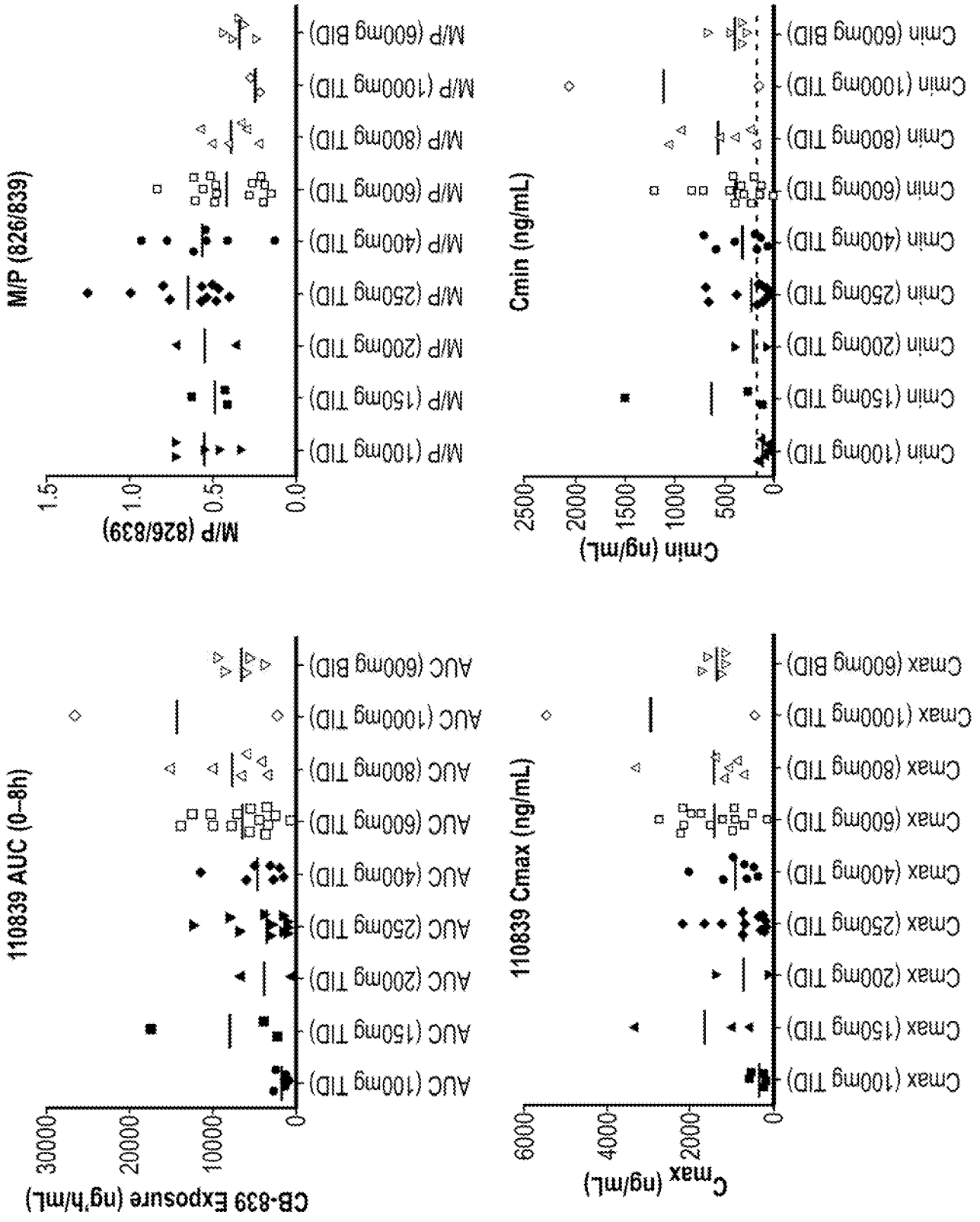

M/P (826/839)
1.5
1.0
0.5
0.0
M/P (100mg TID)
M/P (150mg TID)
M/P (200mg TID)
M/P (250mg TID)
M/P (400mg TID)
M/P (600mg TID)
M/P (800mg TID)
M/P (1000mg TID)
M/P (600mg BID)
Cmin (ng/mL)
2500
2000
1500
1000
500
0
Cmin (100mg TID)
Cmin (150mg TID)
Cmin (200mg TID)
Cmin (250mg TID)
Cmin (400mg TID)
Cmin (600mg TID)
Cmin (800mg TID)
Cmin (1000mg TID)
Cmin (600mg BID)
CB-839 Exposure (ng*h/mL)
30000
20000
10000
0
AUC (100mg TID)
AUC (150mg TID)
AUC (200mg TID)
AUC (250mg TID)
AUC (400mg TID)
AUC (600mg TID)
AUC (800mg TID)
AUC (1000mg TID)
AUC (600mg BID)
Cmax (ng/mL)
6000
4000
2000
0
Cmax (100mg TID)
Cmax (150mg TID)
Cmax (200mg TID)
Cmax (250mg TID)
Cmax (400mg TID)
Cmax (600mg TID)
Cmax (800mg TID)
Cmax (1000mg TID)
Cmax (600mg BID)

