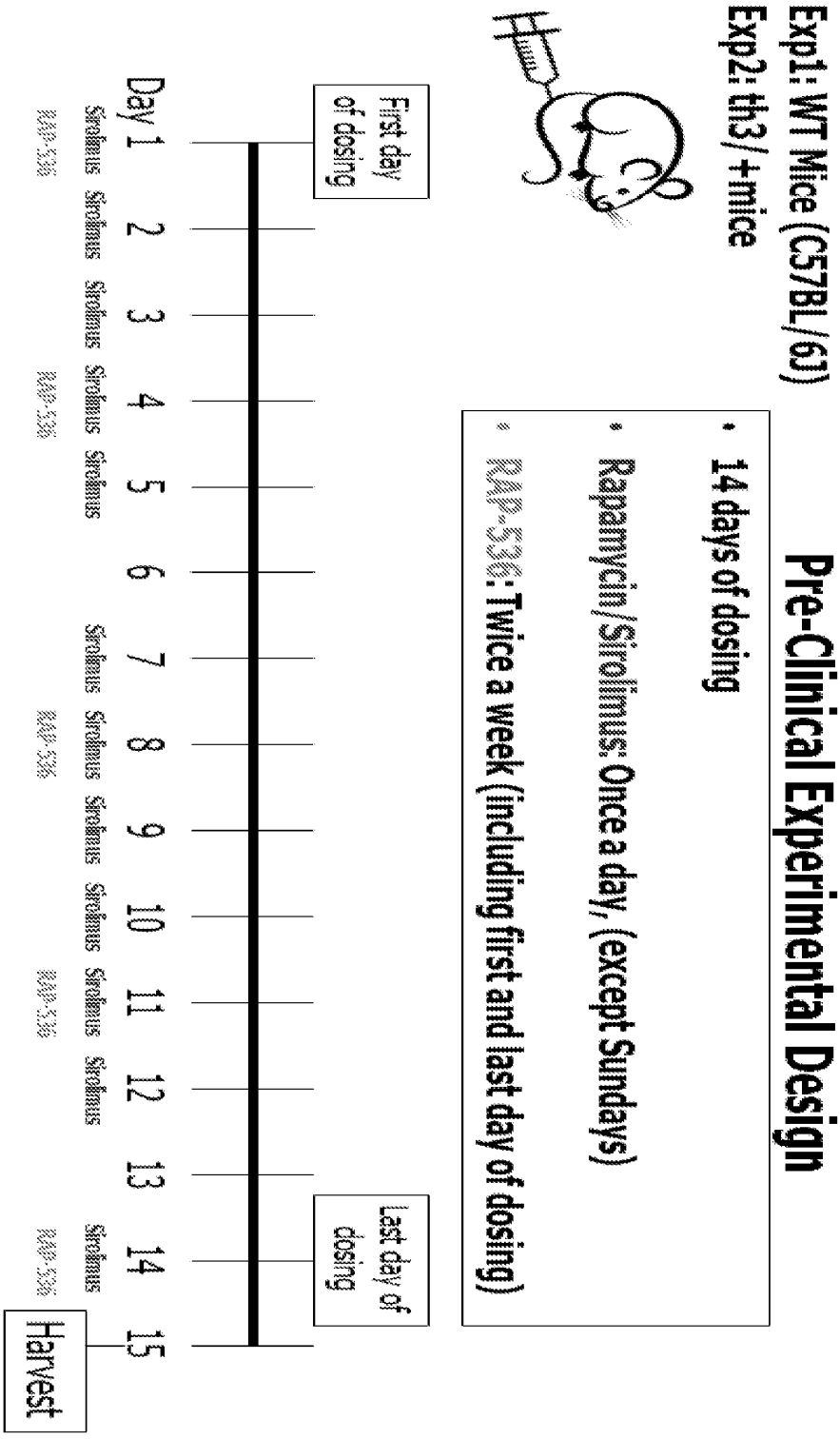
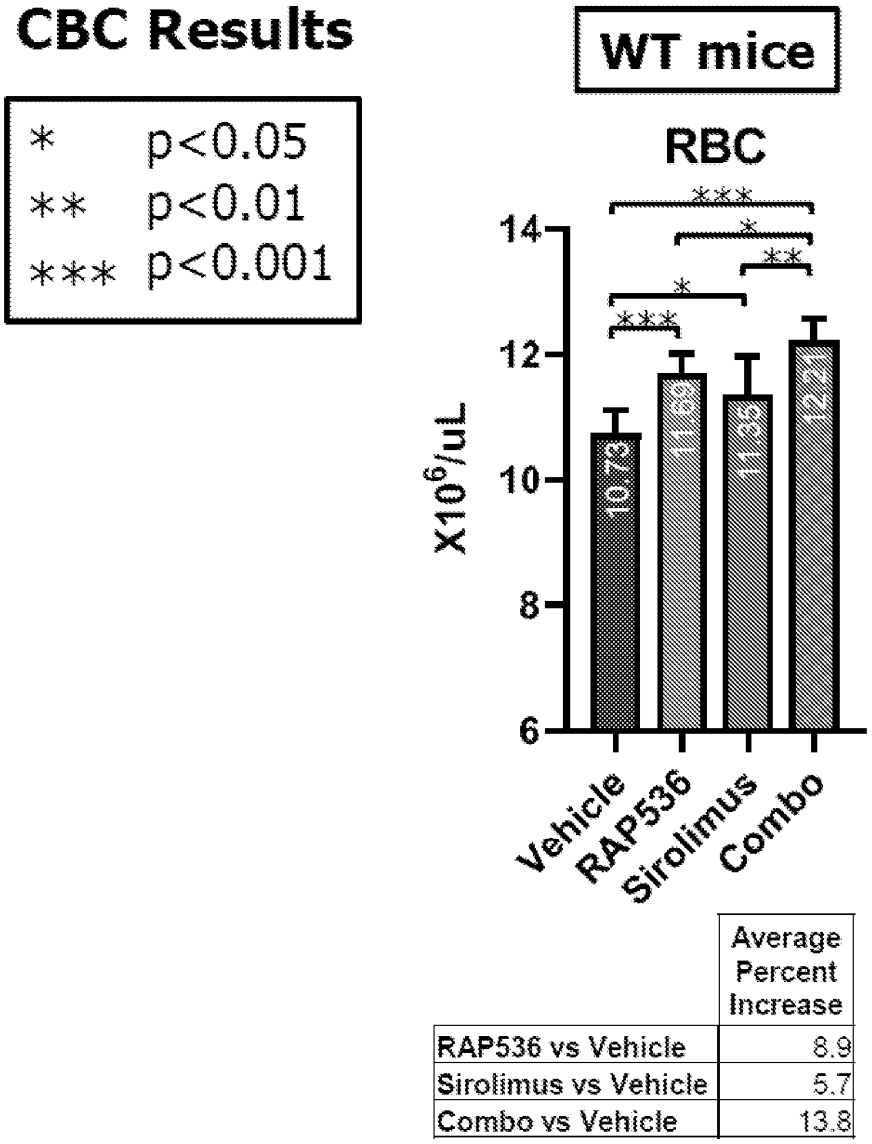
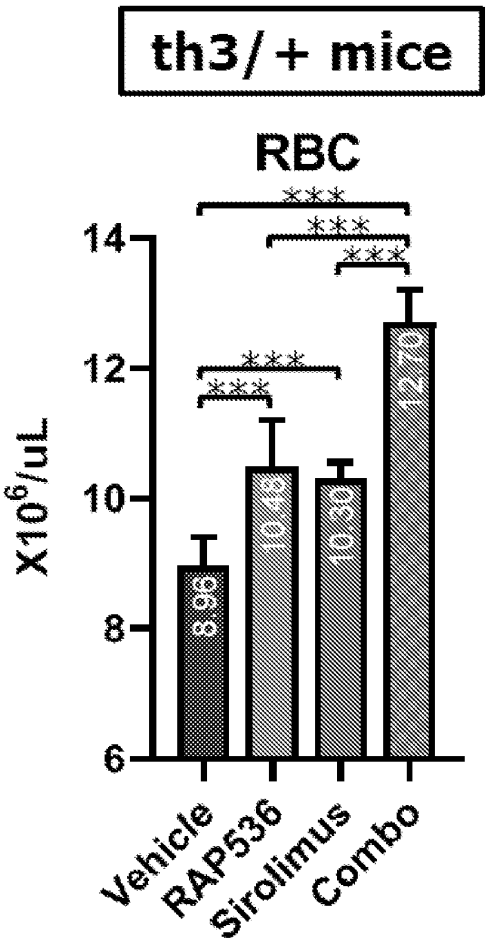

Exp1: WT Mice (C57BL/6J)
Exp2: th3/+mice
Pre-Clinical Experimental Design
14 days of dosing
Rapamycin/Sirolimus: Once a day, (except Sundays)
RAD-530: Twice a week (including first and last day of dosing)
First day of dosing
Last day of dosing
Harvest
Day 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Sirolimus
RAD-530

FIG. 1



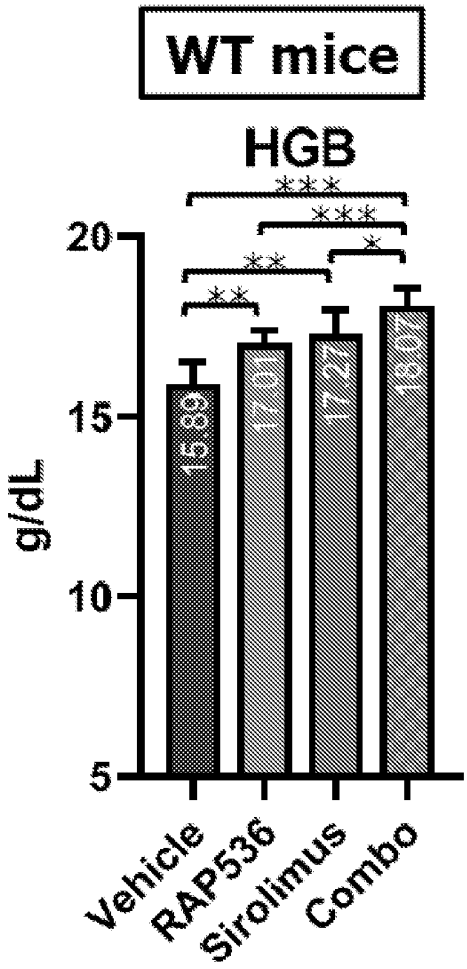
	Average Percent Increase
RAP536 vs Vehicle	8.9
Sirolimus vs Vehicle	5.7
Combo vs Vehicle	13.8

