Figure 1

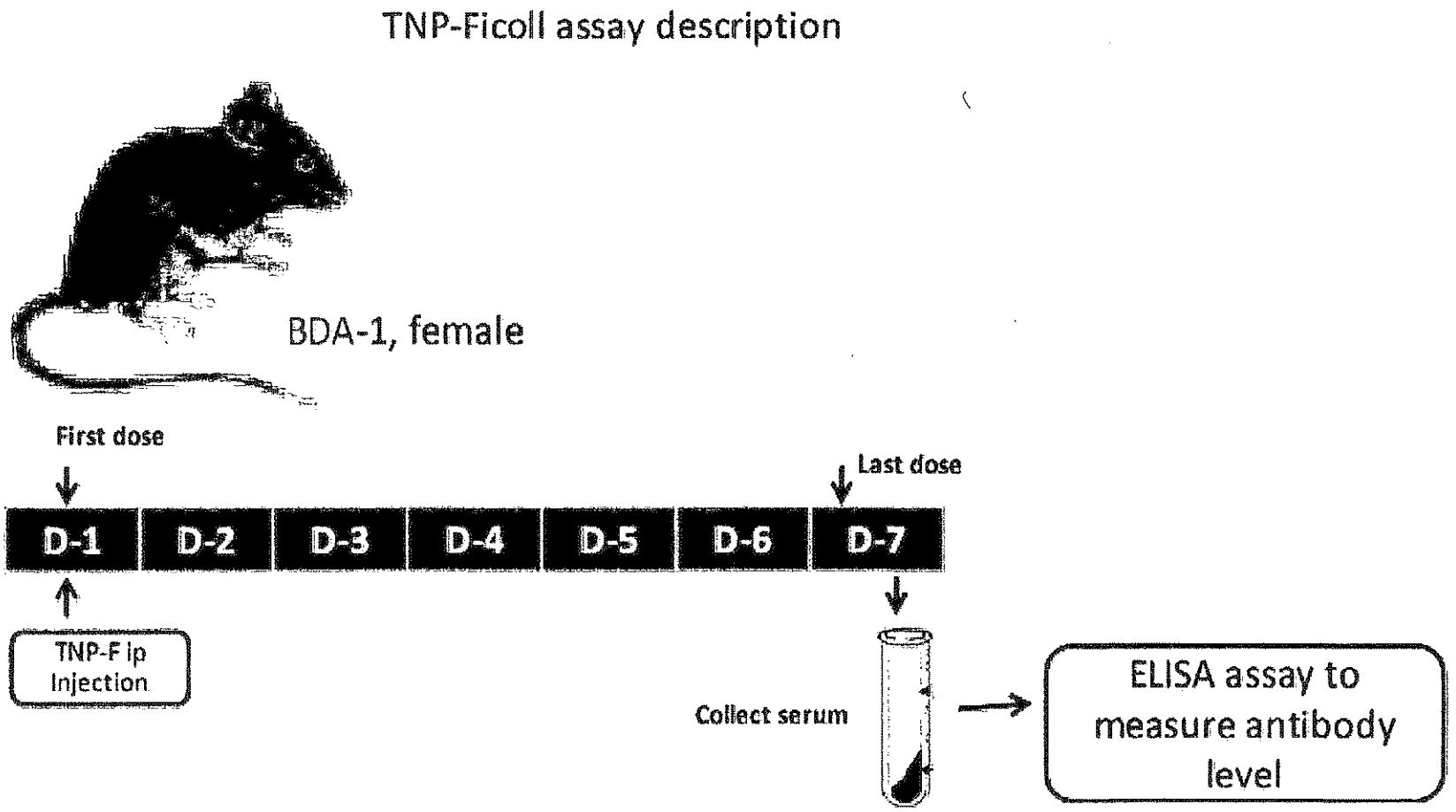

TNP-Ficoll assay description
BDA-1, female
First dose
Last dose
D-1
D-2
D-3
D-4
D-5
D-6
D-7
TNP-F ip Injection
Collect serum
ELISA assay to measure antibody level

Figure 2

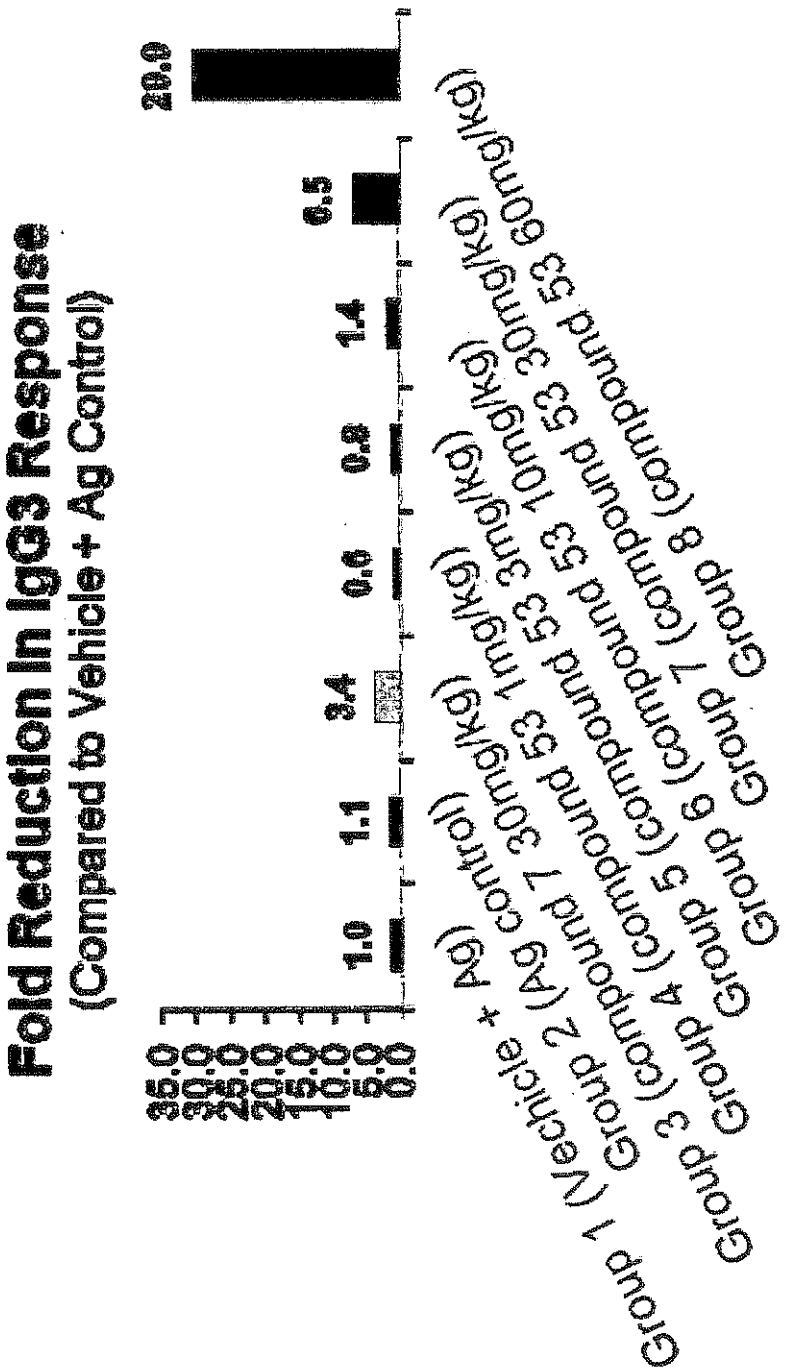
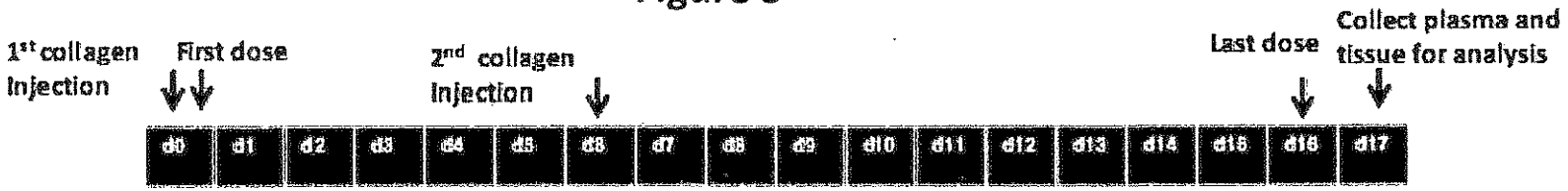

Fold Reduction In IgG3 Response
(Compared to Vehicle + Ag Control)
35.0
30.0
25.0
20.0
15.0
10.0
5.0
0.0
1.0
1.1
3.4
0.6
0.8
1.4
0.5
20.0
Group 1 (Vehicle + Ag control)
Group 2 (Ag control)
Group 3 (Compound 53 30mg/kg)
Group 4 (Compound 53 10mg/kg)
Group 5 (Compound 53 3mg/kg)
Group 6 (Compound 53 1mg/kg)
Group 7 (Compound 53 300mg/kg)
Group 8 (Compound 53 60mg/kg)

Figure 3


1st collagen Injection
First dose
2nd collagen Injection
Last dose
Collect plasma and tissue for analysis
d0
d1
d2
d3
d4
d5
d6
d7
d8
d9
d10
d11
d12
d13
d14
d15
d16
d17

