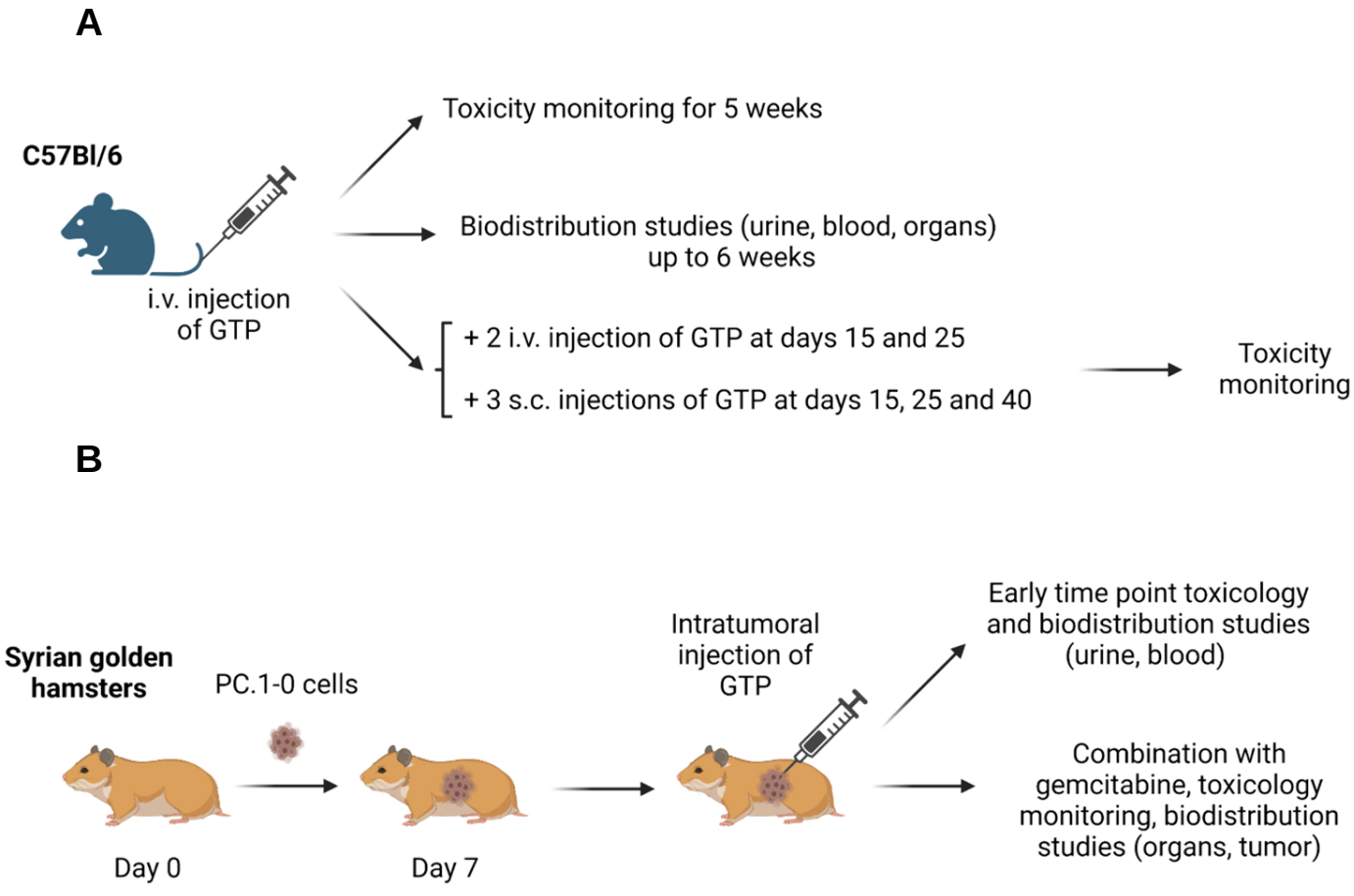
OMTM, Volume *29*

Supplemental information

Preclinical development of non-viral gene therapy for patients with advanced pancreatic cancer

Odile Barbey, Hubert Lulka, Naima Hanoun, Hafid Belhadj-Tahar, Fabienne Vernejoul, Gilles Cambois, Michèle Tiraby, Louis Buscail, Fabian Gross, and Pierre Cordelier

Figure S1



Created with BioRender.com

Figure S1. Schematic description of the preclinical animal models used during the study. Description of the toxicology and biodistribution studies following injection of the gene therapy product (GTP) in C57Bl/6 mice (**A**) and Syrian golden hamsters (**B**).

