

FIG. 1A

ESR1: wild-type

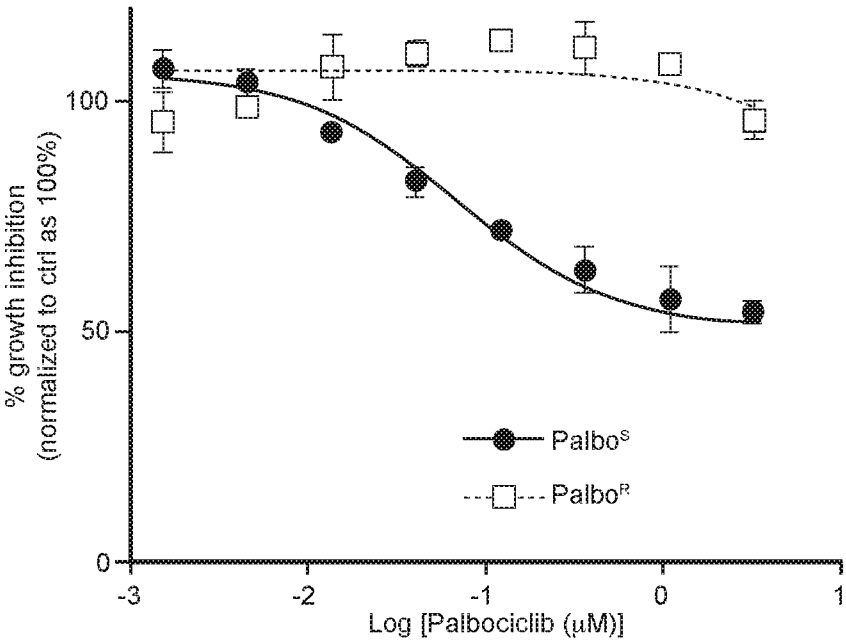


FIG. 1B

ESR1: wild-type

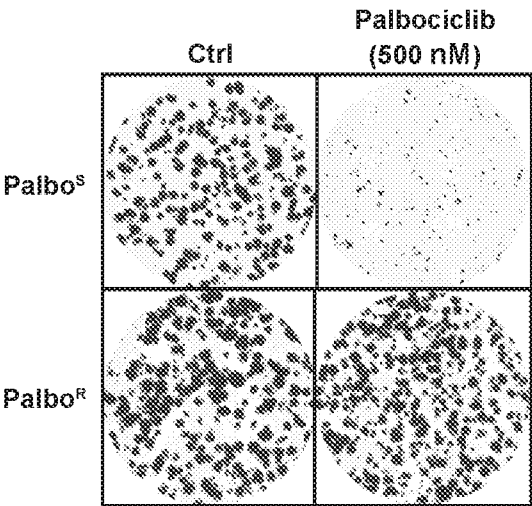


FIG. 1C

ESR1: wild-type

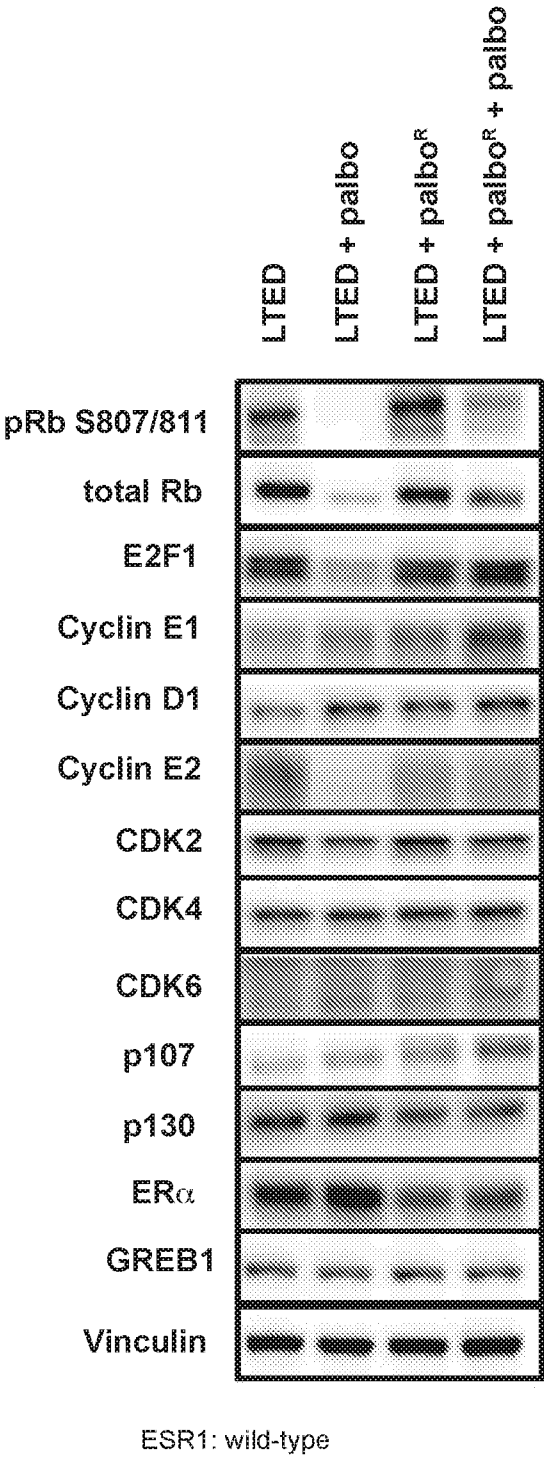
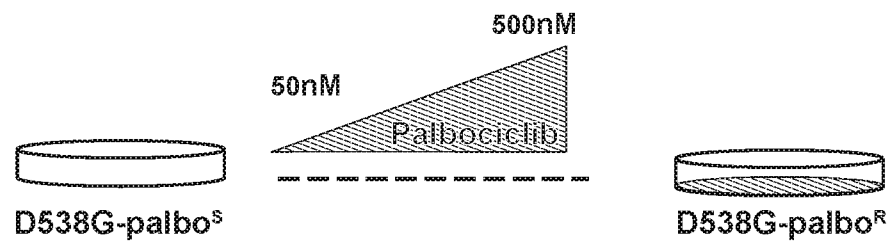
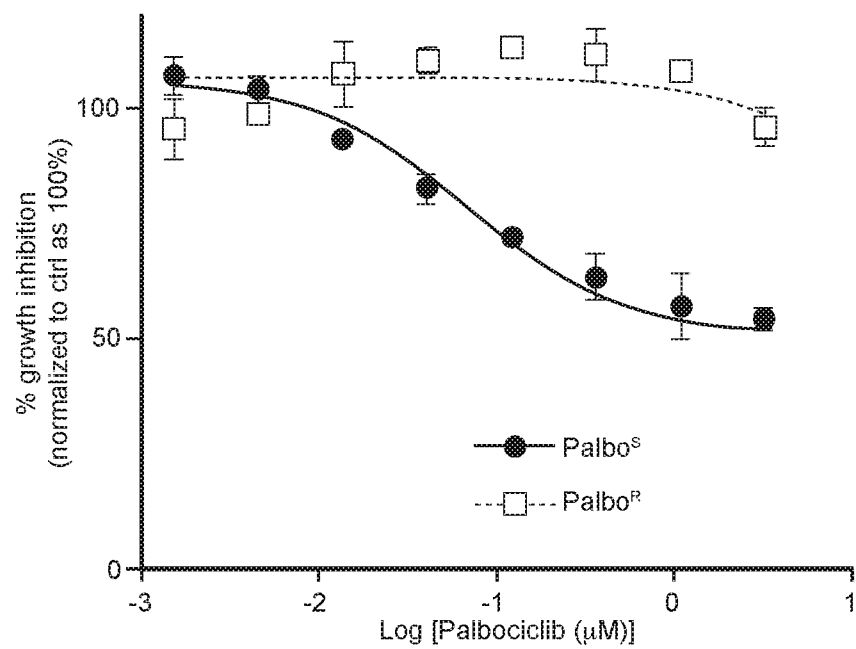


FIG. 1D

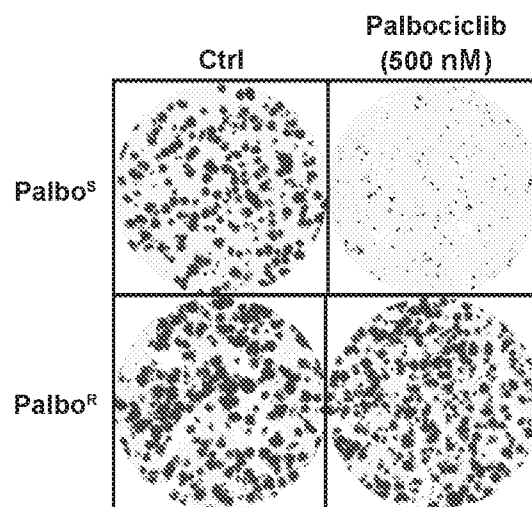
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**FIG. 2A**

