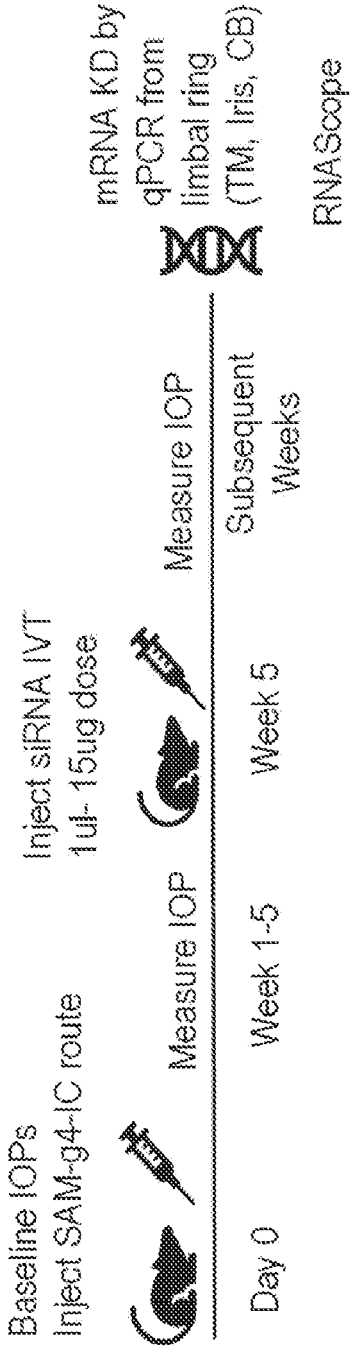

Baseline IOPs
Inject SAM-g4-IC route
Measure IOP
Week 1-5
Inject siRNA IVT
1ul- 15ug dose
Week 5
Measure IOP
Subsequent
Weeks
mRNA KD by
qPCR from
limbal ring
(TM, Iris, CB)
RNAScope
Day 0

FIGURE 1A

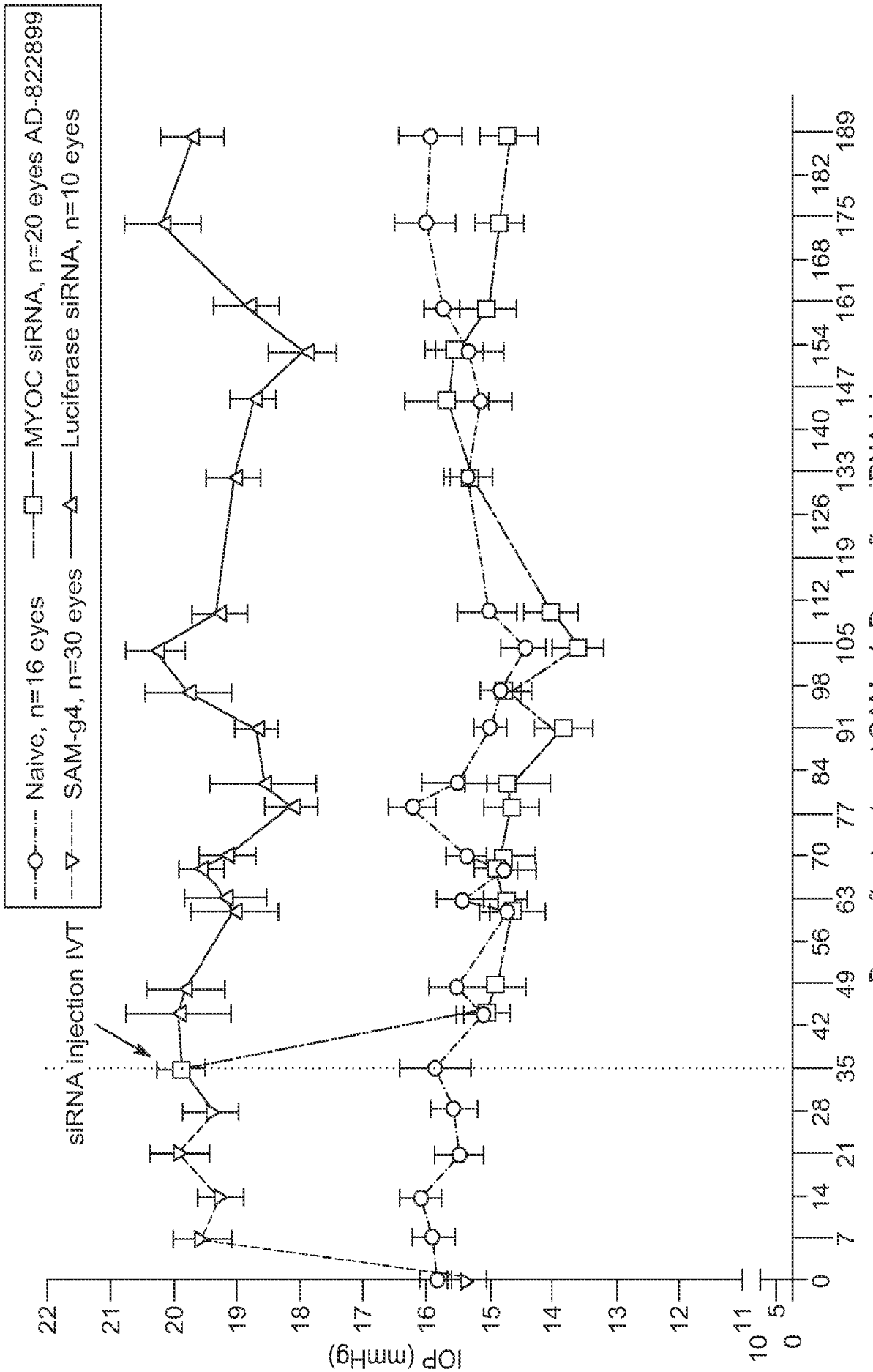

Naive, n=16 eyes
MYOC siRNA, n=20 eyes AD-822899
SAM-g4, n=30 eyes
Luciferase siRNA, n=10 eyes
siRNA injection IVT
IOP (mmHg)
Days after treatment SAM-g4; Days after siRNA inj

