FIG. 1

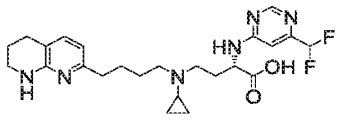
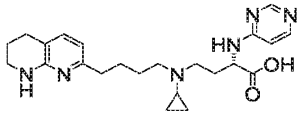
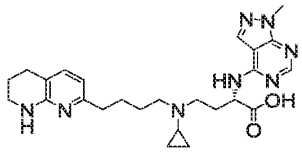
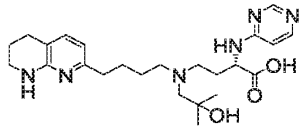
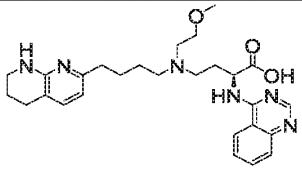
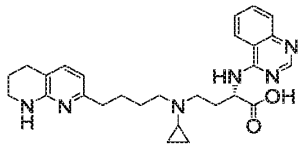
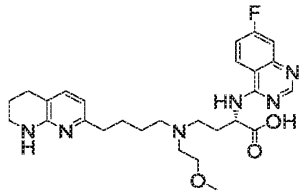
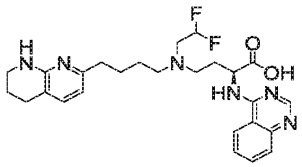
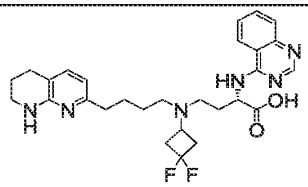
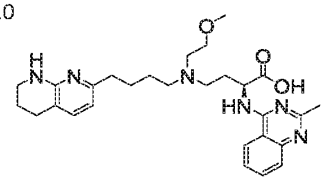
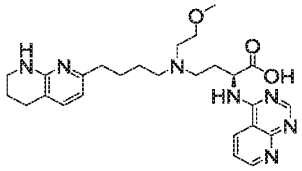
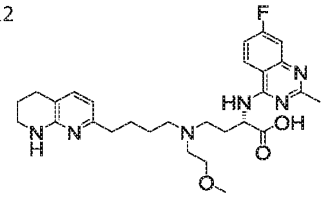
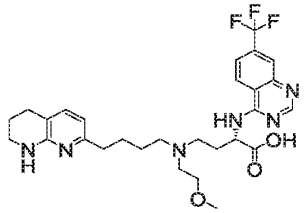
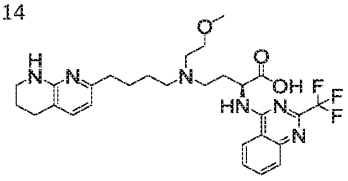
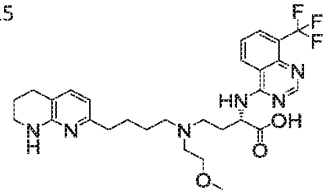
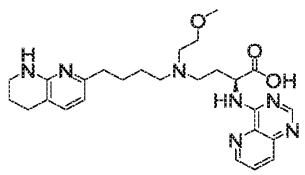
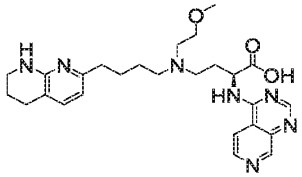
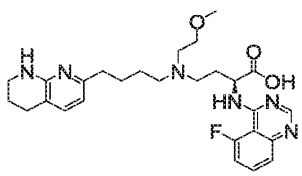
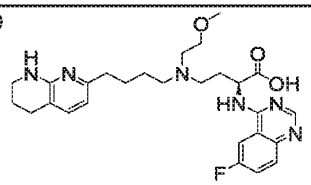
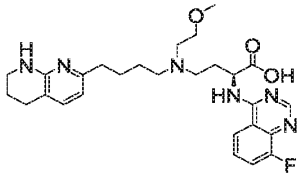
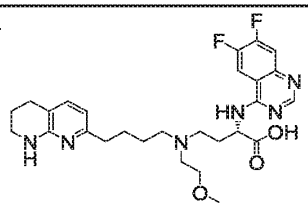
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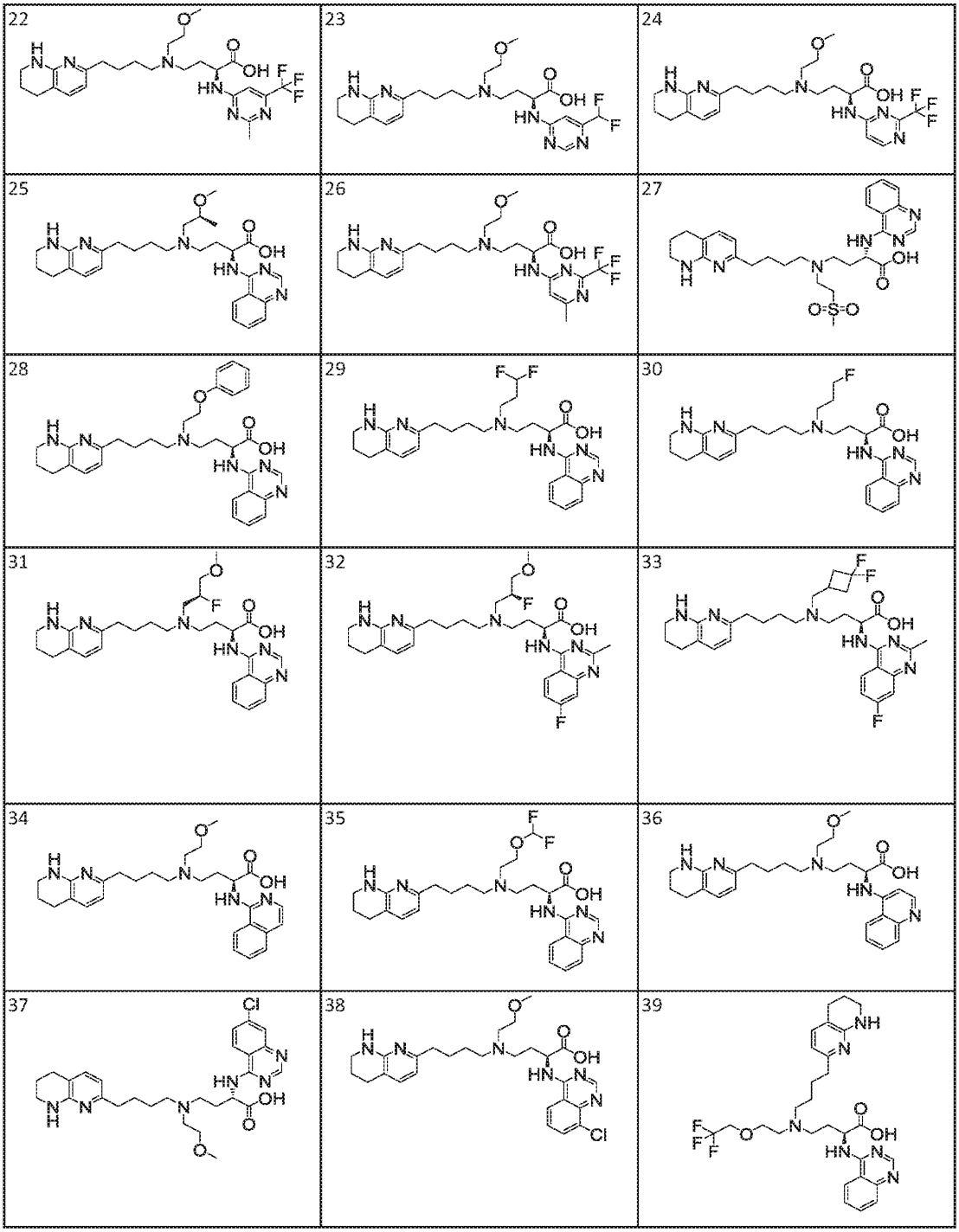


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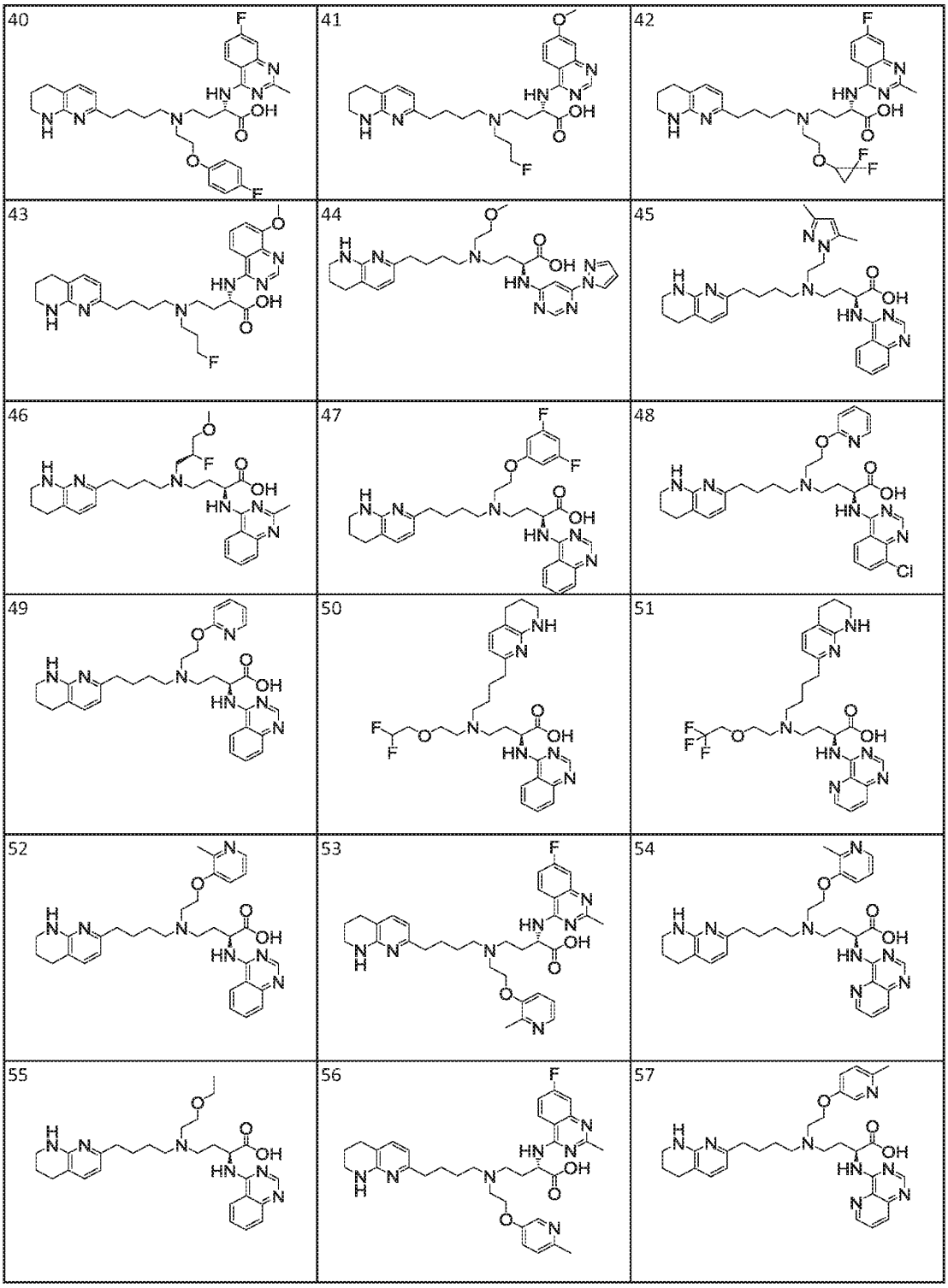


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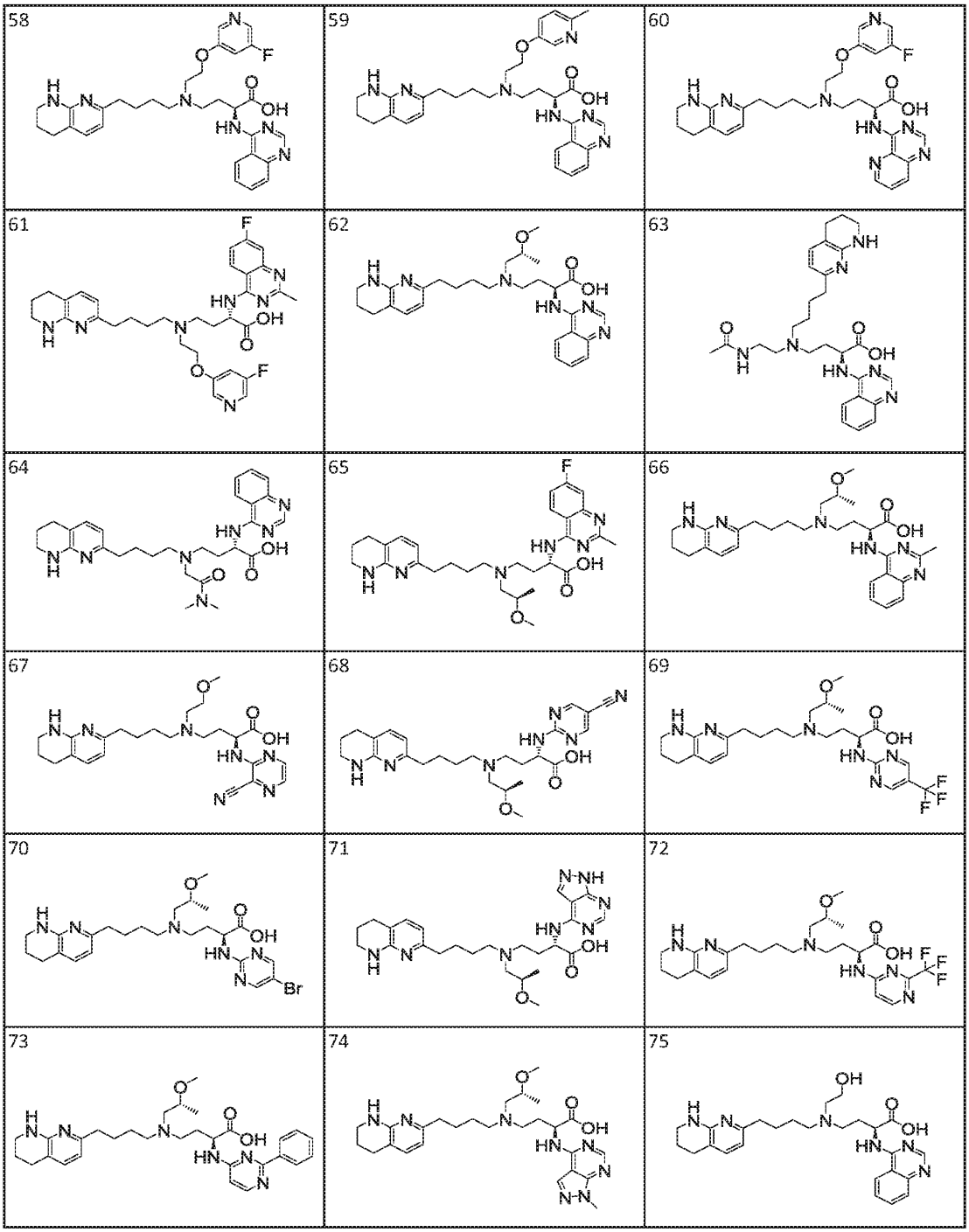


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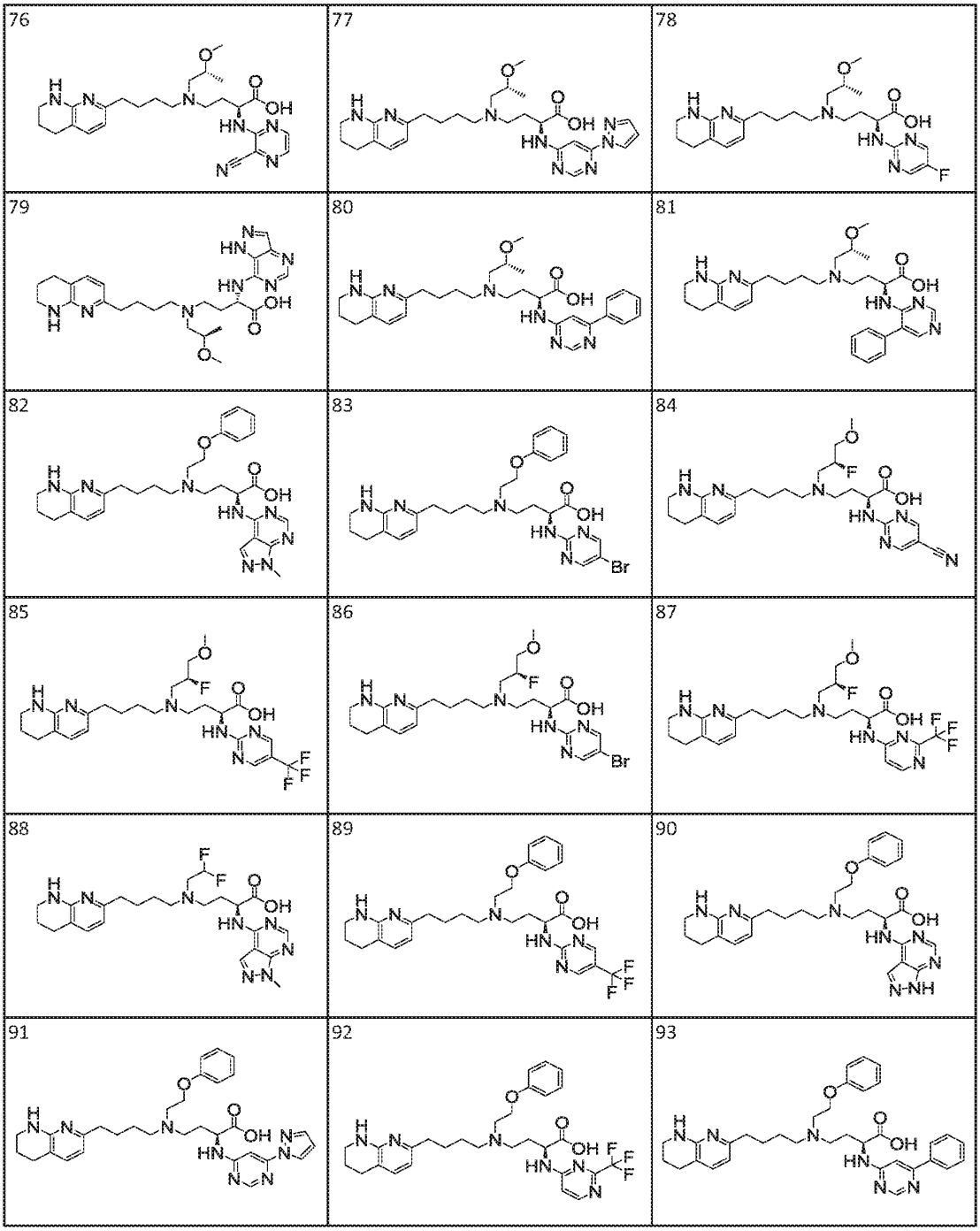


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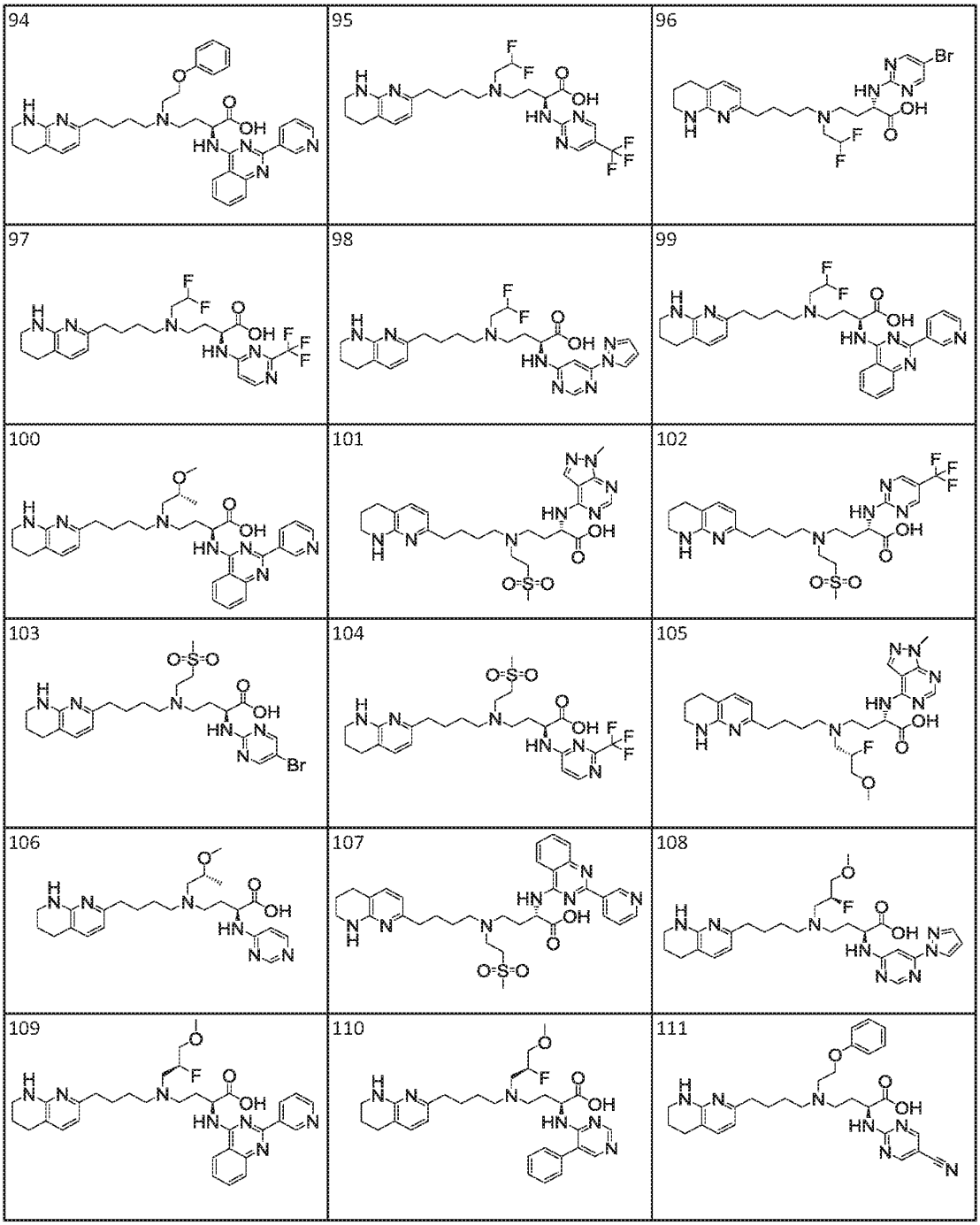


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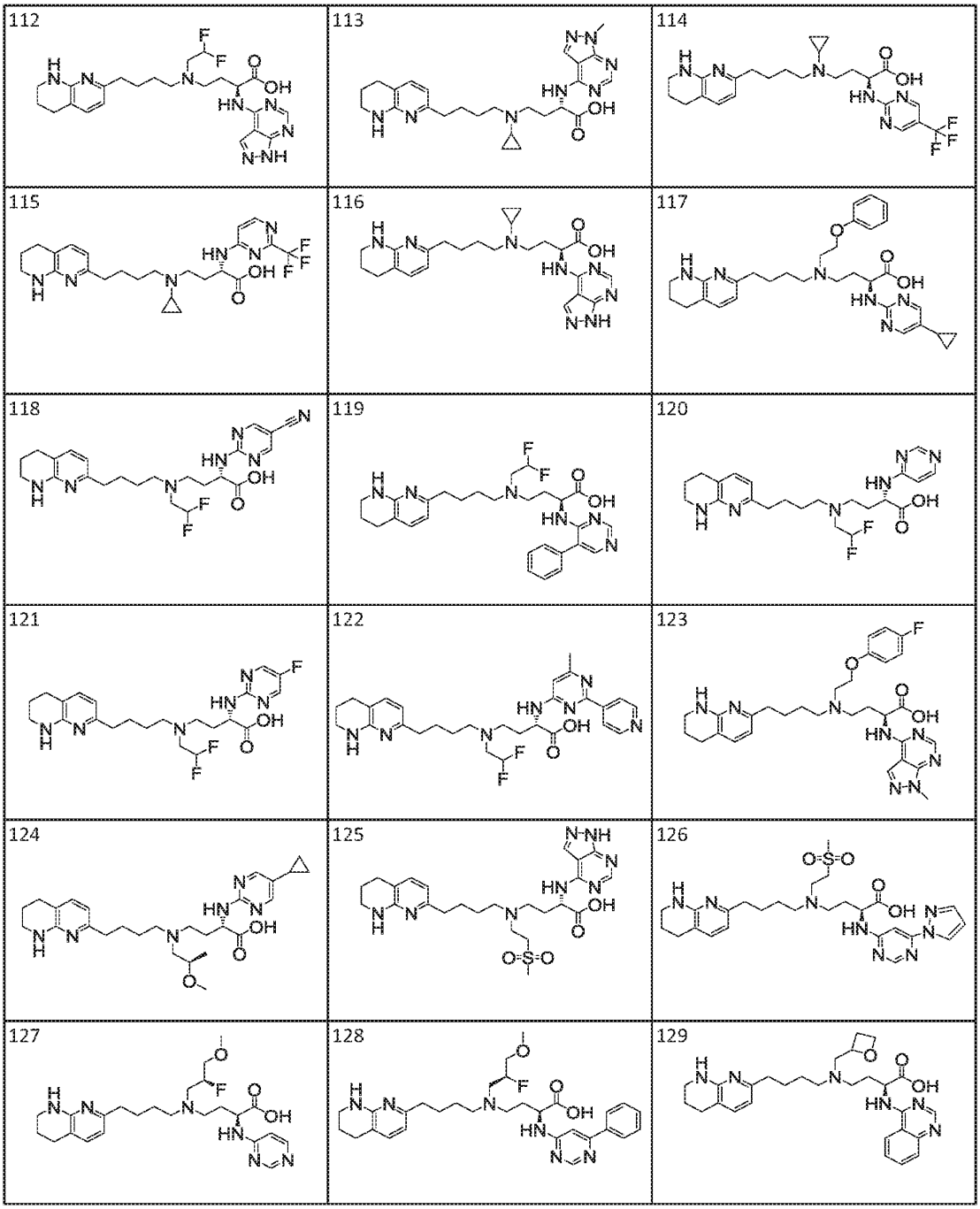

