FIG. 1

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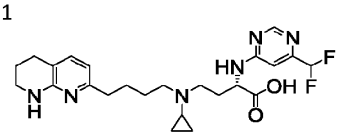
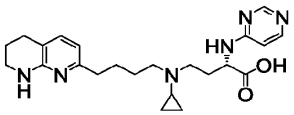
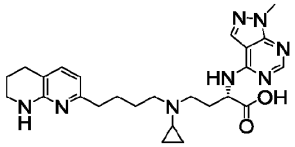
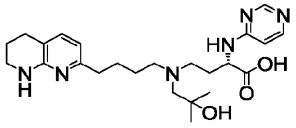
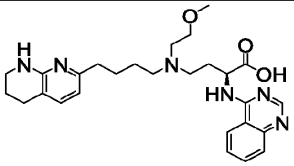
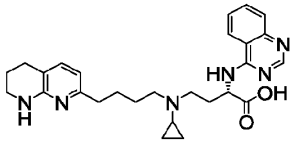
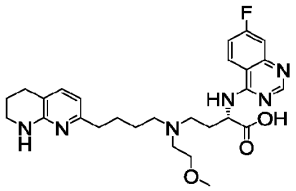
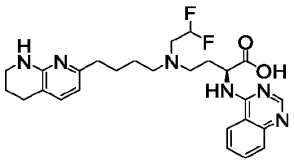
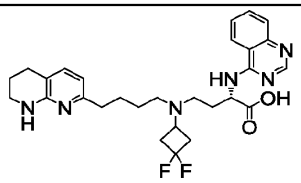
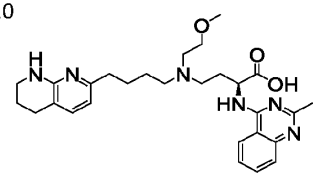
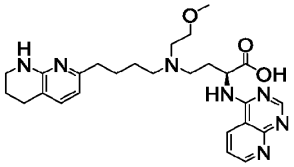
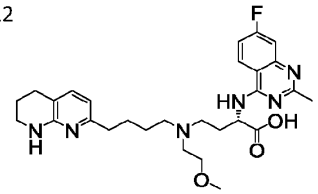
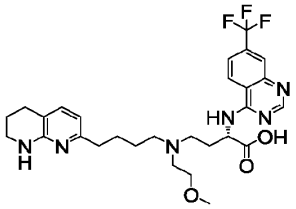
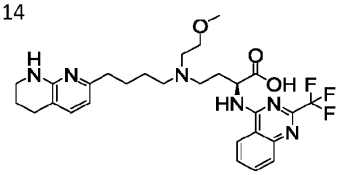
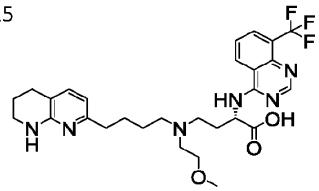
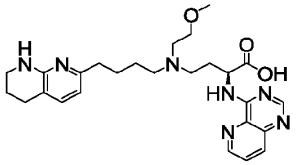
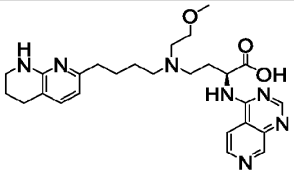
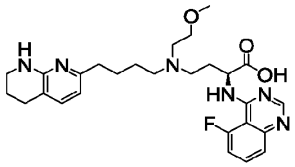
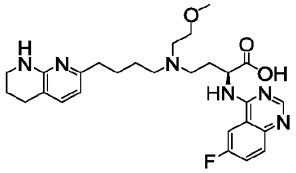
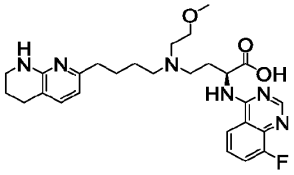
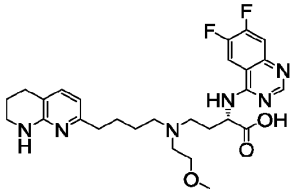
1 	2 	3 
4 	5 	6 
7 	8 	9 
10 	11 	12 
13 	14 	15 
16 	17 	18 
19 	20 	21 

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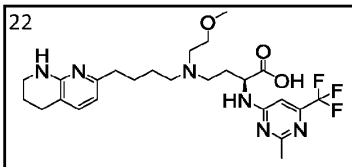
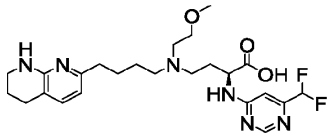
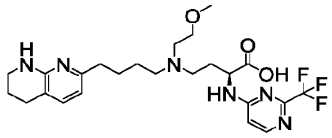
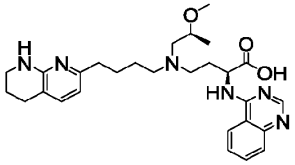
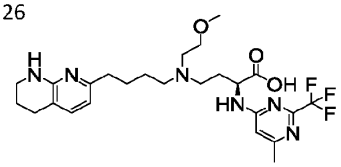
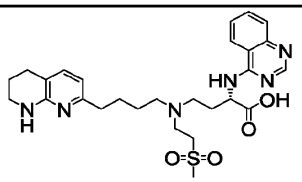
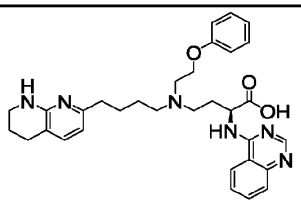
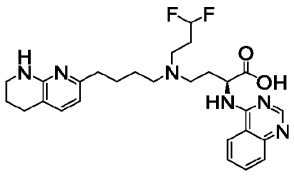
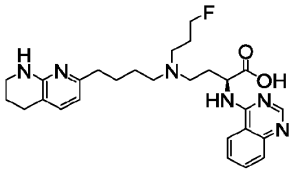
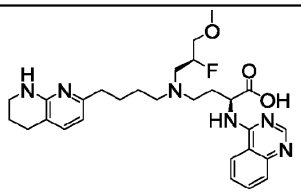
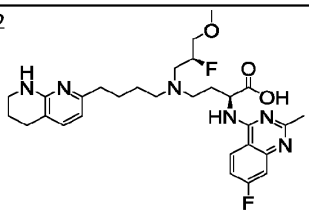
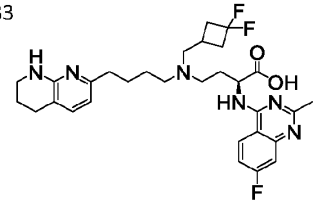
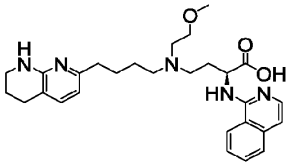
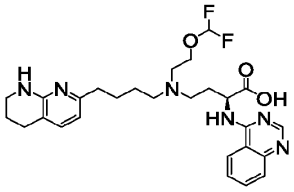
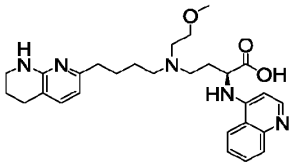
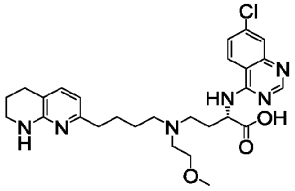
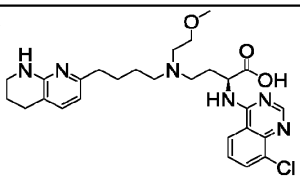
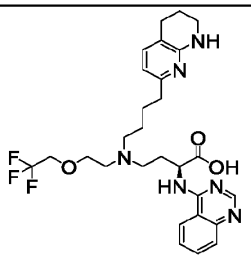
22 	23 	24 
25 	26 	27 
28 	29 	30 
31 	32 	33 
34 	35 	36 
37 	38 	39 

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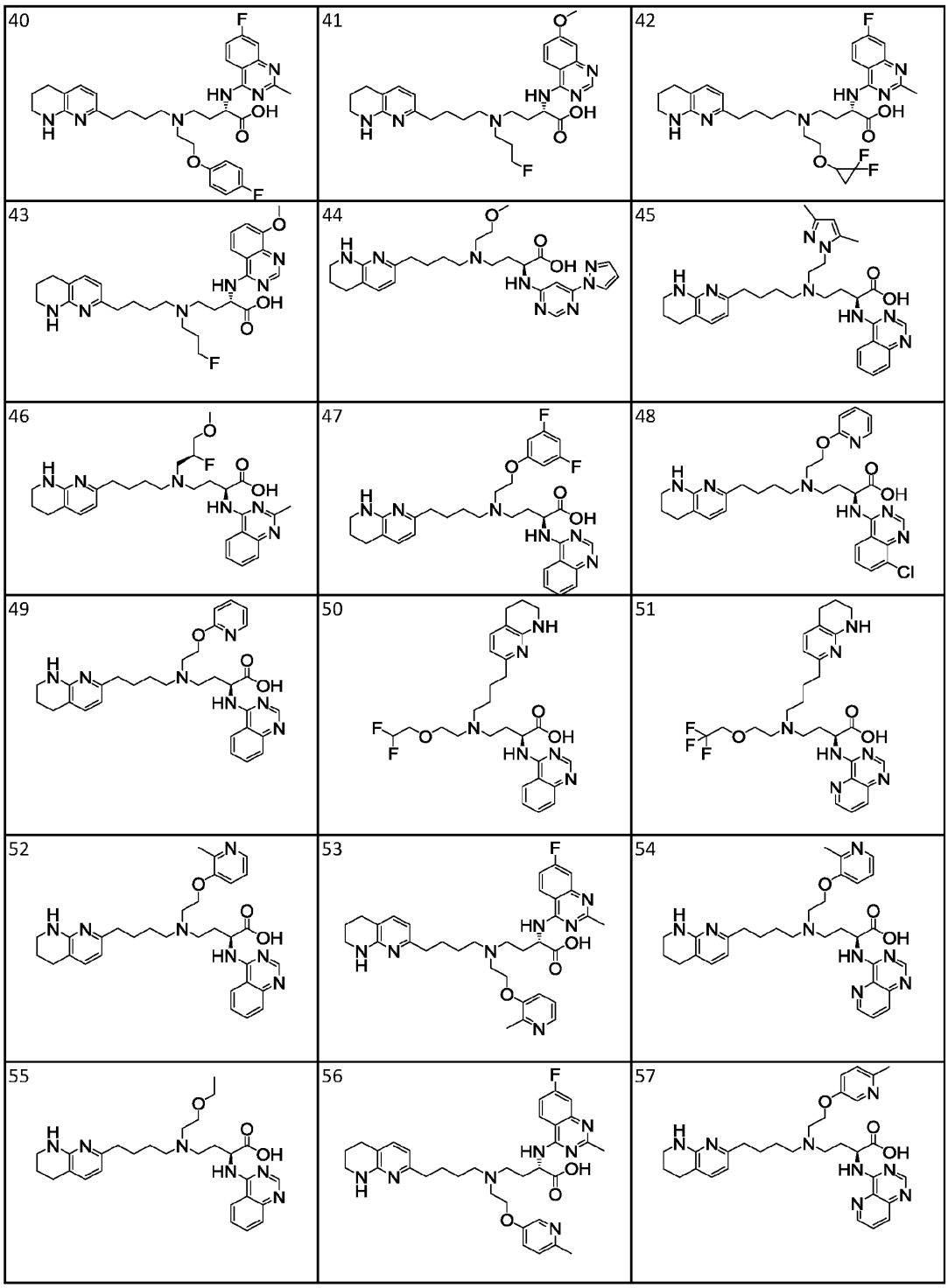

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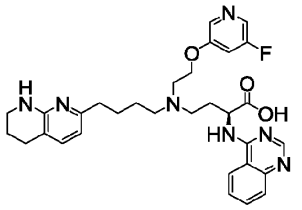
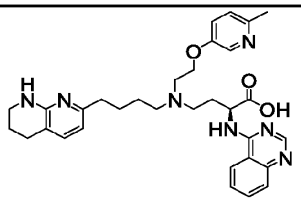
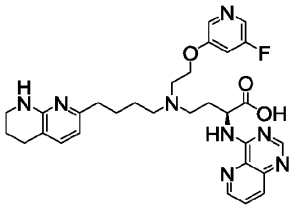
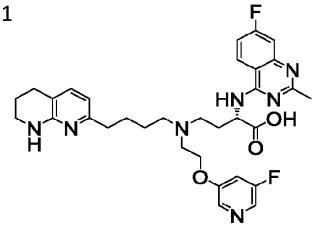
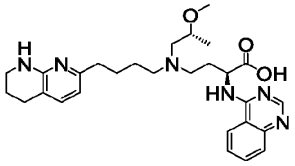
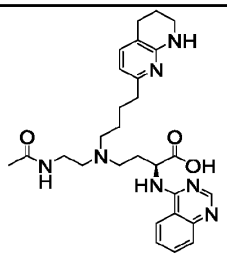
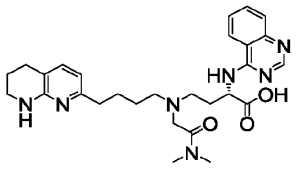
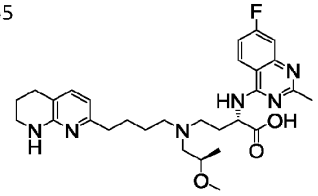
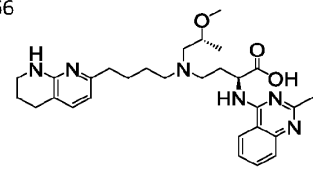
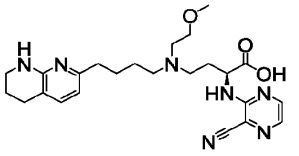
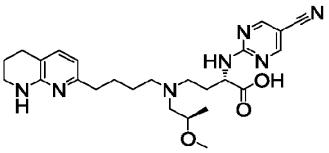
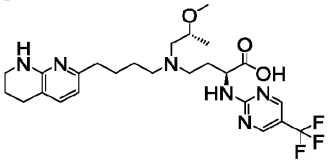
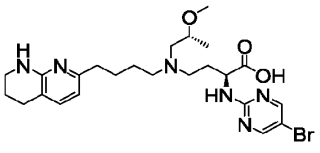
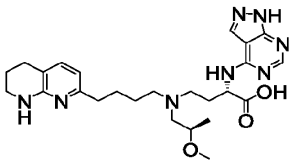
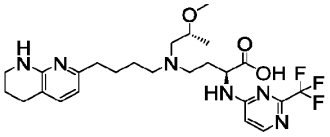
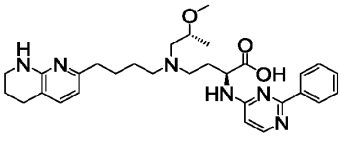
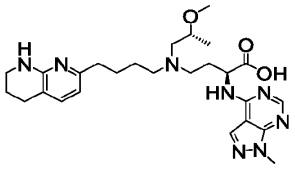
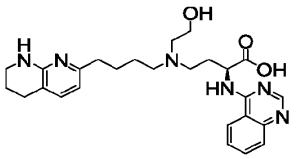
58 	59 	60 
61 	62 	63 
64 	65 	66 
67 	68 	69 
70 	71 	72 
73 	74 	75 

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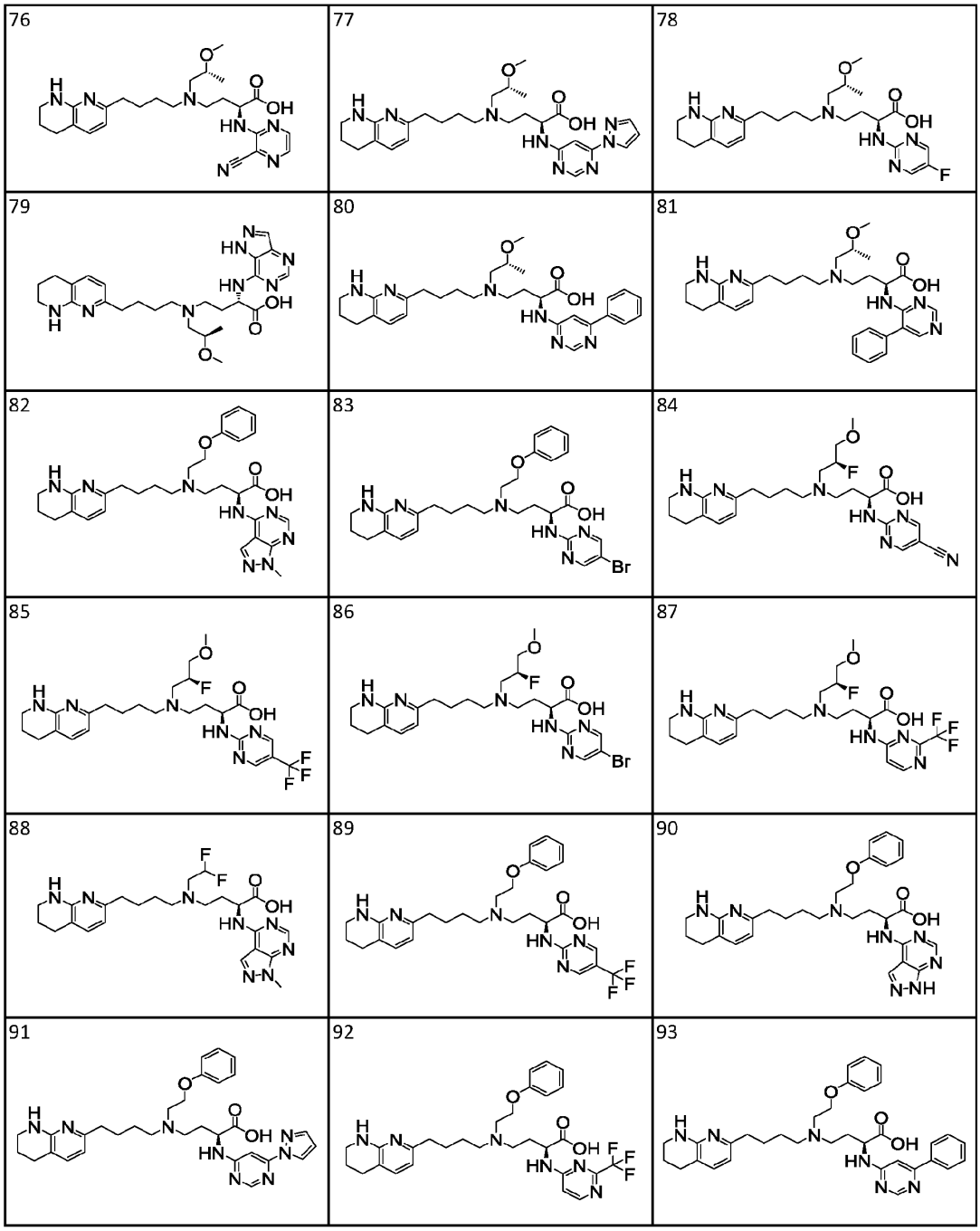

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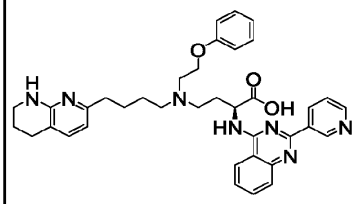
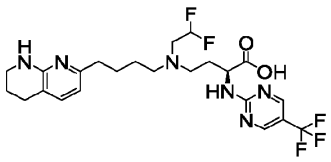
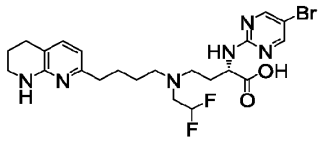
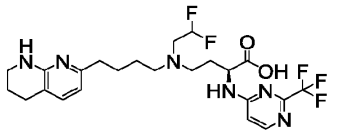
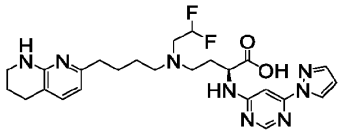
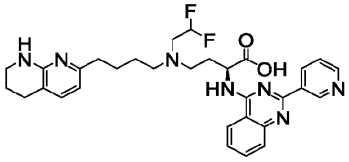
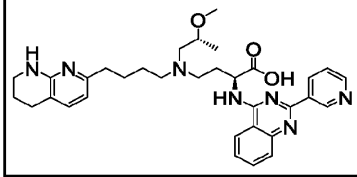
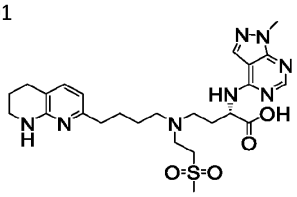
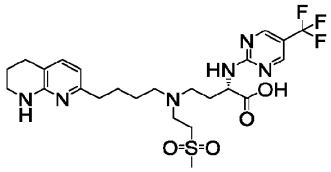
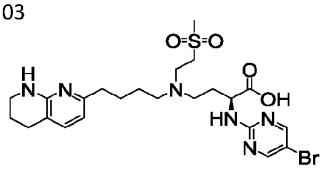
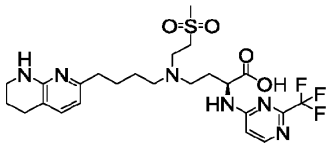
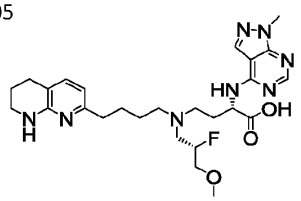
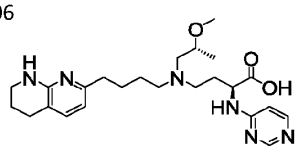
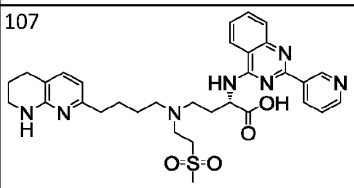
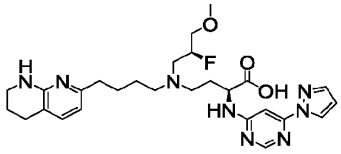
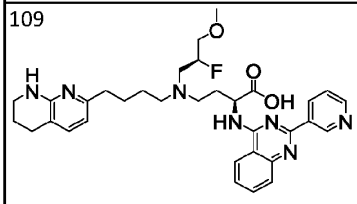
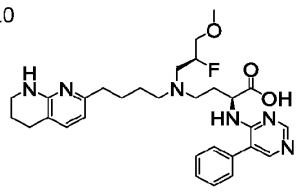
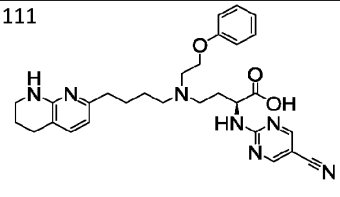
94 	95 	96 
97 	98 	99 
100 	101 	102 
103 	104 	105 
106 	107 	108 
109 	110 	111 

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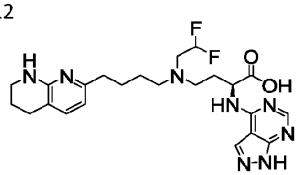
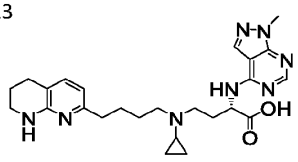
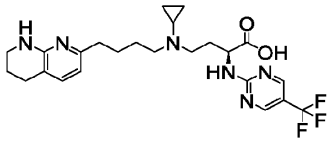
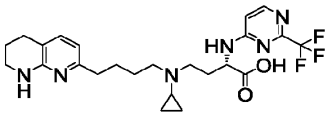
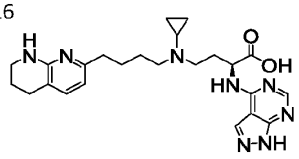
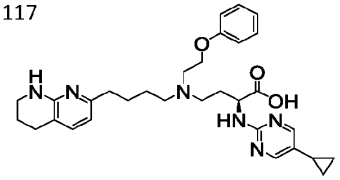
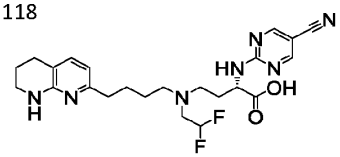
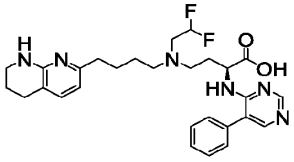
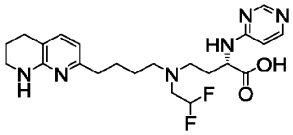
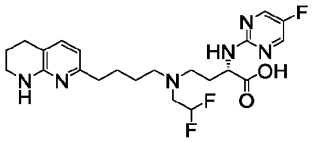
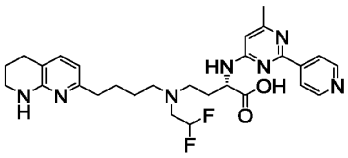
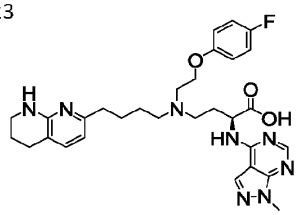
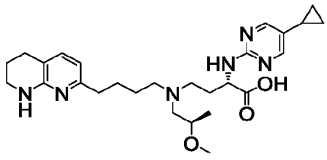
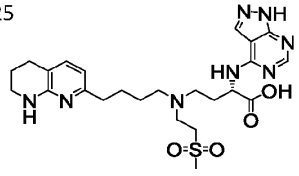
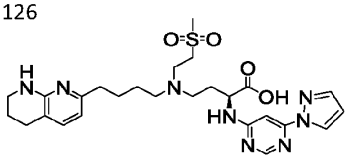
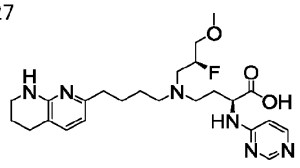
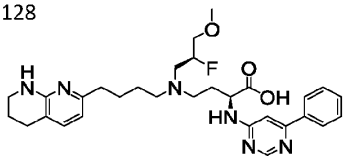
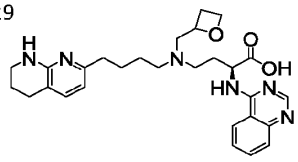
112 	113 	114 
115 	116 	117 
118 	119 	120 
121 	122 	123 
124 	125 	126 
127 	128 	129 

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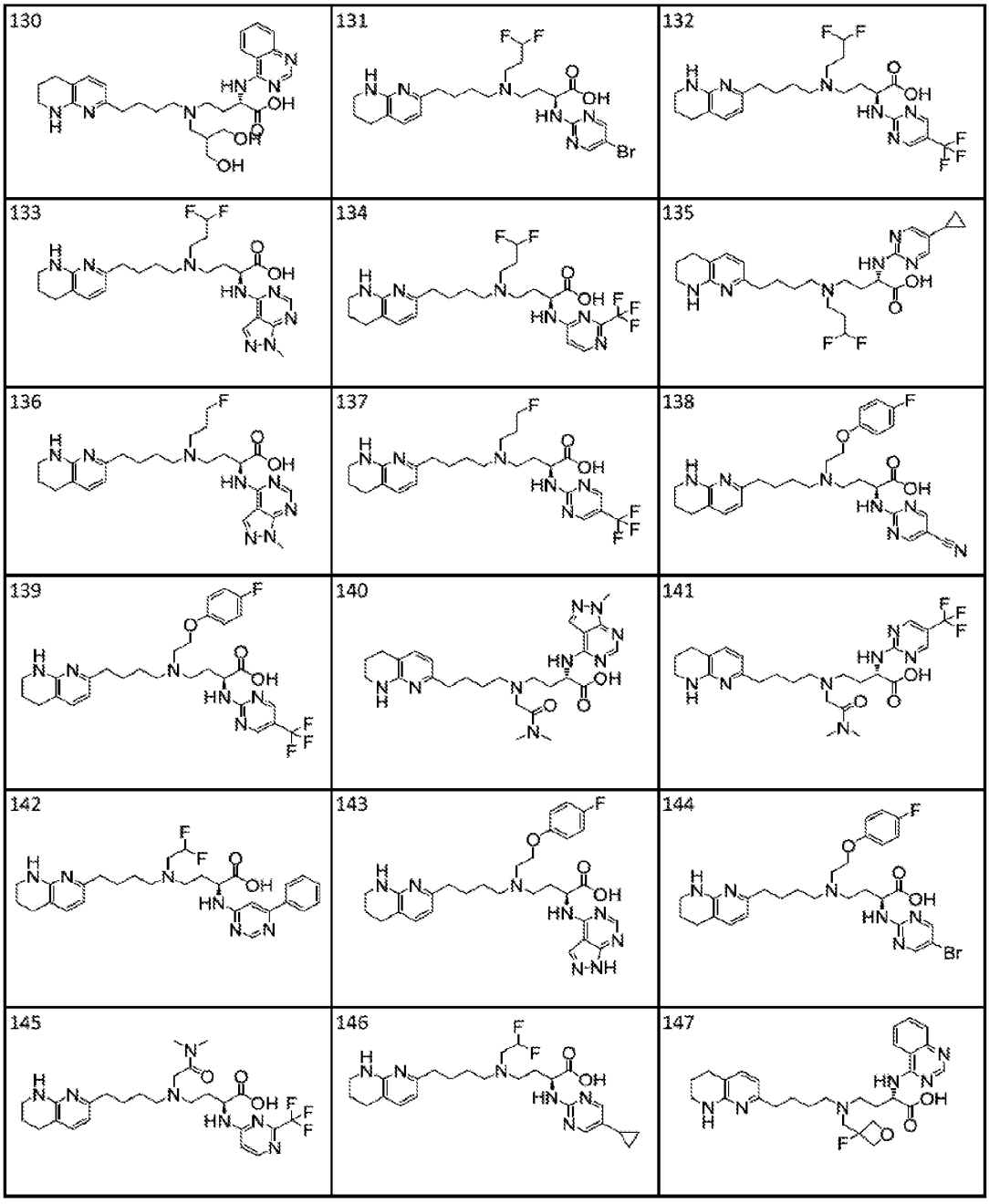
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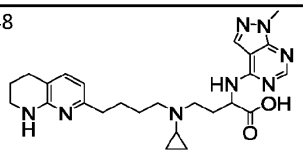
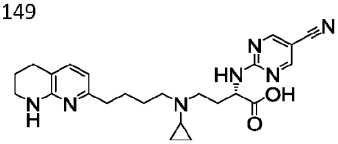
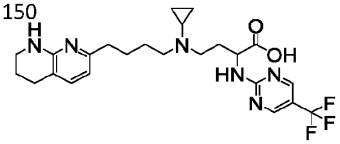
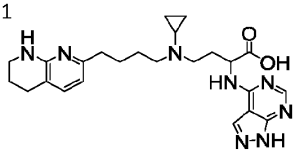
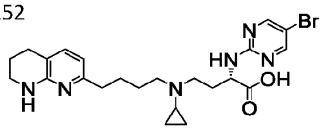
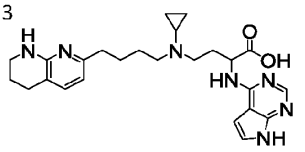
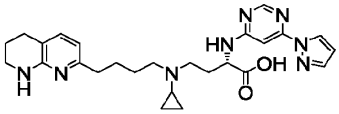
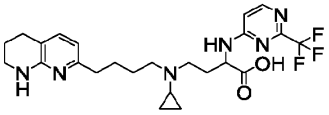
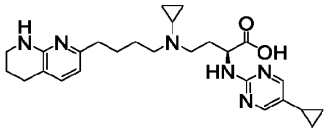
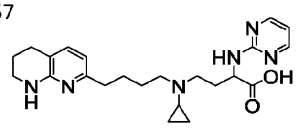
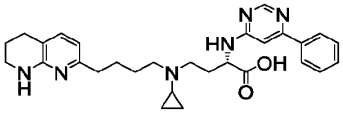
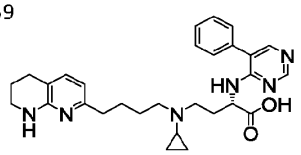
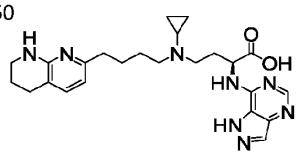
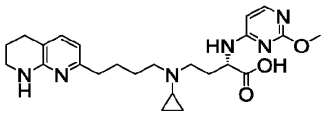
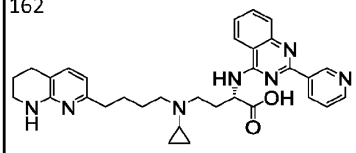
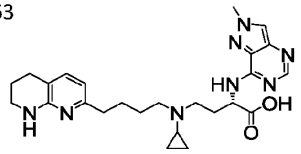
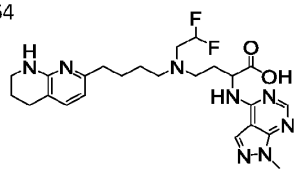
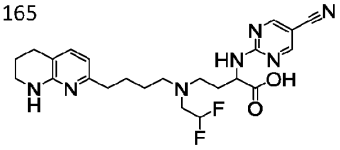
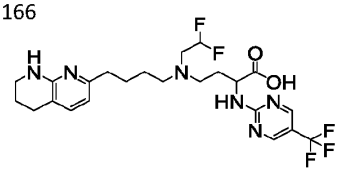
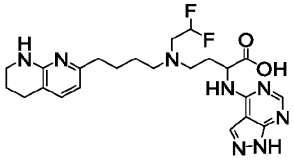
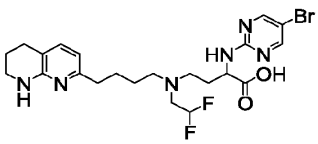
FIG. 1 (cont.)