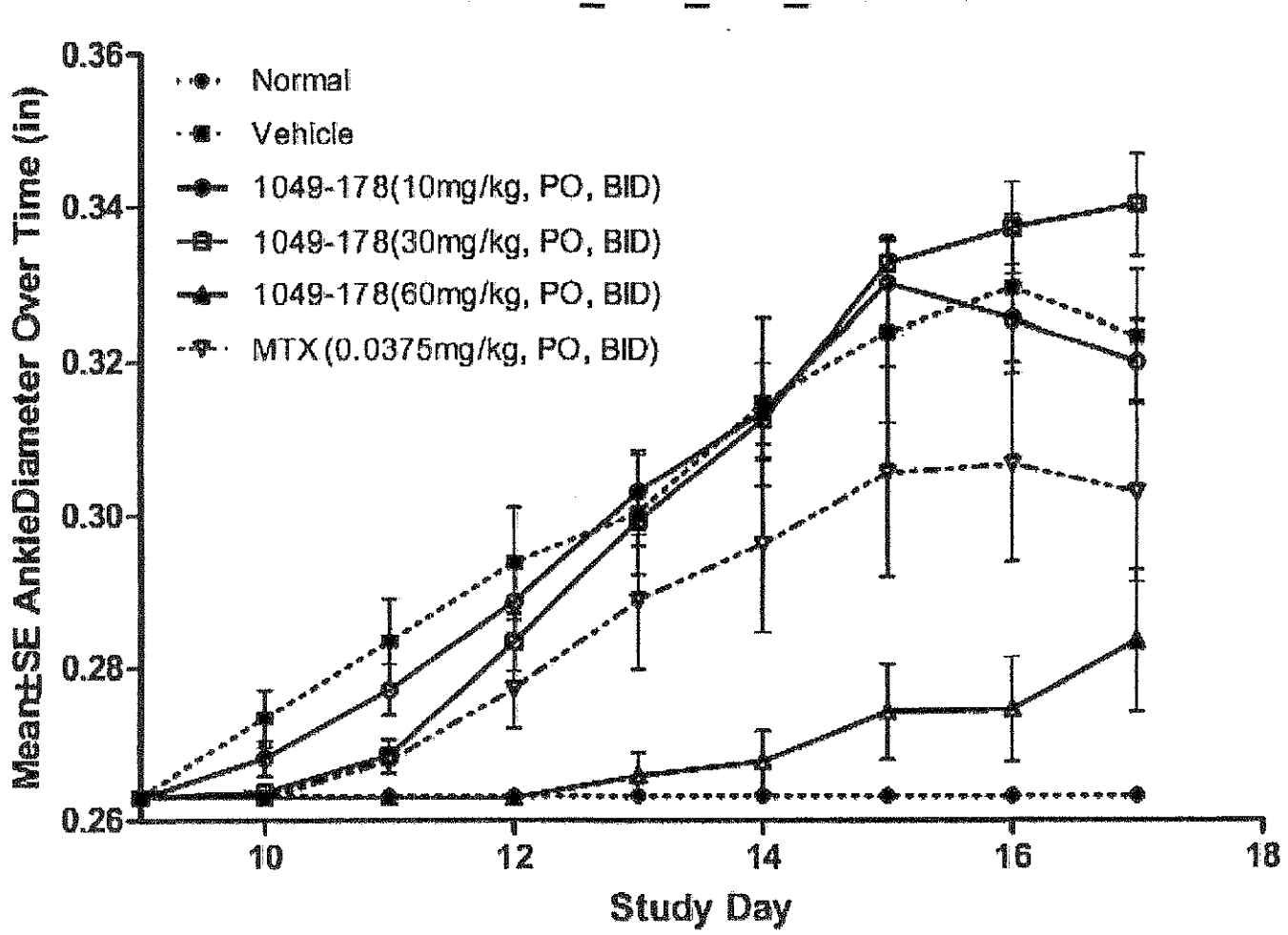

RTTC-IK-1_Ank_BID_Preventive
Normal
Vehicle
1049-178(10mg/kg, PO, BID)
1049-178(30mg/kg, PO, BID)
1049-178(60mg/kg, PO, BID)
MTX (0.0375mg/kg, PO, BID)
Mean±SE AnkleDiameter Over Time (in)
0.36
0.34
0.32
0.30
0.28
0.26
10
12
14
16
18
Study Day

Figure 4

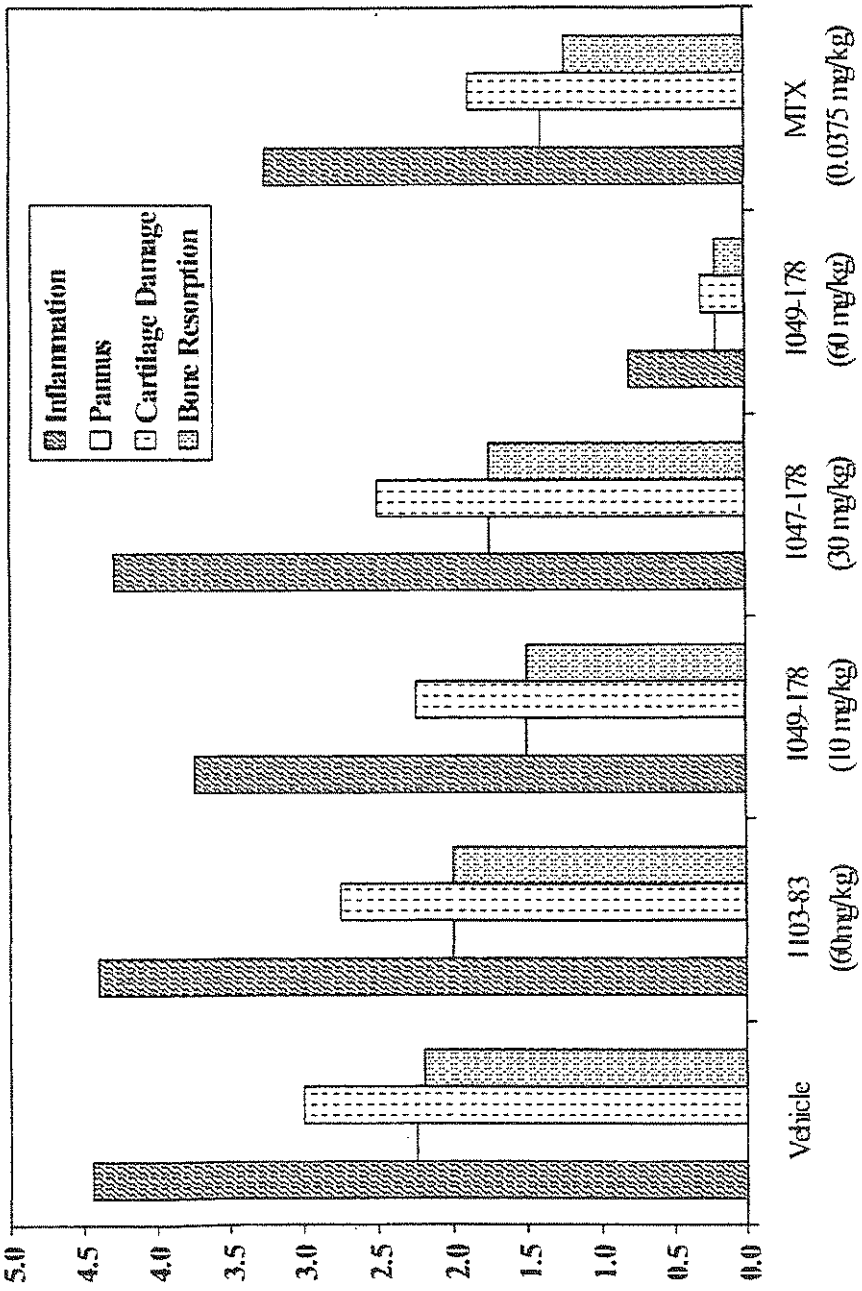

Inflammation
Pannus
Cartilage Damage
Bone Resorption
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
Vehicle
1103-83 (60mg/kg)
1049-178 (10 mg/kg)
1047-178 (30 mg/kg)
1049-178 (60 mg/kg)
MTX (0.0375 mg/kg)
Treatment Group

