

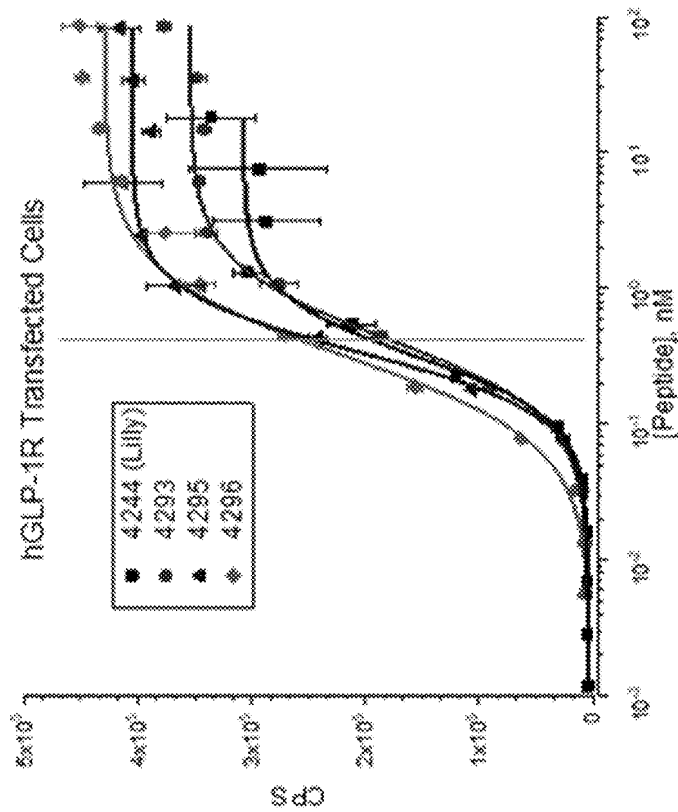
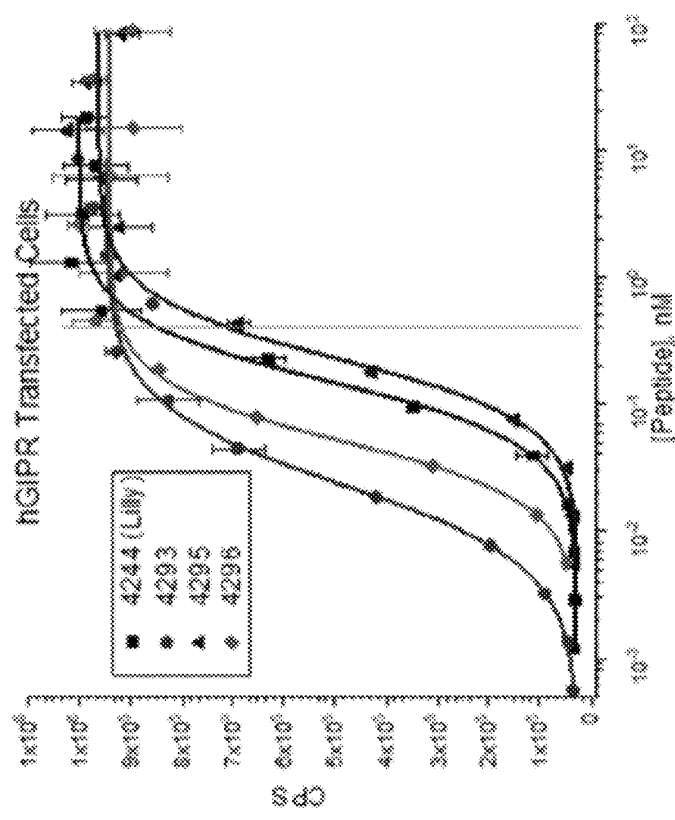


