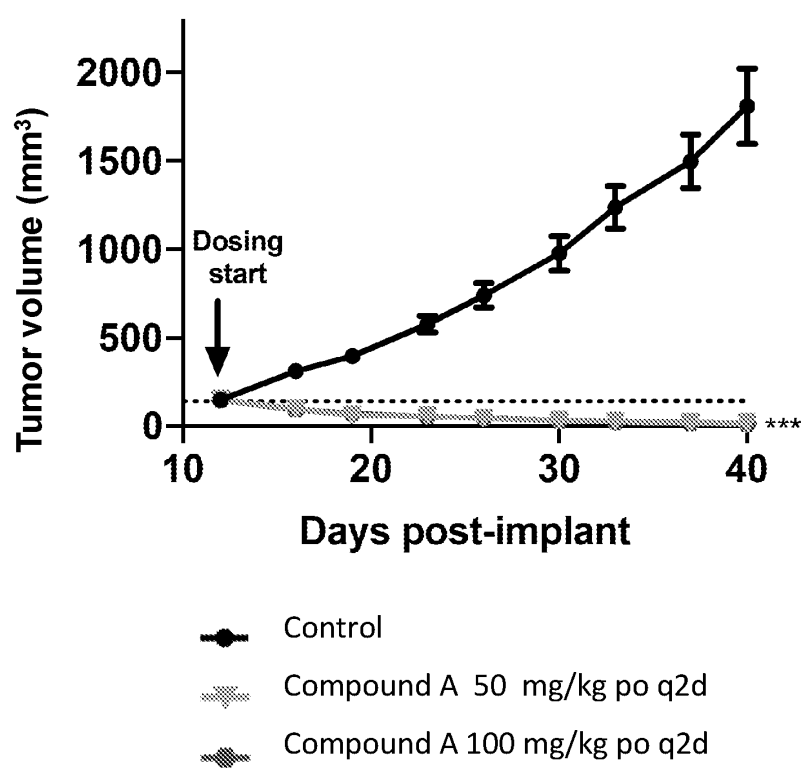


FIG. 1A



n = 10/group \*\*\*p<0.001 All dose levels well tolerated

FIG. 1B

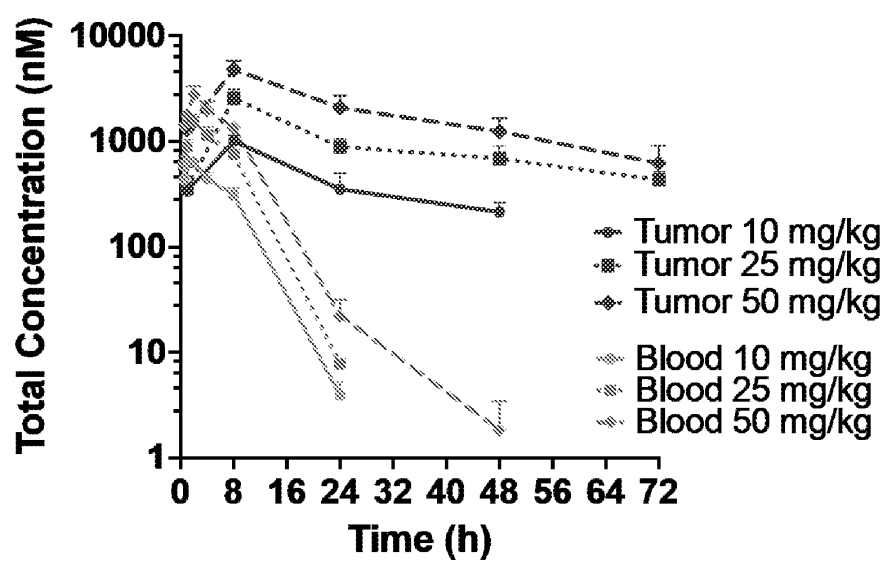


FIG. 1C

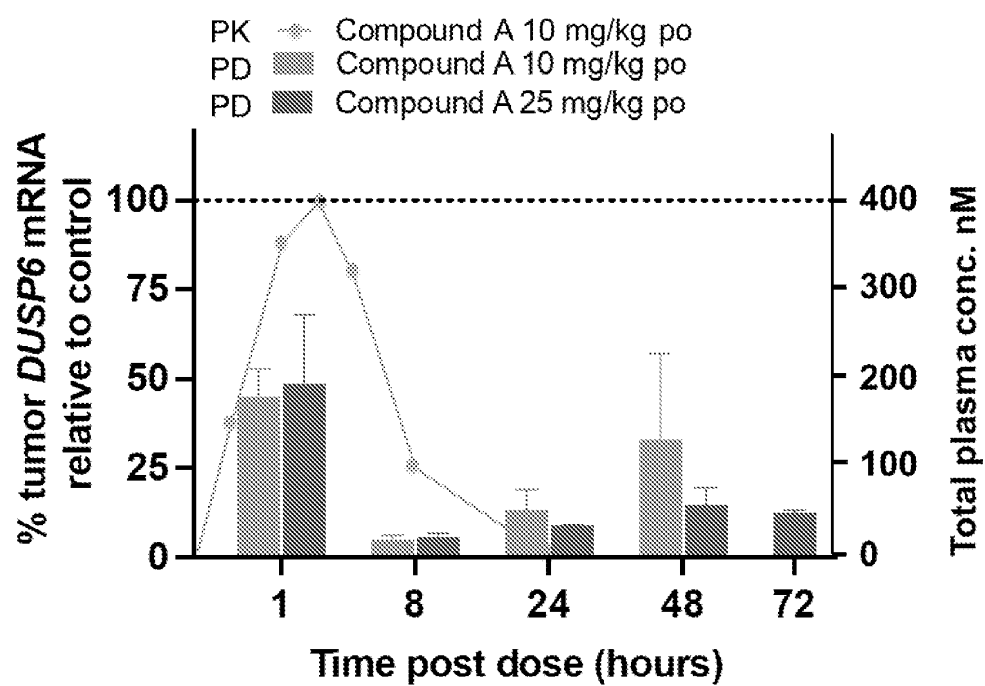


FIG. 1D

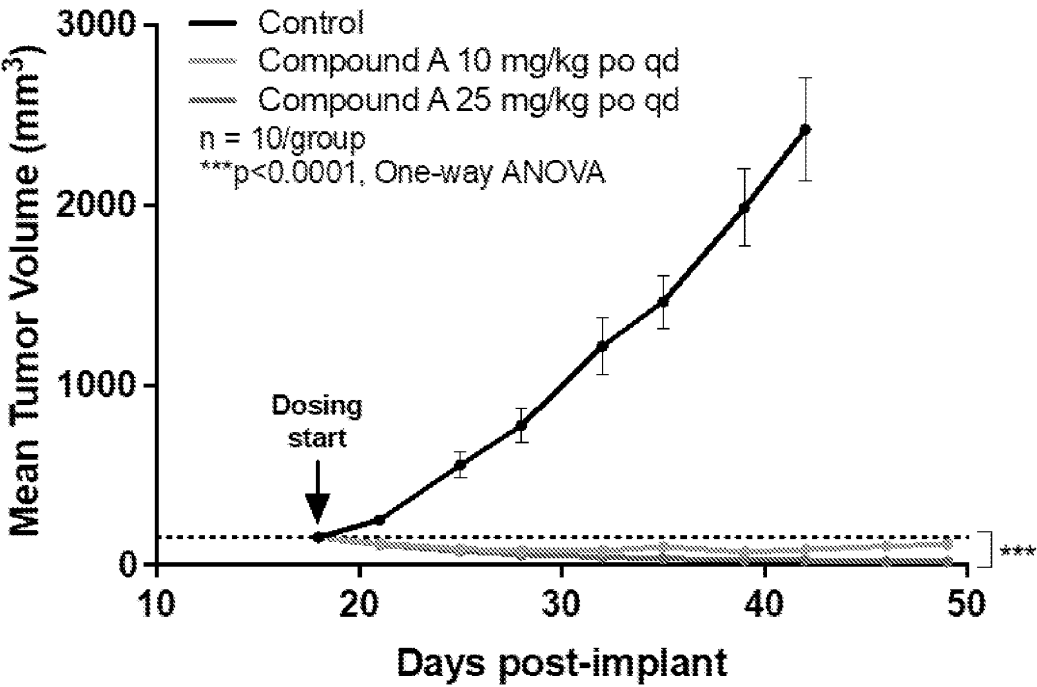


FIG. 1E

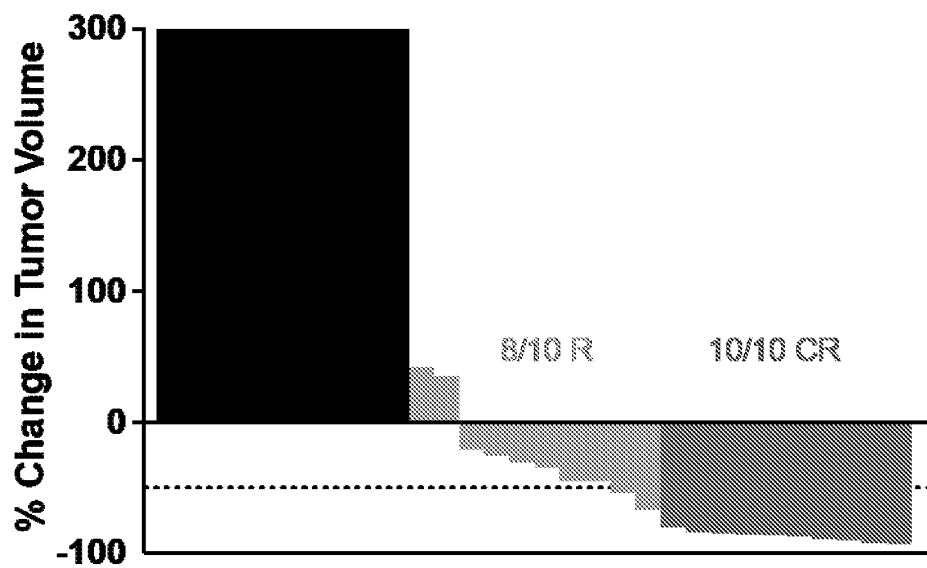


