**Efficacy of AR-V7 inhibition in PCa tissues**

- Table 1: Summary of AR-V7 inhibition in PCa tissues

<table>
<thead>
<tr>
<th>Compound</th>
<th>AR-V7 inhibition activity</th>
<th>AR-V7 expression</th>
<th>AR-V7 driven gene expression</th>
</tr>
</thead>
<tbody>
<tr>
<td>EPI-7386</td>
<td>90%</td>
<td>50%</td>
<td>80%</td>
</tr>
<tr>
<td>Apalutamide</td>
<td>80%</td>
<td>60%</td>
<td>70%</td>
</tr>
<tr>
<td>Enzalutamide</td>
<td>70%</td>
<td>70%</td>
<td>60%</td>
</tr>
<tr>
<td>Bicalutamide</td>
<td>60%</td>
<td>80%</td>
<td>90%</td>
</tr>
</tbody>
</table>

**EPI-7386 demonstrates 20-fold improvement in inhibition of androgen-induced transcriptional activity**

- Figure 2: Efficacy of AR-V7 inhibition in PCa tissues

**AR inhibition is on target through the N-terminal DNA binding domain (DBD)**

- Figure 3: AR activity and sensitivity to AR-V7 inhibition

**EPI-7386 is active in castrated mice bearing enzalutamide-resistant and refractory AR dependent xenografts**

- Figure 4: Efficacy of AR-V7 inhibition in PCa tissues

**EPI-7386 is predicted to display a favorable pharmacokinetic profile in humans and can be dosed as a suspension to support toxicity studies**

- Figure 5: PK parameters for EPI-7386 in various species

**CONCLUSION**

- The next-generation AntiP compound EPI-7386 has been selected as the clinical candidate and displays:
  - Similar potency in vitro to the ‘locastine in full-length AR
  - Activity in several in vitro cell lines, including enzalutamide-resistant models
  - On target NTD inhibition demonstrated by activity on AR-V7-driven gene expression
  - Superior activity to enzalutamide, as single agent, or in combination in the VCaP xenograft tumors an enzalutamide-emerging xenograft tumor
  - Confirmed activity in the enzalutamide refractory xenograft tumors 22Rv1 and LNCaP (NS)
  - No off-target activity noticed in a non-functional AR PC3 xenograft tumor
  - Widespread therapeutic range as demonstrated by the dose response in VCaP xenografts
  - High exposure reachable in toxicology species with drug formulated as a suspension formulation

**First in human study**

- IND filing 1Q 2020, and phase 1 study starting soon thereafter

**Part 1a - Dose Escalation**

- Primary objectives: safety and tolerability of orally administered EPI-7386

**Part 1b - Dose Expansion**

- Primary objective: to further evaluate safety, tolerability, PK and preliminary anti-tumor activity of the NTD at 200 mg/kg of EPI-7386 (as measured by PSA 73rd day) in the LNCaP xenograft model after a single PO dose in male Beagle dogs

**Explanatory objectives: N
tesion, CH of relevant prostate cancer gene: AR, RB1, p53...**

*Chromogranin A, Tumor burden, AR V7 expression*