**RESULTS**

**FAP-2286 Potently and Selectively Binds Human FAP**  
- FAP-2286 demonstrated single-digit nanomolar affinity to FAP in both recombinant protein and cell-based assays.
- FAP-2286 inhibited FAP prostate activity with an IC50 value of 3.2 nM, whereas limited inhibition was observed against the closely related family members DPP4 and PREP.
- FAP-2286 was stable for at least 24 hours at 37°C in human plasma.

**FAP-2286 Biochemical and Cellular Characterisation**

<table>
<thead>
<tr>
<th>Assay Type</th>
<th>Test System</th>
<th>Readout (Units)</th>
<th>FAP-2286</th>
<th>Kd (nM, mean,SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Binding</td>
<td>Recombinant human FAP protein</td>
<td>KD (IC50)</td>
<td>1.4±0.5</td>
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<tr>
<td>Biodistribution</td>
<td>FAP-expressing XE-38</td>
<td>IC50 (nM)</td>
<td>2.7±0.9</td>
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</tr>
<tr>
<td>Inhibition</td>
<td>Human FAP prostate assay</td>
<td>IC50 (nM)</td>
<td>5.2±0.6</td>
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</tr>
<tr>
<td>Inhibition</td>
<td>Human DPP4 prostate assay</td>
<td>IC50 (nM)</td>
<td>&gt;50.0</td>
<td></td>
</tr>
<tr>
<td>Inhibition</td>
<td>Human PREP prostate assay</td>
<td>IC50 (nM)</td>
<td>&gt;3.0±0.0</td>
<td></td>
</tr>
<tr>
<td>Stability</td>
<td>Human plasma (24 h)</td>
<td>Remaining compound</td>
<td>10±0</td>
<td></td>
</tr>
</tbody>
</table>

**FAP-2286 Immunohistochemistry (IHC)**  
- FAP-2286 is expressed in a number of human tumors, and a proportion of sarcomas expressed FAP.

**Antitumour Activity of **$^{177}$Lu-FAP-2286 in FAP-expressing Sarcoma Patient-derived Xenograft Model**  
- In vivo imaging in mice after IV injection showed $^{177}$Lu-FAP-2286 uptake in FAP-positive xenografts at all time points evaluated.
- For sarcoma tumours, 3 hours after 30 or 60 MBq doses of $^{177}$Lu-FAP-2286, tumour uptake was 4.2 and 5.9 %ID/g, respectively.
- The tumour-to-kidney ratios at 3 weeks were 4.4 and 4.9 for the 30 or 60 MBq treated group, respectively (data not shown).

**FAP Immunohistochemistry**  
- IHC confirmed high levels of expression in multiple tumour types including pancreas, breast, and sarcoma.
- Tumor FAP expression is confirmed to the CAF/stroma for most of the epithelial cancers, and a proportion of sarcomas expressed FAP on the tumour cells in addition to the CAFs.
- Expression in normal tissue was limited (data not shown).

**Summary**

- FAP-2286 potently and selectively binds FAP.
- Compelling anti-tumour efficacy of $^{177}$Lu-FAP-2286 was observed in FAP-expressing tumour models.
- Investigational New Drug Application (IND) submission planned for late 2020.
- Clinical studies in a broad spectrum of FAP-positive cancers are planned.