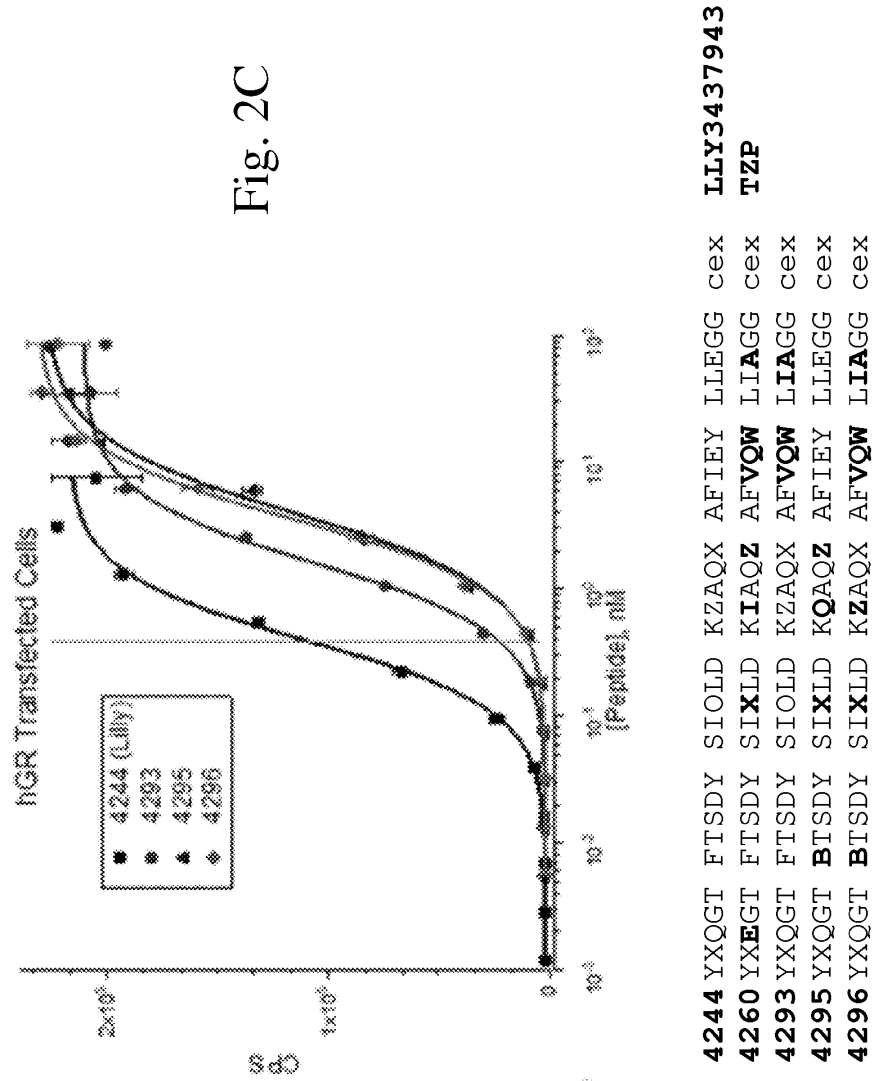
Fig. 2A

4244	YXQGT	FTSDY	SIOLD	KZAQX	AFIEY	LLEGG	LLY3437943
4260	YXEGT	FTSDY	SIXLD	KIAQZ	AFVQW	LIAGG	TZP
4293	YXQGT	FTSDY	SIOLD	KZAQX	AFVQW	LIAGG	LLY3437943
4295	YXQGT	BTSDY	SIXLD	KQAQZ	AFIEY	LLEGG	TZP
4296	YXQGT	BTSDY	SIXLD	KZAQX	AFVQW	LIAGG	LLY3437943

Fig. 2B



4244	YXQGT	FTSDY	SIOLD	KZAQX	AFIEY	LLEGG	ceX	LLY3437943
4260	YXEGT	FTSDY	SIXLD	KIAQZ	AFVQW	LIAGG	ceX	TZP
4293	YXQGT	FTSDY	SIOLD	KZAQX	AFVQW	LIAGG	ceX	
4295	YXQGT	BTSDY	SIXLD	KQAQZ	AFIEY	LLEGG	ceX	
4296	YXQGT	BTSDY	SIXLD	KZAQX	AFVQW	LIAGG	ceX	



		hGcR						hGLP-1R						hGIPR			
		23-Oct		13-Oct		10-Oct		6-Oct		23-Oct		13-Oct		10-Oct		6-Oct	
		Oct		Oct		Oct		Oct		Oct		Oct		Oct		Oct	
4244	LY3437943	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100
4293	MBX 4244, Val23, Gln24, Trp25, Ile27, Ala28	24	26	21	35	76	68	48	153	651	407	206	96				
4296	MBX 4244, alpha-Me-F6, Alb13, Val23, Gln24, Trp25, Ile27, Ala28	11				101				298							
4295	MBX 4244, alpha-Me-F6, Alb13, Gln17, K2Q[2xOEG-yE-diachC20]	10				93				67							

Fig. 2D

% MBX 4244																															
hGcgR												hGLP-1R										hGIPR									
11/14	11/10	11/8	11/6	11/1	10/27	6/13	6/8	11/14	11/10	11/8	11/6	11/1	10/27	6/21	6/8	11/14	11/10	11/8	11/6	11/1	10/27	6/21	6/13	6/8	cmp						
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	1						
74	64	103	164	127		113	67	117	121	217	187	170		90	67	29	26	64	39	35		40	57	22	2						
113	81	66	75					187	143	148	121					238	227	216	156						3						
18	19	10	40	20	22			54	75	56	153	80	61			130	274	142	207	473	115				4						
7					6			126					111			112					82				5						
21								108								165									6						

hGcgR						hGLP-IR						hGIPR							
11/10	11/8	11/6	11/1	6/13	6/8	11/10	11/8	11/6	11/1	6/21	6/8	11/10	11/8	11/6	11/1	6/21	6/13	6/8	cmp
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	1
64	103	164	127	113	67	121	217	187	170	90	67	26	64	39	35	40	57	22	2
81	66	75				143	148	121				227	216	156					3
19	10	40	20			75	56	153	80			274	142	207	473				4
1						178						62							7
25						49						81							8

