Figure 1. Sacituzumab govitecan: a novel antibody-drug conjugate

- SN-38 payload
- SN-38 is more potent than parent compound, irinotecan (TOPO I inhibitor)
- ORR by central review
- OS 10.9 months
- Manageable safety profile
- High drug-to antibody ratio (7:1)
- Directed toward Trop-2, an epithelial marker in cancer
- SN-38 is more potent than parent compound, irinotecan (TOPO I inhibitor)
- Bystander effect on adjacent tumor cells
- Cell death due to DNA damage
- Cancer cell lysis
- Tumor cell death

Study Objective

- Cohort 4 of TROPHY-U-01 is evaluating the safety, tolerability, and activity of SG + cisplatin as induction therapy followed by maintenance therapy with SG + avelumab in cisplatin-ineligible patients with mUC or unresectable locally advanced disease

Figure 2. Cohort 4 study design in TROPHY-U-01, a phase 2, open-label study of sacituzumab govitecan in unresectable locally advanced/metastatic urothelial cancer (mUC)

- Dose escalation 1
- Dose escalation 2
- Dose expansion

Key Eligibility Criteria

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Inclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>&gt; 18 years, with 3-month life expectancy</td>
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<tr>
<td>Histologically documented locally advanced or mUC</td>
<td>Measurable disease by CT or MRI per RECIST 1.1</td>
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<tr>
<td>Cisplatin-eligible</td>
<td>No prior therapy, specifically platinum-based chemotherapy in the metastatic or unresectable locally advanced setting</td>
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<tr>
<td>Adequate blood counts without transfusion or growth factor support within 2 weeks of study drug initiation</td>
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<tr>
<td>Adequate hepatic function, ECOG PS 0-1</td>
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<tr>
<td>Adequate renal function, CrCl ≥ 50 mL/min</td>
<td></td>
</tr>
</tbody>
</table>

Exclusion

- Refractory to platinum (ie, relapse ≤ 12 months after completion of chemotherapy) in neoadjuvant/adjuvant setting
- Prior antitumor monoclonal antibody within 4 weeks of study drug initiation
- Prior chemotherapy, targeted small molecule therapy, or radiation therapy within 2 weeks of study drug initiation
- Active autoimmune disease that required systemic treatment within 2 years of study drug initiation
- History or evidence of intestinal liver disease or non-infectious pneumonitis
- Active CNS metastases and/or carcinomatous meningitis
- Grade ≥ 2 hearing loss
- Grade ≥ 2 peripheral neuropathy
- Active cardiac disease
- Active chronic inflammatory bowel disease or GI perforation within 6 months of entry

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Contact email: GileadClinicalTrials@gilead.com

For more information, please visit https://clinicaltrials.gov/ct2/show/NCT03547973

Study enrollment for TROPHY-U-01 (NCT03547973) Cohort 4 began in February 2021 and is currently ongoing. Overall, enrollment will occur at ~120 sites globally.