

Supplementary Materials

# Preclinical Safety Evaluation of Intraperitoneally Administered Cu-Conjugated Anti-EGFR Antibody NCAB001 for the Early Diagnosis of Pancreatic Cancer using PET

**Table S1-1.** Hematological parameters after intraperitoneal administration of Cu-NCAB001 in male mice.

| Parameters          | Day 1 (n = 10) |                        |                        | Day 14 (n = 5) |              |
|---------------------|----------------|------------------------|------------------------|----------------|--------------|
|                     | Vehicle        | 62.5 µg/kg             | 625 µg/kg              | Vehicle        | 625 µg/kg    |
| RBC 10E4/µL         | 908 ± 33       | 899 ± 46               | 892 ± 37               | 925 ± 23       | 928 ± 55     |
| HGB g/dL            | 14.6 ± 0.4     | 14.5 ± 0.6             | 14.3 ± 0.5             | 14.6 ± 0.2     | 14.8 ± 0.8   |
| HCT %               | 48.3 ± 1.4     | 47.3 ± 1.9             | 47.0 ± 1.3             | 47.0 ± 0.5     | 47.9 ± 2.5   |
| MCV fL              | 53.3 ± 1.6     | 52.7 ± 1.0             | 52.8 ± 1.7             | 50.9 ± 0.8     | 51.5 ± 1.4   |
| MCH pg              | 16.1 ± 0.5     | 16.2 ± 0.4             | 16.0 ± 0.5             | 15.8 ± 0.2     | 15.9 ± 0.6   |
| Reticulocyte %      | 3.3 ± 0.4      | 3.2 ± 0.5              | 3.3 ± 0.5              | 3.3 ± 0.6      | 2.8 ± 0.3    |
| Reticulocyte 10E9/L | 296.4 ± 36.2   | 286.1 ± 45.2           | 293.3 ± 44.8           | 307.9 ± 67.2   | 264.4 ± 33.0 |
| PLT 10E4/µL         | 129.3 ± 31.0   | 130.6 ± 12.6           | 131.5 ± 13.7           | 124.4 ± 27.3   | 119.4 ± 10.1 |
| WBC 10E2/µL         | 51.2 ± 17.0    | 38.2 ± 11.4            | 45.8 ± 12.0            | 34.6 ± 21.3    | 40.0 ± 2.8   |
| LYMP %              | 78.3 ± 7.6     | 75.1 ± 6.6             | 74.7 ± 4.2             | 77.7 ± 4.2     | 74.0 ± 6.9   |
| NEUT %              | 16.9 ± 6.4     | 20.0 ± 5.9             | 20.9 ± 4.3             | 20.0 ± 5.9     | 20.9 ± 4.3   |
| EOS %               | 3.2 ± 1.6      | 3.4 ± 1.2              | 2.7 ± 1.0              | 2.6 ± 0.5      | 3.3 ± 1.1    |
| BASO %              | 0.2 ± 0.1      | 0.1 ± 0.1              | 0.2 ± 0.1              | 0.1 ± 0.1      | 0.1 ± 0.0    |
| MONO %              | 1.1 ± 0.4      | 1.0 ± 0.7              | 1.1 ± 0.5              | 1.4 ± 0.7      | 1.6 ± 0.5    |
| LUC %               | 0.5 ± 0.2      | 0.4 ± 0.2              | 0.4 ± 0.1              | 0.7 ± 0.3      | 0.5 ± 0.2    |
| LYMP 10E2/µL        | 40.6 ± 15.3    | 28.4 ± 8.1             | 34.5 ± 10.6            | 26.5 ± 15.3    | 29.5 ± 3.3   |
| NEUT 10E2/µL        | 8.1 ± 2.6      | 7.8 ± 3.4              | 9.3 ± 1.9              | 6.3 ± 4.9      | 8.2 ± 2.6    |
| EOS 10E2/µL         | 1.6 ± 1.0      | 1.3 ± 0.7              | 1.2 ± 0.4              | 0.9 ± 0.5      | 1.3 ± 0.4    |
| BASO 10E2/µL        | 0.1 ± 0.1      | 0.0 ± 0.1              | 0.0 ± 0.1              | 0.0 ± 0.0      | 0.0 ± 0.0    |
| MONO 10E2/µL        | 0.5 ± 0.2      | 0.4 ± 0.4              | 0.5 ± 0.3              | 0.5 ± 0.5      | 0.6 ± 0.2    |
| LUC 10E2/µL         | 0.2 ± 0.1      | 0.1 ± 0.1 <sup>+</sup> | 0.1 ± 0.1 <sup>+</sup> | 0.3 ± 0.3      | 0.2 ± 0.1    |