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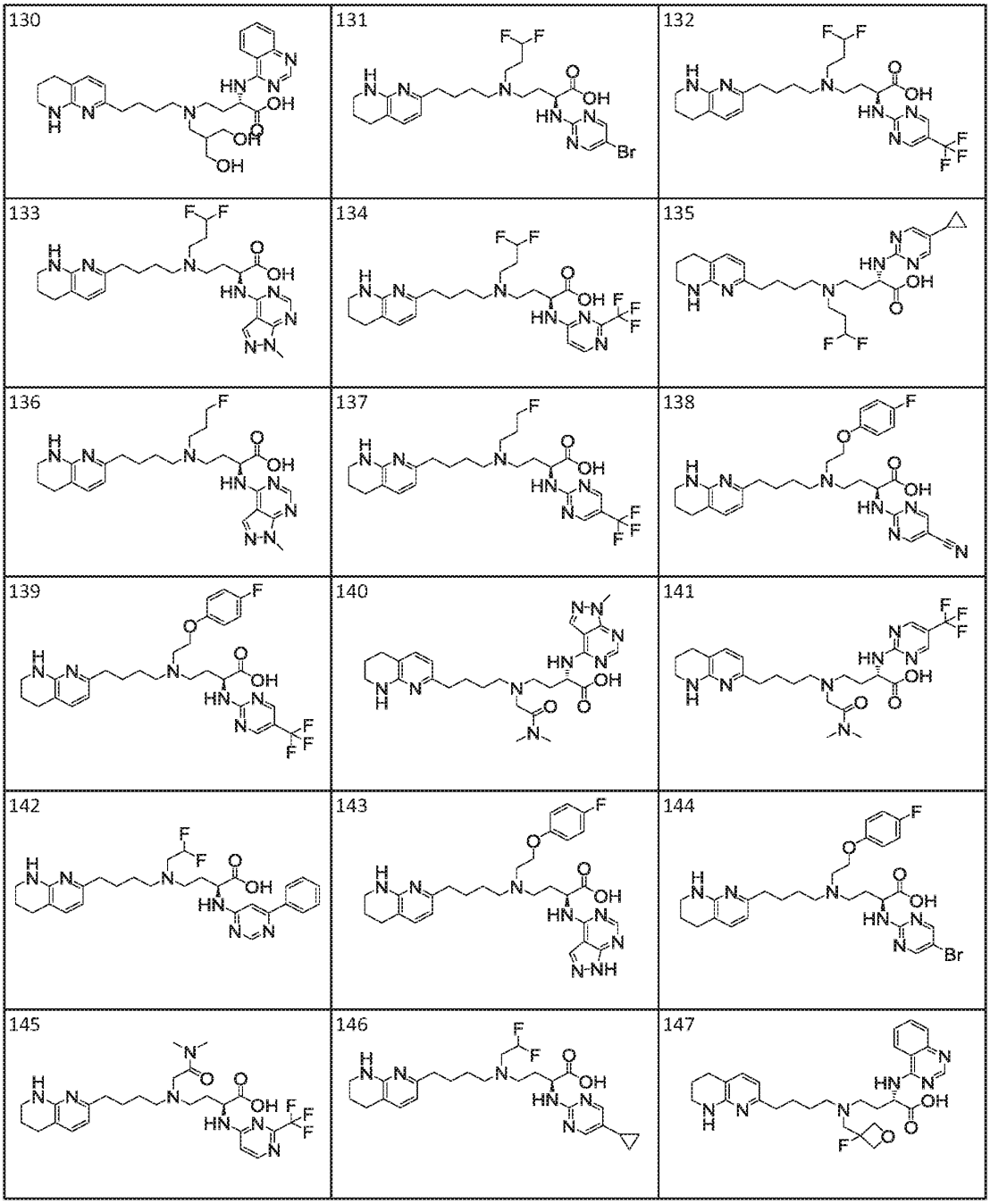

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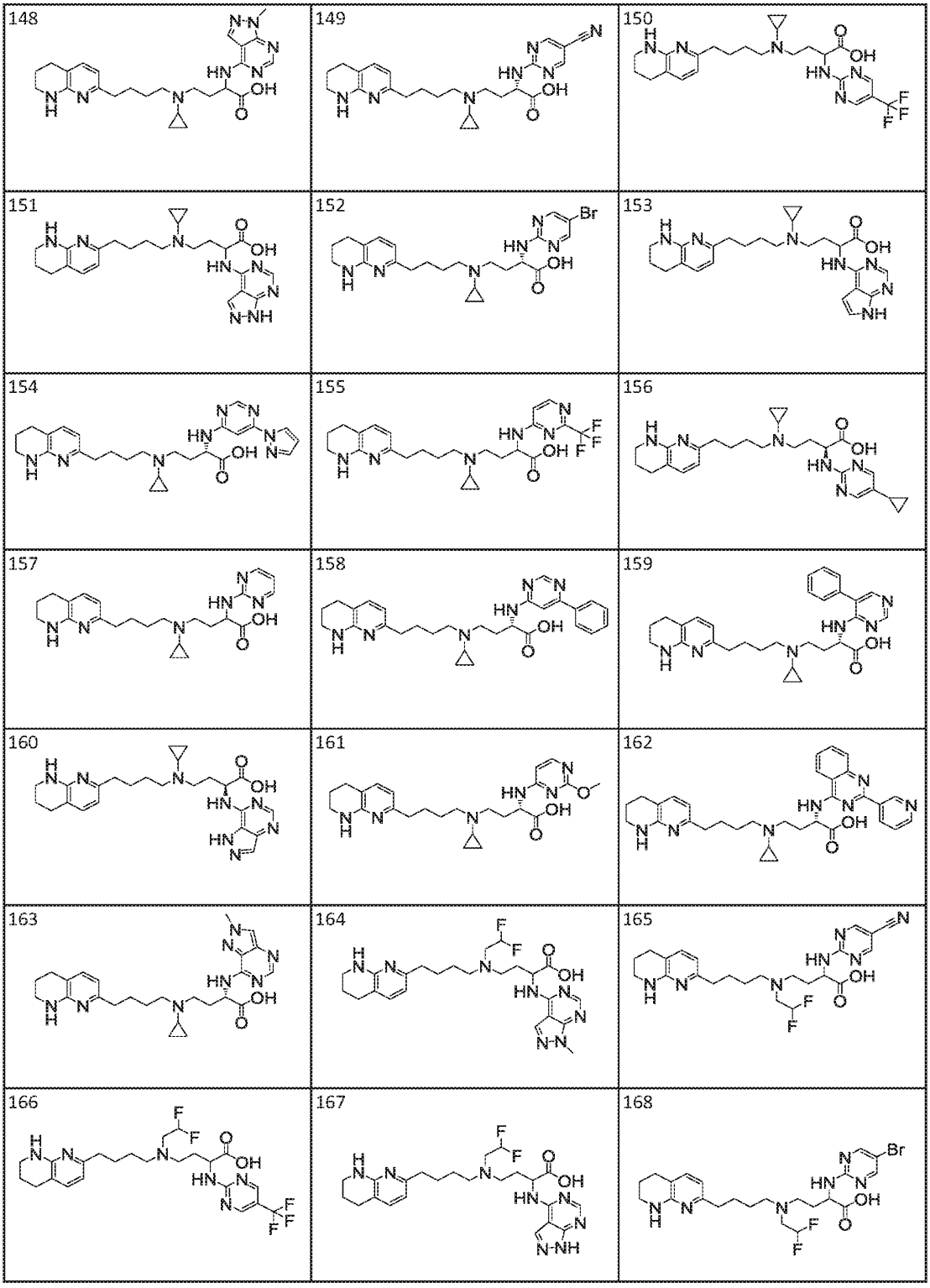

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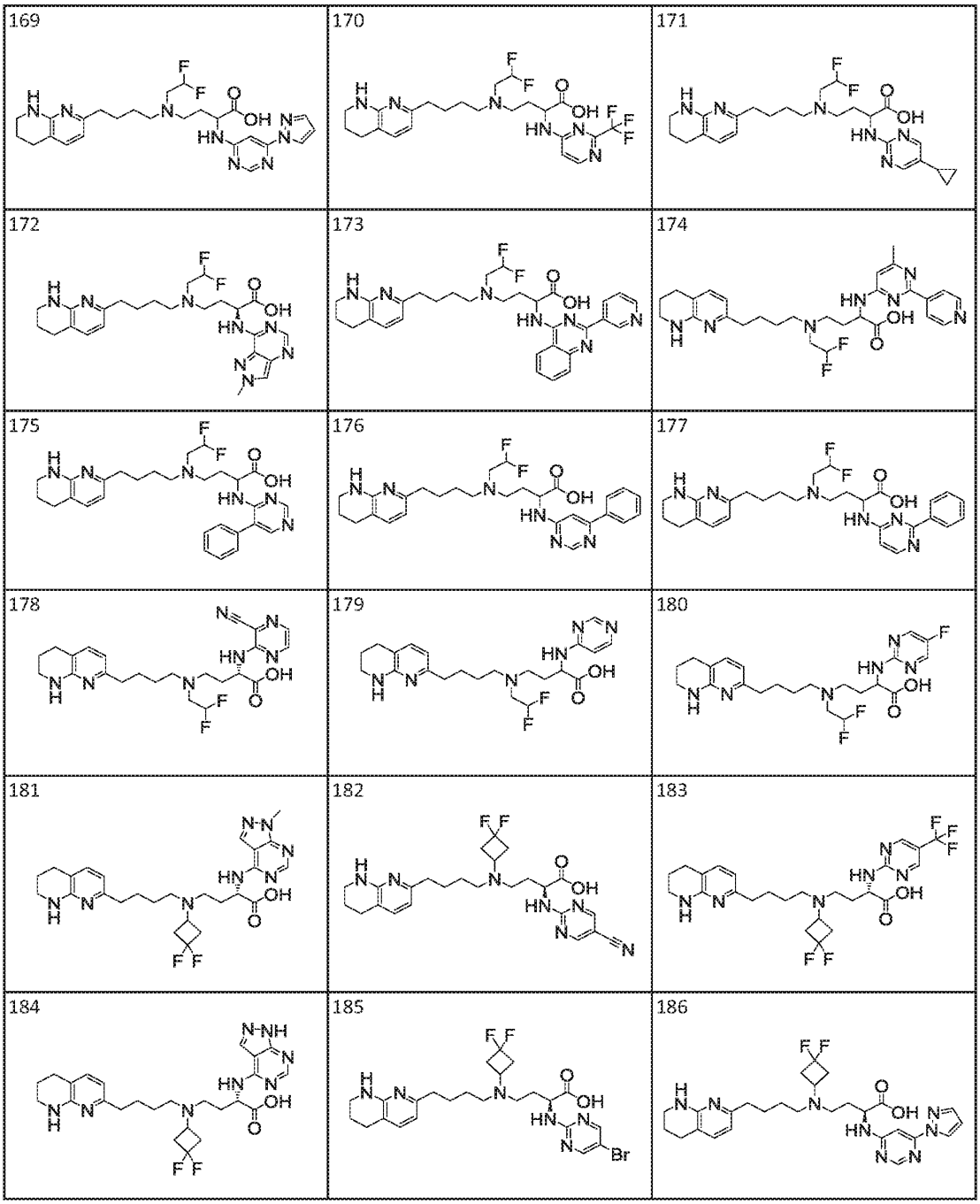

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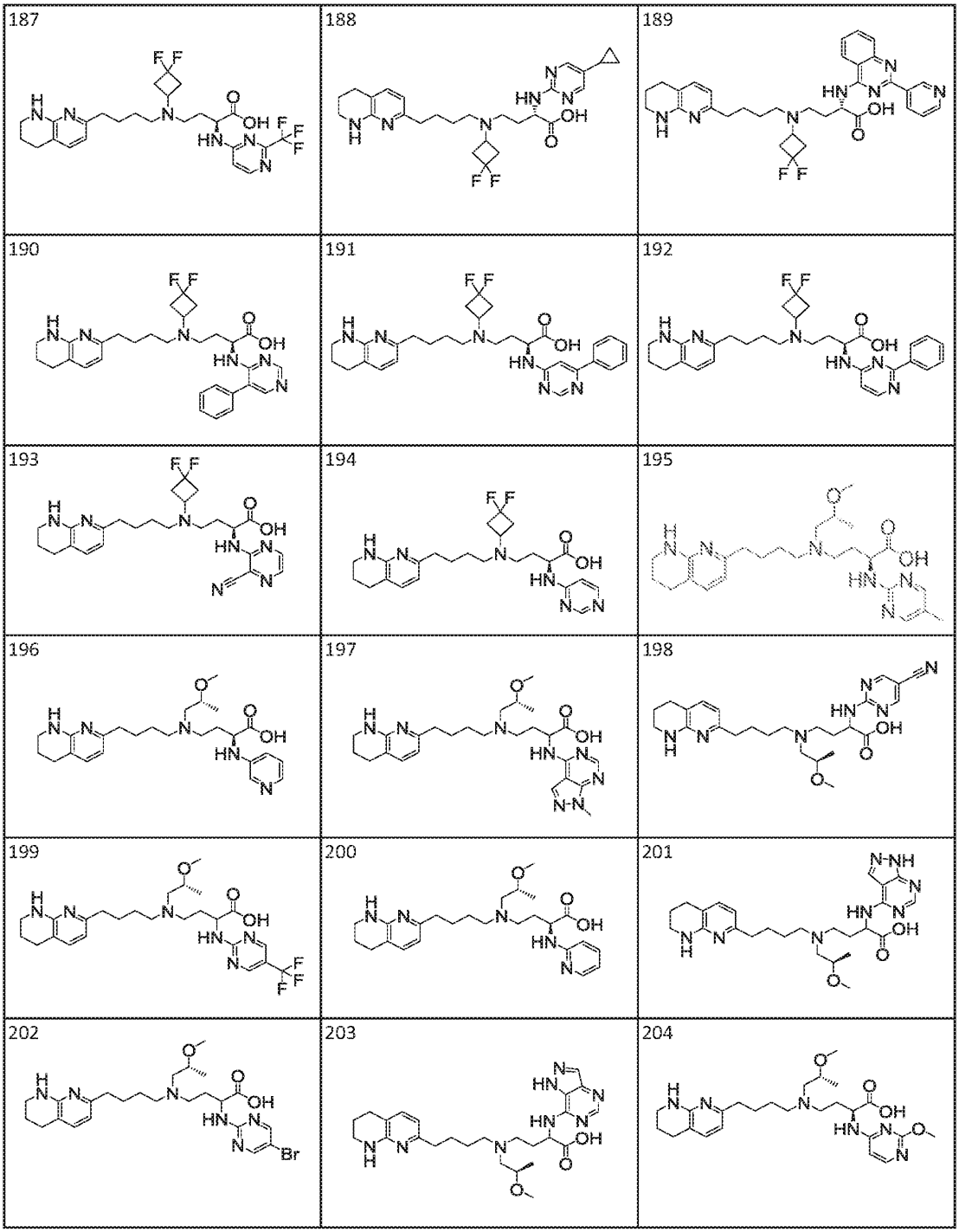

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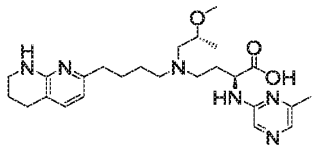
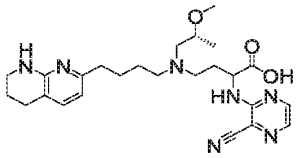
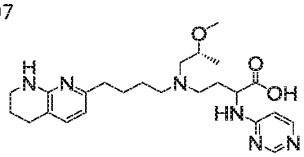
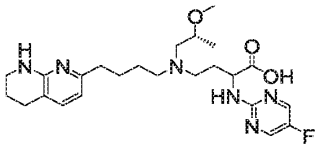
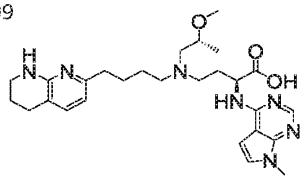
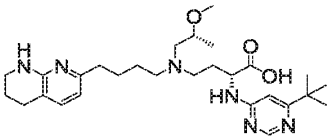
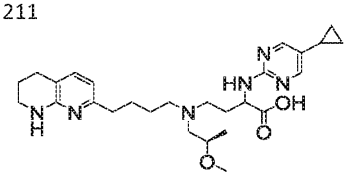
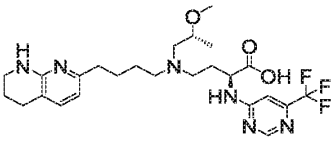
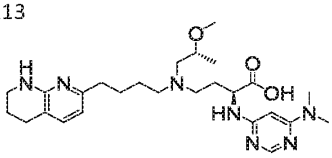
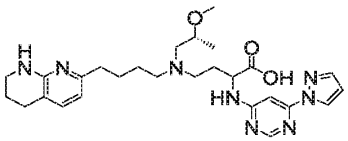
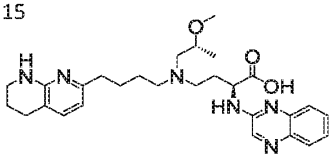
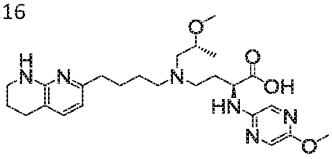
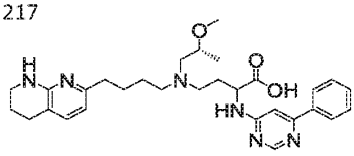
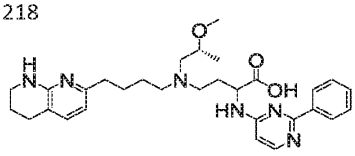
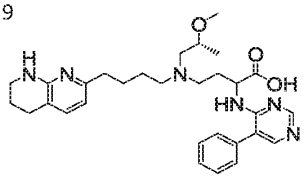
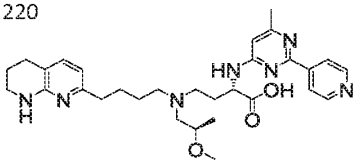
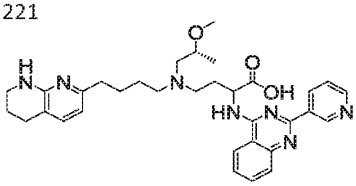
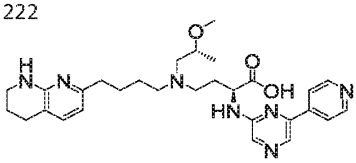
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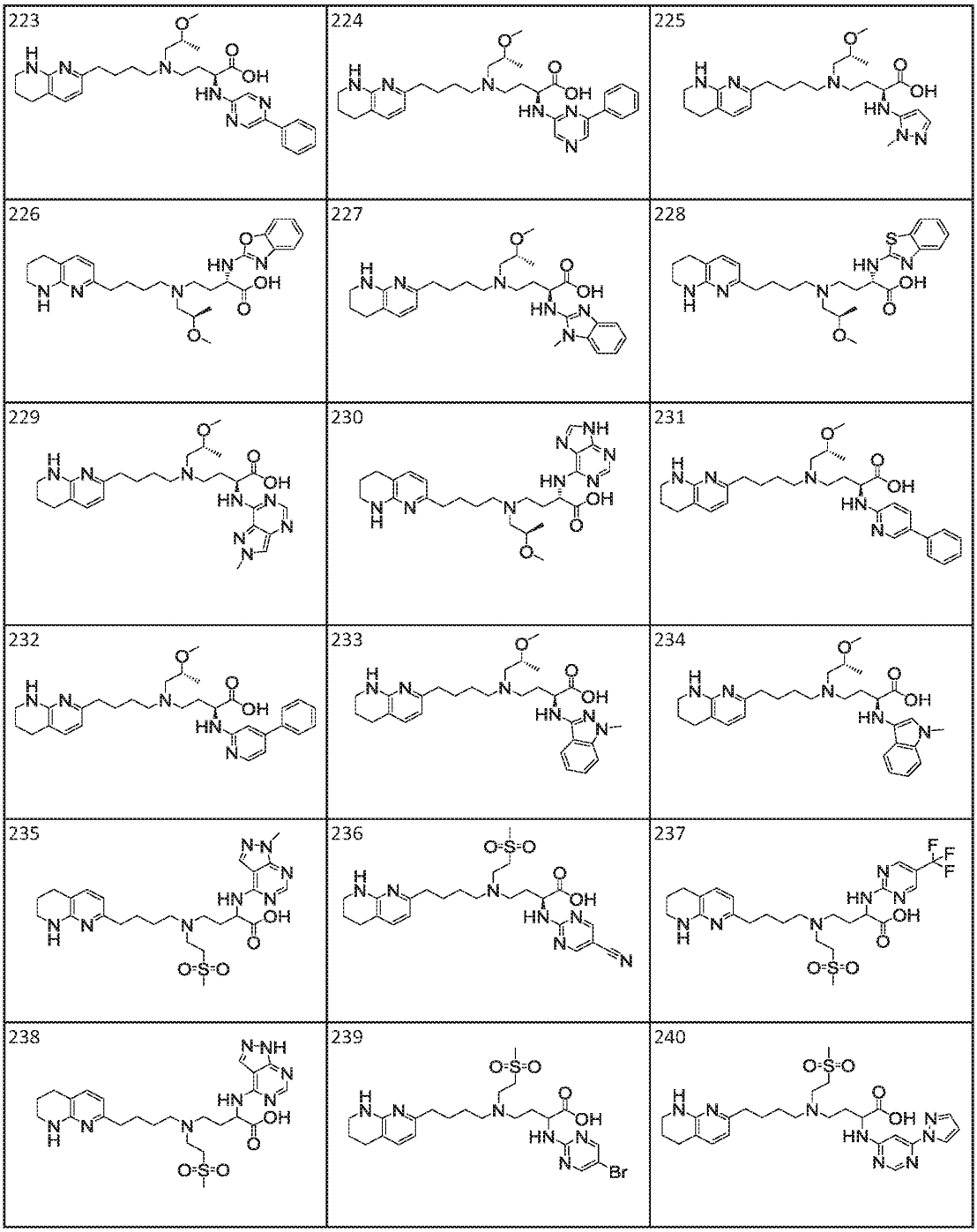