Fig. 3

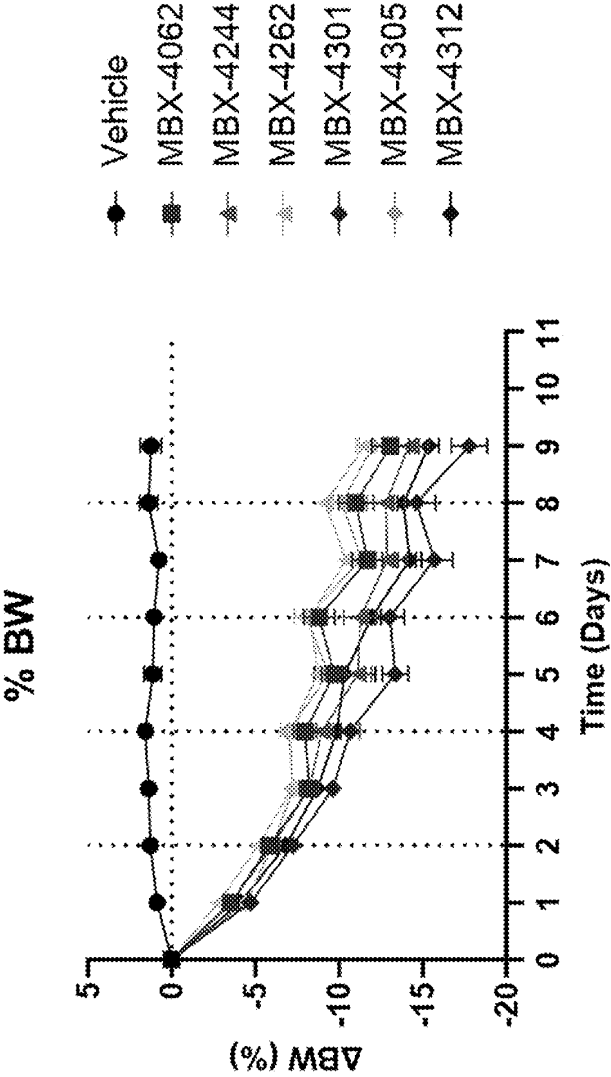


Fig. 4

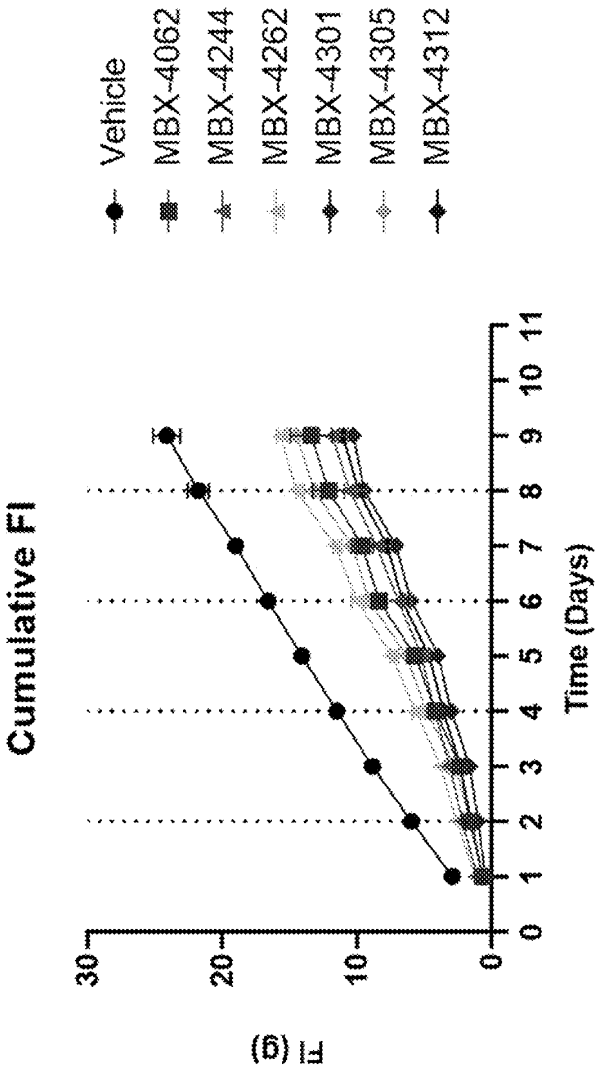


Fig. 5

MBX 4244: LLY3437943

MBX 4244: YXQGTFTSDYSIBLDKZAQXAFIEYLLEGGPSSGAPPPS-amide
X=Aib, B= (aMe)Leu, Z= K(OEG-OEG-γE-COC18H36CO2H)

		% MBX 4244		
		hGcGR	hGLP-1R	hGIPR
4244	LLY3437943	100	100	100
4301	Val23, Gln24, Trp25	86	147	145
4318	Tyr18, Val23, Gln24, Trp25	90	93	145
4320	His1, Tyr18, Val23, Gln24, Trp25	63	171	159
4321	His1, His3, Tyr18, Val23, Gln24, Trp25	187	120	157
4323	IsoVal13, Val23, Gln24, Trp25	17	93	104
4322	aMe,Phe13, Val23, Gln24, Trp25	31	105	63

