

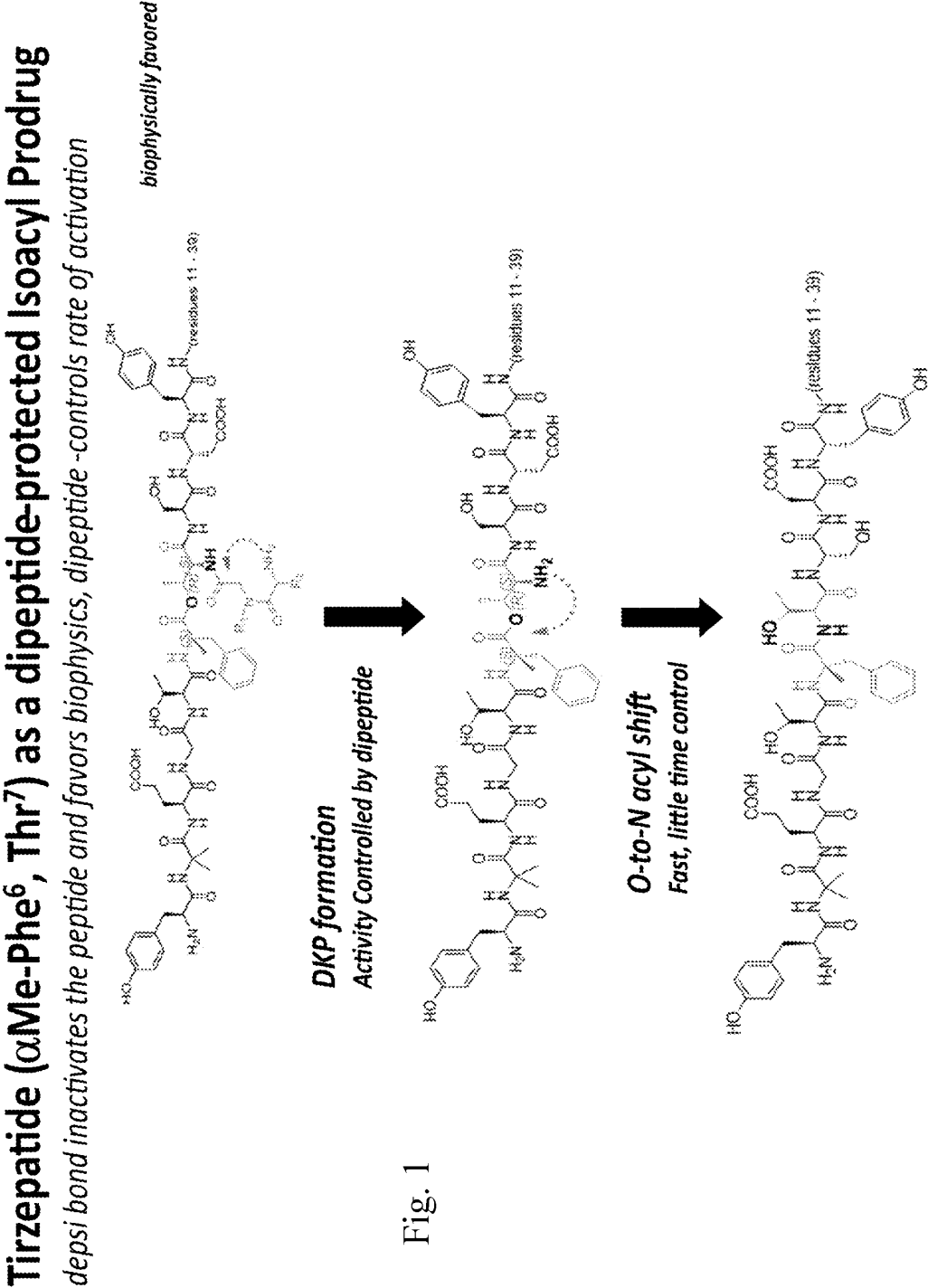
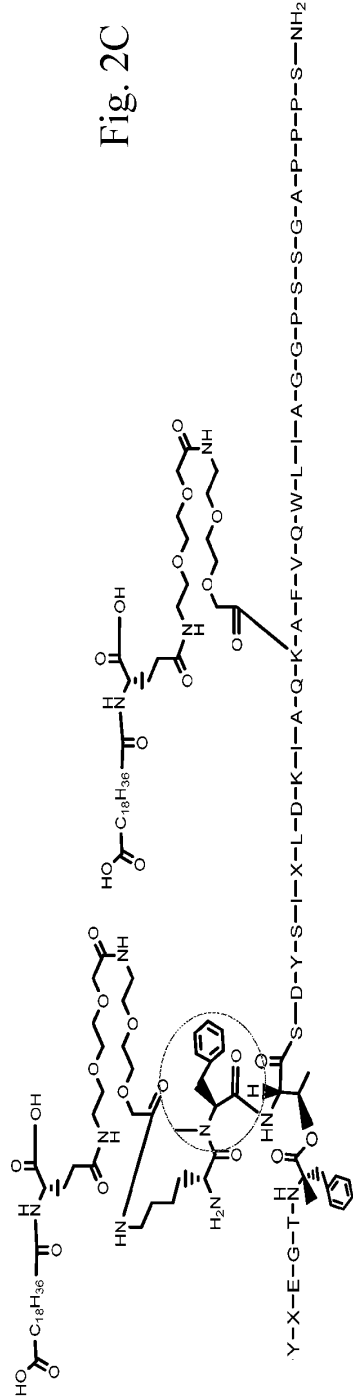
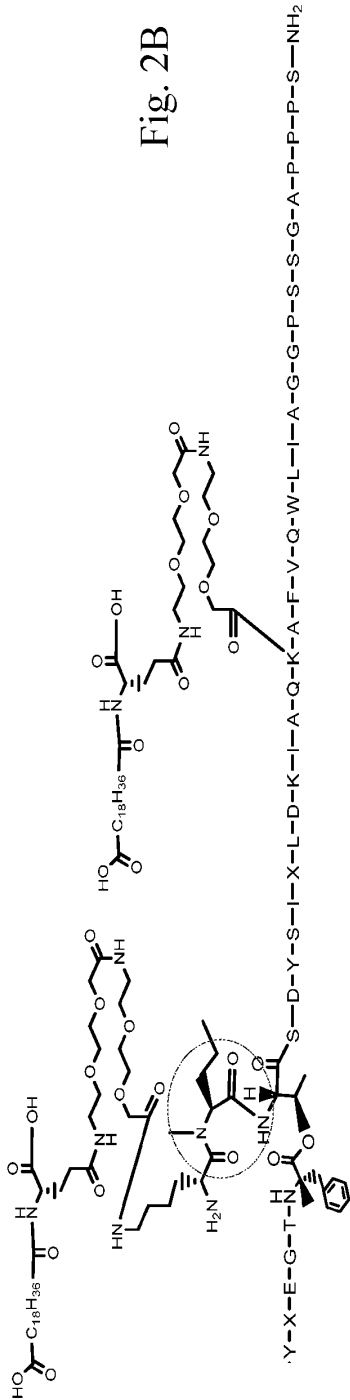
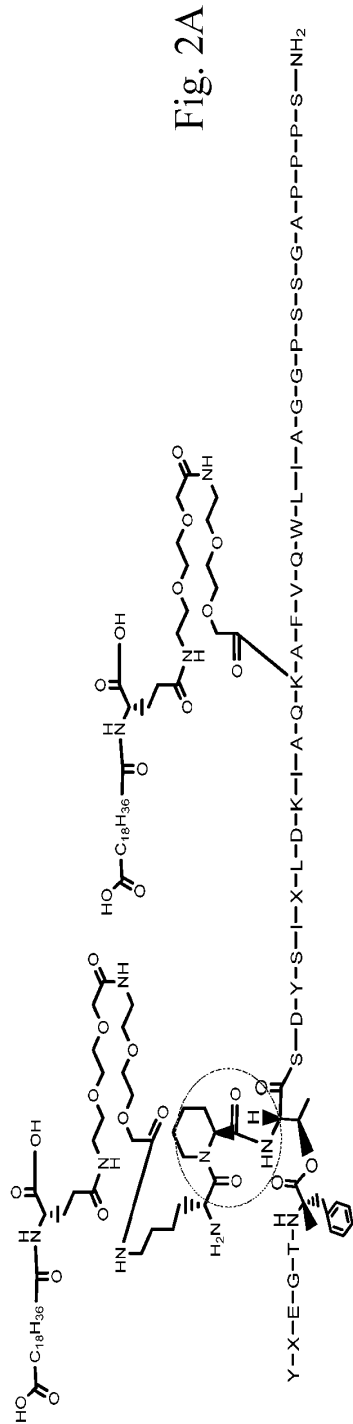
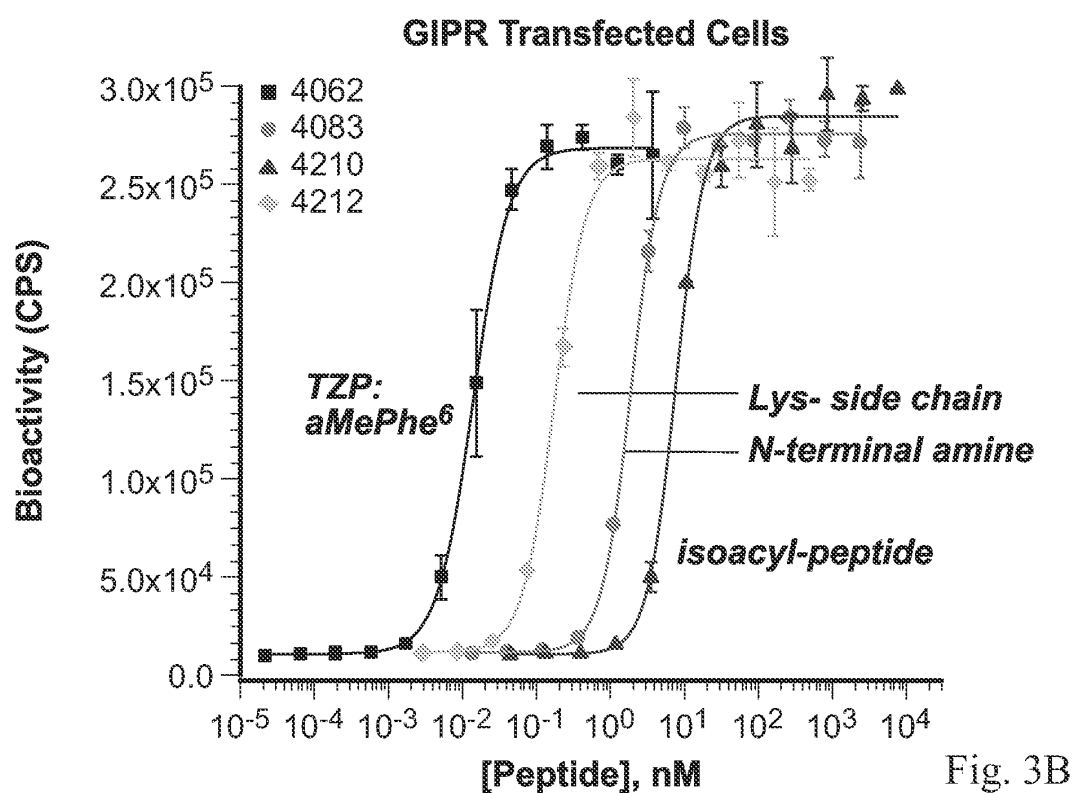
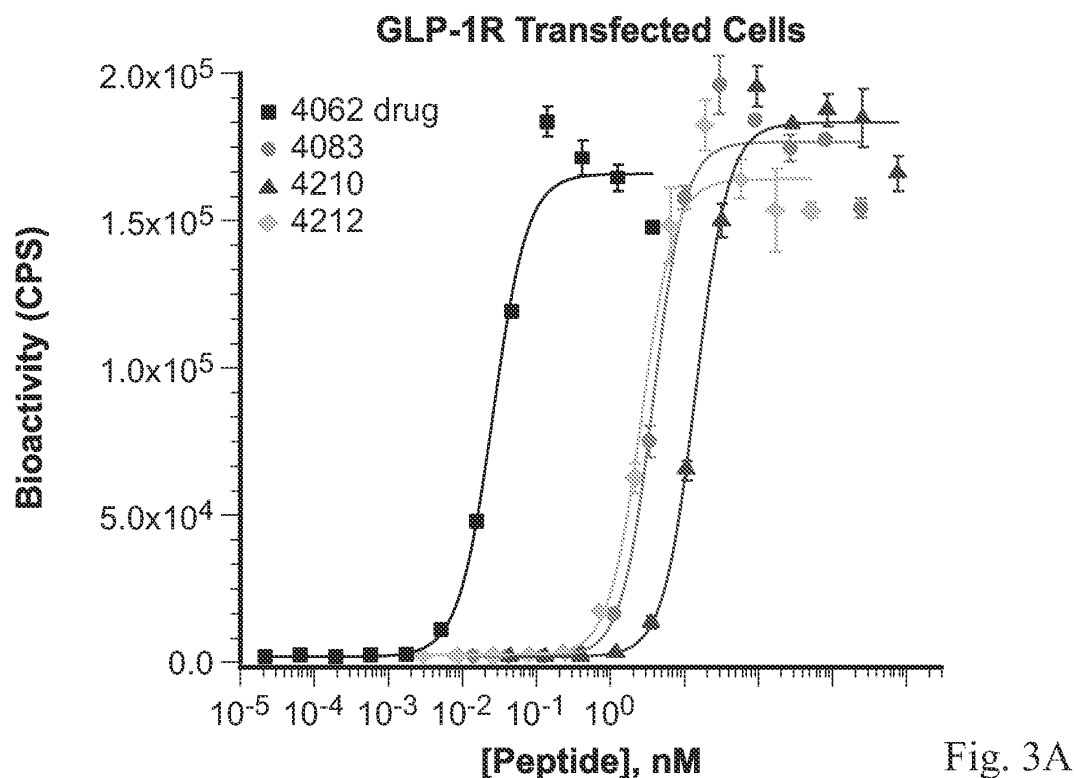


