

Supplementary Table S1: SIRP α , CD47 and EGFR expression levels on indicated cells expressed as the mean specific antibody binding capacity (sABC). N indicates the number of tests performed.

| Cell line / Receptor | SIRP α | | CD47 | | EGFR (panitumumab) | | EGFR (cetuximab) | |
|----------------------|---------------------|---|-----------|---|--------------------|---|------------------|---|
| | Mean sABC | N | Mean sABC | N | Mean sABC | N | Mean sABC | N |
| SW48 (006) | < 3300 [§] | 2 | 53681 | 5 | 104416 | 5 | 118262 | 5 |
| SW48 (115) | < 3300 [§] | 2 | 56096 | 5 | 98710 | 5 | 126366 | 5 |
| SW48 BRAF V600E | < 3300 [§] | 2 | 71094 | 2 | 47841 | 2 | 68095 | 2 |
| SW48 KRAS G12D | < 3300 [§] | 2 | 70397 | 2 | 74716 | 2 | 125488 | 2 |
| SW48 KRAS G13D | < 3300 [§] | 2 | 77390 | 2 | 143566 | 2 | 186522 | 2 |

§: Receptor expression is below the lowest calibration point of the Human IgG calibrator kit, namely 3300 receptors/cell.

Supplementary Table S2: Observed affinities (K_D -obs) for BYON4228-IgG1-L234A/L235A and BYON4228-IgG1 binding to Fc γ Receptors.

| Ligand | BYON4228-IgG1-L234A/L235A Observed affinities (K_D -obs) | SYD5664-IgG1* Observed affinities (K_D -obs) |
|--|--|--|
| Human Fc γ RIIIa (CD16a) | 15.1 μ M | 2.6 μ M |
| Human Fc γ RIIIb (CD16b) | > 16.7 μ M | 7.4 μ M |
| Human Fc γ RIIIa (CD32a H131 or R131) | > 16.7 μ M | 1.4 or 1.6 μ M |
| Human Fc γ RIIb (CD32b) | > 16.7 μ M | 6.5 μ M |
| Human Fc γ RI (CD64) | > 1.67 μ M | 2.5 nM |

* SYD5664 contains the variable domains of BYON4228 but has a wildtype IgG1 constant domain with wildtype effector functions.

Supplementary Table S3: BYON4228 PK in mice after single IV dose.

| Parameter | huSIRP α_{BIT} mice | | | C57BL/6 mice |
|-------------------------------------|----------------------------|----------|----------|--------------|
| | 3 mg/kg | 10 mg/kg | 30 mg/kg | 3 mg/kg |
| C_{max} (μ g/mL) | 44.2 | 197 | 581 | 45.2 |
| AUC _{last} (h* μ g/mL) | 1340 | 9810 | 36700 | 3390 |

Last sample taken at 168 h

Supplementary Table S4: BYON4228 PK in mice after single IP dose.

| Parameter | huSIRP α_{BIT} mice | | | C57BL/6 mice |
|-------------------------------------|----------------------------|----------|----------|--------------|
| | 3 mg/kg | 10 mg/kg | 30 mg/kg | 3 mg/kg |
| C_{max} (μ g/mL) | 21.9 | 78.5 | 311 | 29.8 |
| AUC _{last} (h* μ g/mL) | 940 | 8720 | 33400 | 3730 |

Last sample taken at 168 h

Supplementary Table S5: BYON4228 PK in monkey after a single IV dose

| Parameters | 1 mg/kg BYON4228 | 3 mg/kg BYON4228 | 10 mg/kg BYON4228 | 30 mg/kg BYON4228 | 100 mg/kg BYON4228 |
|--|---------------------|---------------------|----------------------|----------------------|-----------------------|
| $t_{1/2}$ (h) | 105 | 66.8 | 95.6 | 109 | 100 |
| C_{max} ($\mu\text{g/mL}$) | 27.2 | 90.5 | 278 | 930 | 1740 |
| AUC_{last} ($\text{h} \cdot \mu\text{g/mL}$) | 2010 | 5520 | 29100 | 131000 | 426000 |
| AUC_{inf} ($\text{h} \cdot \mu\text{g/mL}$) | 2080 | 6190 | 30400 | 143000 | 449000 |
| CL (mL/h/kg) | 0.496 | 0.485 | 0.329 | 0.218 | 0.229 |
| V_{ss} (mL/kg) | 55.8 | 47.0 | 44.2 | 37.6 | 41.5 |

Cynomolgus monkeys after single IV infusion of BYON4228, animals sampled for 3 weeks following dosing. Values are means of n=2, with one male and one female animal per dose group.

Supplementary Movies: Real-time phagocytosis was visualized using live-cell imaging. Panitumumab-opsonized (40 ng/mL) HT-29 tumor cells were labeled with pHrodo and co-incubated with unlabeled macrophages and BYON4228 (10 $\mu\text{g/mL}$). Images were taken every 3 minutes for 4 hours. The light-red tumor cells become bright red upon phagocytosis by macrophages.