

## Supplementary Tables

### **<sup>177</sup>Lu-EC0800 Combined with the Antifolate Pemetrexed: Preclinical Pilot Study of Folate Receptor Targeted Radionuclide Tumor Therapy**

Josefine Reber,<sup>1</sup> Stephanie Haller,<sup>1</sup> Christopher P. Leamon,<sup>2</sup> and Cristina Müller<sup>1\*</sup>

<sup>1</sup>*Center for Radiopharmaceutical Sciences ETH-PSI-USZ, Paul Scherrer Institute, Villigen-PSI, Switzerland,* <sup>2</sup>*Endocyte Inc., West Lafayette, Indiana, U.S.*

**Supplementary Table S1.** Time-dependent biodistribution data of  $^{177}\text{Lu}$ -EC0800 (3 MBq, 1 nmol) in KB tumor bearing nude mice.

$^{177}\text{Lu}$ -EC0800					
Uptake (% ID/g)	1 h p.i.	4 h p.i.	24 h p.i.	48 h p.i.	72 h p.i.
blood	0.26 ± 0.05	0.11 ± 0.02	0.04 ± 0.04	0.02 ± 0.01	0.03 ± 0.00
lung	1.22 ± 0.05	0.81 ± 0.05	0.62 ± 0.07	0.41 ± 0.05	0.44 ± 0.03
spleen	0.76 ± 0.19	0.89 ± 0.78	0.24 ± 0.06	0.43 ± 0.02	0.67 ± 0.50
<b>kidneys</b>	<b>73.0 ± 11.2</b>	<b>73.7 ± 3.5</b>	<b>58.0 ± 3.8</b>	<b>51.2 ± 6.9</b>	<b>43.3 ± 2.6</b>
stomach	2.25 ± 0.25	1.75 ± 0.14	1.06 ± 0.07	0.92 ± 0.13	0.75 ± 0.16
intestines	0.69 ± 0.08	0.43 ± 0.09	0.30 ± 0.08	0.22 ± 0.04	0.24 ± 0.06
liver	5.13 ± 2.28	2.53 ± 0.57	1.68 ± 0.50	1.90 ± 0.33	2.11 ± 0.15
salivary glands	7.56 ± 0.18	4.88 ± 1.17	2.58 ± 0.57	2.37 ± 0.20	2.15 ± 0.10
muscle	1.21 ± 0.35	1.21 ± 0.15	0.70 ± 0.08	0.44 ± 0.02	0.47 ± 0.10
bone	1.23 ± 0.24	1.17 ± 0.12	0.72 ± 0.16	0.44 ± 0.04	0.50 ± 0.06
<b>tumor</b>	<b>7.05 ± 1.04</b>	<b>7.52 ± 1.15</b>	<b>7.00 ± 1.22</b>	<b>5.05 ± 0.71</b>	<b>3.02 ± 0.38</b>
$^{177}\text{Lu}$ -EC0800					
Ratios	1 h p.i.	4 h p.i.	24 h p.i.	48 h p.i.	72 h p.i.
tumor-to-blood	27.6 ± 3.4	72.5 ± 22.0	161.2 ± 58.6	265.4 ± 52.9	116.3 ± 15.5
tumor-to-liver	1.57 ± 0.63	3.11 ± 0.92	4.14 ± 1.42	2.74 ± 0.65	1.43 ± 0.10
tumor-to-kidney	0.10 ± 0.02	0.10 ± 0.01	0.12 ± 0.03	0.09 ± 0.01	0.07 ± 0.01

**Supplementary Table S2.** Calculation of synergism between PMX and <sup>177</sup>Lu-EC0800.

<b>KB tumor cells</b>					
viability	PMX <sup>1</sup> single agent	PMX <sup>1</sup> in combination	<sup>177</sup> Lu-EC0800 <sup>2</sup> single agent	<sup>177</sup> Lu-EC0800 <sup>2</sup> in combination	Combination Index <sup>3</sup>
55%	(D <sub>single</sub> ) <sub>PMX</sub>	(D <sub>comb</sub> ) <sub>PMX</sub>	(D <sub>single</sub> ) <sub><sup>177</sup>Lu-EC0800</sub>	(D <sub>comb</sub> ) <sub><sup>177</sup>Lu-EC0800</sub>	CI <sub>55</sub>
	1.59	0.15	0.06	0.03	0.63 ± 0.03
	1.59	1.20	0.06	< 0.01	0.70 ± 0.04
70%	(D <sub>single</sub> ) <sub>PMX</sub>	(D <sub>comb</sub> ) <sub>PMX</sub>	(D <sub>single</sub> ) <sub><sup>177</sup>Lu-EC0800</sub>	(D <sub>comb</sub> ) <sub><sup>177</sup>Lu-EC0800</sub>	CI <sub>70</sub>
	3.55	0.15	0.11	0.07	0.65 ± 0.02
	3.55	1.20	0.11	0.02	0.46 ± 0.05
	3.55	2.50	0.11	< 0.01	0.72 ± 0.02
<b>IGROV-1 tumor cells</b>					
viability	PMX <sup>1</sup> single agent	PMX <sup>1</sup> in combination	<sup>177</sup> Lu-EC0800 <sup>2</sup> single agent	<sup>177</sup> Lu-EC0800 <sup>2</sup> in combination	Combination Index <sup>3</sup>
55%	(D <sub>single</sub> ) <sub>PMX</sub>	(D <sub>comb</sub> ) <sub>PMX</sub>	(D <sub>single</sub> ) <sub><sup>177</sup>Lu-EC0800</sub>	(D <sub>comb</sub> ) <sub><sup>177</sup>Lu-EC0800</sub>	CI <sub>55</sub>
	1.86	0.20	1.07	0.56	0.63 ± 0.05
	1.86	0.60	1.07	0.39	0.69 ± 0.04
70%	(D <sub>alone</sub> ) <sub>PMX</sub>	(D <sub>comb</sub> ) <sub>PMX</sub>	(D <sub>alone</sub> ) <sub><sup>177</sup>Lu-EC0800</sub>	(D <sub>comb</sub> ) <sub><sup>177</sup>Lu-EC0800</sub>	CI <sub>70</sub>
	4.68	0.20	2.00	1.12	0.61 ± 0.01
	4.68	0.60	2.00	0.89	0.69 ± 0.03
	4.68	1.20	2.00	0.31	0.41 ± 0.07

<sup>1</sup>) PMX concentrations are indicated in μM, <sup>2</sup>) <sup>177</sup>Lu-EC0800 concentrations are indicated in MBq/mL

<sup>3</sup>) the combination index is calculated according to the formula:  $CI = (D_{comb})_{PMX} / ((D_{single})_{PMX} + (D_{comb})_{^{177}Lu-EC0800} / (D_{single})_{^{177}Lu-EC0800})$