

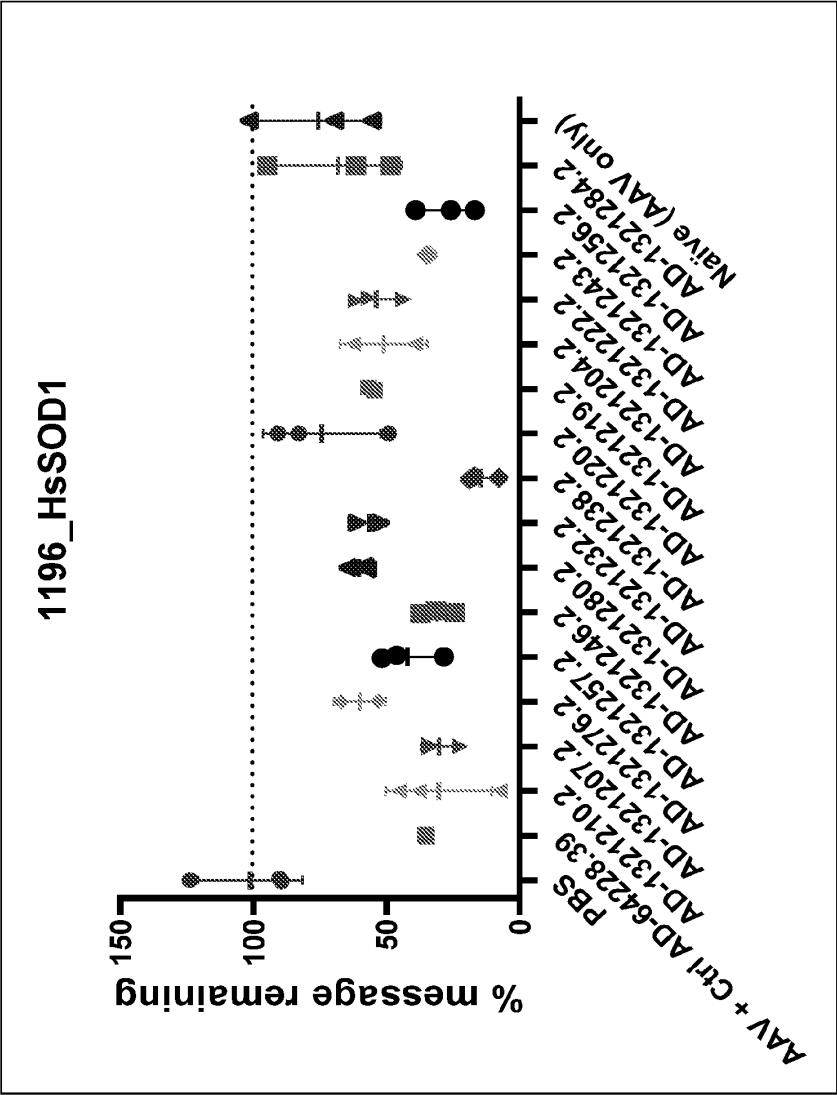


FIG. 1

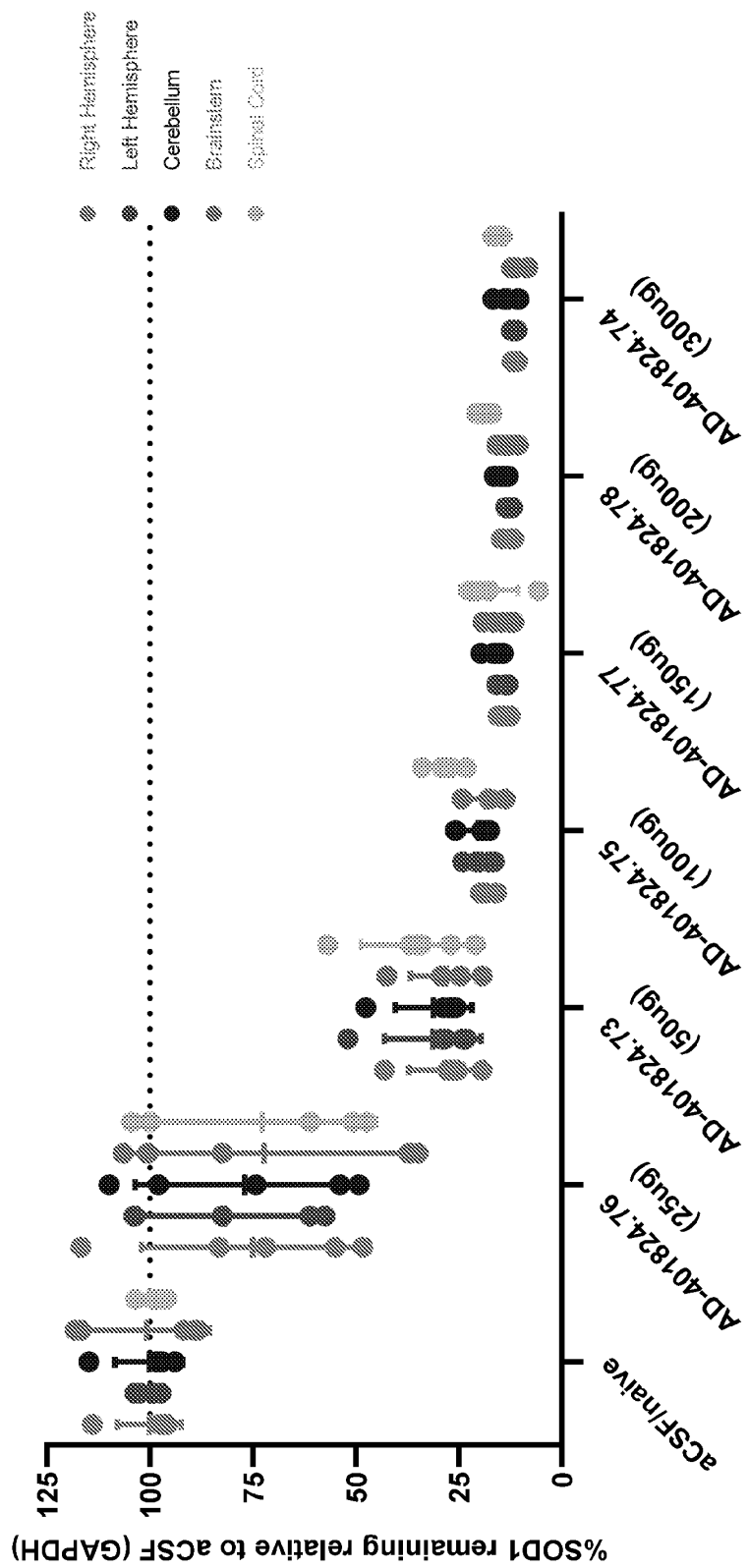


FIG. 2

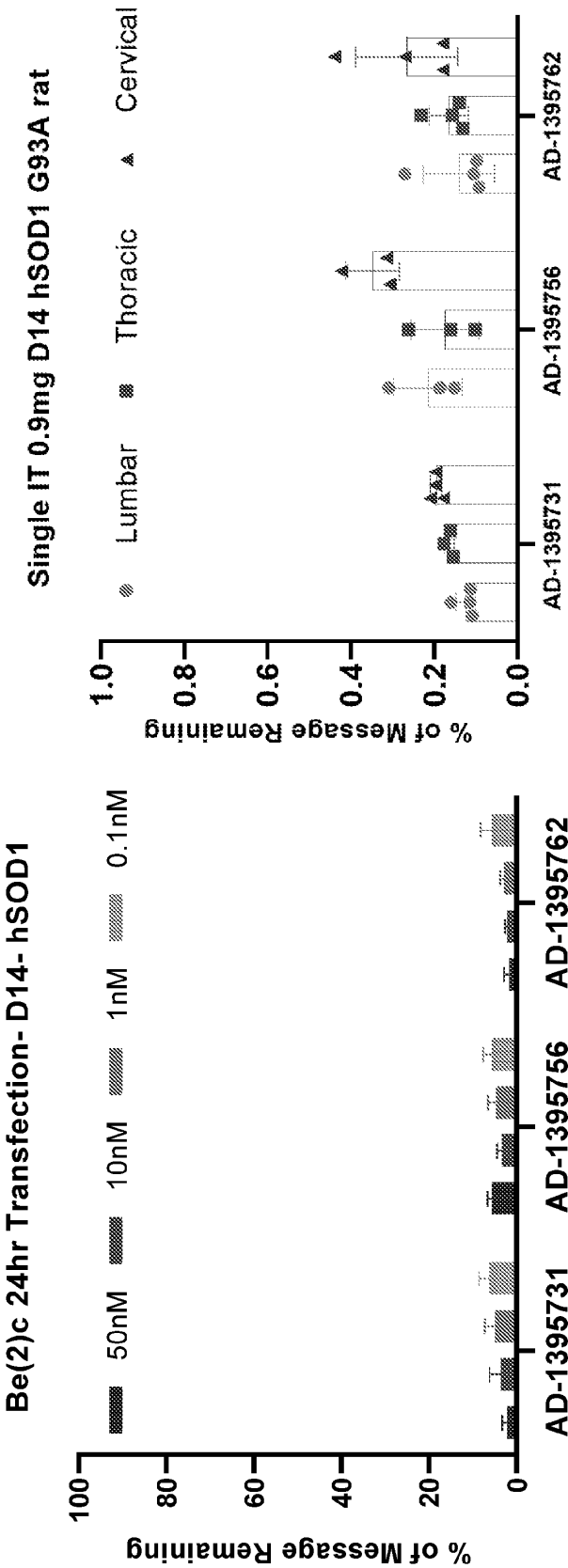


FIG. 3A

FIG. 3B

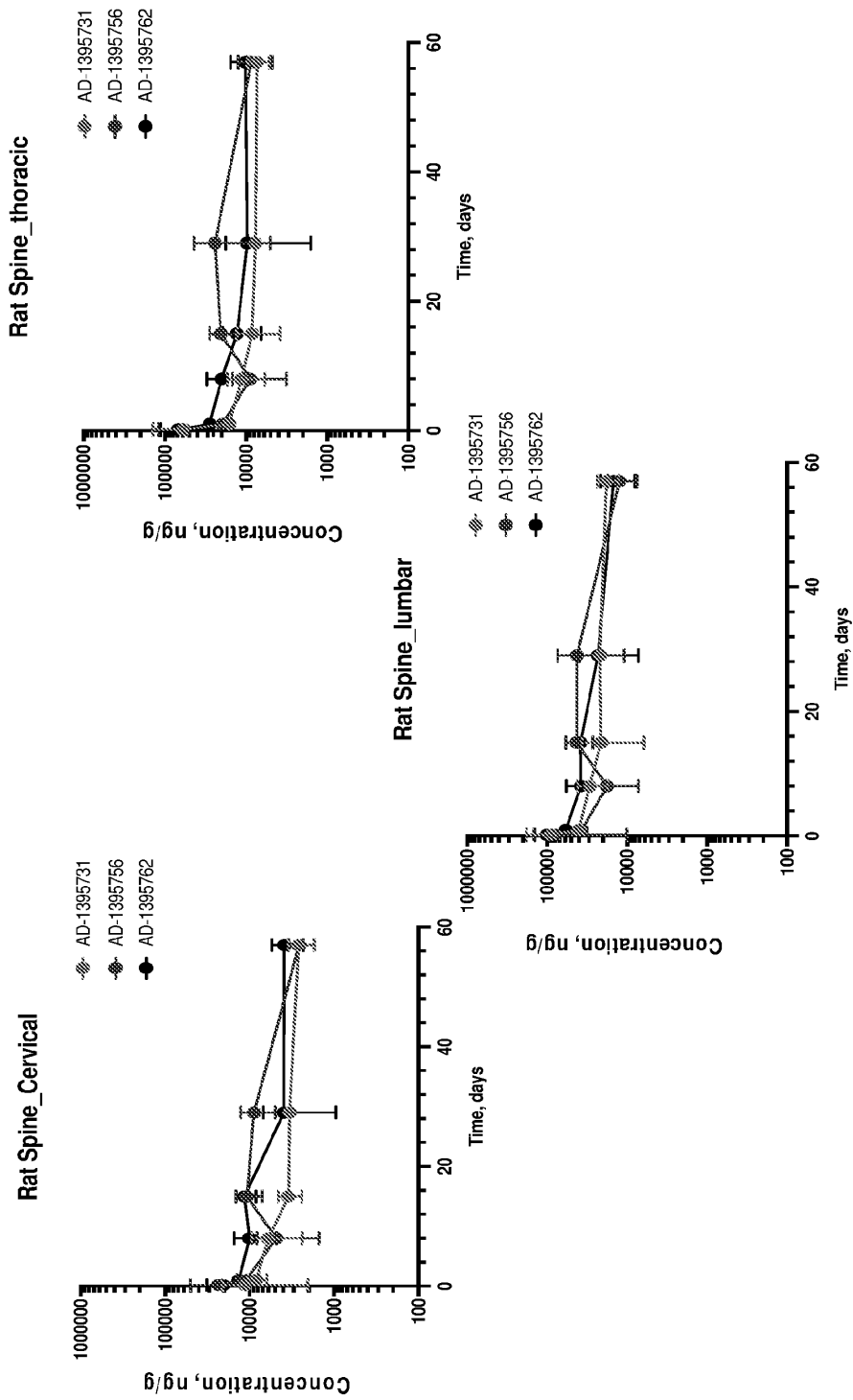


FIG. 4A

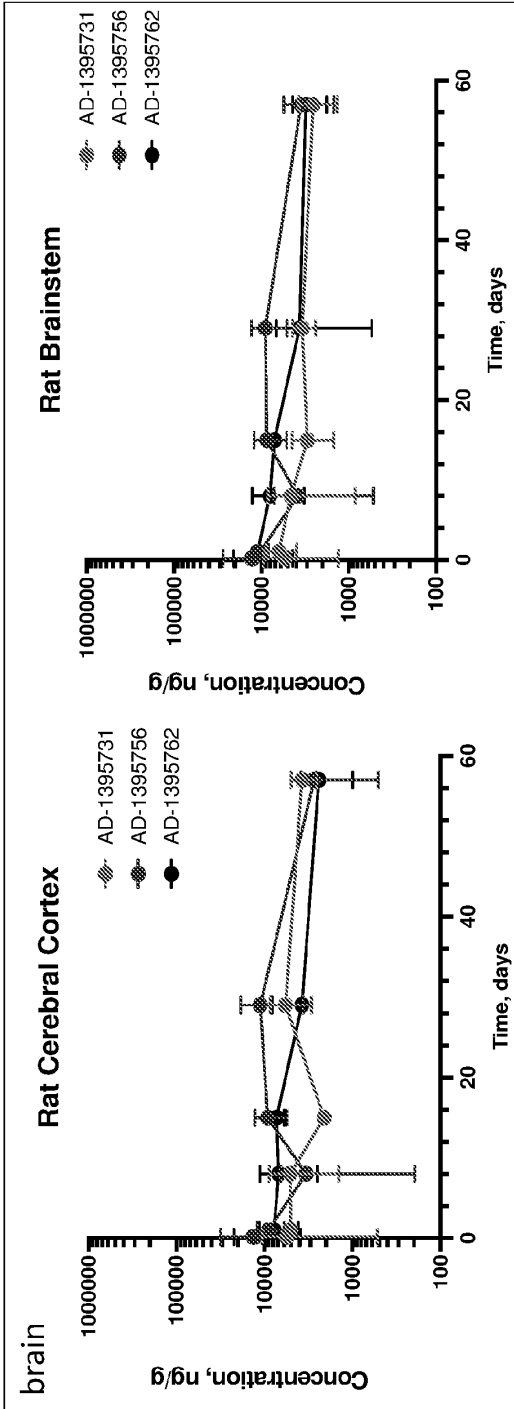


FIG. 4B

| Tissue           | AD-1395731                        | AD-1395756 <sup>a</sup>           | AD-1395762                        |
|------------------|-----------------------------------|-----------------------------------|-----------------------------------|
|                  | AUC <sub>last</sub><br>(day*µg/g) | AUC <sub>last</sub><br>(day*µg/g) | AUC <sub>last</sub><br>(day*µg/g) |
| Cerebral Cortex  | 255                               | 438                               | 276                               |
| Brain stem       | 197                               | 406                               | 299                               |
| Spine (cervical) | 225                               | 431                               | 392                               |
| Spine (Thoracic) | 528                               | 1020                              | 771                               |
| Spine (lumbar)   | 1300                              | 1830                              | 1640                              |

FIG. 4C

[illegible]

**FIG. 5**

| siRNA      | Rat PK <sup>a</sup>                              |                |                     |                     |                   | Met-ID                                     |
