Introduction

- FASN inhibition is a novel approach to cancer treatment.
- Selective disruption of palmitate biosynthesis leads to apoptosis in many tumor cells.
- FASN expression correlates with poor prognosis in certain tumor types including NSCLC (Visca et al., 2004).
- TVB-2640 is the only selective FASN inhibitor in clinical trials.
- Preliminary data show: Broad mono-therapy activity in multiple solid tumors, including 60% (3 of 5) NSCLC KRAS-Mut patients with > 12 weeks SD. Well tolerated with majority grade 1-2 adverse events at the MTD; even when combined with paclitaxel.

FASN: An Integrated Target in Tumor Biology

- Markedly higher in NSCLC patients compared to normal donors.
- NSCLC serum FASN among the highest expression of >10 tumour types tested.

Objective

- Safety, MTX, PK, recommended Phase-2 dose (monotherapy and in combination with chemo) and preliminary activity.
- Biomarkers of response and pharmacodynamic biomarkers.

Study Design & Key Eligibility Criteria

- Oral, once daily; 21 days in monotherapy or 28 days with a taxane; continuous cycles.
- Adult patients (ECOG 0-1), with pathologically confirmed metastatic or advanced-stage solid tumors, standard accepted Ph-1 Inclusion criteria.
- Clinically significant ophthalmologic finding, including history of dry eye, excluded.
- FASN Serum ELISA

Pharmacodynamics

- TVB-2640 inhibits FASN and de novo lipogenesis

NSCLC Preliminary Anti-Tumor Activity

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Response</th>
<th>Previous Taxane Treatment*</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSCLC KRAA-MUT</td>
<td>SD &gt; 12 weeks</td>
<td>3 of 5</td>
<td>N/A 1 KRAA-MUT SD = 42 weeks</td>
</tr>
<tr>
<td>NSCLC KRAA-WT</td>
<td>SD &gt; 12 weeks</td>
<td>0 of 5</td>
<td>N/A</td>
</tr>
<tr>
<td>NSCLC KRAA-MUT</td>
<td>SD &gt; 12 weeks</td>
<td>3 of 5</td>
<td>1 Confirmed PR</td>
</tr>
<tr>
<td>NSCLC KRAA-WT</td>
<td>SD &gt; 12 weeks</td>
<td>3 of 6</td>
<td>3 of 6 1 KRAS-WT SD=16 weeks</td>
</tr>
</tbody>
</table>

* # of average prior regimens (including taxane) #

Conclusions

- TVB-2640 demonstrates a favorable tolerability profile with no significant GI, hematologic or serum chemistry adverse events; no evidence of QTc prolongation by Holter monitoring.
- Biomarker analysis demonstrates target engagement (FASN inhibition), and inhibition of lipogenesis in patients.
- NSCLC KRAA-MUT patients remain on study longer than NSCLC KRAA-WT patients, when treated with TVB-2640 monotherapy.
- Further exploration of biological activity is underway in heavily pretreated ovarian and breast cancer patients in combination with paclitaxel:
  - Breast: 3 confirmed PRs and 8 SDs > 12 weeks.
  - Ovarian/Pelitoneal: 1 confirmed PR and 58-98% decreases in tumor marker CA-125 in n=6 patients.
  - High baseline serum FASN associated with longest duration on study, a potential patient selection marker.

For more information, please contact: Emma.Dean@christie.nhs.uk.

Thank You to the Patients and Their Families

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