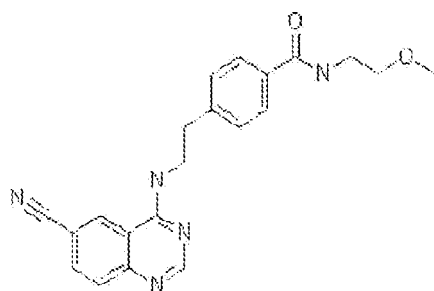
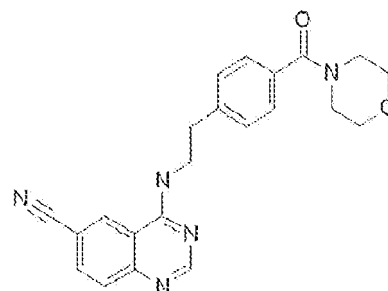


Replacement Sheet

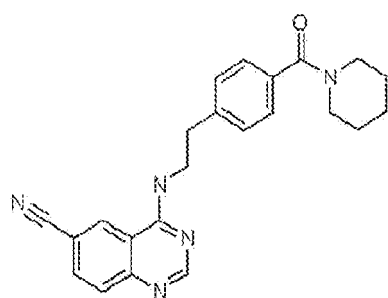
SNX2-1-150



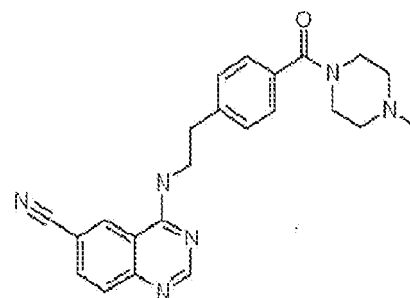
SNX2-1-151



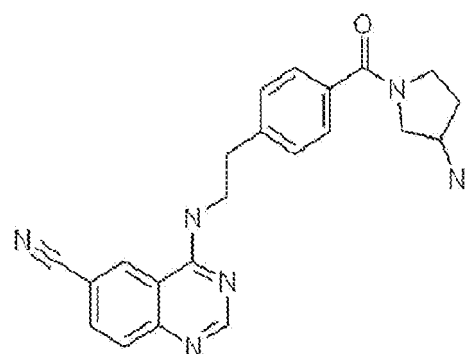
SNX2-1-152



SNX2-1-153



SNX2-1-154



SNX2-1-155

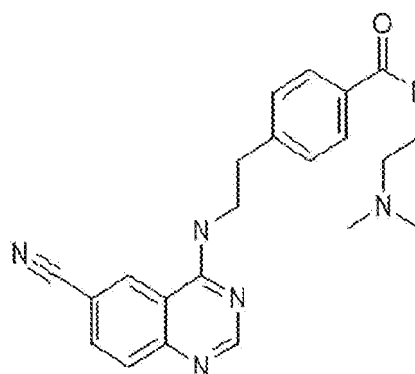
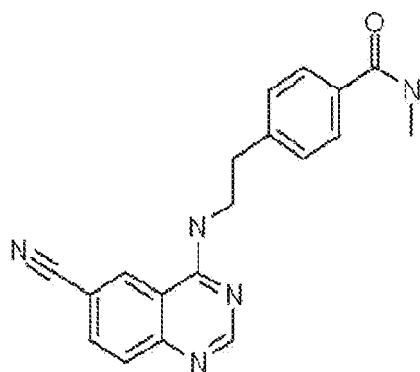