|------------|--------------------------------------------------|----------------|---------------------|---------------------|-------------------|--------------------------------------------|
|            | Tissue exposure (AUC <sub>last</sub> (day*µg/g)) |                |                     |                     |                   | Antisense<br>(4-1344 hr pool) <sup>b</sup> |
|            | Cerebral<br>Cortex                               | Brain-<br>stem | Spine<br>(cervical) | Spine<br>(thoracic) | Spine<br>(lumbar) |                                            |
|            | AD-1395731                                       | 255            | 197                 | 225                 | 528               | 1300                                       |
|            | AD-1395756                                       | 438            | 406                 | 431                 | 1020              | 1830                                       |
| AD-1395762 | 276                                              | 299            | 392                 | 771                 | 1640              | 3' N-1 (30%)                               |

<sup>a</sup> Parents and active metabolites are combined  
<sup>b</sup> mean of cerebral cortex and lumbar spinal cord

FIG. 6

| Group No. | Test Material | Dose Level (mg/dose) | Dose Volume (mL/dose) | Dose Concentration (mg/mL) | Number of Main Study Males |                 |                  |
|-----------|---------------|----------------------|-----------------------|----------------------------|----------------------------|-----------------|------------------|
|           |               |                      |                       |                            | Necropsy Day 31            | Necropsy Day 85 | Necropsy Day 169 |
| 1         | aCSF          | 0                    | 2                     | 0                          | 2                          | 2               | -                |
| 2         | AD-1395731    | 70                   | 2                     | 35                         | 4                          | 4               | 1                |
| 3         | AD-1395756    | 70                   | 2                     | 35                         | 4                          | 4               | 1                |
| 4         | AD-1395762    | 70                   | 2                     | 35                         | 4                          | 4               | 1                |
| 5         | aCSF          | 0                    | 2                     | 0                          | 2                          | 2               | -                |
| 6         | AD-1395731    | 120                  | 2                     | 60                         | 4                          | 4               | -                |

FIG. 7

|                          | AD-1395731 | AD-1395754 | AD-1395762 |
|--------------------------|------------|------------|------------|
| Bad<br>(<1k ng/mL)       | 5 / 9      | 3 / 9      | 1 / 9      |
| Partial<br>(1k-3k ng/mL) | 1 / 9      | 1 / 9      | 1 / 9      |
| Good<br>(>3k ng/mL)      | 3 / 9      | 5 / 9      | 8 / 9      |