Fig. 6

10/26

Fig. 7A

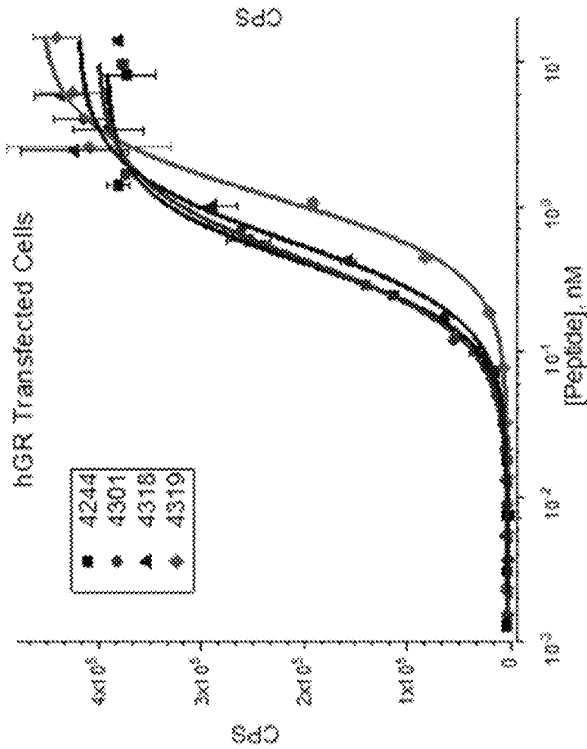


Fig. 7B

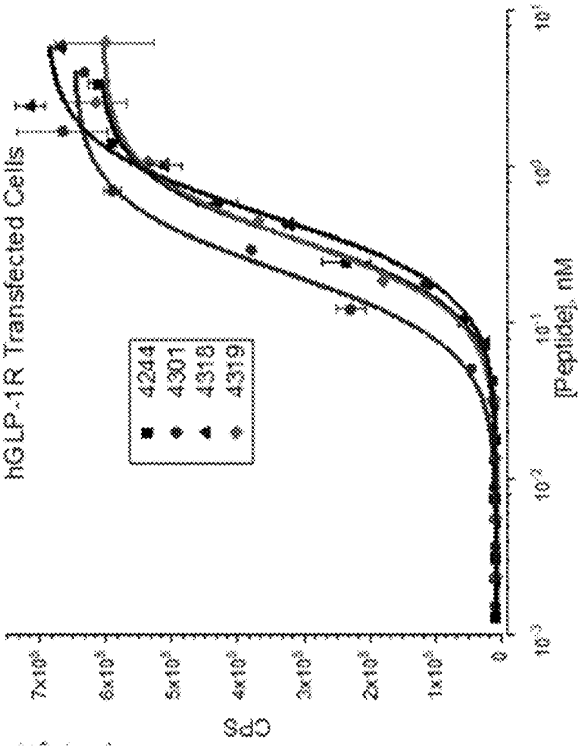
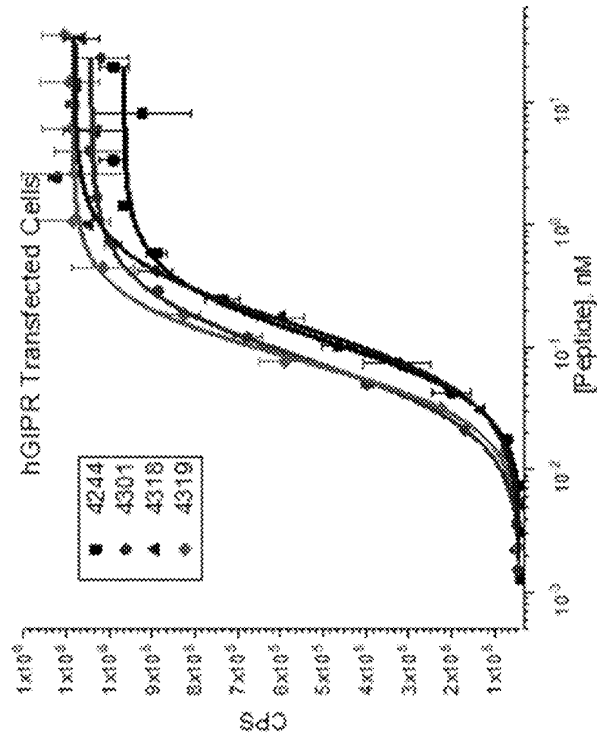


Fig. 7C



MBX 4244: YXQGTFTSDYSIBLDKZAQXAFIEYLLEGGPSSGAPPPS-
amide
X=Aib, B= (aMe)Leu, Z= K(OEG-OEG-γE-COC18H36CO2H)

MBX	Structure	% MBX 4244		
		hGcgR	hGLP-1R	hGIPR
4244	LLY3437943	12/8	12/8	12/8
4301	Val23, Gln24, Trp25	100	100	100
4318	Tyr18, Val23, Gln24, Trp25	92	162	144
4319	Glu21, Val23, Gln24, Trp25	71	71	76
		35	102	144

