

FIG. 1

SUBSTITUTE SHEET (RULE 26)

|                |                                                                                                                            |     |
|----------------|----------------------------------------------------------------------------------------------------------------------------|-----|
| 48. 6-HC-WT    | .....                                                                                                                      | 10  |
| 48. 6-HC-F029E | EVQLQQSGPELVKPGASVKLSCKTSGYTFTETVTHHWKQSHRKKSILEWIGGINTNNGSTGYNOKFKKATITVVKSSSTAYMELRSLTSDSAVYFCARGSLYSYGNSTFYDYGQGLTATVSS | 120 |
| 48. 6-HC-F032D | .....E.....                                                                                                                | 110 |
| 48. 6-HC-F033C | .....D.....                                                                                                                | 100 |
| 48. 6-HC-M034D | .....C.....                                                                                                                | 90  |
| 48. 6-HC-M034E | .....D.....                                                                                                                | 80  |
| 48. 6-HC-M034Y | .....E.....                                                                                                                | 70  |
| 48. 6-HC-G050S | .....Y.....                                                                                                                | 60  |
| 48. 6-HC-F051E | .....S.....                                                                                                                | 50  |
| 48. 6-HC-N052C | .....E.....                                                                                                                | 40  |
| 48. 6-HC-N052L | .....C.....                                                                                                                | 30  |
| 48. 6-HC-N052V | .....L.....                                                                                                                | 20  |
| 48. 6-HC-F053D | .....V.....                                                                                                                | 10  |
| 48. 6-HC-F053E | .....D.....                                                                                                                |     |
| 48. 6-HC-A097I | .....E.....                                                                                                                |     |
| 48. 6-HC-A097M | .....I.....                                                                                                                |     |
| 48. 6-HC-A097S | .....M.....                                                                                                                |     |
| 48. 6-HC-A097T | .....S.....                                                                                                                |     |
| 48. 6-HC-R098H | .....T.....                                                                                                                |     |
| 48. 6-HC-R098Q | .....H.....                                                                                                                |     |
| 48. 6-HC-G099E | .....Q.....                                                                                                                |     |
| 48. 6-HC-L101F | .....E.....                                                                                                                |     |
| 48. 6-HC-S103G | .....F.....                                                                                                                |     |
| 48. 6-HC-G105D | .....G.....                                                                                                                |     |
| 48. 6-HC-N106E | .....D.....                                                                                                                |     |
| 48. 6-HC-D110L | .....E.....                                                                                                                |     |
| 48. 6-HC-Y111C | .....L.....                                                                                                                |     |
| 48. 6-HC-Y111F | .....C.....                                                                                                                |     |
| 48. 6-HC-W112L | .....T.....                                                                                                                |     |
|                | .....L.....                                                                                                                |     |

FIG. 2B



|                |                                                                                                             |       |       |       |       |       |       |       |       |       |       |
|----------------|-------------------------------------------------------------------------------------------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| 48. 6-LC-WT    | QIVLFTQSPALMSASPGKVTITNCSATSSVSVMHWFQKPCCTSPKLIYCTSNLASGVDPARFSCSCSCSTSYSLTISRMEADAATYYCQQRSSYPFTFCQCTKVEIK | 10    | 20    | 30    | 40    | 50    | 60    | 70    | 80    | 90    | 100   |
| 48. 6-LC-V029E | .....                                                                                                       | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... |
| 48. 6-LC-S030D | .....                                                                                                       | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... |
| 48. 6-LC-Y031C | .....                                                                                                       | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... |
| 48. 6-LC-Y031D | .....                                                                                                       | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... |
| 48. 6-LC-H033G | .....                                                                                                       | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... |
| 48. 6-LC-H033L | .....                                                                                                       | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... |
| 48. 6-LC-G049C | .....                                                                                                       | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... |
| 48. 6-LC-G049H | .....                                                                                                       | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... |
| 48. 6-LC-G049P | .....                                                                                                       | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... |
| 48. 6-LC-Q089E | .....                                                                                                       | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... |
| 48. 6-LC-R090H | .....                                                                                                       | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... |
| 48. 6-LC-S092D | .....                                                                                                       | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... |
| 48. 6-LC-S092G | .....                                                                                                       | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... |
| 48. 6-LC-S092I | .....                                                                                                       | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... |
| 48. 6-LC-S092Q | .....                                                                                                       | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... |
| 48. 6-LC-S092V | .....                                                                                                       | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... |
| 48. 6-LC-T096D | .....                                                                                                       | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... |
| 48. 6-LC-F097D | .....                                                                                                       | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... |
| 48. 6-LC-F097E | .....                                                                                                       | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... |