148 	149 	150 
151 	152 	153 
154 	155 	156 
157 	158 	159 
160 	161 	162 
163 	164 	165 
166 	167 	168 

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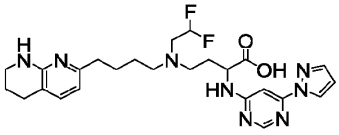
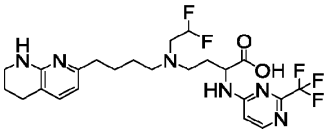
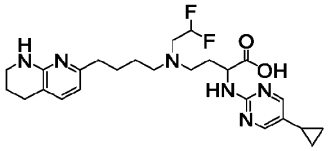
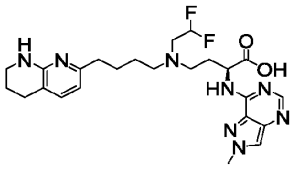
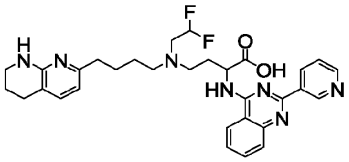
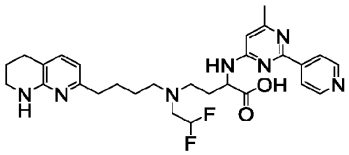
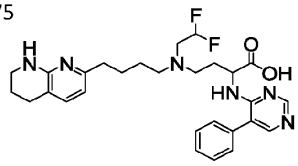
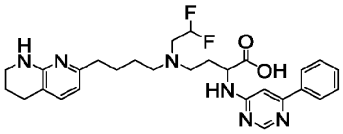
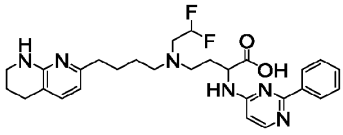
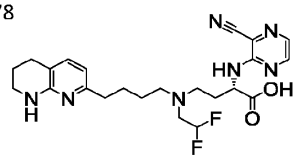
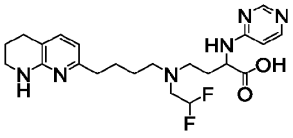
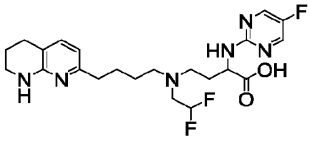
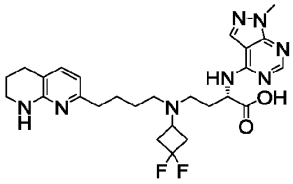
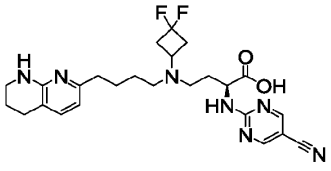
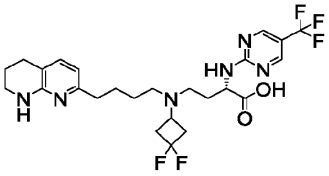
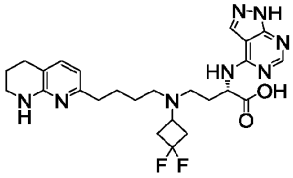
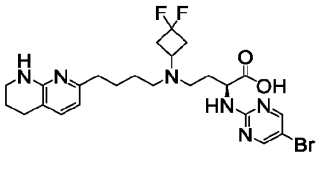
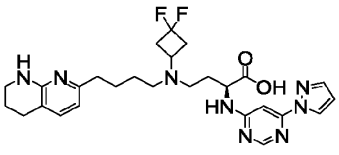
169 	170 	171 
172 	173 	174 
175 	176 	177 
178 	179 	180 
181 	182 	183 
184 	185 	186 

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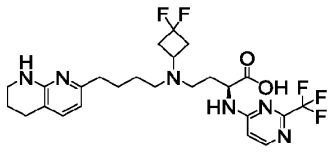
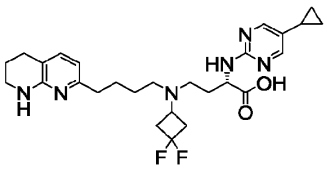
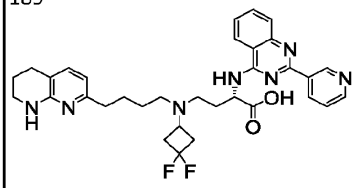
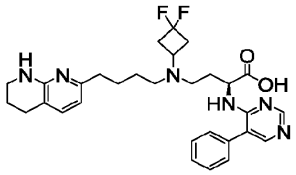
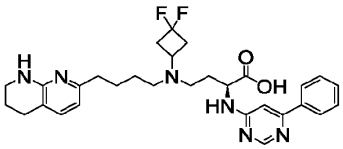
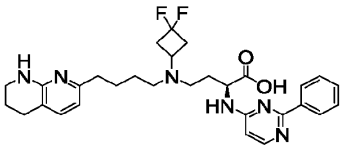
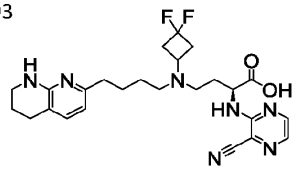
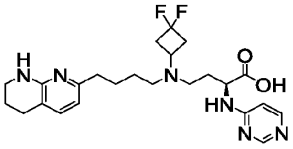
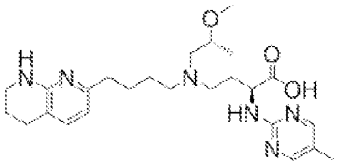
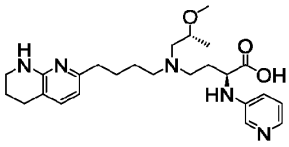
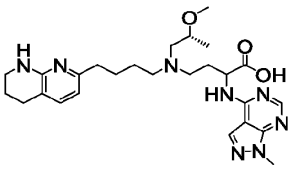
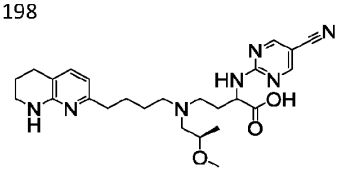
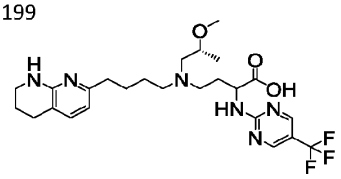
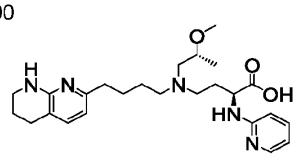
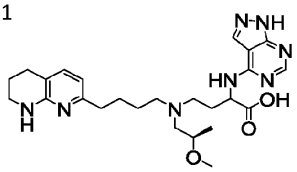
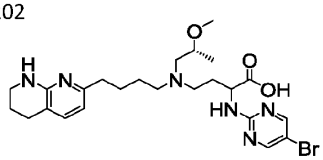
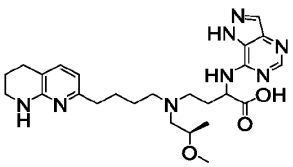
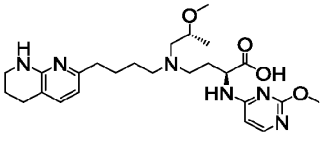
187 	188 	189 
190 	191 	192 
193 	194 	195 
196 	197 	198 
199 	200 	201 
202 	203 	204 

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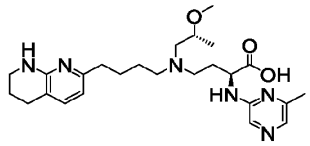
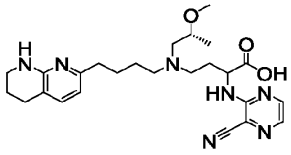
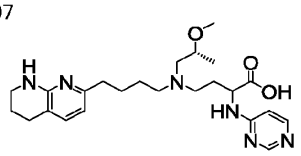
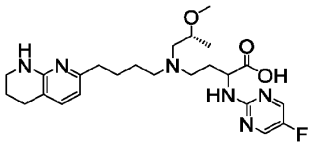
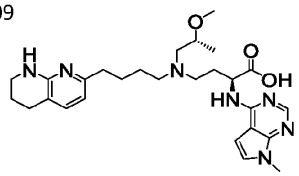
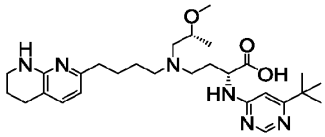
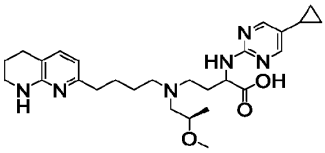
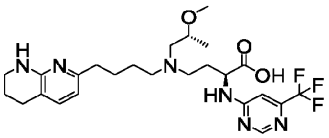
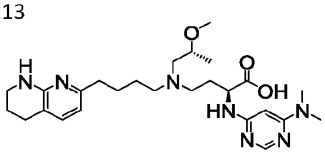
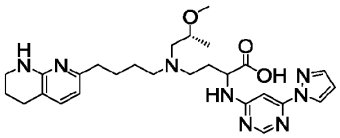
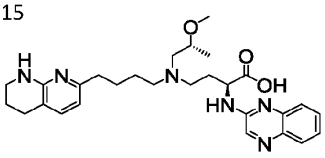
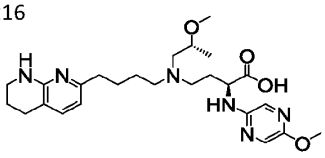
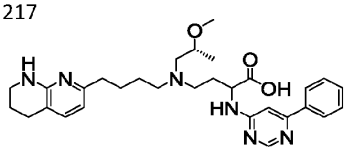
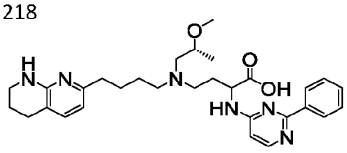
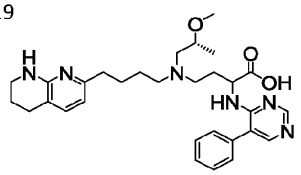
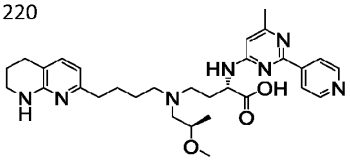
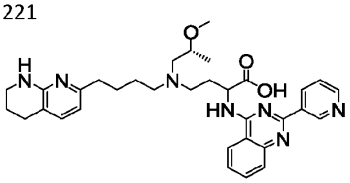
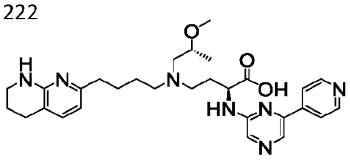
205 	206 	207 
208 	209 	210 
211 	212 	213 
214 	215 	216 
217 	218 	219 
220 	221 	222 

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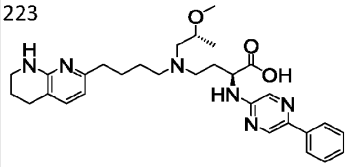
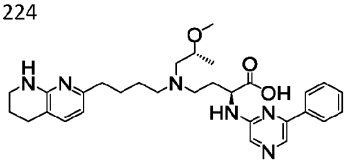
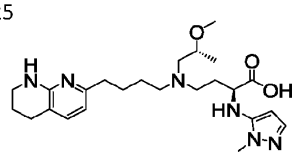
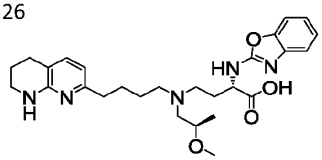
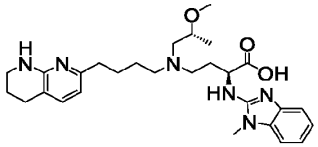
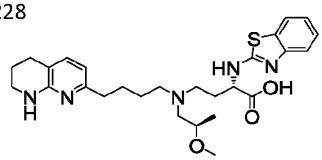
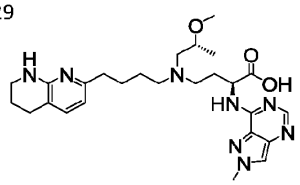
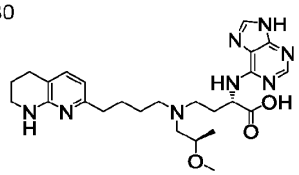
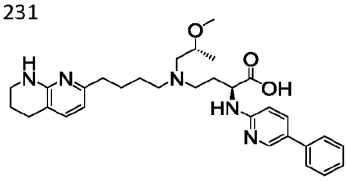
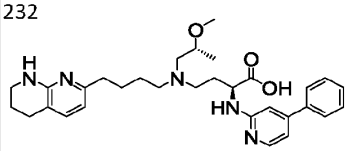
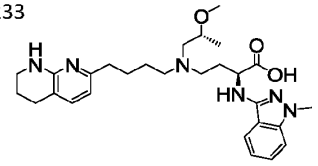
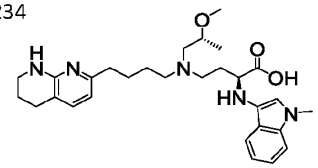
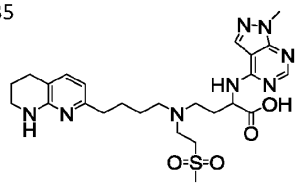
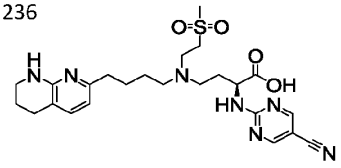
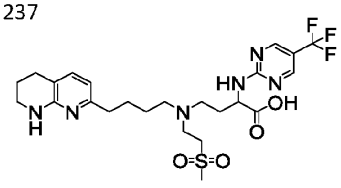
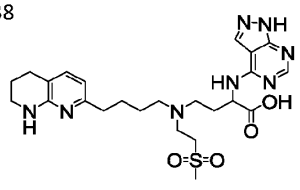
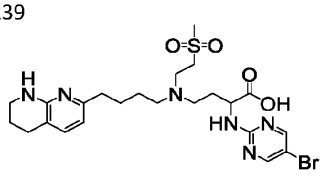
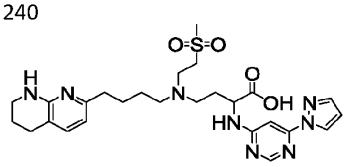
223 	224 	225 
226 	227 	228 
229 	230 	231 
232 	233 	234 
235 	236 	237 
238 	239 	240 

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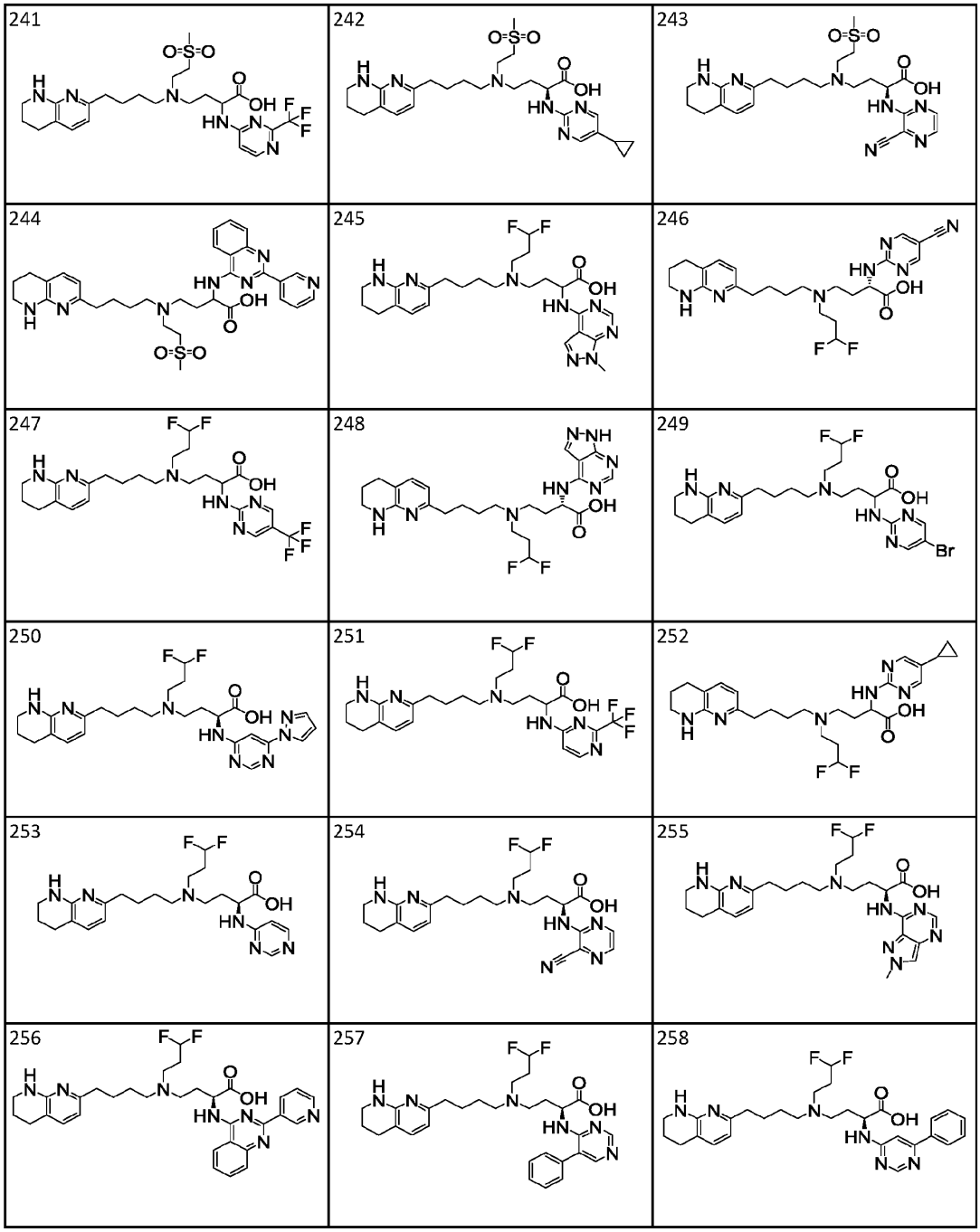
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FIG. 1 (cont.)

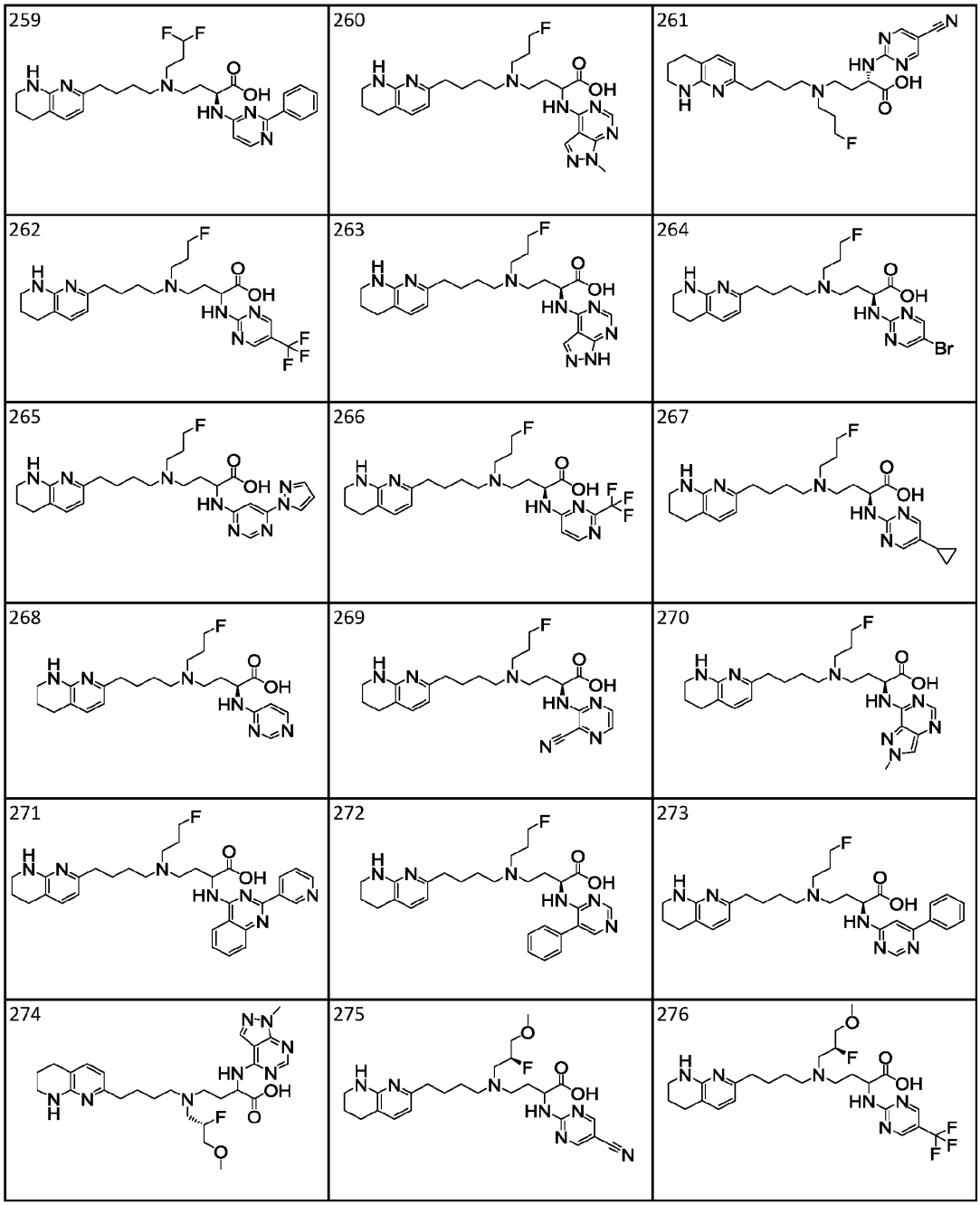
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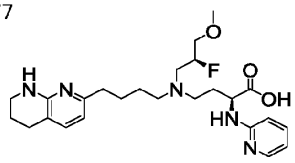
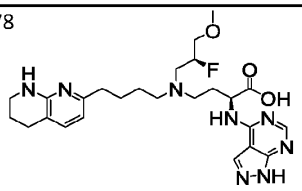
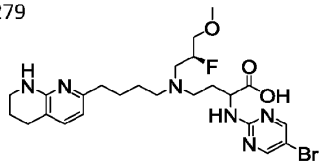
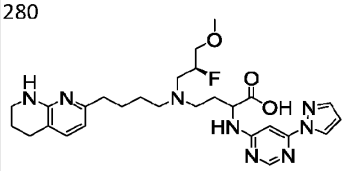
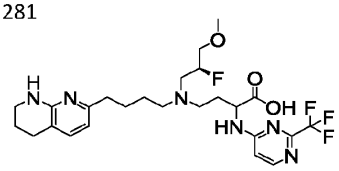
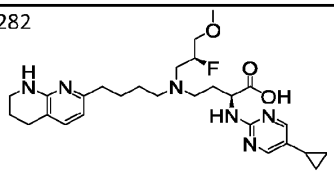
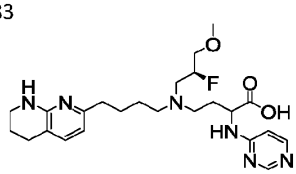
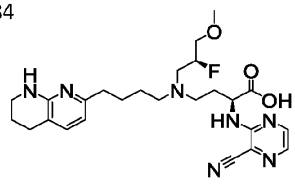
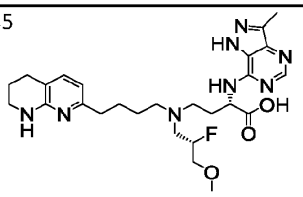
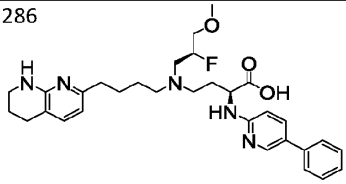
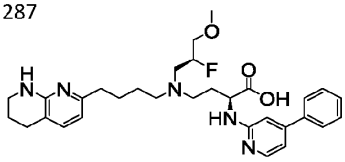
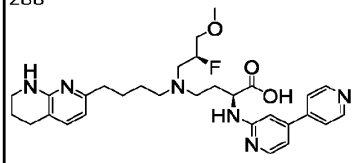
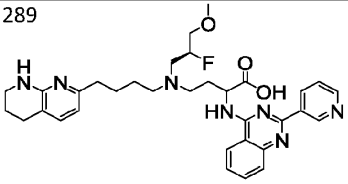
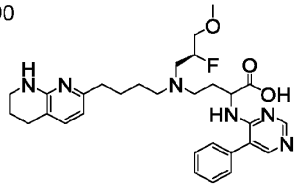
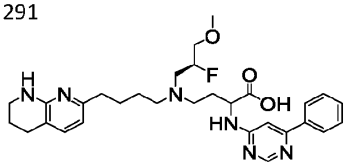
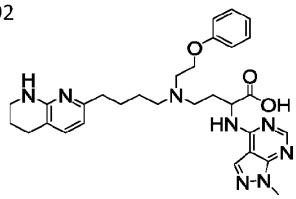
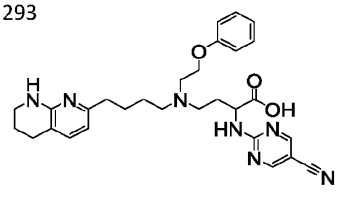
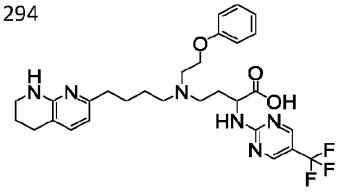
FIG. 1 (cont.)

277 	278 	279 
280 	281 	282 
283 	284 	285 
286 	287 	288 
289 	290 	291 
292 	293 	294 

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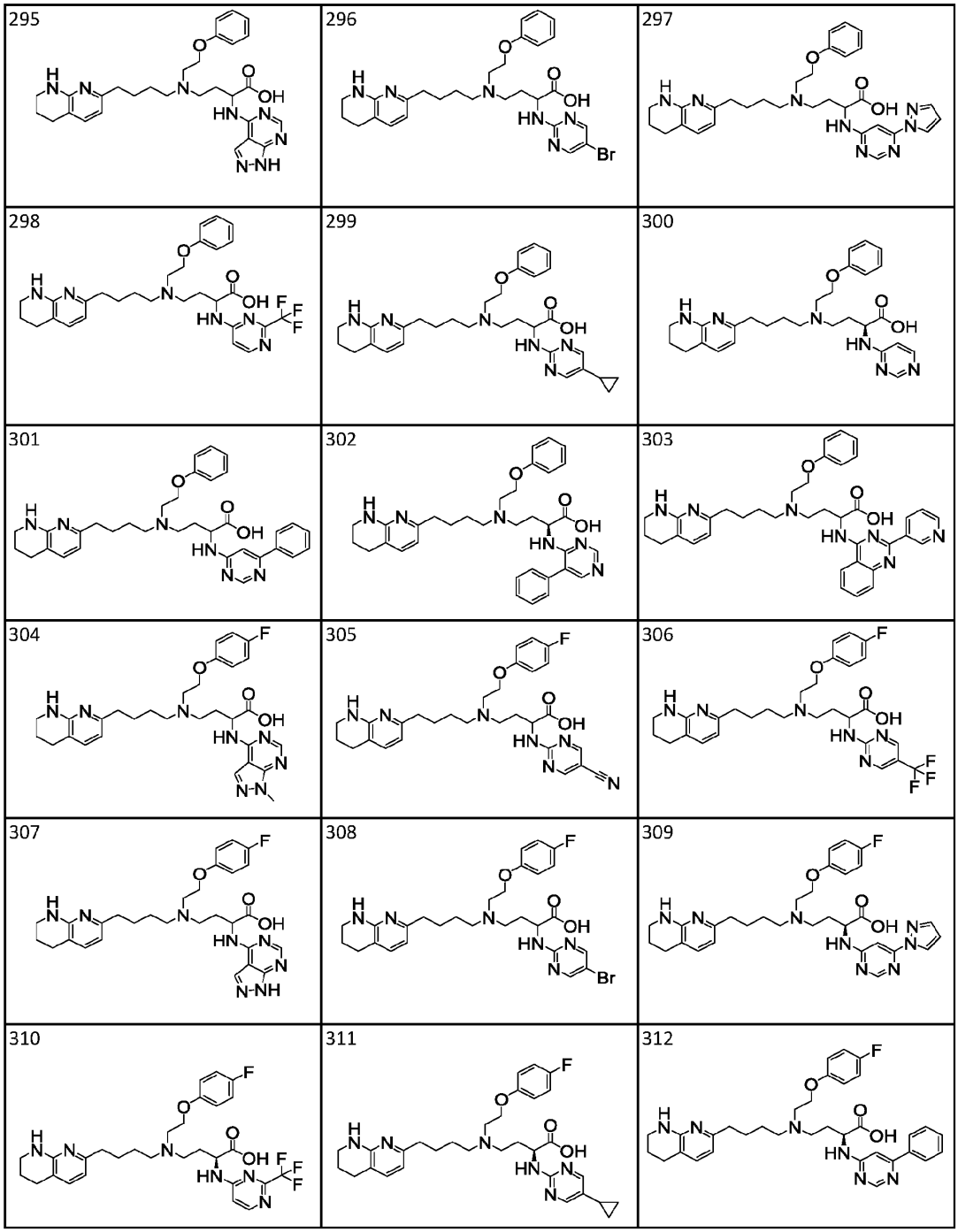
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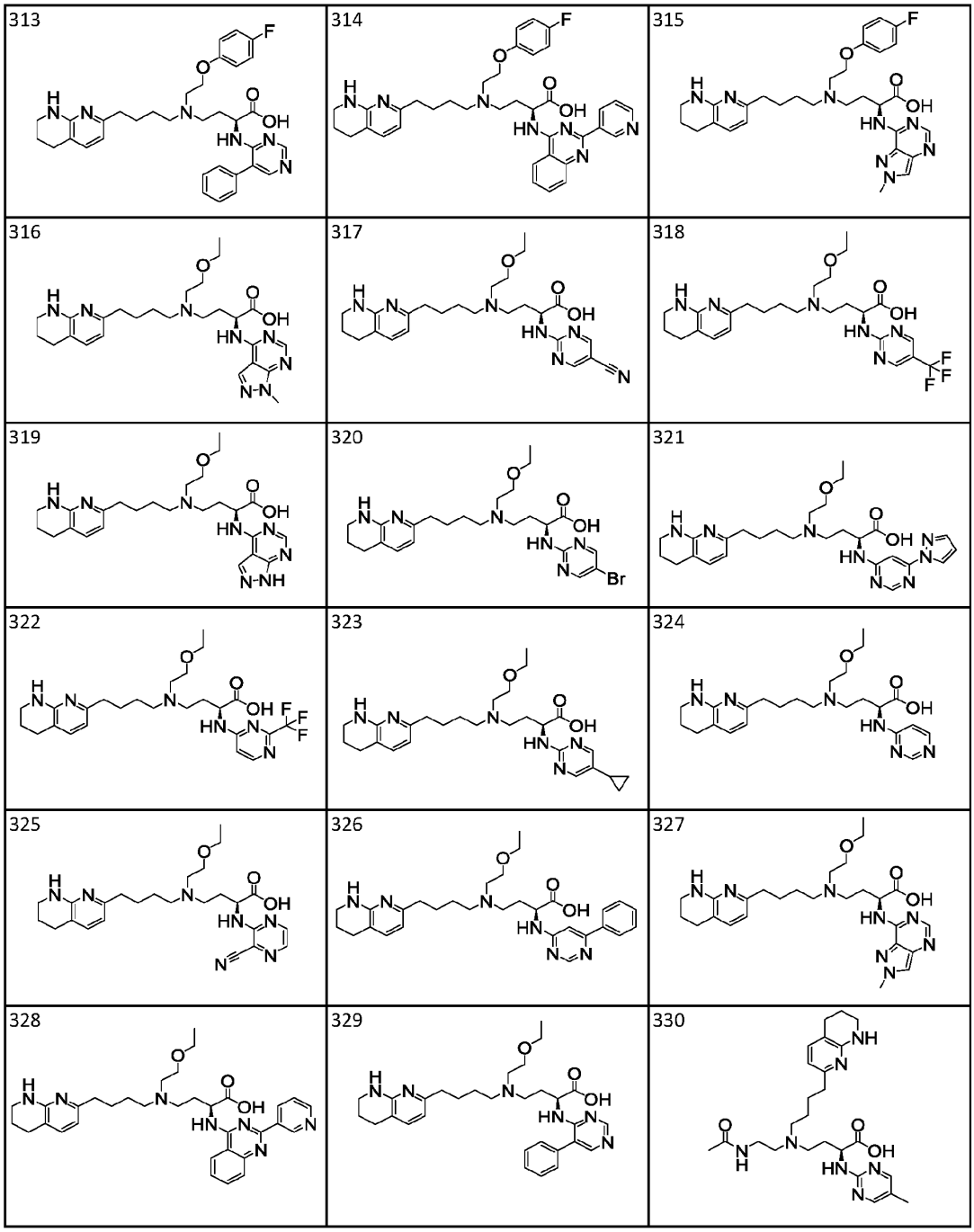
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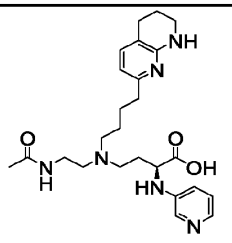
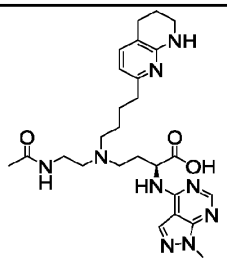
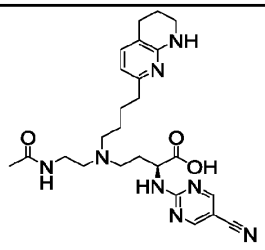
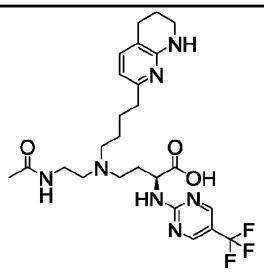
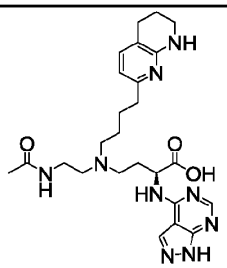
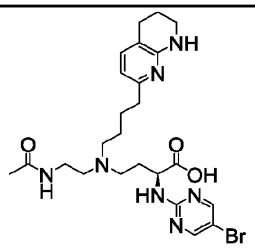
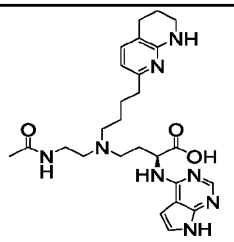
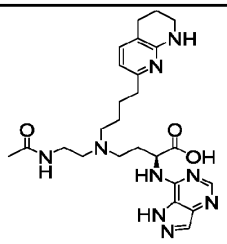
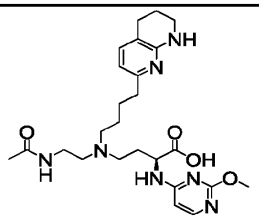
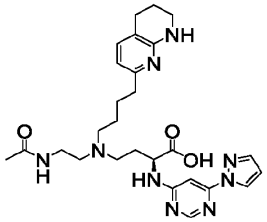
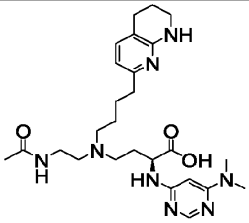
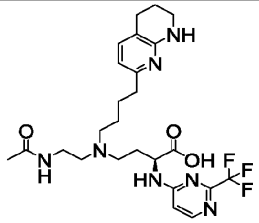
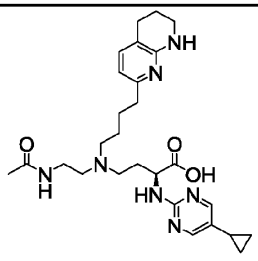
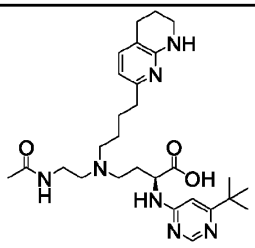
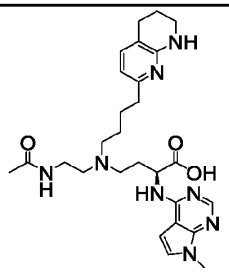
331 	332 	333 
334 	335 	336 
337 	338 	339 
340 	341 	342 
343 	344 	345 