FIG. 1F

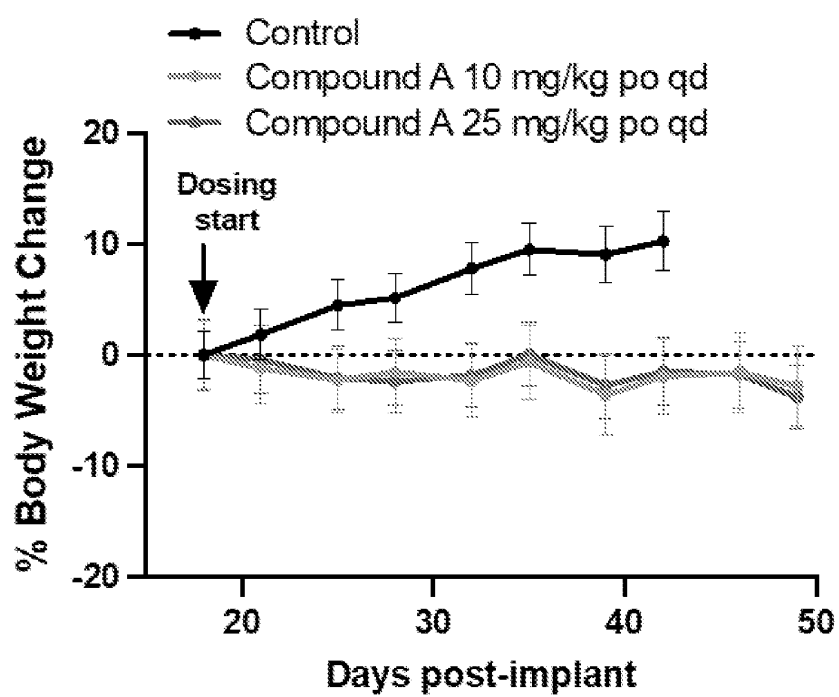


FIG. 2A

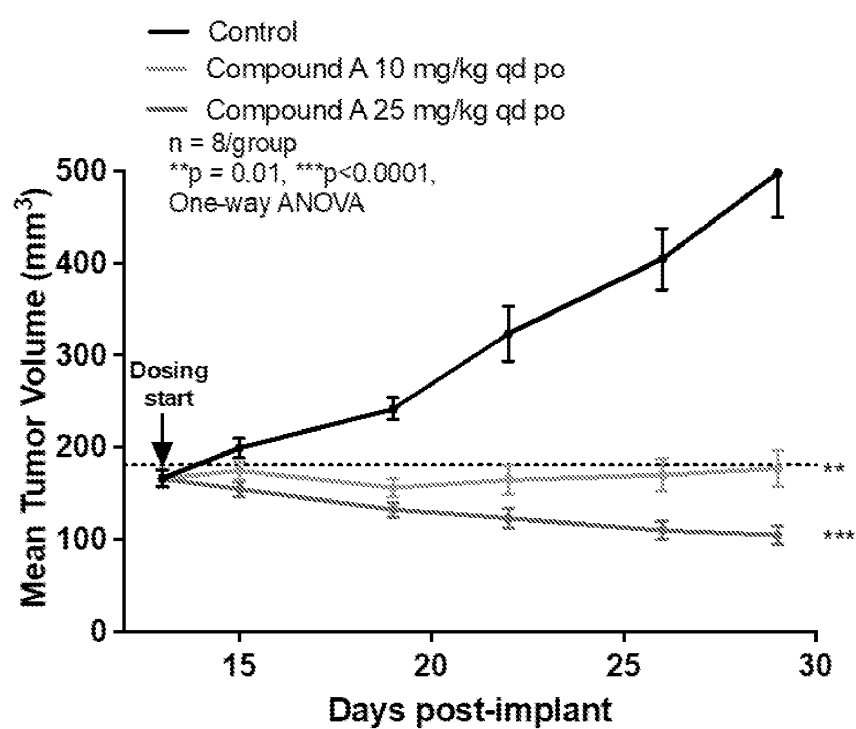


FIG. 2B

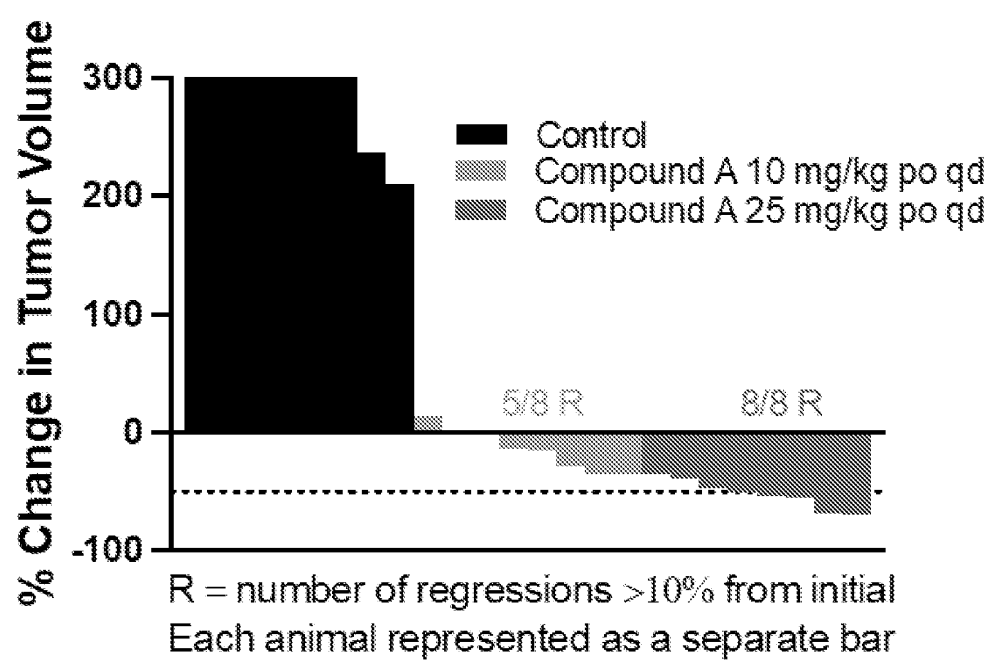


FIG. 2C

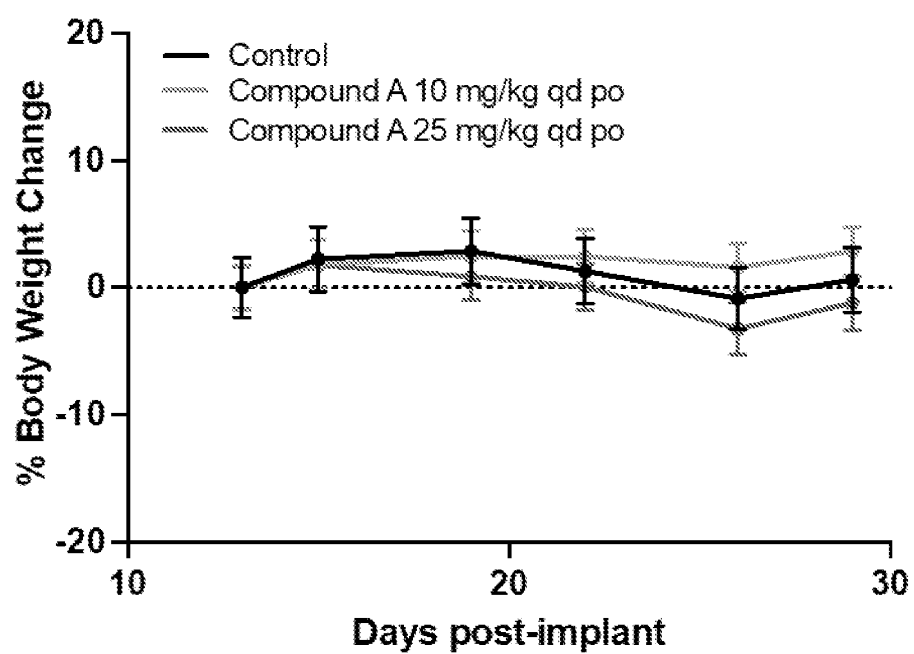


FIG. 2D

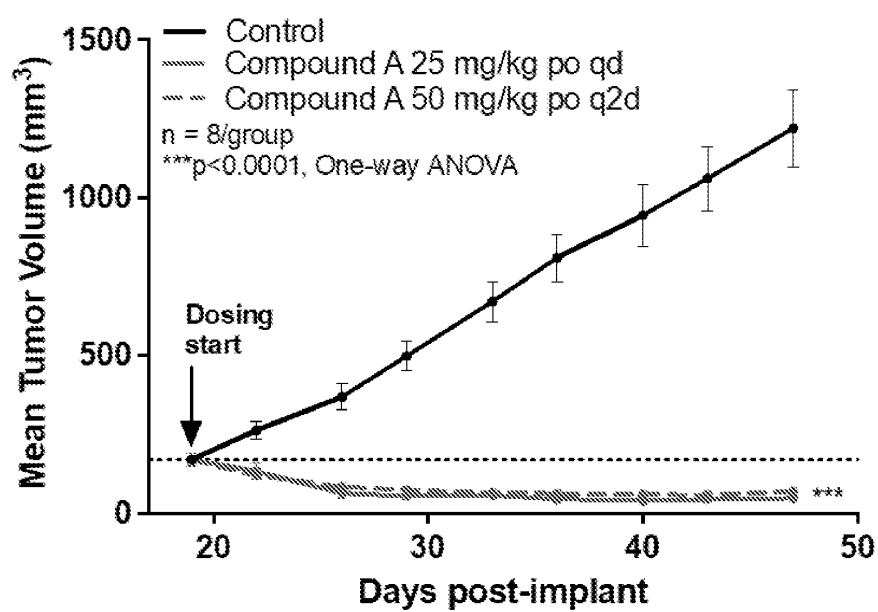


FIG. 2E

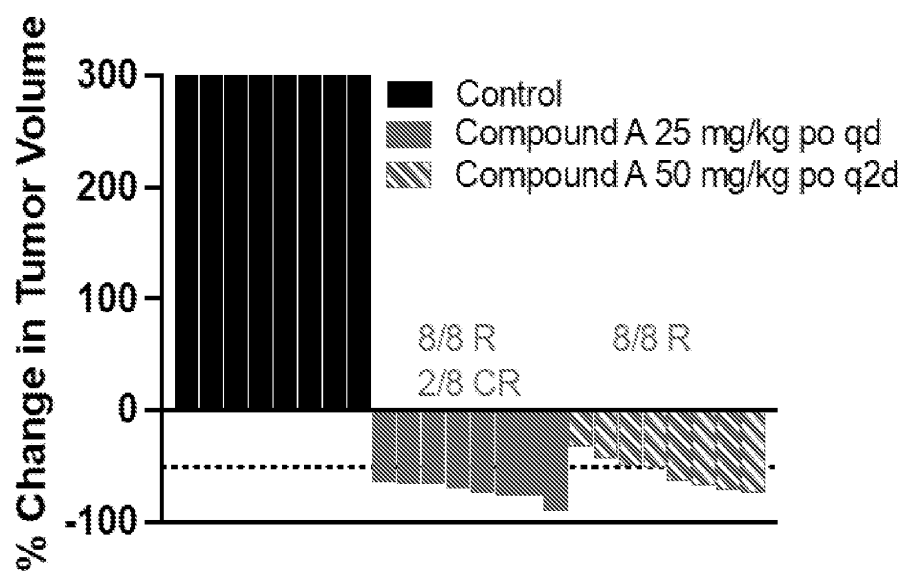


