

FIG. 1a

Compd	Hsp90a (μ M)	Hsp90 β (μ M)	Grp94 (μ M)	Trap-1 (μ M)
PU-H3	>300	>300	1.83 $\pm$ 0.47	13.8 $\pm$ 1.8
PU-H54	>250	>250	11.77 $\pm$ 3.24	54.1 $\pm$ 4.6
PU-H39	>300	>300	0.12 $\pm$ 0.04	145.4 $\pm$ 13.4
PU-H38	>500	>500	2.37 $\pm$ 0.79	9.6 $\pm$ 0.8
PU-H4	>300	>300	11.45 $\pm$ 0.92	157.9 $\pm$ 9.7
PU-H40	>500	>500	0.26 $\pm$ 0.01	83.6 $\pm$ 11.8
PU-H27	>300	>300	1.14 $\pm$ 0.14	203.7 $\pm$ 11.0
PU-H42	60.4 $\pm$ 3.6	>100	0.53 $\pm$ 0.10	5.1 $\pm$ 4.2
PU-W513	27.3 $\pm$ 3.5	41.8 $\pm$ 1.3	0.22 $\pm$ 0.08	7.3 $\pm$ 0.5
PU-H61	>300	>200	0.17 $\pm$ 0.11	78.4 $\pm$ 8.9
PU-H52	112.2 $\pm$ 0.6	>200	2.08 $\pm$ 1.49	19.5 $\pm$ 0.2
PU-H36	>500	>500	2.10 $\pm$ 0.56	65.5 $\pm$ 1.3
PU-H71	0.043 $\pm$ 0.006	0.042 $\pm$ 0.003	0.030 $\pm$ 0.005	0.205 $\pm$ 0.006

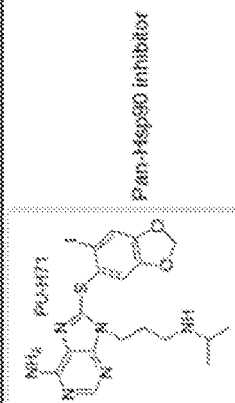


FIG. 1b

Compd	Hsp90α (μM)	Hsp90β (μM)	Grp94 (μM)	Trap-1 (μM)
pu-27	>500	>200	59.30±2.69	>300
pu-34	>500	>250	91.13±2.16	327.3±6.6

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Compd	Grp94:Hsp90 α selectivity	Grp94:Trap-1 selectivity
PU-H3	>100	10
PU-H54	>25	5
PU-H39	>100	>100
PU-H38	>100	4
PU-H4	>100	15
PU-H40	>100	>100
PU-H27	>100	>100
PU-H42	>100	10
PU-WS13	140	35
PU-H51	>100	>100
PU-H52	50	10
PU-H36	>100	35
PU-27	>10	>10
PU-34	>10	3

FIG. 1c

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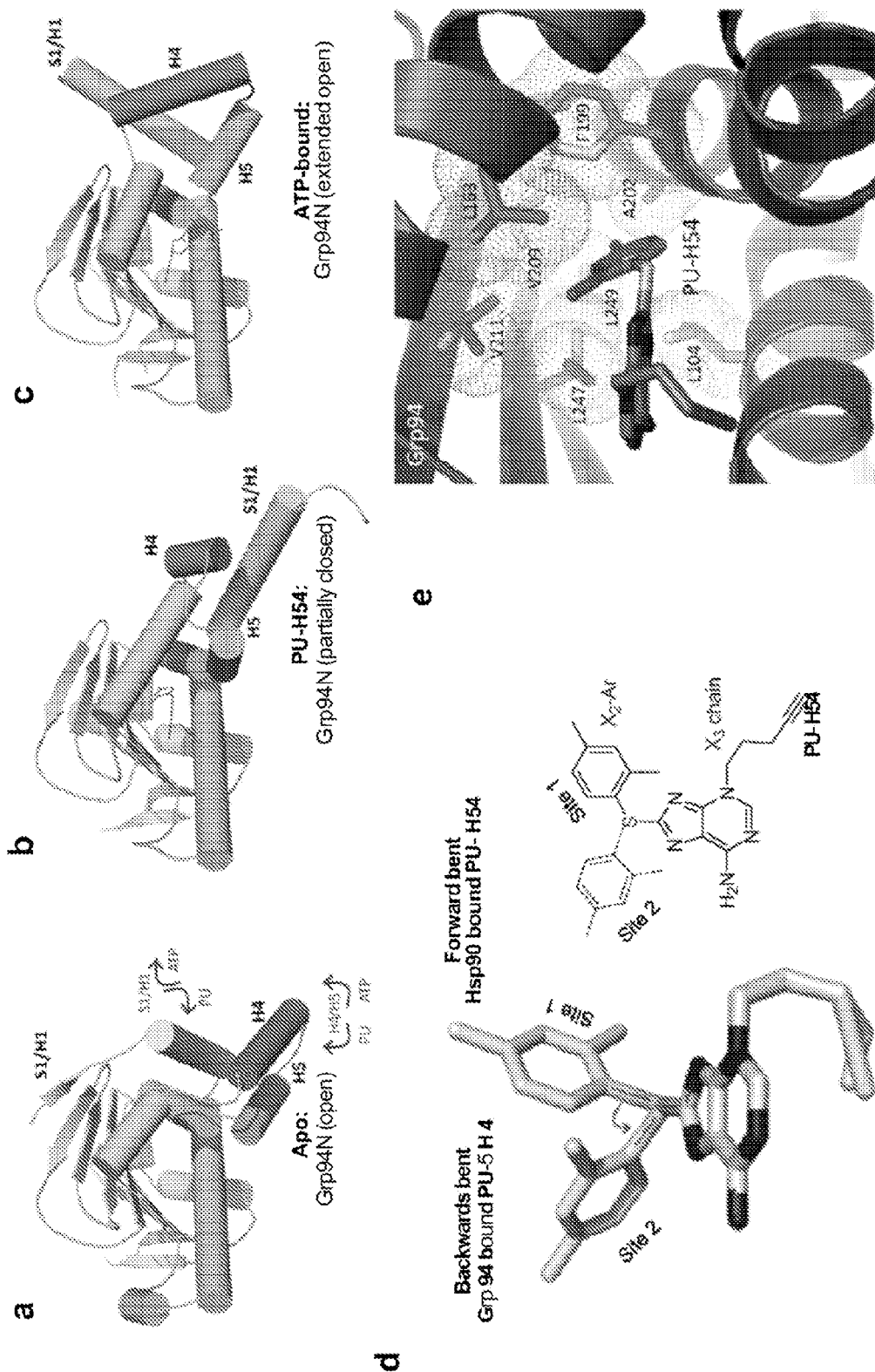


FIG. 2

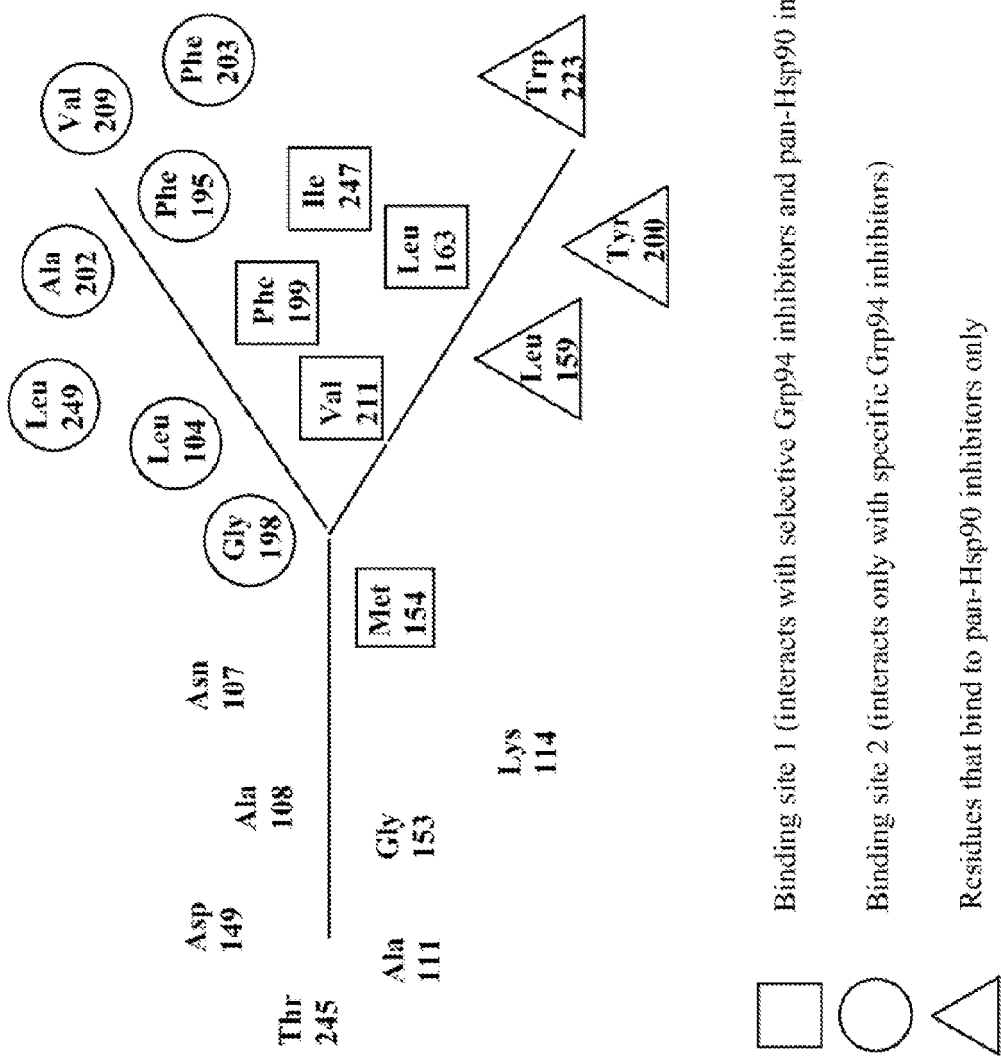


FIG. 2f

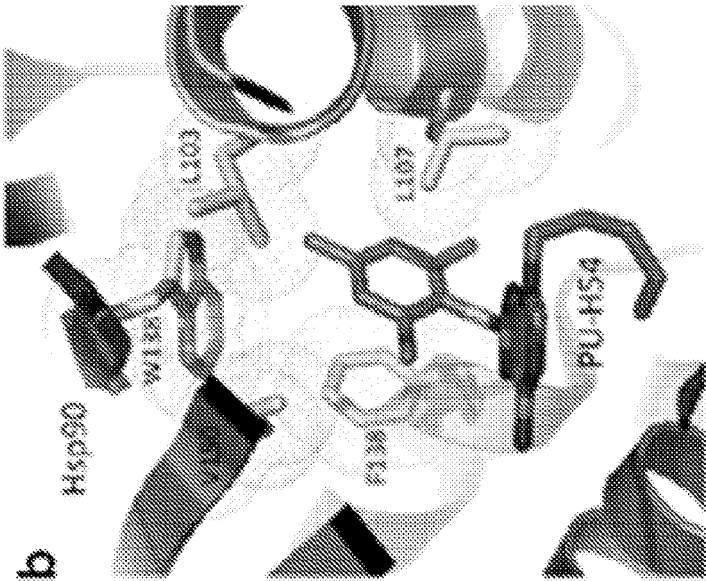
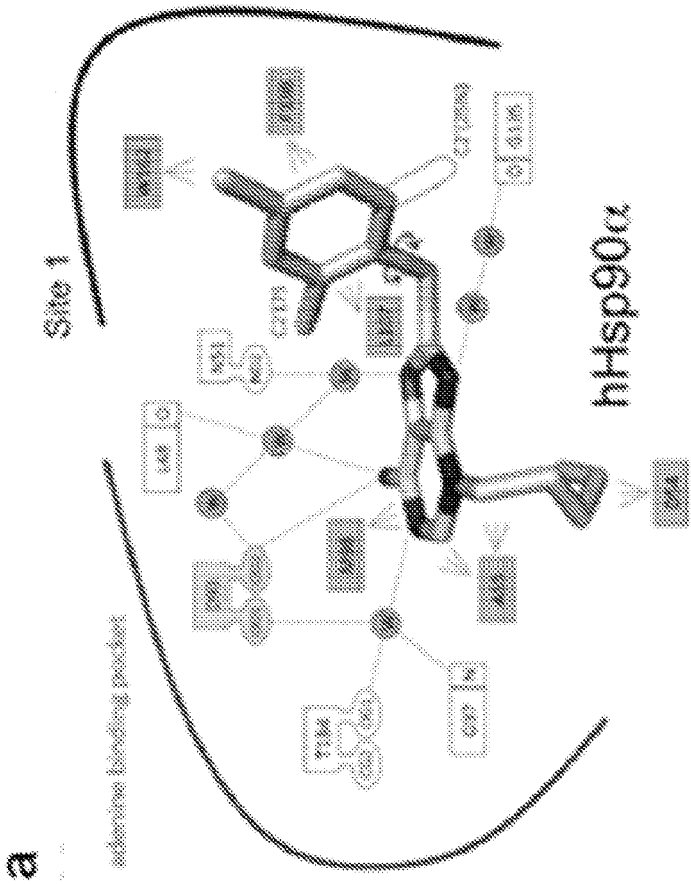


FIG. 3b



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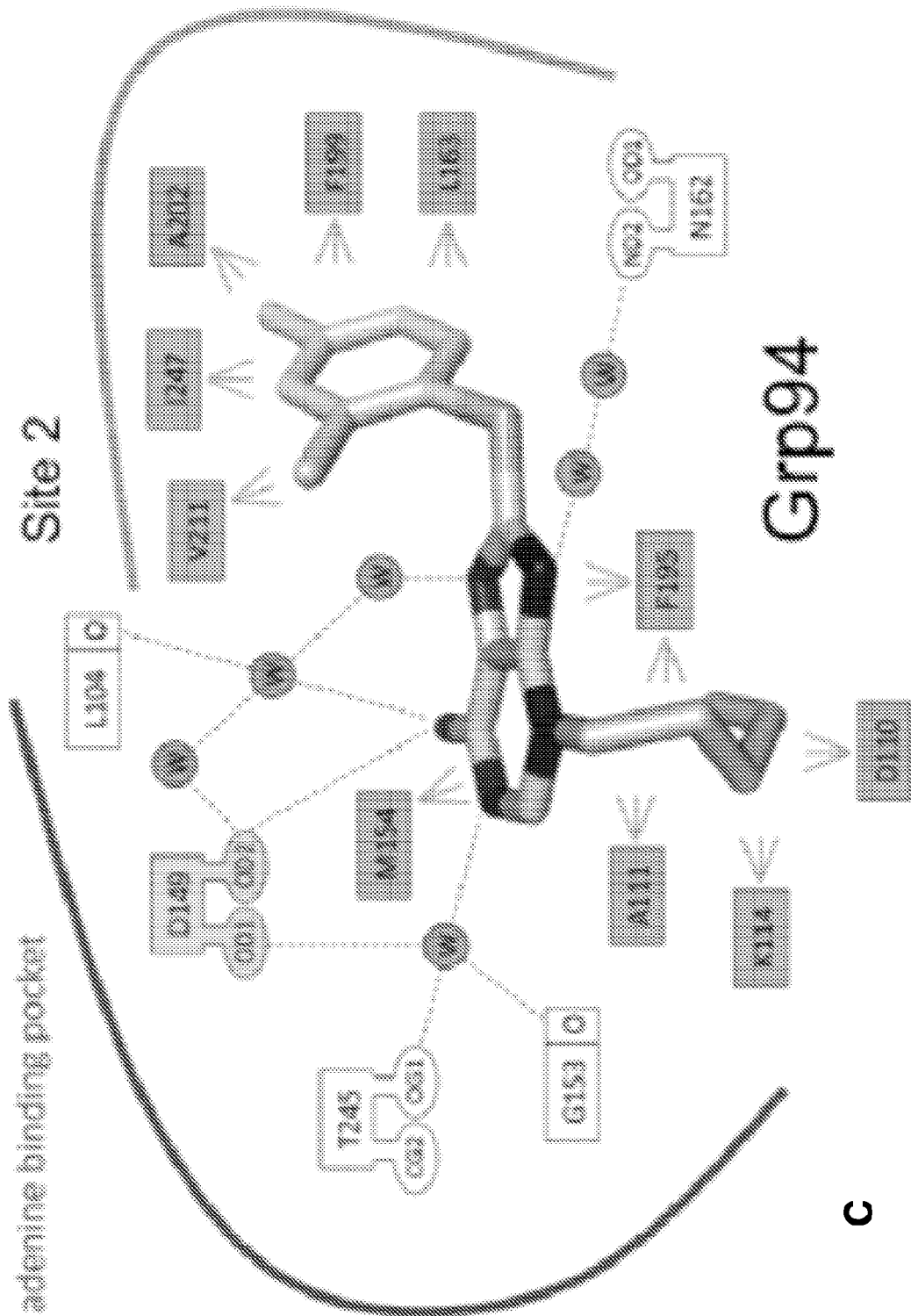
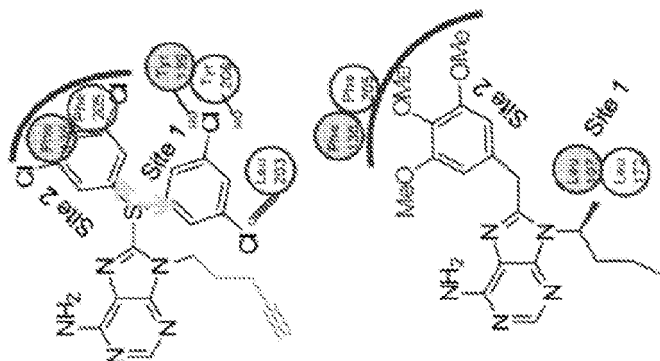
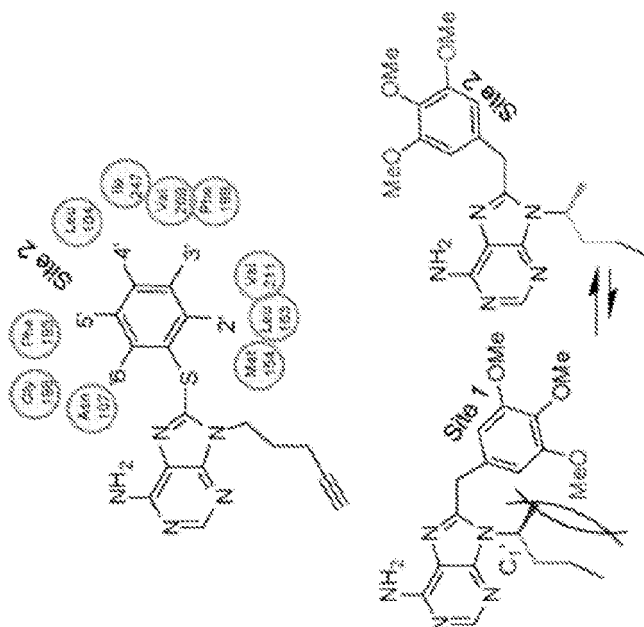
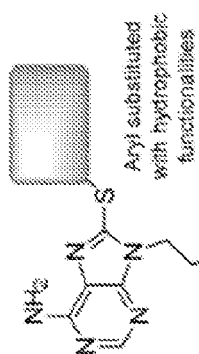
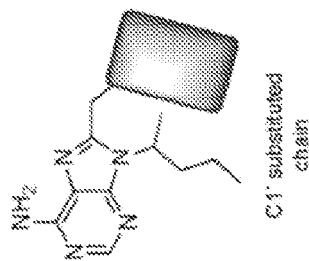


FIG. 3c

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Hsp90 α/β and Trap-1
binding