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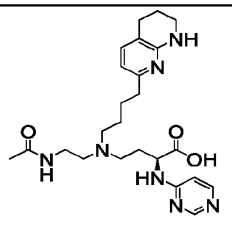
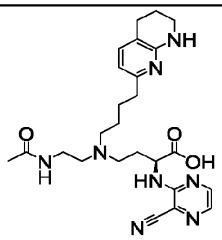
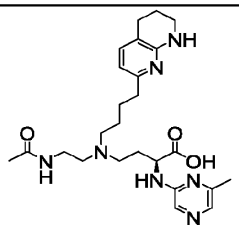
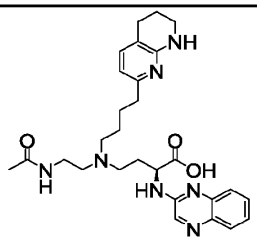
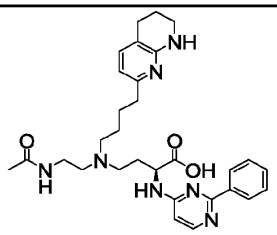
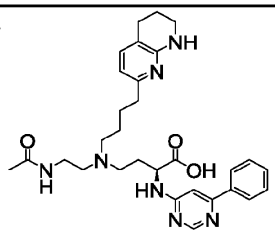
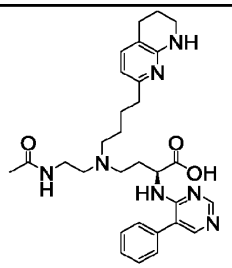
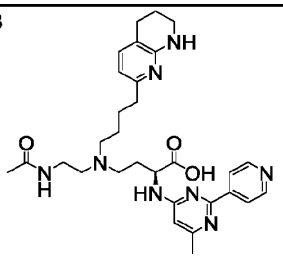
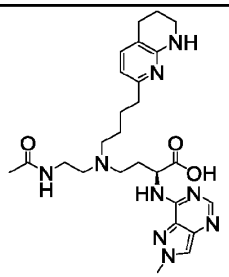
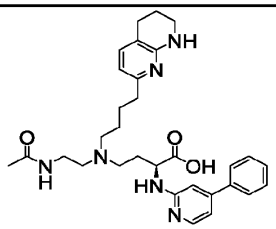
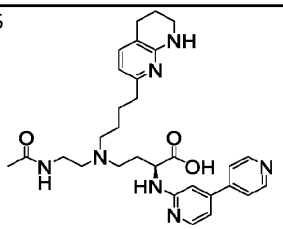
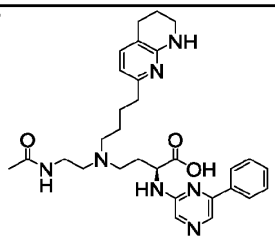
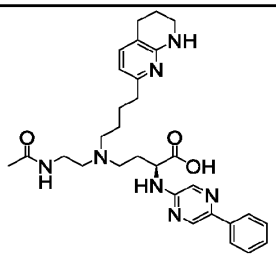
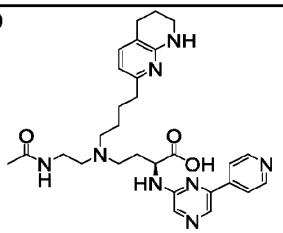
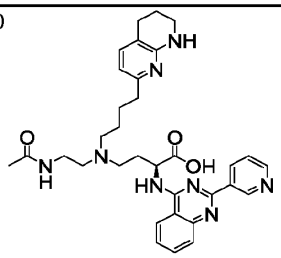
346 	347 	348 
349 	350 	351 
352 	353 	354 
355 	356 	357 
358 	359 	360 

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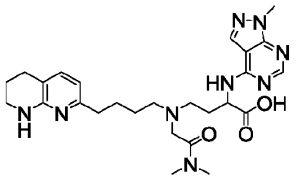
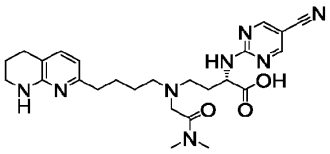
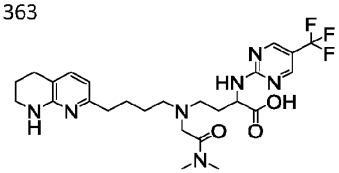
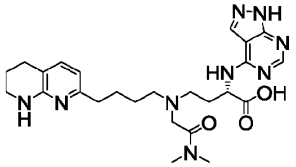
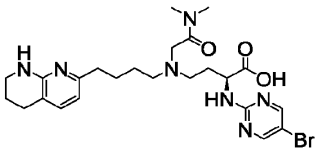
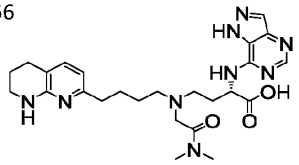
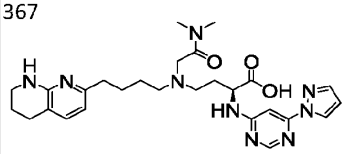
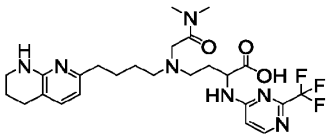
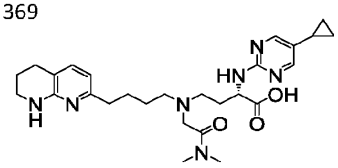
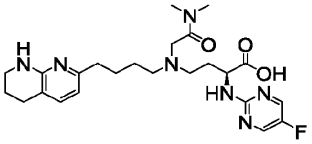
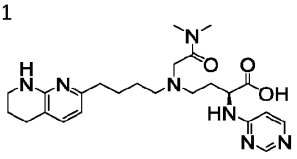
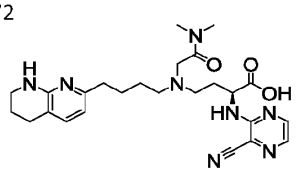
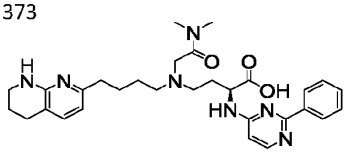
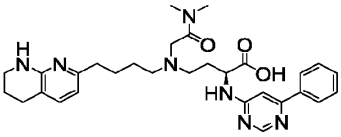
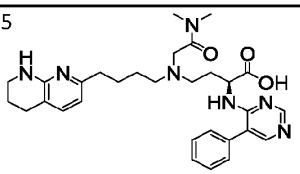
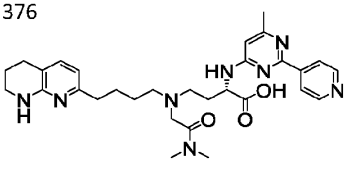
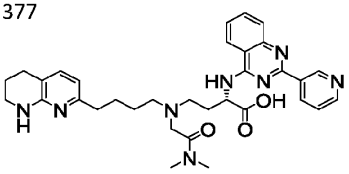
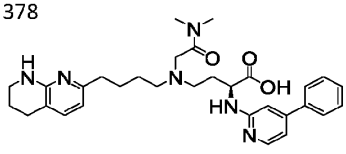
361 	362 	363 
364 	365 	366 
367 	368 	369 
370 	371 	372 
373 	374 	375 
376 	377 	378 

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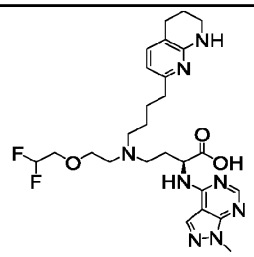
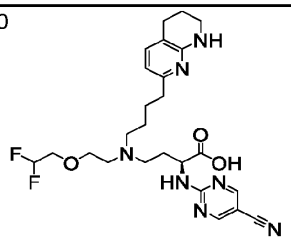
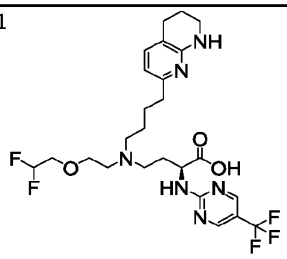
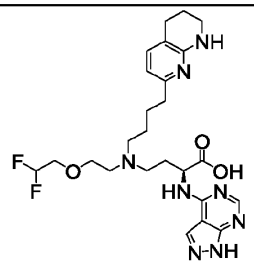
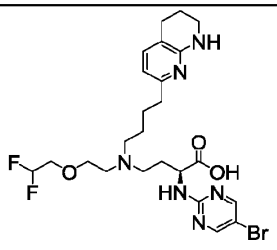
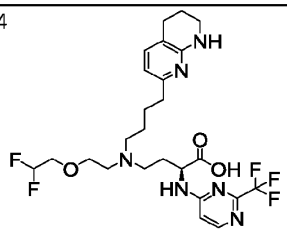
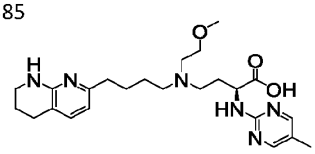
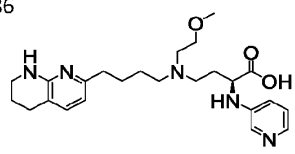
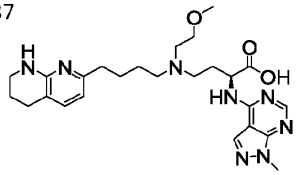
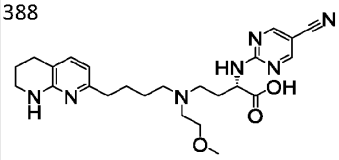
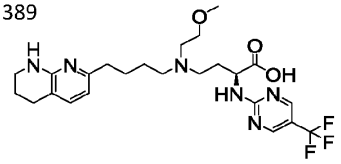
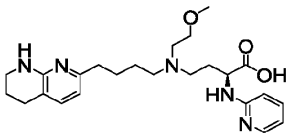
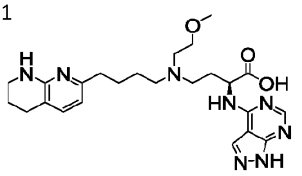
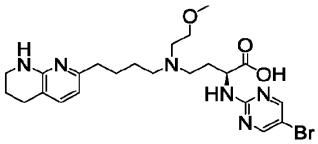
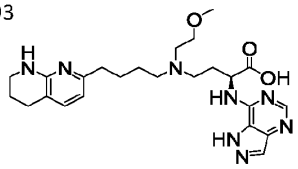
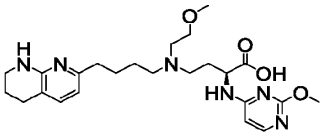
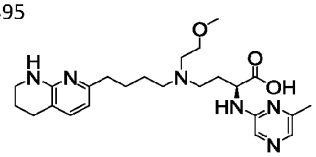
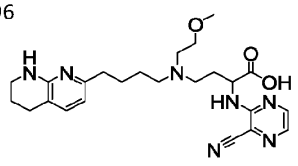
379 	380 	381 
382 	383 	384 
385 	386 	387 
388 	389 	390 
391 	392 	393 
394 	395 	396 

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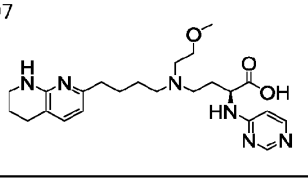
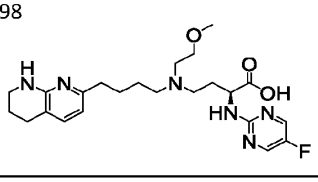
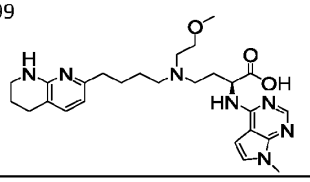
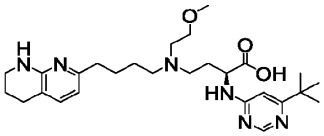
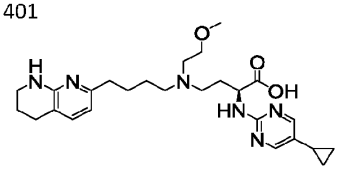
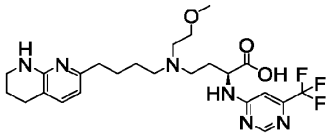
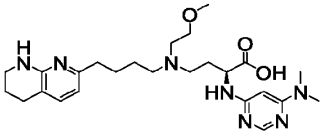
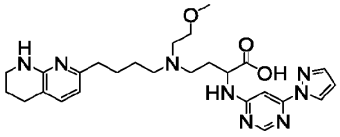
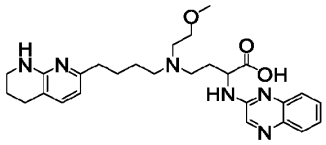
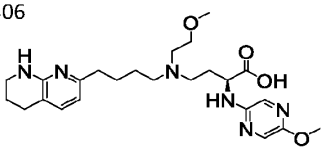
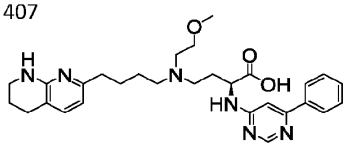
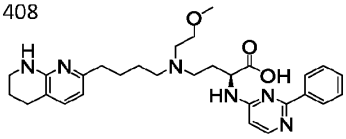
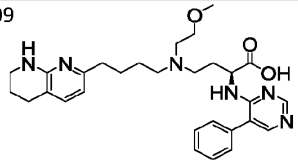
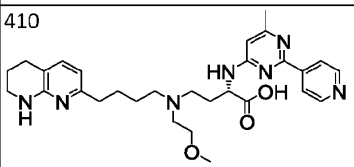
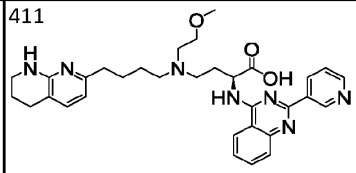
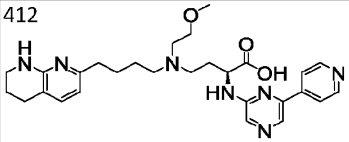
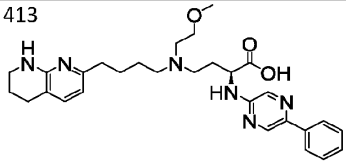
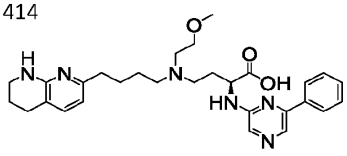
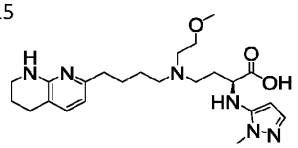
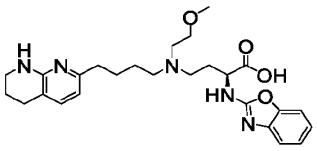
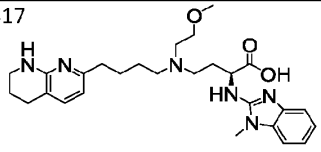
397 	398 	399 
400 	401 	402 
403 	404 	405 
406 	407 	408 
409 	410 	411 
412 	413 	414 
415 	416 	417 

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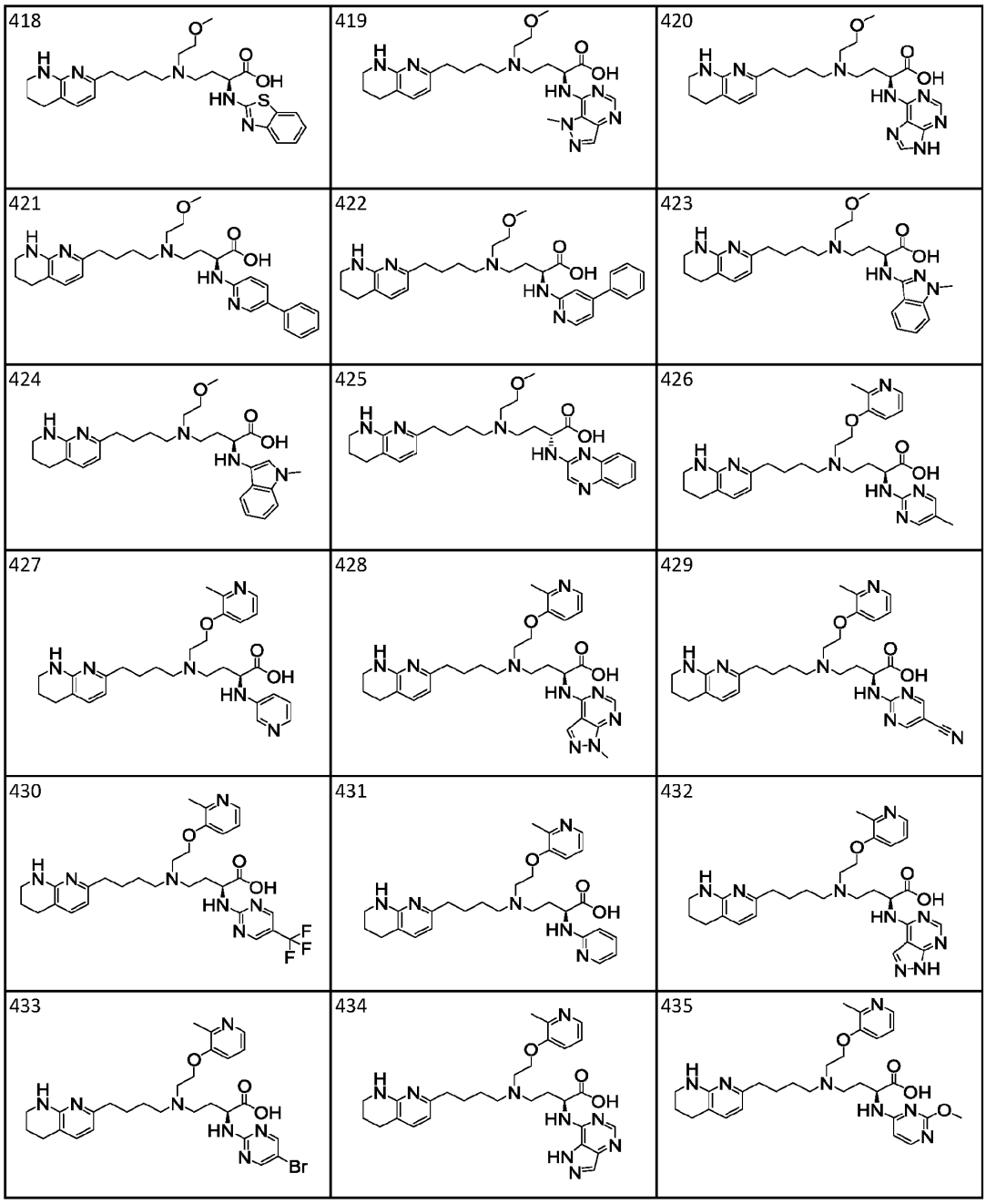
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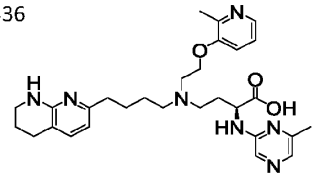
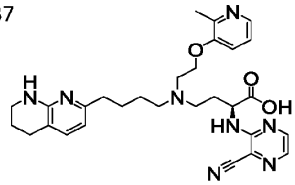
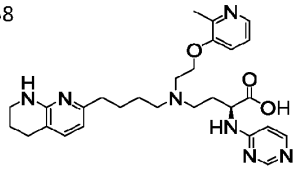
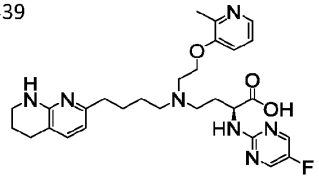
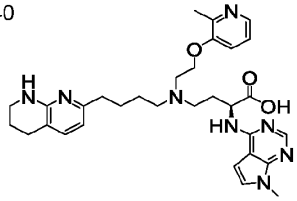
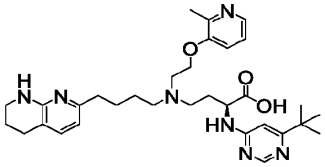
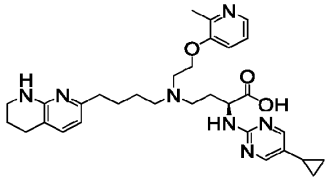
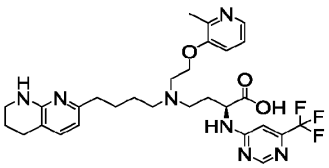
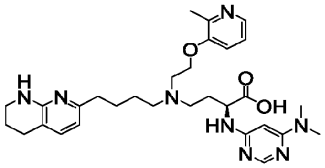
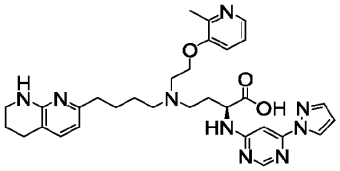
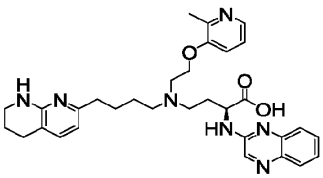
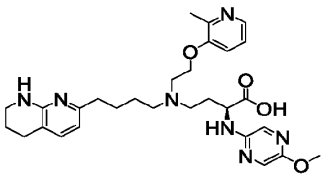
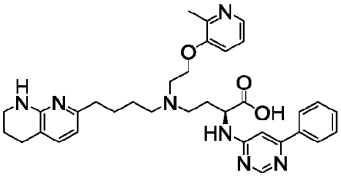
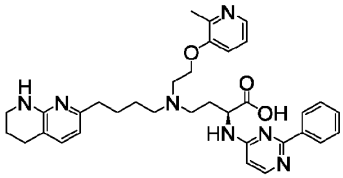
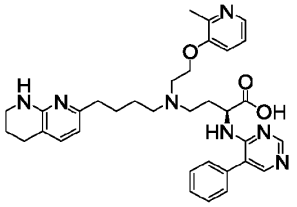
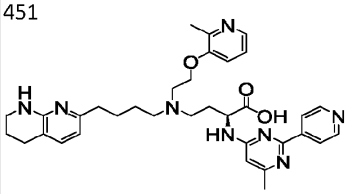
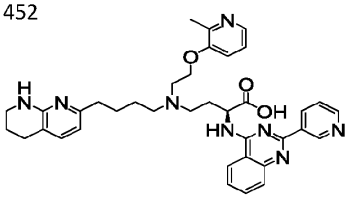
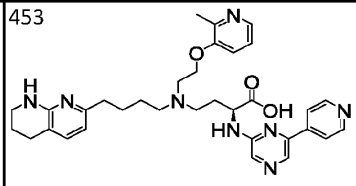
FIG. 1 (cont.)

436 	437 	438 
439 	440 	441 
442 	443 	444 
445 	446 	447 
448 	449 	450 
451 	452 	453 

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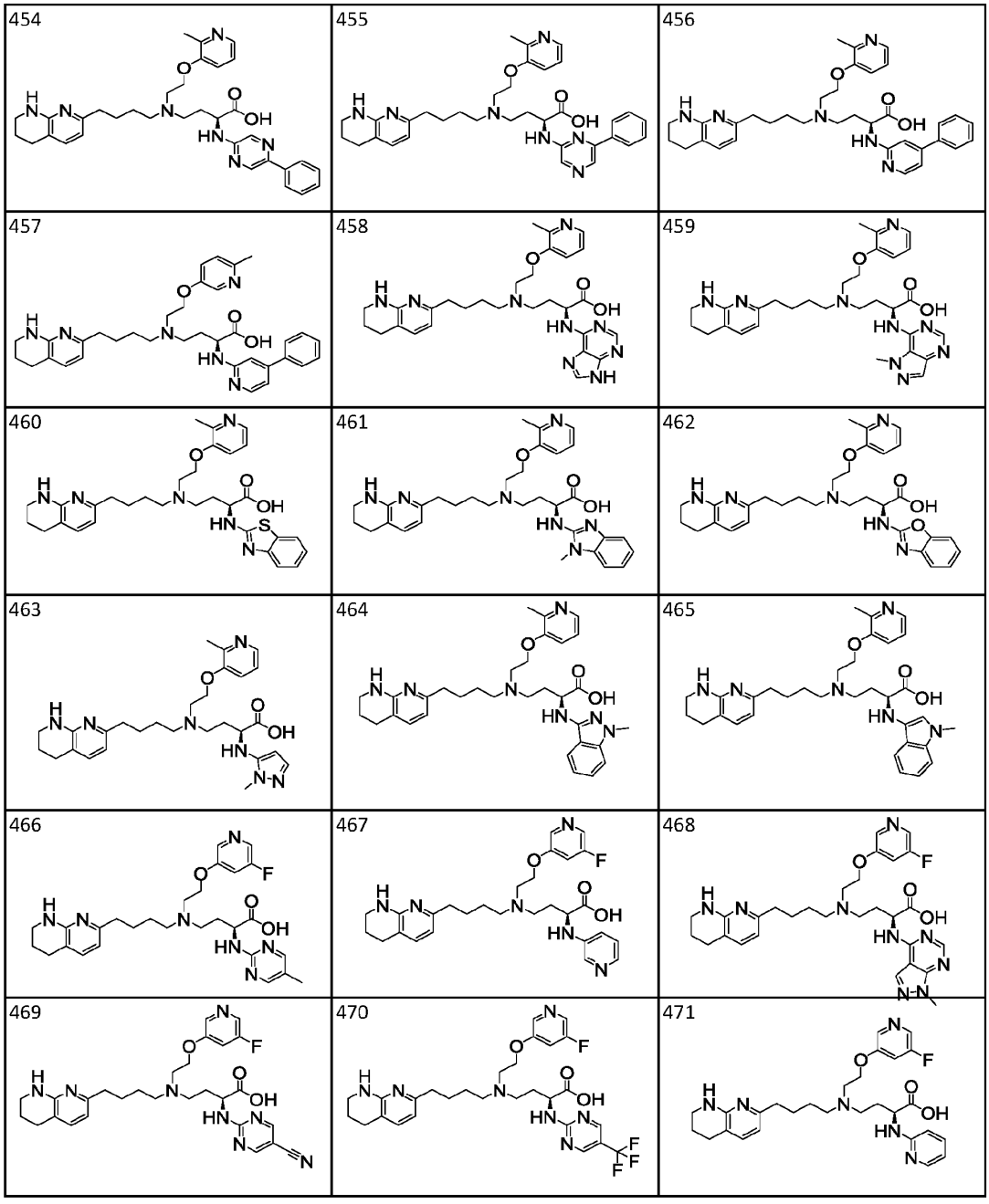
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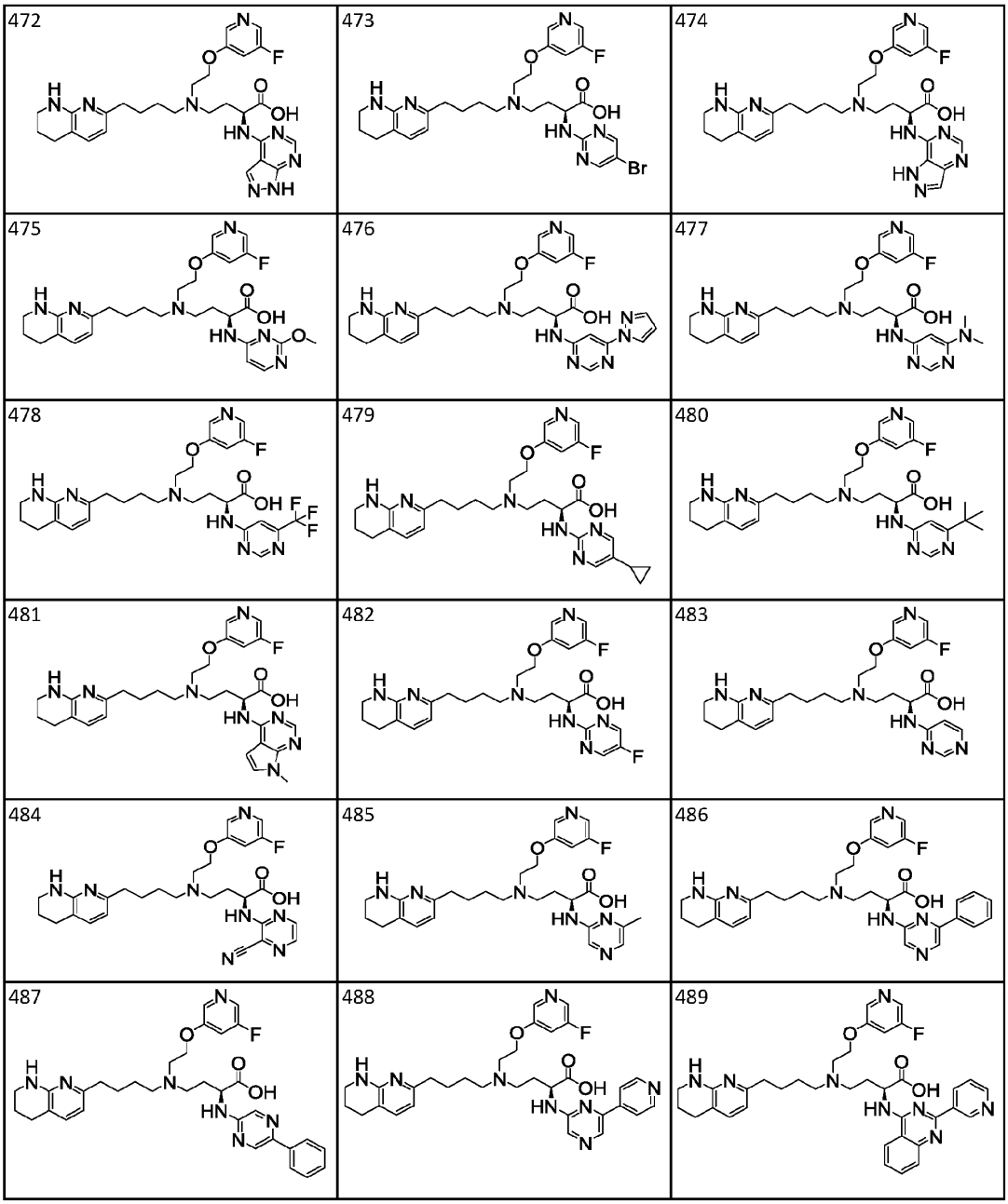
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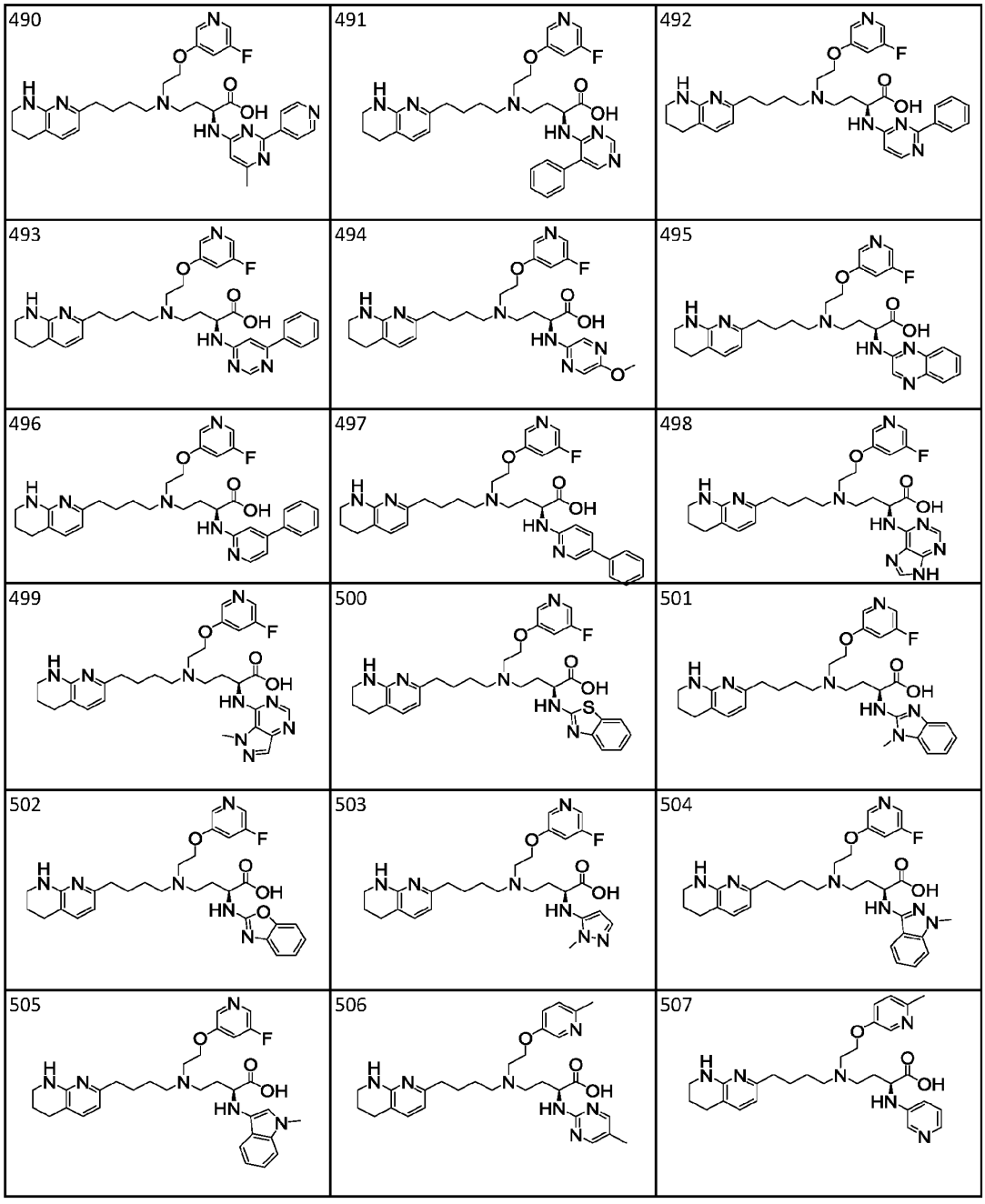
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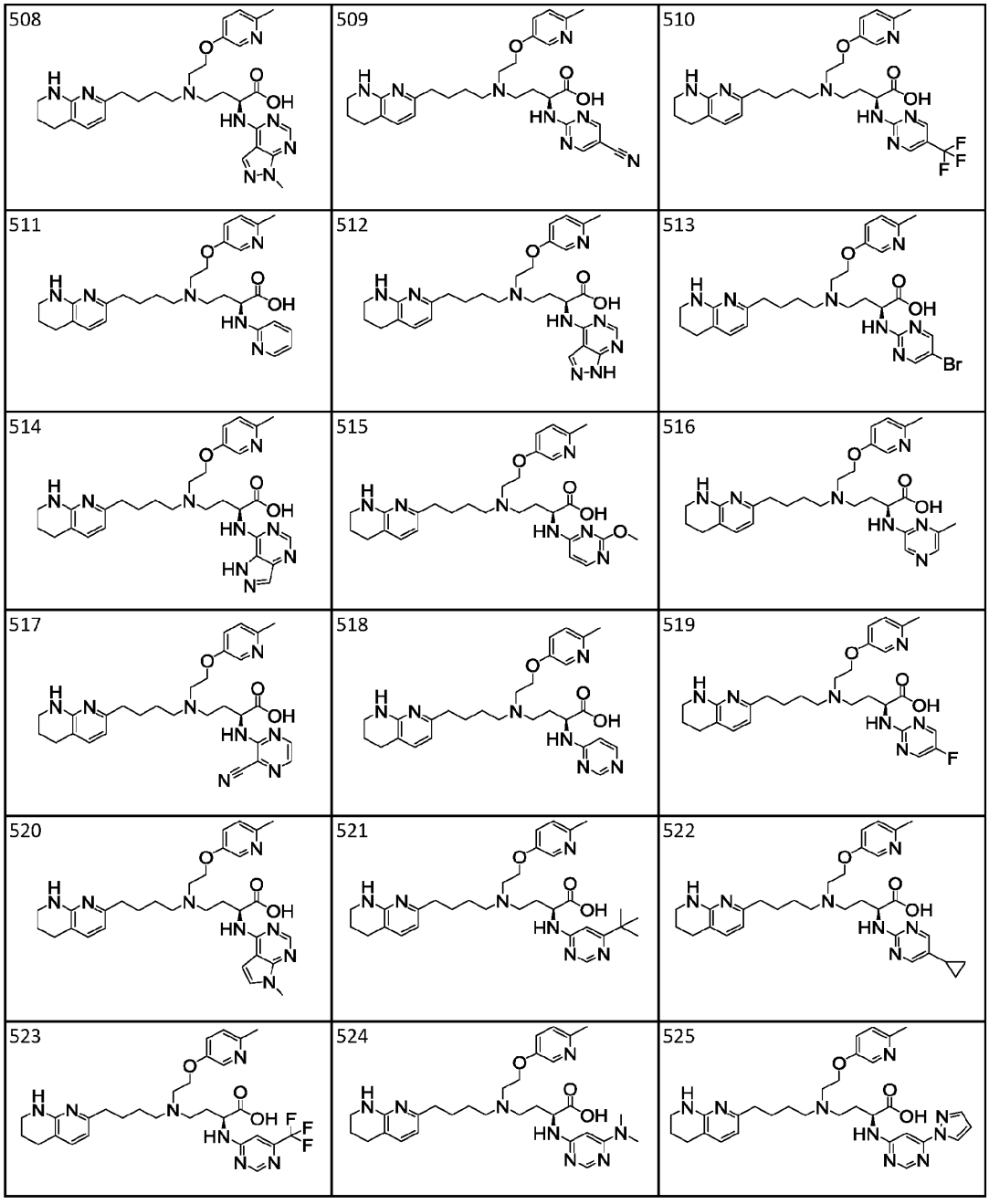
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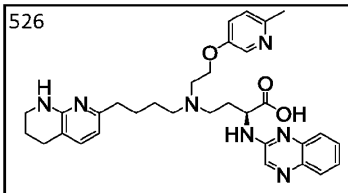
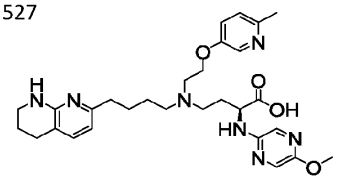
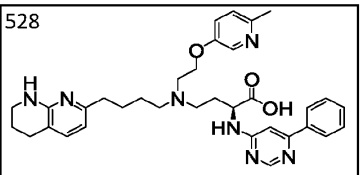
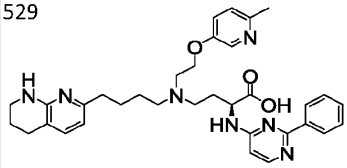
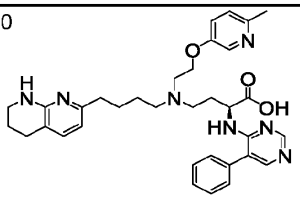
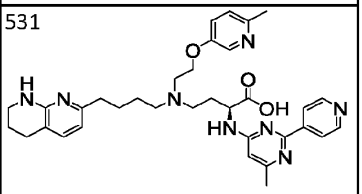
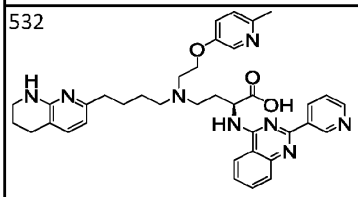
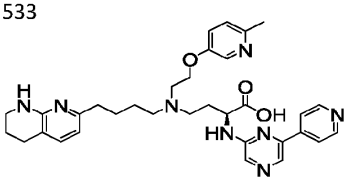
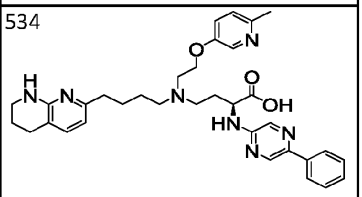
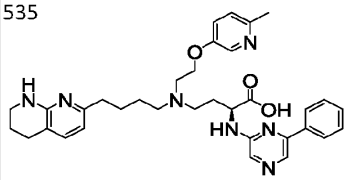
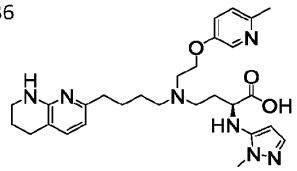
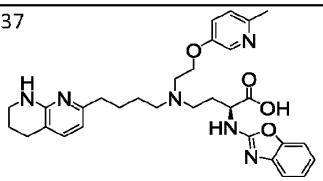
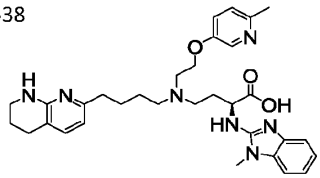
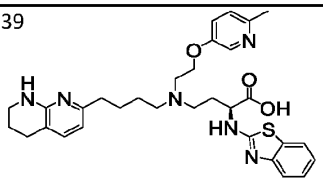
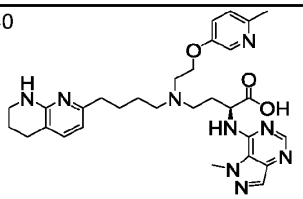
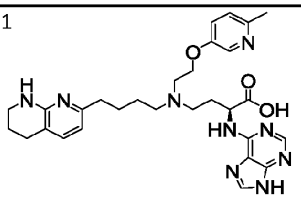
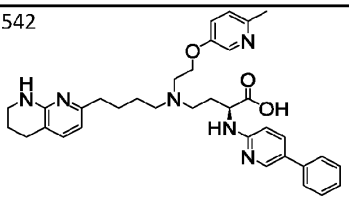
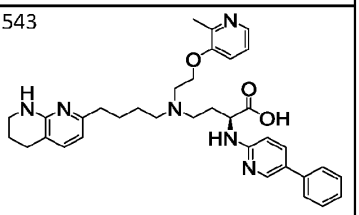
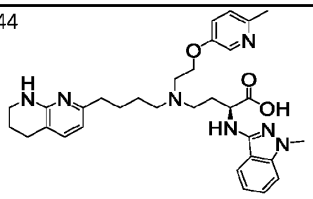
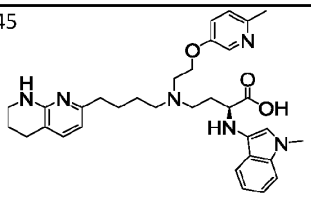
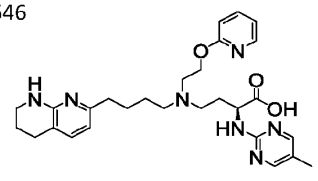
526 	527 	528 
529 	530 	531 
532 	533 	534 
535 	536 	537 
538 	539 	540 
541 	542 	543 
544 	545 	546 

