■ Vehicle twice weekly, ▼3 mg/kg BT1718 twice weekly, ▲10 mg/kg BT1718 twice weekly.

LU-010-0046 lung PDX
High MT1-MMP expression

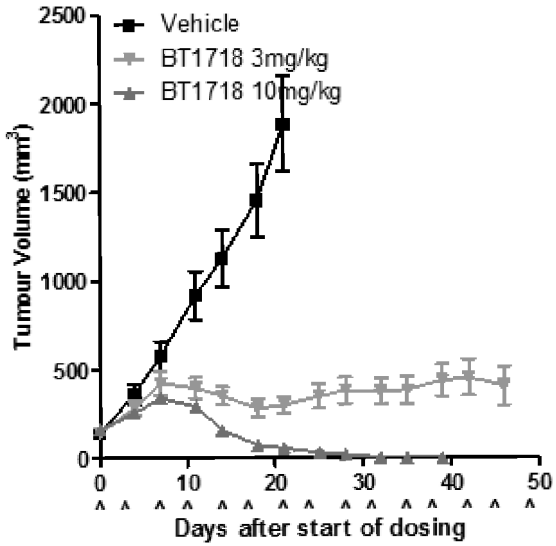


Fig. 1A

LU-010-0251 lung PDX
High MT1-MMP expression

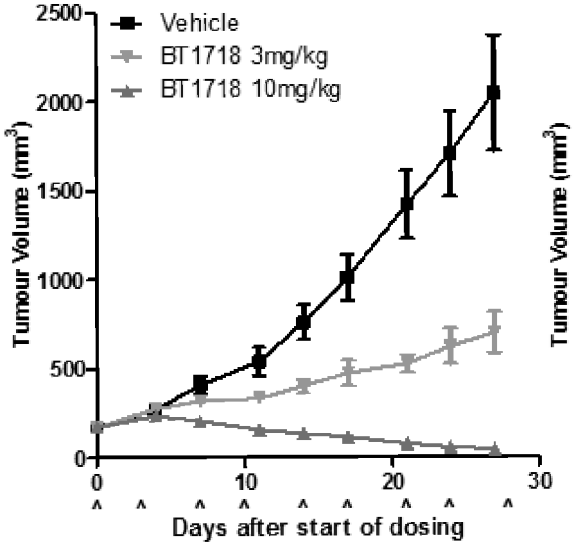


Fig. 1B

LU-010-0486 lung PDX
Low MT1-MMP expression

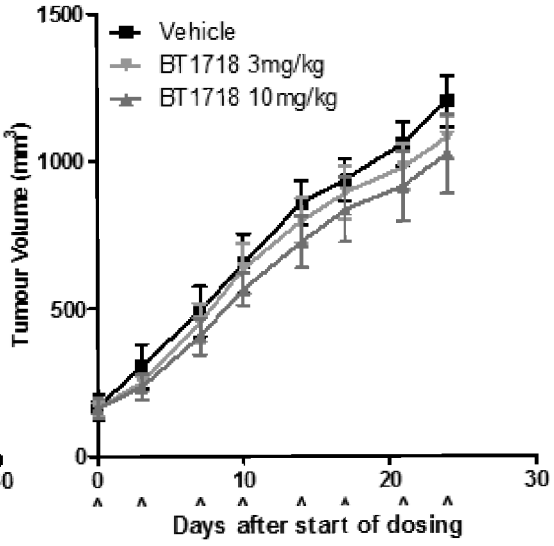


Fig. 1C

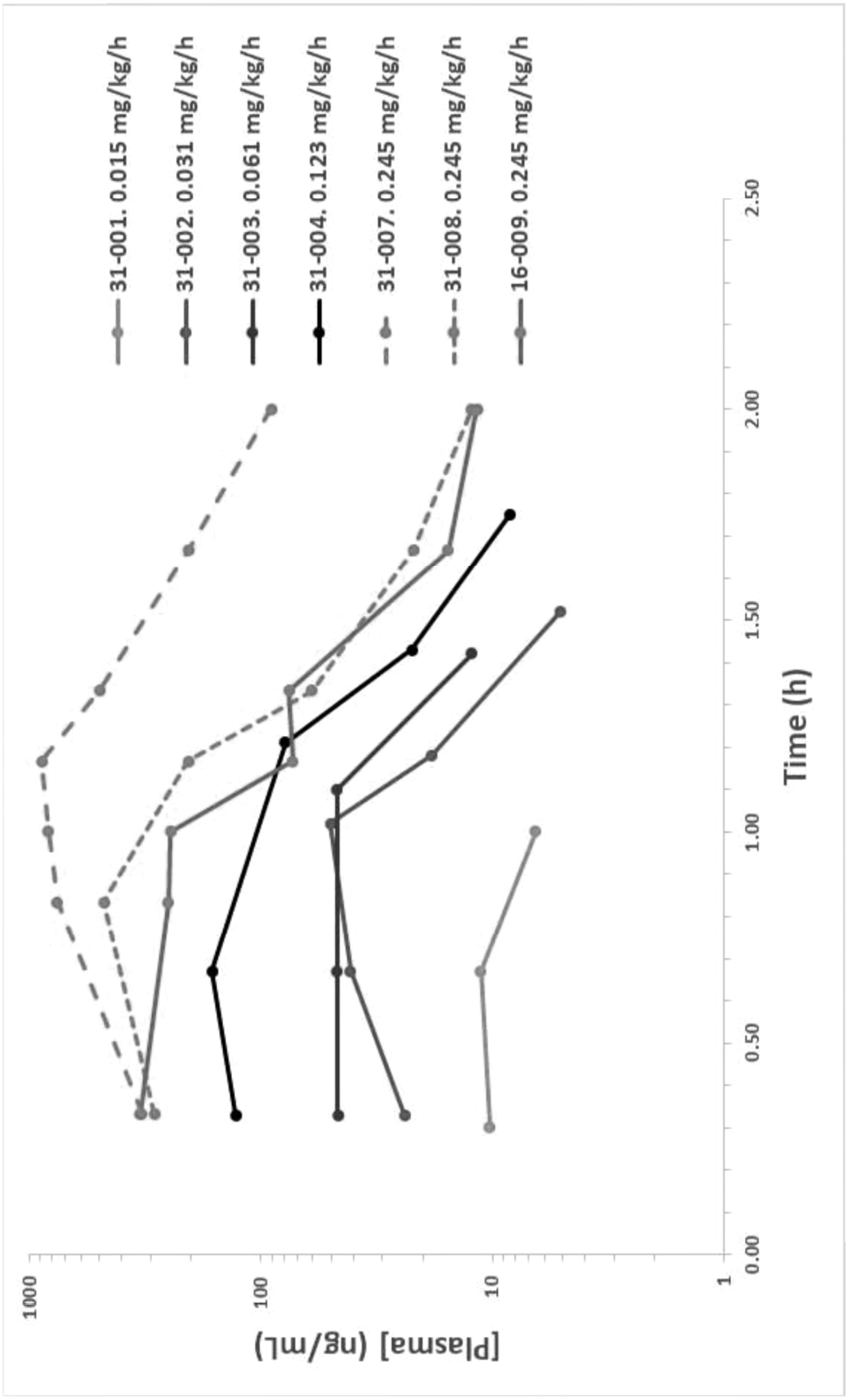

31-001. 0.015 mg/kg/h
31-002. 0.031 mg/kg/h
31-003. 0.061 mg/kg/h
31-004. 0.123 mg/kg/h
31-007. 0.245 mg/kg/h
31-008. 0.245 mg/kg/h
16-009. 0.245 mg/kg/h
[Plasma] (ng/mL)
1000
100
10
1
0.00
0.50
1.00
1.50
2.00
2.50
Time (h)

