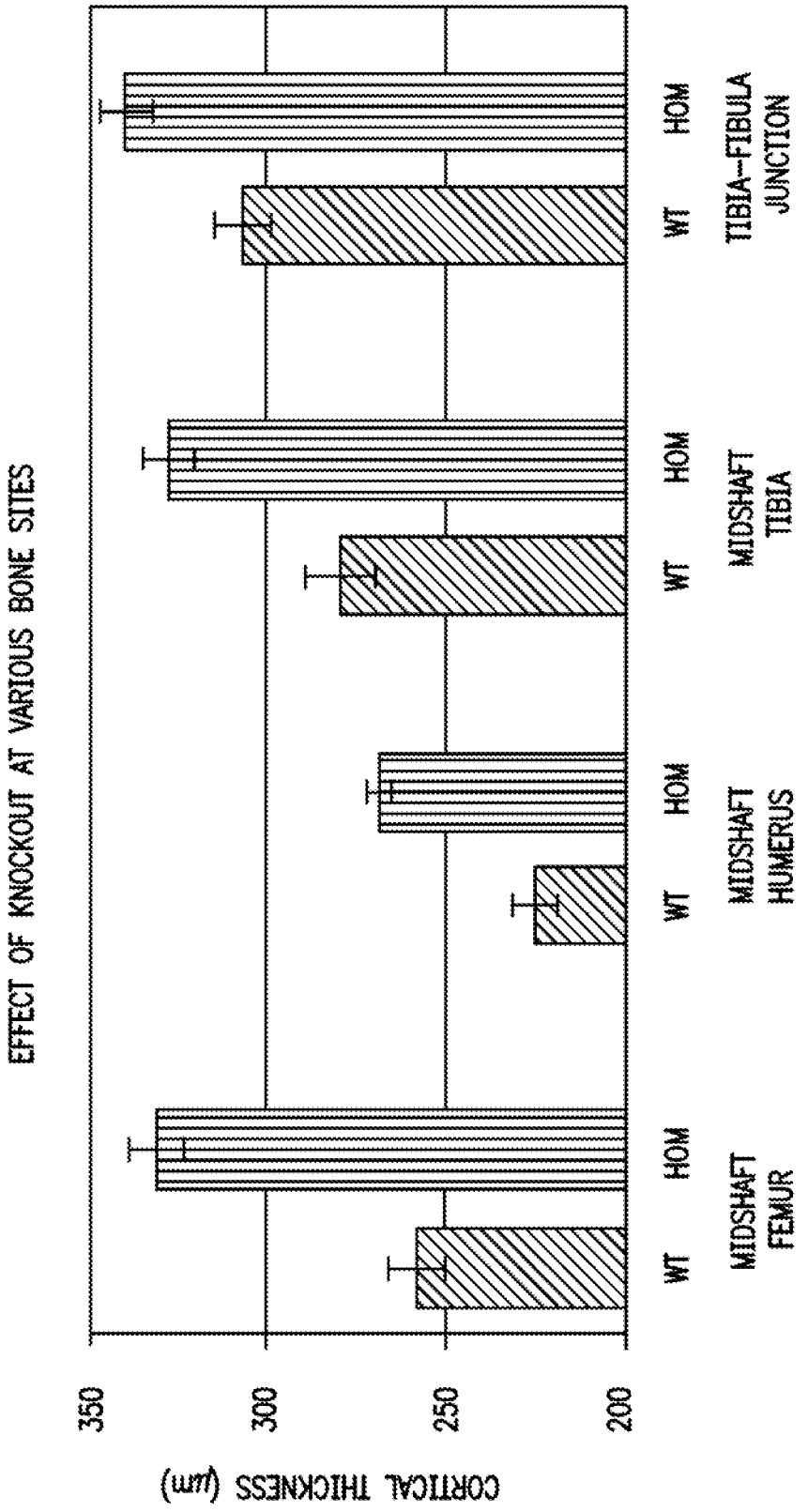

EFFECT OF KNOCKOUT AT VARIOUS BONE SITES
CORTICAL THICKNESS (μm)
350
300
250
200
WT
HOM
MIDSHAFT FEMUR
MIDSHAFT HUMERUS
MIDSHAFT TIBIA
TIBIA-FIBULA JUNCTION

