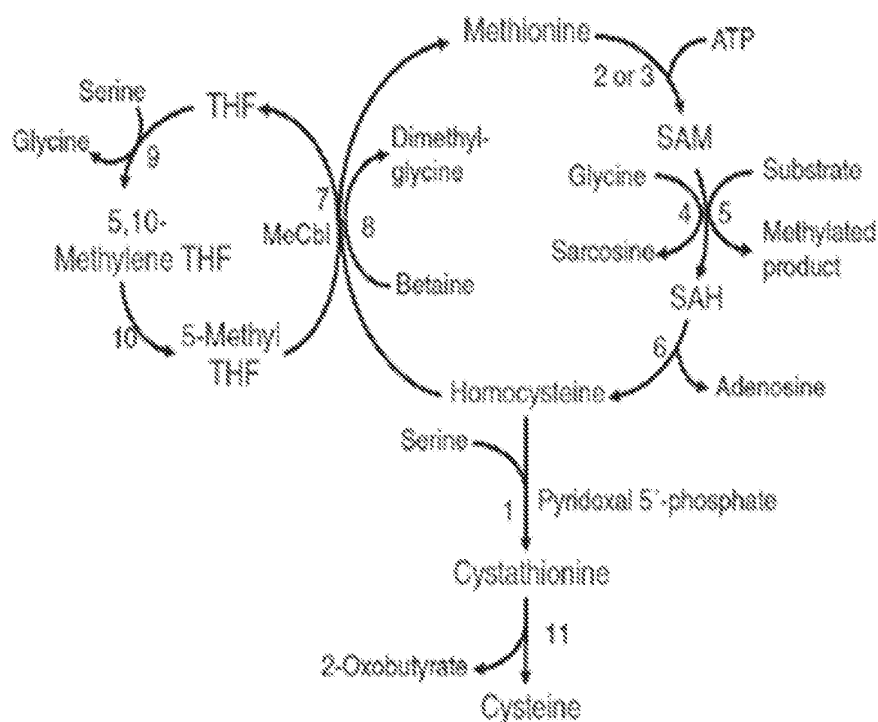


Fig. 1



Pathways of methionine metabolism. SAM, S-adenosylmethionine; SAH, S-adenosylhomocysteine; THF, tetrahydrofolate; MeCbl, methylcobalamin. 1, cystathionine beta-synthase; 2, methionine adenosyltransferase I/III; 3, methionine adenosyltransferase II; 4, glycine N-methyltransferase; 5, numerous methyltransferases; 6, S-adenosylhomocysteine hydrolase; 7, methionine synthase; 8, betaine-homocysteine methyltransferase; 9, Serine hydroxymethyltransferase; 10, methylenetetrahydrofolate reductase; 11, cystathionine gamma-lyase (Morris, Kozich et al. 2017).

Fig. 2A

SEQ ID NO: 1

MQEKDASSQGFLPHFQHFATQAIHVGQDPEQWTSRAVVPPISLSTTFKQG
APGQHSGFEYSRSGNPTRNCLEKAVAALDGAKYCLAFASGLAATVTITHL
LKAGDQIICMDDVYGGTNRYFRQVASEFGLKISFVDCSKIKLLEAAITPE
TKLVWIETPTNPTQKVIDIEGCAHIVHKHGDIIILVVDNTFMSPYFQRPLA
LGADISMYSATKYMNGHSDVVMGLVSVNCESLHNRLRFLQNSLGAVPSP I
DCYLCNRGLKTLHVRMEKHFKNGMAVAQFLESNPWVEKVIYPGLPSHPQH
ELVKRQCTGCTG MVTFYIKGTLQHAEIFLKNLKLFTLAESLGGFESLAEL
PAIMTHASVLKND RDVLGISDTLIRLSVGLEDEEDLLEDLDQALKAHPP
SGSHS

Fig. 2B

SEQ ID NO: 2

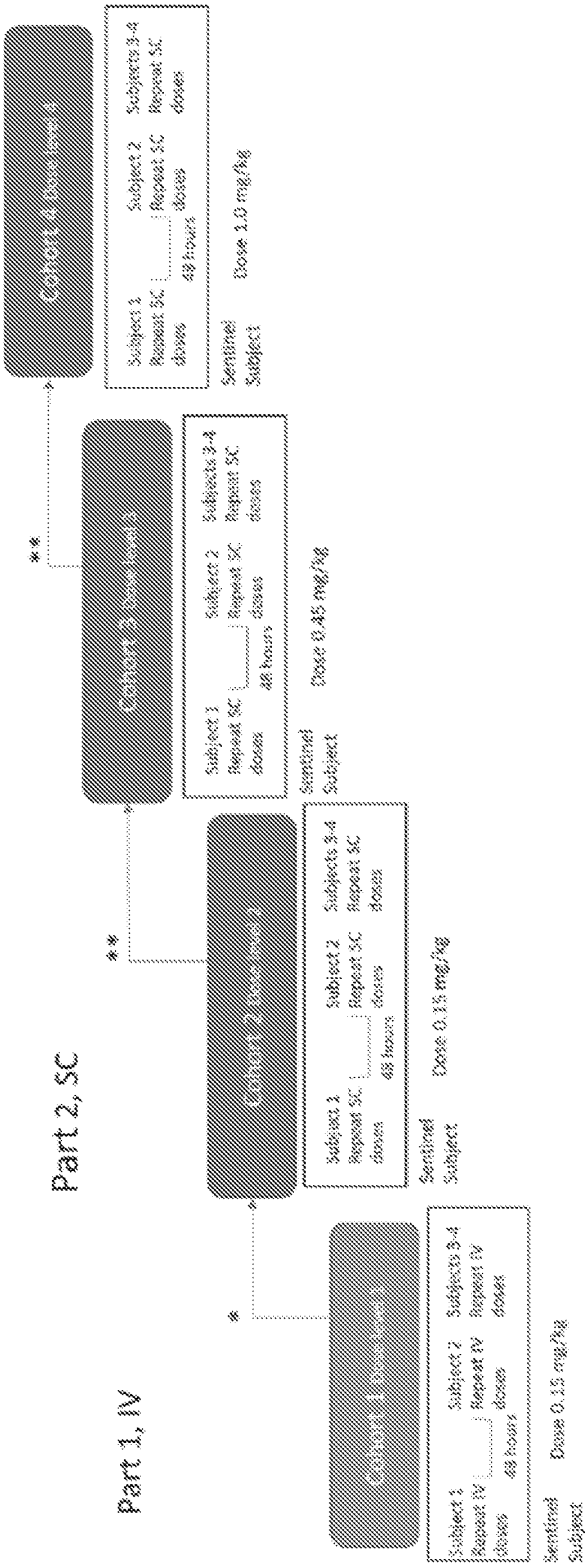
MQEKDASSQGFLPHFQHFATQAIHVGQDPEQWTSRAVVPPISLSTTFKQG
APGQHSGFEYSRSGNPTRNCLEKAVAALDGAKYCLAFASGLAATVTITHL
LKAGDQIICMDDVYGGTNRYFRQVASEFGLKISFVDCSKIKLLEAAITPE
TKLVWIETPTNPTQKVIDIEGCAHIVHKHGDIIILVVDNTFMSPYFQRPLA
LGADISMYSATKYMNGHSDVVMGLVSVNCESLHNRLRFLQNSLGAVPSP I
DCYLCNRGLKTLHVRMEKHFKNGMAVAQFLESNPWVEKVIYPGLPSHPQH
ELVKRQCTGCTG MVTFYIKGTLQHAEIFLKNLKLFTLAESLGGFESLAEL
PAIMTHASVLKND RDVLGISDTLIRLSVGLEDEEDLLEDLDQALKAHPP
SGSHS