Values are shown as the mean ± SD. <sup>+</sup>p ≤ 0.05 vs. vehicle group (Dunnett test, two-side). RBC: Red Blood Cells, HGB: Hemoglobin, HCT: Hematocrit, MCV: Mean Red Blood Cell Volume, MCH: Mean Red Blood Cell Hemoglobin, PLT: Platelets, WBC: White Blood Cells, LYMP: Lymphocytes, NEUT: Neutrophils, EOS: Eosinophils, BASO: Basophils, MONO: Monocytes, LUC: Large Unstained Cells.

**Table S1-2.** Hematological parameters after intraperitoneal administration of Cu-NCAB001 in female mice.

| Parameters          | Day 1 (n = 10) |              |              | Day 14 (n = 5) |              |
|---------------------|----------------|--------------|--------------|----------------|--------------|
|                     | Vehicle        | 62.5 µg/kg   | 625 µg/kg    | Vehicle        | 625 µg/kg    |
| RBC 10E4/µL         | 918 ± 40       | 936 ± 45     | 926 ± 53     | 927 ± 16       | 937 ± 70     |
| HGB g/dL            | 14.7 ± 0.5     | 15.0 ± 0.7   | 14.7 ± 0.5   | 14.5 ± 0.4     | 14.7 ± 0.7   |
| HCT %               | 47.7 ± 1.8     | 48.6 ± 1.9   | 48.2 ± 1.4   | 47.0 ± 1.0     | 48.2 ± 2.2   |
| MCV fL              | 52.0 ± 1.7     | 52.0 ± 1.2   | 52.1 ± 1.8   | 50.7 ± 0.5     | 51.5 ± 1.6   |
| MCH pg              | 16.1 ± 0.6     | 16.1 ± 0.5   | 16.0 ± 0.5   | 15.6 ± 0.5     | 15.8 ± 0.6   |
| Reticulocyte %      | 3.1 ± 0.6      | 3.4 ± 0.7    | 3.2 ± 1.0    | 3.3 ± 0.3      | 3.9 ± 1.1    |
| Reticulocyte 10E9/L | 288.0 ± 51.5   | 313.9 ± 66.1 | 290.2 ± 86.0 | 307.2 ± 27.6   | 358.2 ± 81.4 |