Figure 5

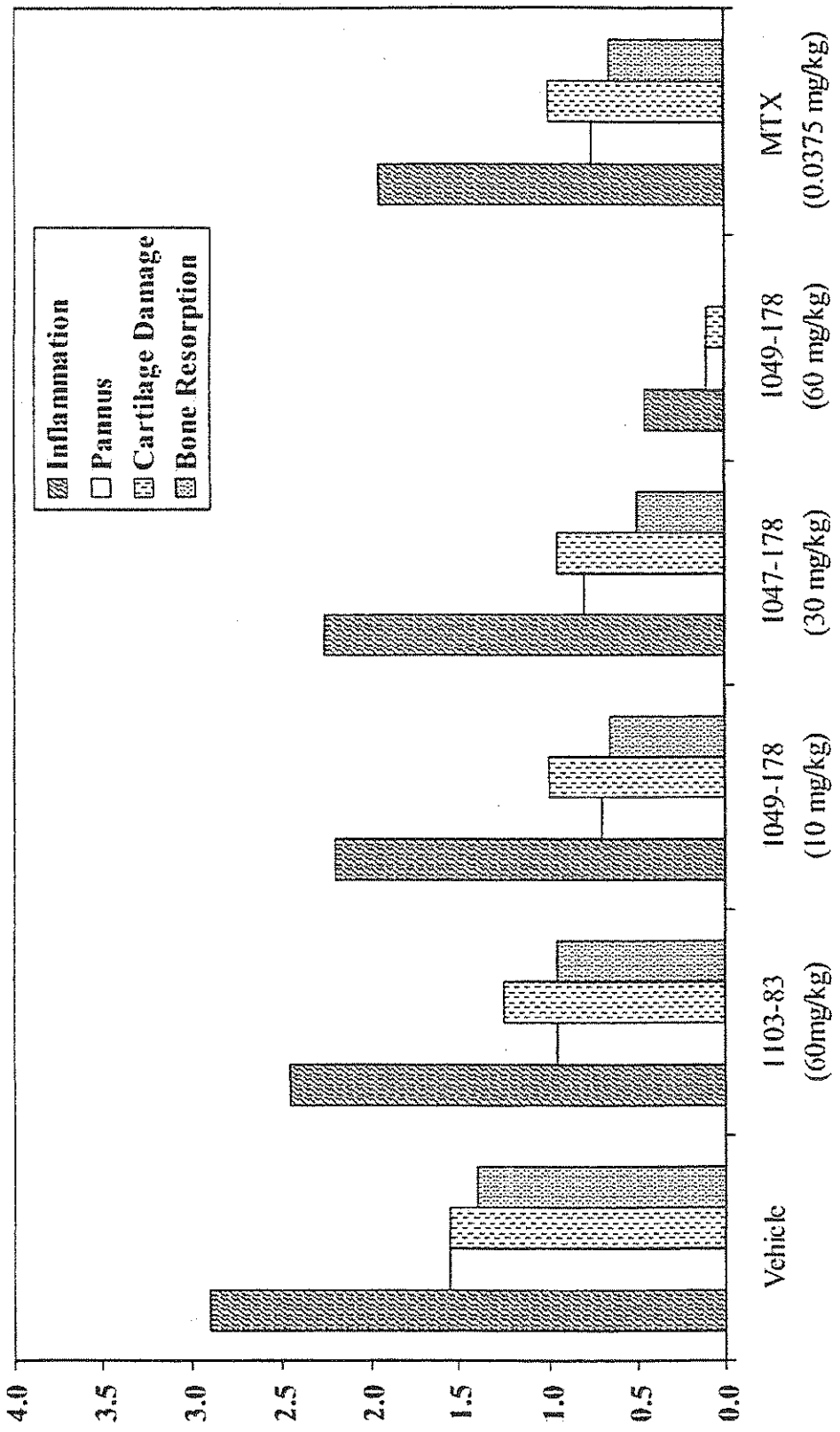

Inflammation
Pannus
Cartilage Damage
Bone Resorption
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
Vehicle
1103-83 (60mg/kg)
1049-178 (10 mg/kg)
1047-178 (30 mg/kg)
1049-178 (60 mg/kg)
MTX (0.0375 mg/kg)
Treatment Group

Figure 6

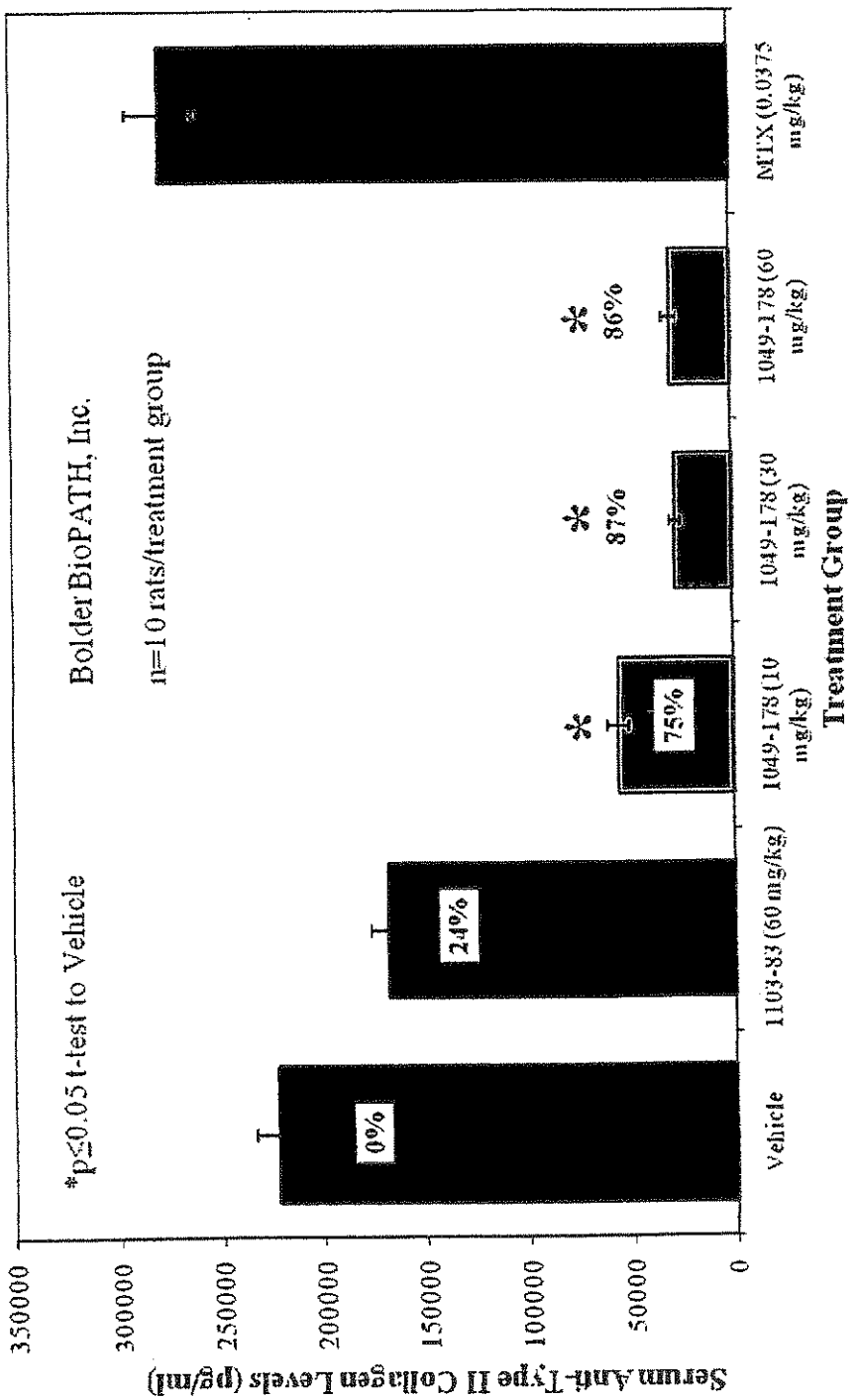

*p≤0.05 t-test to Vehicle
Bolder BioPATH, Inc.
n=10 rats/treatment group
Serum Anti-Type II Collagen Levels (pg/ml)
350000
300000
250000
200000
150000
100000
50000
0
0%
24%
75%
87%
86%
Vehicle
1103-83 (60 mg/kg)
1049-178 (10 mg/kg)
1049-178 (30 mg/kg)
1049-178 (60 mg/kg)
MTX (0.0375 mg/kg)
Treatment Group

Figure 7

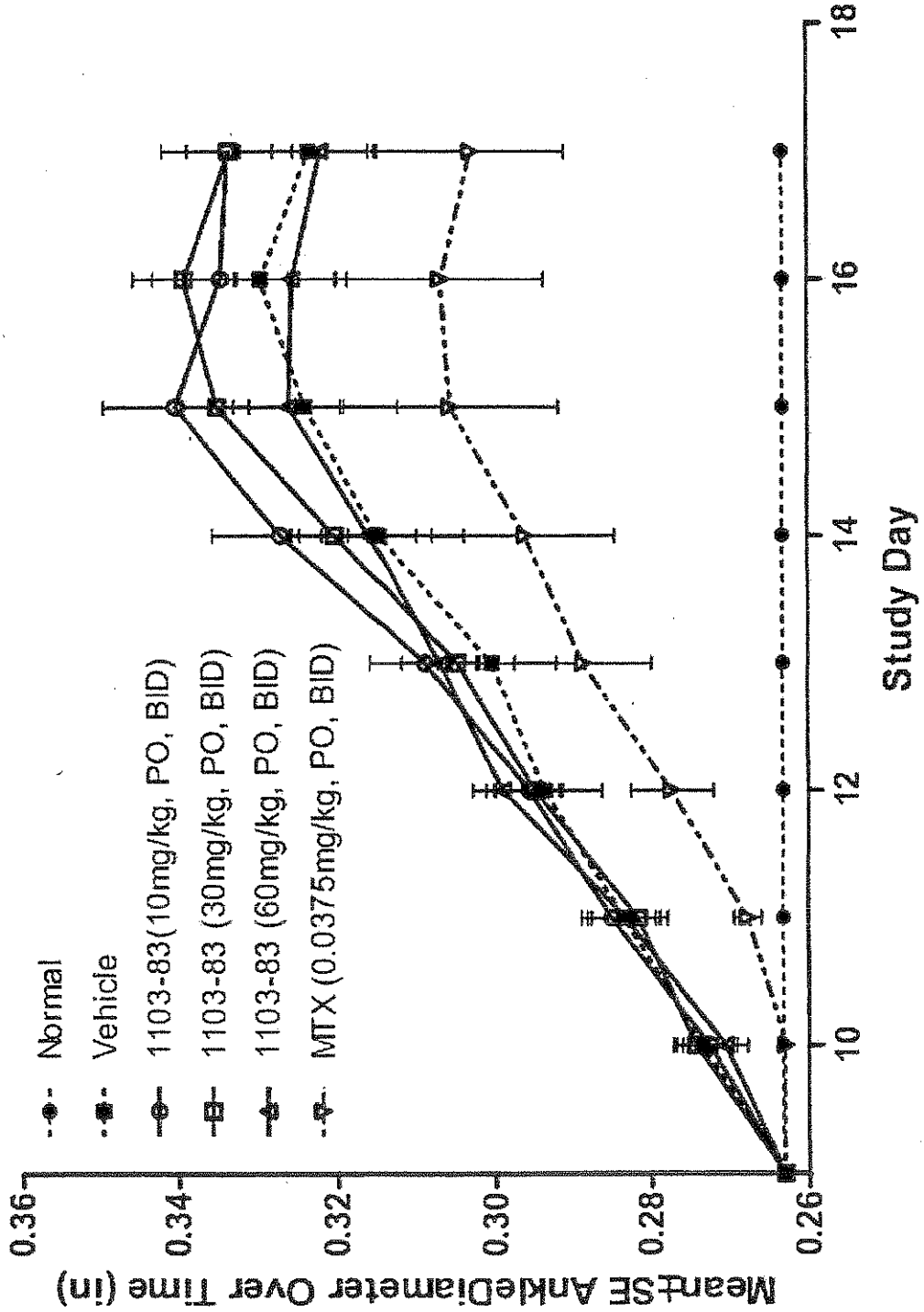

RTTC-IK-1_Ank_BID_Preventive
Normal
Vehicle
1103-83(10mg/kg, PO, BID)
1103-83 (30mg/kg, PO, BID)
1103-83 (60mg/kg, PO, BID)
MTX (0.0375mg/kg, PO, BID)
Mean±SE AnkleDiameter Over Time (in)
0.36
0.34
0.32
0.30
0.28
0.26
10
12
14
16
18
Study Day