Grp94 binding

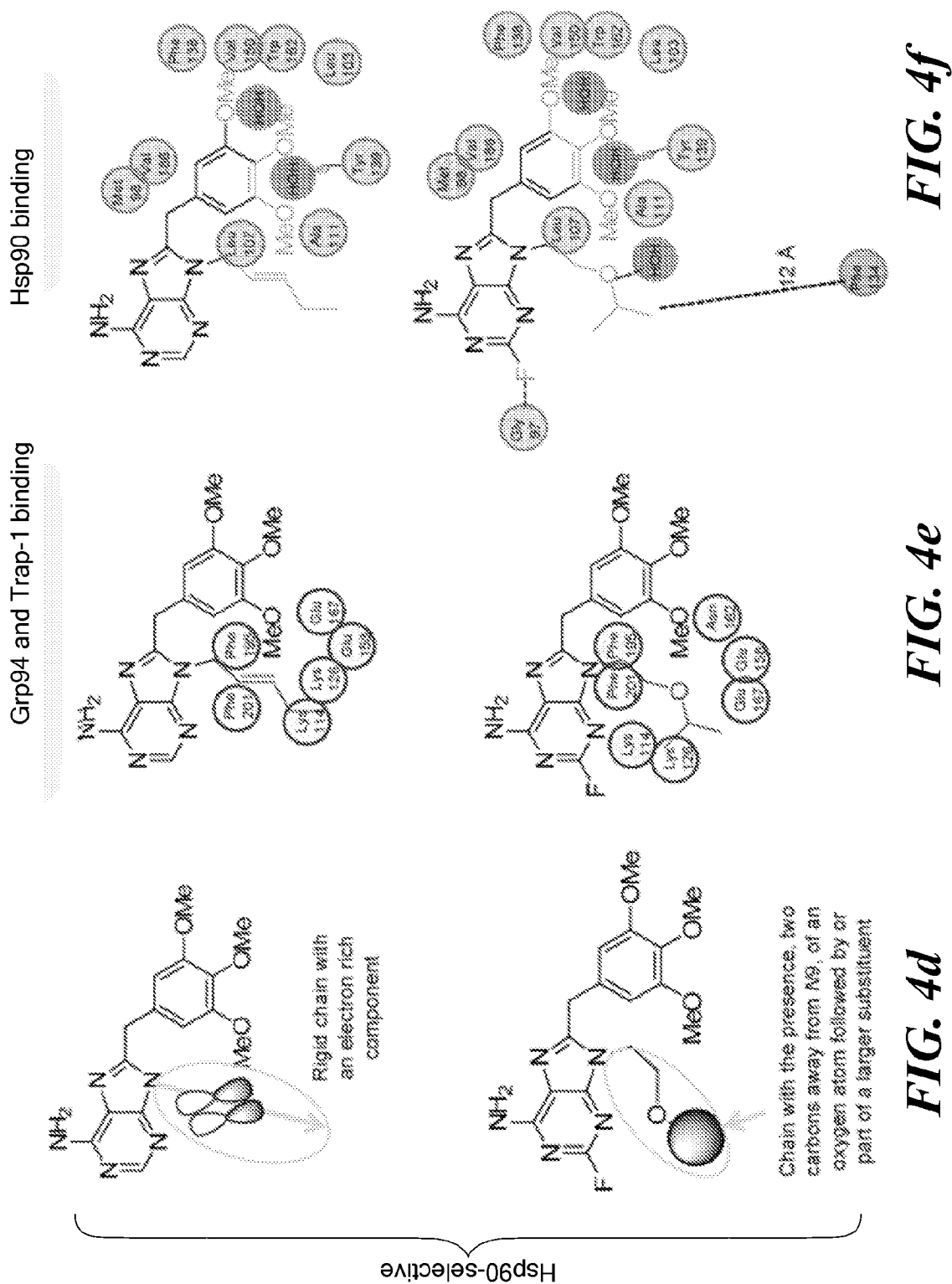
Ar-X₂-dependent subtypeX₂-dependent subtype

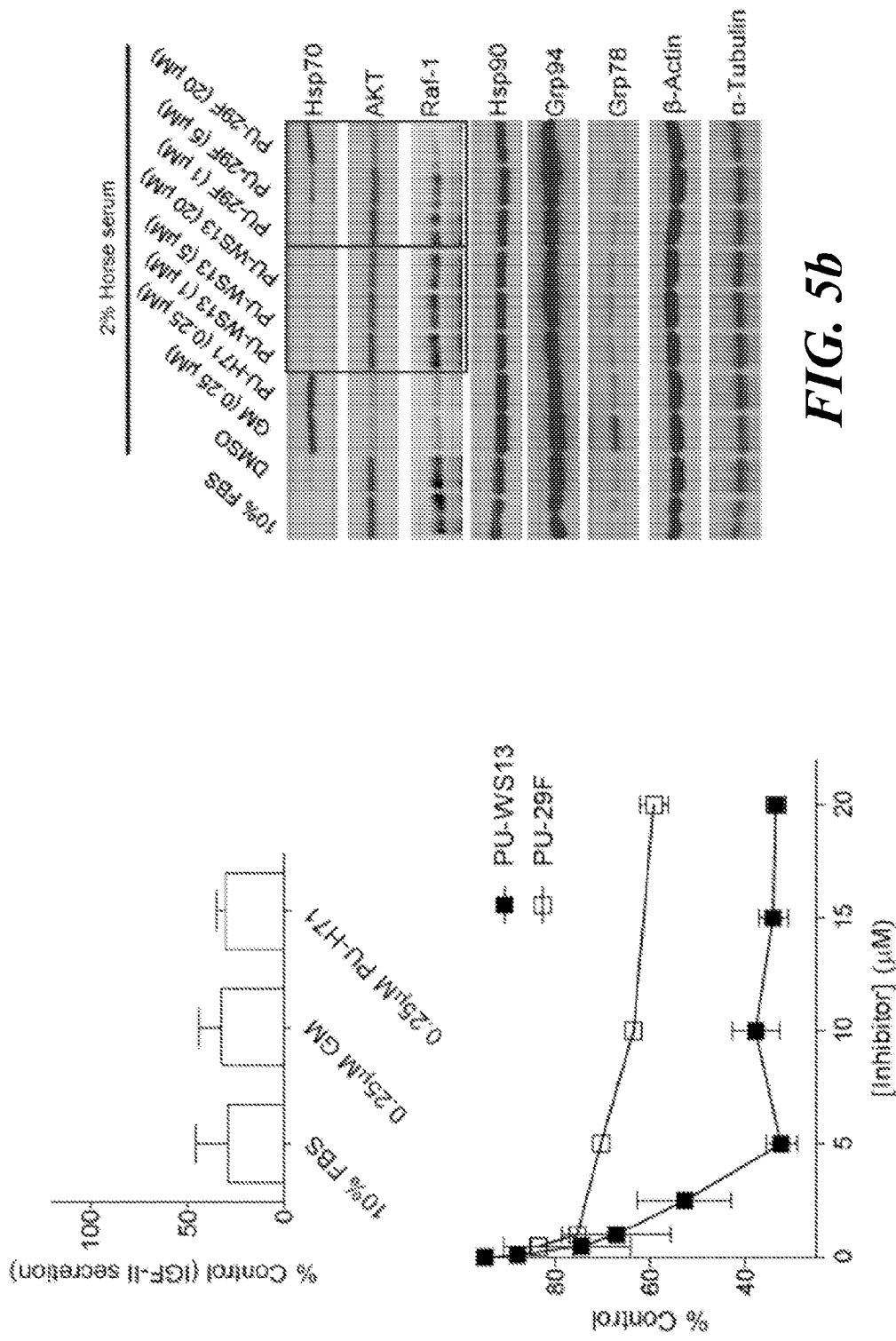
Grp94-selective

FIG. 4c

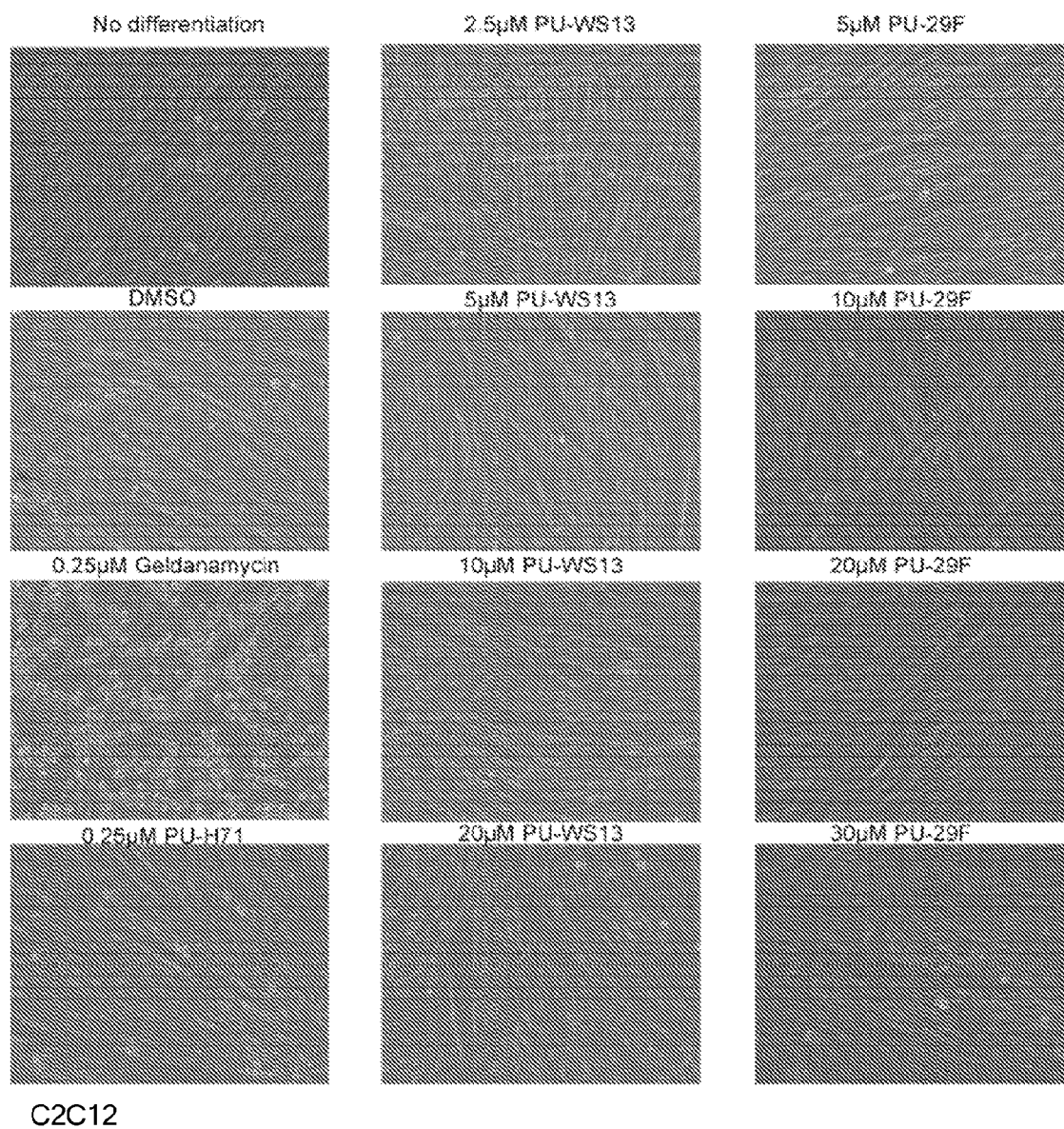
FIG. 4b

FIG. 4a





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**FIG. 5c**

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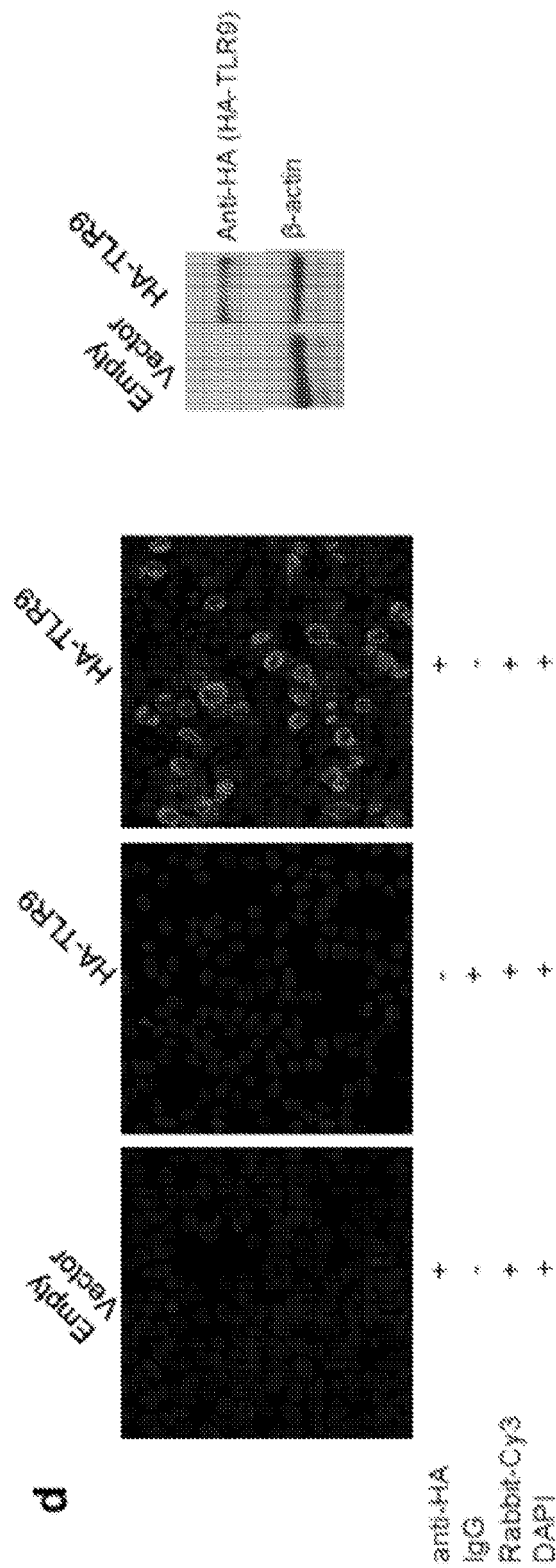
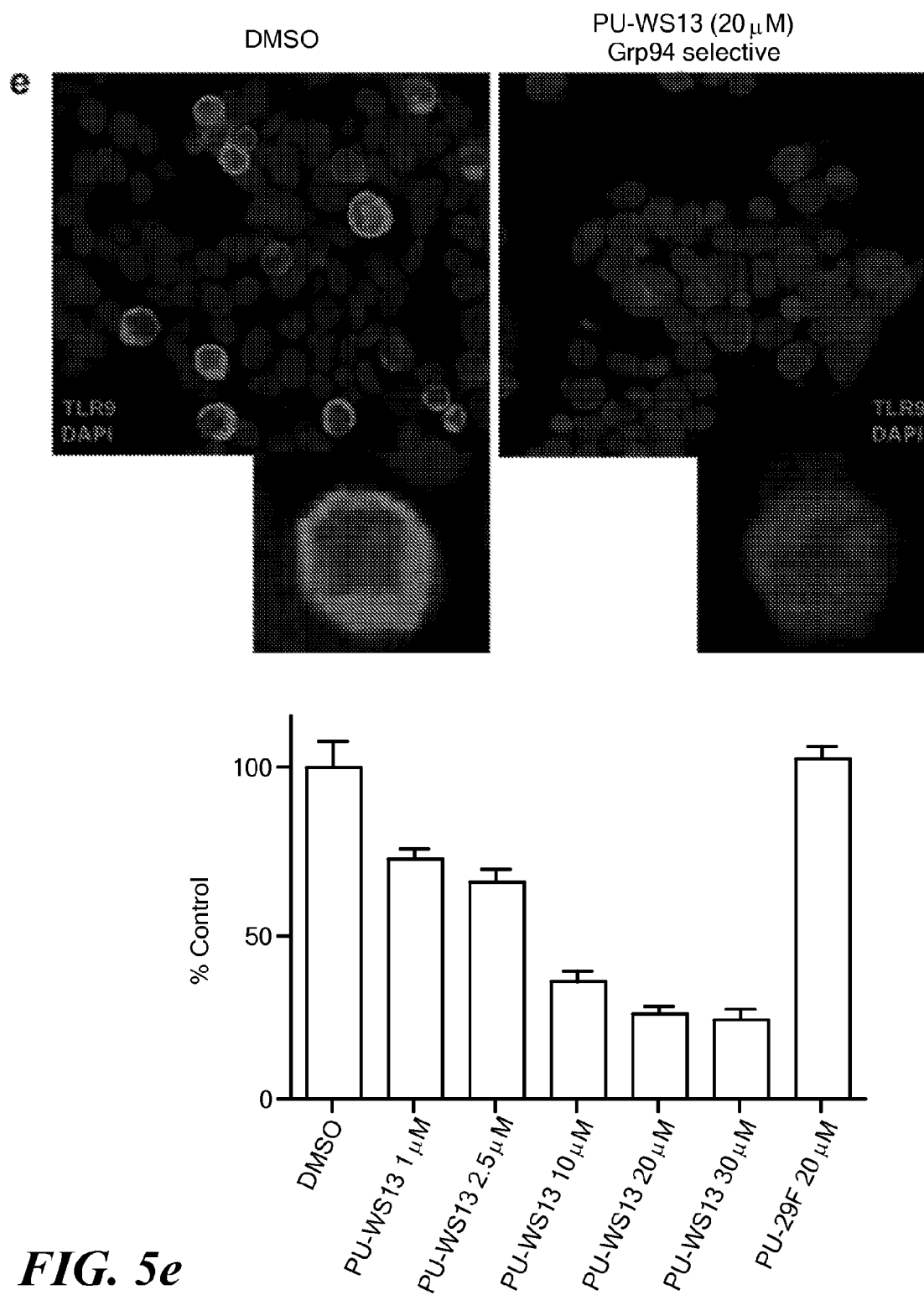