FIGURE S2

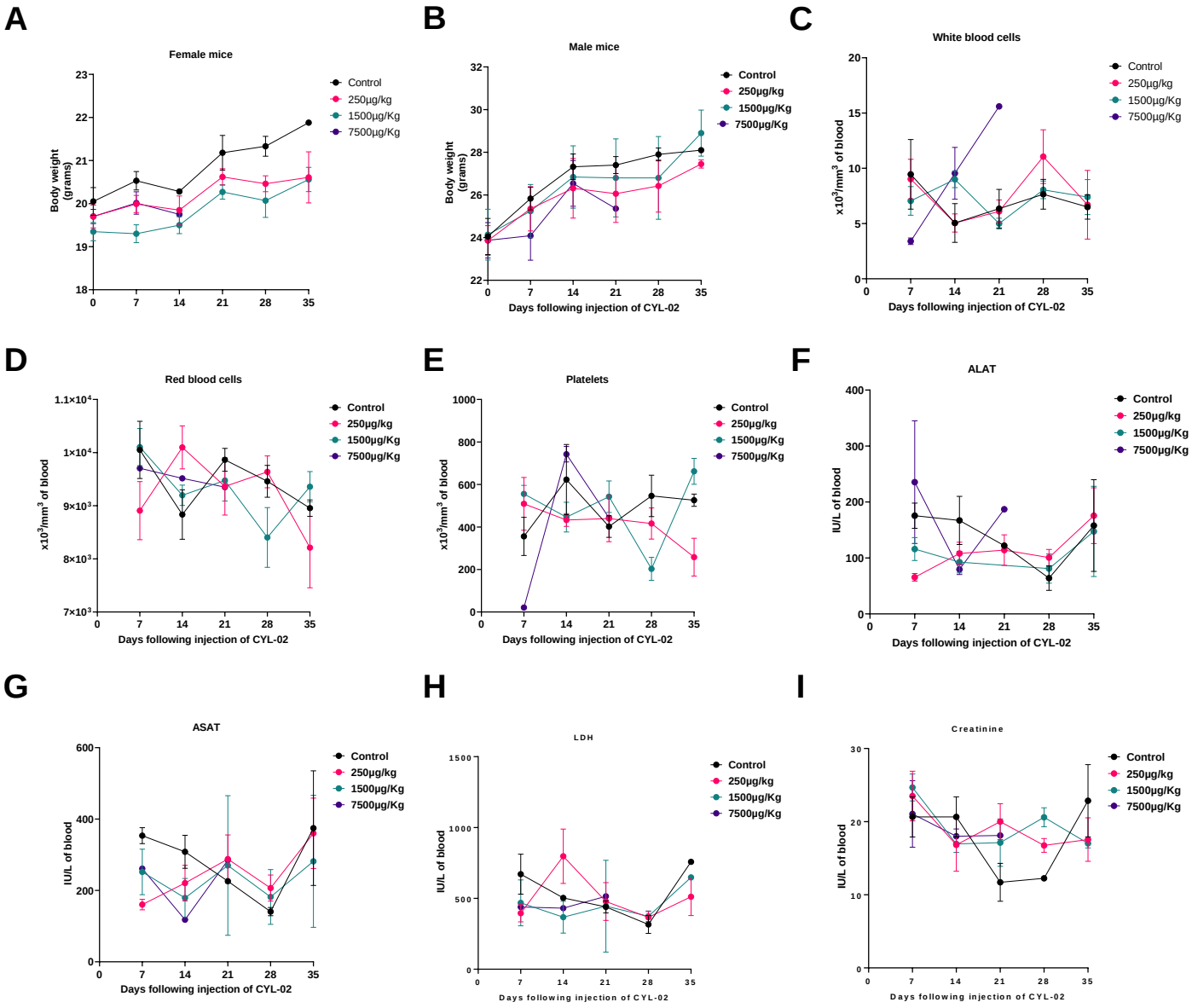


Figure S2. Toxicology monitoring in mice receiving an i.v. injection of CYL-01. 250µg/kg, 500µg/kg and 7500µg/kg of first generation CYL-01 was administered i.v. in C57Bl/6 mice from both sex. Body weight of female (**A**), or male mice (**B**), white (**C**), red (**D**) blood cells and platelets (**E**) counts, ALAT (**F**), ASAT (**G**), LDH (**H**) and creatinine (**I**) levels were monitored at the time indicated following injection of CYL-01. Results are mean ± SD of n=5 animals per group.