FIG. 2A



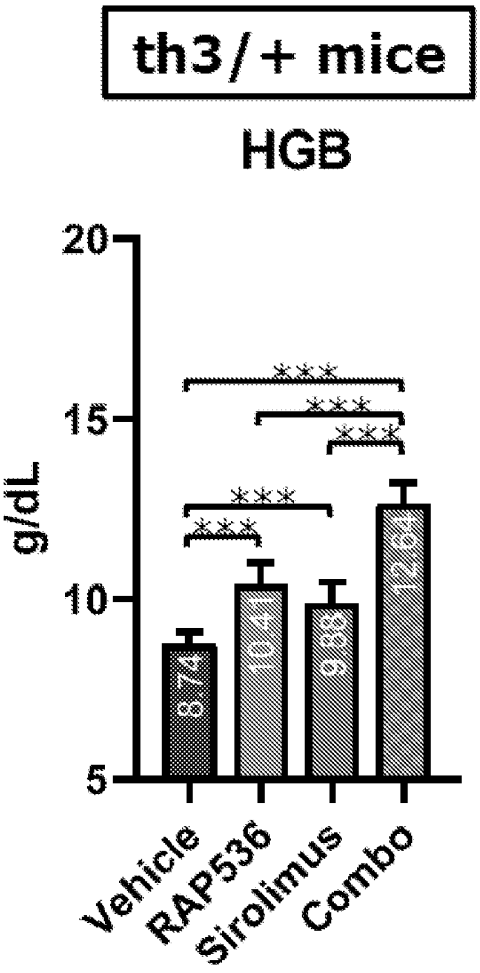
	Average Percent Increase
RAP536 vs Vehicle	17.0
Sirolimus vs Vehicle	15.0
Combo vs Vehicle	41.8

FIG. 2B



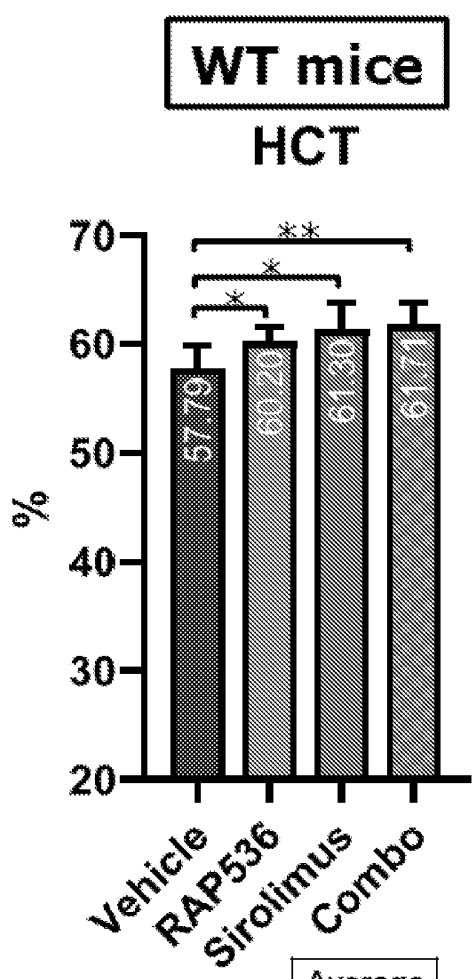
	Average Percent Increase
RAP536 vs Vehicle	7.1
Sirolimus vs Vehicle	8.7
Combo vs Vehicle	13.8

FIG. 3A



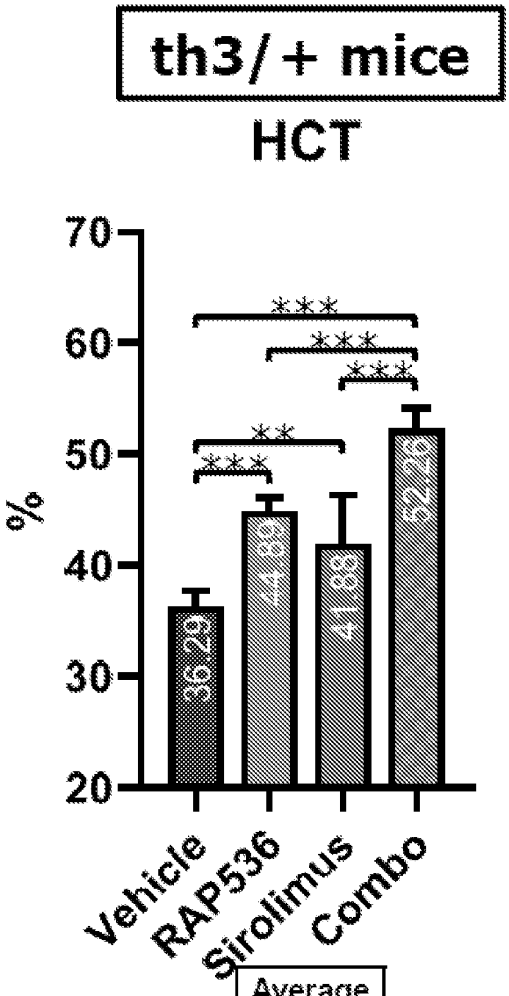
	Average Percent Increase
RAP536 vs Vehicle	19.2
Sirolimus vs Vehicle	13.0
Combo vs Vehicle	44.7

FIG. 3B



	Average Percent Increase
RAP536 vs Vehicle	4.2
Sirolimus vs Vehicle	6.1
Combo vs Vehicle	6.8

FIG. 4A



	Average Percent Increase
RAP536 vs Vehicle	23.7
Sirolimus vs Vehicle	15.4
Combo vs Vehicle	44.0

FIG. 4B

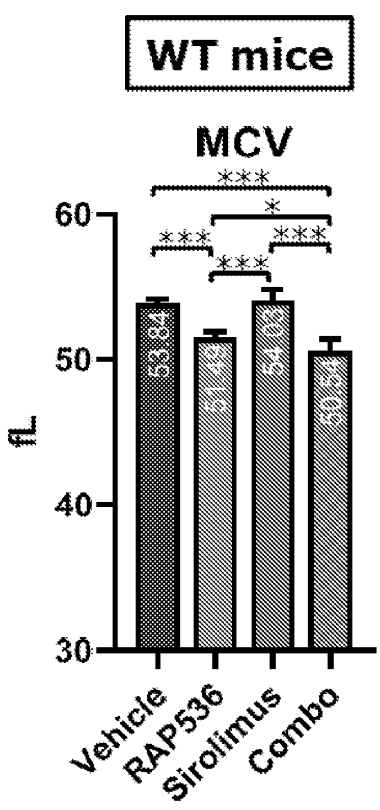

WT mice
MCV
fL
60
50
40
30
***
*
***
***
***
53.84
51.47
54.03
50.51
Vehicle
RAP536
Sirolimus
Combo

FIG. 5A

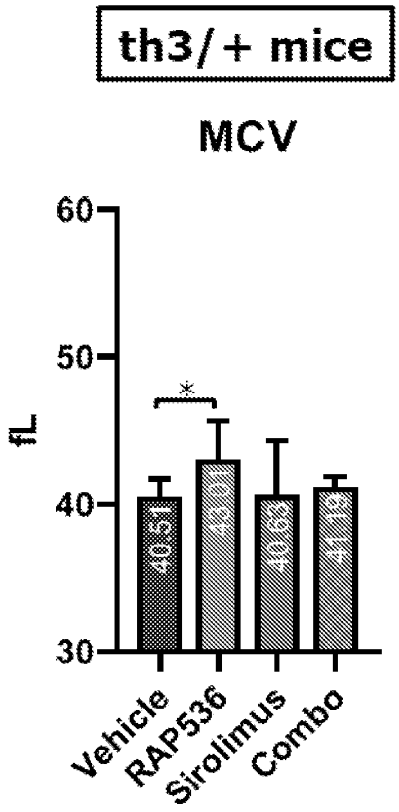

th3/+ mice
MCV
fL
60
50
40
30
*
40.51
43.01
40.63
41.19
Vehicle
RAP536
Sirolimus
Combo

FIG. 5B

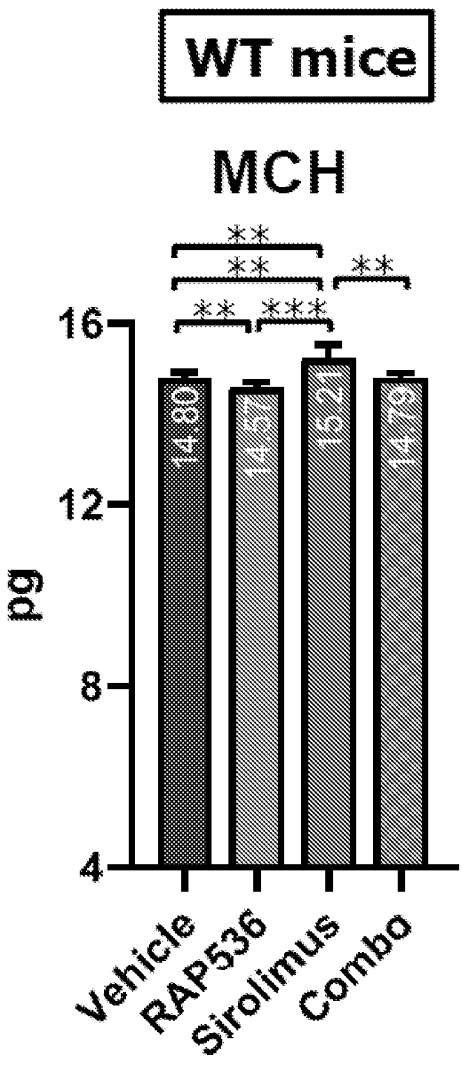

WT mice
MCH
pg
16
12
8
4
14.80
14.57
15.21
14.79
**
**
**
**
***
Vehicle
RAP536
Sirolimus
Combo