FIG. 2F

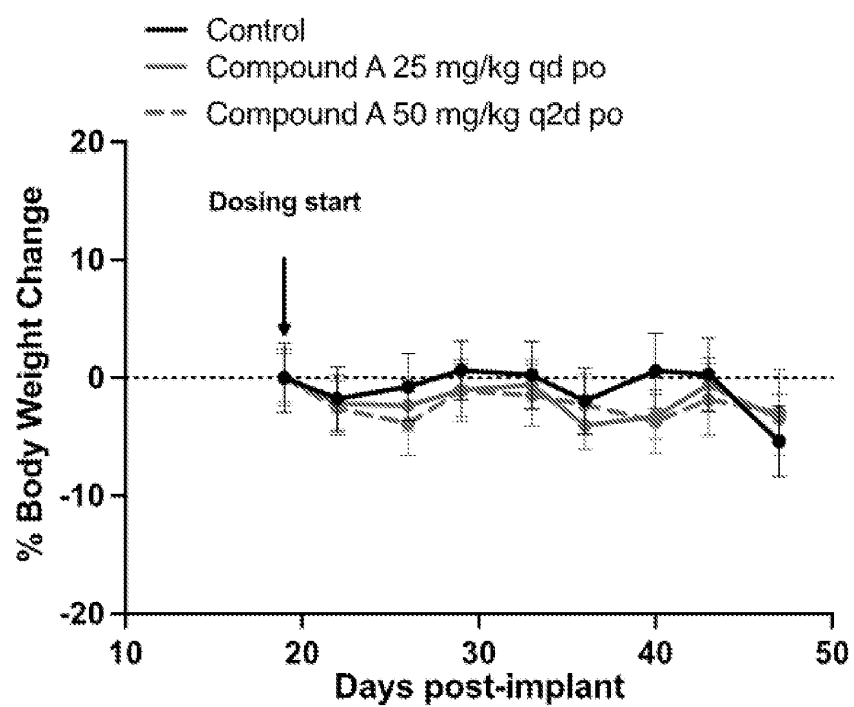


FIG. 3A

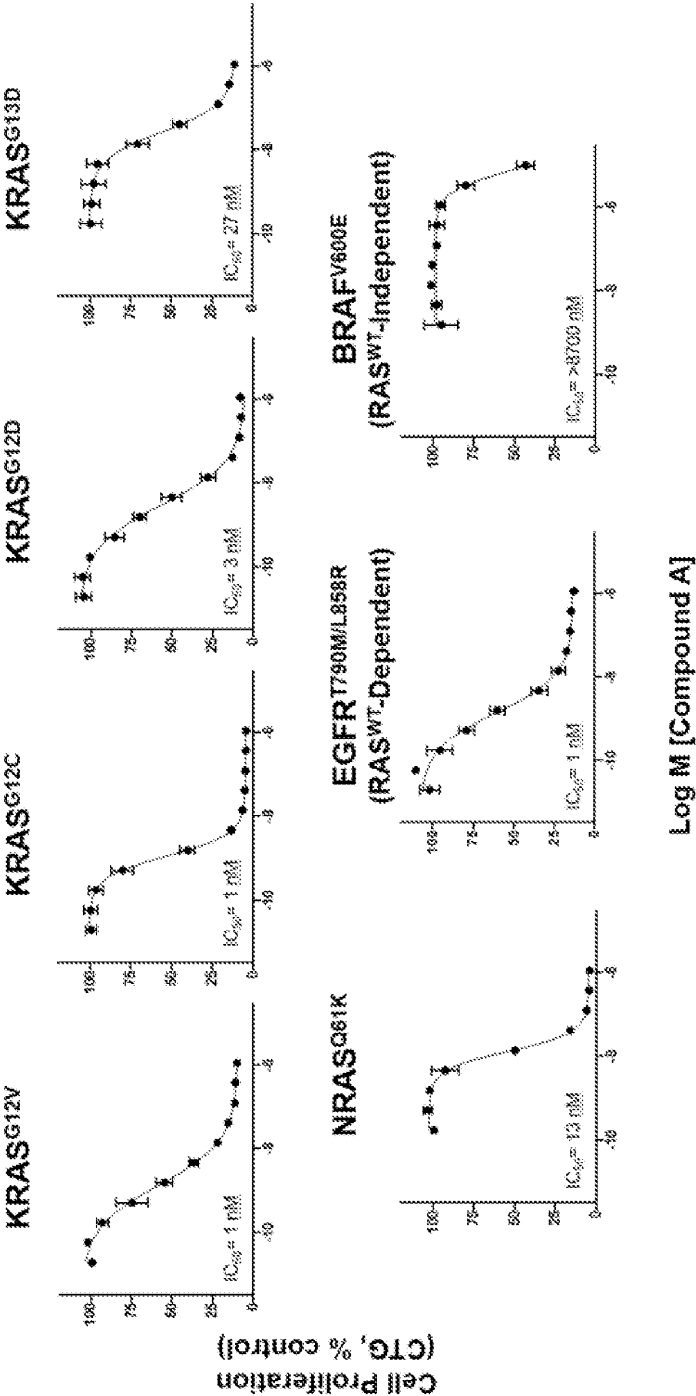


FIG. 3B

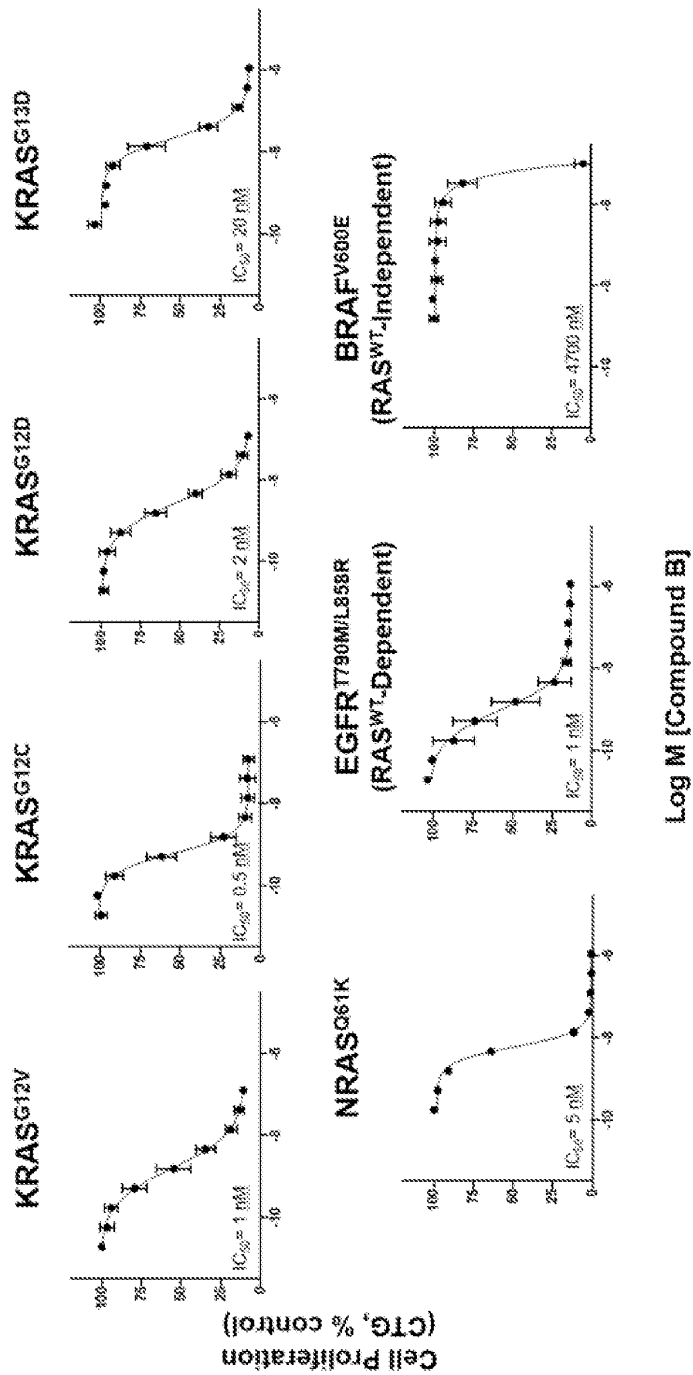


FIG. 3C

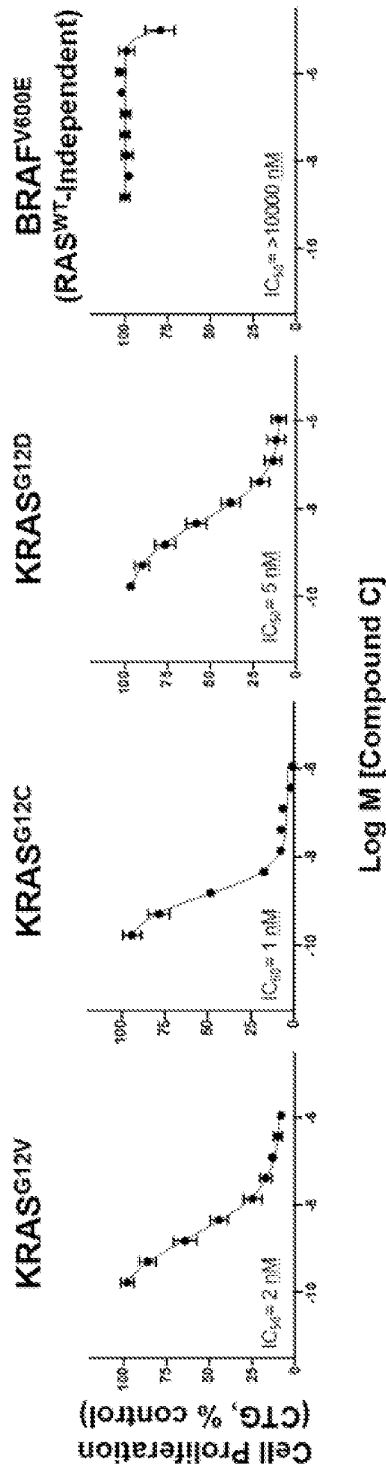


FIG. 4A

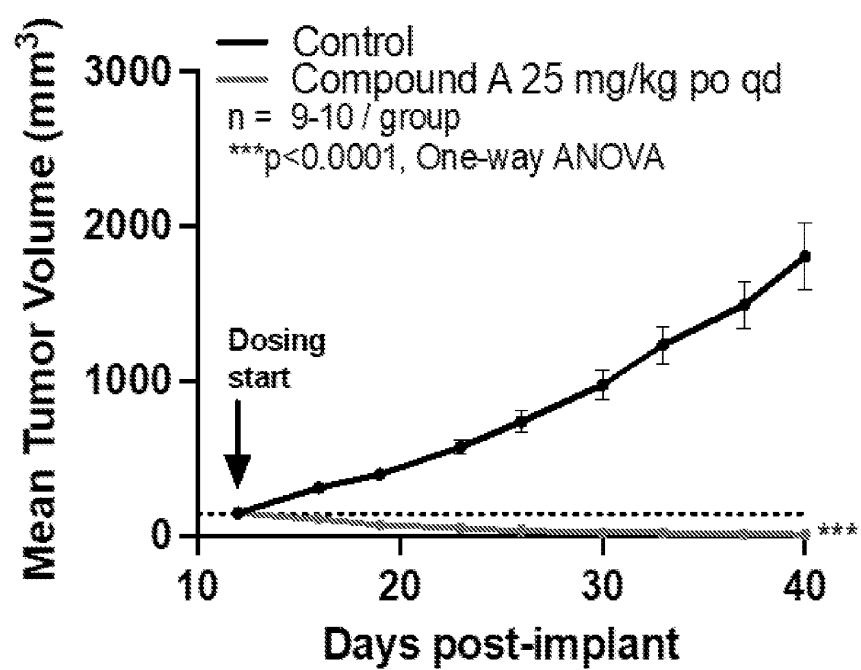


FIG. 4B

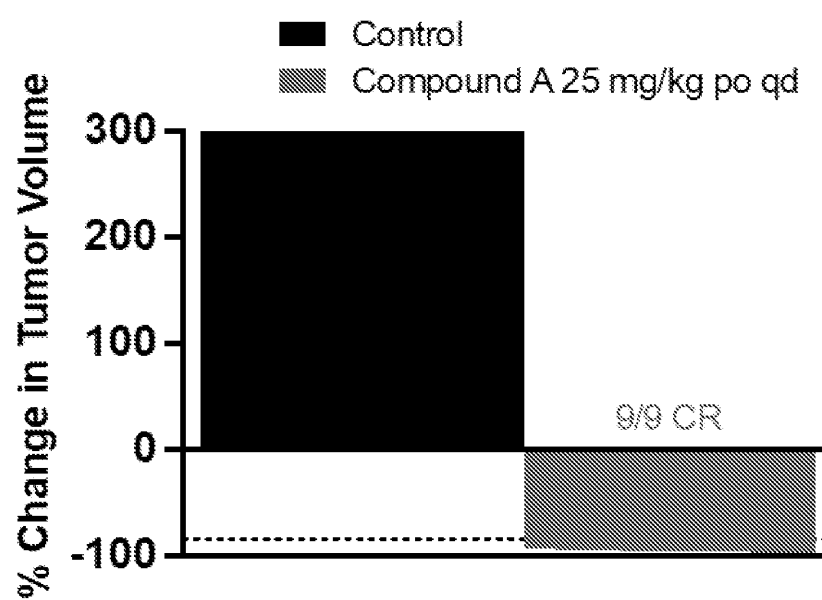