FIG. 8A

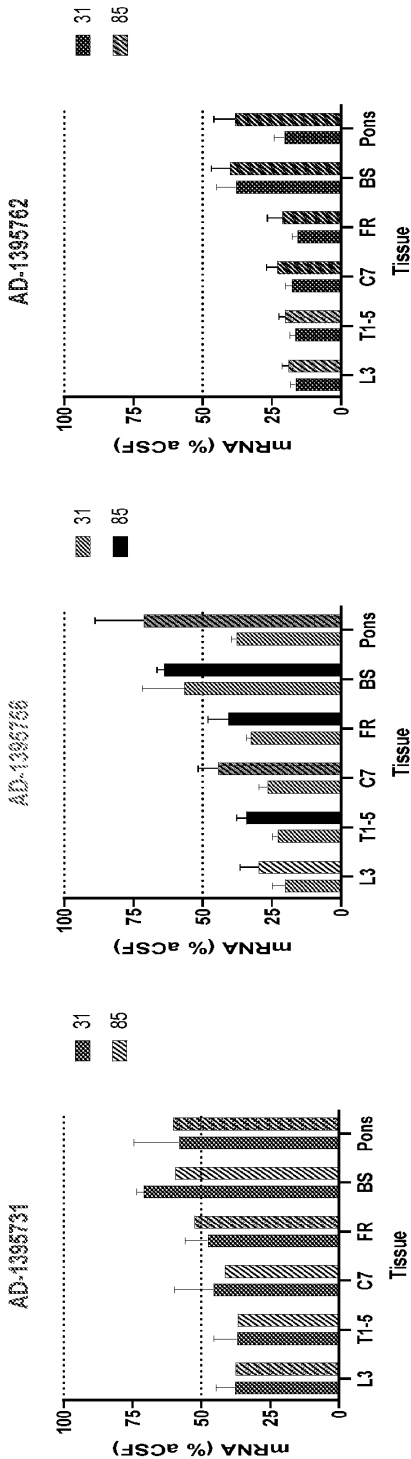
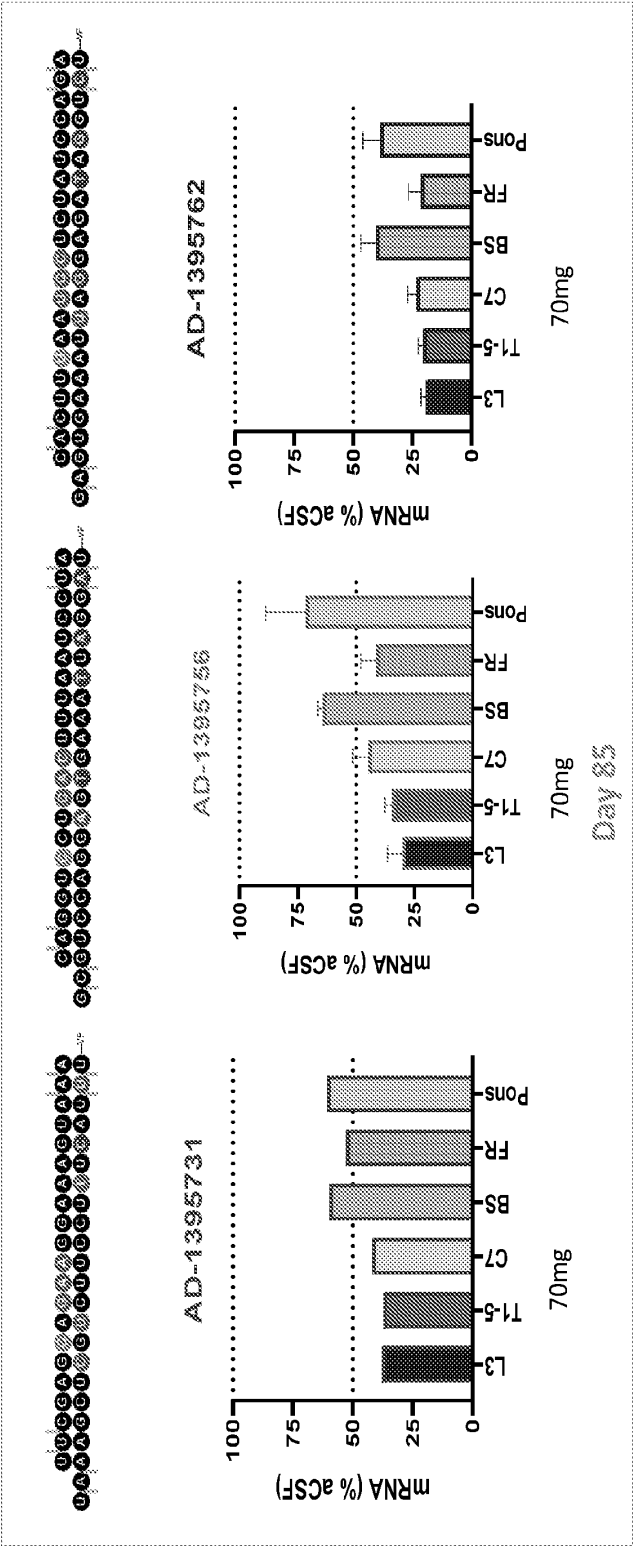
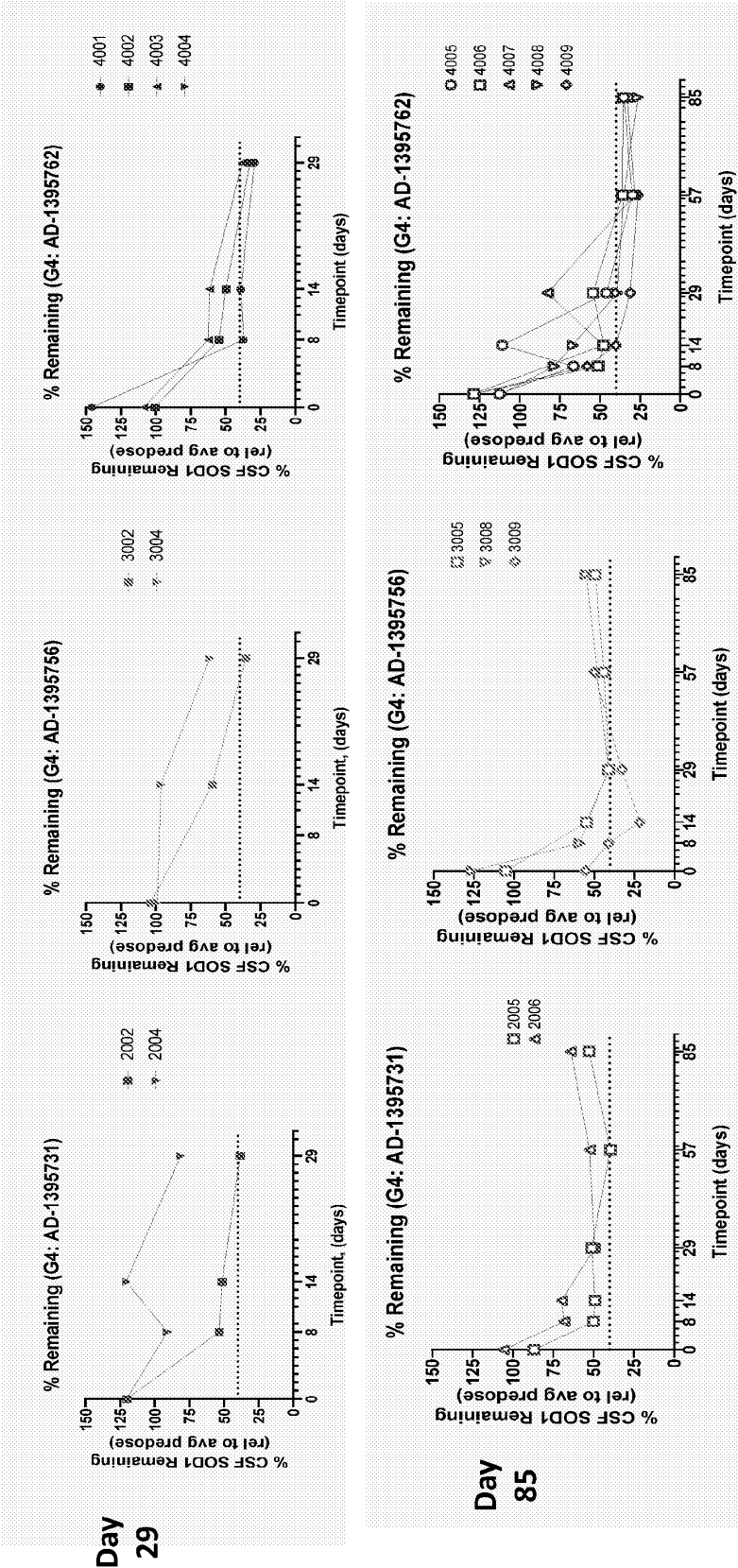


FIG. 8B



\*Samples removed from graphs if drug exposure levels at 24hrs in CSF were lower than 1500 ng/ml, these are considered suboptimal doses

