

SEQUENCE LISTING

<110> Revolution Medicines, Inc.
 <120> C26-Linked Rapamycin Analogs as mTOR Inhibitors
 <130> REME-009/01WO 323913-2133
 <150> US 62/836,040
 <151> 2019-04-18
 <150> US 62/752,881
 <151> 2018-10-30
 <150> US 62/665,426
 <151> 2018-05-01
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 <170> PatentIn version 3.5
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 <212> PRT
 <213> Homo sapiens
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Thr Met Glu Leu Arg Glu Met Ser Gln Glu Glu Ser Thr Arg Phe Tyr
 50 55 60

Asp Gln Leu Asn His His Ile Phe Glu Leu Val Ser Ser Ser Asp Ala
 65 70 75 80

Asn Glu Arg Lys Gly Gly Ile Leu Ala Ile Ala Ser Leu Ile Gly Val
 85 90 95

Glu Gly Gly Asn Ala Thr Arg Ile Gly Arg Phe Ala Asn Tyr Leu Arg
 100 105 110

Asn Leu Leu Pro Ser Asn Asp Pro Val Val Met Glu Met Ala Ser Lys
 115 120 125

Ala Ile Gly Arg Leu Ala Met Ala Gly Asp Thr Phe Thr Ala Glu Tyr
 130 135 140

Val	Glu	Phe	Glu	Val	Lys	Arg	Ala	Leu	Glu	Trp	Leu	Gly	Ala	Asp	Arg	145	150	155	160
Asn	Glu	Gly	Arg	Arg	His	Ala	Ala	Val	Leu	Val	Leu	Arg	Glu	Leu	Ala	165	170	175	
Ile	Ser	Val	Pro	Thr	Phe	Phe	Phe	Gln	Gln	Val	Gln	Pro	Phe	Phe	Asp	180	185	190	
Asn	Ile	Phe	Val	Ala	Val	Trp	Asp	Pro	Lys	Gln	Ala	Ile	Arg	Glu	Gly	195	200	205	
Ala	Val	Ala	Ala	Leu	Arg	Ala	Cys	Leu	Ile	Leu	Thr	Thr	Gln	Arg	Glu	210	215	220	
Pro	Lys	Glu	Met	Gln	Lys	Pro	Gln	Trp	Tyr	Arg	His	Thr	Phe	Glu	Glu	225	230	235	240
Ala	Glu	Lys	Gly	Phe	Asp	Glu	Thr	Leu	Ala	Lys	Glu	Lys	Gly	Met	Asn	245	250	255	
Arg	Asp	Asp	Arg	Ile	His	Gly	Ala	Leu	Leu	Ile	Leu	Asn	Glu	Leu	Val	260	265	270	
Arg	Ile	Ser	Ser	Met	Glu	Gly	Glu	Arg	Leu	Arg	Glu	Glu	Met	Glu	Glu	275	280	285	
Ile	Thr	Gln	Gln	Gln	Leu	Val	His	Asp	Lys	Tyr	Cys	Lys	Asp	Leu	Met	290	295	300	
Gly	Phe	Gly	Thr	Lys	Pro	Arg	His	Ile	Thr	Pro	Phe	Thr	Ser	Phe	Gln	305	310	315	320
Ala	Val	Gln	Pro	Gln	Gln	Ser	Asn	Ala	Leu	Val	Gly	Leu	Leu	Gly	Tyr	325	330	335	
Ser	Ser	His	Gln	Gly	Leu	Met	Gly	Phe	Gly	Thr	Ser	Pro	Ser	Pro	Ala	340	345	350	
Lys	Ser	Thr	Leu	Val	Glu	Ser	Arg	Cys	Cys	Arg	Asp	Leu	Met	Glu	Glu	355	360	365	
Lys	Phe	Asp	Gln	Val	Cys	Gln	Trp	Val	Leu	Lys	Cys	Arg	Asn	Ser	Lys	370	375	380	
Asn	Ser	Leu	Ile	Gln	Met	Thr	Ile	Leu	Asn	Leu	Leu	Pro	Arg	Leu	Ala	385	390	395	400