FIG. 5d

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**FIG. 5e**

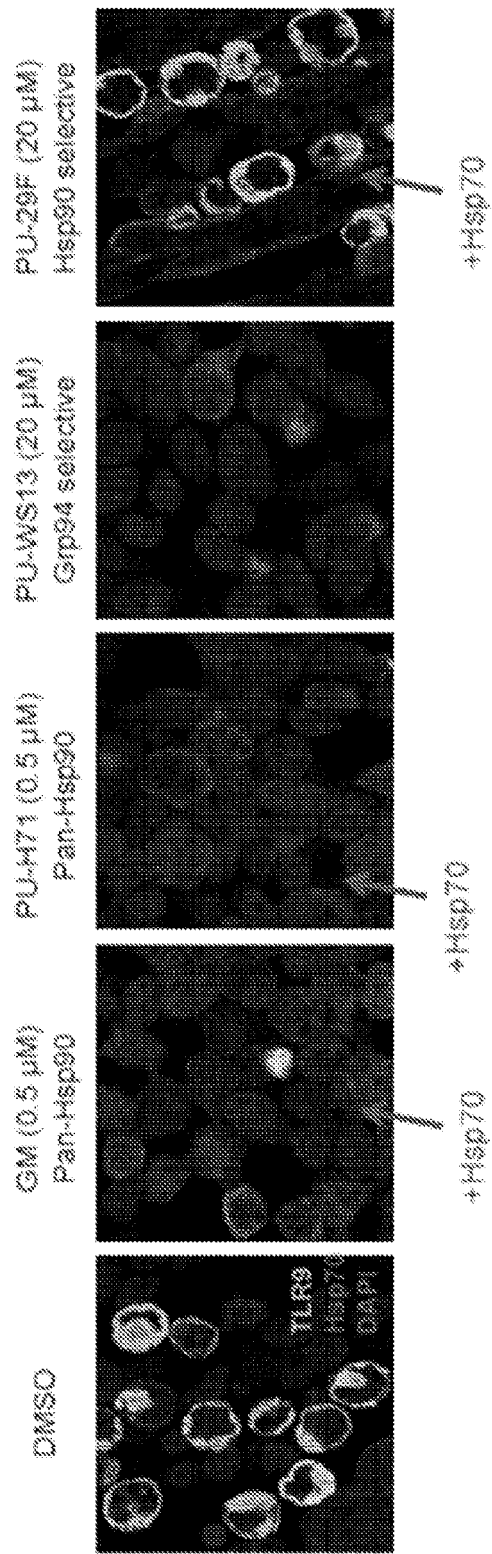


FIG. 5f

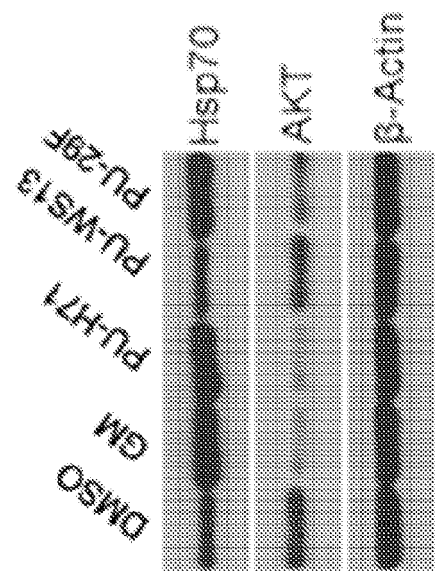


FIG. 5g

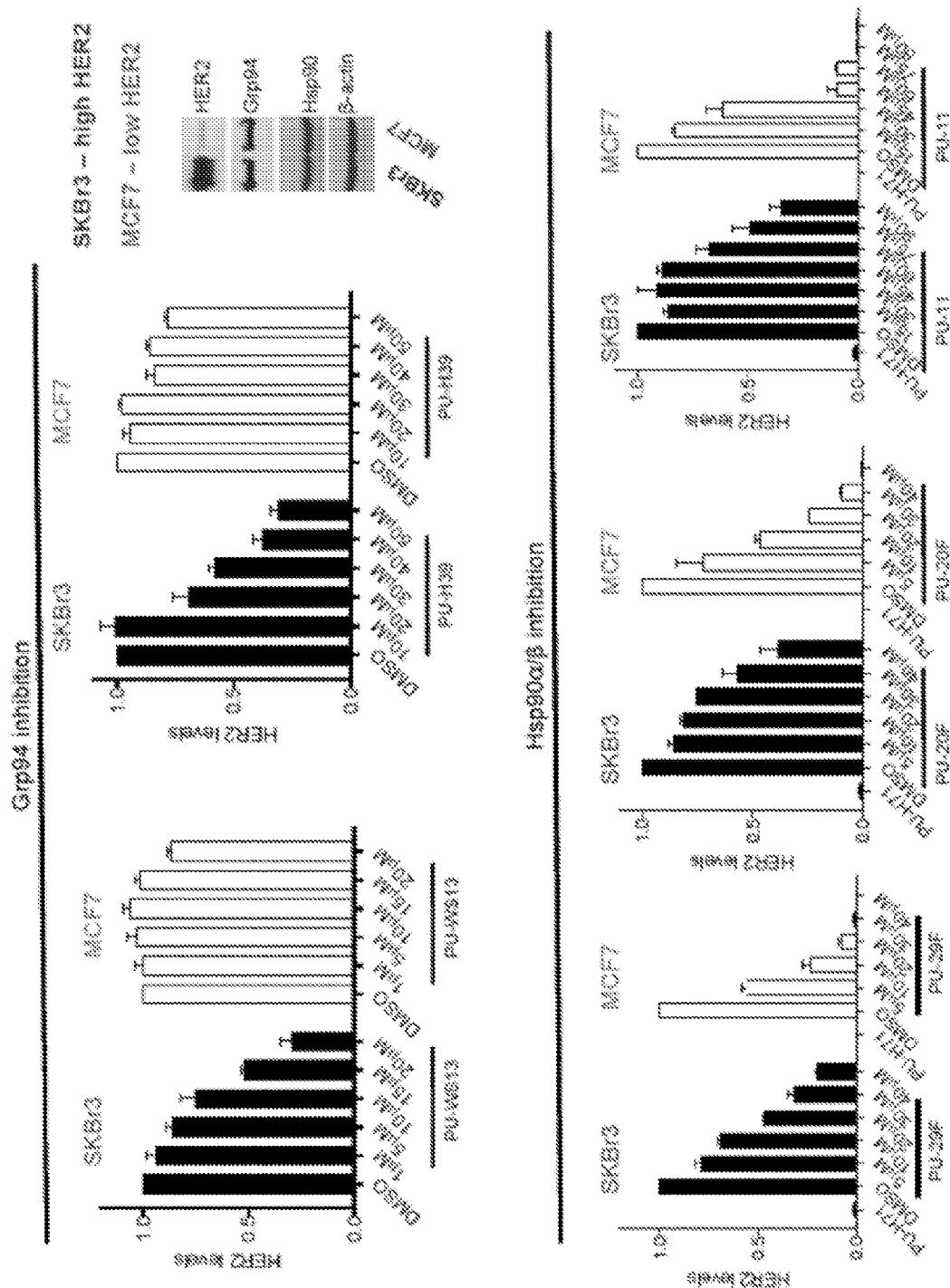


FIG. 6a

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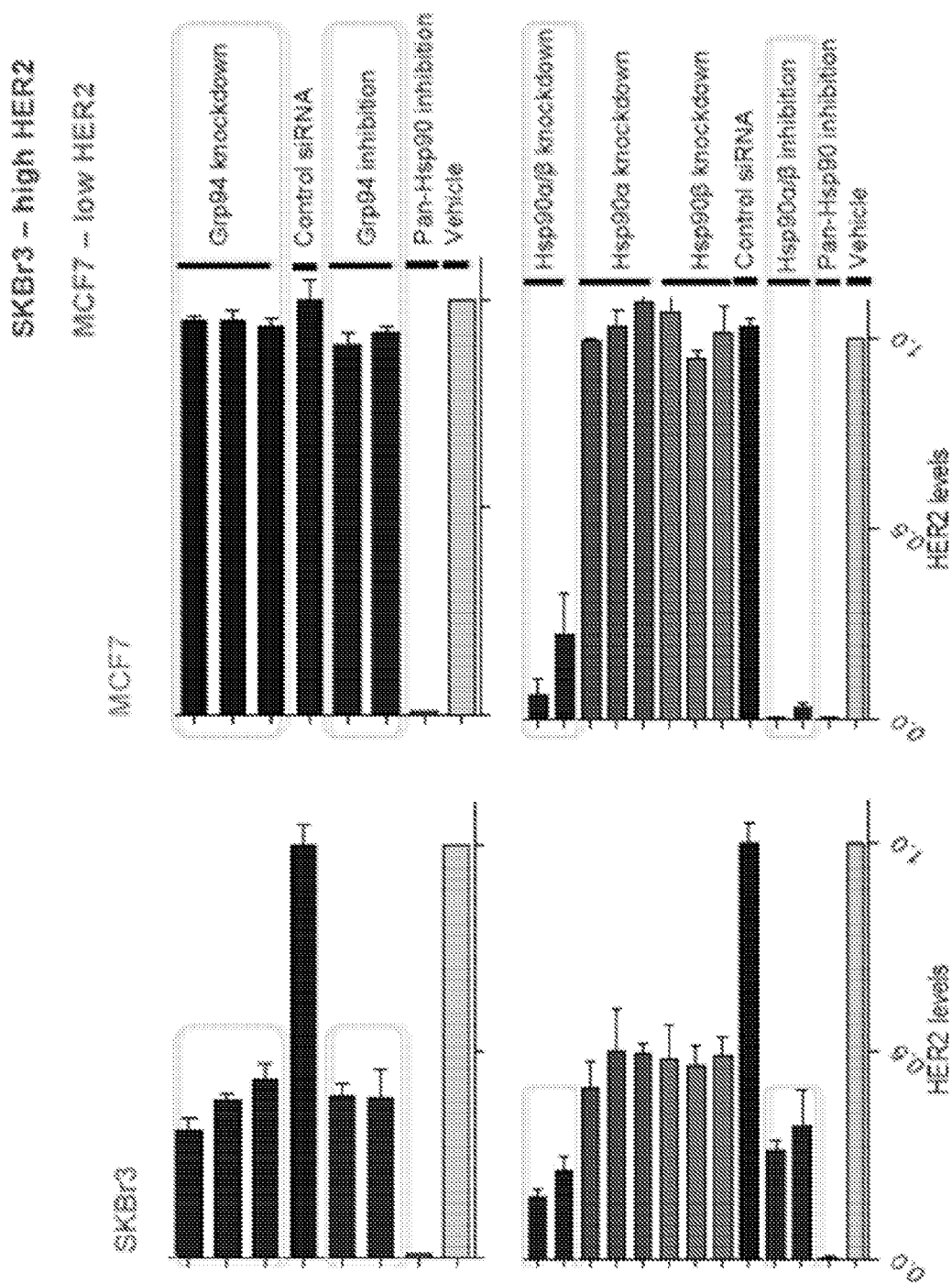


FIG. 6b

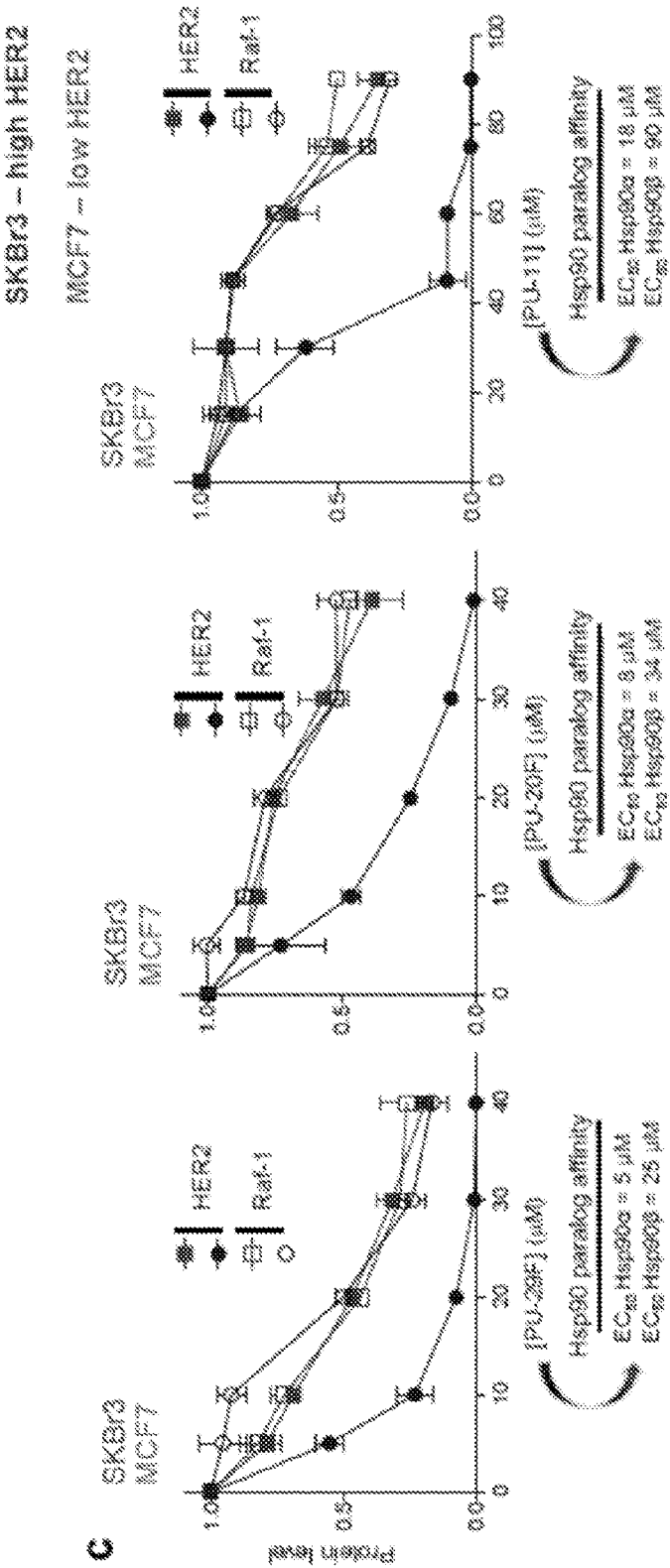


FIG. 6c

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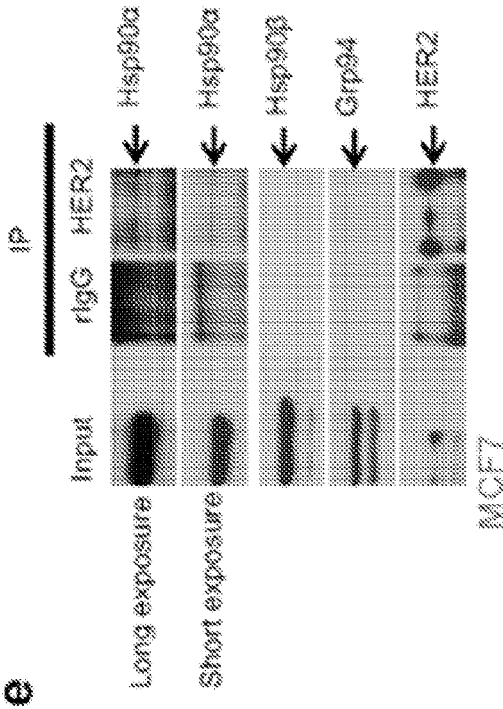


