BACKGROUND
• Multiple lines of evidence suggest that invariant NKT (iNKT) cells generate an inflammatory cascade that promotes and sustains sickle cell vasoincision.
• In prior studies of mouse models and patients with sickle cell disease (SCD), iNKT cells are increased in number and more likely to be activated compared to controls. Depleting

OBJECTIVE
To determine the safety, maximum tolerated dose, pharmacokinetics, and pharmacodynamics of NKTT120 in steady state adult with SCD. The optimal dose for a phase 1 study of NKTT120 will deplete iNKT cells for approximately 3 months allowing for periodic dosing.

METHODS
• Phase 1 study utilizing a 3+3 design to evaluate single doses escalated over a range from: 0.001 mg/kg to 1.0 mg/kg (0.001, 0.003, 0.01, 0.03, and 0.10 mg/kg)
• Primary outcome measure:
  • Dose limiting toxicity is defined as an adverse event grade 3 or higher on NCI-CTCAE version 4.0 with exceptions for SCD and NKTT specific events.
• Secondary outcome measures:
  • Pain: analog scale, quality of life (QoL), pulmonary function
  • During a screening run-in period and after dosing of NKTT120, subjects will maintain a daily smartphone eDiary (eDiPaP) to report pain, respiratory symptoms and analog use. ASCO-N and PROMIS QoL questionnaires will be administered at clinic visits. The screening run-in outcomes will be used as baseline comparison for values obtained post dosing.

RESULTS
• Eleven patients have been dosed to date.
  • 20 dose cohort (1) (0.01 mg/kg) subjects have recovered iNKT cells to baseline levels.
  • Currently in fourth dosing cohort (0.03 mg/kg).
  • No observed dose limiting toxicities, events of interest or serious adverse events.

Table 1. NKTT safety data. Eleven participants have been dosed with NKTT120 and 9 participants have recovered % iNKT cells to baseline.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Occurrence</th>
<th>Subject Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose limiting toxicities</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Events of interest</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Serious adverse events</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Adverse events</td>
<td>17</td>
<td>[1 were possibly or probably related: Subject 100-010 (dose cohort 1) dizziness, pruritus x 2</td>
</tr>
<tr>
<td>Lab safety signals</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

Table 1: NKTT safety data. Eleven participants have been dosed with NKTT120 and 9 participants have recovered % iNKT cells to baseline.

CONCLUSIONS
In stable adult patients with SCD:
• NKTT120 rapidly depletes iNKT cells.
• No dose limiting toxicities, events of interest or serious adverse events have been observed in 11 subjects.
• In two subjects with a lower baseline % of iNKT cells, plasma levels of NKTT120 were higher and time to recovery of iNKT cells was longer compared to other subjects with a higher % of iNKT cells at baseline.
• The relationship between NKTT120 dose and % of iNKT cells at baseline will be explored with additional subjects. Potentially, dosing of NKTT120 will differ depending on baseline % of iNKT cells.
• NKTT120 holds promise for reducing inflammation and preventing vaso-occlusion in patients with SCD.

Figure 1. Effect of NKTT120 on % iNKT cells of CD3+ T cells. Three NKTT120 dose cohorts have had iNKT cell recovery following dosing. NKTT120 depletes iNKT cell % below lower limit of quantification (LLOQ) generally in 6 hours.

Figure 2. Pharmacokinetics of NKTT120. Pharmacokinetics of NKTT120 in dose cohorts 1, 2 and 3. Subjects 101-003 and 100-010 demonstrated higher levels of NKTT120.

Figure 3. Pharmacodynamics of NKTT120. Pharmacodynamics of NKTT120 in the 8 subjects that have recovered iNKT cell levels to baseline. Subjects 101-003 and 100-010 with lower baseline iNKT cell percentage had longer time to recovery of iNKT cells. Some subjects achieved higher peak concentrations as shown in Figure 2.