Figure 1

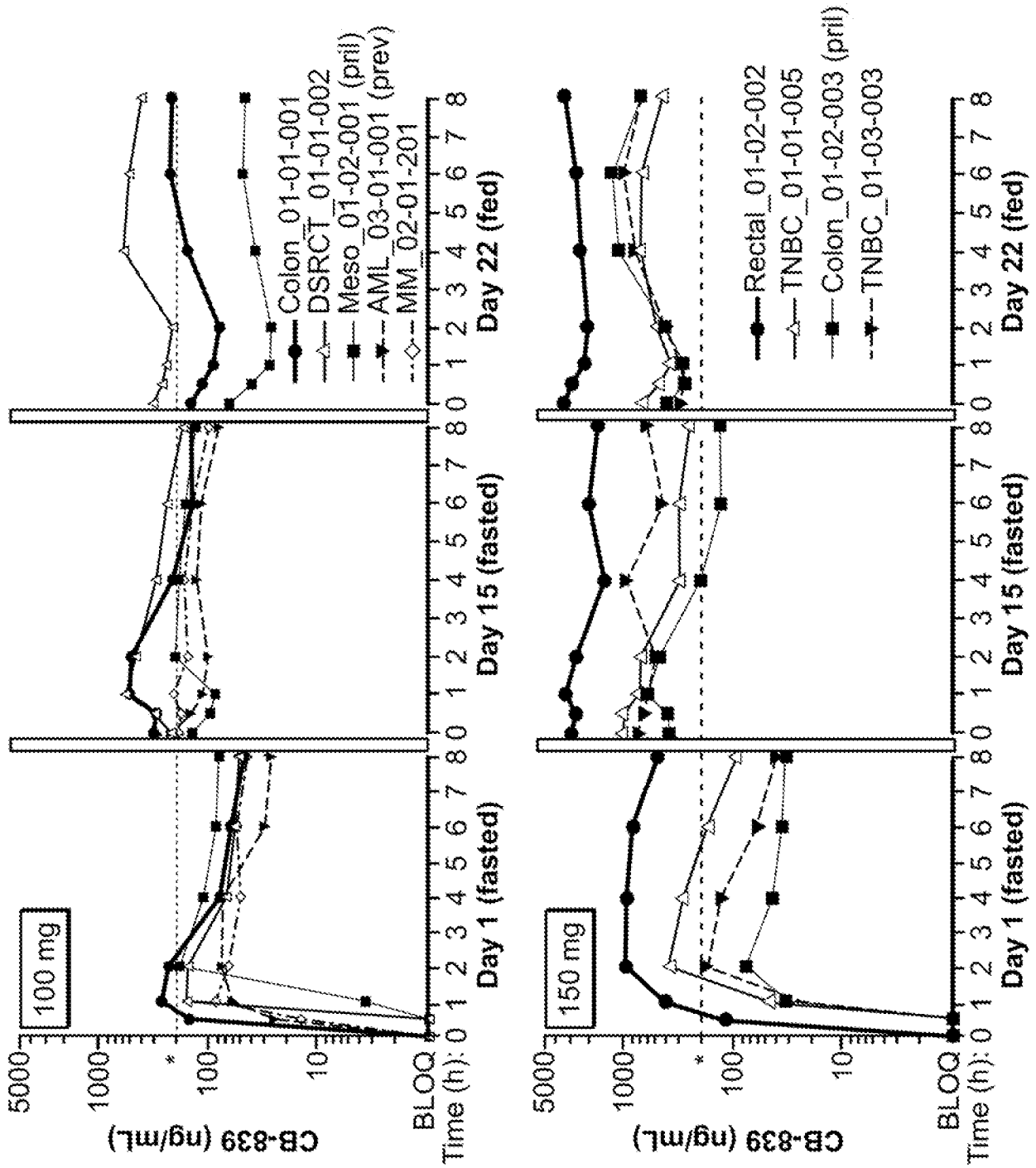

100 mg
150 mg
CB-839 (ng/mL)
5000
1000
100
10
*
BLOQ
Time (h): 0 1 2 3 4 5 6 7 8 0 1 2 3 4 5 6 7 8 0 1 2 3 4 5 6 7 8
Day 1 (fasted)
Day 15 (fasted)
Day 22 (fed)
Colon_01-01-001
DSRCT_01-01-002
Meso_01-02-001 (pril)
AML_03-01-001 (prev)
MM_02-01-201
Rectal_01-02-002
TNBC_01-01-005
Colon_01-02-003 (pril)
TNBC_01-03-003