Fig. 1





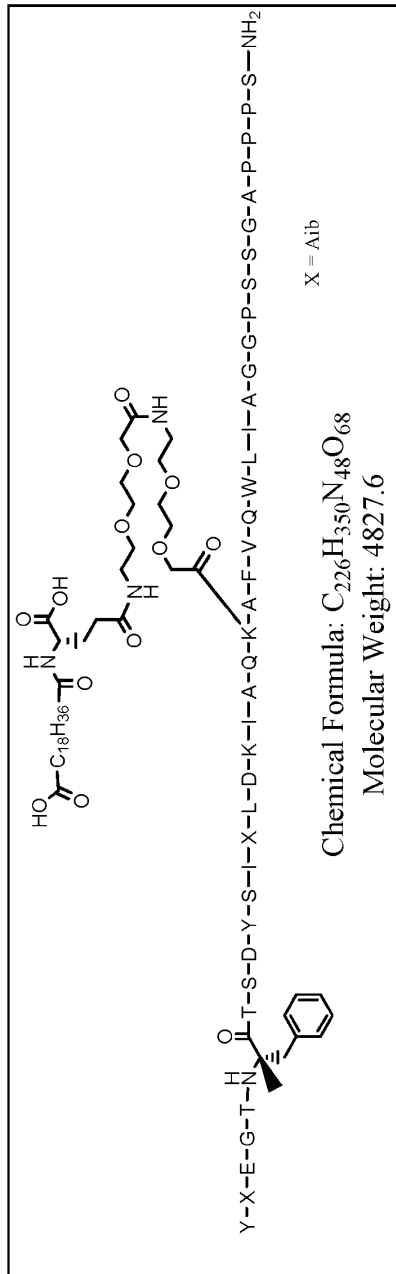


Fig. 4A

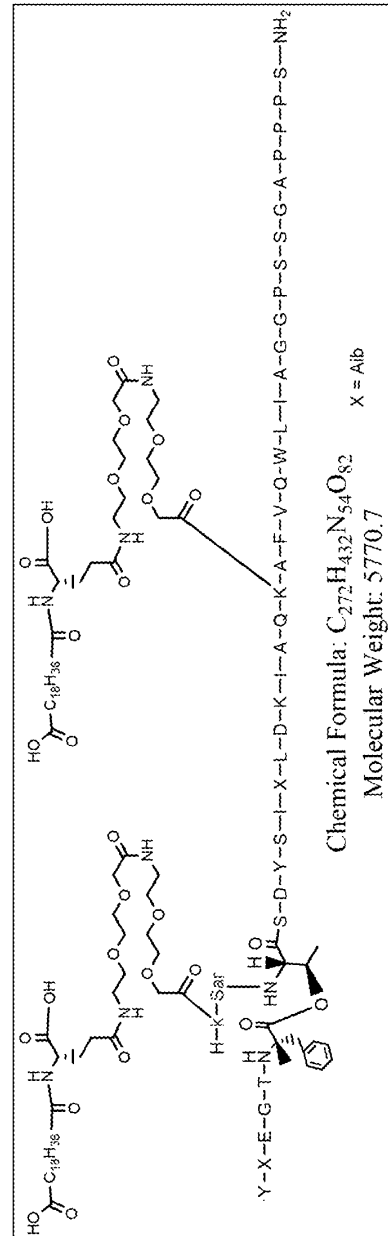


Fig. 4B

Single Dose Effect of Prodrugs in DIO Mice

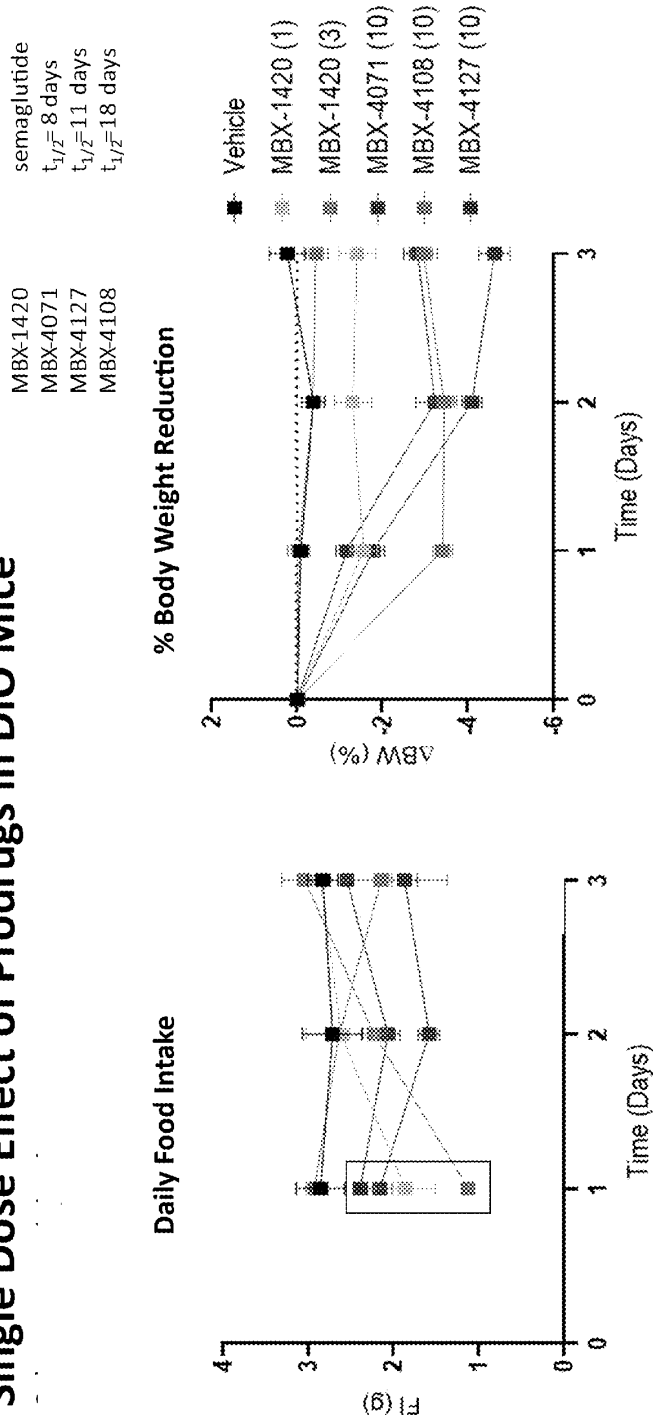


Fig. 5A

Fig. 5B

Repeat Daily Dose Effect of Pre-prodrugs in DIO Mice

Three daily subcutaneous injections

MBX-4071 t_{1/2} = 8 days
MBX-4127 t_{1/2} = 11 days
MBX-4129 t_{1/2} = 20 days

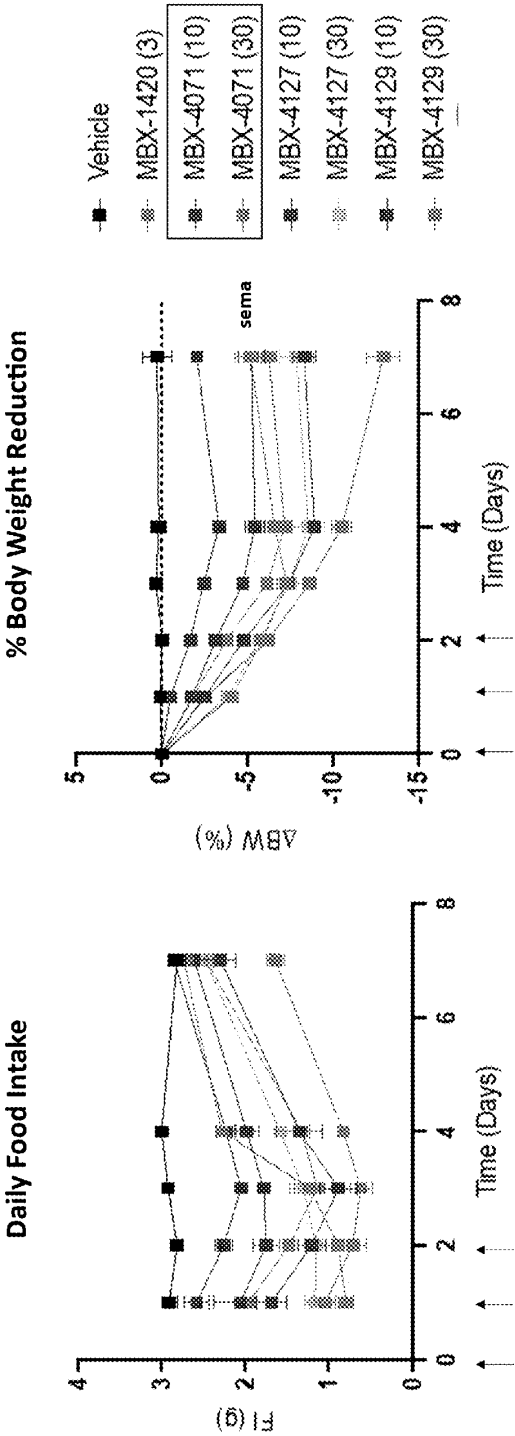


Fig. 6B

Ten Days Daily Doses in DIO-Mice with Co-agonists & its Prodrug

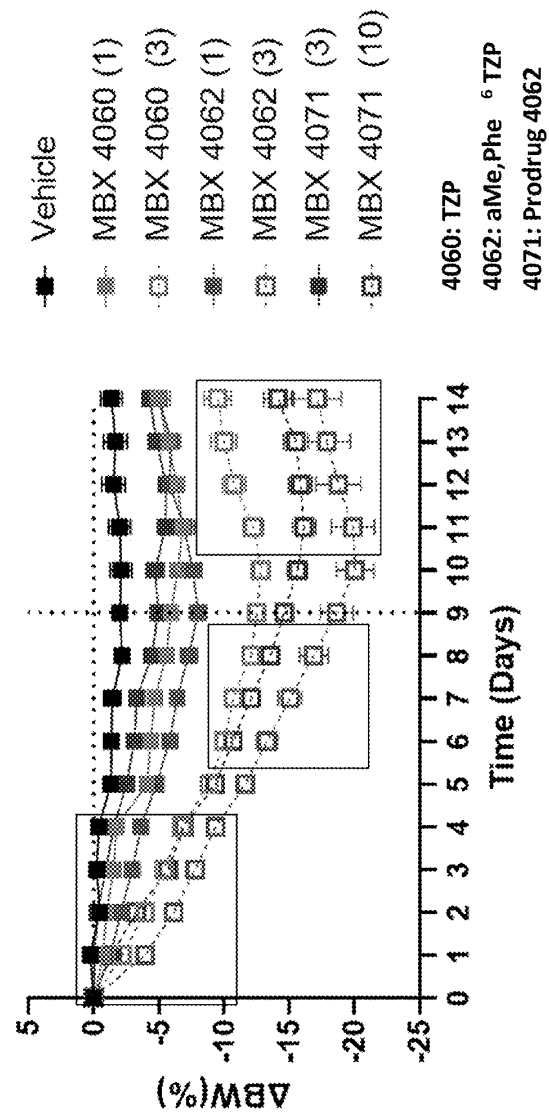


Fig. 7

Ten Days Daily Doses in DIO-Rats with Co-agonists & its Prodrug

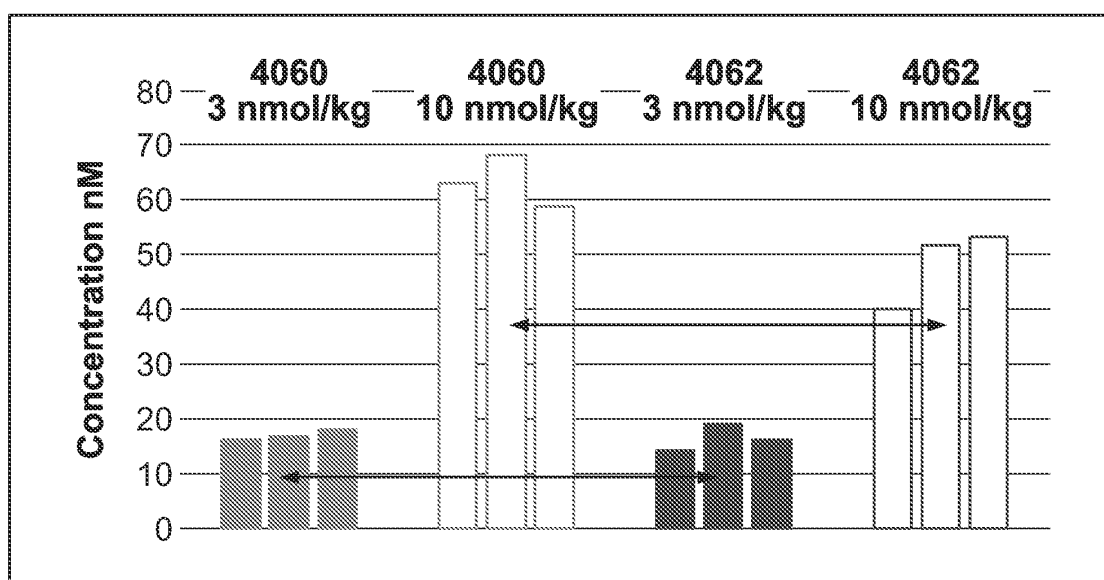
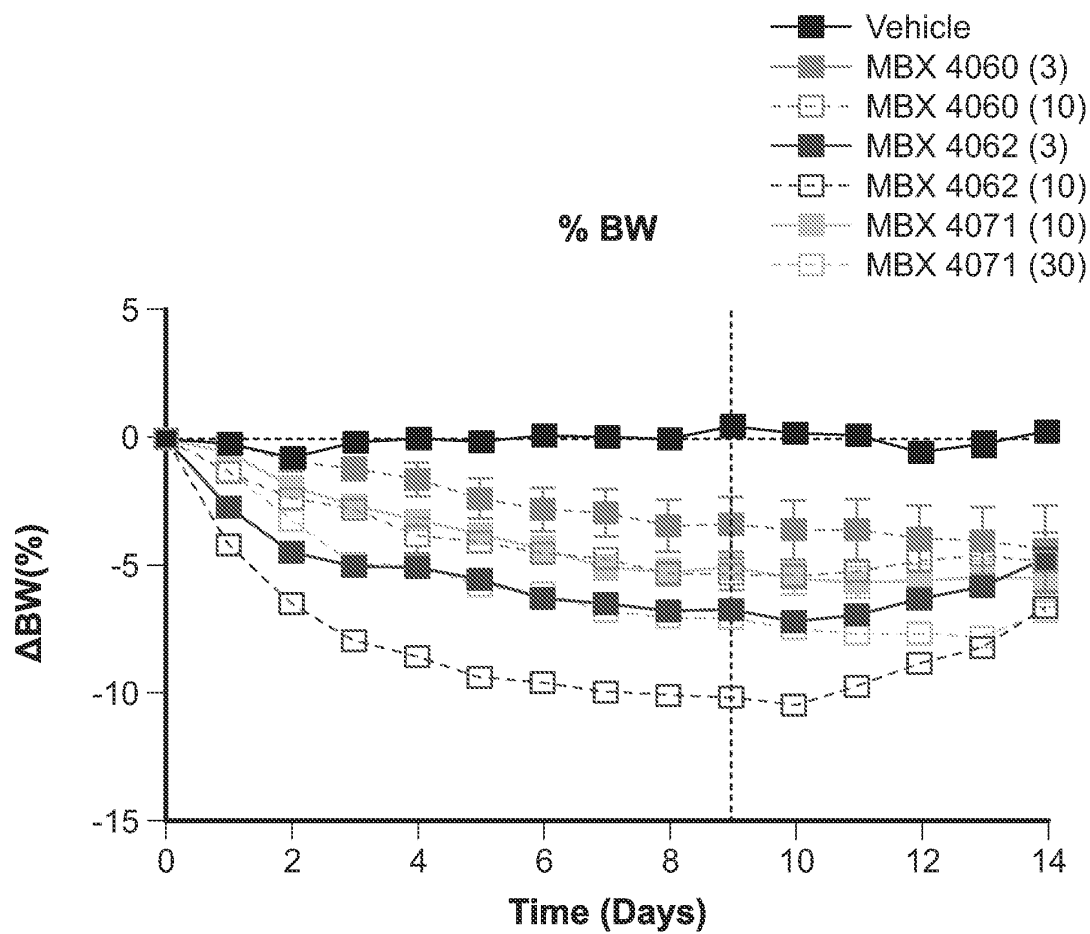