Fig. 2C

SEQ ID NO: 3

QEKDASSQGFLPHFQHFATQAIHVGQDPEQWTSRAVVPPISLSTTFKQGA
PGQHS~~GF~~EYSRSGNPTRNCLEKAVAALDGAKYCLAFASGLAATVTITHLL
KAGDQIIICMDDVYGGTNRYFRQVASEFGLKISFVDCSKIKLLEAAITPET
KLVWIETPTNPTQKVIDIEGCAHIVHKHGDIIILVVDNTFMSPYFQRPLAL
GADISMYSATKYMNGHSDVVMGLVSVNCESLHNRLRFLQNSLGAVPSPID
CYLCNRGLKTLHVRMEKHFKNGMAVAQFLESNPWVEKVIYPGLPSHPQHE
LVKRQCTGCTTGMVTFYIKGTLQHAEIFLKNLKLFTLAESLGGFESLAELP
AIMTHASVLKNDRDVLGISDTLIRLSVGLLEDEEDLLEDLDQALKAHPPS
GSHS

Fig.3



Each Cohort has a sentinel subject
*Transition from Cohort 1 to Cohort 2 may occur after 2 patients in Cohort 1 have received 4 doses each (8 doses total) and safety data have been reviewed; Cohort 2 may then open at the same dose level as Cohort 1.
**Transition from Cohort 2 to Cohort 3 and from Cohort 3 to Cohort 4 may occur after at least 2 subjects in the previous cohort have received all 4 planned once-weekly doses and the safety and tolerability profile is considered acceptable.

4
K
5
6

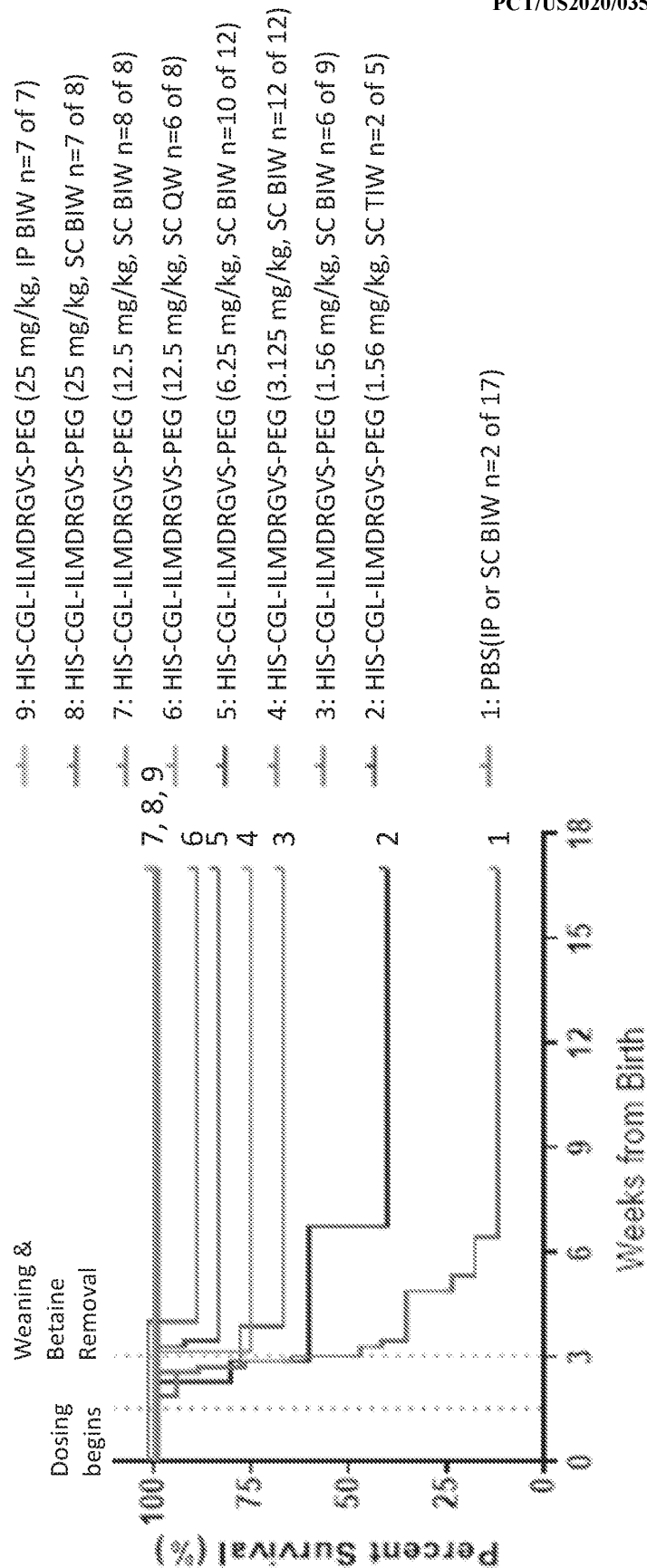
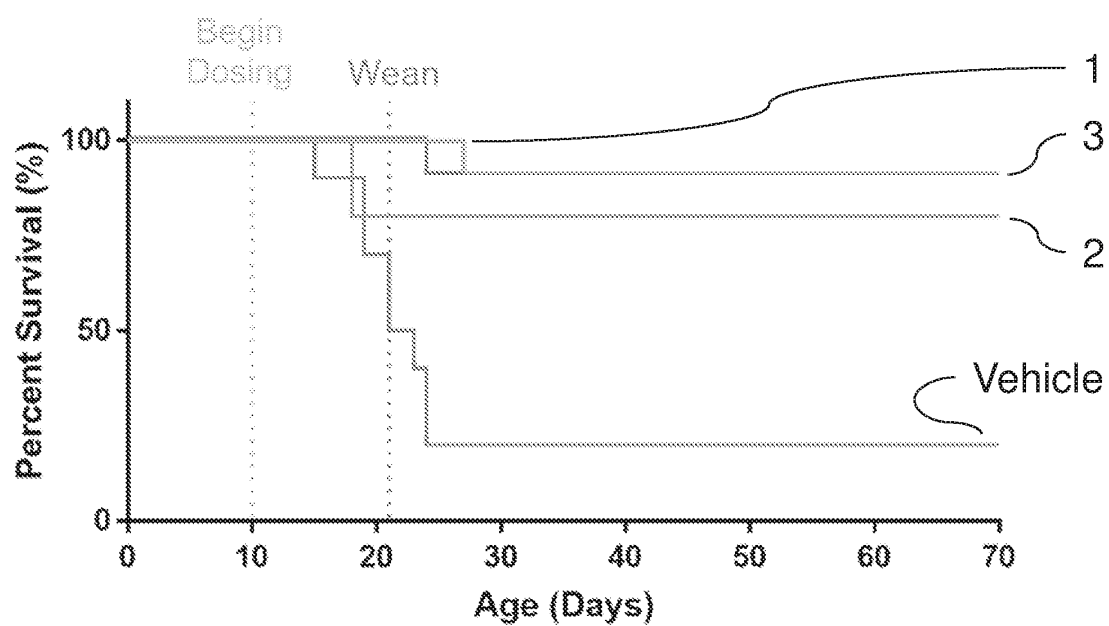