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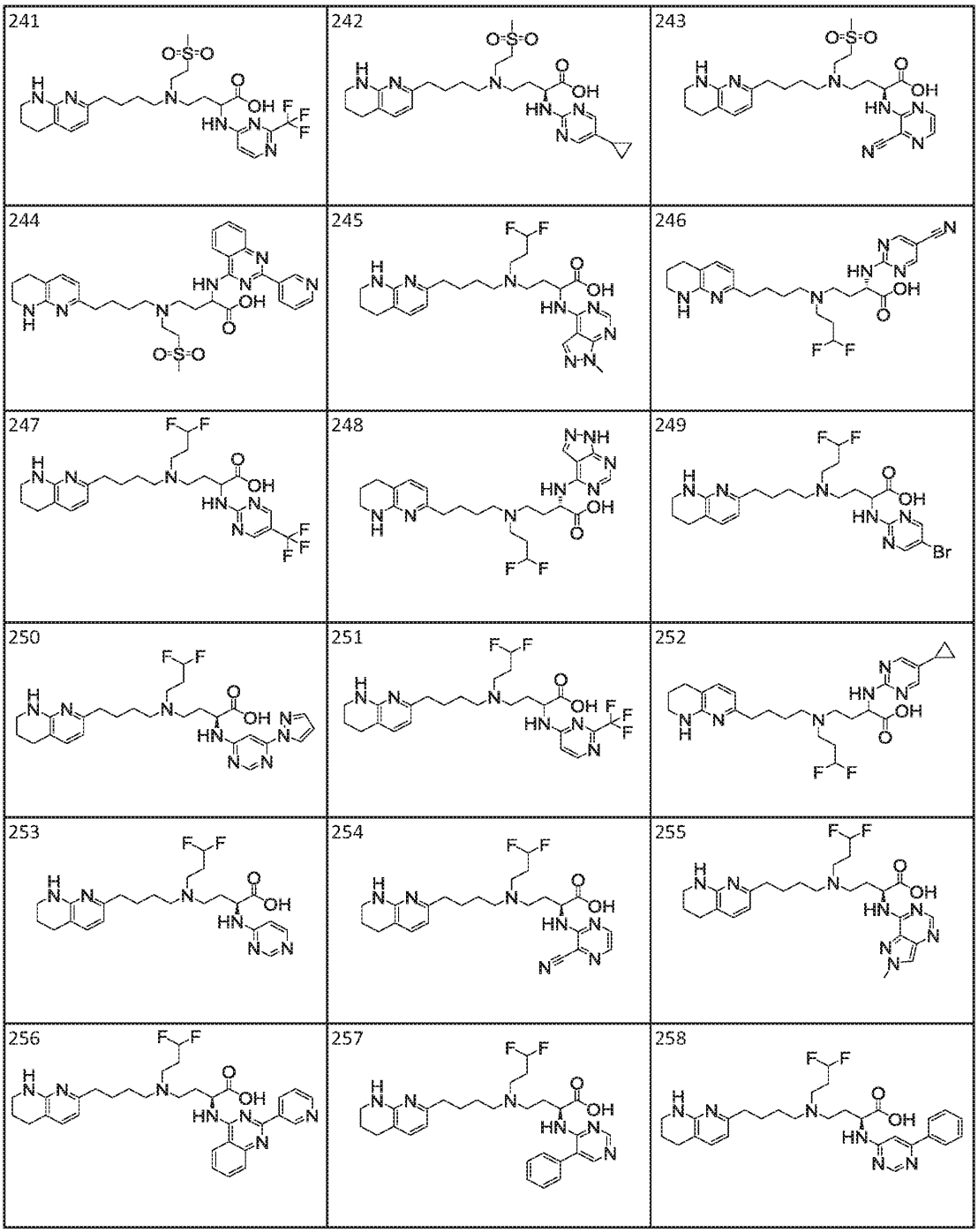

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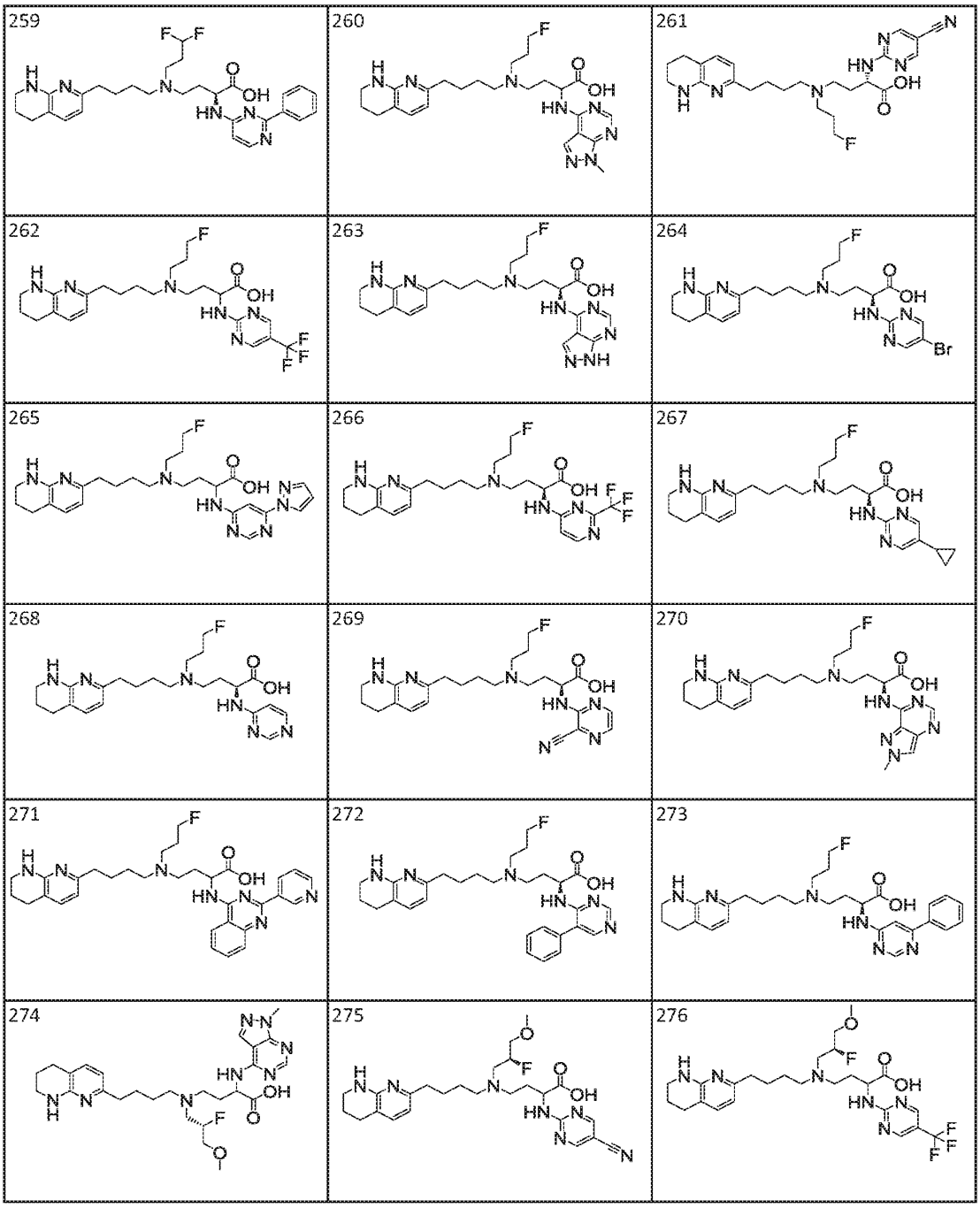

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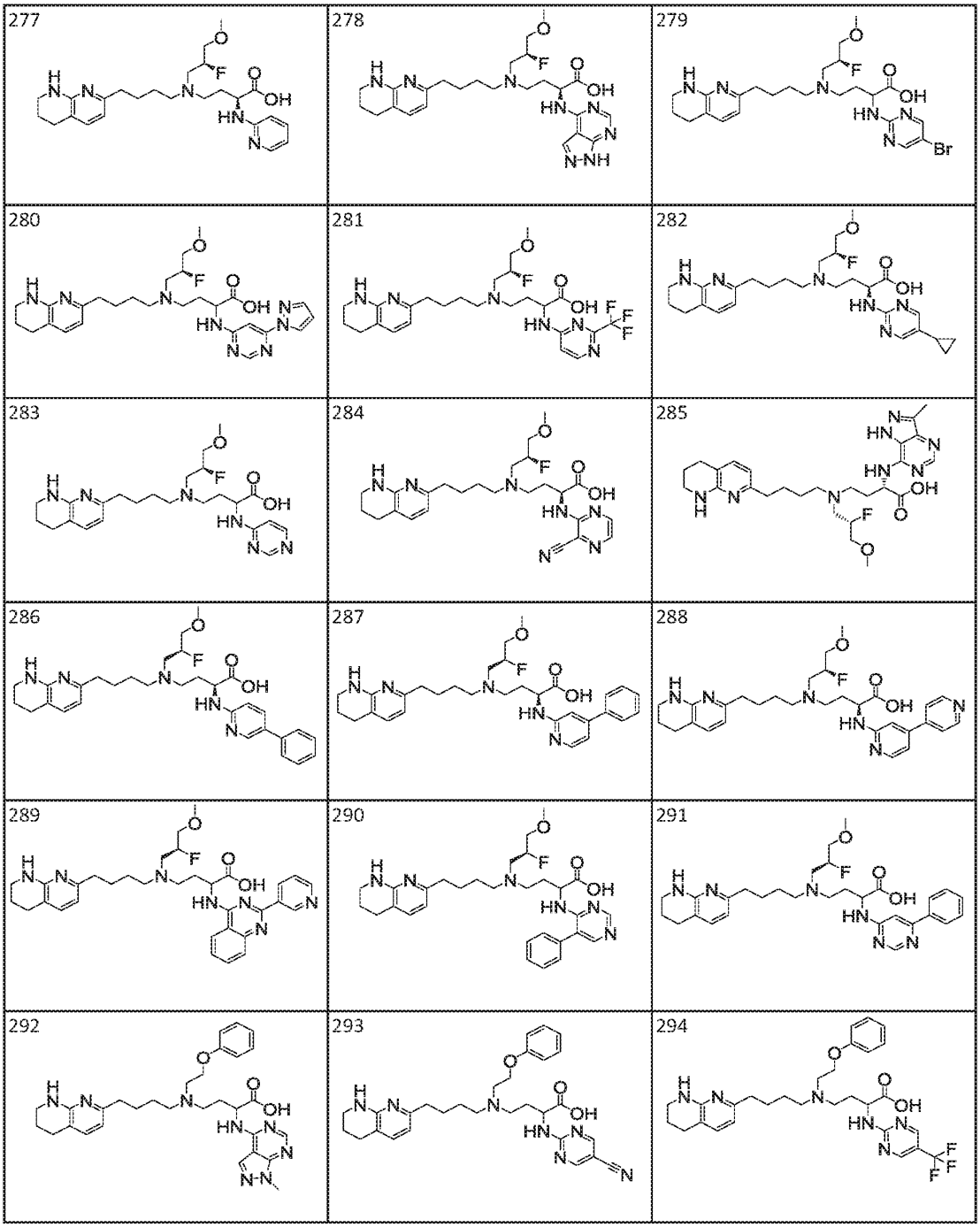

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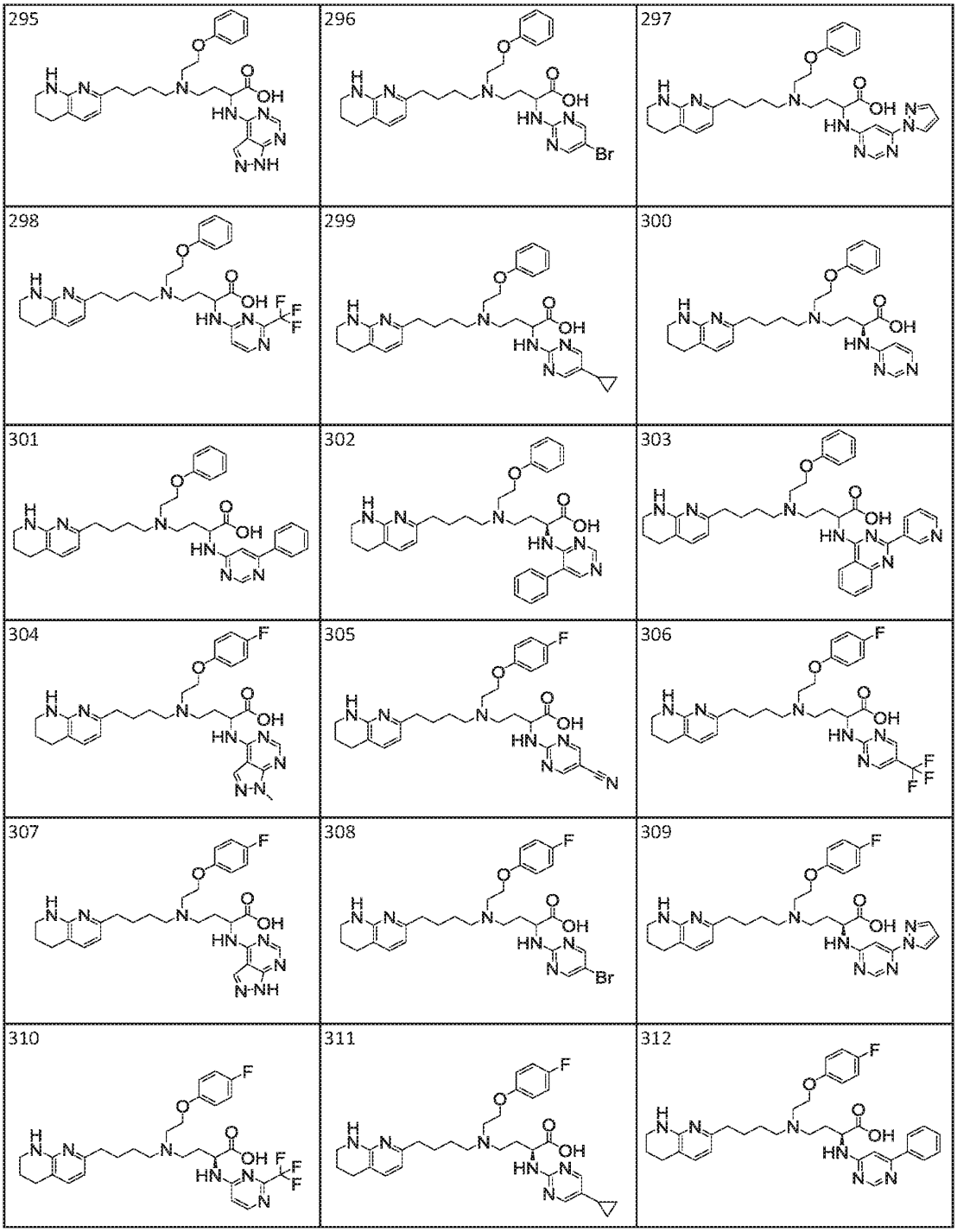

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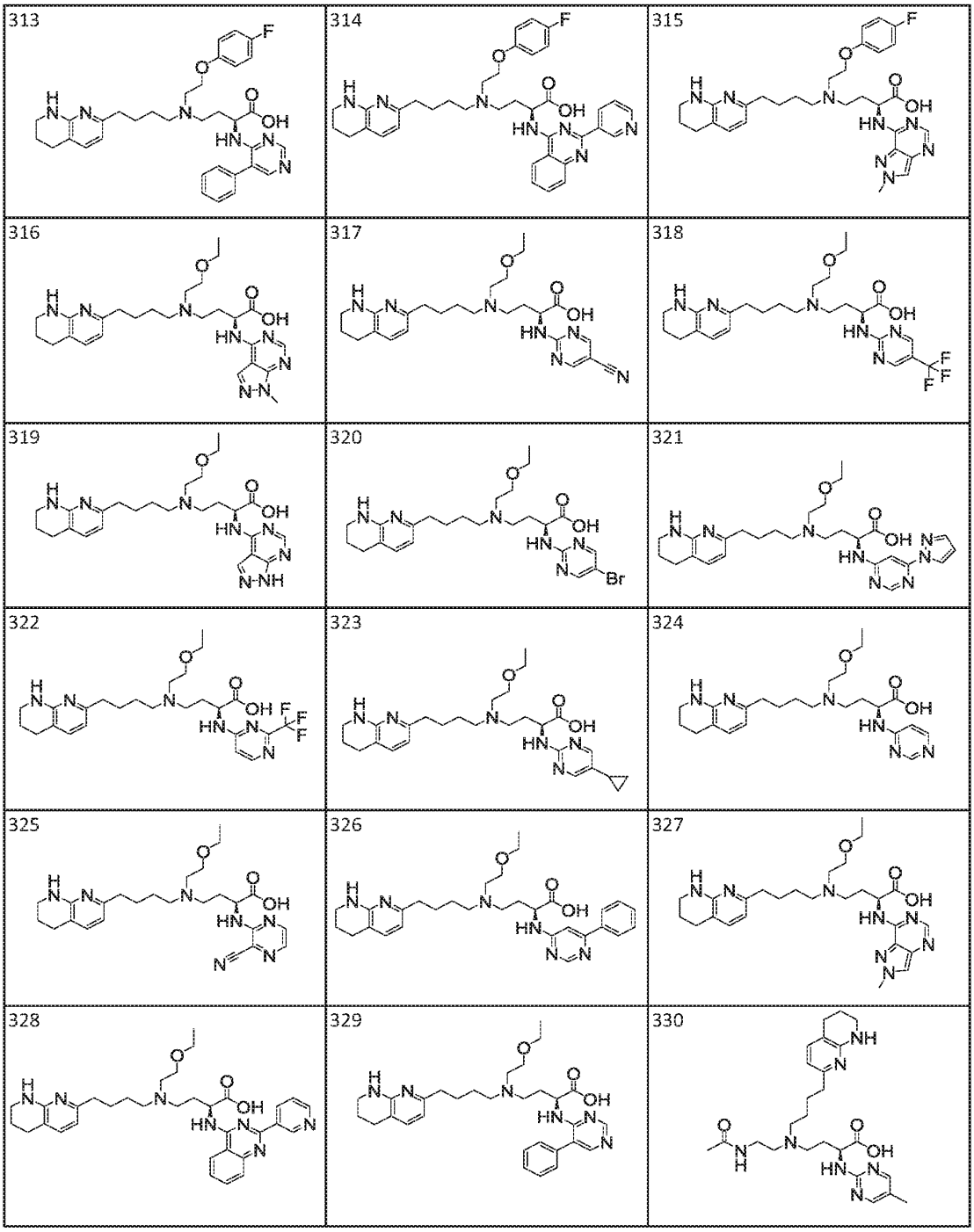

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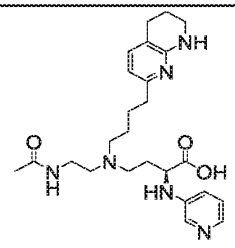
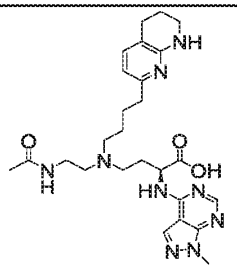
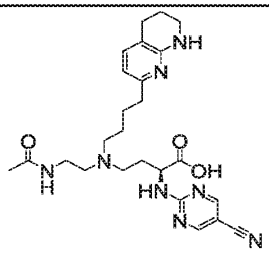
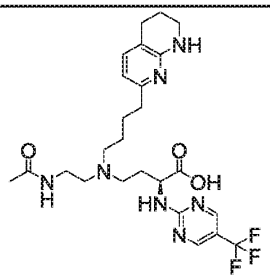
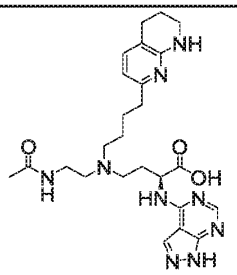
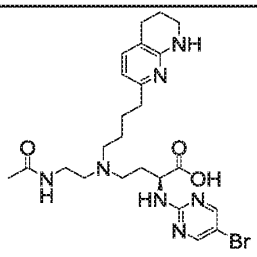
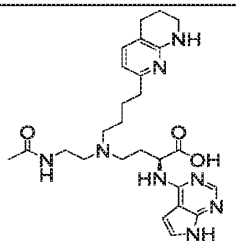
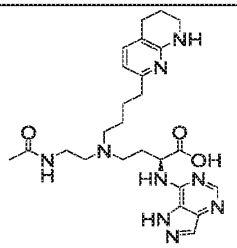
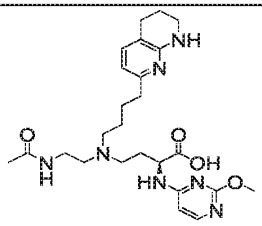
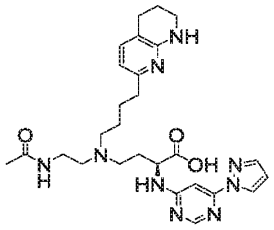
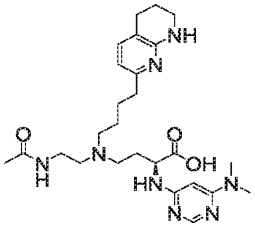
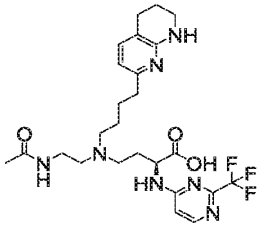
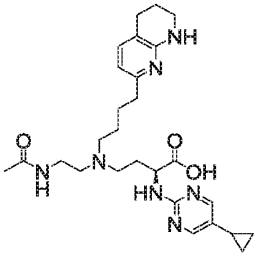
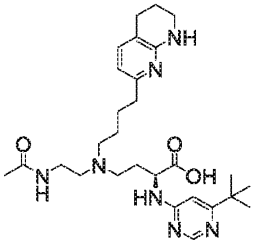
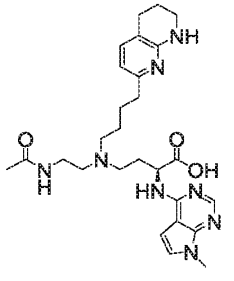
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FIG. 1 (cont.)

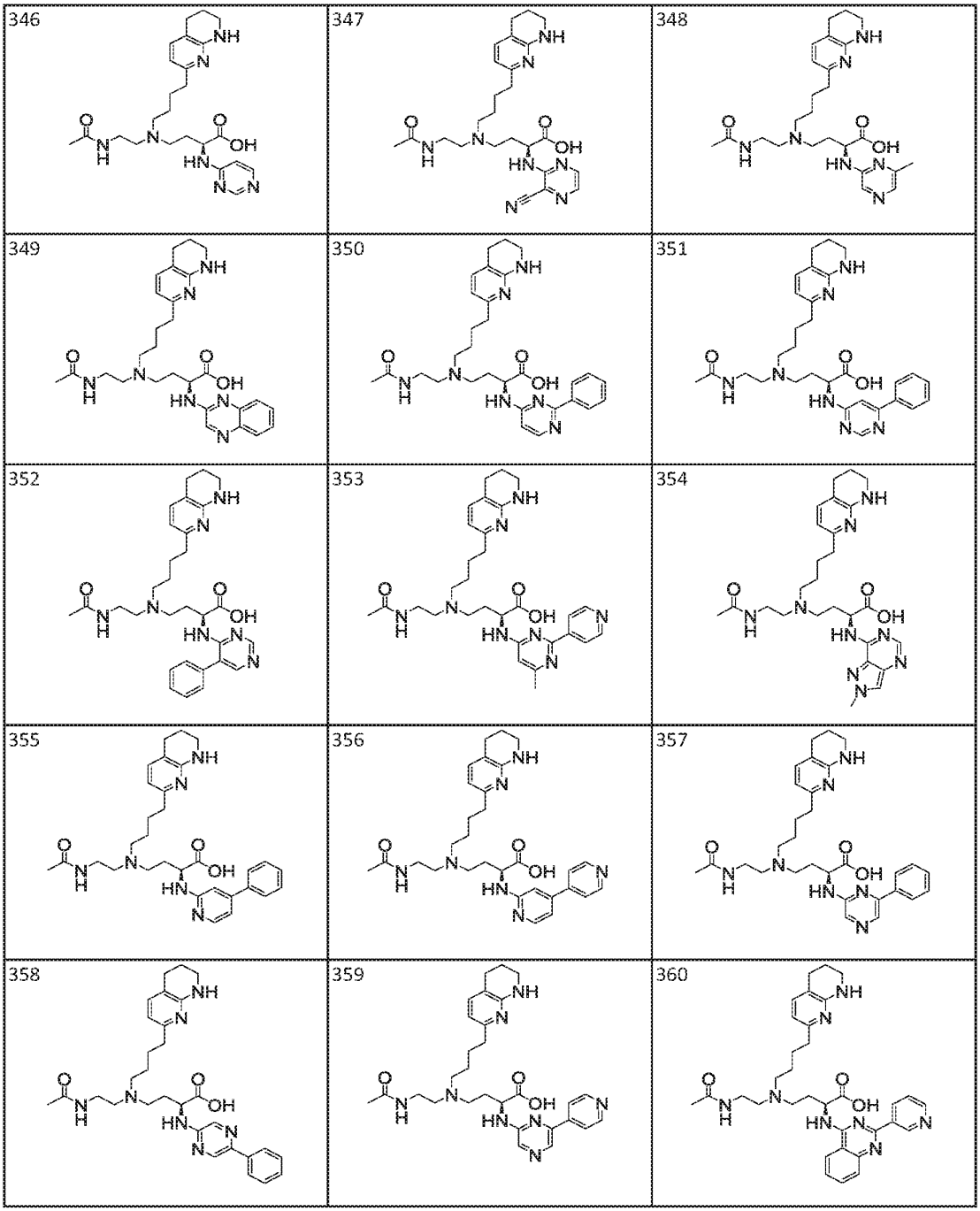


FIG. 1 (cont.)