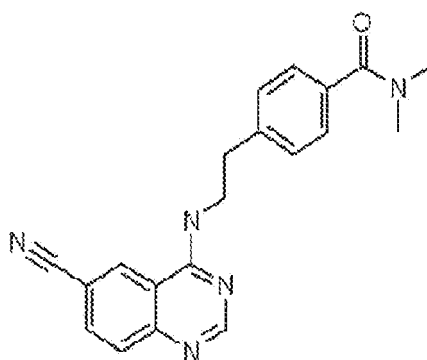
Fig. 1A

Replacement Sheet

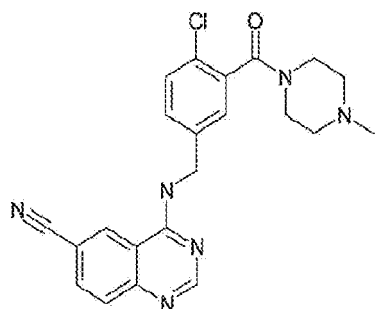
SNX2-1-157



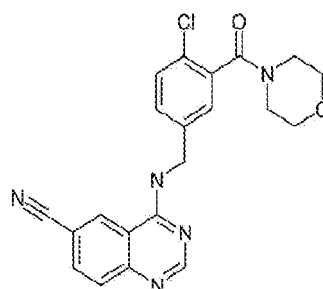
SNX2-1-158



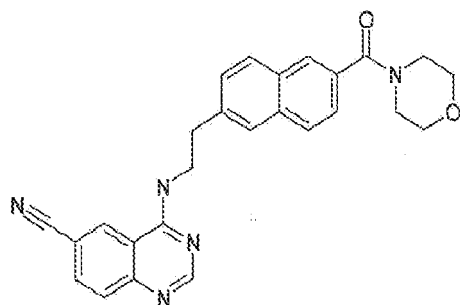
SNX2-1-162



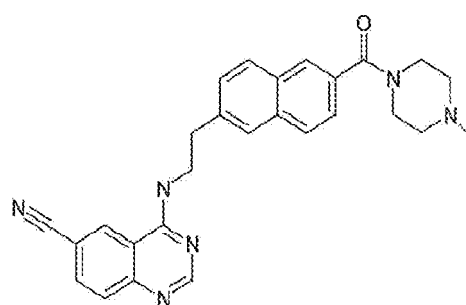
SNX2-1-163



SNX2-1-164

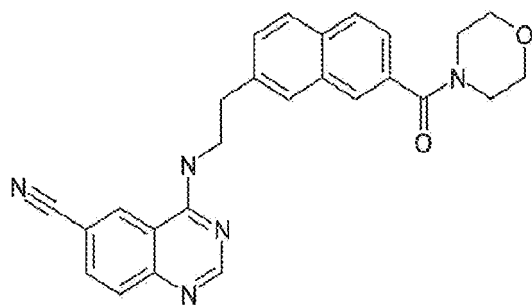


SNX2-1-165

**Fig. 1B**

Replacement Sheet

SNX2-1-166



SNX2-1-167

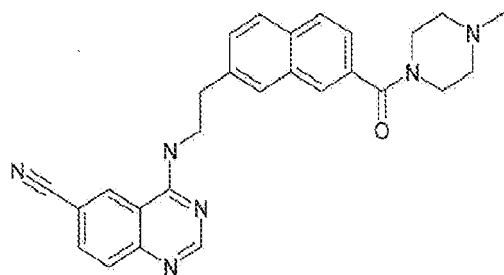
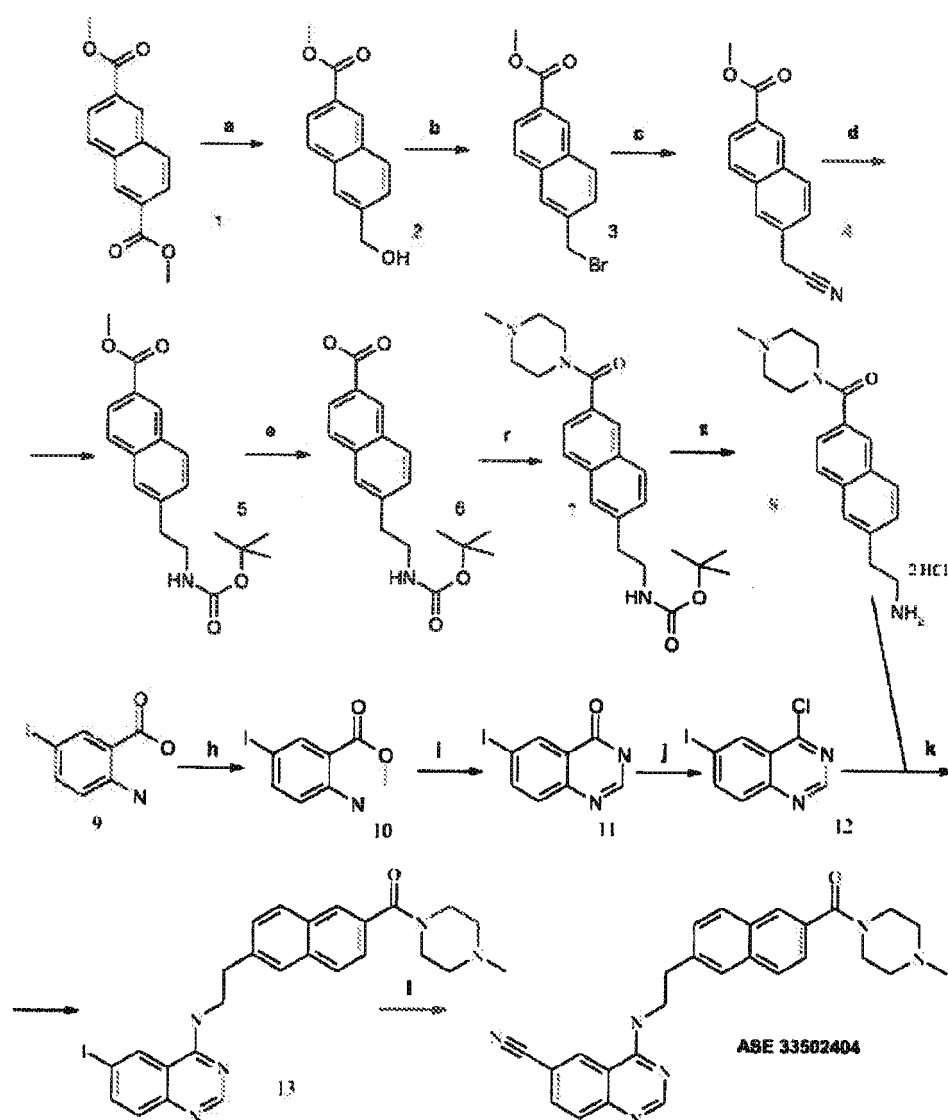


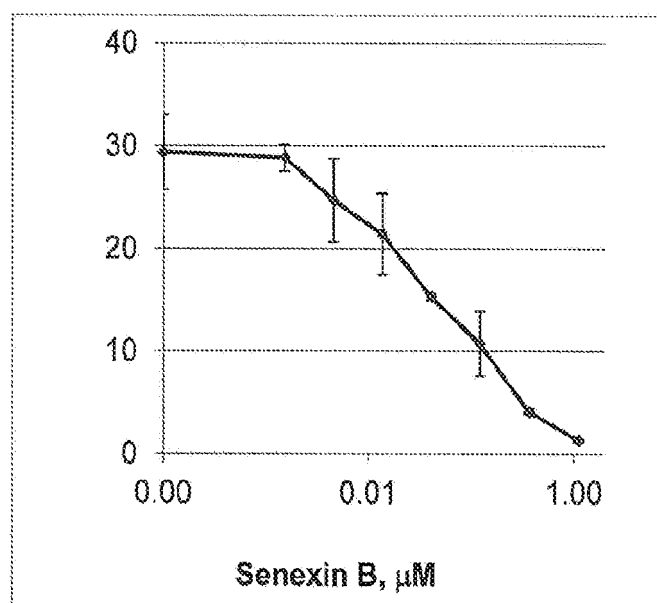
Fig. 1C

FIGURE 2



Scheme 1. a. NaBH_4 , THF, MeOH, 60°C , 6 h; b. CBr_4 , Ph_3P , DCM, r.t., 12 h; c. NaCN , $\text{CH}_3\text{CN}/\text{H}_2\text{O}$, reflux, 12 h; d. Boc_2O , NaBH_4 , $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$, MeOH, r.t., 12 h; e. NaOH , THF/ H_2O , r.t., 4 h; f. 1-methyl-piperazine, NEt_3 , TBTU, DCM, r.t., 6 h; g. HCl /dioxane, THF, r.t., 3 h; h. MeI , K_2CO_3 , DMF, r.t., 12 h; i. formamide, reflux, 2-3 h; j. SOCl_2 , reflux, 2 h; k. [6-(2-Amino-ethyl)-naphthalen-2-yl]-(4-methyl-piperazin-1-yl)-methanone dihydrochloride (**8**), NEt_3 , CH_3CN , reflux, 1 h; l. $\text{Zn}(\text{CN})_2$, (1,1'-bis(diphenyl-phosphino)ferrocene)-dichloro-palladium (II), N,N -dimethylacetamide, 120°C , 2 h