FIG. 6e

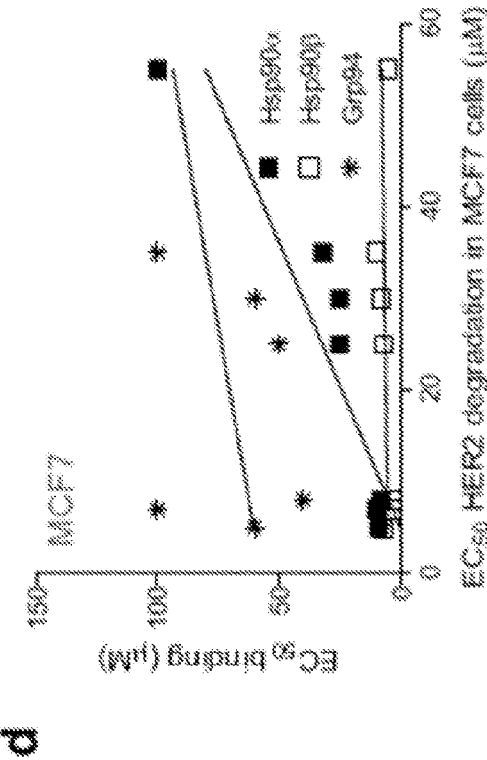


FIG. 6d

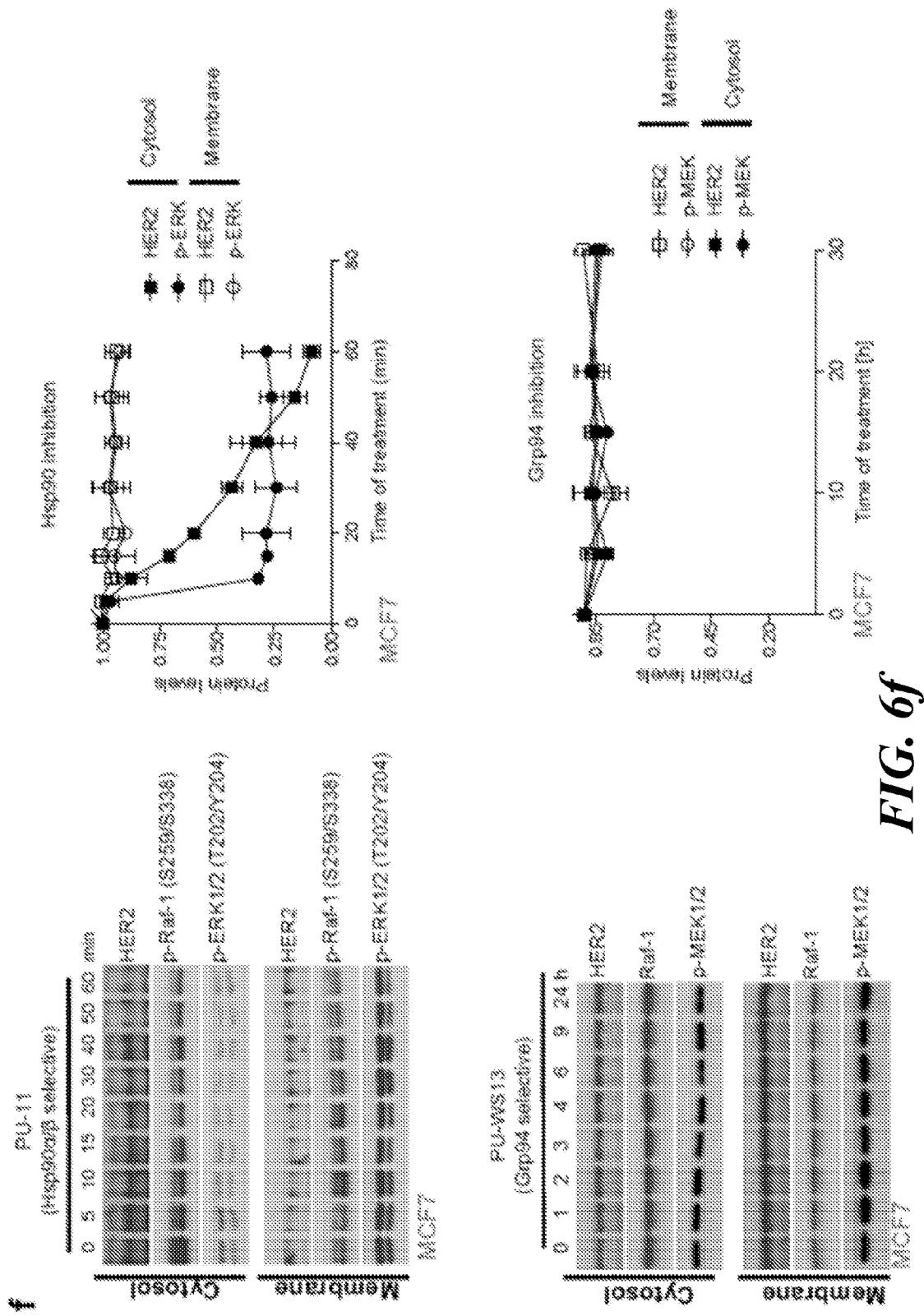


FIG. 6f

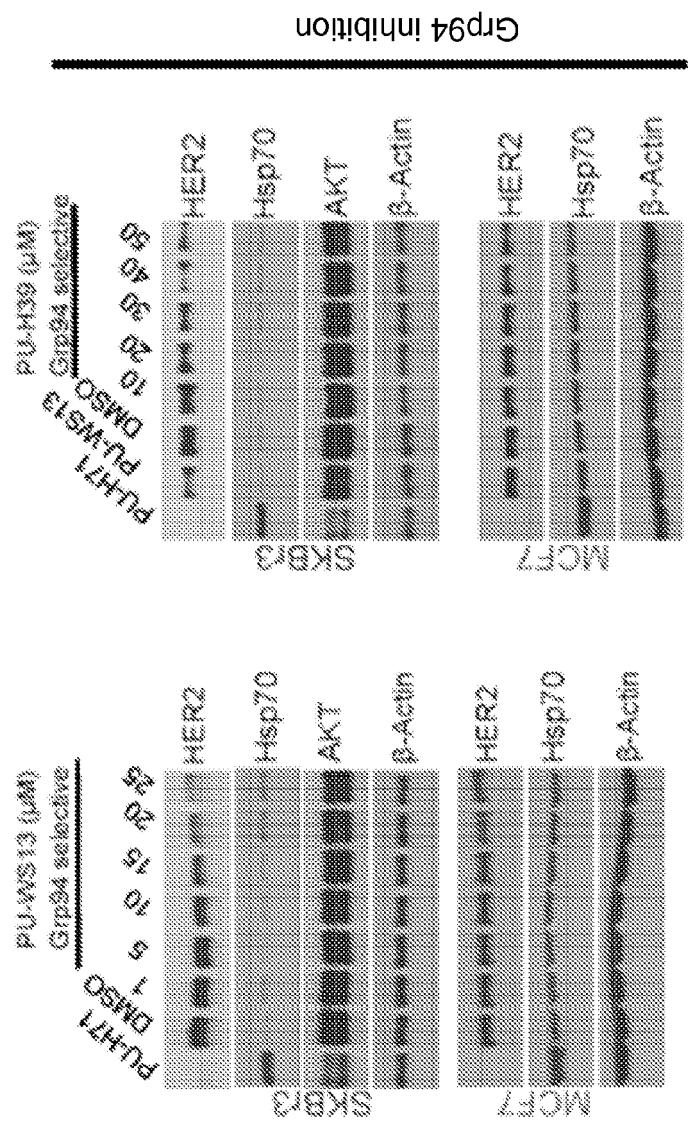


FIG. 7a-1

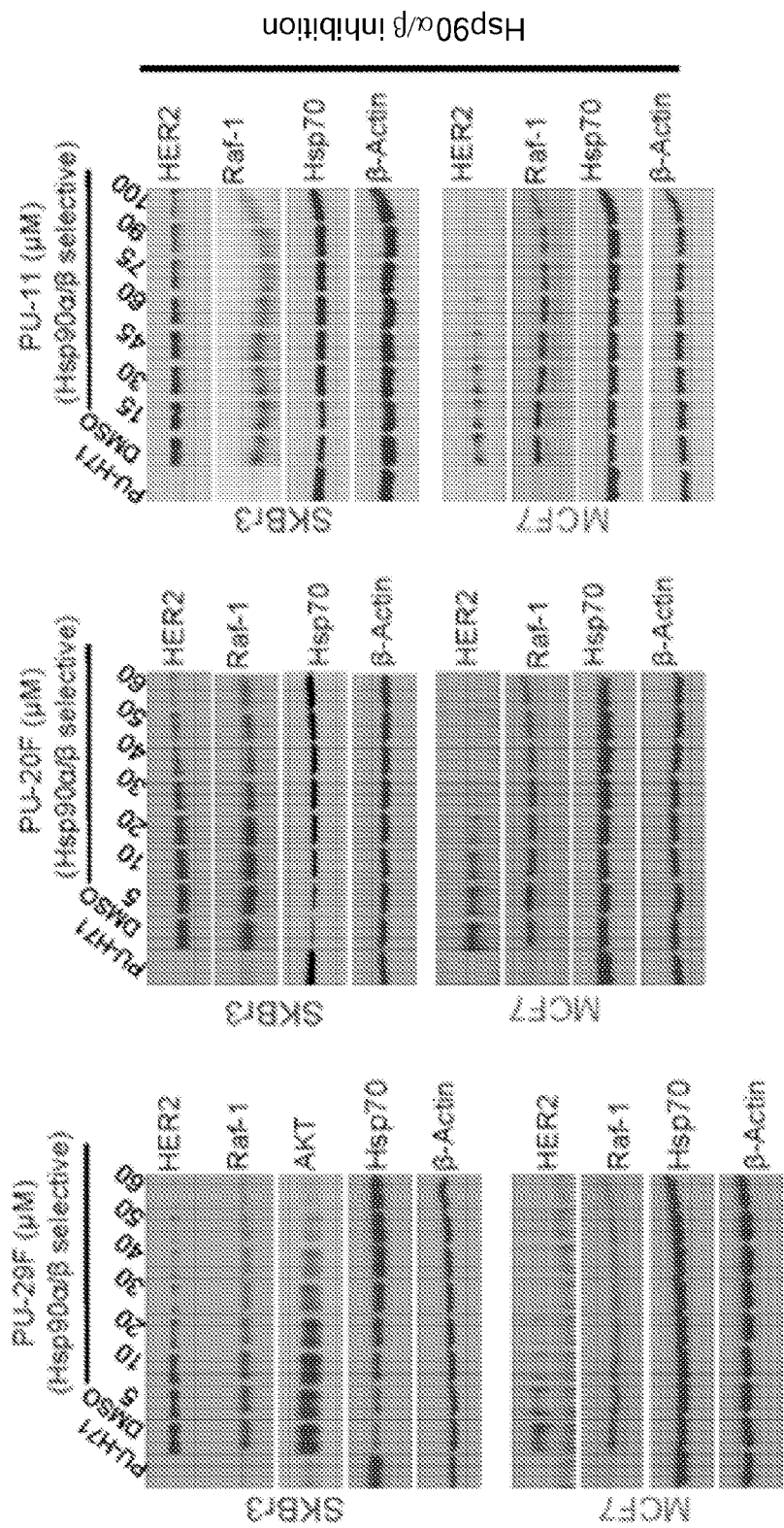


FIG. 7a-2

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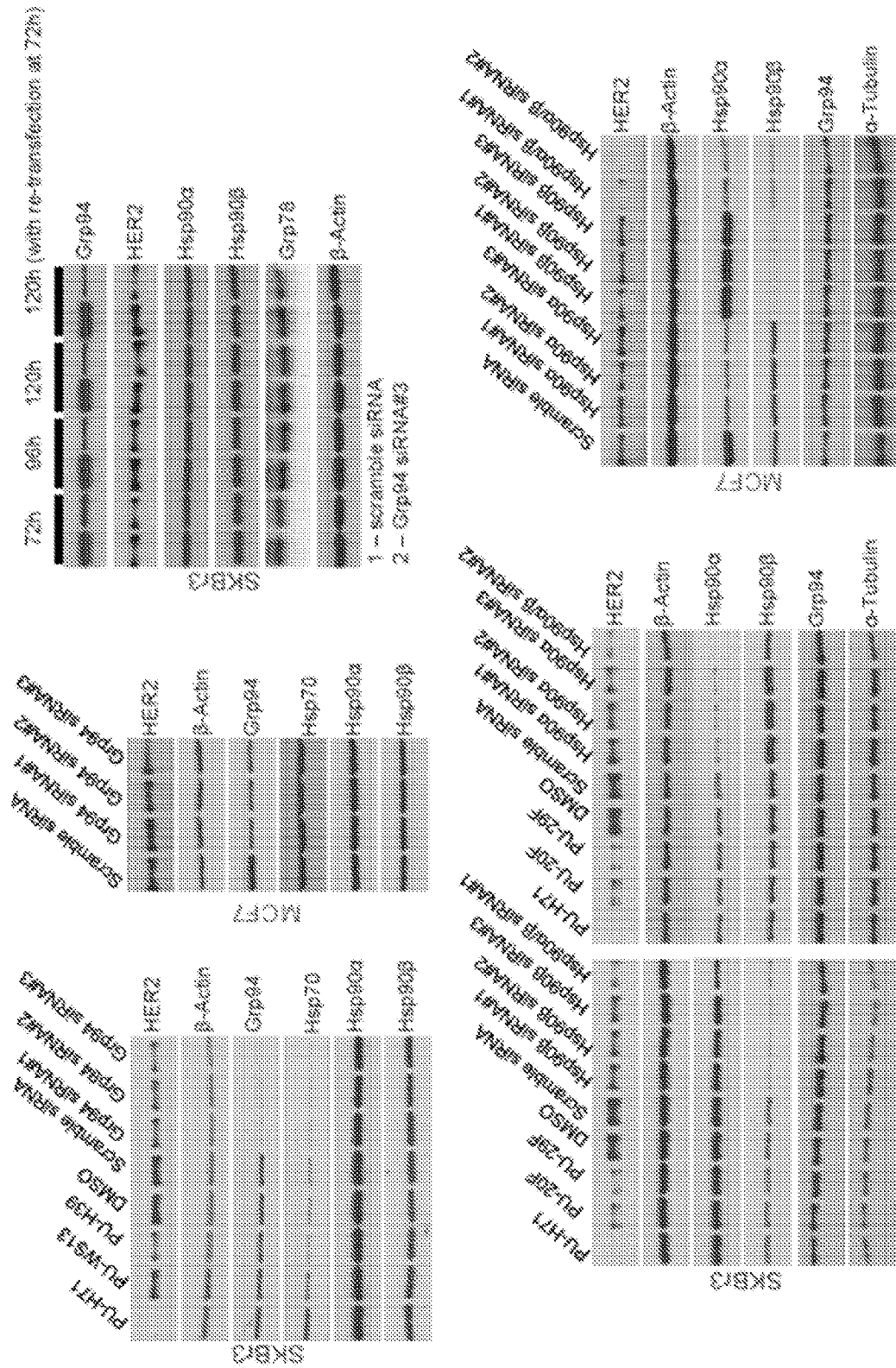


FIG. 7b



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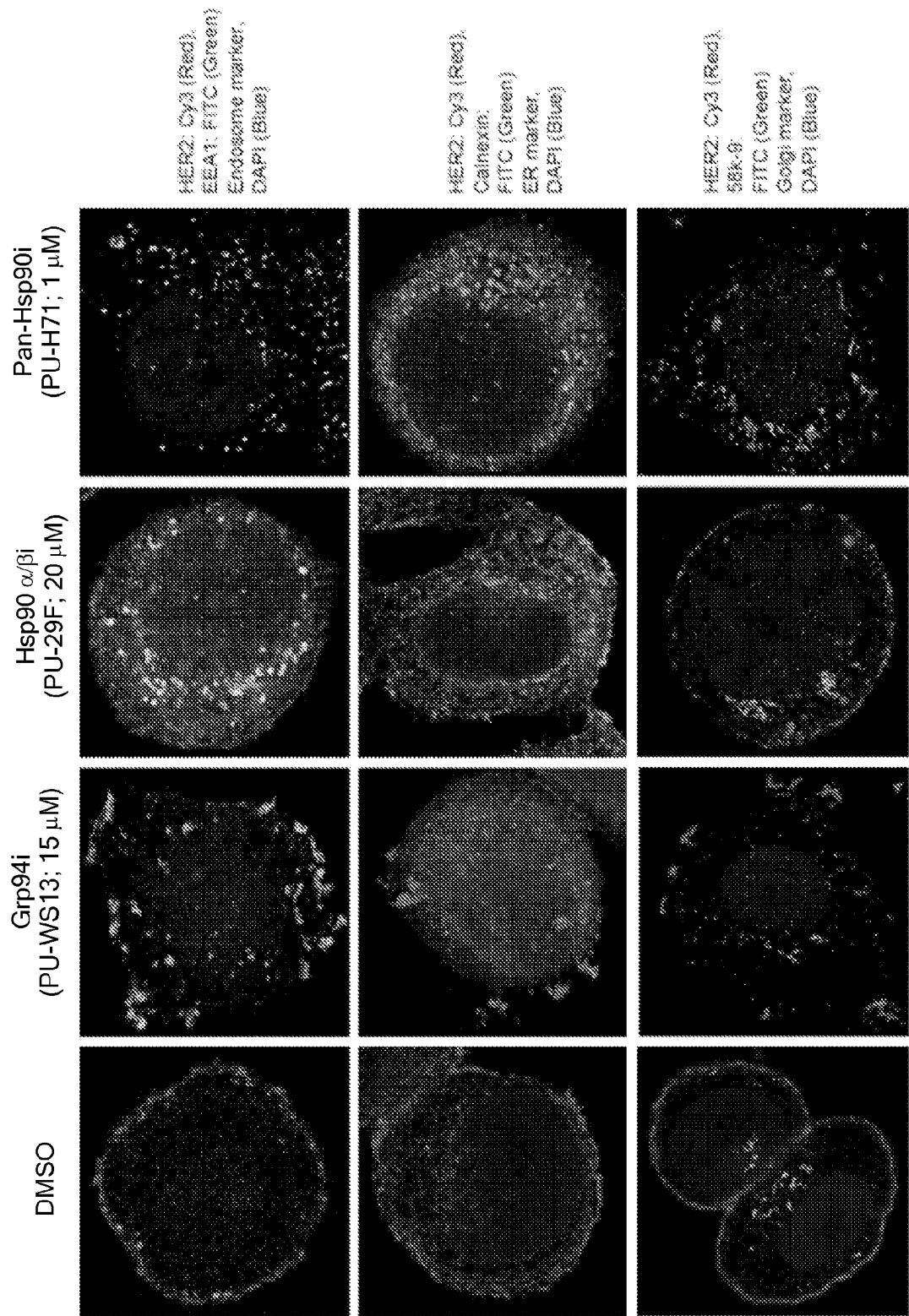
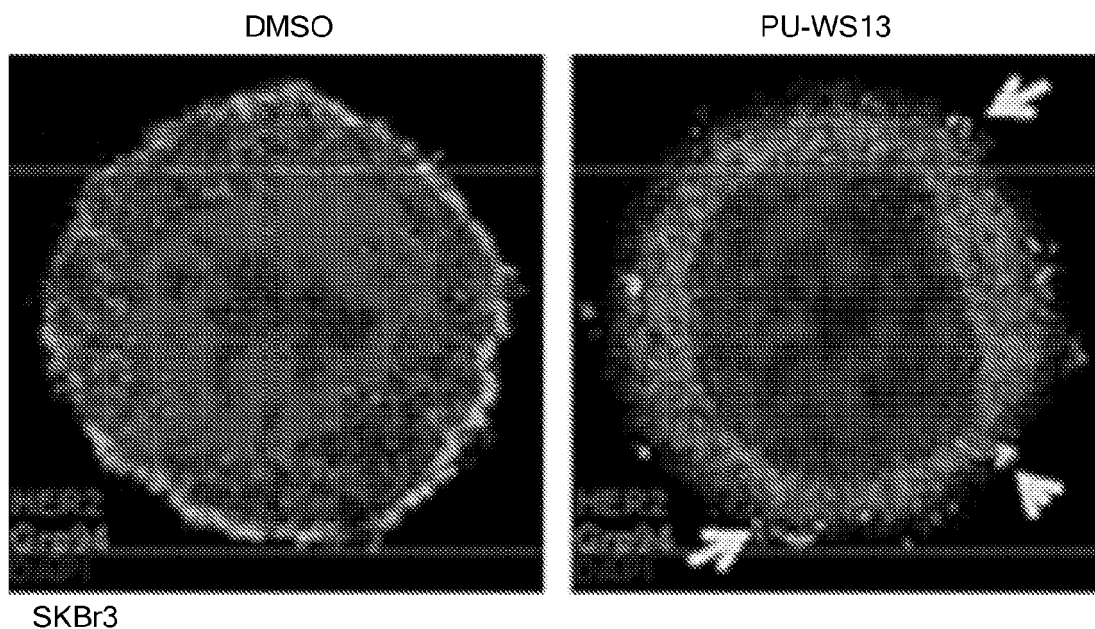
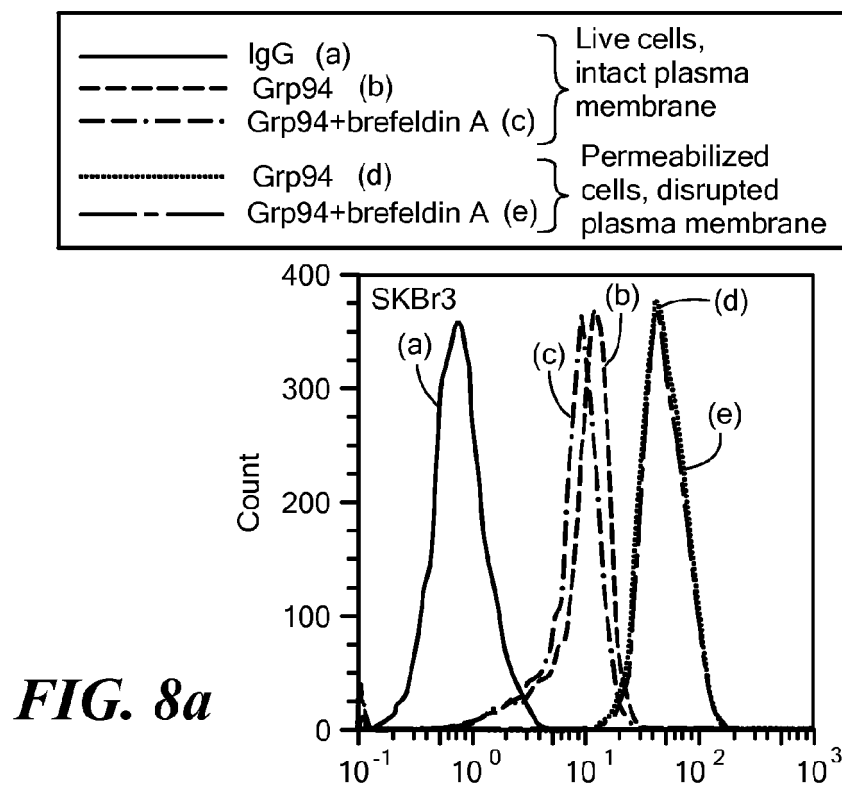
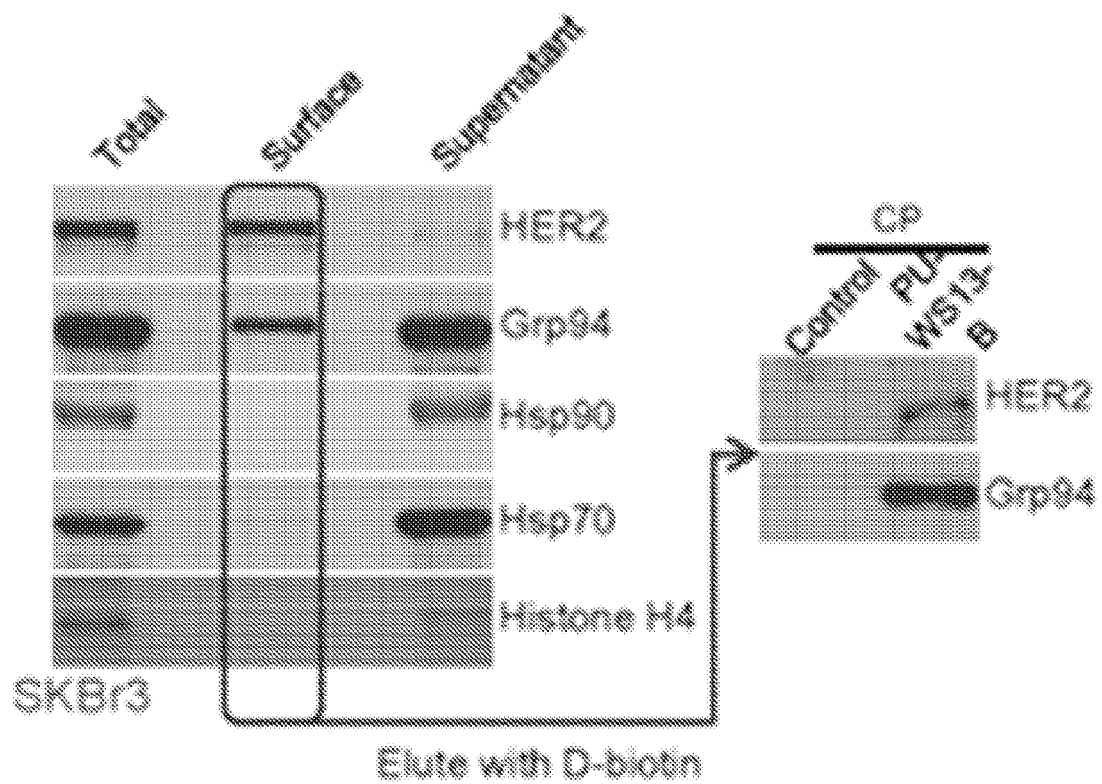


FIG. 7d

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**FIG. 8c**

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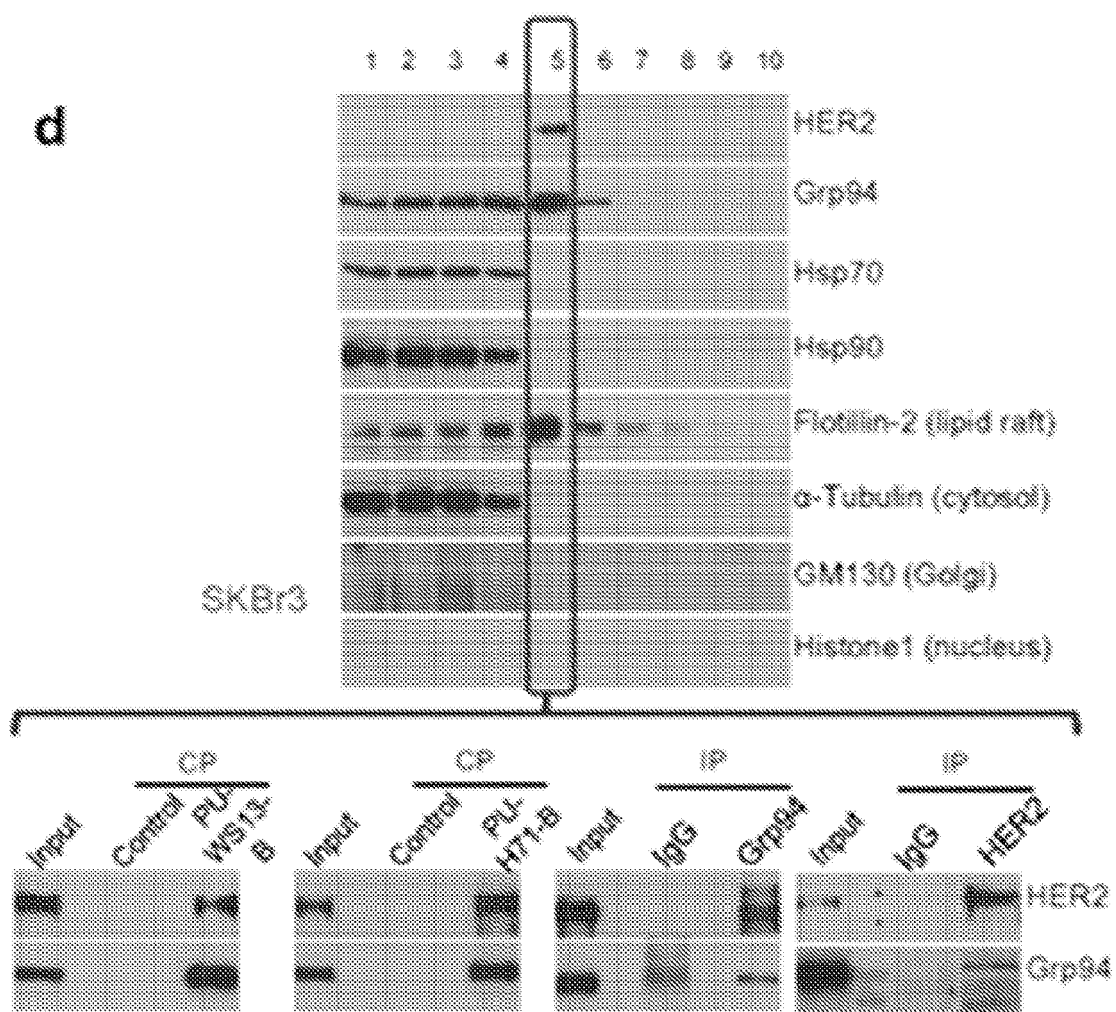