FIG. 6A

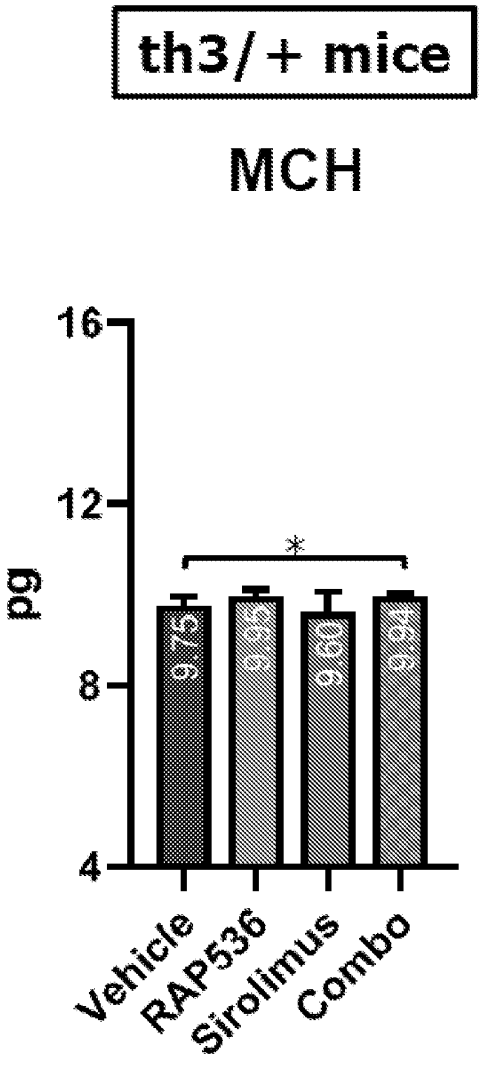

th3/+ mice
MCH
pg
16
12
8
4
9.75
9.96
9.60
9.94
*
Vehicle
RAP536
Sirolimus
Combo

FIG. 6B

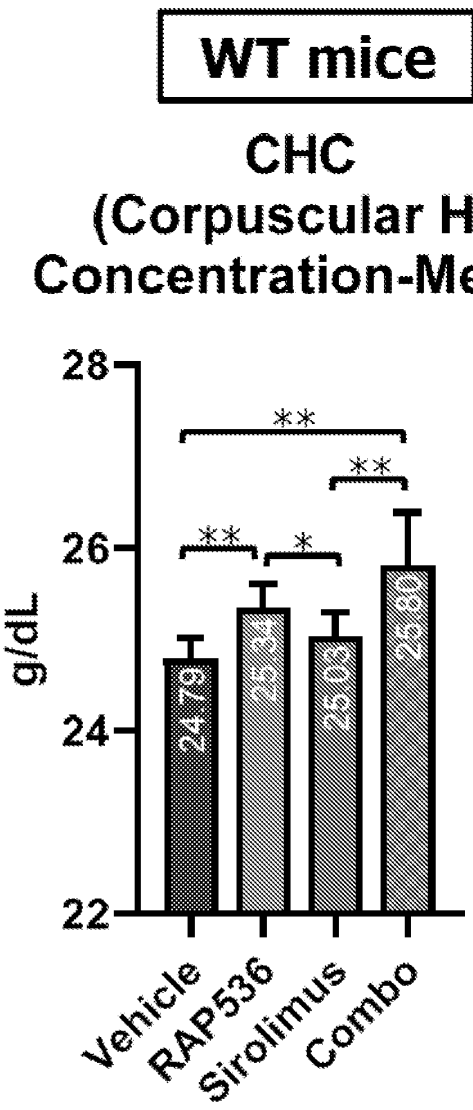

WT mice
CHC
(Corpuscular Hb
Concentration-Mean)
g/dL
28
26
24
22
**
**
**
*
24.78
25.34
25.03
25.80
Vehicle
RAP536
Sirolimus
Combo

FIG. 7A

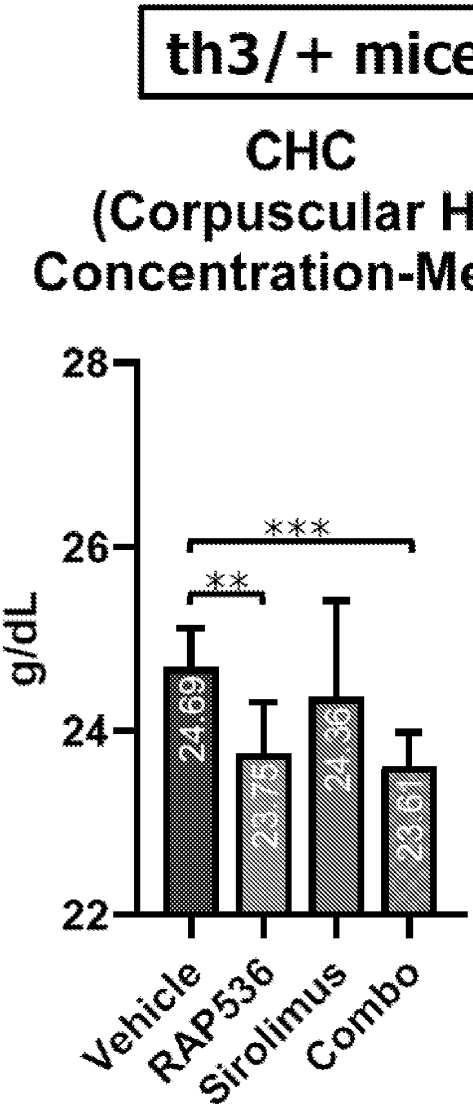

th3/+ mice
CHC
(Corpuscular Hb
Concentration-Mean)
g/dL
28
26
24
22
***
**
24.69
23.75
24.36
23.61
Vehicle
RAP536
Sirolimus
Combo

FIG. 7B

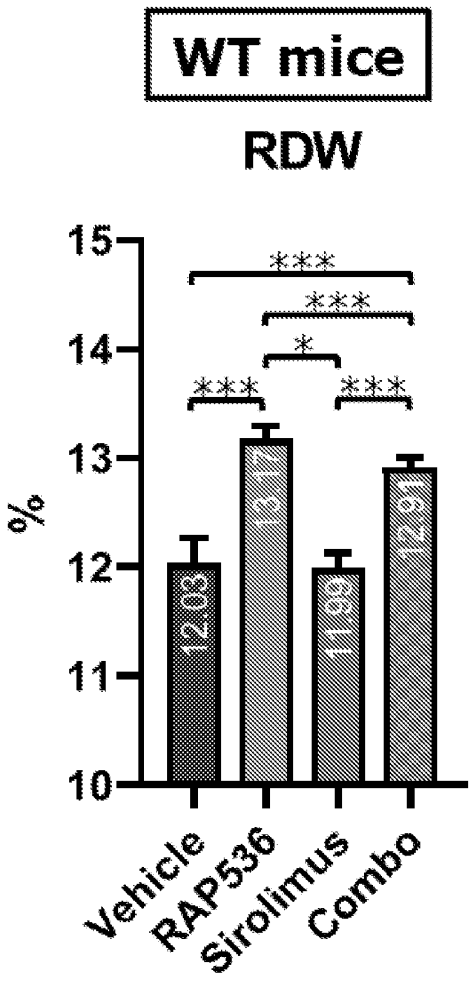

WT mice
RDW
%
15
14
13
12
11
10
***
***
*
***
***
12.03
13.17
11.99
12.91
Vehicle
RAP536
Sirolimus
Combo

FIG. 8A

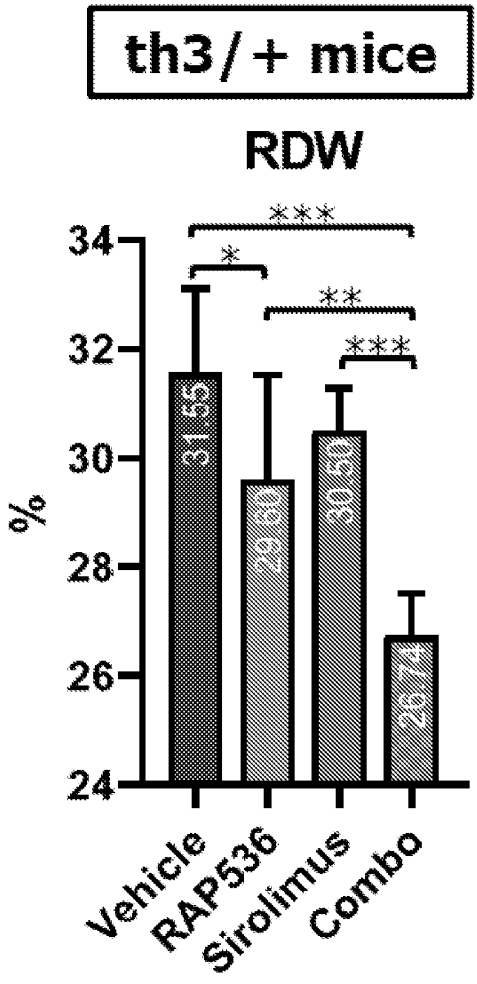

th3/+ mice
RDW
%
34
32
30
28
26
24
***
*
**
***
31.55
29.80
30.50
26.74
Vehicle
RAP536
Sirolimus
Combo

