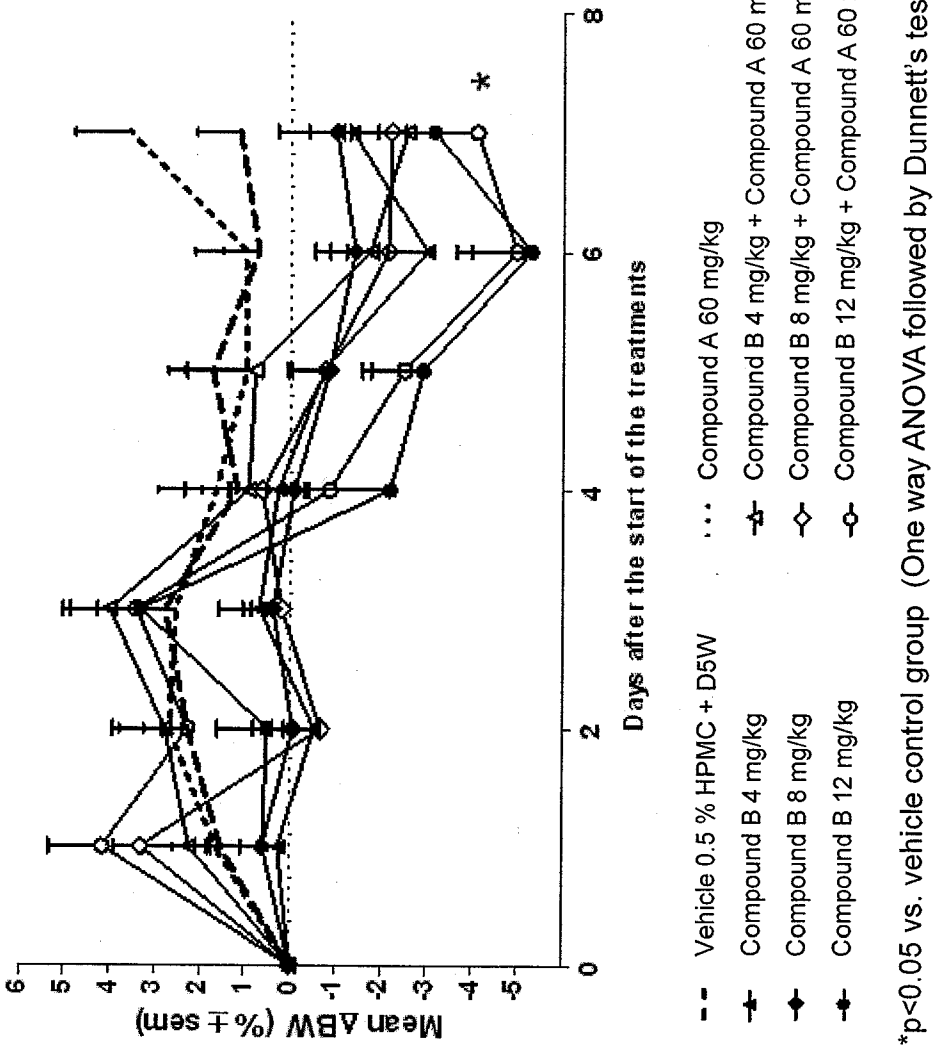
Figure 1


Mean ΔBW (% ± sem)
6
5
4
3
2
1
0
-1
-2
-3
-4
-5
0
2
4
6
8
Days after the start of the treatments
*
Vehicle 0.5 % HPMC + D5W
Compound A 60 mg/kg
Compound B 4 mg/kg
Compound B 4 mg/kg + Compound A 60 mg/kg
Compound B 8 mg/kg
Compound B 8 mg/kg + Compound A 60 mg/kg
Compound B 12 mg/kg
Compound B 12 mg/kg + Compound A 60 mg/kg
*p<0.05 vs. vehicle control group (One way ANOVA followed by Dunnett's test)

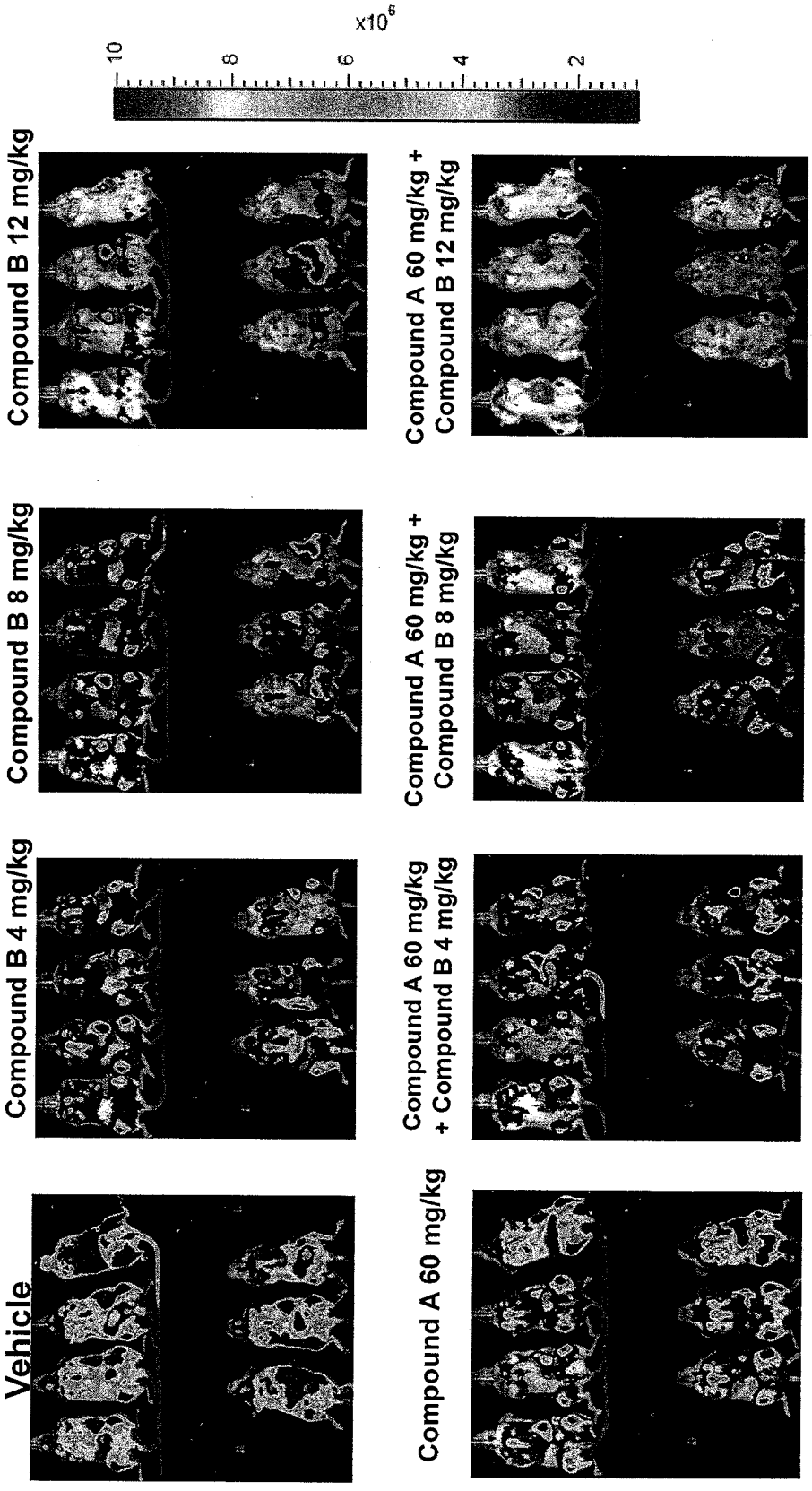

x10^6
10
8
6
4
2
Vehicle
Compound B 4 mg/kg
Compound B 8 mg/kg
Compound B 12 mg/kg
Compound A 60 mg/kg
Compound A 60 mg/kg + Compound B 4 mg/kg
Compound A 60 mg/kg + Compound B 8 mg/kg
Compound A 60 mg/kg + Compound B 12 mg/kg