ESR1: Mutant (D538G)

**FIG. 2B**

ESR1: Mutant (D538G)

**FIG. 2C**

ESR1: Mutant (D538G)

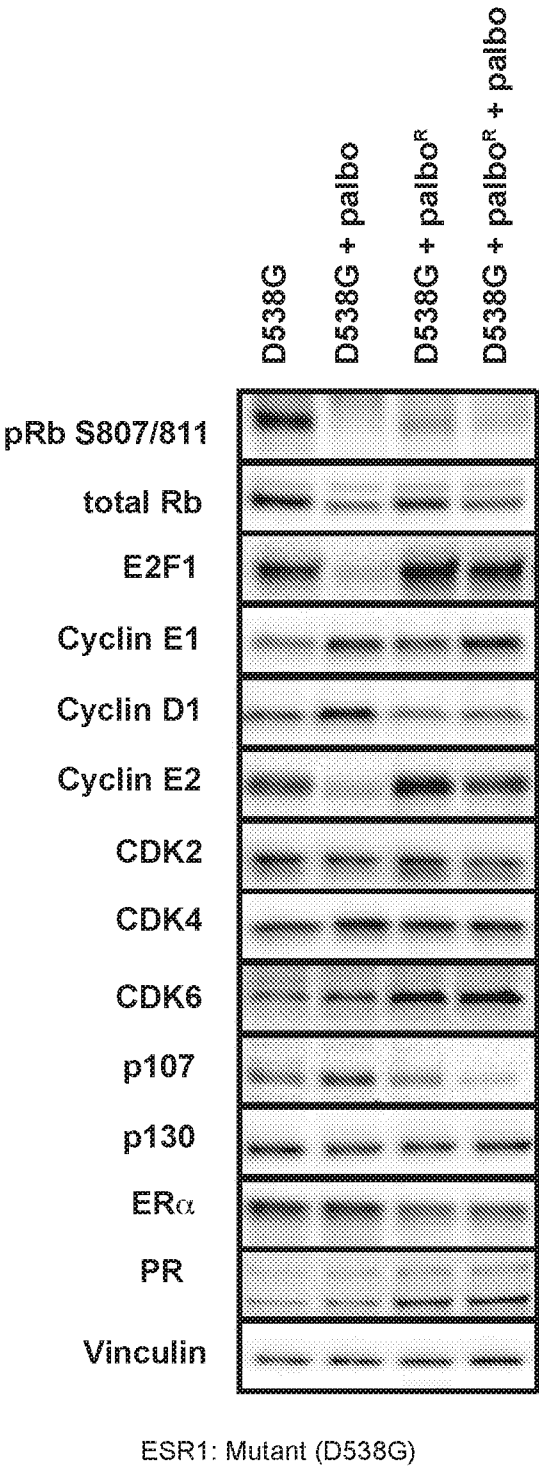
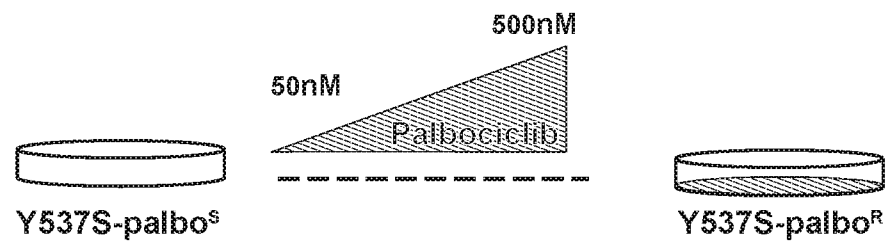
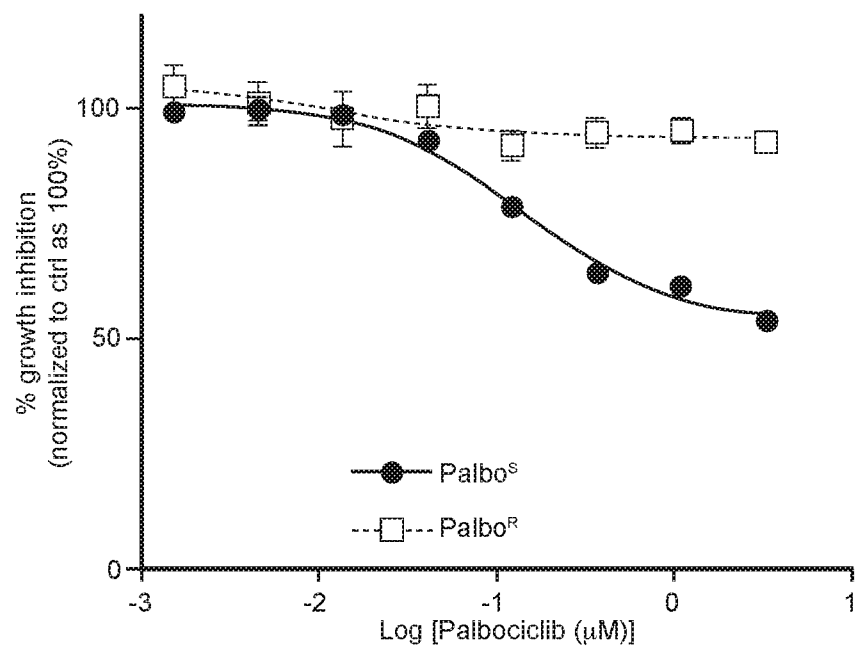
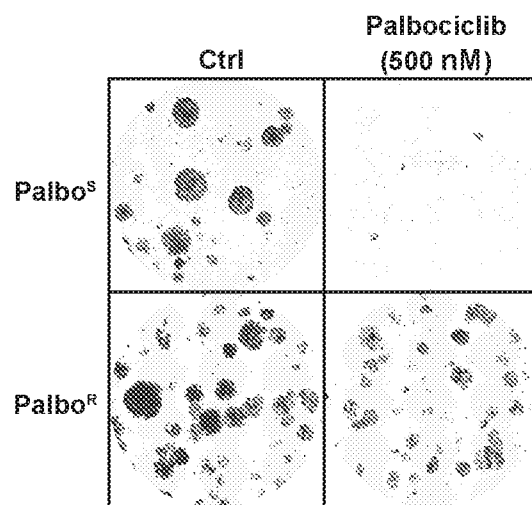


FIG. 2D

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**FIG. 3A****FIG. 3B****FIG. 3C**

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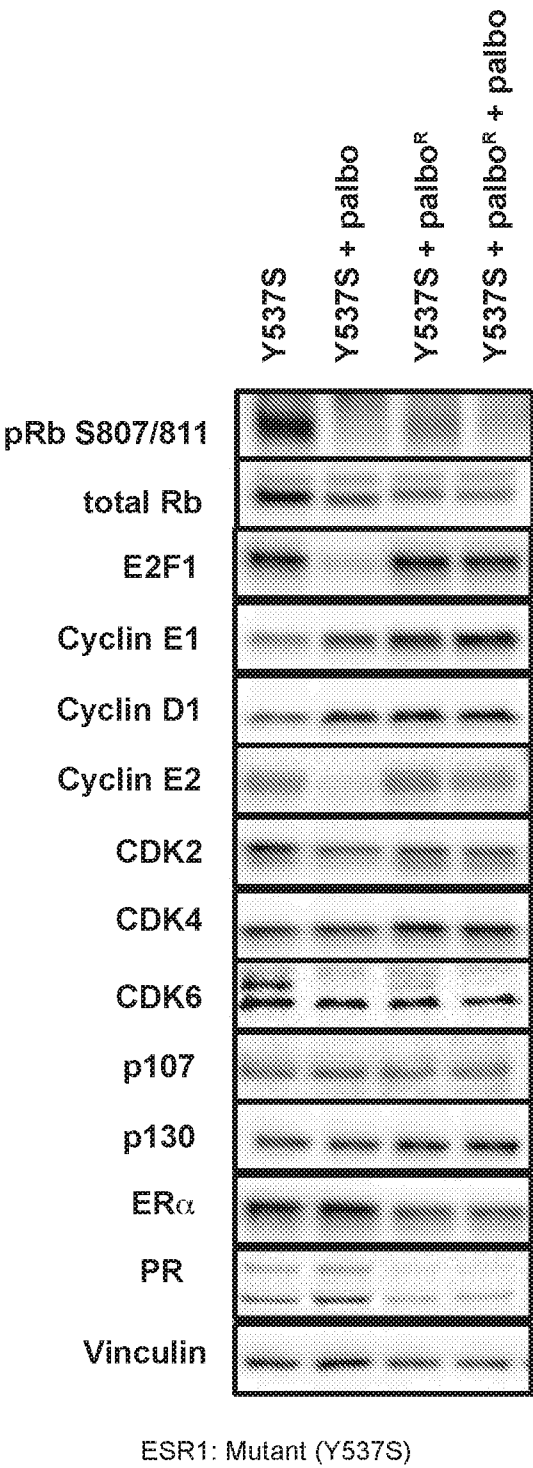