Fig. 2

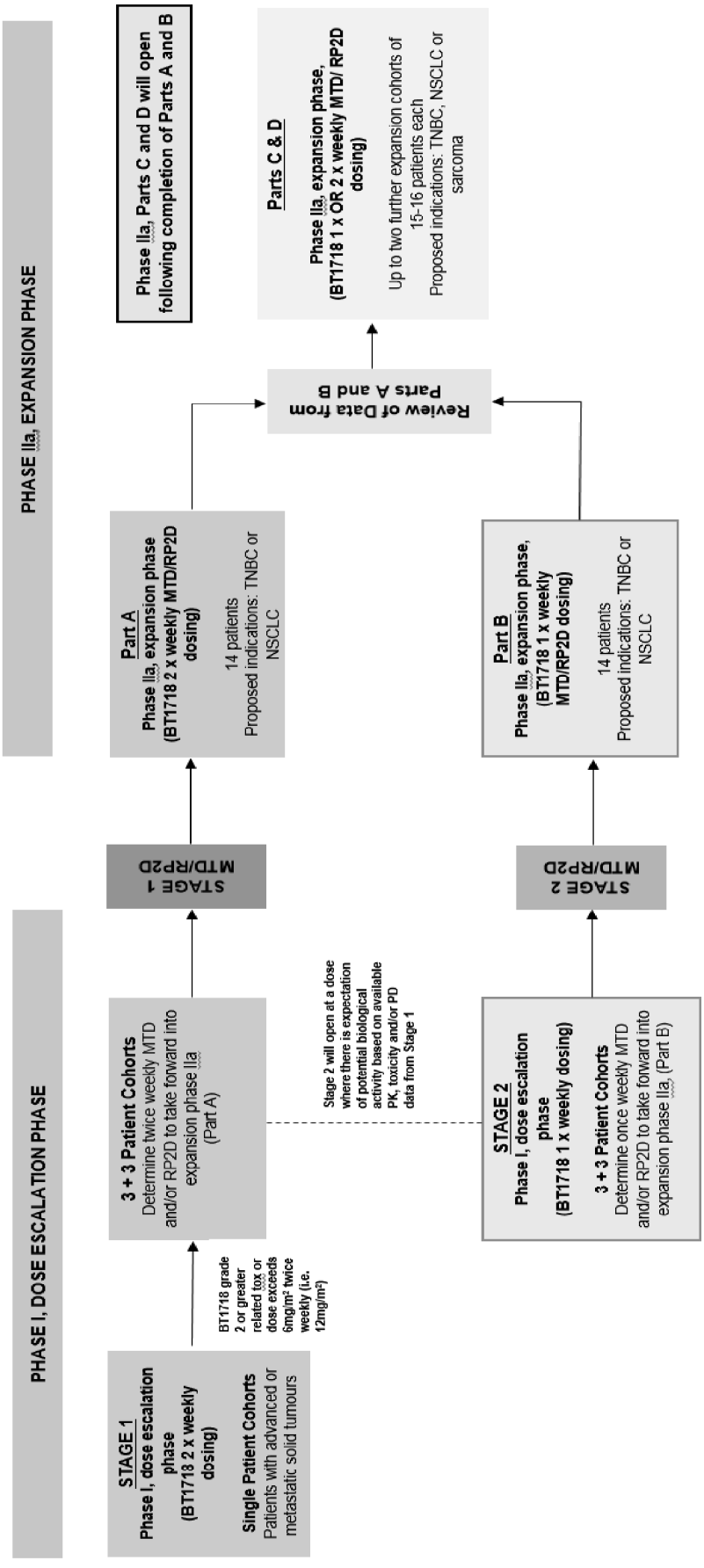

PHASE I, DOSE ESCALATION PHASE
PHASE IIa, EXPANSION PHASE
STAGE 1
Phase I, dose escalation phase
(BT1718 2 x weekly dosing)
Single Patient Cohorts
Patients with advanced or metastatic solid tumours
BT1718 grade 2 or greater related tox or dose exceeds 6mg/m² twice weekly (i.e. 12mg/m²)
3 + 3 Patient Cohorts
Determine twice weekly MTD and/or RP2D to take forward into expansion phase IIa (Part A)
STAGE 1 MTD/RP2D
Part A
Phase IIa, expansion phase (BT1718 2 x weekly MTD/RP2D dosing)
14 patients
Proposed indications: TNBC or NSCLC
Stage 2 will open at a dose where there is expectation of potential biological activity based on available PK, toxicity and/or PD data from Stage 1
STAGE 2
Phase I, dose escalation phase
(BT1718 1 x weekly dosing)
3 + 3 Patient Cohorts
Determine once weekly MTD and/or RP2D to take forward into expansion phase IIa, (Part B)
STAGE 2 MTD/RP2D
Part B
Phase IIa, expansion phase, (BT1718 1 x weekly MTD/RP2D dosing)
14 patients
Proposed indications: TNBC or NSCLC
Review of Data from Parts A and B
Parts C & D
Phase IIa, expansion phase, (BT1718 1 x OR 2 x weekly MTD/ RP2D dosing)
Up to two further expansion cohorts of 15-16 patients each
Proposed indications: TNBC, NSCLC or sarcoma
Phase IIa, Parts C and D will open following completion of Parts A and B