Figure 2

Figure 3

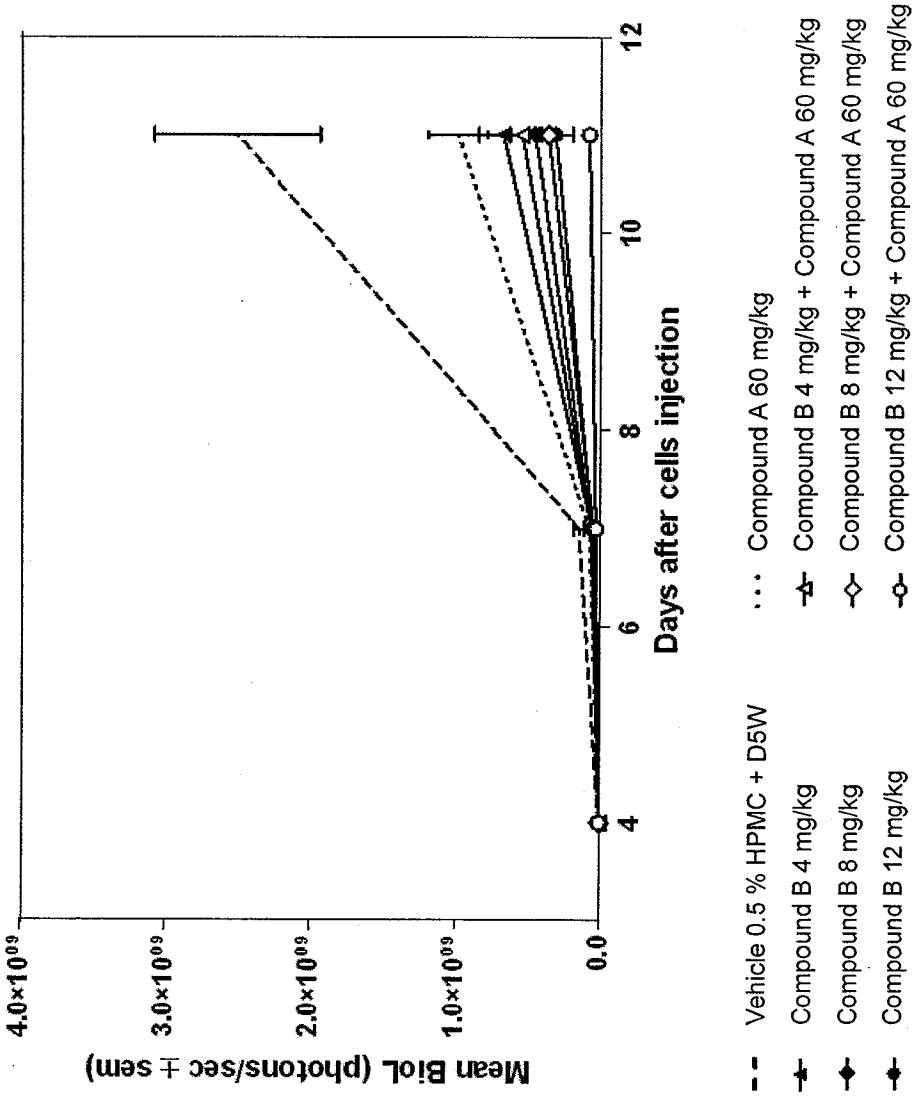
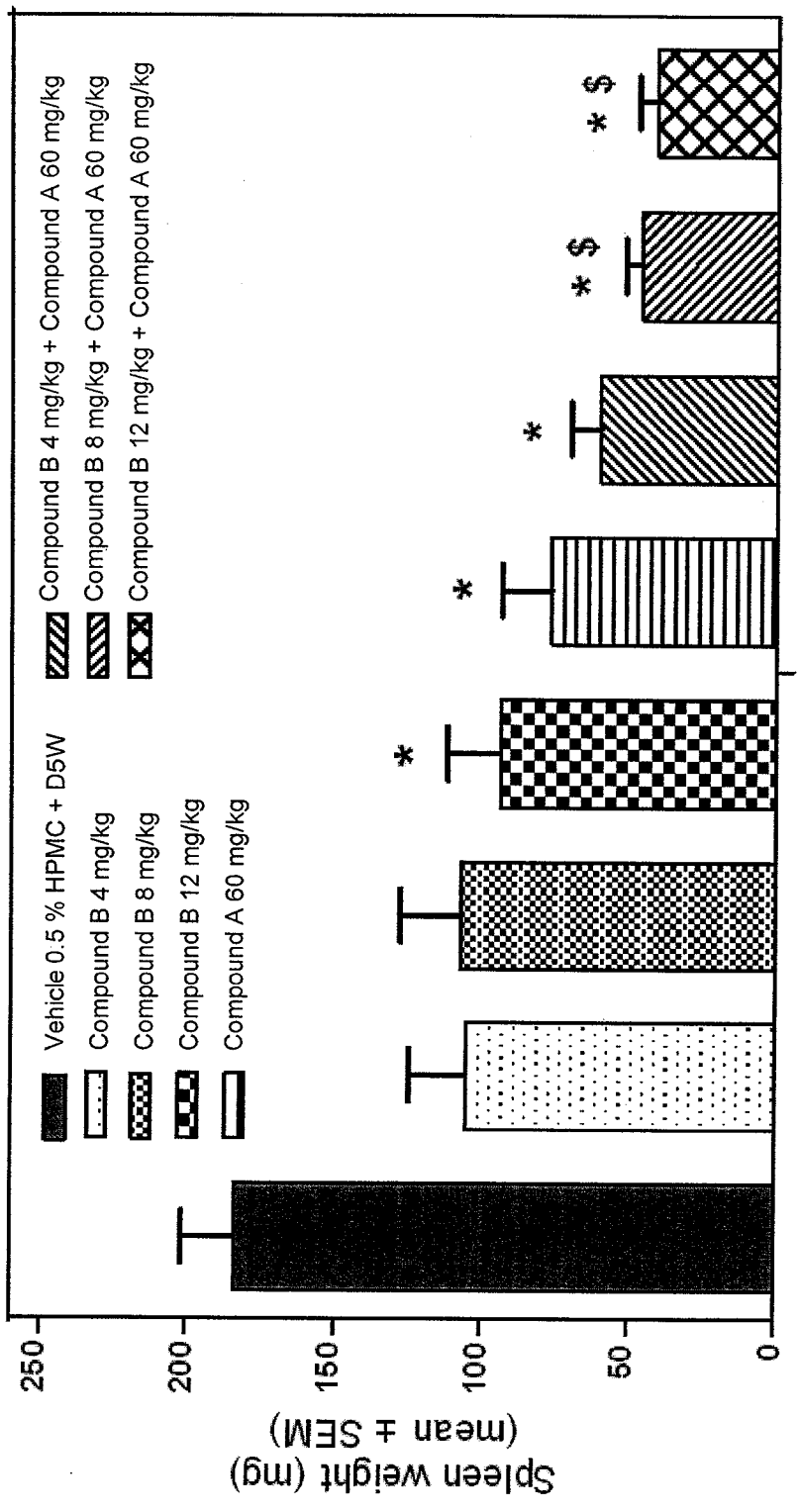

Mean BioL (photons/sec ± sem)
4.0×10^09
3.0×10^09
2.0×10^09
1.0×10^09
0.0
4
6
8
10
12
Days after cells injection
Vehicle 0.5 % HPMC + D5W
Compound A 60 mg/kg
Compound B 4 mg/kg
Compound B 4 mg/kg + Compound A 60 mg/kg
Compound B 8 mg/kg
Compound B 8 mg/kg + Compound A 60 mg/kg
Compound B 12 mg/kg
Compound B 12 mg/kg + Compound A 60 mg/kg

Figure 4



*p<0.05 vs. Vehicle control group
$p<0.05 vs. Compound B same dose

Note: statistical analysis done on log-transformed values with ANOVA one way followed by Tukey's test for multiple comparisons with all groups.

Figure 5

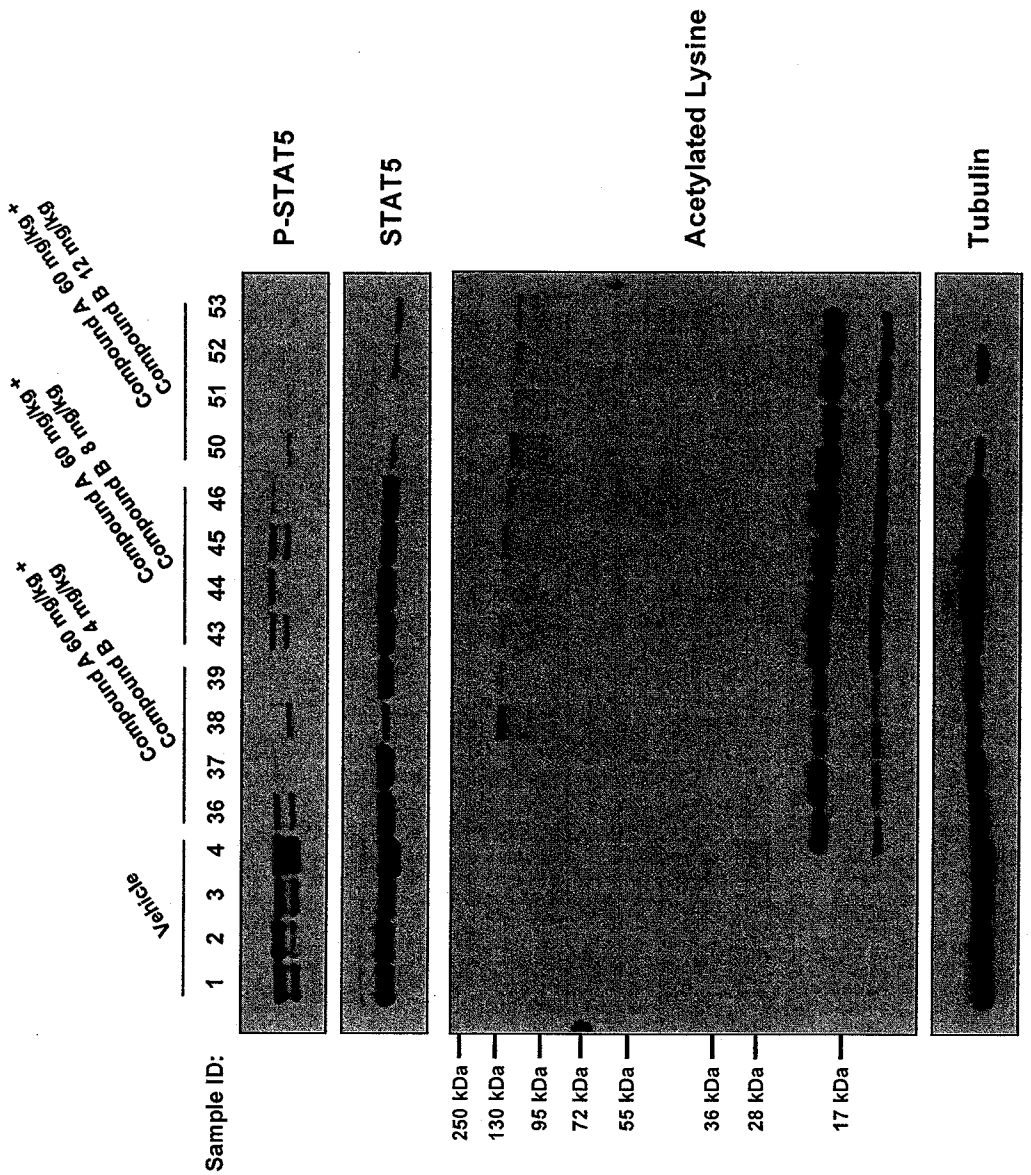

P-STAT5
STAT5
Acetylated Lysine
Tubulin
Sample ID:
1 2 3 4 36 37 38 39 43 44 45 46 50 51 52 53
Vehicle
Compound A 60 mg/kg + Compound B 4 mg/kg
Compound A 60 mg/kg + Compound B 8 mg/kg
Compound A 60 mg/kg + Compound B 12 mg/kg
250 kDa
130 kDa
95 kDa
72 kDa
55 kDa
36 kDa
28 kDa
17 kDa