FIGURE S3

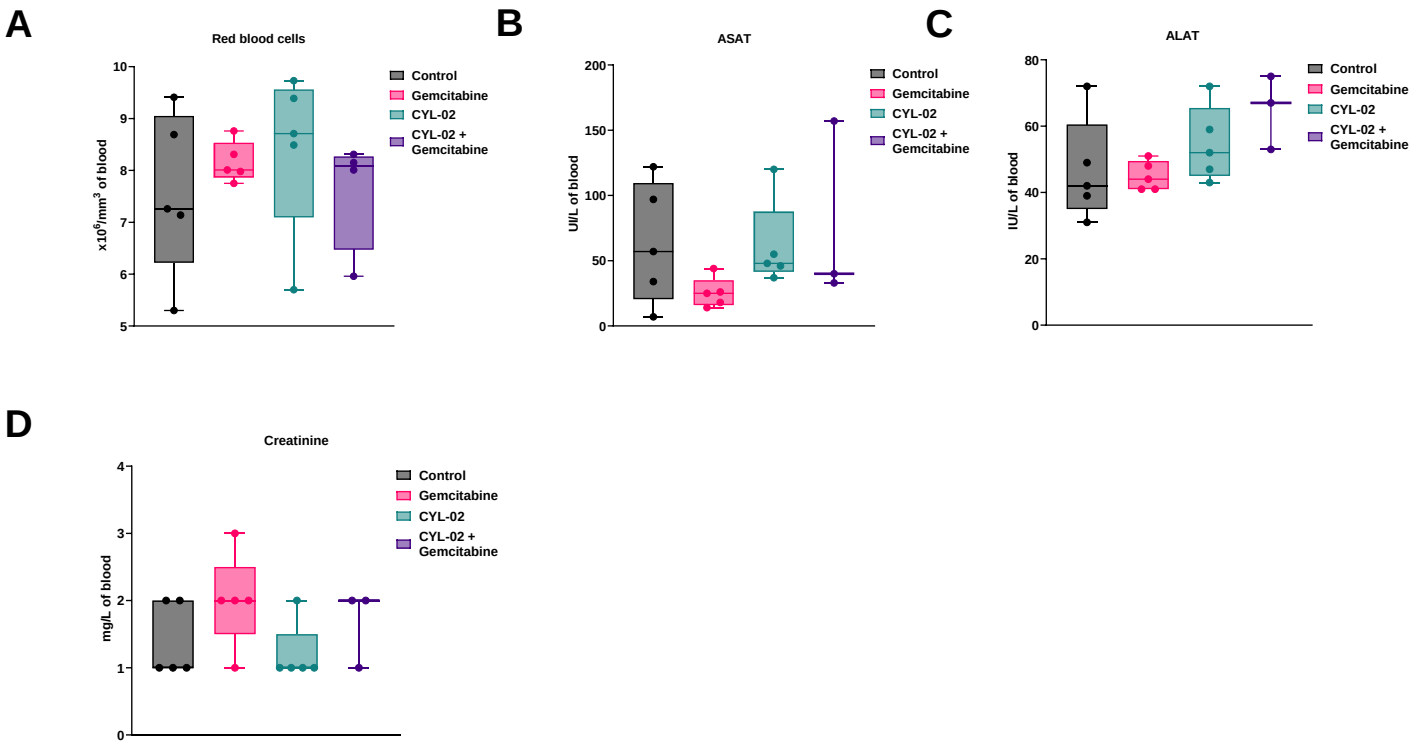


Figure S3. Toxicology monitoring in hamsters receiving an intratumoral injection of CYL-02 combined with gemcitabine treatment. Experimental orthotopic PDAC tumors were induced as described in Materials and Methods. Eight days later, 900µg/kg of second generation CYL-02 was administered in exponentially growing tumors, when control animals received 5% glucose. Gemcitabine was given at 80mg/kg i.p. every 2 days for a week. $NaCl9^{0/00}$ was given i.p. as control. Red blood cells count (**A**), ASAT (**B**), ALAT (**C**), and creatinine (**D**) levels were monitored 7 days following injection of CYL-02 and treatment with gemcitabine. Results are mean ± SD of n=5 animals per group