FIGURE. 1B

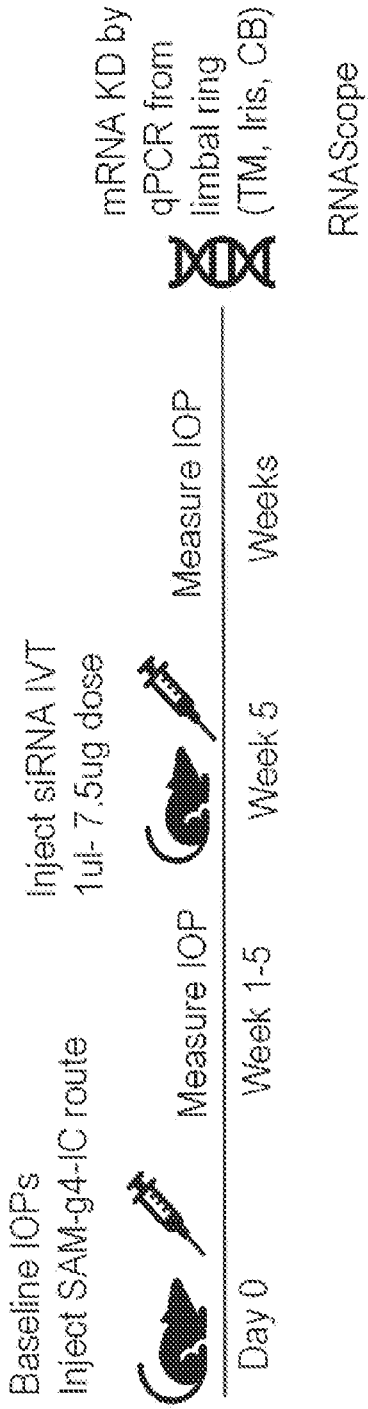

Baseline IOPs
Inject SAM-g4-IC route
Inject siRNA IVT
1ul- 7.5ug dose
mRNA KD by
qPCR from
limbal ring
(TM, Iris, CB)
Measure IOP
Measure IOP
RNAScope
Day 0
Week 1-5
Week 5
Weeks

FIGURE 2A

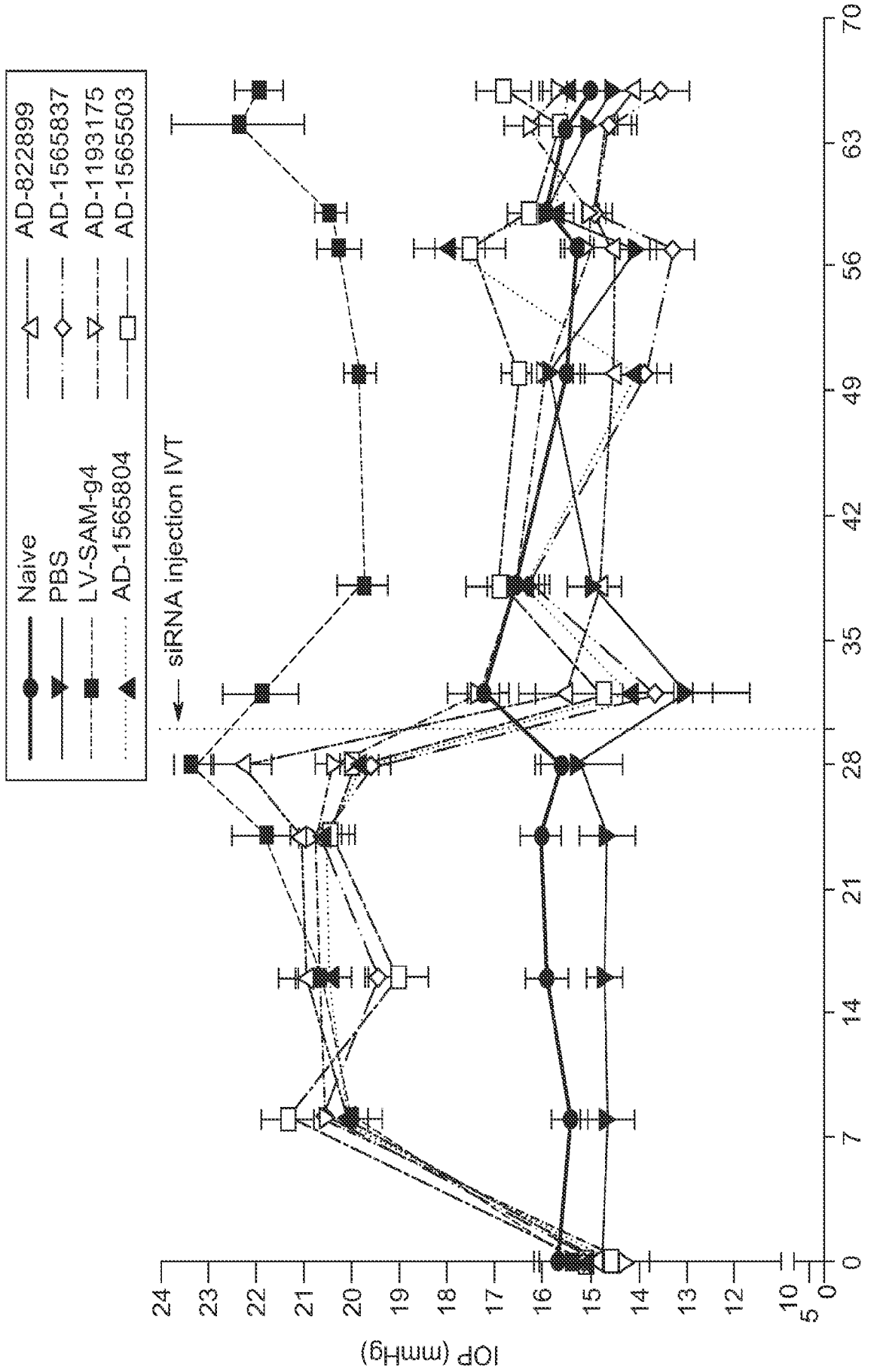

Naive
PBS
LV-SAM-g4
AD-1565804
AD-822899
AD-1565837
AD-1193175
AD-1565503
siRNA injection IVT
IOP (mmHg)
Days after treatment SAM-g4; Days after siRNA inj