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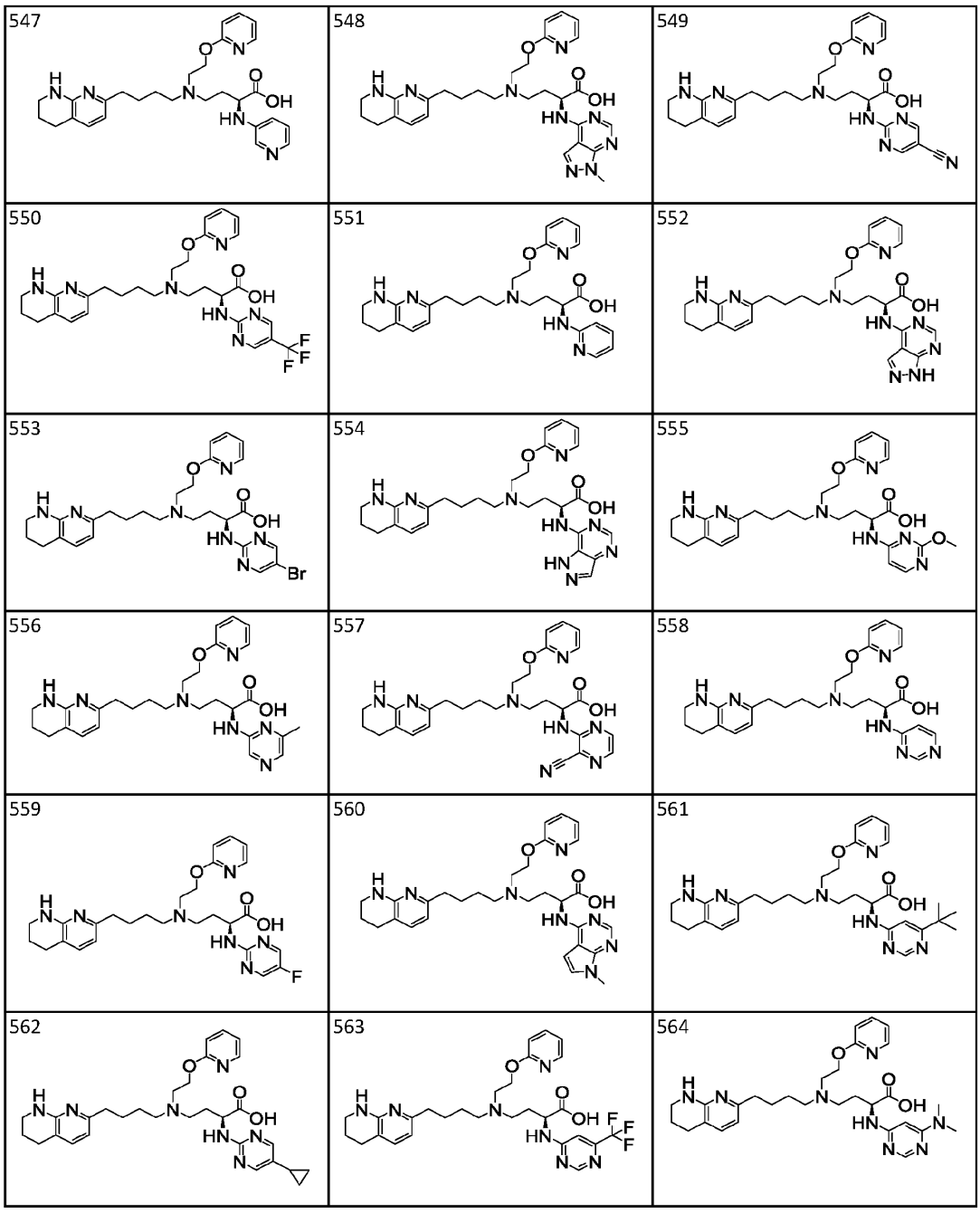
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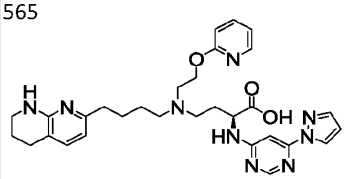
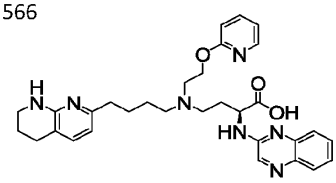
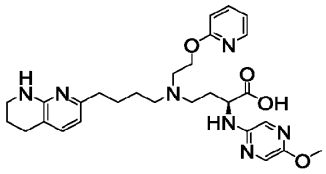
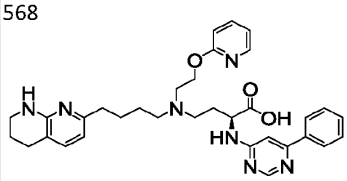
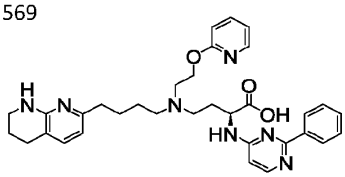
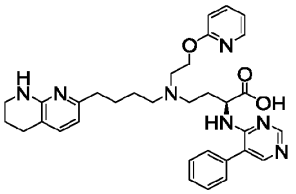
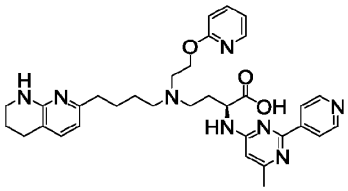
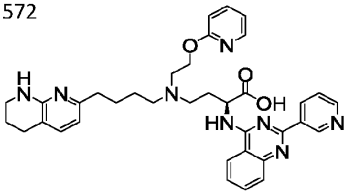
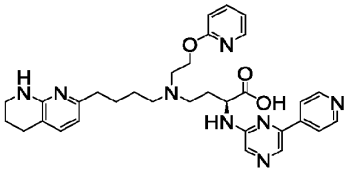
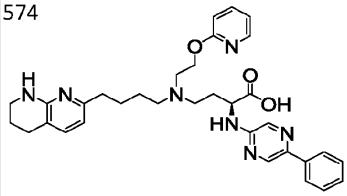
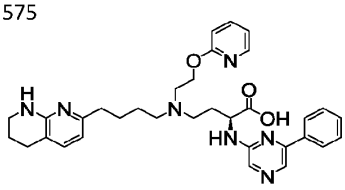
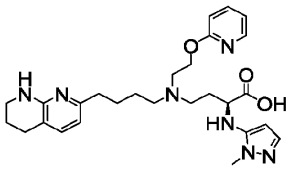
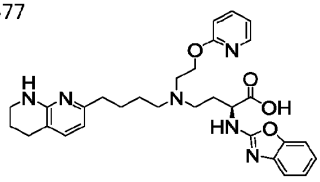
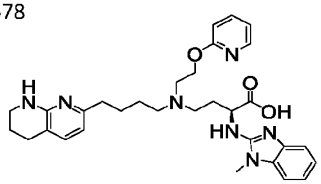
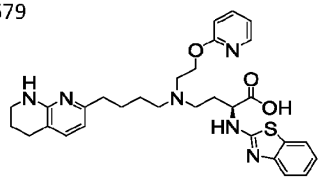
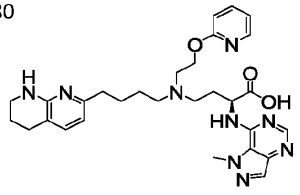
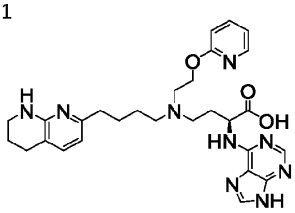
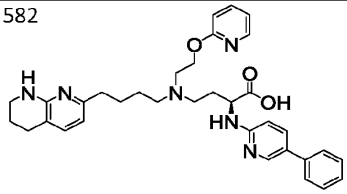
FIG. 1 (cont.)

565 	566 	567 
568 	569 	570 
571 	572 	573 
574 	575 	576 
577 	578 	579 
580 	581 	582 

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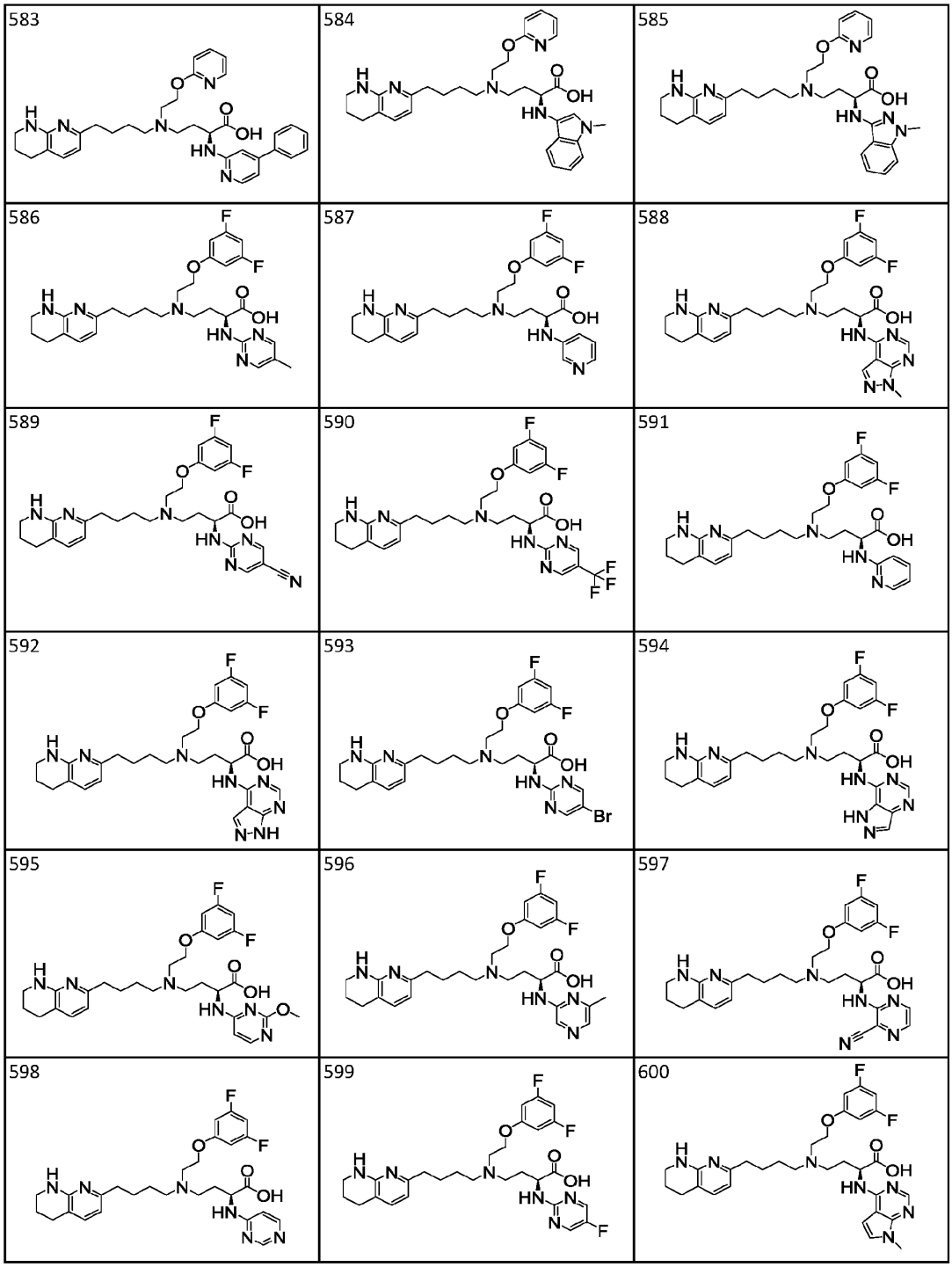
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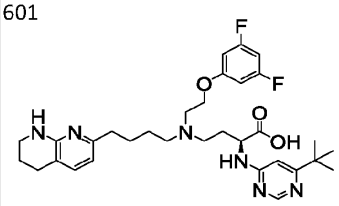
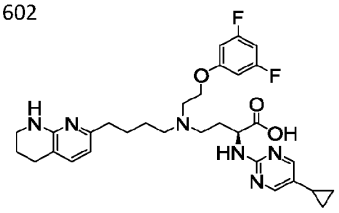
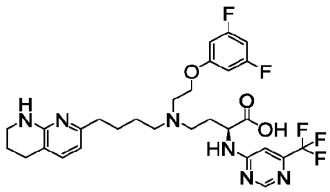
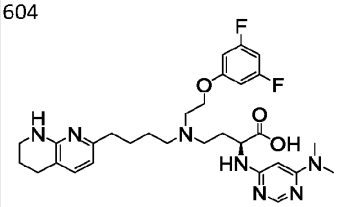
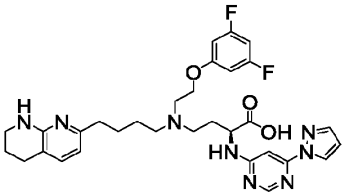
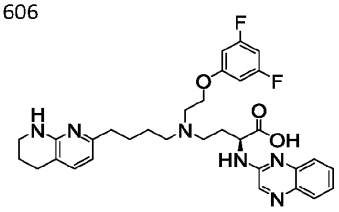
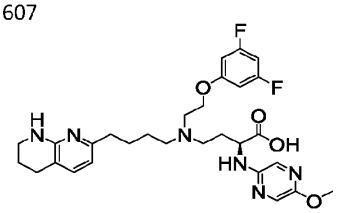
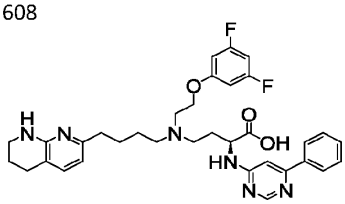
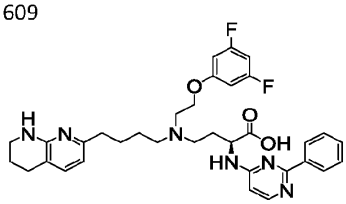
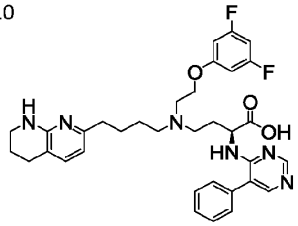
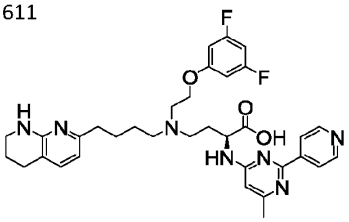
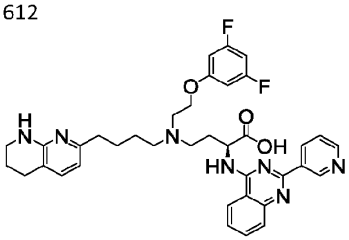
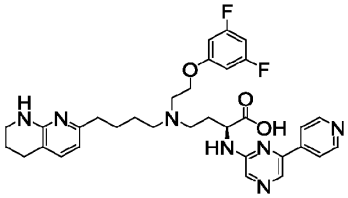
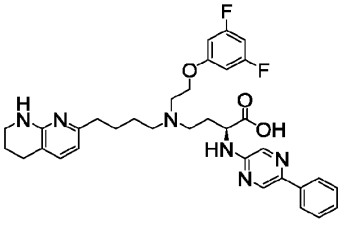
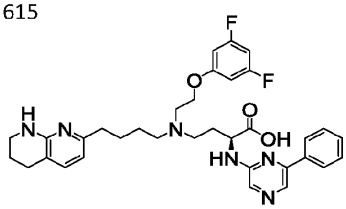
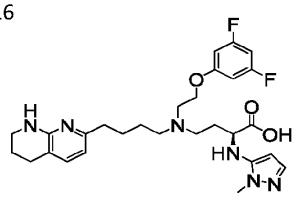
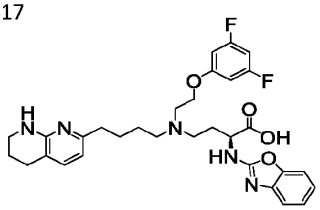
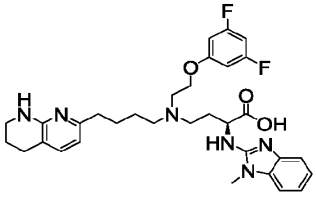
FIG. 1 (cont.)

601 	602 	603 
604 	605 	606 
607 	608 	609 
610 	611 	612 
613 	614 	615 
616 	617 	618 

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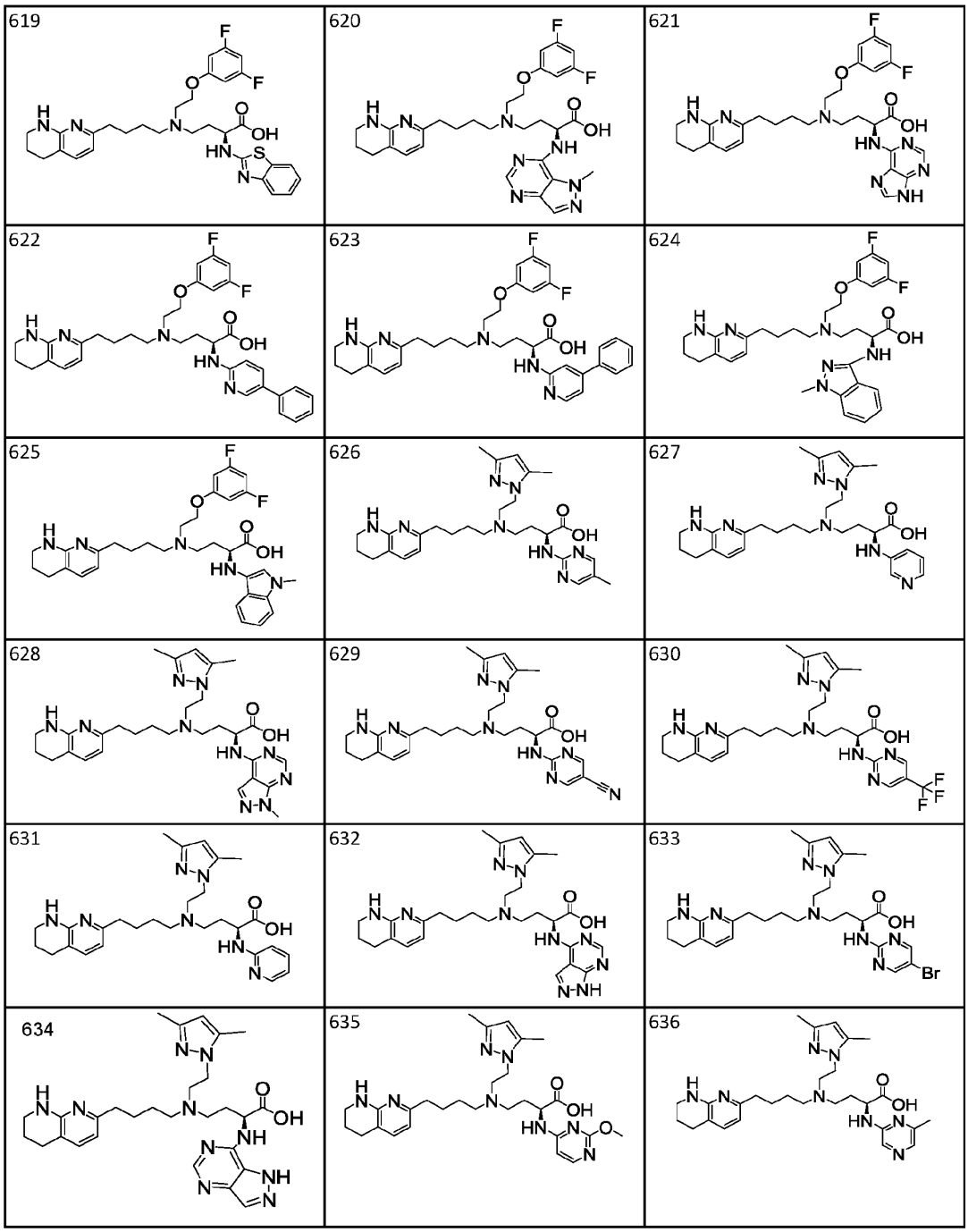
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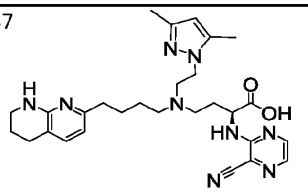
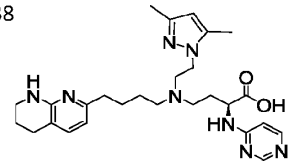
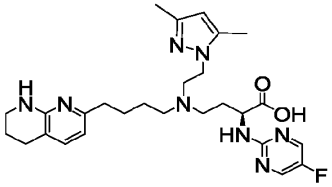
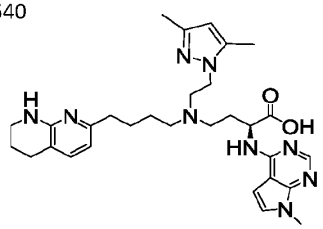
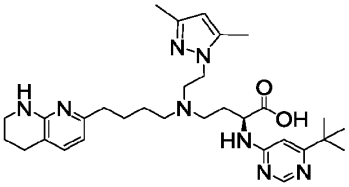
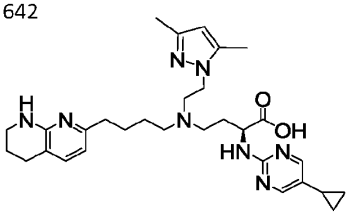
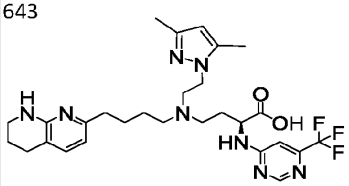
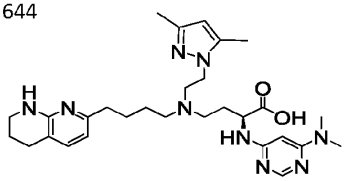
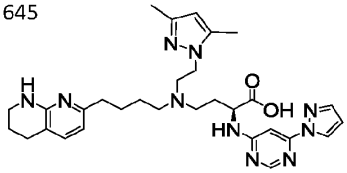
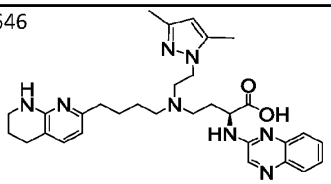
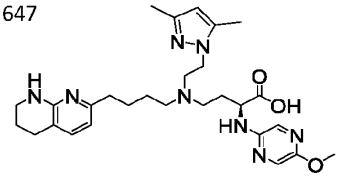
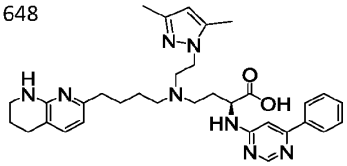
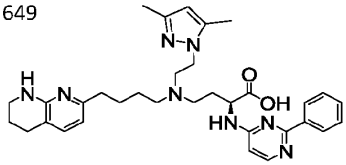
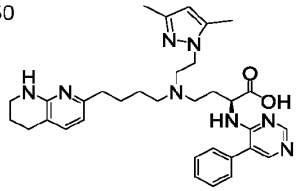
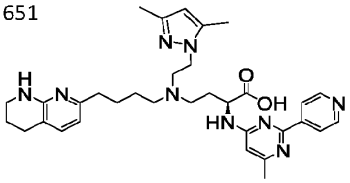
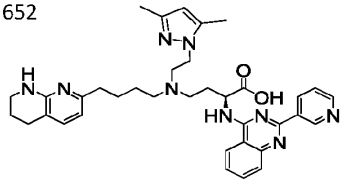
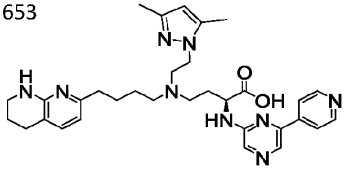
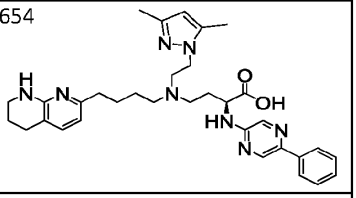
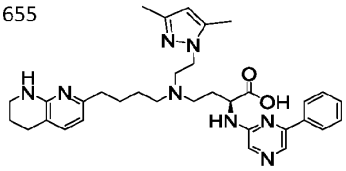
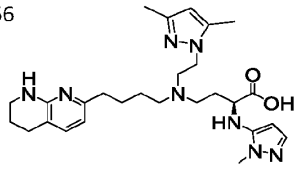
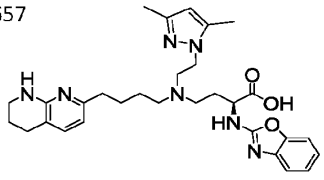
FIG. 1 (cont.)

637 	638 	639 
640 	641 	642 
643 	644 	645 
646 	647 	648 
649 	650 	651 
652 	653 	654 
655 	656 	657 

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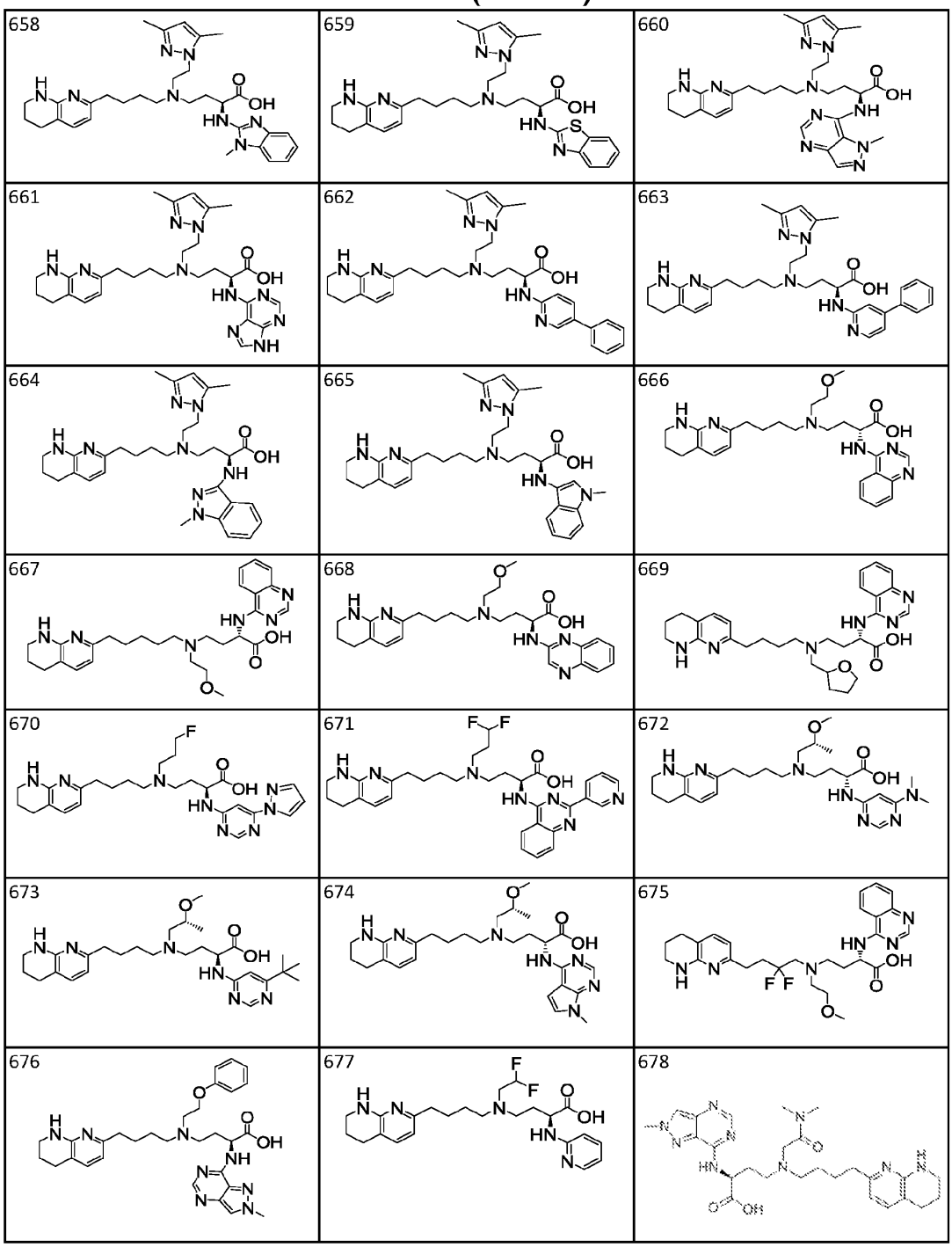
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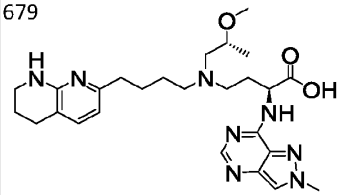
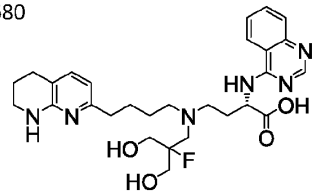
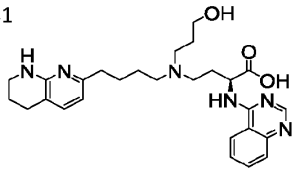
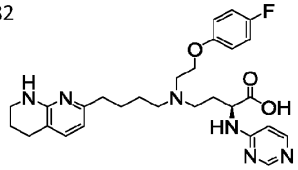
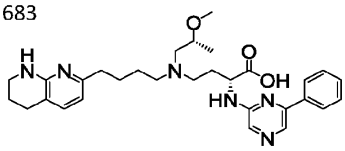
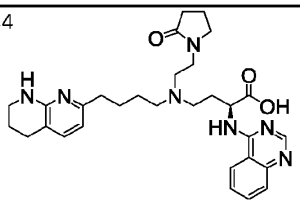
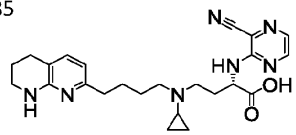
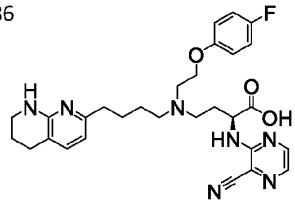
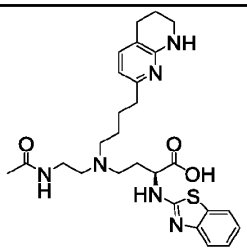
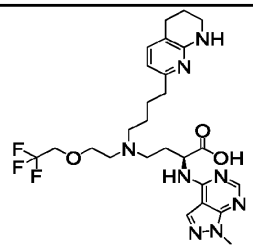
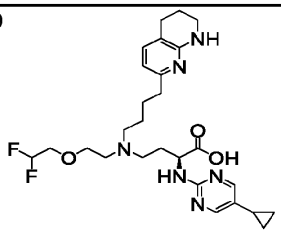
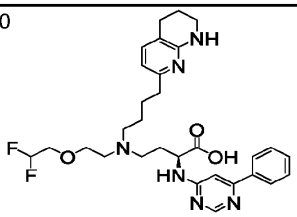
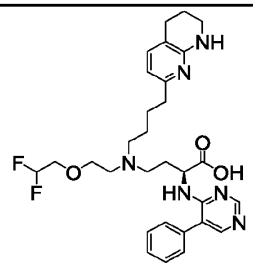
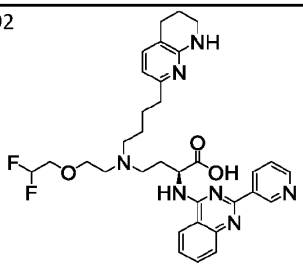
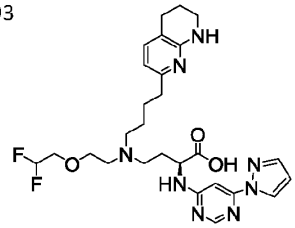
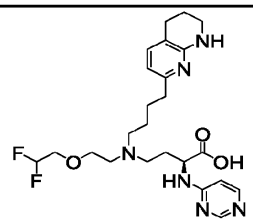
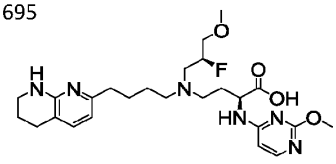
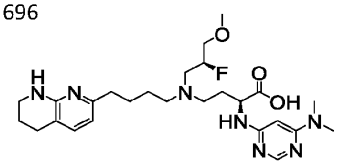
FIG. 1 (cont.)