FIG. 3B

6 / 21

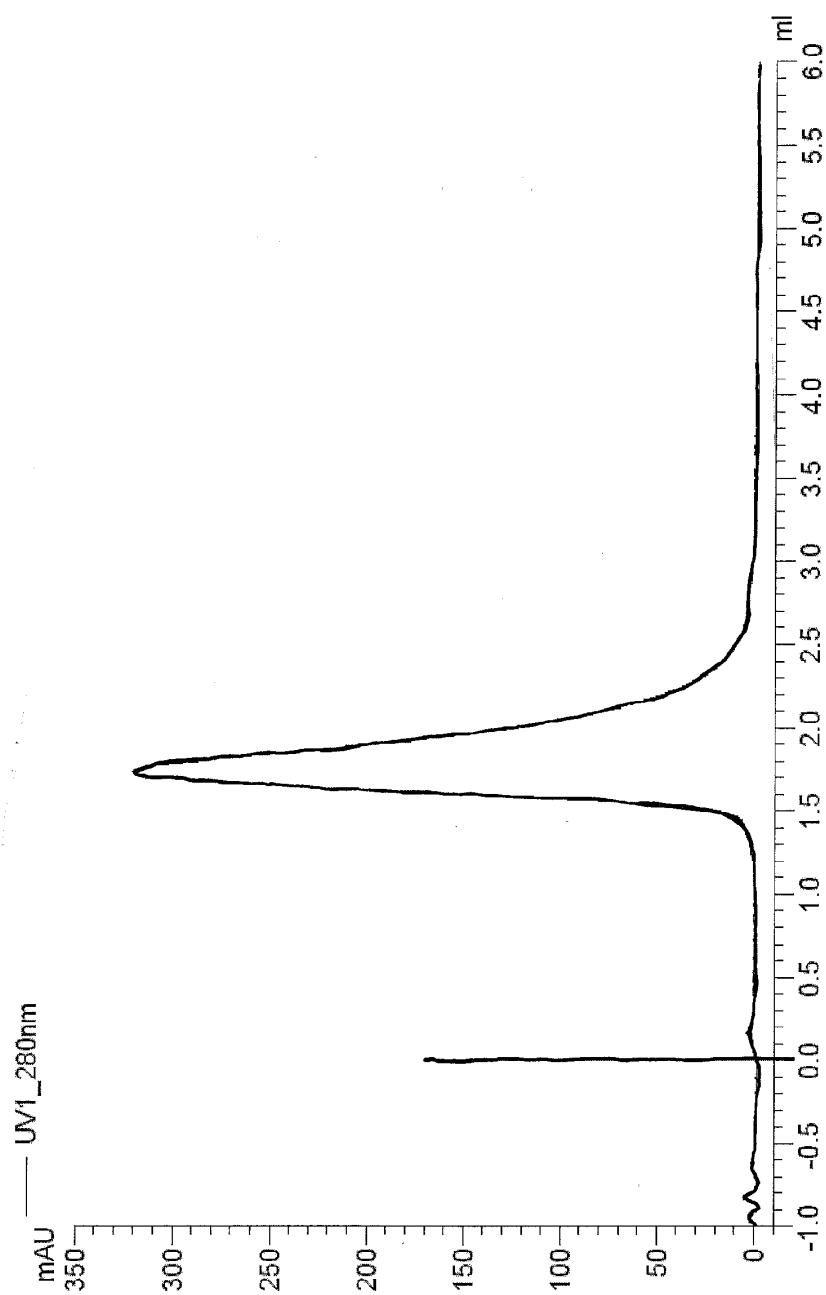
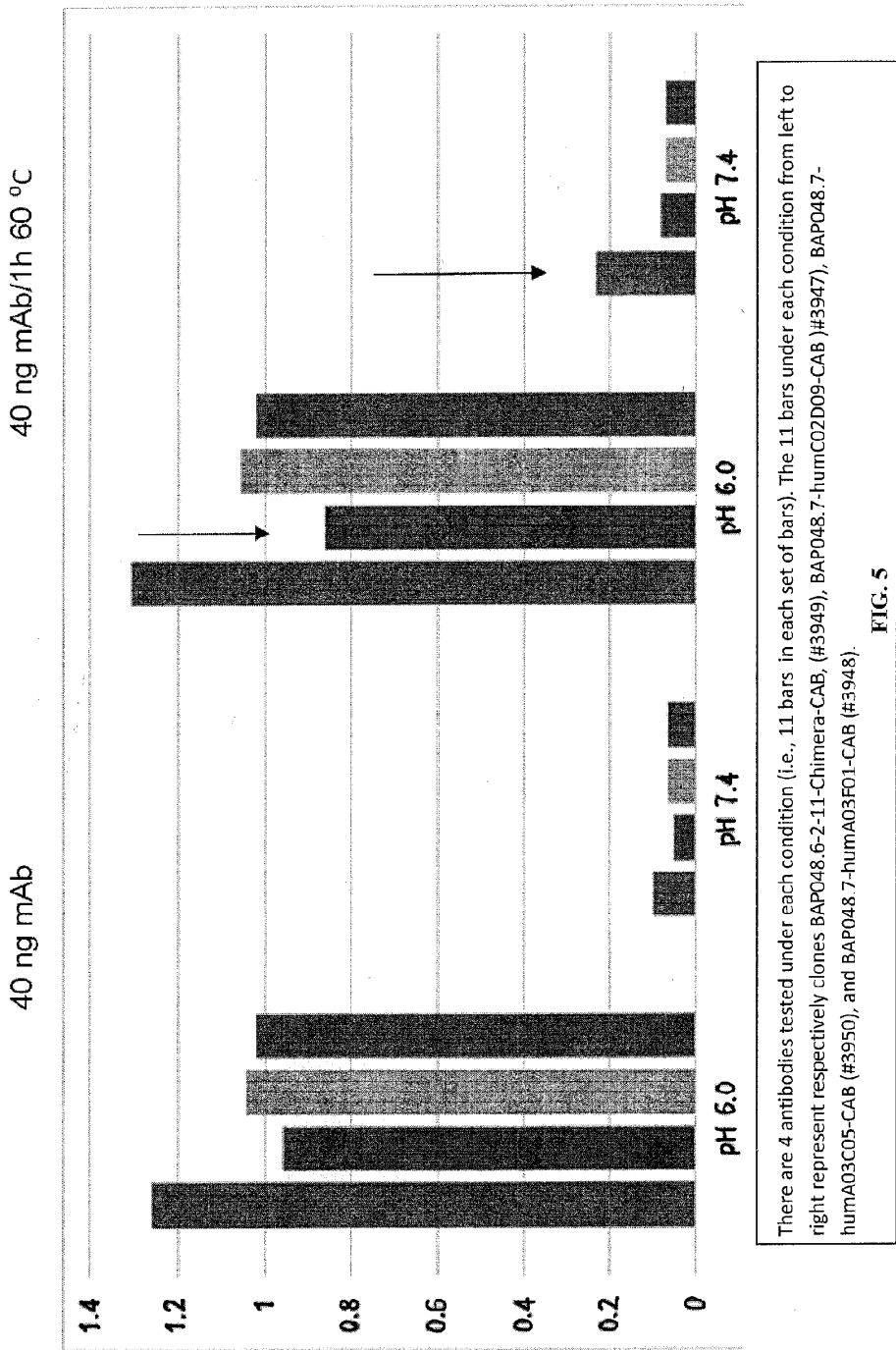


FIG. 4



Tumor environment (pH6.0)