FIG. 8C



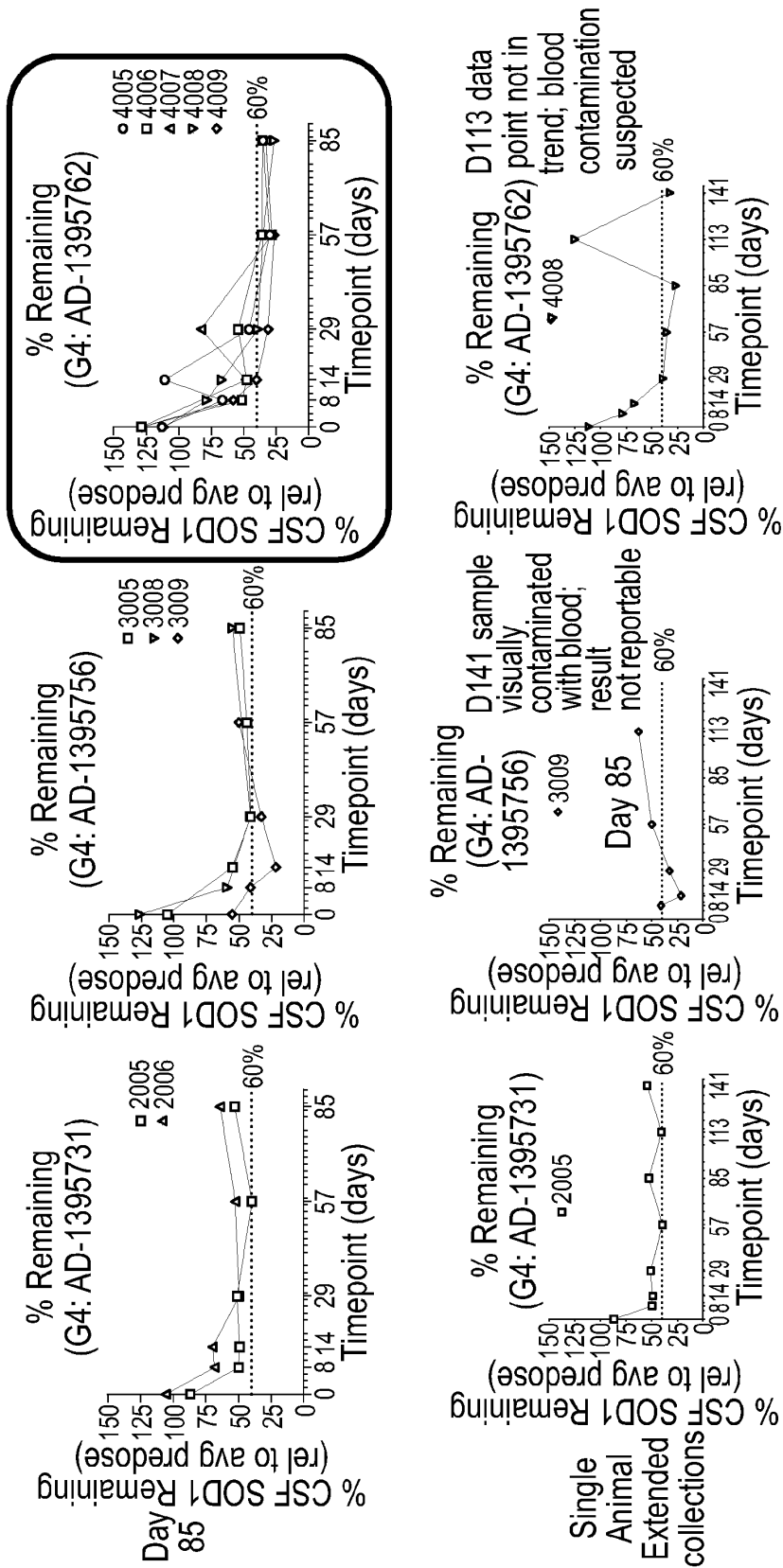
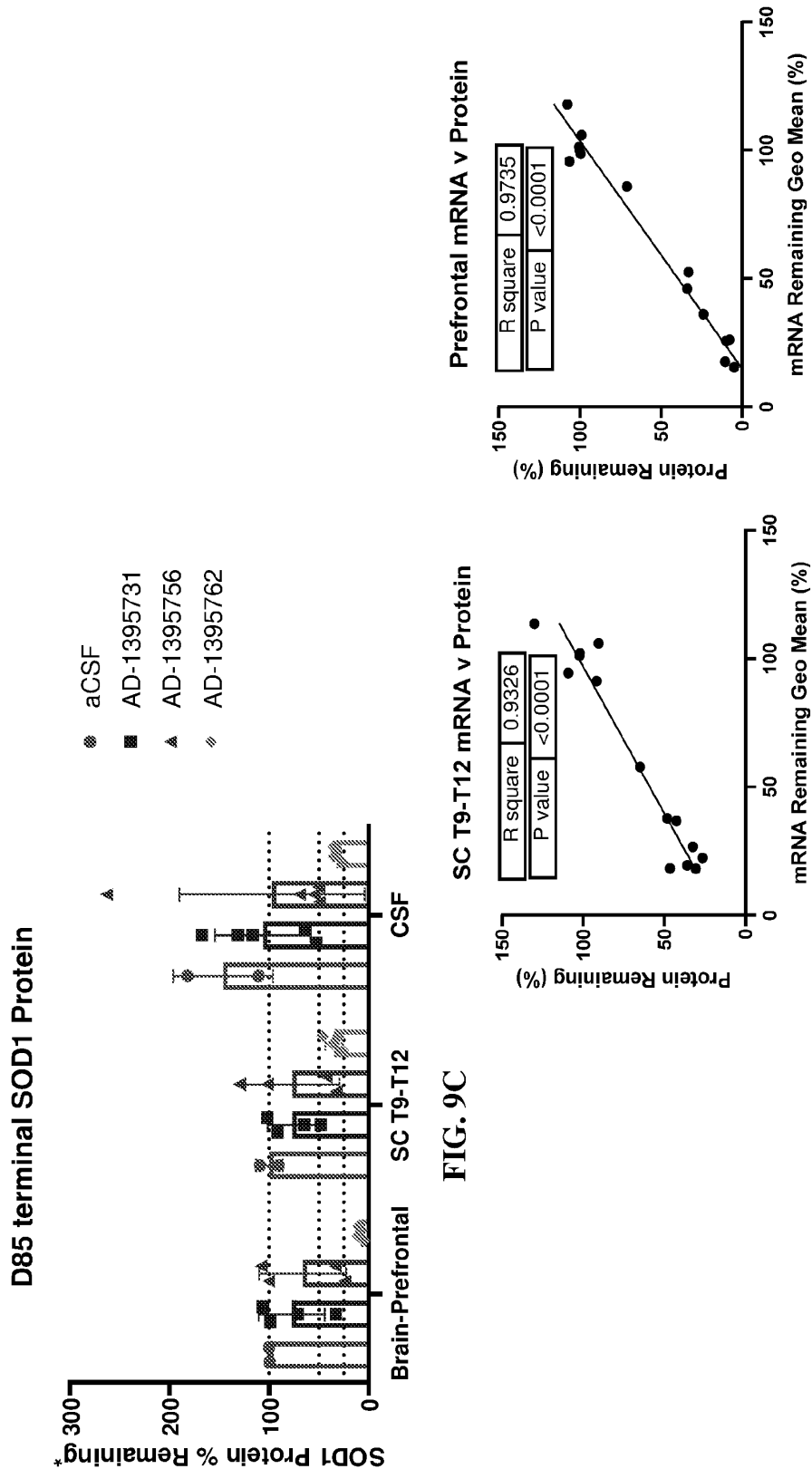
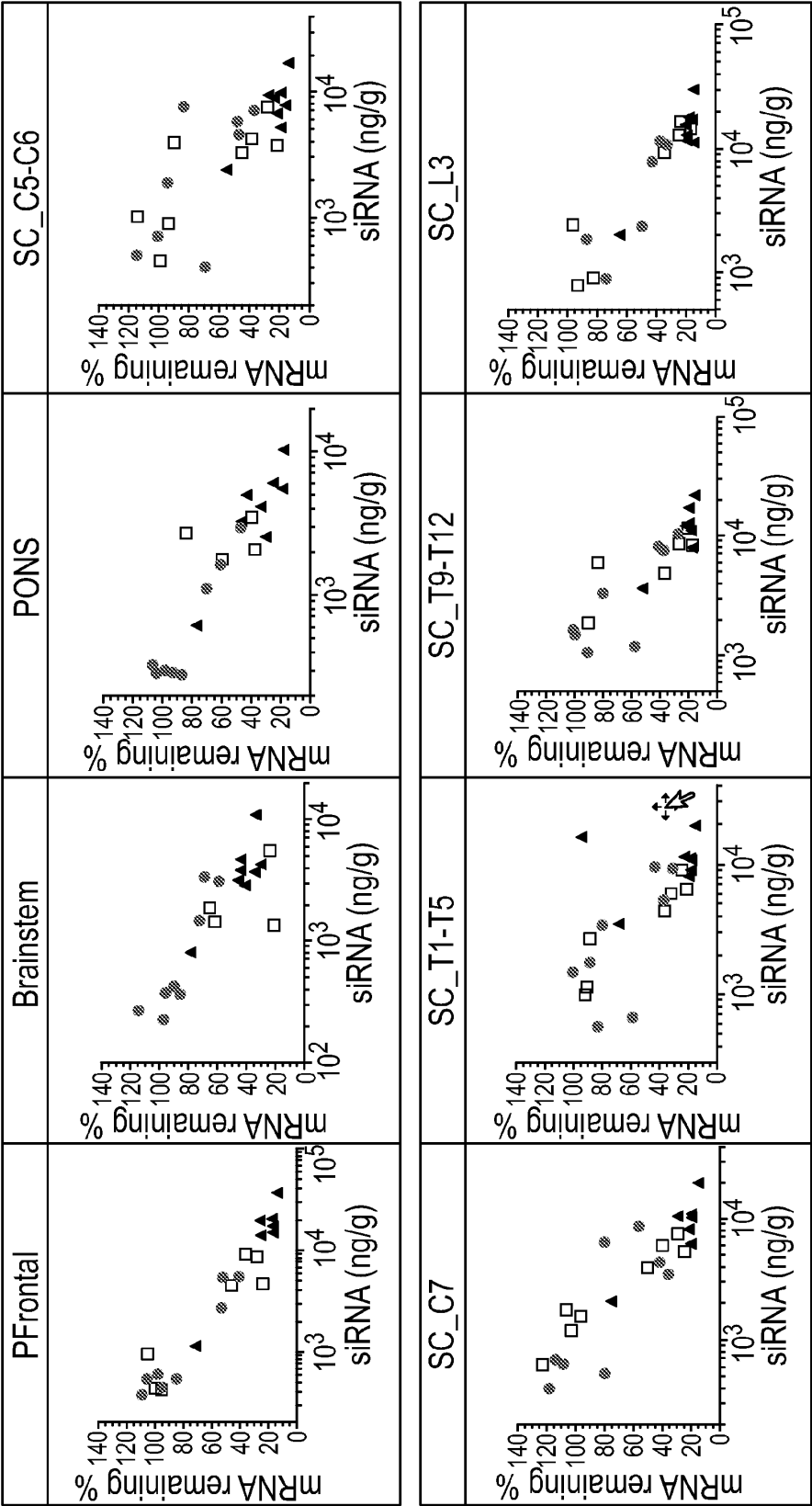