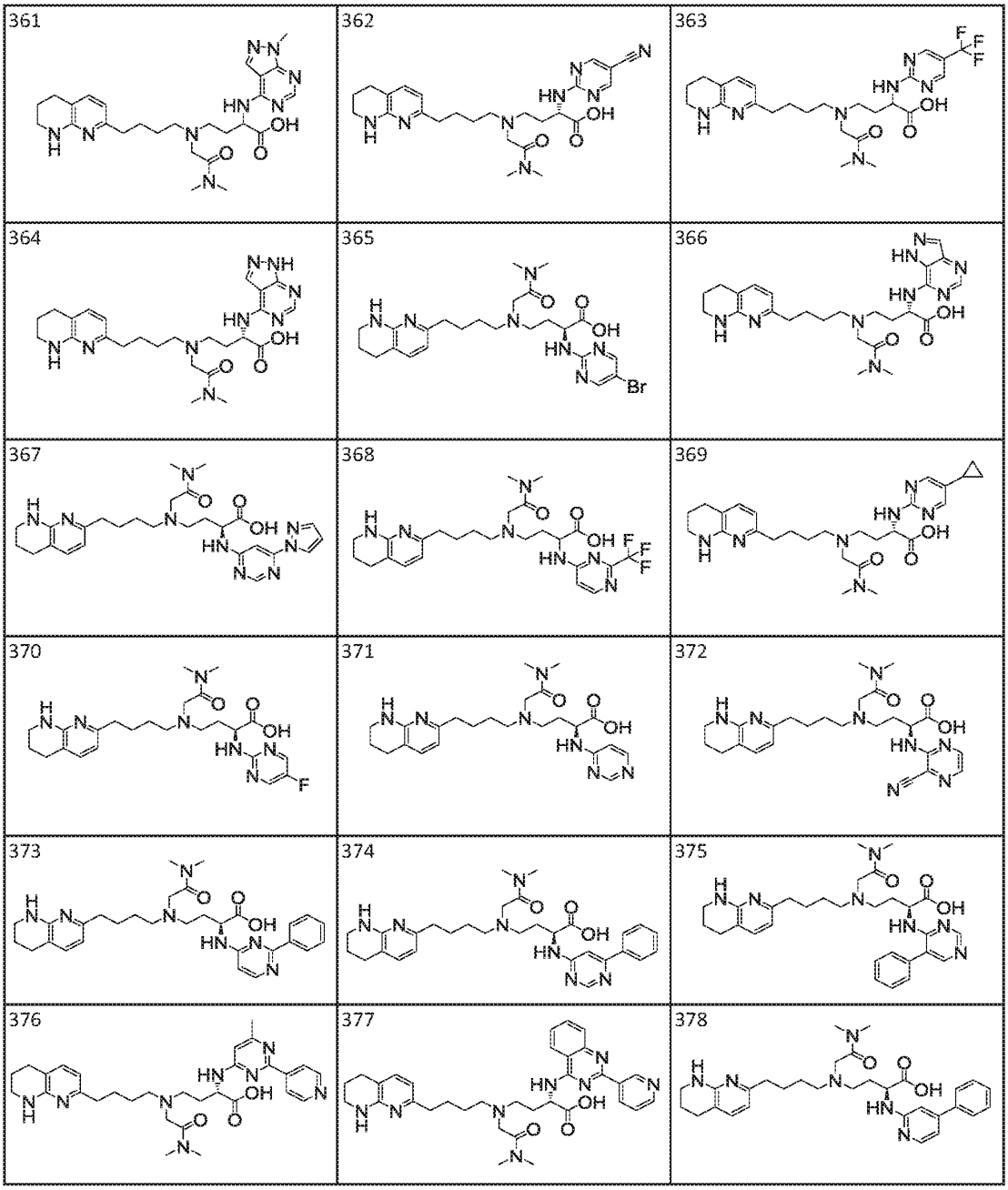

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FIG. 1 (cont.)

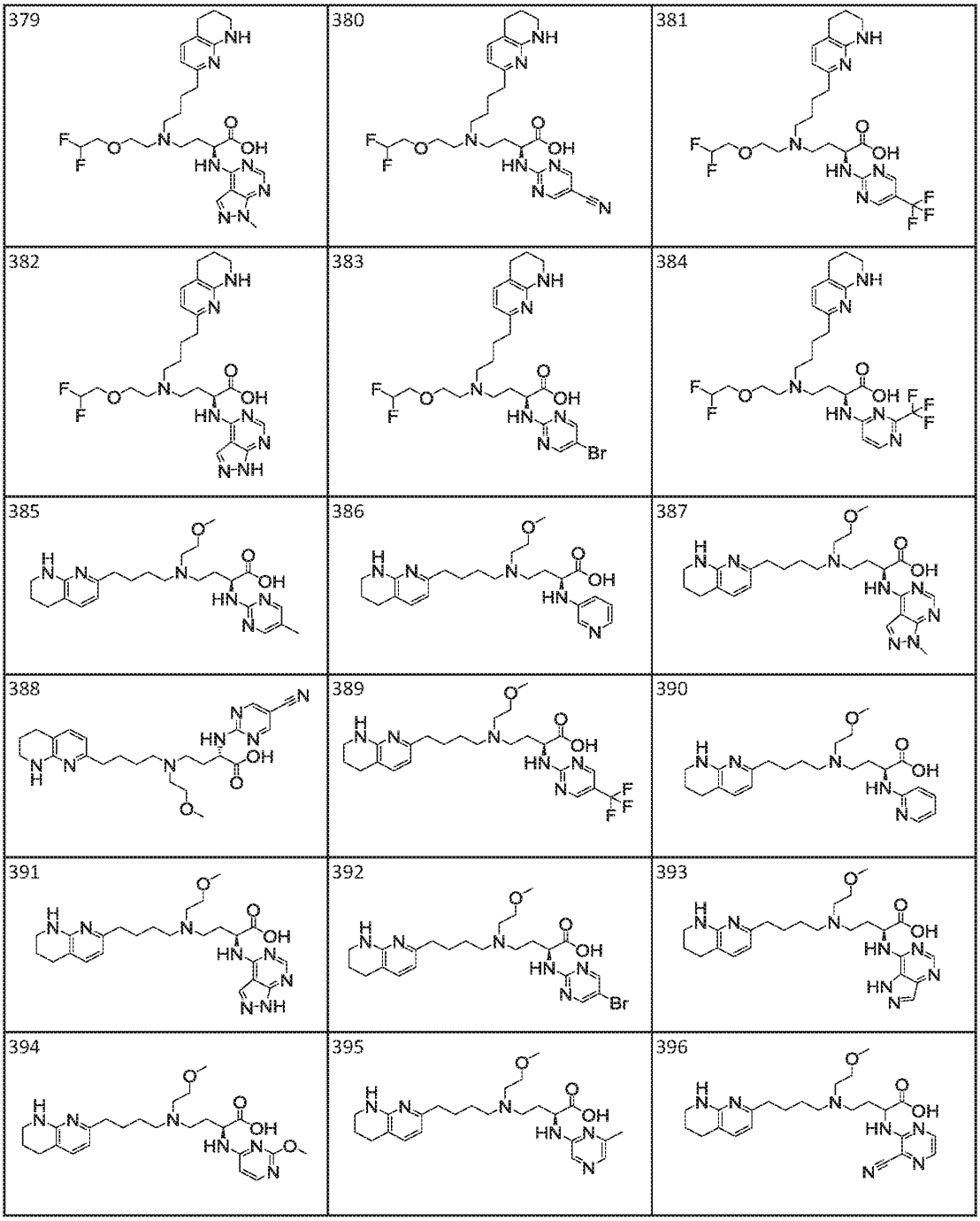

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FIG. 1 (cont.)

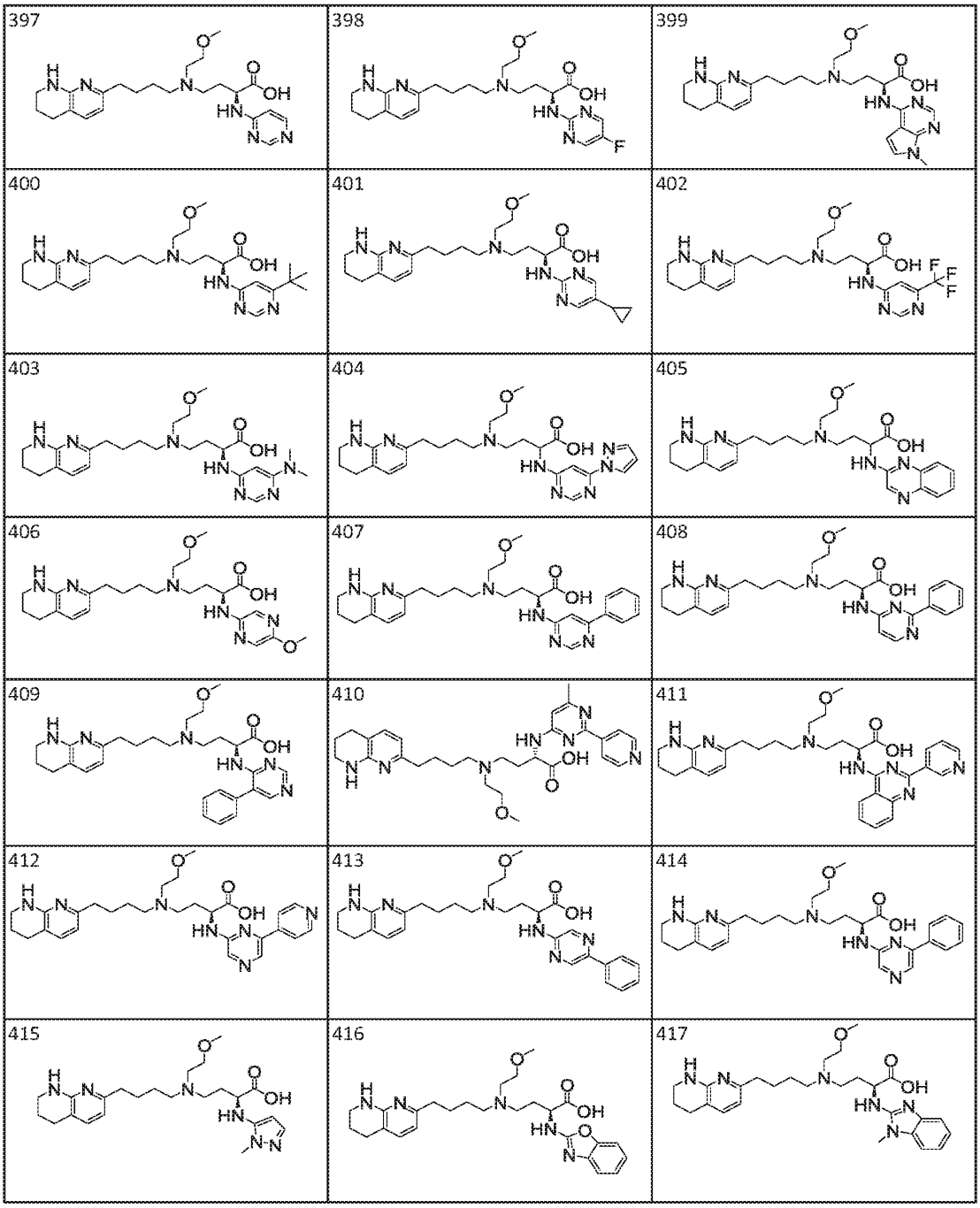

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FIG. 1 (cont.)

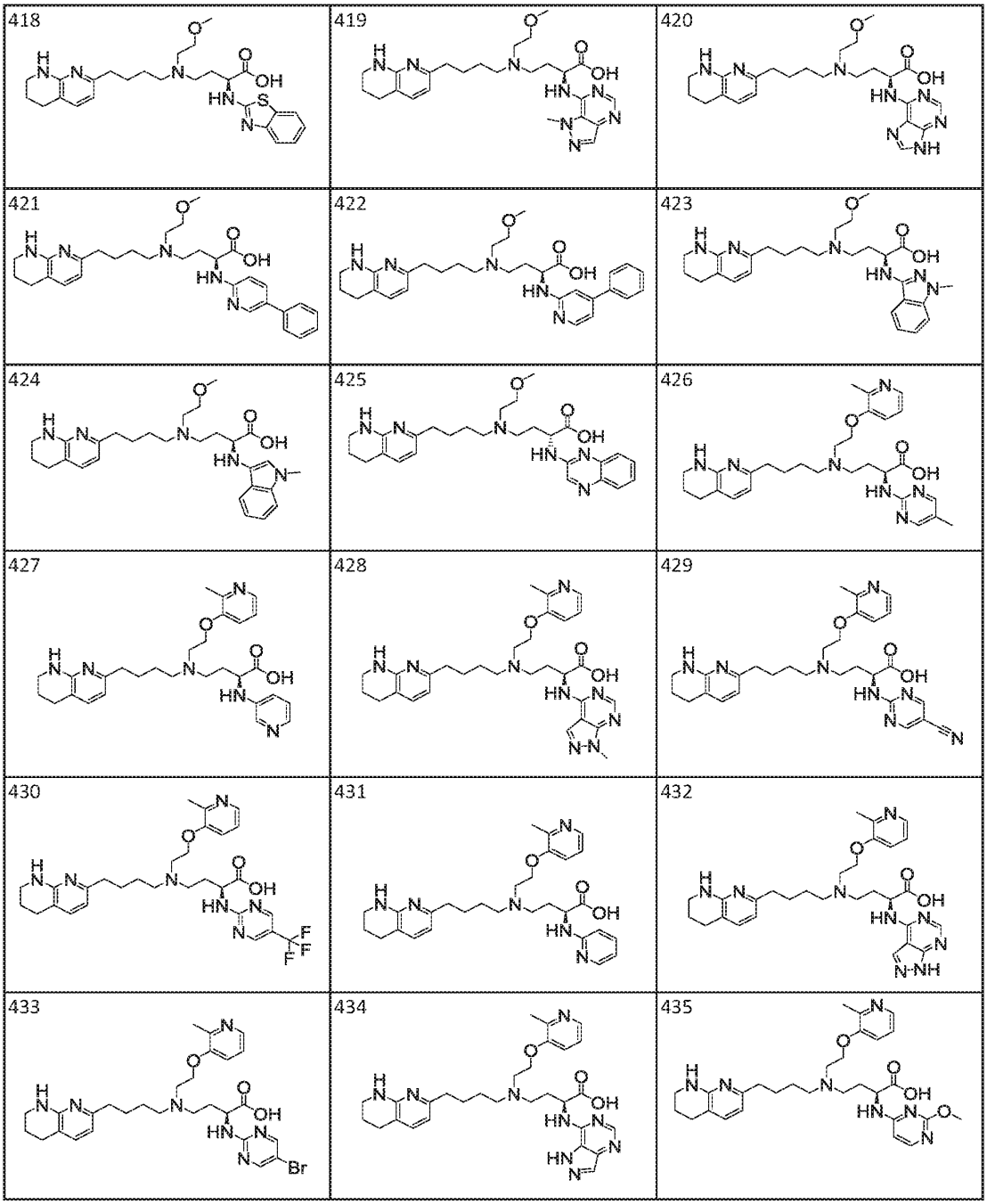

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FIG. 1 (cont.)

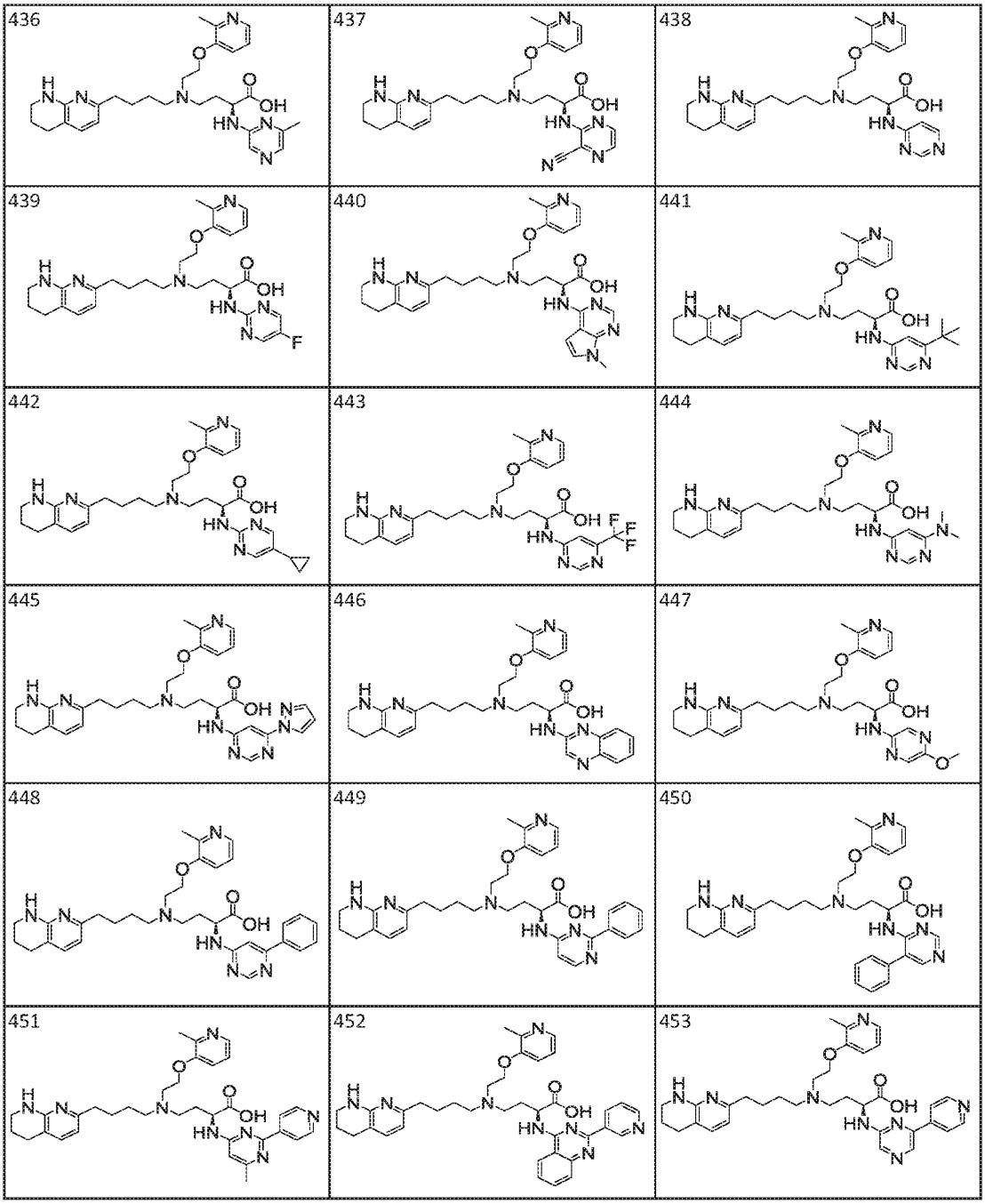

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FIG. 1 (cont.)

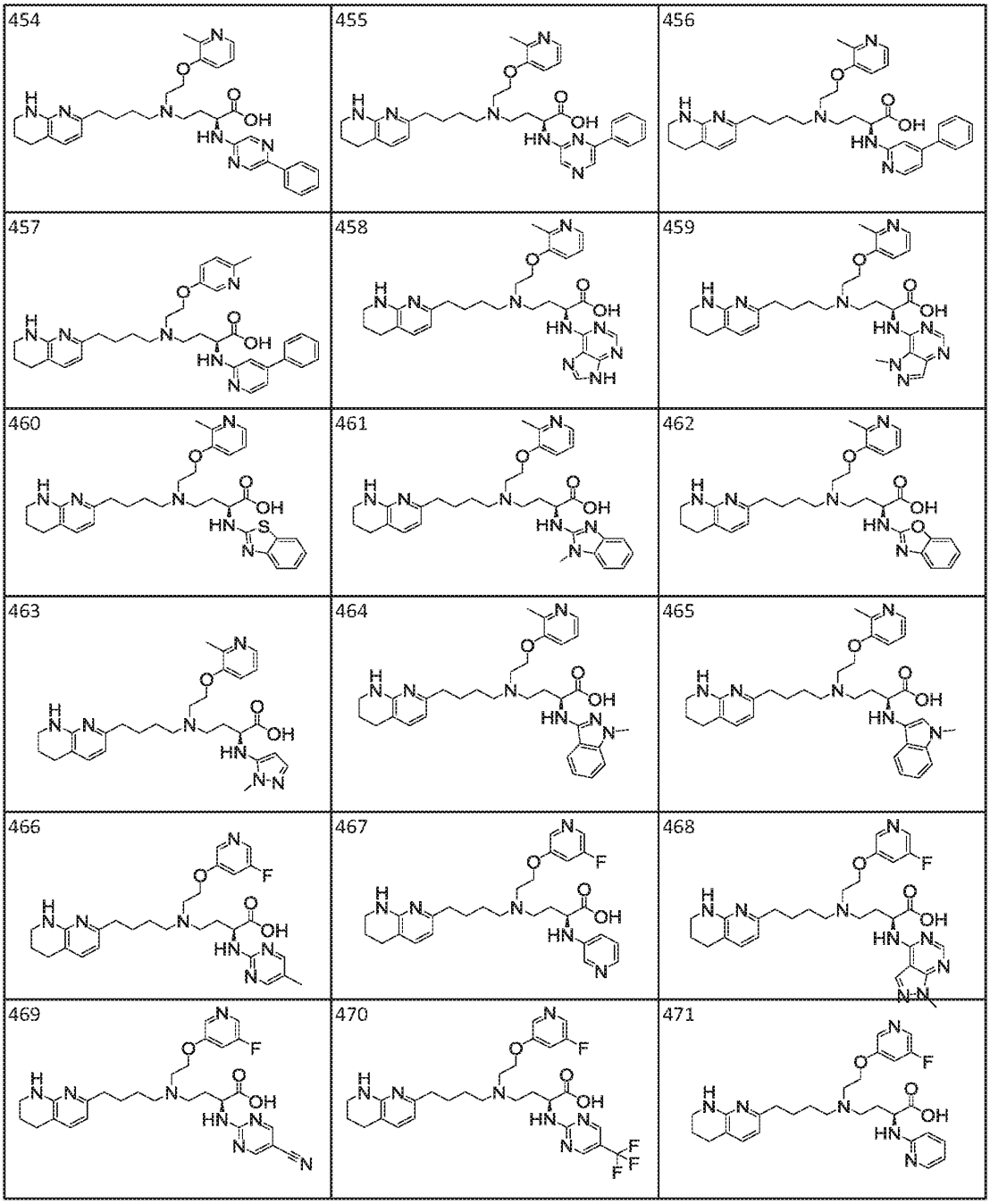

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FIG. 1 (cont.)

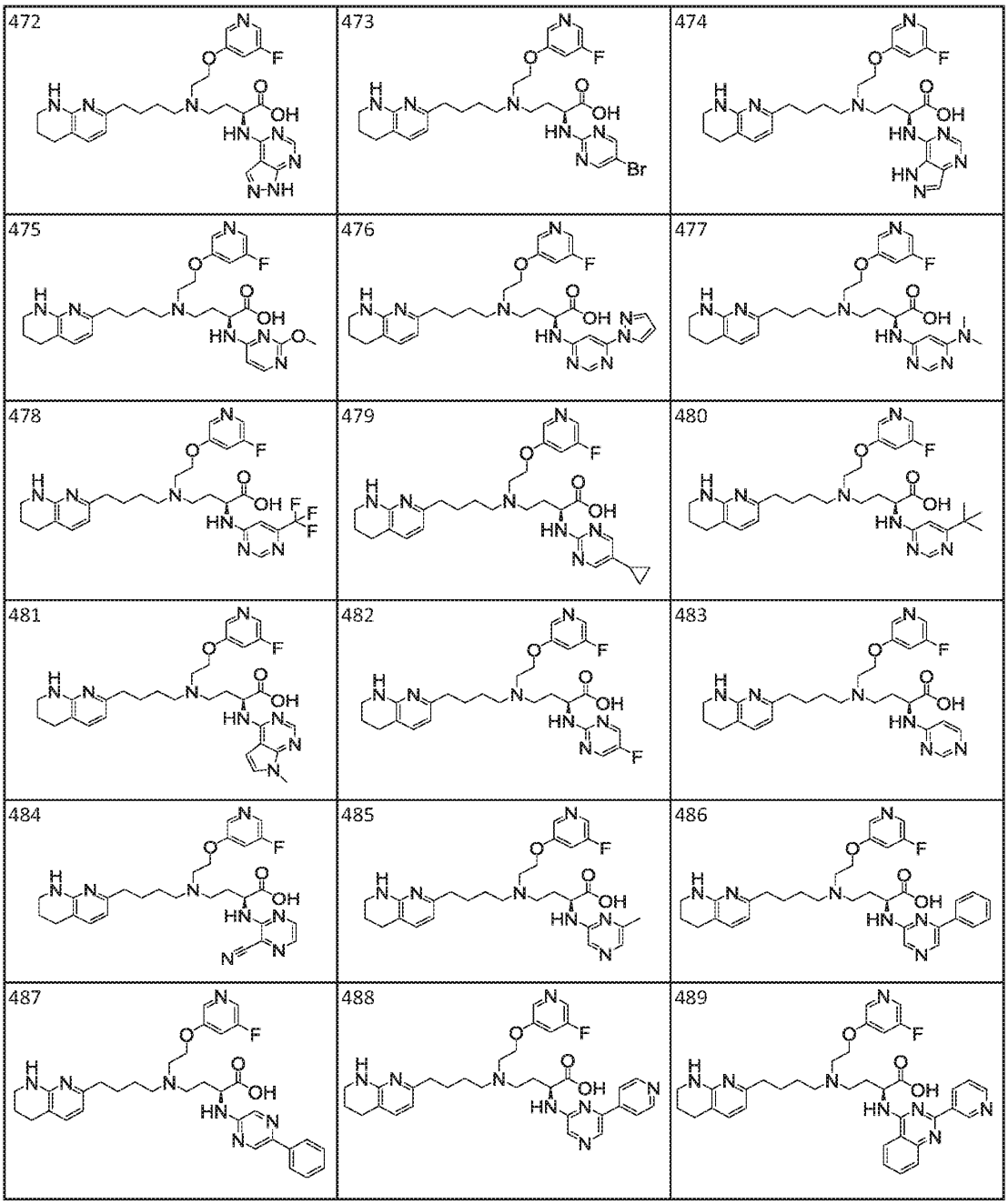

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FIG. 1 (cont.)