FIG. 1

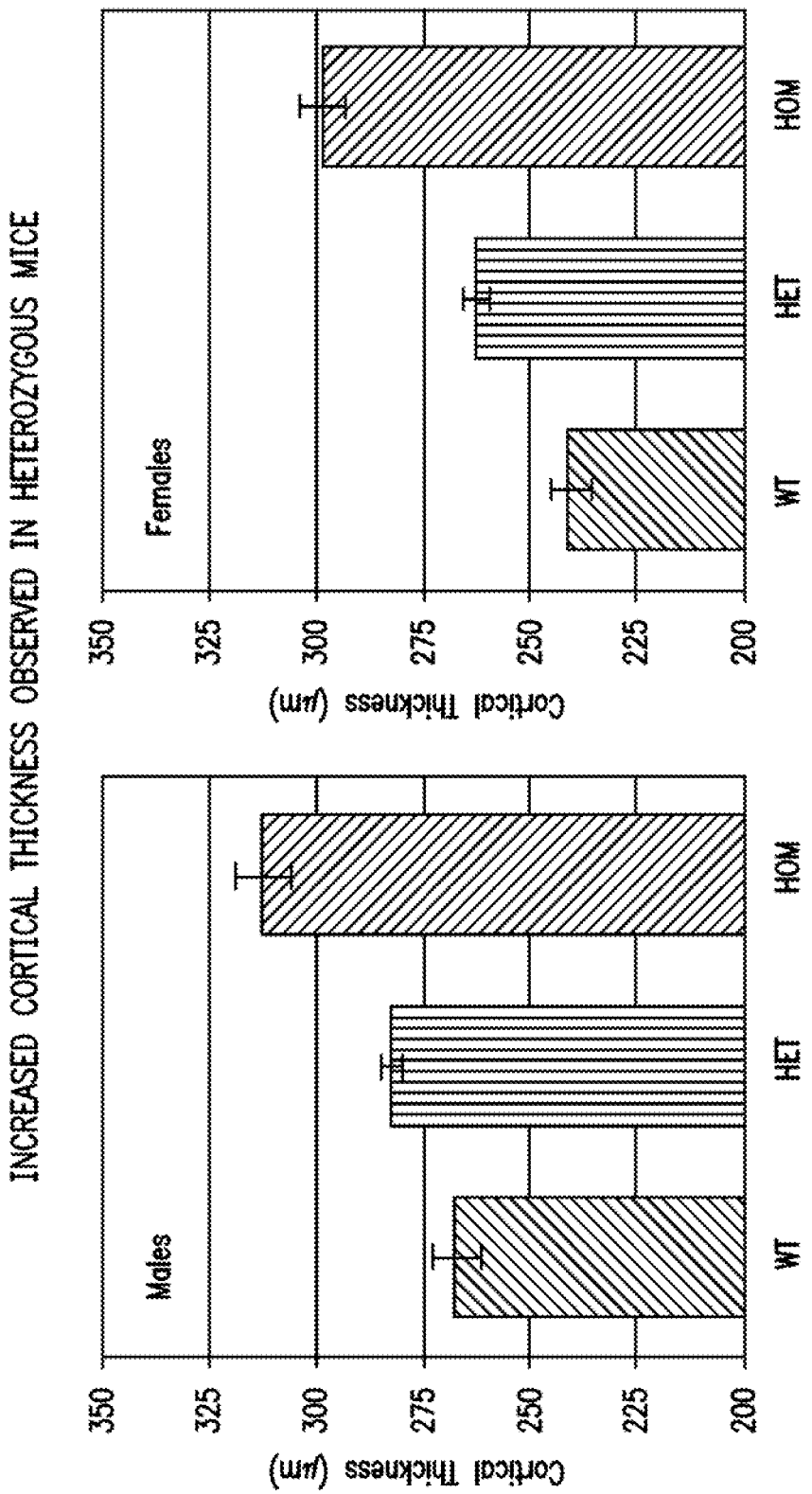

INCREASED CORTICAL THICKNESS OBSERVED IN HETEROZYGOUS MICE
Males
Females
Cortical Thickness (μm)
350
325
300
275
250
225
200
WT
HET
HOM

FIG. 2

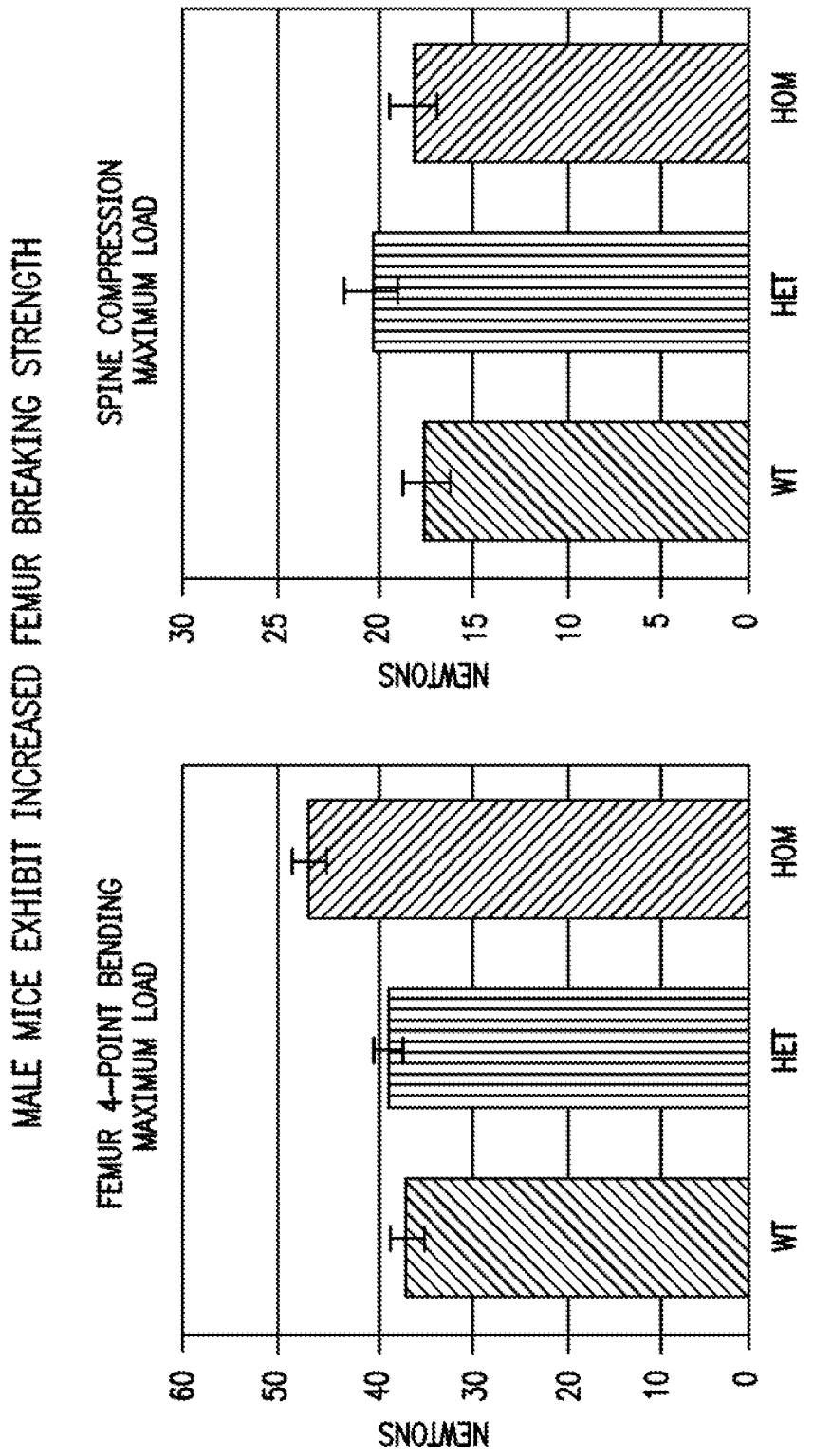

MALE MICE EXHIBIT INCREASED FEMUR BREAKING STRENGTH
FEMUR 4-POINT BENDING
MAXIMUM LOAD
NEWTONS
60
50
40
30
20
10
0
WT
HET
HOM
SPINE COMPRESSION
MAXIMUM LOAD
NEWTONS
30
25
20
15
10
5
0
WT
HET
HOM