Fig. 3

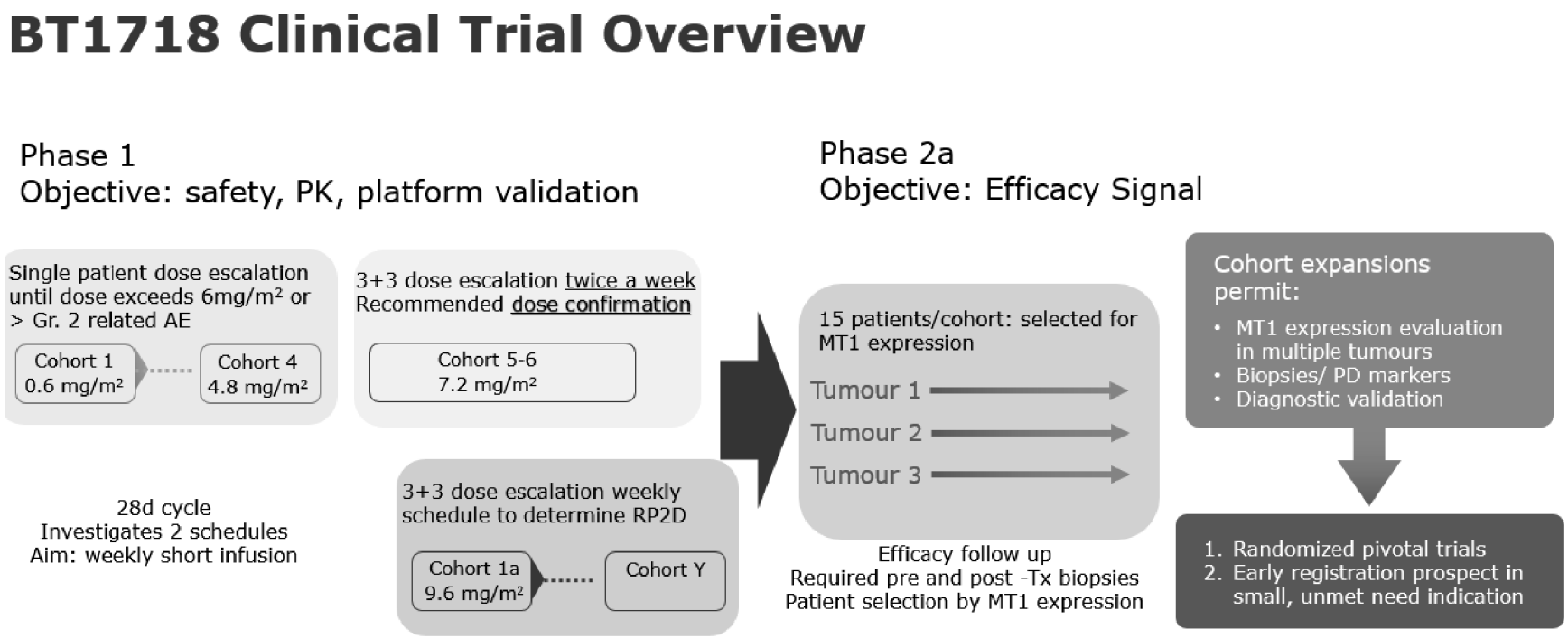

BT1718 Clinical Trial Overview
Phase 1
Objective: safety, PK, platform validation
Single patient dose escalation until dose exceeds 6mg/m² or > Gr. 2 related AE
Cohort 1 0.6 mg/m²
Cohort 4 4.8 mg/m²
3+3 dose escalation twice a week Recommended dose confirmation
Cohort 5-6 7.2 mg/m²
28d cycle
Investigates 2 schedules
Aim: weekly short infusion
3+3 dose escalation weekly schedule to determine RP2D
Cohort 1a 9.6 mg/m²
Cohort Y
Phase 2a
Objective: Efficacy Signal
15 patients/cohort: selected for MT1 expression
Tumour 1
Tumour 2
Tumour 3
Efficacy follow up
Required pre and post -Tx biopsies
Patient selection by MT1 expression
Cohort expansions permit:
• MT1 expression evaluation in multiple tumours
• Biopsies/ PD markers
• Diagnostic validation
1. Randomized pivotal trials
2. Early registration prospect in small, unmet need indication

Fig. 4

- Phase 1: safety, PK, platform validation
- Investigates 2 schedules; weekly short infusion preferred