FIGURE. 2B

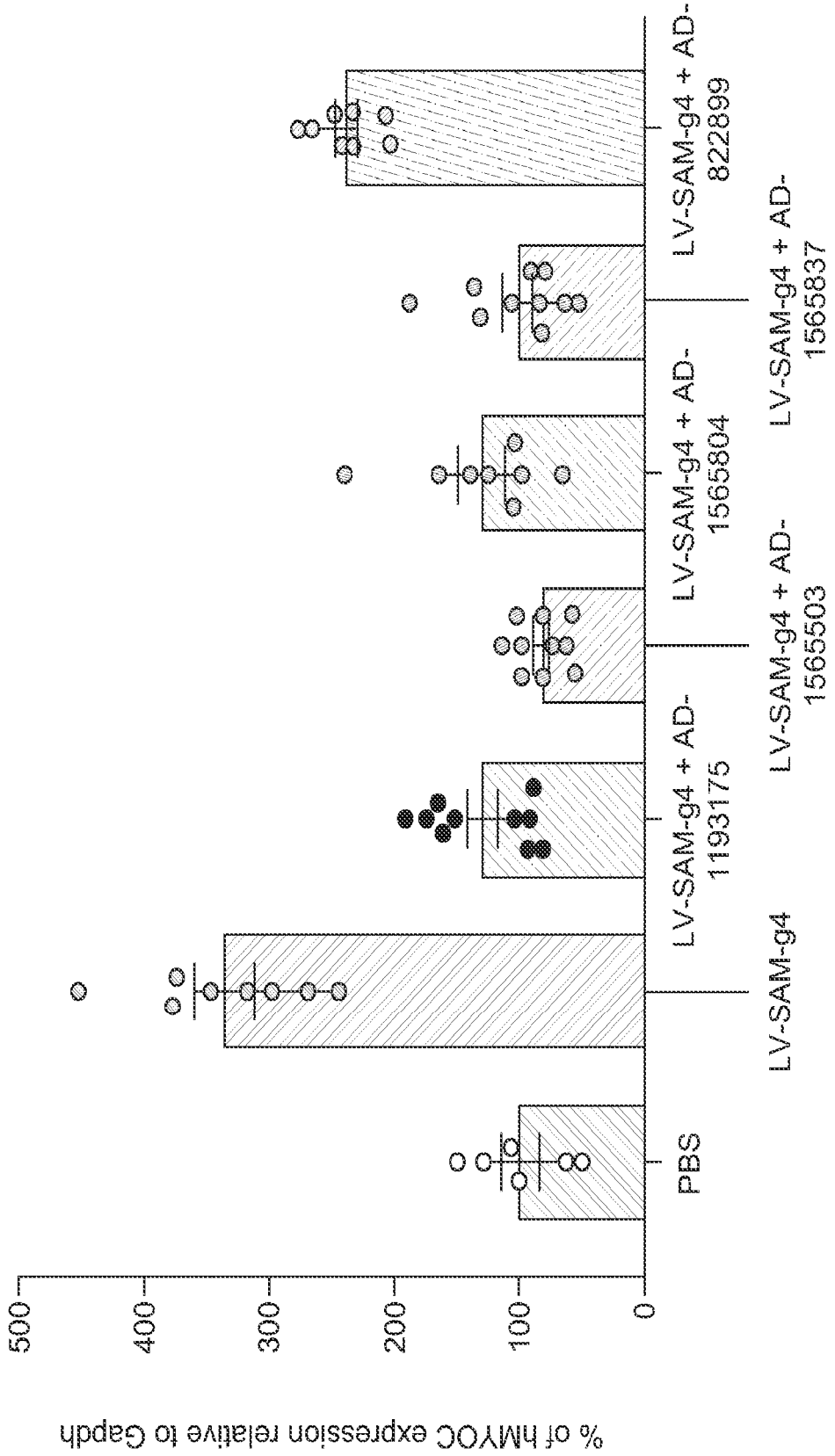

% of hMYOC expression relative to Gapdh
500
400
300
200
100
0
PBS
LV-SAM-g4
LV-SAM-g4 + AD-1193175
LV-SAM-g4 + AD-1565503
LV-SAM-g4 + AD-1565804
LV-SAM-g4 + AD-1565837
LV-SAM-g4 + AD-822899