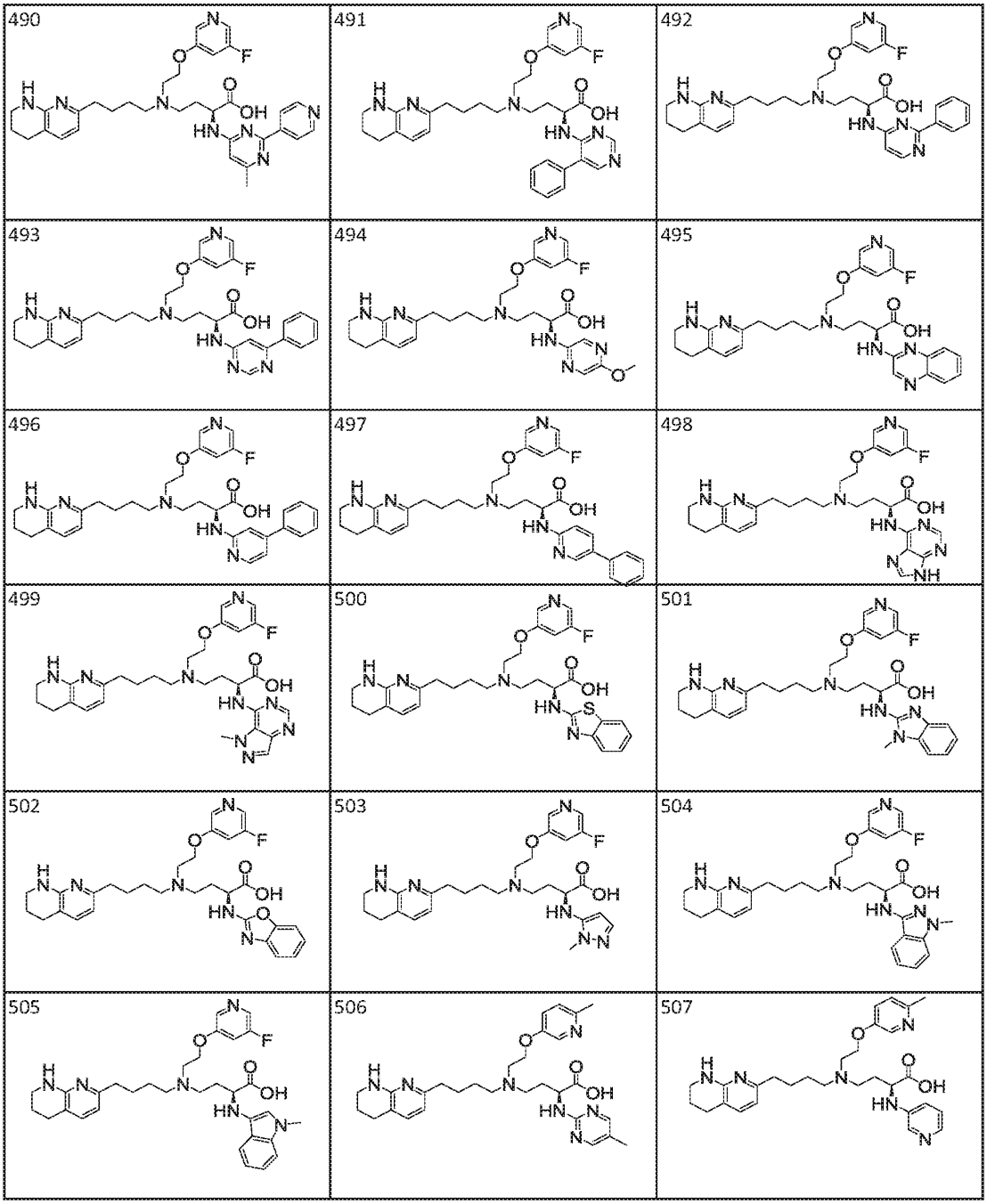

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FIG. 1 (cont.)

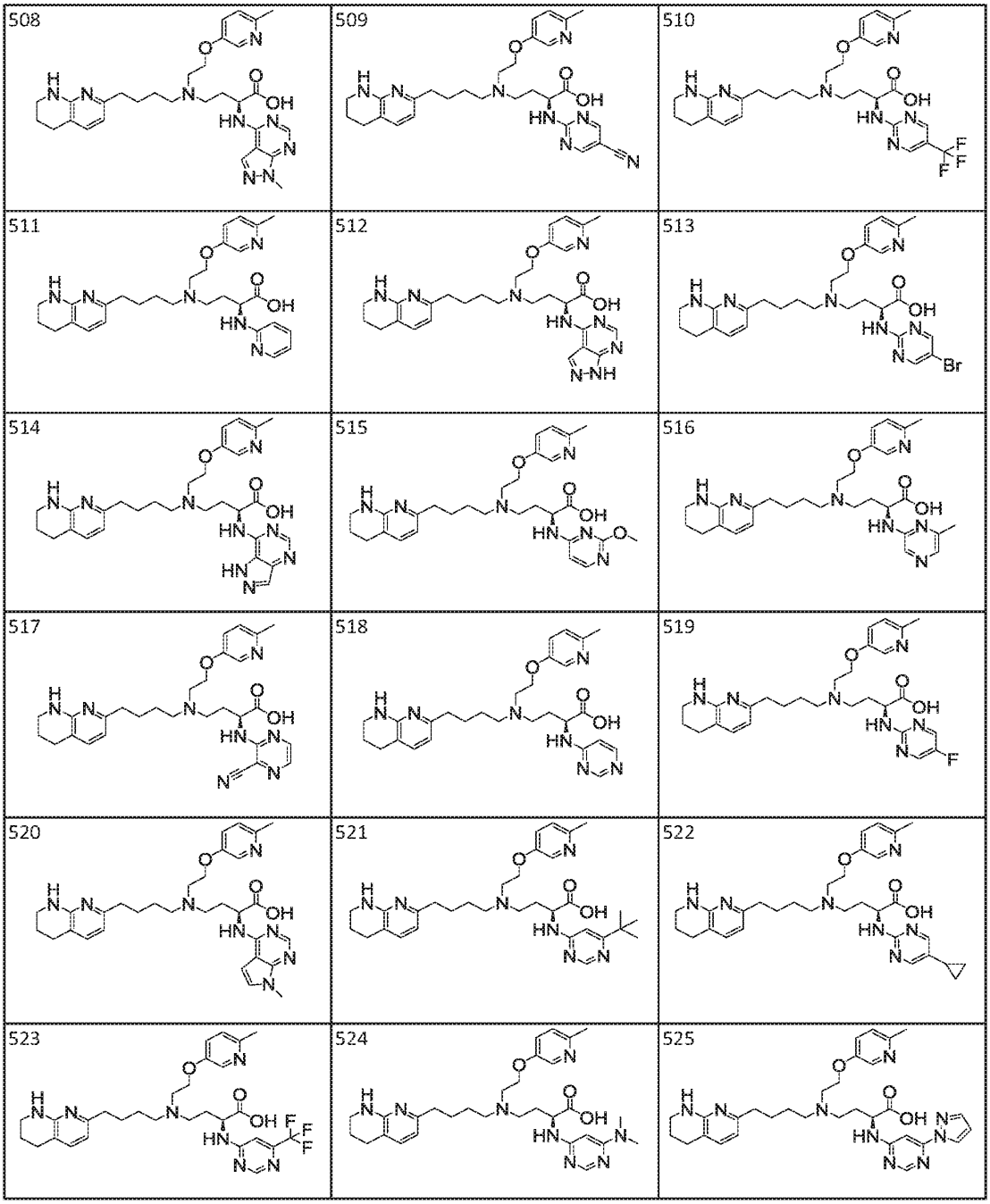

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FIG. 1 (cont.)

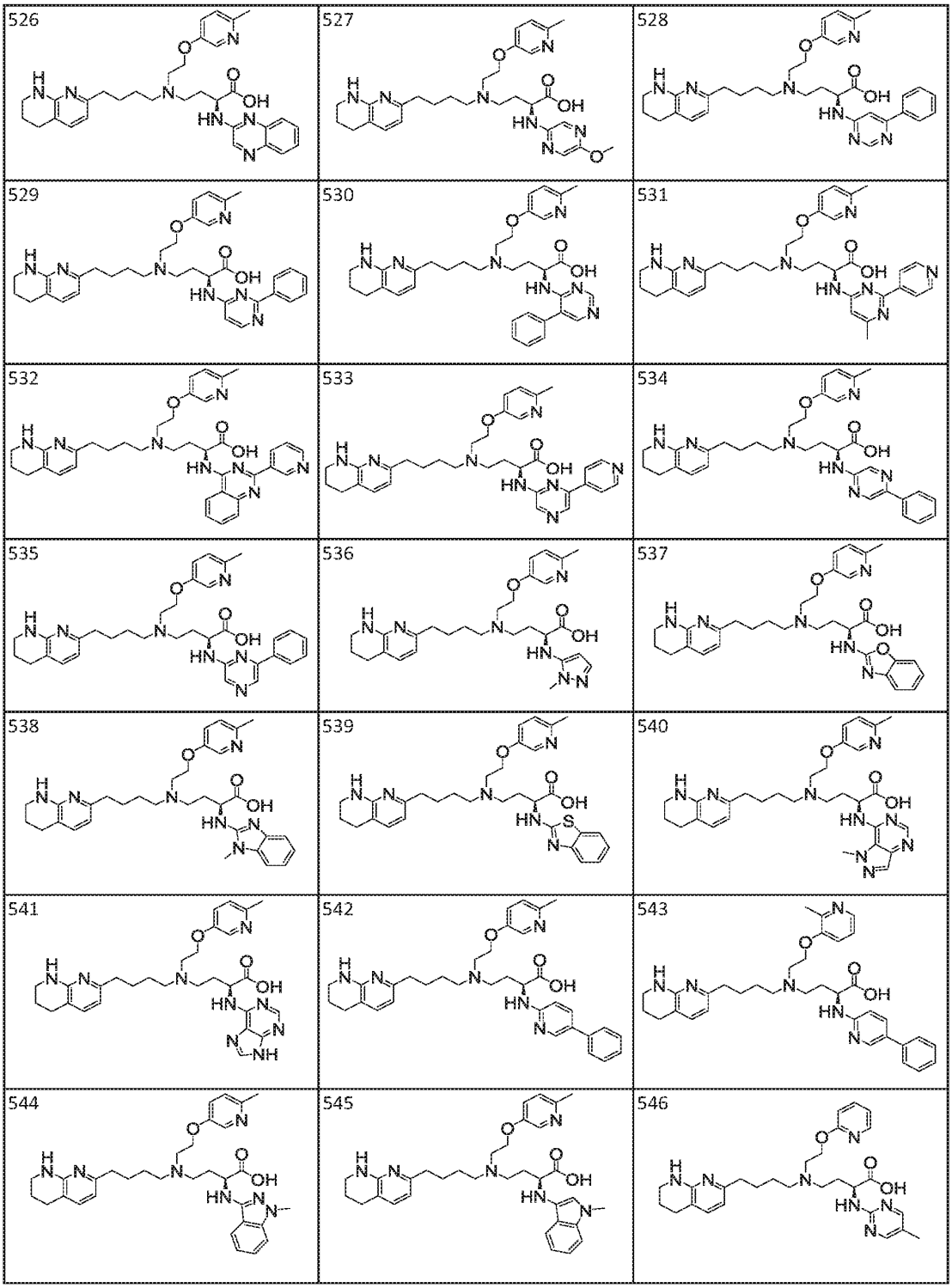

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FIG. 1 (cont.)

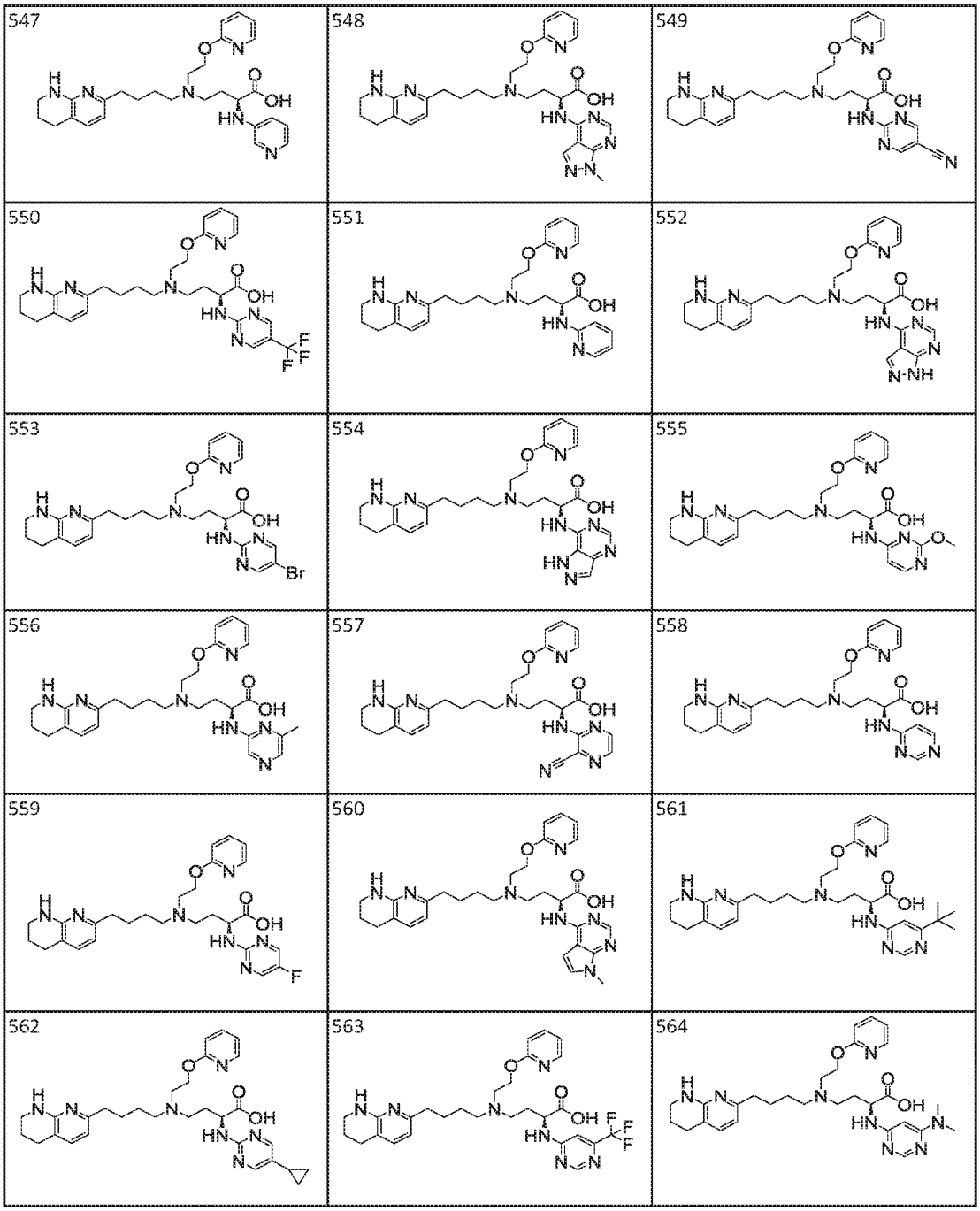

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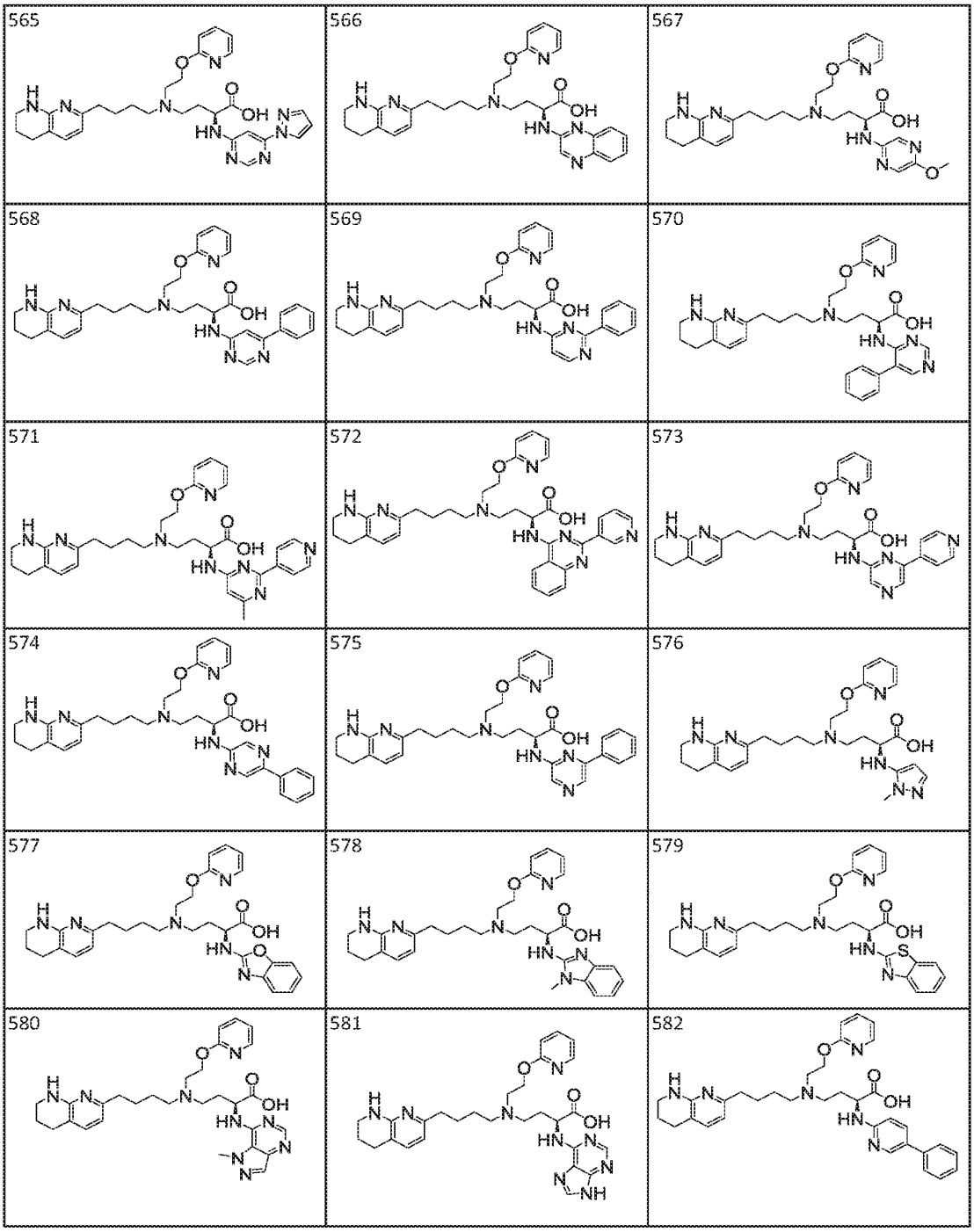

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FIG. 1 (cont.)

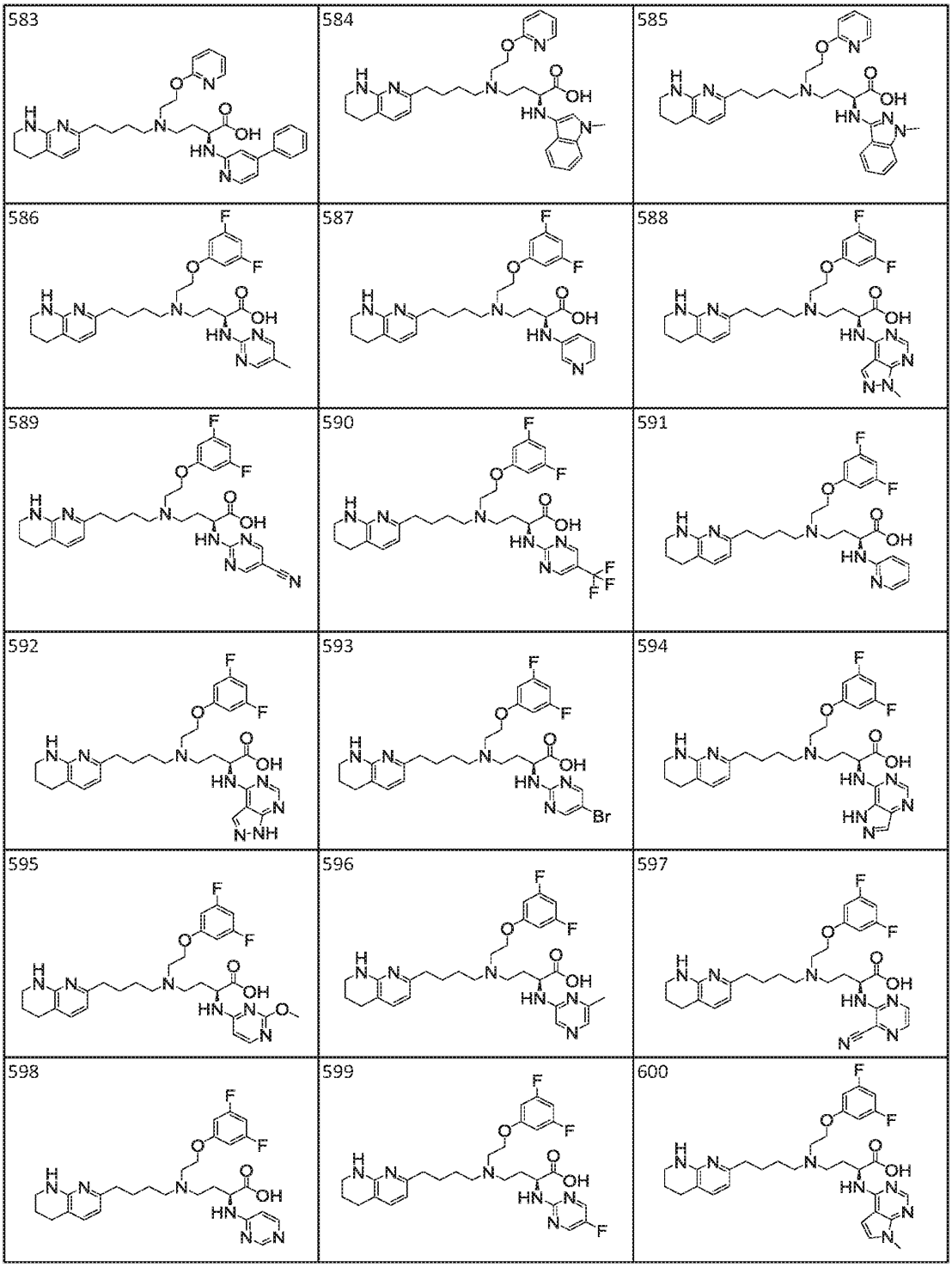

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FIG. 1 (cont.)