FIG. 8d

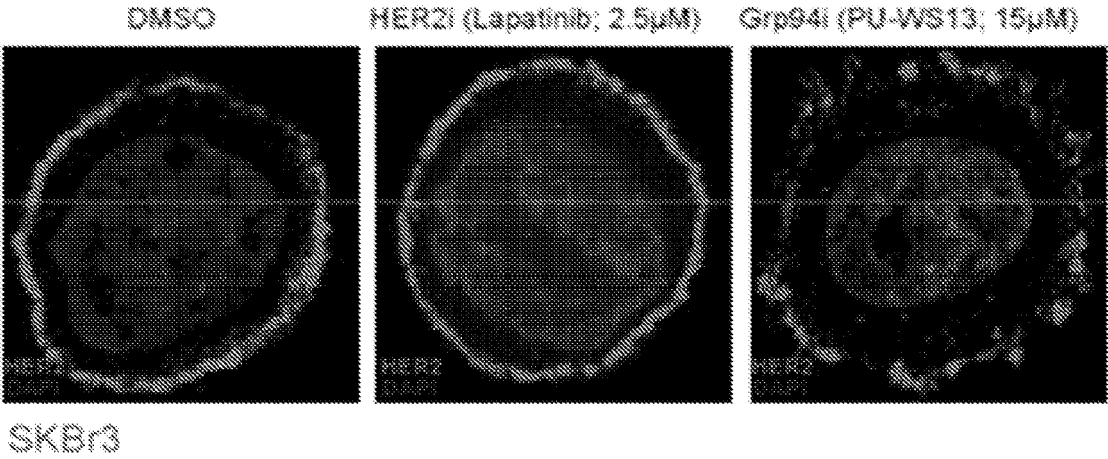


FIG. 8f

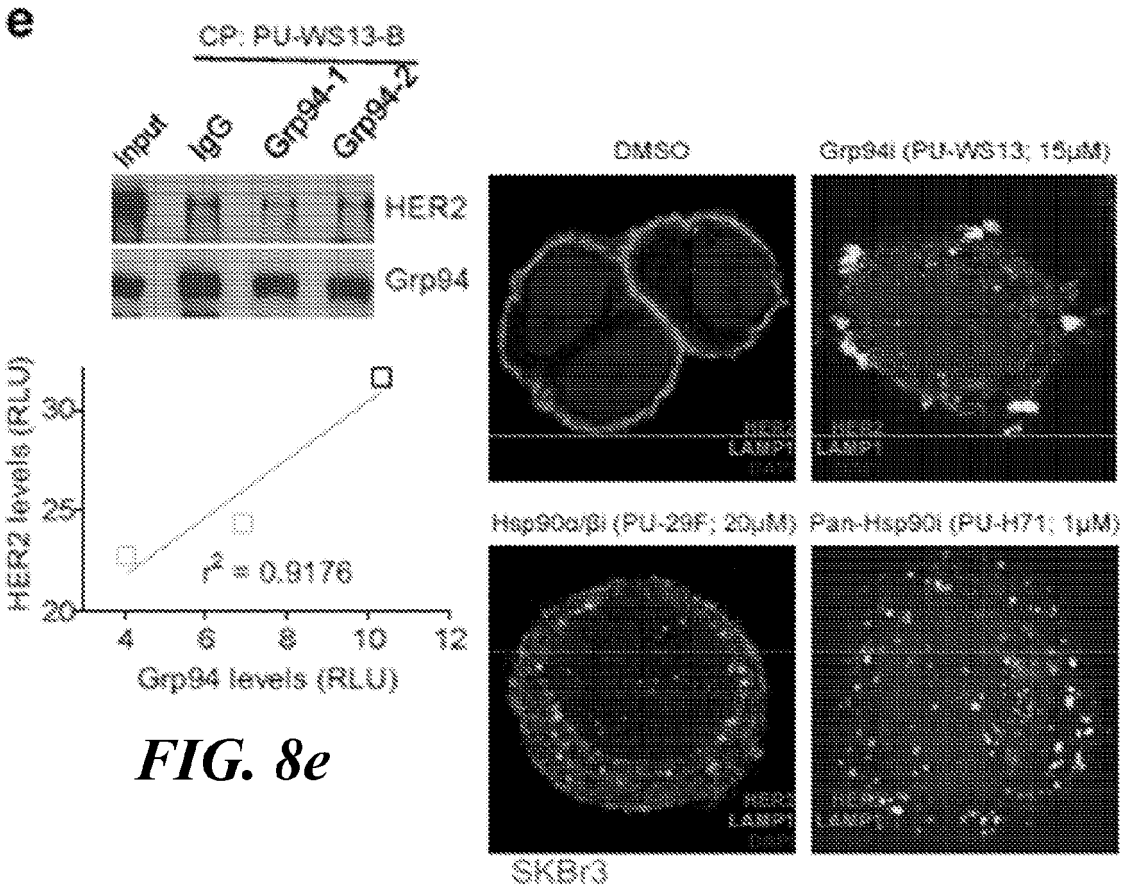


FIG. 8e

FIG. 8g

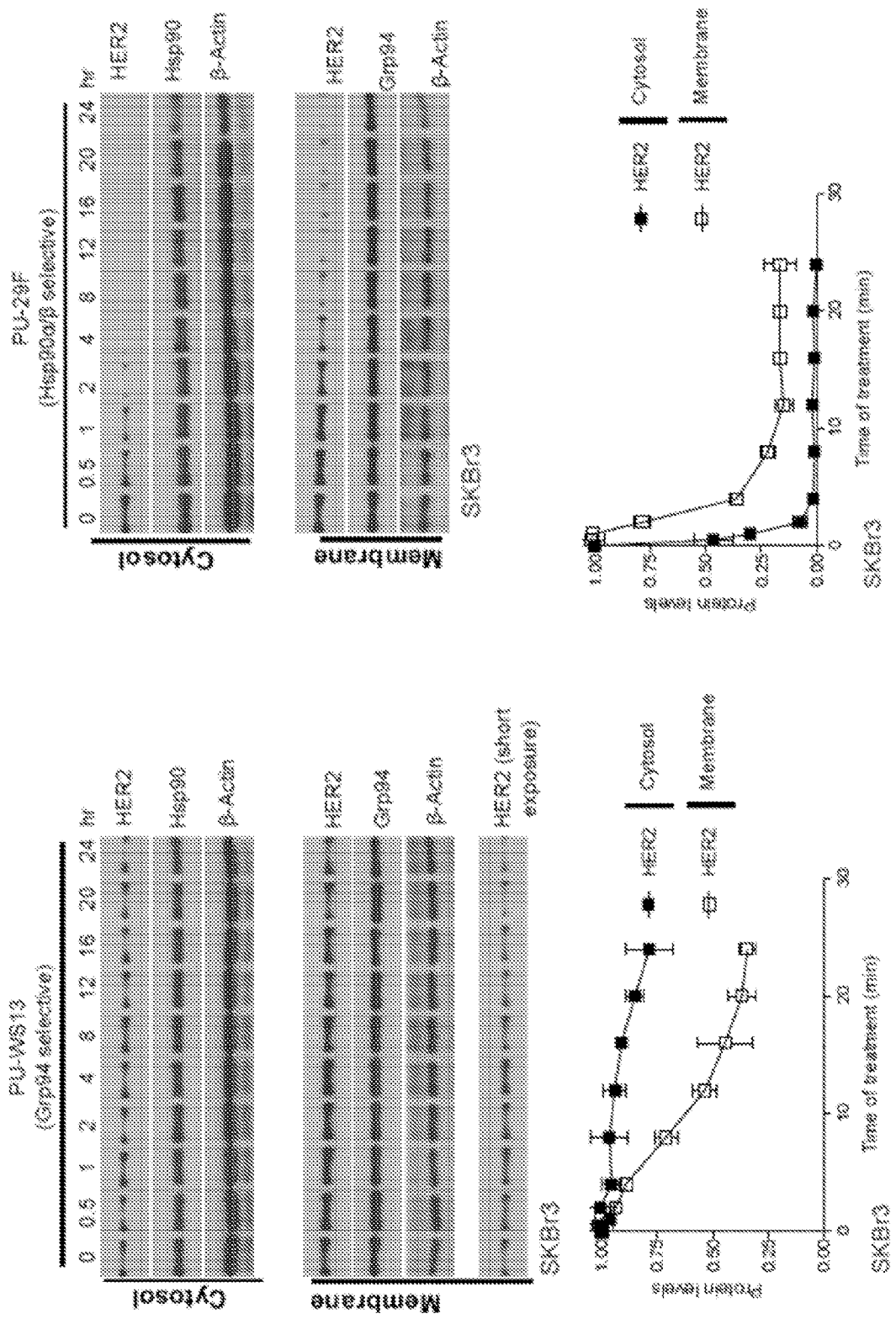
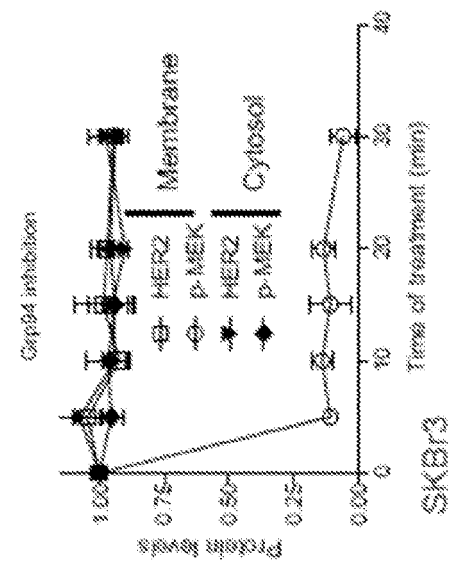
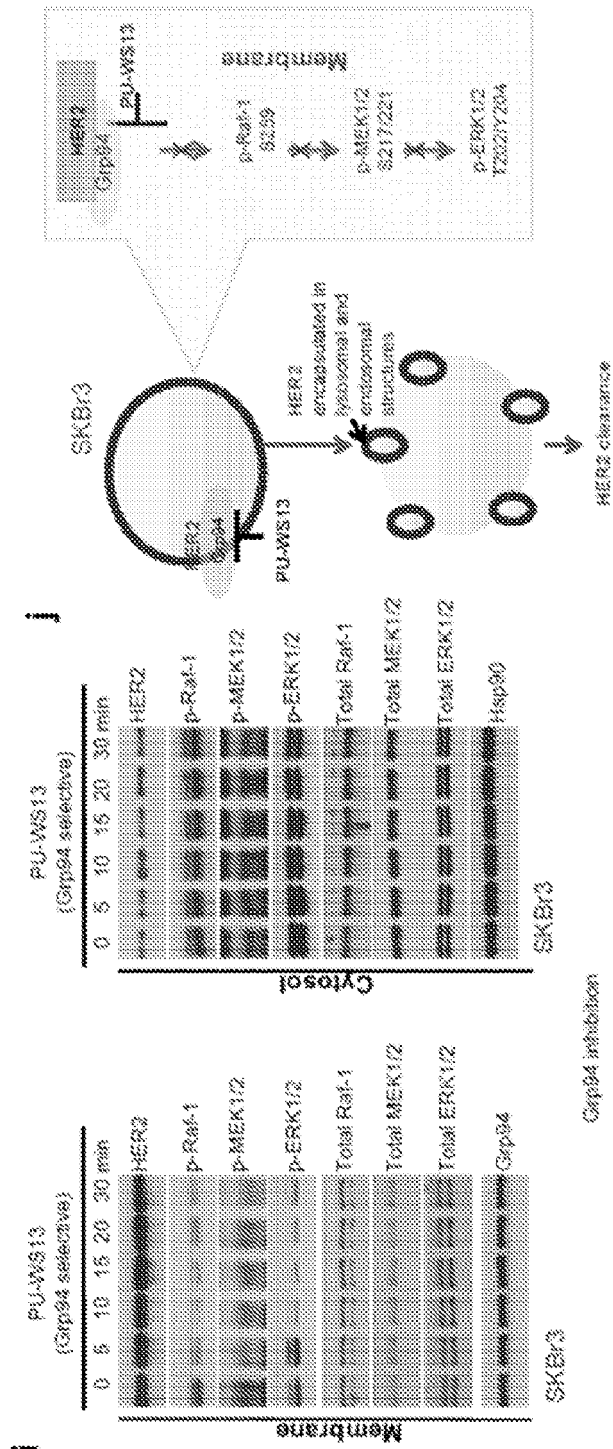


FIG. 8h



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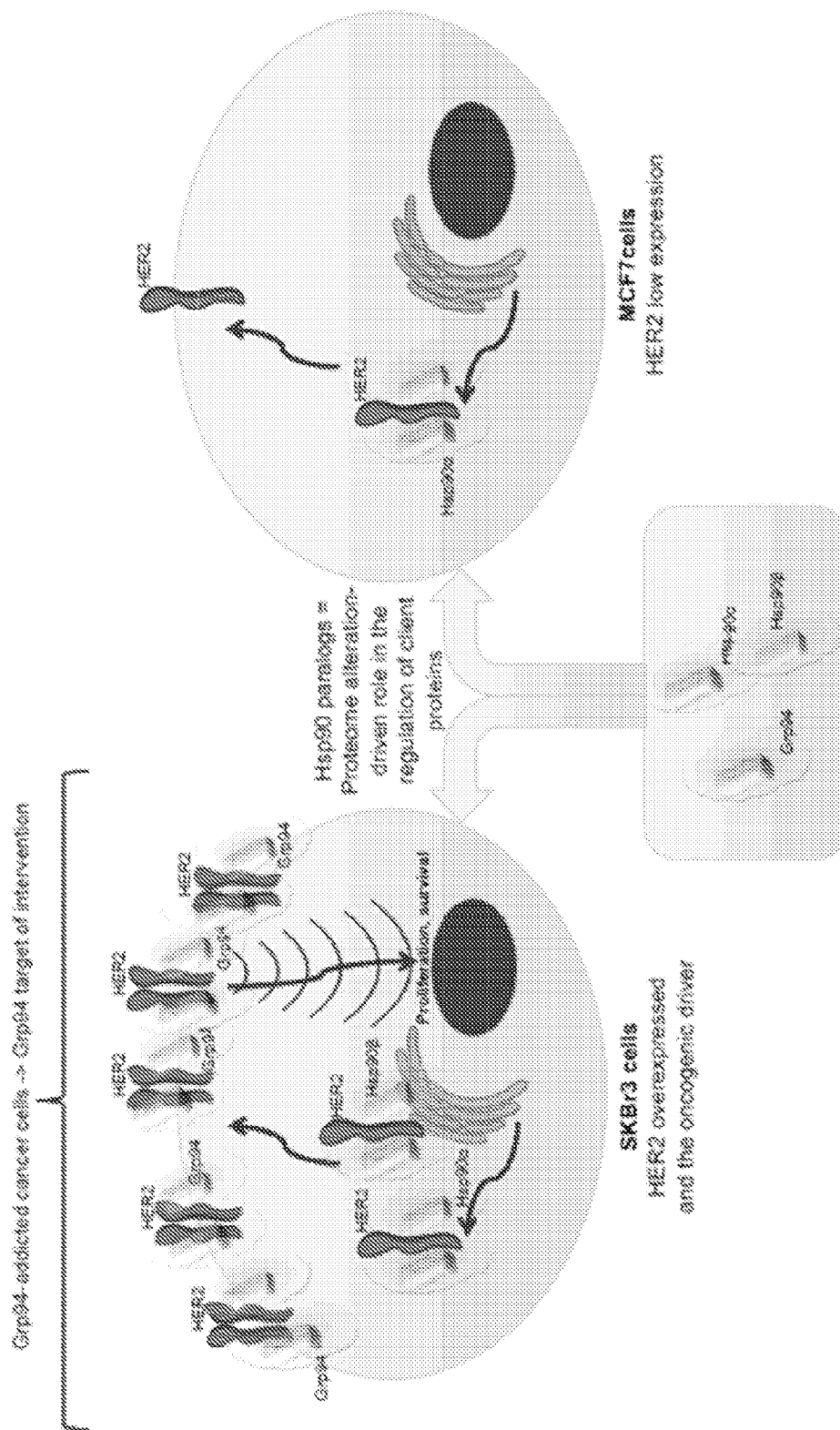
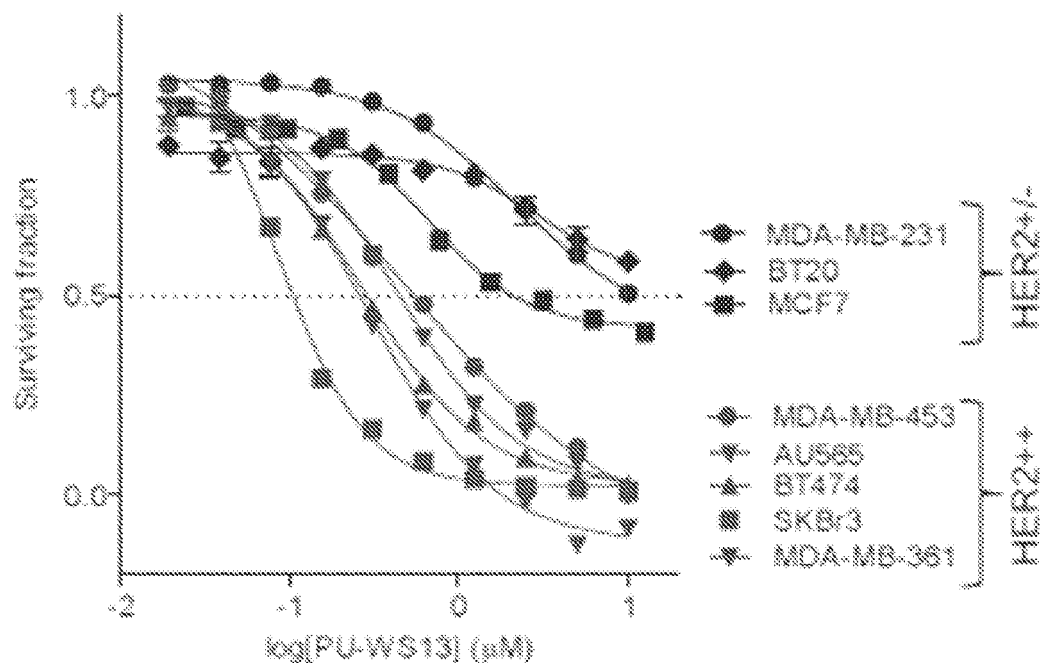
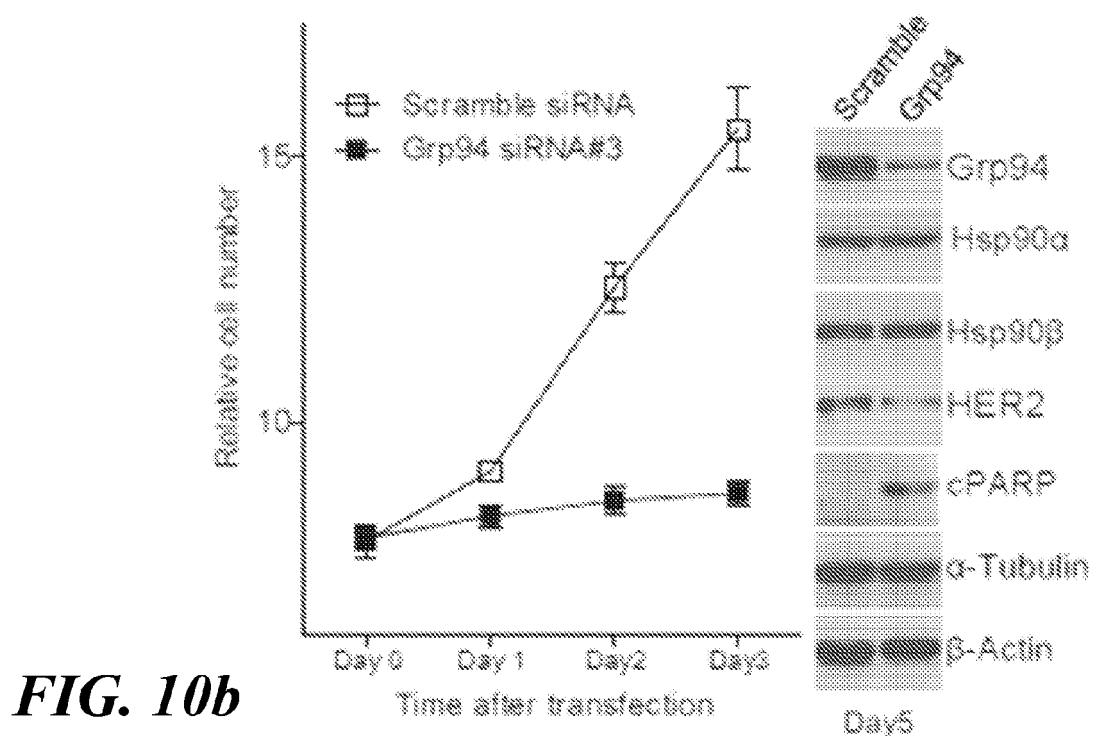