Replacement Sheet

**Fig. 3**

Replacement Sheet

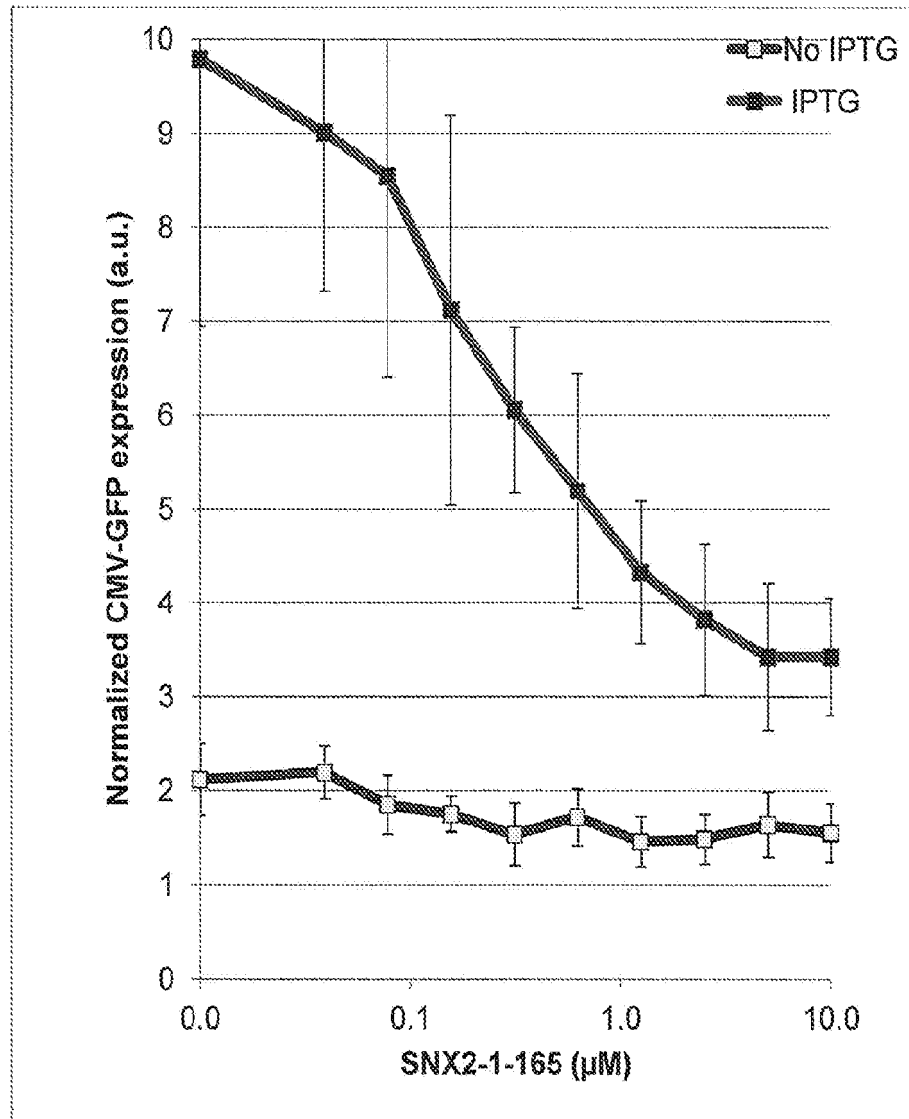
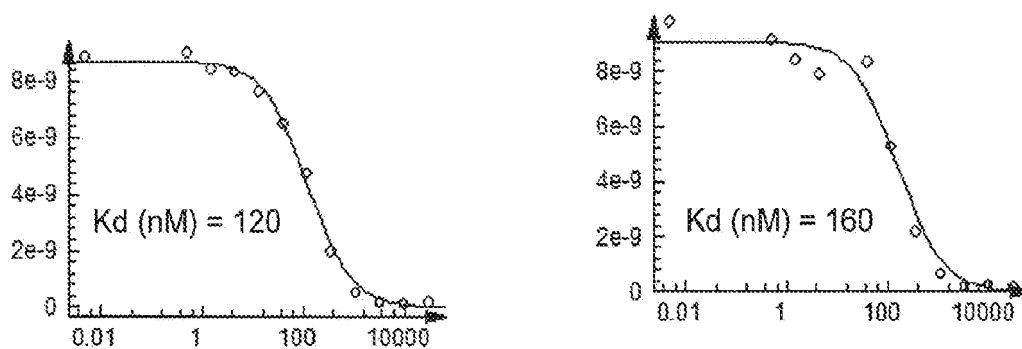