FIG. 8B

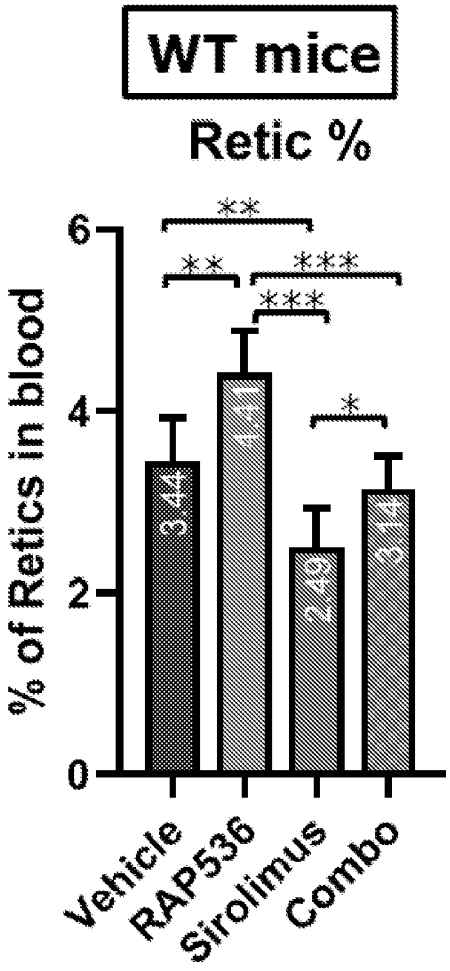

WT mice
Retic %
% of Retics in blood
0
2
4
6
3.44
4.41
2.49
3.14
**
**
***
***
*
Vehicle
RAP536
Sirolimus
Combo

FIG. 9A

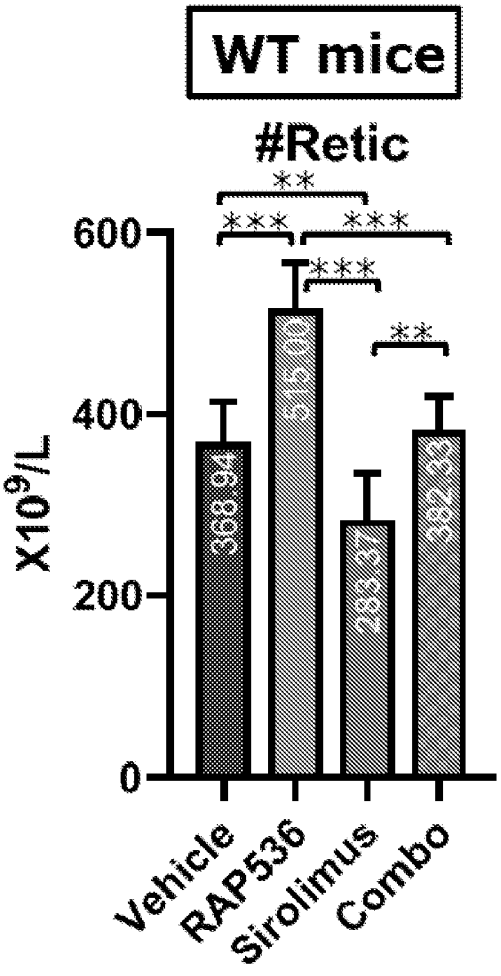

WT mice
#Retic
X10^9/L
0
200
400
600
368.94
516.08
283.37
382.32
**
***
***
***
**
Vehicle
RAP536
Sirolimus
Combo