FIG. 9

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**FIG. 10a****FIG. 10b**

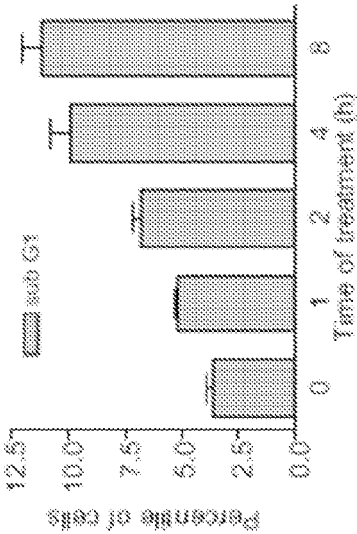


FIG. 10c

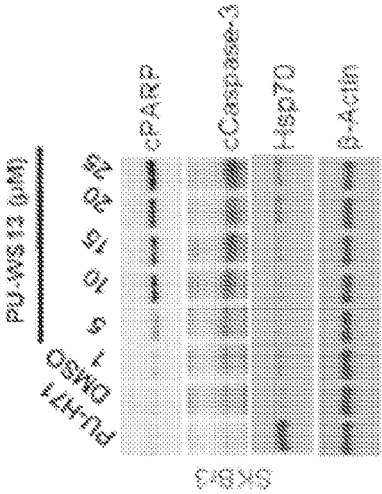


FIG. 10d

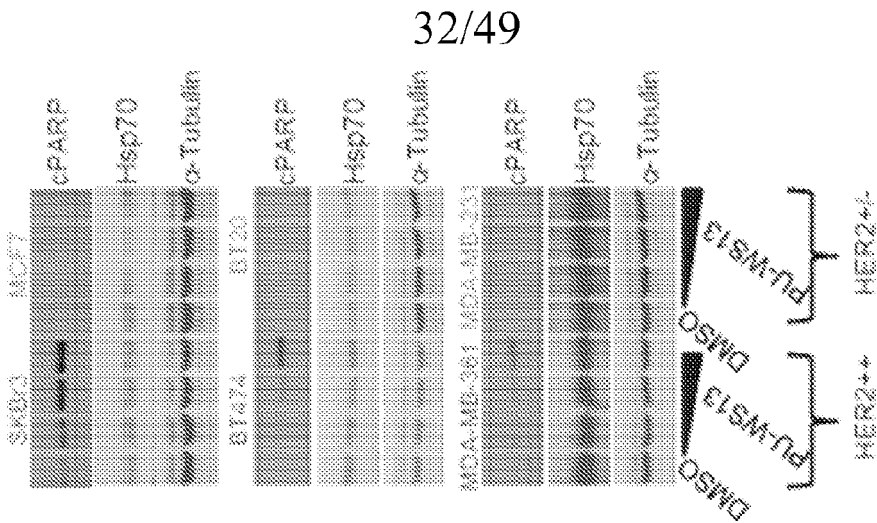


FIG. 10e

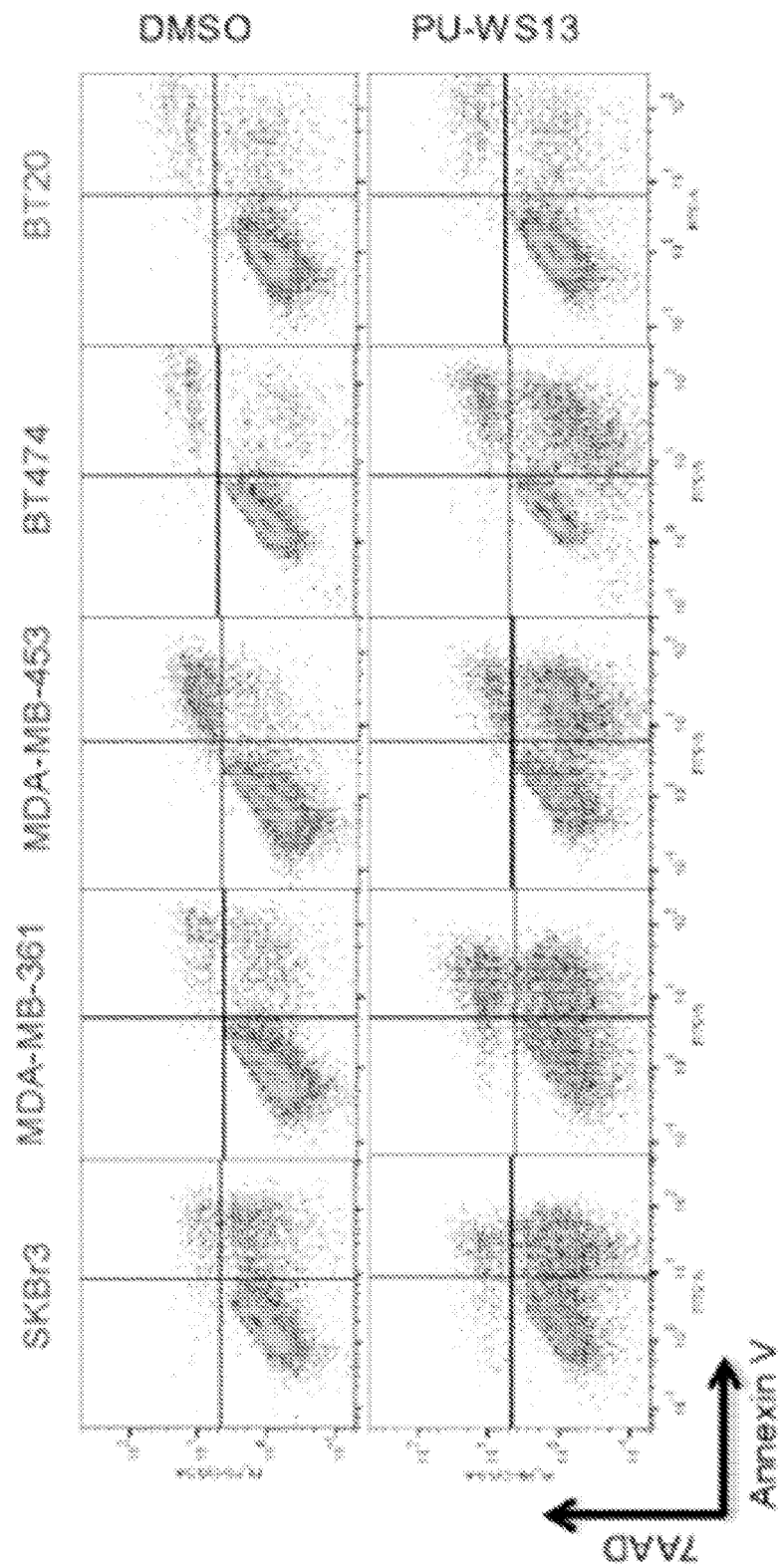


FIG. 10f

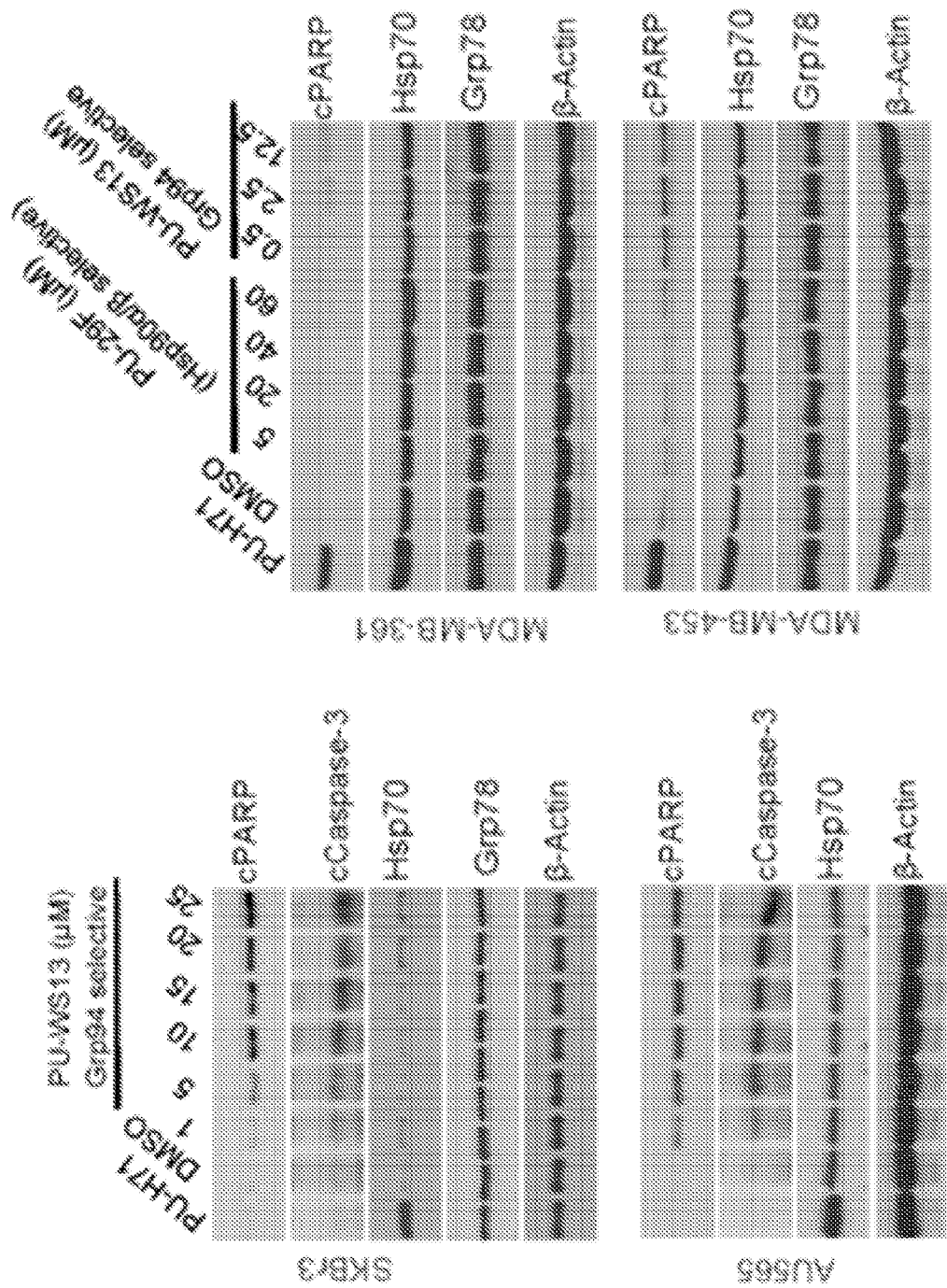


FIG. 11a

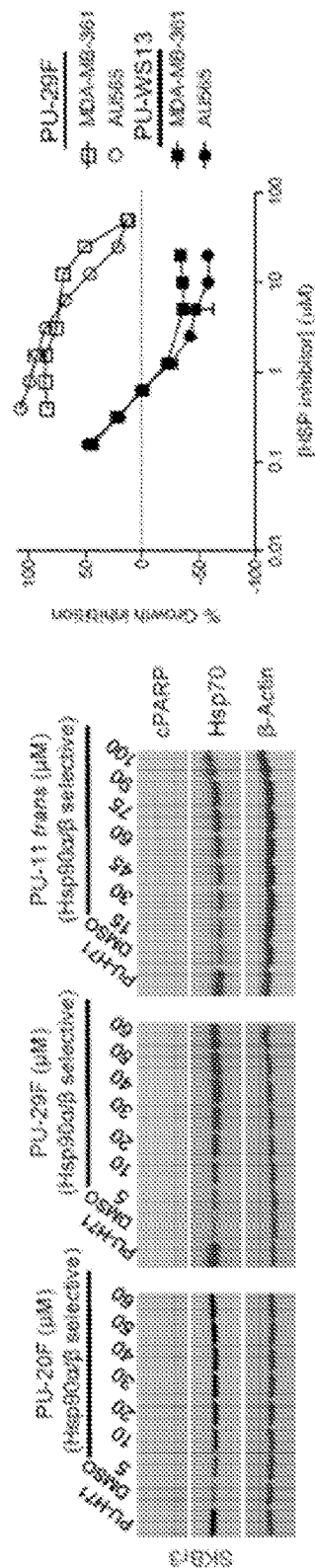


FIG. 11c

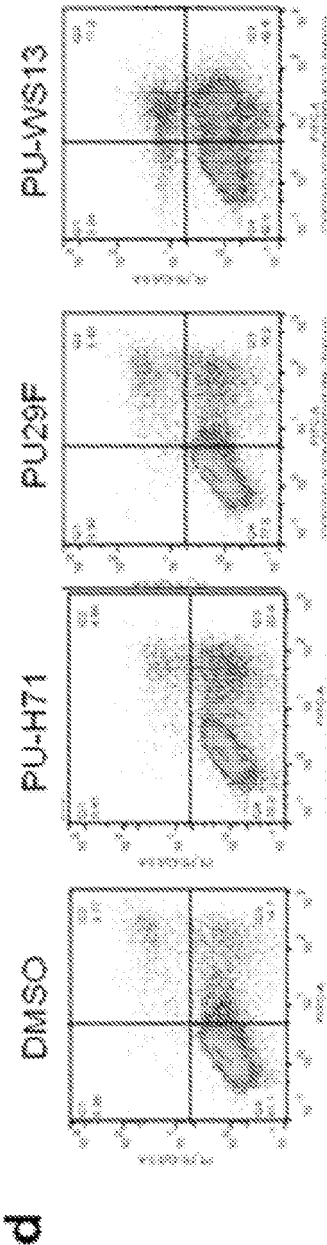


FIG. 11d

Treatment of HER2-overexpressing SKBr3 breast cancer cells with the Grp94 inhibitor PU-WS13 is more potent at killing these cells through apoptosis than is inhibition of Hsp90 alone by PU-29F or pan-Hsp90 inhibition by PU-H71.

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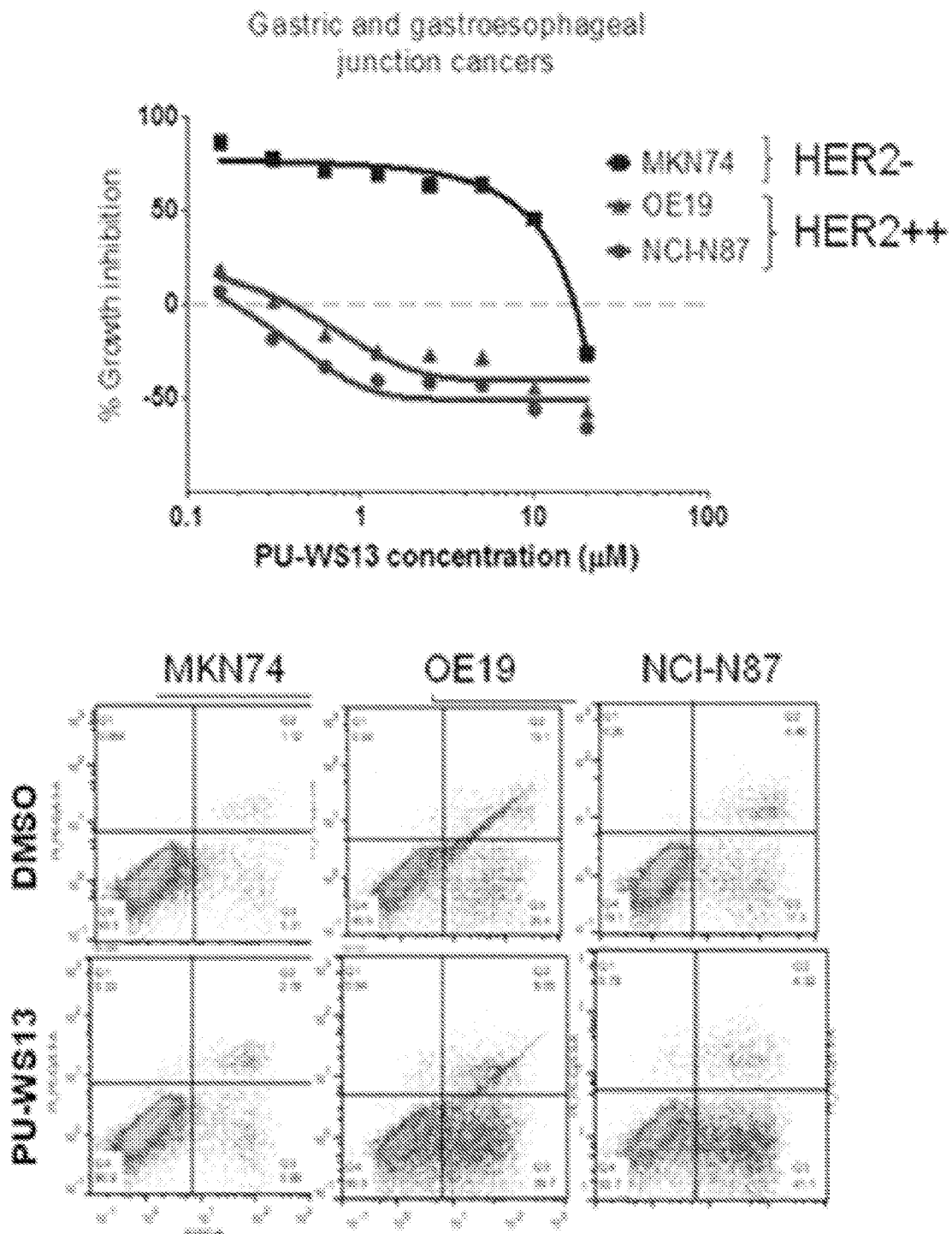
**FIG. 12**

FIG. 13a

EGFR overexpressing breast cancer cells are sensitive to Grp94 inhibition

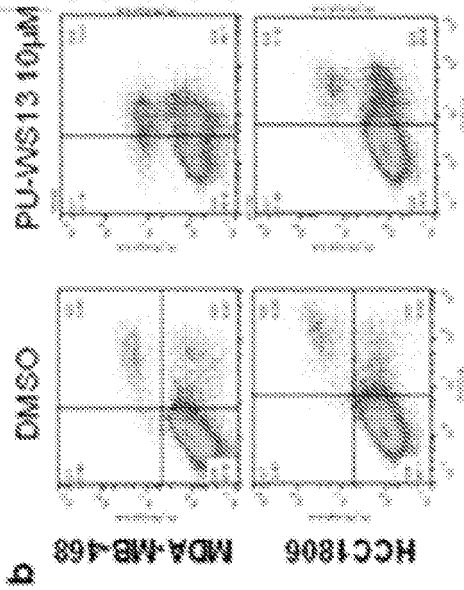
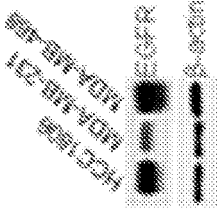
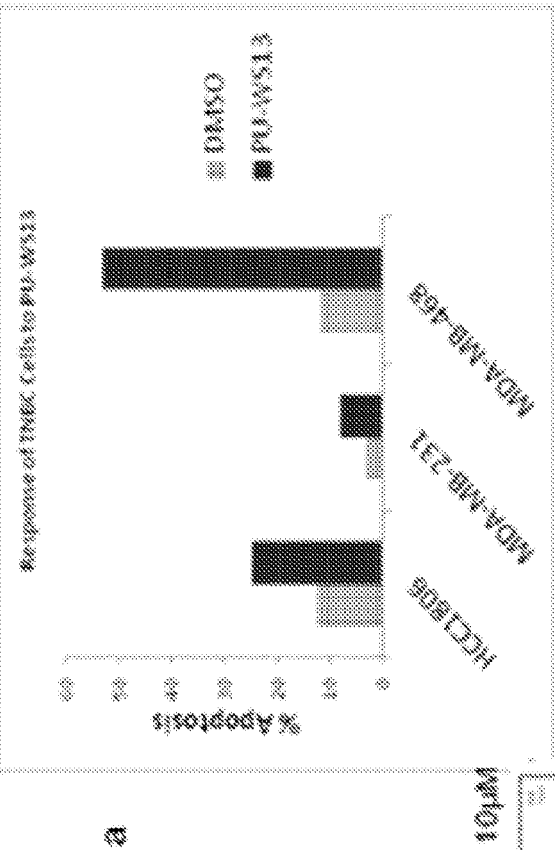