|                    |                  |                  |                 |                 |                  |
|--------------------|------------------|------------------|-----------------|-----------------|------------------|
| PLT 10E4/ $\mu$ L  | 114.8 $\pm$ 11.9 | 110.0 $\pm$ 14.4 | 113.4 $\pm$ 7.9 | 102.9 $\pm$ 6.5 | 106.2 $\pm$ 10.9 |
| WBC 10E2/ $\mu$ L  | 36.9 $\pm$ 16.9  | 45.7 $\pm$ 17.6  | 45.8 $\pm$ 15.7 | 39.3 $\pm$ 22.1 | 37.7 $\pm$ 9.6   |
| LYMP %             | 75.8 $\pm$ 6.9   | 73.9 $\pm$ 6.2   | 72.5 $\pm$ 6.3  | 73.1 $\pm$ 7.0  | 74.4 $\pm$ 4.3   |
| NEUT %             | 18.6 $\pm$ 7.7   | 20.5 $\pm$ 6.5   | 22.0 $\pm$ 6.5  | 19.8 $\pm$ 7.1  | 17.6 $\pm$ 2.6   |
| EOS %              | 4.0 $\pm$ 1.9    | 3.7 $\pm$ 1.2    | 3.6 $\pm$ 0.8   | 4.6 $\pm$ 2.0   | 5.7 $\pm$ 1.4    |
| BASO %             | 0.1 $\pm$ 0.1    | 0.1 $\pm$ 0.1    | 0.1 $\pm$ 0.1   | 0.1 $\pm$ 0.1   | 0.1 $\pm$ 0.1    |
| MONO %             | 1.0 $\pm$ 0.4    | 1.2 $\pm$ 0.7    | 1.3 $\pm$ 0.7   | 1.7 $\pm$ 0.9   | 1.8 $\pm$ 0.8    |
| LUC %              | 0.6 $\pm$ 0.4    | 0.6 $\pm$ 0.3    | 0.6 $\pm$ 0.3   | 0.7 $\pm$ 0.5   | 0.4 $\pm$ 0.2    |
| LYMP 10E2/ $\mu$ L | 28.4 $\pm$ 14.3  | 34.1 $\pm$ 13.7  | 33.4 $\pm$ 12.2 | 28.9 $\pm$ 16.2 | 28.2 $\pm$ 7.9   |
| NEUT 10E2/ $\mu$ L | 6.4 $\pm$ 2.5    | 9.1 $\pm$ 4.0    | 9.9 $\pm$ 4.3   | 7.6 $\pm$ 5.1   | 6.7 $\pm$ 1.8    |
| EOS 10E2/ $\mu$ L  | 1.5 $\pm$ 1.1    | 1.7 $\pm$ 0.7    | 1.6 $\pm$ 0.8   | 1.9 $\pm$ 1.3   | 2.1 $\pm$ 0.6    |
| BASO 10E2/ $\mu$ L | 0.0 $\pm$ 0.0    | 0.0 $\pm$ 0.1    | 0.0 $\pm$ 0.1   | 0.0 $\pm$ 0.1   | 0.0 $\pm$ 0.0    |
| MONO 10E2/ $\mu$ L | 0.3 $\pm$ 0.2    | 0.6 $\pm$ 0.4    | 0.5 $\pm$ 0.2   | 0.6 $\pm$ 0.4   | 0.6 $\pm$ 0.3    |
| LUC 10E2/ $\mu$ L  | 0.2 $\pm$ 0.2    | 0.3 $\pm$ 0.2    | 0.5 $\pm$ 0.2   | 0.2 $\pm$ 0.2   | 0.1 $\pm$ 0.1    |

Values are shown as the mean  $\pm$  SD. No significant difference in any treated groups from vehicle group. RBC: Red Blood Cells, HGB: Hemoglobin, HCT: Hematocrit, MCV: Mean Red Blood Cell Volume, MCH: Mean Red Blood Cell Hemoglobin, PLT: Platelets, WBC: White Blood Cells, LYMP: Lymphocytes, NEUT: Neutrophils, EOS: Eosinophils, BASO: Basophils, MONO: Monocytes, LUC: Large Unstained Cells.