FIG. 9B

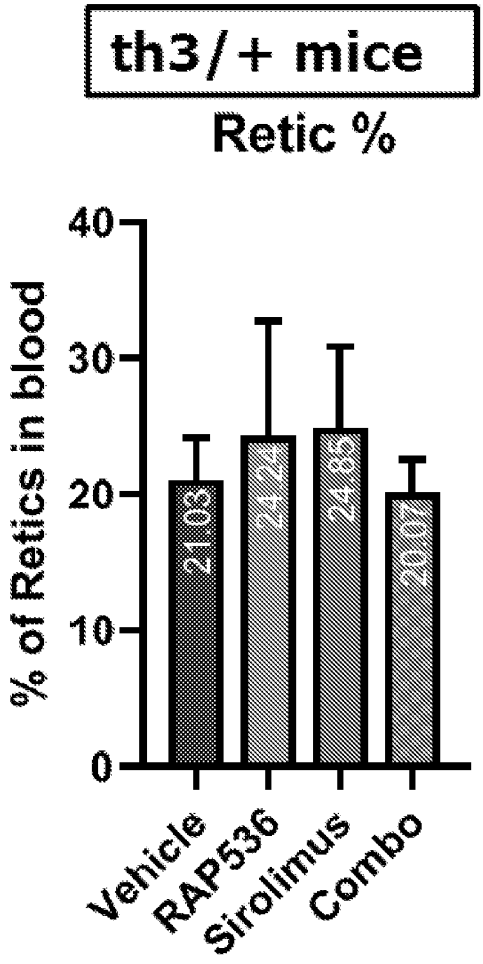


FIG. 10A

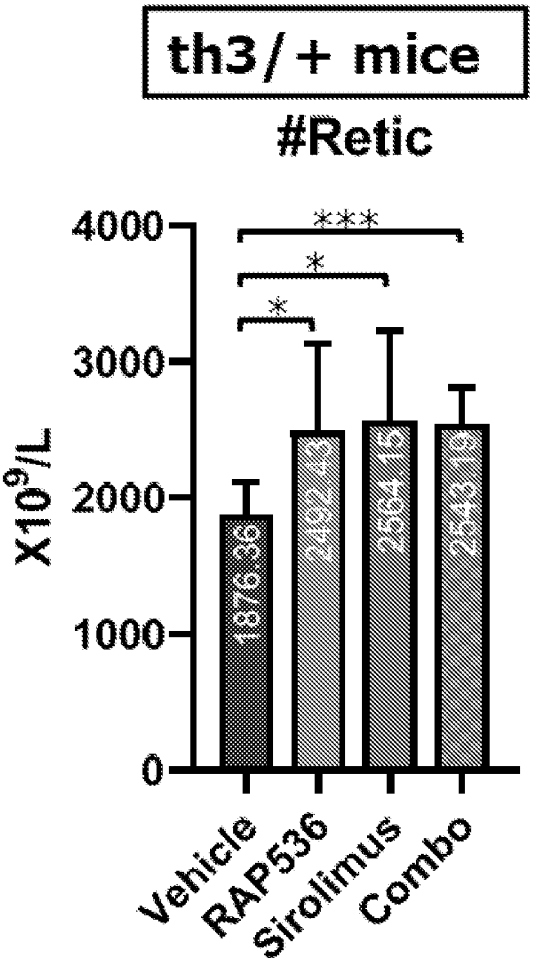


FIG. 10B

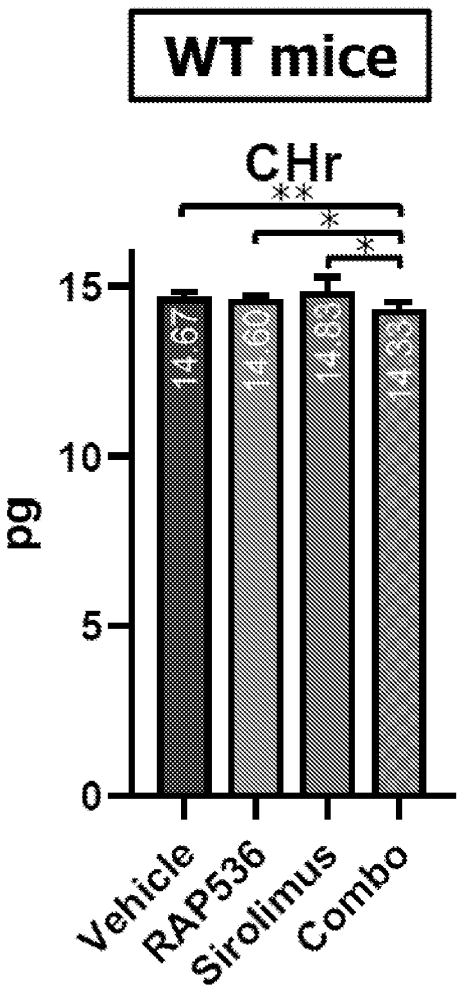


FIG. 11A

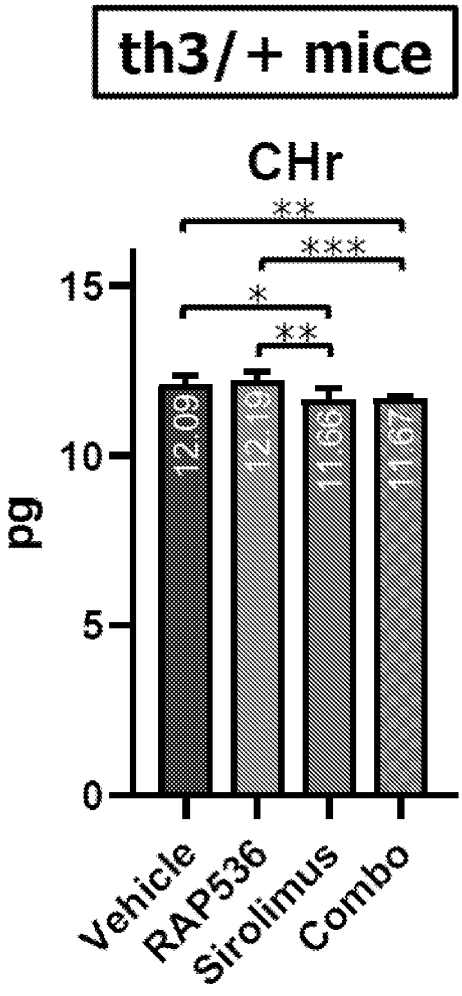


FIG. 11B

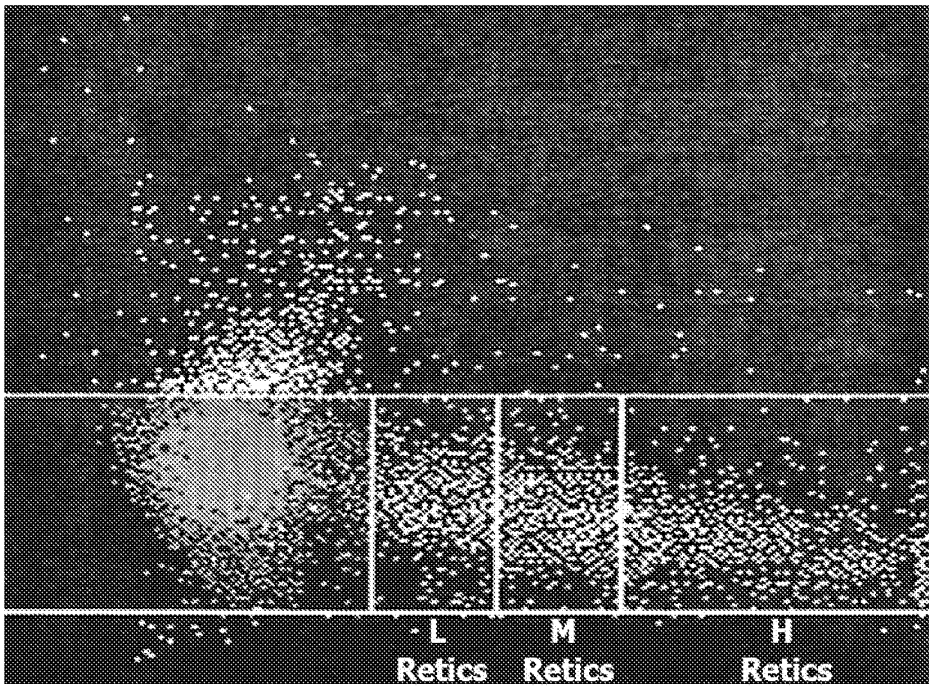


FIG. 12