FIGURE S4

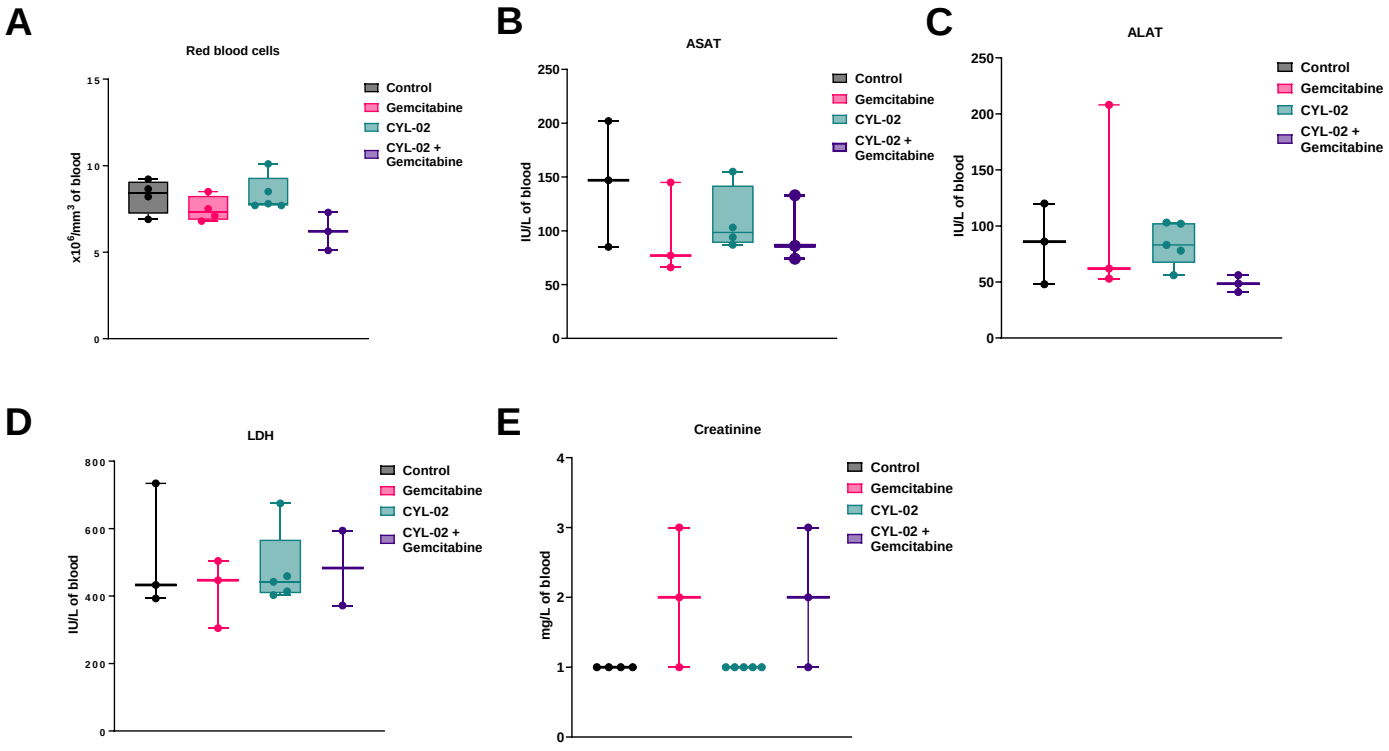


Figure S4. Toxicology monitoring in hamsters receiving two intratumoral injection of CYL-02 combined with gemcitabine treatment. Experimental orthotopic PDAC tumors were induced as described in Materials and Methods. 900µg/kg of second generation CYL-02 was administered at days 0 and 7 in exponentially growing tumors, when control animals received 5% glucose. Gemcitabine was given at 80mg/kg i.p. every 2 days for a week following each injection. NaCl9$^{0/00}$ was given i.p. as control. Red blood cells count (**A**), ASAT (**B**), ALAT (**C**), LDH (**D**) and creatinine (**E**) levels were monitored 14 days following the first injection of CYL-02 combined with gemcitabine treatment. Results are mean ± SD of n=3 to 5 animals per group.

FIGURE S5

A

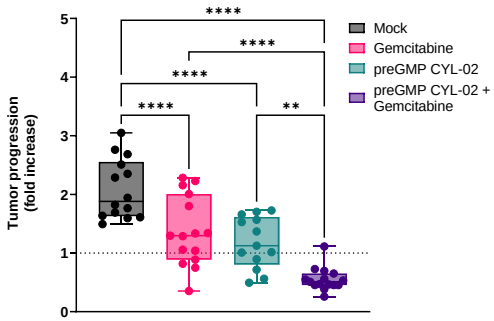


Figure S5. preclinical characterization of CYL-02 activity and antitumoral efficacy in orthotopic pancreatic tumors in Syrian golden hamsters. A. Experimental orthotopic PDAC tumors were induced as described in Materials and Methods. Eight days later, 900µg/kg of preGMP CYL-02 were administered in exponentially growing tumors, when control animals received 5% glucose. Gemcitabine was given at 80mg/kg i.p. every 2 days for a week. $NaCl9^{0/00}$ was given i.p. as control. Tumor progression at endpoint between the different groups. Results are mean fold ± SD of tumor progression in n=14 to 15 animals per group, sum of 3 independent experiments. **: $p<0.01$, ***: $p<0.005$, ****: $p<0.0001$