**Table S2-1.** Serum biochemical parameters after intraperitoneal administration of Cu-NCAB001 in male mice.

| Parameters  | Day 1 (n = 10)  |                 |                 | Day 14 (n = 5)  |                 |
|-------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|             | Vehicle         | 62.5 $\mu$ g/kg | 625 $\mu$ g/kg  | Vehicle         | 625 $\mu$ g/kg  |
| AST IU/L    | 38 $\pm$ 7      | 37 $\pm$ 6      | 43 $\pm$ 5      | 46 $\pm$ 12     | 41 $\pm$ 3      |
| ALT IU/L    | 24 $\pm$ 4      | 25 $\pm$ 5      | 27 $\pm$ 7      | 38 $\pm$ 14     | 28 $\pm$ 4      |
| LDH IU/L    | 173 $\pm$ 60    | 186 $\pm$ 63    | 189 $\pm$ 48    | 175 $\pm$ 80    | 155 $\pm$ 21    |
| CPK IU/L    | 49 $\pm$ 5      | 54 $\pm$ 17     | 54 $\pm$ 14     | 44 $\pm$ 8      | 44 $\pm$ 9      |
| ALP IU/L    | 340 $\pm$ 78    | 366 $\pm$ 138   | 358 $\pm$ 59    | 217 $\pm$ 15    | 281 $\pm$ 63    |
| T-CHO mg/dL | 159 $\pm$ 28    | 168 $\pm$ 23    | 153 $\pm$ 9     | 143 $\pm$ 29    | 132 $\pm$ 17    |
| TG mg/dL    | 65 $\pm$ 35     | 47 $\pm$ 22     | 68 $\pm$ 48     | 72 $\pm$ 11     | 54 $\pm$ 18     |
| T-BIL mg/dL | 0.1 $\pm$ 0.0   | 0.1 $\pm$ 0.0   | 0.1 $\pm$ 0.0   | 0.1 $\pm$ 0.0   | 0.2 $\pm$ 0.1   |
| GUL mg/dL   | 195 $\pm$ 27    | 205 $\pm$ 15    | 205 $\pm$ 15    | 219 $\pm$ 32    | 200 $\pm$ 13    |
| BUN mg/dL   | 18 $\pm$ 2      | 16 $\pm$ 2      | 17 $\pm$ 3      | 20 $\pm$ 4      | 19 $\pm$ 2      |
| CRNN mg/dL  | 0.10 $\pm$ 0.02 | 0.08 $\pm$ 0.01 | 0.09 $\pm$ 0.01 | 0.13 $\pm$ 0.02 | 0.13 $\pm$ 0.02 |
| Na mmol/L   | 151 $\pm$ 1     | 150 $\pm$ 1     | 150 $\pm$ 1     | 151 $\pm$ 1     | 151 $\pm$ 1     |
| K mmol/L    | 4.7 $\pm$ 0.5   | 4.7 $\pm$ 0.4   | 4.4 $\pm$ 0.3   | 4.6 $\pm$ 0.2   | 4.6 $\pm$ 0.3   |
| Cl mmol/L   | 115 $\pm$ 2     | 114 $\pm$ 1     | 114 $\pm$ 2     | 114 $\pm$ 3     | 114 $\pm$ 1     |
| Ca mg/dL    | 9.7 $\pm$ 0.3   | 9.6 $\pm$ 0.2   | 9.5 $\pm$ 0.4   | 9.1 $\pm$ 0.2   | 9.0 $\pm$ 0.3   |
| P mg/dL     | 8.3 $\pm$ 0.9   | 8.9 $\pm$ 0.7   | 8.3 $\pm$ 0.7   | 7.6 $\pm$ 0.7   | 7.7 $\pm$ 0.8   |
| TP g/dL     | 5.1 $\pm$ 0.3   | 5.1 $\pm$ 0.3   | 5.1 $\pm$ 0.2   | 4.9 $\pm$ 0.1   | 5.0 $\pm$ 0.2   |
| ALB g/dL    | 3.4 $\pm$ 0.2   | 3.4 $\pm$ 0.3   | 3.4 $\pm$ 0.2   | 3.3 $\pm$ 0.1   | 3.4 $\pm$ 0.1   |
| A/G         | 2.0 $\pm$ 0.2   | 2.0 $\pm$ 0.2   | 2.0 $\pm$ 0.2   | 2.0 $\pm$ 0.1   | 2.1 $\pm$ 0.2   |

Values are shown as the mean  $\pm$  SD. No significant difference in any treated groups from vehicle group. AST: Aspartic Aminotransferase, ALT: Alanine Aminotransferase, LDH: Lactate Dehydrogenase, CPK: Creatine Phosphokinase, ALP: Alkaline Phosphatase, T-CHO: Total Cholesterol, TG: Triglyceride, T-BIL: Total Bilirubin, GUL: Glucose, BUN: Blood Urea Nitrogen, CRNN: Creatinine, TP: Total Protein, ALB: Albumin, A/G: Albumin/Globulin ratio.