FIG. 3D

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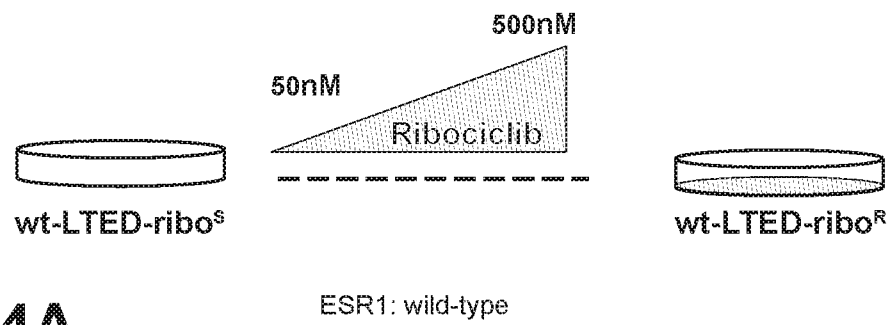


FIG. 4A

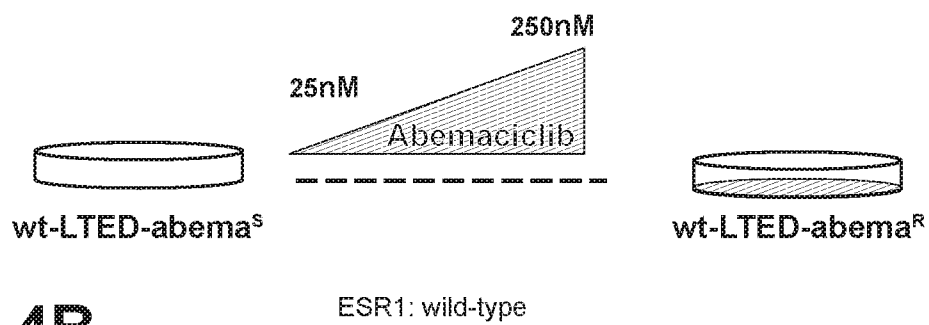


FIG. 4B

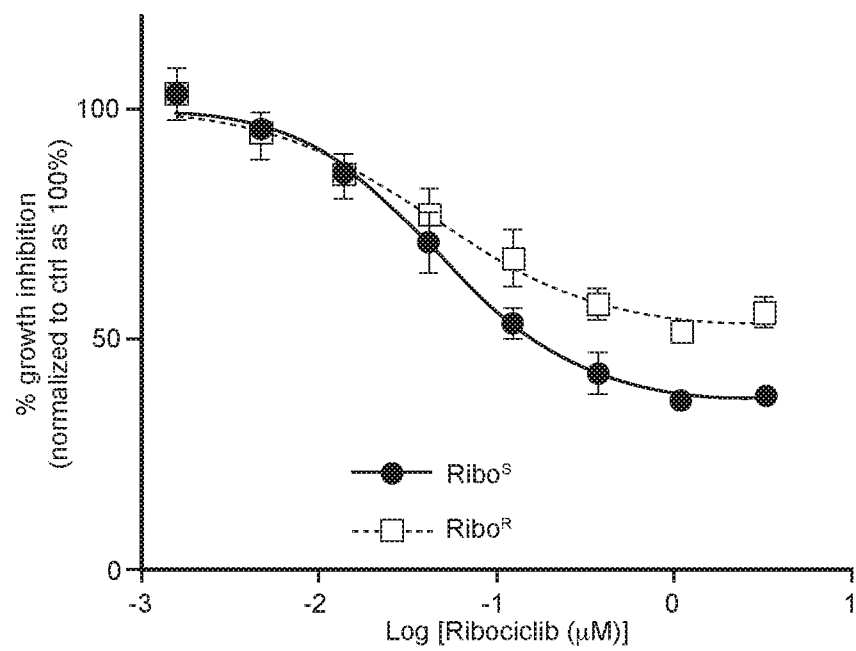


FIG. 4C

ESR1: wild-type

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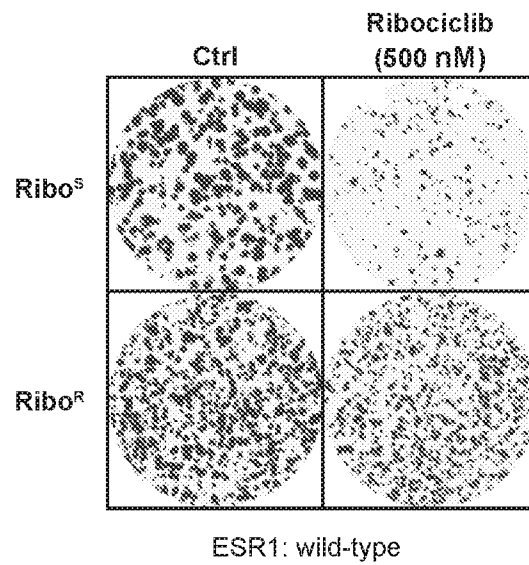


