VELOCITY-Lung A Phase 2 Study Evaluating Safety and Efficacy of Sacituzumab Govitecan + Zimberelimab + Etrumadenant in Patients With Advanced or Metastatic Non-Small Cell Lung Cancer (NSCLC) Progressing on or After Platinum-Based Chemotherapy and Checkpoint Inhibitors

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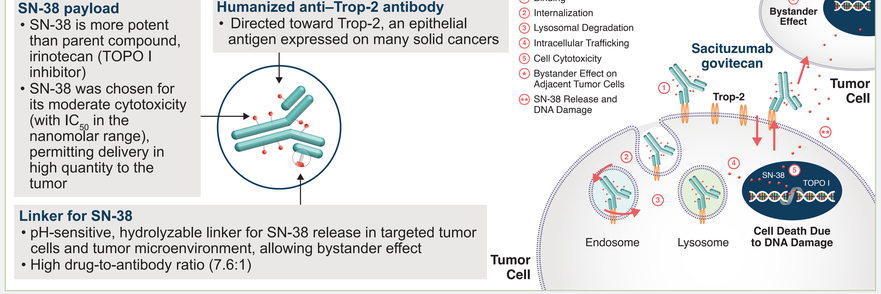
Background

- Lung cancer (of which non-small cell lung cancer [NSCLC] makes up 85%) is the leading cause of cancer-related deaths in the United States, with a 5-year survival rate of 6% for patients diagnosed with distant metastases[1,2]
- Single-agent chemotherapy is the standard of care for patients with metastatic NSCLC progressing on or after platinum-based chemotherapy and checkpoint inhibitors (CPI) but is associated with poor outcomes[2,3]
- Sacituzumab govitecan is an antibody-drug conjugate (**Figure 1**) approved by the US Food and Drug Administration (FDA) for patients with metastatic triple-negative breast cancer who received ≥2 prior chemotherapies (≥1 in the metastatic setting) and has FDA-accelerated approval for patients with locally advanced or metastatic urothelial cancer who have previously received a platinum-containing chemotherapy and either programmed cell death receptor-1 (anti–PD-1) or programmed cell death-ligand 1 (anti-PDL-1) inhibitor[4]
- Sacituzumab govitecan monotherapy demonstrated an objective response rate of 17%, with a manageable safety profile in 54 patients with metastatic NSCLC who had multiple prior therapies,[5] and a phase 3 study is currently ongoing in this population (NCT05089734)
- Zimberelimab (anti–PD-1) and etrumadenant (dual adenosine receptor antagonist) (**Figure 2**) are under clinical investigation for antitumor activity[6]; combination treatment including zimberelimab + etrumadenant has been well tolerated, with a manageable safety profile[7]
- Here, we describe the design of substudy-02 of the VELOCITY-Lung phase 2 platform study (NCT05633667), which will evaluate efficacy and safety of novel treatment combinations, including sacituzumab govitecan + zimberelimab + etrumadenant, in patients with advanced or metastatic NSCLC progressing on or after platinum-based chemotherapy and CPI

Figure 1. Sacituzumab Govitecan: A Novel[6] Antibody-Drug Conjugate[8-11]



Adapted from Rugo HS, et al. TROPiCS-02: A Phase III study investigating sacituzumab govitecan in the treatment of HR+/HER2- metastatic breast cancer. *Future Oncol.* 2020;16:705-715.
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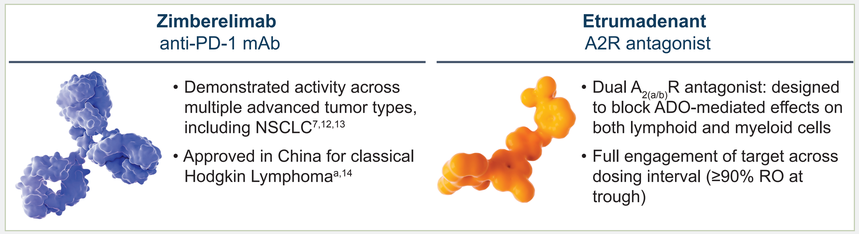
IC_{50}, half maximal inhibitory concentration; TOPO I, topoisomerase I; Trop-2, trophoblast cell surface antigen 2.