Figure 8

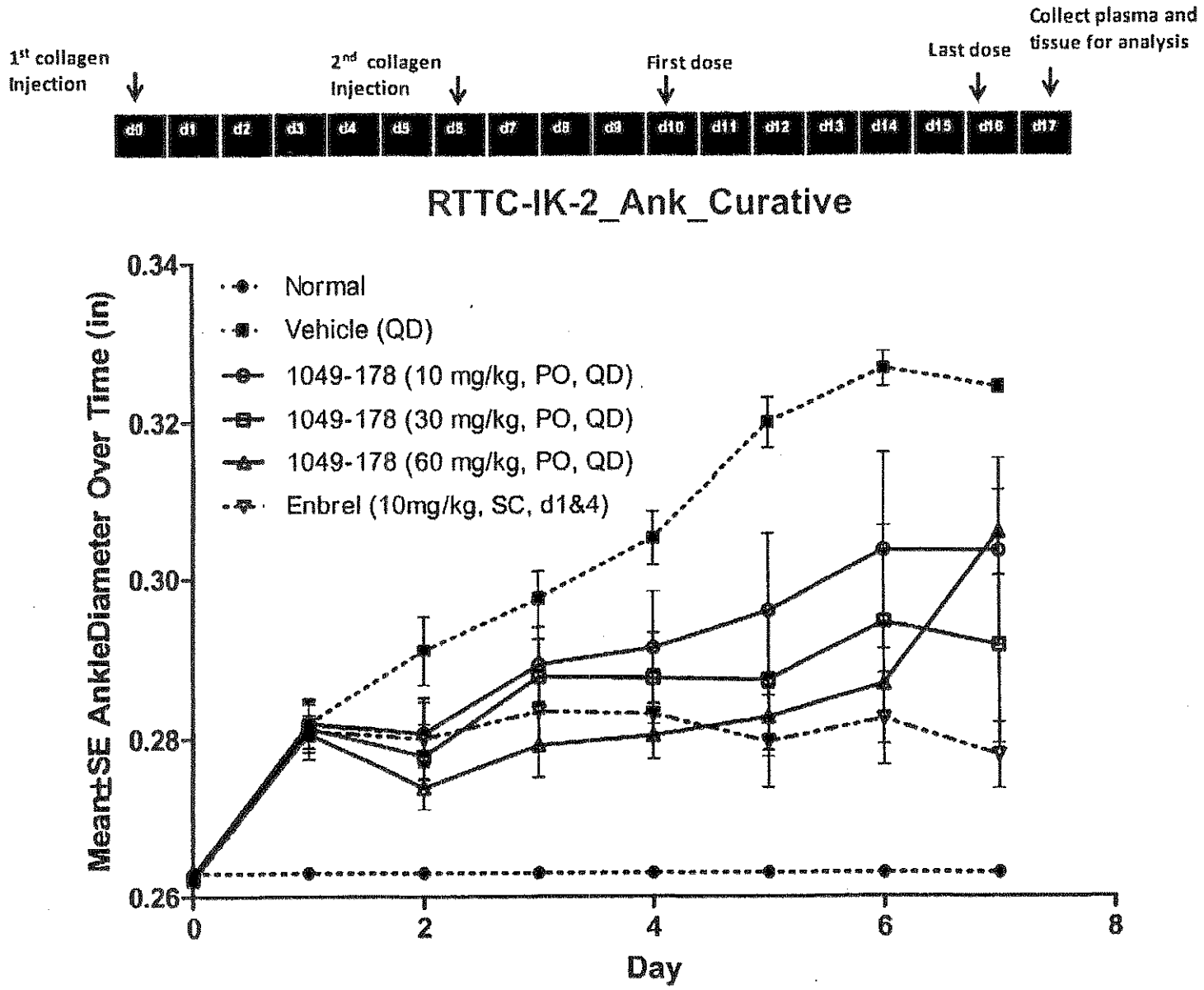

1st collagen Injection
2nd collagen Injection
First dose
Last dose
Collect plasma and tissue for analysis
d0
d1
d2
d3
d4
d5
d6
d7
d8
d9
d10
d11
d12
d13
d14
d15
d16
d17
RTTC-IK-2_Ank_Curative
Normal
Vehicle (QD)
1049-178 (10 mg/kg, PO, QD)
1049-178 (30 mg/kg, PO, QD)
1049-178 (60 mg/kg, PO, QD)
Enbrel (10mg/kg, SC, d1&4)
Mean±SE AnkleDiameter Over Time (in)
0.34
0.32
0.30
0.28
0.26
0
2
4
6
8
Day

Figure 9

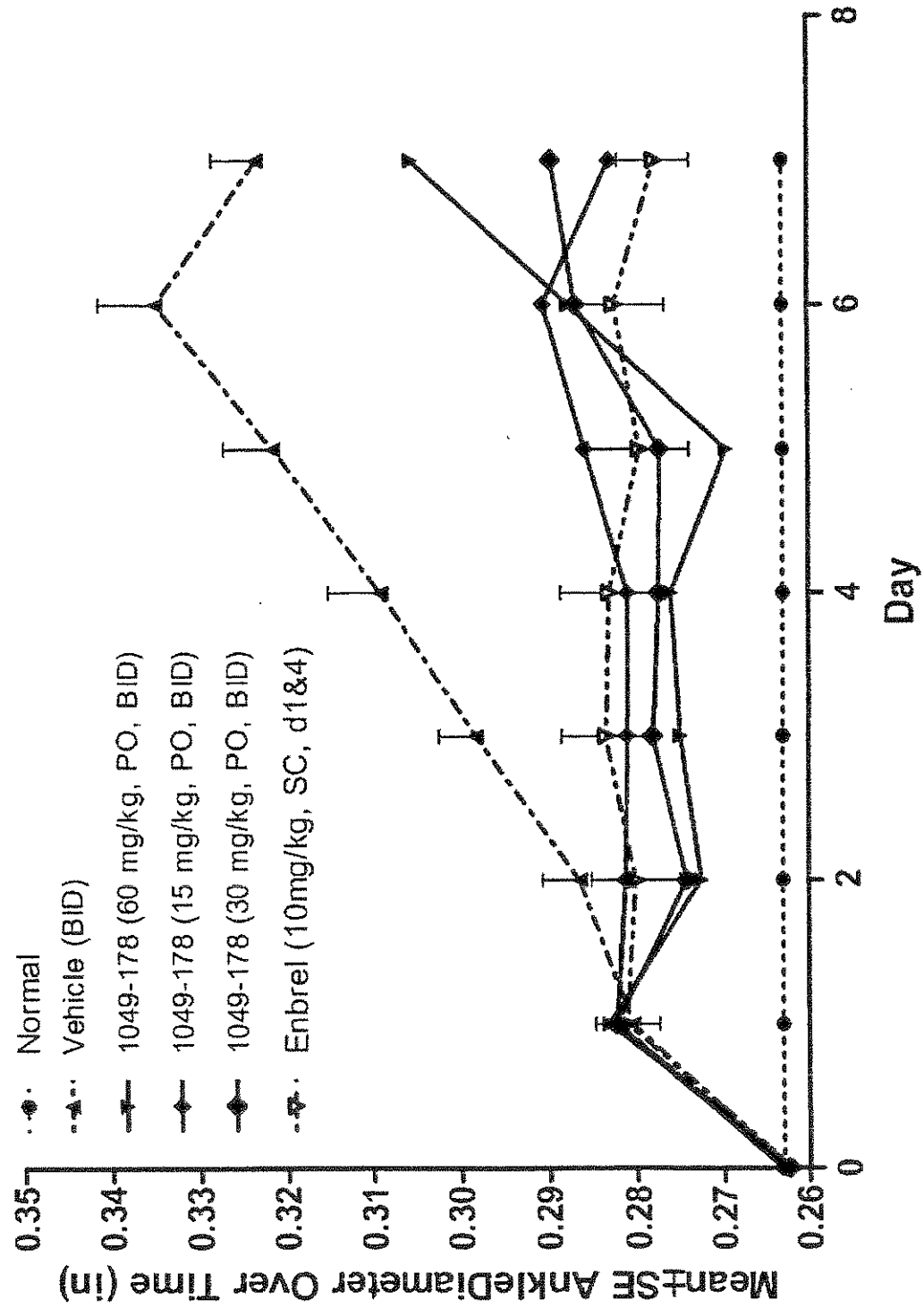

RTTC-IK-2_Ank_Curative
Normal
Vehicle (BID)
1049-178 (60 mg/kg, PO, BID)
1049-178 (15 mg/kg, PO, BID)
1049-178 (30 mg/kg, PO, BID)
Enbrel (10mg/kg, SC, d1&4)
Mean±SE AnkleDiameter Over Time (in)
0.35
0.34
0.33
0.32
0.31
0.30
0.29
0.28
0.27
0.26
0
2
4
6
8
Day

