Supporting Information

The i.v. administration of $^{14}$C-Q[7] as bolus injections in Rats.

Plasma Radioactivity vs Time Data:

**Table S1.** Pharmacokinetic parameters determined following i.v. administration of $^{14}$C-Q[7] in rats.

<table>
<thead>
<tr>
<th>Dose Route</th>
<th>Rat #</th>
<th>$k_{\text{elim}}$ (h$^{-1}$)</th>
<th>$t_{1/2}$ (h)</th>
<th>$C_{\text{max}}$ (dpm)</th>
<th>$T_{\text{max}}$ (h)</th>
<th>CL (L/h/kg)</th>
<th>Vd (L/kg)</th>
<th>AUC$_{0-\text{inf}}$ (dpm.h/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>i.v.</td>
<td>1</td>
<td>0.0571</td>
<td>12.1</td>
<td>12416</td>
<td>0.033</td>
<td>0.426</td>
<td>7.46</td>
<td>151732</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>0.0456</td>
<td>15.2</td>
<td>12730</td>
<td>0.033</td>
<td>0.398</td>
<td>8.73</td>
<td>162317</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>0.063</td>
<td>11.0</td>
<td>11274</td>
<td>0.033</td>
<td>0.374</td>
<td>5.94</td>
<td>172685</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>0.053</td>
<td>13.0</td>
<td>13242</td>
<td>0.033</td>
<td>0.365</td>
<td>6.88</td>
<td>177317</td>
</tr>
<tr>
<td><strong>Mean</strong></td>
<td></td>
<td><strong>0.0547</strong></td>
<td><strong>12.8</strong></td>
<td><strong>12416</strong></td>
<td><strong>0.033</strong></td>
<td><strong>0.391</strong></td>
<td><strong>7.25</strong></td>
<td><strong>166013</strong></td>
</tr>
</tbody>
</table>

$k_{\text{elim}}$ = terminal elimination rate constant; $t_{1/2}$ = terminal elimination half life; $C_{\text{max}}$ = the maximum plasma concentration; $T_{\text{max}}$ = time of the maximum plasma concentration; CL = clearance (i.e. volume of blood cleared of Q[7] per unit time); Vd = volume of distribution; and AUC$_{0-\text{inf}}$ = area under the plasma concentration versus time curve from time 0 to infinity.

**Figure S1.** Radioactivity (DPM) for Q[7] plasma concentration in rats after administration of $^{14}$C-Q[7] by i.v. as bolus injections.
Urine Radioactivity vs Time Data

Table S2. Radioactivity (DPM) in urine samples following i.v. administration of $^{14}$C-Q7 as bolus injections.

<table>
<thead>
<tr>
<th></th>
<th>0-4 h</th>
<th>4-8 h</th>
<th>8-24 h</th>
<th>24-48 h</th>
<th>Cage Washing</th>
<th>Total Recovery</th>
<th>Percent of Dose Excreted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rat 1</td>
<td>4852866</td>
<td>4142859</td>
<td>2022073</td>
<td>377471</td>
<td>72897</td>
<td>11468167</td>
<td>59.5</td>
</tr>
<tr>
<td>Rat 2</td>
<td>12854798</td>
<td>2480755</td>
<td>1412505</td>
<td>152982</td>
<td>45173</td>
<td>16946212</td>
<td>87.6</td>
</tr>
<tr>
<td>Rat 3</td>
<td>5752995</td>
<td>2365865</td>
<td>2022817</td>
<td>418883</td>
<td>96703</td>
<td>10657263</td>
<td>55.5</td>
</tr>
<tr>
<td>Rat 4</td>
<td>11204991</td>
<td>1343240</td>
<td>2720213</td>
<td>675977</td>
<td>169972</td>
<td>16114394</td>
<td>84.0</td>
</tr>
<tr>
<td>Mean</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>71.6</td>
</tr>
<tr>
<td>SD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>16.5</td>
</tr>
</tbody>
</table>

Oral-dosed Rats $^{14}$C-Q[8]

Table S3. Pharmacokinetic parameters determined following oral administration of $^{14}$C-Q[8] (plasma)