FIG. 3

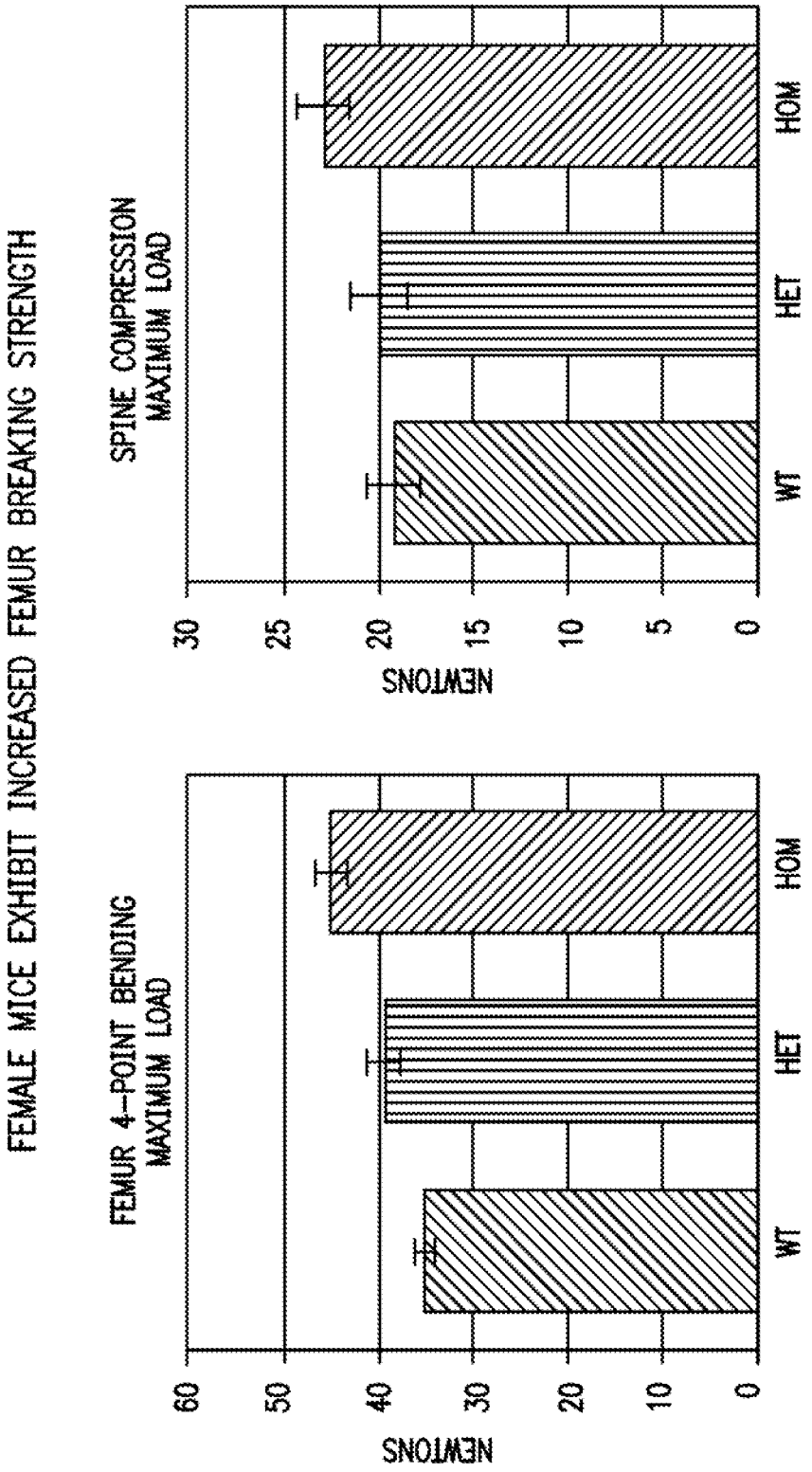

FEMALE MICE EXHIBIT INCREASED FEMUR BREAKING STRENGTH
FEMUR 4-POINT BENDING
MAXIMUM LOAD
NEWTONS
60
50
40
30
20
10
0
WT
HET
HOM
SPINE COMPRESSION
MAXIMUM LOAD
NEWTONS
30
25
20
15
10
5
0
WT
HET
HOM

FIG. 4

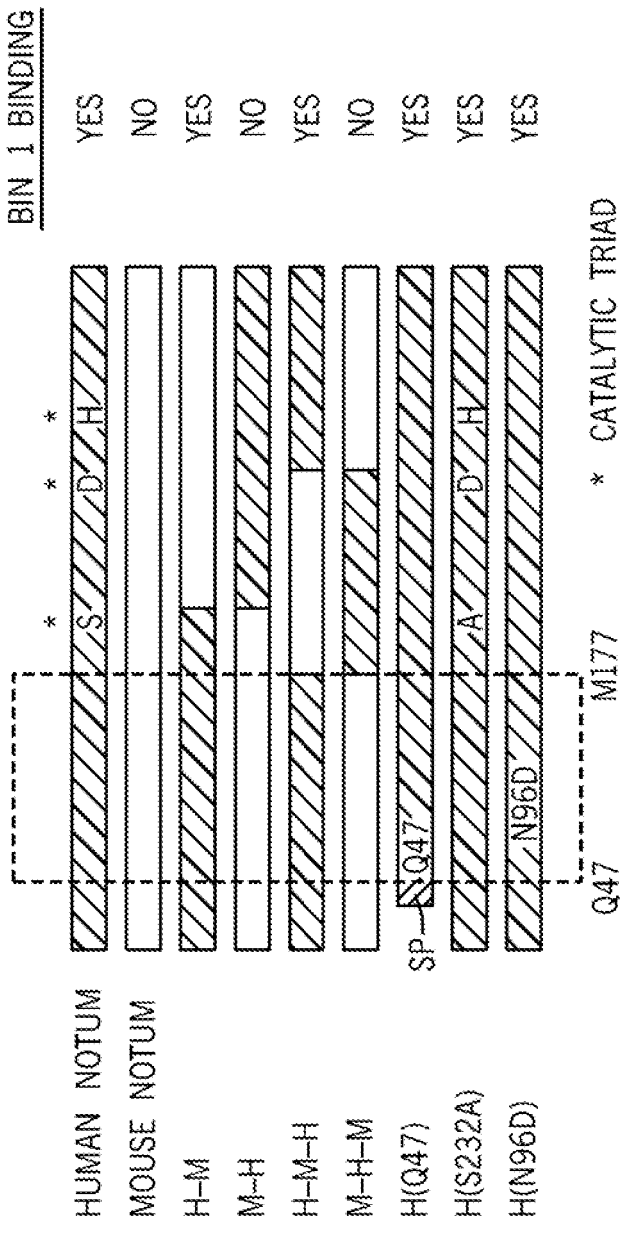

BIN 1 BINDING
HUMAN NOTUM
MOUSE NOTUM
H–M
M–H
H–M–H
M–H–M
H(Q47)
H(S232A)
H(N96D)
YES
NO
YES
NO
YES
NO
YES
YES
YES
SP
Q47
M177
* CATALYTIC TRIAD