FIGURE. 2C

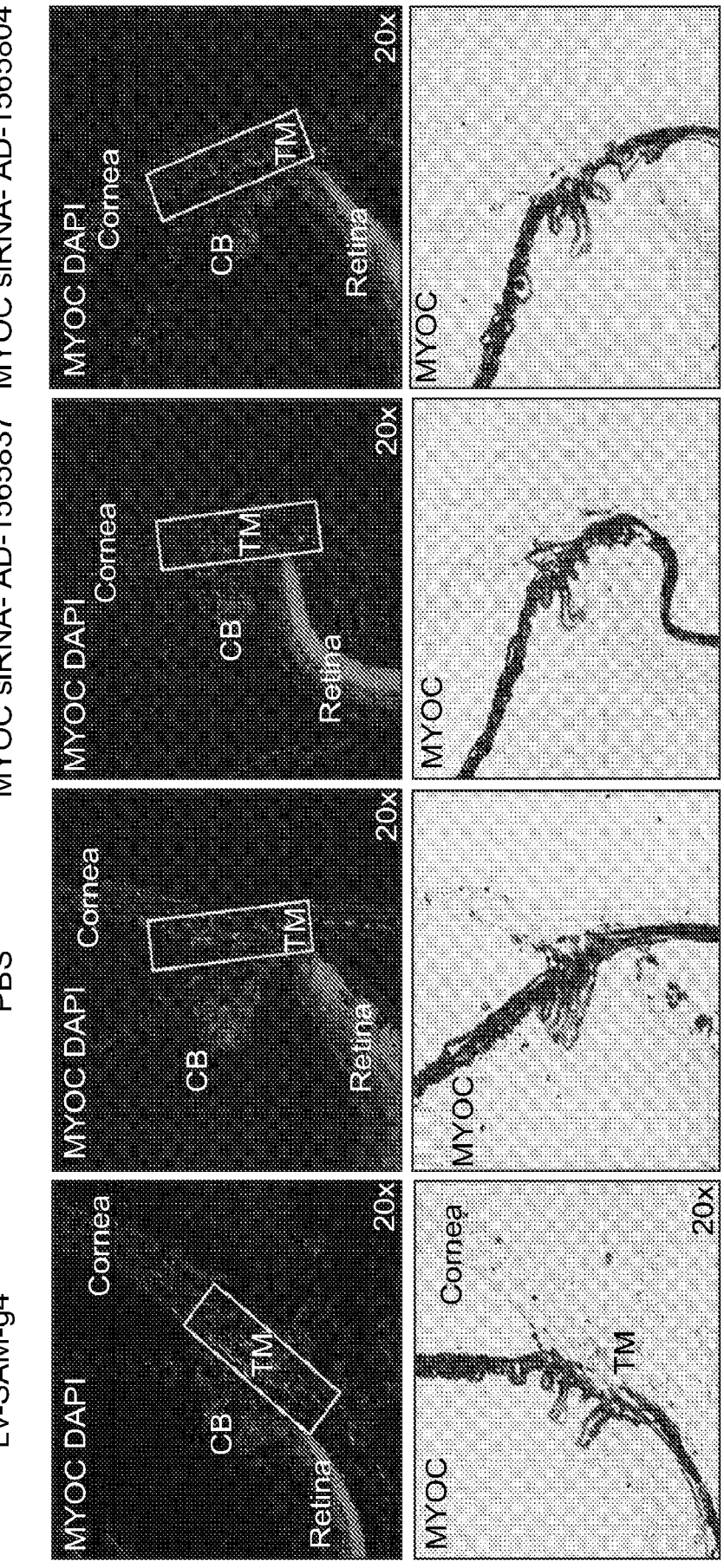

Lv-SAM-g4
PBS
MYOC siRNA- AD-1565837
MYOC siRNA- AD-1565804
MYOC DAPI
Cornea
CB
TM
Retina
20x
MYOC

FIGURE. 2D

Baseline IOPs
Inject SAM-g4-IC route
Inject siRNA IVT
1ul- 3.75ug, 1.87ug dose
Measure IOP
Measure IOP
mRNA KD by
qPCR from
limbal ring
(TM, Iris, CB)
RNAScope
Day 0
Week 1-5
Week 5
Weeks

FIGURE 3A

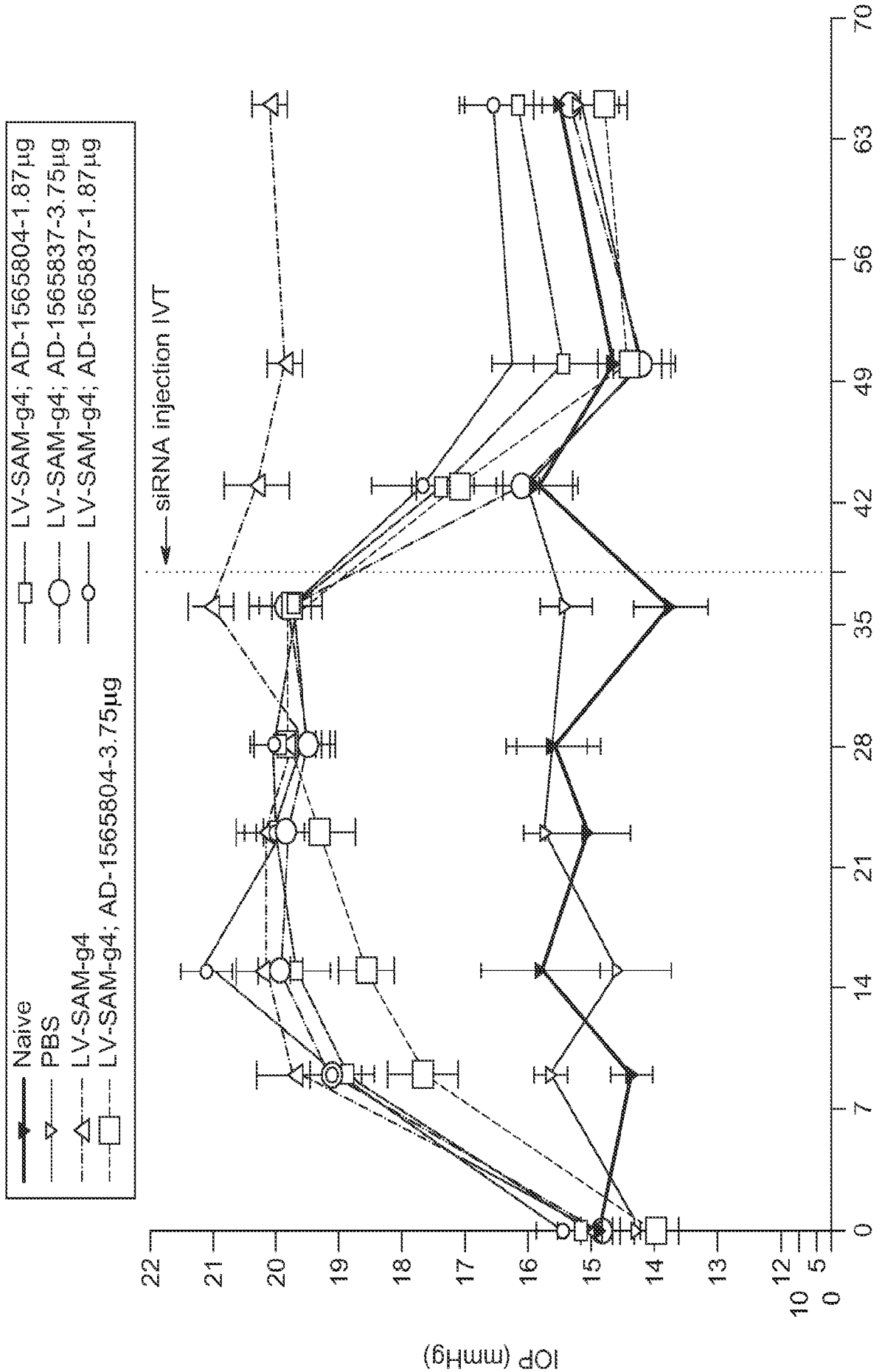

Naive
PBS
LV-SAM-g4
LV-SAM-g4; AD-1565804-3.75µg
LV-SAM-g4; AD-1565804-1.87µg
LV-SAM-g4; AD-1565837-3.75µg
LV-SAM-g4; AD-1565837-1.87µg
siRNA injection IVT
IOP (mmHg)
Days after treatment
0
7
14
21
28
35
42
49
56
63
70
22
21
20
19
18
17
16
15
14
13
12
10
5
0