Figure 6

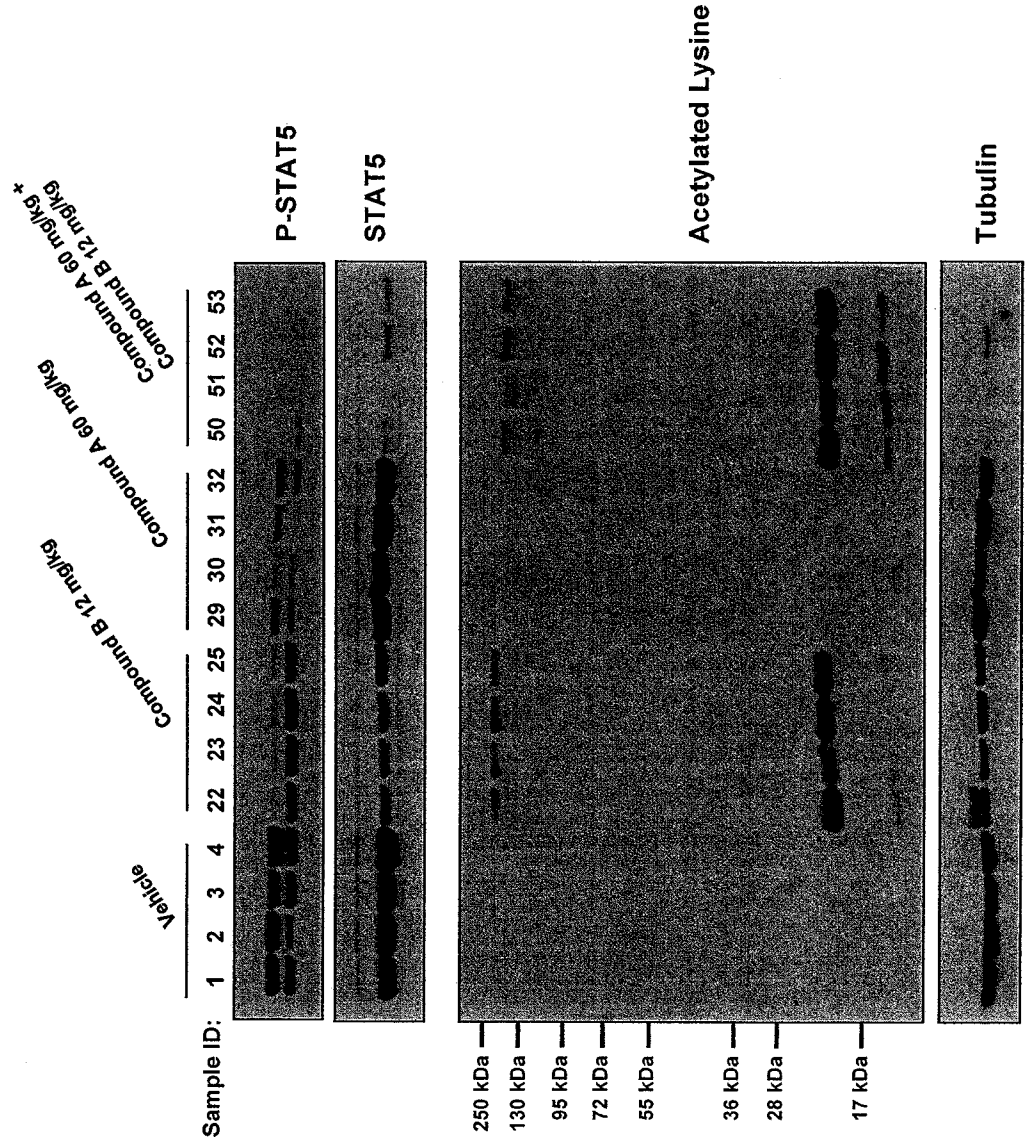

Sample ID:
1
2
3
4
22
23
24
25
29
30
31
32
50
51
52
53
Vehicle
Compound B 12 mg/kg
Compound A 60 mg/kg
Compound A 60 mg/kg + Compound B 12 mg/kg
P-STAT5
STAT5
Acetylated Lysine
Tubulin
250 kDa
130 kDa
95 kDa
72 kDa
55 kDa
36 kDa
28 kDa
17 kDa

Figure 7 Change in body weight post-therapy

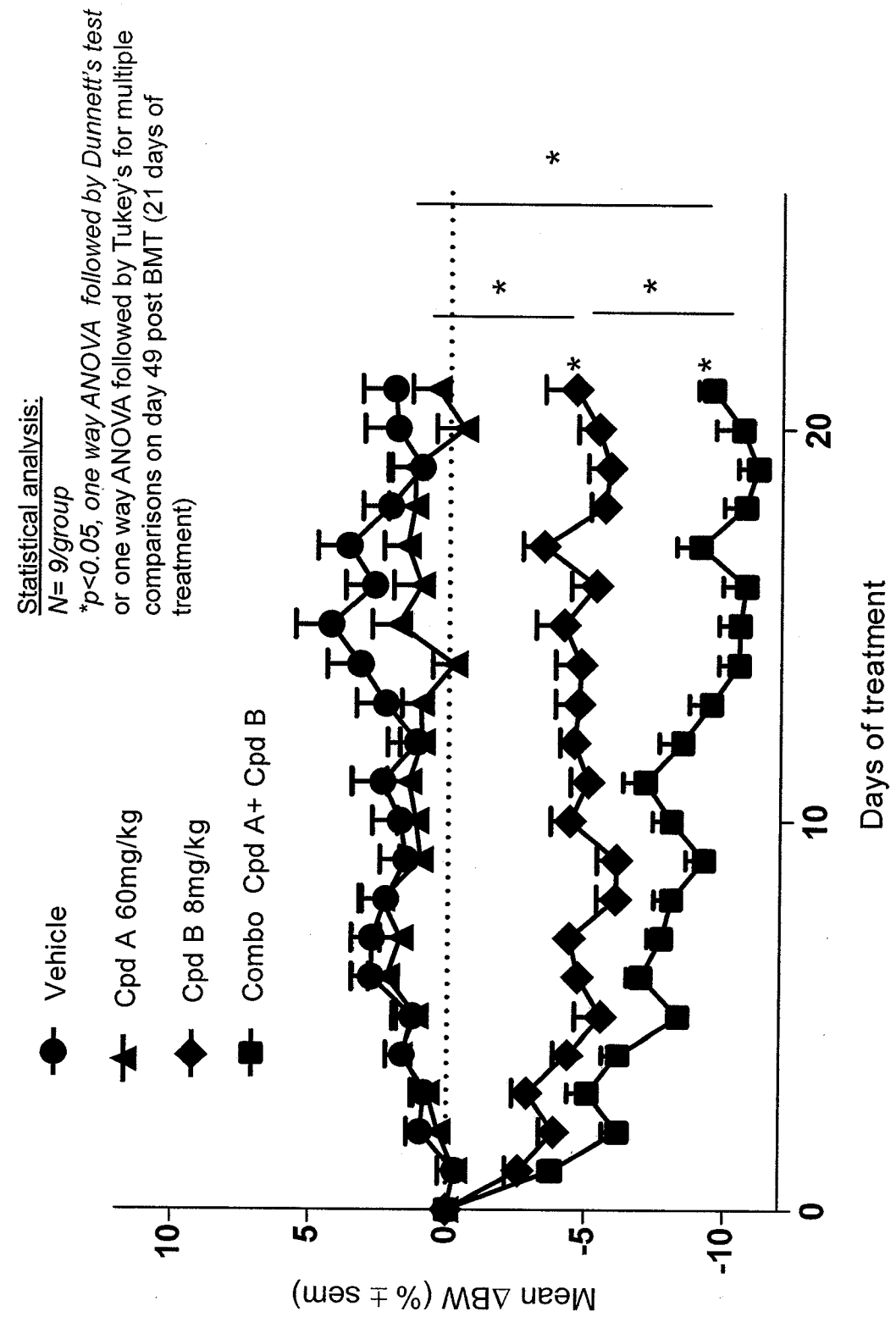
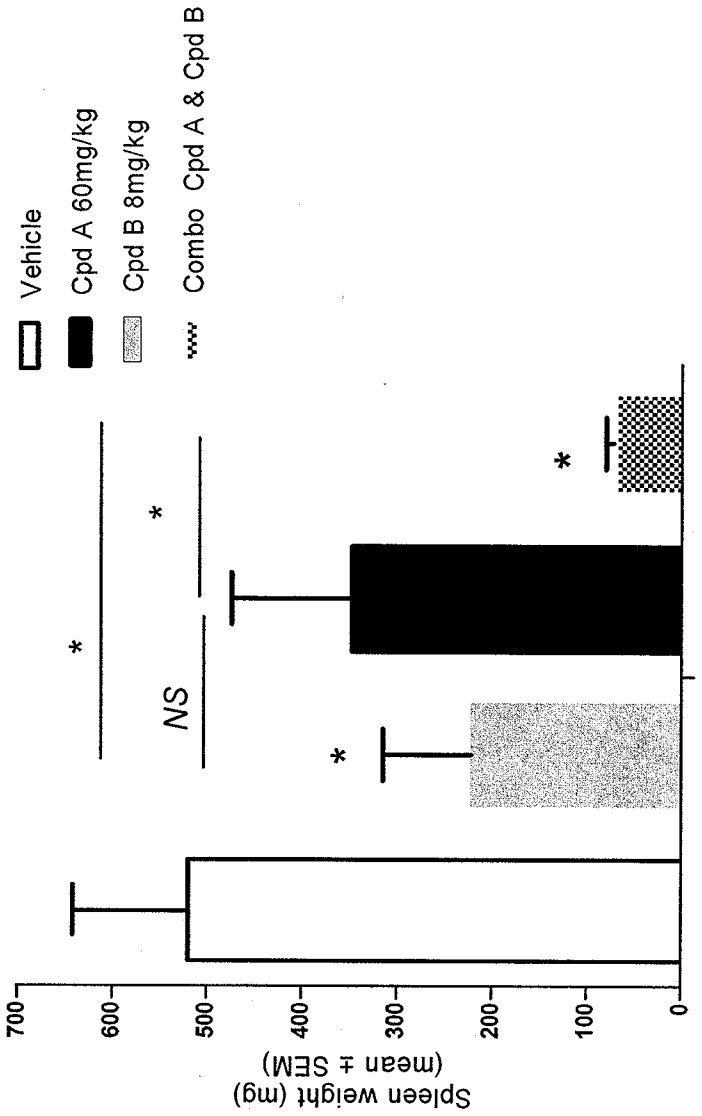