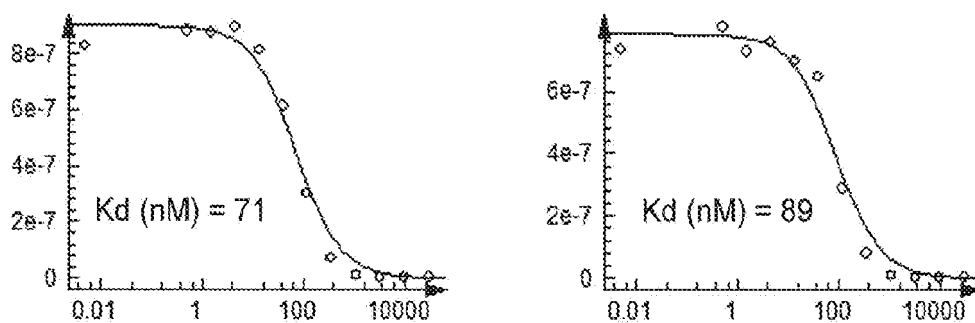
Fig. 4

Replacement Sheet

CDK8



CDK19



CDK9

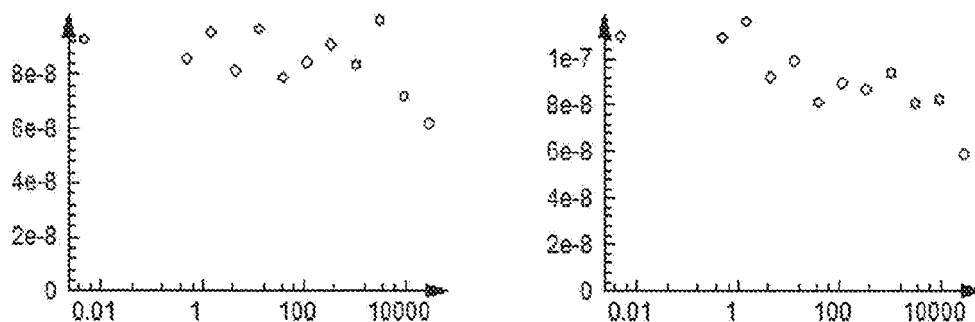
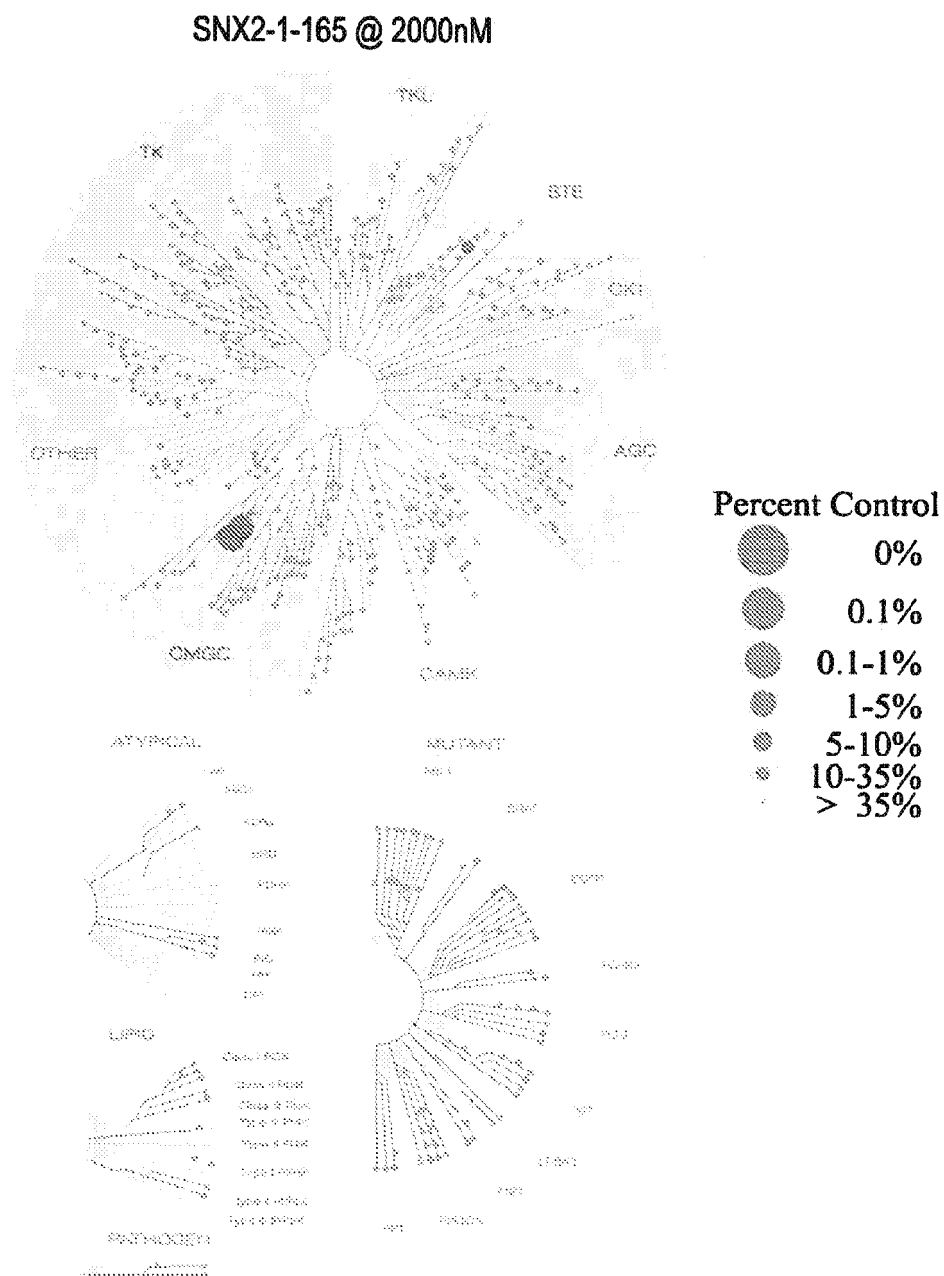