FIGURE. 3B

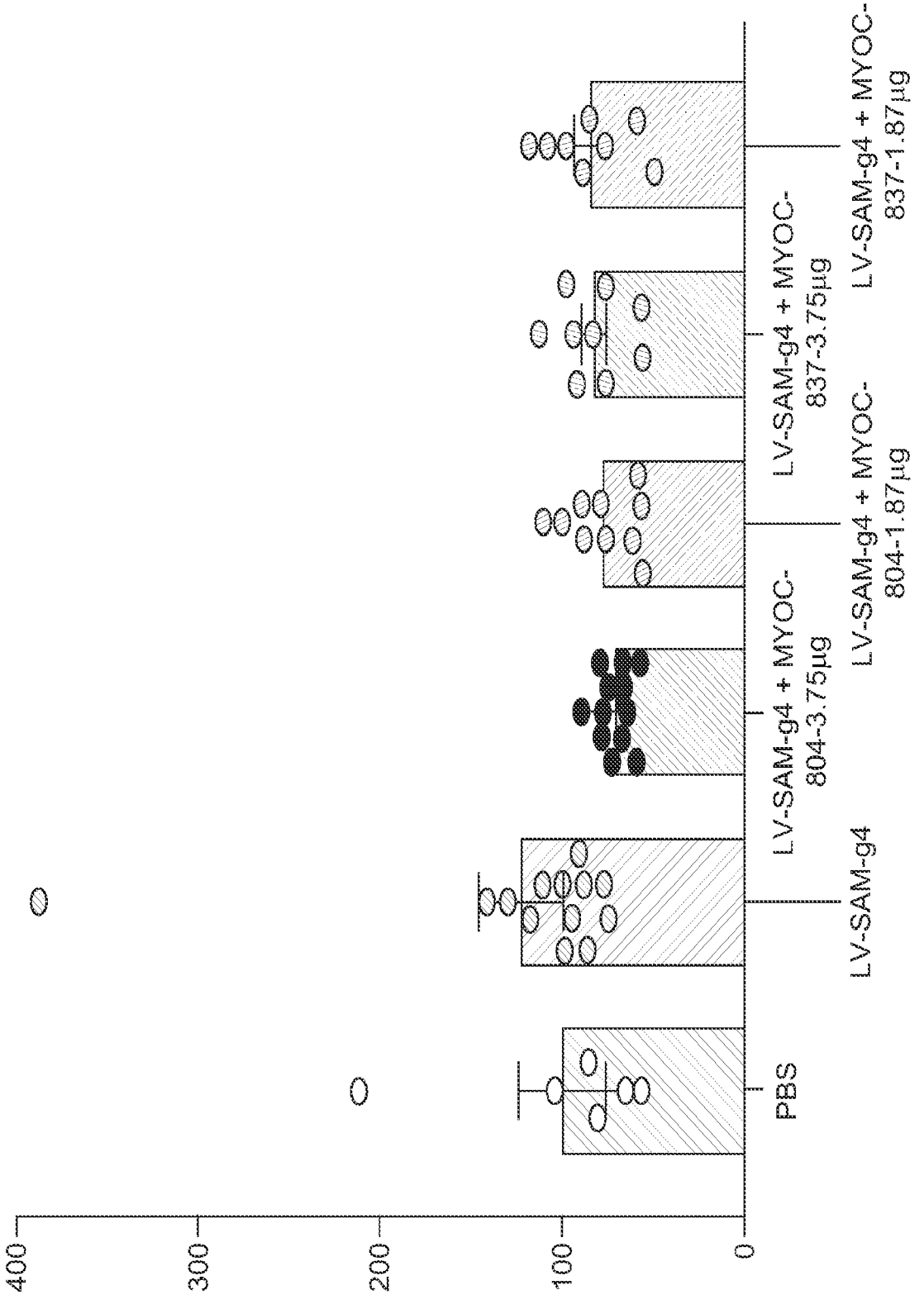

% of hMYOC expression relative to Gapdh
400
300
200
100
0
PBS
LV-SAM-g4
LV-SAM-g4 + MYOC-804-3.75µg
LV-SAM-g4 + MYOC-804-1.87µg
LV-SAM-g4 + MYOC-837-3.75µg
LV-SAM-g4 + MYOC-837-1.87µg