679 	680 	681 
682 	683 	684 
685 	686 	687 
688 	689 	690 
691 	692 	693 
694 	695 	696 

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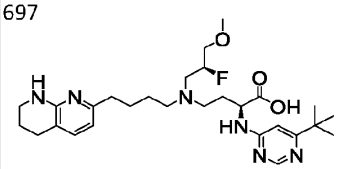
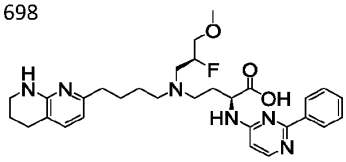
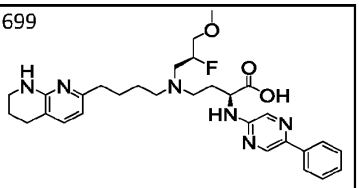
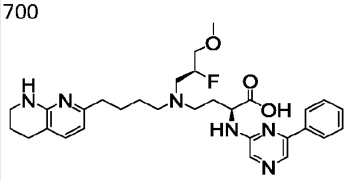
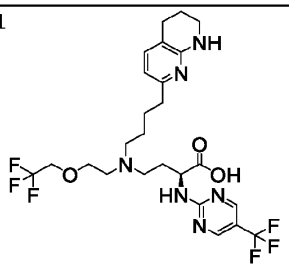
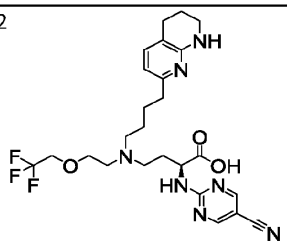
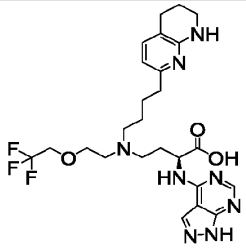
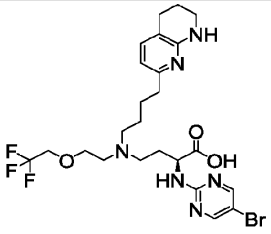
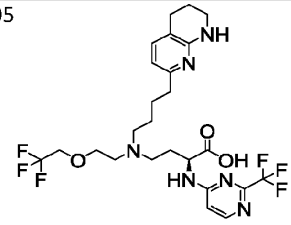
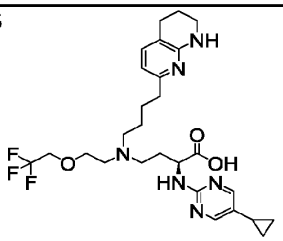
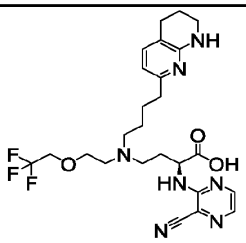
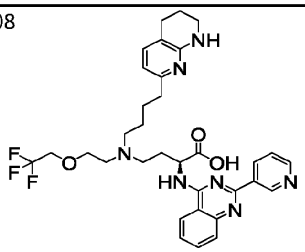
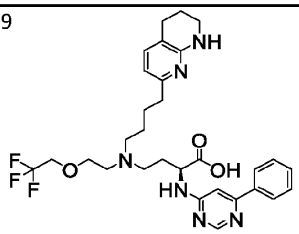
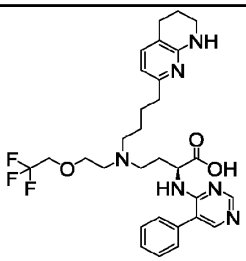
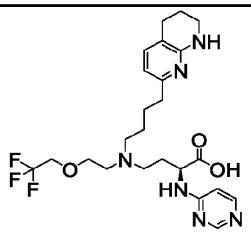
697 	698 	699 
700 	701 	702 
703 	704 	705 
706 	707 	708 
709 	710 	711 

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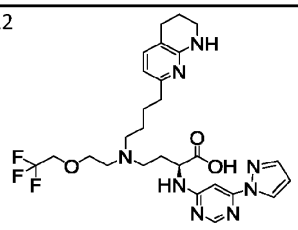
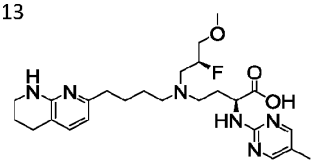
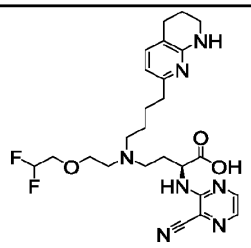
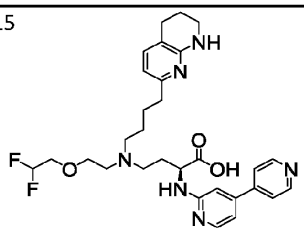
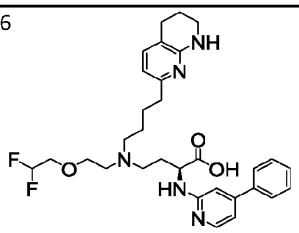
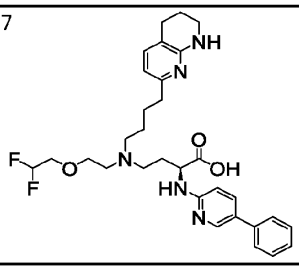
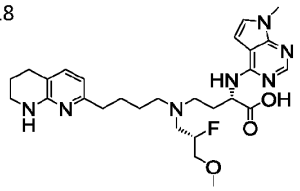
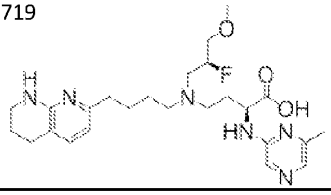
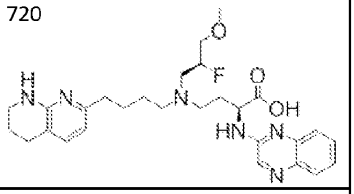
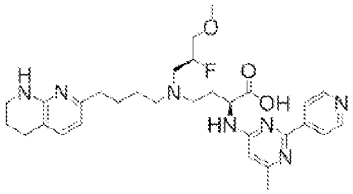
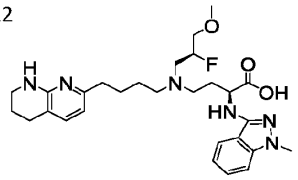
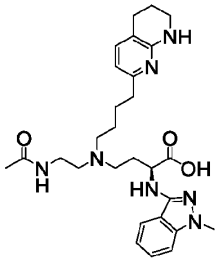
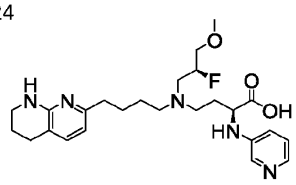
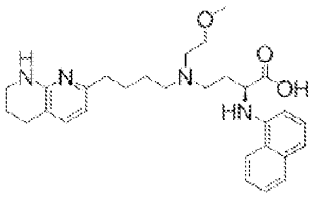
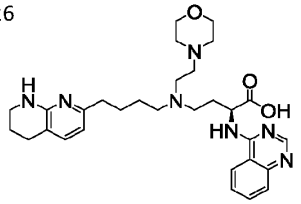
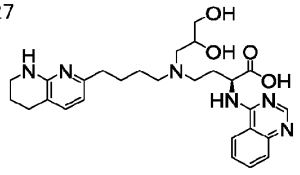
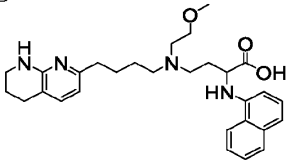
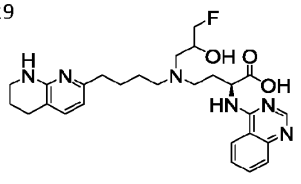
712 	713 	714 
715 	716 	717 
718 	719 	720 
721 	722 	723 
724 	725 	726 
727 	728 	729 

FIG. 1 (cont.)

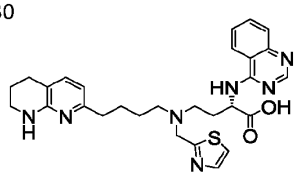
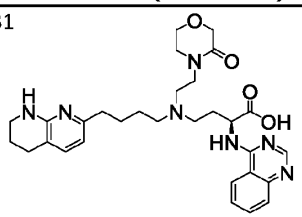
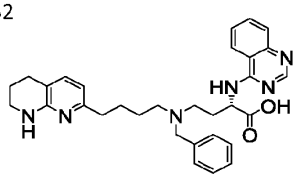
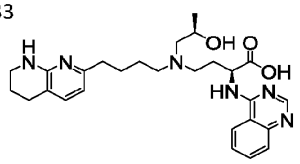
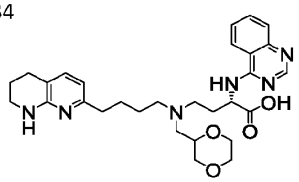
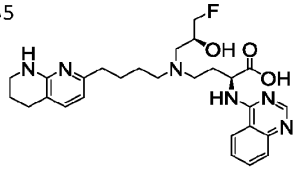
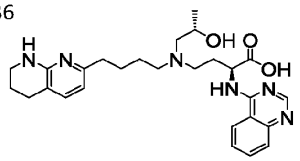
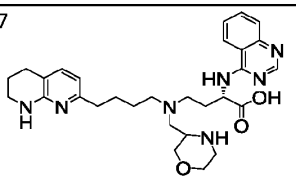
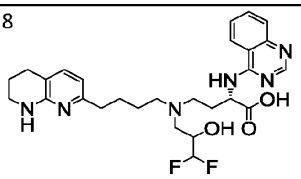
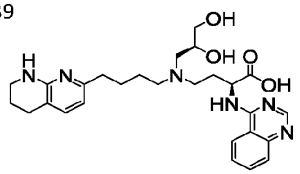
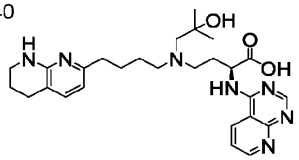
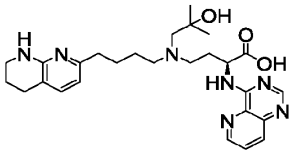
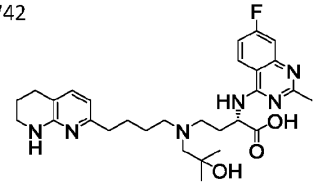
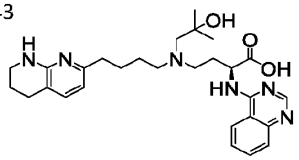
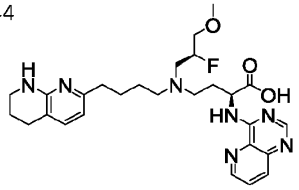
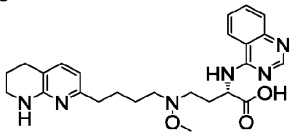
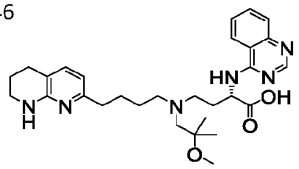
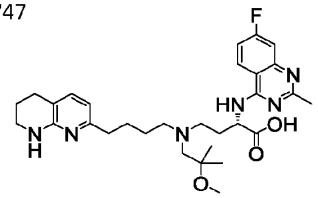
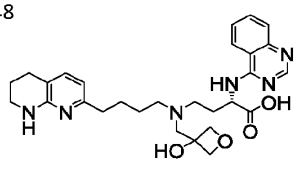
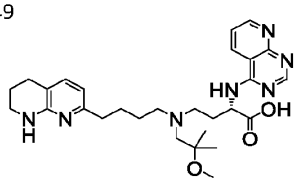
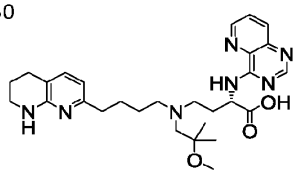
730 	731 	732 
733 	734 	735 
736 	737 	738 
739 	740 	741 
742 	743 	744 
745 	746 	747 
748 	749 	750 

FIG. 1 (cont.)

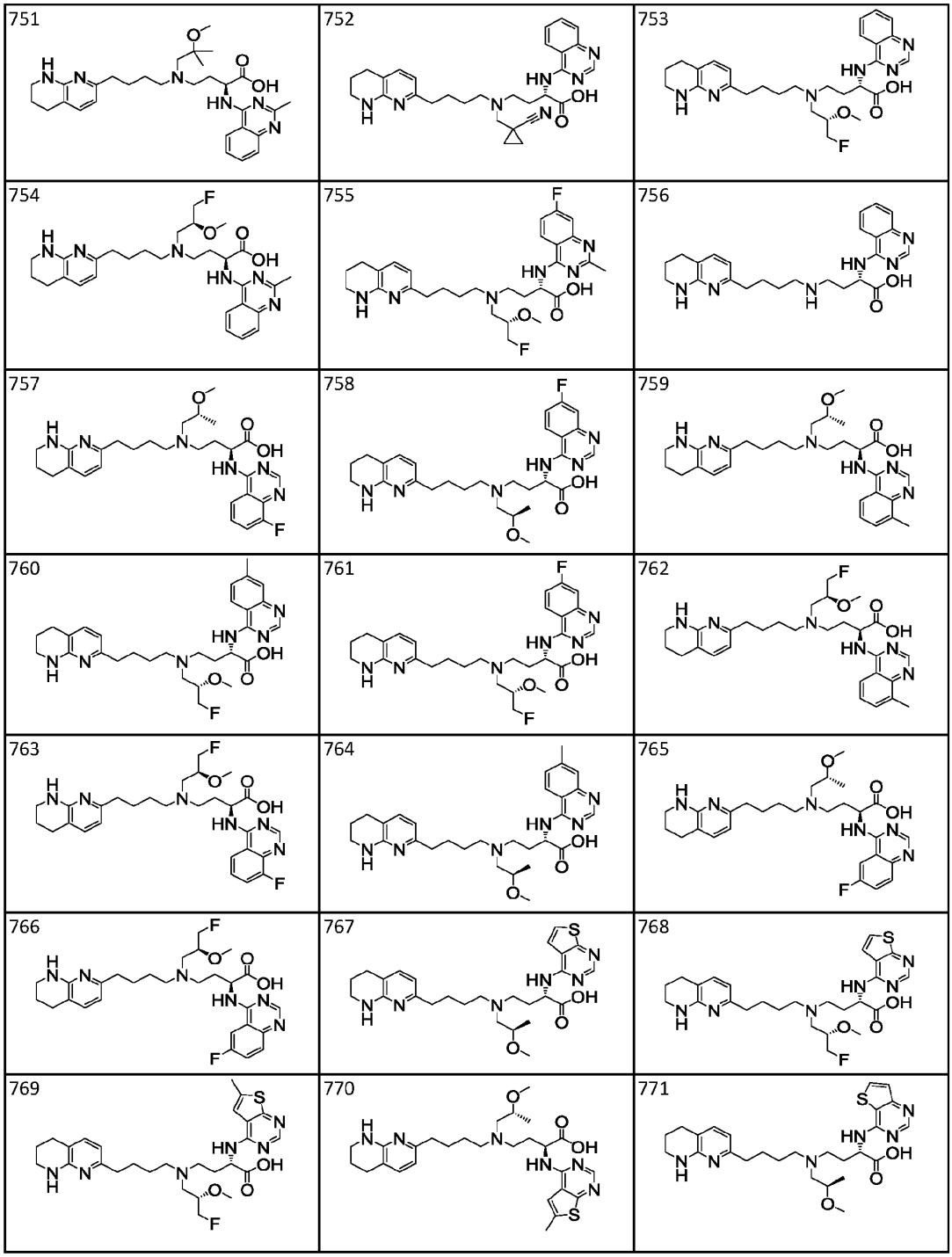

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FIG. 1 (cont.)

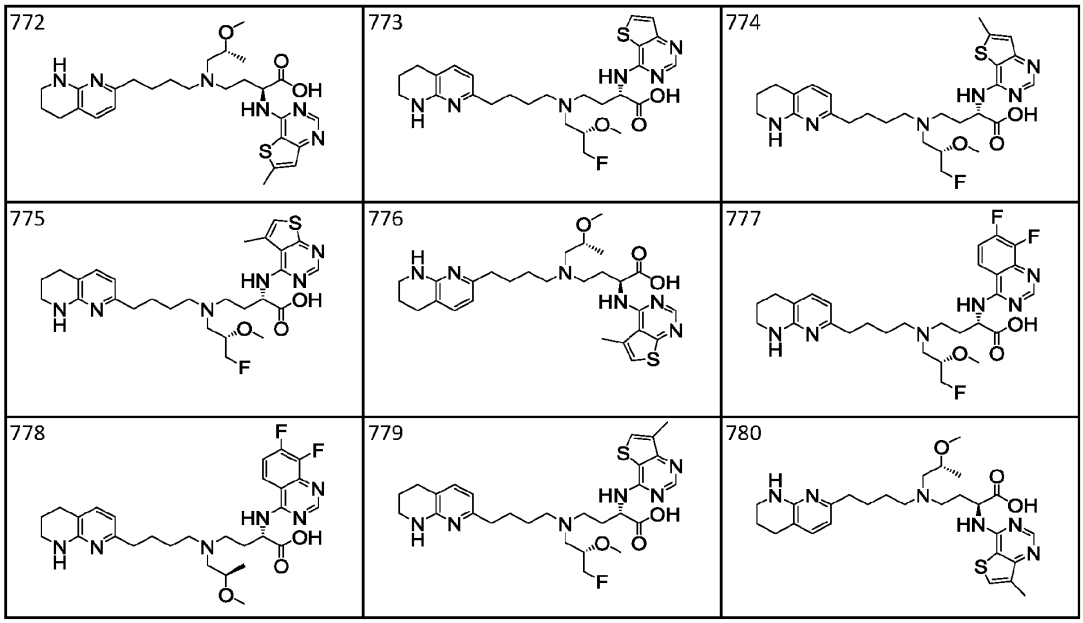


FIG. 2

Table B-3

	Solid phase assay		Proximity-based assay			Solid phase assay		Proximity-based assay	
	$\alpha v\beta_1$	$\alpha v\beta_6$	$\alpha v\beta_1$	$\alpha v\beta_6$		$\alpha v\beta_1$	$\alpha v\beta_6$	$\alpha v\beta_1$	$\alpha v\beta_6$
1	>1000	250-1000		50-250	41		<50		<50
2	>1000	250-1000		>1000	42	<50	<50		<50
3	>1000	50-250		250-1000	43		<50		
4	>1000	50-250	>1000	50-250	44	<50	<50		
5	<50	<50			45	50-250	<50		
6		50-250		<50	46		<50	<50	<50
7		<50		<50	47		<50		<50
8		50-250		<50	48		<50		<50
9		>1000		50-250	49		<50		<50
10	<50	<50			50		<50		<50
11	<50	<50		<50	51		<50		<50
12	<50	<50		<50	52		<50		<50
13		50-250		<50	53		<50	50-250	<50
14		<50		<50	54		<50		<50
15		<50		<50	55		<50		<50
16	<50	<50		<50	56		<50		<50
17		<50		<50	57		<50		<50
18		<50		<50	58		<50		<50
19		<50		<50	59		<50		<50
20		<50		<50	60		<50		<50
21		<50		<50	61		<50		<50
22	<50	<50		<50	62	<50	<50		<50
23	<50	<50		<50	63		<50	50-250	<50
24	250-1000	<50		<50	64		<50		<50
25	250-1000	<50	50-250	<50	65	<50	<50	<50	<50
26		<50		<50	66	<50	<50	<50	<50
27		<50		<50	67	<50	<50		
28	<50	<50		<50	68		<50		<50
29		<50		<50	69		<50		<50
30	50-250	<50		<50	70		<50		<50
31	50-250	<50		<50	71		<50		<50
32	50-250	<50		<50	72		<50		<50
33		<50		<50	73		<50		50-250
34		>1000		>1000	74		<50	<50	<50
35	<50	<50		<50	75		<50		<50
36		>1000		>1000	76		<50		<50
37		50-250		<50	77		<50		<50
38	<50	<50		<50	78		<50		<50
39	<50	<50		<50	79		<50	<50	<50
40	<50	<50		<50	80		<50		<50

FIG. 2 (cont.)

	Solid phase assay		Proximity-based assay			Solid phase assay		Proximity-based assay	
	$\alpha v\beta_1$	$\alpha v\beta_6$	$\alpha v\beta_1$	$\alpha v\beta_6$		$\alpha v\beta_1$	$\alpha v\beta_6$	$\alpha v\beta_1$	$\alpha v\beta_6$
81		<50		<50	121		>1000		>1000
82		<50		<50	122		250-1000		250-1000
83		<50		<50	123		<50		<50
84		250-1000		50-250	124		<50		<50
85		250-1000		<50	125		50-250		<50
86		50-250		50-250	126		>1000		250-1000
87		250-1000		50-250	127		250-1000		50-250
88		>1000		>1000	128		>1000		50-250
89		<50		<50	129		<50	<50	<50
90		<50		<50	130		<50		<50
91		<50		<50	131		50-250		50-250
92		<50			132		50-250		50-250
93		<50			133		50-250		<50
94		<50			134		50-250		250-1000
95		>1000		>1000	135		50-250		50-250
96		>1000		>1000	136		<50		<50
97		>1000		>1000	137		<50		50-250
98		>1000		>1000	138		<50		<50
99		250-1000		250-1000	139		<50		<50
100		<50		<50	140		<50		<50
101		50-250		50-250	141		50-250		50-250
102		>1000		250-1000	142		>1000		
103		>1000		250-1000	143		50-250		
104		>1000		250-1000	144		50-250		
105		<50		<50	145		<50		50-250
106		<50		<50	146		>1000		>1000
107		250-1000		<50	147		50-250		<50
108		>1000		250-1000	149		50-250		250-1000
109		<50		<50	152		>1000		250-1000
110		<50		<50	154		>1000		250-1000
111		<50		<50	156		50-250		250-1000
112		250-1000		250-1000	158		>1000		250-1000
113		250-1000		50-250	159		>1000		50-250
114		<50		250-1000	162		<50		<50
115		50-250		250-1000	163		>1000		50-250
116		50-250		50-250	172		>1000		250-1000
117		<50		<50	178		>1000		250-1000
118		>1000		>1000	181	>1000	>1000		>1000
119		>1000			182	>1000	>1000		>1000
120	>1000	>1000		>1000	183	>1000	>1000		>1000

FIG. 2 (cont.)

	Solid phase assay		Proximity-based assay			Solid phase assay		Proximity-based assay	
	$\alpha v\beta_1$	$\alpha v\beta_6$	$\alpha v\beta_1$	$\alpha v\beta_6$		$\alpha v\beta_1$	$\alpha v\beta_6$	$\alpha v\beta_1$	$\alpha v\beta_6$
185	>1000	>1000		>1000	264	250-1000	>1000		50-250
186	>1000	>1000		>1000	266	>1000	50-250		50-250
187	>1000	>1000		>1000	267		<50		
188	>1000	>1000		>1000	268		50-250		<50
190	>1000	>1000		>1000	269	<50	50-250		<50
191	>1000	>1000		>1000	270		<50		
192	>1000	>1000		50-250	272		250-1000		
193	>1000	>1000		>1000	273		50-250		
194	>1000	>1000		>1000	278		<50		<50
195		<50		<50	282		>1000		
196		>1000		50-250	284		<50		50-250
200		<50		<50	287	250-1000	250-1000		50-250
204	<50	<50		<50	288	50-250	<50		50-250
205		<50		<50	302		<50		<50
209		50-250		50-250	309		50-250		<50
210		<50			310		<50		<50
213		>1000		50-250	311		<50		<50
215		<50		<50	312	<50	50-250		<50
220		<50		<50	313	<50	<50		<50
222		50-250		<50	314		50-250		<50
224		>1000		50-250	315		<50		<50
228	<50	<50		<50	316		<50		<50
229		<50		<50	317	<50	<50		<50
230		<50		<50	318		<50		<50
231		<50		<50	319		<50		<50
232		<50		<50	320		<50		<50
233	>1000	>1000		>1000	321	<50	50-250		<50
236		<50			322	>1000	50-250		<50
243	250-1000	>1000		250-1000	323	<50	<50		<50
246	>1000	250-1000		50-250	324	<50	<50		<50
248		<50		<50	325	<50	<50		<50
250	>1000	50-250		50-250	326	<50	<50		<50
253		50-250		<50	327	<50	<50		<50
254	<50	<50		50-250	328	250-1000	50-250		<50
255		<50		<50	329	<50	<50		<50
256	>1000	50-250		<50	330	>1000	50-250		<50
257		50-250		50-250	332		50-250		<50
258		>1000		50-250	334		50-250		<50
261	>1000	>1000		50-250	335		<50		<50
263		<50		<50	336		50-250		<50

FIG. 2 (cont.)

	Solid phase assay		Proximity-based assay			Solid phase assay		Proximity-based assay	
	$\alpha v\beta_1$	$\alpha v\beta_6$	$\alpha v\beta_1$	$\alpha v\beta_6$		$\alpha v\beta_1$	$\alpha v\beta_6$	$\alpha v\beta_1$	$\alpha v\beta_6$
340	>1000	50-250		<50	677		>1000		250-1000
341	>1000	>1000		<50	678		<50		<50
342		50-250		250-1000	679		<50		<50
343		50-250		<50	680			>1000	<50
344	250-1000	<50		<50	681			<50	<50
345	50-250	50-250		<50	682	<50	<50	<50	<50
346		250-1000		<50	683	50-250	<50		
347	50-250	>1000		<50	684	250-1000	<50		<50
348	>1000	250-1000		50-250	685	250-1000	>1000		250-1000
349	250-1000	50-250		<50	686	<50	<50		<50
350	>1000	>1000		250-1000	687	>1000	>1000		<50
352	>1000	>1000		<50	688	<50	<50		<50
353	>1000	>1000		50-250	689	<50	<50		<50
354		<50	<50	<50	690	<50	50-250		<50
357	>1000	>1000		50-250	691	<50	<50		<50
360	>1000	<50		<50	692	>1000	50-250		<50
362	>1000	>1000		50-250	693	50-250	50-250		<50
364		<50		<50	694	<50	<50		<50
365		50-250		50-250	695	250-1000	50-250		50-250
369		50-250		<50	696	50-250	50-250		50-250
371		50-250		50-250	697	50-250	50-250		<50
372		50-250		<50	698	250-1000	>1000		50-250
375		<50		<50	699	>1000	>1000		50-250
377		<50		<50	700	>1000	250-1000		50-250
379	<50	<50		<50	701	<50	<50		<50
381	<50	<50	<50	<50	702	50-250	<50		<50
382	<50	<50		<50	703	<50	<50		<50
383	<50	<50		<50	704	<50	<50		<50
384	>1000	250-1000		50-250	705	>1000	50-250		250-1000
666	50-250	<50			706	<50	<50		<50
667	50-250	<50			707	<50	<50		
668	<50	<50		<50	708	>1000	<50		
669	<50	<50	<50	<50	709	<50	<50		
670	>1000	50-250		<50	710	<50	<50	<50	<50
671	250-1000	50-250		<50	711	<50	<50	50-250	<50
672		<50			712	50-250	<50	50-250	<50
673		<50		<50	713	250-1000	<50	250-1000	50-250
674		<50			714	<50	<50	<50	<50
675	>1000	>1000		>1000	715	<50	<50	<50	<50
676		<50		<50	716	<50	50-250	50-250	<50

FIG. 2 (cont.)

	Solid phase assay		Proximity-based assay	
	$\alpha v\beta_1$	$\alpha v\beta_6$	$\alpha v\beta_1$	$\alpha v\beta_6$
717	<50	<50	50-250	<50
718	<50	<50	<50	<50
719	>1000	<50	250-1000	50-250
720	250-1000	<50	250-1000	<50
721	250-1000	<50	50-250	50-250
722	>1000	50-250	>1000	250-1000
723	>1000	50-250	>1000	<50
724	>1000	250-1000	>1000	250-1000
725	>1000	250-1000	250-1000	50-250
726	50-250	<50	50-250	<50
727	<50	<50		<50
728			>1000	50-250
729			<50	<50
730			250-1000	50-250
731			250-1000	<50
732			250-1000	<50
733			<50	<50
734			<50	<50
735			<50	<50
736			<50	<50
737			>1000	50-250
738			50-250	<50
739			<50	<50
740			250-1000	<50
741			250-1000	<50
742			50-250	<50
743				
744				
745			50-250	50-250
746			50-250	<50
747			50-250	<50
748			<50	<50
749			50-250	<50
750			250-1000	<50
751			50-250	<50
752			50-250	<50
753			<50	<50
754			<50	<50
755			<50	<50
756				

	Solid phase assay		Proximity-based assay	
	$\alpha v\beta_1$	$\alpha v\beta_6$	$\alpha v\beta_1$	$\alpha v\beta_6$
757			<50	<50
758			<50	<50
759			<50	<50
760			<50	<50
761			<50	<50
762			<50	<50
763			<50	<50
764			<50	<50
765			<50	<50
766			<50	<50
767			<50	<50
768			<50	<50
769			50-250	<50
770			<50	<50
771			<50	<50
772			<50	<50
773			<50	<50
774			<50	<50
775			<50	<50
776			<50	<50
777			<50	<50
778			<50	<50
779			<50	<50
780			<50	<50

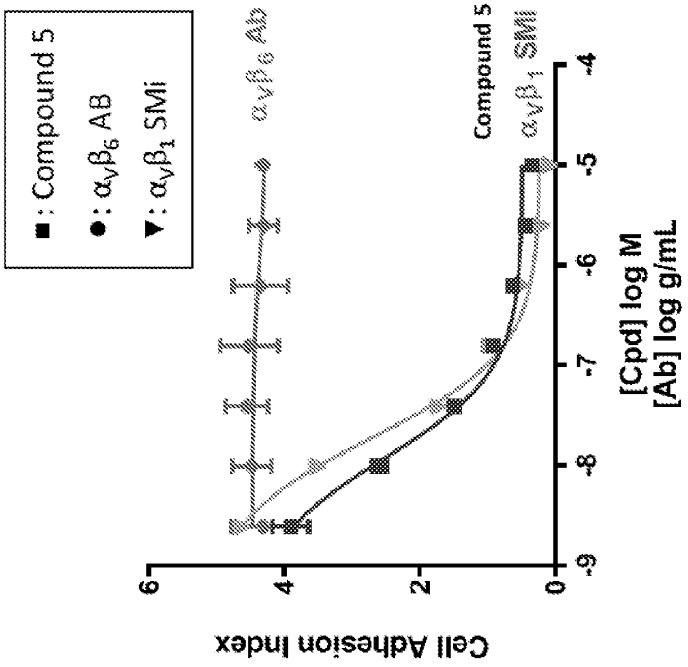

■: Compound 5
●: $\alpha_v\beta_6$ AB
▼: $\alpha_v\beta_1$ SMi
$\alpha_v\beta_6$ Ab
Compound 5
$\alpha_v\beta_1$ SMi
Cell Adhesion Index
[Cpd] log M
[Ab] log g/mL

FIG. 3B

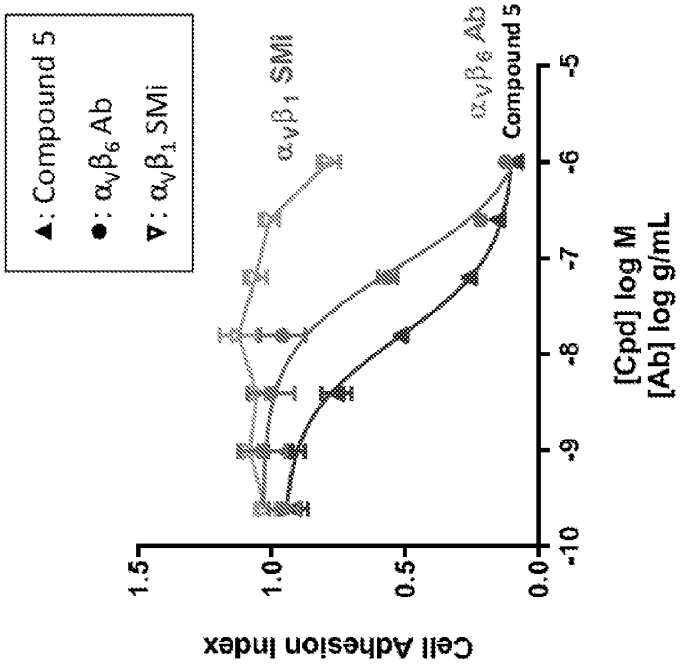

▲: Compound 5
●: $\alpha_v\beta_6$ Ab
▼: $\alpha_v\beta_1$ SMi
$\alpha_v\beta_1$ SMi
$\alpha_v\beta_6$ Ab
Compound 5
Cell Adhesion Index
[Cpd] log M
[Ab] log g/mL