FIG. 9B





● AD-1395731  
□ AD-1395756  
▲ AD-1395762

FIG. 11A

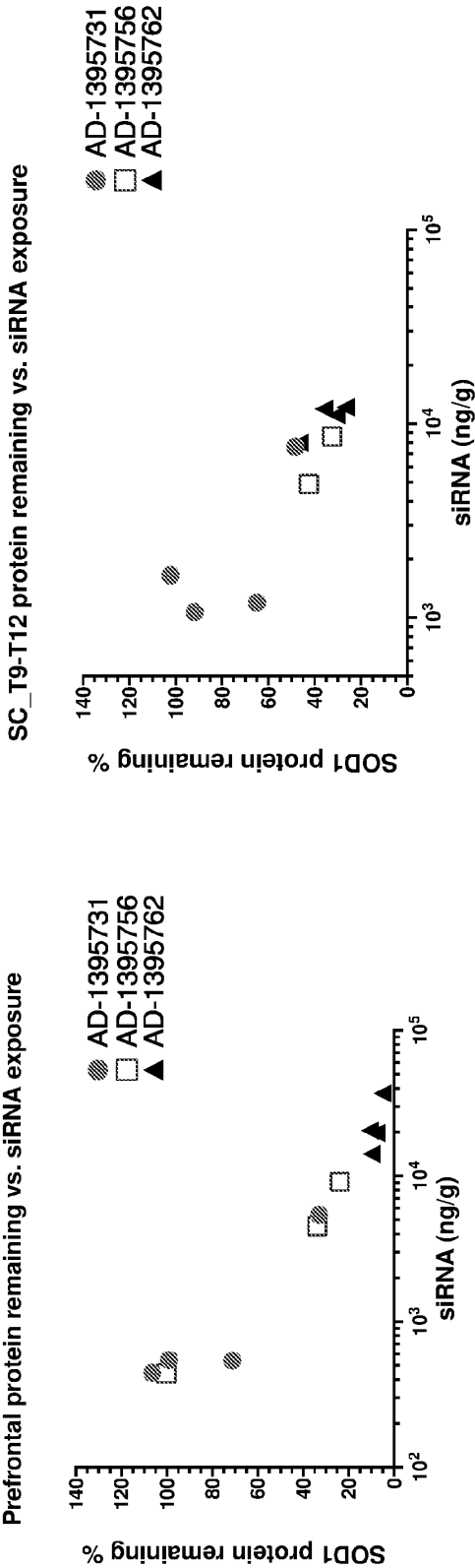


FIG. 11B

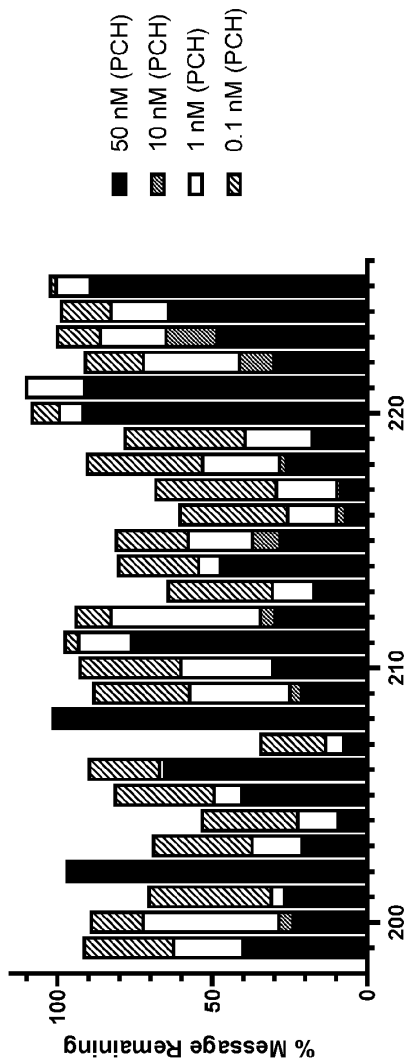