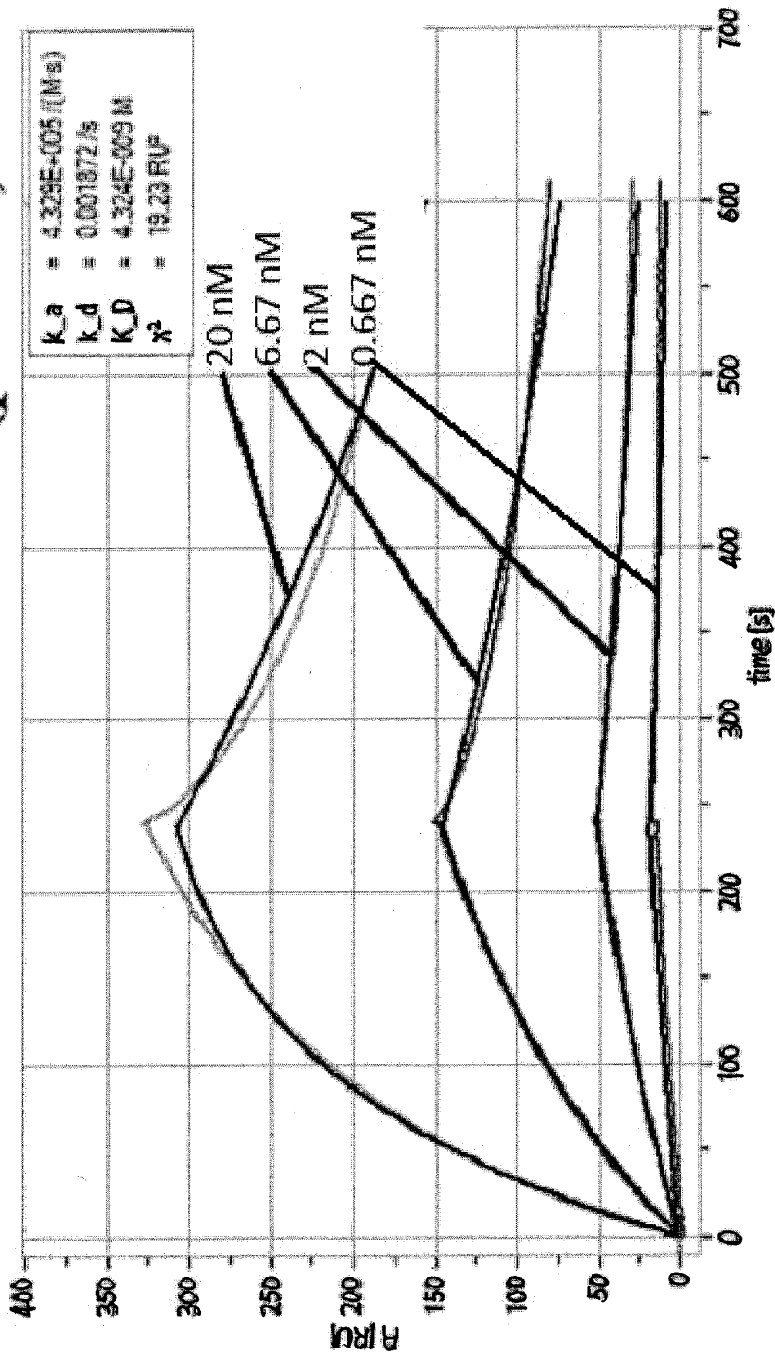


FIG. 6A

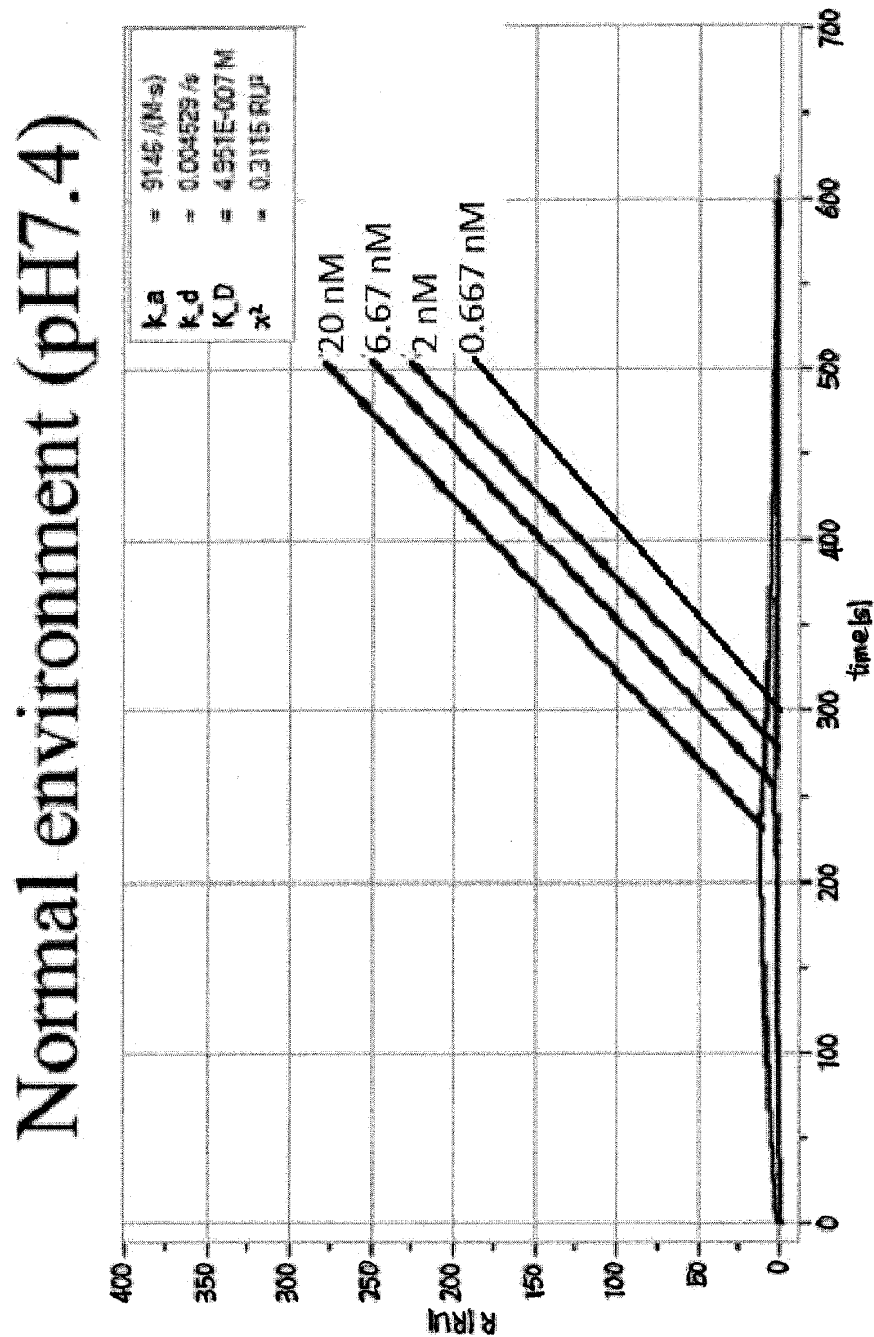