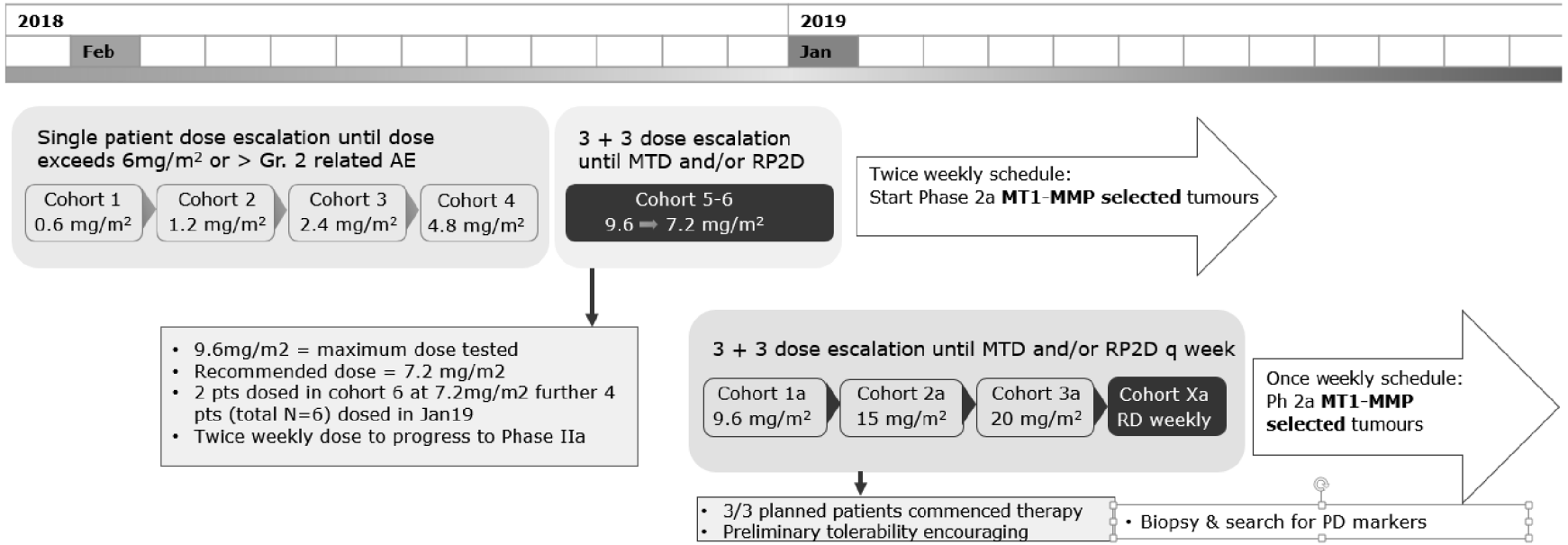


Fig. 5

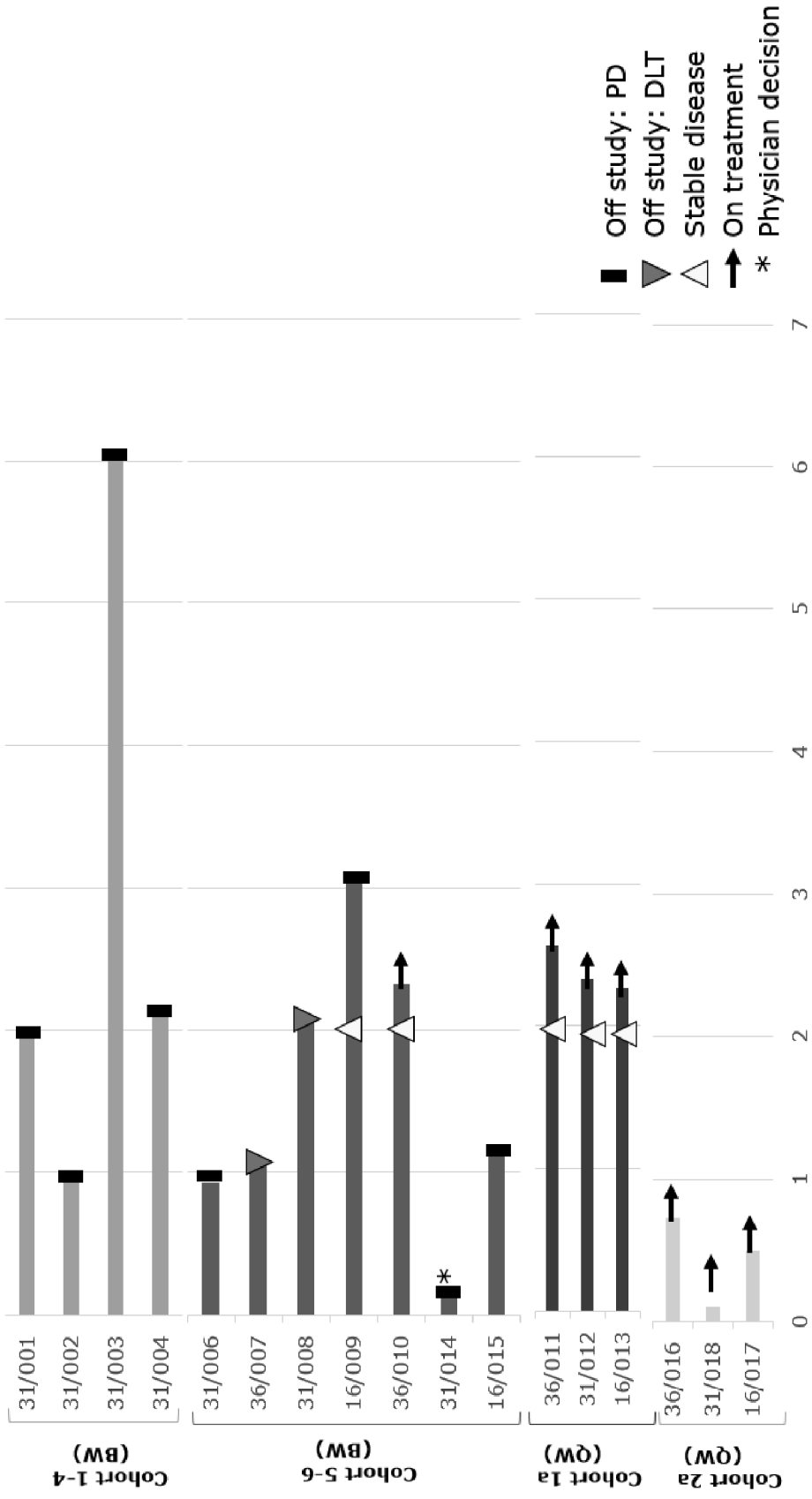

Off study: PD
Off study: DLT
Stable disease
On treatment
* Physician decision
0
1
2
3
4
5
6
7
Months
Cohort 1-4 (BW)
31/001
31/002
31/003
31/004
Cohort 5-6 (BW)
31/006
36/007
31/008
16/009