FIG. 12A

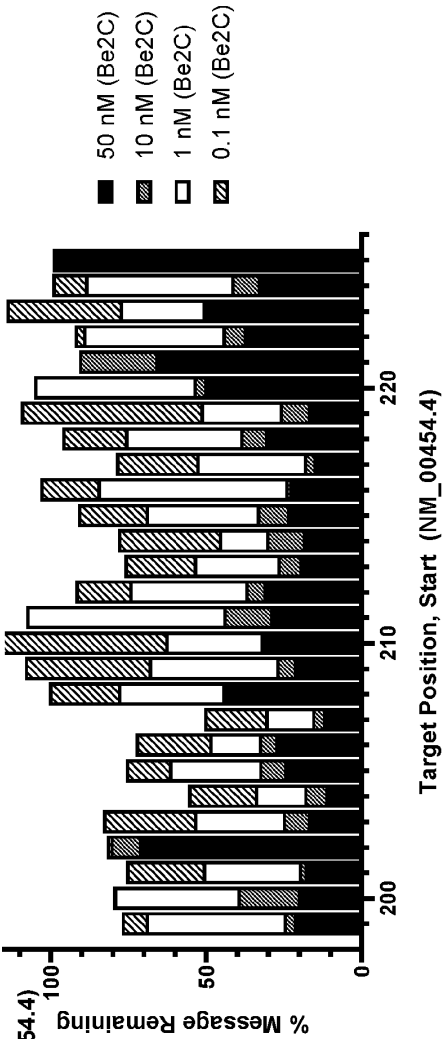


FIG. 12B

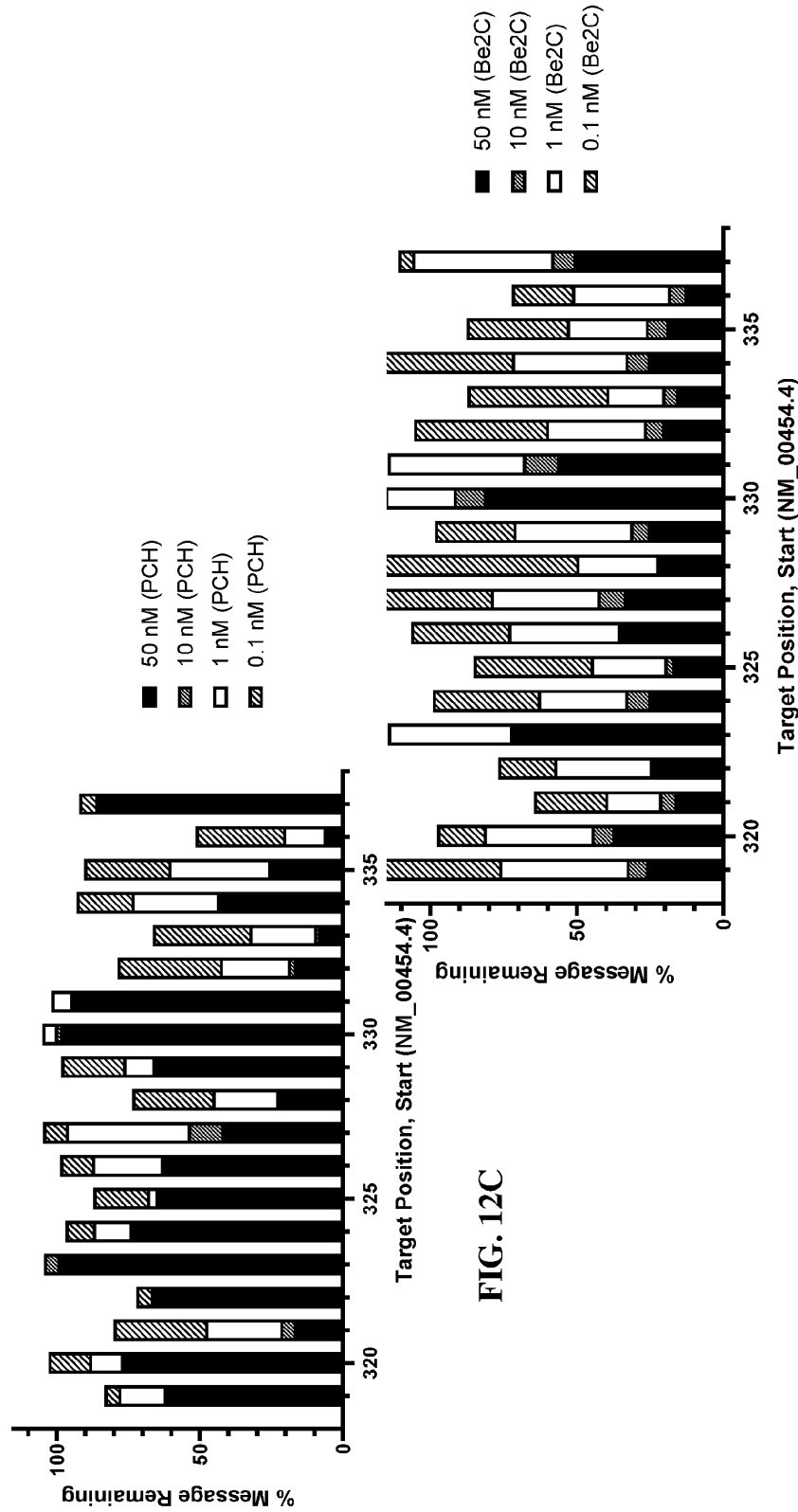


FIG. 12C

FIG. 12D