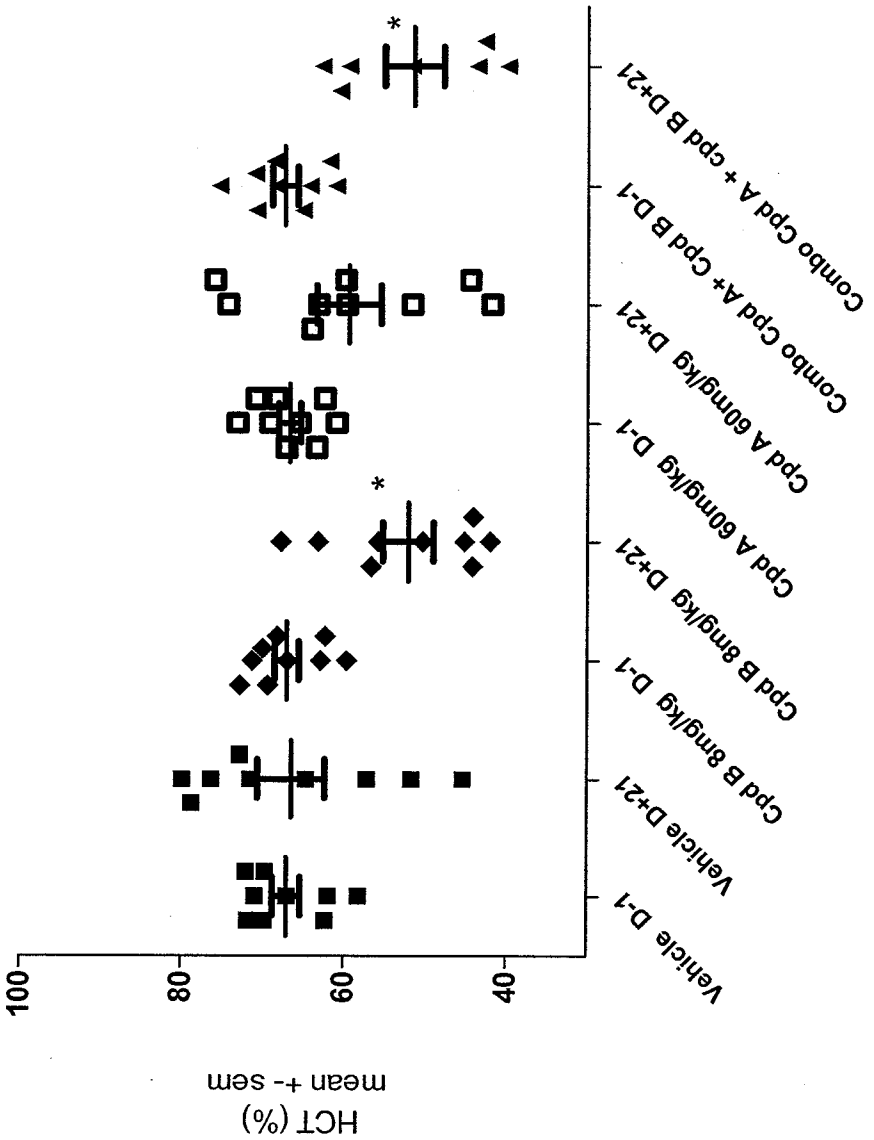
Figure 8

Effect of treatment on splenomegaly in mJAK2^{V617F} transplanted mice



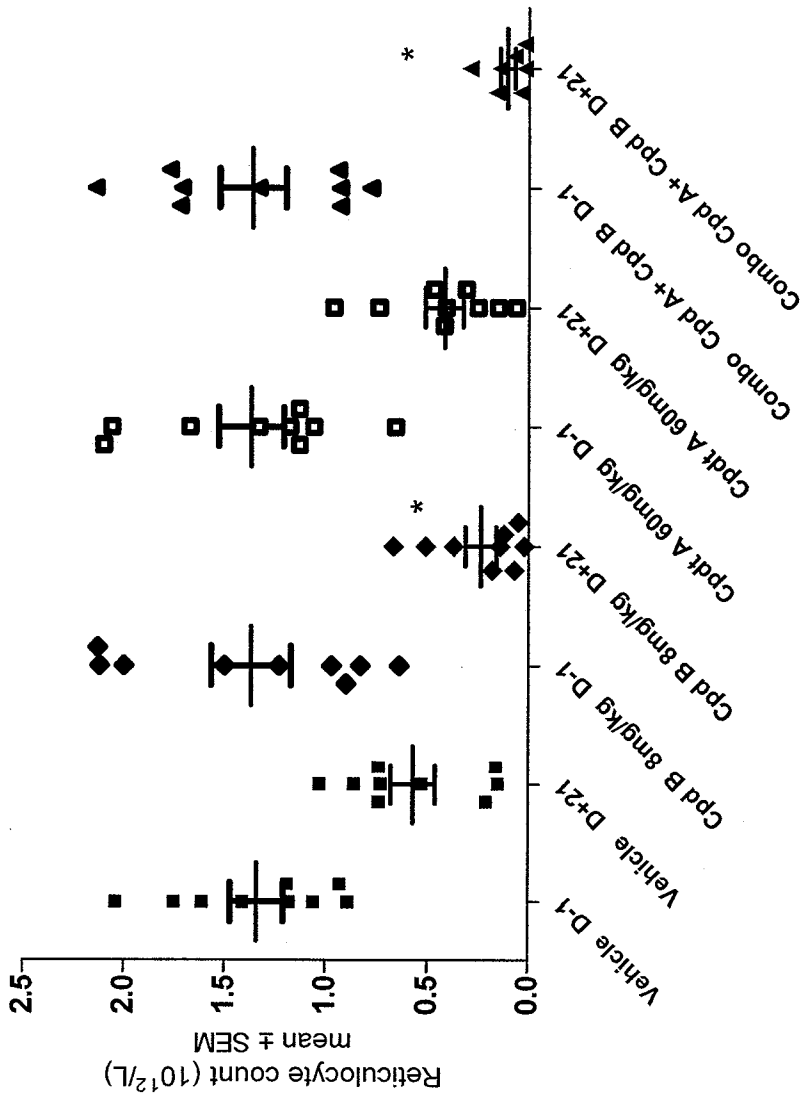
Statistical analysis:
N= 9/group
*p< 0.05 one-way ANOVA on transformed values followed by Dunnett's test or one way ANOVA followed by Tukey's test for multiple comparison

Figure 9



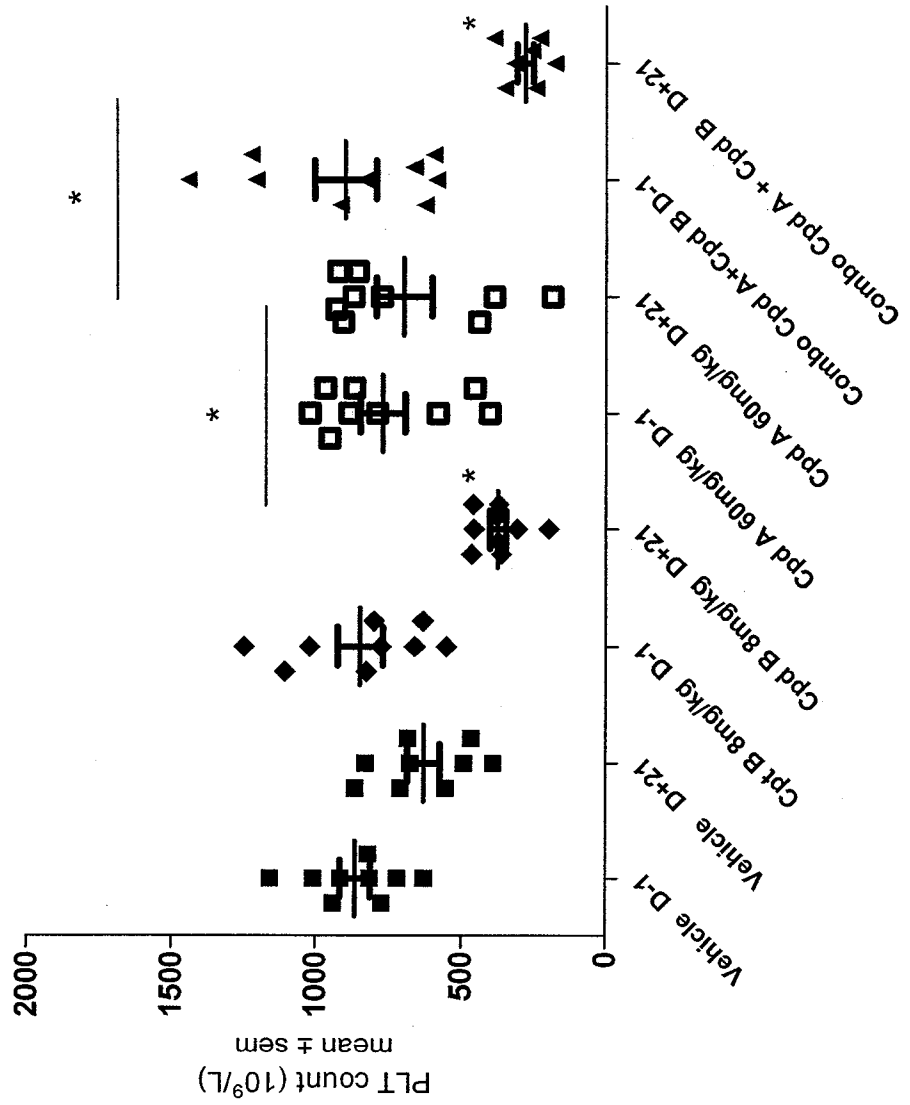
Statistical analysis:
N= 9/group 7 samples were available for analysis for the combo group
*p< 0.05 *vs. vehicle group*, One-way ANOVA followed by Dunnett's test on day of sacrifice
NS between single or combo treatments

Figure 10



Statistical analysis:
N= 9/group 7 samples were available for analysis for the combo group
*p< 0.05 *vs. vehicle group*, One-way ANOVA followed by Dunnett's test on day of sacrifice
NS between single or combo treatments