Fig. 7D

Fig. 8A

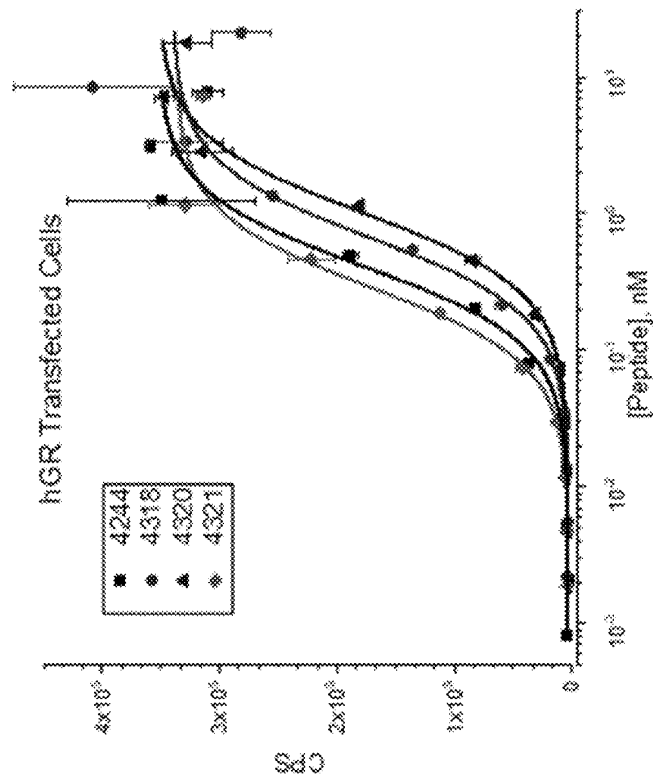


Fig. 8B

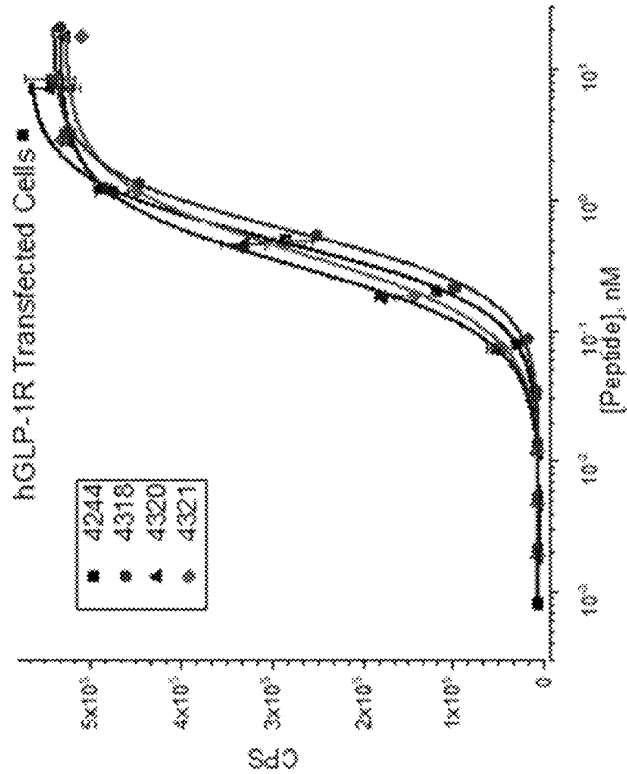
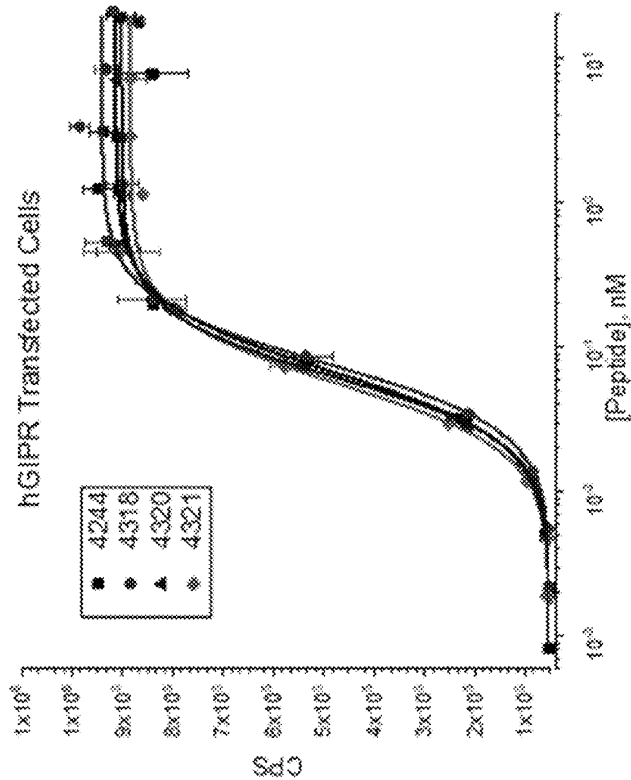


Fig. 8C



MBX 4244: YXQGTFTSDYSIBLDKZAQXAFIEYLLEGGPSSGAPPPS-amide
X=Aib, B= (aMe)Leu, Z= K(OEG-OEG-γE-COC18H36CO2H)

MBX 4244: LLY3437943

		% MBX 4244			
		hGcGR	hGLP-1R	hGIPR	
		12/19	12/19	12/19	12/19
4244	LLY3437943	100	100	100	100
4301	Val23, Gln24, Trp25	113	153	197	197
4319	Glu21, Val23, Gln24, Trp25	45	133	225	225
4318	Tyr18, Val23, Gln24, Trp25	157	134	212	212
4320	His1, Tyr18, Val23, Gln24, Trp25	85	187	208	208
4321	His1, His3, Tyr18, Val23, Gln24, Trp25	229	118	191	191