FIGURE. 3C

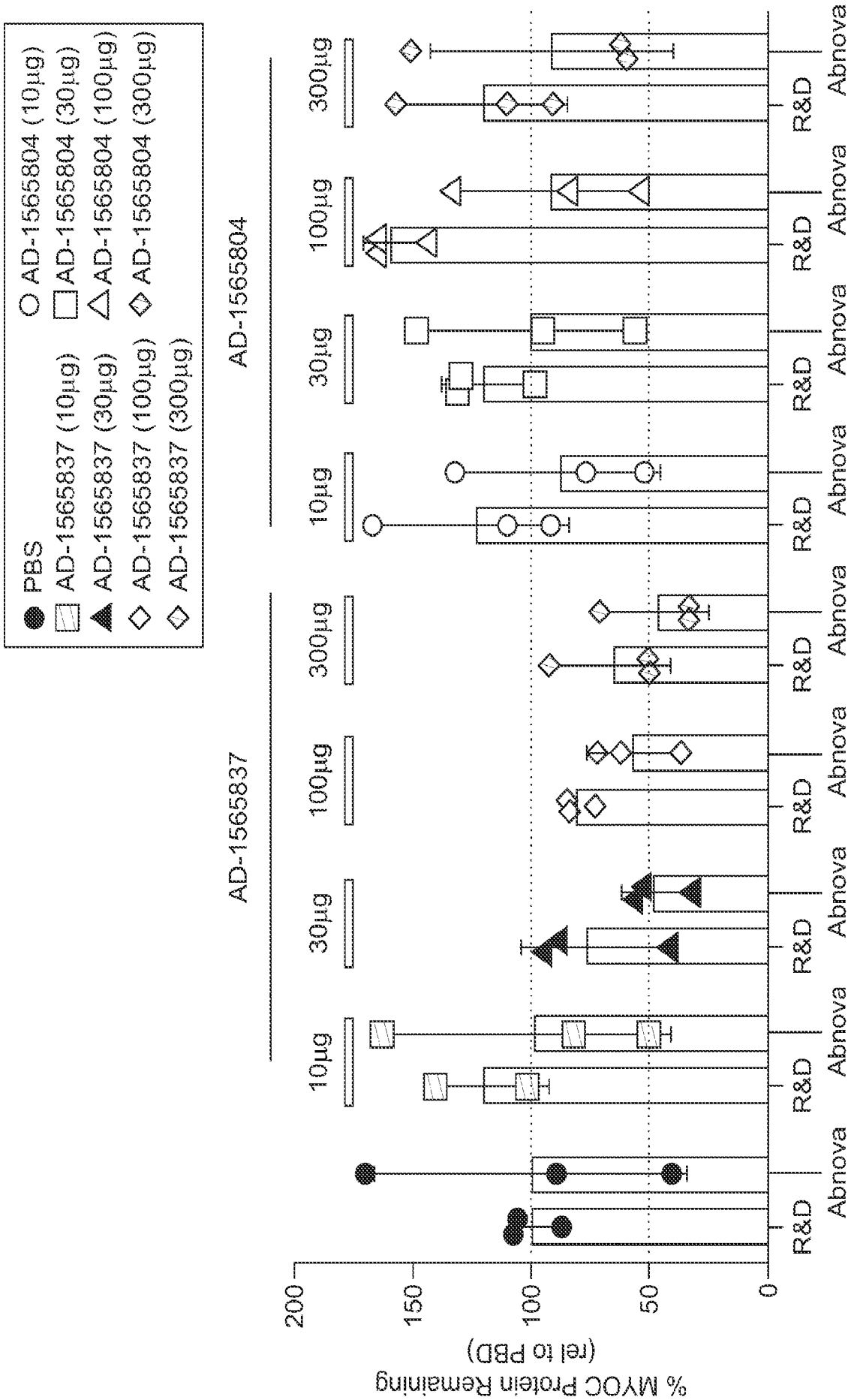

PBS
AD-1565837 (10µg)
AD-1565837 (30µg)
AD-1565837 (100µg)
AD-1565837 (300µg)
AD-1565804 (10µg)
AD-1565804 (30µg)
AD-1565804 (100µg)
AD-1565804 (300µg)
AD-1565837
AD-1565804
10µg
30µg
100µg
300µg
R&D
Abnova
% MYOC Protein Remaining
(rel to PBD)
200
150
100
50
0

FIGURE. 4

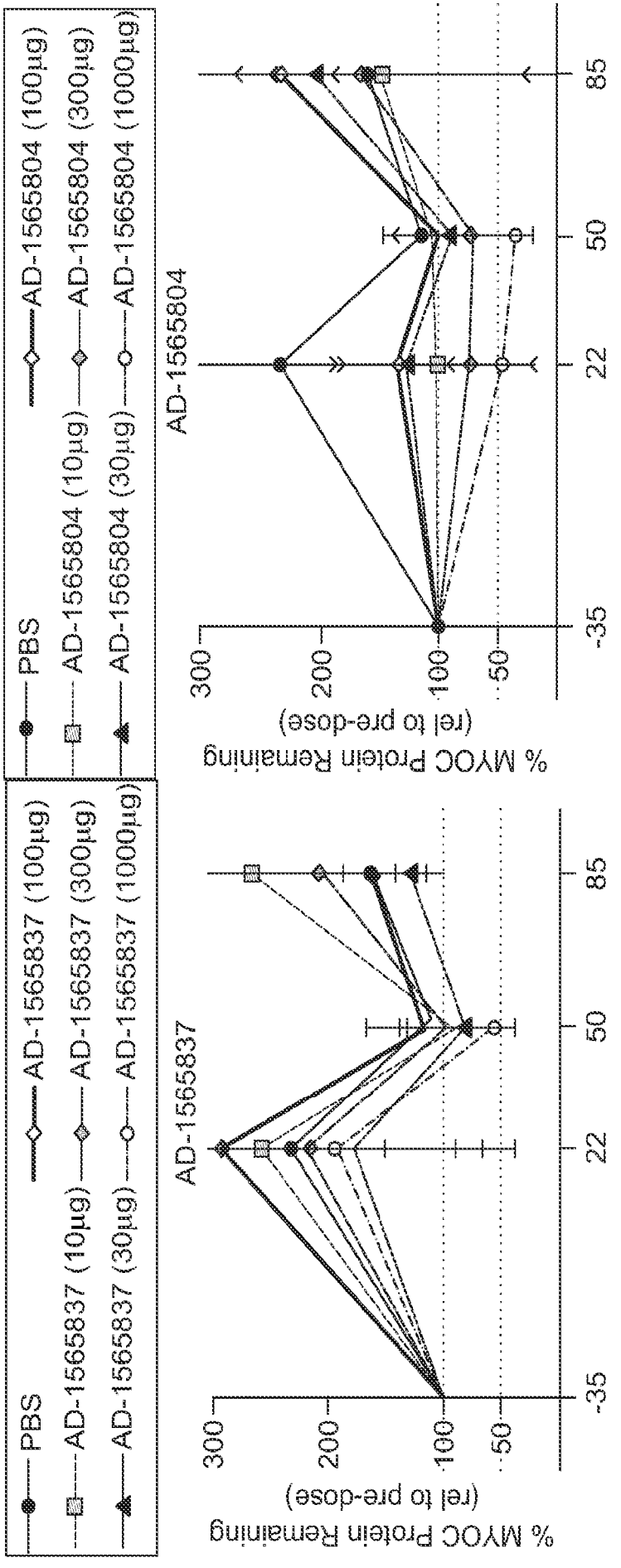

PBS
AD-1565837 (100µg)
AD-1565837 (10µg)
AD-1565837 (300µg)
AD-1565837 (30µg)
AD-1565837 (1000µg)
AD-1565804 (100µg)
AD-1565804 (10µg)
AD-1565804 (300µg)
AD-1565804 (30µg)
AD-1565804 (1000µg)
AD-1565837
AD-1565804
% MYOC Protein Remaining (rel to pre-dose)
300
200
100
50
-35
22
50
85
Timepoint (days)
Abnova RbPAb + Abnova Ms PAb