Ala	Phe	Arg	Pro	Ser	Ala	Phe	Thr	Asp	Thr	Gln	Tyr	Leu	Gln	Asp	Thr	405	410	415	
Met	Asn	His	Val	Leu	Ser	Cys	Val	Lys	Lys	Glu	Lys	Glu	Arg	Thr	Ala	420	425	430	
Ala	Phe	Gln	Ala	Leu	Gly	Leu	Leu	Ser	Val	Ala	Val	Arg	Ser	Glu	Phe	435	440	445	
Lys	Val	Tyr	Leu	Pro	Arg	Val	Leu	Asp	Ile	Ile	Arg	Ala	Ala	Leu	Pro	450	455	460	
Pro	Lys	Asp	Phe	Ala	His	Lys	Arg	Gln	Lys	Ala	Met	Gln	Val	Asp	Ala	465	470	475	480
Thr	Val	Phe	Thr	Cys	Ile	Ser	Met	Leu	Ala	Arg	Ala	Met	Gly	Pro	Gly	485	490	495	
Ile	Gln	Gln	Asp	Ile	Lys	Glu	Leu	Leu	Glu	Pro	Met	Leu	Ala	Val	Gly	500	505	510	
Leu	Ser	Pro	Ala	Leu	Thr	Ala	Val	Leu	Tyr	Asp	Leu	Ser	Arg	Gln	Ile	515	520	525	
Pro	Gln	Leu	Lys	Lys	Asp	Ile	Gln	Asp	Gly	Leu	Leu	Lys	Met	Leu	Ser	530	535	540	
Leu	Val	Leu	Met	His	Lys	Pro	Leu	Arg	His	Pro	Gly	Met	Pro	Lys	Gly	545	550	555	560
Leu	Ala	His	Gln	Leu	Ala	Ser	Pro	Gly	Leu	Thr	Thr	Leu	Pro	Glu	Ala	565	570	575	
Ser	Asp	Val	Gly	Ser	Ile	Thr	Leu	Ala	Leu	Arg	Thr	Leu	Gly	Ser	Phe	580	585	590	
Glu	Phe	Glu	Gly	His	Ser	Leu	Thr	Gln	Phe	Val	Arg	His	Cys	Ala	Asp	595	600	605	
His	Phe	Leu	Asn	Ser	Glu	His	Lys	Glu	Ile	Arg	Met	Glu	Ala	Ala	Arg	610	615	620	
Thr	Cys	Ser	Arg	Leu	Leu	Thr	Pro	Ser	Ile	His	Leu	Ile	Ser	Gly	His	625	630	635	640
Ala	His	Val	Val	Ser	Gln	Thr	Ala	Val	Gln	Val	Val	Ala	Asp	Val	Leu	645	650	655	

Ser Lys Leu Leu Val Val Gly Ile Thr Asp Pro Asp Pro Asp Ile Arg
 660 665 670

Tyr Cys Val Leu Ala Ser Leu Asp Glu Arg Phe Asp Ala His Leu Ala
 675 680 685

Gln Ala Glu Asn Leu Gln Ala Leu Phe Val Ala Leu Asn Asp Gln Val
 690 695 700

Phe Glu Ile Arg Glu Leu Ala Ile Cys Thr Val Gly Arg Leu Ser Ser
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Met Asn Pro Ala Phe Val Met Pro Phe Leu Arg Lys Met Leu Ile Gln
 725 730 735

Ile Leu Thr Glu Leu Glu His Ser Gly Ile Gly Arg Ile Lys Glu Gln
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Ser Ala Arg Met Leu Gly His Leu Val Ser Asn Ala Pro Arg Leu Ile
 755 760 765

Arg Pro Tyr Met Glu Pro Ile Leu Lys Ala Leu Ile Leu Lys Leu Lys
 770 775 780

Asp Pro Asp Pro Asp Pro Asn Pro Gly Val Ile Asn Asn Val Leu Ala
 785 790 795 800

Thr Ile Gly Glu Leu Ala Gln Val Ser Gly Leu Glu Met Arg Lys Trp
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Val Asp Glu Leu Phe Ile Ile Ile Met Asp Met Leu Gln Asp Ser Ser
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Leu Leu Ala Lys Arg Gln Val Ala Leu Trp Thr Leu Gly Gln Leu Val
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Ala Ser Thr Gly Tyr Val Val Glu Pro Tyr Arg Lys Tyr Pro Thr Leu
 850 855 860

Leu Glu Val Leu Leu Asn Phe Leu Lys Thr Glu Gln Asn Gln Gly Thr
 865 870 875 880

Arg Arg Glu Ala Ile Arg Val Leu Gly Leu Leu Gly Ala Leu Asp Pro
 885 890 895

Tyr Lys His Lys Val Asn Ile Gly Met Ile Asp Gln Ser Arg Asp Ala
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Ser Ala Val Ser Leu Ser Glu Ser Lys Ser Ser Gln Asp Ser Ser Asp
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Tyr Ser Thr Ser Glu Met Leu Val Asn Met Gly Asn Leu Pro Leu Asp
 930 935 940