Fig. 8D

Fig. 9A

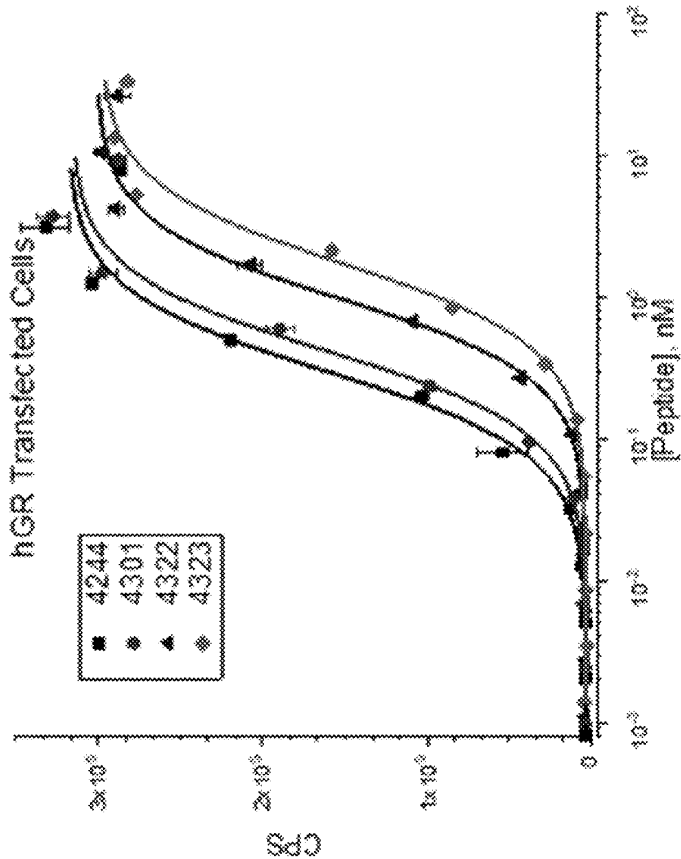


Fig. 9B

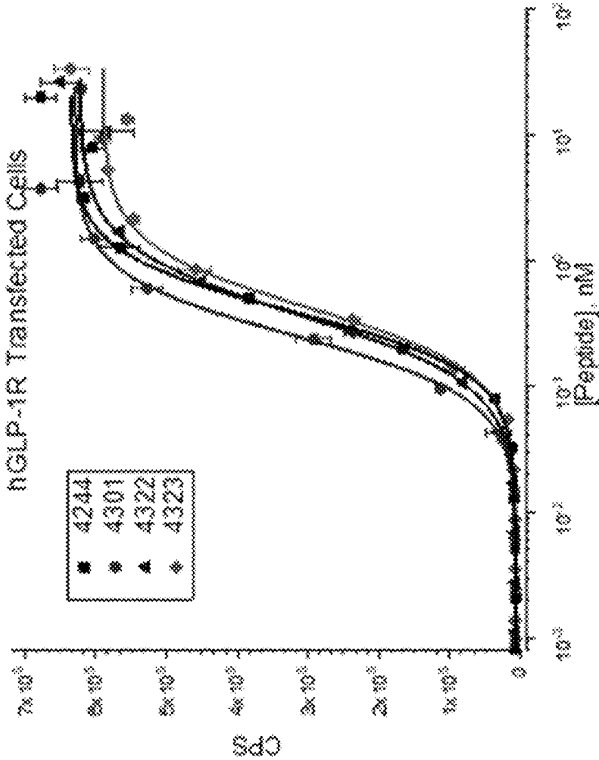
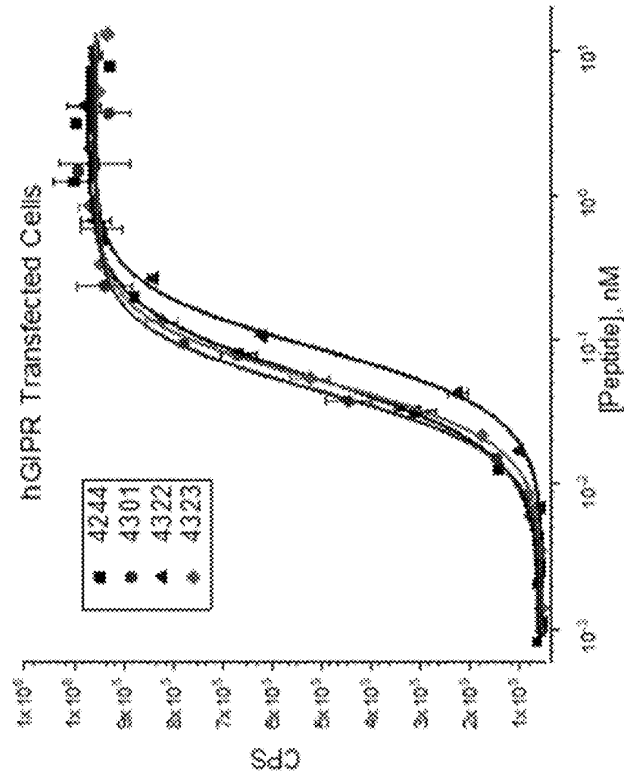


Fig. 9C



MBX 4244: YXQGTFTSDYSIBLDKZAQXAFIEYLLEGGPSSGAPPPS-amide
X=Aib, B= (aMe)Leu, Z= K(**OEG-OEG**-γE-COC18H36CO2H)

MBX 4244: LLY3437943

% MBX 4244																	
		hGcGR						hGLP-1R						hGIPR			
		12/22	12/22	12/19	12/14	12/8	12/22	12/22	12/19	12/14	12/8	12/19	12/19	12/19	12/14	12/8	
4244	LLY3437943	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	
4301	Val23, Gln24, Trp25	73		113	66	92	155		153	117	162	123		197	115	144	
4318	Tyr18, Val23, Gln24, Trp25		62	157	68	71		84	134	81	71		88	212	94	76	
4320	His1, Tyr18, Val23, Gln24, Trp25		41	85				155	187				109	208			
4321	His1, His3, Tyr18, Val23, Gln24, Trp25		144	229				122	118				122	191			
4323	isoVal13, Val23, Gln24, Trp25	17					93					104					
4322	aMe,Phe13, Val23, Gln24, Trp25	31					105					63					