FIG. 6B

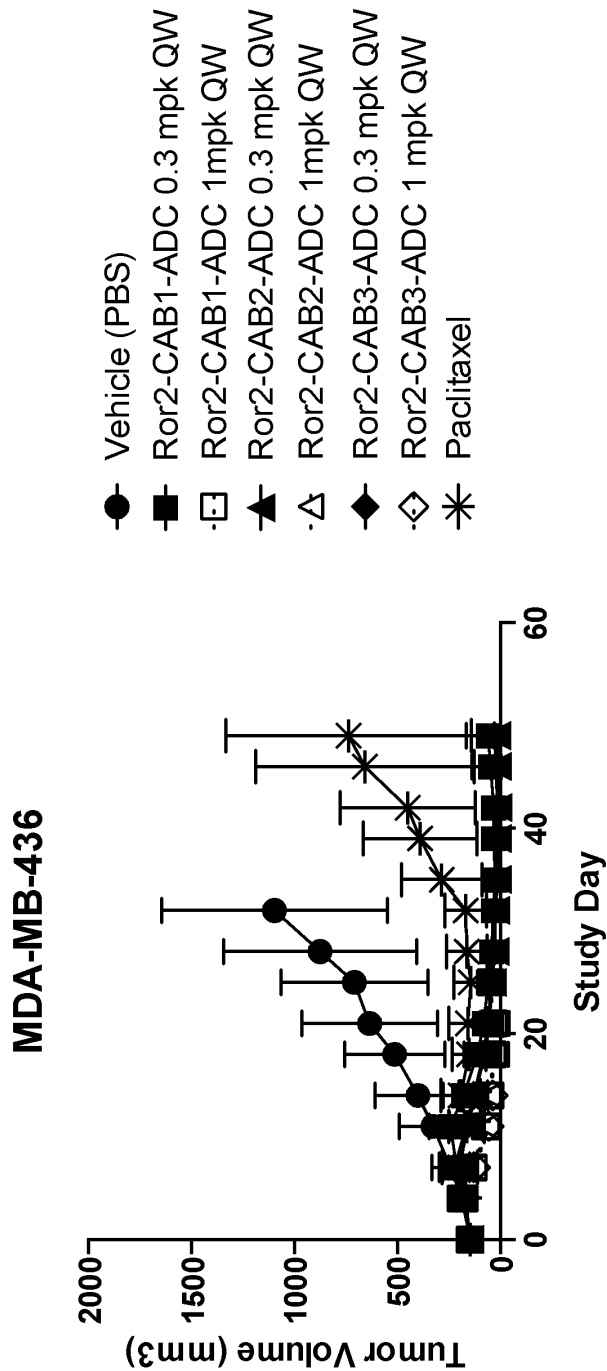


FIG. 7A

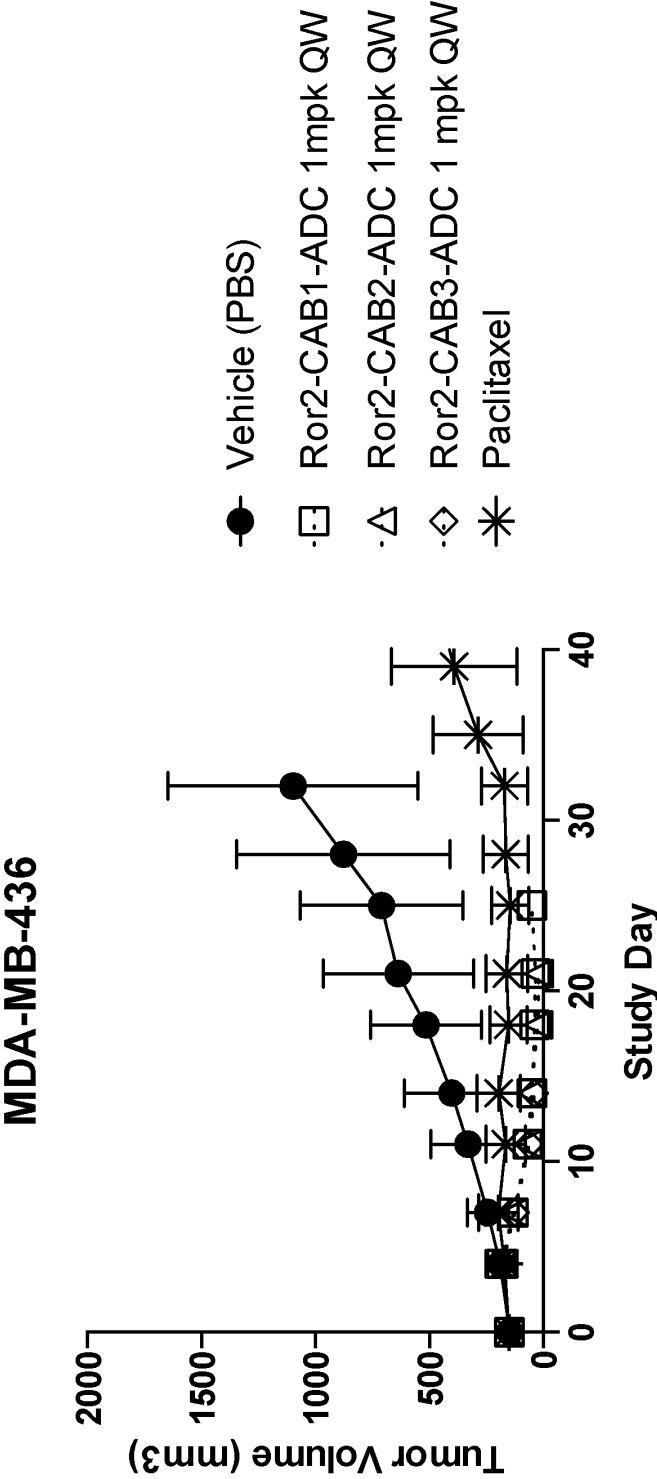