Figure 10

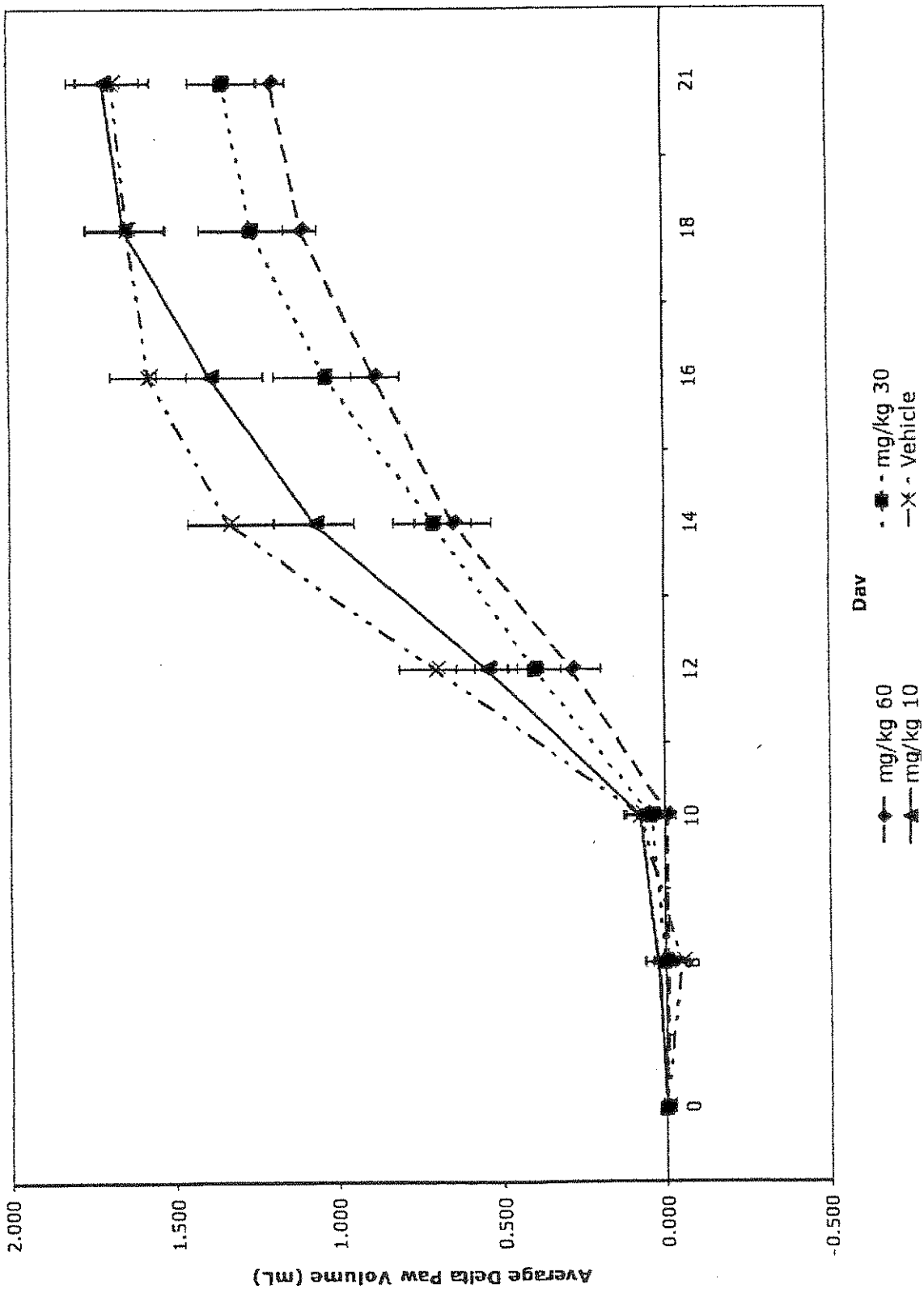

Average Delta Paw Volume with PI3K γδ Inhibitor Treatment
Average Delta Paw Volume (mL)
2.000
1.500
1.000
0.500
0.000
-0.500
0
10
12
14
16
18
21
Day
mg/kg 60
mg/kg 30
mg/kg 10
Vehicle

Figure 11

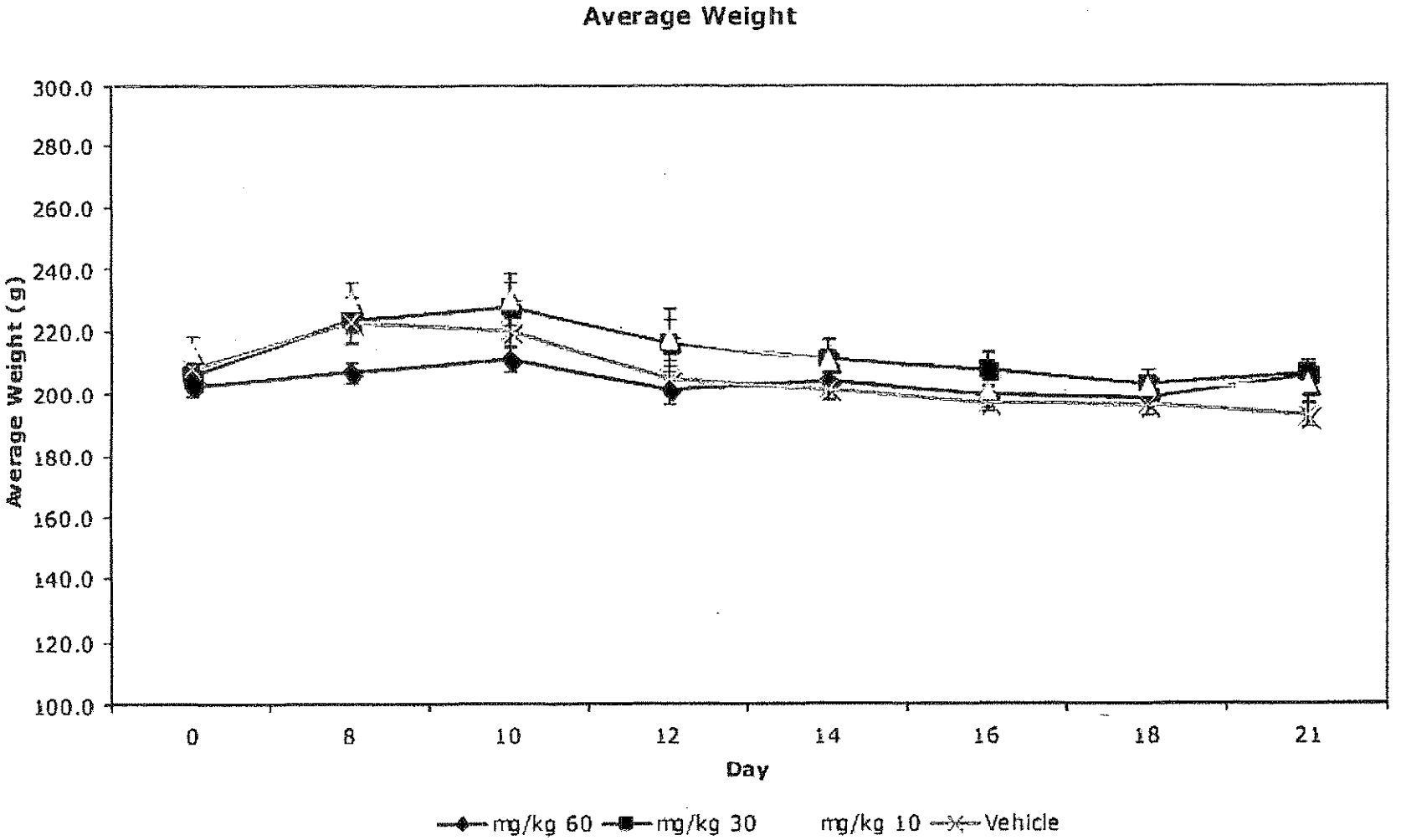

Average Weight
Average Weight (g)
300.0
280.0
260.0
240.0
220.0
200.0
180.0
160.0
140.0
120.0
100.0
0
8
10
12
14
16
18
21
Day
mg/kg 60
mg/kg 30
mg/kg 10
Vehicle

Figure 12

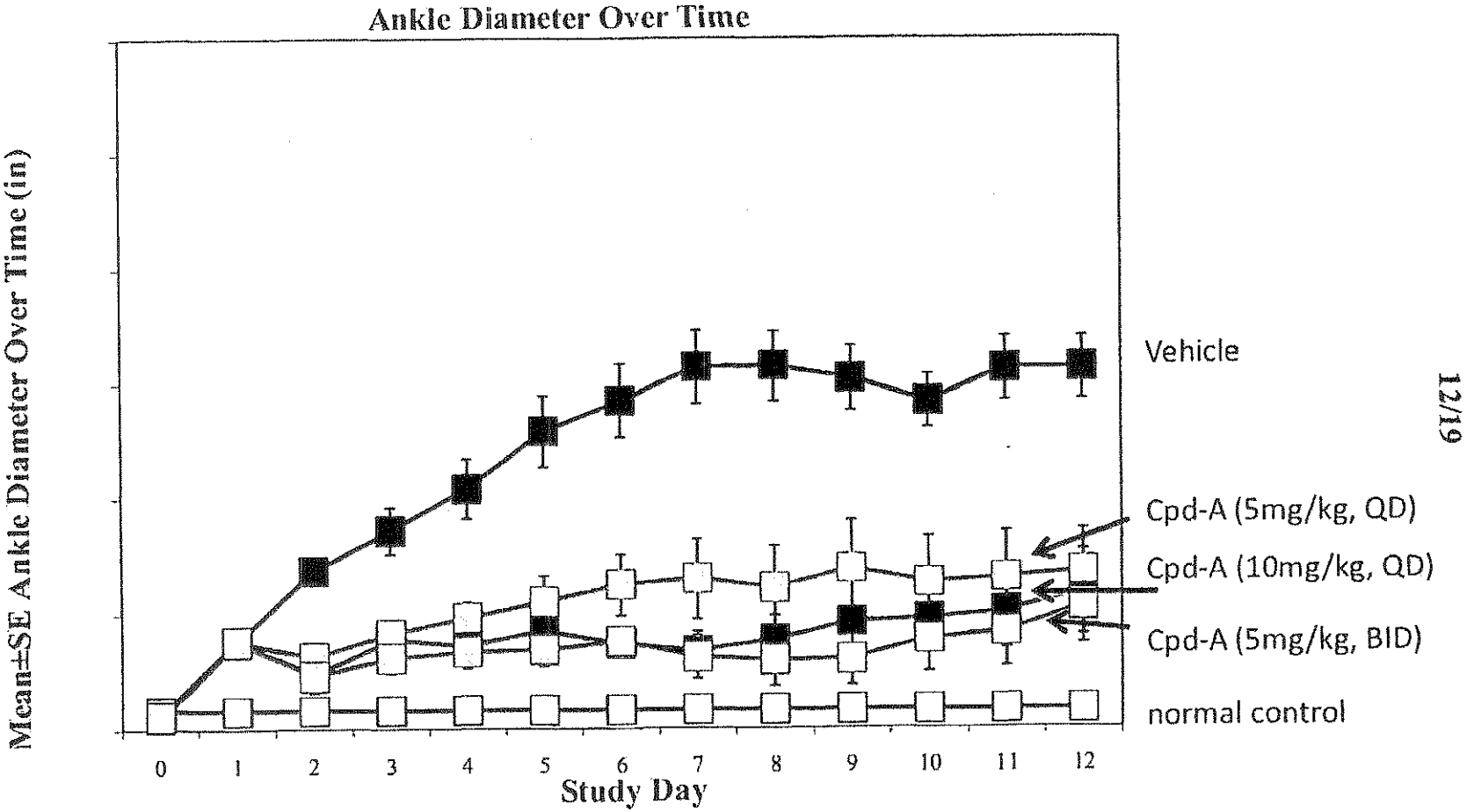

Ankle Diameter Over Time
Mean±SE Ankle Diameter Over Time (in)
0
1
2
3
4
5
6
7
8
9
10
11
12
Study Day
Vehicle
Cpd-A (5mg/kg, QD)
Cpd-A (10mg/kg, QD)
Cpd-A (5mg/kg, BID)
normal control