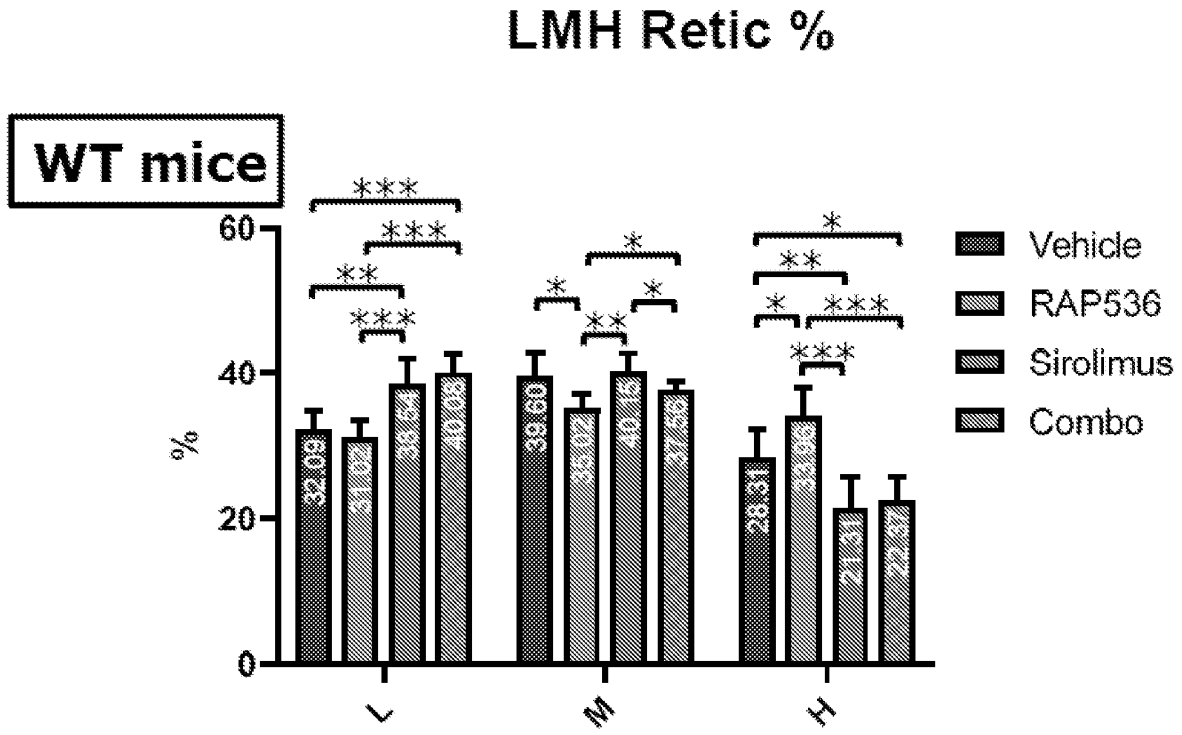


FIG. 13A

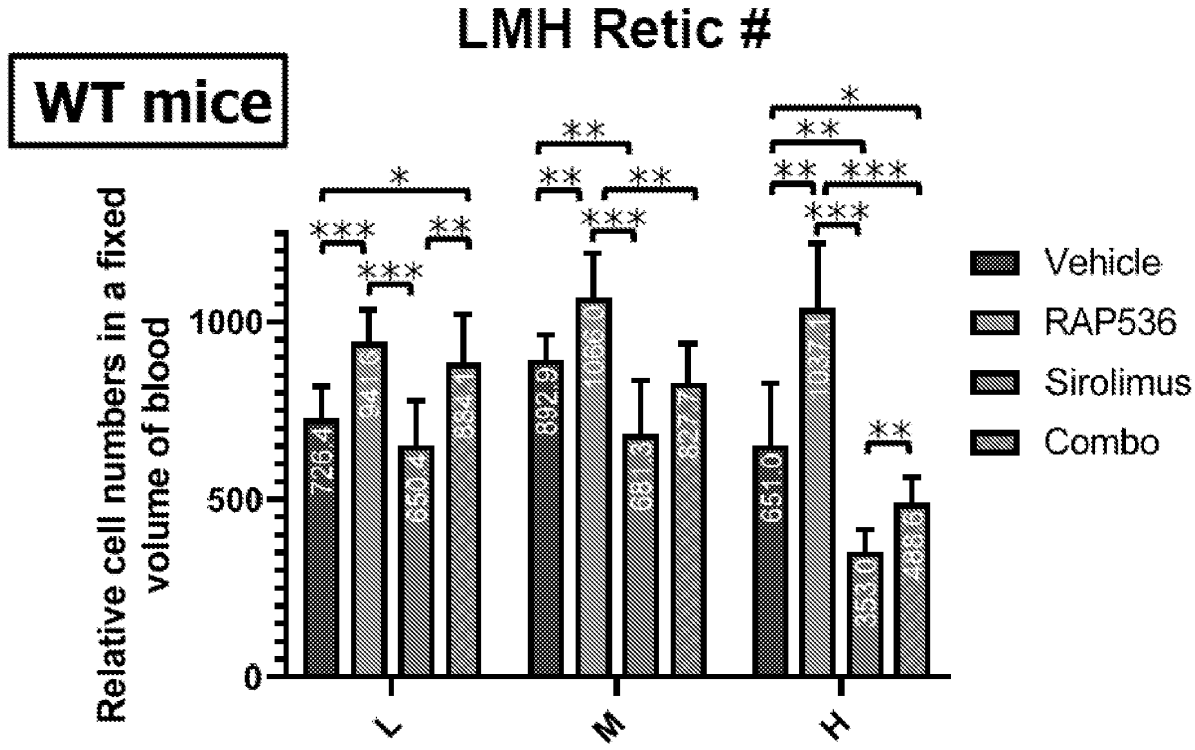


FIG. 13B

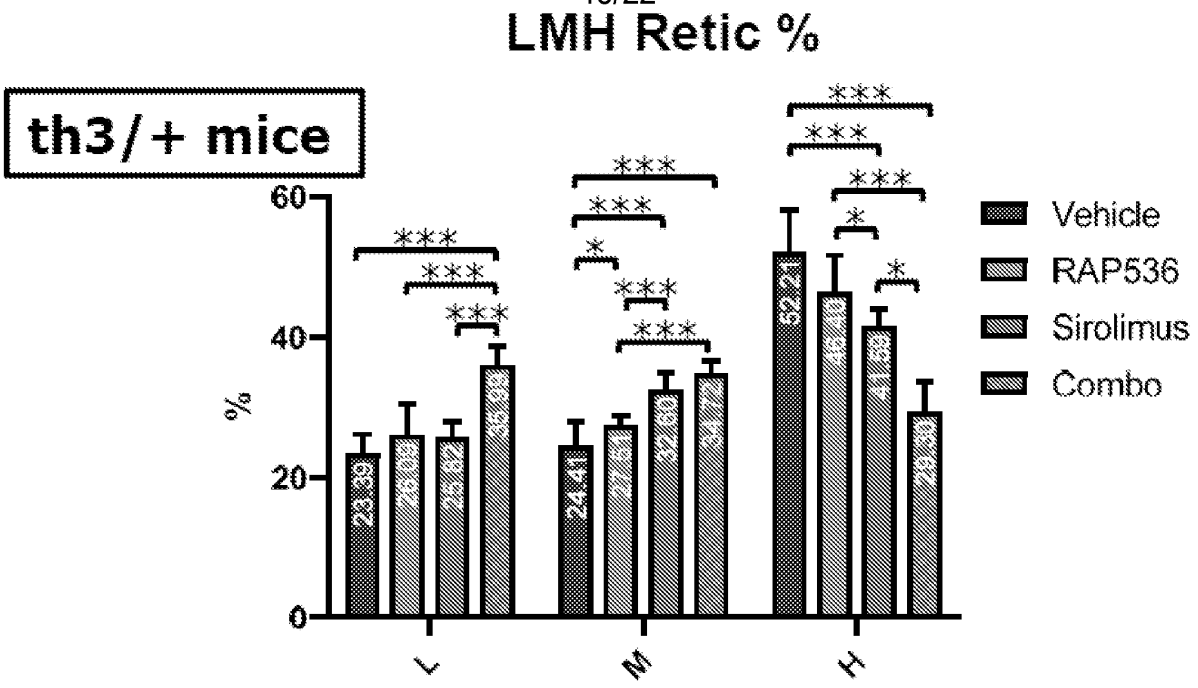


FIG. 14A

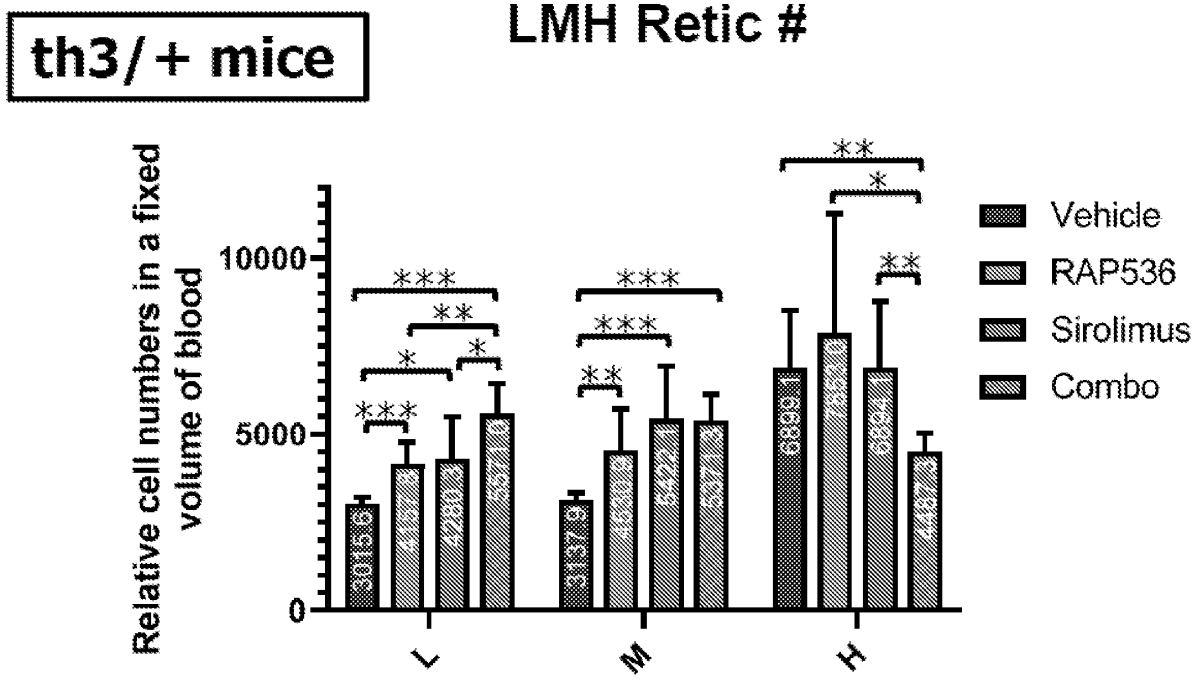


FIG. 14B

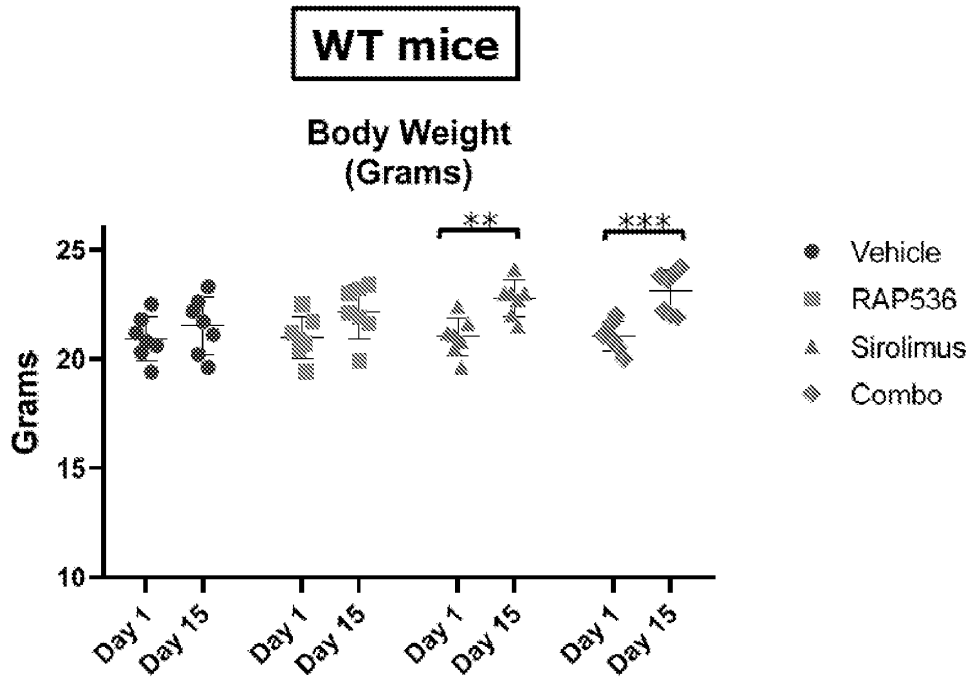


FIG. 15A

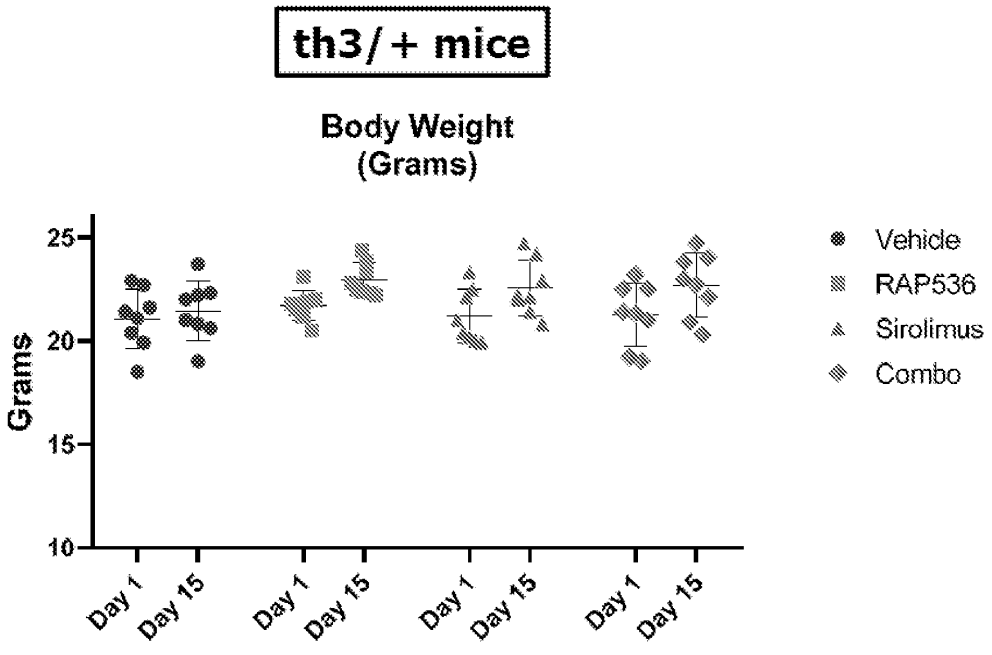