FIG. 3A

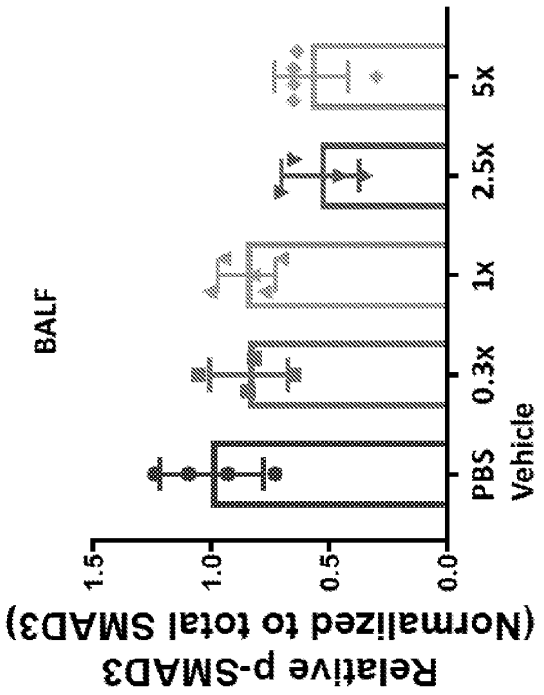

BALF
Relative p-SMAD3
(Normalized to total SMAD3)
1.5
1.0
0.5
0.0
PBS
Vehicle
0.3x
1x
2.5x
5x

FIG. 4B

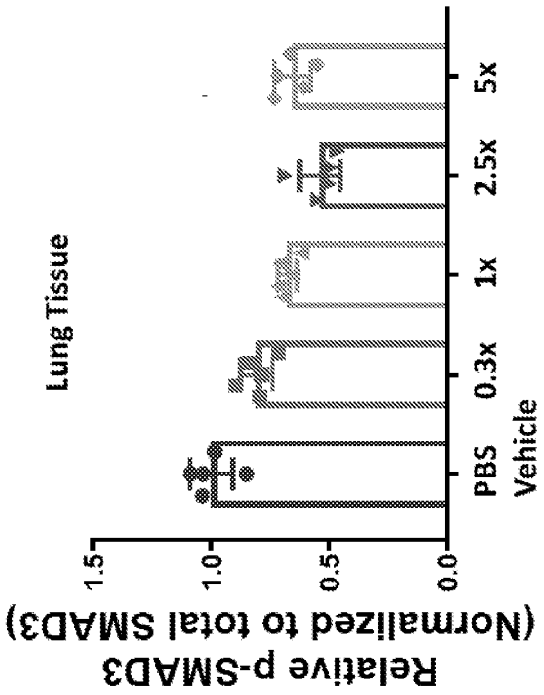

Lung Tissue
Relative p-SMAD3
(Normalized to total SMAD3)
1.5
1.0
0.5
0.0
PBS
Vehicle
0.3x
1x
2.5x
5x

FIG. 4A

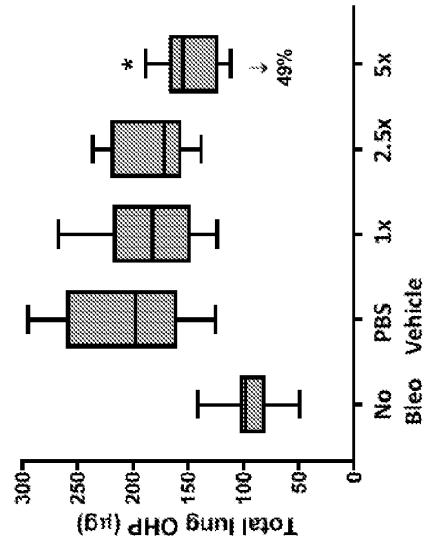


FIG. 4E

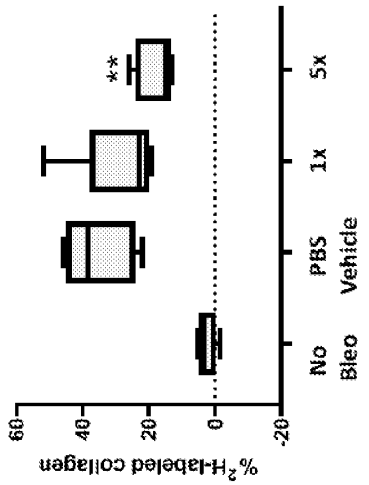


FIG. 4D

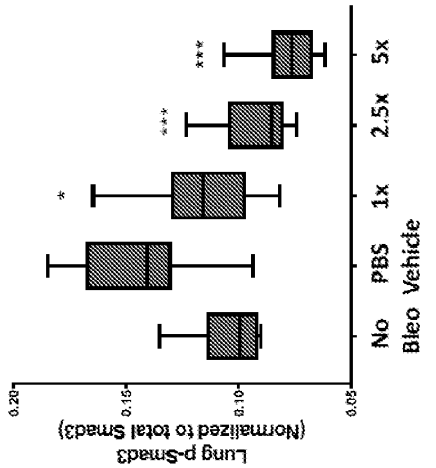


FIG. 4C

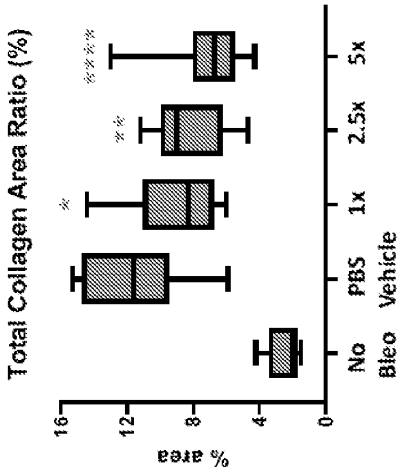


FIG. 4I

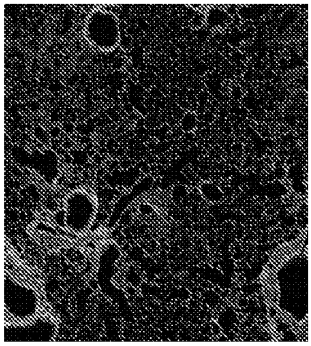


FIG. 4H

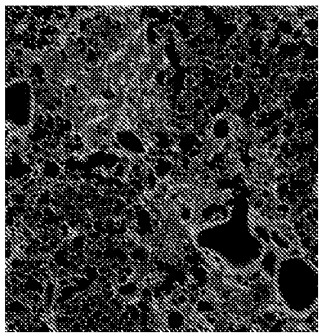


FIG. 4G

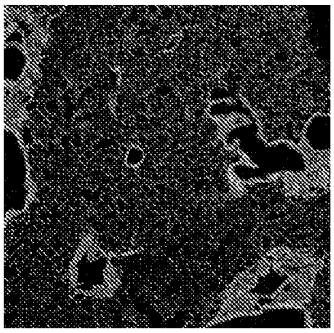


FIG. 4F

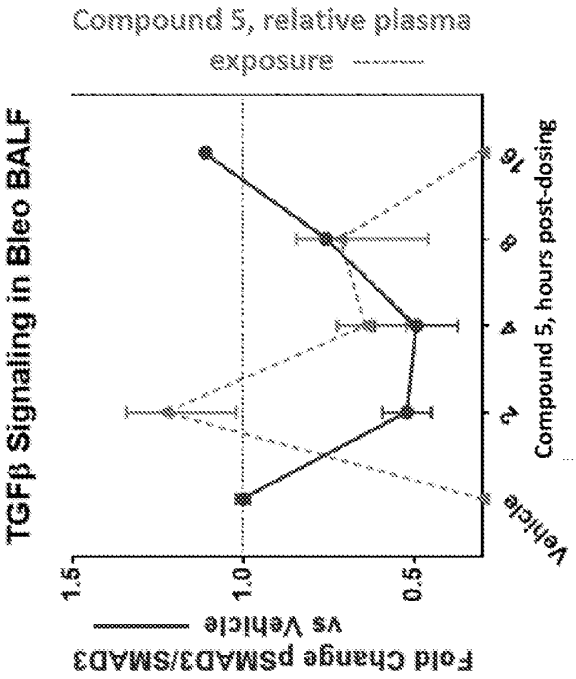

TGFβ Signaling in Bleo BALF
Compound 5, relative plasma exposure
Fold Change pSMAD3/SMAD3 vs Vehicle
1.5
1.0
0.5
Vehicle
2
4
8
16
Compound 5, hours post-dosing

FIG. 4K

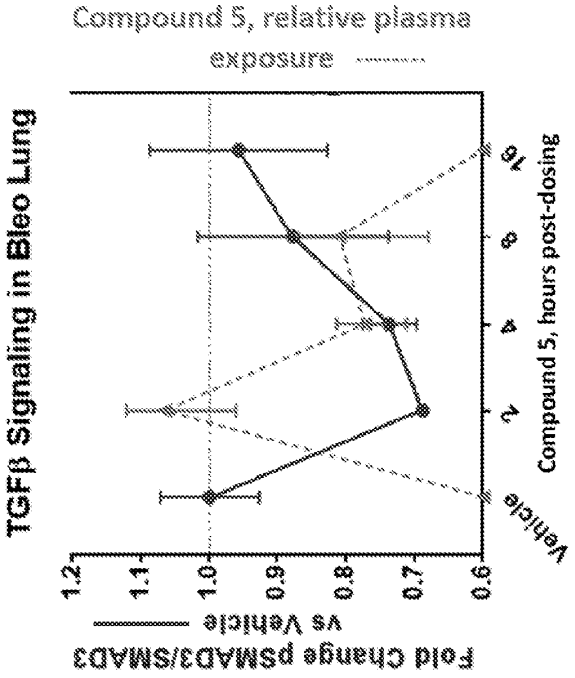

TGFβ Signaling in Bleo Lung
Compound 5, relative plasma exposure
Fold Change pSMAD3/SMAD3 vs Vehicle
1.2
1.1
1.0
0.9
0.8
0.7
0.6
Vehicle
2
4
8
16
Compound 5, hours post-dosing

FIG. 4J

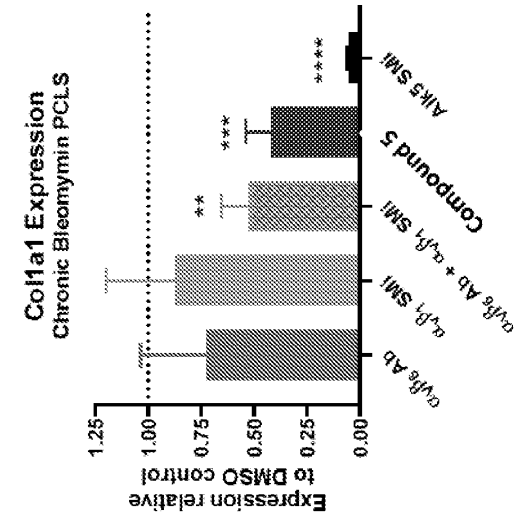

Col1a1 Expression
Chronic Bleomymin PCLS
Expression relative to DMSO control
1.25
1.00
0.75
0.50
0.25
0.00
**
**
***
****
αvβ6 Ab
αvβ1 SMI
αvβ6 Ab + αvβ1 SMI
Compound 5
AIK5 SMI

FIG. 5B

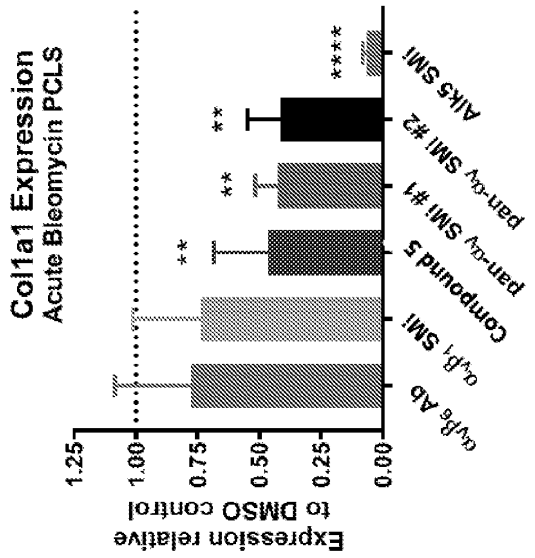

Col1a1 Expression
Acute Bleomycin PCLS
Expression relative to DMSO control
1.25
1.00
0.75
0.50
0.25
0.00
**
**
**
****
αvβ6 Ab
αvβ1 SMI
Compound 5
pan-αv SMI #1
pan-αv SMI #2
AIK5 SMI

FIG. 5A

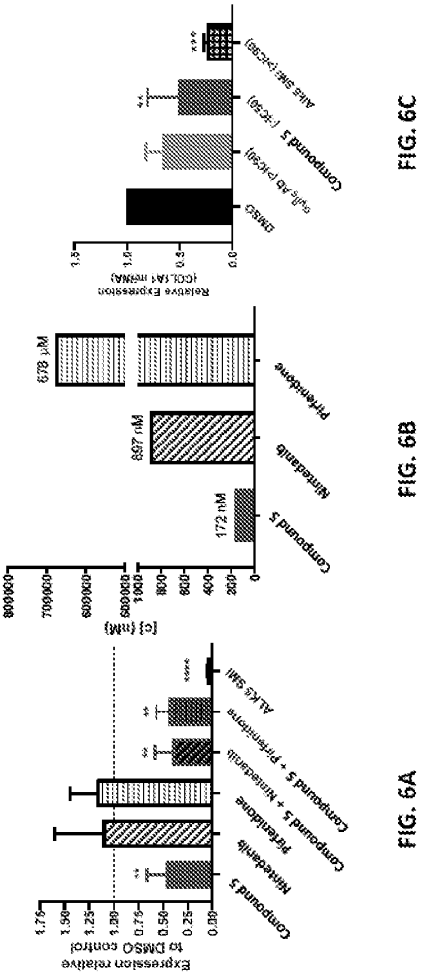


FIG. 6A

FIG. 6B

FIG. 6C

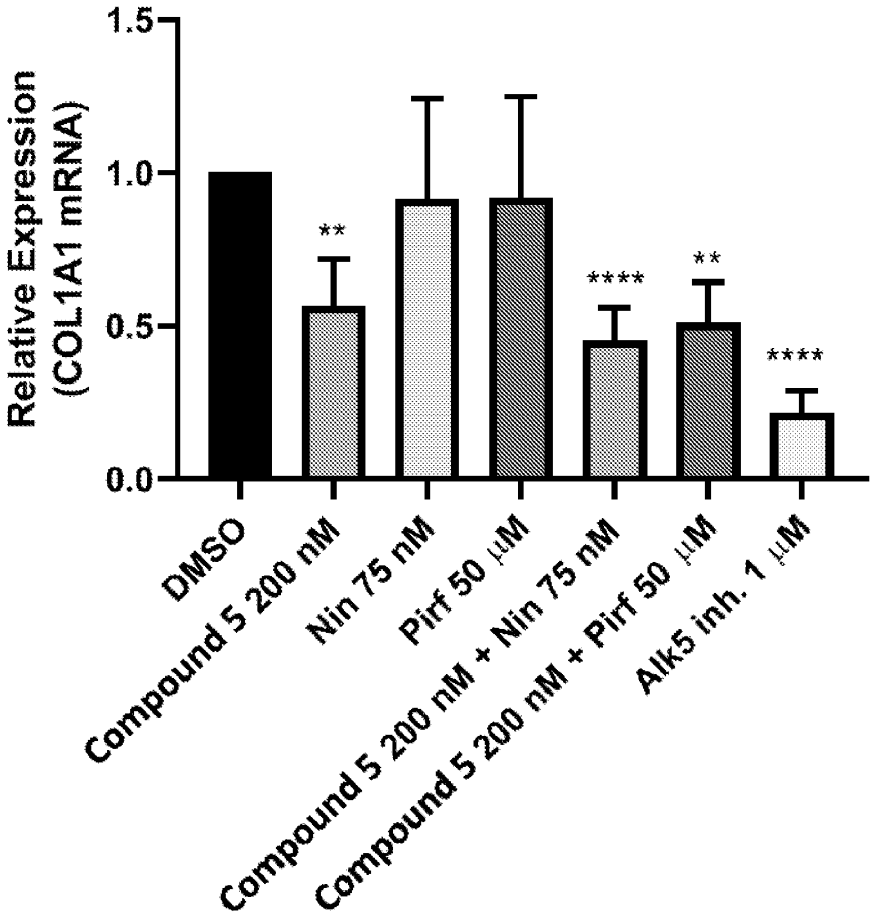

Relative Expression
(COL1A1 mRNA)
1.5
1.0
0.5
0.0
**
****
**
****
DMSO
Compound 5 200 nM
Nin 75 nM
Pirf 50 μM
Compound 5 200 nM + Nin 75 nM
Compound 5 200 nM + Pirf 50 μM
Alk5 inh. 1 μM

FIG. 6D

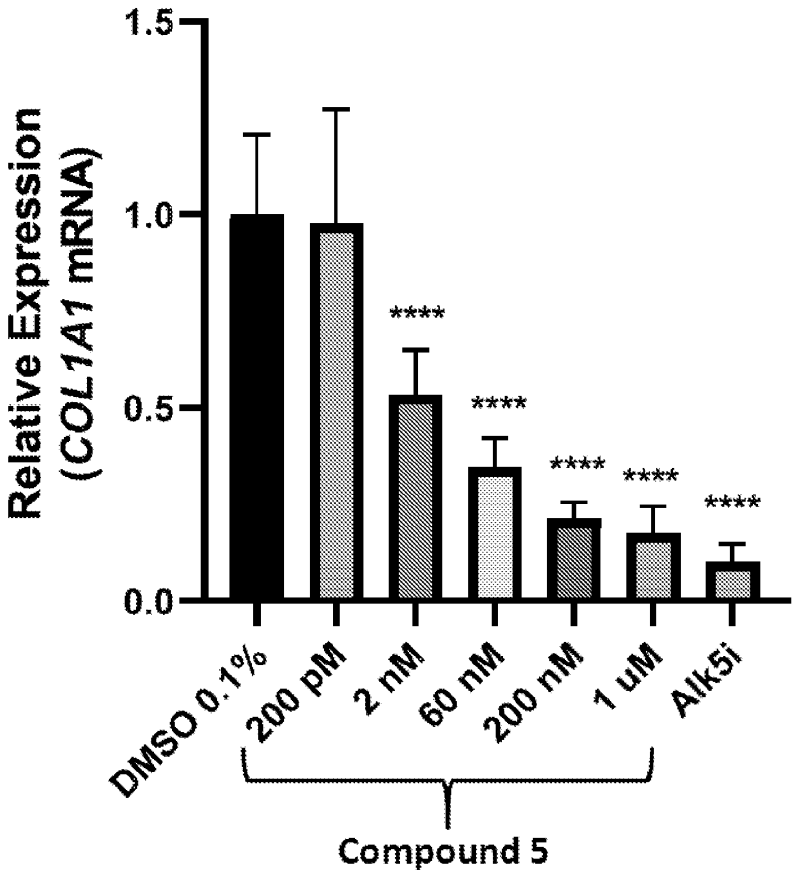

Relative Expression
(COL1A1 mRNA)
1.5
1.0
0.5
0.0
****
****
****
****
****
DMSO 0.1%
200 pM
2 nM
60 nM
200 nM
1 uM
Alk5i
Compound 5

FIG. 6E

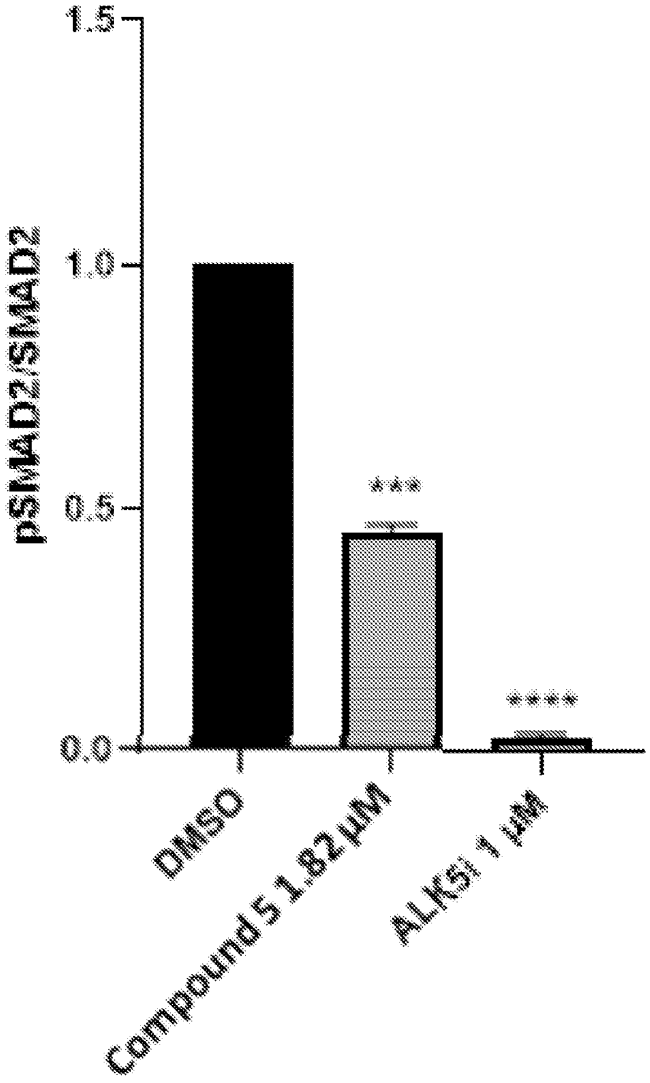


FIG. 6F

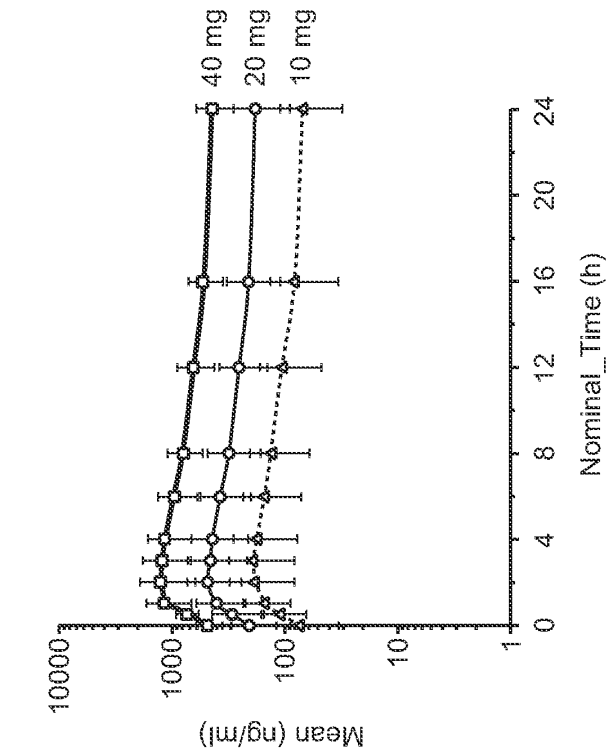
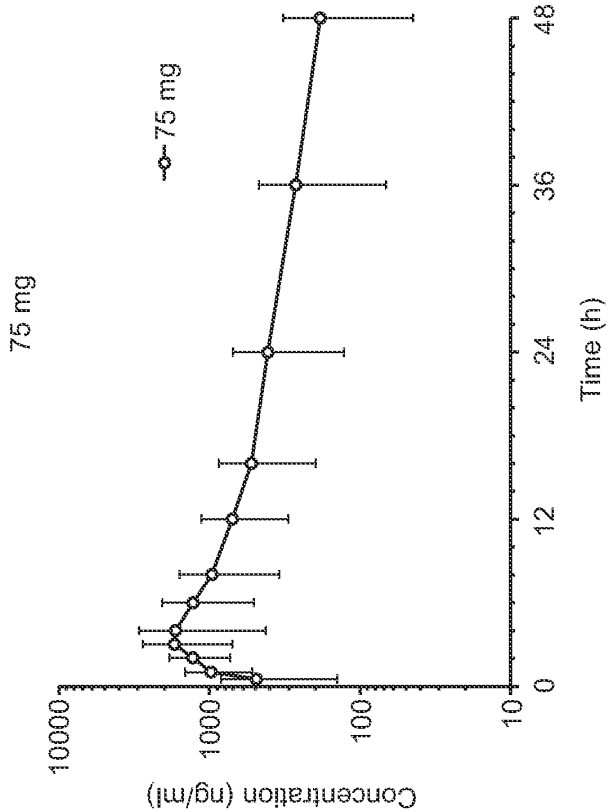


FIG. 7B



Parameter	75 mg
Tmax (h)	2.9±1.0 (34%)
Cmax (ng/mL)	1869±1241 (66%)
AUC0-24 (ng.h/mL)	19653±10860 (55%)
AUC0-48 (ng.h/mL)	22464±15679 (59%)
Thalf (h)	20.0±3.6 (18%)

FIG. 7A

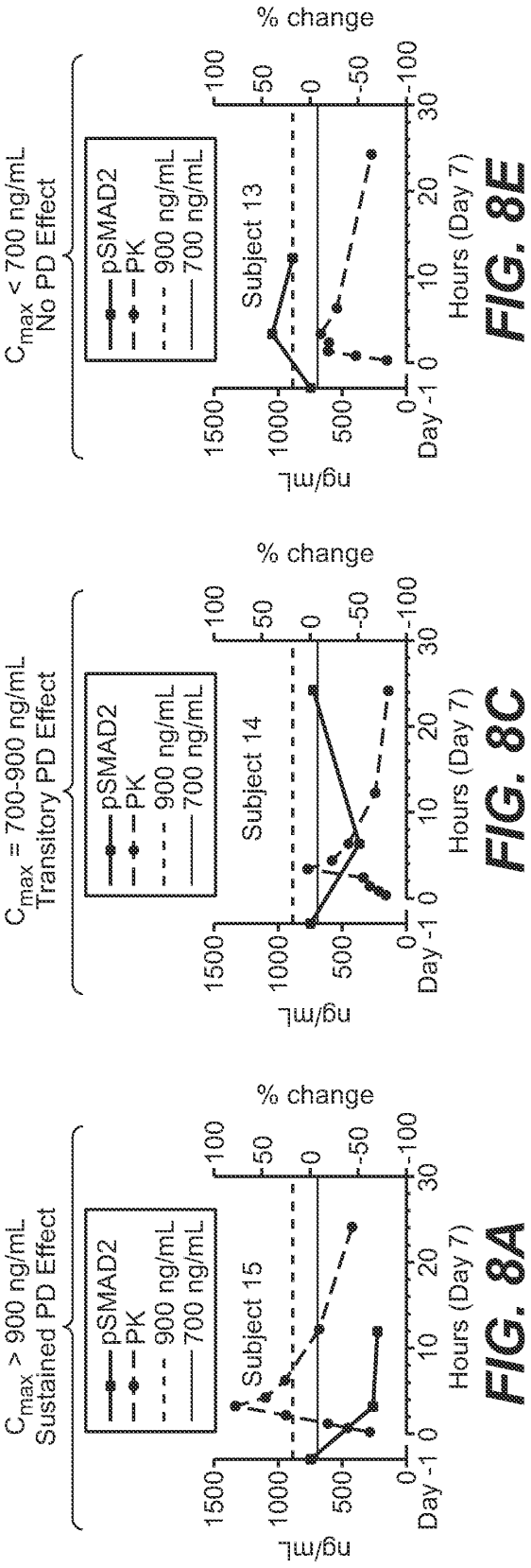


FIG. 8A

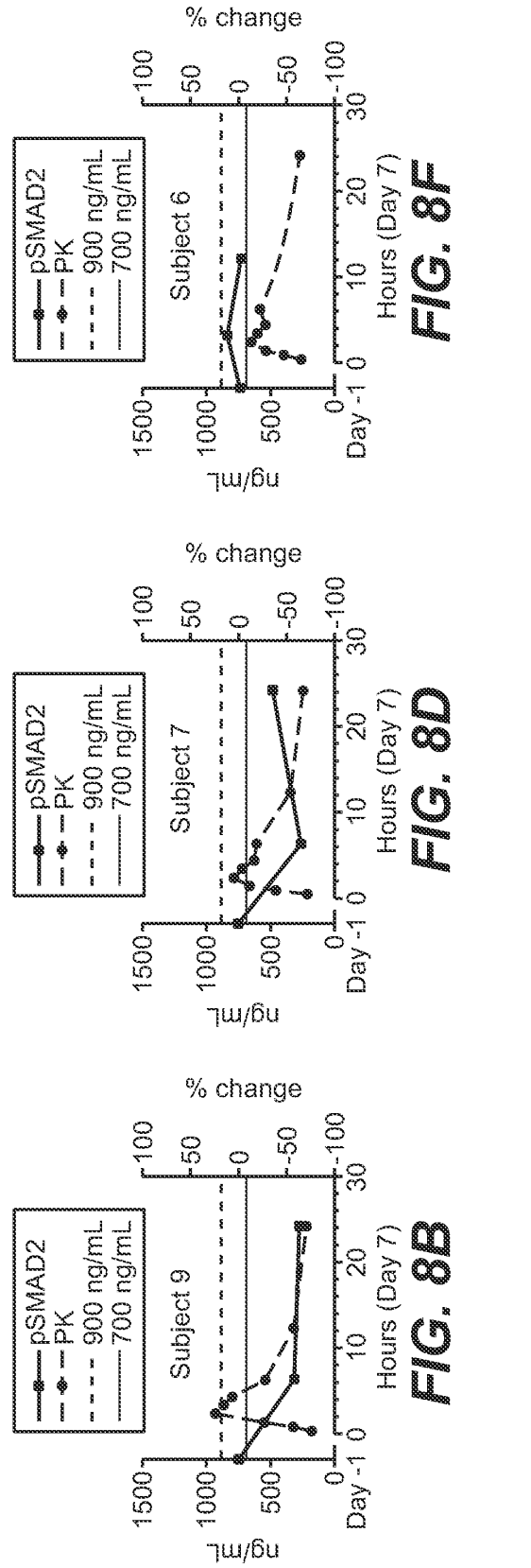


FIG. 8B

FIG. 8C

FIG. 8D

FIG. 8E

FIG. 8F

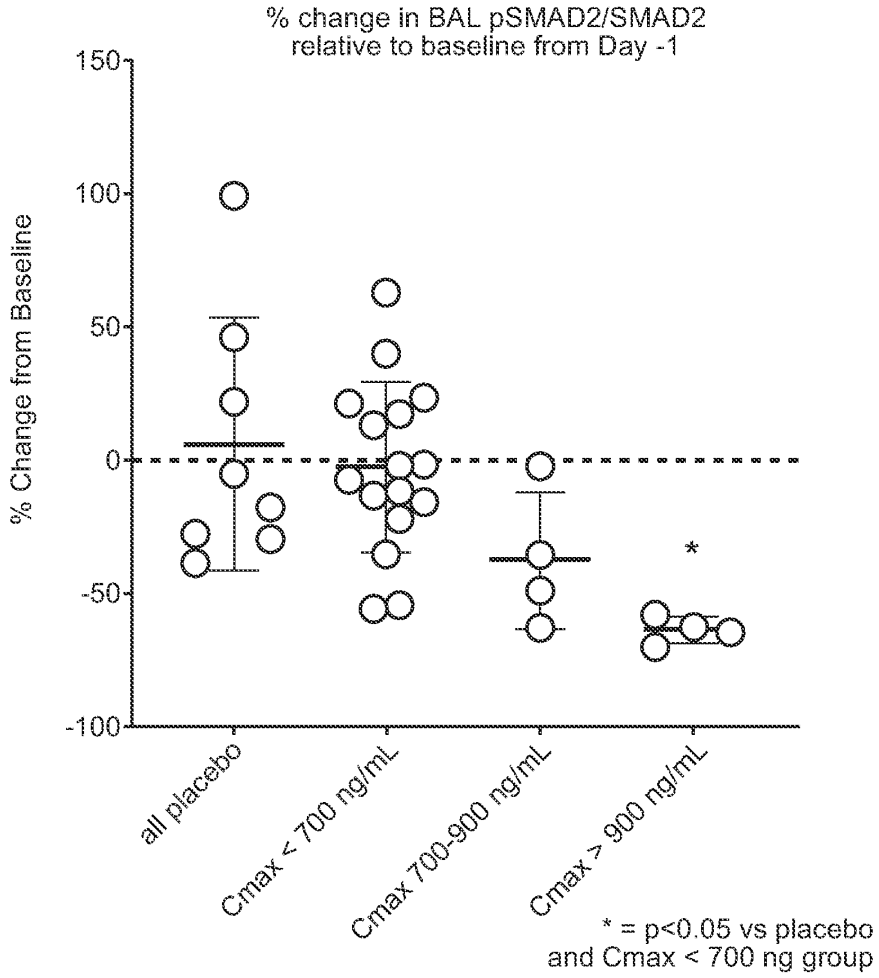

% change in BAL pSMAD2/SMAD2
relative to baseline from Day -1
% Change from Baseline
150
100
50
0
-50
-100
*
all placebo
Cmax < 700 ng/mL
Cmax 700-900 ng/mL
Cmax > 900 ng/mL
* = p<0.05 vs placebo
and Cmax < 700 ng group

FIG. 8G

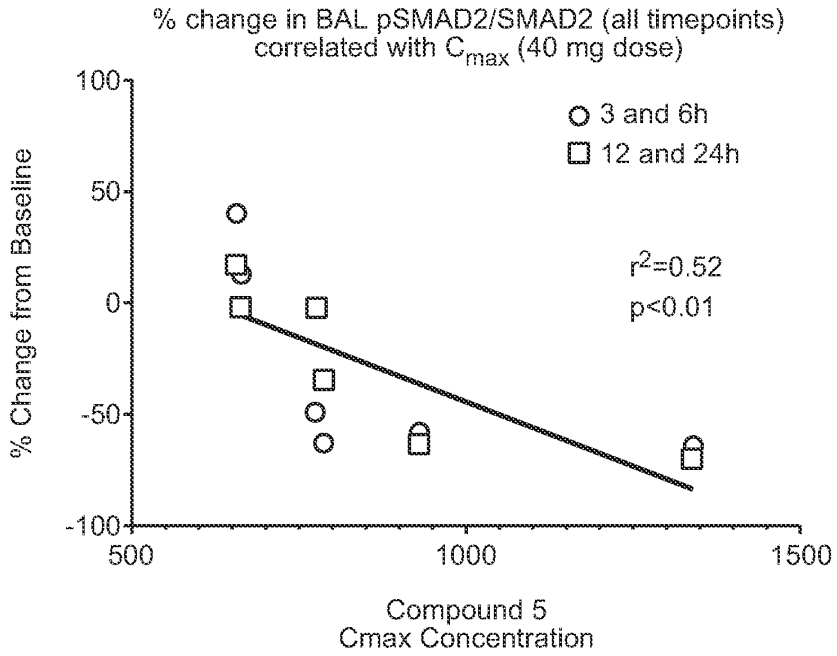

% change in BAL pSMAD2/SMAD2 (all timepoints)
correlated with C_{max} (40 mg dose)
3 and 6h
12 and 24h
r^2=0.52
p<0.01
% Change from Baseline
100
50
0
-50
-100
500
1000
1500
Compound 5
Cmax Concentration