Figure 11

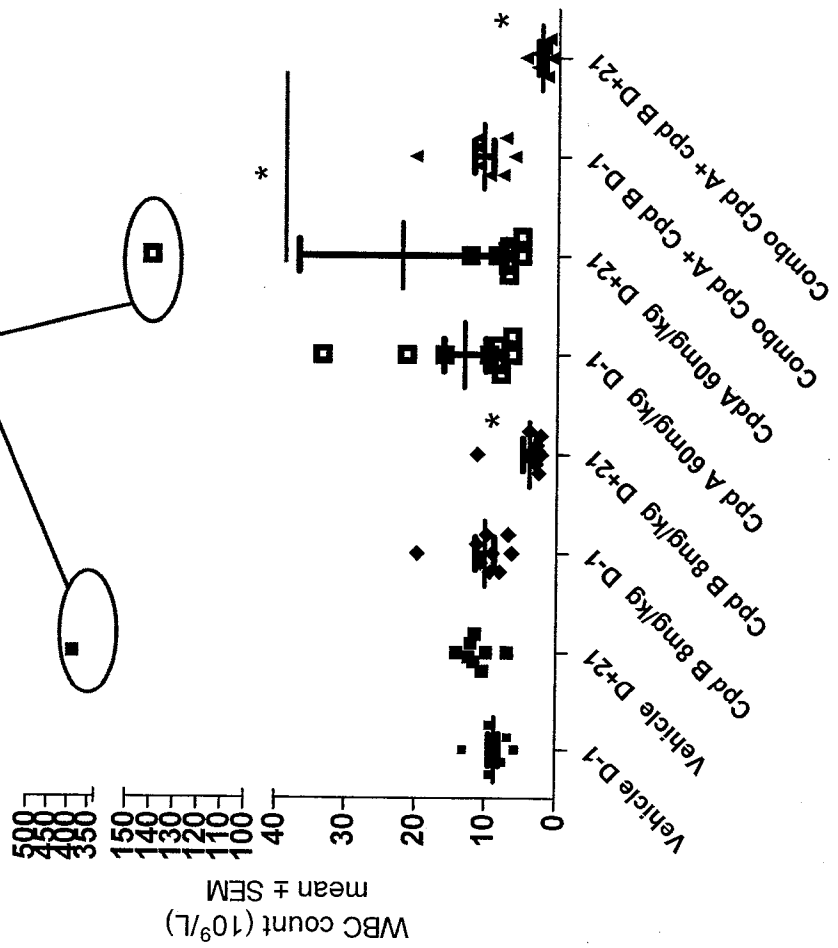


Statistical analysis:

N= 9/group 7 samples were available for analysis for the combo group

*p< 0.05 one-way ANOVA followed by Dunnett's test ot Tukey's test for multiple comparisons on log transforme values on day of sacrifice

Figure 12



Statistical analysis:
N= 9/group 7 samples were available for analysis for the combo group
*p< 0.05 one-way ANOVA followed by Dunnett's test on log transformed values or one way ANOVA followed by Tukey's test for multiple comparison on day of sacrifice.