Fig. 5



- 1: CGL-ILMDRGVS-PEG (10 mg/kg SC BIW, n=11 of 12)
- 2: CGL-ILMDRGVS-PEG (3 mg/kg SC BIW, n=8 of 10)
- 3: CGL-ILMDRGVS-PEG (1.0 mg/kg SC BIW, n=10 of 11)
- Vehicle (SC BIW, n=2 of 10)

Fig. 6

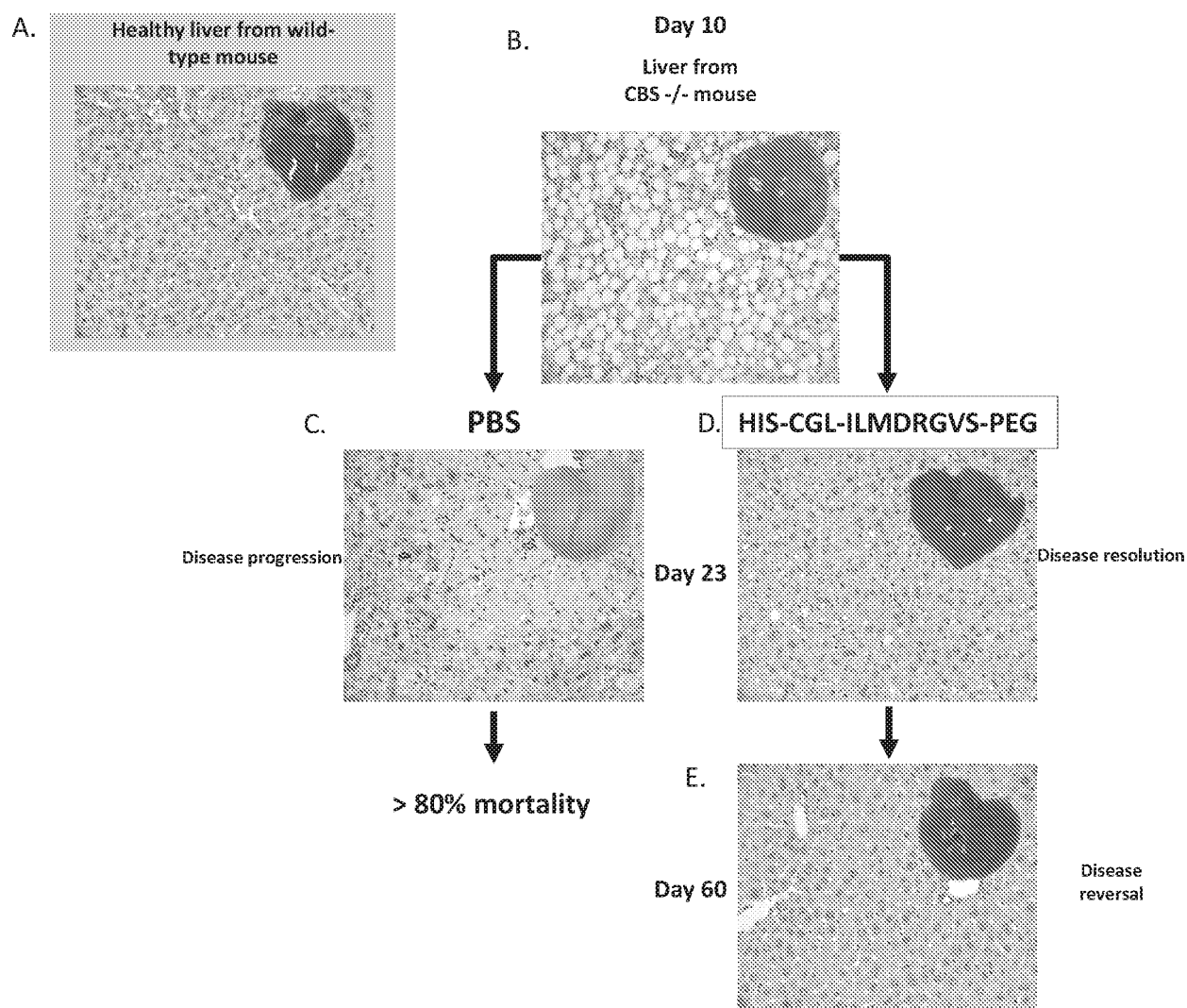


Fig. 7