FIG. 8H

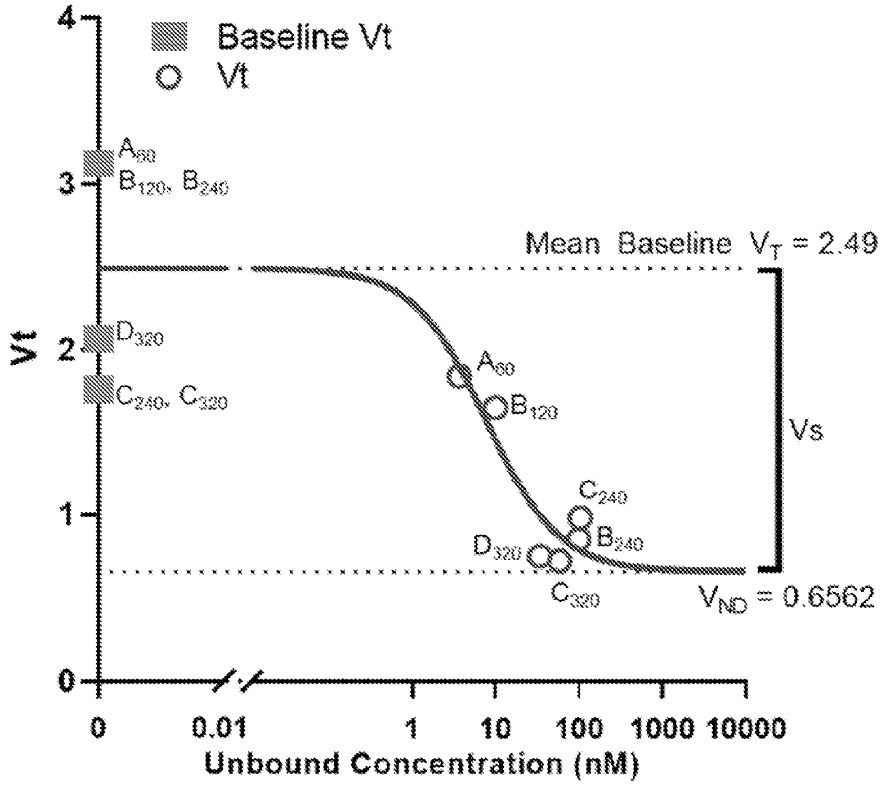
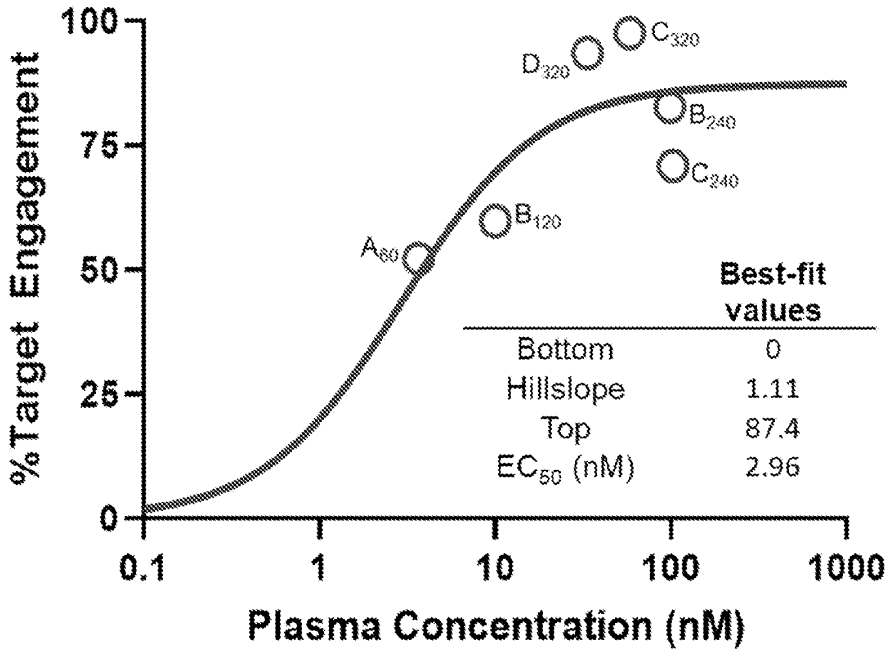

Baseline Vt
Vt
A60
B120, B240
D320
C240, C320
Mean Baseline VT = 2.49
Vs
A60
B120
C240
B240
D320
C320
VND = 0.6562
Vt
4
3
2
1
0
0
0.01
1
10
100
1000
10000
Unbound Concentration (nM)

FIG. 9



Y axis = % target engagement, X axis = Unbound Plasma Concentration
Non-linear regression using 4-parameter [agonist] vs response (variable slope)
Y=Bottom + (X^Hillslope)*(Top-Bottom)/(X^HillSlope + EC50^HillSlope)

FIG. 10

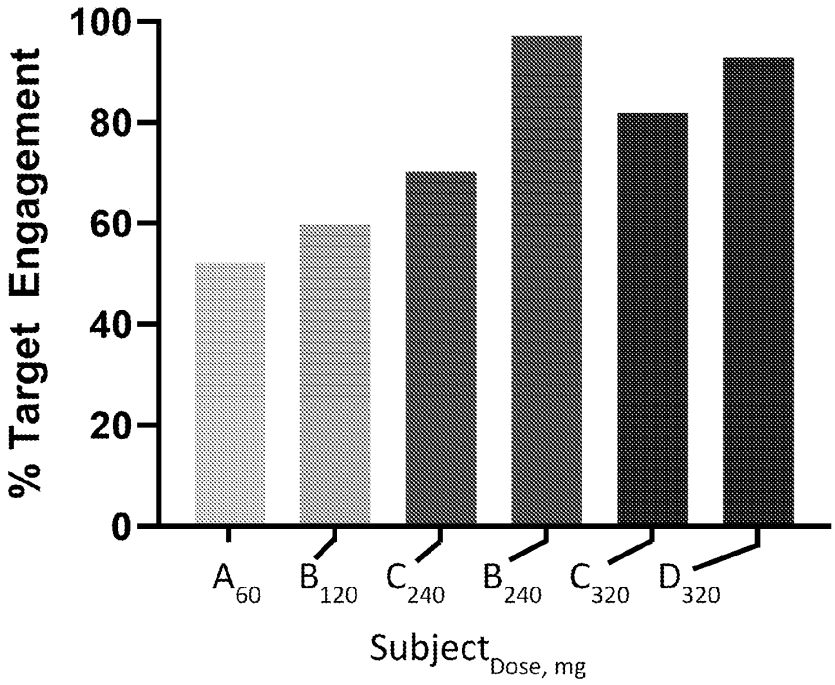

% Target Engagement
100
80
60
40
20
0
A60
B120
C240
B240
C320
D320
SubjectDose, mg

FIG. 11

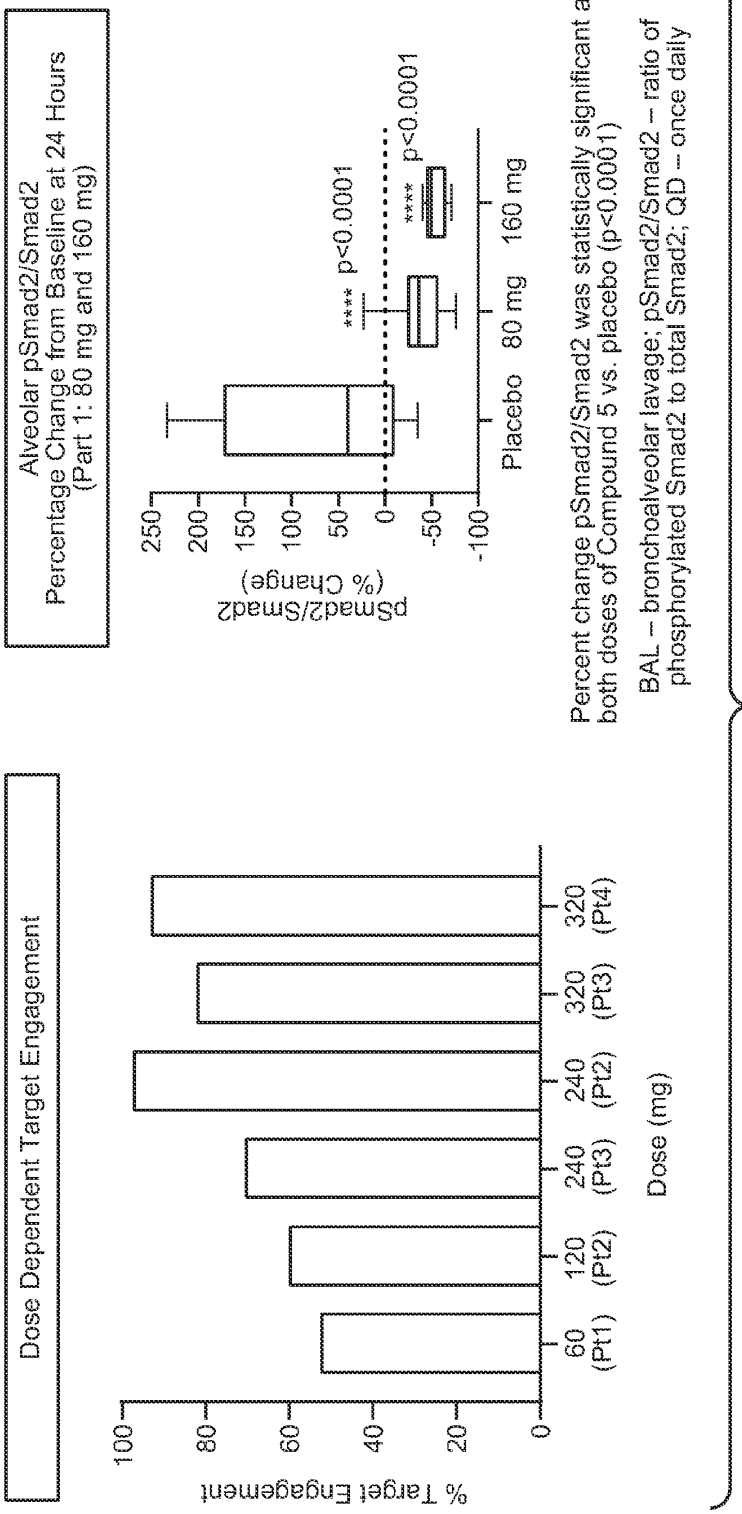

Dose Dependent Target Engagement
% Target Engagement
100
80
60
40
20
0
60 (Pt1)
120 (Pt2)
240 (Pt3)
240 (Pt2)
320 (Pt3)
320 (Pt4)
Dose (mg)
Alveolar pSmad2/Smad2
Percentage Change from Baseline at 24 Hours
(Part 1: 80 mg and 160 mg)
pSmad2/Smad2
(% Change)
250
200
150
100
50
0
-50
-100
**** p<0.0001
**** p<0.0001
Placebo
80 mg
160 mg
Percent change pSmad2/Smad2 was statistically significant at both doses of Compound 5 vs. placebo (p<0.0001)
BAL – bronchoalveolar lavage; pSmad2/Smad2 – ratio of phosphorylated Smad2 to total Smad2; QD – once daily

FIG. 12

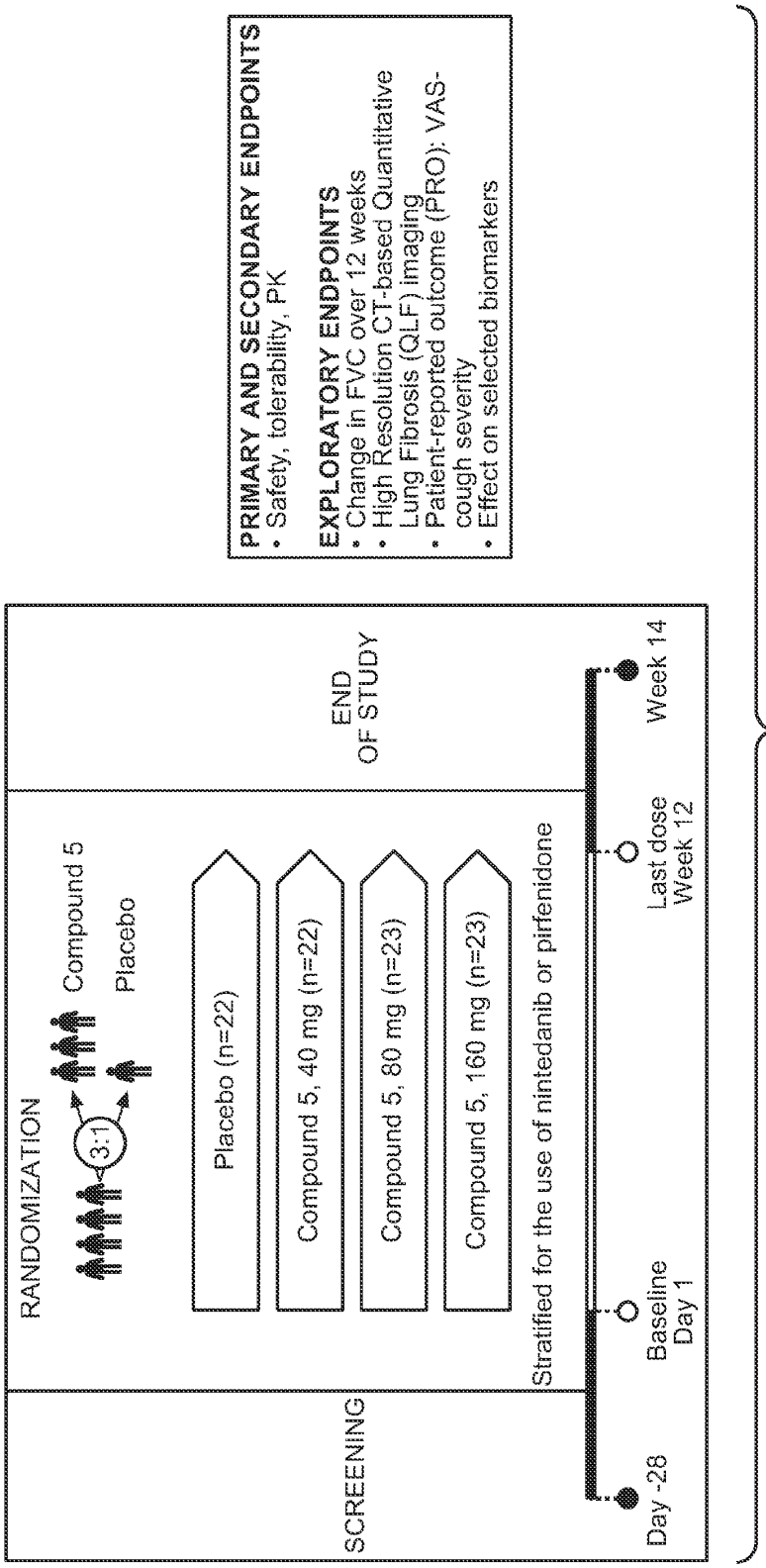

SCREENING
RANDOMIZATION
3:1
Compound 5
Placebo
Placebo (n=22)
Compound 5, 40 mg (n=22)
Compound 5, 80 mg (n=23)
Compound 5, 160 mg (n=23)
Stratified for the use of nintedanib or pirfenidone
END OF STUDY
Day -28
Baseline Day 1
Last dose Week 12
Week 14
PRIMARY AND SECONDARY ENDPOINTS
• Safety, tolerability, PK
EXPLORATORY ENDPOINTS
• Change in FVC over 12 weeks
• High Resolution CT-based Quantitative Lung Fibrosis (QLF) imaging
• Patient-reported outcome (PRO): VAS-cough severity
• Effect on selected biomarkers

FIG. 13

Compound 5 Safe and Well Tolerated Over 12 Weeks of Treatment

- Most TEAEs were mild or moderate in severity
- No premature discontinuations due to AEs
- No deaths or drug-related SAEs

Compound 5-Treated Patients Experienced an 80% Reduction in FVC Decline Over 12 Weeks (-15.1 mL, Pooled Active Groups) Compared to Placebo (-74.1 mL)

- Compound 5 treatment effect was evident with and without use of standard-of-care agents
- An improvement in FVC (+24.6 mL) was observed in Compound 5, 80 mg dose cohort
- Dose-dependent reduction in proportion of patients with FVCpp decline of ≥10%, a well-established predictor of death and disease progression in IPF

Other Exploratory Endpoints

- Compound 5 decreased Serum biomarkers of collagen synthesis of PROC3 and 6 relative to placebo

FIG. 14

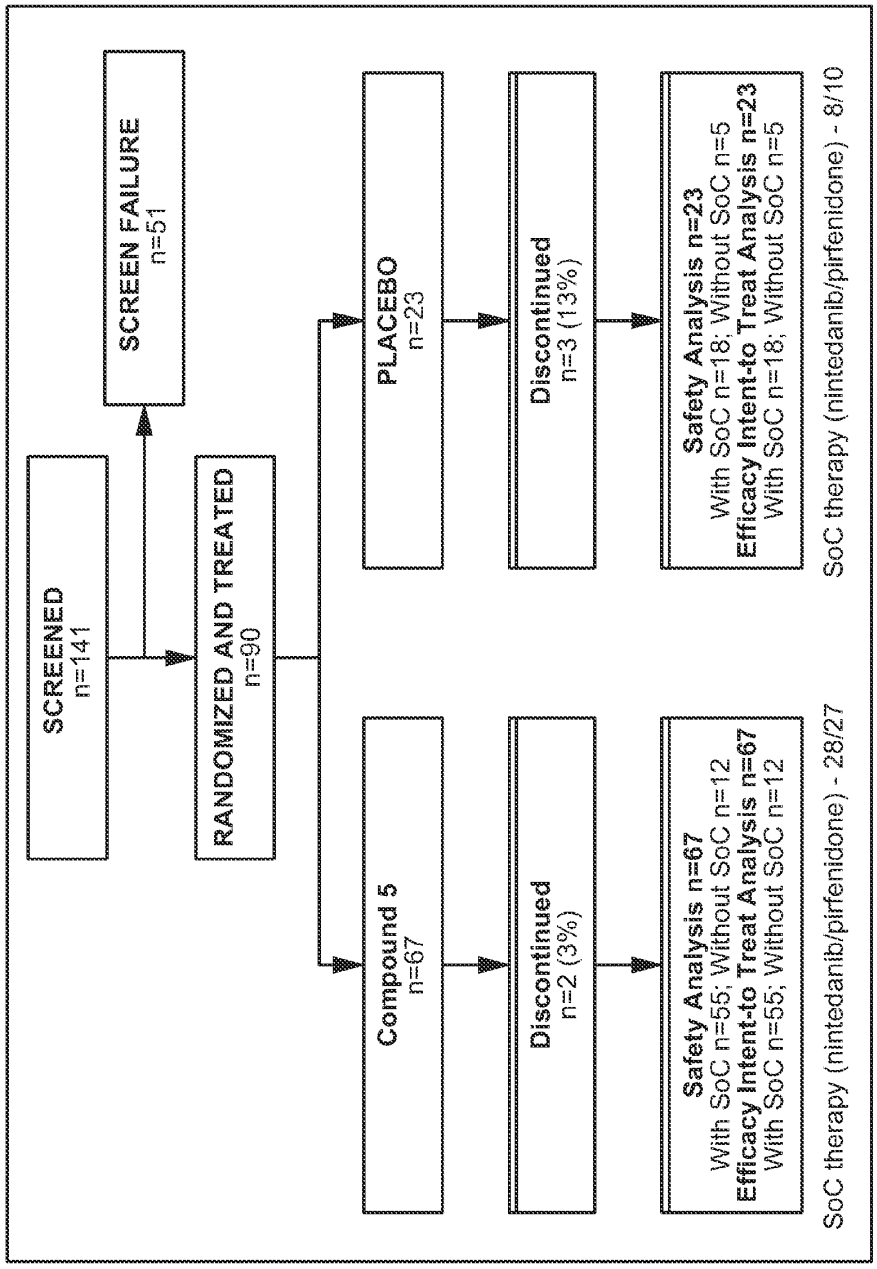

SCREENED
n=141
SCREEN FAILURE
n=51
RANDOMIZED AND TREATED
n=90
Compound 5
n=67
PLACEBO
n=23
Discontinued
n=2 (3%)
Discontinued
n=3 (13%)
Safety Analysis n=67
With SoC n=55; Without SoC n=12
Efficacy Intent-to Treat Analysis n=67
With SoC n=55; Without SoC n=12
Safety Analysis n=23
With SoC n=18; Without SoC n=5
Efficacy Intent-to Treat Analysis n=23
With SoC n=18; Without SoC n=5
SoC therapy (nintedanib/pirfenidone) - 28/27
SoC therapy (nintedanib/pirfenidone) - 8/10
SoC = Standard of Care

FIG. 15

Characteristic	Compound 5 40mg (n=22)	Compound 5 80mg (n=23)	Compound 5 160mg (n=22)	Compound 5 All (n=67)	Placebo (n=23)
Male sex – no. (%)	18 (81.8)	19 (82.6)	16 (72.7)	53 (79.1)	22 (95.7)
Female sex – no. (%)	4 (18.2)	4 (17.4)	6 (27.3)	14 (20.9)	1 (4.3)
Age – yr (SD)	69.2 (7.11)	74.2 (4.70)	71.5 (6.63)	71.7 (6.45)	71.7 (5.61)
Race – no. (%)					
White	22 (100.0)	21 (91.3)	22 (100.0)	65 (97.0)	22 (95.7)
Asian	0	1 (4.3)	0	1 (1.5)	1 (4.3)
Not Reported / Unknown	0	1 (4.3)	0	1 (1.5)	0
Weight – kg, Mean (SD)	86.09 (18.223)	85.89 (14.949)	85.37 (13.507)	85.79 (15.437)	85.23 (10.743)
Body-mass index (kg/m^2), Mean (SD)	27.67 (4.205)	28.54 (5.790)	29.28 (4.663)	28.50 (4.915)	27.43 (2.488)

SD = Standard deviation; BMI = Body Mass Index; FVC = Forced Vital Capacity; DLCO = Diffusing capacity for carbon monoxide; SD = standard deviation
Duration since diagnosis at screening is calculated from the first reported date for preferred terms of Idiopathic Pulmonary Fibrosis, Pulmonary Fibrosis or Interstitial Lung Disease.
Percentages are based on the number of participants in the Safety Population by treatment group.
GAP Stage I = GAP Index 0-3; GAP Stage II = GAP Index 4-5; GAP Stage III = GAP Index 6-8.
GAP Index score (0-8) derived from Gender, Age, FVC, % Predicted and DLCO, % Predicted.

FIG. 16

Characteristic	Compound 5 40mg (n=22)	Compound 5 80mg (n=23)	Compound 5 160mg (n=22)	Compound 5 All (n=67)	Placebo (n=23)
Time since diagnosis of IPF – yr, Mean (SD)	1.78 (0.925)	2.39 (1.422)	2.13 (1.083)	2.10 (1.176)	2.62 (1.378)
Standard of Care Use	17 (77.3)	19 (82.6)	19 (86.4)	55 (82.1)	18 (78.3)
None	5 (22.72)	4 (17.39)	3 (13.63)	12 (17.91)	5 (21.74)
Nintedanib	12 (54.5)	9 (39.1)	7 (31.8)	28 (41.8)	8 (34.8)
Pirfenidone	5 (22.7)	10 (43.5)	12 (54.5)	27 (40.3)	10 (43.5)
Duration of Standard of Care at Randomization (months), Mean, (SD)	19.47 (11.527)	20.21 (11.523)	20.07 (11.632)	19.93 (11.350)	24.12 (17.295)
FVC					
Mean – mL (SD)	2976.5 (861.01)	3128.7 (814.20)	2863.0 (725.39)	2991.5 (797.76)	3211.7 (792.68)
Median – mL	2937.0	2929.0	2702.5	2806.0	3282.0
Percent of predicted value, Mean (SD)	74.81 (14.698)	82.67 (13.471)	78.75 (16.356)	78.80 (14.995)	78.30 (15.859)
Percent of predicted DLCO, corrected for the hemoglobin level, Mean (SD)	57.200 (14.7434)	51.782 (14.6690)	48.615 (15.1082)	52.521 (15.0362)	50.335 (16.2161)
GAP Stage					
GAP Stage I, n (%)	11 (50.0)	8 (34.8)	7 (31.8)	26 (38.8)	7 (30.4)
GAP Stage II, n (%)	10 (45.5)	15 (65.2)	13 (59.1)	38 (56.7)	13 (56.5)
GAP Stage III, n (%)	1 (4.5)	0	2 (9.1)	3 (4.5)	3 (13.0)

SD = Standard deviation; BMI = Body Mass Index; FVC = Forced Vital Capacity; DLCO = Diffusing capacity for carbon monoxide;
SD = standard deviation GAP Stage I = GAP Index 0-3; GAP Stage II = GAP Index 4-5; GAP Stage III = GAP Index 6-8.
Duration since diagnosis at screening is calculated from the first reported date for preferred terms of Idiopathic Pulmonary Fibrosis, Pulmonary Fibrosis or Interstitial Lung Disease. GAP Index score (0-8) derived from Gender, Age, FVC, % Predicted and DLCO, % Predicted.
Percentages are based on the number of participants in the Safety Population by treatment group.

FIG. 17

AE, n (%) of Participants Reporting	Compound 5 40mg (n=22)	Compound 5 80mg (n=23)	Compound 5 160mg (n=22)	Compound 5 All (n=67)	Placebo (n=23)
Any AEs	16 (72.7)	15 (65.2)	15 (68.1)	46 (68.7)	14 (60.9)
TEAE	16 (72.7)	15 (65.2)	14 (63.6)	45 (67.2)	14 (60.9)
Related to study drug	4 (18.2)	7 (30.4)	4 (18.2)	15 (22.4)	8 (34.8)
Serious TEAE	1 (4.5)	0	2 (9.1)	3 (4.5)	2 (8.7)
Related to study drug	0	0	0	0	0
TEAE of CTCAE Grade 3 or Higher	2 (9.1)	0	2 (9.1)	4 (6.0)	1 (4.3)
Related to study drug	0	0	1 (4.5)	1 (1.5)	0
TEAE Leading to Interruption of Study Drug	0	0	1 (4.5)	1 (1.5)	0
TEAE Leading to Withdrawal of Study Drug	0	0	0	0	2 (8.7)
TEAE Leading to Early Termination from Study	0	0	0	0	1 (4.3)
TEAE Leading to Death	0	0	0	0	0

AE = Adverse Event; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Events. Adverse events coded using MedDRA v. 24.0.
TEAE is defined as any AE starting (or worsening) on or after the date of first dose.

FIG. 18

AE, n (%) of Participants Reporting	Without Background SoC (n=17)		With Background SoC (n=73)	
	Compound 5 (n=12)	Placebo (n=5)	Compound 5 (n=55)	Placebo (n=18)
Any AEs	8 (66.7)	3 (60.0)	38 (69.1)	11 (61.1)
TEAE	8 (66.7)	3 (60.0)	37 (67.3)	11 (61.1)
Related to study drug	2 (16.7)	2 (40.0)	13 (23.6)	6 (33.3)
Serious TEAE	0	0	3 (5.5)	2 (11.1)
Related to study drug	0	0	0	0
TEAE of CTCAE Grade 3 or Higher	0	0	4 (7.3)	1 (5.6)
Related to study drug	0	0	1 (1.8)	0
TEAE Leading to Interruption of Study Drug	1 (8.3)	0	0	0
TEAE Leading to Withdrawal of Study Drug	0	1 (20.0)	0	1 (5.6)
TEAE Leading to Early Termination from Study	0	1 (20.0)	0	0
TEAE Leading to death	0	0	0	0

TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Events. Adverse events coded using MedDRA version 24.0.
TEAE is defined as any AE starting (or worsening) on or after the date of first dose.
SOC = standard of care, nintedanib or pirfenidone

FIG. 19

AE, n (%) of Participants Reporting	Compound 5 40mg (n=22)	Compound 5 80mg (n=23)	Compound 5 160mg (n=22)	Compound 5 All (n=67)	Placebo (n=23)
Most frequent TEAEs (≥10% in at least one arm)					
Diarrhea	2 (9.1)	5 (21.7)	5 (22.7)	12 (17.9)	1 (4.3)
Related to study drug	1 (4.5)	3 (13.0)	4 (18.2)	8 (11.9)	1 (4.3)

* All TEAEs of diarrhea occurred in participants on SoC
  - 12 of 13 participants with diarrhea were taking nintedanib
  - All but one event were mild to moderate in severity

TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Events. Adverse events coded using MedDRA version 24.0.
TEAE is defined as any AE starting (or worsening) on or after the date of first dose

FIG. 20

Study Part Treatment Group Part c pant Number	System Organ C ass Preferred Term Verbat m Term	Standard Tox c ty Grade	Any a ternat ve cause or confound ng factors?	Act on Taken	Outcome
Part B 40mg 01018-103	Resp ratory, thorac c and med ast na d sorders Acute resp ratory fa ure Acute on chron c resp ratory fa ure	GRADE 3 (SEVERE)	N	DOSE NOT CHANGED	RECOVERED / RESOLVED
Part B 40mg 01018-103	Infect ons and nfestat ons Pneumon a Pneumon a	GRADE 2 (MODERATE)	Y Removed carpet from home w thout a mask	DOSE NOT CHANGED	RECOVERED / RESOLVED
Part B P acebo 01018-105	Resp ratory, thorac c and med ast na d sorders Resp ratory fa ure Acute on chron c resp ratory fa ure w th hypoxem a	GRADE 3 (SEVERE)	Y Coronary Artery d sease w th tr p e vesse d sease	NOT APPLICABLE Ear y term nat on from the study	RECOVERED / RESOLVED WITH SEQUELAE
Part C 160mg 01002-111	Resp ratory, thorac c and med ast na d sorders Id opath c pu monary f bros s Acute exacerbat on of d opath c pu monary f bros s	GRADE 3 (SEVERE)	Y Under y ng d sease and af b	NOT APPLICABLE Hosp ta zat on	NOT RECOVERED / NOT RESOLVED
Part C (160 mg) 01014-109	Card ac d sorders Atr a f utter Atr a f utter	GRADE 3 (SEVERE)	Y Under y ng d sease	NOT APPLICABLE Hosp ta zat on	RECOVERED / RESOLVED
Part C P acebo 01013-112	Rena and ur nary d sorders B adder d atat on D stended B adder due to Ur nary Retent on	GRADE 2 (MODERATE)	N	DOSE NOT CHANGED Fo ey Catheter p aced	RECOVERED / RESOLVED WITH SEQUELAE

TEAE = Treatment Emergent Adverse Event; Adverse events coded using MedDRA version 24.0.
TEAE is defined as any AE starting (or worsening) on or after the date of first dose.