**Table S2-2.** Serum biochemical parameters after intraperitoneal administration of Cu-NCAB001 in female mice.

| Parameters  | Day 1 (n=10) |             |             | Day 14 (n=5) |                       |
|-------------|--------------|-------------|-------------|--------------|-----------------------|
|             | Vehicle      | 62.5 µg/kg  | 625 µg/kg   | Vehicle      | 625 µg/kg             |
| AST IU/L    | 46 ± 6       | 48 ± 9      | 50 ± 13     | 48 ± 4       | 47 ± 3                |
| ALT IU/L    | 23 ± 5       | 22 ± 4      | 28 ± 12     | 27 ± 3       | 26 ± 2                |
| LDH IU/L    | 185 ± 70     | 169 ± 43    | 210 ± 82    | 136 ± 31     | 215 ± 63 <sup>†</sup> |
| CPK IU/L    | 368 ± 96     | 395 ± 75    | 392 ± 151   | 47 ± 8       | 55 ± 9                |
| ALP IU/L    | 368 ± 96     | 395 ± 75    | 392 ± 151   | 344 ± 119    | 333 ± 20              |
| T-CHO mg/dL | 106 ± 22     | 106 ± 16    | 106 ± 20    | 87 ± 9       | 119 ± 33              |
| TG mg/dL    | 42 ± 24      | 46 ± 15     | 48 ± 25     | 64 ± 9       | 66 ± 14               |
| T-BIL mg/dL | 0.1 ± 0.0    | 0.1 ± 0.0   | 0.1 ± 0.0   | 0.1 ± 0.0    | 0.1 ± 0.0             |
| GUL mg/dL   | 191 ± 8      | 196 ± 26    | 197 ± 22    | 191 ± 22     | 199 ± 16              |
| BUN mg/dL   | 18 ± 3       | 18 ± 4      | 18 ± 2      | 19 ± 3       | 15 ± 3                |
| CRNN mg/dL  | 0.11 ± 0.02  | 0.11 ± 0.01 | 0.10 ± 0.01 | 0.15 ± 0.03  | 0.15 ± 0.02           |
| Na mmol/L   | 150 ± 2      | 150 ± 2     | 150 ± 1     | 151 ± 1      | 150 ± 1               |
| K mmol/L    | 4.2 ± 0.4    | 4.3 ± 0.6   | 4.4 ± 0.2   | 4.1 ± 0.4    | 3.9 ± 0.3             |
| Cl mmol/L   | 116 ± 2      | 116 ± 2     | 115 ± 2     | 115 ± 1      | 115 ± 2               |
| Ca mg/dL    | 9.6 ± 0.3    | 9.4 ± 0.2   | 9.6 ± 0.2   | 9.0 ± 0.1    | 8.9 ± 0.1             |
| P mg/dL     | 7.9 ± 0.9    | 7.9 ± 0.9   | 8.4 ± 1.0   | 6.8 ± 0.2    | 7.3 ± 0.6             |
| TP g/dL     | 5.1 ± 0.3    | 4.9 ± 0.2   | 4.9 ± 0.2   | 4.9 ± 0.2    | 5.0 ± 0.2             |
| ALB g/dL    | 3.6 ± 0.2    | 3.5 ± 0.1   | 3.5 ± 0.1   | 3.6 ± 0.1    | 3.6 ± 0.2             |
| A/G         | 2.5 ± 0.3    | 2.6 ± 0.3   | 2.6 ± 0.2   | 2.7 ± 0.2    | 2.6 ± 0.3             |