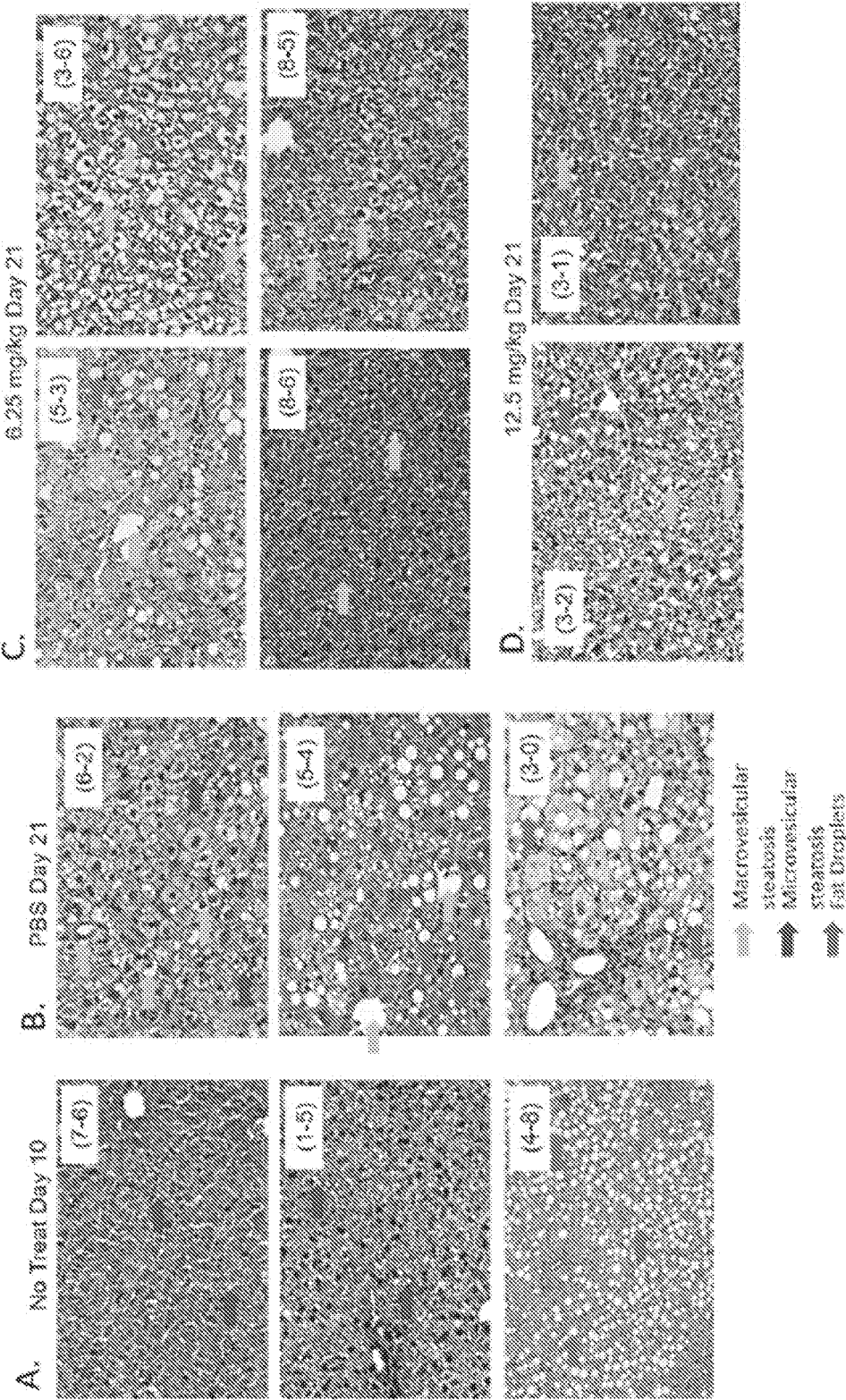


Fig. 8

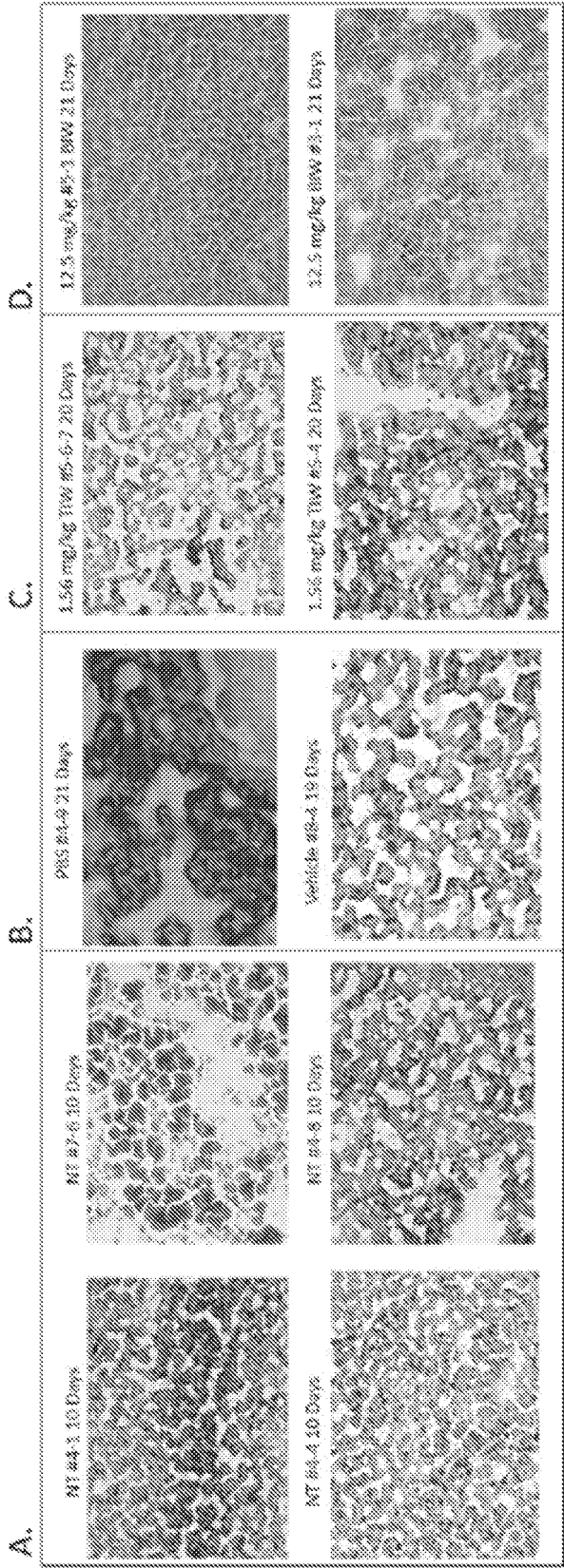


Fig. 9

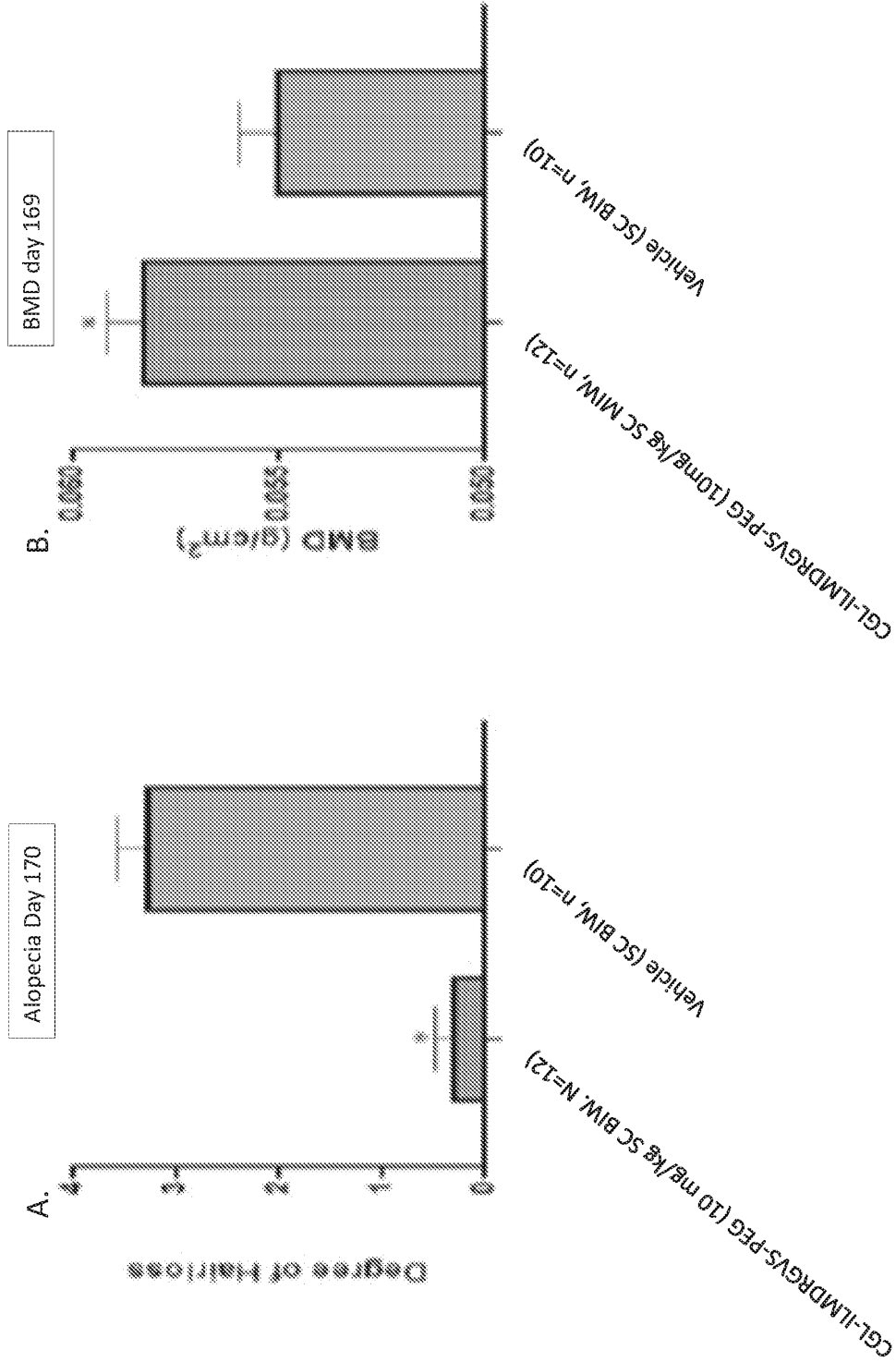