FIG. 4C

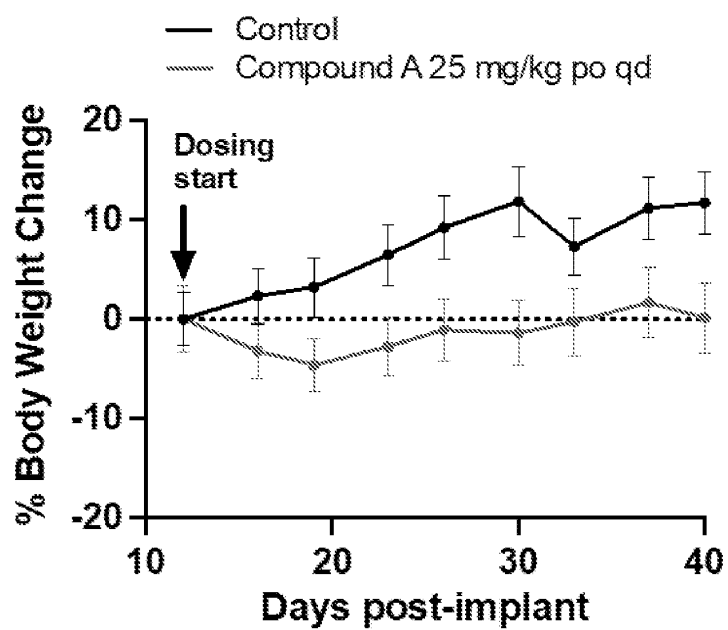


FIG. 4D

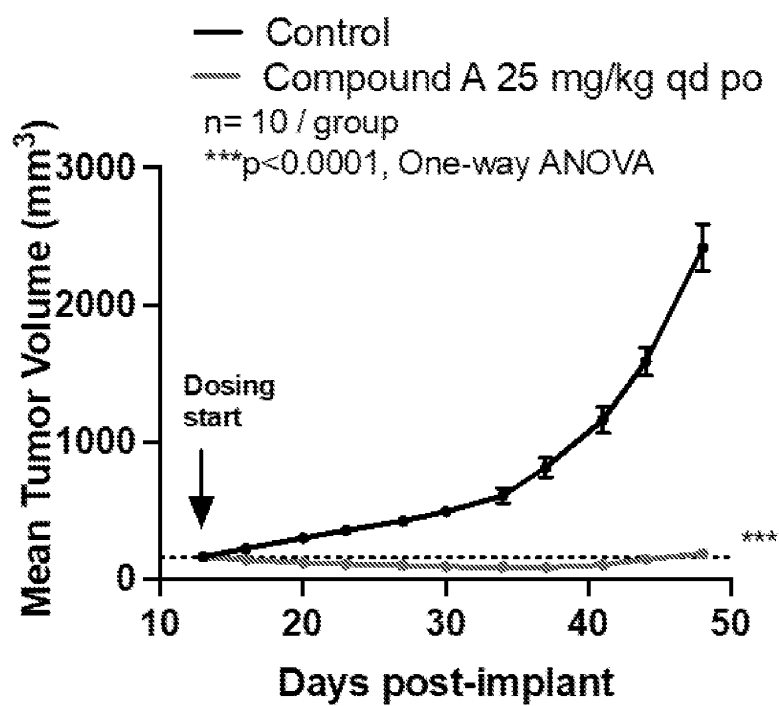


FIG. 4E

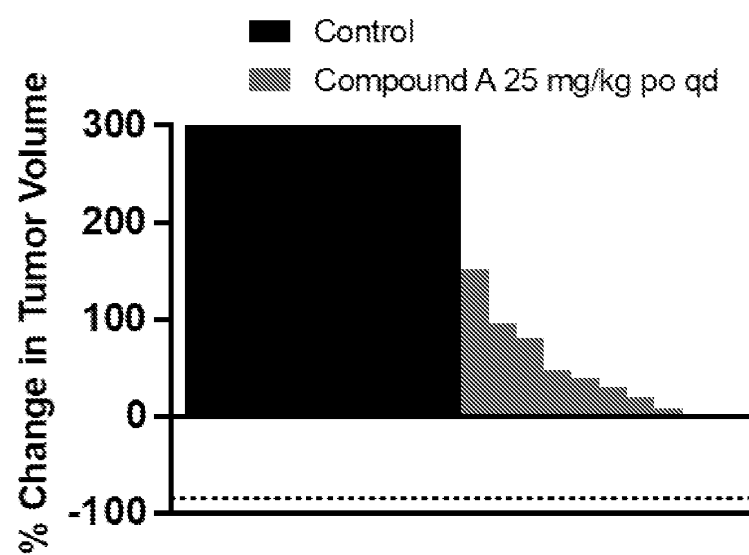


FIG. 4F

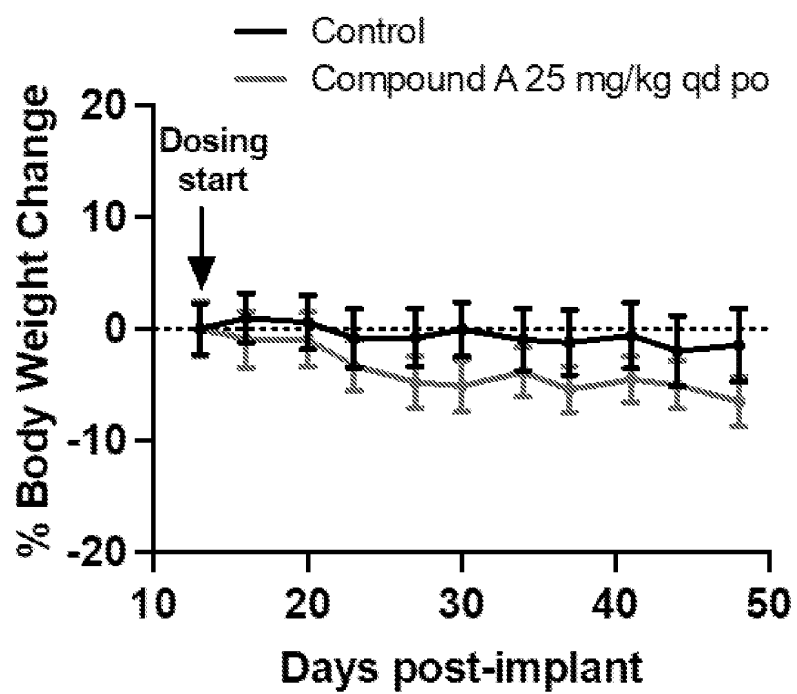


FIG. 5A

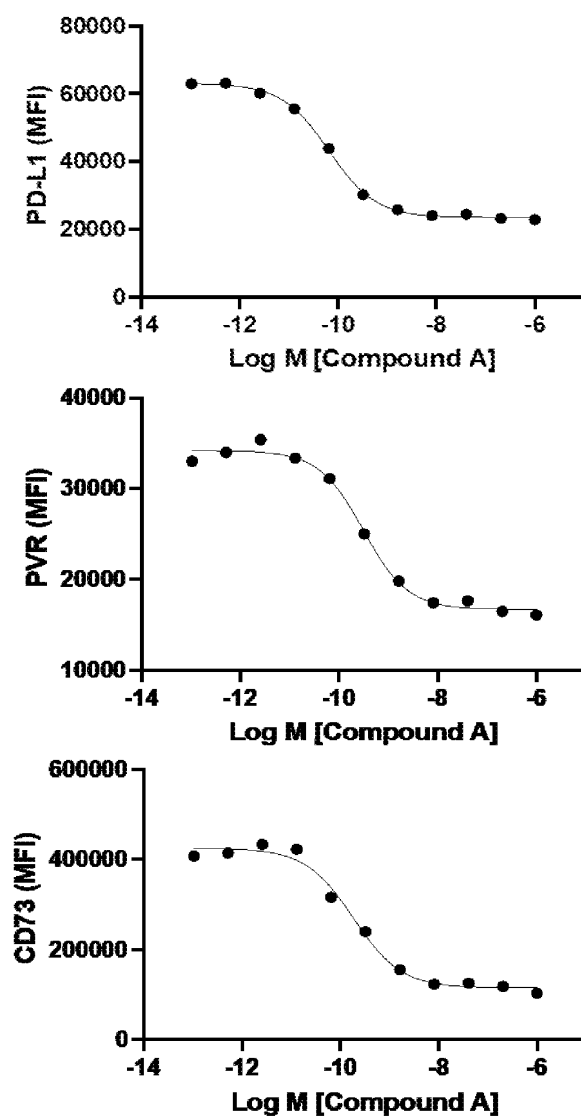


FIG. 5B