Fig. 8

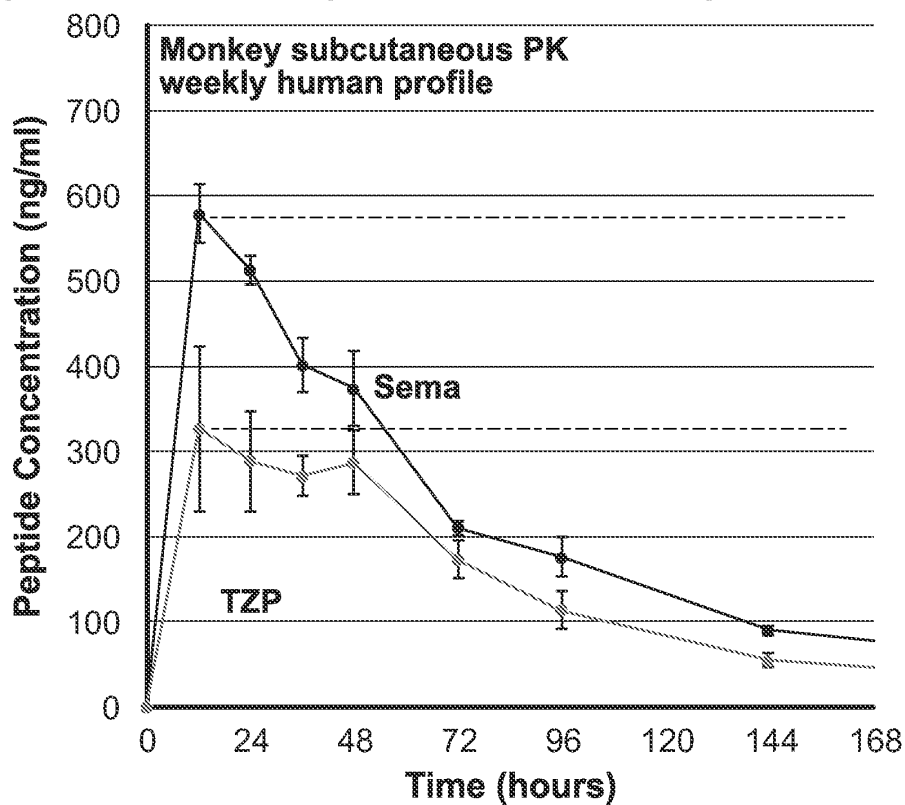


Fig. 9A

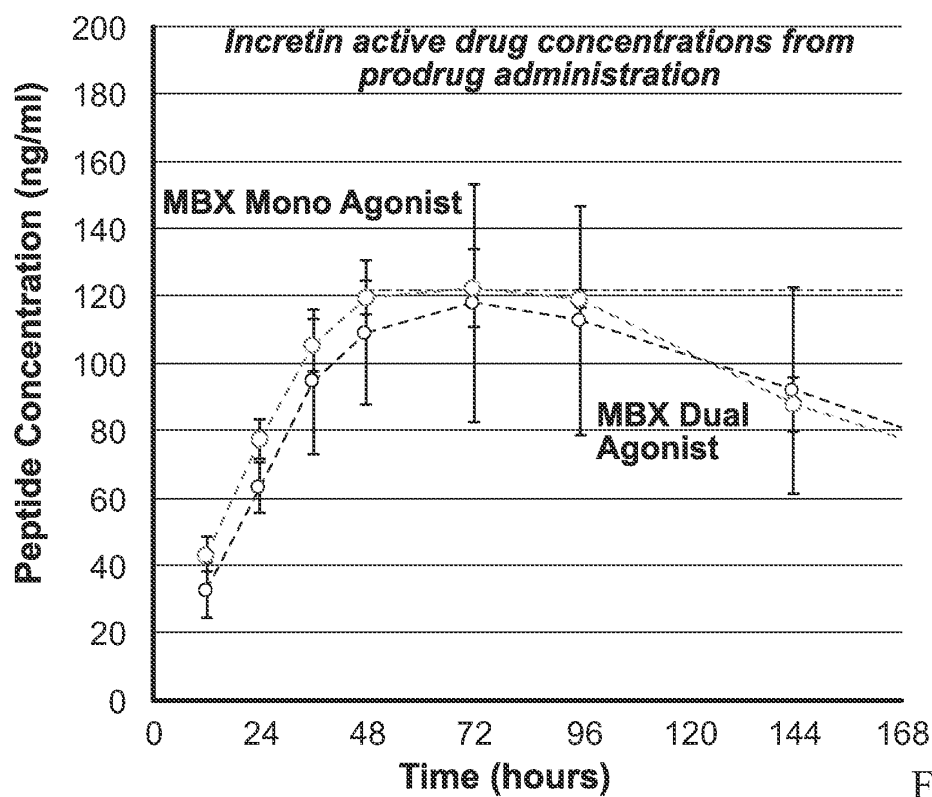


Fig. 9B

Monkey PK of Co-Agonist Prodrug

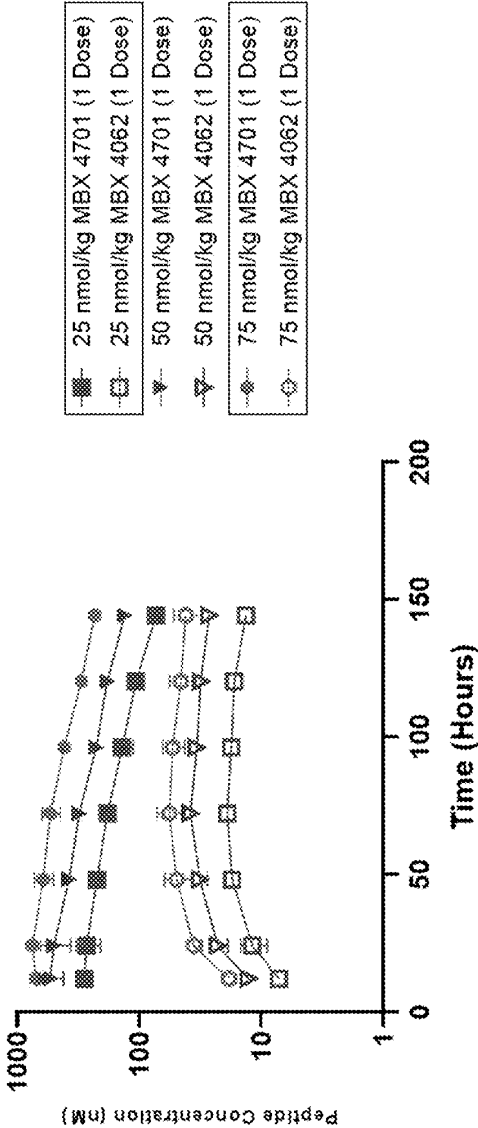


Fig. 10A

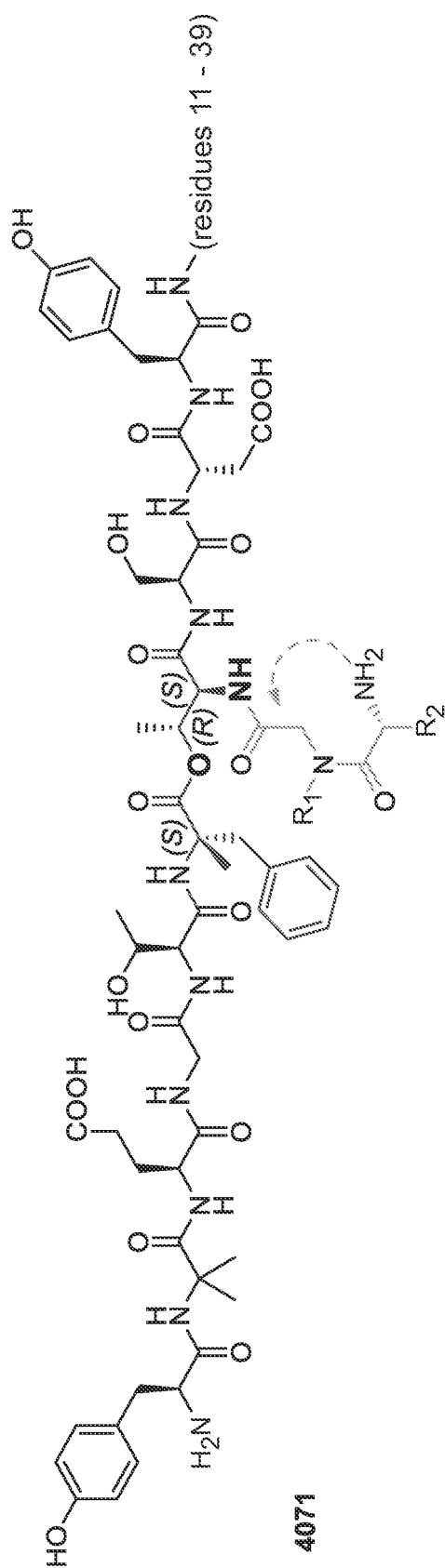


Fig. 10B

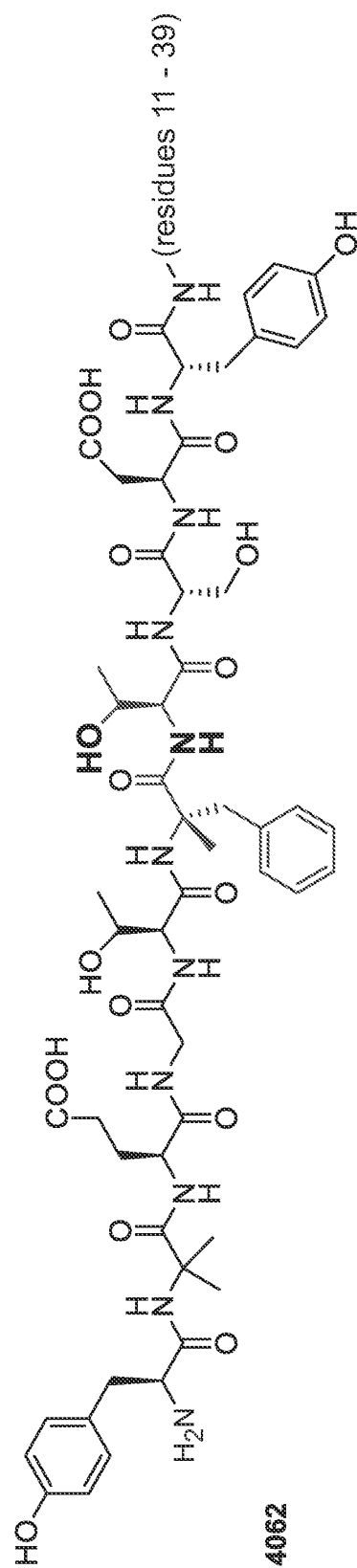


Fig. 10C

Alanine Scan in TZP (w/o lipid)

	MBX	Structure	GLP-1R EC50 pM	% to 4051 no substitution	GIPR EC50 pM	% to 4051 no substitution	EC50 GLP- 1R/EC50 GIPR
4116	(Y)L10-Tirzepatide		0.76	89%	0.27	48%	2.8 x
4117	(L)Nle14-Tirzepatide		0.69	99%	0.1	130%	6.9 x
4118	(D)E15-Tirzepatide		0.36	189%	0.16	81%	2.3 x
4119	(K)Orn16-Tirzepatide		0.64	106%	0.11	118%	5.8 x
4120	(I)V17-Tirzepatide		0.72	94%	0.13	100%	5.5 x
4121	(A)E21-Tirzepatide		0.7	97%	0.06	217%	11.7 x
4122	(V)I23-Tirzepatide		0.69	99%	0.18	72%	3.8 x
4123	(Q)A24-Tirzepatide		0.98	69%	0.33	39%	3.0 x
4124	(I)V27-Tirzepatide		0.96	71%	0.13	100%	7.4 x
4125	(A)E28-Tirzepatide		0.59	115 %	0.19	68%	3.1 x

Fig. 11

Tirzepatide (MBX 4060) vs aMe,Phe⁶ TZIP Analogs (MBX 4062, 4189, 4190)
EC50 measurements (pM) and relative potency to MBX 4060 in parenthesis

<u>MBX #</u>		<u>hGLP-1</u>	<u>hGIP</u>	<u>mGLP-1</u>	<u>mGIP</u>
4060	TZIP	0.157	0.056	0.170	0.930
4062	aMe,Phe ⁶	0.088 (1.78x)	0.026 (2.15x)	0.110 (1.55x)	0.120 (7.7x)
4063	AIB ¹⁶ , Thr ¹⁷	0.740 (0.20x)	0.153 (0.37x)		
4169	Ile ¹² , Tyr ¹³ , Glu ¹⁵ , AIB ¹⁶ , Thr ¹⁷ , Ala ¹⁹	0.197 (0.80x)	0.146 (0.38x)		
4178	Glu ¹⁵ , AIB ¹⁶ , Thr ¹⁷	0.074 (2.12x)	0.430 (0.13x)		
4189	aMe,Phe ⁶ , Glu ¹⁵ , AIB ¹⁶ , Thr ¹⁷	0.101 (1.55x)	0.065 (0.86x)	0.093 (1.83x)	0.289 (3.2x)
4190	aMe,Phe ⁶ , Glu ¹⁵ , AIB ¹⁶ , Thr ¹⁷ , Ala ¹⁹	0.101 (1.55x)	0.048 (1.16x)	0.093 (1.83x)	0.508 (1.8x)

Fig. 12

Body Weight Lowering in DIO-Mice of MBX Incretin Co-agonists
MBX-4060, 4062, 4189, 1 & 3nmol/kg

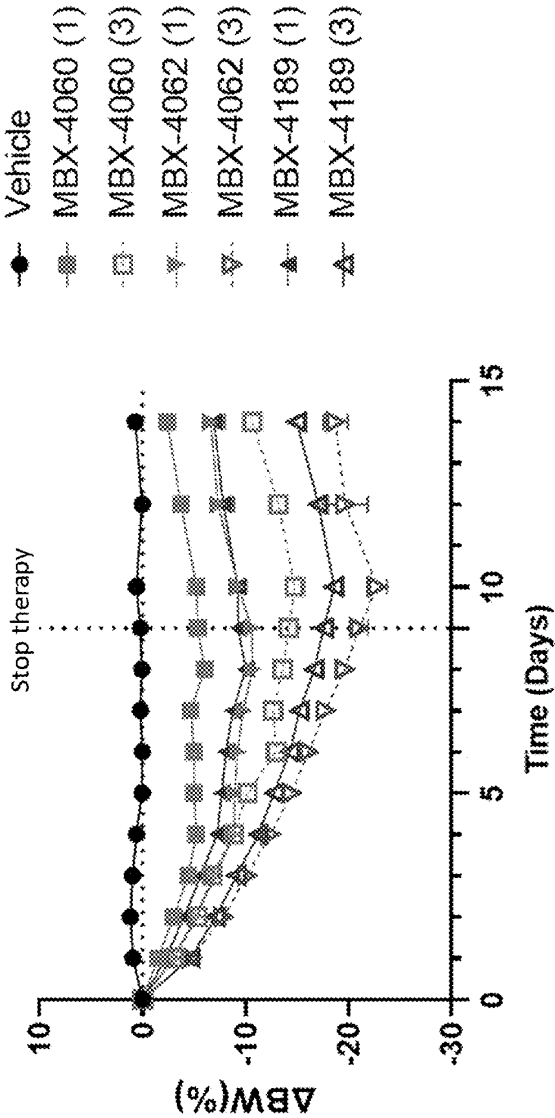


Fig. 13

Food Intake Analysis in DIO-Mice of MBX Incretin Co-agonists
MBX-4060, 4062, 4189, 1 & 3nmol/kg

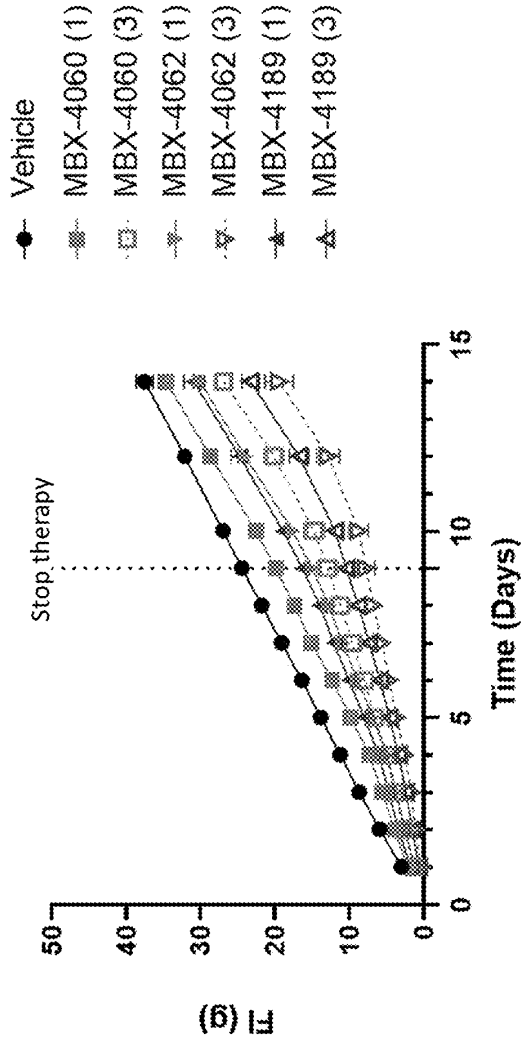


Fig. 14

MBX 4274: Tirzepatide, alpha -Me-F6, Glu15, Thr17, Ala19 analog

Double Agonism: GLP-1 & GIP

TZP = 4060	hGLP-1R (EC50)				% of 4060				hGIPR (% of 4060)				% of 4060			
	4060	4189	4190	4274	4189	4190	4274	4060	4189	4190	4274	4060	4189	4190	4274	
10-Oct-23	0.68	0.34	0.33	0.77	197	203	89									
4-Oct-23	0.51	0.27	0.48	0.70	187	106	73	0.05	0.08	0.06	0.06		67	88	99	
26-Sep-23	1.34	0.42	0.39	0.59	320	348	227	0.03	0.11	0.06	0.04		28	52	83	
21-Sep-23	0.38	0.39	0.32	0.40	98	118	96	0.15	0.26	0.15	0.13		58	100	111	
19-Sep-23	0.42	0.31	0.27	0.34	138	160	125	0.16	0.23	0.14	0.14		69	112	113	
Mean					226	224	122						56	88	101	