Fig. 5

Figure 6



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Replacement Sheet

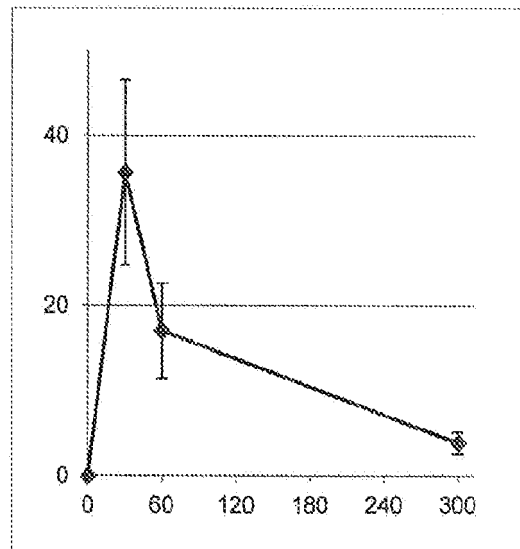


Fig. 7A

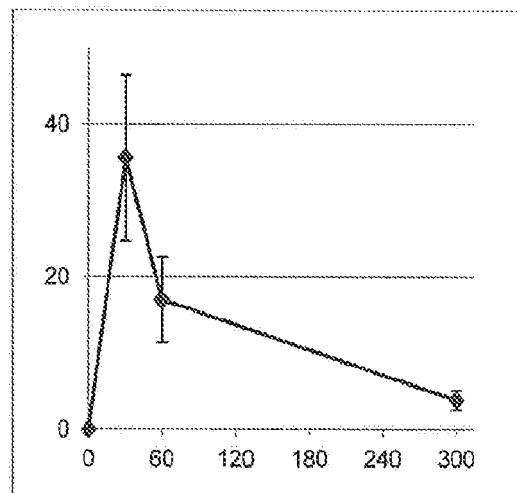
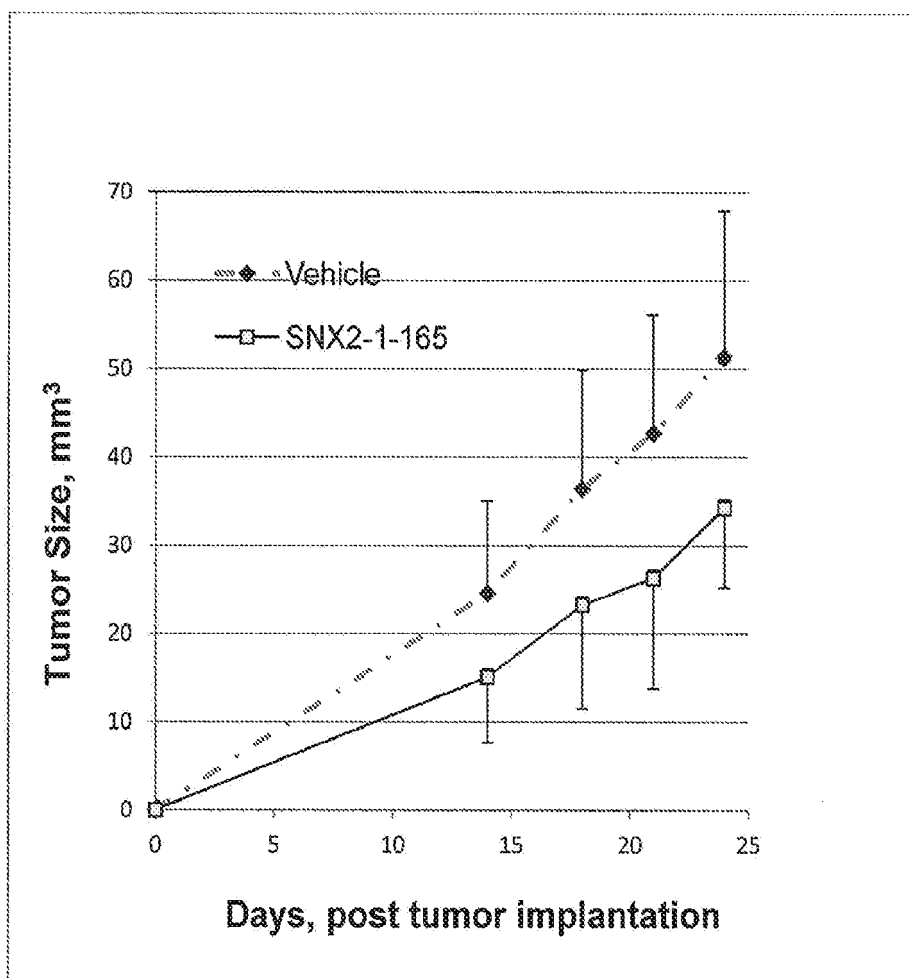


Fig. 7B

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Replacement Sheet

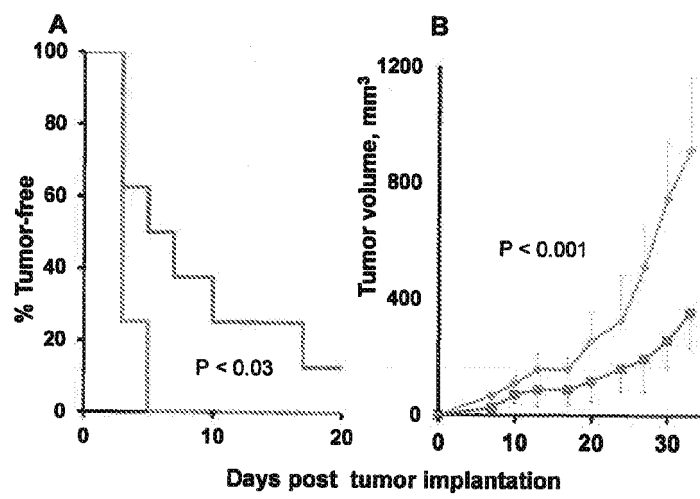


Day	P-value
14	0.017431
18	0.017349
21	0.006626
24	0.006534

Fig. 8

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Figure 9.