36/010
31/014
16/015
Cohort 1a (QW)
36/011
31/012
16/013
Cohort 2a (QW)
36/016
31/018
16/017

Fig. 6

9.6 mg/m^2 QW Schedule

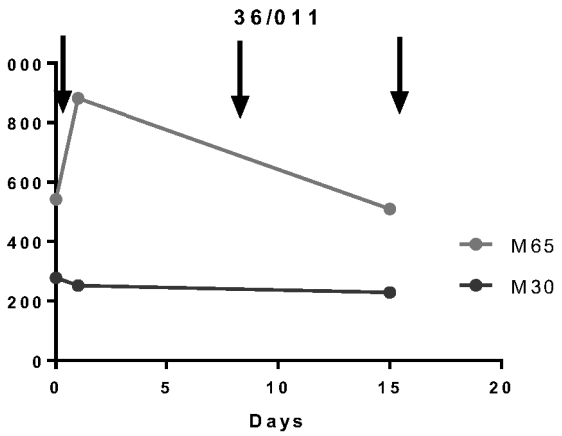
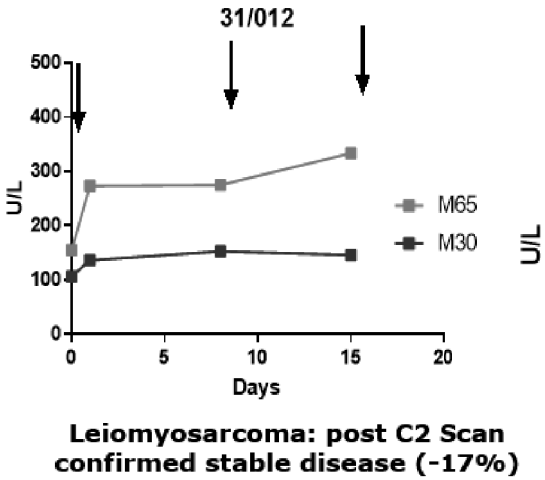


Fig. 7A



Leiomyosarcoma: post C2 Scan confirmed stable disease (-17%)