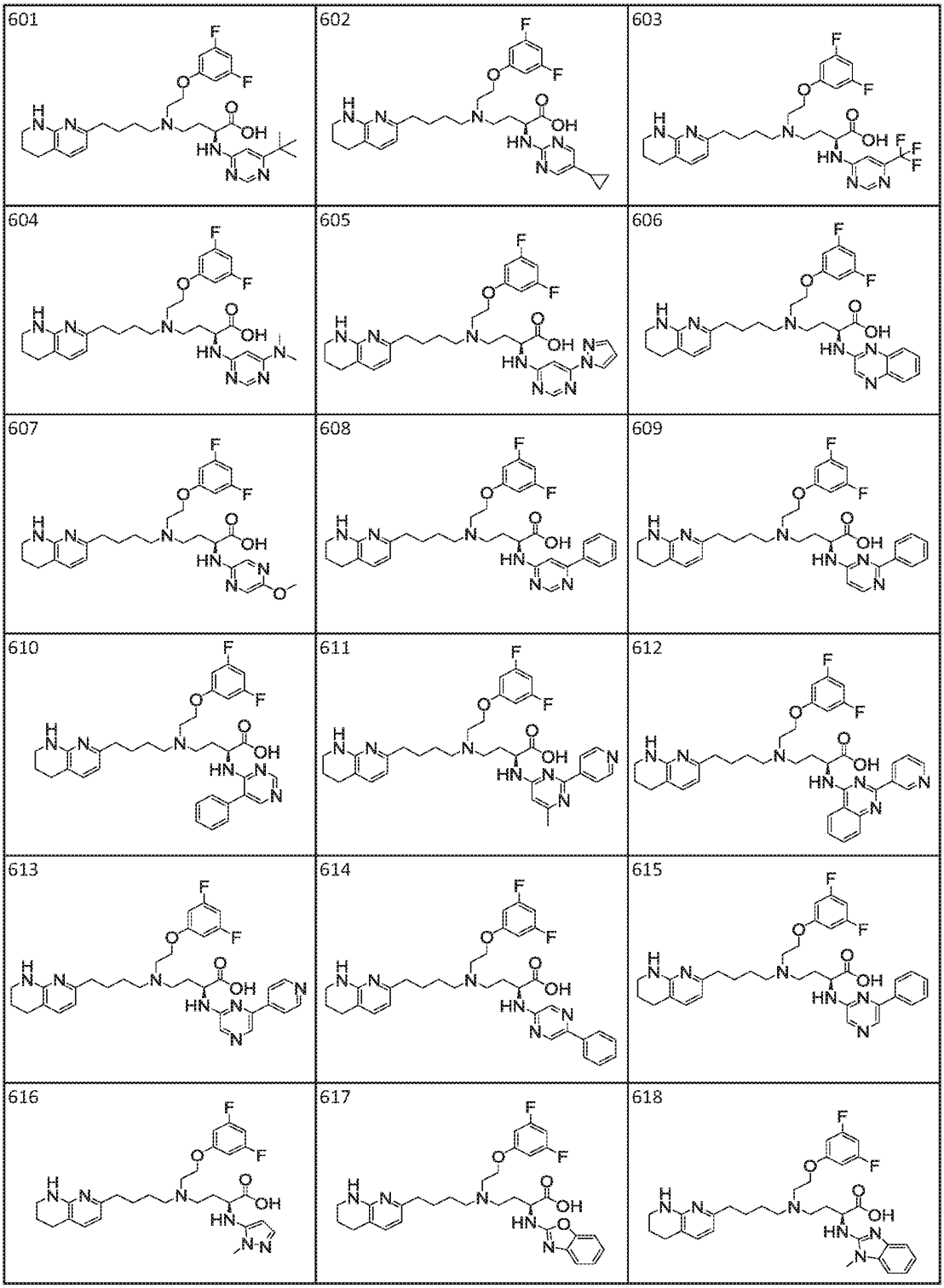

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FIG. 1 (cont.)

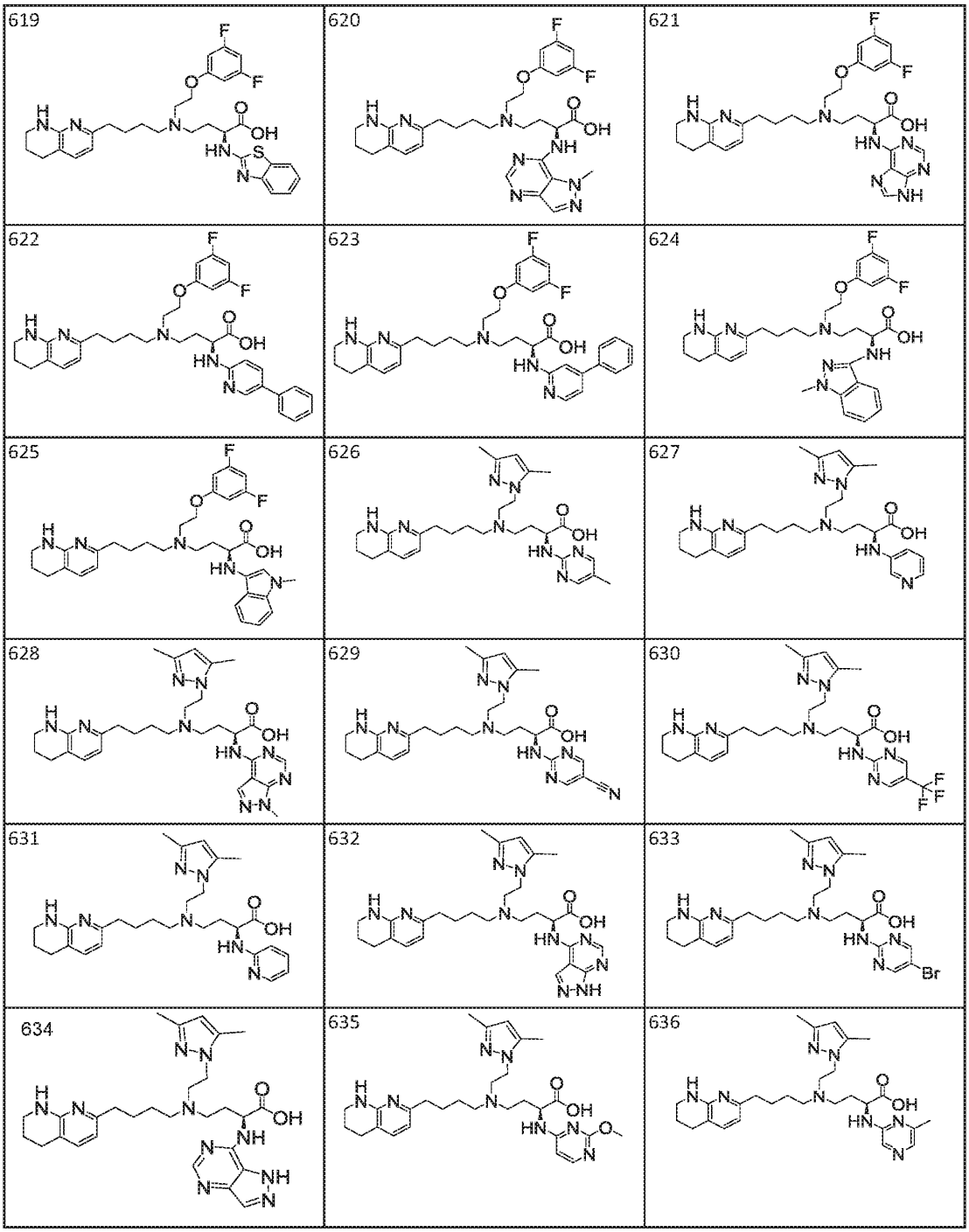

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FIG. 1 (cont.)

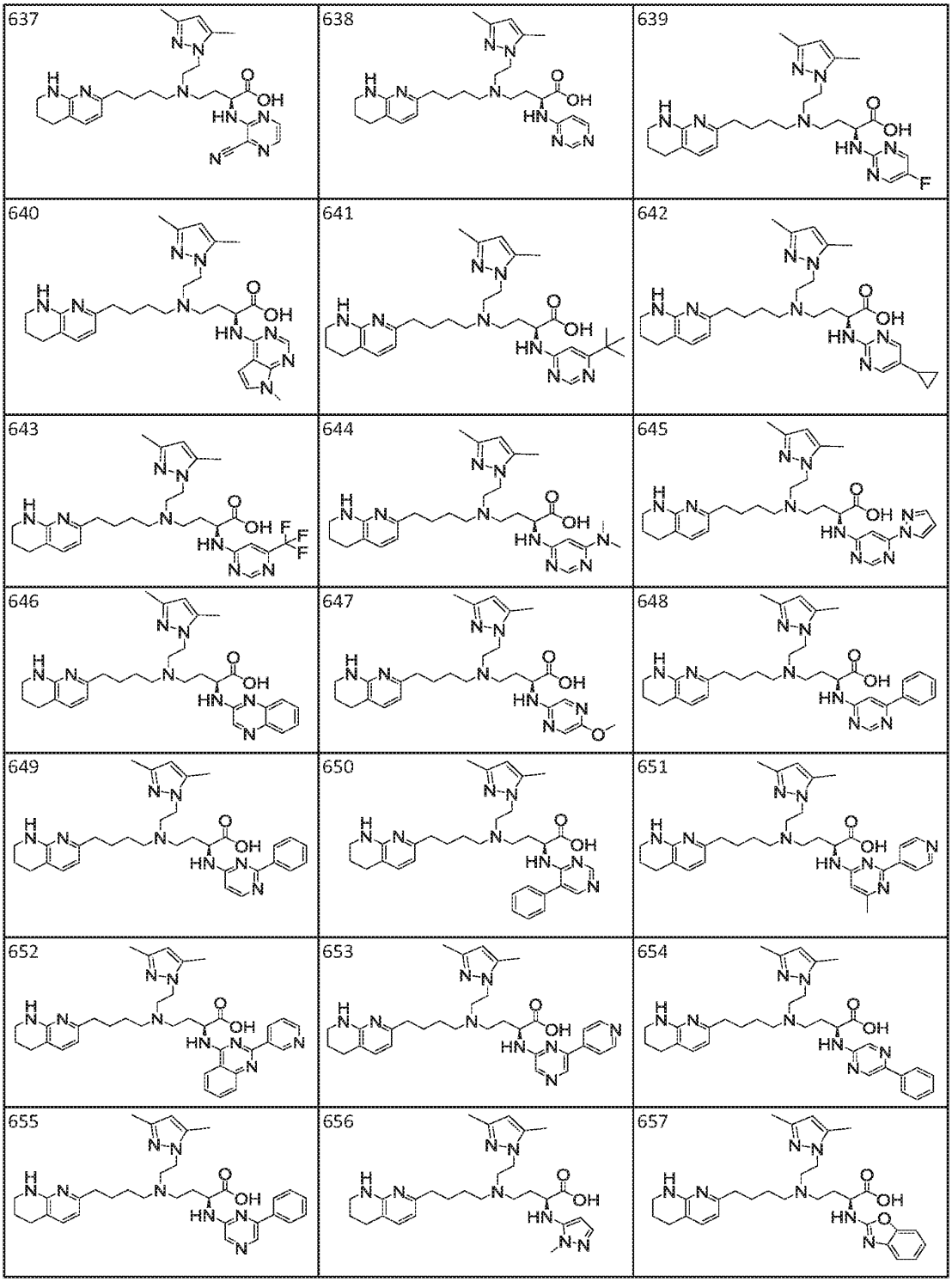

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FIG. 1 (cont.)

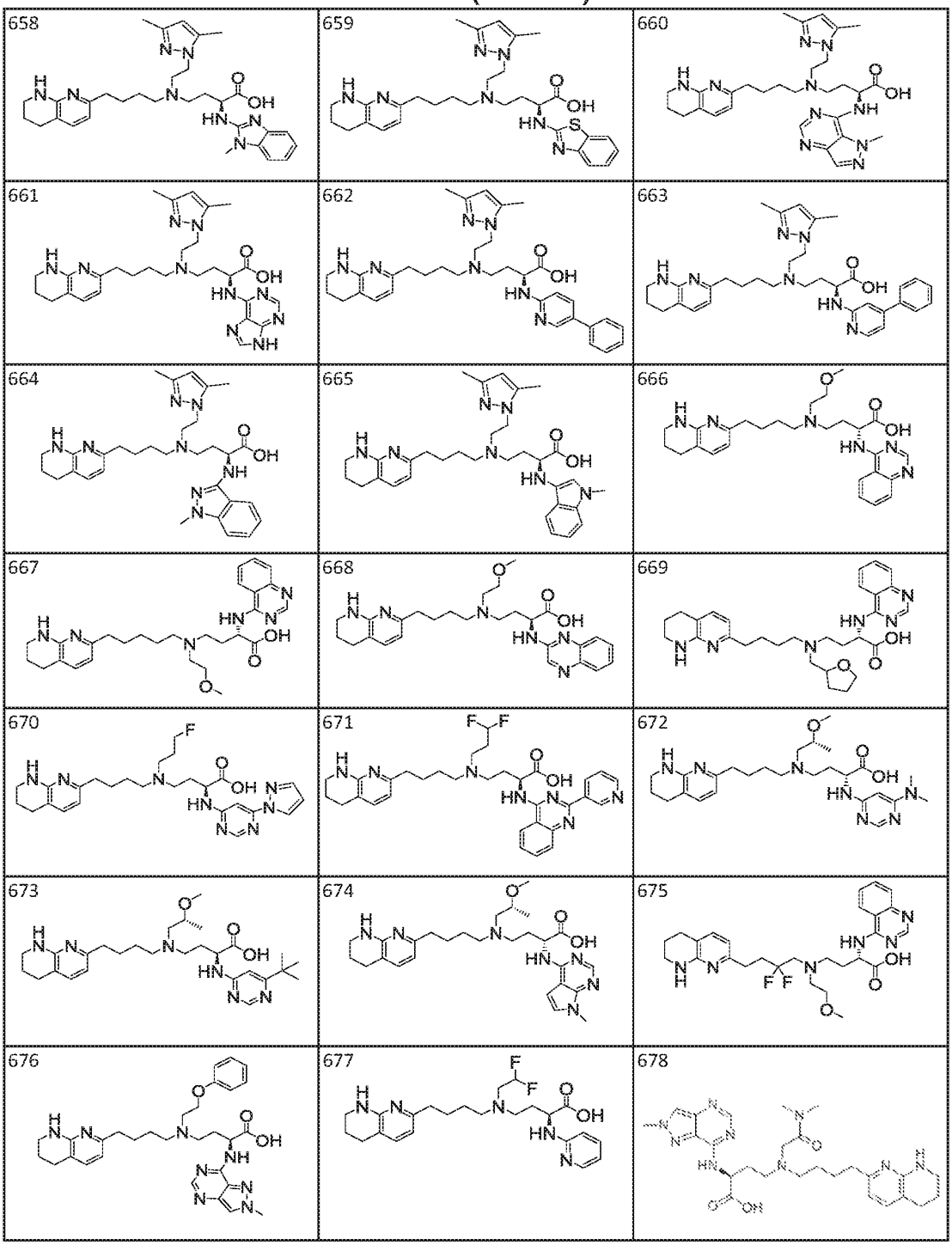

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FIG. 1 (cont.)

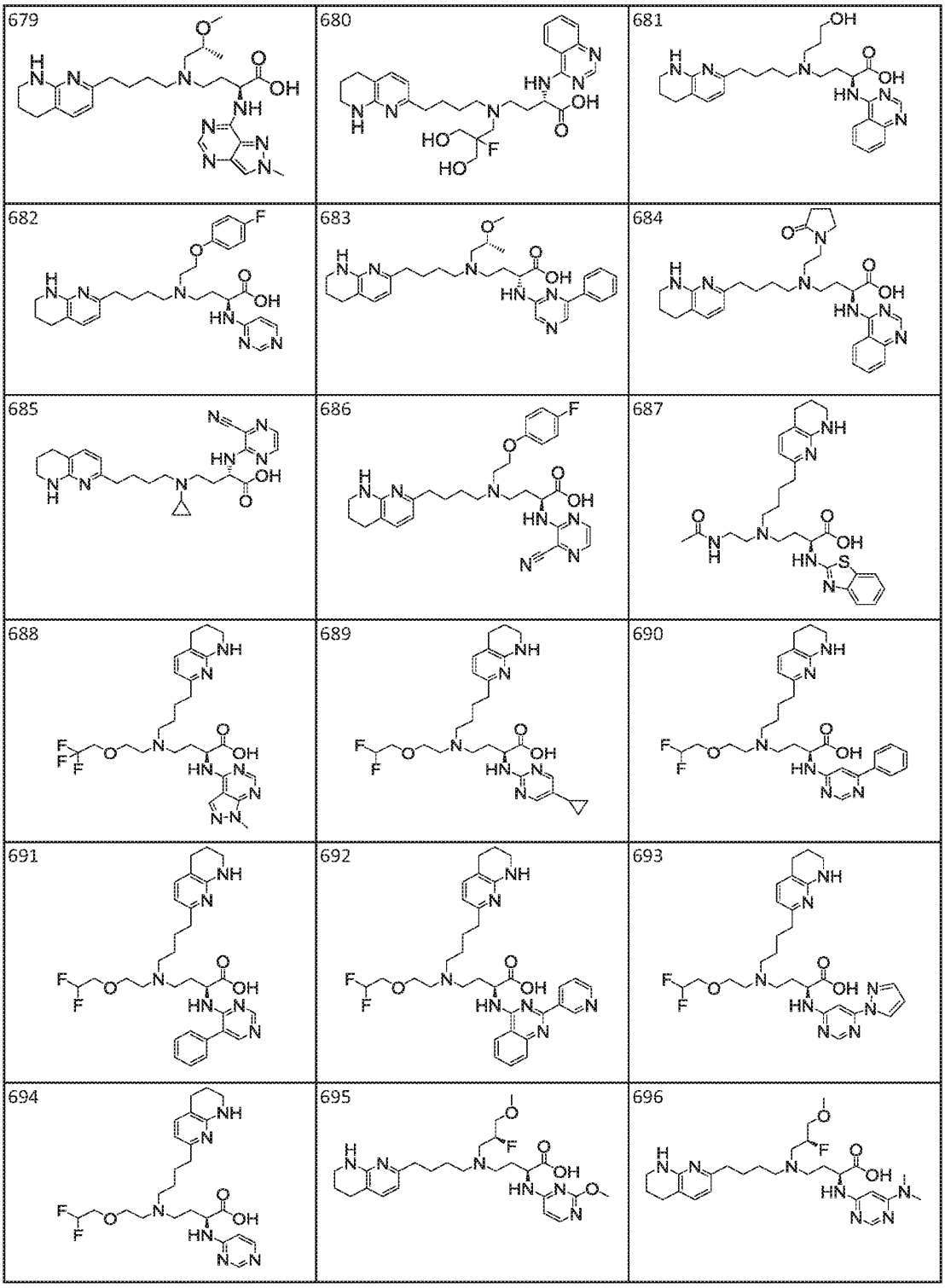

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FIG. 1 (cont.)

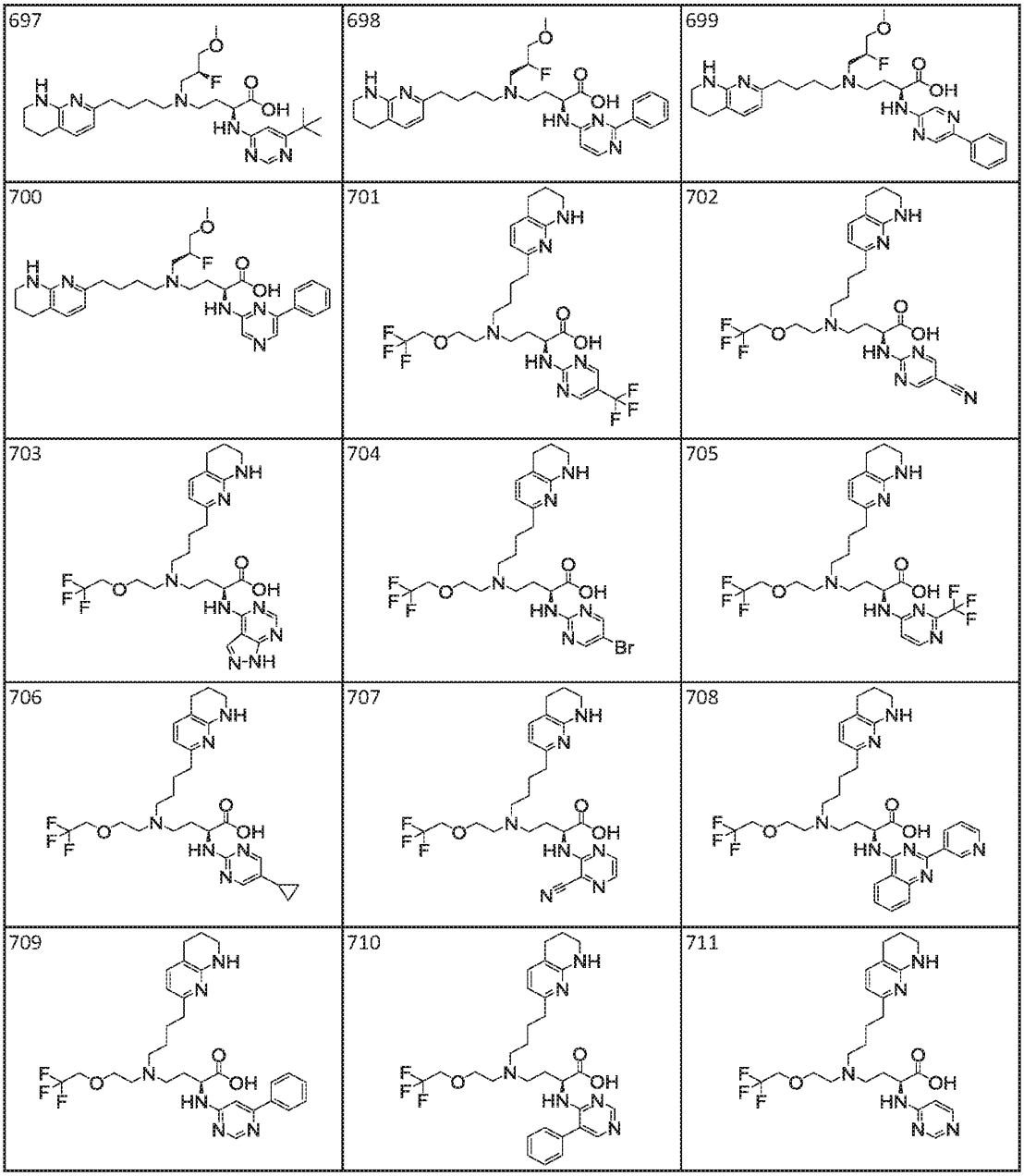


FIG. 1 (cont.)

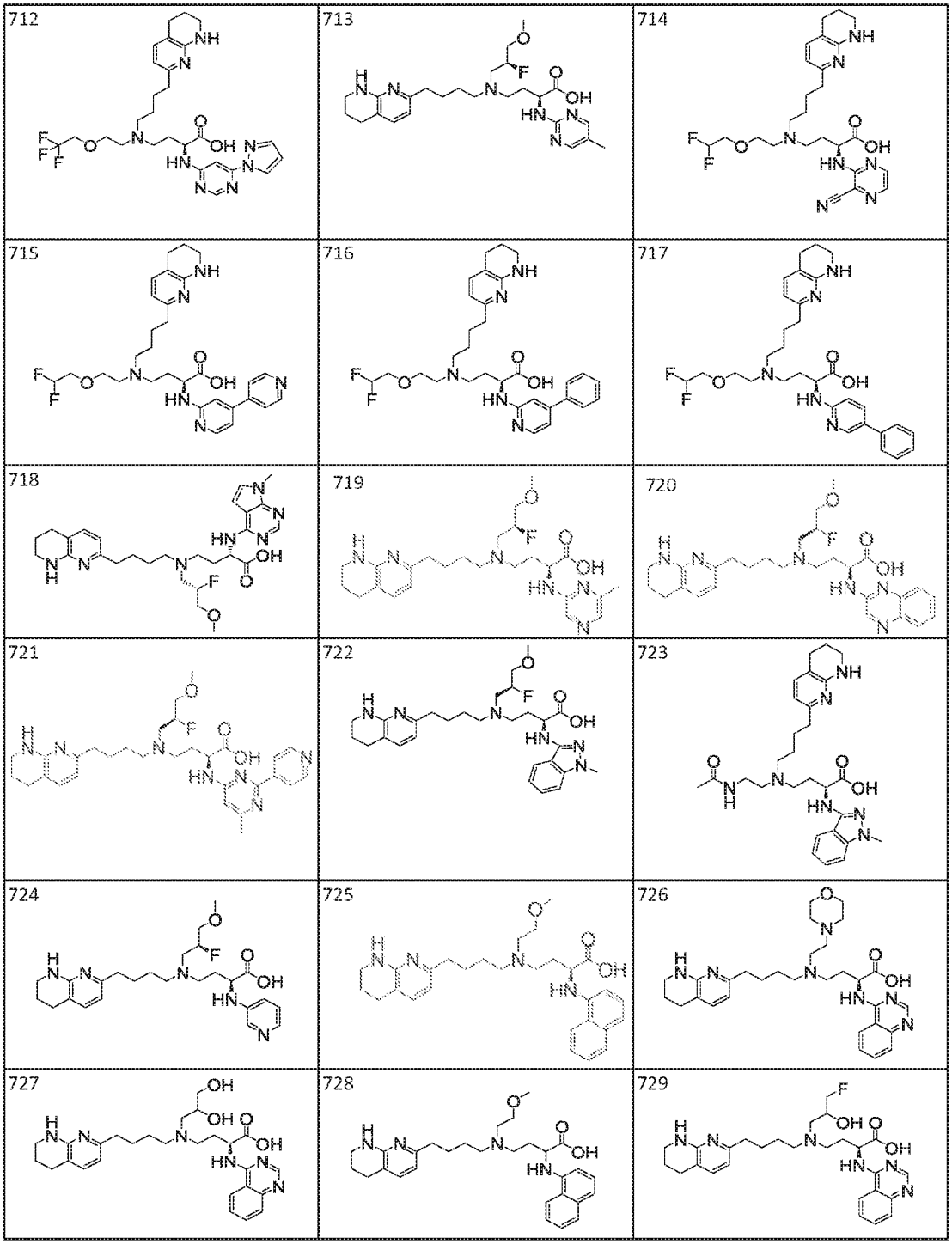

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FIG. 1 (cont.)