FIG. 4D

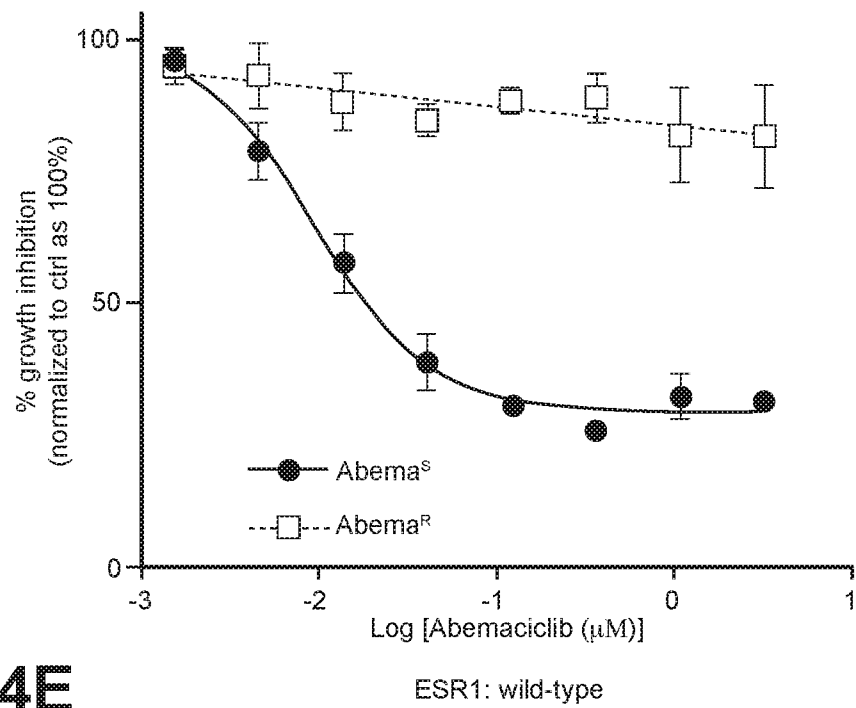


FIG. 4E

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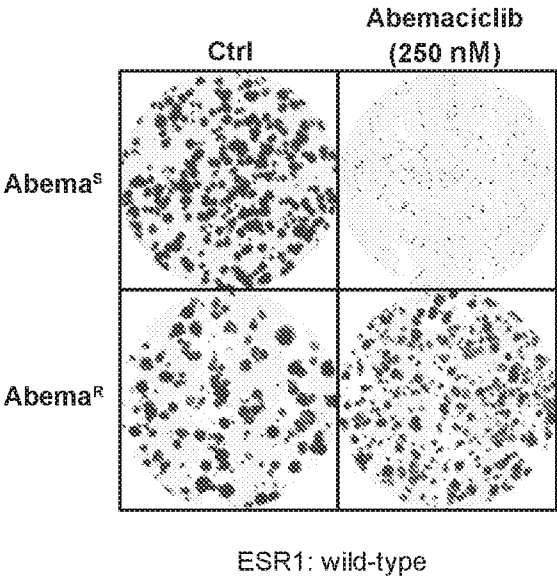
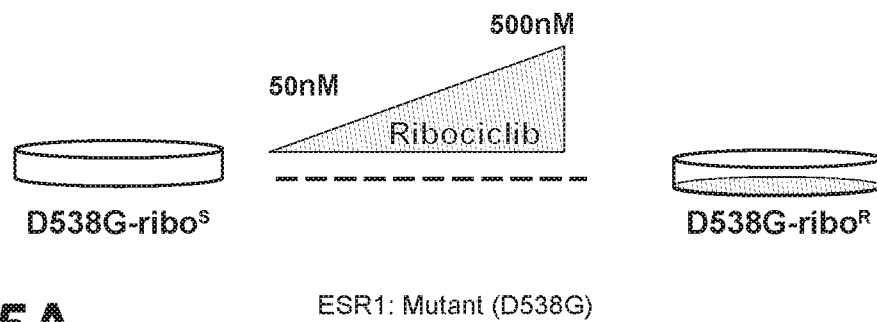
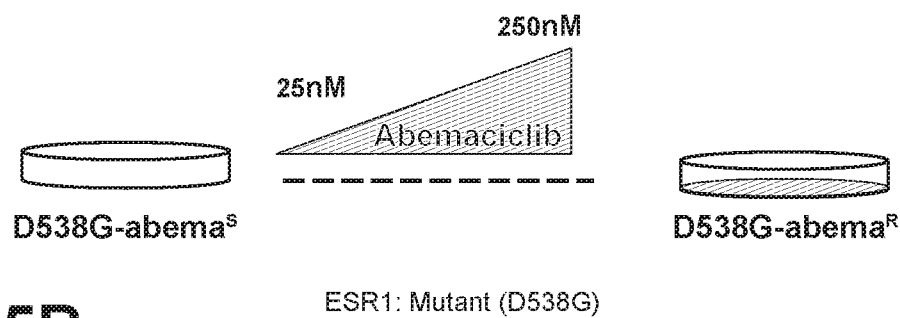
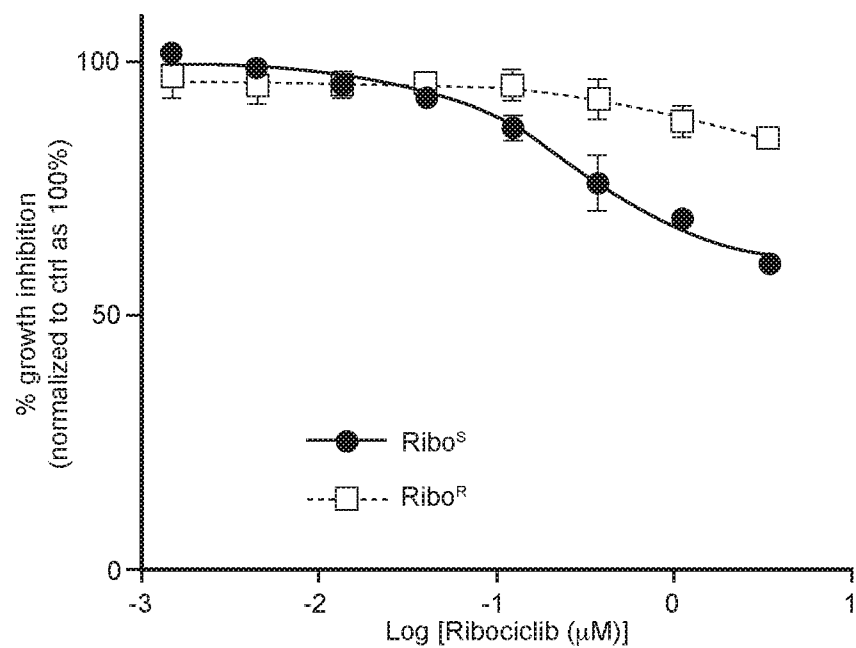
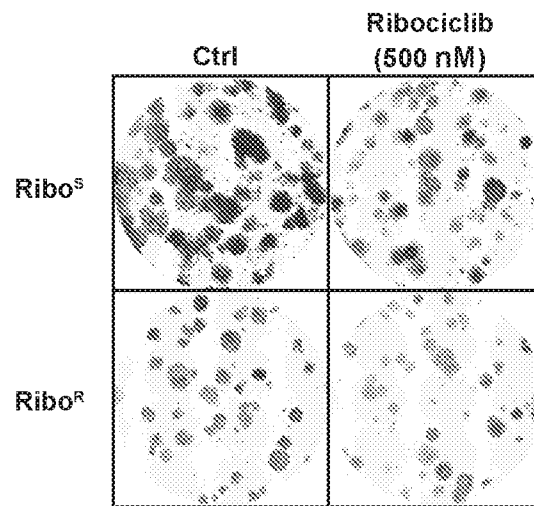


FIG. 4F

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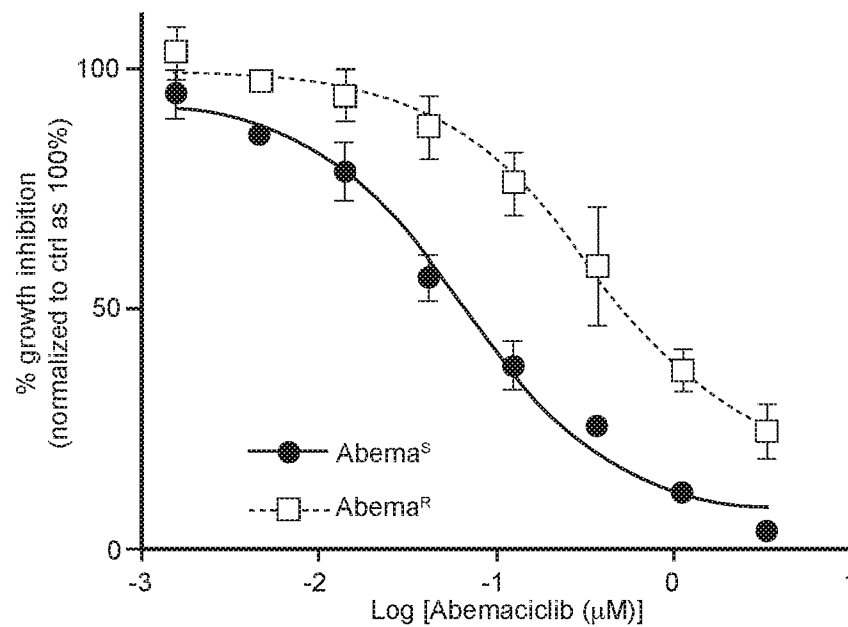
**FIG. 5A****FIG. 5B****FIG. 5C**

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ESR1: Mutant (D538G)

FIG. 5D



ESR1: Mutant (D538G)