<table>
<thead>
<tr>
<th>Dose Route</th>
<th>Rat #</th>
<th>$k_{elum}$ (h$^{-1}$)</th>
<th>$t_1/2$ (h)</th>
<th>$C_{max}$ (dpm)</th>
<th>$T_{max}$ (h)</th>
<th>CL (L/h/kg)</th>
<th>Vd (L/kg)</th>
<th>AUC$_{0-inf}$ (dpm.h/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>oral</td>
<td>1</td>
<td>0.042</td>
<td>16.4</td>
<td>71.3</td>
<td>2</td>
<td>1.74</td>
<td>41.5</td>
<td>14090</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>0.036</td>
<td>19.4</td>
<td>72.5</td>
<td>2</td>
<td>1.59</td>
<td>44.2</td>
<td>154</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>0.031</td>
<td>22.4</td>
<td>71.3</td>
<td>0.5</td>
<td>1.21</td>
<td>38.9</td>
<td>20360</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>0.032</td>
<td>21.9</td>
<td>68.4</td>
<td>2</td>
<td>1.19</td>
<td>37.1</td>
<td>20660</td>
</tr>
<tr>
<td>Mean</td>
<td>0.035</td>
<td>20.0</td>
<td>70.9</td>
<td>2</td>
<td>1.43</td>
<td>40.4</td>
<td>17635</td>
<td></td>
</tr>
</tbody>
</table>
Figure S2. $^{14}$C-Q[8] (DPM) following oral administration of Q[8] (unlabeled and labeled) as a bolus injection.

Table S4. Radioactivity (DPM) in faeces samples following oral administration of $^{14}$C-Q[8] as a single bolus dose.

<table>
<thead>
<tr>
<th>Faeces Recovery (DPM)</th>
<th>Percent of Dose Excreted</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0-4 h</td>
</tr>
<tr>
<td>Rat 5</td>
<td>*</td>
</tr>
<tr>
<td>Rat 6</td>
<td>*</td>
</tr>
<tr>
<td>Rat 7</td>
<td>*</td>
</tr>
<tr>
<td>Rat 8</td>
<td>145</td>
</tr>
<tr>
<td>Mean</td>
<td></td>
</tr>
<tr>
<td>SD</td>
<td></td>
</tr>
</tbody>
</table>

*No sample available
Organ Radioactivity Recovery

**Table S5.** Radioactivity excreted in organs 2h following oral administration of $[^{14}C]$-Q8 as bolus injections.

<table>
<thead>
<tr>
<th>Organ</th>
<th>Rat 9</th>
<th>Rat 10</th>
<th>Rat 11</th>
<th>Rat 12</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>µCi/g tissue</td>
<td>% of dose</td>
<td>µCi/g tissue</td>
<td>% of dose</td>
<td>µCi/g tissue</td>
<td>% of dose</td>
</tr>
<tr>
<td>Stomach</td>
<td>0.306</td>
<td>48.63</td>
<td>0.267</td>
<td>62.59</td>
<td>0.173</td>
<td>45.82</td>
</tr>
<tr>
<td>Small Intestine</td>
<td>0.222</td>
<td>81.72</td>
<td>0.272</td>
<td>97.17</td>
<td>0.120</td>
<td>56.66</td>
</tr>
<tr>
<td>Large Intestine</td>
<td>0.001</td>
<td>0.19</td>
<td>0.001</td>
<td>0.22</td>
<td>0.001</td>
<td>0.14</td>
</tr>
<tr>
<td>Liver</td>
<td>0.001</td>
<td>0.22</td>
<td>0.000</td>
<td>0.16</td>
<td>0.001</td>
<td>0.22</td>
</tr>
<tr>
<td>Kidney</td>
<td>0.001</td>
<td>0.06</td>
<td>0.001</td>
<td>0.07</td>
<td>0.001</td>
<td>0.06</td>
</tr>
<tr>
<td>Spleen</td>
<td>0.000</td>
<td>0.01</td>
<td>0.001</td>
<td>0.02</td>
<td>0.001</td>
<td>0.02</td>
</tr>
<tr>
<td>Brain</td>
<td>0.002</td>
<td>0.10</td>
<td>0.000</td>
<td>0.01</td>
<td>0.000</td>
<td>0.01</td>
</tr>
<tr>
<td>Bladder</td>
<td>0.008</td>
<td>0.05</td>
<td>0.006</td>
<td>0.12</td>
<td>0.006</td>
<td>0.09</td>
</tr>
<tr>
<td>Total Recovery</td>
<td>130.97</td>
<td>160.37</td>
<td>103.0</td>
<td></td>
<td>131.45</td>
<td>28.68</td>
</tr>
</tbody>
</table>

