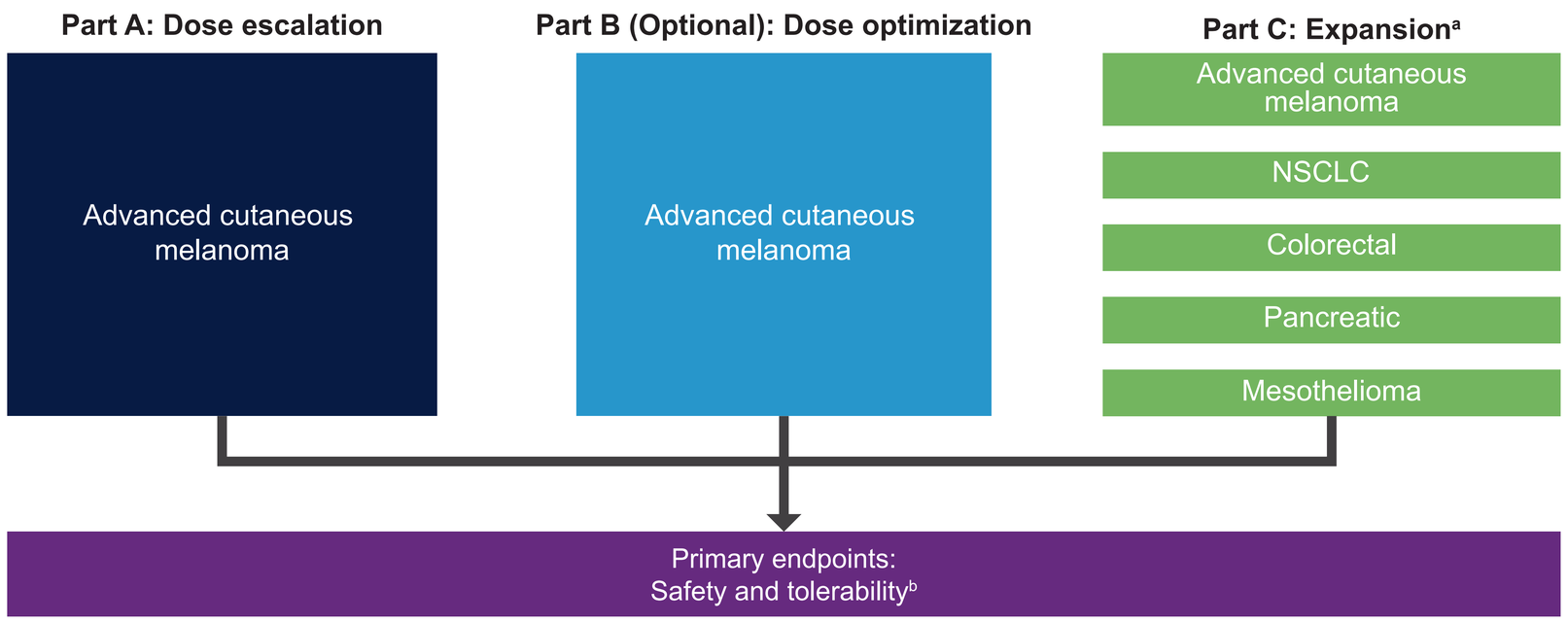
Key Inclusion Criteria

- Adults aged ≥18 years with histologically or cytologically confirmed metastatic or advanced cutaneous melanoma (Parts A, B, C) or histologically or cytologically confirmed metastatic NSCLC, colorectal cancer, pancreatic cancer, or mesothelioma (Part C only)
  - For patients with cutaneous melanoma, prior treatment with an anti-PD-1 or anti-PD-L1 agent, and for those with targetable BRAF mutation, treatment with BRAF/MEK targeted therapy unless intolerant or declined
- Disease that is relapsed, refractory, or intolerant to standard-of-care therapies and no other therapeutic options known to provide clinical benefit, per investigator assessment
- ECOG performance status score of 0 or 1