FIG. 5E

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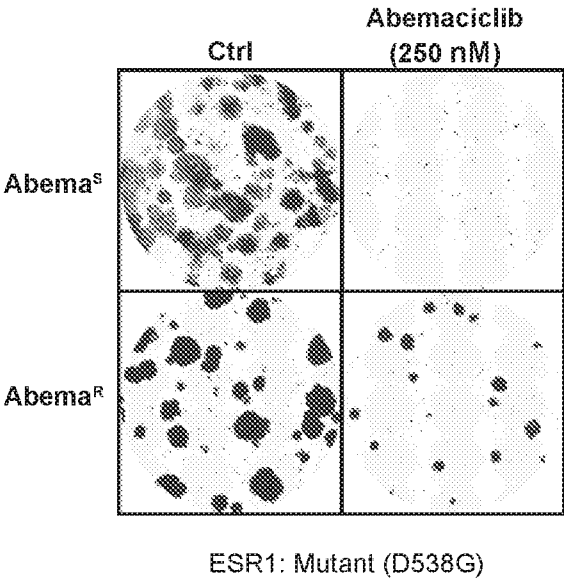
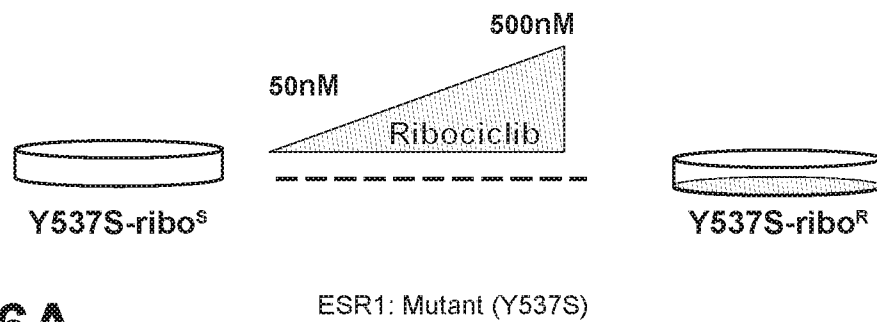
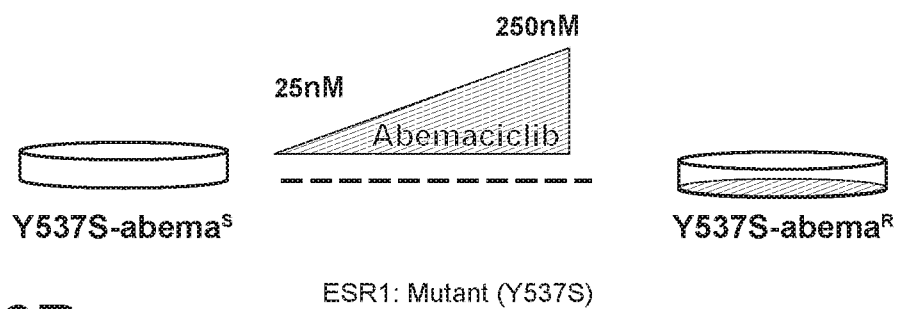
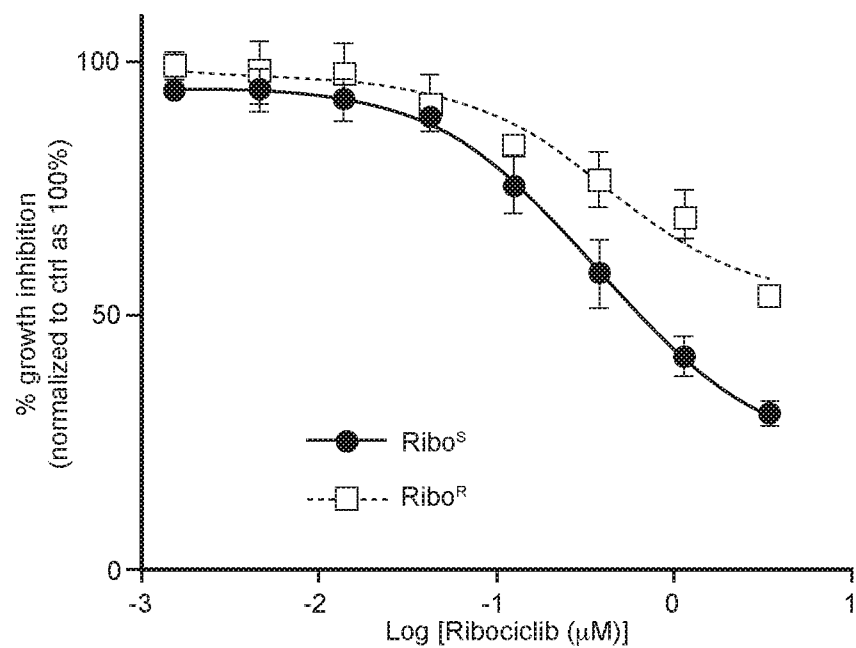


FIG. 5F

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**FIG. 6A****FIG. 6B****FIG. 6C**

ESR1: Mutant (Y537S)

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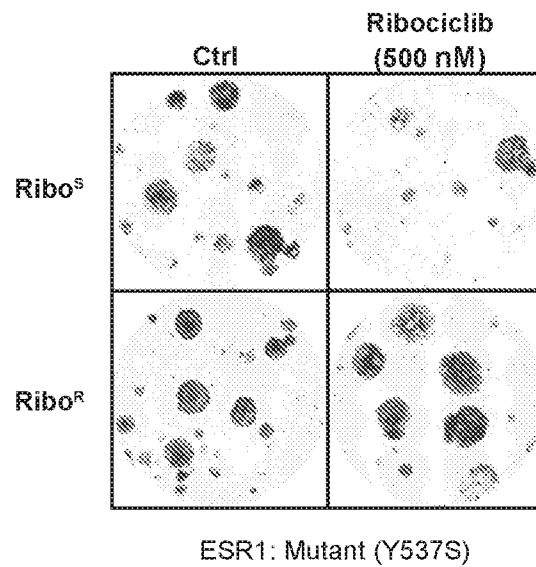


FIG. 6D

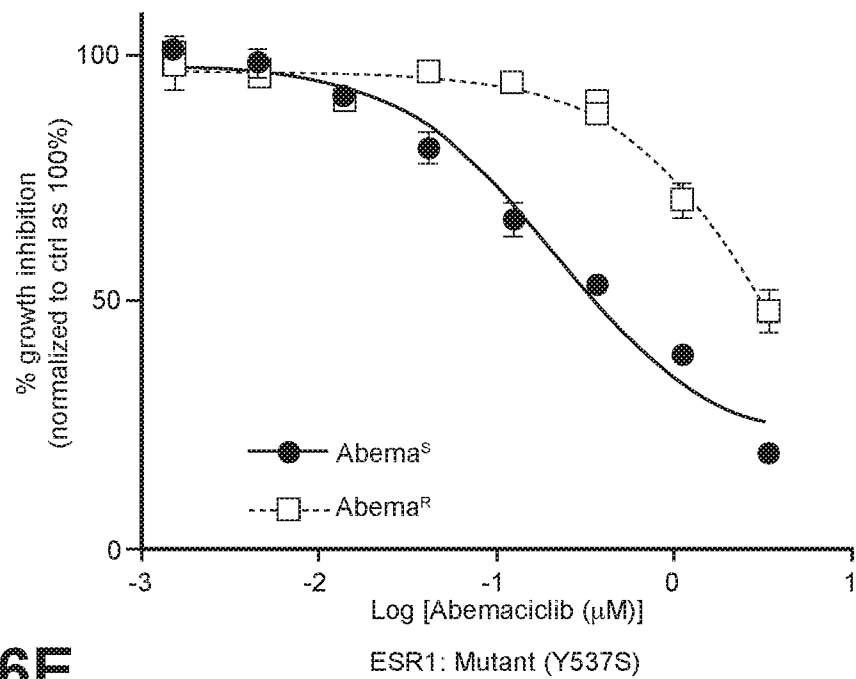


FIG. 6E

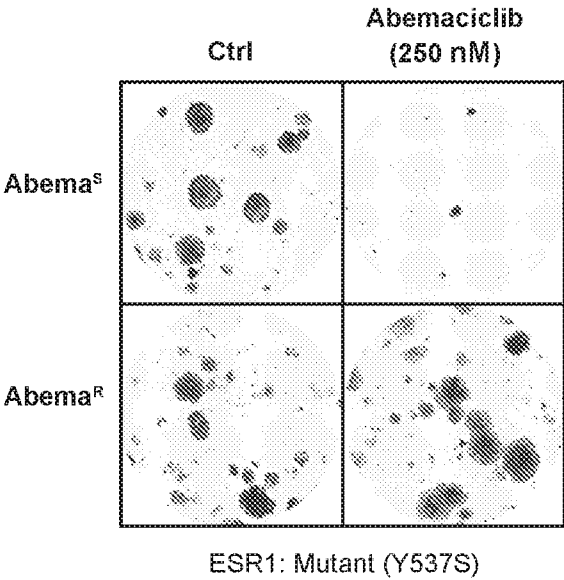
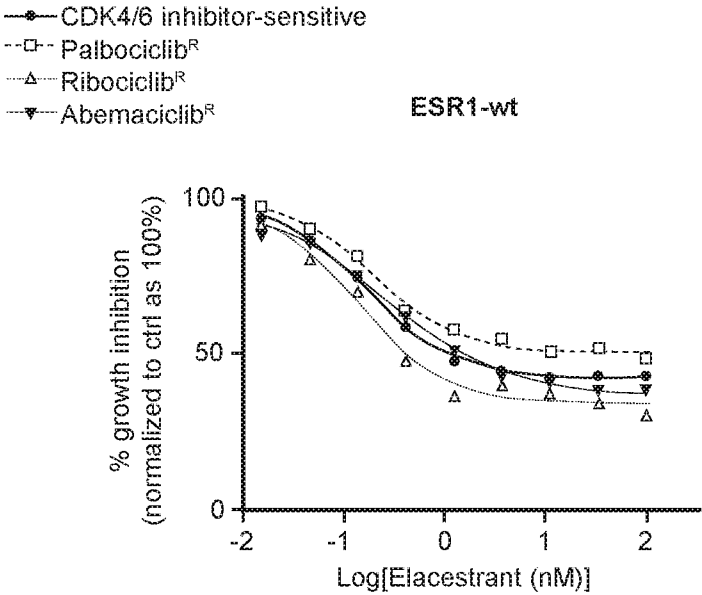
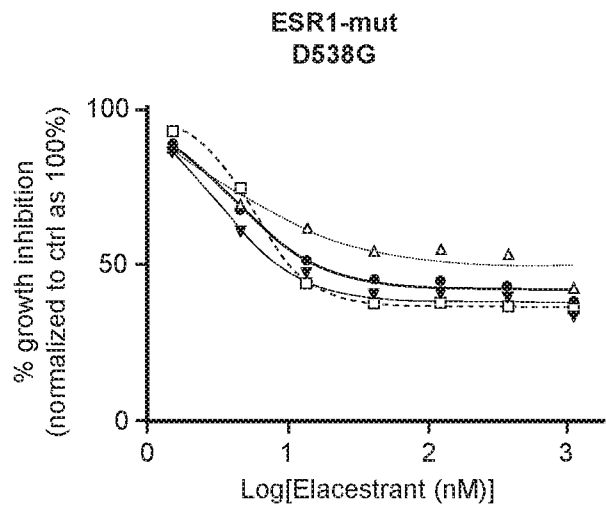