FIG. 7B

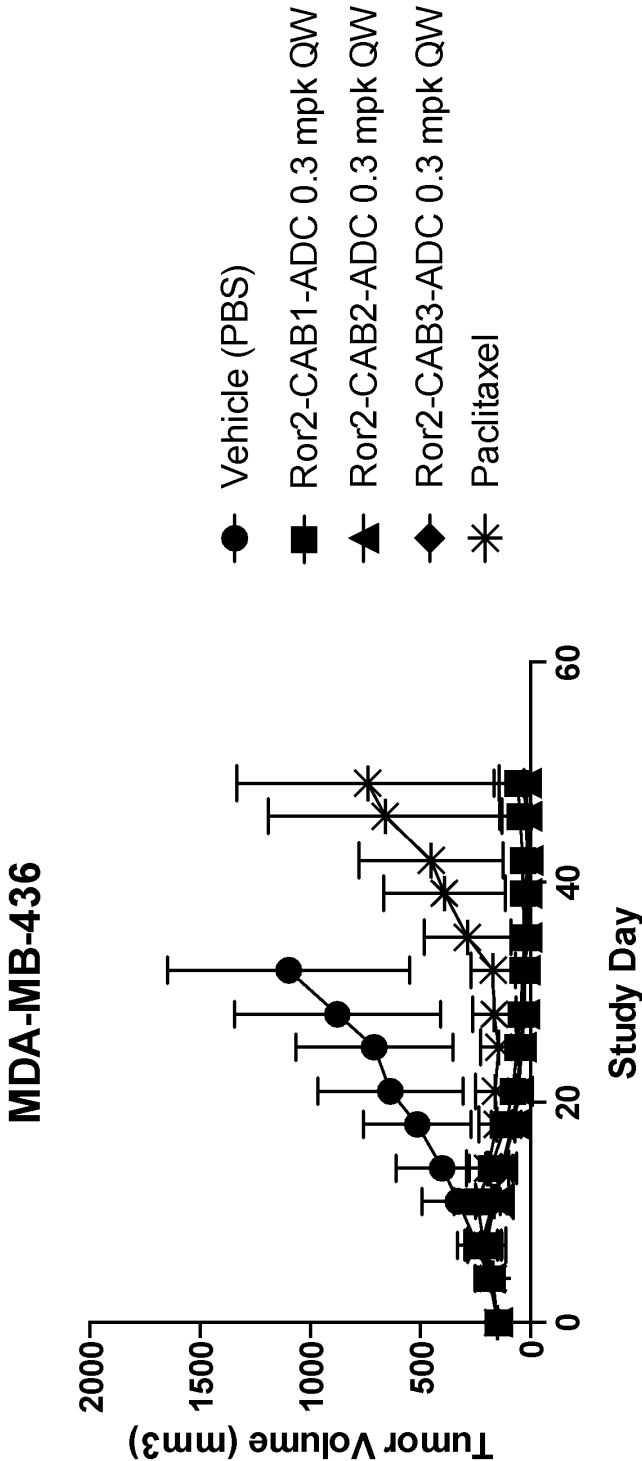
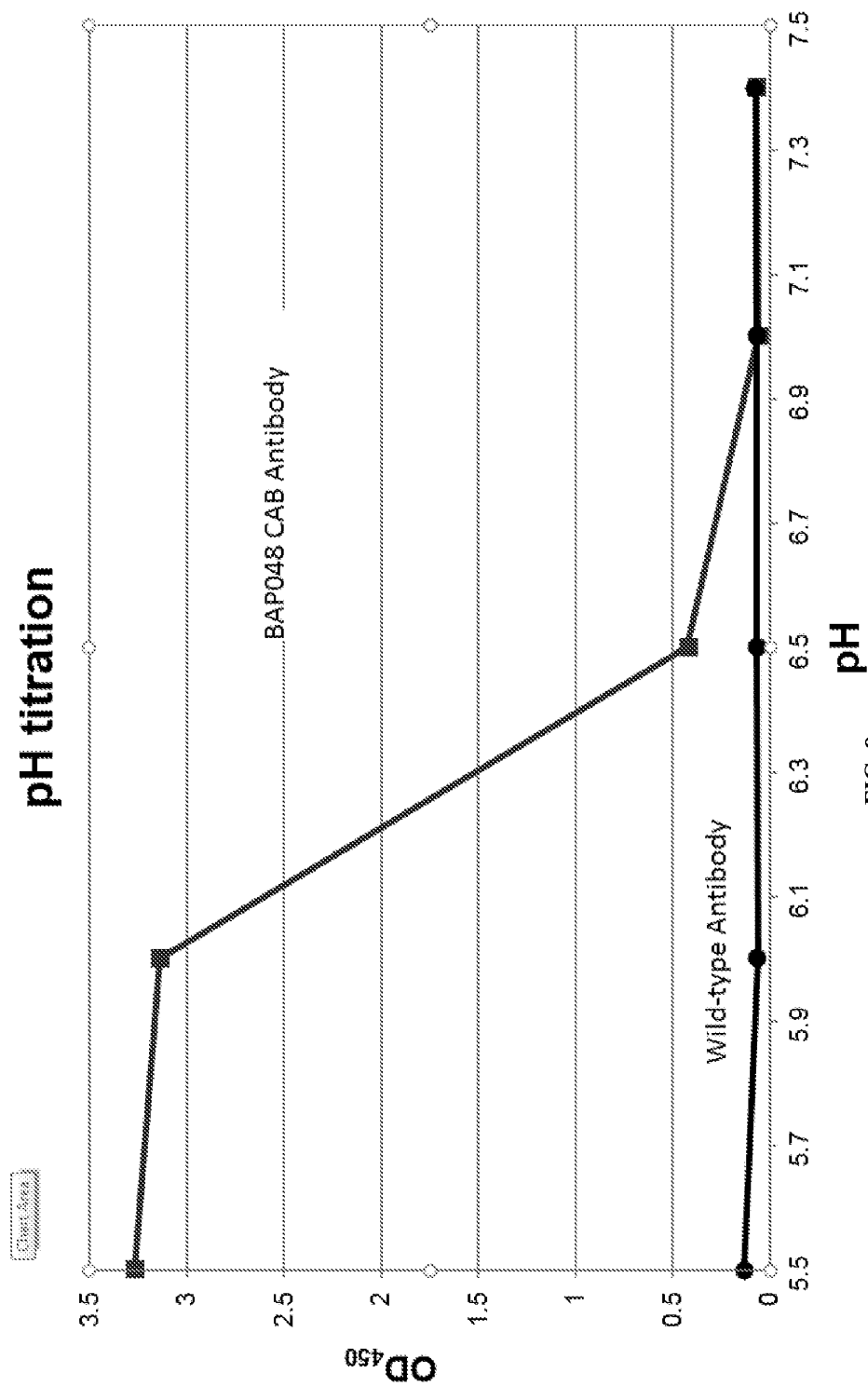