Figure 2

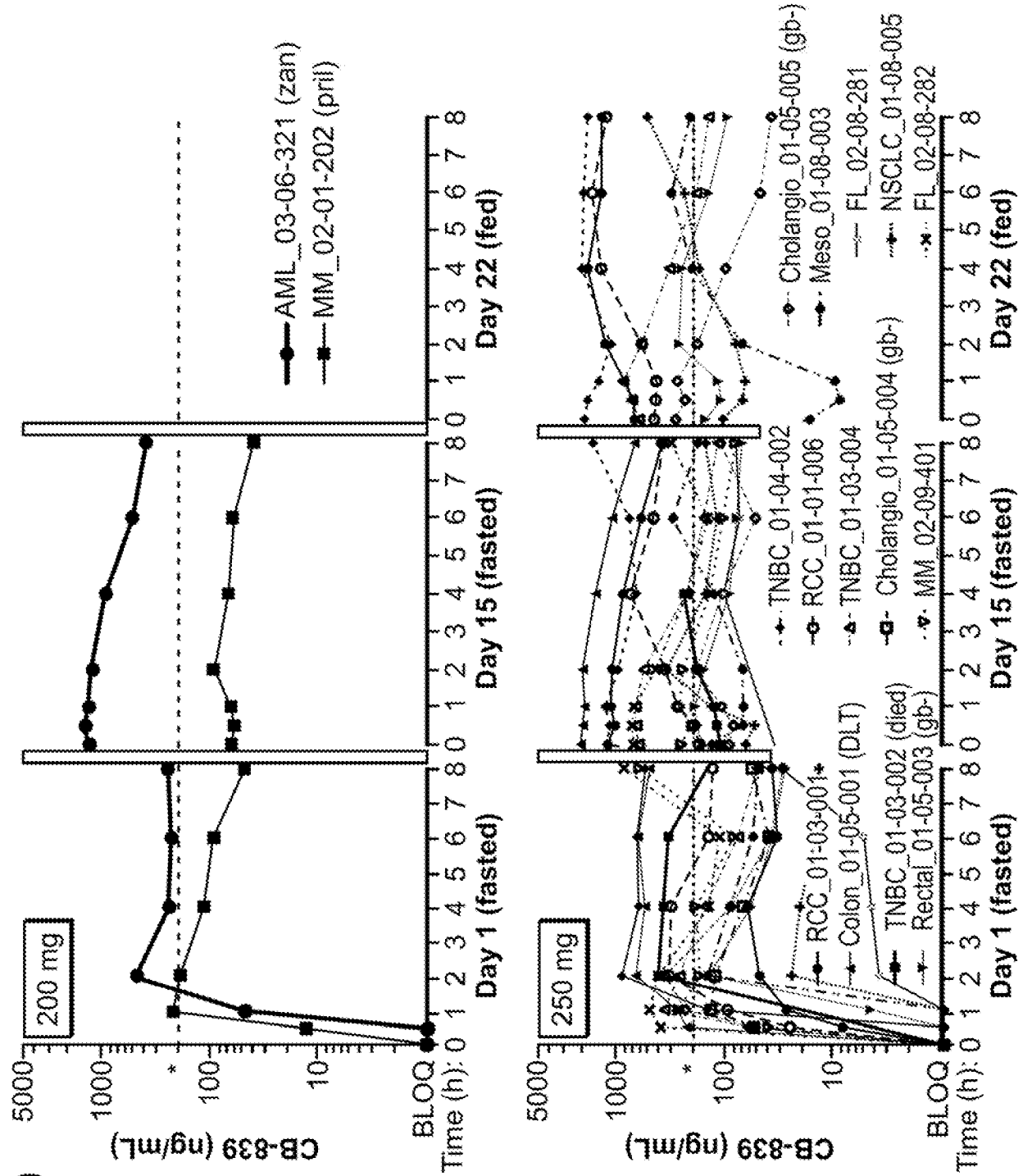


Figure 2 (cont.)