Fig. 15

Double Agonism: GLP-1 & GIP, dailysc-DIO Mice

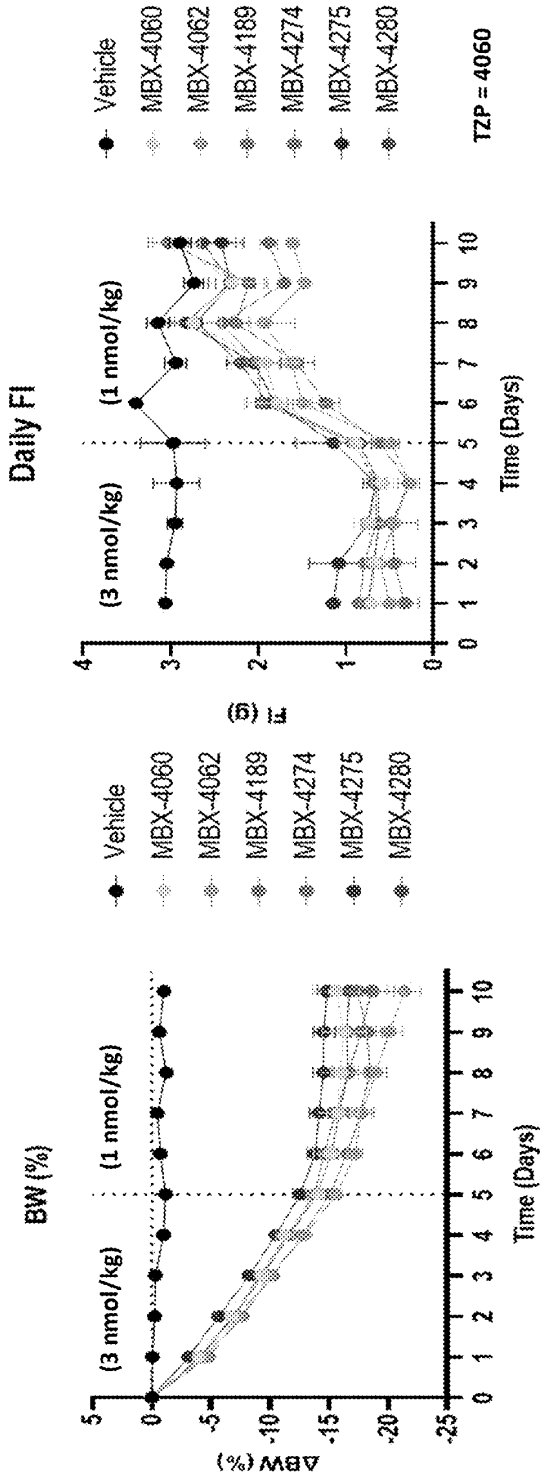


Fig. 16A

Fig. 16B

Inotiv NHP PK Analysis Study 2687-2301854

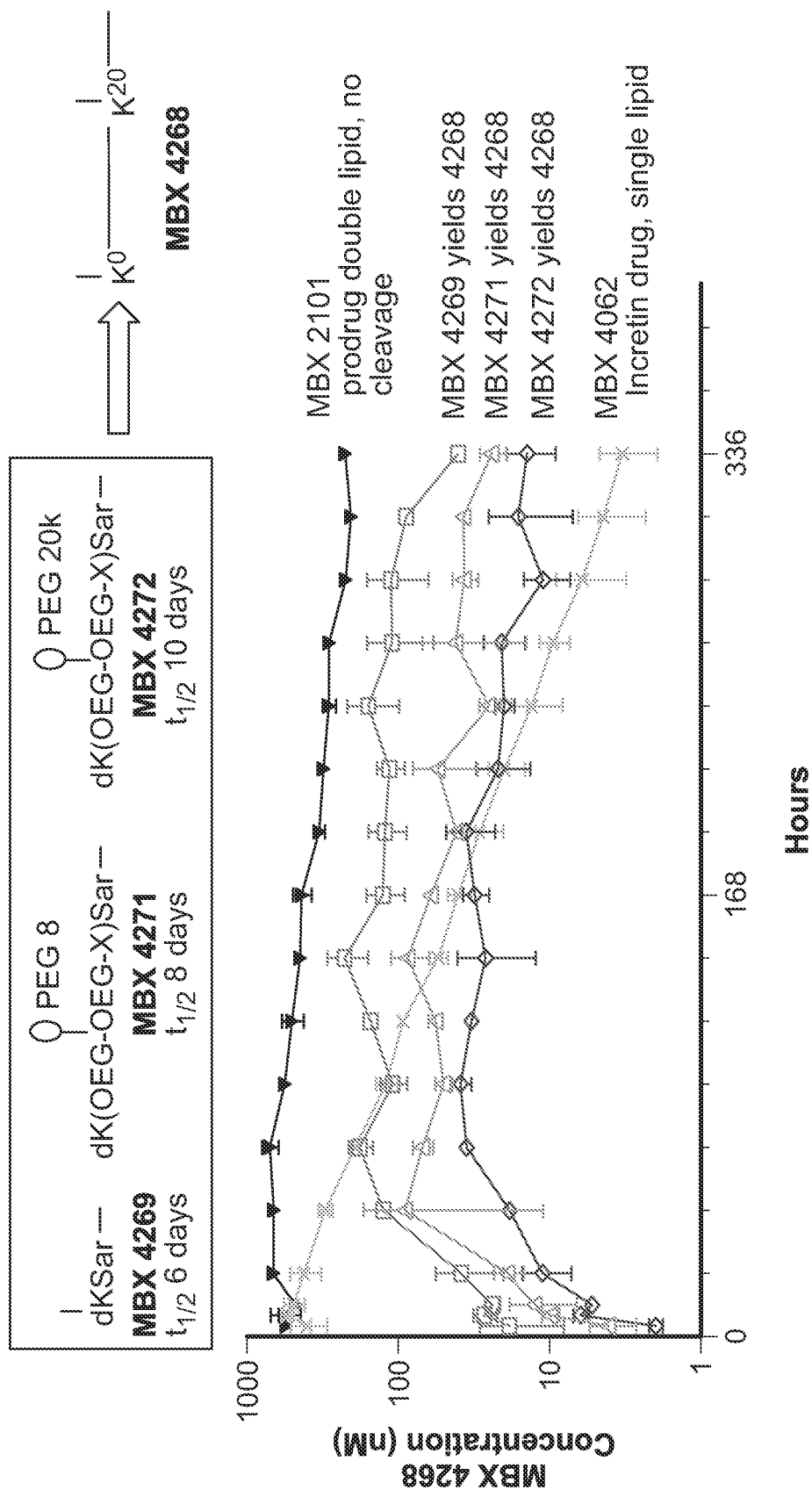
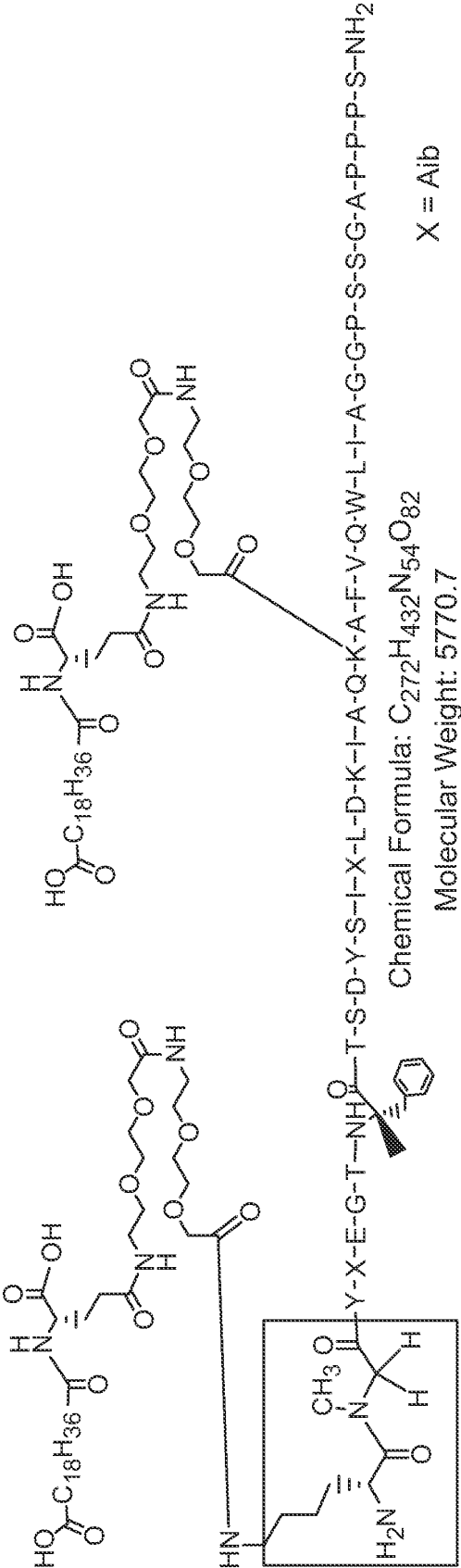


Fig. 17

Analysis of Conversion of MBX 4083 to MBX 4062 in PBS, by LCMS

MBX4083



Time (d)	Drug MBX4062 (%)	Prodrug MBX4083 (%)	Total peak area
0	0	1395.3 (100 %)	1395.3
1	136.9 (10 %)	1263.3 (90 %)	1400.2
3	353.7 (26 %)	1003.7 (74 %)	1357.4
7	651.1 (48 %)	695.4 (52 %)	1346.5
11	786 (59 %)	539.8 (41 %)	1325.8

Fig. 18

PK Analysis in NHP, Study 2687-2301854

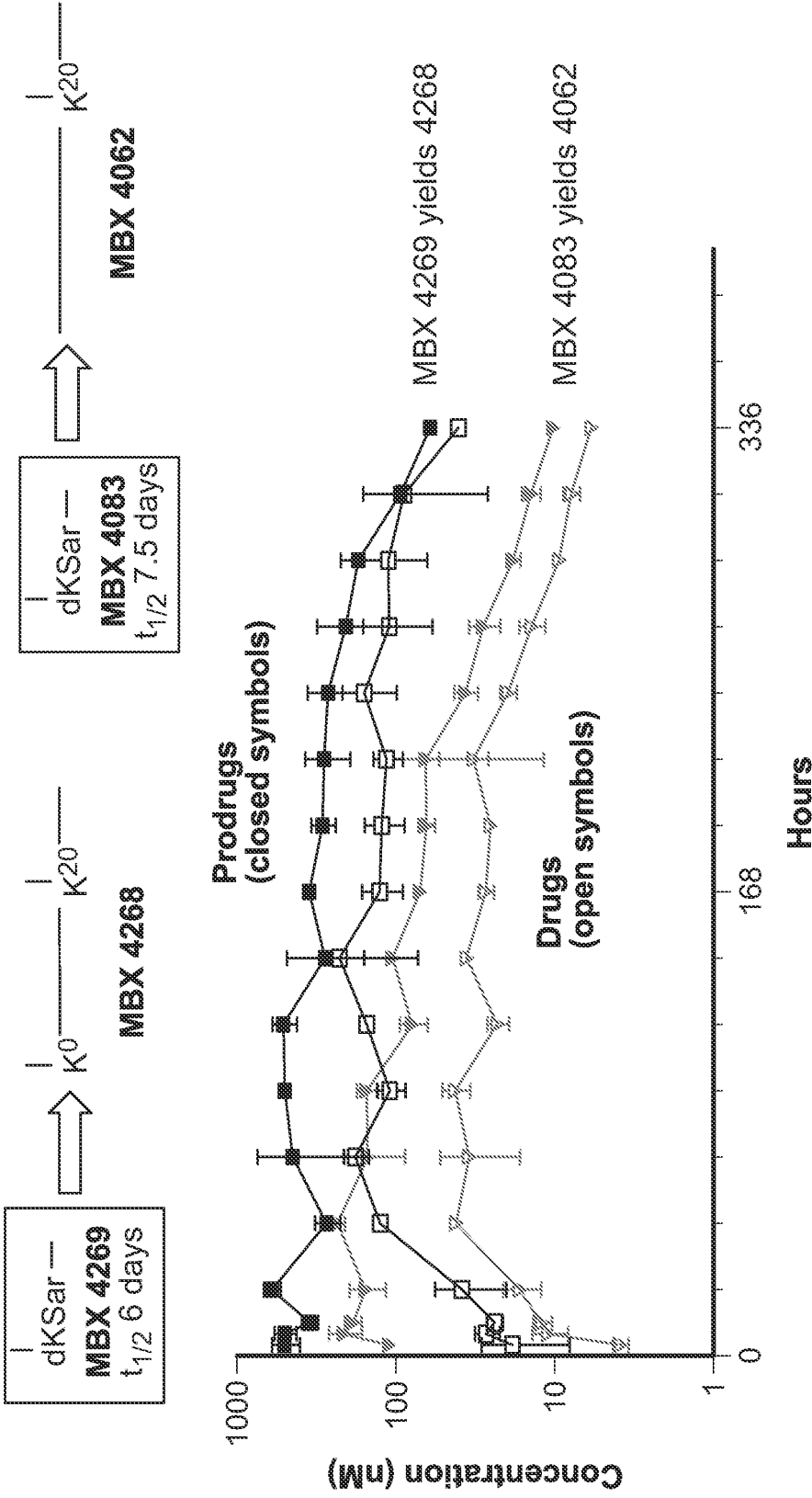


Fig. 19

Analysis of Conversion of Deuterated Prodrugs to MBX 4062 in PBS, by LCMS

	MBX4083 N(CH3)CH2	MBX4232 N(CD3)CD2	MBX4265 N(CH3)CD2	MBX4266 N(CD3)CH2
Half-life	8.3 (21d)	15.3	10.9	11.1
0 d	1408.5	1445.9	14440.9	1523.2
1 d	132.8+1310.8=1443.6 (90.8 % prodrug)	101.2+1324.6=1425.8 (92.9 % prodrug)	126.9+1336=1462.9 (91.3 % prodrug)	133.3+1378.5=1511.8 (91.2 % prodrug)
3 d	380.5+1080.6=1461.1 (74.0 % prodrug)	252.8+1160.3=1413.1 (82.1 % prodrug)	319.5+1159.8=1479.3 (78.4 % prodrug)	334.6+1186.8=1521.4 (78.0 % prodrug)
5 d	566.1+888.6=1454.7 (61.1 % prodrug)	369.5+1013.2=1382.7 (73.3 % prodrug)	464.5+957.1=1421.6 (67.3 % prodrug)	480.1+981=1461.1 (67.1 % prodrug)
7 d	728+766.4=1494.4 (51.3 % prodrug)	458.8+911=1369.8 (66.5 % prodrug)	583+823.3=1406.3 (58.5 % prodrug)	610.4+872.4=1482.8 (58.8 % prodrug)
10 d	885+583.1=1468.1 (39.7 % prodrug)	552.8+785.2=1338 (58.7 % prodrug)	718.1+676.8=1394.9 (48.5 % prodrug)	734.4+714.8=1449.2 (49.3 % prodrug)
14 d	1024.2+419.8=1444 (29.1 % prodrug)	659.8+684.2=1344 (50.9 % prodrug)	843.4+538.3=1381.7 (39.0 % prodrug)	858.8+565.9=1424.7 (39.7 % prodrug)
21 d	1112.5+280.6=1393.1 (20.1 % prodrug)	713.5+555.4=1268.9 (43.8 % prodrug)	928.7+400.8=1329.5 (30.1 % prodrug)	921.9+407.7=1329.6 (30.7 % prodrug)

Fig. 20

Analysis of Conversion of Lysine¹⁶ Prodrugs to MBX 4062 in PBS, by LCMS

Peptides	dipeptide	1d	7 d	14 d	Half-life in PBS 37 °C
MBX4206	dLys-Sar	-	24.7 % prodrug	9.6 % prodrug	4.0 d
MBX4220	lLys-dPro	20 h 89.2 % prodrug	46.0 % prodrug	24.7 % prodrug	6.3 d
MBX4221	lLys-dPro C18	20 h 90.5 % prodrug	48.4 % prodrug	28.4 % prodrug	7.3 d
MBX4213	dLys-lPro	20 h 90.3 % prodrug	44.9 % prodrug	22.9 % prodrug	6.5 d
MBX4212	lLys-lPro	94.6 % prodrug	72.2 % prodrug	19 d 46.3 % prodrug	18.2 d
MBX4218	dLys-trans-3-OH-lPro	-	78.9 % prodrug	64.5 % prodrug	18.0 d
MBX4217	lLys-trans-3-OH-lPro	-	87.5 % prodrug	77.3 % prodrug	30.8 d
MBX4215	dLys-Gly	100 % prodrug	99.0 % prodrug	98.4 % prodrug	~5600 d