Figure 13

H&E staining, Bone marrow pictures

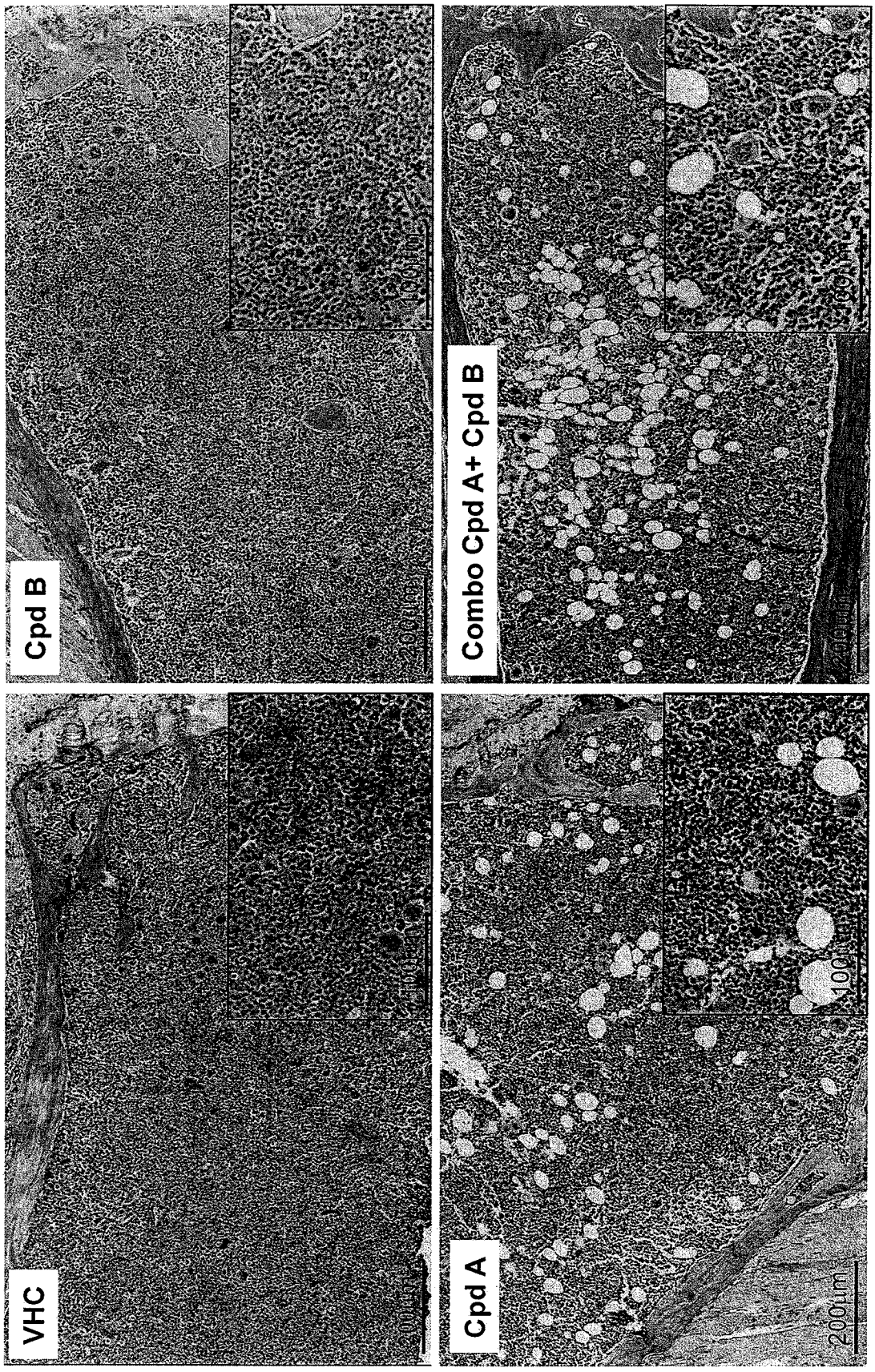


Figure 14

Reticuline staining, Bone marrow pictures

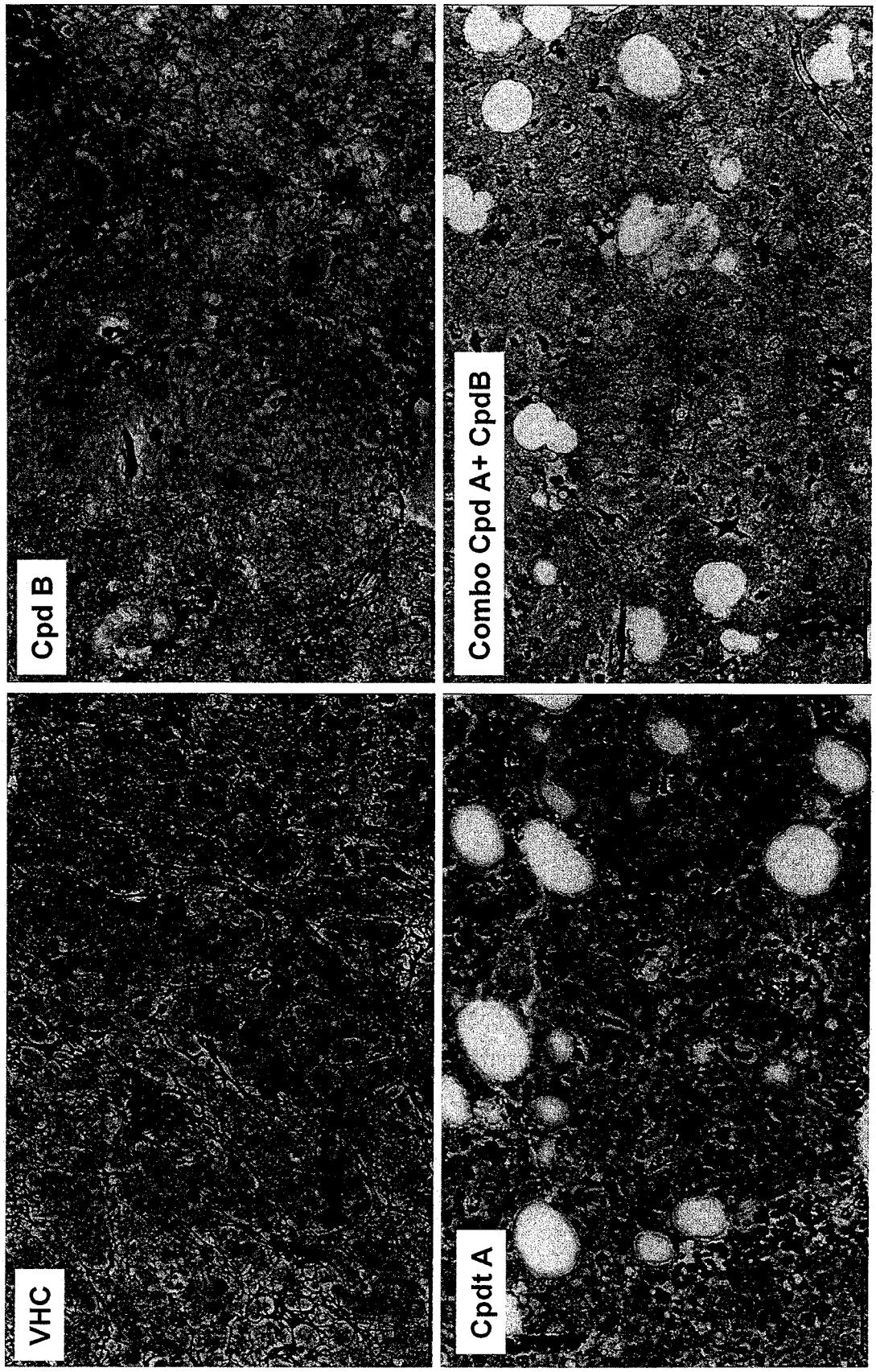


Figure 15
Stat5p, Bone marrow pictures

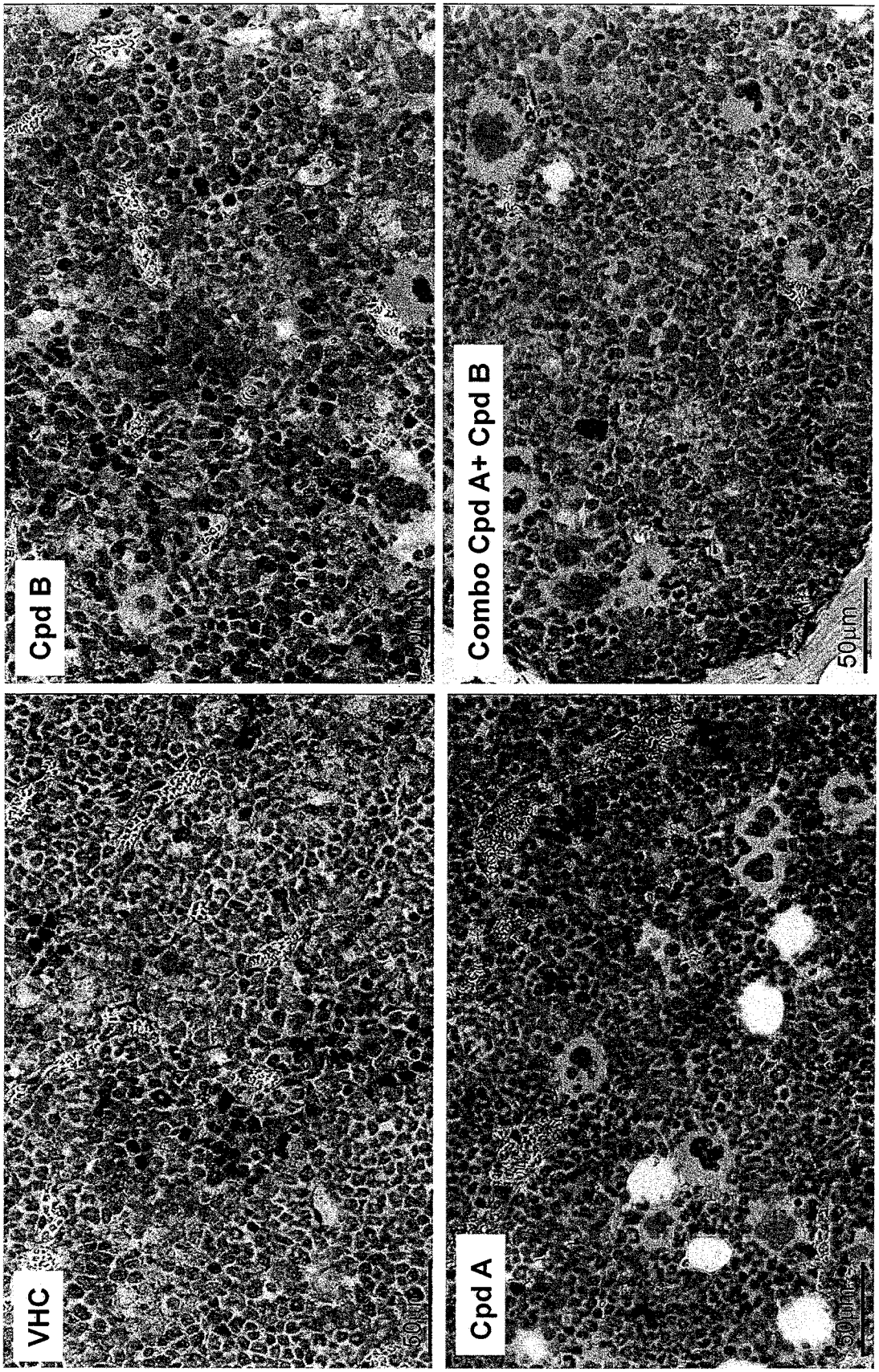


Figure 16

Ac Histone H3, Bone marrow pictures