Glu Phe Tyr Pro Ala Val Ser Met Val Ala Leu Met Arg Ile Phe Arg
 945 950 955 960

Asp Gln Ser Leu Ser His His His Thr Met Val Val Gln Ala Ile Thr
 965 970 975

Phe Ile Phe Lys Ser Leu Gly Leu Lys Cys Val Gln Phe Leu Pro Gln
 980 985 990

Val Met Pro Thr Phe Leu Asn Val Ile Arg Val Cys Asp Gly Ala Ile
 995 1000 1005

Arg Glu Phe Leu Phe Gln Gln Leu Gly Met Leu Val Ser Phe Val
 1010 1015 1020

Lys Ser His Ile Arg Pro Tyr Met Asp Glu Ile Val Thr Leu Met
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Arg Glu Phe Trp Val Met Asn Thr Ser Ile Gln Ser Thr Ile Ile
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Leu Leu Ile Glu Gln Ile Val Val Ala Leu Gly Gly Glu Phe Lys
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Leu Tyr Leu Pro Gln Leu Ile Pro His Met Leu Arg Val Phe Met
 1070 1075 1080

His Asp Asn Ser Pro Gly Arg Ile Val Ser Ile Lys Leu Leu Ala
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Ala Ile Gln Leu Phe Gly Ala Asn Leu Asp Asp Tyr Leu His Leu
 1100 1105 1110

Leu Leu Pro Pro Ile Val Lys Leu Phe Asp Ala Pro Glu Ala Pro
 1115 1120 1125

Leu Pro Ser Arg Lys Ala Ala Leu Glu Thr Val Asp Arg Leu Thr
 1130 1135 1140

Glu Ser Leu Asp Phe Thr Asp Tyr Ala Ser Arg Ile Ile His Pro
 1145 1150 1155

Ile Val	Arg Thr	Leu Asp	Gln Ser	Pro Glu	Leu Arg	Ser Thr	Ala
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Gln Ile	Phe Ile	Pro Met	Val Asn	Lys Val	Leu Val	Arg His	Arg
1190			1195		1200		
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Gly Tyr	Thr Leu	Ala Asp	Glu Glu	Glu Asp	Pro Leu	Ile Tyr	Gln
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His Arg	Met Leu	Arg Ser	Gly Gln	Gly Asp	Ala Leu	Ala Ser	Gly
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Pro Val	Glu Thr	Gly Pro	Met Lys	Lys Leu	His Val	Ser Thr	Ile
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1280			1285		1290		
Asp Ser	Ser Ser	Pro Ser	Leu Arg	Ser Cys	Trp Ala	Leu Ala	Gln
1295			1300		1305		
Ala Tyr	Asn Pro	Met Ala	Arg Asp	Leu Phe	Asn Ala	Ala Phe	Val
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Ser Cys	Trp Ser	Glu Leu	Asn Glu	Asp Gln	Gln Asp	Glu Leu	Ile
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Arg Ser	Ile Glu	Leu Ala	Leu Thr	Ser Gln	Asp Ile	Ala Glu	Val
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Thr Gln	Thr Leu	Leu Asn	Leu Ala	Glu Phe	Met Glu	His Ser	Asp
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Lys Gly	Pro Leu	Pro Leu	Arg Asp	Asp Asn	Gly Ile	Val Leu	Leu
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Gly Glu	Arg Ala	Ala Lys	Cys Arg	Ala Tyr	Ala Lys	Ala Leu	His
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Ala	Leu	Val	Ala	Tyr	Asp	Lys	Lys	Met	Asp	Thr	Asn	Lys	Asp	Asp
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Pro	Glu	Leu	Met	Leu	Gly	Arg	Met	Arg	Cys	Leu	Glu	Ala	Leu	Gly
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Ala	Ala	Trp	Gly	Leu	Gly	Gln	Trp	Asp	Ser	Met	Glu	Glu	Tyr	Thr
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Cys	Met	Ile	Pro	Arg	Asp	Thr	His	Asp	Gly	Ala	Phe	Tyr	Arg	Ala
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Val	Leu	Ala	Leu	His	Gln	Asp	Leu	Phe	Ser	Leu	Ala	Gln	Gln	Cys
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Ile	Asp	Lys	Ala	Arg	Asp	Leu	Leu	Asp	Ala	Glu	Leu	Thr	Ala	Met
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Ala	Gly	Glu	Ser	Tyr	Ser	Arg	Ala	Tyr	Gly	Ala	Met	Val	Ser	Cys
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His	Met	Leu	Ser	Glu	Leu	Glu	Glu	Val	Ile	Gln	Tyr	Lys	Leu	Val
1595						1600					1605			
Pro	Glu	Arg	Arg	Glu	Ile	Ile	Arg	Gln	Ile	Trp	Trp	Glu	Arg	Leu
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Gln	Gly	Cys	Gln	Arg	Ile	Val	Glu	Asp	Trp	Gln	Lys	Ile	Leu	Met
1625						1630					1635			