Key Exclusion Criteria

- History of another malignancy within 3 years before the first dose of study drug or any evidence of residual disease from a previously diagnosed malignancy
- Known active CNS metastases or leptomeningeal disease
  - Patients with previously treated brain metastases may participate if they have been clinically stable for at least 4 weeks prior to study entry after brain metastasis treatment, have no new or enlarging brain metastases, and are off corticosteroids prescribed for a minimum of 7 days prior to the first dose of the study drug
- Prior treatment with CD228 or 4-1BB-targeted drugs
- Immunotherapy, biologics, and/or other approved or investigational antitumor treatment that is not completed 4 weeks prior to the first dose of study drug or within 2 weeks prior to the first dose of study drug if the underlying disease has progressed on treatment

Study Design



[a]Part C will further characterize safety, tolerability, PK, and antitumor activity of SGN-BB228 in disease-specific cohorts
[b]Patients may continue on treatment until confirmed progressive disease per immune-based therapeutics iRECIST, unacceptable toxicity, withdrawal of consent, initiation of subsequent therapy, or study termination, whichever occurs first

Objectives

Primary Objectives	Primary Endpoints
To evaluate the safety and tolerability of SGN-BB228	• Type, incidence, severity, seriousness, and relatedness of AEs and type, incidence, and severity of laboratory abnormalities
To identify the MTD of SGN-BB228	• Incidence of DLTs
To identify a recommended dose and schedule for SGN-BB228	• Incidence of DLTs and cumulative safety by dose level
Secondary Objectives	**Secondary Endpoints**
To assess the immunogenicity of SGN-BB228	• Incidence of ADAs
To assess the PK of SGN-BB228	• Estimates of PK parameters including AUC, C_{max}, T_{max}, apparent terminal $t_{1/2}$, and C_{trough}. Additional analytes may be evaluated, as necessary
To assess the antitumor activity of SGN-BB228	• ORR (per RECIST v1.1), DOR, PFS, and OS

Assessments

- Safety assessments include recording of AEs, concomitant medications, physical examination findings, and laboratory tests, presented as descriptive statistics
- MTD and/or recommended dose of SGN-BB228 will be identified through the modified Toxicity Probability Interval design[6]
- Response will be assessed by radiographic tumor evaluation at screening and every 6 weeks and at EOT, through progressive disease or initiation of subsequent therapy
- Antitumor activity will be determined by ORR as defined by RECIST v1.1
- DOR, PFS, and OS will be estimated by using the Kaplan-Meier method
- Blood samples for PK and ADA analyses will be collected at protocol-defined time points for PK and immunogenicity assessments
- Safety and antitumor activity will be summarized by using the all treated subjects analysis set

Summary

- The SGNBB228-001 (NCT05571839) study is evaluating the safety, tolerability, PK, and antitumor activity of SGN-BB228 in patients with advanced melanoma and other solid tumors
- SGN-BB228 is an investigational costimulatory antibody Anticalin (Mabcalin) bispecific molecule directed to CD228 and 4-1BB
- Enrollment is ongoing in the USA and planned for Europe and Canada

References

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Abbreviations

4-1BB, CD137; ADA, antidrug antibody; AE, adverse event; AUC, area under the curve; BRAF, B-Raf proto-oncogene, serine/threonine kinase; CD, cluster of differentiation; CD228, melanotransferrin; C_{max}, maximum serum concentration; CNS, central nervous system; C_{trough}, trough concentration; DLT, dose-limiting toxicity; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; MEK, mitogen-activated protein kinase kinase; MHC, major histocompatibility complex; MTD, maximum tolerated dose; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PD-1, programmed cell death protein 1; PD-L1, programmed cell death-ligand protein 1; PFS, progression-free survival; PK, pharmacokinetic; RECIST, Response Evaluation Criteria in Solid Tumors; $t_{1/2}$, half life; TCR, T-cell receptor; T_{max}, time to maximum serum concentration; USA, United States of America

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