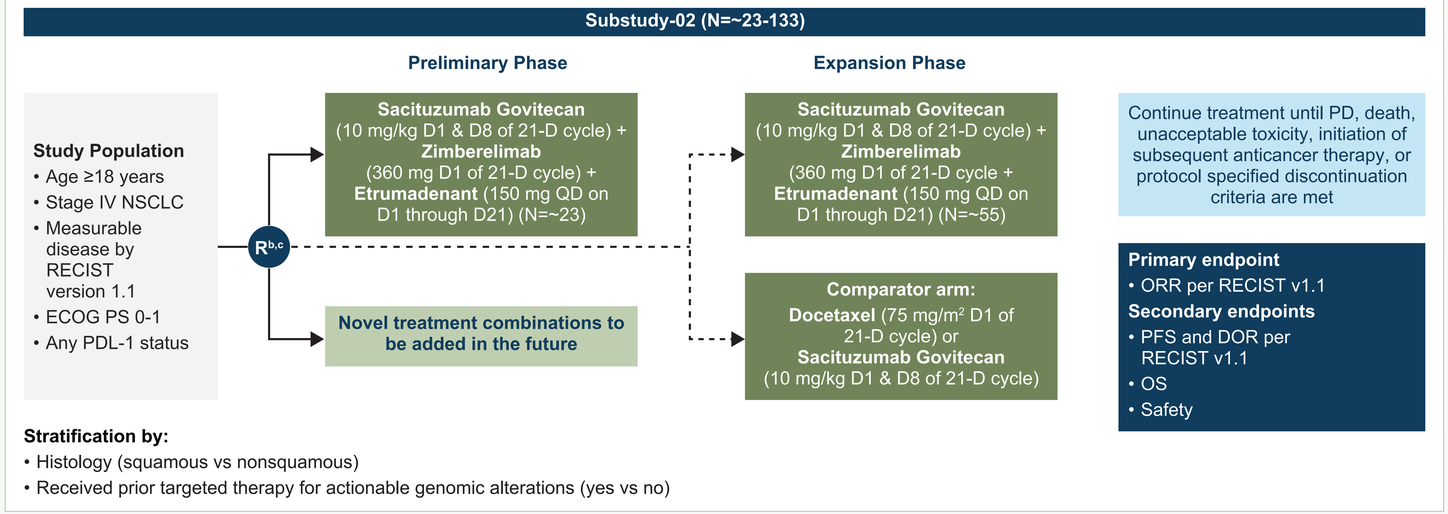
Figure 2. Combined Inhibition of PD-1, and the Adenosine (ADO) Axis May Enhance Anti-Cancer Immune Responses



[a]Gloria Biosciences secured approval in China for zimberelimab and conducts its activities independently of Arcus.
ADO, adenosine; A2R, adenosine 2a and 2b receptor; mAb, monoclonal antibody; NSCLC, non-small cell lung cancer; PD-1, programmed cell death protein 1; RO, receptor occupancy.

Methods

Figure 3: VELOCITY-Lung: An Open-Label, Multicenter, Randomized, Phase 2 Platform Study of Novel Treatment Combinations in Patients With Advanced or Metastatic NSCLC Progressing on or After PT-Based Chemotherapy and CPI (NCT05633667)[a]



[a]Substudy-01 evaluates novel treatment combinations in treatment-naive mNSCLC. [b]Subjects will be recruited and randomized to the expansion phase treatment and comparator arms only if the treatment passes preliminary stage.
[c]The randomization ratio will be determined by the sponsor depending on the number of experimental arms initiated in the expansion stage, the comparator arm, and any newly added preliminary stage treatment arms.
CPI, checkpoint inhibitor; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PD, progressive disease; PDL-1, programmed cell death ligand 1; PFS, progression-free survival; PT, platinum; R, randomization; RECIST, Response Evaluation Criteria in Solid Tumors.

Key Eligibility Criteria (Substudy-02)

Inclusion

- ✓ Patients with nonsquamous histology must have *EGFR* and *ALK* alterations evaluated
- ✓ Patients with actionable gene mutations must have received 1 previous approved targeted therapy appropriate to the genomic alteration
- ✓ Progression or recurrence after PT-based chemotherapy and CPI given either in combination or sequentially

Exclusion

- ✗ Mixed SCLC and NSCLC histology
- ✗ Previous topo-1 inhibitor (including as ADC), Trop-2 targeting agent, docetaxel
- ✗ Known active CNS metastases and/or carcinomatous meningitis[a]
- ✗ Active autoimmune disease or secondary malignancy

[a]Patients with previously treated brain metastases with stable CNS disease for at least 4 weeks are permitted.
ADC, antibody-drug conjugate; ALK, anaplastic lymphoma kinase; CNS, central nervous system; CPI, checkpoint inhibitor; EGFR, epidermal growth factor receptor; NSCLC, non-small cell lung cancer; PT, platinum; RECIST, Response Evaluation Criteria in Solid Tumors; SCLC, small-cell lung cancer; TOPO-I, topoisomerase type 1; Trop-2, trophoblast cell surface antigen 2.

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VELOCITY-Lung Contacts

- Enrollment for VELOCITY-Lung Trial (NCT05633667) is currently ongoing
- For more information, please visit www.clinicaltrials.gov
- Contact email: mmm@gilead.com

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