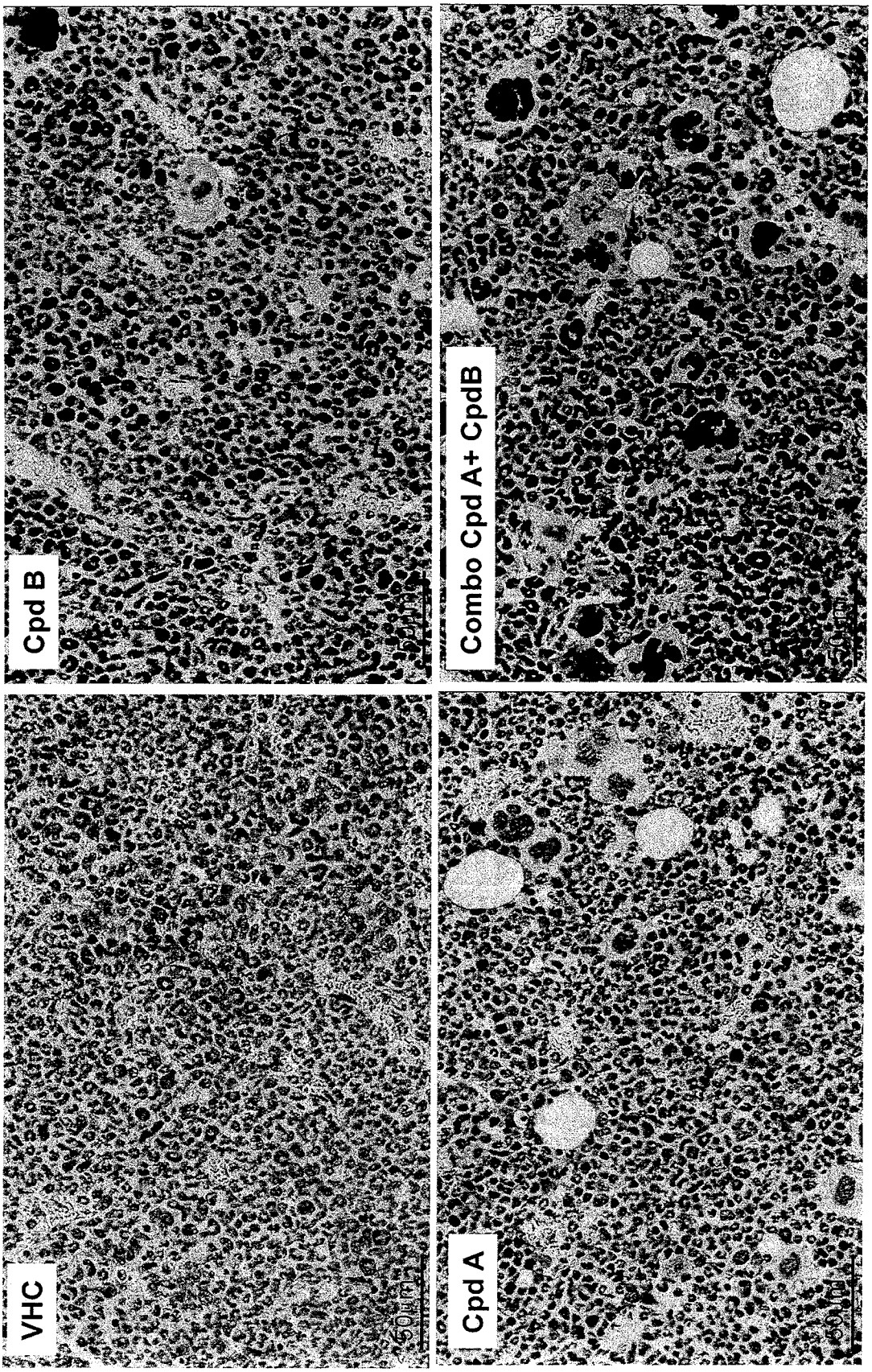


Figure 17
H&E staining, Spleen pictures

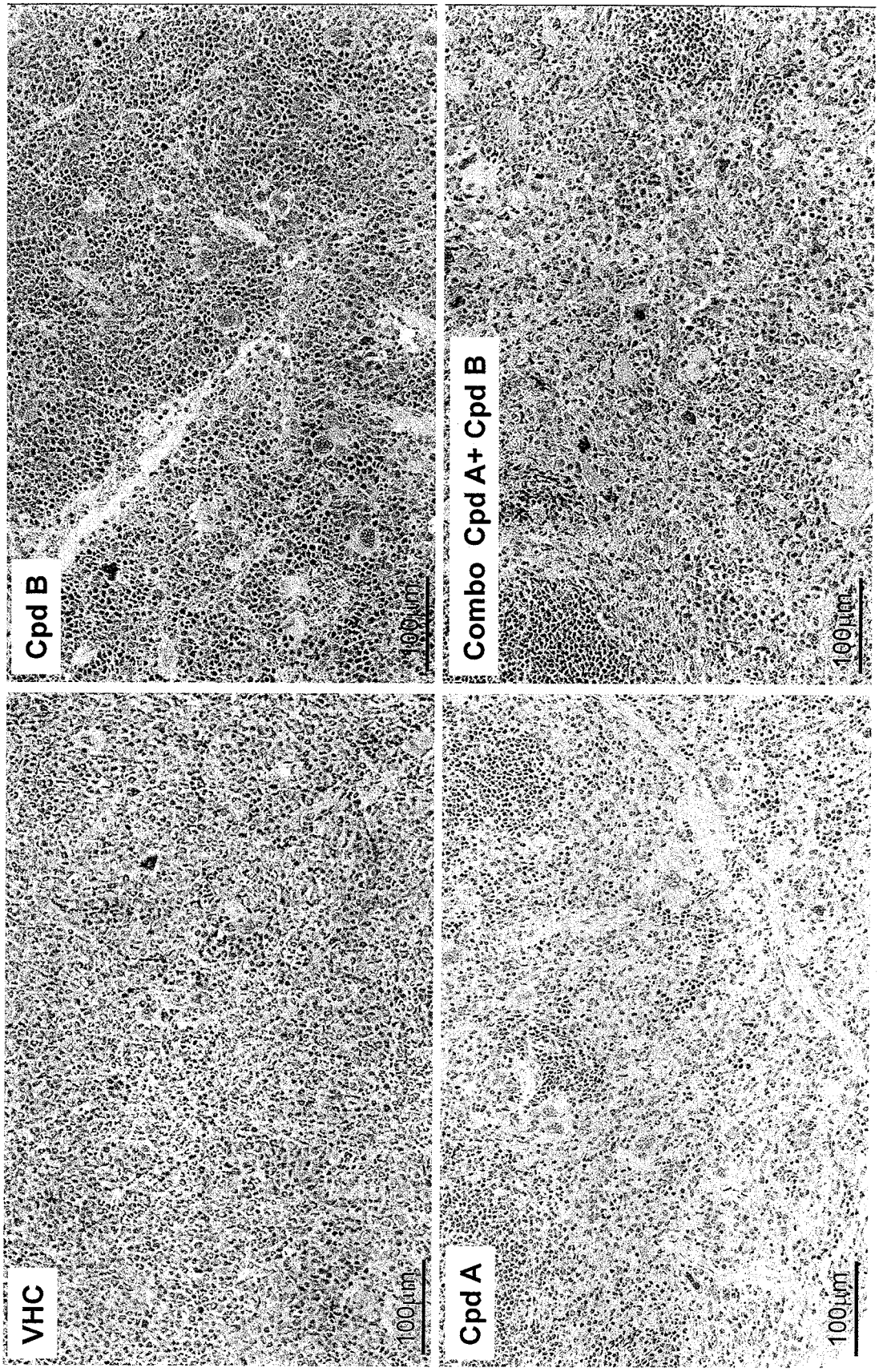


Figure 18
Stat5p, Spleen pictures

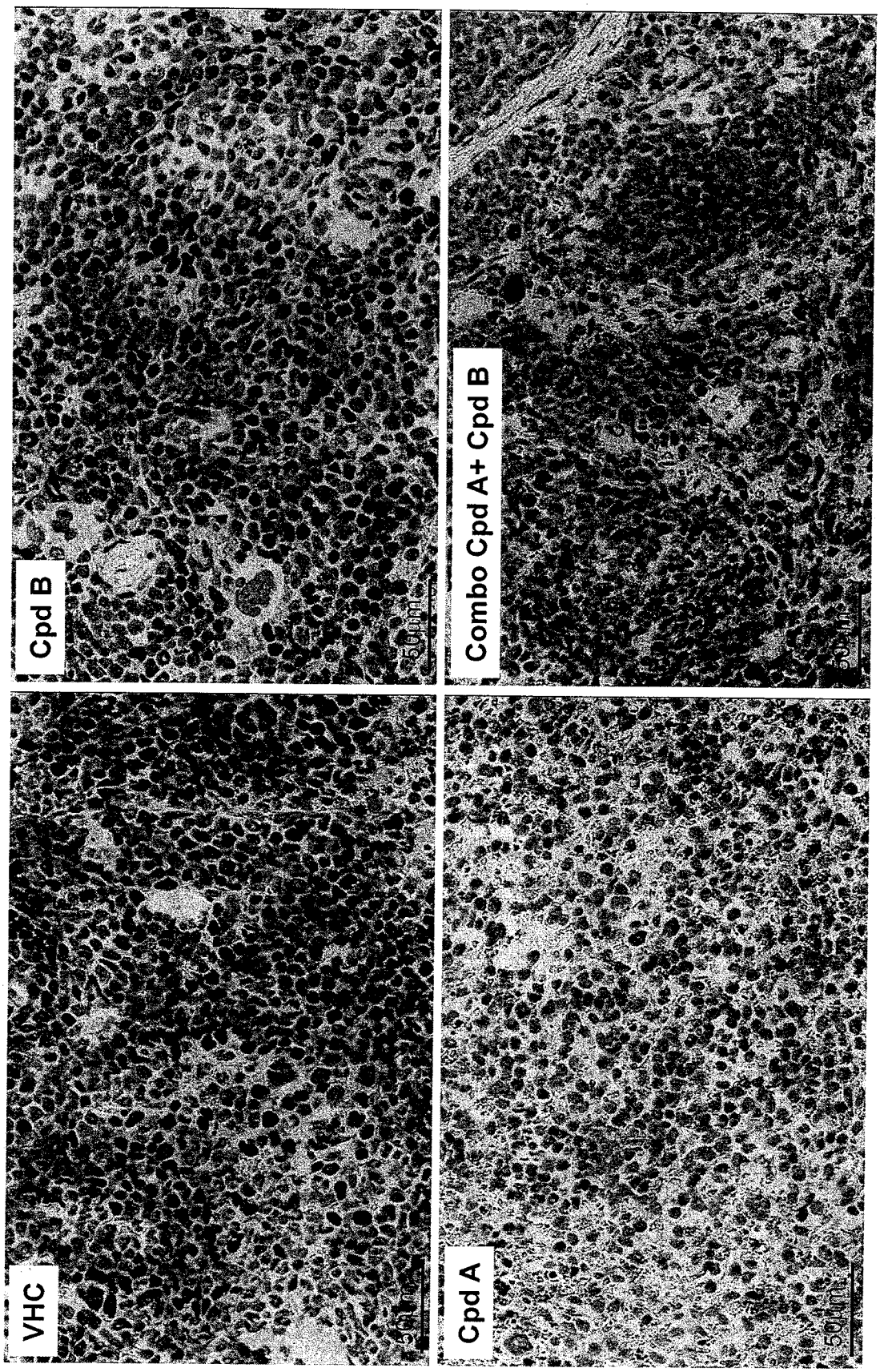


Figure 19

Ac Histone H3, Spleen pictures

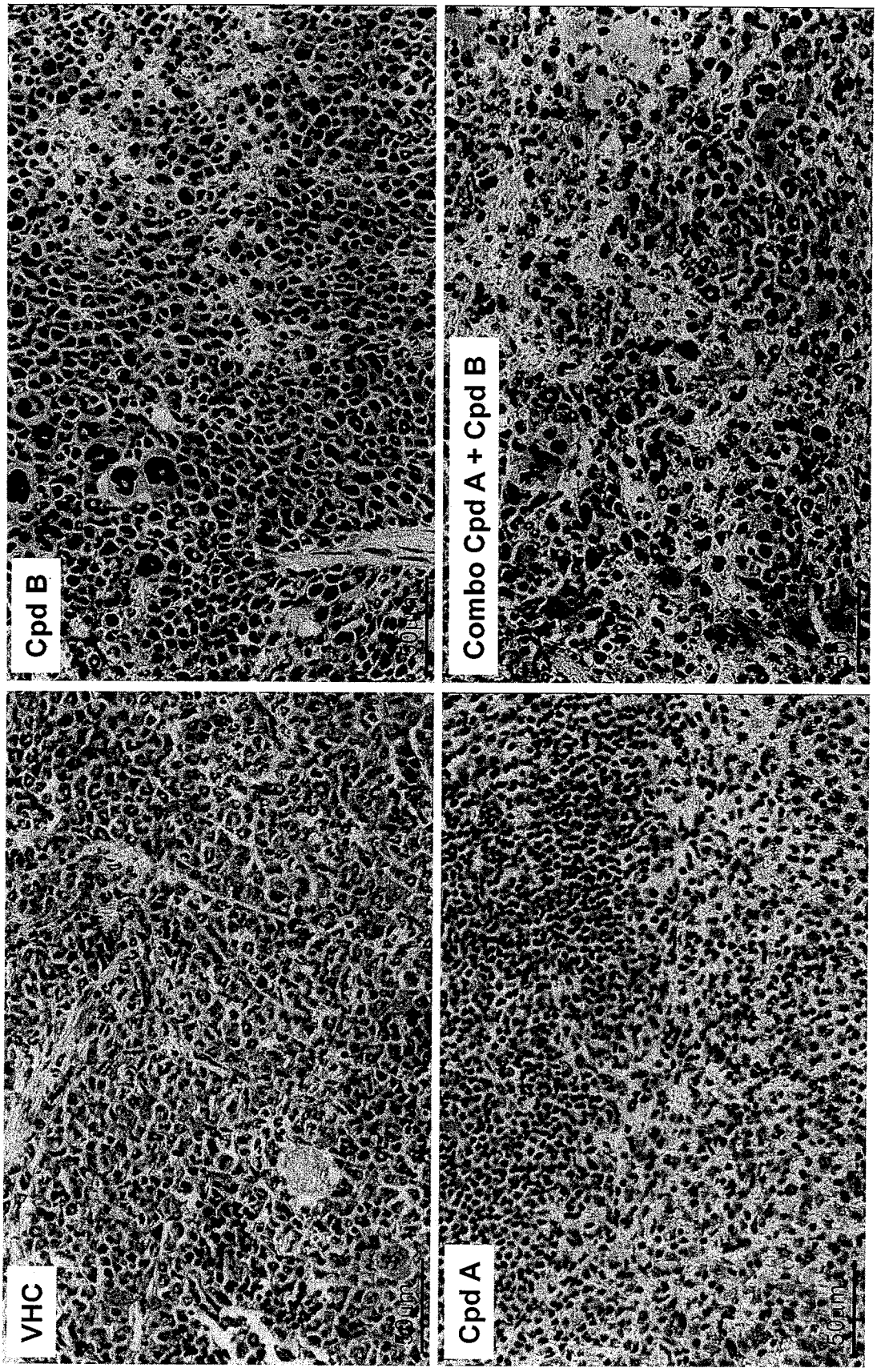
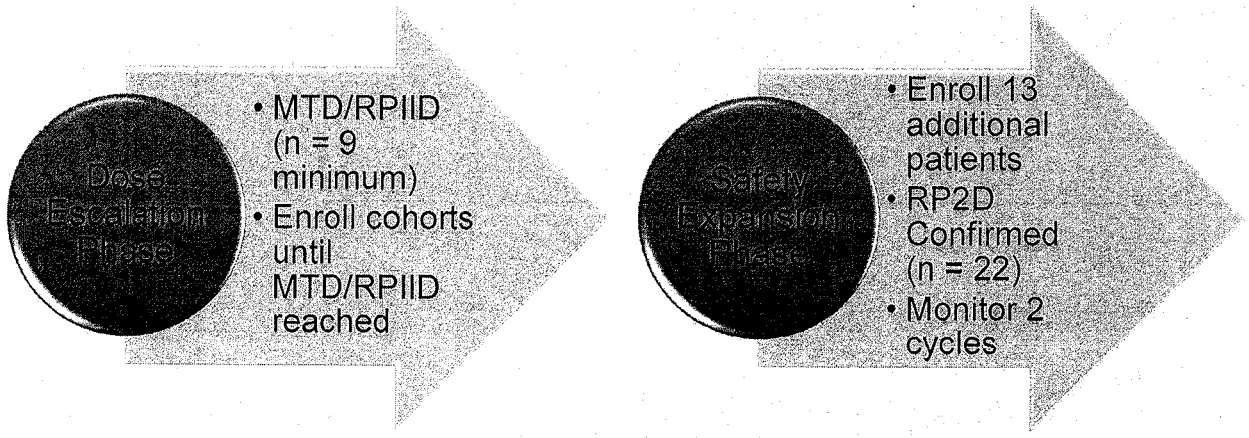