FIG. 6F



Growth inhibition, EG ₅₀ (nM)	
ESR1 wild-type	
CDK4/6 inhibitor-sensitive	0.17
Palbociclib ^R	0.19
Ribociclib ^R	0.13
Abemaciclib ^R	0.25

FIG. 7A



Growth inhibition, EG ₅₀ (nM)	
ESR1 mutant (D538G)	
CDK4/6 inhibitor-sensitive	4.2
Palbociclib ^R	5.6
Ribociclib ^R	4.1
Abemaciclib ^R	3.4

FIG. 7B

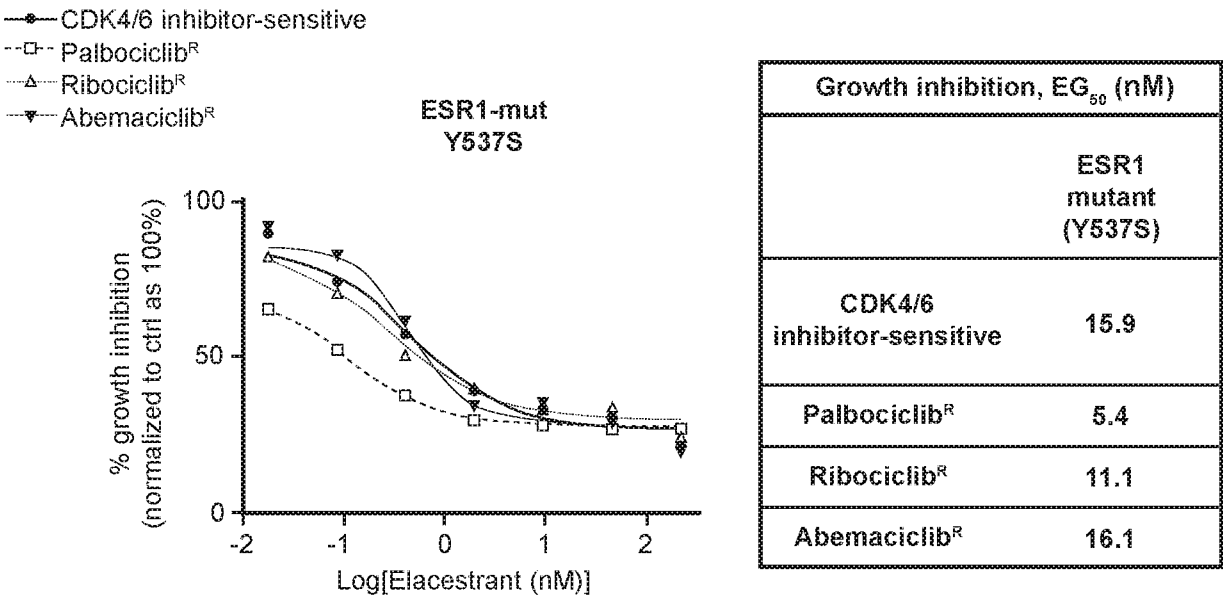


FIG. 7C

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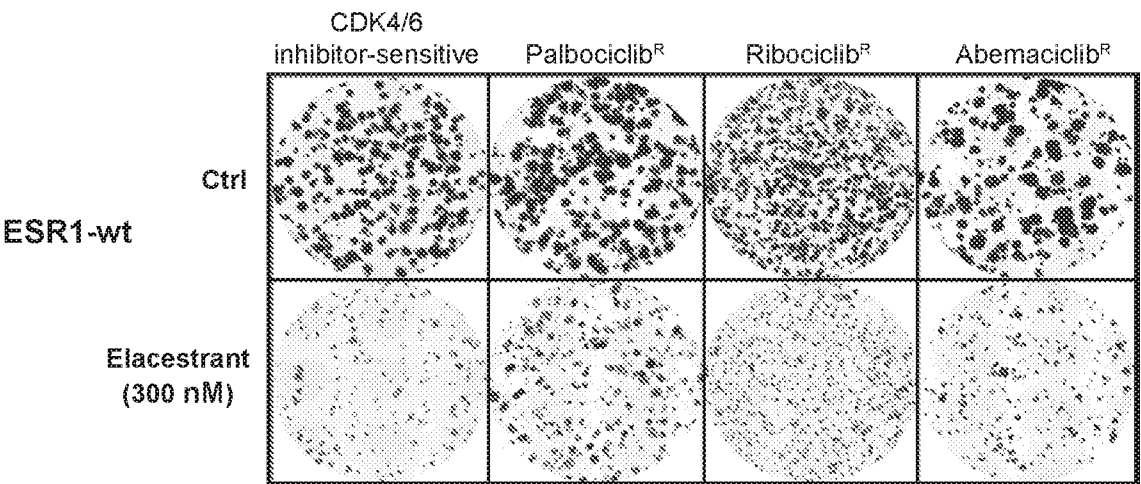