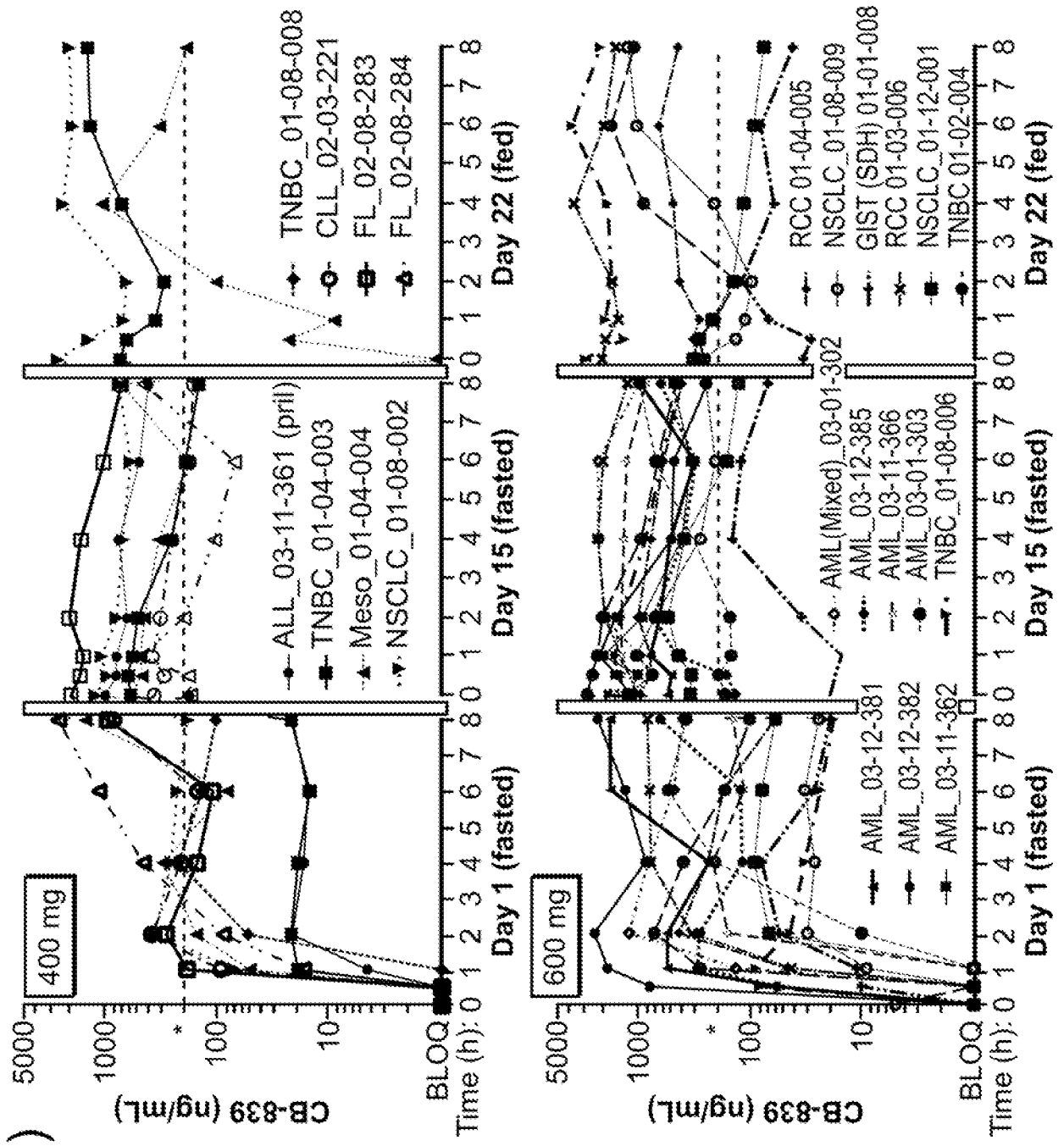


Figure 2 (cont.)

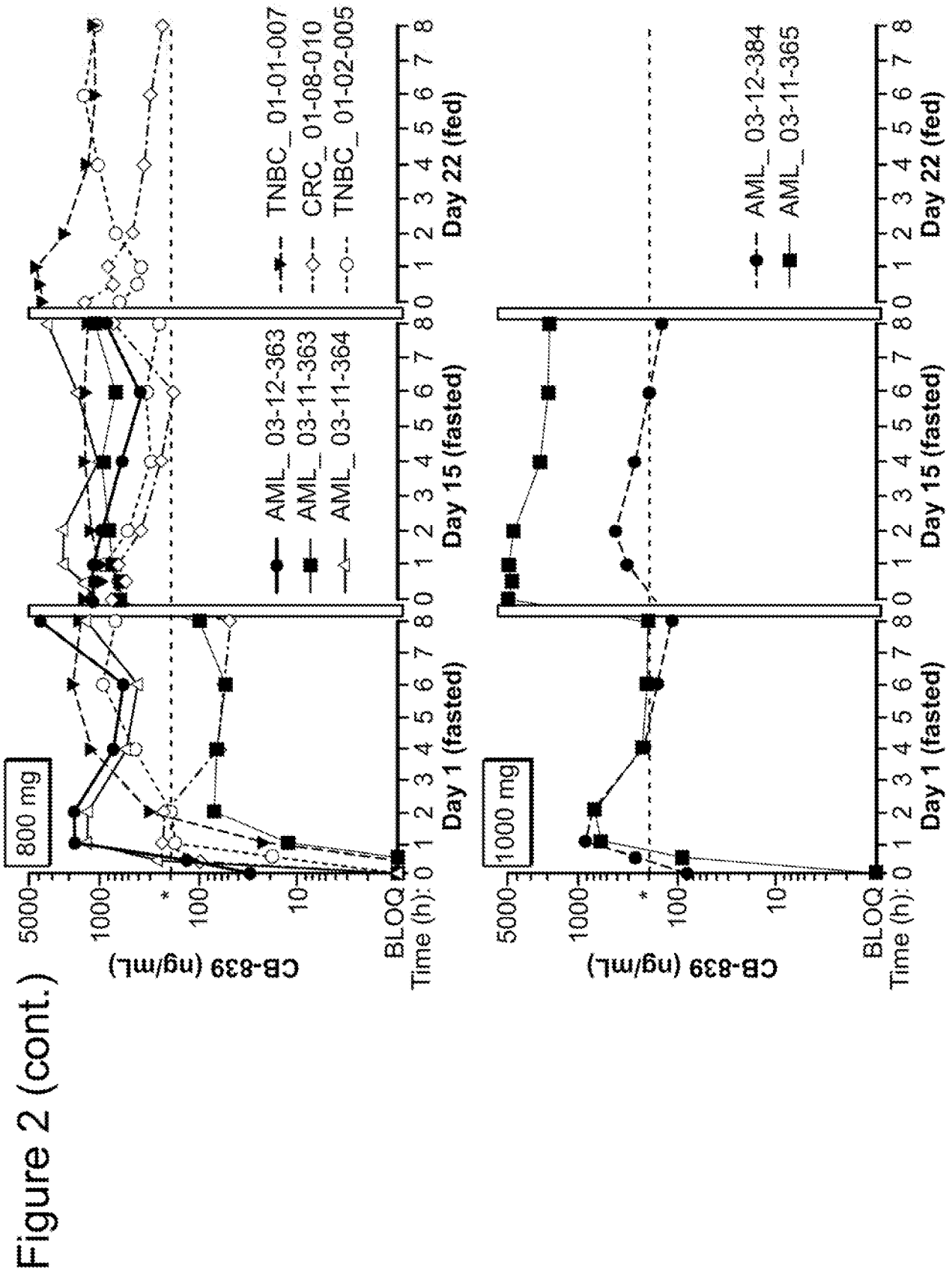


Figure 2 (cont.)