Fig. 7B

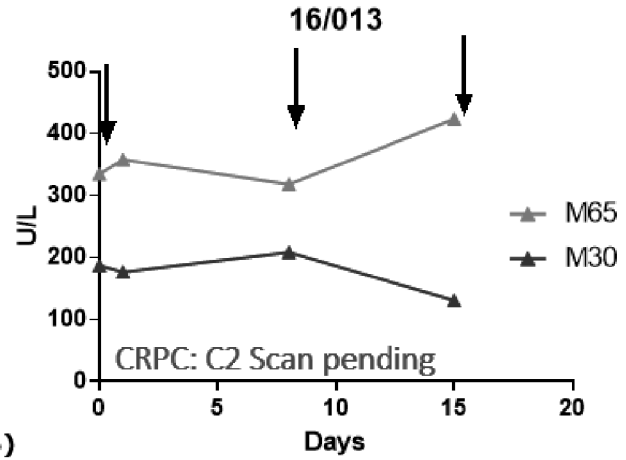
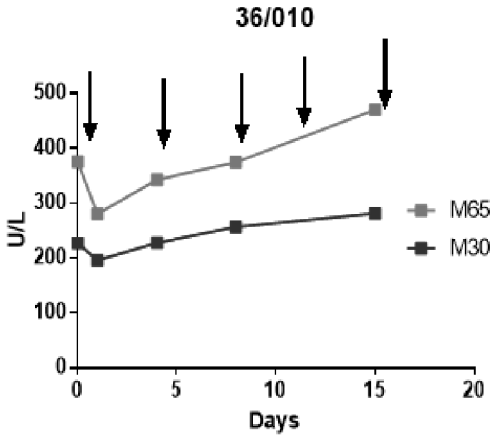