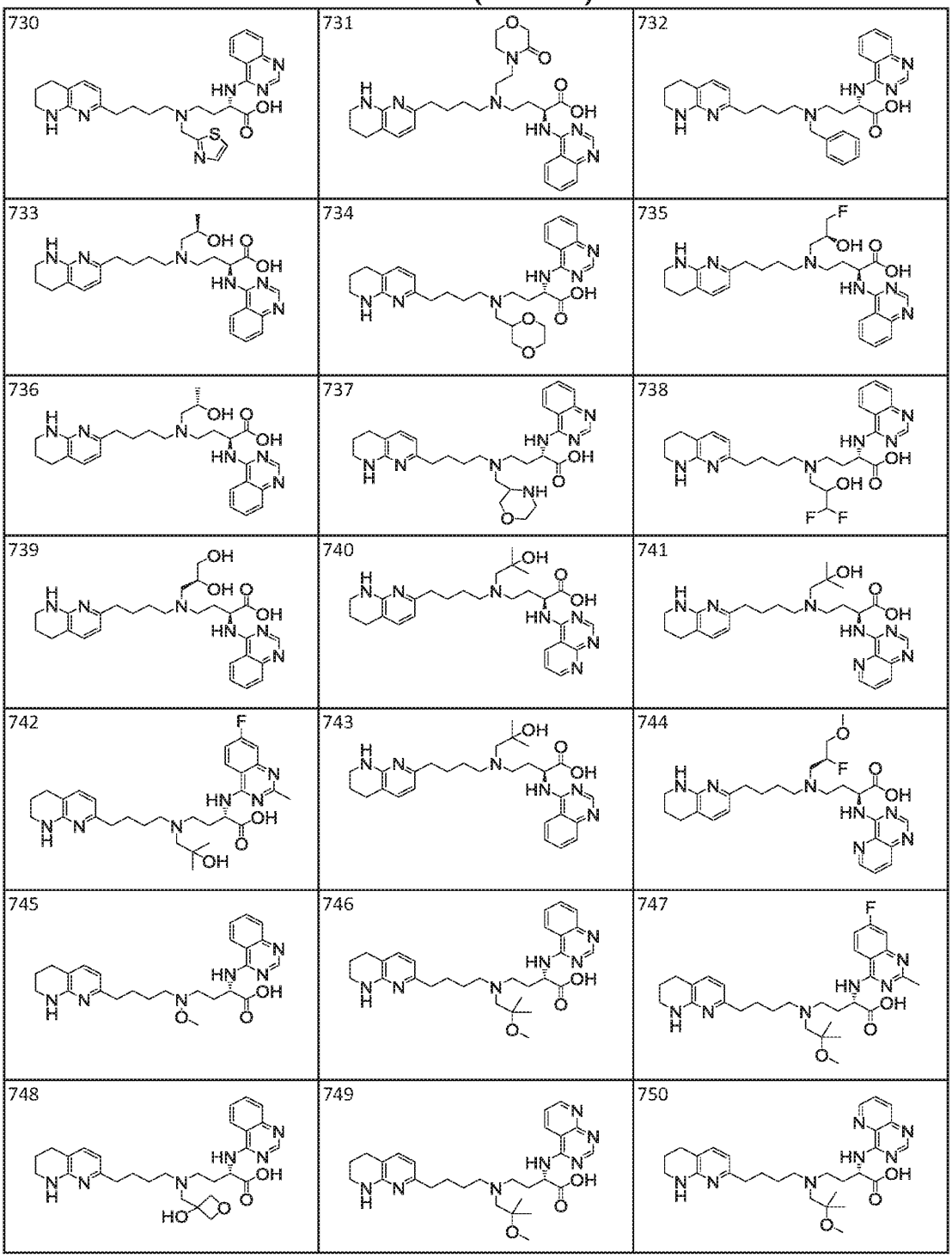

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FIG. 1 (cont.)

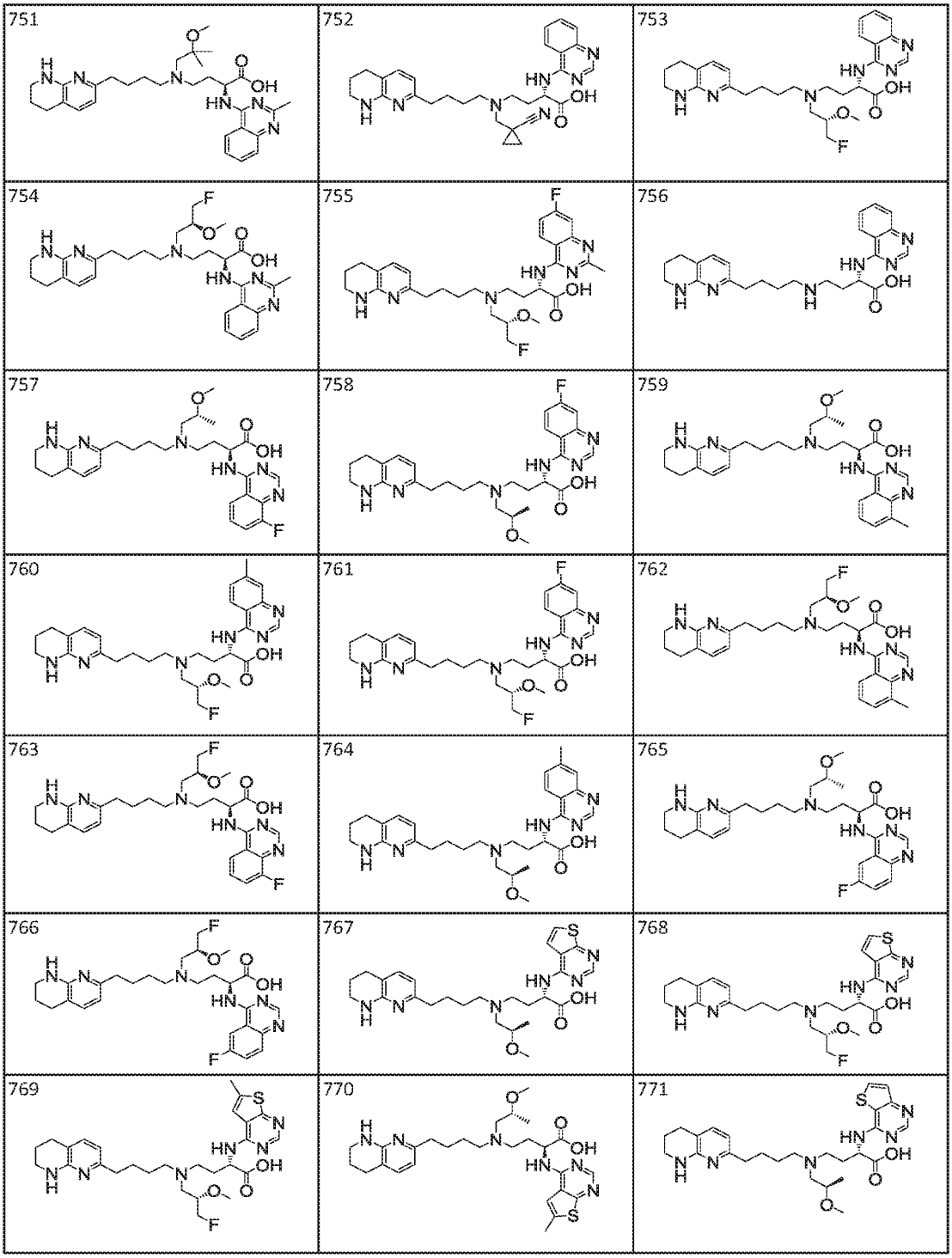

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FIG. 1 (cont.)

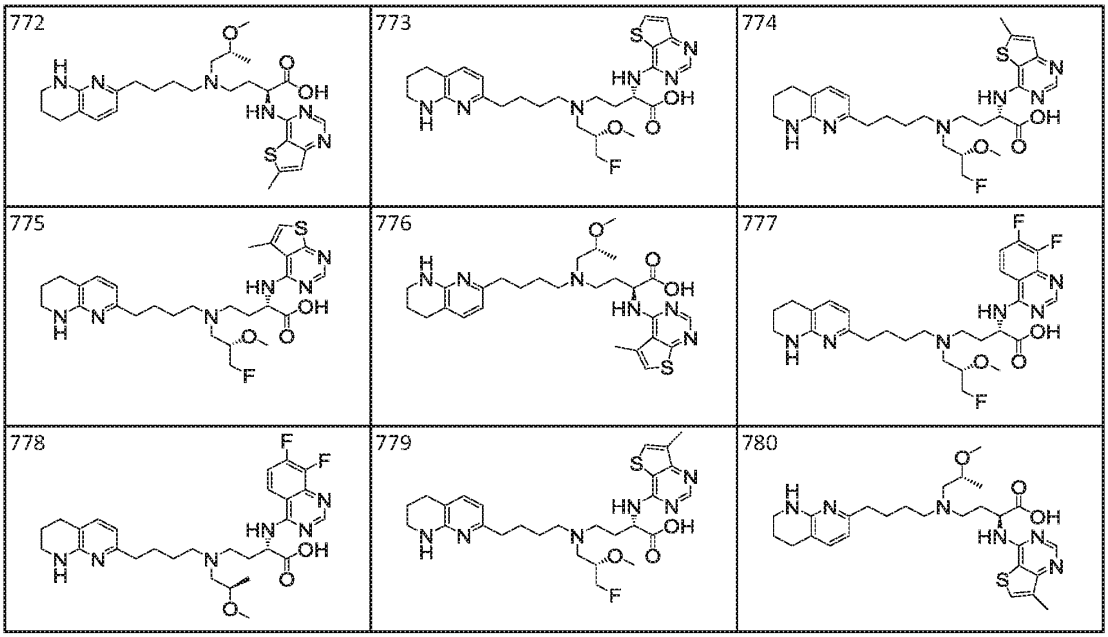


FIG. 2

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

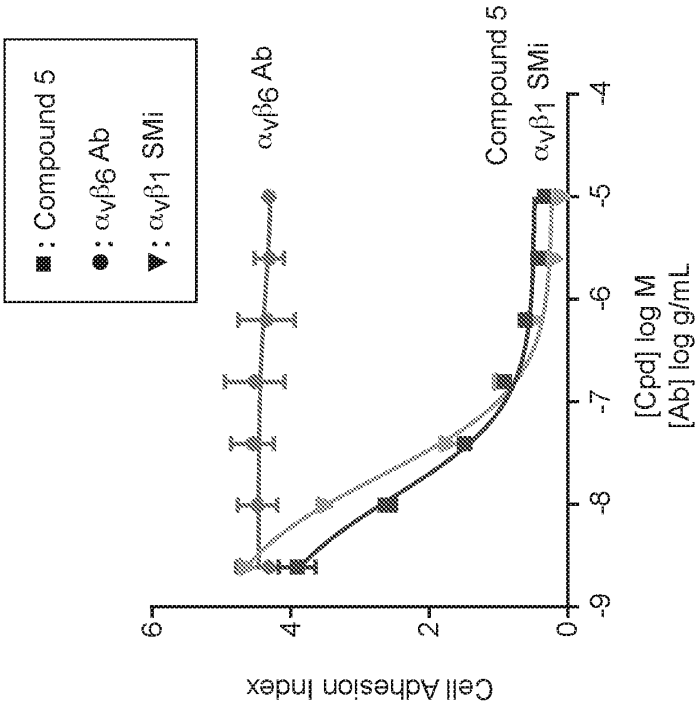

■: Compound 5
●: αvβ6 Ab
▼: αvβ1 SMi
αvβ6 Ab
Compound 5
αvβ1 SMi
Cell Adhesion Index
6
4
2
0
-9
-8
-7
-6
-5
-4
[Cpd] log M
[Ab] log g/mL

FIG. 3B

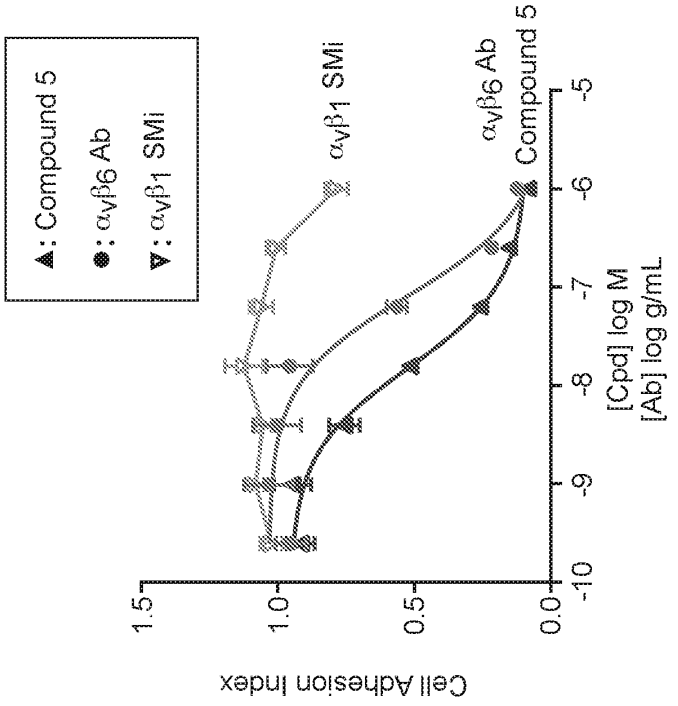

▲: Compound 5
●: αvβ6 Ab
▼: αvβ1 SMi
αvβ1 SMi
αvβ6 Ab
Compound 5
Cell Adhesion Index
1.5
1.0
0.5
0.0
-10
-9
-8
-7
-6
-5
[Cpd] log M
[Ab] log g/mL

FIG. 3A

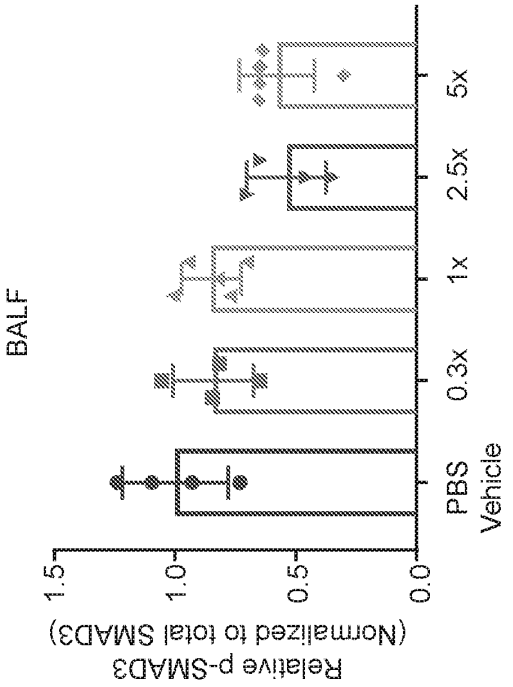

BALF
Relative p-SMAD3
(Normalized to total SMAD3)
1.5
1.0
0.5
0.0
PBS
Vehicle
0.3x
1x
2.5x
5x

FIG. 4B

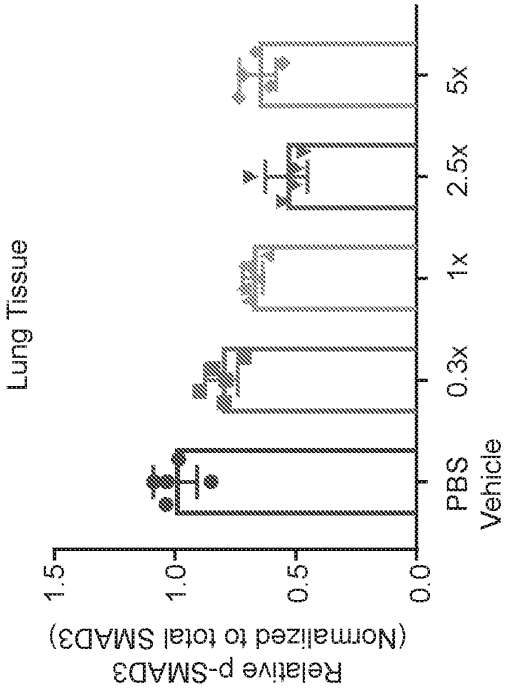

Lung Tissue
Relative p-SMAD3
(Normalized to total SMAD3)
1.5
1.0
0.5
0.0
PBS
Vehicle
0.3x
1x
2.5x
5x

FIG. 4A

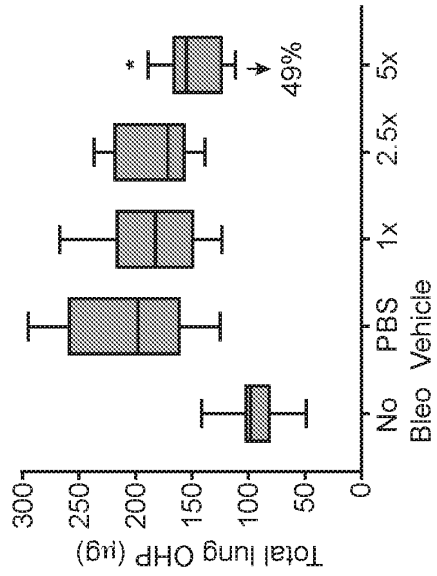


FIG. 4E

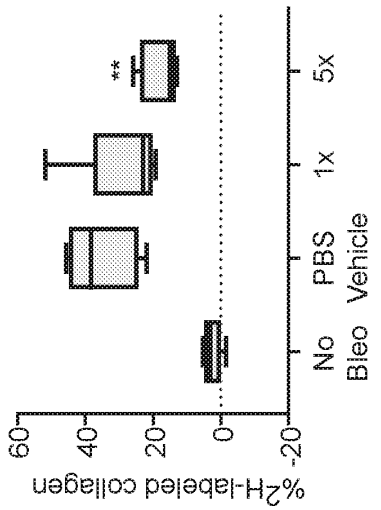


FIG. 4D

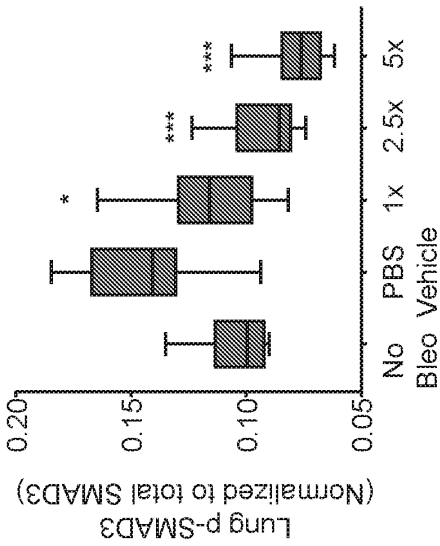


FIG. 4C

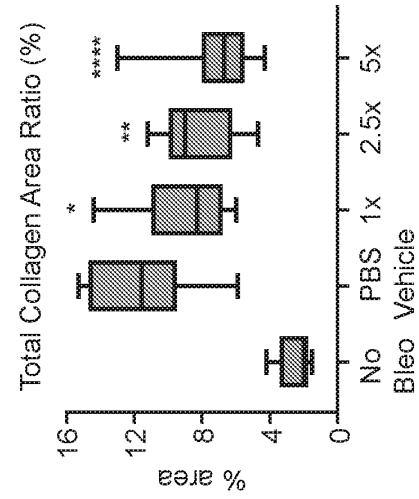


FIG. 4I

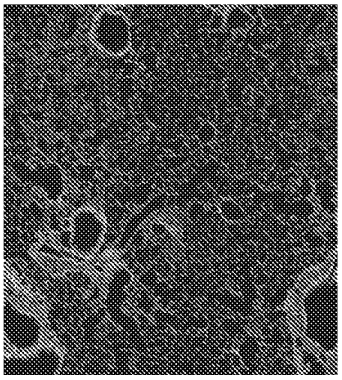


FIG. 4H

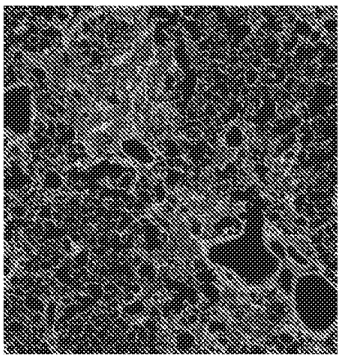


FIG. 4G

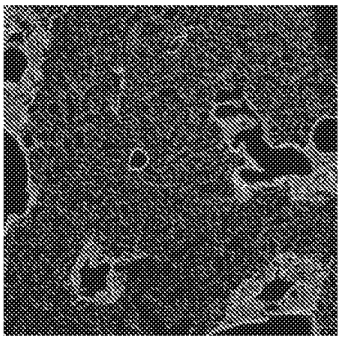


FIG. 4F

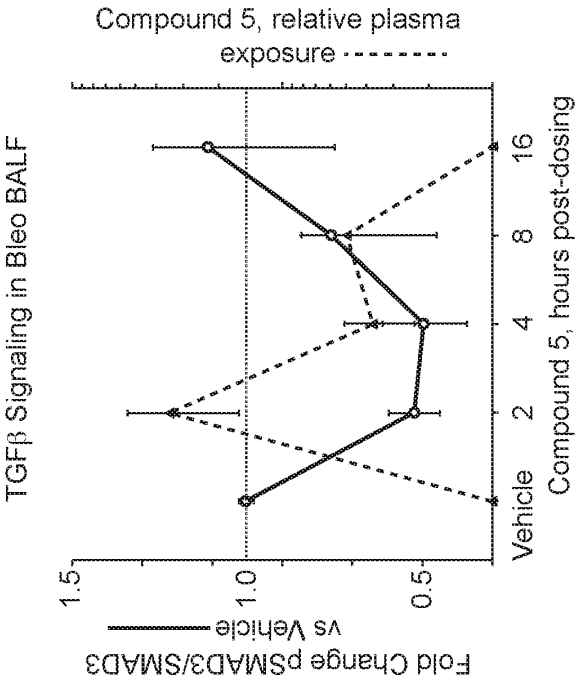

Compound 5, relative plasma exposure
TGFβ Signaling in Bleo BALF
Fold Change pSMAD3/SMAD3 vs Vehicle
1.5
1.0
0.5
Vehicle
2
4
8
16
Compound 5, hours post-dosing

FIG. 4K

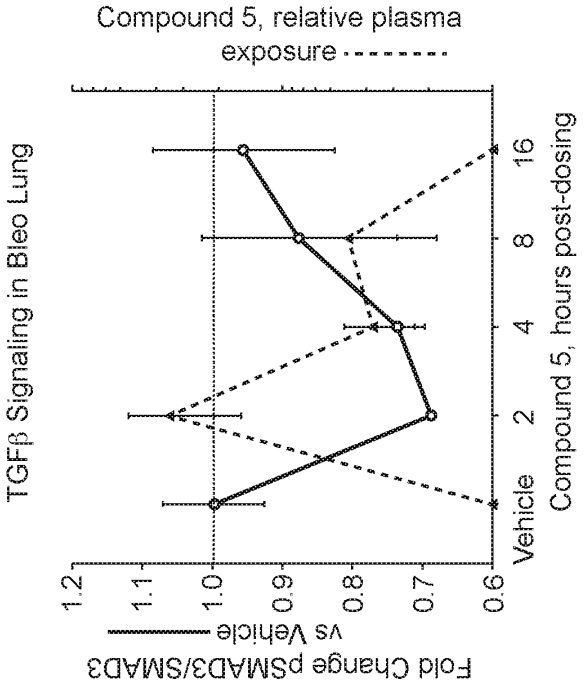

Compound 5, relative plasma exposure
TGFβ Signaling in Bleo Lung
Fold Change pSMAD3/SMAD3 vs Vehicle
1.2
1.1
1.0
0.9
0.8
0.7
0.6
Vehicle
2
4
8
16
Compound 5, hours post-dosing

FIG. 4J

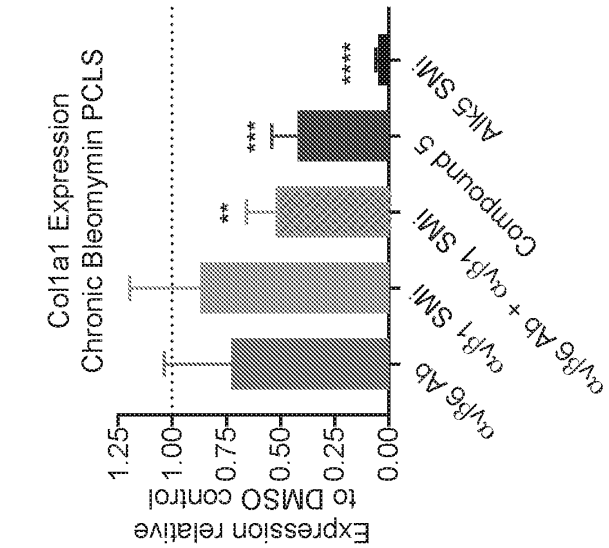

Col1a1 Expression
Chronic Bleomymin PCLS
Expression relative
to DMSO control
1.25
1.00
0.75
0.50
0.25
0.00
**
**
***
****
αvβ6 Ab
αvβ1 SMI
αvβ6 Ab + αvβ1 SMI
Compound 5
Alk5 SMI