Figure 3

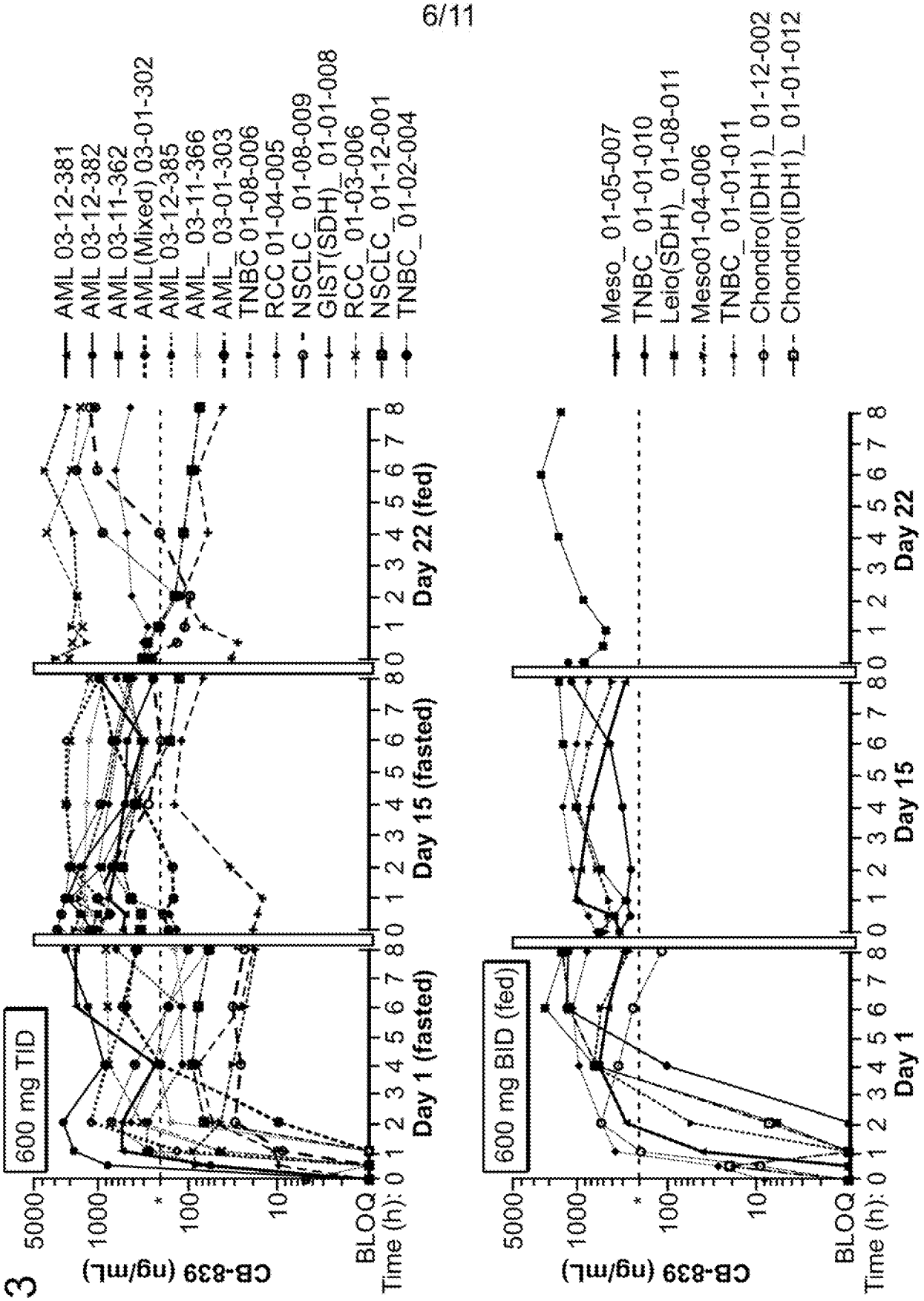
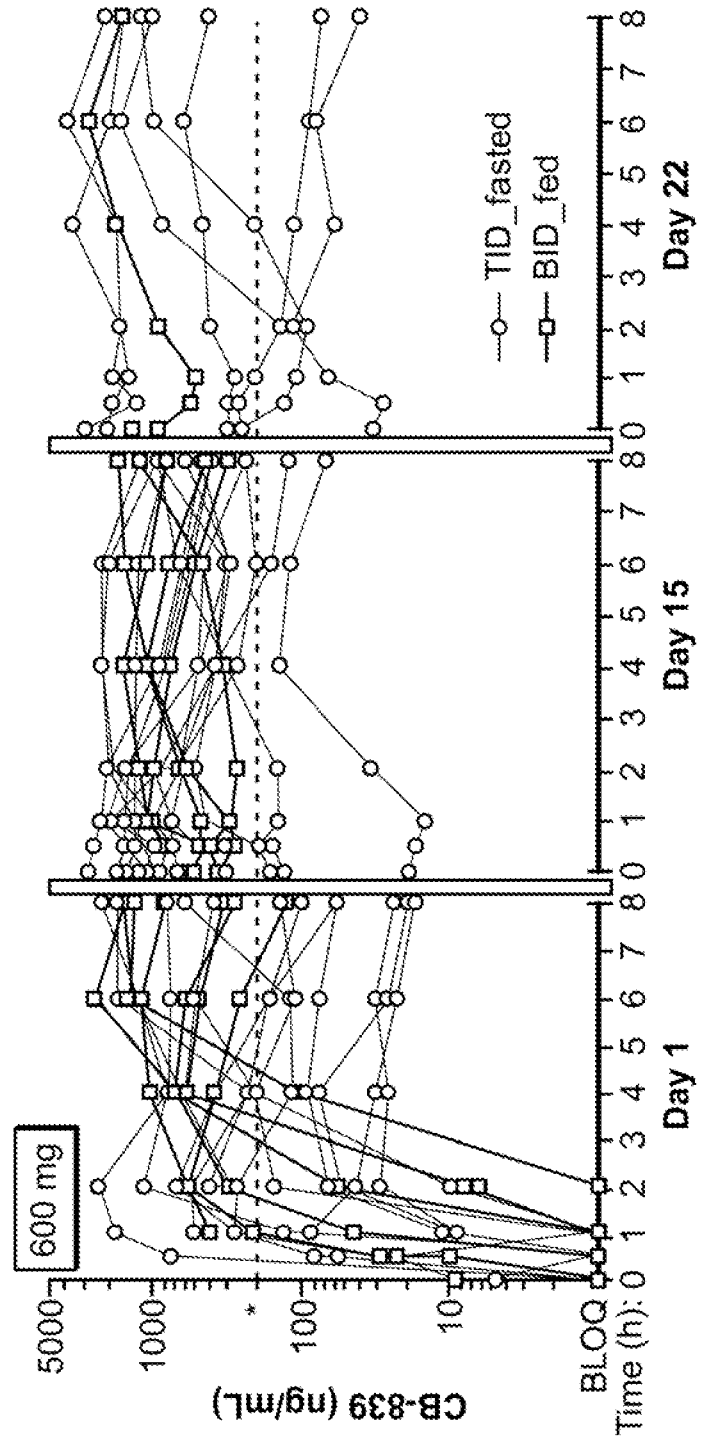