FIG. 7C



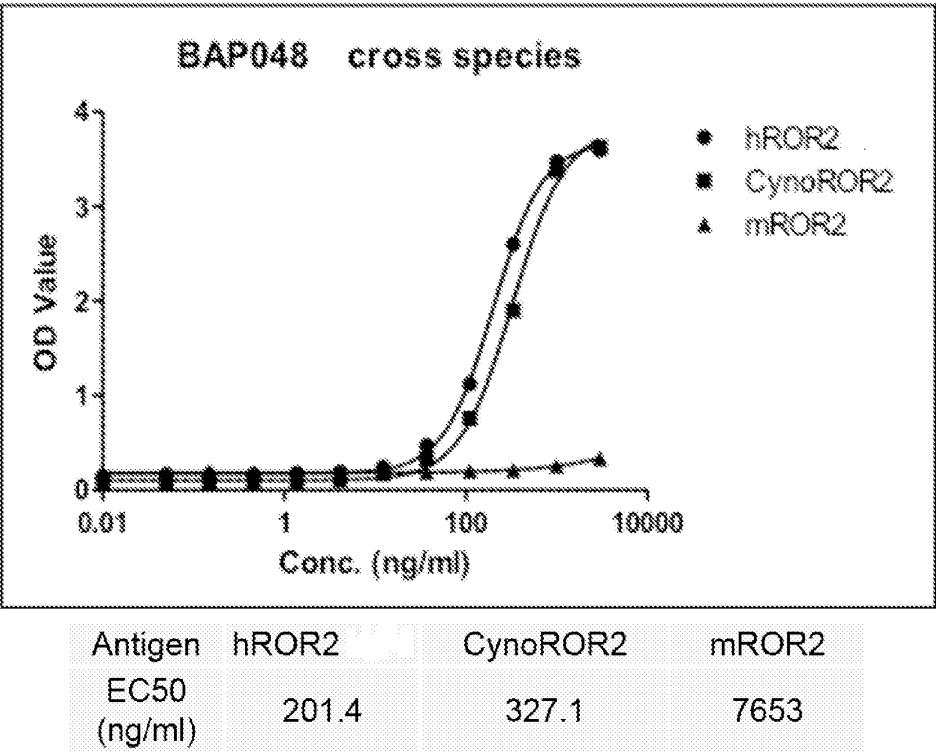


FIG. 9

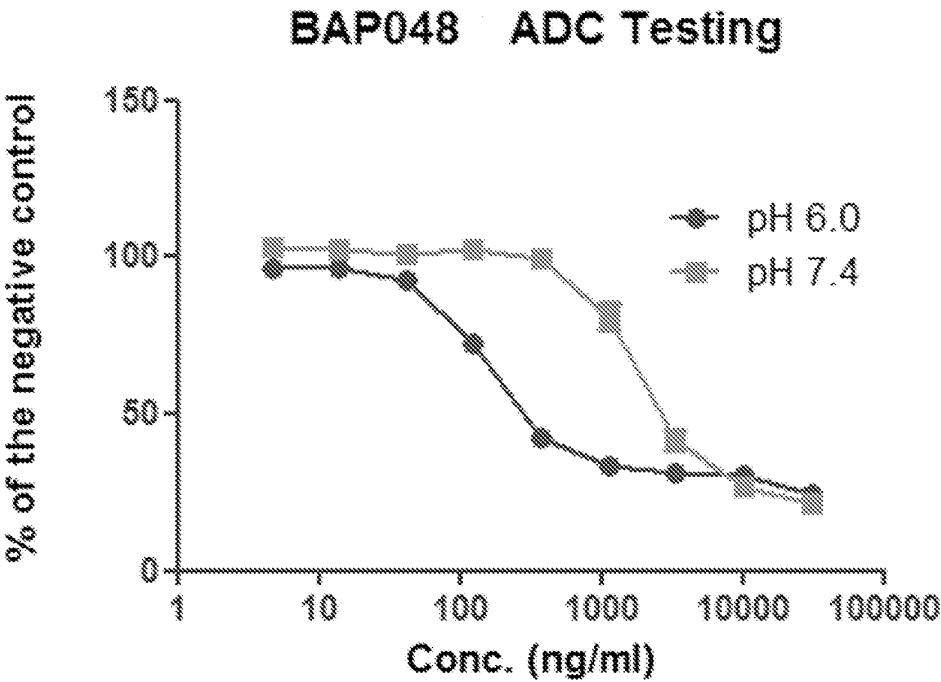


FIG. 10

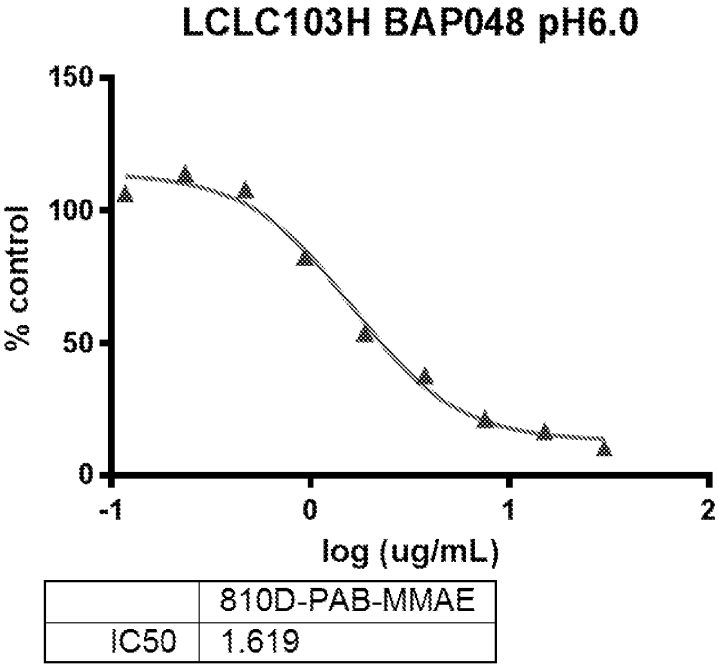


FIG. 11A

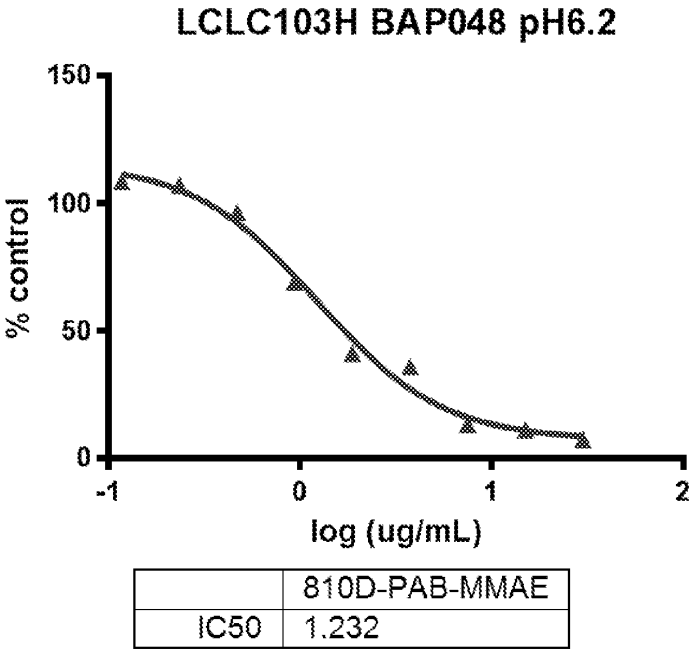