Figure 13

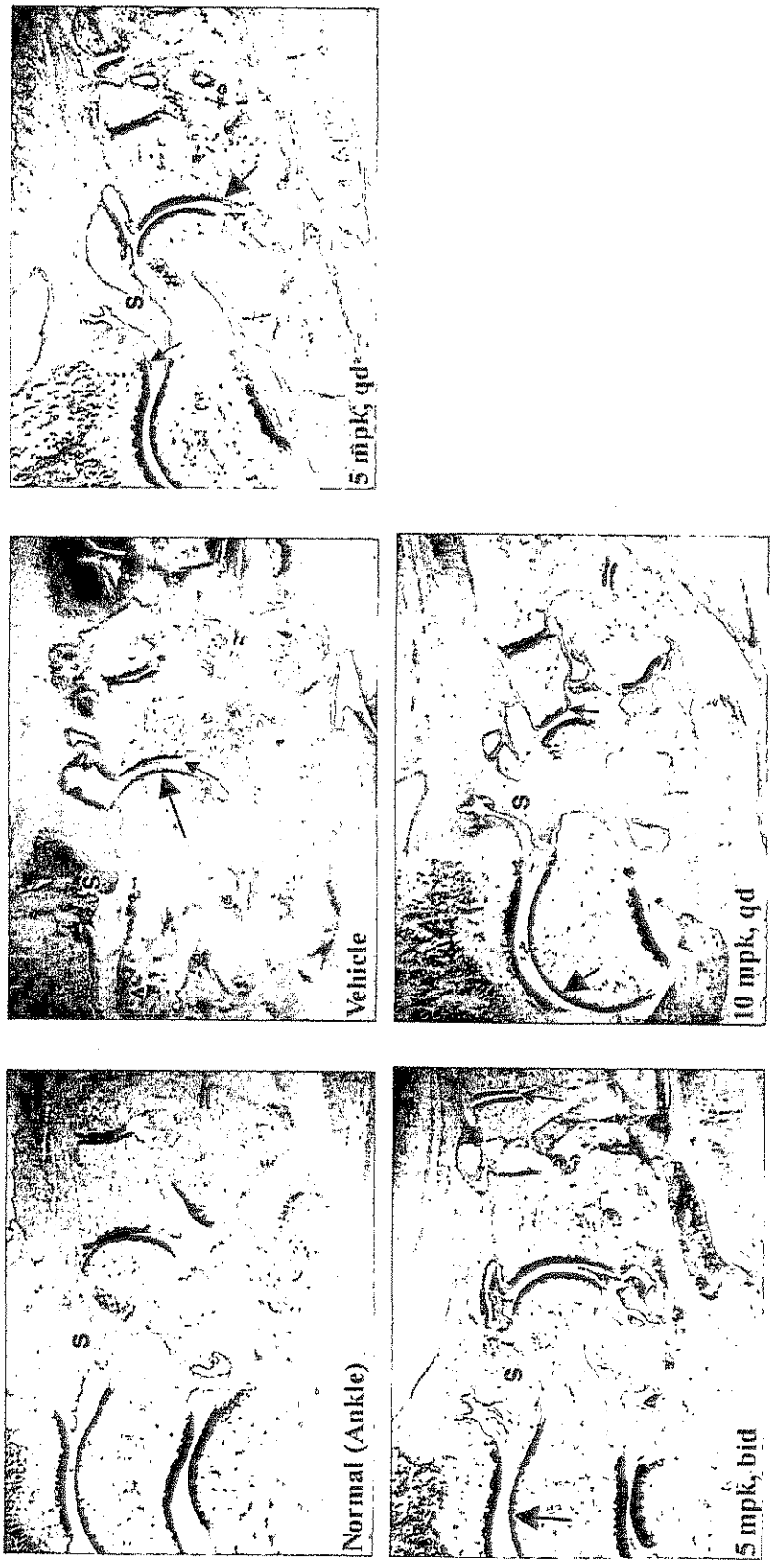


Figure 14

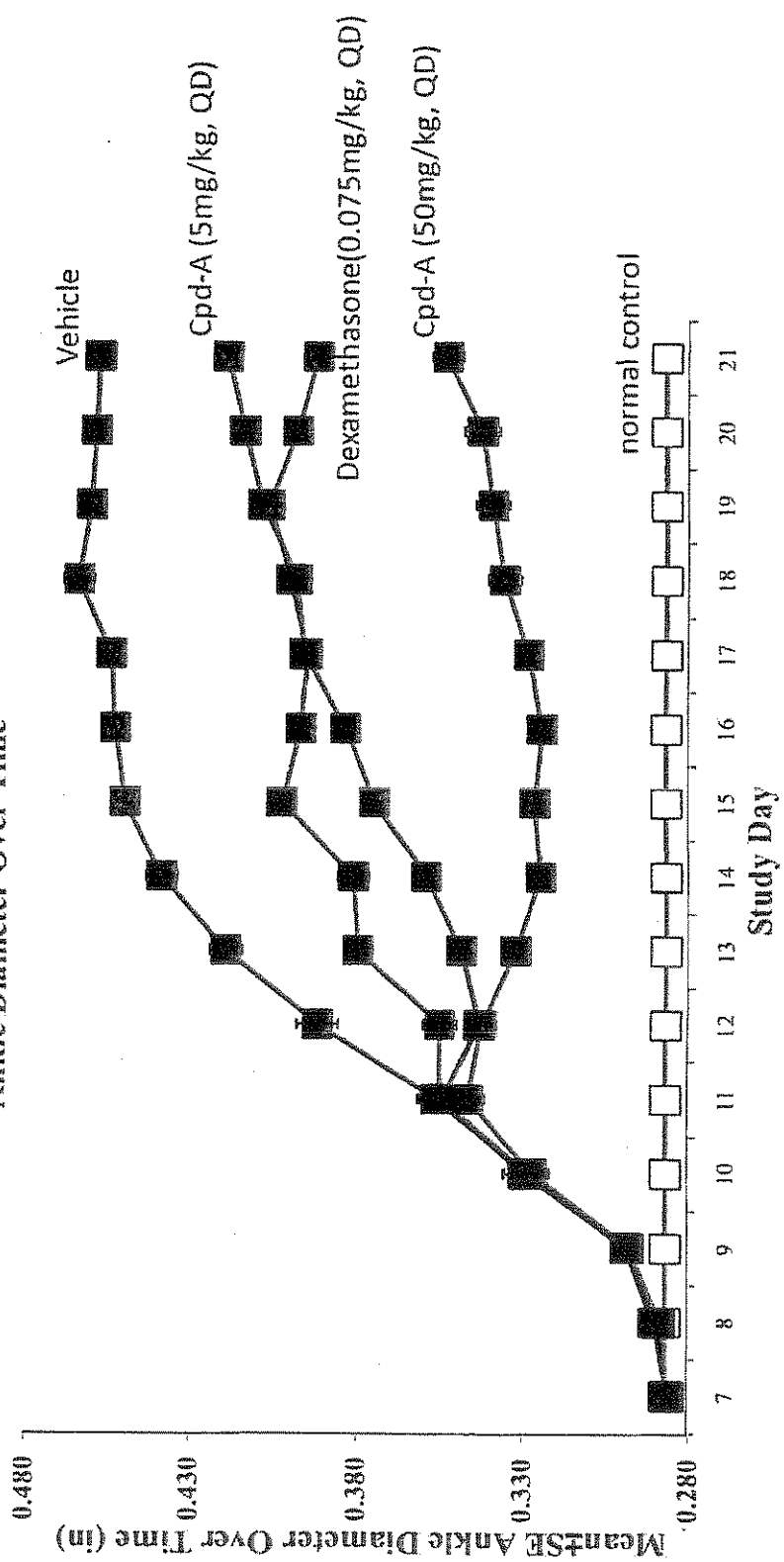

Ankle Diameter Over Time
Vehicle
Cpd-A (5mg/kg, QD)
Dexamethasone(0.075mg/kg, QD)
Cpd-A (50mg/kg, QD)
normal control
Mean±SE Ankle Diameter Over Time (in)
0.480
0.430
0.380
0.330
0.280
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
Study Day