Fig. 21

PK Analysis in NHP, of Lysine¹⁶ Prodrugs to MBX 4062 in PBS, by LCMS

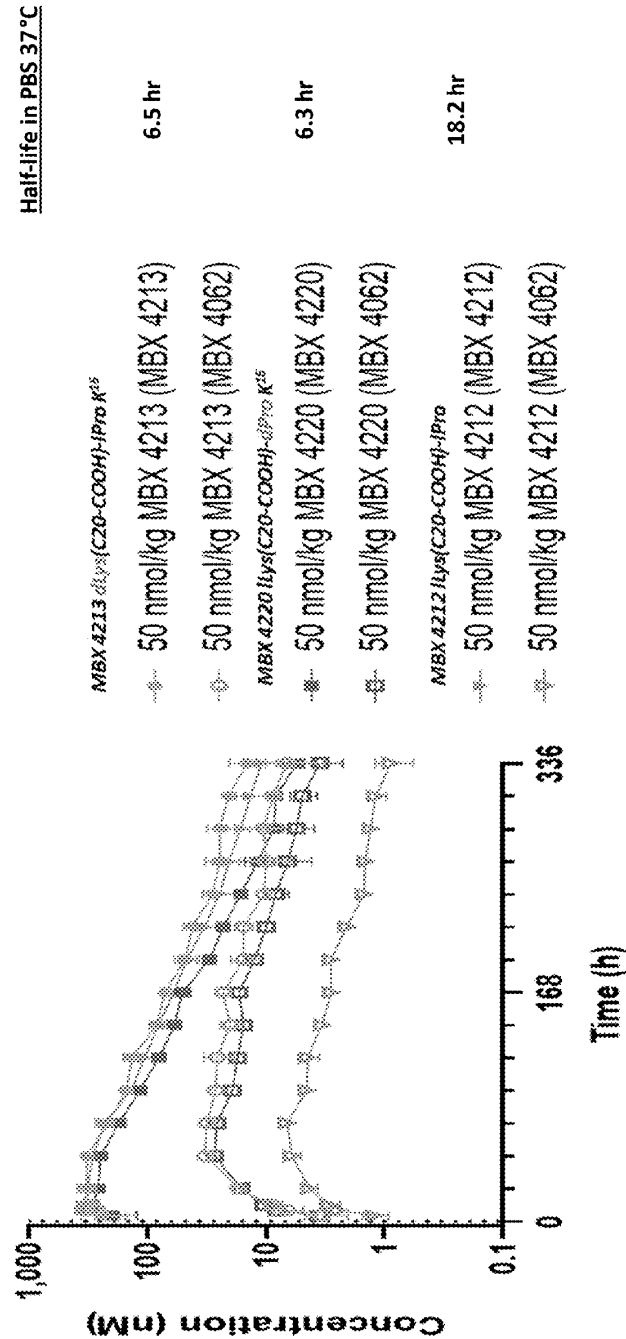


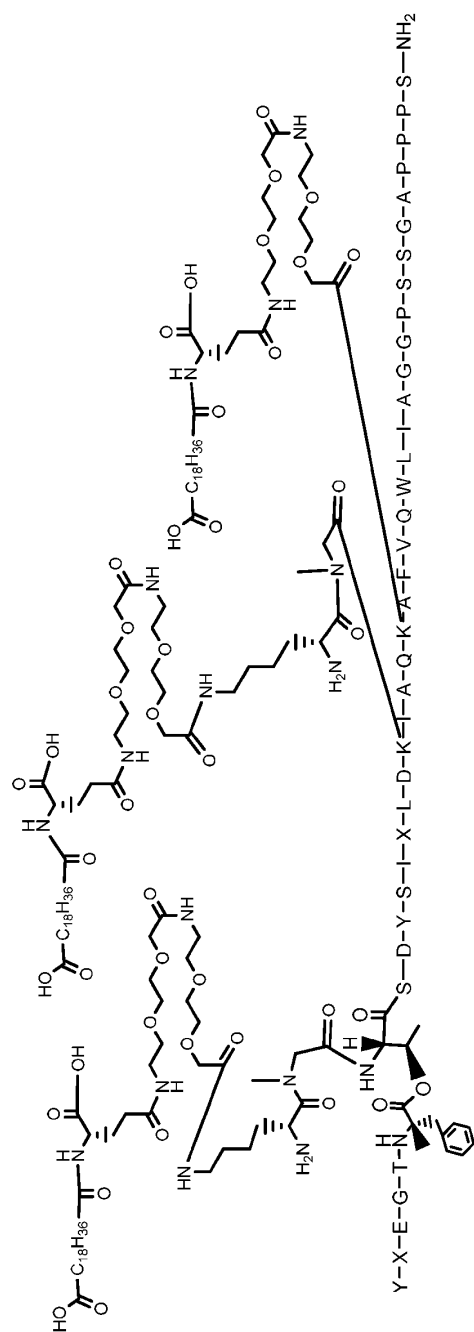
Fig. 22

Analysis of Conversion of N-terminal vs Lysine¹⁶ Prodrugs to MBX 4062 in PBS, by LCMS

	MBX4239 dK-I3,4-dehydroP at Y1	MBX4240 IK-I3,4-dehydroP at Y1	MBX4241 dK-I3,4-dehydroP at K16	MBX4242 IK-I3,4-dehydroP at K16
Half-life	54.6 d	53.7 d	8.5 d	14.8 d
0 d	1440.8	1472.8	1449.4	1454.7
3 d	46.7+1372.3 (97 % prodrug)	46.9+1379.5 (97 % prodrug)	326.4+1130.3 (78 % prodrug)	171.5+1251.0 (88 % prodrug)
7 d	116.8+1270.7 (92 % prodrug)	108.1+1308 (92 % prodrug)	617.9+22.8(DKP)+758.3 (54 % prodrug)	379.6+15.3(DKP)+1003.4 (72 % prodrug)
10 d	171.8+1173.8 (87 % prodrug)	164.8+1213.6 (88 % prodrug)	751.9+47.3(DKP)+600.1 (43 % prodrug)	503.8+25.4(DKP) +917.8 (63 % prodrug)
14 d	191.4+969.7 (84 % prodrug)	203.7+10.9(DKP)+1071.2 (83 % prodrug)	791.9+63.2(DKP)+370.2 (30 % prodrug)	606.8+42.4(DKP)+675.9 (51 % prodrug)
21 d	232+13(DKP)+818.6 (77 % prodrug)	294.5+19.4(DKP)+997.4 (76 % prodrug)	873.4+115.7(DKP)+234.2 (19 % prodrug)	787.6+83.5(DKP)+528.7 (38 % prodrug)

← Slow and equal $t_{1/2} > 21$ days → Faster than Y1 and d_j > than I_j → $t_{1/2} \sim 7$ days $t_{1/2} \sim 14$ days

Fig. 23



Chemical Formula: C₃₁₈H₅₁₄N₆₀O₉₆ X = Aib

Molecular Weight: 6713.93

Fig. 24A

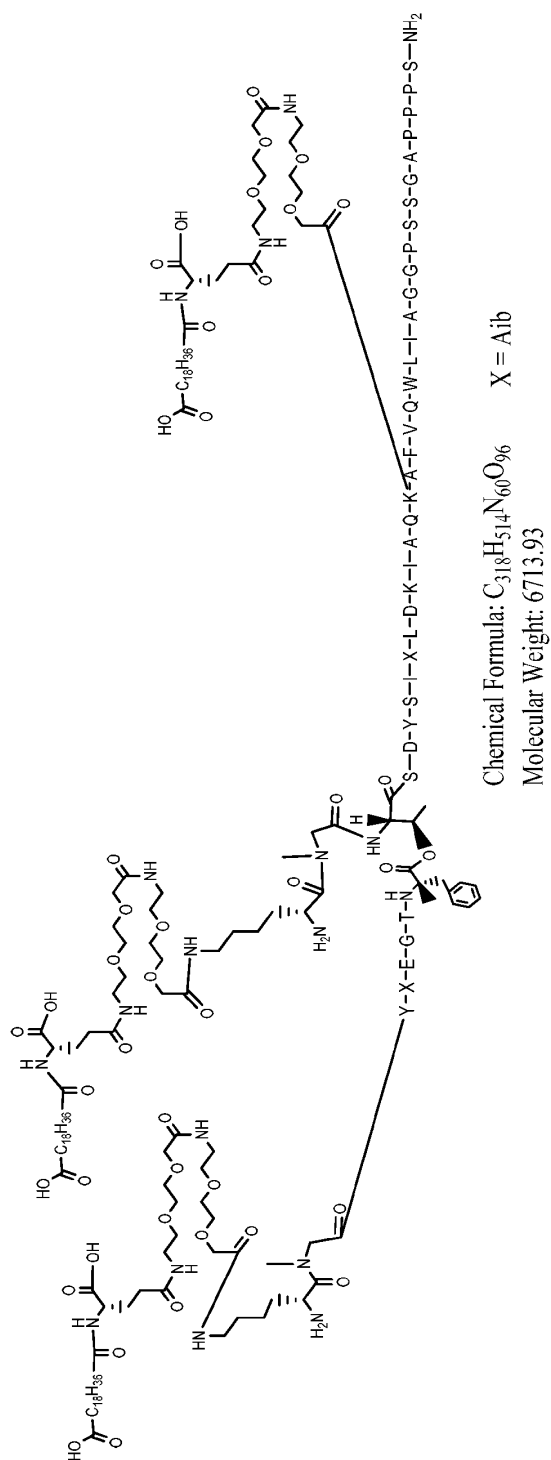


Fig. 24B

	1 lipid drug	2 lipids prodrug	3 lipids prodrug	Hydrolysis/byproduct
MBX4223 2d	8%	46%	41%	6%
MBX4224 2d	3%	24%	65%	8%
MBX4225 2d	10%	50%	39%	0%
MBX4223 3d	14%	56% (ratio 4:1)	25%	5%
MBX4224 3d	5%	33%(ratio 1:1:4)	48%	13%
MBX4225 3d	18%	56%(ratio 1:4)	26%	0%
MBX4223 4d	21%	55% (ratio 4:1)	18%	6%
MBX4224 4d	11%	36% (ratio 1:1:3)	38%	14%
MBX4225 4d	24%	57% (ratio 1:4)	19%	0%
MBX4223 7d	39%	47%	8%	6%
MBX4224 7d	26%	37%	23%	15%
MBX4225 7d	41%	51%	8%	0%

Fig. 25

Analysis of Conversion of Sequential Prodrugs to MBX 4062 in PBS, by LCMS



Time (d)	Drug MBX4062 (%)	2 lipids prodrug MBX4083 (%)	3 lipids prodrug MBX4234 (%)	Total peak area
0	0 (0 %)	0 (0 %)	1444.4 (100 %)	1444.4
1	13.1 (1 %)	209 (15 %)	1171 (84 %)	1393.1
3	80.5 (6 %)	417.9 (31 %)	841.4 (63 %)	1339.8
7	322.3 (24 %)	542.7 (41 %)	474.8 (35 %)	1339.8
10	497.5 (37 %)	516.6 (39 %)	323 (24 %)	1337.1
14	642.9 (51 %)	400.9 (32 %)	206.5 (17 %)	1250.3
21	839.2 (69 %)	250 (21 %)	126.1 (10 %)	1215.3
28	918.8 (79 %)	145.6 (13 %)	92.6 (8 %)	1157