Fig. 9D

Fig. 10A

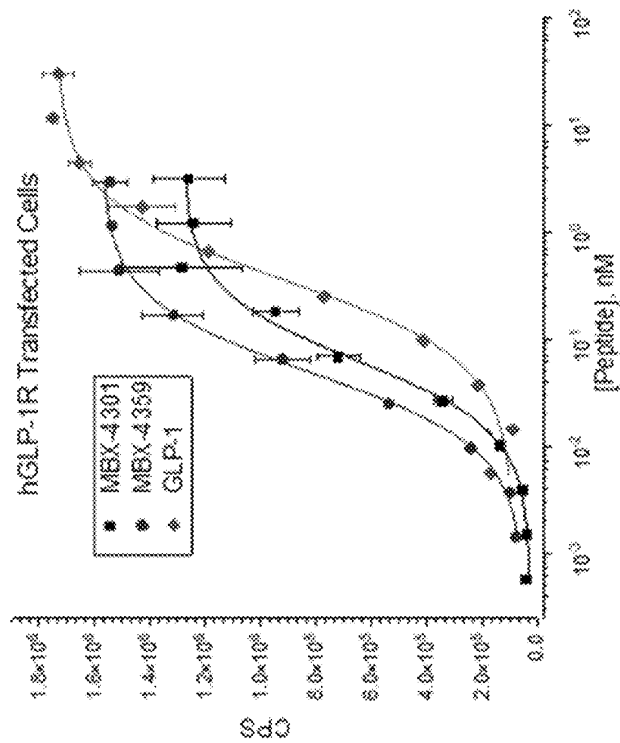


Fig. 10B

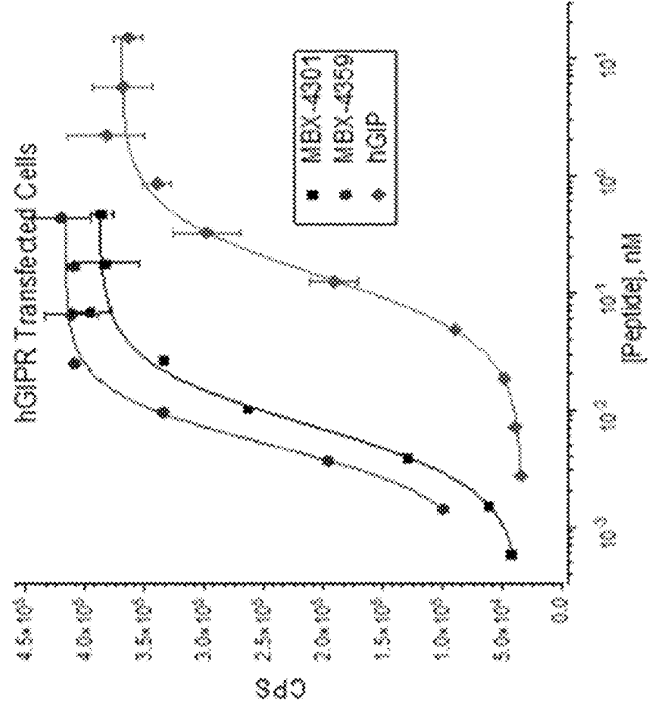
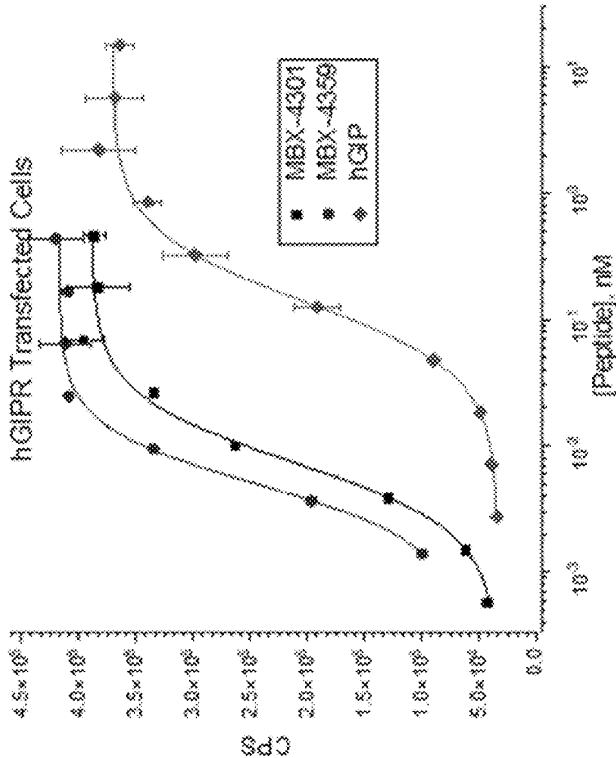