FIG. 5

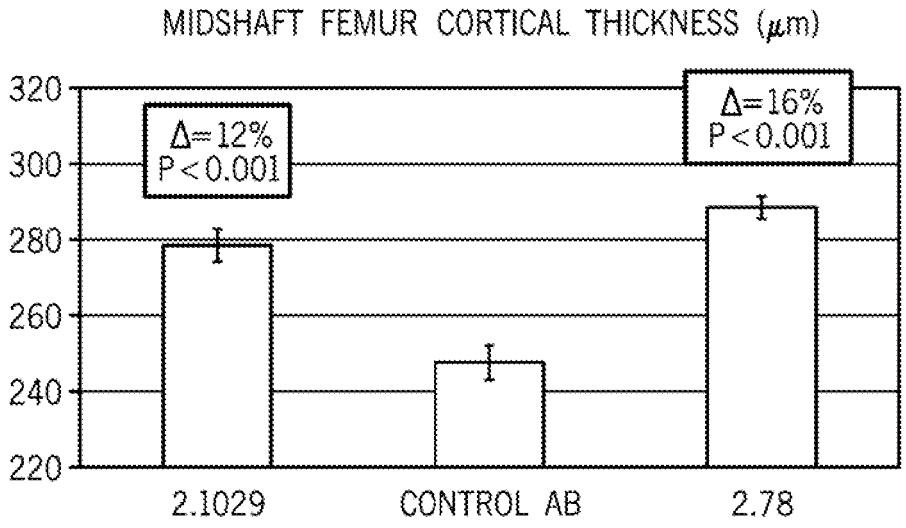

MIDSHAFT FEMUR CORTICAL THICKNESS (μm)
320
300
280
260
240
220
Δ=12%
P<0.001
Δ=16%
P<0.001
2.1029
CONTROL AB
2.78

FIG. 6

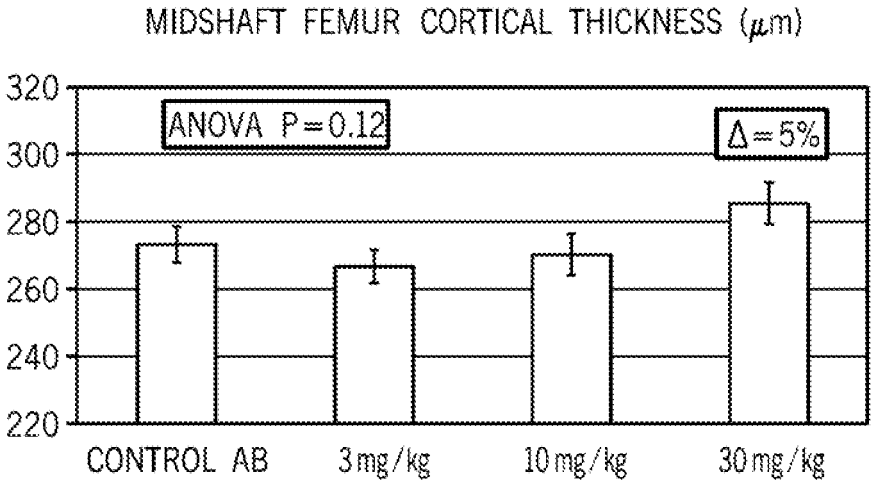

MIDSHAFT FEMUR CORTICAL THICKNESS (μm)
320
300
280
260
240
220
ANOVA P=0.12
Δ=5%
CONTROL AB
3mg/kg
10mg/kg
30mg/kg

FIG. 7

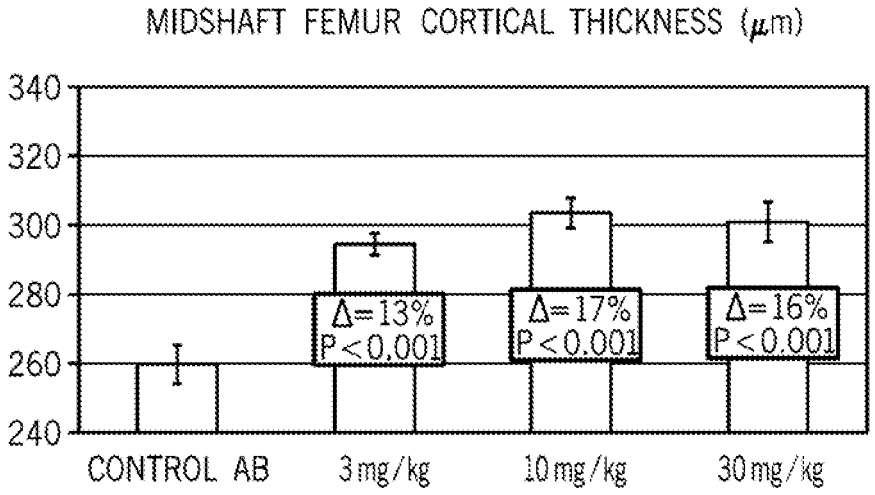

MIDSHAFT FEMUR CORTICAL THICKNESS (μm)
340
320
300
280
260
240
Δ=13%
P<0.001
Δ=17%
P<0.001
Δ=16%
P<0.001
CONTROL AB
3mg/kg
10mg/kg
30mg/kg

FIG. 8A

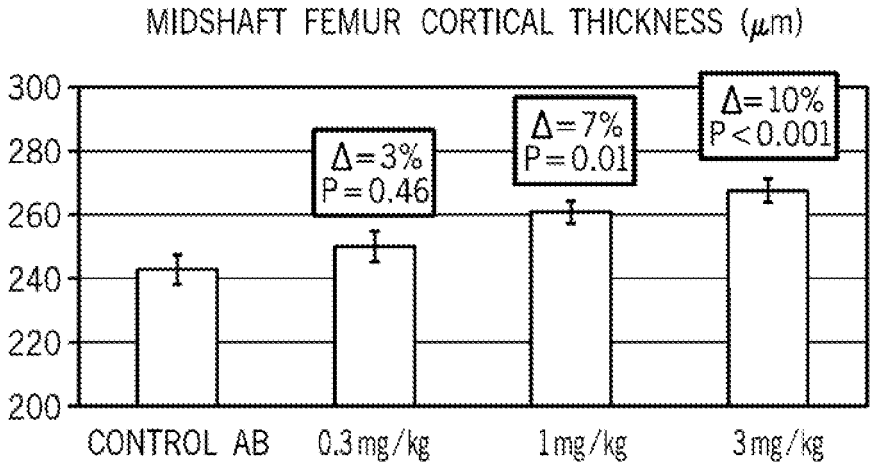

MIDSHAFT FEMUR CORTICAL THICKNESS (μm)
300
280
260
240
220
200
Δ=3%
P=0.46
Δ=7%
P=0.01
Δ=10%
P<0.001
CONTROL AB
0.3mg/kg
1mg/kg
3mg/kg