FIG. 8A

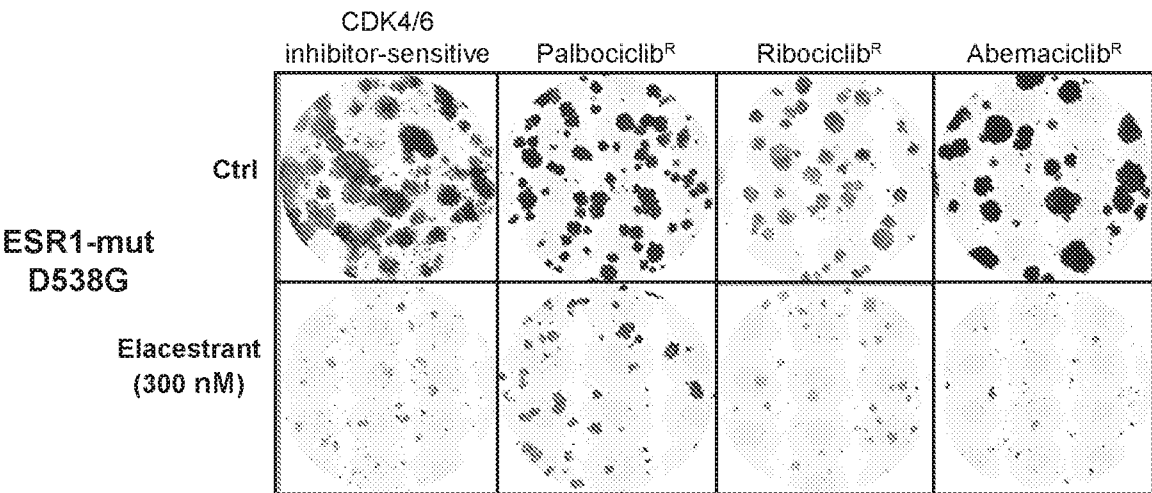


FIG. 8B

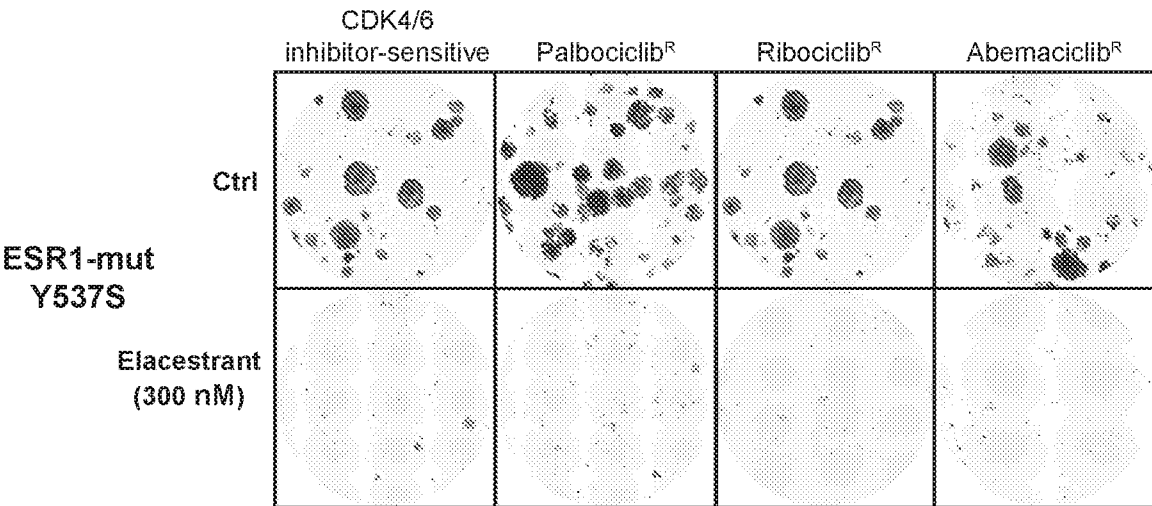


FIG. 8C

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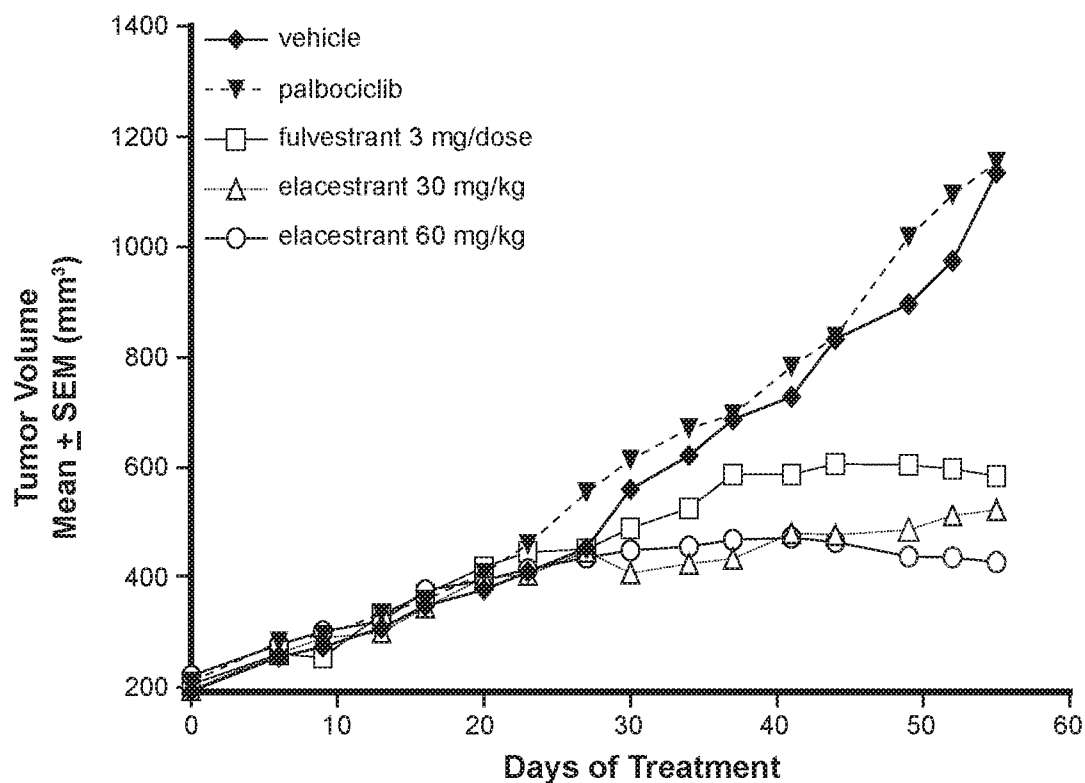


FIG. 9A

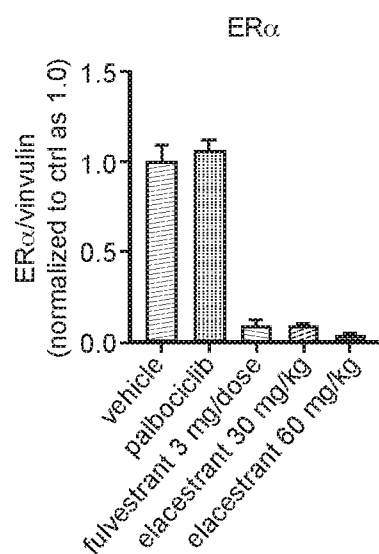


FIG. 9B

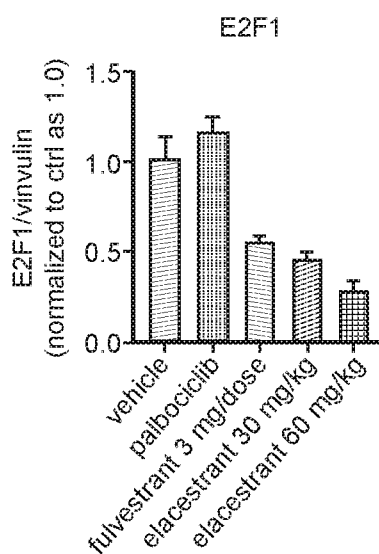


FIG. 9C

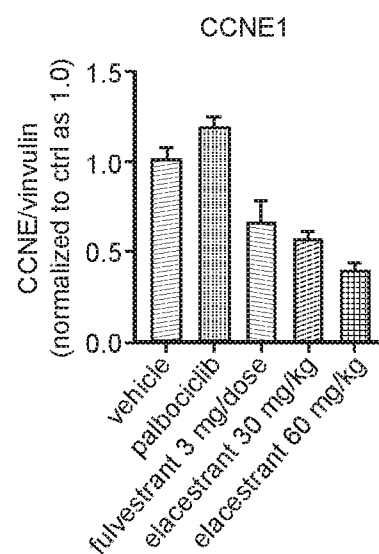


FIG. 9D

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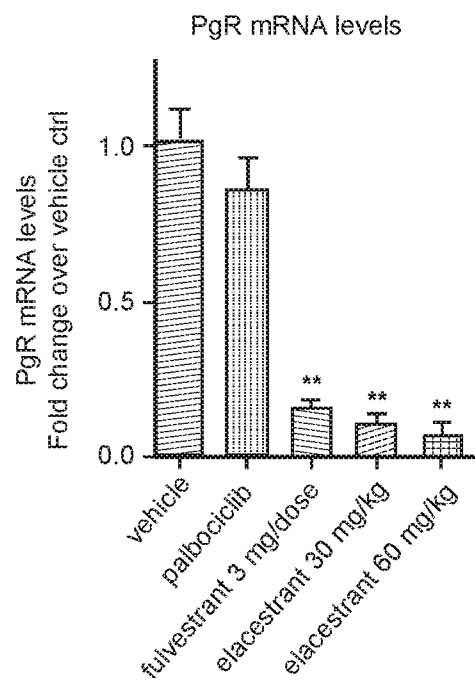