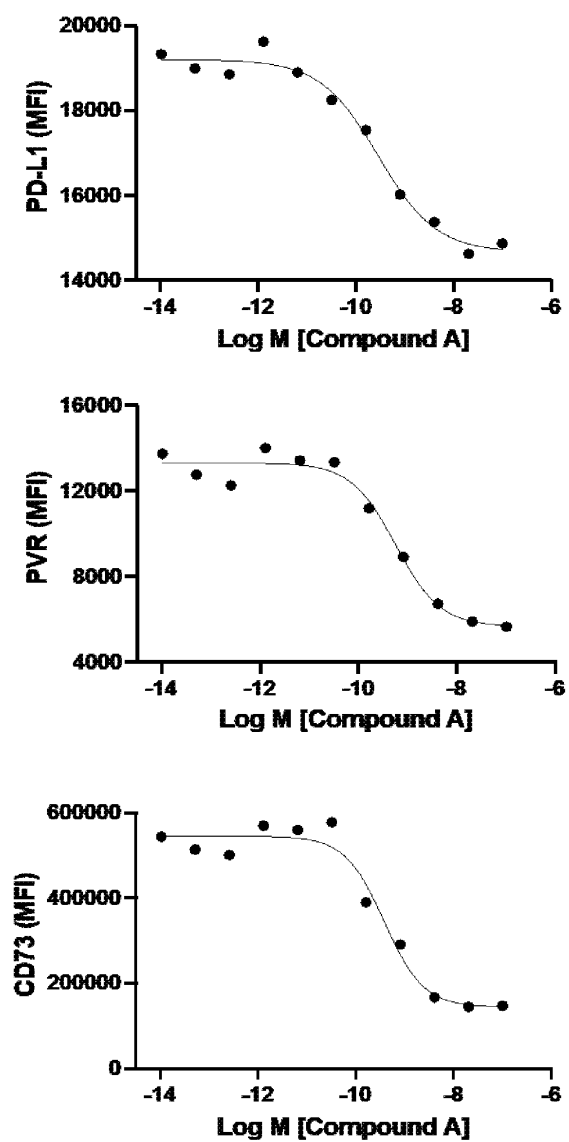


FIG. 5C

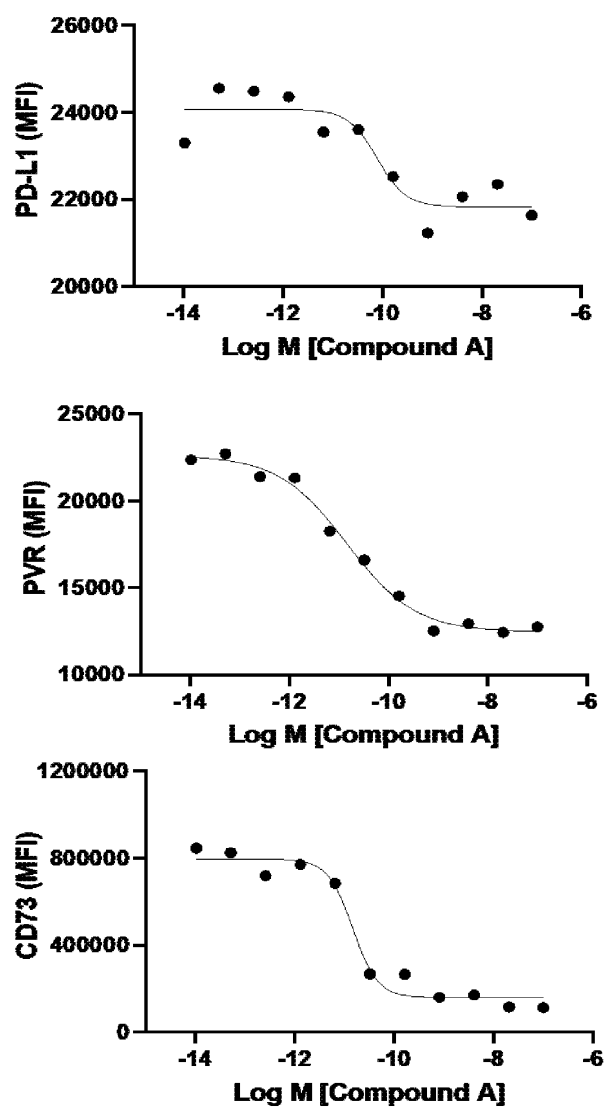


FIG. 6A

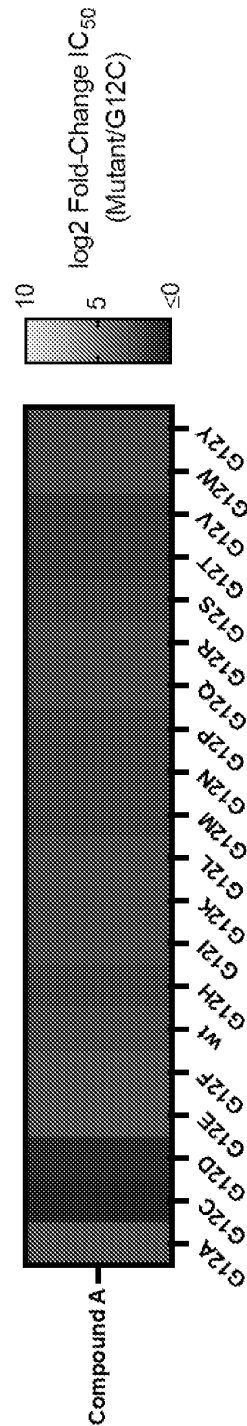


FIG. 6B

|            |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |
|------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|            | G12A | G12C | G12D | G12E | G12F | wt   | G12H | G12I | G12J | G12K | G12L | G12M | G12N | G12O | G12P | G12Q | G12R | G12S | G12T | G12V | G12W | G12X | G12Y |
| Compound A | 1.72 | 0.00 | 0.23 | 1.62 | 1.60 | 1.44 | 1.02 | 1.20 | 1.47 | 1.40 | 0.87 | 0.88 | 1.00 | 1.04 | 1.33 | 1.39 | 0.78 | 1.04 | 0.78 | 0.70 | 1.39 | 1.39 | 1.54 |