FIG. 11B

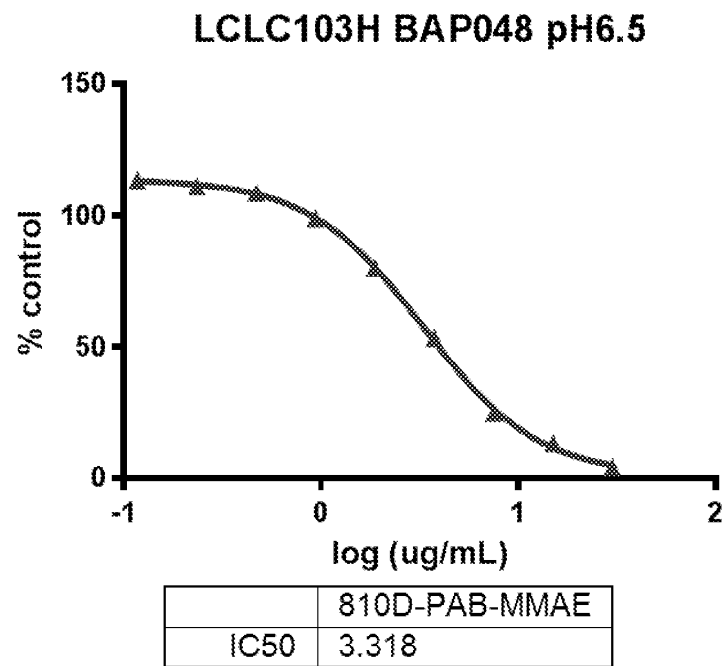


FIG. 11C

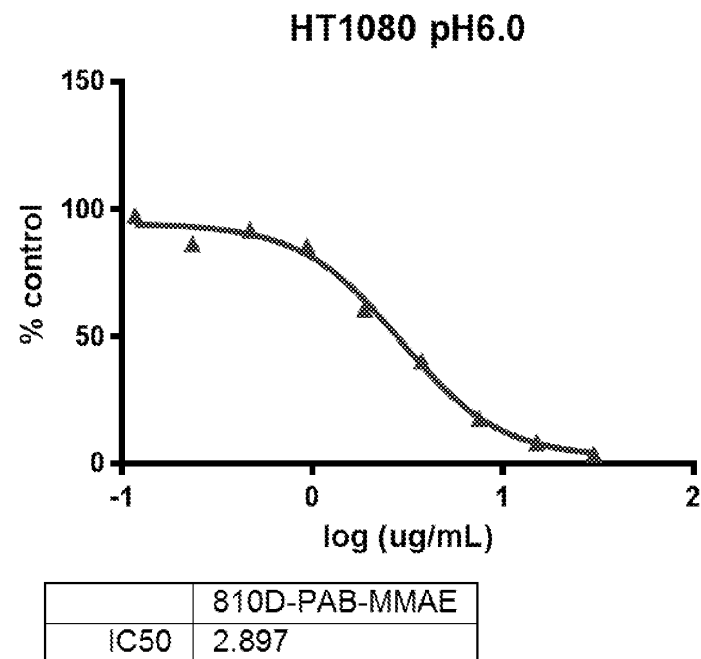


FIG. 12A

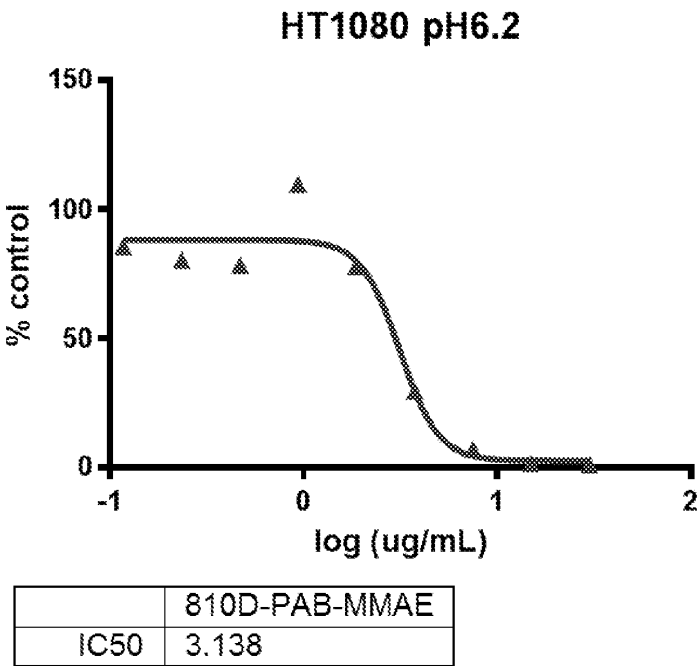


FIG. 12B

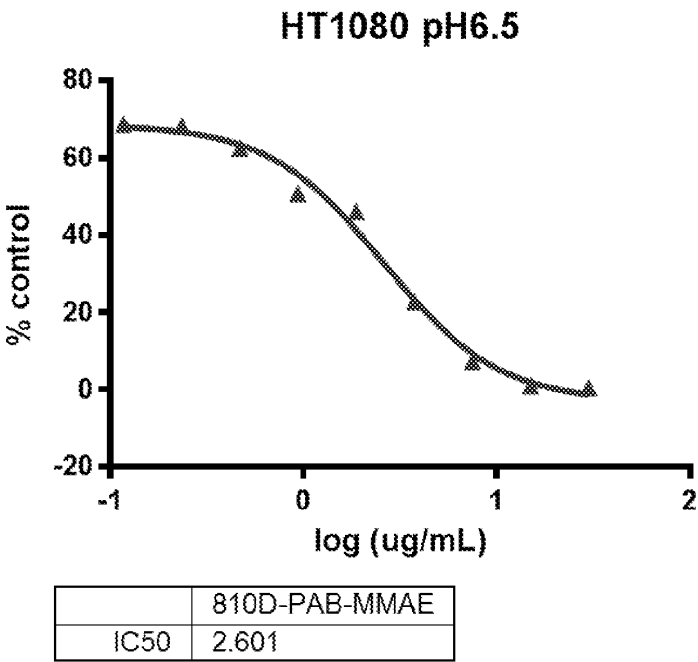