Fig. 10C



Biopotency of Peptide-Drugs with Different Fatty Acids

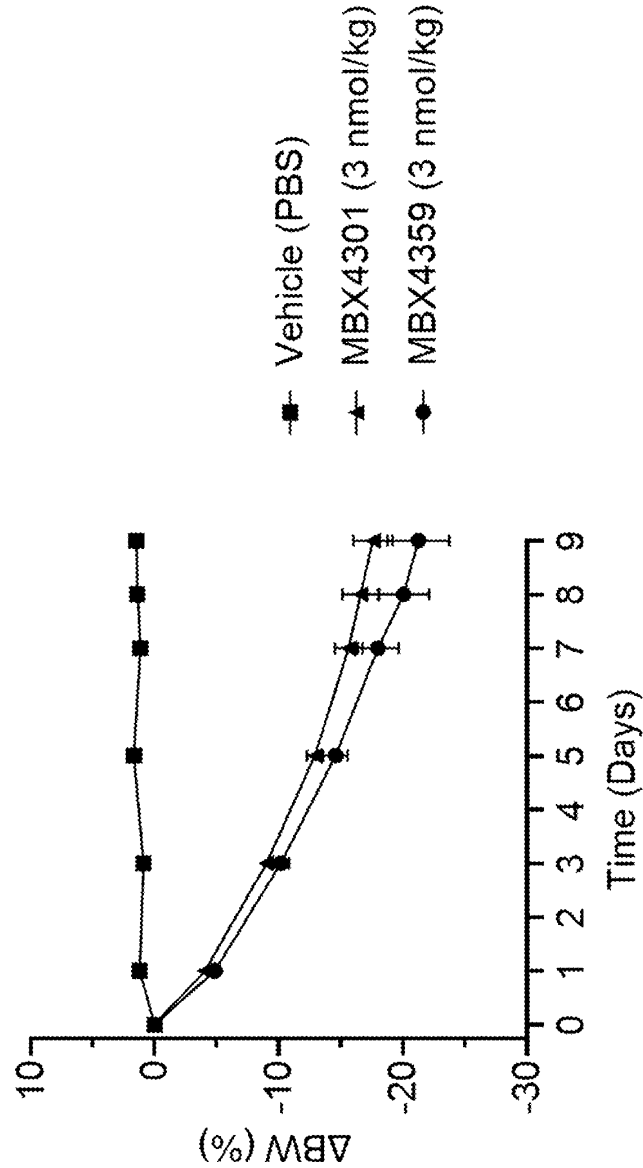


Fig. 11

MBX	SEQ ID NO:	Sequence
4244	8	Y-Aib-QGTFTSDYSI- α Me, L-LDKK (miniPEG- γ E-COC18H36CO2H) AQ-Aib-AFIEYLLEGGPSSGAPPPS-amide
4262	9	Y-Aib-QGTFTSDYSIYLEK (ϵ K- ϵ K- γ E-COC18H36CO2H) QAA-Aib-EFVQWLLEGGPSSGAPPPS-amide
4293	10	Y-Aib-QGTFTSDYSI- α Me, L-LDKK (miniPEG- γ E-COC18H36CO2H) AQ-Aib-AFVQWLIAGGPSSGAPPPS-amide
4295	11	Y-Aib-QGT- α Me, F-TSDYSI-Aib-LDKQAQK ((miniPEG) 2- γ E-COC18H36CO2H) AFIEYLLEGGPSSGAPPPS-amide
4296	12	Y-Aib-QGT- α Me, F-TSDYSI-Aib-LDKK ((miniPEG) 2- γ E-COC18H36CO2H) AQ-Aib-AFVQWLIAGGPSSGAPPPS-amide
4298	13	Y-Aib-QGTFTSDYSI- α Me, L-LDKK ((miniPEG) 2- γ E-COC18H36CO2H) AQ-Aib-AFVQWLIAGGPSSGAPPPS-amide
4301	14	Y-Aib-QGTFTSDYSI- α Me, L-LDKK ((miniPEG) 2- γ E-COC18H36CO2H) AQ-Aib-AFVQWLLEGGPSSGAPPPS-amide
4303	15	Y-Aib-QGTFTSDYSI- α Me, L-LDKK ((ϵ K- ϵ K- γ E-COC18H36CO2H) AQ-Aib-AFVQWLLEGGPSSGAPPPS-amide
4304	16	Y-Aib-QGTFTSDYSI-Aib-LDK ((ϵ K- ϵ K- γ E-COC18H36CO2H) KAQ-Aib-AFVQWLIAGGPSSGAPPPS-amide
4305	17	H-Aib-HGTFTSDYSI- α Me, L-LDKK ((miniPEG) 2- γ E-COC18H36CO2H) AQ-Aib-AFVQWLIAGGPSSGAPPPS-amide
4312	18	Y-Aib-QGTFTSDYSY- α Me, L-LDKK ((miniPEG) 2- γ E-COC18H36CO2H) AQ-Aib-AFVQWLLEGGPSSGAPPPS-amide
4318	19	Y-Aib-QGTFTSDYSI- α Me, L-LDKK ((miniPEG) 2- γ E-COC18H36CO2H) YQ-Aib-AFVQWLLEGGPSSGAPPPS-amide
4319	20	Y-Aib-QGTFTSDYSI- α Me, L-LDKK ((miniPEG) 2- γ E-COC18H36CO2H) AQ-Aib-EFVQWLLEGGPSSGAPPPS-amide
4320	21	H-Aib-QGTFTSDYSI- α Me, L-LDKK ((miniPEG) 2- γ E-COC18H36CO2H) YQ-Aib-AFVQWLLEGGPSSGAPPPS-amide
4321	22	H-Aib-HGTFTSDYSI- α Me, L-LDKK ((miniPEG) 2- γ E-COC18H36CO2H) YQ-Aib-AFVQWLLEGGPSSGAPPPS-amide
4322	23	Y-Aib-QGTFTSDYSI- α Me, F-LDKK ((miniPEG) 2- γ E-COC18H36CO2H) AQ-Aib-AFVQWLLEGGPSSGAPPPS-amide
4323	24	Y-Aib-QGTFTSDYSI- α Et, A-LLDKK ((miniPEG) 2- γ E-COC18H36CO2H) AQ-Aib-AFVQWLLEGGPSSGAPPPS-amide
4359	25	Y-Aib-QGTFTSDYSI- α Me, L-LDKK ((miniPEG) 2- γ E-COC18H36-PO3H) AQ-Aib-AFVQWLLEGGPSSGAPPPS-amide

α Et, A: α -Ethylalanine (2-Amino-2-methylbutyric acid)

Fig. 12