FIG. 13b

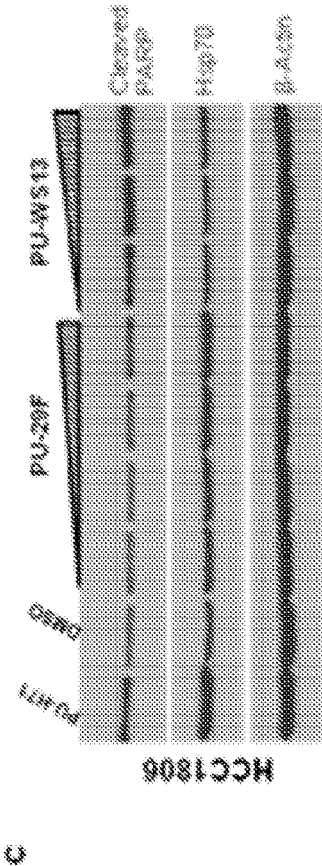


FIG. 13c

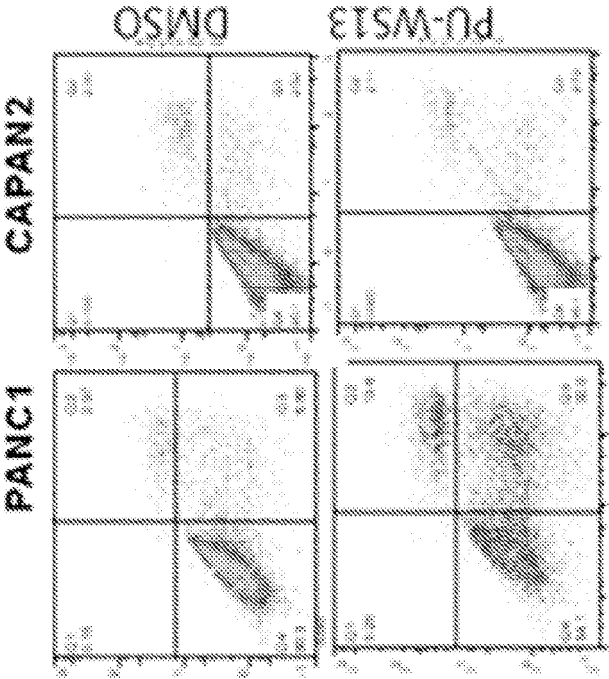


FIG. 14b

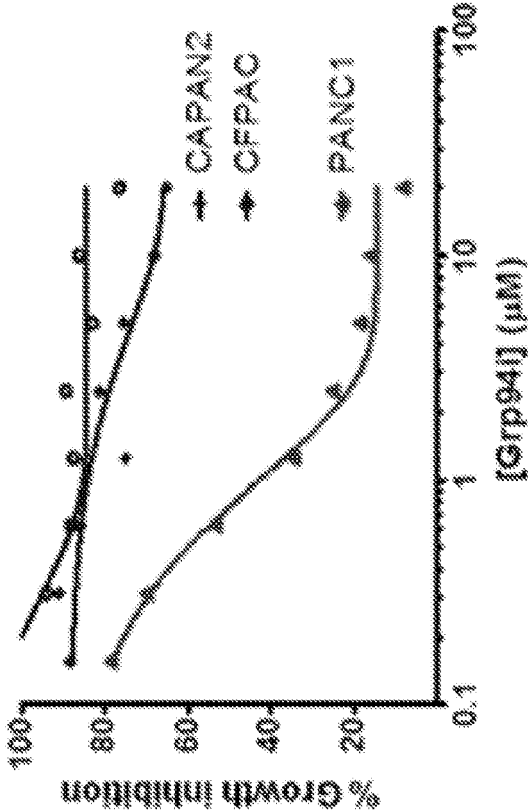
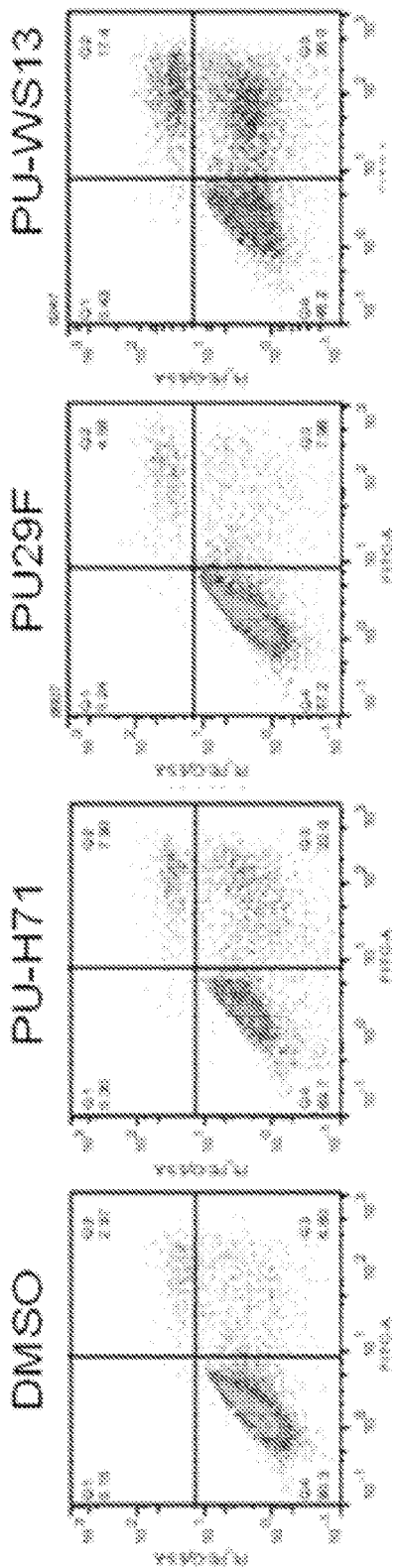


FIG. 14a

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Treatment of EGFR-overexpressing PANC-1 cells with the Grp94 inhibitor PU-WS13 is more potent at killing these cells through apoptosis than is inhibition of Hsp90 alone by PU-29F or pan-Hsp90 inhibition by PU-H71.

FIG. 15

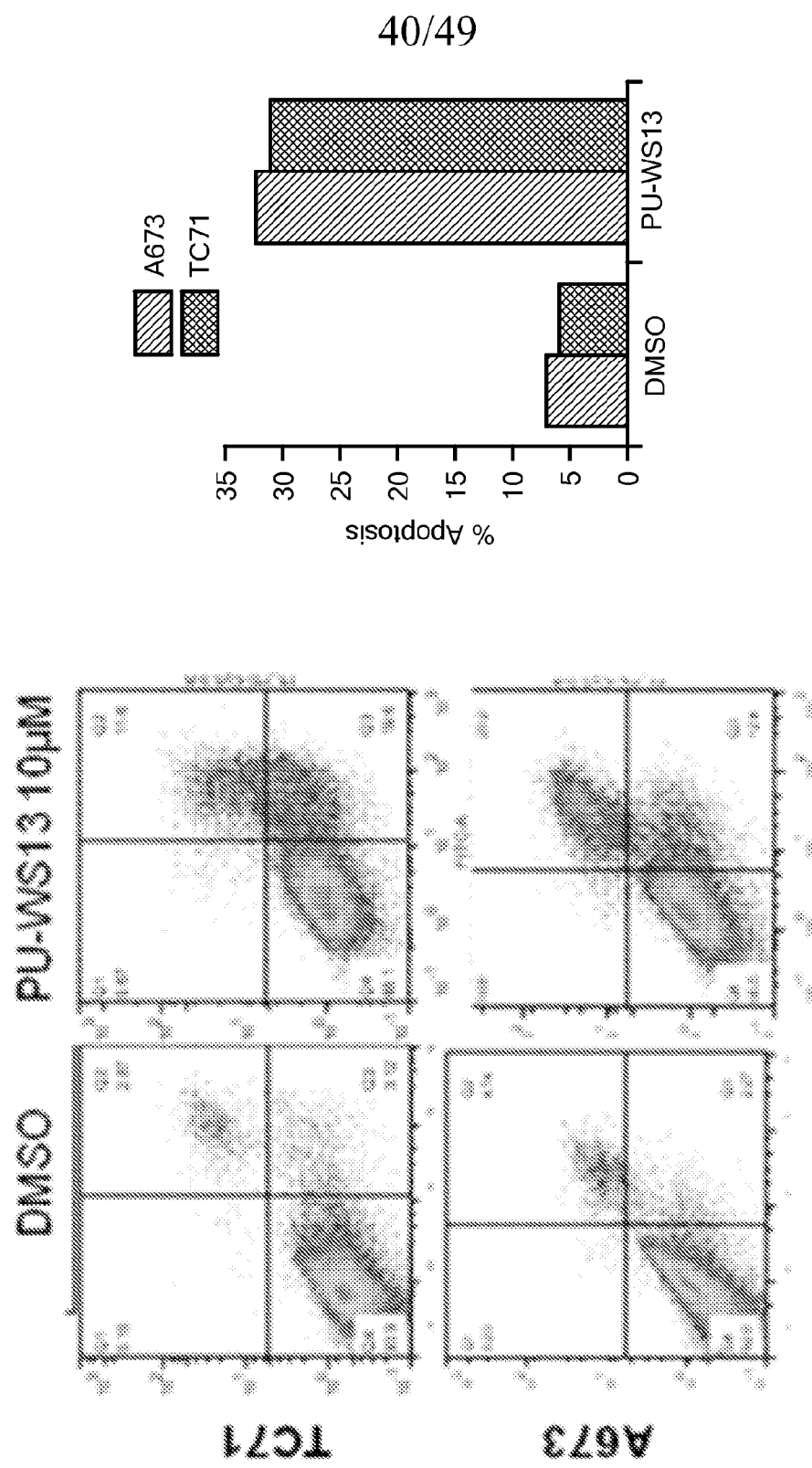
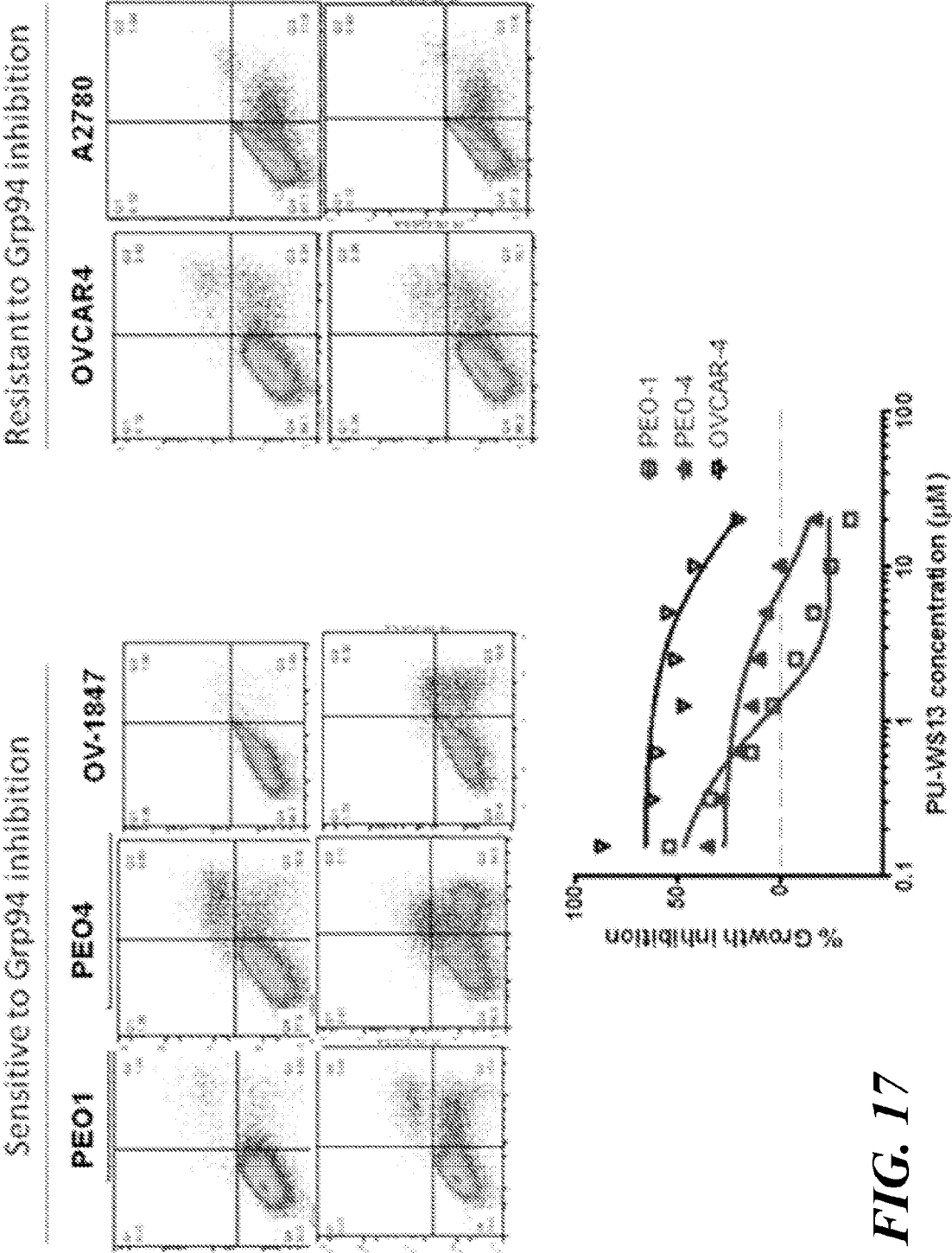
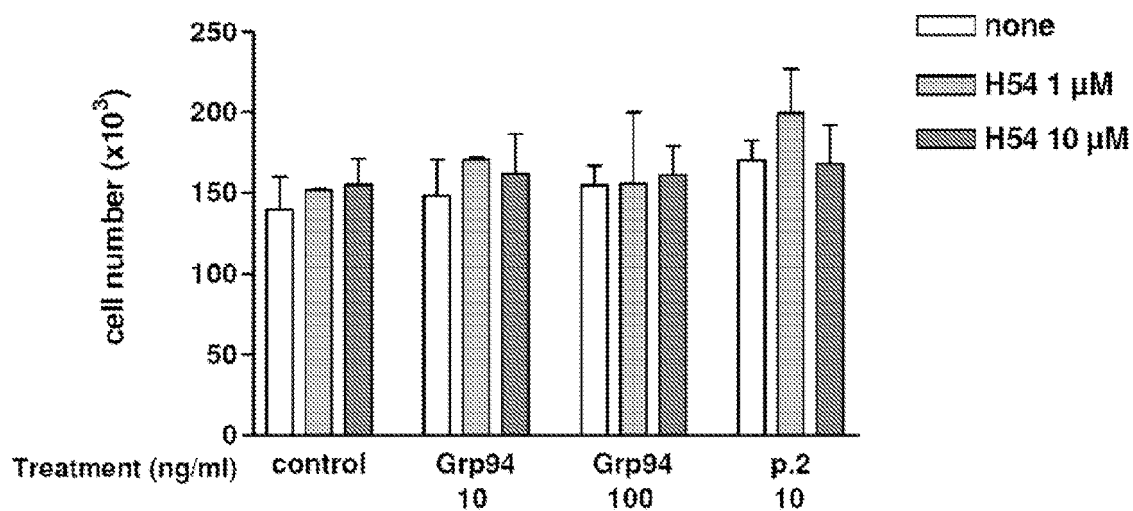
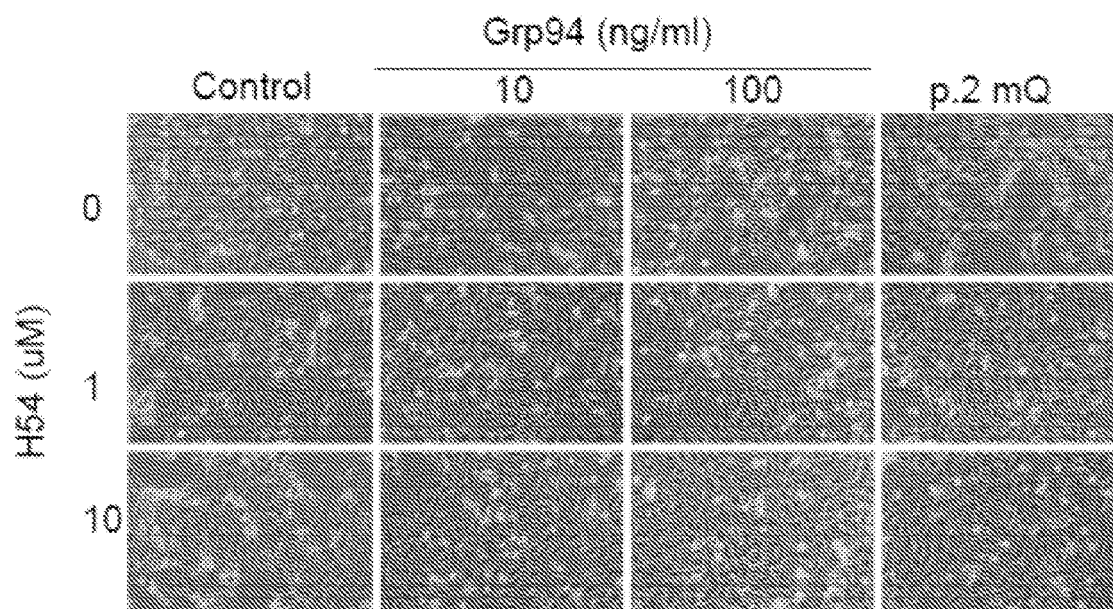


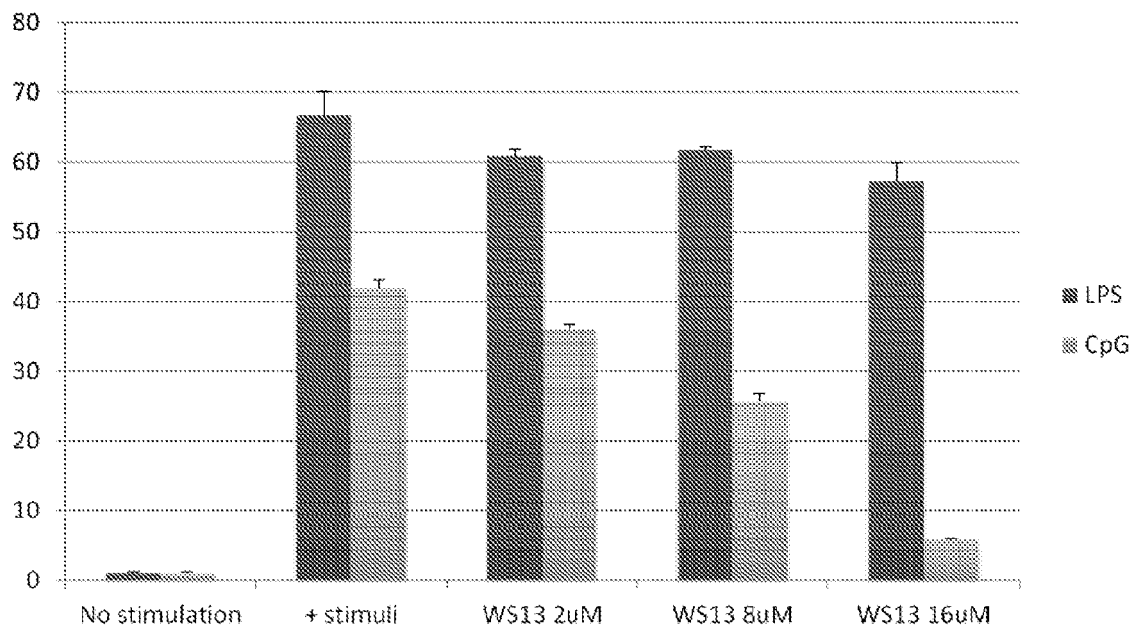
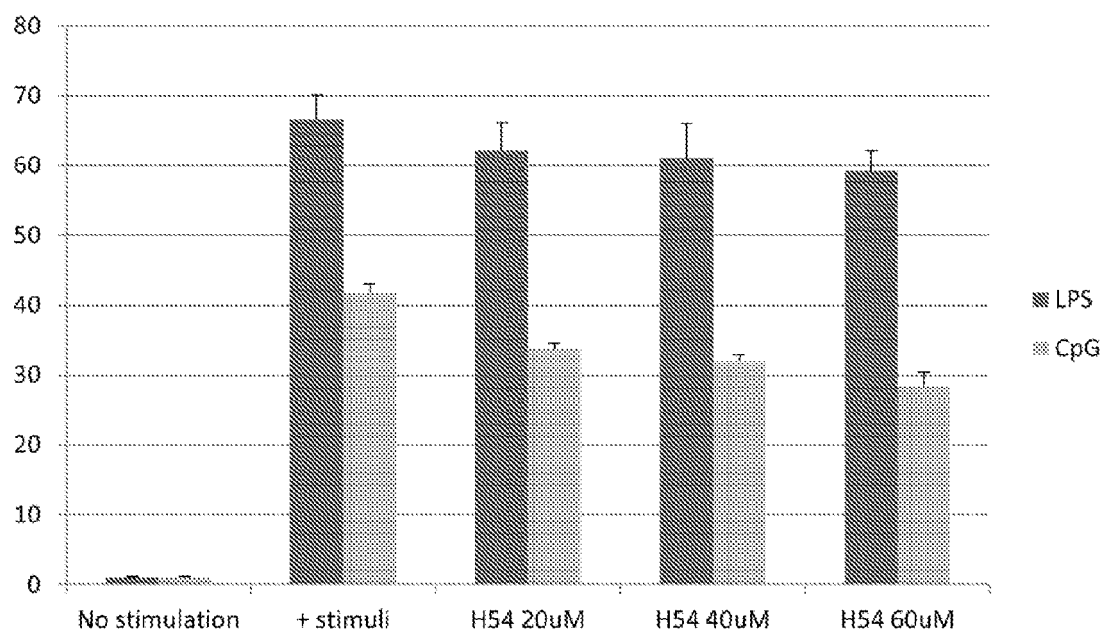
FIG. 16