Fig. 10

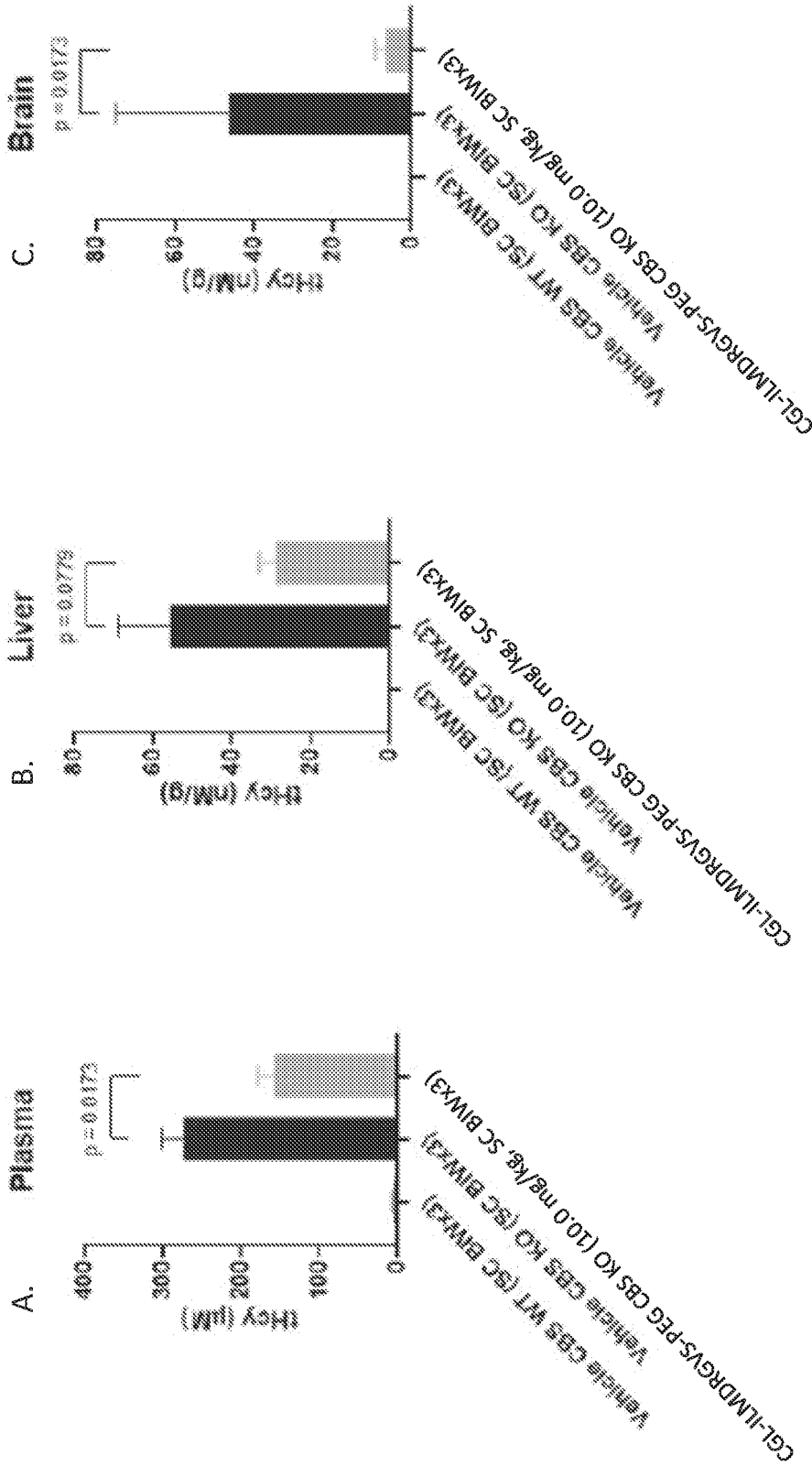


Fig. 11

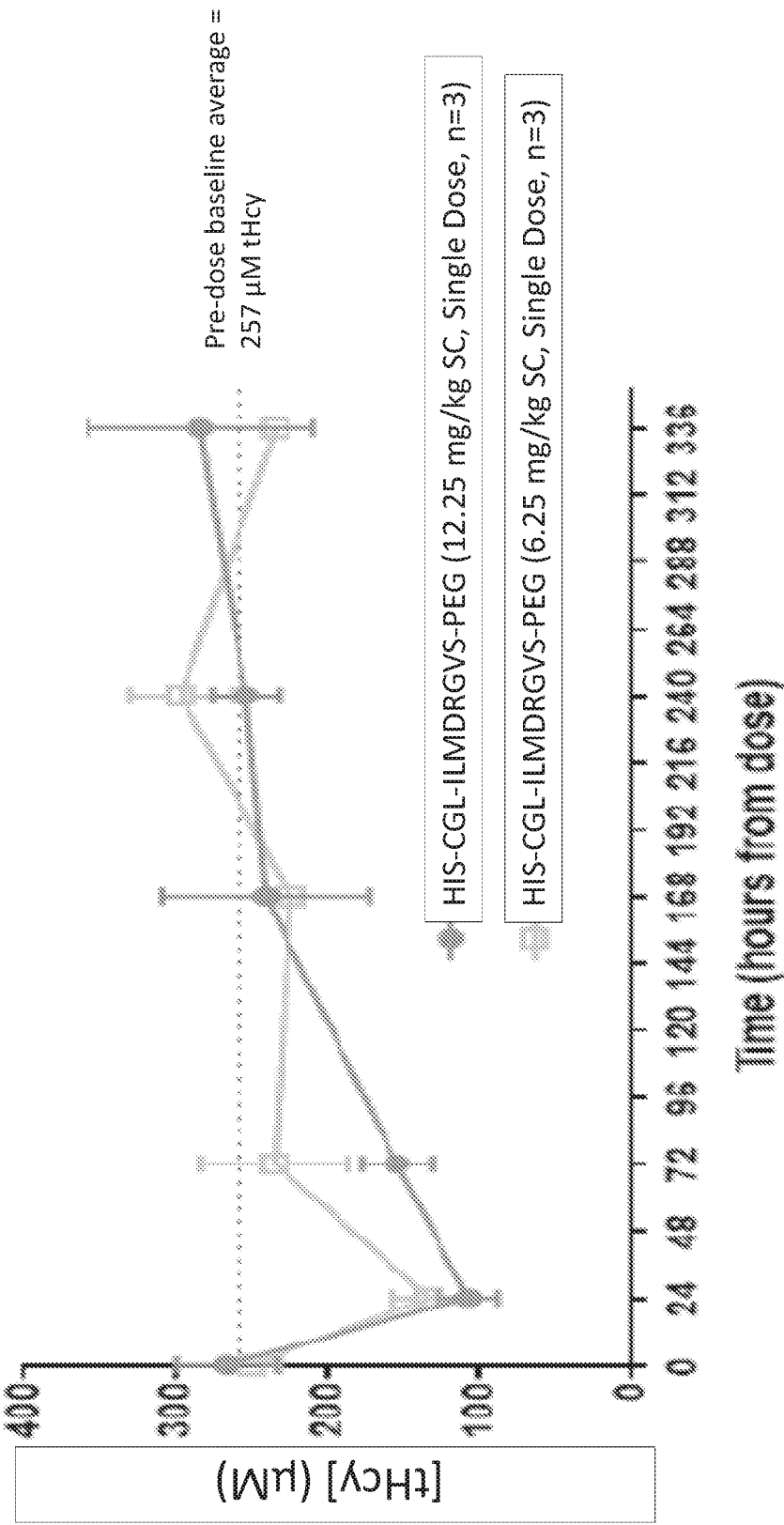


Fig. 12