FIG. 9E

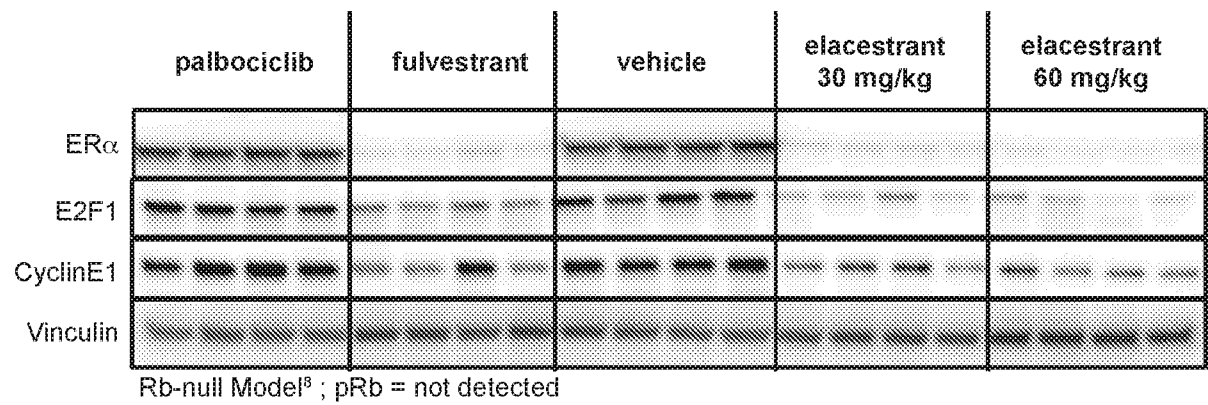


FIG. 9F

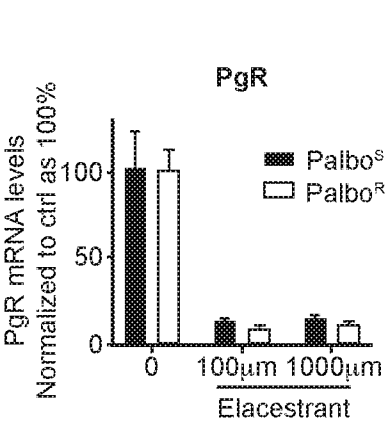


FIG. 10A

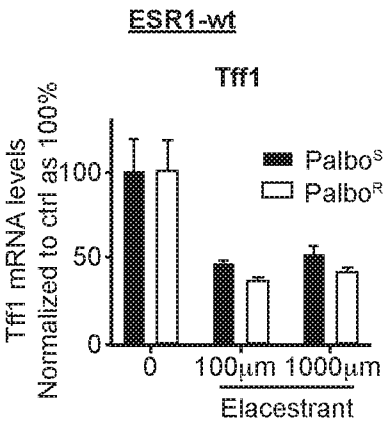


FIG. 10B

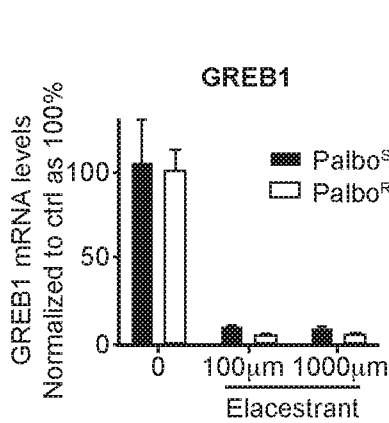


FIG. 10C

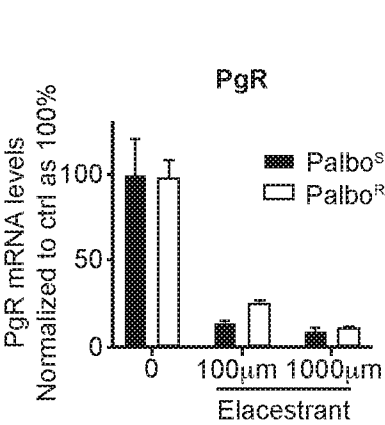


FIG. 11A

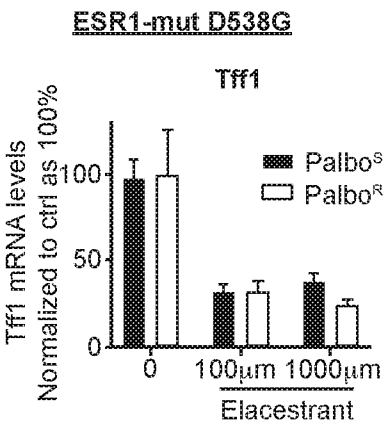


FIG. 11B

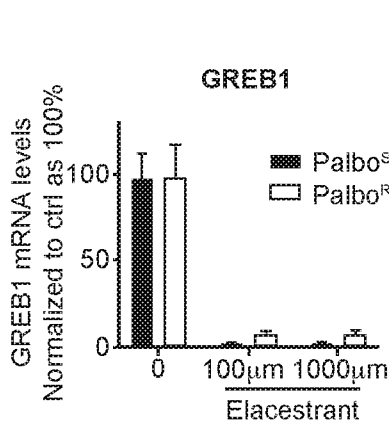


FIG. 11C

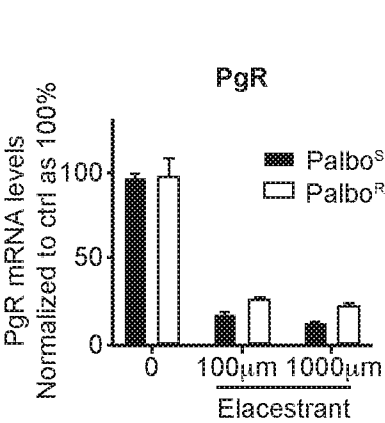


FIG. 12A

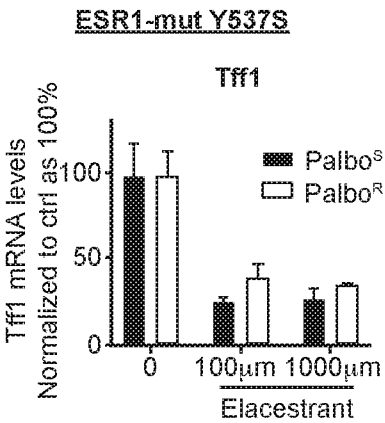


FIG. 12B

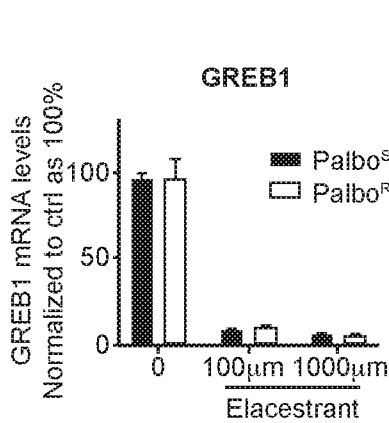
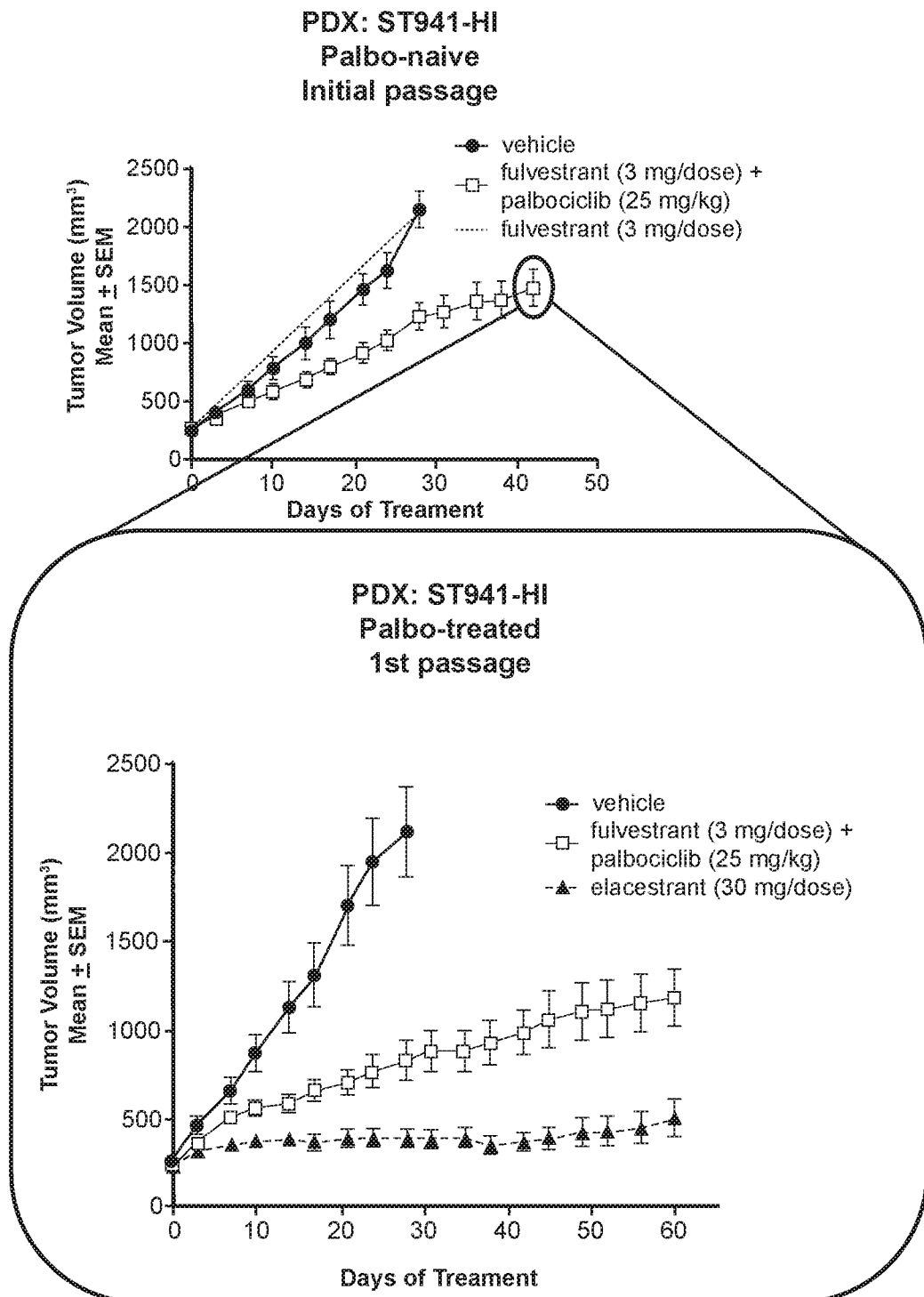


FIG. 12C

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**FIG. 13**