Figure 15

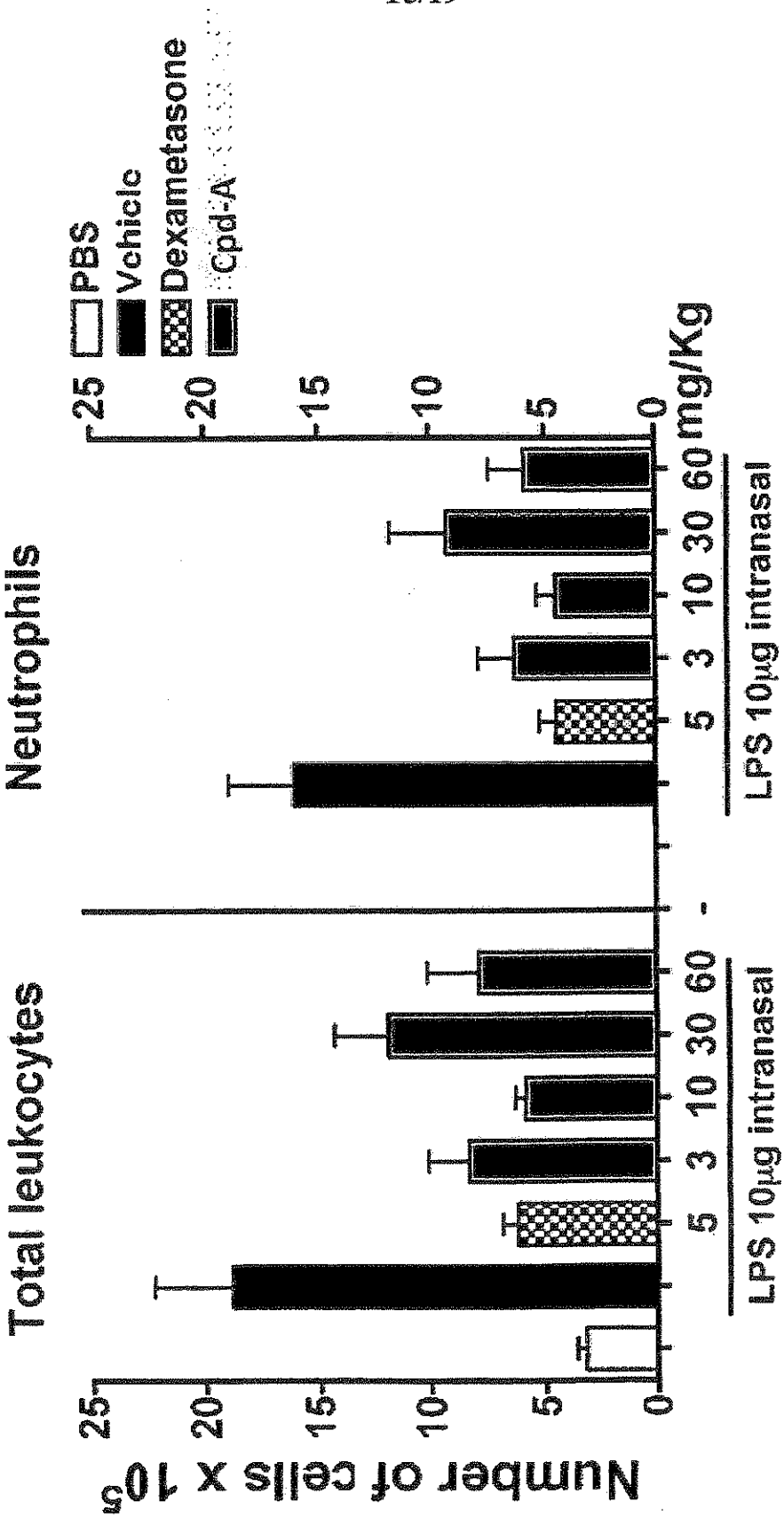

Number of cells x 10⁵
Total leukocytes
Neutrophils
PBS
Vehicle
Dexametasone
Cpd-A
mg/Kg
LPS 10μg intranasal
LPS 10μg intranasal
0
5
10
15
20
25
-
5
3
10
30
60

Figure 16

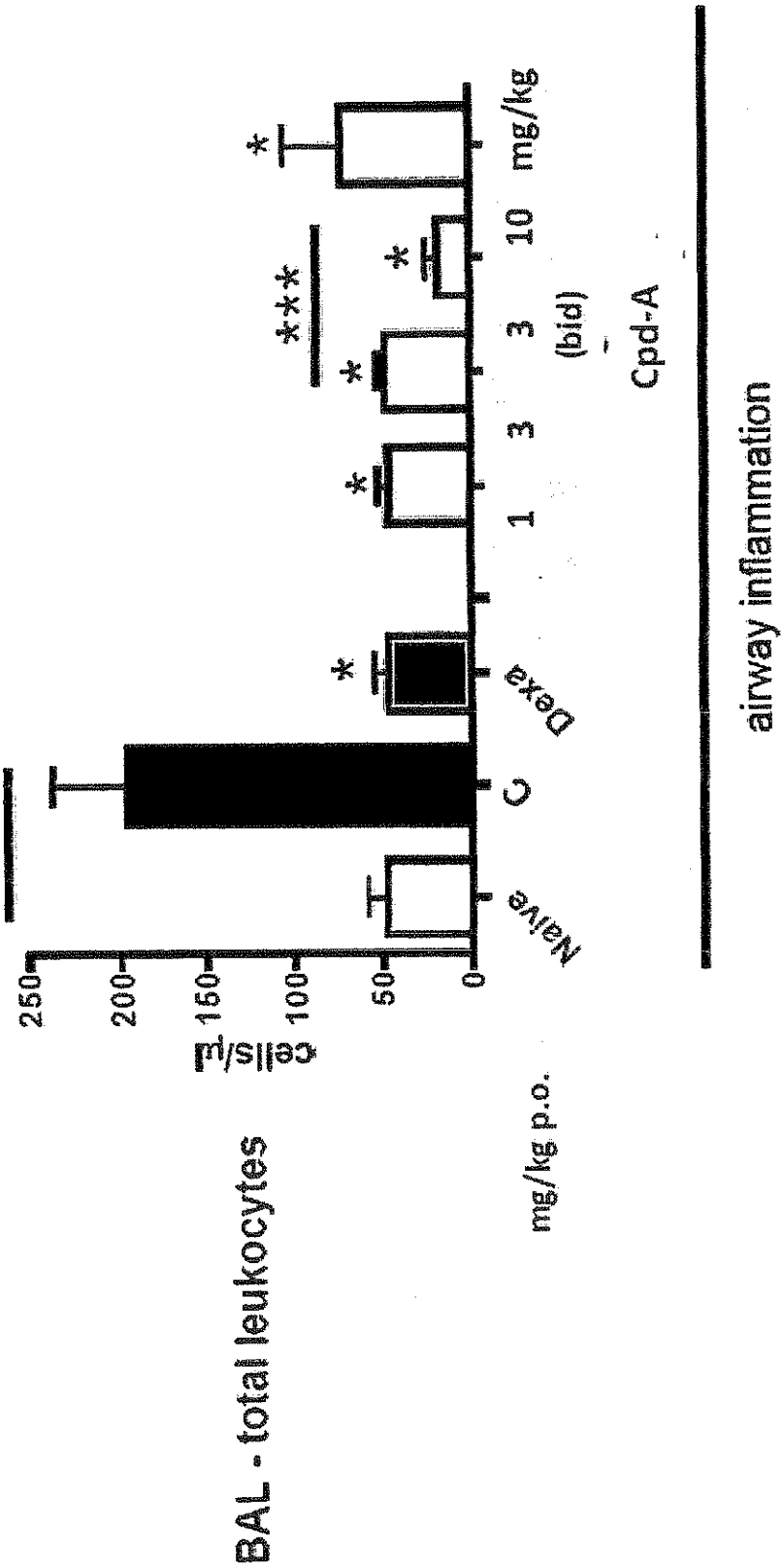

BAL - total leukocytes
cells/µl
250
200
150
100
50
0
Naïve
C
Dexa
1
3
3
10
mg/kg
(bid)
mg/kg p.o.
Cpd-A
airway inflammation