Fig. 7C

7.2 mg/m^2 BIW Schedule



CRPC: post C2 Scan confirmed stable disease

Fig. 7D

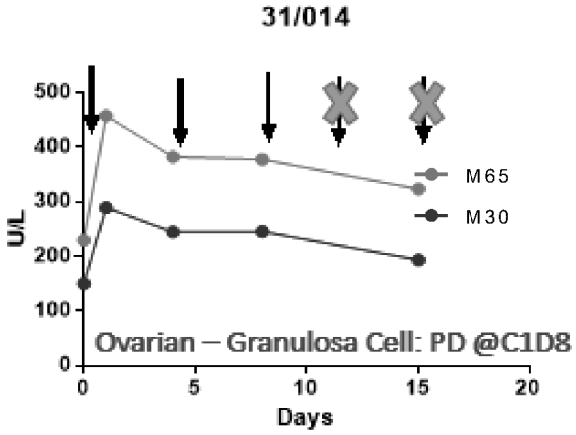


Fig. 7E

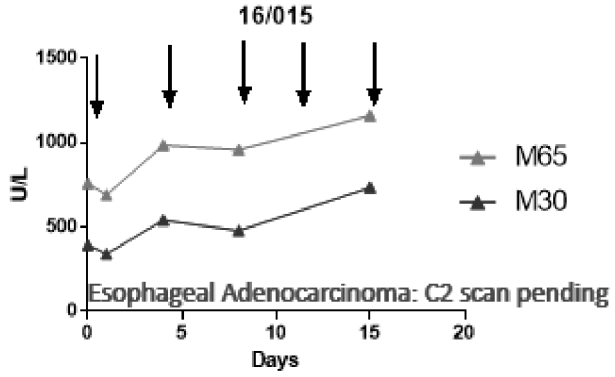


Fig. 7F

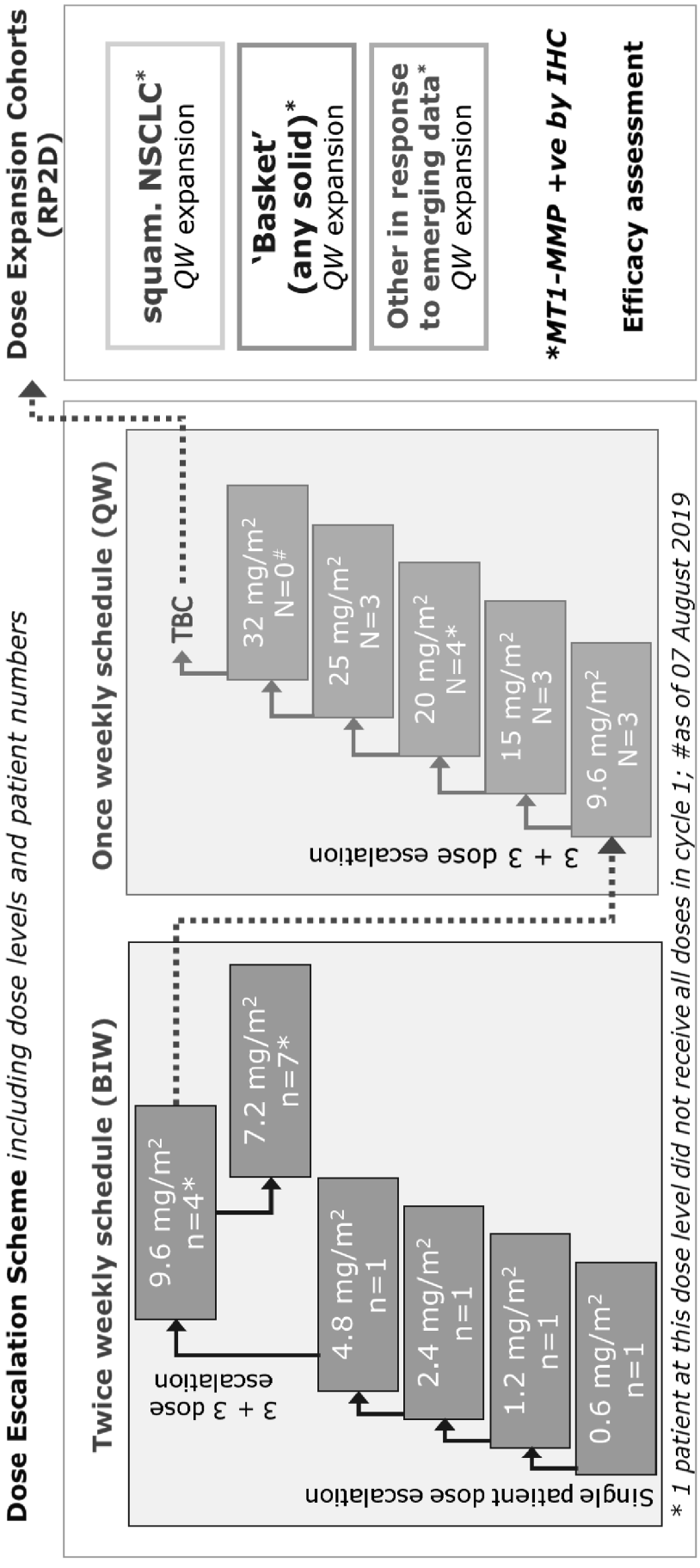

Dose Escalation Scheme including dose levels and patient numbers
Twice weekly schedule (BIW)
Single patient dose escalation
0.6 mg/m² n=1
1.2 mg/m² n=1
2.4 mg/m² n=1
4.8 mg/m² n=1
3 + 3 dose escalation
9.6 mg/m² n=4*
7.2 mg/m² n=7*
Once weekly schedule (QW)
3 + 3 dose escalation
9.6 mg/m² N=3
15 mg/m² N=3
20 mg/m² N=4*
25 mg/m² N=3
TBC
32 mg/m² N=0#
* 1 patient at this dose level did not receive all doses in cycle 1; #as of 07 August 2019
Dose Expansion Cohorts (RP2D)
squam. NSCLC* QW expansion
'Basket' (any solid)* QW expansion
Other in response to emerging data* QW expansion
*MT1-MMP +ve by IHC
Efficacy assessment