FIG. 7A

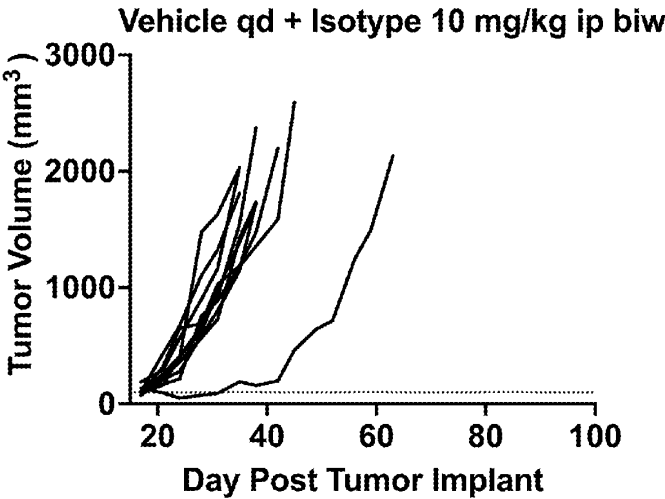


FIG. 7B

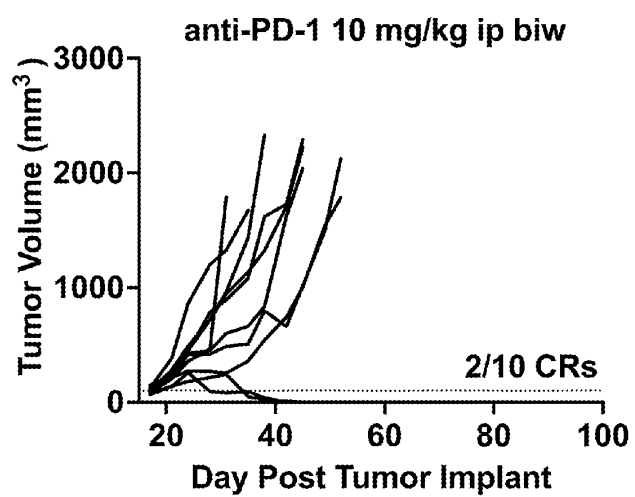


FIG. 7C

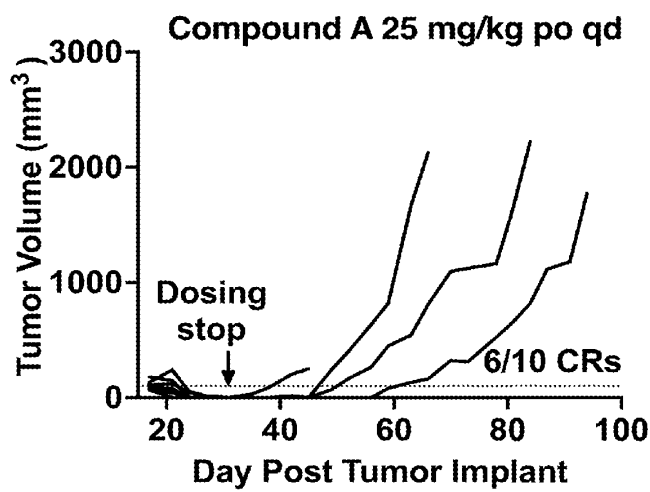


FIG. 7D

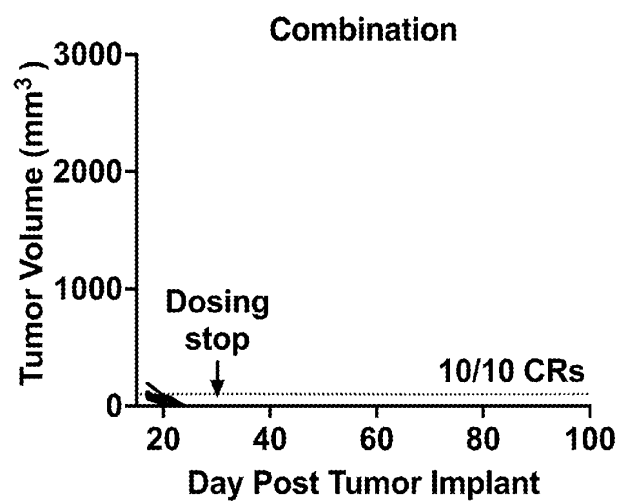


FIG. 8

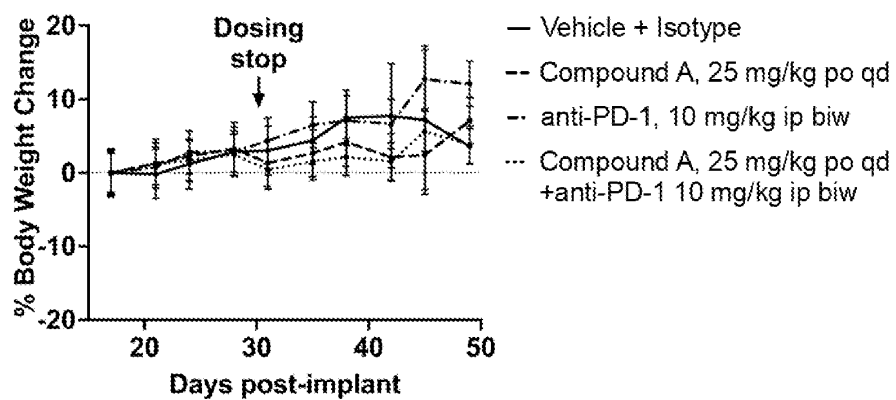


FIG. 9A

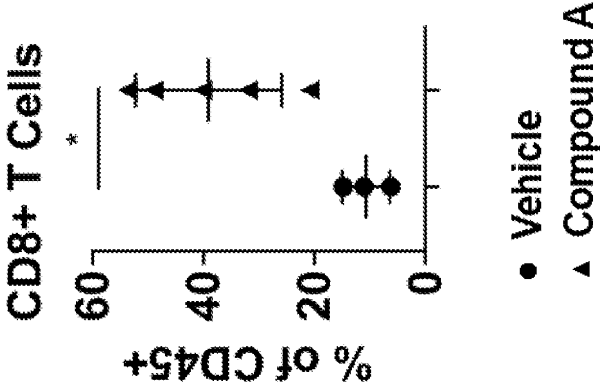


FIG. 9B

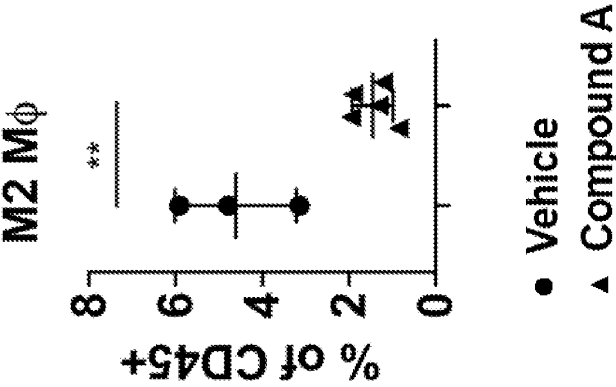


FIG. 9C

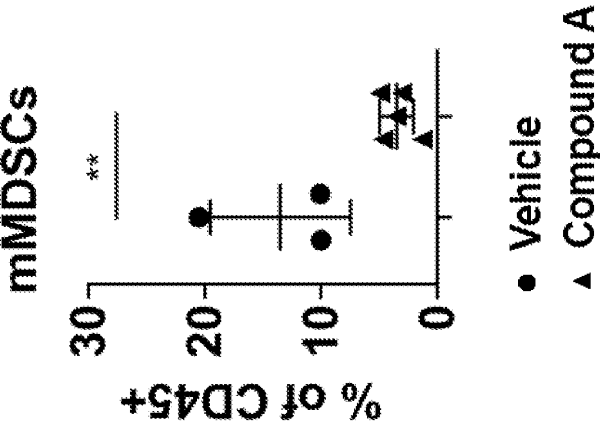