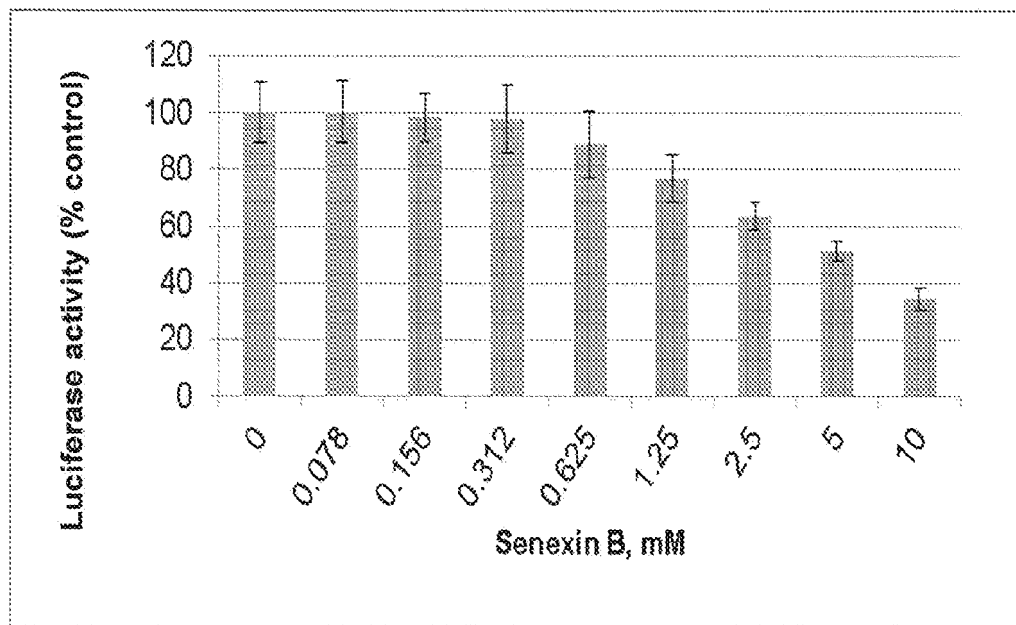
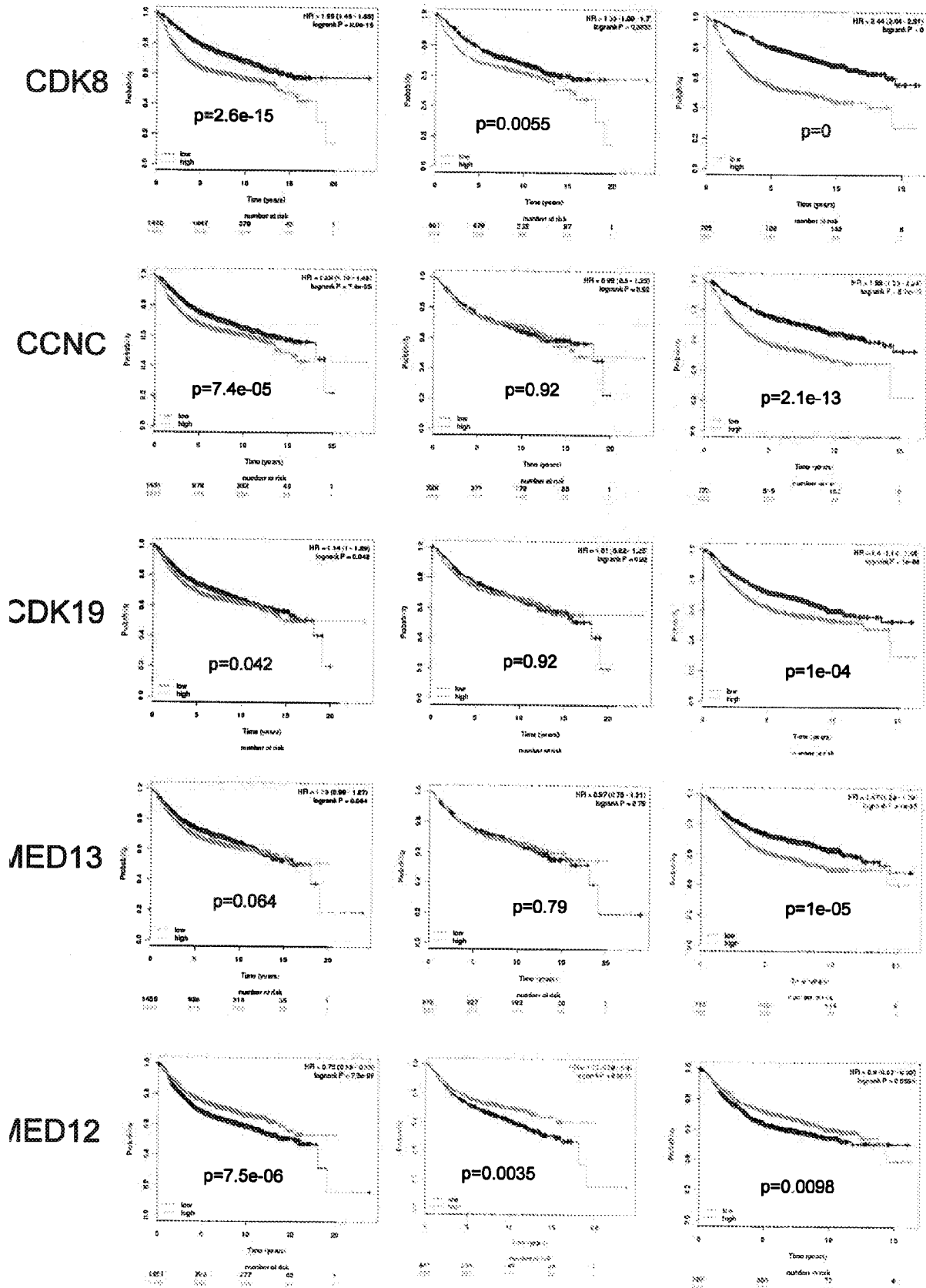
**Fig. 10**

FIG. 11 All patients
(n=2896)Untreated
(n=995)Treated
(n=1465)