Fig. 8

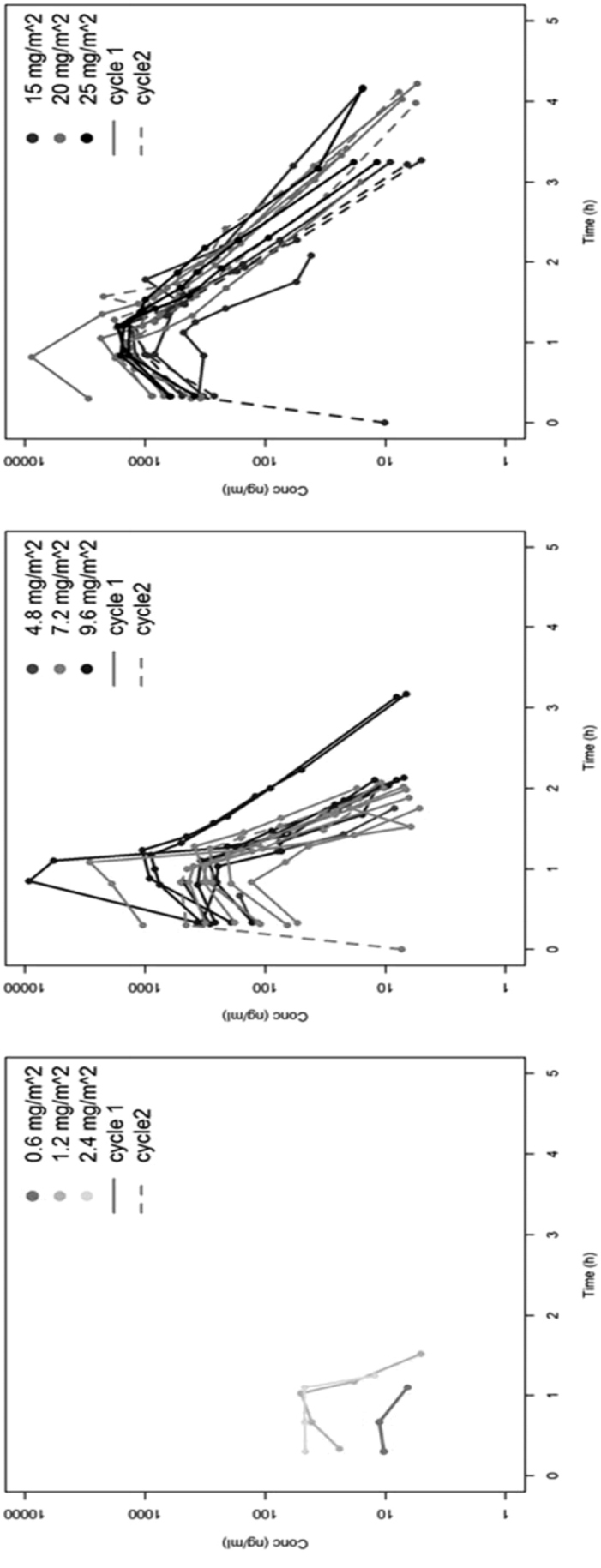


Fig. 9A

Fig. 9B

Fig. 9C

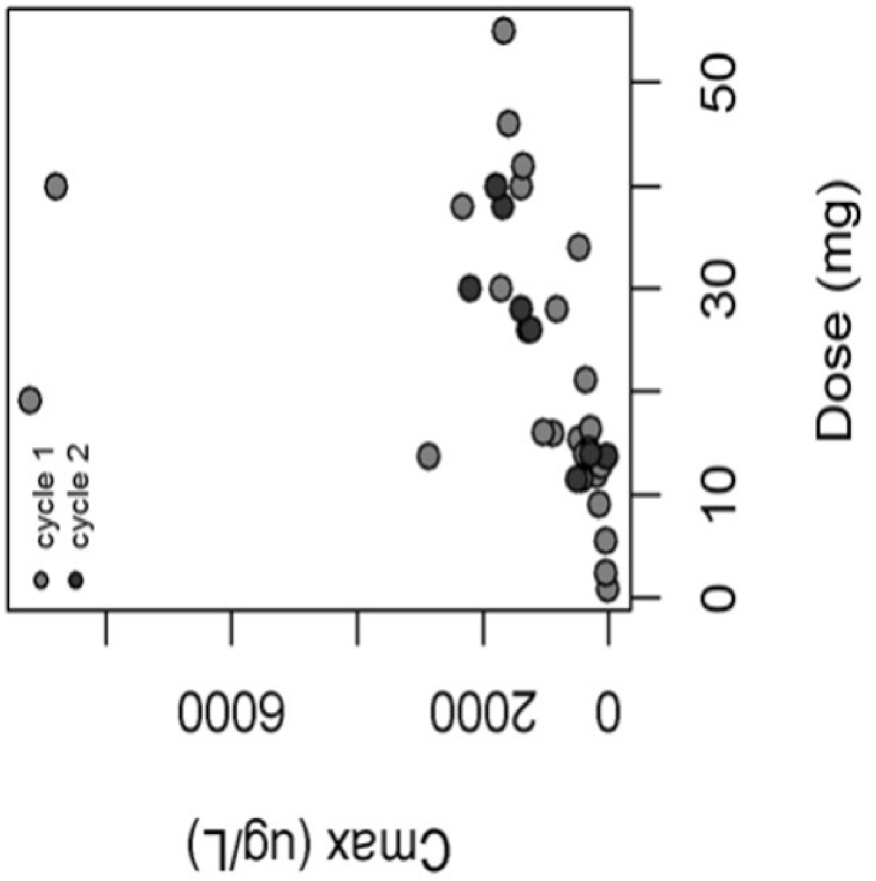


Fig. 10B

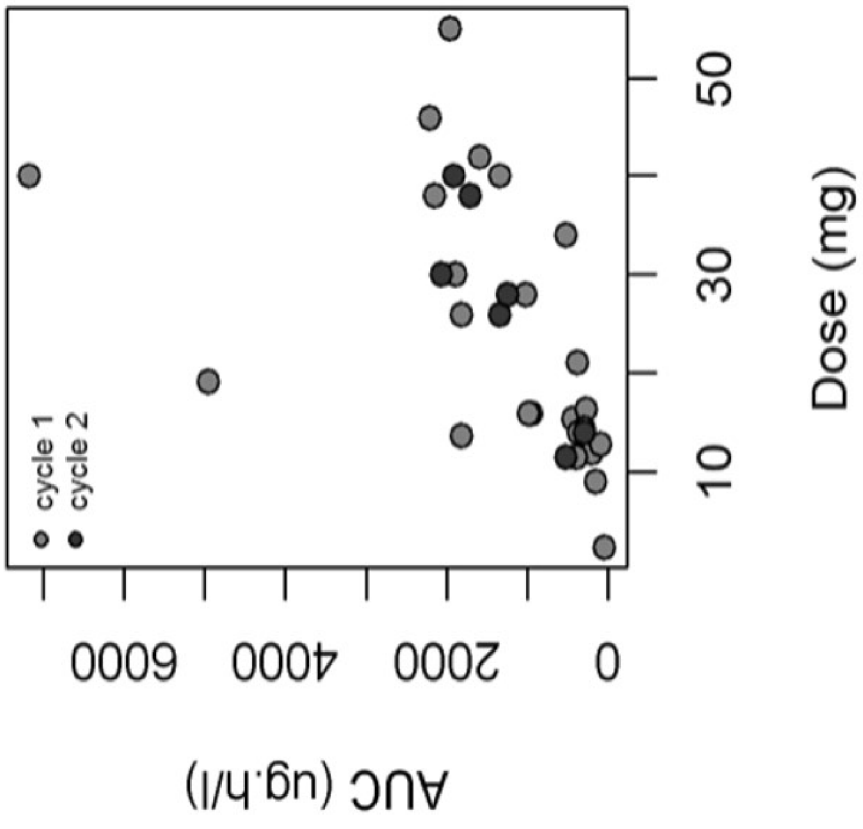


Fig. 10A