Fig. 26A

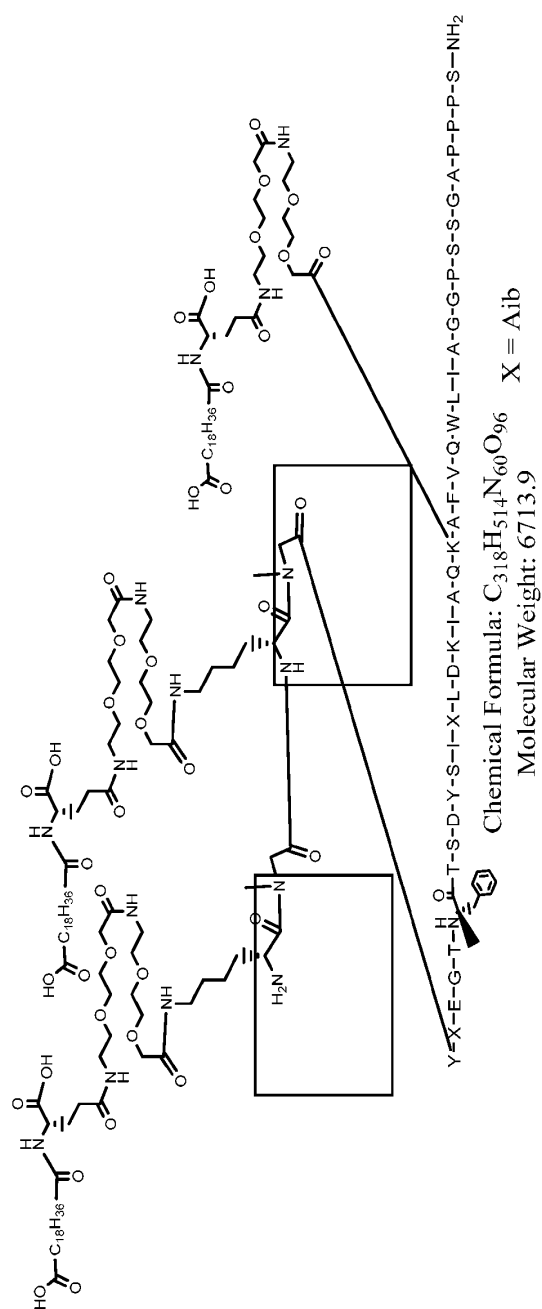


Fig. 26B

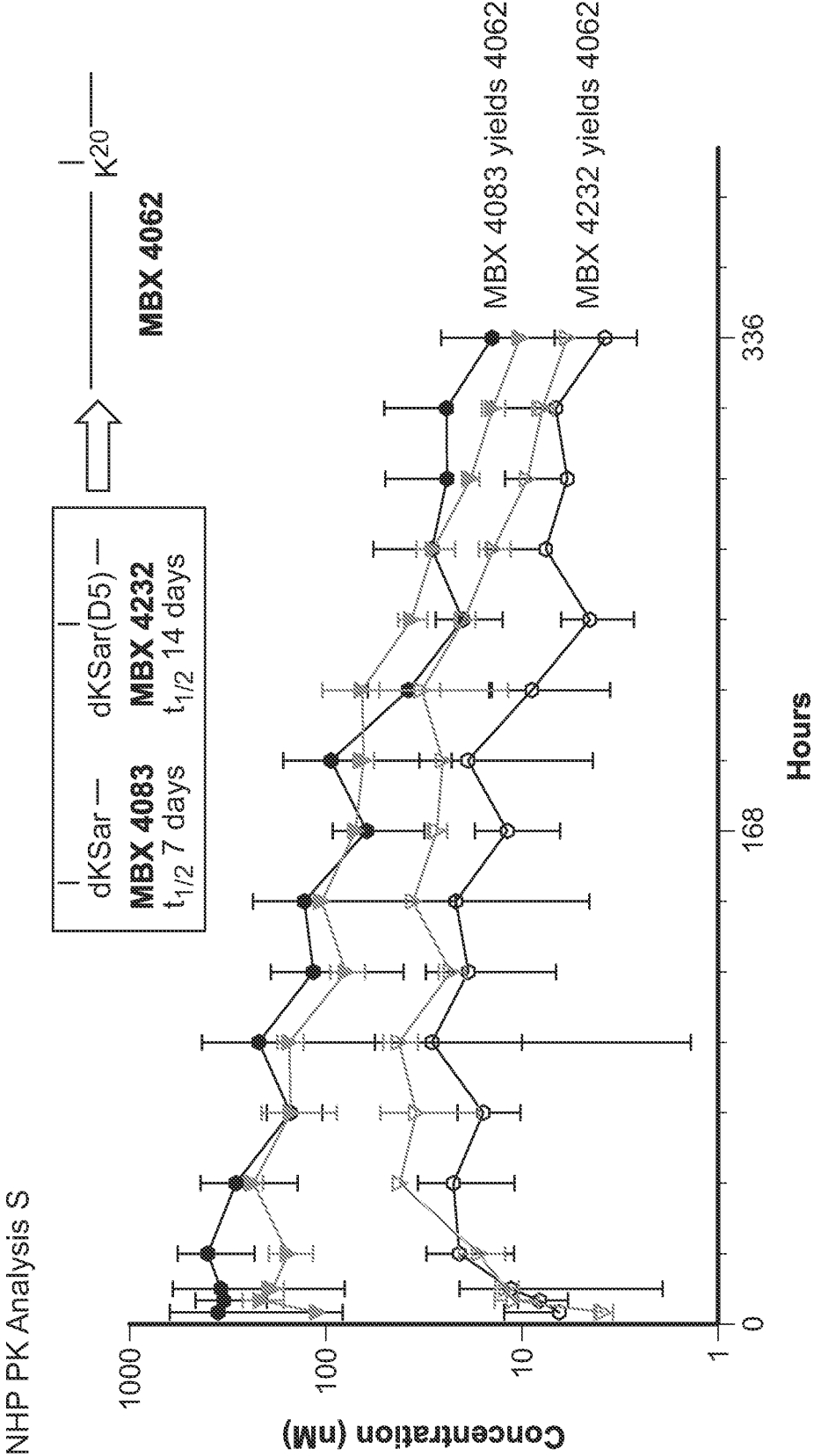


Fig. 27

Comparative NHP PK Analysis of Single vs Sequential Prodrug Cleavage

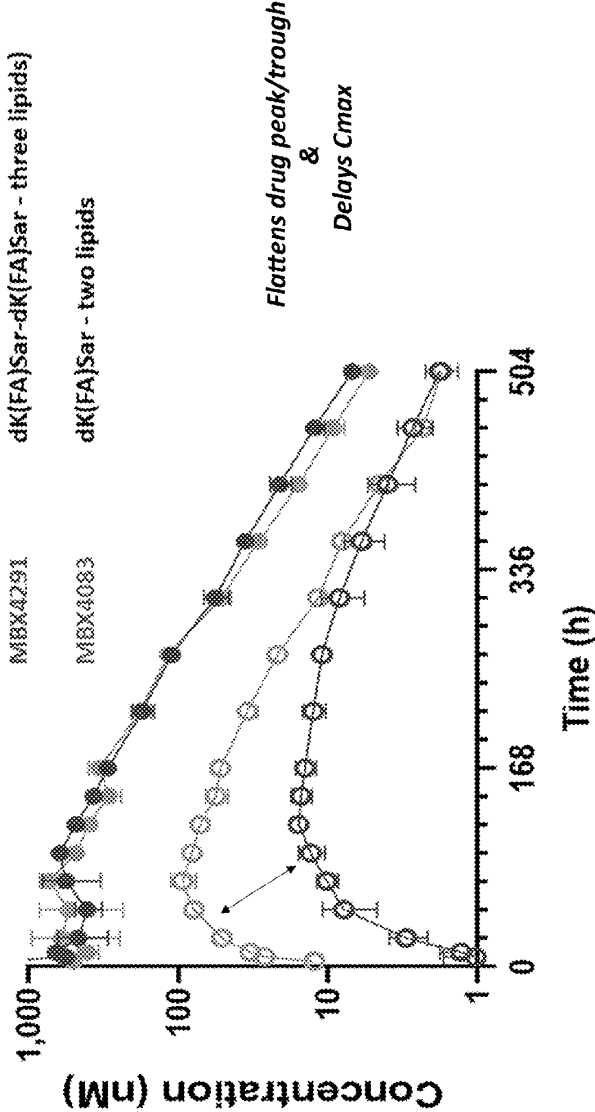


Fig. 28

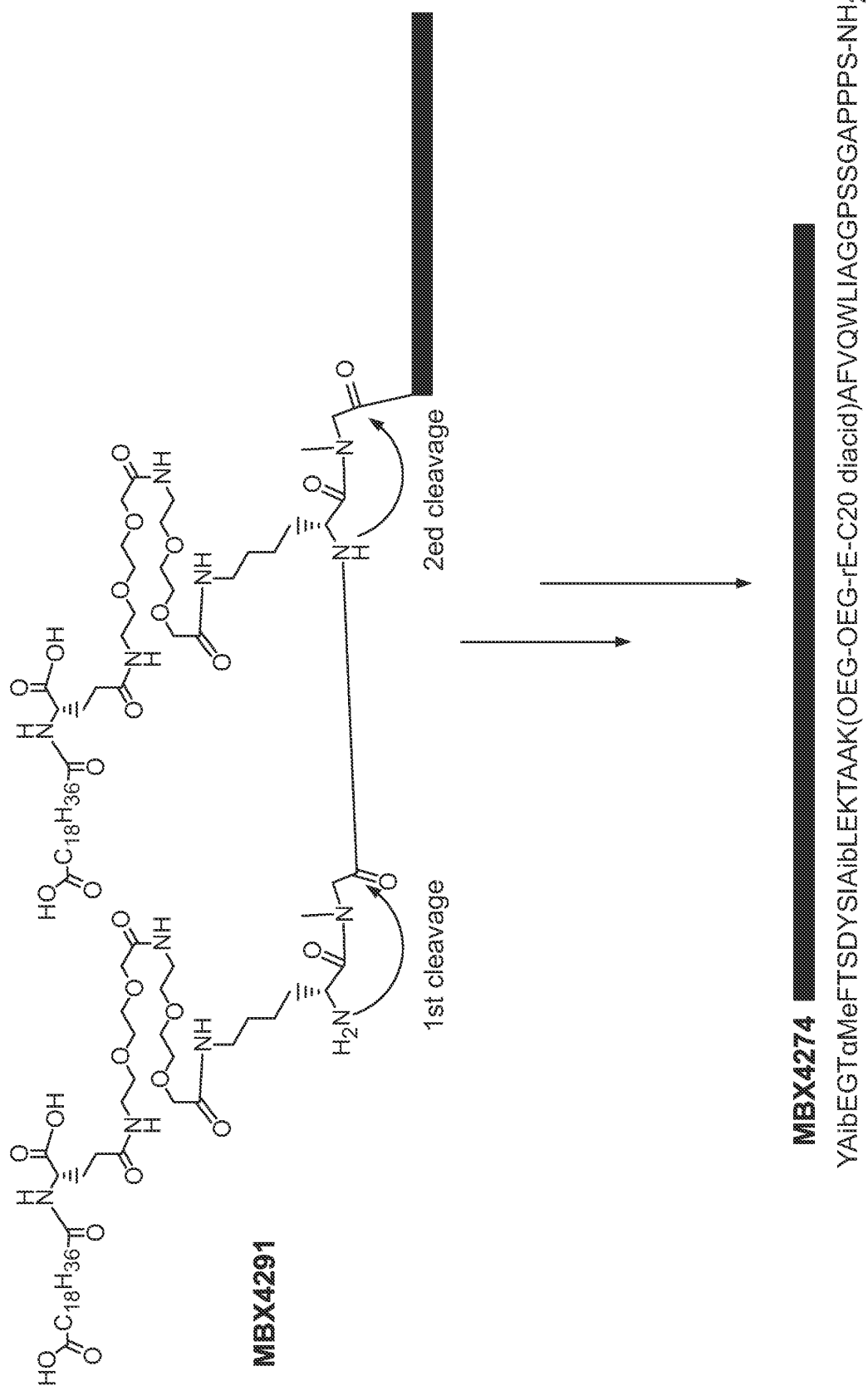


Fig. 29

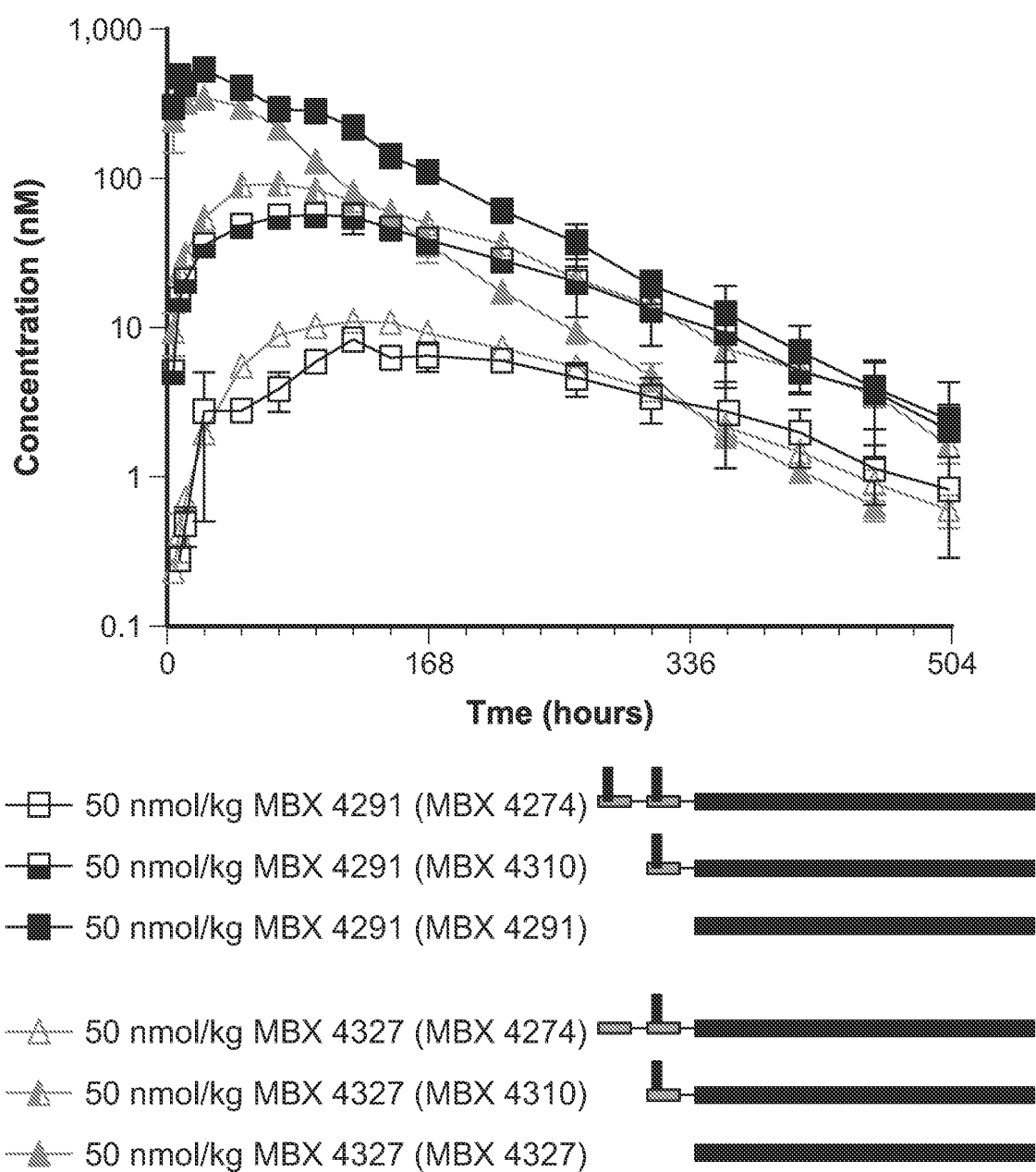


Fig. 30

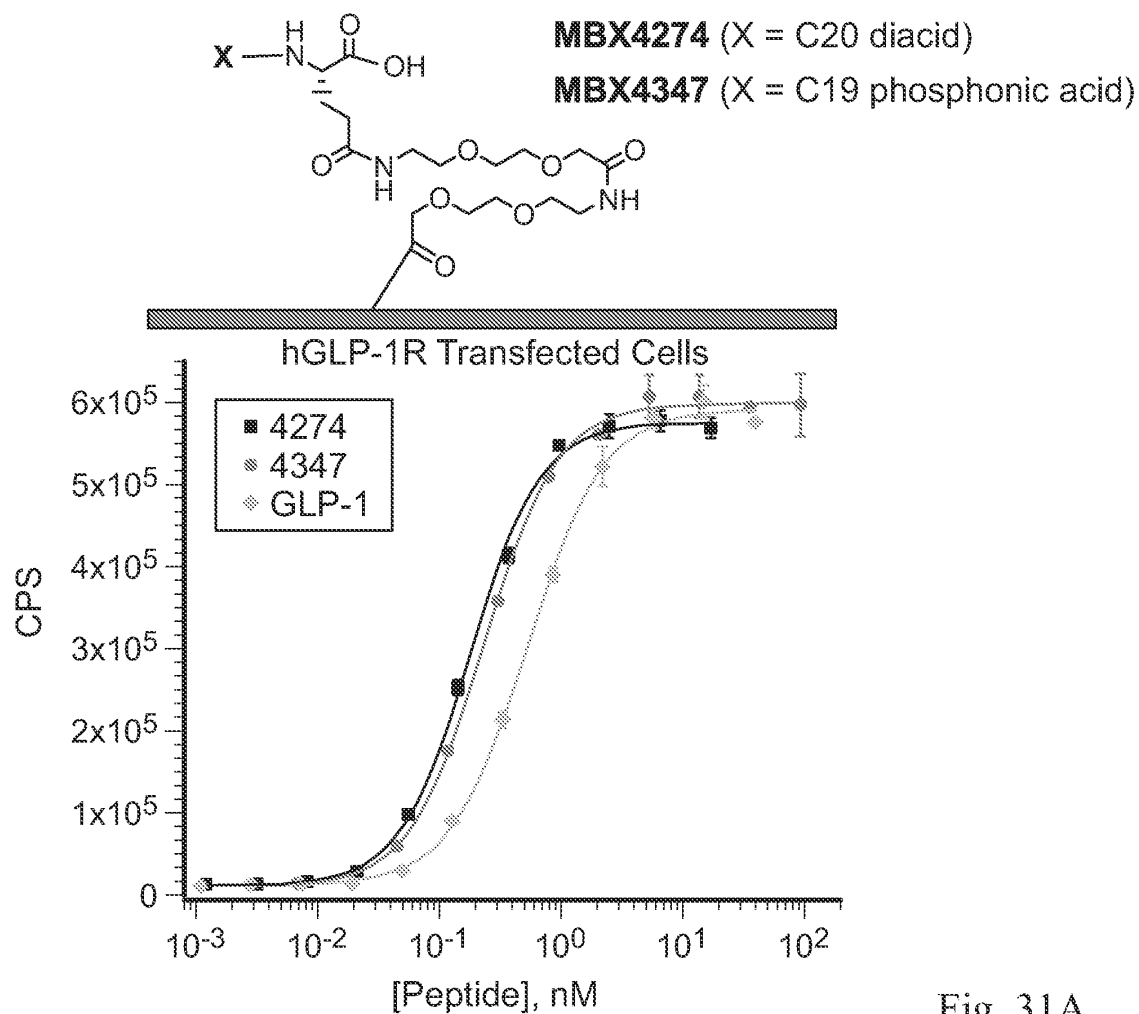


Fig. 31A

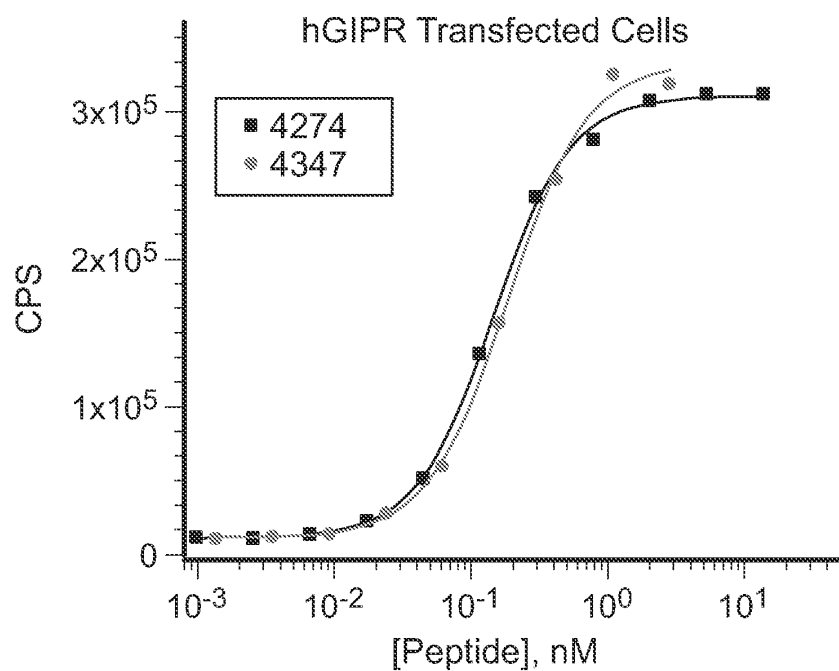


Fig. 31B

Pharmacokinetics in Cynomolgus Monkeys of Peptide-Drugs with Different Fatty Acids

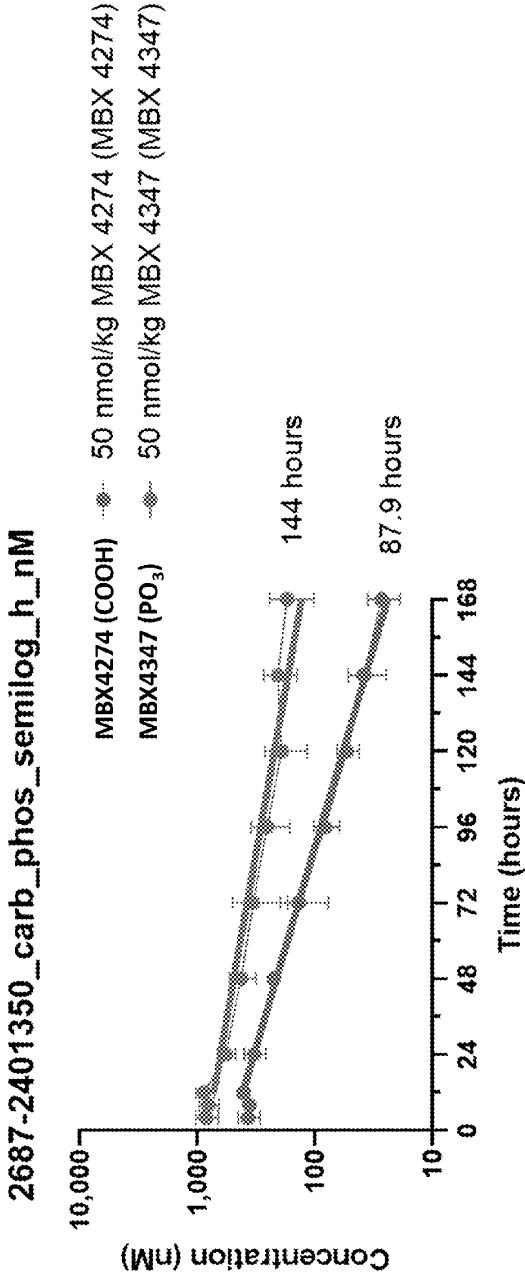


Fig. 32

A family of Sequential Dipeptide Prodrugs with Fatty Carboxylic or Fatty Phosphonic Acids