FIG. 21

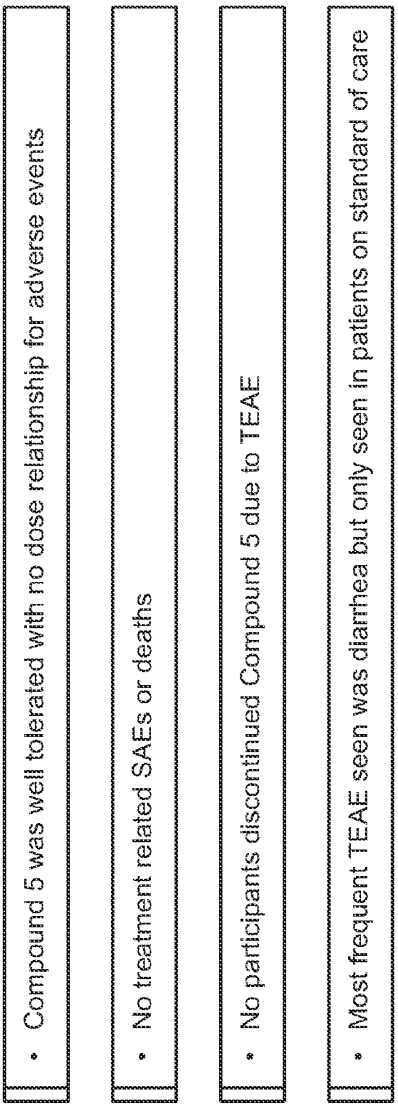

• Compound 5 was well tolerated with no dose relationship for adverse events
• No treatment related SAEs or deaths
• No participants discontinued Compound 5 due to TEAE
• Most frequent TEAE seen was diarrhea but only seen in patients on standard of care

FIG. 22

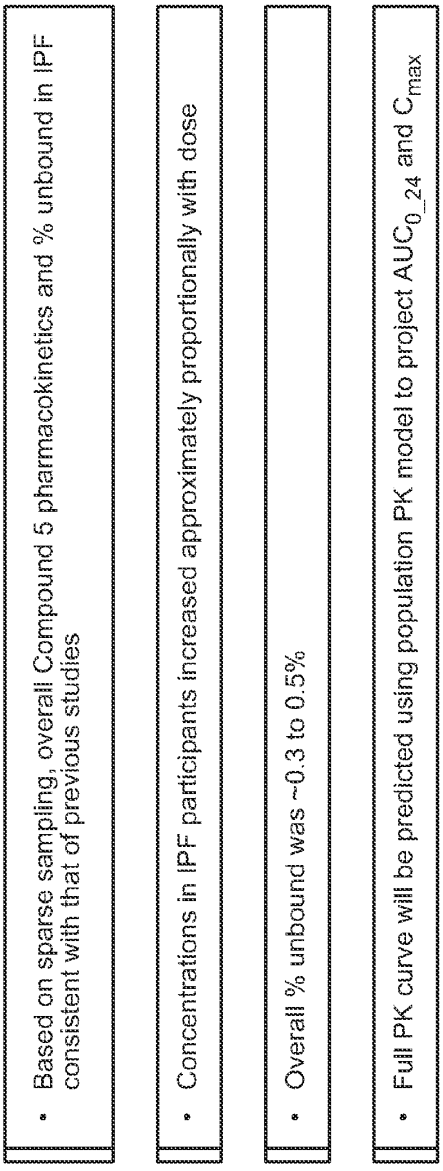
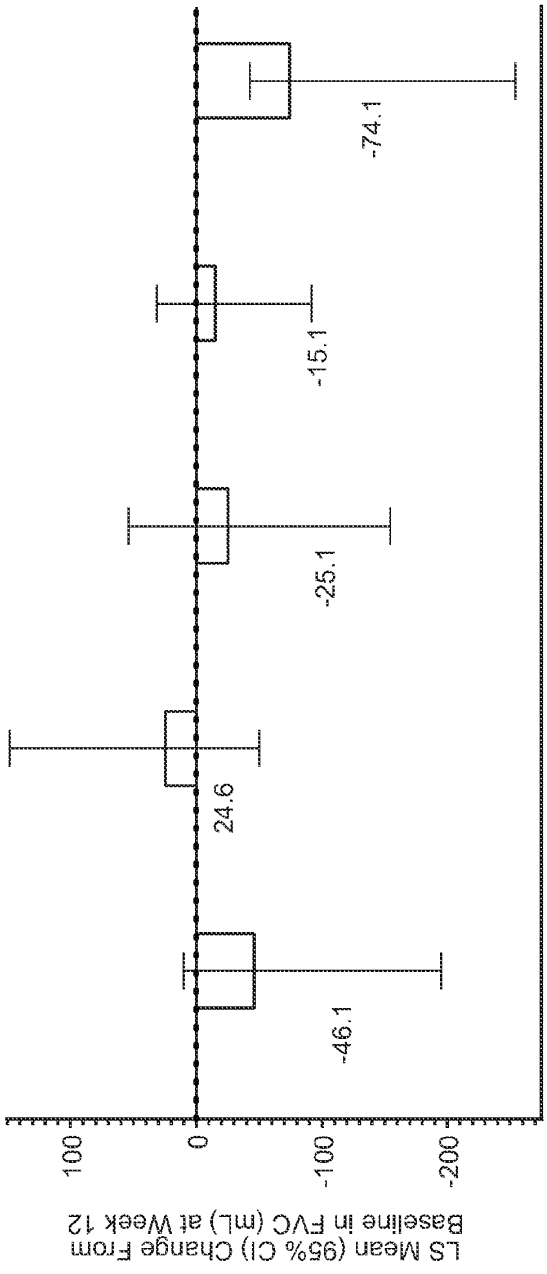
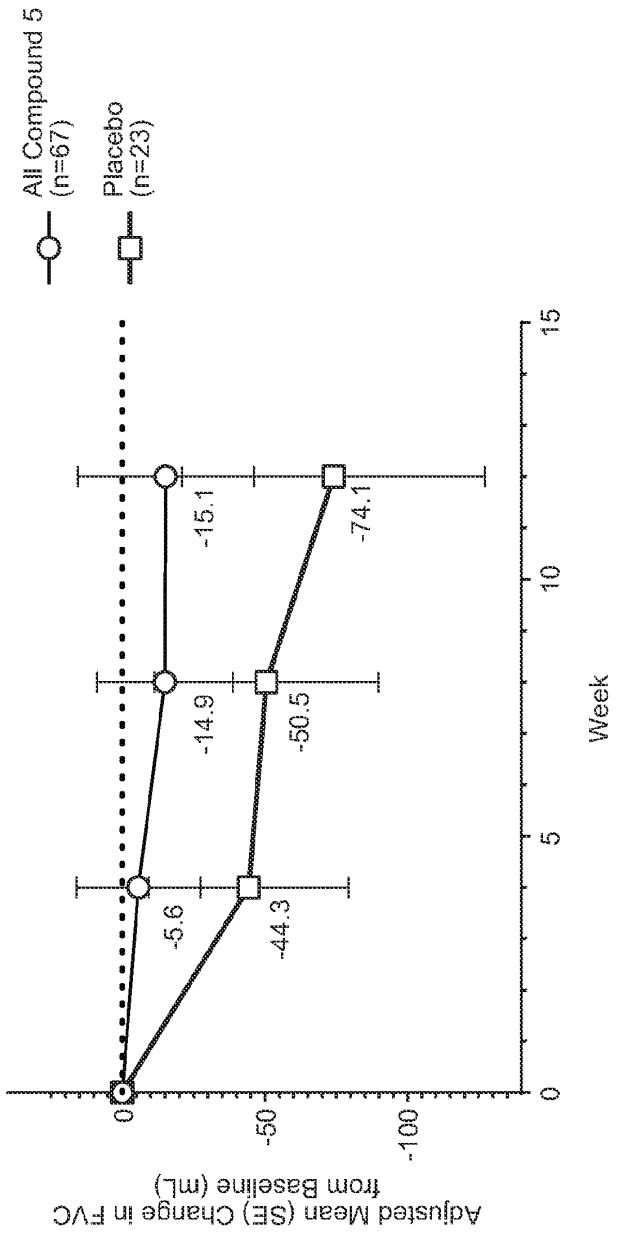

• Based on sparse sampling, overall Compound 5 pharmacokinetics and % unbound in IPF consistent with that of previous studies
• Concentrations in IPF participants increased approximately proportionally with dose
• Overall % unbound was ~0.3 to 0.5%
• Full PK curve will be predicted using population PK model to project AUC_{0_24} and C_{max}

FIG. 23



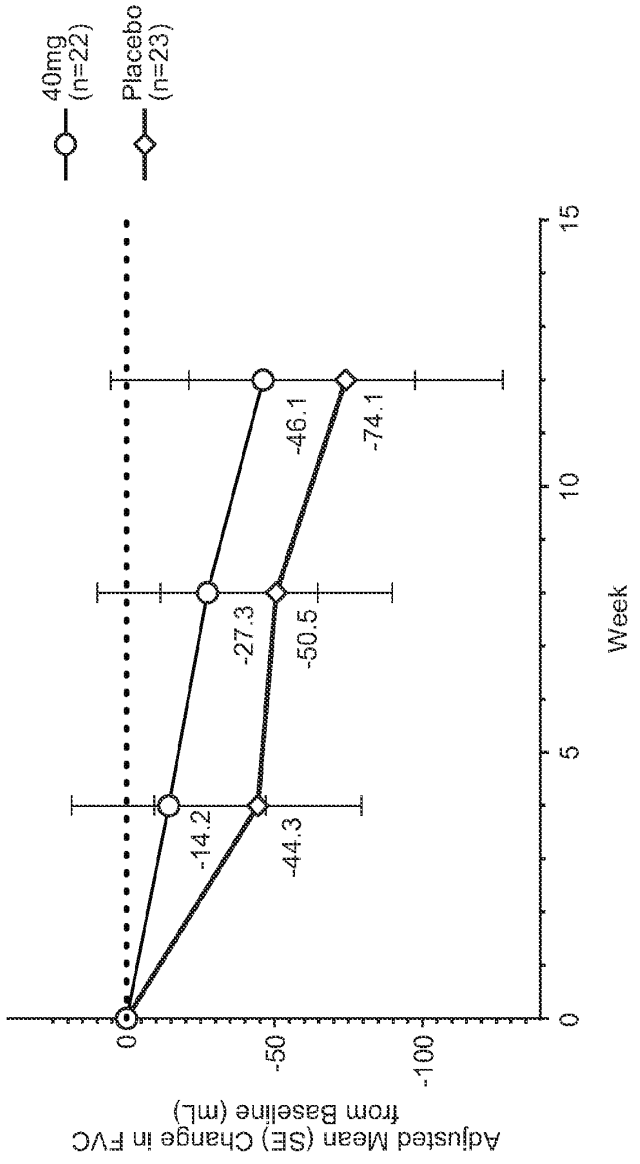
Change from baseline analyzed using a mixed model for repeated measures with terms for treatment group, SOC (Y/N), visit, baseline value, and treatment-by-visit interaction. An unstructured covariance (UN) structure was used.

FIG. 24



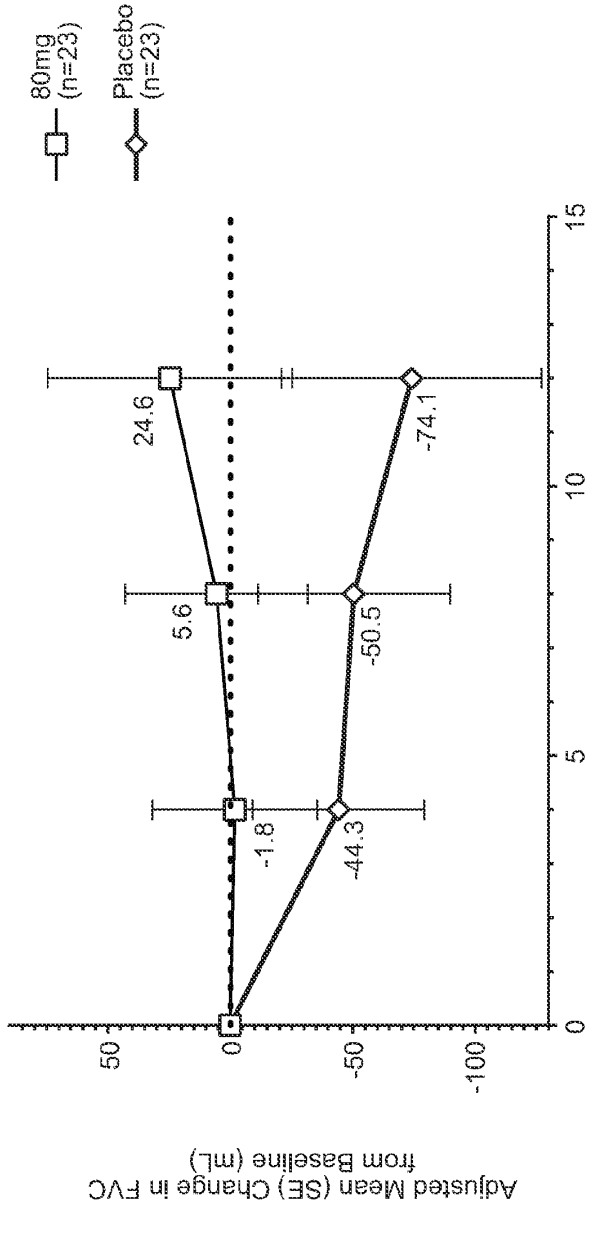
FVC = Forced Vital Capacity
MMRM = Mixed Model Repeat Measures.

FIG. 25



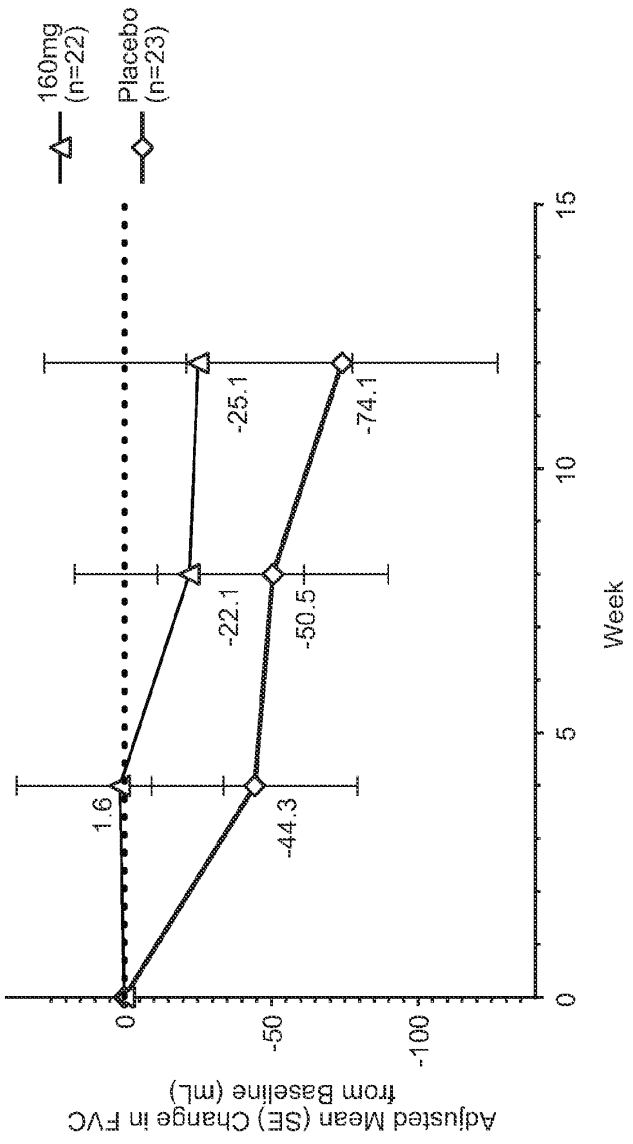
FVC = Forced Vital Capacity
MMRM = Mixed Model Repeat Measures.

FIG. 26



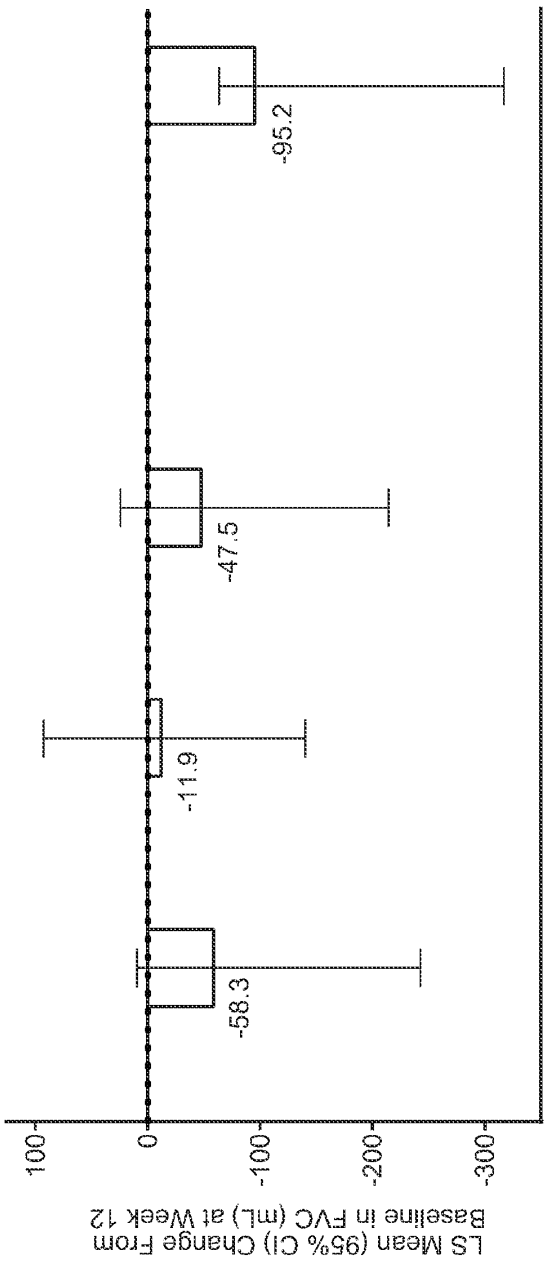
FVC = Forced Vital Capacity
MMRM = Mixed Model Repeat Measures.

FIG. 27



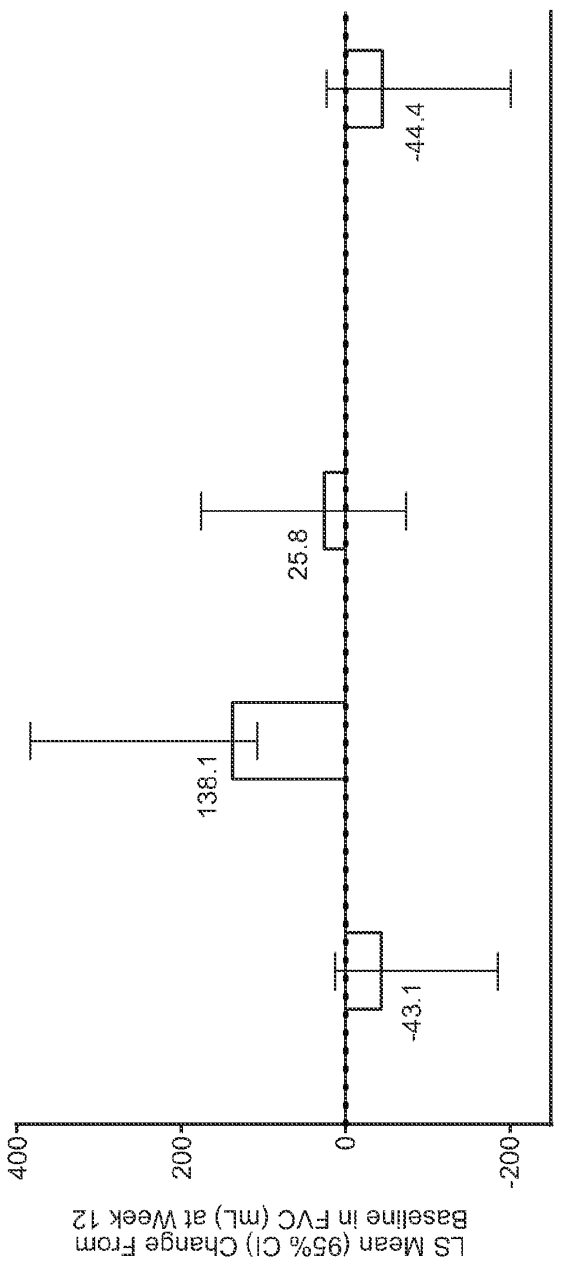
FVC = Forced Vital Capacity
MMRM = Mixed Model Repeat Measures.

FIG. 28



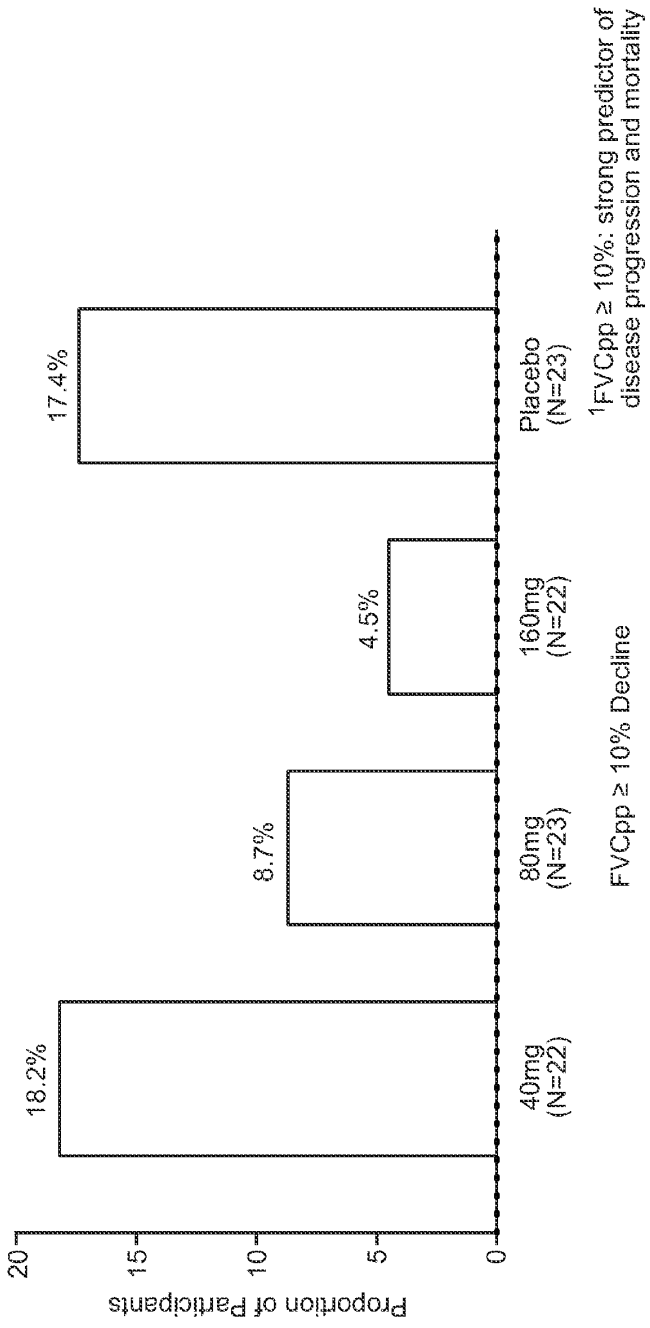
Change from baseline analyzed using a mixed model for repeated measures with terms for treatment group, SOC (Y/N), visit, baseline value, and treatment-by-visit interaction. An unstructured covariance (UN) structure was used. FVC = Forced Vital Capacity

FIG. 29



Change from baseline analyzed using a mixed model for repeated measures with terms for treatment group, SOC (Y/N), visit, baseline value, and treatment-by-visit interaction. An unstructured covariance (UN) structure was used. FVC = Forced Vital Capacity

FIG. 30



FVCpp = Forced Vital Capacity (% Predicted)
[1]Ann Am Thorac Soc. 2017 Sep;14(9):1395-1402.

FIG. 31

- Compound 5-treated participants experienced a benefit in FVC change from Baseline to Week 12 (-15.1 mL for pooled Compound 5 group) compared to those on placebo (-74.1 mL)[1]

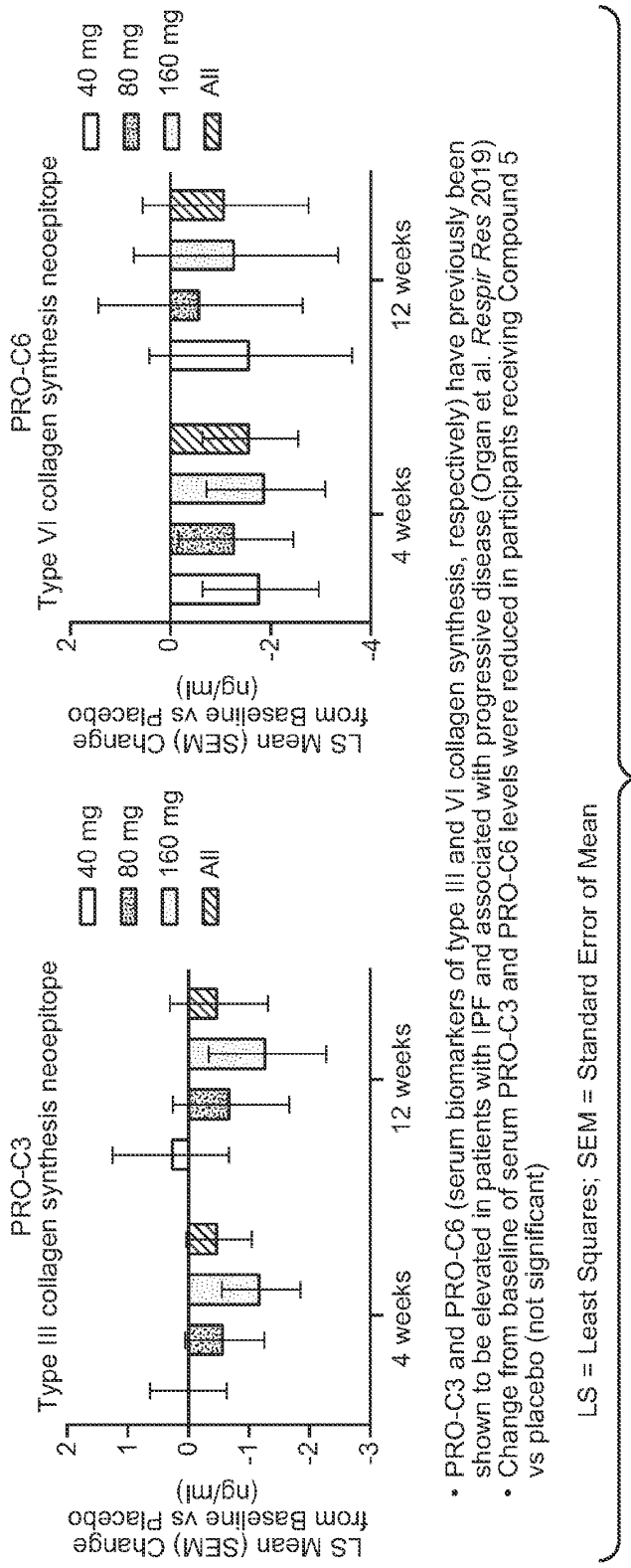
- Compound 5 treatment effect was evident with and without use of standard of care

- Compound 5 80 mg dose demonstrated an improvement in FVC (+24.6 mL)

- Dose-dependent reduction in proportion of participants with FVCpp decline of ≥10%

[1] MMRM analysis ITT population

FIG. 32



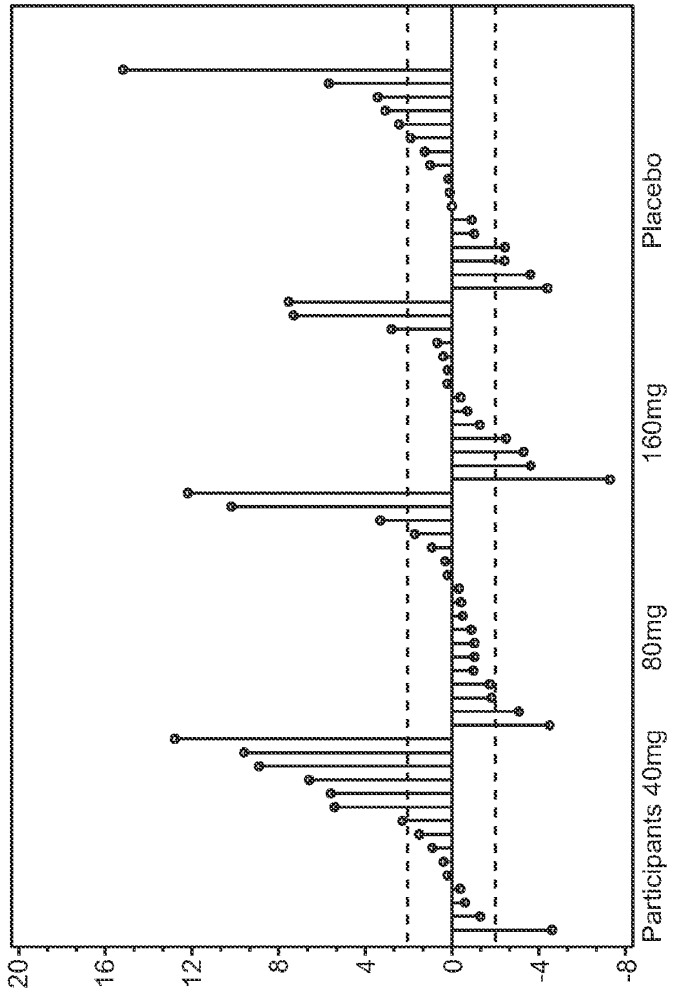
- PRO-C3 and PRO-C6 (serum biomarkers of type III and VI collagen synthesis, respectively) have previously been shown to be elevated in patients with IPF and associated with progressive disease (Organ et al. *Respir Res* 2019)
- Change from baseline of serum PRO-C3 and PRO-C6 levels were reduced in participants receiving Compound 5 vs placebo (not significant)

LS = Least Squares; SEM = Standard Error of Mean

FIG. 33

- The data from the INTEGRIS-IPF trial exceeded our expectations showing a favorable safety and tolerability profile and a treatment effect on FVC, the current registrational endpoint in IPF. Importantly, the treatment effect was also observed on top of standard of care therapy.
- Pliant recently completed enrollment in the 320 mg cohort of the INTEGRIS-IPF Phase 2a trial. Interim data from this trial is anticipated in early 2023
- Pliant intends on sharing today's data with regulatory authorities in the near future to discuss the late-stage development of Compound 5.

FIG. 34



Participants, Sorted by QLF Extent Changes

	40mg (N=15)	80 mg (N=18)	160 mg (N=14)	Placebo (N=17)
Improvers< -2%, N (%)	1 (6.6%)	2 (11.1%)	4 (28.6%)	4 (23.5%)
Stable [- 2, 2%), N (%)	7 (46.7%)	13 (72.2%)	7 (50.0%)	8 (47.1%)
Worse > 2%, N (%)	7 (46.7%)	3 (16.7%)	3 (21.4%)	5 (29.4%)
Mean Difference (SD)	3.15% (4.80)	0.70% (4.19)	0.00% (3.96)	1.15% (4.47)
Median	1.50%	-0.45%	-0.10%	0.20%

QLF = quantitative lung fibrosis

FIG. 35

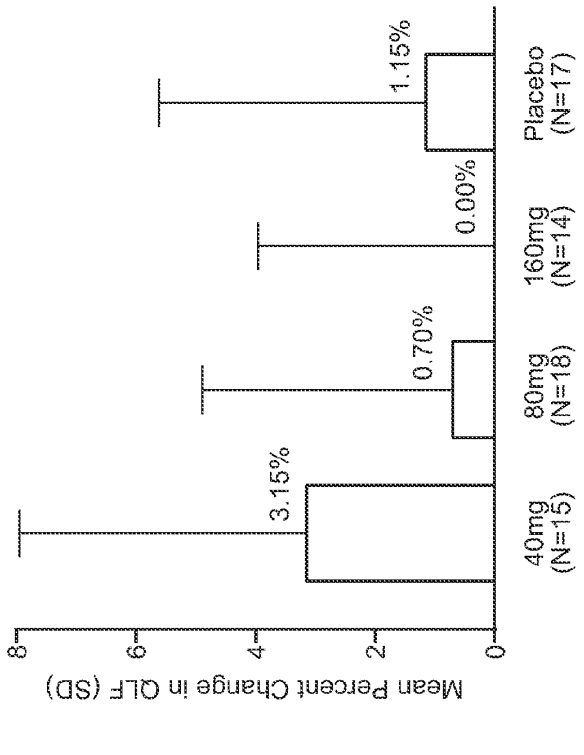

Mean Percent Change in QLF (SD)
8
6
4
2
0
3.15%
0.70%
0.00%
1.15%
40mg (N=15)
80mg (N=18)
160mg (N=14)
Placebo (N=17)
QLF = quantitative lung fibrosis

FIG. 36

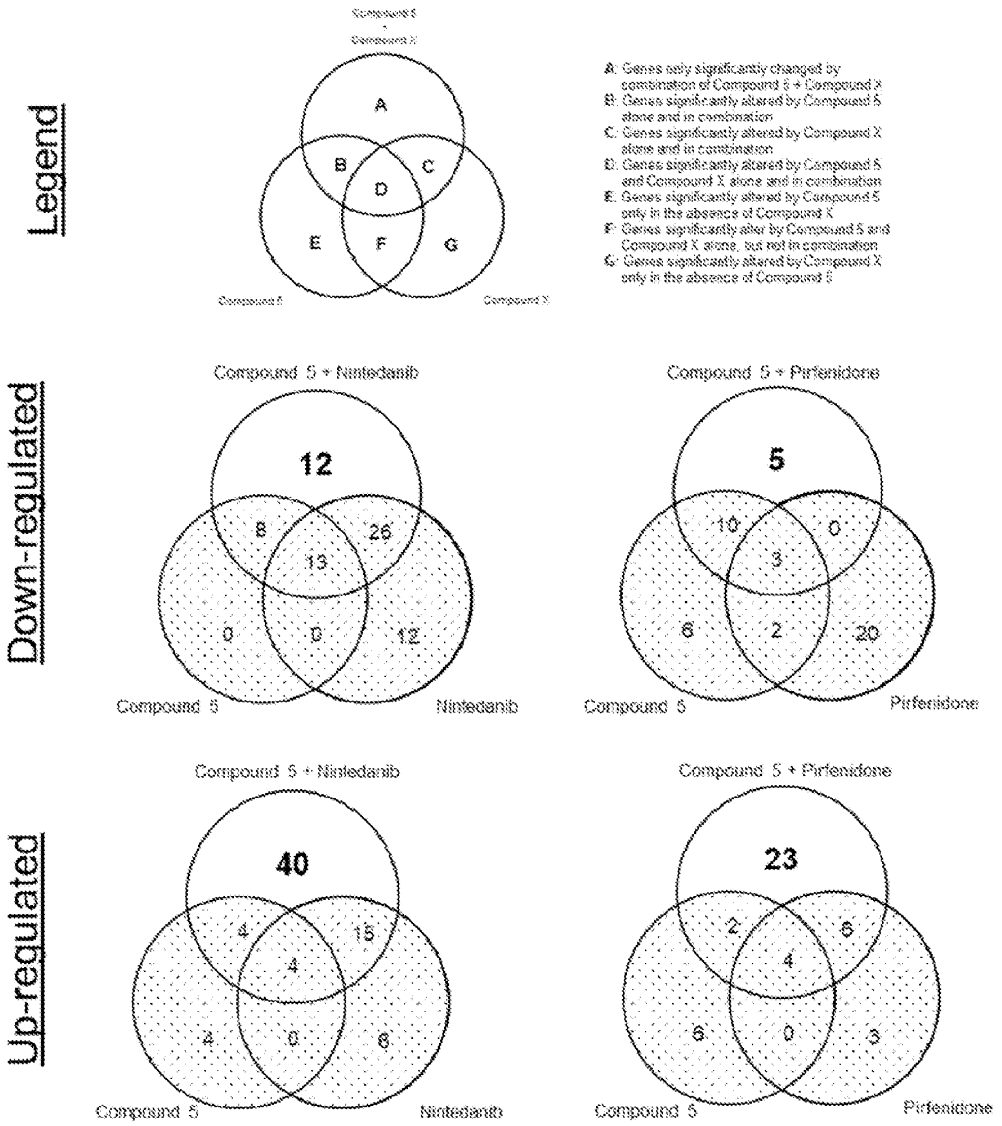

Legend
A
B
C
D
E
F
G
A: Genes only significantly changed by combination of Compound 5 + Compound X
B: Genes significantly altered by Compound 5 alone and in combination
C: Genes significantly altered by Compound X alone and in combination
D: Genes significantly altered by Compound 5 and Compound X alone and in combination
E: Genes significantly altered by Compound 5 only in the absence of Compound X
F: Genes significantly alter by Compound 5 and Compound X alone, but not in combination
G: Genes significantly altered by Compound X only in the absence of Compound 5
Down-regulated
Compound 5 + Nintedanib
12
8
26
13
0
0
12
Compound 5
Nintedanib
Compound 5 + Pirfenidone
5
10
0
3
6
2
20
Compound 5
Pirfenidone
Up-regulated
Compound 5 + Nintedanib
40
4
15
4
4
0
6
Compound 5
Nintedanib
Compound 5 + Pirfenidone
23
2
6
4
6
0
3
Compound 5
Pirfenidone

FIG. 37

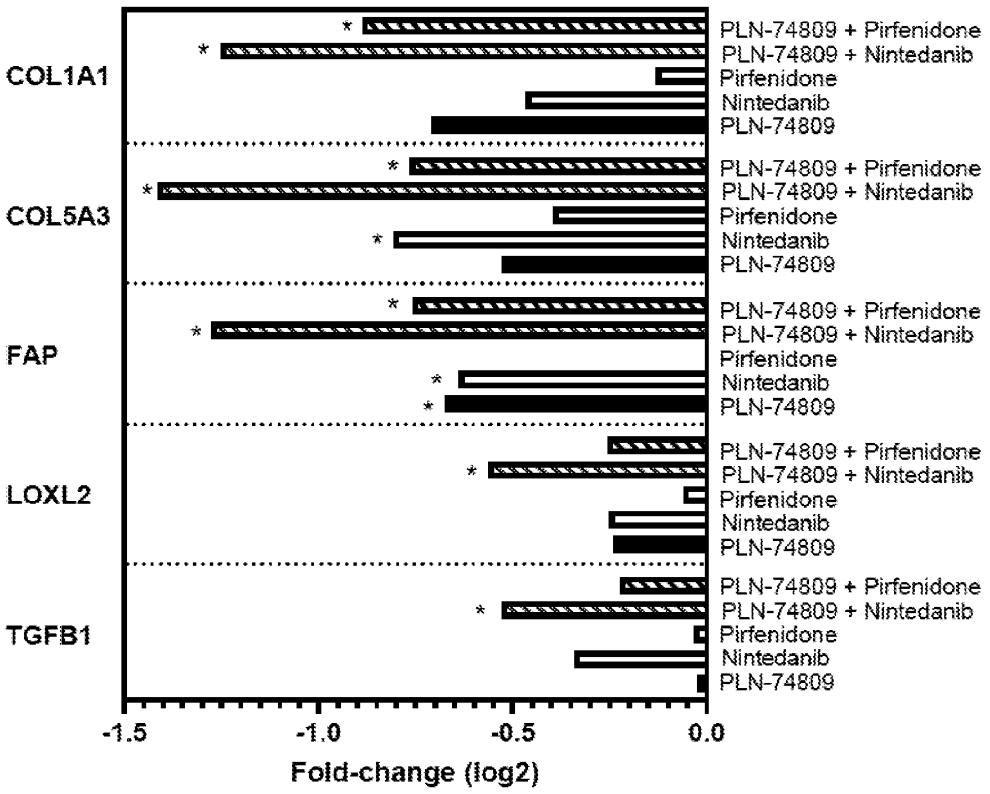

COL1A1
COL5A3
FAP
LOXL2
TGFB1
PLN-74809 + Pirfenidone
PLN-74809 + Nintedanib
Pirfenidone
Nintedanib
PLN-74809
-1.5
-1.0
-0.5
0.0
Fold-change (log2)

FIG. 38