Values are shown as the mean ± SD. <sup>†</sup>  $p \leq 0.05$  vs. vehicle group (t test, two-side). AST: Aspartic Aminotransferase, ALT: Alanine Aminotransferase, LDH: Lactate Dehydrogenase, CPK: Creatine Phosphokinase, ALP: Alkaline Phosphatase, T-CHO: Total Cholesterol, TG: Triglyceride, T-BIL: Total Bilirubin, GUL: Glucose, BUN: Blood Urea Nitrogen, CRNN: Creatinine, TP: Total Protein, ALB: Albumin, A/G: Albumin/Globulin ratio.

**Table S3-1.** Organ weights after intraperitoneal administration of Cu-NCAB001 in male mice.

| Parameters   | Day 1 (n=10) |             |             | Day 14 (n=5) |             |
|--------------|--------------|-------------|-------------|--------------|-------------|
|              | Vehicle      | 62.5 µg/kg  | 625 µg/kg   | Vehicle      | 625 µg/kg   |
| Brain mg     | 475 ± 19     | 484 ± 24    | 479 ± 25    | 476 ± 18     | 489 ± 9     |
| Thymus mg    | 50 ± 17      | 58 ± 9      | 55 ± 10     | 48 ± 8       | 54 ± 7      |
| Heart mg     | 142 ± 11     | 143 ± 10    | 138 ± 9     | 153 ± 23     | 159 ± 10    |
| Lung mg      | 180 ± 16     | 178 ± 9     | 185 ± 31    | 198 ± 22     | 193 ± 23    |
| Liver g      | 1.49 ± 0.15  | 1.59 ± 0.12 | 1.51 ± 0.13 | 1.78 ± 0.21  | 1.68 ± 0.17 |
| Spleen mg    | 78 ± 11      | 83 ± 13     | 84 ± 16     | 92 ± 26      | 96 ± 23     |
| Kidney-RL mg | 453 ± 49     | 462 ± 27    | 455 ± 38    | 507 ± 29     | 510 ± 47    |
| Testis-RL mg | 201 ± 49     | 200 ± 26    | 202 ± 30    | 243 ± 42     | 243 ± 30    |

Values are shown as the mean ± SD. No significant difference in any treated groups from vehicle group. RL: Right and Left.

**Table S3-2.** Organ weights after intraperitoneal administration of Cu-NCAB001 in female mice.

| Parameters   | Day 1 (n=10) |             |                       | Day 14 (n=5) |             |
|--------------|--------------|-------------|-----------------------|--------------|-------------|
|              | Vehicle      | 62.5 µg/kg  | 625 µg/kg             | Vehicle      | 625 µg/kg   |
| Brain mg     | 470 ± 21     | 476 ± 26    | 469 ± 13              | 485 ± 18     | 481 ± 23    |
| Thymus mg    | 57 ± 17      | 53 ± 14     | 61 ± 12               | 55 ± 9       | 49 ± 9      |
| Heart mg     | 116 ± 12     | 118 ± 6     | 121 ± 12              | 140 ± 14     | 131 ± 15    |
| Lung mg      | 159 ± 13     | 160 ± 18    | 157 ± 14              | 170 ± 12     | 169 ± 10    |
| Liver g      | 1.14 ± 0.14  | 1.13 ± 0.10 | 1.20 ± 0.16           | 1.32 ± 0.07  | 1.39 ± 0.21 |
| Spleen mg    | 75 ± 13      | 85 ± 15     | 88 ± 21               | 93 ± 16      | 100 ± 13    |
| Kidney-RL mg | 293 ± 30     | 300 ± 24    | 322 ± 22 <sup>†</sup> | 333 ± 26     | 334 ± 42    |

Values are shown as the mean ± SD. <sup>†</sup>  $p \leq 0.05$  vs. vehicle group (Dunnett test, two-side). RL: Right and Left.