FIG. 5B

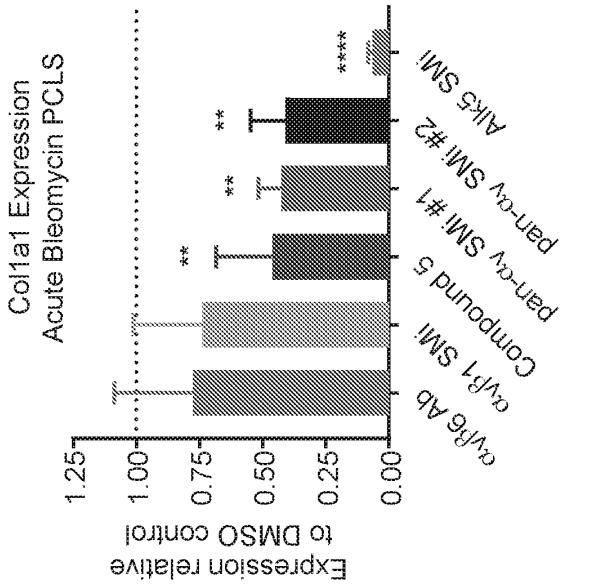

Col1a1 Expression
Acute Bleomycin PCLS
Expression relative
to DMSO control
1.25
1.00
0.75
0.50
0.25
0.00
**
**
**
****
αvβ6 Ab
αvβ1 SMI
Compound 5
pan-αv SMI #1
pan-αv SMI #2
Alk5 SMI

FIG. 5A

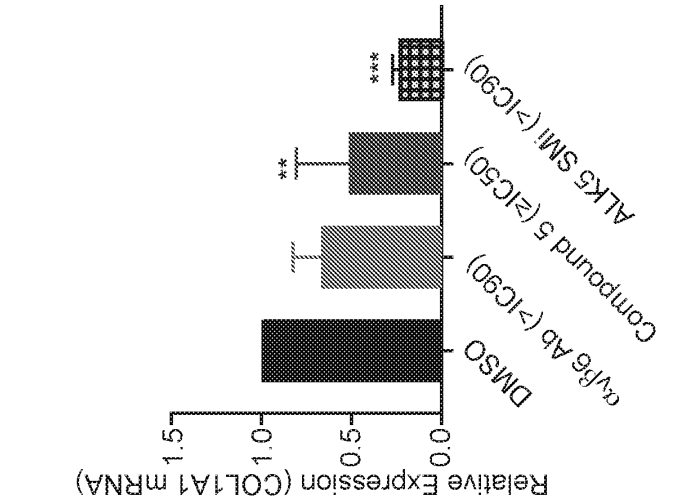


FIG. 6C

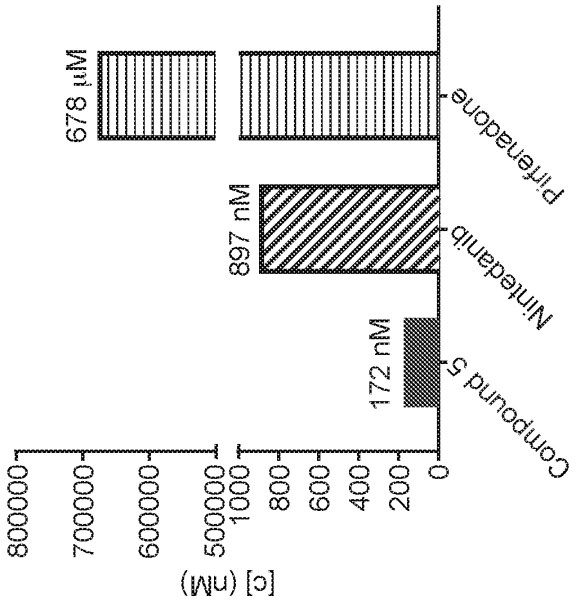


FIG. 6B

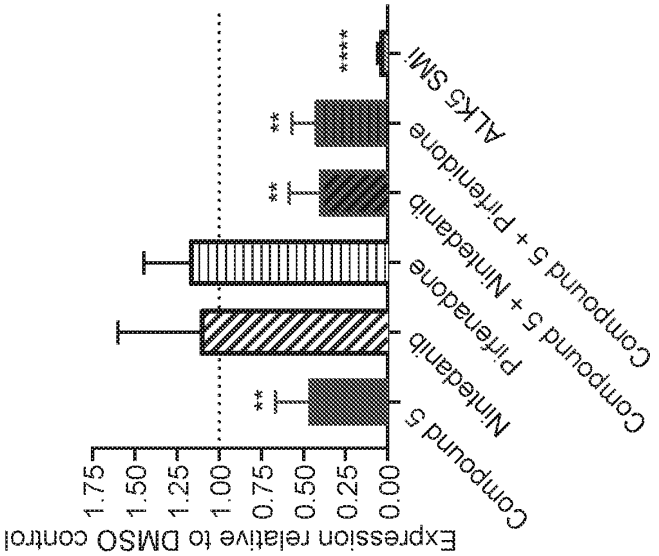


FIG. 6A

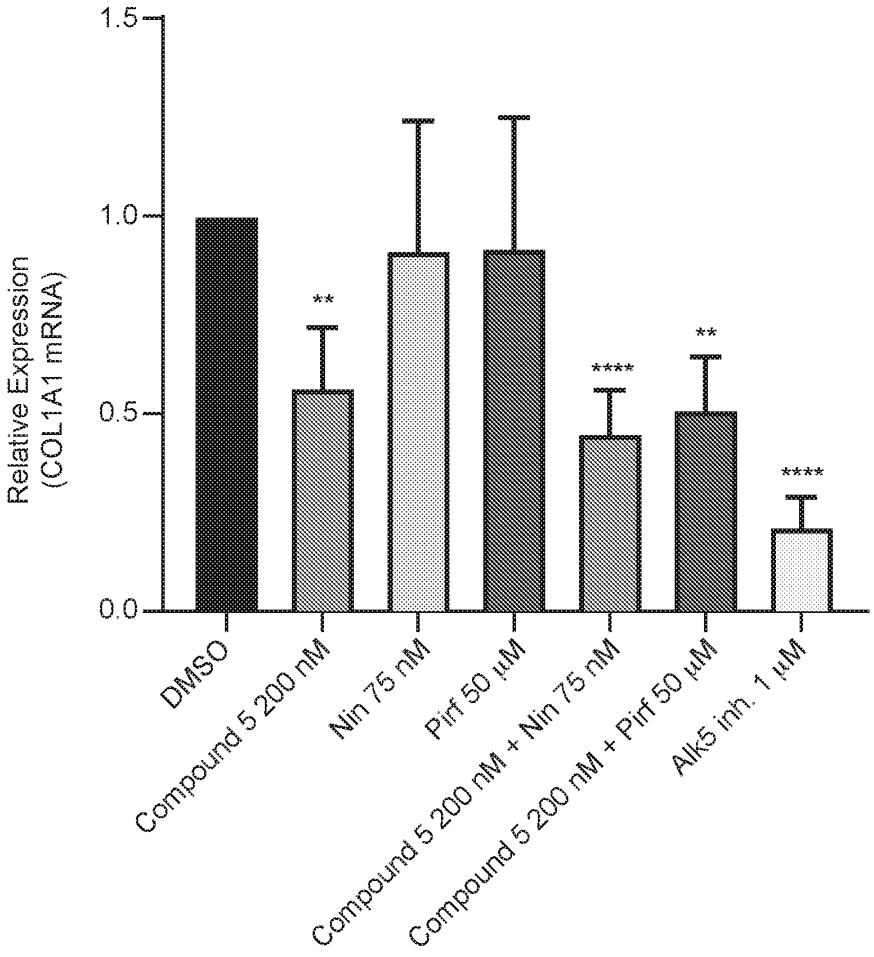

1.5
1.0
0.5
0.0
Relative Expression
(COL1A1 mRNA)
**
****
**
****
DMSO
Compound 5 200 nM
Nin 75 nM
Pirf 50 µM
Compound 5 200 nM + Nin 75 nM
Compound 5 200 nM + Pirf 50 µM
Alk5 inh. 1 µM

FIG. 6D

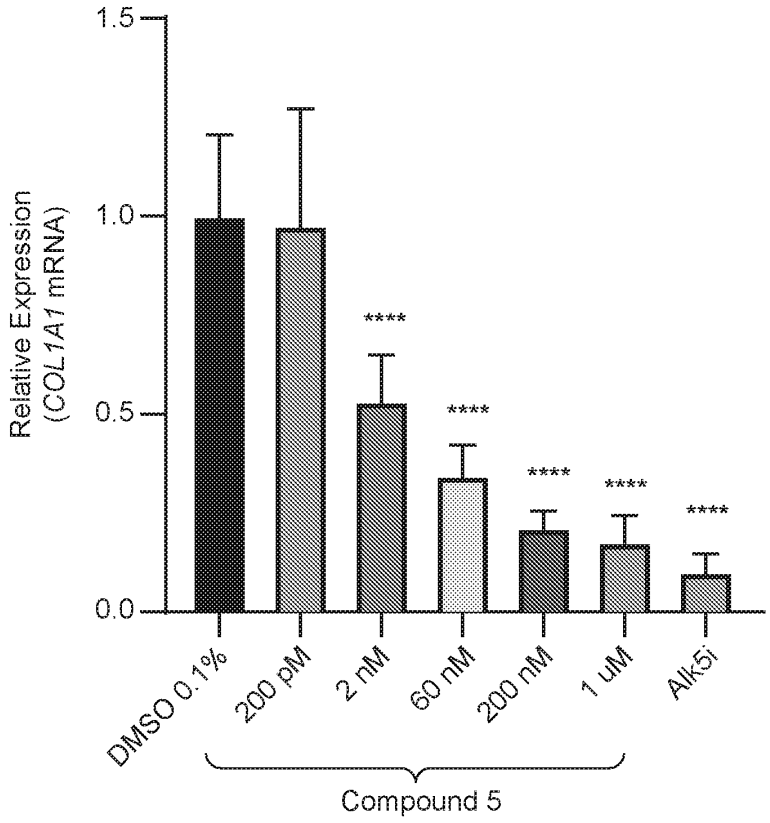

1.5
1.0
0.5
0.0
Relative Expression
(COL1A1 mRNA)
****
****
****
****
****
DMSO 0.1%
200 pM
2 nM
60 nM
200 nM
1 uM
Alk5i
Compound 5

FIG. 6E

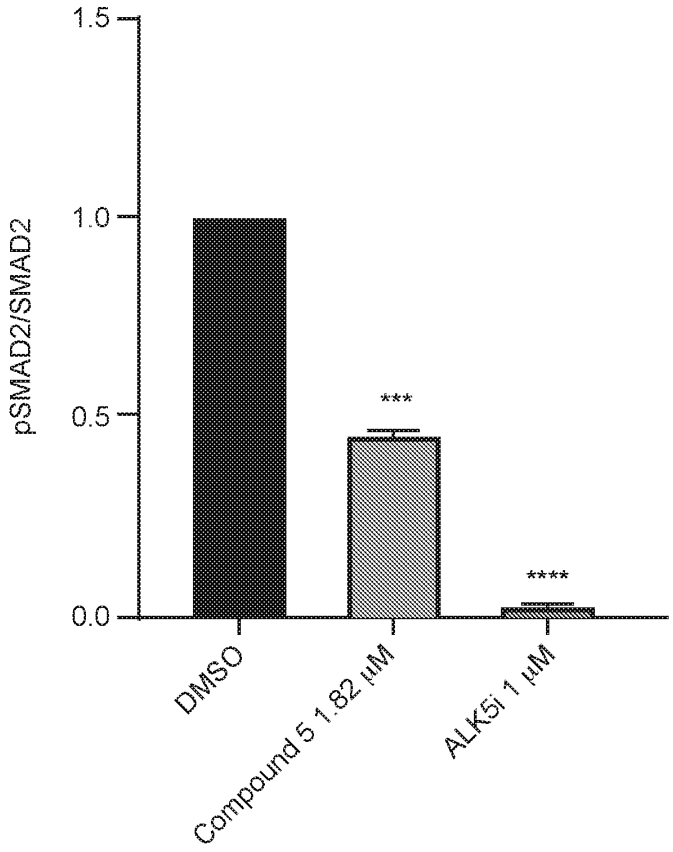


FIG. 6F

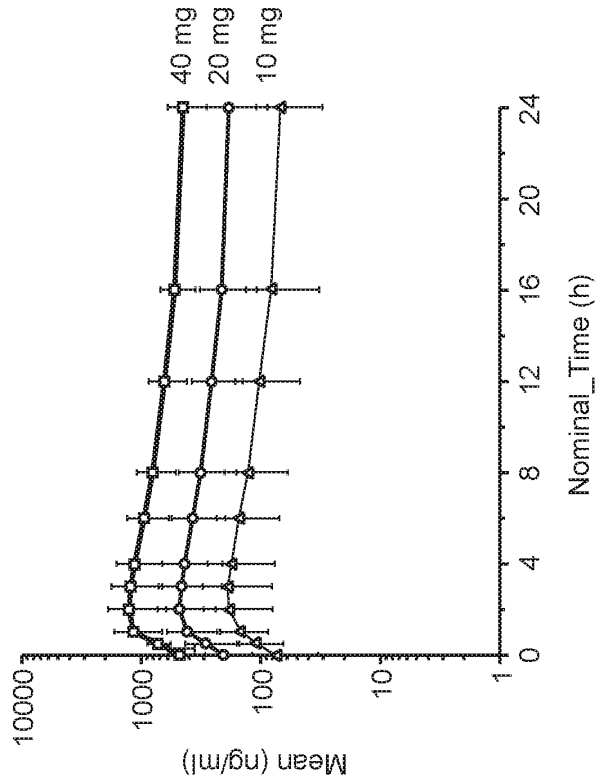
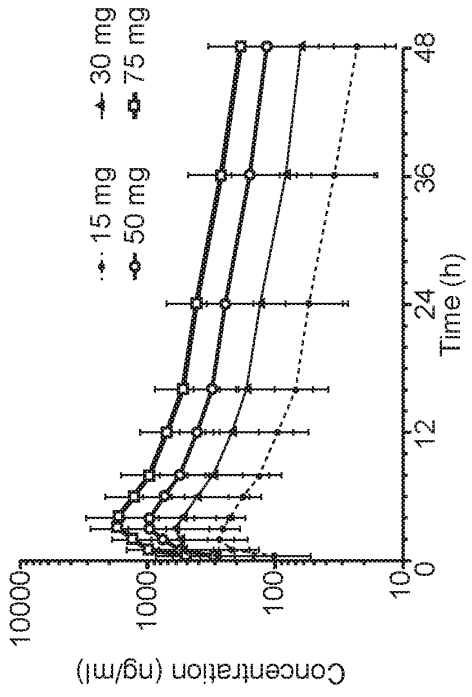


FIG. 7B



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

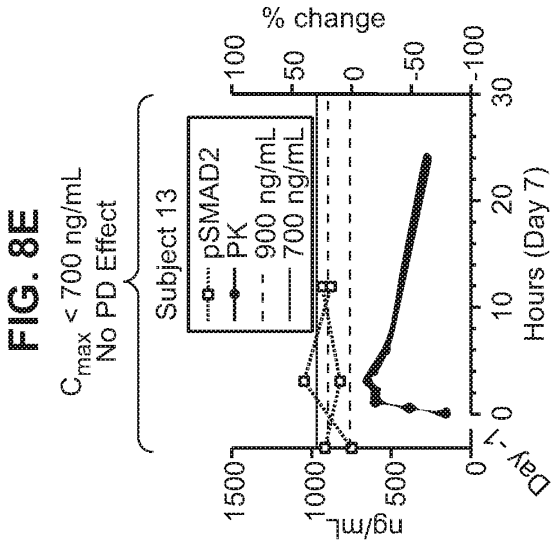


FIG. 8E

C_{max} < 700 ng/mL
No PD Effect

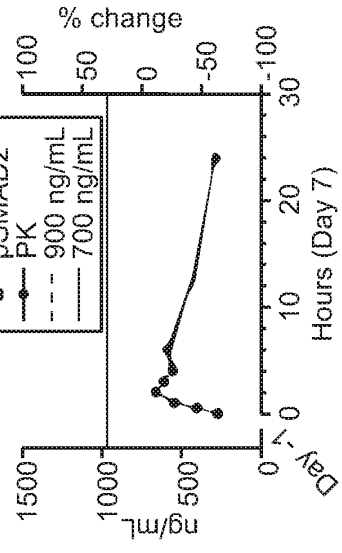


FIG. 8F

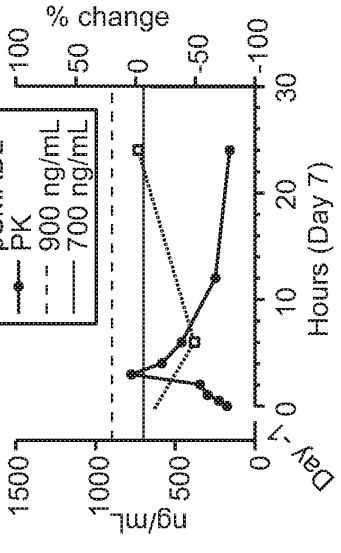


FIG. 8C

C_{max} = 700-900 ng/mL
Transitory PD Effect

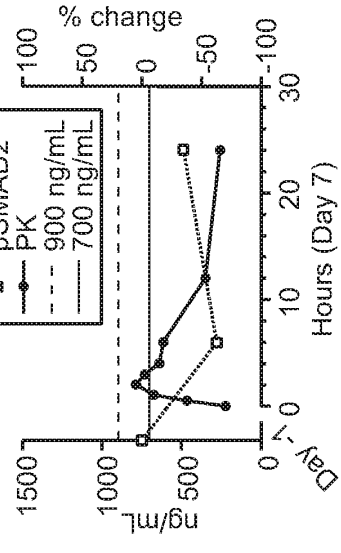


FIG. 8D

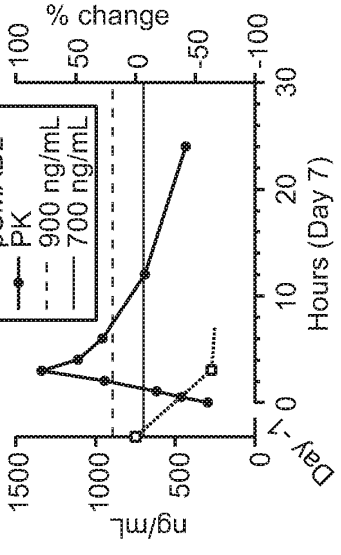


FIG. 8A

C_{max} > 900 ng/mL
Sustained PD Effect

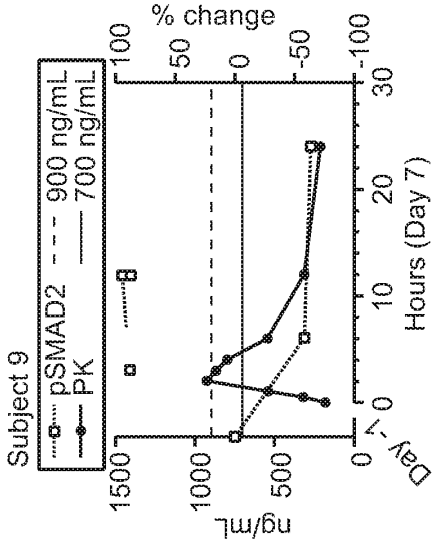


FIG. 8B

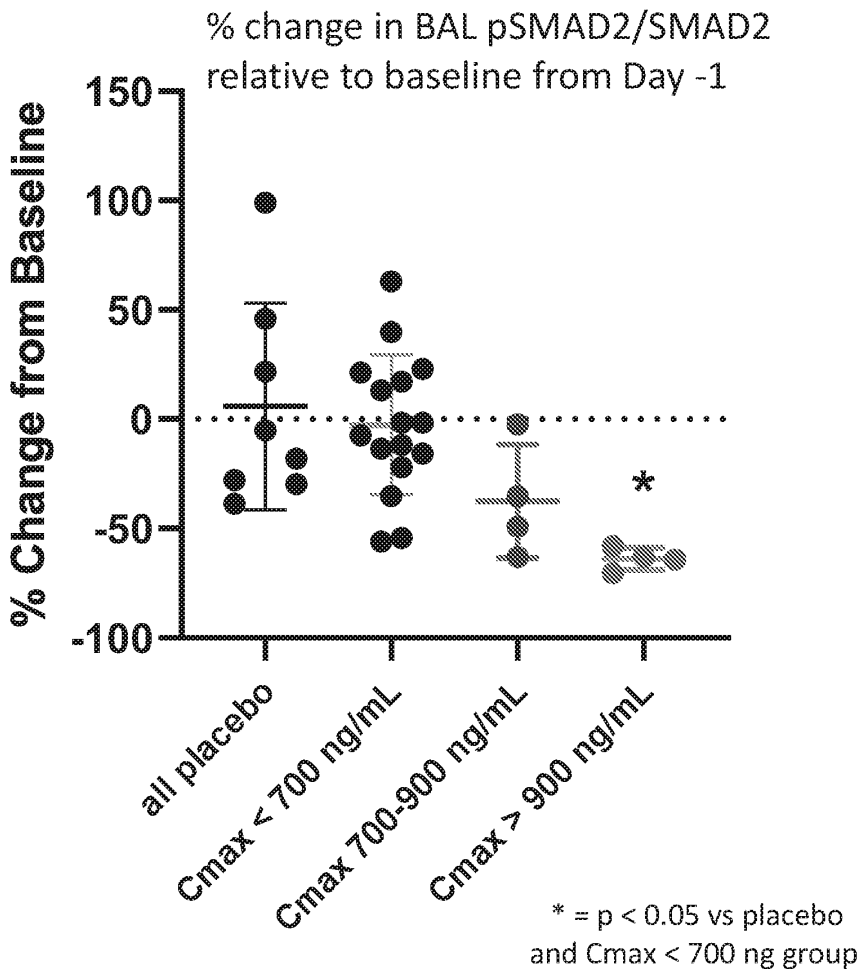

% change in BAL pSMAD2/SMAD2
relative to baseline from Day -1
% Change from Baseline
150
100
50
0
-50
-100
*
all placebo
Cmax < 700 ng/mL
Cmax 700-900 ng/mL
Cmax > 900 ng/mL
* = p < 0.05 vs placebo
and Cmax < 700 ng group

FIG. 8G

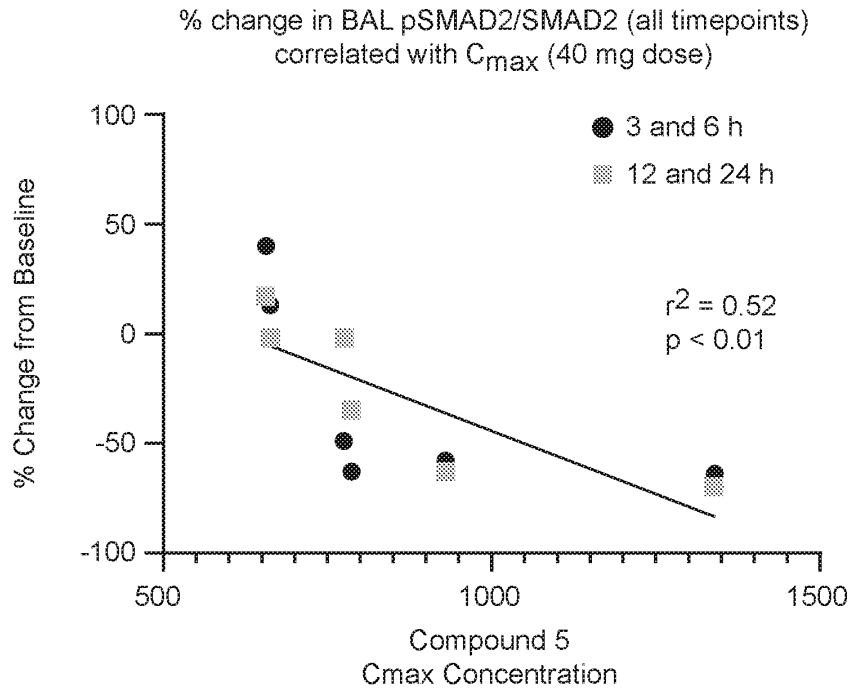

% change in BAL pSMAD2/SMAD2 (all timepoints)
correlated with C_{max} (40 mg dose)
3 and 6 h
12 and 24 h
r^2 = 0.52
p < 0.01
% Change from Baseline
100
50
0
-50
-100
500
1000
1500
Compound 5
Cmax Concentration

FIG. 8H