FIG. 15B

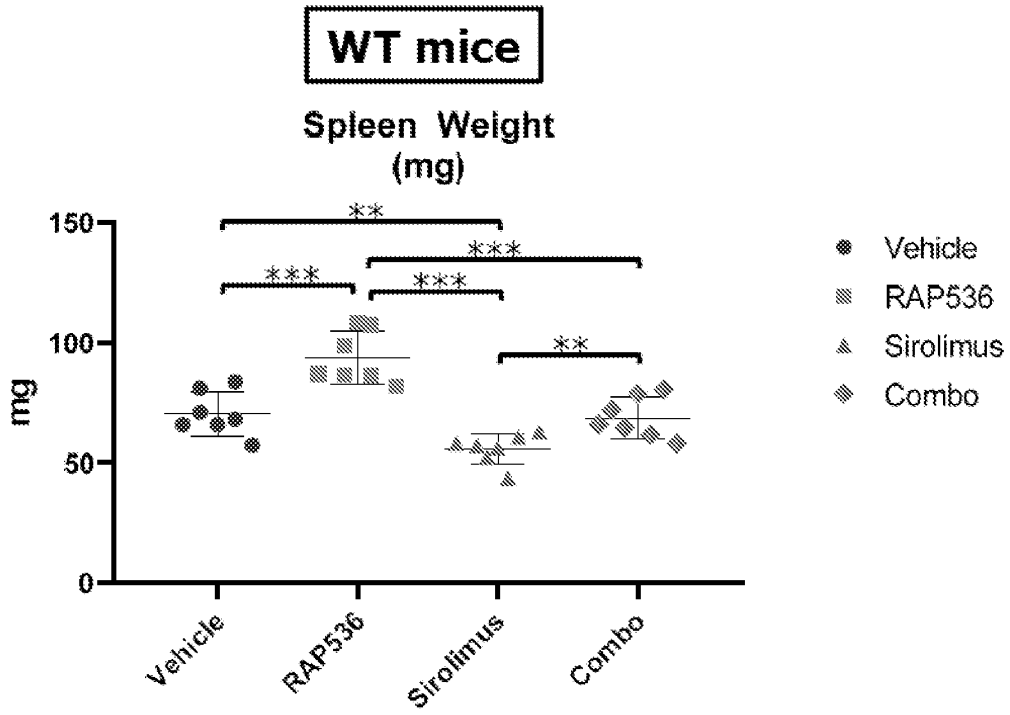


FIG. 16A

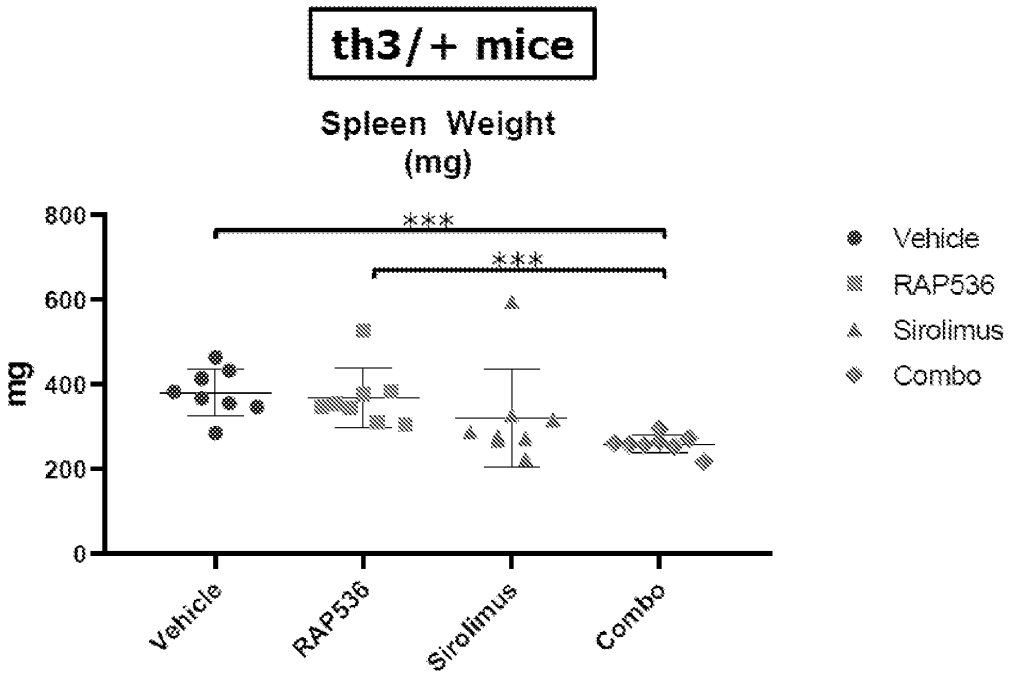


FIG. 16B

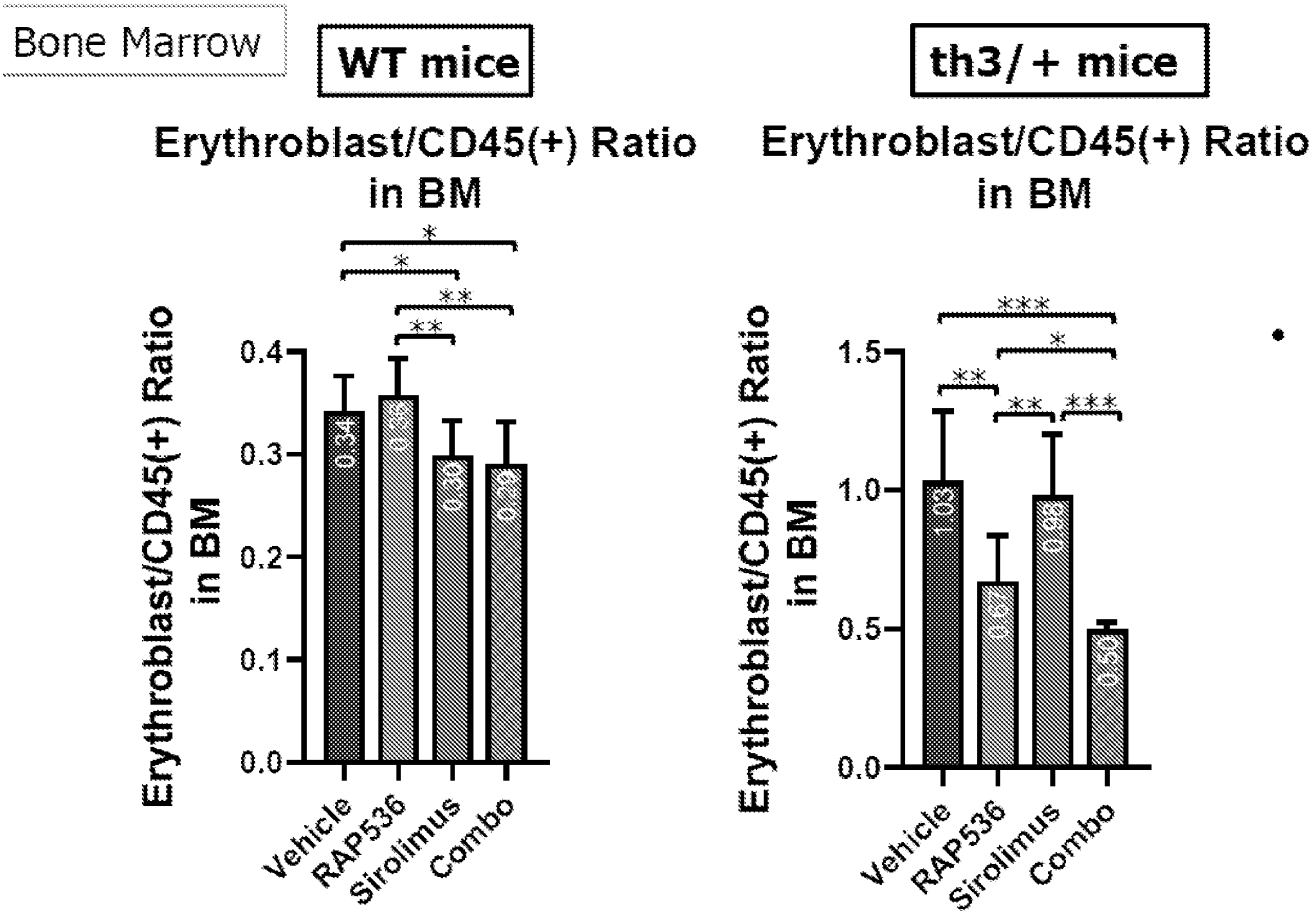


FIG. 17A

FIG. 17B

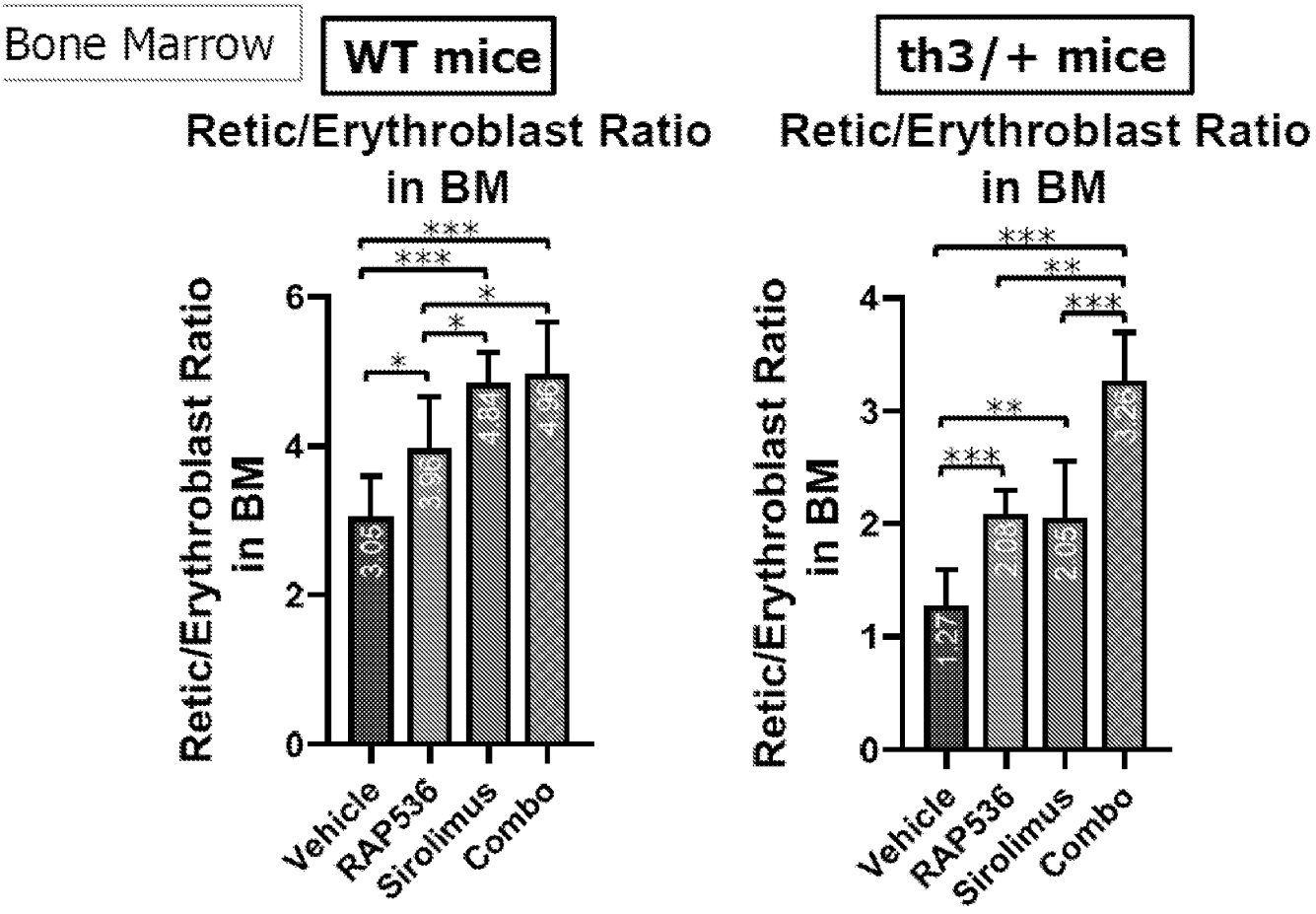


FIG. 18A

FIG. 18B

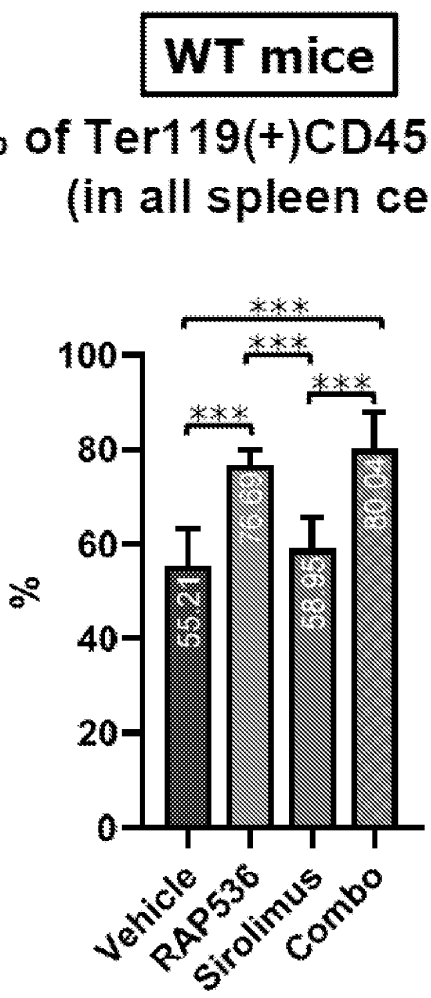