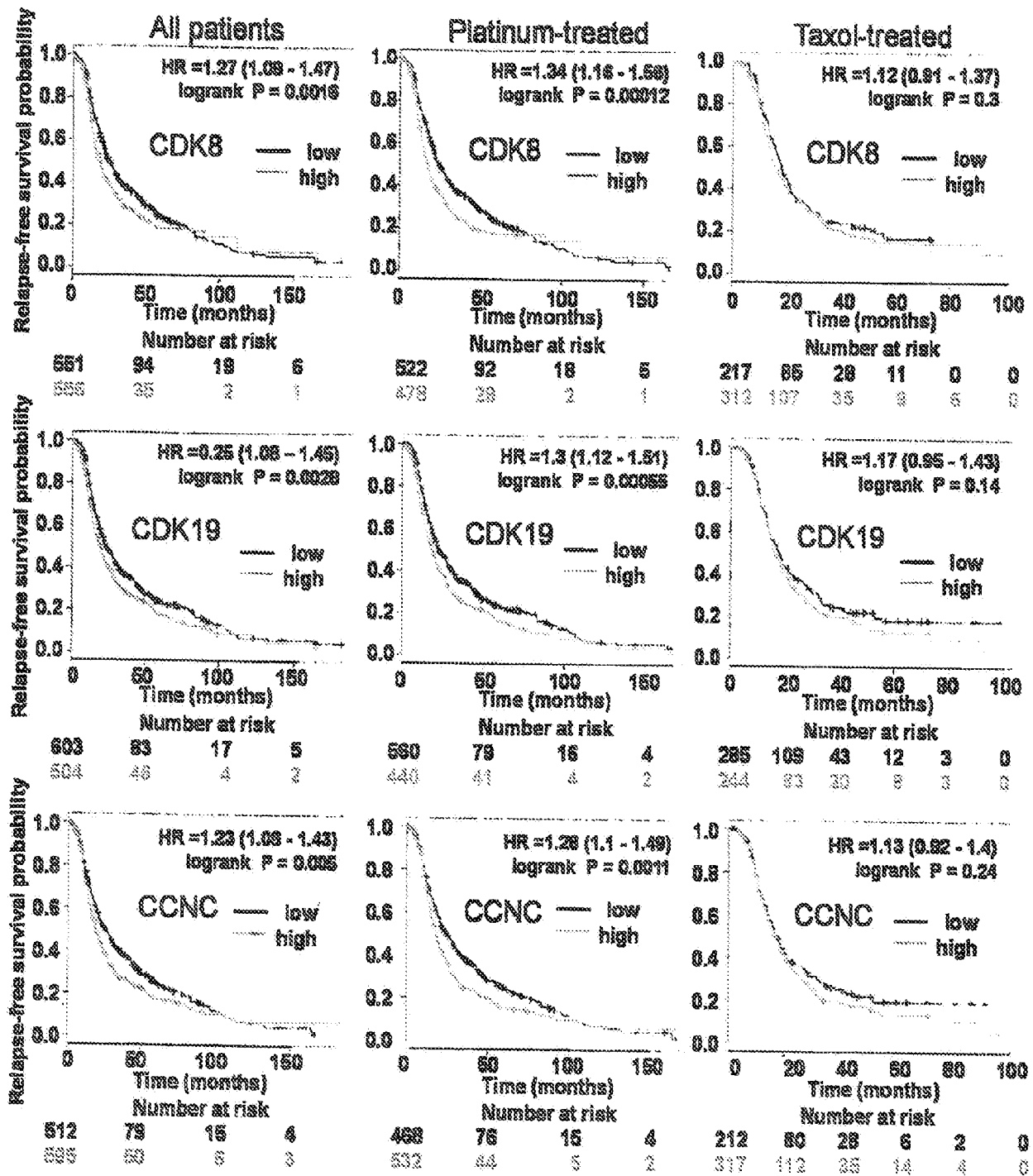


Fig. 12

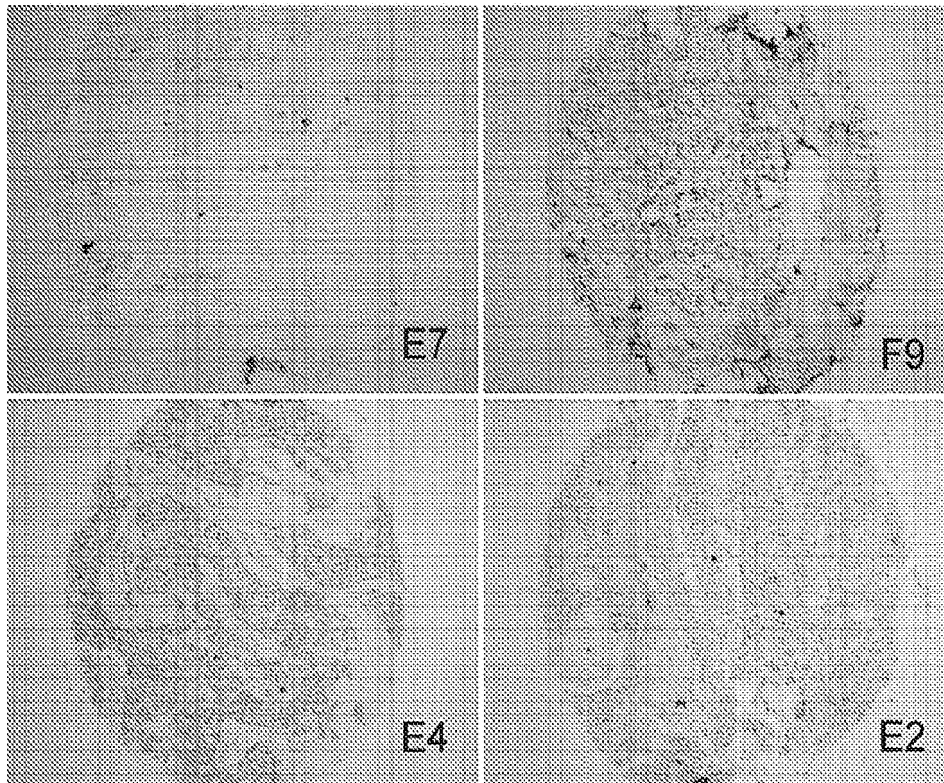


Fig. 13A

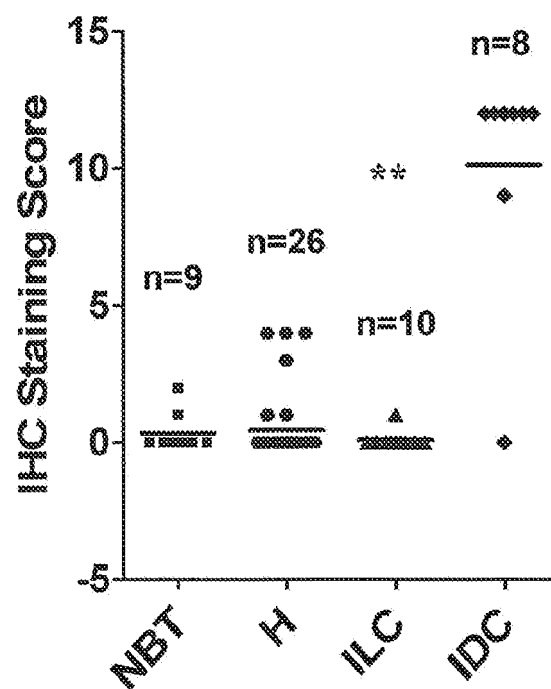
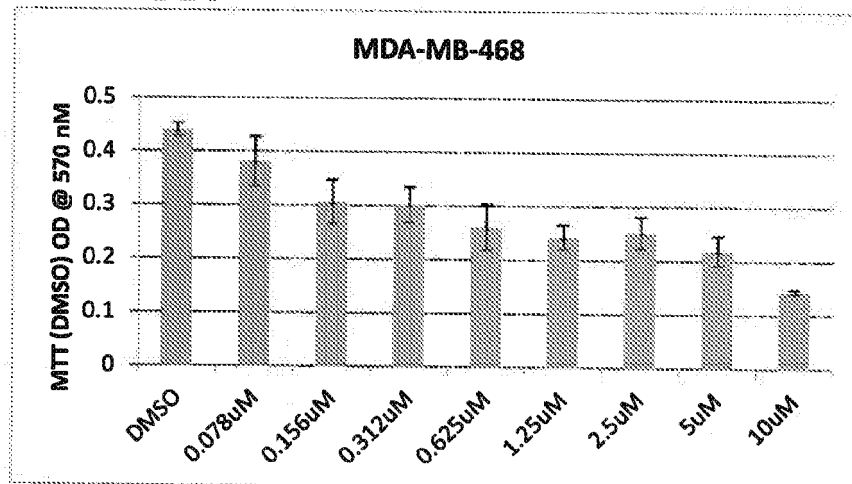
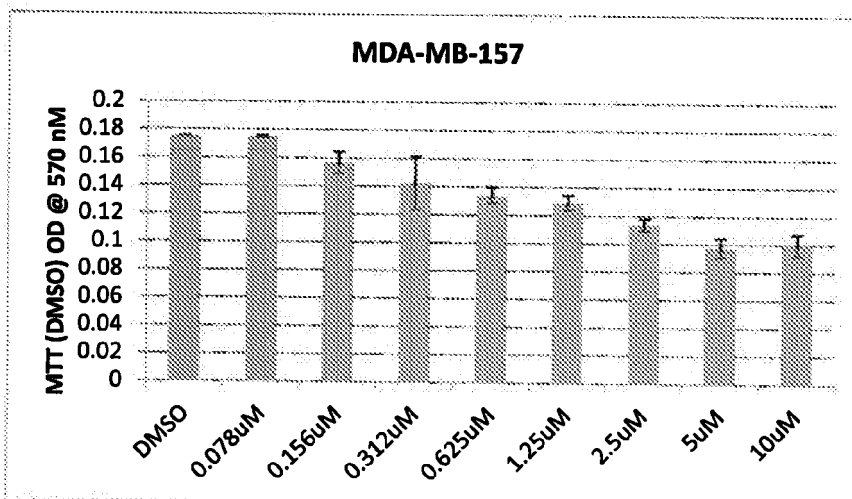
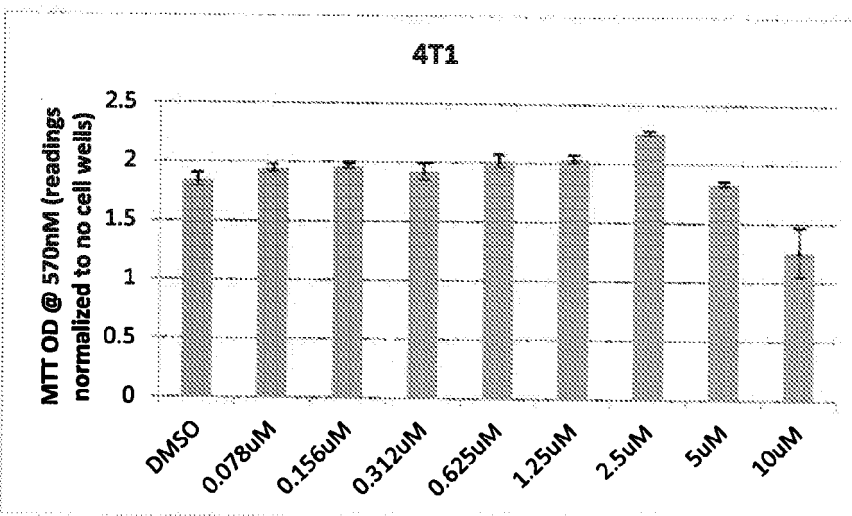