Figure 17

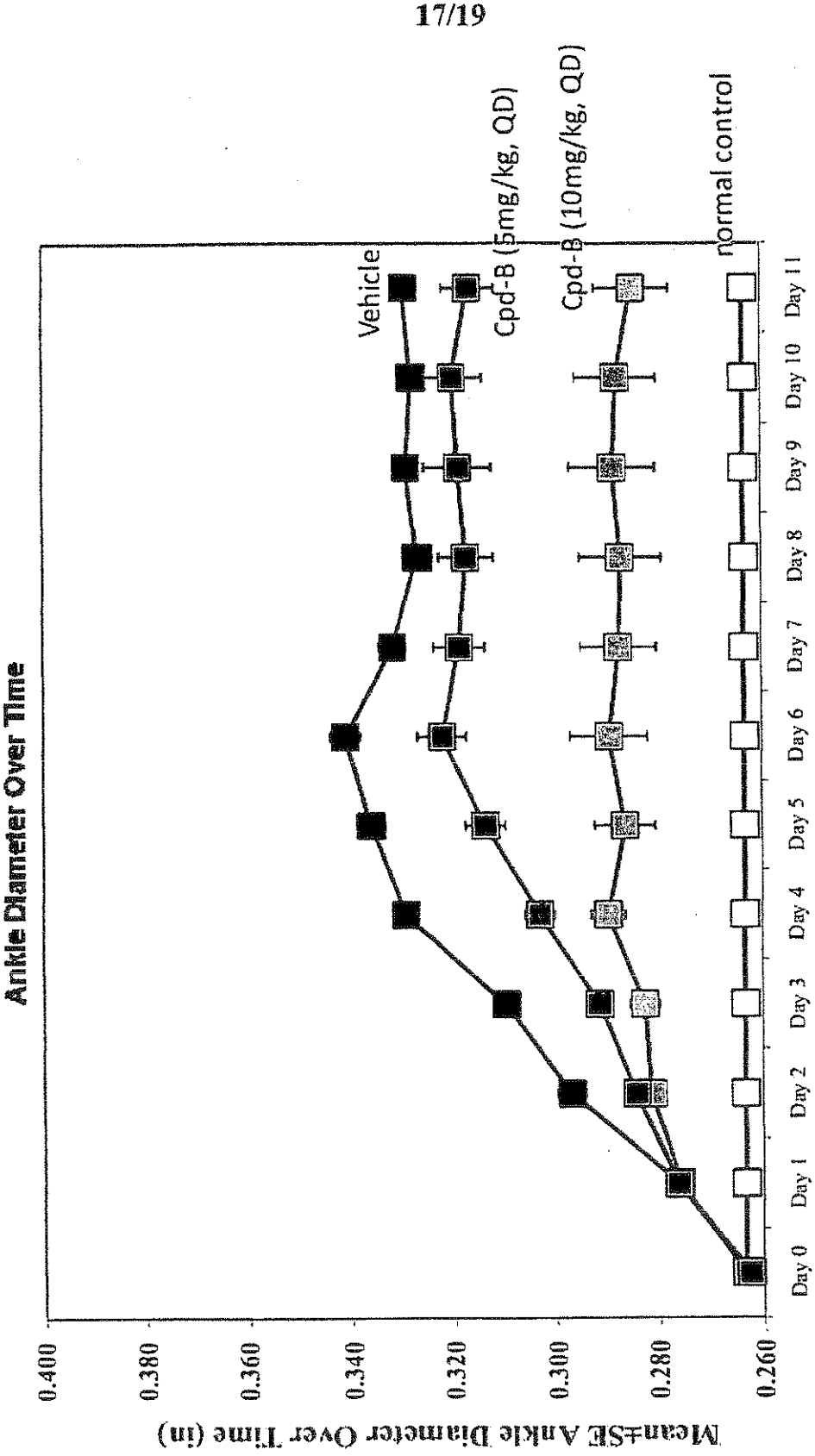

Ankle Diameter Over Time
Mean±SE Ankle Diameter Over Time (in)
0.400
0.380
0.360
0.340
0.320
0.300
0.280
0.260
Day 0
Day 1
Day 2
Day 3
Day 4
Day 5
Day 6
Day 7
Day 8
Day 9
Day 10
Day 11
Study Day
Vehicle
Cpd-B (5mg/kg, QD)
Cpd-B (10mg/kg, QD)
normal control

Figure 18

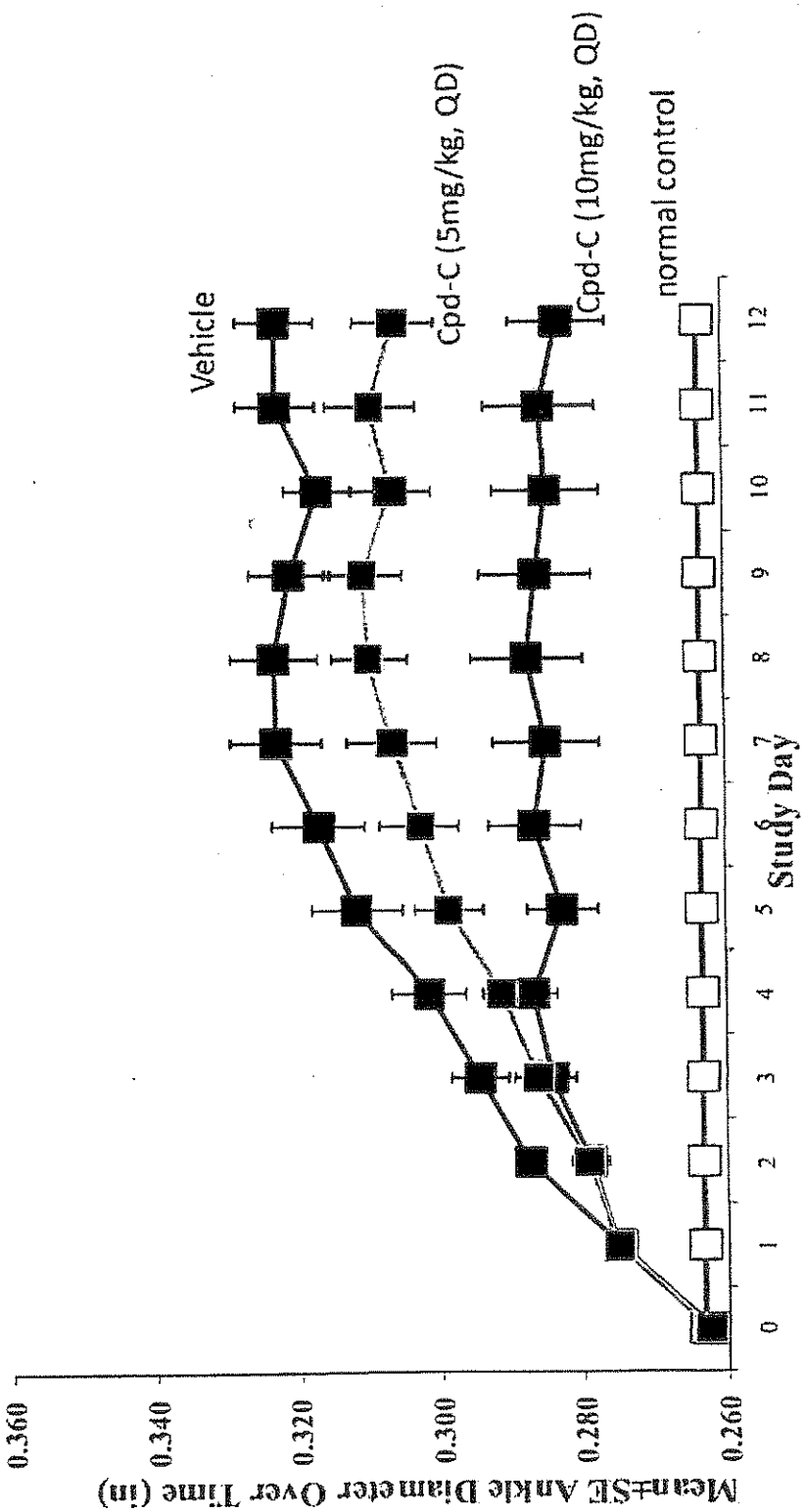
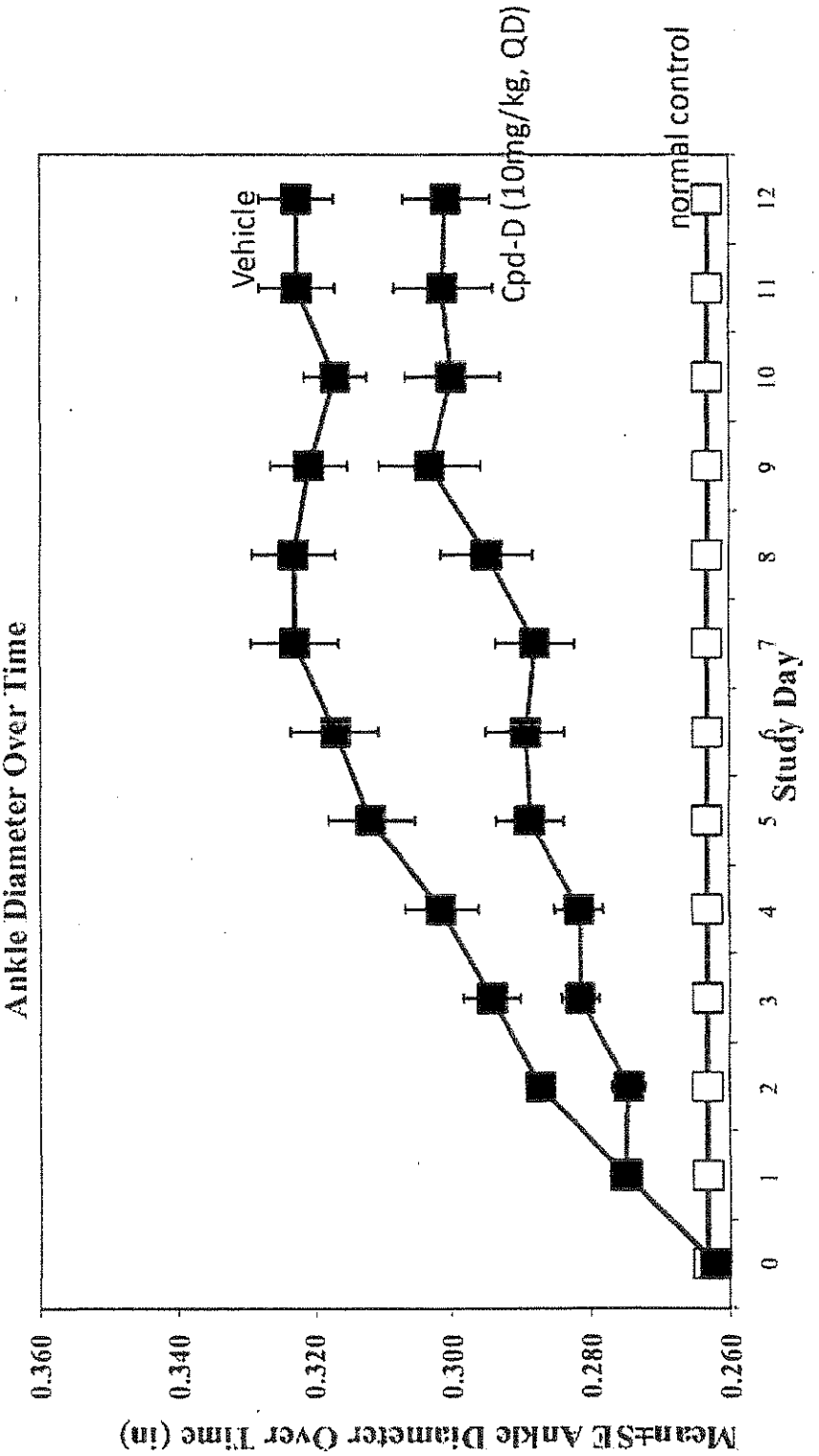

Ankle Diameter Over Time
Mean±SE Ankle Diameter Over Time (in)
0.360
0.340
0.320
0.300
0.280
0.260
0
1
2
3
4
5
6
7
8
9
10
11
12
Study Day
Vehicle
Cpd-C (5mg/kg, QD)
Cpd-C (10mg/kg, QD)
normal control

Figure 19


Ankle Diameter Over Time
Mean±SE Ankle Diameter Over Time (in)
0.360
0.340
0.320
0.300
0.280
0.260
0
1
2
3
4
5
6
7
8
9
10
11
12
Study Day
Vehicle
Cpd-D (10mg/kg, QD)
normal control