600 mg TID
600 mg BID (fed)
CB-839 (ng/mL)
5000
1000
100
10
BLOQ
Time (h): 0 1 2 3 4 5 6 7 8 0 1 2 3 4 5 6 7 8 0 1 2 3 4 5 6 7 8
Day 1 (fasted)
Day 15 (fasted)
Day 22 (fed)
Day 1
Day 15
Day 22
AML 03-12-381
AML 03-12-382
AML 03-11-362
AML(Mixed) 03-01-302
AML 03-12-385
AML_ 03-11-366
AML_ 03-01-303
TNBC 01-08-006
RCC 01-04-005
NSCLC_ 01-08-009
GIST(SDH)_ 01-01-008
RCC_ 01-03-006
NSCLC_ 01-12-001
TNBC_ 01-02-004
Meso_ 01-05-007
TNBC_ 01-01-010
Leio(SDH)_ 01-08-011
Meso01-04-006
TNBC_ 01-01-011
Chondro(IDH1)_ 01-12-002
Chondro(IDH1)_ 01-01-012

Figure 4


600 mg
CB-839 (ng/mL)
5000
1000
100
10
*
BLOQ
Time (h): 0 1 2 3 4 5 6 7 8 0 1 2 3 4 5 6 7 8 0 1 2 3 4 5 6 7 8
Day 1
Day 15
Day 22
TID_fasted
BID_fed

