**Introduction and Highlights**

- SL 801 is a reversible XPO1 inhibitor that offers the potential for improved safety profile / therapeutic window.
- Initial results from this ongoing Phase 1 dose escalation trial indicate that SL 801 demonstrates a manageable safety and tolerability profile, with minimal 1/3 dose escalations (AEs) seen to date.
- No maximum tolerated dose (MTD) reached; Dose escalation ongoing: 100 mg (5 mg/day) currently enrolling.
- Multiple cases of stable disease (SD) in a heavily pretreated solid tumor patient population.
- Pharmacokinetic (PK) analyses suggest dose dependent increases in exposure; studies ongoing.
- Select ideal therapeutic dosing is yet to be determined as dose escalation continues.
- Given favorable data profile thus far with SL 801, coupled with clinical validation of the XPO1 target, additional SL 801 trials, including in hematologic cancers and combination studies, planned.

**Background**

**SL-801 Background**

- SL 801 is orally administered, novel small molecule XPO1 (Exportin 1) inhibitor.
- SL 801 is a key nuclear transport oncoprotein overexpressed in a variety of cancers.
- Initiation of XPO1 has been clinically validated in multiple phase 1 trials.
- SL 801 demonstratedpotential in vitro and in vivo activity against a wide array of solid and hematologic cancer models.
- SL 801 reversibly inhibits XPO1 offering the potential for a favorable therapeutic window.
- A Phase 1 Trial of SL 801 monotherapy in patients with advanced solid tumors is underway.
- Results from the ongoing dose escalation trial are reported here.

**XPO1 Background**

- XPO1 is the key mediator of nuclear-cytoplasmic transport and is involved in the export of most of 200 nuclear proteins, including:
  - tumor suppressor proteins (p53, ARF, Rb, BRCA1, FOXO family proteins)
  - cell cycle inhibitors (p16, p21, p27)
  - transcription factors (HIF)
  - cytoprotective proteins (CASP-8, DFF40)
  - immune response regulators (IκB)
  - molecular chaperones (hsp60)
- XPO1 also exports specific subset of messenger riboncucleic acid (mRNA) via export adaptor proteins
- Mislocalization of a nuclear protein into the cytoplasm can result in poor efficacy as a tumor suppressor
- XPO1 is overexpressed in various solid tumors, including breast, ovarian, and pancreatic cancers, gliomas, gliomas, and melanomas, as well as hematologic malignancies, including acute myelogenous leukemia, chronic lymphocytic leukemia, multiple myeloma, and lymphomas.
- XPO1 overexpression has been associated with drug resistance, including being correlated with tumor grade, size, metastasis, resistance to chemotherapy, as well as shorter progression-free survival (PFS) and overall survival (OS).

**Mechanism of Action and Rational**

- SL 801 is a reversible XPO1 inhibitor: Potential for improved safety profile / therapeutic window.
- Potentially profi tive in vitro and vivo activity against multiple cancer types.

**Study Design**

**Inclusion / Exclusion Criteria**

- Select inclusion criteria
  - Patients with locally advanced and/or unresectable or metastatic solid tumors with histologically confirmed diagnosis
  - Age ≥ 18 years
  - Eastern Cooperative Oncology Group (ECOG) PS 0-1
  - Adequate hematologic and organ function
- Select exclusion criteria
  - Prior treatment with SL 801
  - Measurable disease and evaluable by RECIST 1.1
- Select inclusion criteria
  - Advanced (metastatic or locally advanced and unresectable) relapsed or refractory solid tumors with histologically confirmed diagnosis
  - Adequate hematologic and organ function
- Select exclusion criteria
  - Prior treatment with SL 801
  - Measurable disease and evaluable by RECIST 1.1
- Patients with locally advanced and/or unresectable or metastatic solid tumors with histologically confirmed diagnosis

**Safety and Tolerability**

**Treatment Related Adverse Events (AEs) (n=42 patients)**

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Febrile neutropenia</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>4 (9%)</td>
<td>1 (2%)</td>
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<tr>
<td>Hostile neutropenia</td>
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<td>2 (4%)</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
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<tr>
<td>Dysphagia</td>
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<tr>
<td>Osteopenia/Osteoporosis</td>
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<td>1 (2%)</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
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<tr>
<td>Increased AST</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
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</tbody>
</table>

**Pharmacokinetics**

- Pharmacokinetic (PK) analysis suggests dose dependent increases in SL 801 exposure.
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**Overview of Disease Control**

- Treatment Duration
  - Median duration of treatment: 14 cycles (46.9 wks).
  - Median duration of follow-up: 6 mo.

**Patient CT Scans**

- Imaging criteria: Response assessment was conducted using Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 and per investigator assessment.
- Imaging modality: Baseline and subsequent CT scans were obtained at the start of therapy and every 3 mo thereafter.

**References**