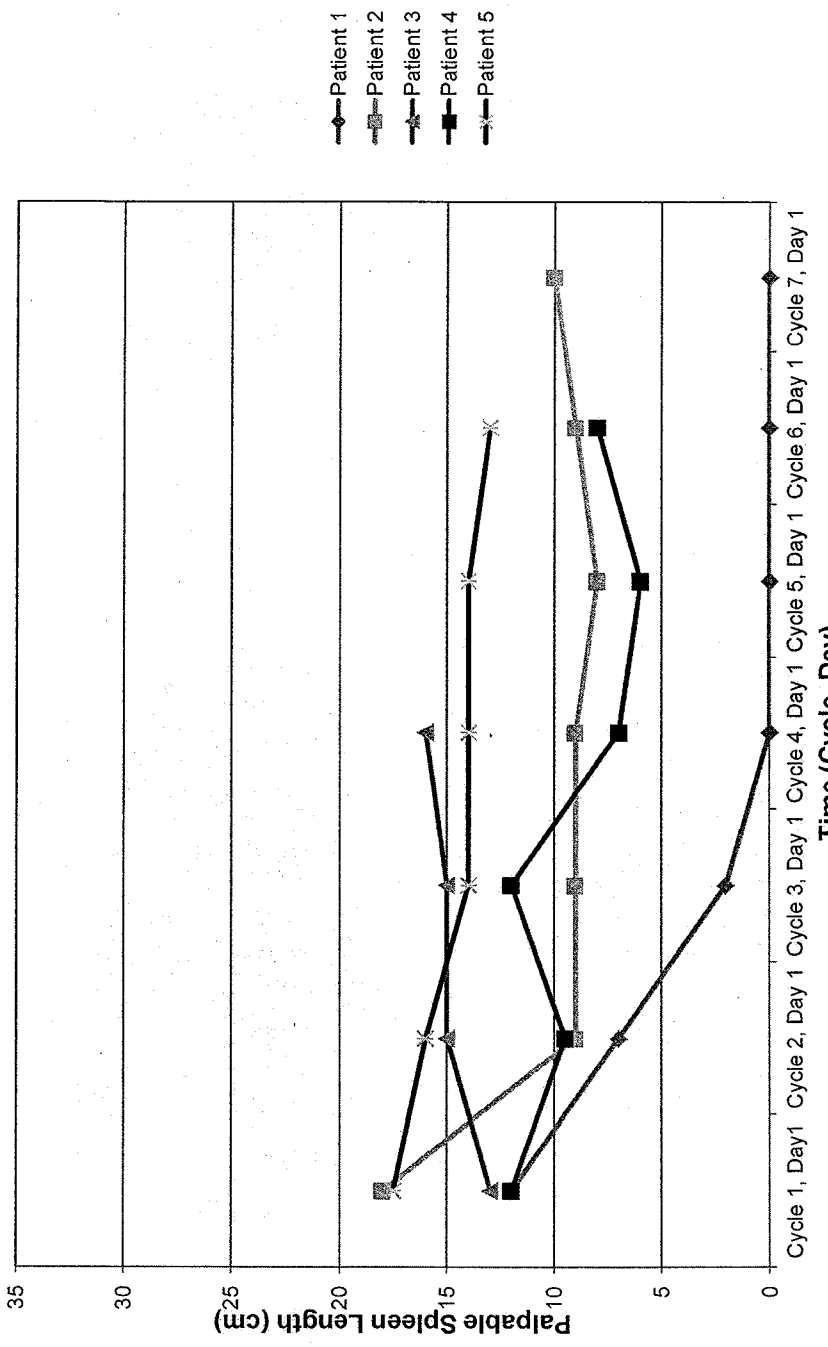
Figure 20. Phase 1b Trial Study Design and Methods



Proposed Dose level	Proposed combination treatment dose
1	Ruxolitinib 5 mg BID, Panobinostat 10 mg TIW QOW
2	Ruxolitinib 10 mg BID, Panobinostat 10 mg TIW QOW
3	Ruxolitinib 15 mg BID, Panobinostat 10 mg TIW QOW
4	Ruxolitinib 15 mg BID, Panobinostat 15 mg TIW QOW
5	Ruxolitinib 15 mg BID, Panobinostat 20 mg TIW QOW
6	Ruxolitinib 15 mg BID, Panobinostat 25 mg TIW QOW
7	Ruxolitinib 15 mg BID, Panobinostat 30 mg TIW QOW

MTD = Maximum tolerated dose; RP2D = Recommended phase 2 dose

Figure 21. Palpable Spleen Length Over Time in Cohort 1



1 cycle = 28 days – Data from patient profiles

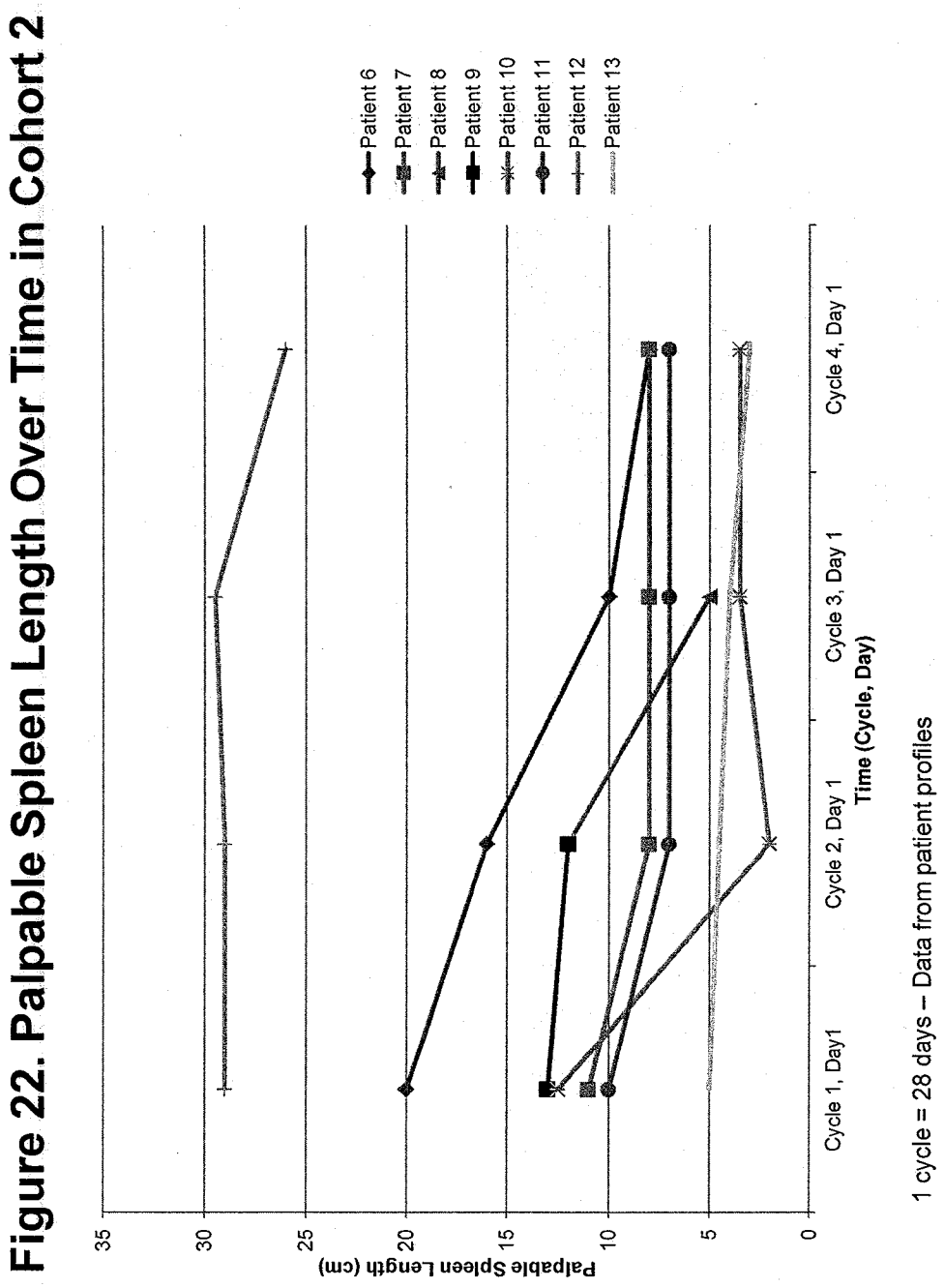

Figure 22. Palpable Spleen Length Over Time in Cohort 2
Patient 6
Patient 7
Patient 8
Patient 9
Patient 10
Patient 11
Patient 12
Patient 13
Palpable Spleen Length (cm)
35
30
25
20
15
10
5
0
Cycle 1, Day1
Cycle 2, Day 1
Cycle 3, Day 1
Cycle 4, Day 1
Time (Cycle, Day)
1 cycle = 28 days -- Data from patient profiles

Figure 23. Palpable Spleen Length Over Time in Cohort 3