*Animal died following dosing

**Table S6.** Radioactivity excreted in organs 6h following oral administration of $[^{14}C]$-Q8 as Bolus Injections.

<table>
<thead>
<tr>
<th>Organ</th>
<th>Rat 13</th>
<th>Rat 14</th>
<th>Rat 15</th>
<th>Rat 16</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>µCi/g tissue</td>
<td>% of dose</td>
<td>µCi/g tissue</td>
<td>% of dose</td>
<td>µCi/g tissue</td>
<td>% of dose</td>
</tr>
<tr>
<td>Stomach</td>
<td>0.086</td>
<td>11.28</td>
<td>0.438</td>
<td>56.58</td>
<td>0.110</td>
<td>13.81</td>
</tr>
<tr>
<td>Small Intestine</td>
<td>0.070</td>
<td>26.21</td>
<td>0.041</td>
<td>17.29</td>
<td>0.044</td>
<td>14.83</td>
</tr>
<tr>
<td>Large Intestine</td>
<td>0.283</td>
<td>75.64</td>
<td>0.098</td>
<td>26.26</td>
<td>0.370</td>
<td>88.64</td>
</tr>
<tr>
<td>Liver</td>
<td>0.001</td>
<td>0.21</td>
<td>0.001</td>
<td>0.29</td>
<td>0.001</td>
<td>0.44</td>
</tr>
<tr>
<td>Kidney</td>
<td>0.001</td>
<td>0.05</td>
<td>0.001</td>
<td>0.07</td>
<td>0.002</td>
<td>0.14</td>
</tr>
<tr>
<td>Spleen</td>
<td>0.001</td>
<td>0.03</td>
<td>0.002</td>
<td>0.05</td>
<td>0.002</td>
<td>0.04</td>
</tr>
<tr>
<td>Brain</td>
<td>0.000</td>
<td>0.02</td>
<td>0.001</td>
<td>0.03</td>
<td>0.000</td>
<td>0.02</td>
</tr>
<tr>
<td>Bladder</td>
<td>0.004</td>
<td>0.03</td>
<td>0.001</td>
<td>0.01</td>
<td>0.000</td>
<td>0.00</td>
</tr>
<tr>
<td>Total Recovery</td>
<td>113.5</td>
<td>100.6</td>
<td>117.7</td>
<td>111.2</td>
<td>110.73</td>
<td>7.29</td>
</tr>
</tbody>
</table>
Table S7. Radioactivity excreted in organs 24h following oral administration of $^{[14C]}$-Q8 as bolus injections.

<table>
<thead>
<tr>
<th>Organ</th>
<th>Rat 17</th>
<th>Rat 18</th>
<th>Rat 19</th>
<th>Rat 20*</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>µCi/g tissue</td>
<td>% of dose</td>
<td>µCi/g tissue</td>
<td>% of dose</td>
<td>µCi/g tissue</td>
<td>% of dose</td>
</tr>
<tr>
<td>Stomach</td>
<td>0.000</td>
<td>0.02</td>
<td>0.000</td>
<td>0.02</td>
<td>0.000</td>
<td>0.10</td>
</tr>
<tr>
<td>Small Intestine</td>
<td>0.001</td>
<td>0.38</td>
<td>0.001</td>
<td>0.25</td>
<td>0.001</td>
<td>0.29</td>
</tr>
<tr>
<td>Large Intestine</td>
<td>0.017</td>
<td>5.61</td>
<td>0.036</td>
<td>10.96</td>
<td>0.025</td>
<td>8.62</td>
</tr>
<tr>
<td>Liver</td>
<td>0.000</td>
<td>0.10</td>
<td>0.000</td>
<td>0.06</td>
<td>0.000</td>
<td>0.09</td>
</tr>
<tr>
<td>Kidney</td>
<td>0.000</td>
<td>0.01</td>
<td>0.000</td>
<td>0.02</td>
<td>0.001</td>
<td>0.08</td>
</tr>
<tr>
<td>Spleen</td>
<td>0.000</td>
<td>0.01</td>
<td>0.000</td>
<td>0.00</td>
<td>0.003</td>
<td>0.08</td>
</tr>
<tr>
<td>Brain</td>
<td>0.000</td>
<td>0.01</td>
<td>0.000</td>
<td>0.00</td>
<td>0.000</td>
<td>0.00</td>
</tr>
<tr>
<td>Bladder</td>
<td>0.000</td>
<td>0.00</td>
<td>0.000</td>
<td>0.00</td>
<td>0.000</td>
<td>0.00</td>
</tr>
<tr>
<td>Total Recovery</td>
<td>6.13</td>
<td></td>
<td>11.3</td>
<td></td>
<td>9.3</td>
<td></td>
</tr>
</tbody>
</table>

*Animal died following dosing

Figure S3. Time course for Q[8] to traverse the GIT