FIG. 12C

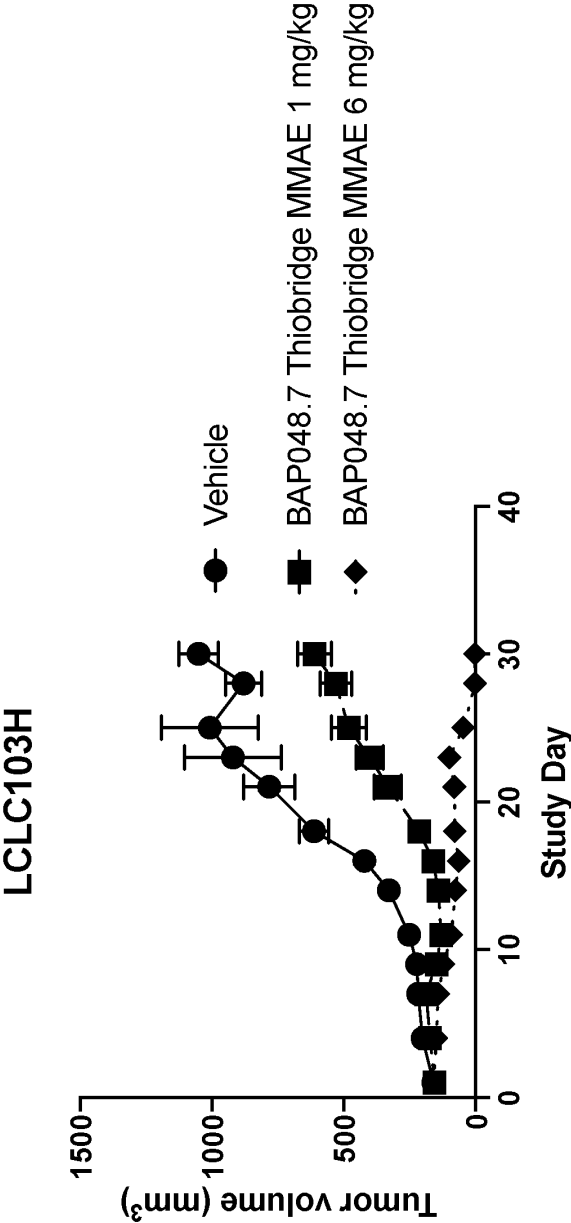


FIG. 13

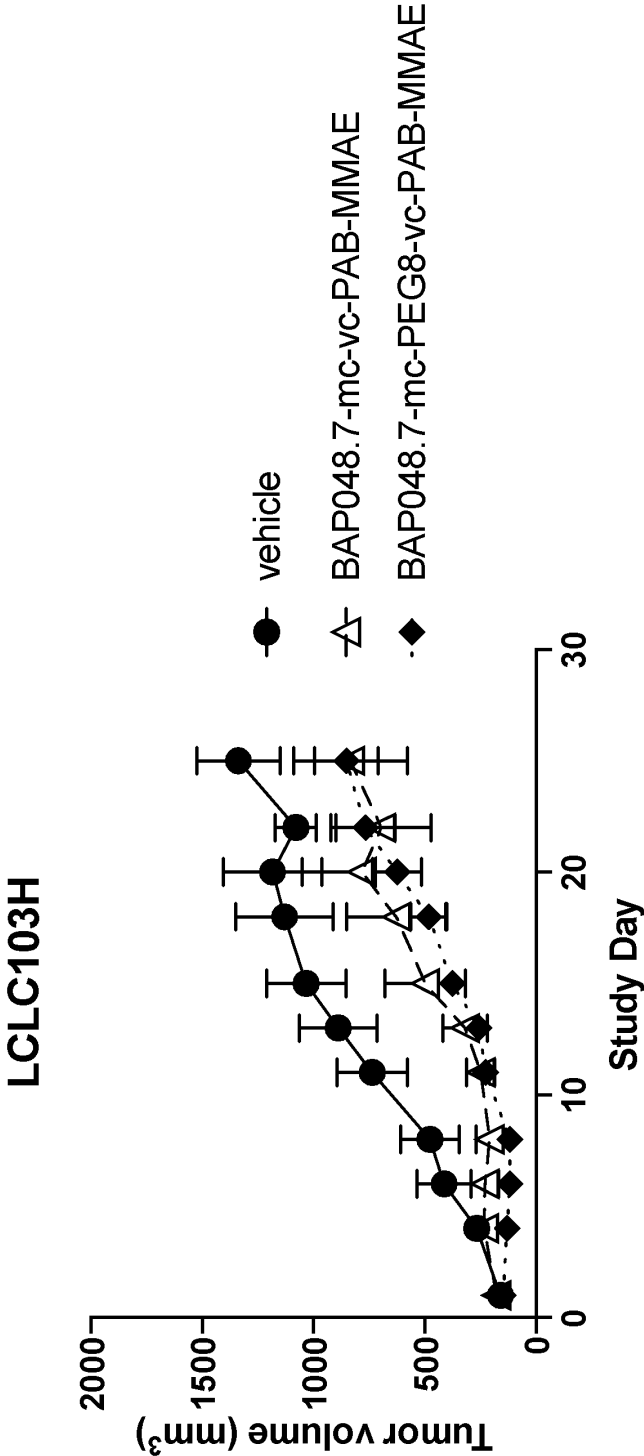


FIG. 14

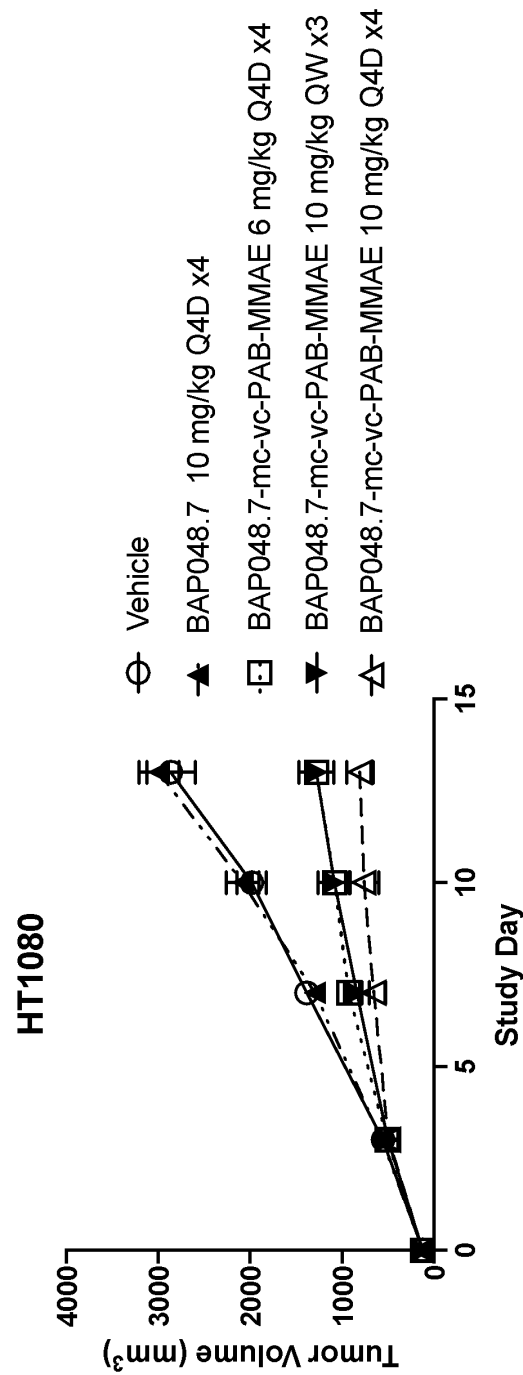


FIG. 15A

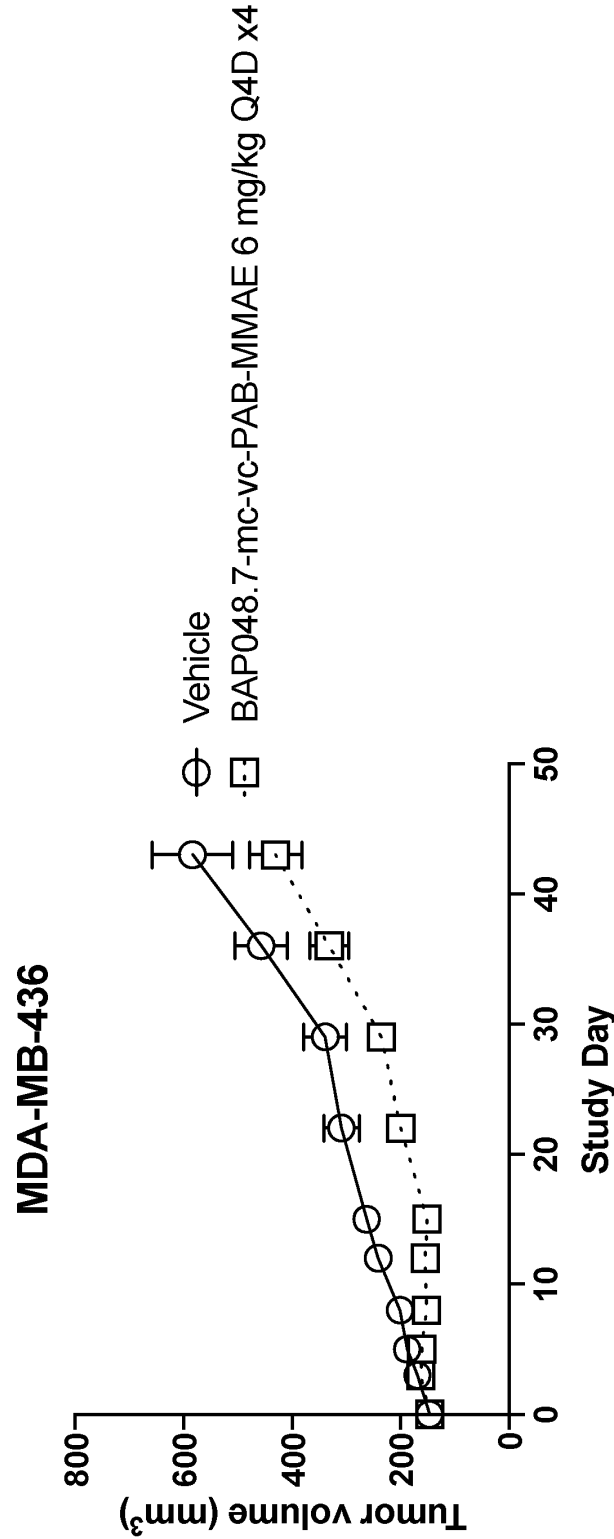


FIG. 15B