FIG. 19A

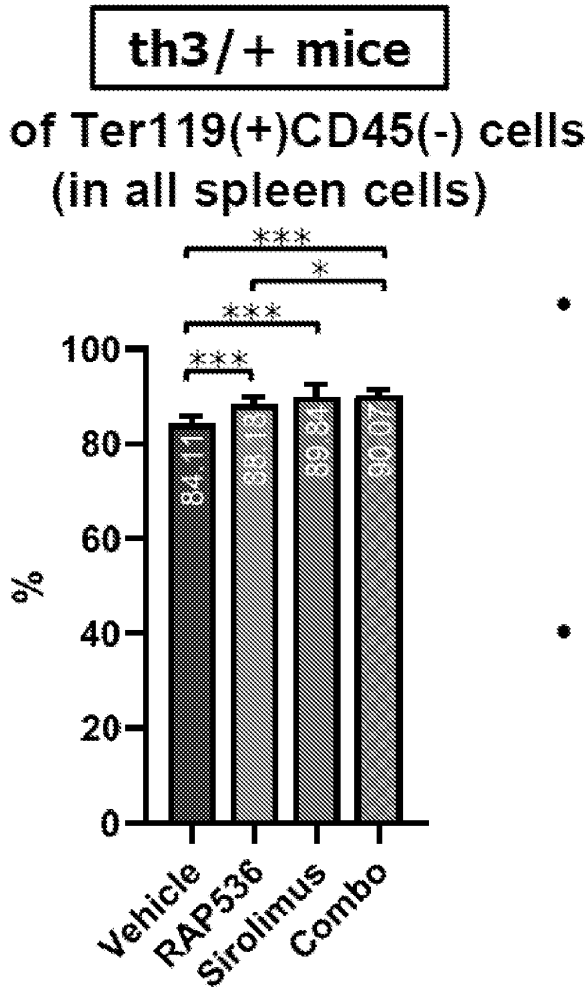


FIG. 19B

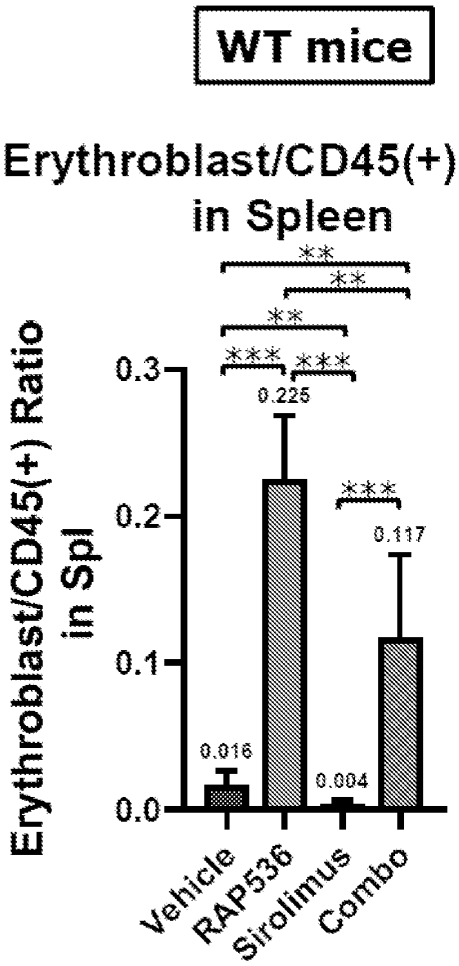


FIG. 20A

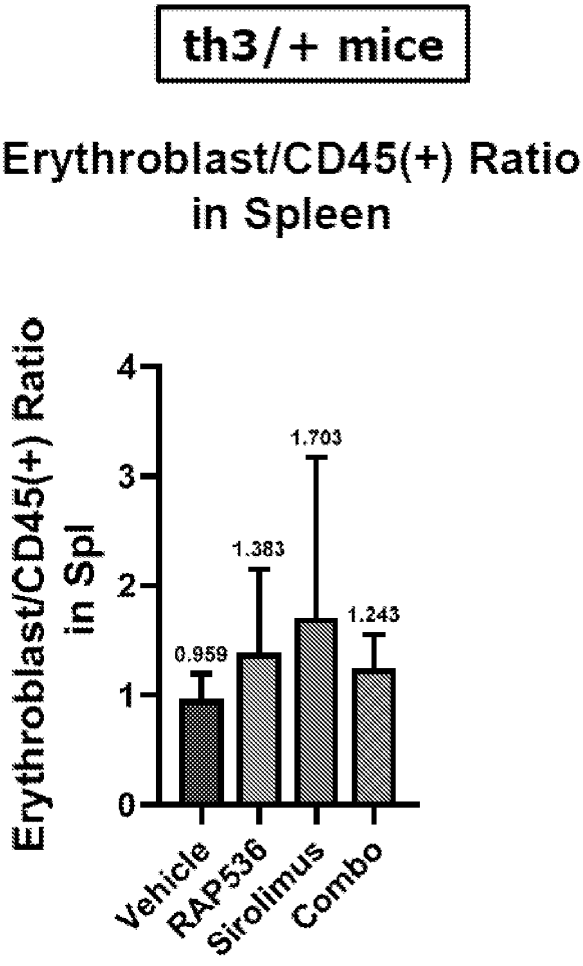


FIG. 20B

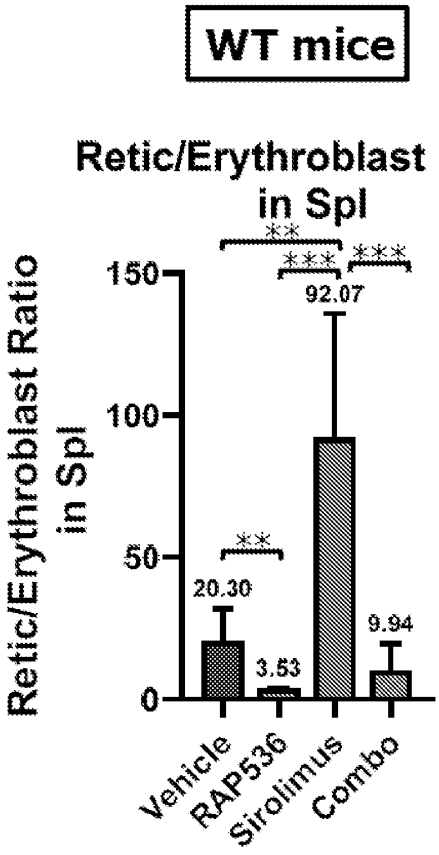


FIG. 21A

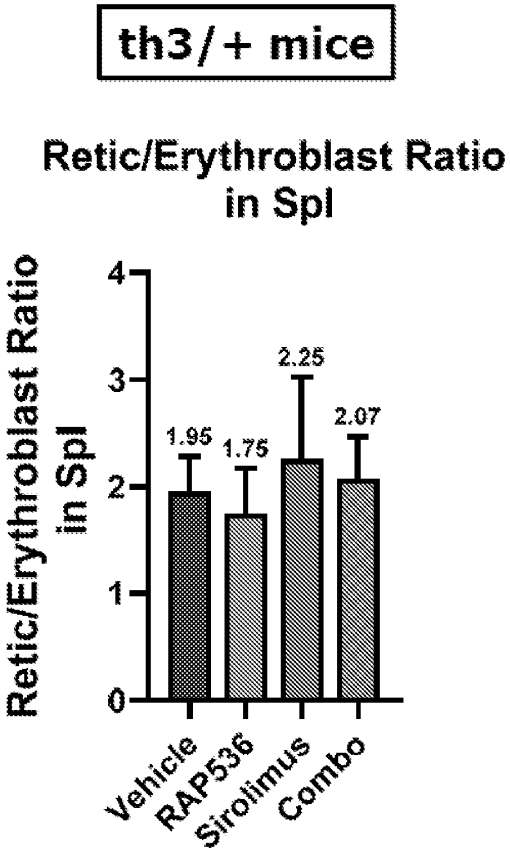


FIG. 21B