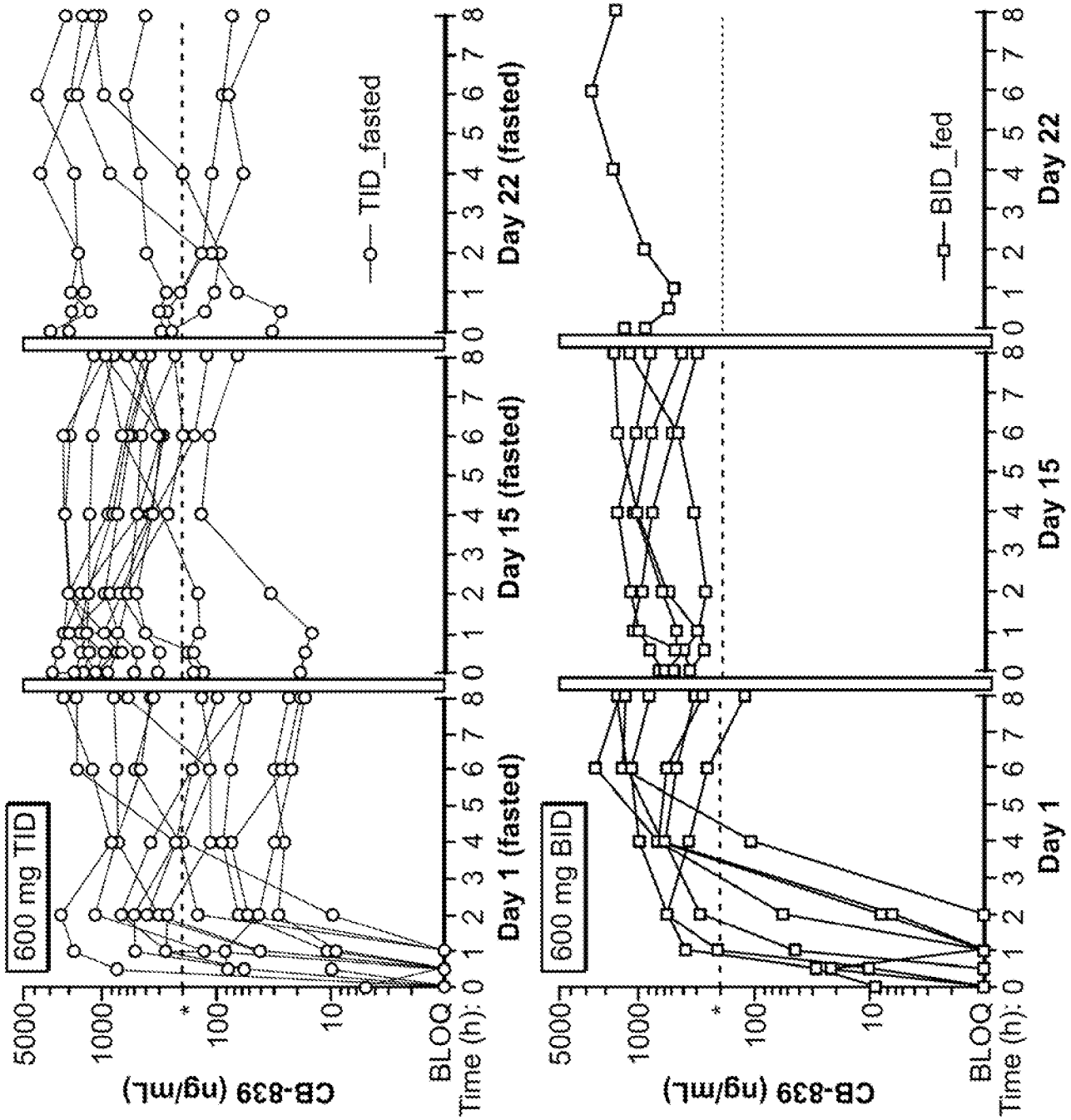

600 mg TID
600 mg BID
TID_fasted
BID_fed
CB-839 (ng/mL)
5000
1000
100
10
*
BLOQ
Time (h): 0 1 2 3 4 5 6 7 8 0 1 2 3 4 5 6 7 8 0 1 2 3 4 5 6 7 8
Day 1 (fasted)
Day 15 (fasted)
Day 22 (fasted)
Day 1
Day 15
Day 22

Figure 5

Figure 6

	Dose (mg)	100	150	250	400	600	800	600
	Schedule	TID	TID	TID	TID	TID	TID	BID
	N	3	4	10	3	7	3	8
AUC (0-8h) (ng*hr/mL)	Average	1980	7167	3852	3959	6125	5575	6201
	Variation (%CV)	33%	98%	101%	46%	70%	72%	34%
C_{max} (ng/mL)	Average	432	1467	778	846	1366	1019	1291
	Variation (%CV)	46%	87%	89%	38%	68%	35%	23%
C_{min} (ng/mL)	Average	134	585	241	306	400	457	366
	Variation (%CV)	32%	108%	105%	80%	98%	92%	35%