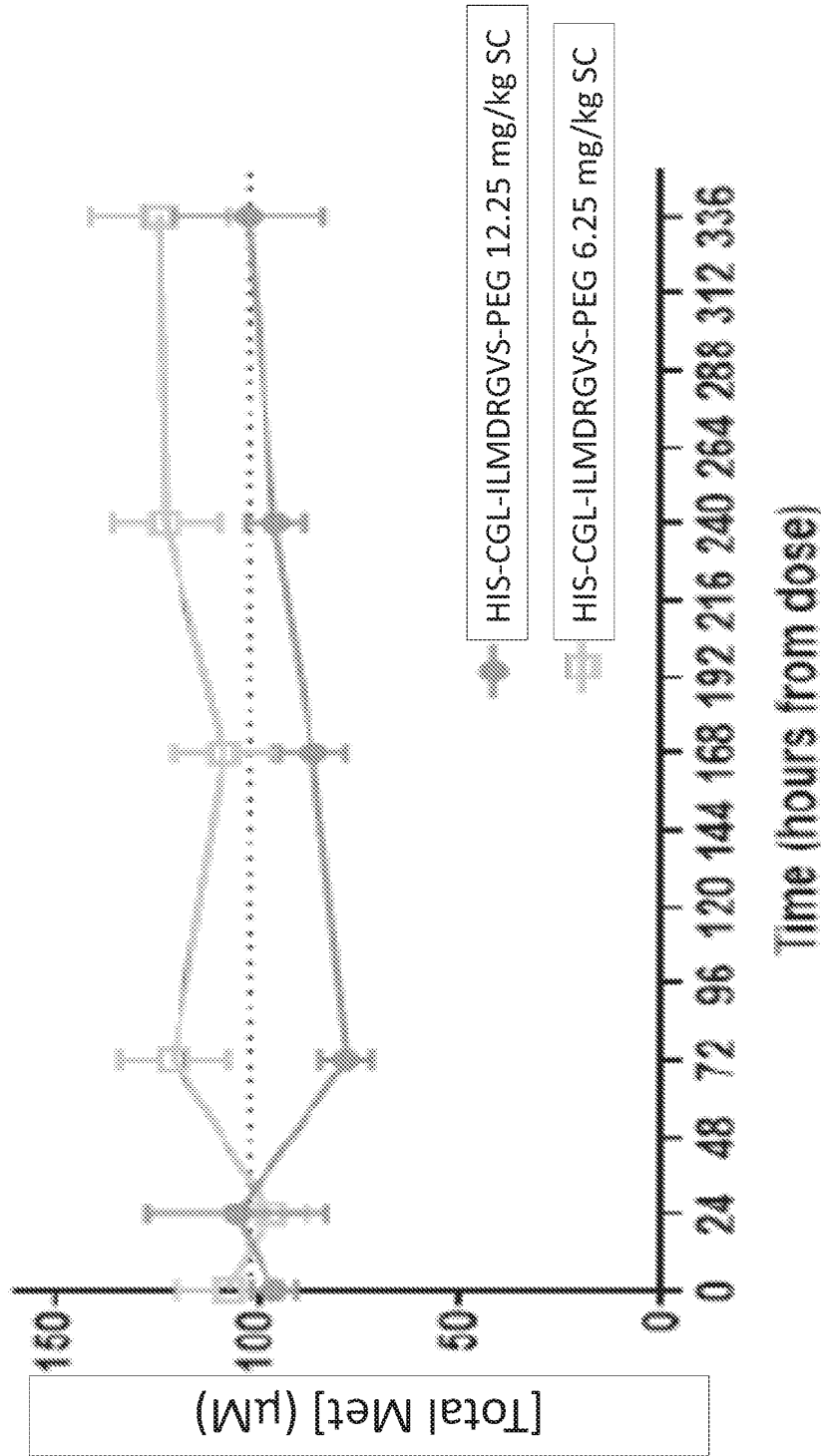


Fig. 13

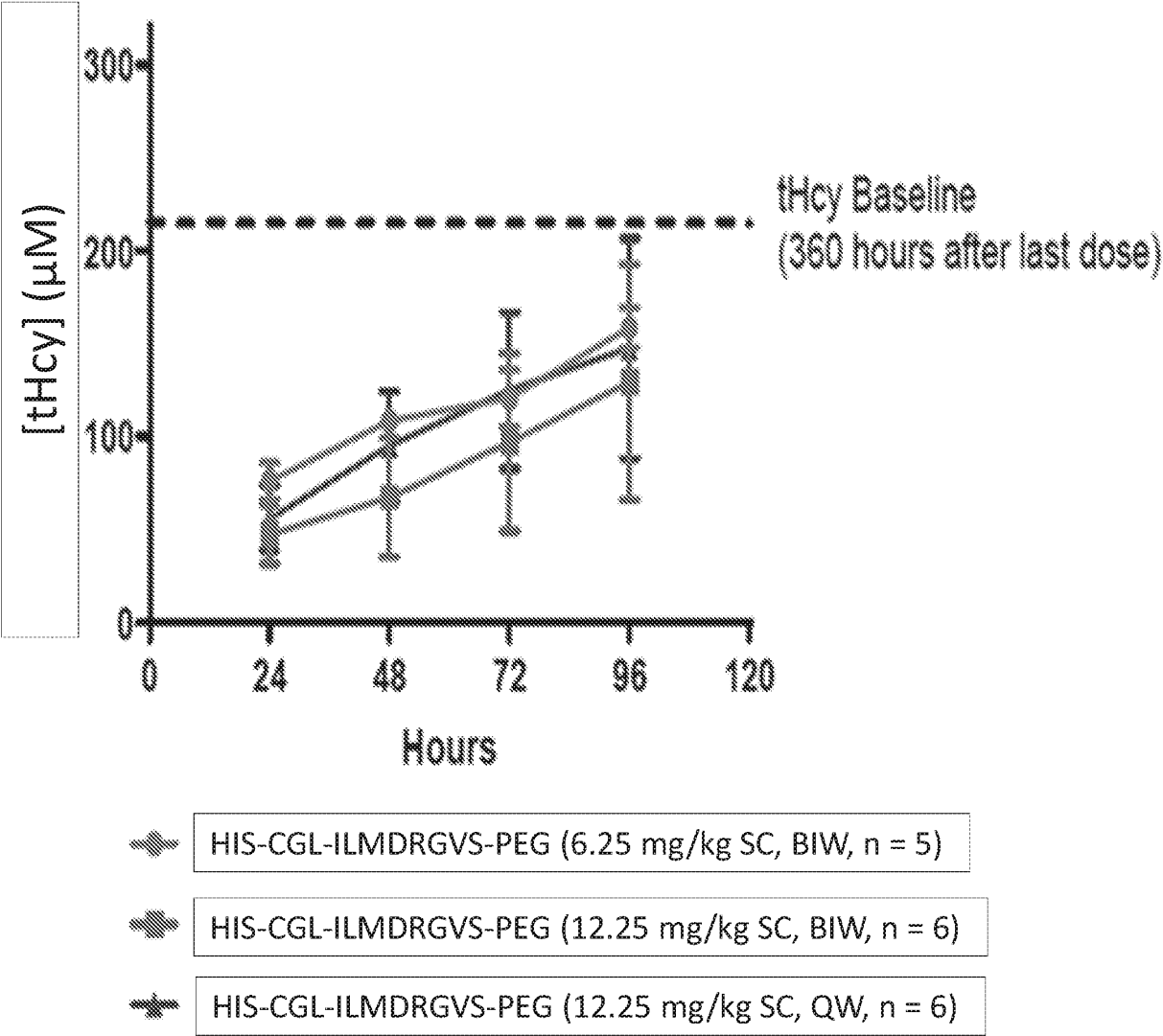


Fig. 14

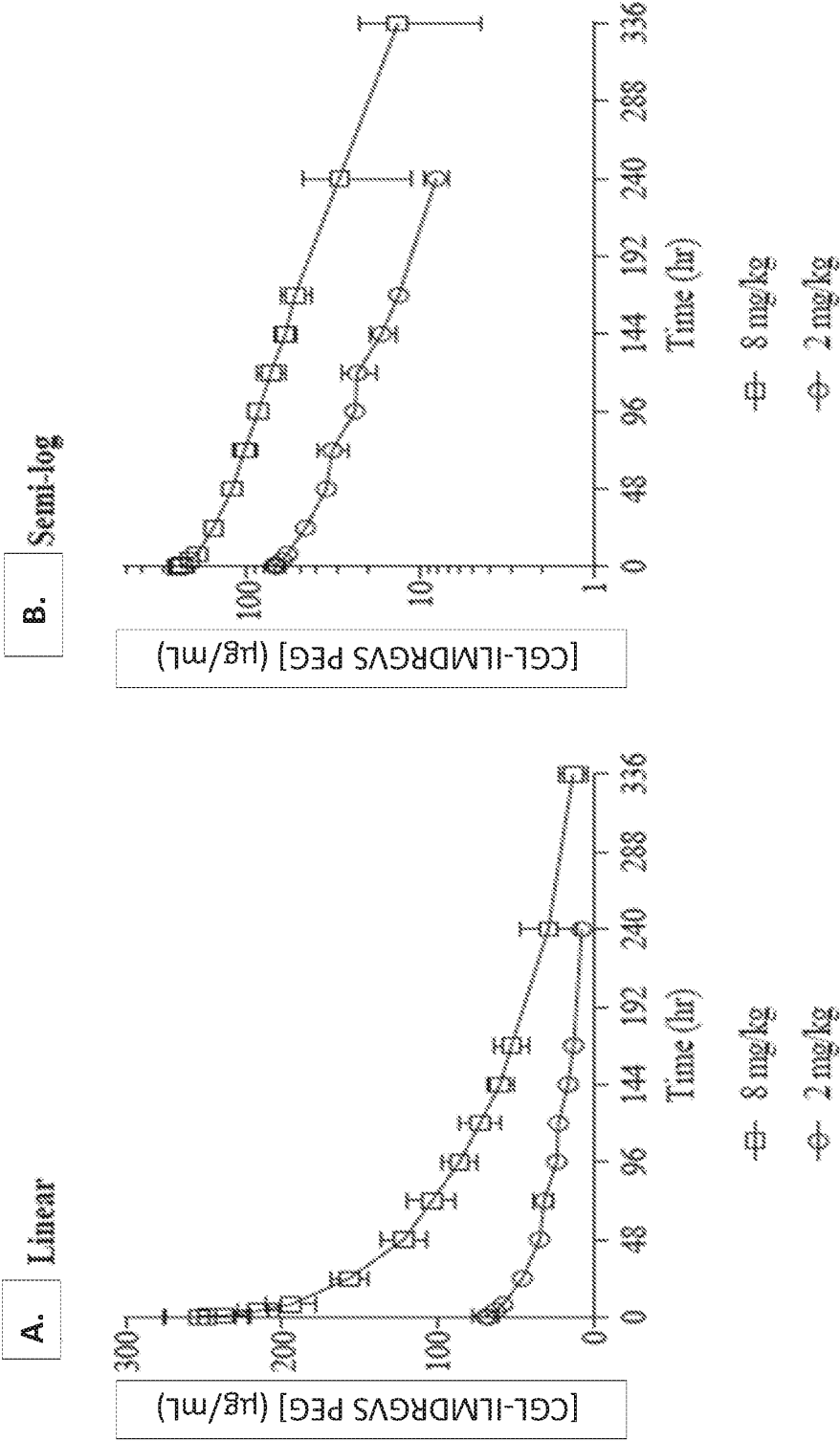