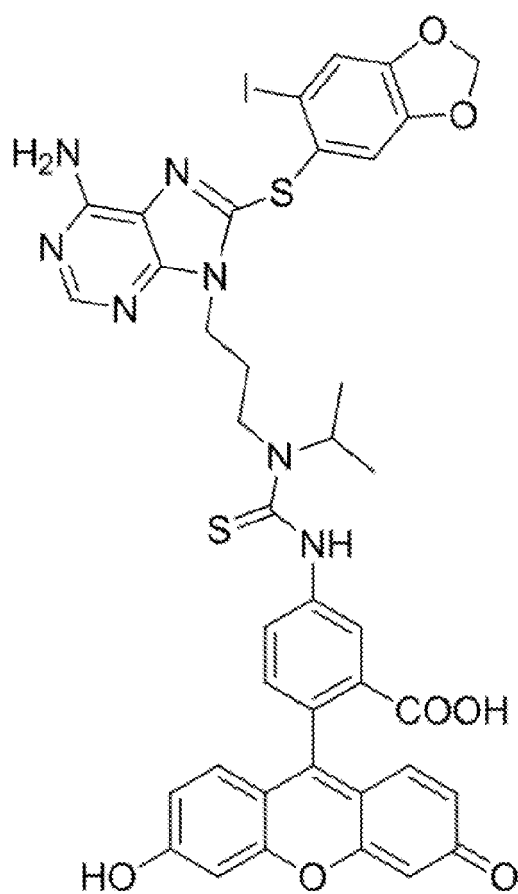
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**FIG. 18a****FIG. 18b**

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**FIG. 19a****FIG. 19b**

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COMPOUND 40

FIG. 20

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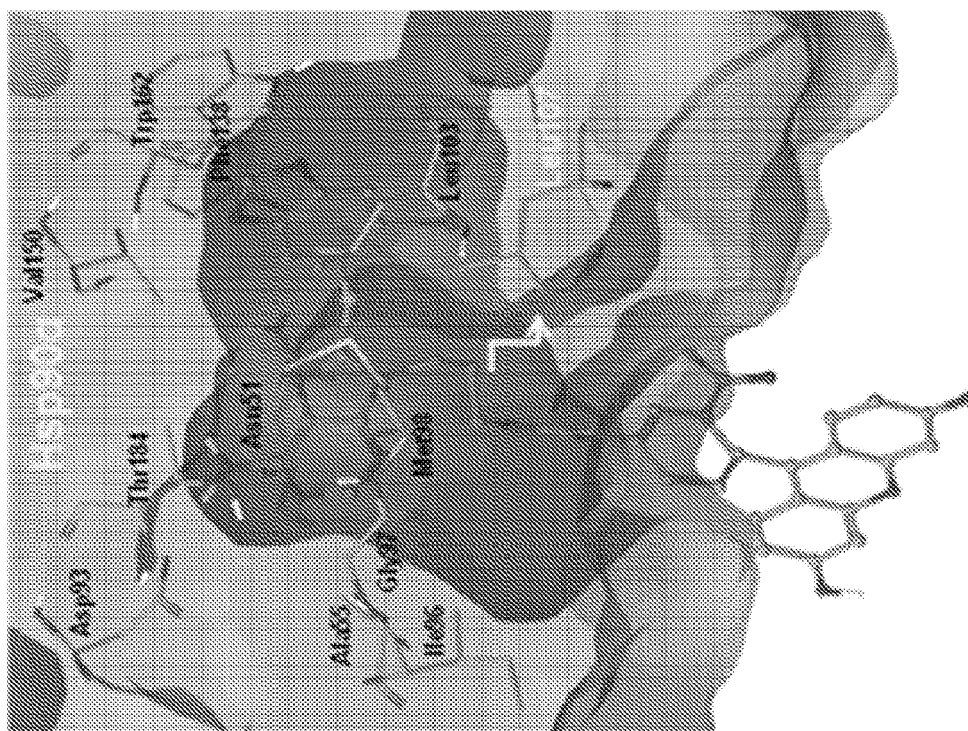


FIG. 21b

b

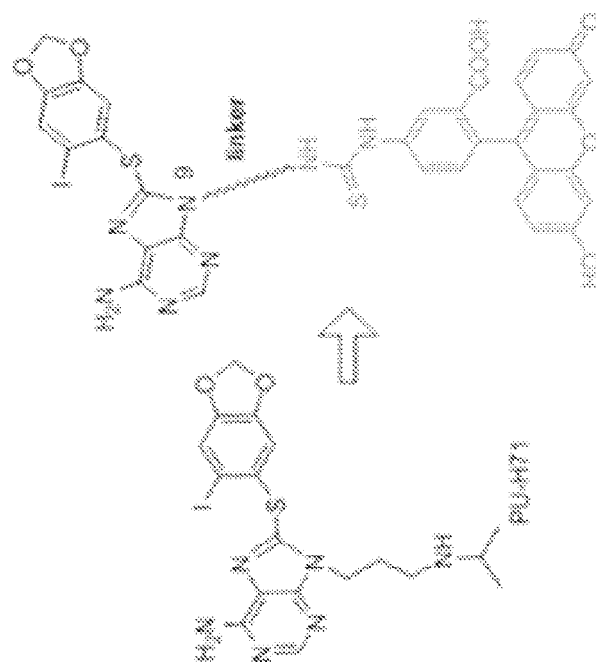


FIG. 21a

a

FIG. 22b

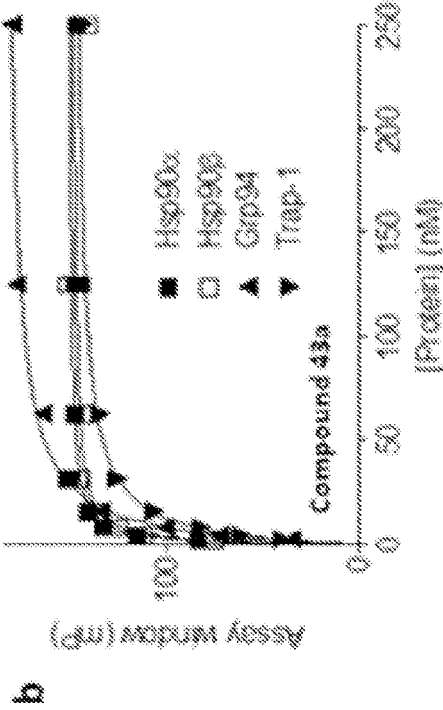


FIG. 22a

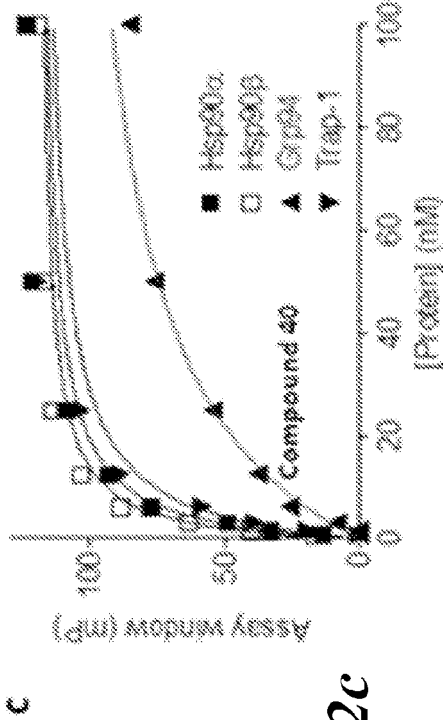
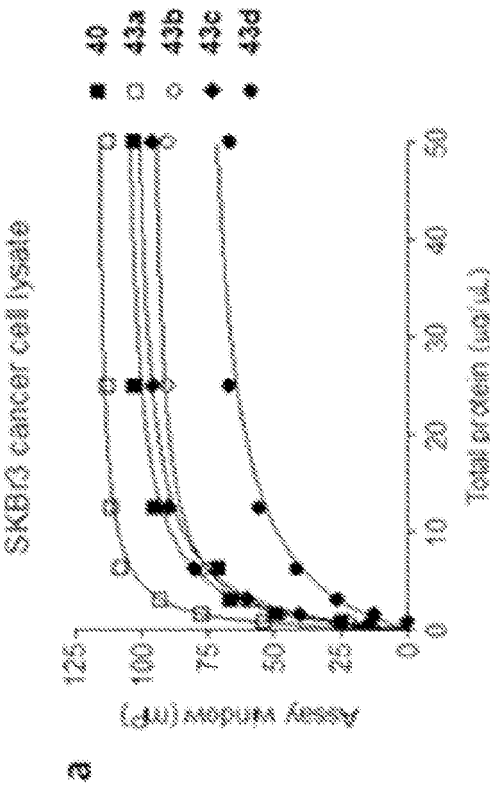
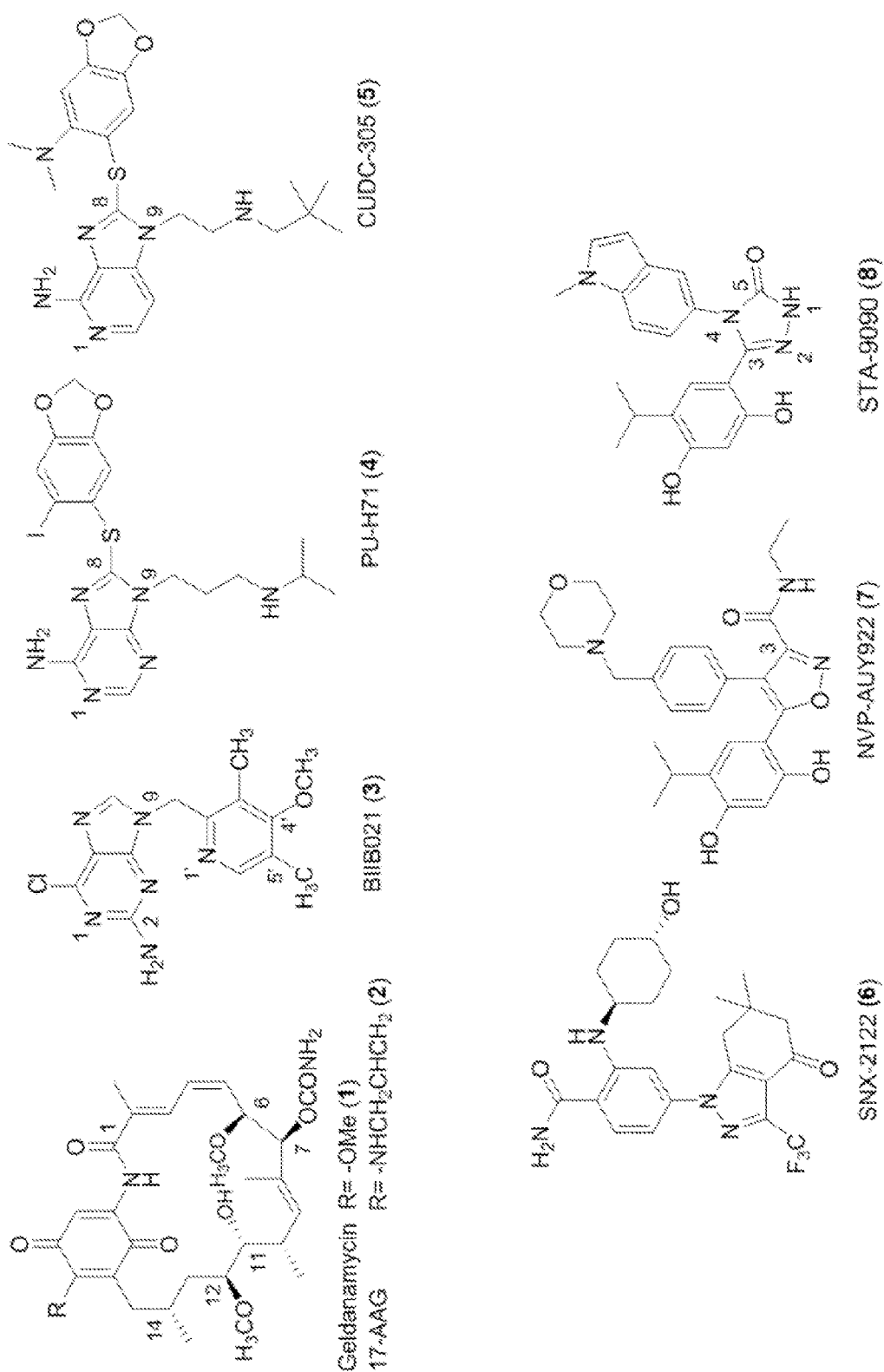


FIG. 22c

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**FIG. 23**

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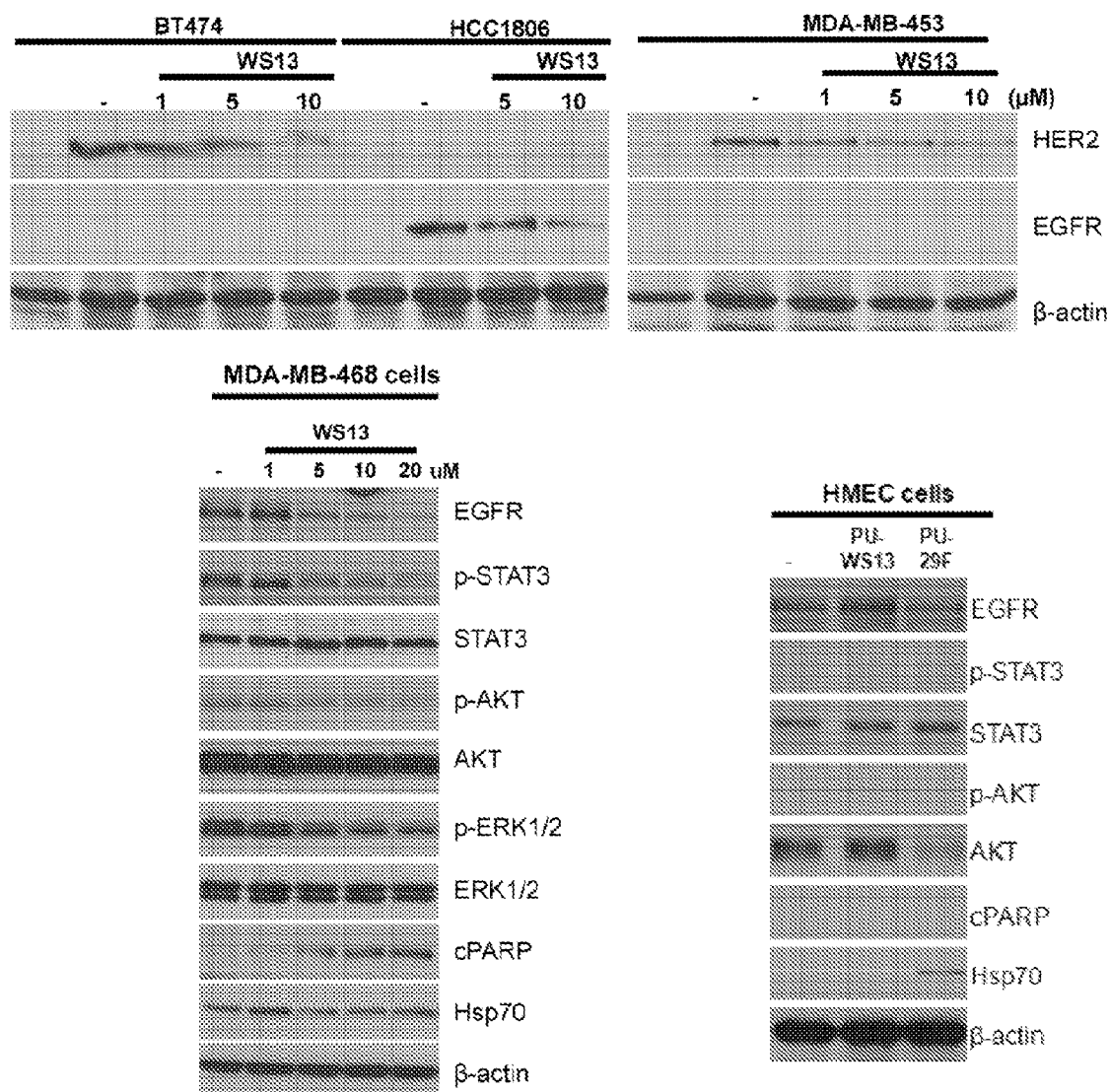
**FIG. 24**

FIG. 25a

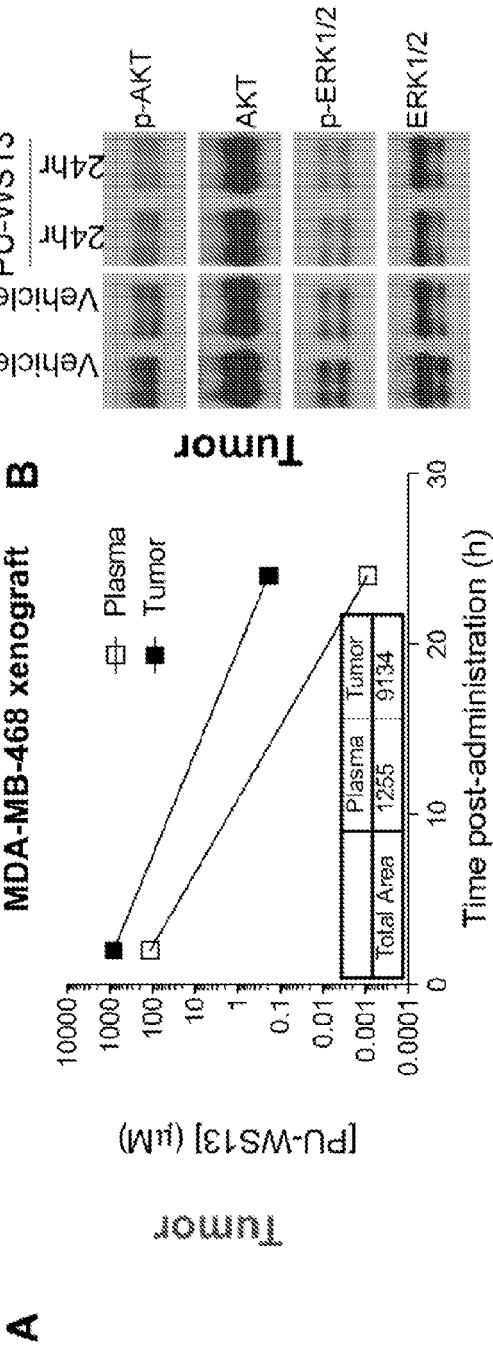


FIG. 25b

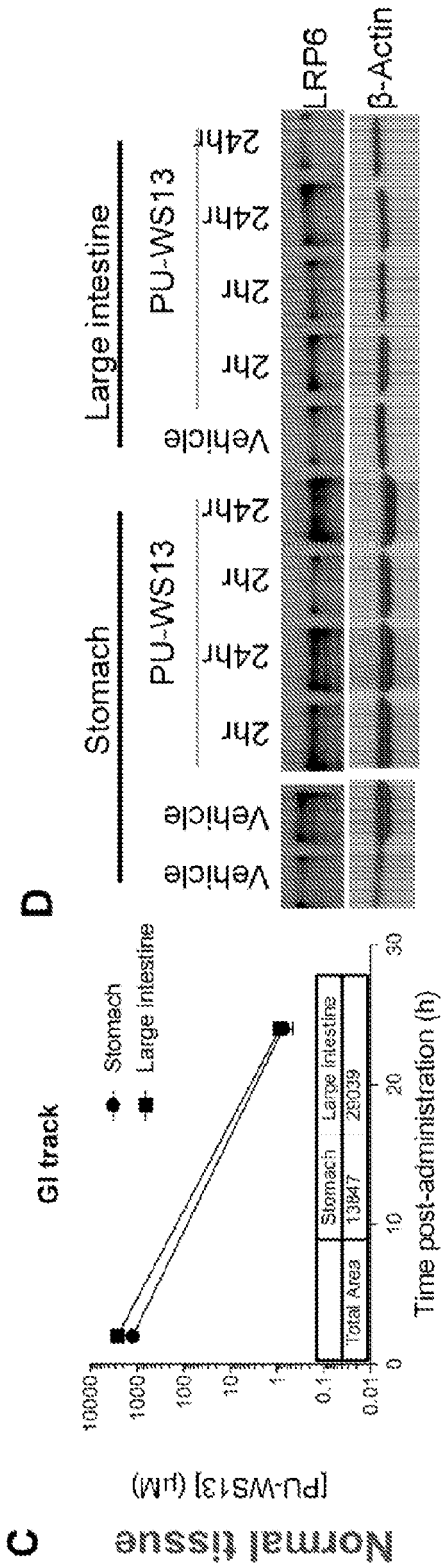


FIG. 25c

FIG. 25d