FIGURE. 5

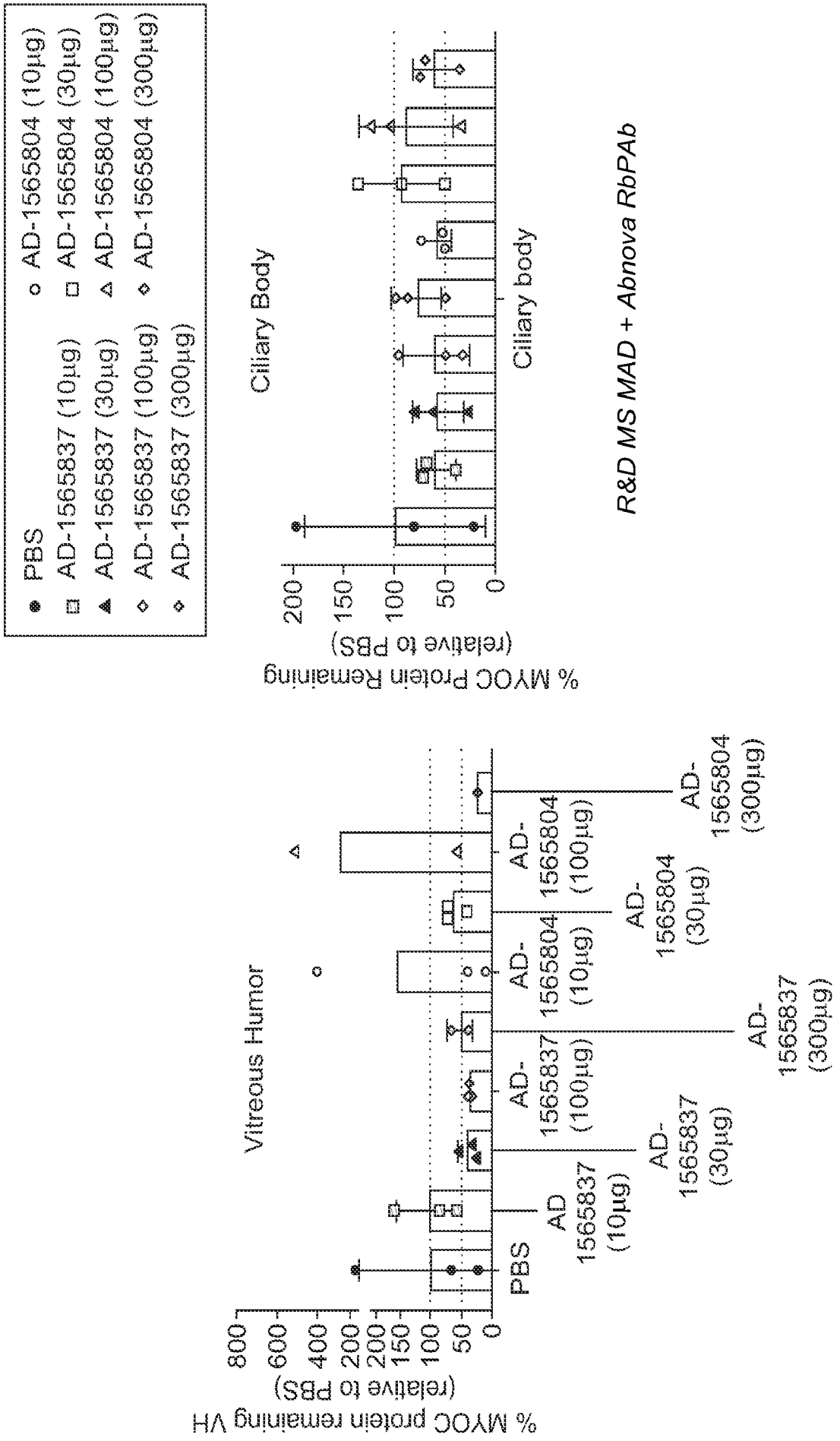

PBS
AD-1565837 (10µg)
AD-1565837 (30µg)
AD-1565837 (100µg)
AD-1565837 (300µg)
AD-1565804 (10µg)
AD-1565804 (30µg)
AD-1565804 (100µg)
AD-1565804 (300µg)
Ciliary Body
% MYOC Protein Remaining (relative to PBS)
Ciliary body
R&D MS MAD + Abnova RbPAb
Vitreous Humor
% MYOC protein remaining VH (relative to PBS)
PBS
AD 1565837 (10µg)
AD-1565837 (30µg)
AD-1565837 (100µg)
AD-1565837 (300µg)
AD-1565804 (10µg)
AD-1565804 (30µg)
AD-1565804 (100µg)
AD-1565804 (300µg)