Fig. 13B

FIGURE 14

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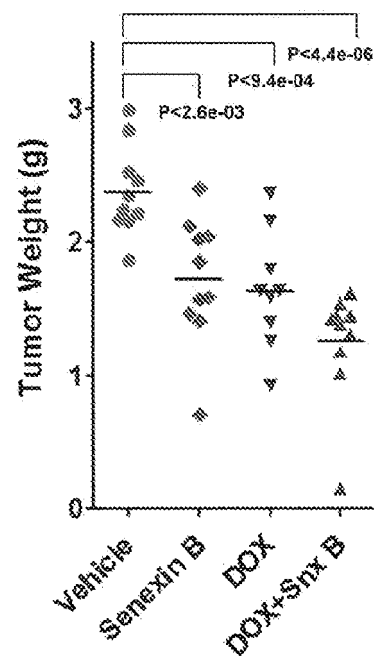


Fig. 15A

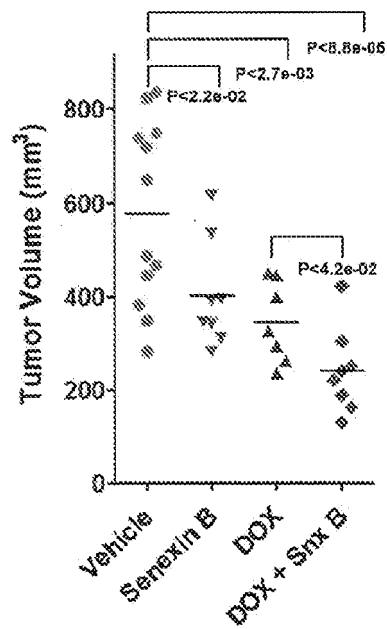
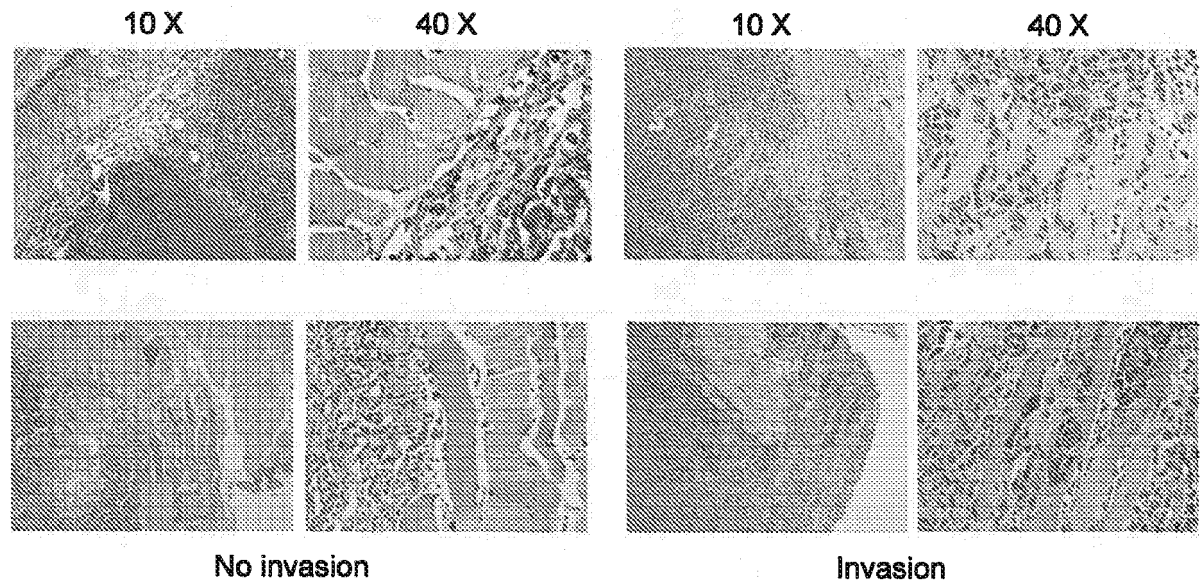


Fig. 15B

Figure 16.**A.****B.**