FIG. 8B

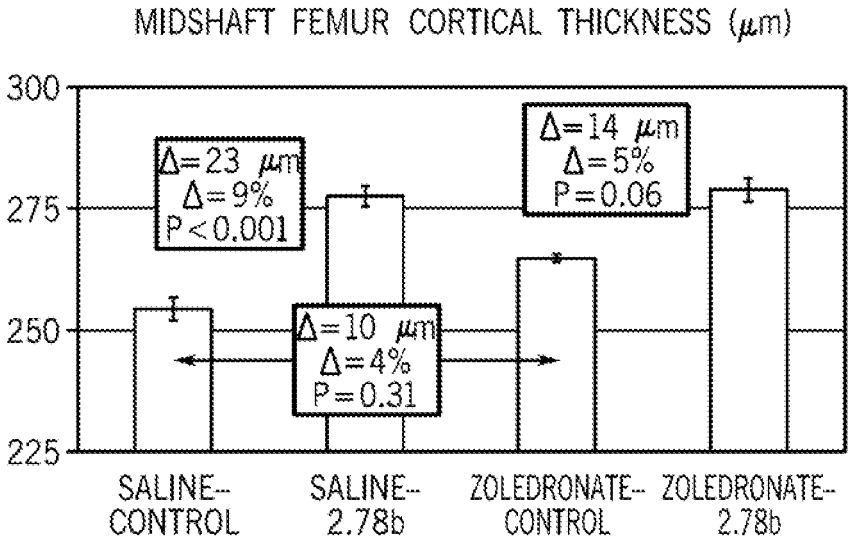

MIDSHAFT FEMUR CORTICAL THICKNESS (μm)
300
275
250
225
Δ=23 μm
Δ=9%
P<0.001
Δ=10 μm
Δ=4%
P=0.31
Δ=14 μm
Δ=5%
P=0.06
SALINE-- CONTROL
SALINE-- 2.78b
ZOLEDRONATE-- CONTROL
ZOLEDRONATE-- 2.78b

FIG. 9A

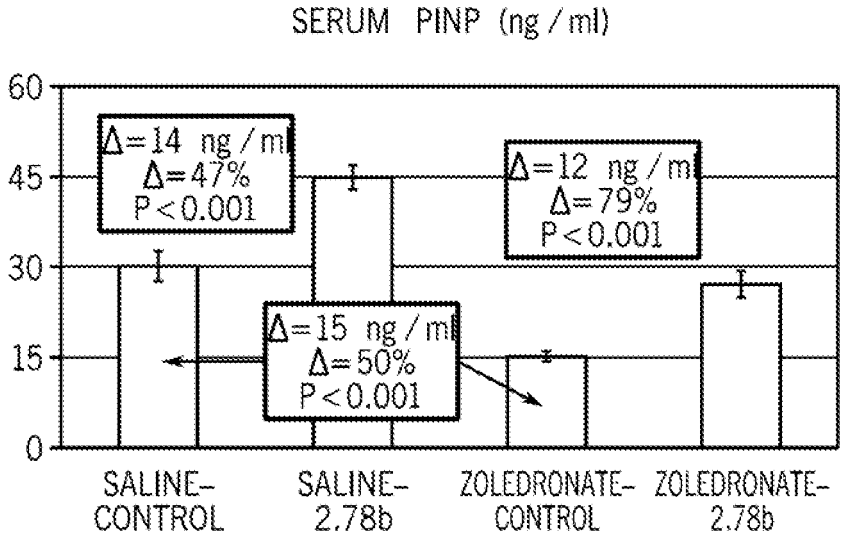

SERUM PINP (ng / ml)
60
45
30
15
0
Δ=14 ng / ml
Δ=47%
P<0.001
Δ=15 ng / ml
Δ=50%
P<0.001
Δ=12 ng / ml
Δ=79%
P<0.001
SALINE- CONTROL
SALINE- 2.78b
ZOLEDRONATE- CONTROL
ZOLEDRONATE- 2.78b