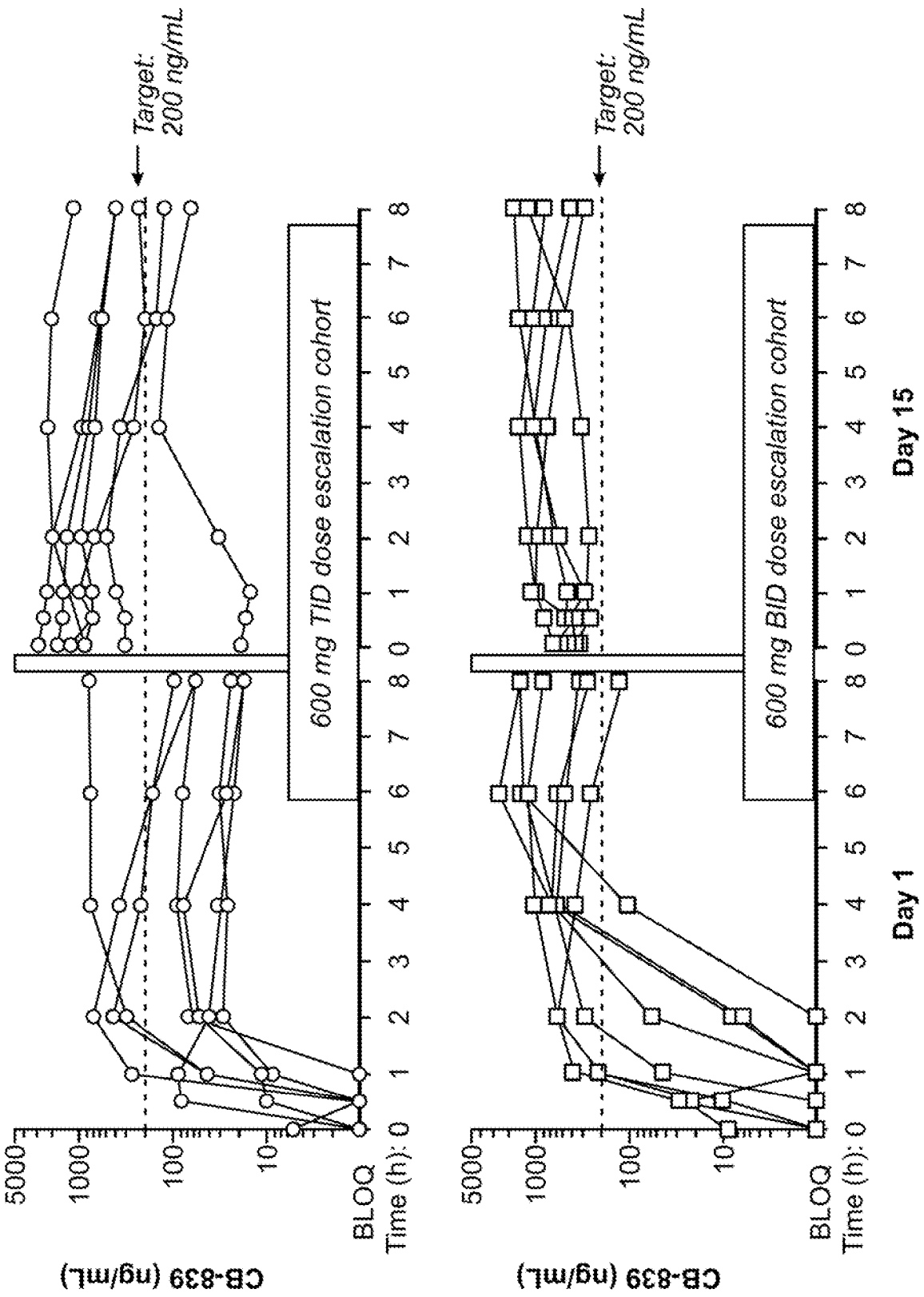
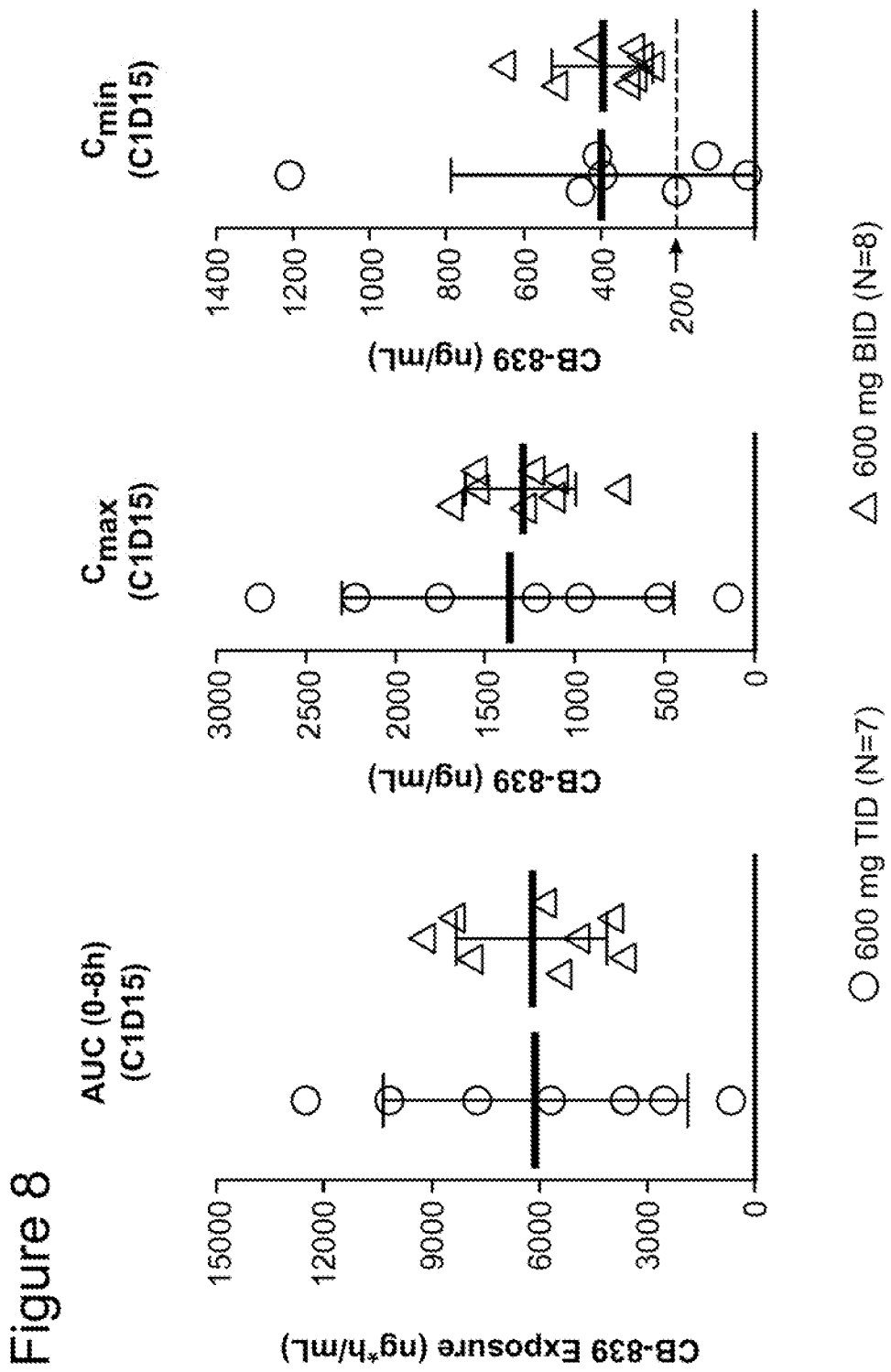

Target:
200 ng/mL
600 mg TID dose escalation cohort
600 mg BID dose escalation cohort
Day 1
Day 15
CB-839 (ng/mL)
5000
1000
100
10
BLOQ
Time (h): 0 1 2 3 4 5 6 7 8 0 1 2 3 4 5 6 7 8

Figure 7

Figure 8


AUC (0-8h) (C1D15)
CB-839 Exposure (ng*h/mL)
15000
12000
9000
6000
3000
0
C_{max} (C1D15)
CB-839 (ng/mL)
3000
2500
2000
1500
1000
500
0
C_{min} (C1D15)
CB-839 (ng/mL)
1400
1200
1000
800
600
400
200
○ 600 mg TID (N=7)
△ 600 mg BID (N=8)