

**Table S1 Efficacy of H5B14-Mediated RON Internalization in  
Comparison with Other Anti-RON mAbs**

| Cancer cell lines<br>(RON receptors<br>per cell)           | IE <sub>50</sub> values of different anti-RON mAbs in induction of<br>cell surface RON internalization (hours)* |                       |                  |                  |                       |                     |
|------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------|-----------------------|------------------|------------------|-----------------------|---------------------|
|                                                            | PCM5B14<br>(PSI domain)                                                                                         | H5B14<br>(PSI domain) | Zt/g4<br>(Sema)  | Zt/f12<br>(Sema) | Zt/c1<br>(IPT domain) | Zt/c11<br>(unknown) |
| <b>Colon LoVo<br/>(<math>&lt;100 \pm 13</math>)</b>        | No effect                                                                                                       | No effect             | No effect        | No effect        | No effect             | ND                  |
| <b>Colon HT-29<br/>(<math>18,793 \pm 278</math>)</b>       | $7.35 \pm 0.33$                                                                                                 | $5.32 \pm 0.53$       | $11.02 \pm$      | $19.11 \pm 1.88$ | $19.32 \pm 0.94$      | No effect           |
| <b>Colon DLD1<br/>(<math>4,480 \pm 352</math>)</b>         | $11.40 \pm 1.42$                                                                                                | $10.48 \pm 1.47$      | $15.81 \pm 2.44$ | $21.75 \pm 2.56$ | $27.83 \pm 1.11$      | ND                  |
| <b>Lung H1993<br/>(<math>2,152 \pm 208</math>)</b>         | $12.34 \pm 1.26$                                                                                                | $13.51 \pm 1.73$      | $24.72 \pm 3.84$ | $20.61 \pm 2.24$ | No effect             | ND                  |
| <b>Lung H2228<br/>(<math>10,207 \pm 278</math>)</b>        | $9.43 \pm 0.47$                                                                                                 | $8.62 \pm 0.68$       | $9.84 \pm 0.88$  | $11.43 \pm 1.67$ | $16.78 \pm 0.79$      | No effect           |
| <b>Lung H358<br/>(<math>15,286 \pm 366</math>)</b>         | $7.04 \pm 0.55$                                                                                                 | $7.84 \pm 0.69$       | $7.47 \pm 0.63$  | $13.47 \pm 0.78$ | $18.44 \pm 1.37$      | No effect           |
| <b>Pancreatic Panc-1<br/>(<math>&lt;100 \pm 4</math>)</b>  | No effect                                                                                                       | No effect             | No effect        | No effect        | No effect             | ND                  |
| <b>Pancreatic L3.6pl<br/>(<math>16,628 \pm 245</math>)</b> | $6.68 \pm 0.76$                                                                                                 | $8.24 \pm 0.61$       | $14.14 \pm 1.54$ | $18.46 \pm 1.22$ | $18.82 \pm 1.43$      | No effect           |
| <b>Pancreatic BxPC-3<br/>(<math>10,214 \pm 310</math>)</b> | $5.73 \pm 0.65$                                                                                                 | $7.52 \pm 0.49$       | $12.77 \pm 0.82$ | $14.56 \pm 0.83$ | $16.77 \pm 2.18$      | Not effect          |
| <b>Breast T-47D<br/>(<math>15,756 \pm 314</math>)</b>      | $9.34 \pm 0.84$                                                                                                 | $8.6 \pm 0.49$        | $23.46 \pm 2.88$ | $17.58 \pm 1.24$ | $21.34 \pm 1.39$      | ND                  |
| <b>Average</b>                                             | $8.66 \pm 2.36$                                                                                                 | $8.77 \pm 2.39$       | $14.90 \pm 6.23$ | $17.12 \pm 3.62$ | $19.90 \pm 3.83$      | No effect           |

\*Individual cell lines ( $1 \times 10^6$  cells per culture dish in triplicate) were treated at 37°C with 5 µg/ml of different anti-RON mAbs. Cells were collected at different time points, washed with acidic buffer to remove cell surface-bound IgG and then incubated with anti-RON mAb Zt/f2 as previously described [1]. Cell surface immunofluorescence was analyzed by a flow cytometer using FITC-coupled goat anti-human or mouse IgG, respectively. Immunofluorescence from cells treated with anti-RON mAbs at 4°C was set as 100%. Internalization efficacy was calculated as previously described [1-3].