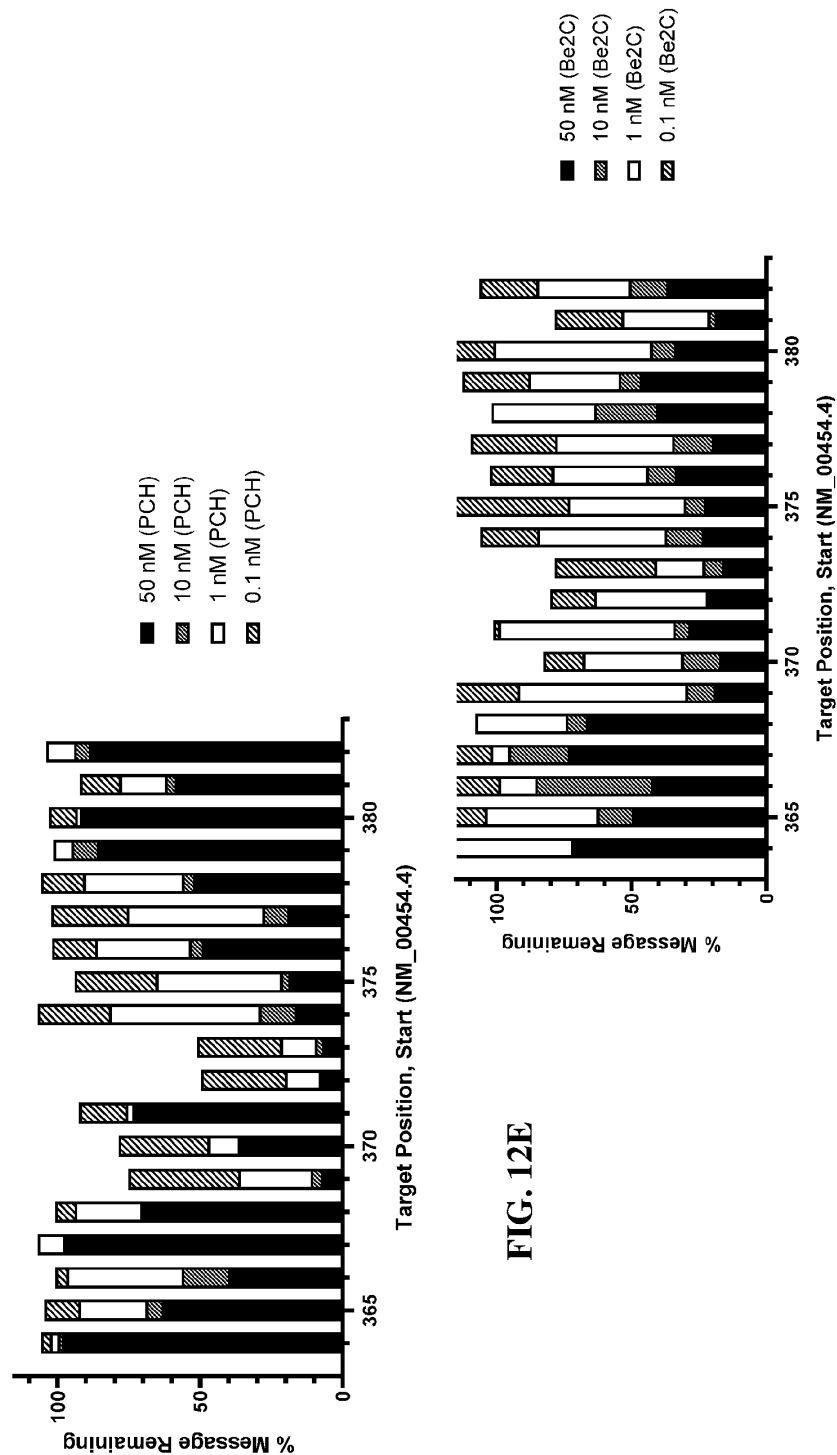


FIG. 12F

FIG. 12E

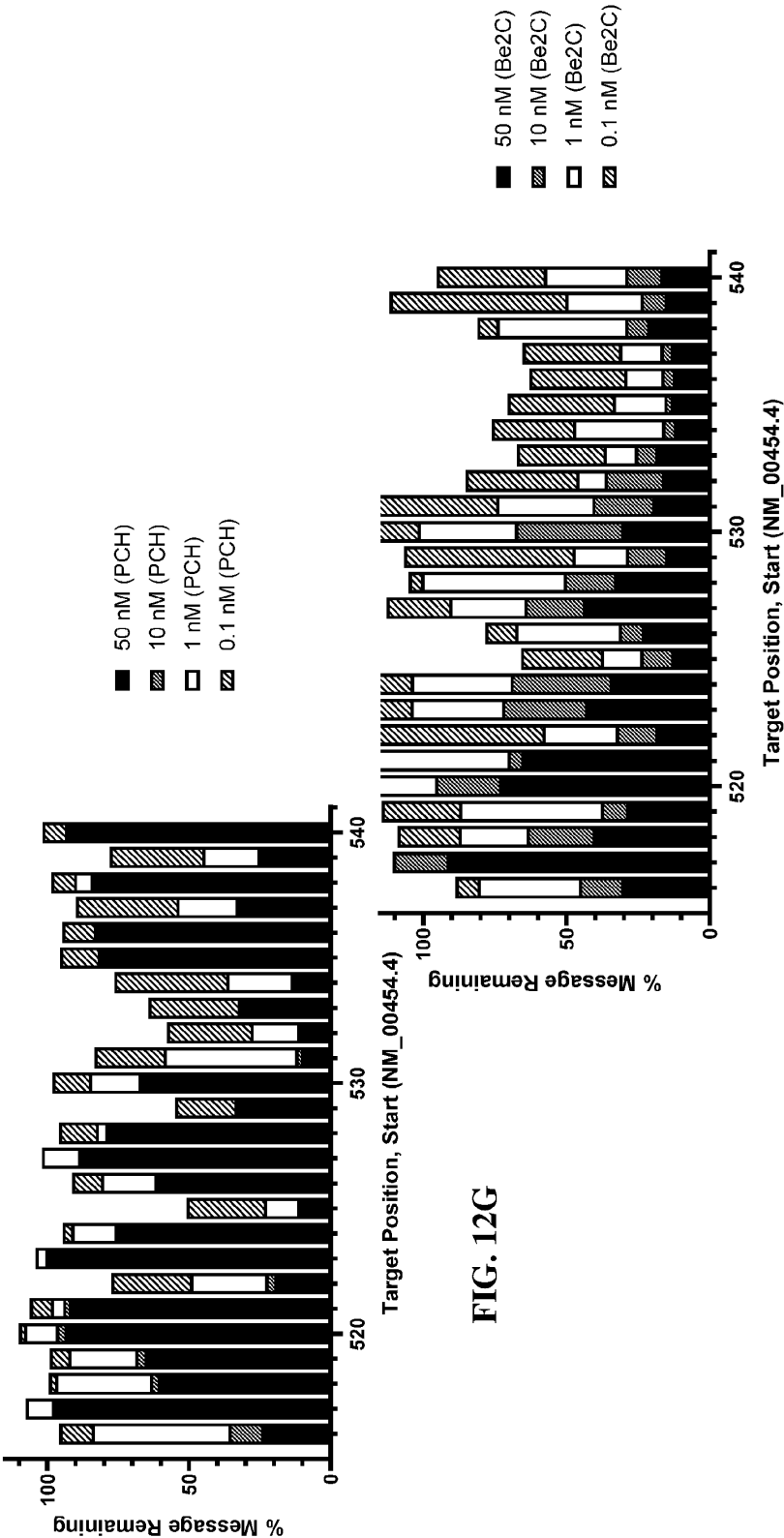


FIG. 12H

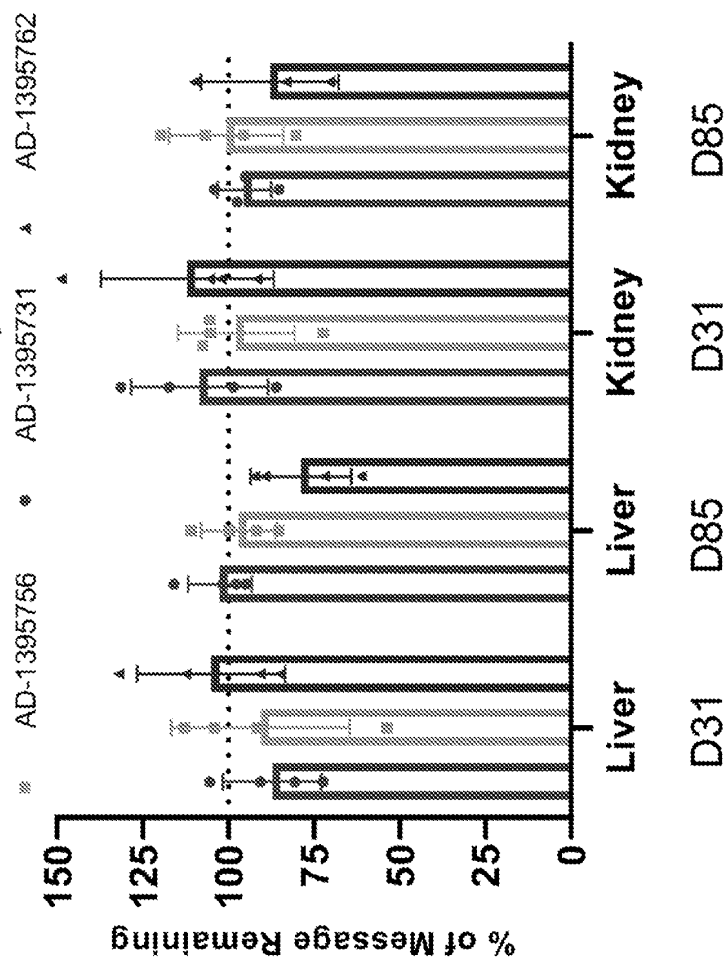


FIG. 13