Fig.15

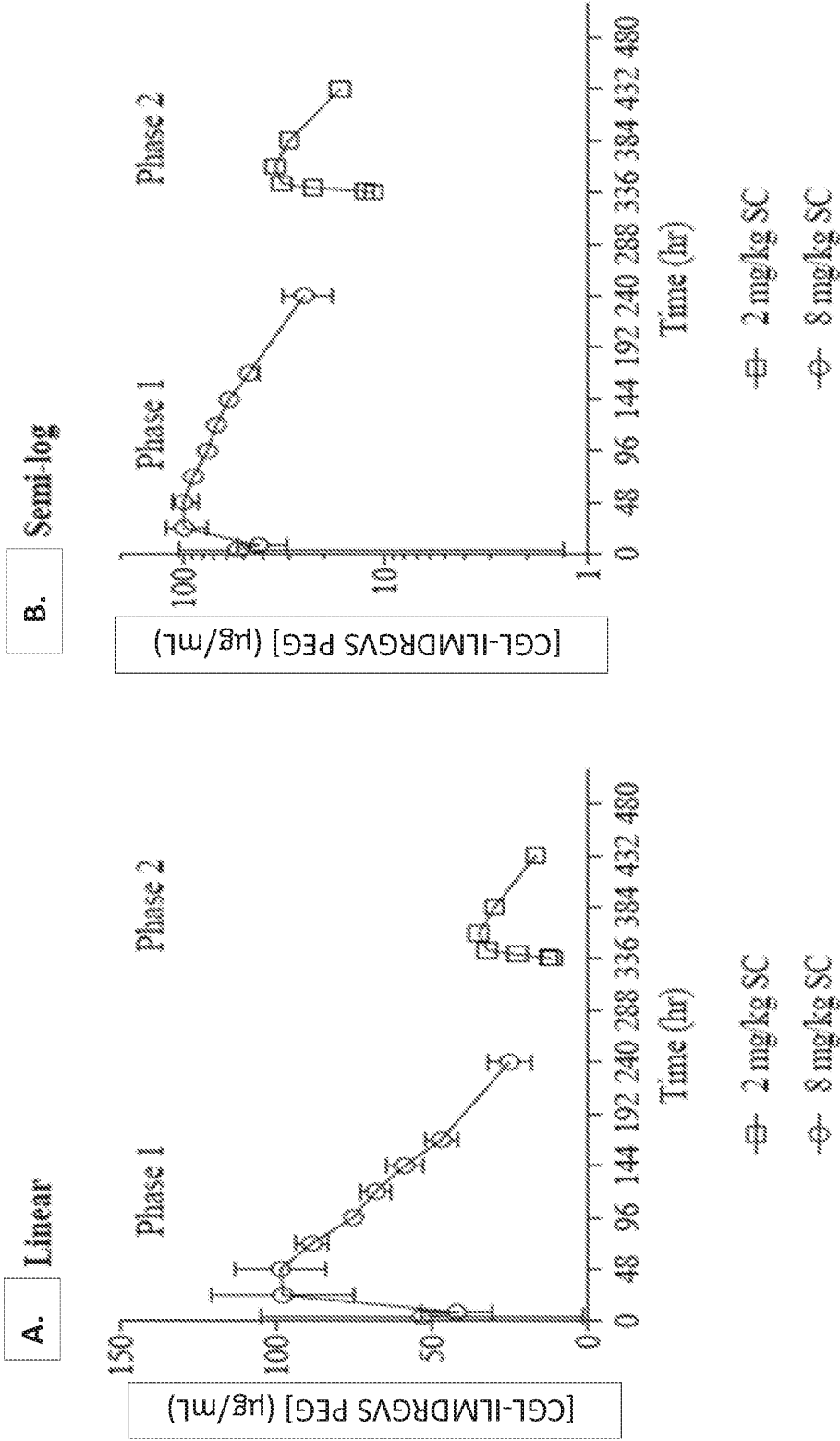


Fig.16

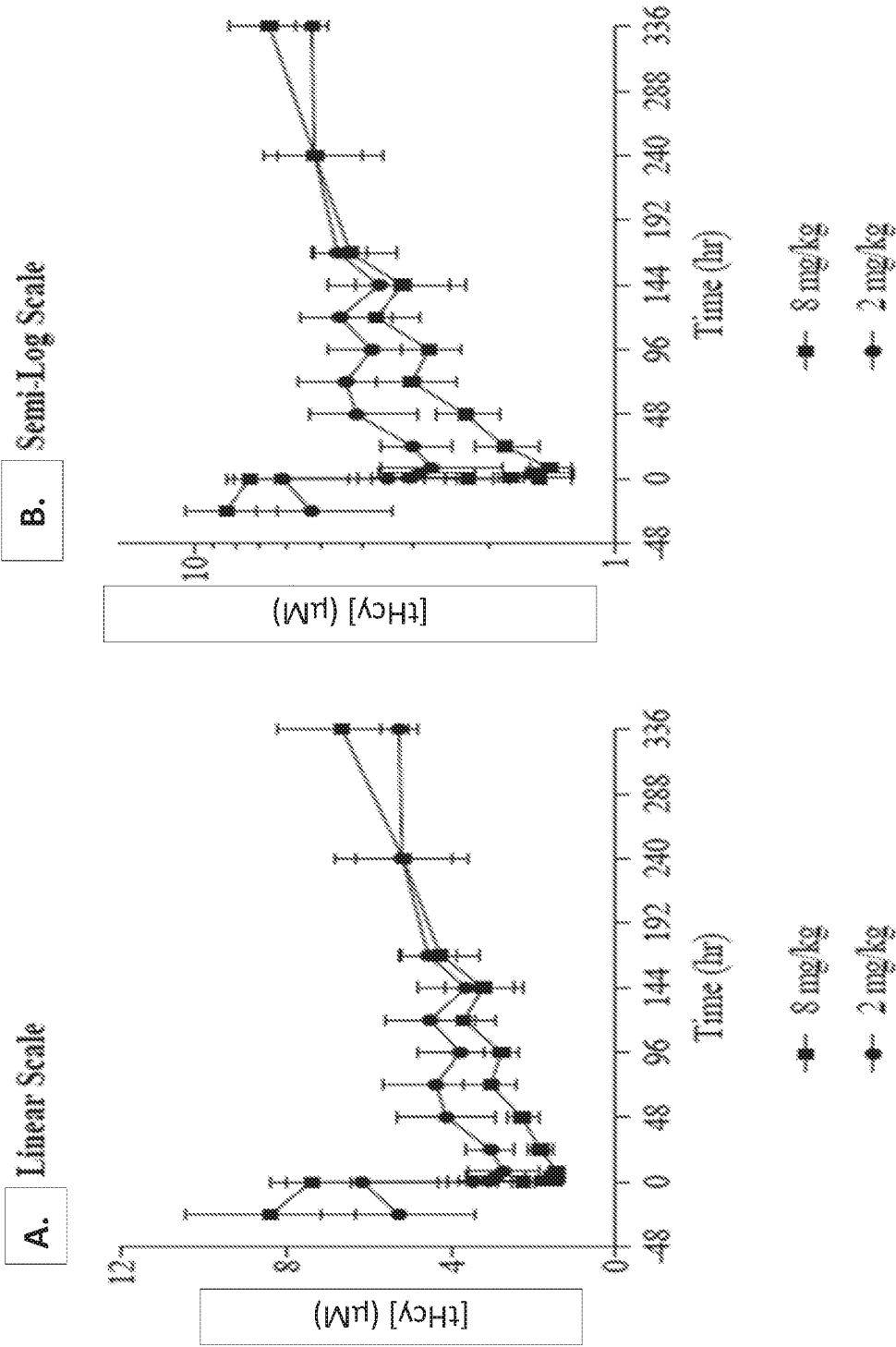


Fig.17