FIG. 10A

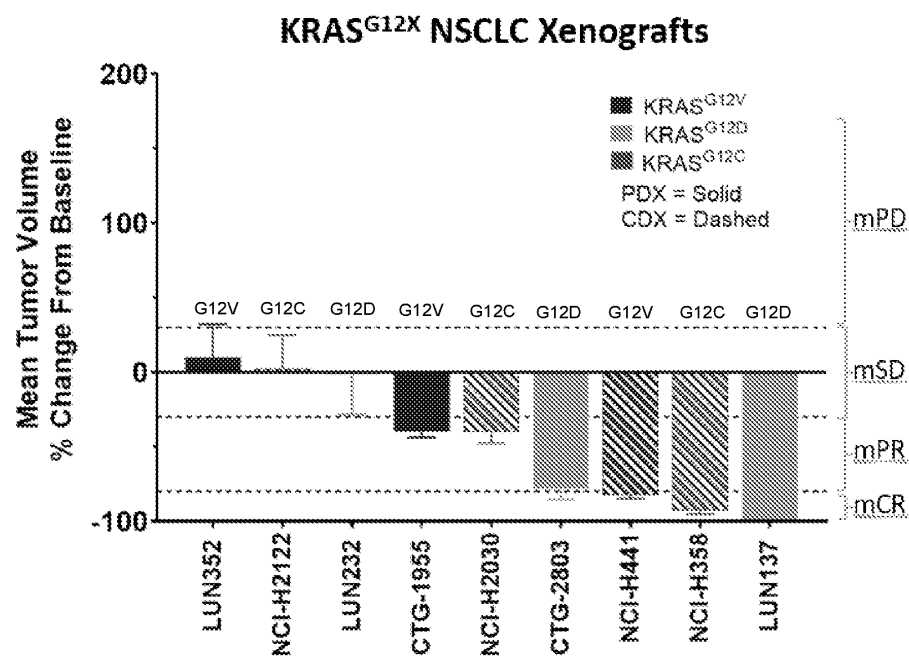


FIG. 10B

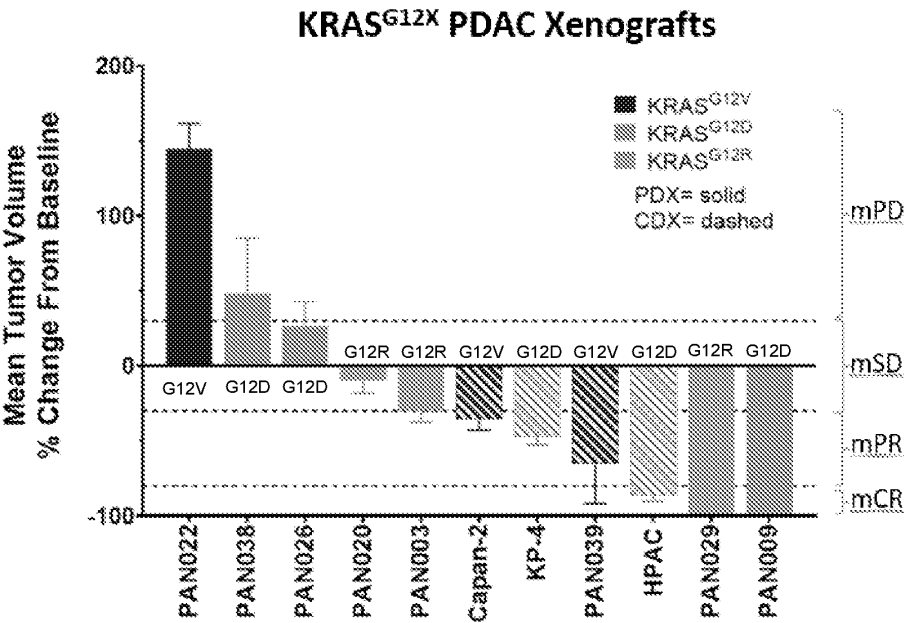


FIG. 11

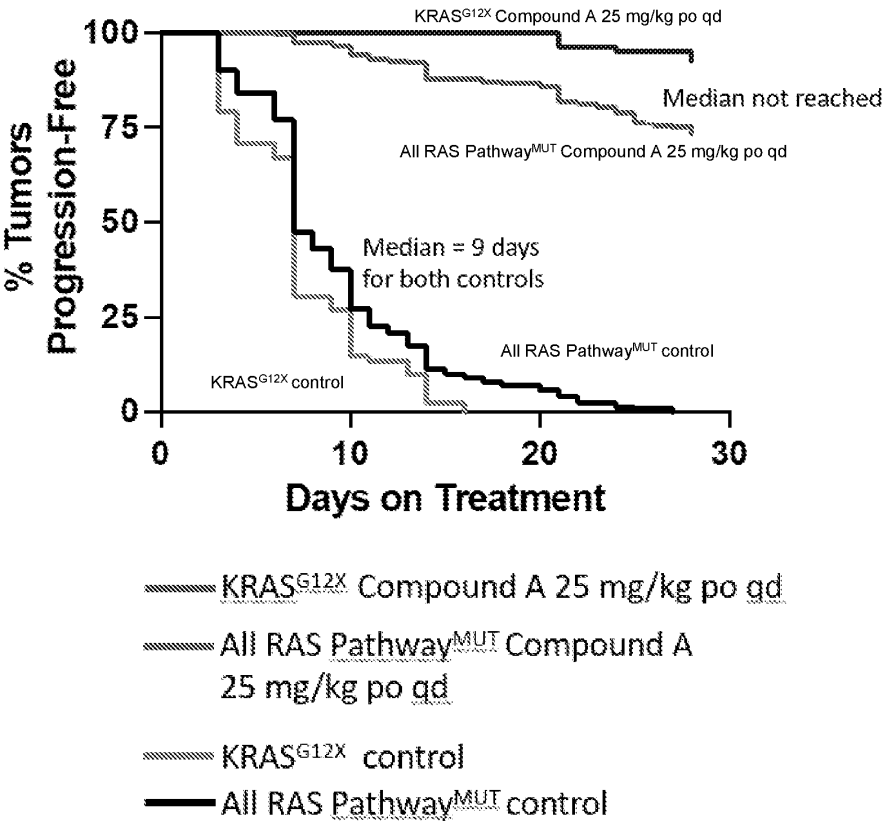


FIG. 12A

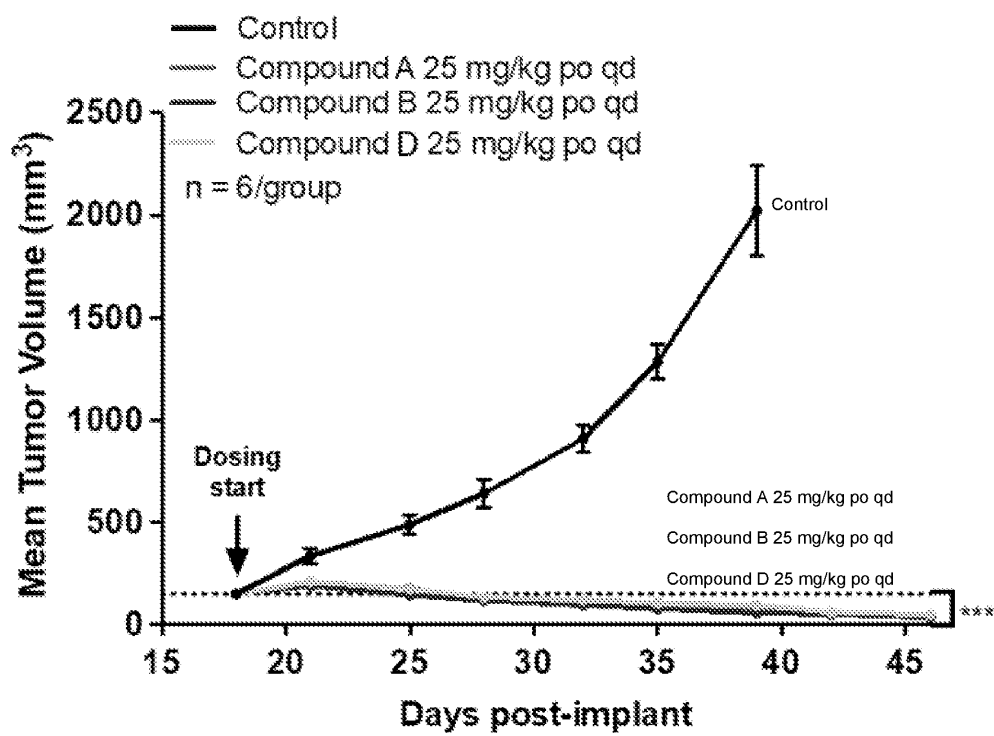


FIG. 12B

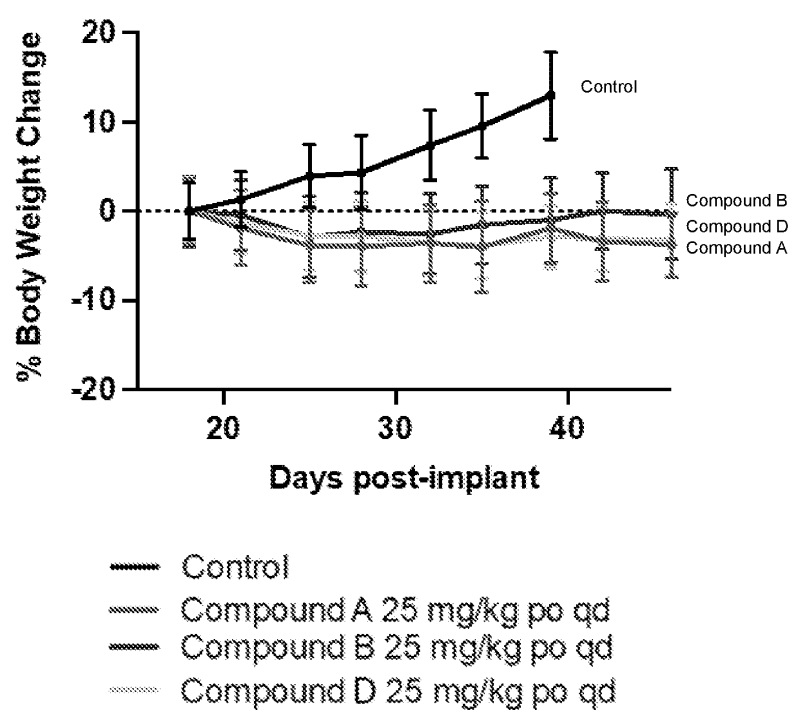


FIG. 12C

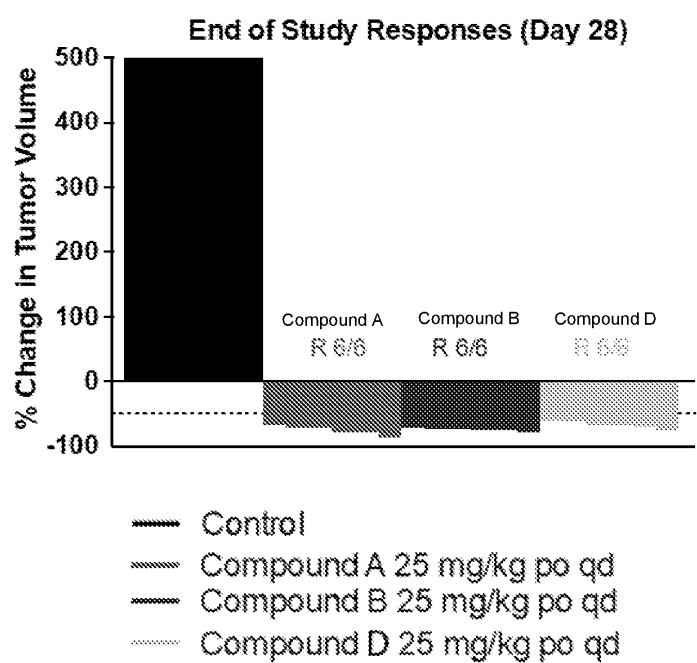


FIG. 13A

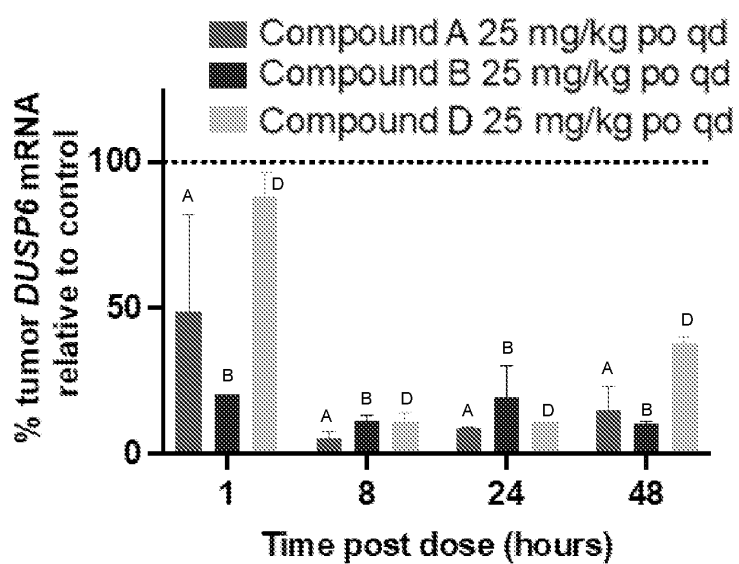


FIG. 13B