Val	Arg	Ser	Leu	Val	Val	Ser	Pro	His	Glu	Asp	Met	Arg	Thr	Trp
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Leu	Lys	Tyr	Ala	Ser	Leu	Cys	Gly	Lys	Ser	Gly	Arg	Leu	Ala	Leu
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Ala	His	Lys	Thr	Leu	Val	Leu	Leu	Leu	Gly	Val	Asp	Pro	Ser	Arg
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Gln	Leu	Asp	His	Pro	Leu	Pro	Thr	Val	His	Pro	Gln	Val	Thr	Tyr
1685						1690					1695			
Ala	Tyr	Met	Lys	Asn	Met	Trp	Lys	Ser	Ala	Arg	Lys	Ile	Asp	Ala
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Phe	Gln	His	Met	Gln	His	Phe	Val	Gln	Thr	Met	Gln	Gln	Gln	Ala
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1790						1795					1800			
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Leu	Trp	Phe	Asp	Tyr	Gly	His	Trp	Pro	Asp	Val	Asn	Glu	Ala	Leu
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Val	Glu	Gly	Val	Lys	Ala	Ile	Gln	Ile	Asp	Thr	Trp	Leu	Gln	Val
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Thr	Thr	Ala	Arg	His	Asn	Ala	Ala	Asn	Lys	Ile	Leu	Lys	Asn	Met
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Cys	Glu	His	Ser	Asn	Thr	Leu	Val	Gln	Gln	Ala	Met	Met	Val	Ser
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Glu	Glu	Leu	Ile	Arg	Val	Ala	Ile	Leu	Trp	His	Glu	Met	Trp	His
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Tyr	Tyr	His	Val	Phe	Arg	Arg	Ile	Ser	Lys	Gln	Leu	Pro	Gln	Leu
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Pro	Ile	Ile	Arg	Ile	Gln	Ser	Ile	Ala	Pro	Ser	Leu	Gln	Val	Ile
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Trp	Val	Pro	His	Cys	Asp	Thr	Leu	His	Ala	Leu	Ile	Arg	Asp	Tyr
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Met	Val	Gly	Tyr	Ile	Leu	Gly	Leu	Gly	Asp	Arg	His	Pro	Ser	Asn
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Leu	Met	Leu	Asp	Arg	Leu	Ser	Gly	Lys	Ile	Leu	His	Ile	Asp	Phe
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Gly	Asp	Cys	Phe	Glu	Val	Ala	Met	Thr	Arg	Glu	Lys	Phe	Pro	Glu
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Lys	Ile	Pro	Phe	Arg	Leu	Thr	Arg	Met	Leu	Thr	Asn	Ala	Met	Glu
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Val	Thr	Gly	Leu	Asp	Gly	Asn	Tyr	Arg	Ile	Thr	Cys	His	Thr	Val
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Glu	Ala	Phe	Val	Tyr	Asp	Pro	Leu	Leu	Asn	Trp	Arg	Leu	Met	Asp
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Tyr	Ser	Ala	Gly	Gln	Ser	Val	Glu	Ile	Leu	Asp	Gly	Val	Glu	Leu
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Gly	Glu	Pro	Ala	His	Lys	Lys	Thr	Gly	Thr	Thr	Val	Pro	Glu	Ser
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Ile	His	Ser	Phe	Ile	Gly	Asp	Gly	Leu	Val	Lys	Pro	Glu	Ala	Leu
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Gln	Val	Glu	Leu	Leu	Ile	Lys	Gln	Ala	Thr	Ser	His	Glu	Asn	Leu
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gatgcttgga accggacctg ccgccgccac caccgctgcc accacatcta gcaatgtgag	180

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cgccaaggag	ctccagcact	atgtcaccat	ggaactccga	gagatgagtc	aagaggagtc	300
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Asp Gly Lys Lys Phe Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
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Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
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Gly Thr Arg Ile Ile Tyr Asp Arg Lys Phe Leu Met Glu Cys Arg Asn
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Ser Pro Val Thr Lys Thr Pro Pro Arg Asp Leu Pro Thr Ile Pro Gly
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Gln Phe Glu Met Asp Ile
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Glu Ala Pro Leu Asn Asn Phe Ser Val Ala Gln Cys Gln Leu Met Lys
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Gln	Glu	Glu	Glu	Glu	Met	Asp	Phe	Arg	Ser	Gly	Ser	Pro	Ser	Asp	Asn	115	120	125	
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