FIG. 9B

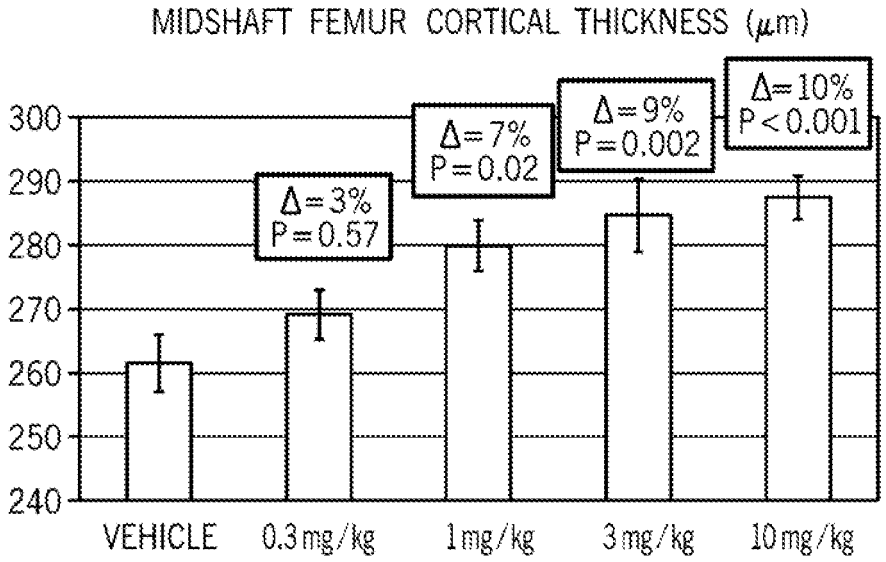


FIG. 10

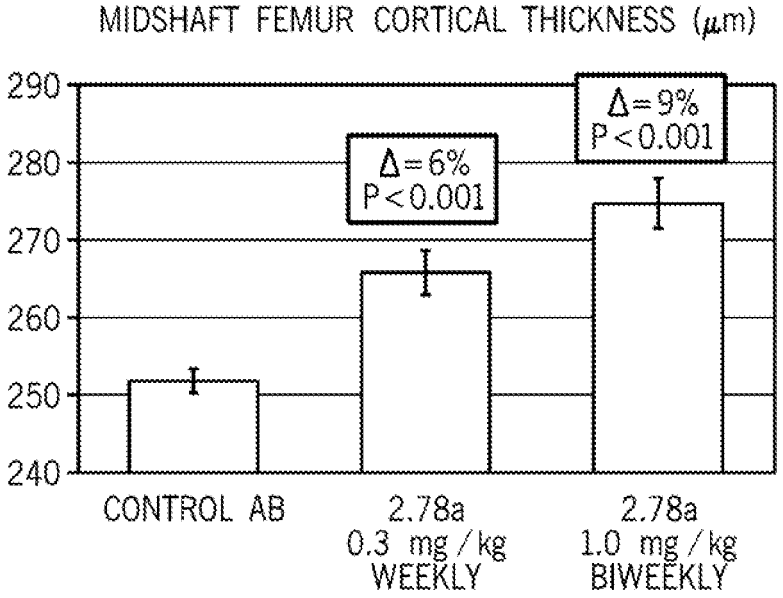


FIG. 11A

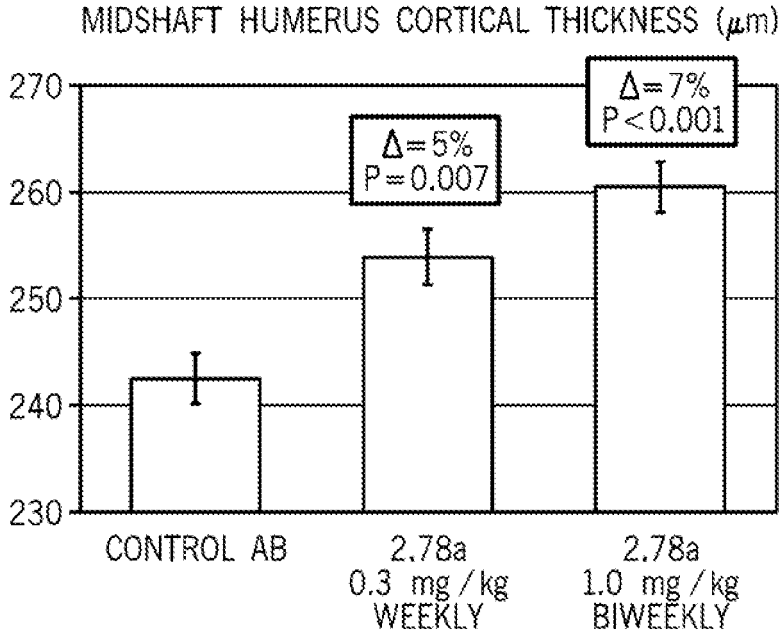


FIG. 11B

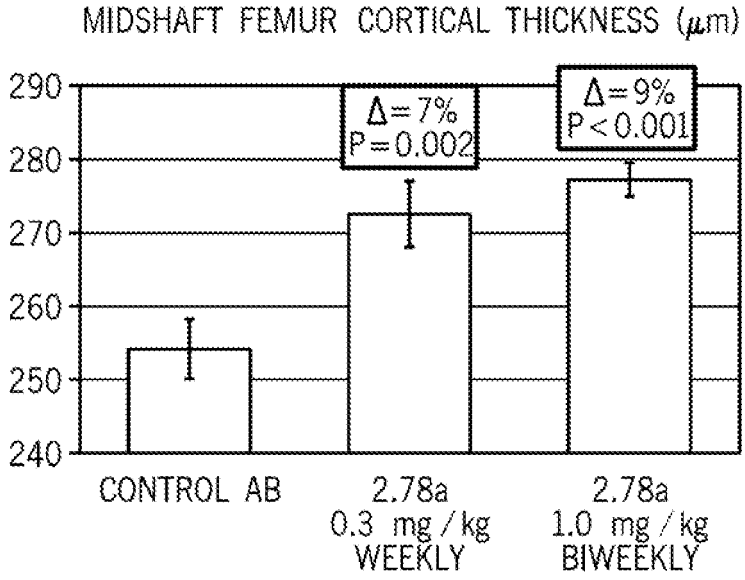


FIG. 12A

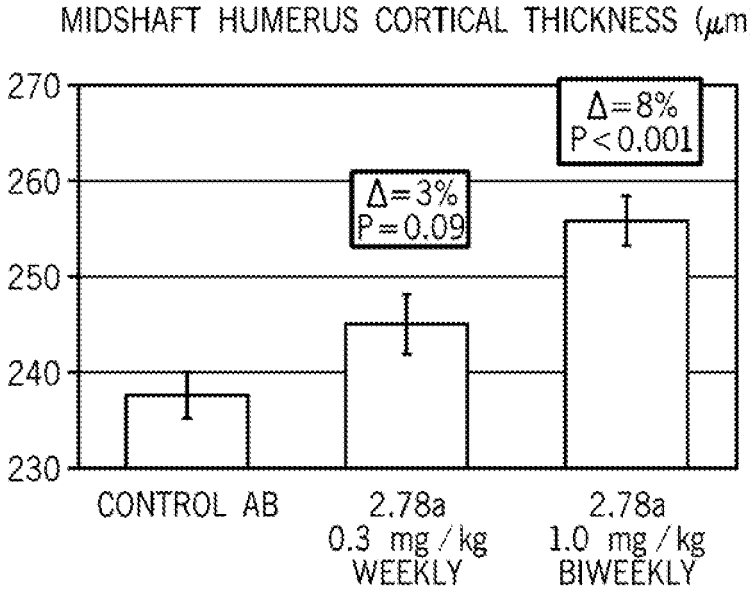


FIG. 12B

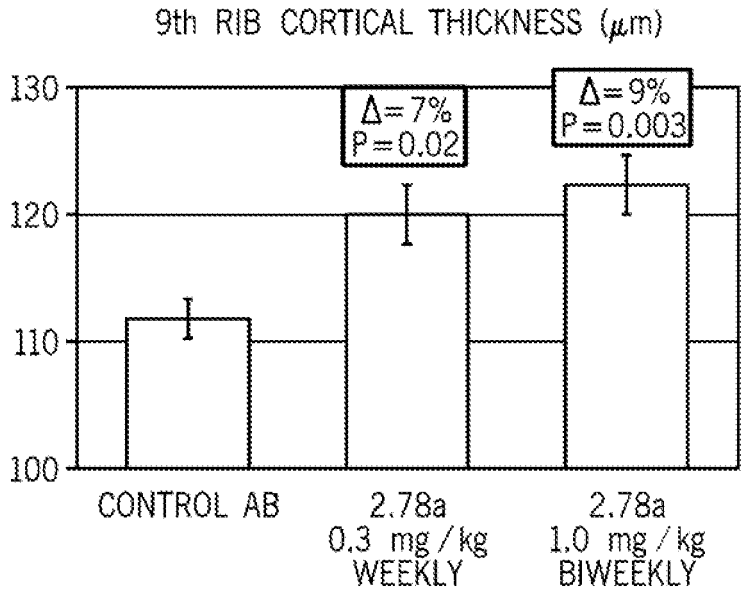


FIG. 12C