FIGURE. 6A

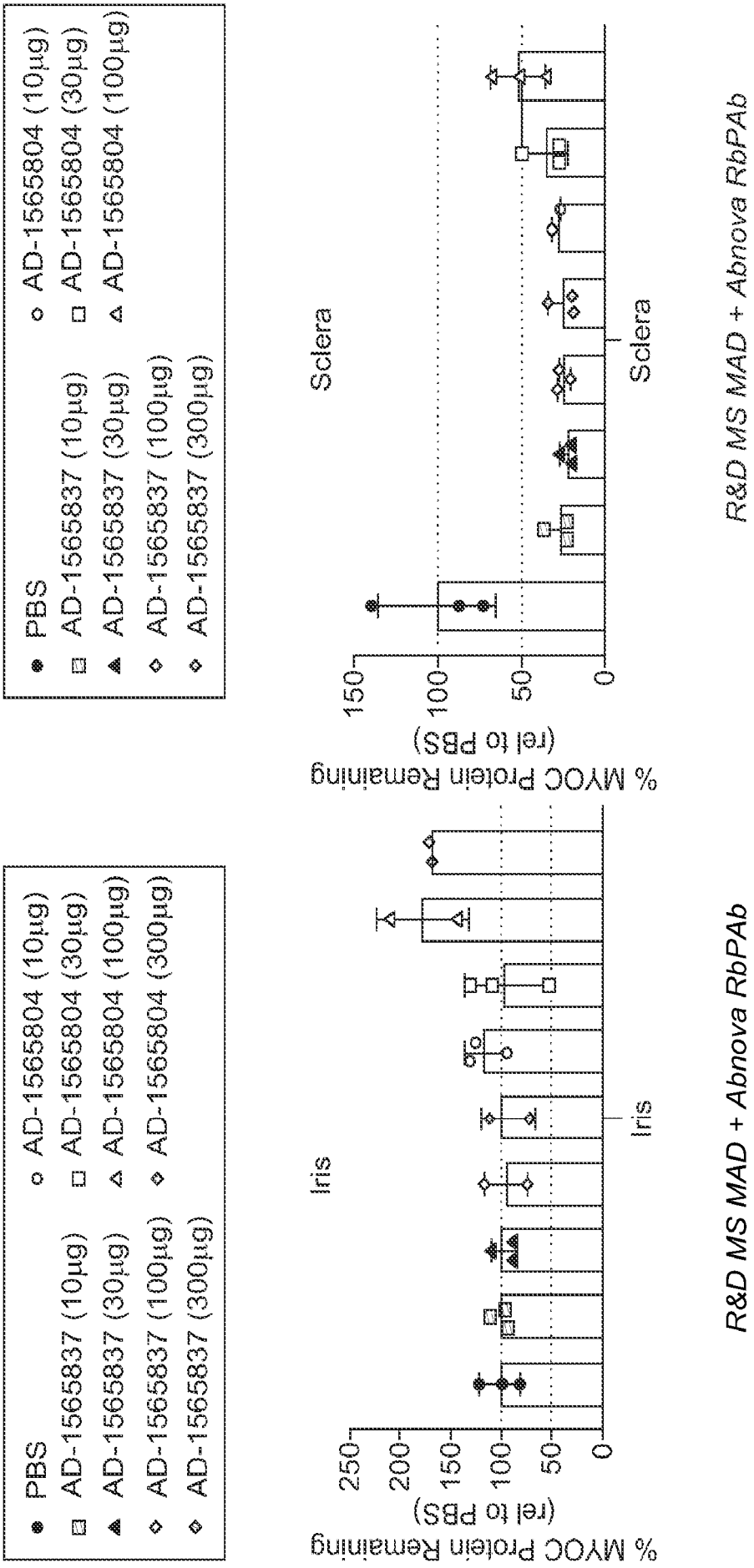

PBS
AD-1565804 (10µg)
AD-1565837 (10µg)
AD-1565804 (30µg)
AD-1565837 (30µg)
AD-1565804 (100µg)
AD-1565837 (100µg)
AD-1565804 (300µg)
AD-1565837 (300µg)
Sclera
Sclera
% MYOC Protein Remaining (rel to PBS)
150
100
50
0
Iris
Iris
% MYOC Protein Remaining (rel to PBS)
250
200
150
100
50
0
R&D MS MAD + Abnova RbPAb
R&D MS MAD + Abnova RbPAb

FIGURE. 6B

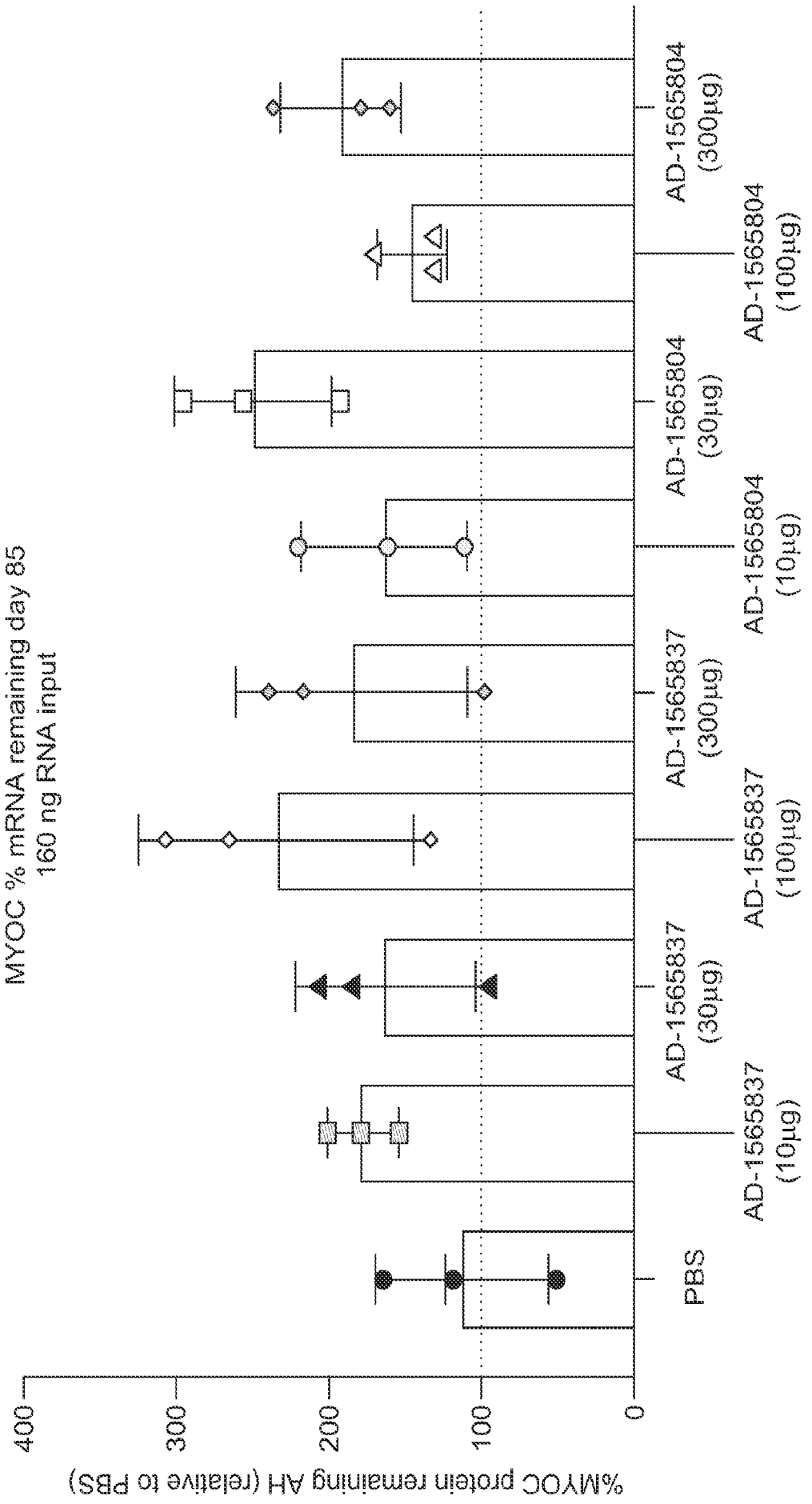

MYOC % mRNA remaining day 85
160 ng RNA input
%MYOC protein remaining AH (relative to PBS)
400
300
200
100
0
PBS
AD-1565837 (10µg)
AD-1565837 (30µg)
AD-1565837 (100µg)
AD-1565837 (300µg)
AD-1565804 (10µg)
AD-1565804 (30µg)
AD-1565804 (100µg)
AD-1565804 (300µg)

FIGURE. 7