	Peptide	1 st dipeptide	2 nd dipeptide	Active drug
CCC	MBX4291	dK(OEG-OEG-rE-C20 diacid)Sar	dK(OEG-OEG-rE-C20 diacid)Sar	4274
CC	MBX4310	absent	dK(OEG-OEG-rE-C20 diacid)Sar	4274
HCC	MBX4327	dKSar	dK(OEG-OEG-rE-C20 diacid)Sar	4274
HCCC	MBX4328	dKSar	dK(OEG-OEG-rE-C20 diacid)Sar	4274
HPC	MBX4350	dKSar	dK(OEG-OEG-rE-C19 phosphonic acid)Sar	4274
PC	MBX4351	absent	dK(OEG-OEG-rE-C19 phosphonic acid)Sar	4274
CPC	MBX4349	dK(OEG-OEG-rE-C20 diacid)Sar	dK(OEG-OEG-rE-C19 phosphonic acid)Sar	4274
PPC	MBX4357	dK(OEG-OEG-rE-C19 phosphonic acid)Sar	dK(OEG-OEG-rE-C19 phosphonic acid)Sar	4274
PPP	MBX4363	dK(OEG-OEG-rE-C19 phosphonic acid)Sar	dK(OEG-OEG-rE-C19 phosphonic acid)Sar	4347
CPP	MBX4365	dK(OEG-OEG-rE-C20 diacid)Sar	dK(OEG-OEG-rE-C19 phosphonic acid)Sar	4347
HPP	MBX4362	dKSar	dK(OEG-OEG-rE-C19 phosphonic acid)Sar	4347
HCP	MBX4364	dKSar	dK(OEG-OEG-rE-C20 diacid)Sar	4347
PP	MBX4361	absent	dK(OEG-OEG-rE-C19 phosphonic acid)Sar	4347
CP	MBX4368	absent	dK(OEG-OEG-rE-C20 diacid)Sar	4347

Fig. 33

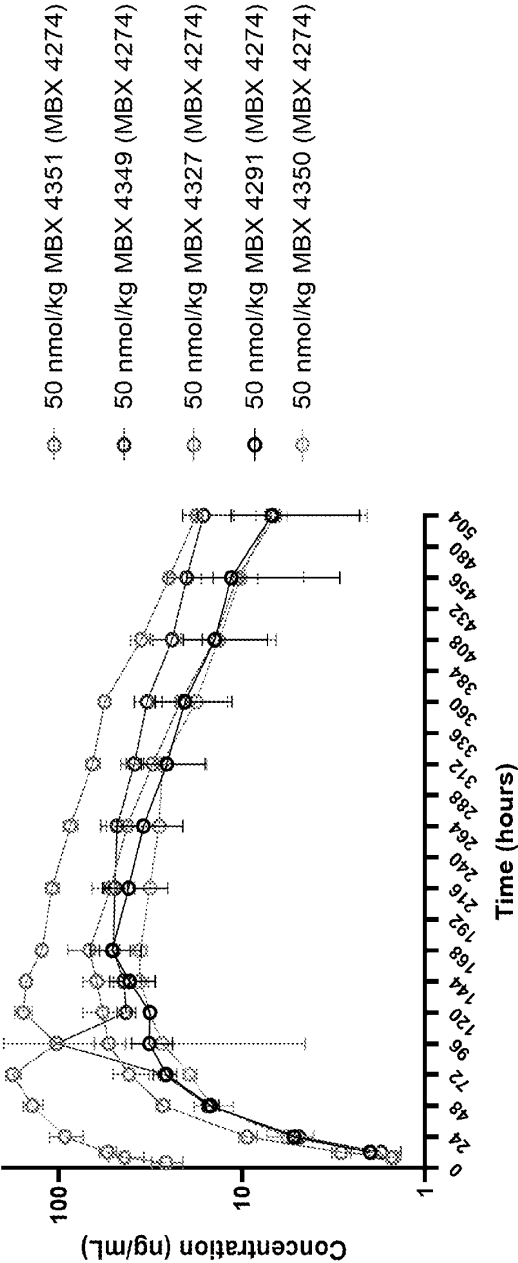


Fig. 34

A family of Sequential Dipeptide Macromolecular Prodrugs with Peg-Polymers

	Peptide	1 st dipeptide	2 nd dipeptide	Active drug
XC	MBX4306	absent	dK(OEG-OEG-A(triazole-PEG 40k)Sar-	4062
XXC	MBX4307	dK(OEG-OEG-A(triazole-PEG 20k)Sar	dK(OEG-OEG-A(triazole-PEG 20k)Sar-	4062
XXC	MBX4308	dK(OEG-OEG-A(triazole-PEG 40k)Sar	dK(OEG-OEG-A(triazole-PEG 40k)Sar-	4062
XC	MBX4308	absent	dK(OEG-OEG-A(triazole-PEG 20k)Sar-	4062
XC	MBX4329	absent	dK(OEG-OEG-A(triazole-PEG 40k)Sar-	4274
HXC	MBX4330	dKSar	dK(OEG-OEG-A(triazole-PEG 40k)Sar-	4274
XXC	MBX4331	dK(OEG-OEG-A(triazole-PEG 20k)Sar	dK(OEG-OEG-A(triazole-PEG 20k)Sar-	4274
HXC	MBX4338	dKSar	dK(OEG-OEG-A(triazole-PEG 20k)Sar-	4274
XC	MBX4348	absent	dK(OEG-OEG-A(triazole-PEG 20k)Sar-	4274
HXC	MBX4339	dKSar	dK(4x(OEG-OEG-A(triazole-PEG 3k))Sar	4274
HXC	MBX4340	dKSar	dK(4x(OEG-OEG-A(triazole-PEG 10k))Sar	4274
XC	MBX4353	absent	dK(4x(OEG-OEG-C(\$-PEG 10k)-Ac)Sar	4274
XC	MBX4354	absent	dK(4x(OEG-OEG-C(\$-PEG 3k)-Ac)Sar	4274
XC	MBX4356	absent	dK(4x(OEG-OEG-Pen(\$-PEG 10k)-Ac)Sar	4274
XP		absent	dK(OEG-OEG-A(triazole-PEG 40k)Sar	4347

Fig. 35

	MBX4329	MBX4274
0 d	100 %	-
1 d	95 %	5.0 %
3 d	84.2 %	15.8 %
5 d	74.9 %	25.1 %
7 d	67.0 %	33.0 %
10 d	56.2 %	43.8 %
14 d	45.5 %	54.5 %
21 d	31.6 %	68.4 %

Fig. 36

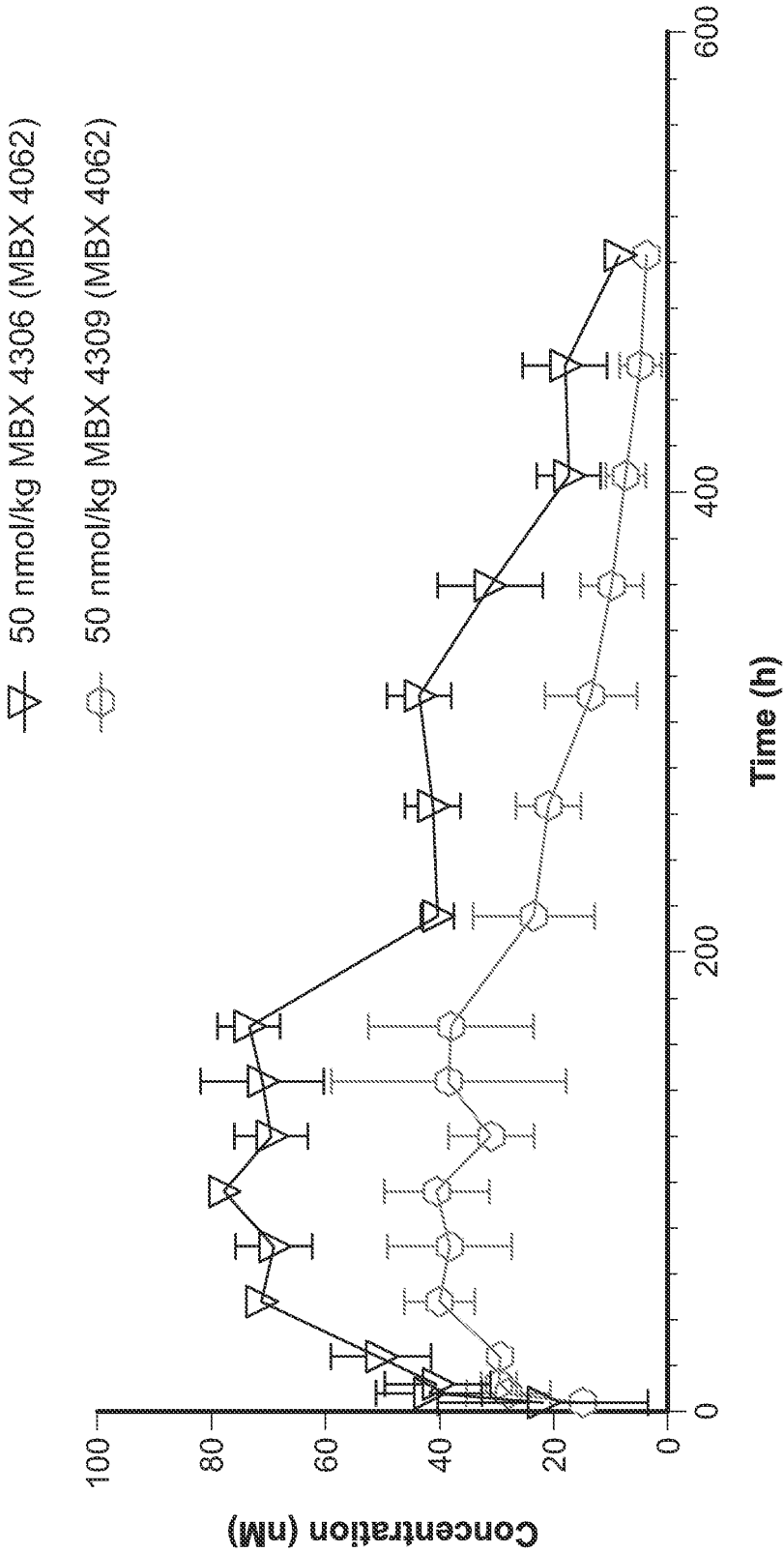


Fig. 37

Pharmacokinetics in Cynomolgus Monkeys of Prodrugs with Time Protractors

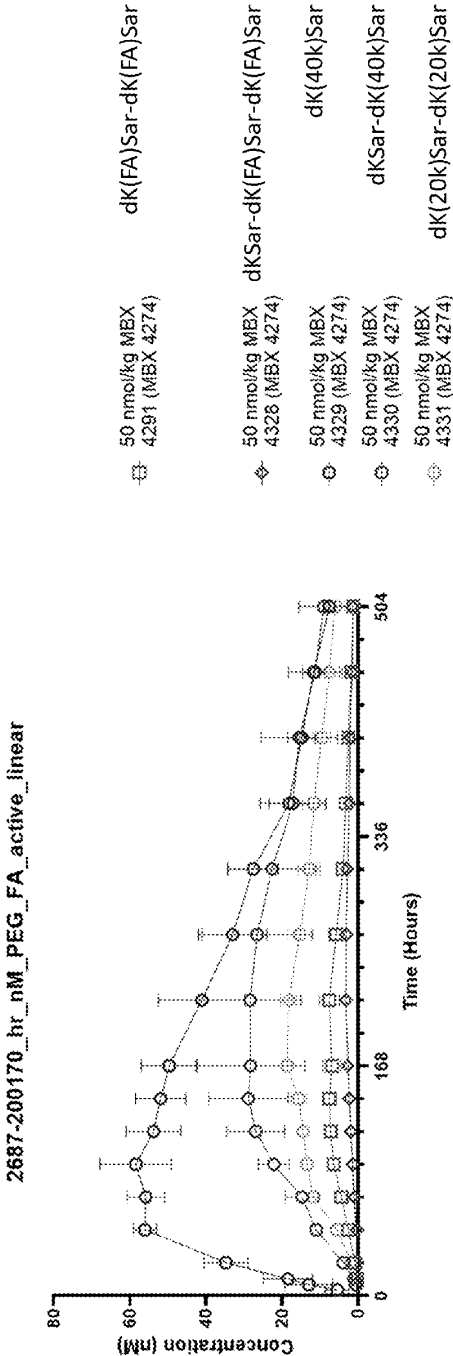


Fig. 38

Fig. 40

MBX		Sequence
1420	SEQ ID NO: 7	H-Aib-EGTFTSDVSSYLEGQAAK((miniPeg)2-γE-COC16H32CO2H)EFIAWLVRGRG-acid
2101	SEQ ID NO: 8	k(γE-(miniPEG)2-γE-COC16H32CO2H)GSVSEIQLMHNLGKHLNSMERVEWLRKKLQDVHK(γE-(miniPEG)2-γE-COC16H32CO2H)-acid
4051	SEQ ID NO: 9 SEQ ID NO: 10	T*(Y-Aib-EGTF)SDYSI-Aib-LDKIAQKAFVQWLIAGGPSSGAPPPS-amide
4062	SEQ ID NO: 11	Y-Aib-EGT-αMe,F-TSDYSI-Aib-LDKIAQK((miniPEG)2-γE-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4063	SEQ ID NO: 12	Y-Aib-EGTFTSDYSI-Aib-LD-Aib-TAQK((miniPEG)2-γE-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4071	SEQ ID NO: 13 SEQ ID NO: 14	T*[k((miniPEG)2-γE-COC18H36CO2H)-Sar-Y-Aib-EGT-αMe,F]SDYSI-Aib-LDKIAQK((miniPEG)2-γE-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4083	SEQ ID NO: 15	k((miniPEG)2-γE-COC18H36CO2H)-Sar-Y-Aib-EGT-αMe,F-TSDYSI-Aib-LDKIAQK((miniPEG)2-γE-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4108	SEQ ID NO: 16 SEQ ID NO: 17	T*[k((miniPEG)2-γE-COC16H32CO2H)-Sar-H-Aib-EGTFTSDVSSYLE-Aib]AAK((miniPEG)2-γE-COC16H32CO2H)EFIAWLVRGRGPPSSGAPPPS-amide
4116	SEQ ID NO: 18	Y-Aib-EGTFTSDLSI-Aib-LDKIAQKAFVQWLIAGGPSSGAPPPS-amide
4117	SEQ ID NO: 19	Y-Aib-EGTFTSDYSI-Aib-Nle-DKIAQKAFVQWLIAGGPSSGAPPPS-amide
4118	SEQ ID NO: 20	Y-Aib-EGTFTSDYSI-Aib-LEKIAQKAFVQWLIAGGPSSGAPPPS-amide
4119	SEQ ID NO: 21	Y-Aib-EGTFTSDYSI-Aib-LD-Orn-IAQKAFVQWLIAGGPSSGAPPPS-amide
4120	SEQ ID NO: 22	Y-Aib-EGTFTSDYSI-Aib-LDKVAQKAFVQWLIAGGPSSGAPPPS-amide
4121	SEQ ID NO: 23	Y-Aib-EGTFTSDYSI-Aib-LDKIAQKEFVQWLIAGGPSSGAPPPS-amide
4122	SEQ ID NO: 24	Y-Aib-EGTFTSDYSI-Aib-LDKIAQKAFIQWLIAGGPSSGAPPPS-amide
4123	SEQ ID NO: 25	Y-Aib-EGTFTSDYSI-Aib-LDKIAQKAFVAWLIAGGPSSGAPPPS-amide
4124	SEQ ID NO: 26	Y-Aib-EGTFTSDYSI-Aib-LDKIAQKAFVQWL VAGGPSSGAPPPS-amide
4125	SEQ ID NO: 27	Y-Aib-EGTFTSDYSI-Aib-LDKIAQKAFVQWLI EGGPSSGAPPPS-amide
4127	SEQ ID NO: 28 SEQ ID NO: 29	T*[k((miniPEG)2-γE-COC16H32CO2H)-Sar-H-Aib-EGTFTSD-Aib]SYLEGQAAK((miniPEG)2-γE-COC16H32CO2H)EFIAWLVRGRGPPSSGAPPPS-amide
4129	SEQ ID NO: 30 SEQ ID NO: 31	T*[k((miniPEG)2-γE-COC18H36CO2H)-Sar-Y-Aib-EGT-αMe,F-TSDYSI-Aib-LDKI-Aib]K((miniPEG)2-γE-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4178	SEQ ID NO: 32	Y-Aib-EGTFTSDYSI-Aib-LE-Aib-TAQK((miniPEG)2-γE-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4189	SEQ ID NO: 33	Y-Aib-EGT-αMe,F-TSDYSI-Aib-LE-Aib-TAAK((miniPEG)2-γE-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4190	SEQ ID NO: 34	Y-Aib-EGT-αMe,F-TSDYSI-Aib-LE-Aib-TAQK((miniPEG)2-γE-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4206	SEQ ID NO: 35	Y-Aib-EGT-αMe,F-TSDYSI-Aib-LDK(k((miniPEG)2-γE-COC18H36CO2H)-Sar)IAQK((miniPEG)2-γE-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide