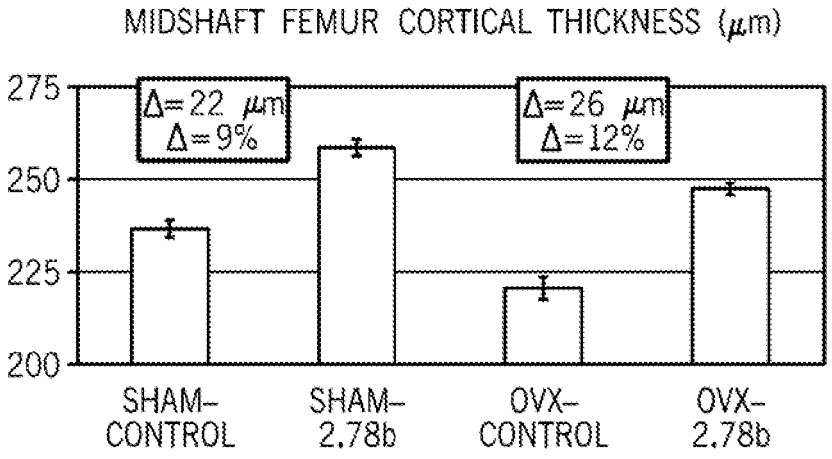


FIG. 13A

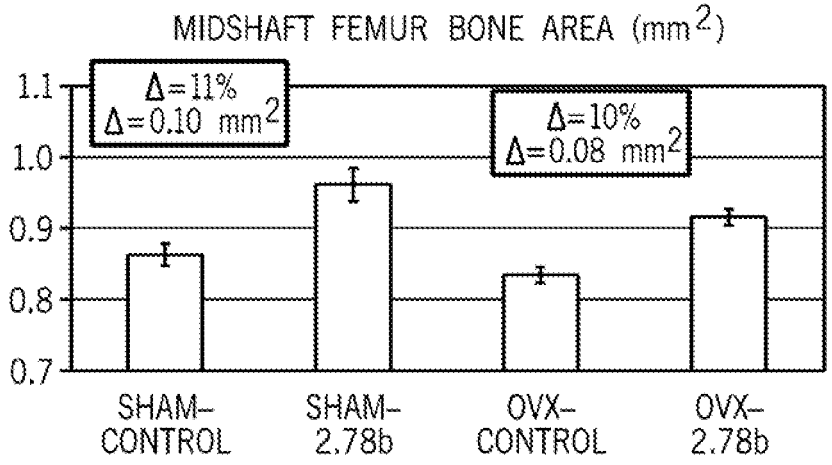


FIG. 13B

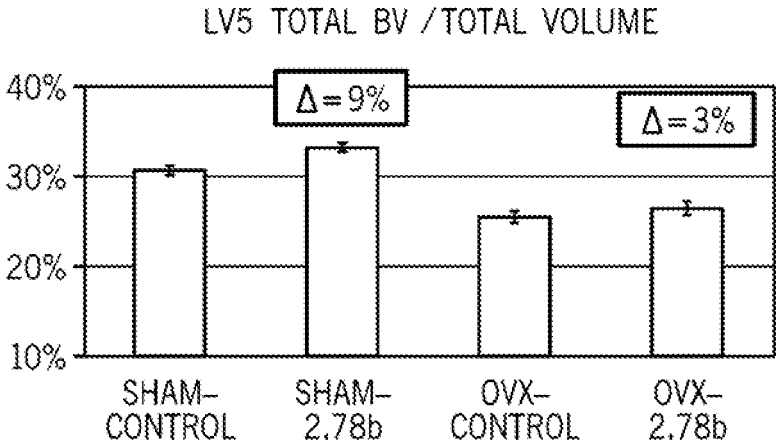


FIG. 14A

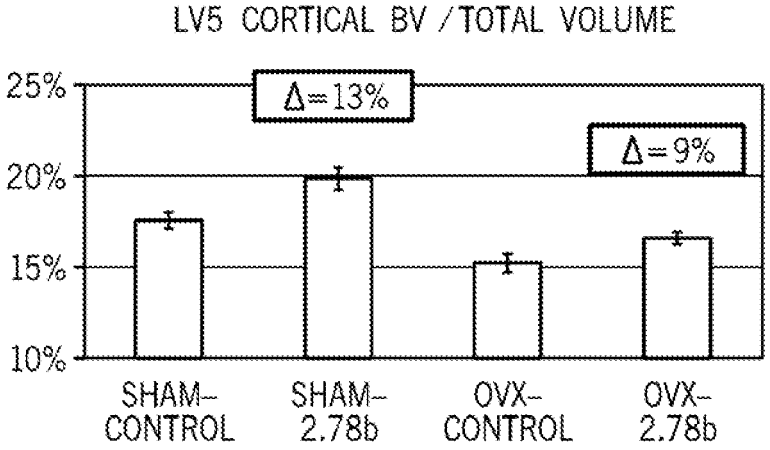


FIG. 14B

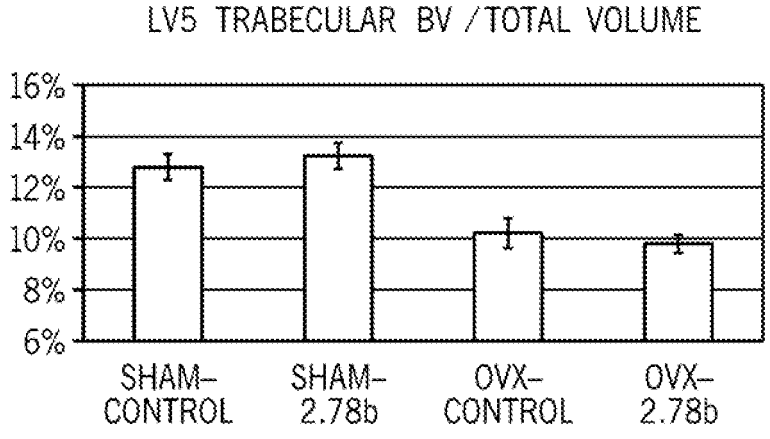


FIG. 14C

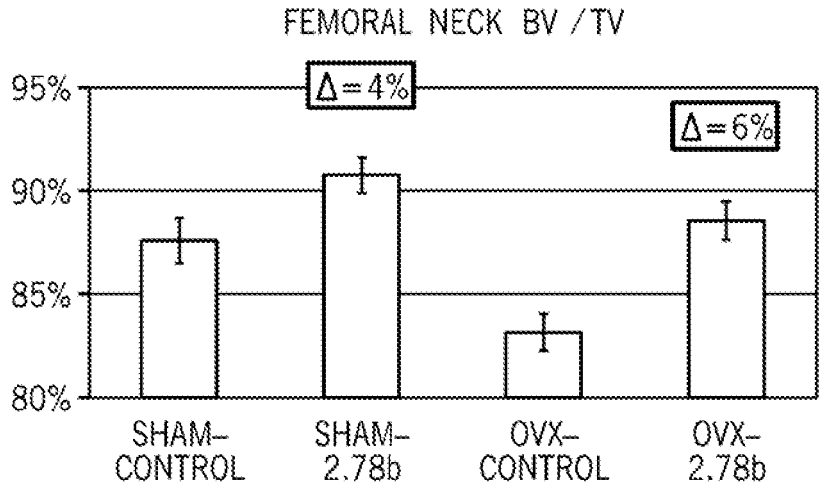

FEMORAL NECK BV / TV
95%
90%
85%
80%
Δ=4%
Δ=6%
SHAM–
CONTROL
SHAM–
2.78b
OVX–
CONTROL
OVX–
2.78b

FIG. 15

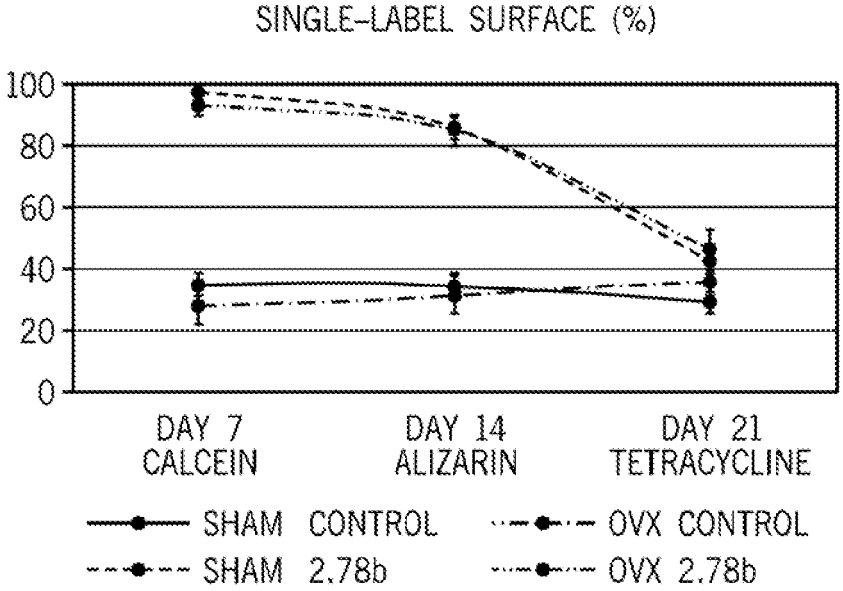

SINGLE-LABEL SURFACE (%)
100
80
60
40
20
0
DAY 7
CALCEIN
DAY 14
ALIZARIN
DAY 21
TETRACYCLINE
SHAM CONTROL
OVX CONTROL
SHAM 2.78b
OVX 2.78b

FIG. 16

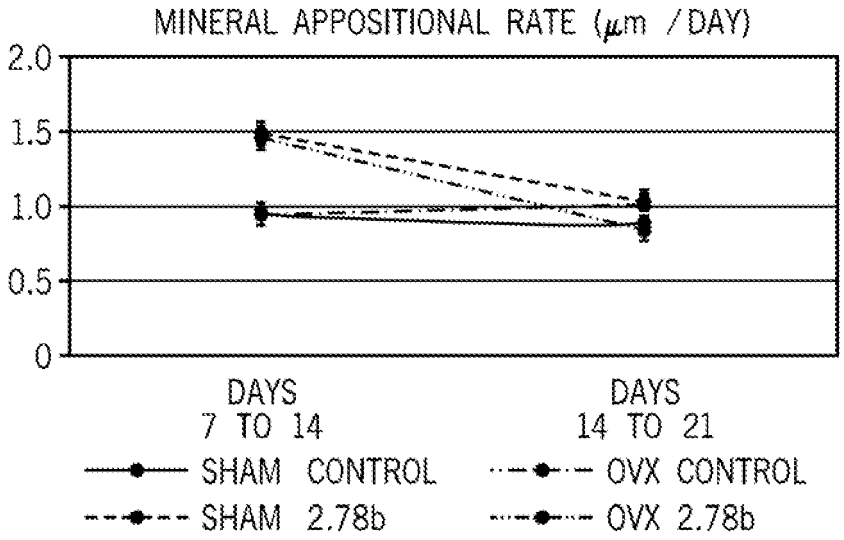


FIG. 17A

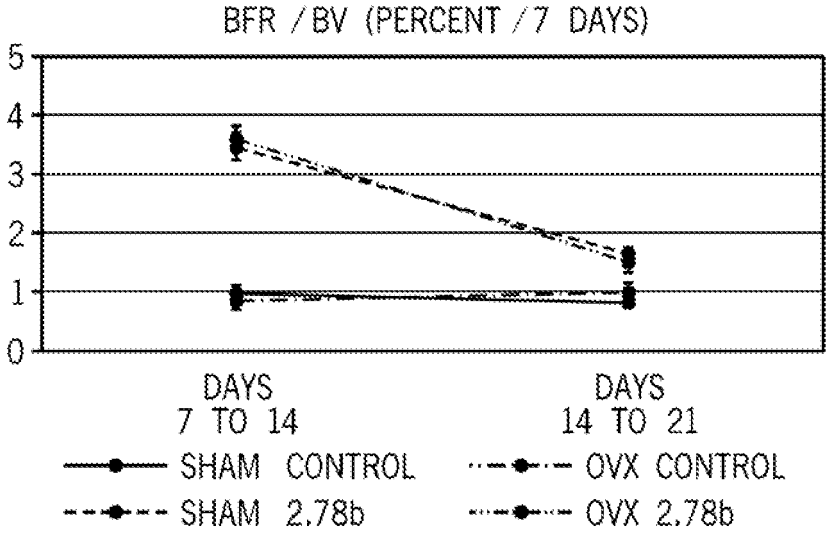


FIG. 17B