Fig. 40 Continued

4209	SEQ ID NO: 36 SEQ ID NO: 37	T*[<i>k</i> ((miniPEG)2- γ E-COC18H36CO2H)-hPro-Y-Aib-EGT- α Me,F]SDYSI-Aib-LDKIAQK((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGG PSSGAPPPS-amide
4210	SEQ ID NO: 38 SEQ ID NO: 39	T*[<i>k</i> ((miniPEG)2- γ E-COC18H36CO2H)-NMe,nVal-Y-Aib-EGT- α Me,F]SDYSI-Aib-LDKIAQK((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGG PSSGAPPPS-amide
4211	SEQ ID NO: 40 SEQ ID NO: 41	T*[<i>k</i> ((miniPEG)2- γ E-COC18H36CO2H)-NMe,Phc-Y-Aib-EGT- α Me,F]SDYSI-Aib-LDKIAQK((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGG PSSGAPPPS-amide
4212	SEQ ID NO: 42	Y-Aib-EGT- α Me,F-TSDYSI-Aib-LDK(<i>k</i> ((miniPEG)2- γ E-COC18H36CO2H)P)IAQK((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4213	SEQ ID NO: 43	Y-Aib-EGT- α Me,F-TSDYSI-Aib-LDK(<i>k</i> ((miniPEG)2- γ E-COC18H36CO2H)P)IAQK((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4215	SEQ ID NO: 44	Y-Aib-EGT- α Me,F-TSDYSI-Aib-LDK(<i>k</i> ((miniPEG)2- γ E-COC18H36CO2H)G)IAQK((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4217	SEQ ID NO: 45	Y-Aib-EGT- α Me,F-TSDYSI-Aib-LDK(<i>k</i> ((miniPEG)2- γ E-COC18H36CO2H)-trans,3Hyp)IAQK((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGG PSSGAPPPS-amide
4218	SEQ ID NO: 46	Y-Aib-EGT- α Me,F-TSDYSILDK(<i>k</i> ((miniPEG)2- γ E-COC18H36CO2H)-trans,3Hyp)IAQK((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGG PSSGAPPPS-NH2
4220	SEQ ID NO: 47	Y-Aib-EGT- α Me,F-TSDYSI-Aib-LDK(<i>k</i> ((miniPEG)2- γ E-COC18H36CO2H)-p)IAQK((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4221	SEQ ID NO: 48	Y-Aib-EGT- α Me,F-TSDYSI-Aib-LDK(<i>k</i> ((miniPEG)2- γ E-COC16H32CO2H)-p)IAQK((miniPEG)2- γ E-COC16H32CO2H)AFVQWLIAGGPSSGAPPPS-amide
4223	SEQ ID NO: 49 SEQ ID NO: 50	T*[<i>k</i> ((miniPEG)2- γ E-COC18H36CO2H)-Sar-Y-Aib-EGT- α Me,F]SDYSI-Aib-LDK(<i>k</i> ((miniPEG)2- γ E-COC18H36CO2H)-Sar)IAQK((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4224	SEQ ID NO: 51 SEQ ID NO: 52	<i>k</i> ((miniPEG)2- γ E-COC18H36CO2H)-Sar-T*[<i>k</i> ((miniPEG)2- γ E-COC18H36CO2H)-Sar-Y-Aib-EGT- α Me,F]SDYSI-Aib-LDKIAQK((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-NH2
4225	SEQ ID NO: 53	<i>k</i> ((miniPEG)2- γ E-COC18H36CO2H)-Sar—Y-Aib-EGT- α Me,F-TSDYSI-Aib-LDK(<i>k</i> ((miniPEG)2- γ E-COC18H36CO2H)-Sar)IAQK((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4232	SEQ ID NO: 54	<i>k</i> ((miniPEG)2- γ E-COC18H36CO2H)-N-CD3,Gly(D2)-Y-Aib-EGT- α Me,F-TSDYSI-Aib-LDKIAQK((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGG PSSGAPPPS-amide

Fig. 40 Continued

4234	SEQ ID NO: 55	<i>k</i> ((miniPEG)2- γ E-COC18H36CO2H)-Sar- <i>k</i> ((miniPEG)2- γ E-COC18H36CO2H)-Sar-GY-Aib-EGT- α Me,F-TSDYSI-Aib-LDKIAQK((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4239	SEQ ID NO: 56	<i>k</i> ((miniPEG)2- γ E-COC18H36CO2H)-3,4dehydro-P)Y-Aib-EGT- α Me,F-TSDYSI-Aib-LDKIAQK((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGG-amide
4240	SEQ ID NO: 57	K((miniPEG)2- γ E-COC18H36CO2H)-3,4dehydro-P)Y-Aib-EGT- α Me,F-TSDYSI-Aib-LDKIAQK((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4241	SEQ ID NO: 58	Y-Aib-EGT- α Me,F-TSDYSI-Aib-LDK(<i>k</i> ((miniPEG)2- γ E-COC18H36CO2H)-3,4dehydro-P))IAQK((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4242	SEQ ID NO: 59	Y-Aib-EGT- α Me,F-TSDYSI-Aib-LDK(K((miniPEG)2- γ E-COC18H36CO2H)-3,4dehydro-P))IAQK((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4265	SEQ ID NO: 60	<i>k</i> ((miniPEG)2- γ E-COC18H36CO2H)-N-Me,Gly(D2)-Y-Aib-EGT- α Me,F-TSDYSI-Aib-LDKIAQK((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4266	SEQ ID NO: 61	<i>k</i> ((miniPEG)2- γ E-COC18H36CO2H)-N-CD3,Gly-Y-Aib-EGT- α Me,F-TSDYSI-Aib-LDKIAQK((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4268	SEQ ID NO: 62	K((miniPEG)2- γ E-COC18H36CO2H)-Y-Aib-EGTFTSDYSI-Aib-LDKIAQK((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4269	SEQ ID NO: 63	<i>k</i> ((miniPEG)2- γ E-COC18H36CO2H)-Sar-K((miniPEG)2- γ E-COC18H36CO2H)Y-Aib-EGTFTSDYSI-Aib-LDKIAQK((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4271	SEQ ID NO: 64	<i>k</i> ((miniPEG)2-Ala(triazole-PEG8))-Sar-K((miniPEG)2- γ E-COC18H36CO2H)Y-Aib-EGTFTSDYSI-Aib-LDKIAQK((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4272	SEQ ID NO: 65	<i>k</i> ((miniPEG)2-Ala(triazole-PEG20k))-Sar-K((miniPEG)2- γ E-COC18H36CO2H)Y-Aib-EGTFTSDYSI-Aib-LDKIAQK((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4274	SEQ ID NO: 66	Y-Aib-EGT- α Me,F-TSDYSI-Aib-LEKTAAK((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4275	SEQ ID NO: 67	Y-Aib-EGT- α Me,F-TSDYSI-Aib-LEKTAAK((miniPEG)2- γ E-COC18H36CO2H)AFIEWLLEGGPSSGAPPPS-amide
4280	SEQ ID NO: 68	Y-Aib-EGT- α Me,F-TSDYSI-Aib-LEKTAAK((miniPEG)2- γ E-COC18H36CO2H)AFINWLVEGGPSSGAPPPS-amide
4291	SEQ ID NO: 69	<i>k</i> ((miniPEG)2- γ E-COC18H36CO2H)-Sar- <i>k</i> ((miniPEG)2- γ E-COC18H36CO2H)-Sar-Y-Aib-EGT- α Me,F-TSDYSI-Aib-LEKTAAK((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4306	SEQ ID NO: 70	<i>k</i> ((miniPEG)2-Ala(triazole-PEG40k)-Sar-Y-Aib-EGT- α Me,F-TSDYSI-Aib-LDKIAQK((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide

Fig. 40 Continued

4307	SEQ ID NO: 71	<i>k</i> ((miniPEG)2-Ala(triazole-PEG20k))-Sar- <i>k</i> ((miniPEG)2-Ala(triazole-PEG20k))-Sar-Y-Aib-EGT- α Me,F-TSDYSI-Aib-LDKIAQ K((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4308	SEQ ID NO: 72	<i>k</i> ((miniPEG)2-Ala(triazole-PEG40k))-Sar- <i>k</i> ((miniPEG)2-Ala(triazole-PEG40k))-Sar-Y-Aib-EGT- α Me,F-TSDYSI-Aib-LDKIAQ K((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4309	SEQ ID NO: 73	<i>k</i> ((miniPEG)2-Ala(triazole-PEG20k))-Sar-Y-Aib-EGT- α Me,F-TSDYSI-Aib-LDKIAQK((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4310	SEQ ID NO: 74	<i>k</i> ((miniPEG)2- γ E-COC18H36CO2H)-Sar-Y-Aib-EGT- α Me,F-TSDYSI-Aib-LEKTAAK((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4327	SEQ ID NO: 75	<i>k</i> -Sar- <i>k</i> ((miniPEG)2- γ E-COC18H36CO2H)-Sar-Y-Aib-EGT- α Me,F-TSDYSI-Aib-LEKTAAK((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4328	SEQ ID NO: 76	<i>k</i> -Sar- <i>k</i> ((miniPEG)2- γ E-COC18H36CO2H)-Sar- <i>k</i> ((miniPEG)2- γ E-COC18H36CO2H)-Sar-Y-Aib-EGT- α Me,F-TSDYSI-Aib-LEKTAAK((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4329	SEQ ID NO: 77	<i>k</i> ((miniPEG)2-Ala(triazole-PEG40k))-Sar-Y-Aib-EGT- α Me,F-TSDYSI-Aib-LEKTAAK((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4330	SEQ ID NO: 78	<i>k</i> -Sar- <i>k</i> ((miniPEG)2-Ala(triazole-PEG40k))-Sar-Y-Aib-EGT- α Me,F-TSDYSI-Aib-LEKTAAK((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4331	SEQ ID NO: 79	<i>k</i> ((miniPEG)2-Ala(triazole-PEG20k))-Sar- <i>k</i> ((miniPEG)2-Ala(triazole-PEG20k))-Sar-Y-Aib-EGT- α Me,F-TSDYSI-Aib-LEKTAAK((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4338	SEQ ID NO: 80	<i>k</i> -Sar- <i>k</i> ((miniPEG)2-Ala(triazole-PEG20k))-Sar-Y-Aib-EGT- α Me,F-TSDYSI-Aib-LEKTAAK((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4339	SEQ ID NO: 81	<i>k</i> -Sar- <i>k</i> ((K(K(miniPEG)2-Ala(triazole-PEG5k)2)2)-Sar-Y-Aib-EGT- α Me,F-TSDYSI-Aib-LEKTAAK((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4340	SEQ ID NO: 82	<i>k</i> -Sar- <i>k</i> ((K(K(miniPEG)2-Ala(triazole-PEG10k)2)2)-Sar-Y-Aib-EGT- α Me,F-TSDYSI-Aib-LEKTAAK((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4347	SEQ ID NO: 83	Y-Aib-EGT- α Me,F-TSDYSI-Aib-LEKTAAK((miniPEG)2- γ E-COC18H36PO3H2)AFVQWLIAGGPSSGAPPPS-amide
4348	SEQ ID NO: 84	<i>k</i> ((miniPEG)2-Ala(triazole-PEG20k))-Sar-Y-Aib-EGT- α Me,F-TSDYSI-Aib-LEKTAAK((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4349	SEQ ID NO: 85	<i>k</i> ((miniPEG)2- γ E-COC18H36CO2H)-Sar- <i>k</i> ((miniPEG)2- γ E-COC18H36-PO3H2)-Sar-Y-Aib-EGT- α Me,F-TSDYSI-Aib-LEKTAAK((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4350	SEQ ID NO: 86	<i>k</i> -Sar- <i>k</i> ((miniPEG)2- γ E-COC18H36-PO3H)-Sar-Y-Aib-EGT- α Me,F-TSDYSI-Aib-LEKTAAK((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide

4351	SEQ ID NO: 87	<i>k</i> ((miniPEG)2- γ E-COC18H36-PO3H)-Sar-Y-Aib-EGT- α Me,F-TSDYSI-Aib-LEKTAAG((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGG PSSGAPPPS-amide
4353	SEQ ID NO: 88	<i>k</i> -Sar- <i>k</i> ((K(K((miniPEG)2-Cys-SS-PEG10k)2)2)-Sar-Y-Aib-EGT- α Me,F-TSDYSI-Aib-LEKTAAG((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-NH2
4354	SEQ ID NO: 89	<i>k</i> -Sar- <i>k</i> ((K(K((miniPEG)2-Cys-SS-PEG5k)2)2)-Sar-Y-Aib-EGT- α Me,F-TSDYSI-Aib-LEKTAAG((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4356	SEQ ID NO: 90	<i>k</i> -Sar- <i>k</i> ((K(K((miniPEG)2-Pen-SS-PEG10k)2)2)-Sar-Y-Aib-EGT- α Me,F-TSDYSI-Aib-LEKTAAG((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4357	SEQ ID NO: 91	<i>k</i> ((miniPEG)2- γ E-COC18H36-PO3H)-Sar- <i>k</i> ((miniPEG)2- γ E-COC18H36-PO3H)-Sar-Y-Aib-EGT- α Me,F-TSDYSI-Aib-LEKTAAG((miniPEG)2- γ E-COC18H36CO2H)AFVQWLIAGGPSSGAPPPS-amide
4360	SEQ ID NO: 92	<i>k</i> ((miniPEG)2-Ala(triazole-PEG40k))-Sar-Y-Aib-EGT- α Me,F-TSDYSI-Aib-LEKTAAG((miniPEG)2- γ E-COC18H36-PO3H)AFVQWLIAGG PSSGAPPPS-amide
4361	SEQ ID NO: 93	<i>k</i> ((miniPEG)2- γ E-COC18H36-PO3H)-Sar-Y-Aib-EGT- α Me,F-TSDYSI-Aib-LEKTAAG((miniPEG)2- γ E-COC18H36-PO3H)AFVQWLIAGG PSSGAPPPS-amide
4362	SEQ ID NO: 94	<i>k</i> -Sar- <i>k</i> ((miniPEG)2- γ E-COC18H36-PO3H)-Sar-Y-Aib-EGT- α Me,F-TSDYSI-Aib-LEKTAAG((miniPEG)2- γ E-COC18H36-PO3H)AFVQWLIAGG PSSGAPPPS-amide
4363	SEQ ID NO: 95	<i>k</i> ((miniPEG)2- γ E-COC18H36-PO3H)-Sar- <i>k</i> ((miniPEG)2- γ E-COC18H36-PO3H)-Sar-Y-EGT- α Me,F-TSDYSI-Aib-LEKTAAG((miniPEG)2- γ E-COC18H36-PO3H)AFVQWLIAGGPSSGAPPPS-amide
4364	SEQ ID NO: 96	<i>k</i> -Sar- <i>k</i> ((miniPEG)2- γ E-COC18H36-PO3H)-Sar-Y-Aib-EGT- α Me,F-TSDYSI-Aib-LEKTAAG((miniPEG)2- γ E-COC18H36-PO3H)AFVQWLIAGG PSSGAPPPS-amide
4365	SEQ ID NO: 97	<i>k</i> ((miniPEG)2- γ E-COC18H36CO2H)-Sar- <i>k</i> ((miniPEG)2- γ E-COC18H36-PO3H)-Sar-Y-Aib-EGT- α Me,F-TSDYSI-Aib-LEKTAAG((miniPEG)2- γ E-COC18H36-PO3H)AFVQWLIAGGPSSGAPPPS-amide
4368	SEQ ID NO: 98	<i>k</i> ((miniPEG)2- γ E-COC18H36-PO3H)-Sar-Y-Aib-EGT- α Me,F-TSDYSI-Aib-LEKTAAG((miniPEG)2- γ E-COC18H36-PO3H)AFVQWLIAGG PSSGAPPPS-amide
TZP	SEQ ID NO: 99	Tyr-Aib-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Tyr-Ser-Ile-Aib-Leu-Asp-Lys-Ile-Ala-Gln-Lys(Eicosanedioyl-isoGlu-PEG-PEG)-Ala-Phe-Val-Gln-Trp-Leu-Ile-Ala-Gly-Gly-Pro-Ser-Ser-Gly-Ala-Pro-Pro-Ser

Where T* = isoacyl threonine

Fig. 40 Continued