

FIGURE 1

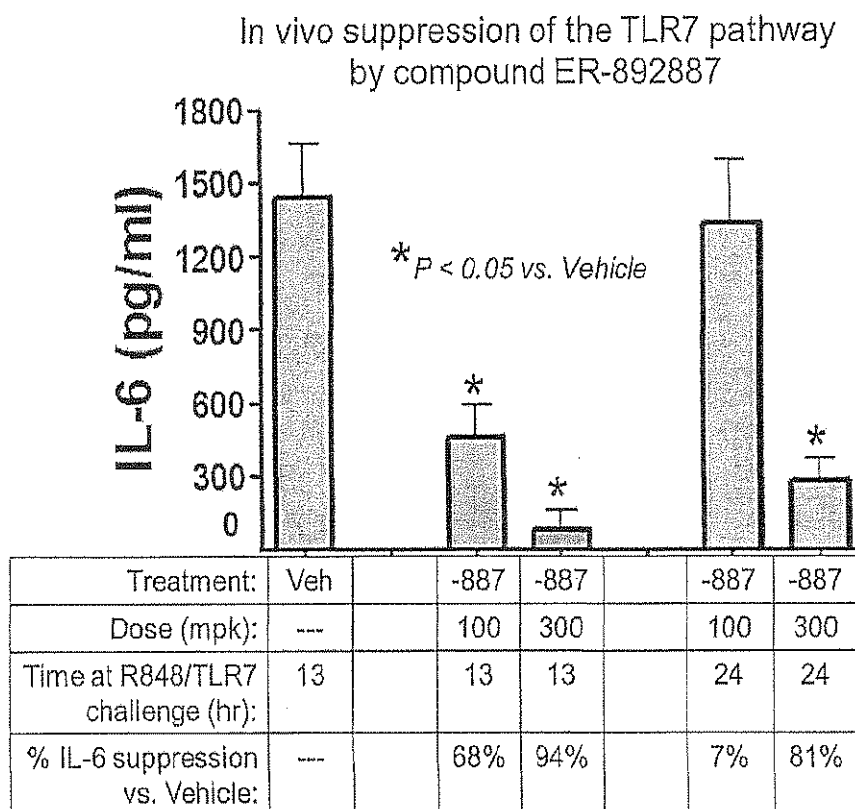


FIGURE 2

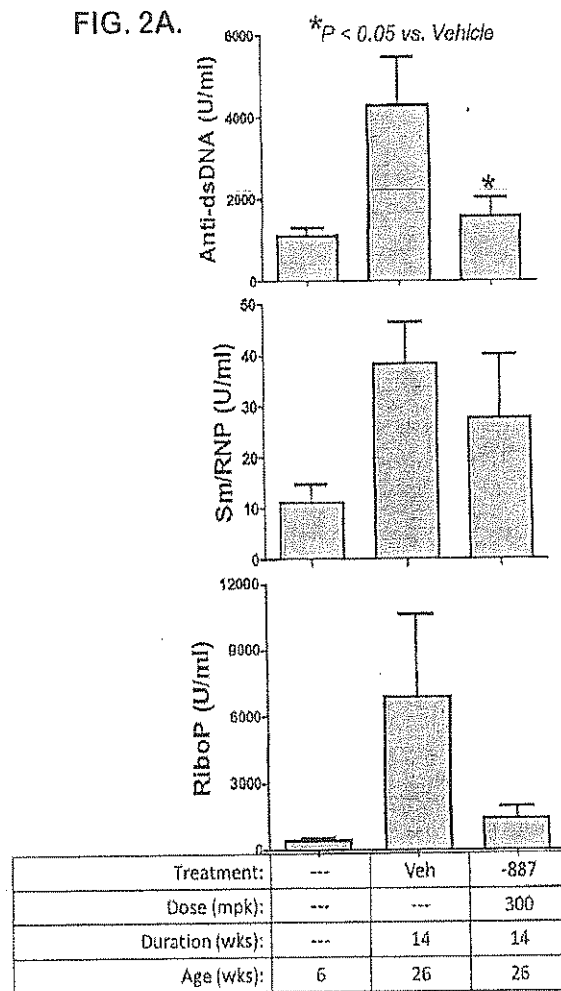


FIGURE 2

FIG. 2B.

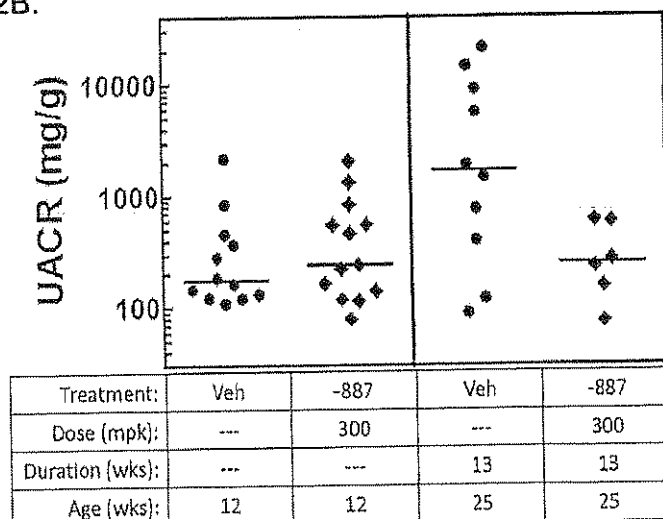


FIG. 2C.

Glomerulonephritis (GN) Evaluation in BXSB-Yaa Strain			
		Vehicle	ER-892887 (300mpk)
Total Mice Examined:		10	7
GN Score:	0/1	1	2
	2	1	5
	3	6	0
	4	2	0
Percent combined incidence of Grade 3 and 4		80%	0%
Grade 0/1: within normal limits; Grade 2: MILD; Grade 3: MODERATE; Grade 4: MARKED			

FIG. 2D.

BXSB-Yaa Study Treatment:	Vehicle	ER-892887
Mortality (# deaths/total group #):	3/13	6/13
Dosing duration at death (days):	24, 31, 56	4, 10, 14, 32, 47, >81d

FIGURE 3

FIG. 3A.

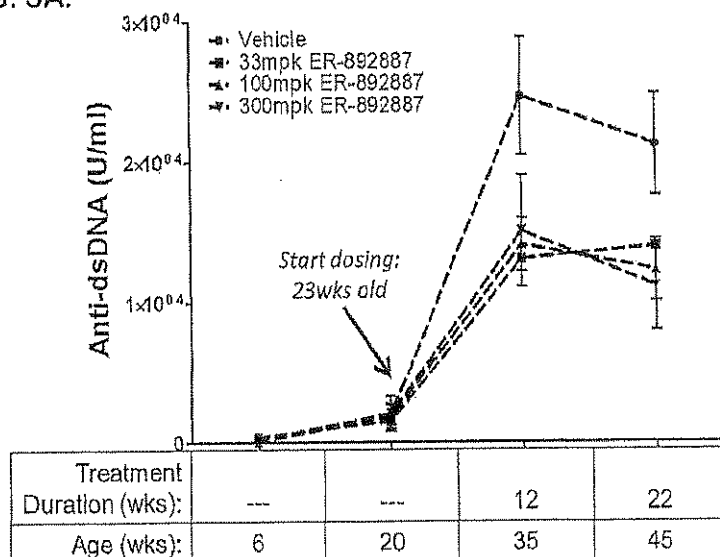


FIG. 3B.

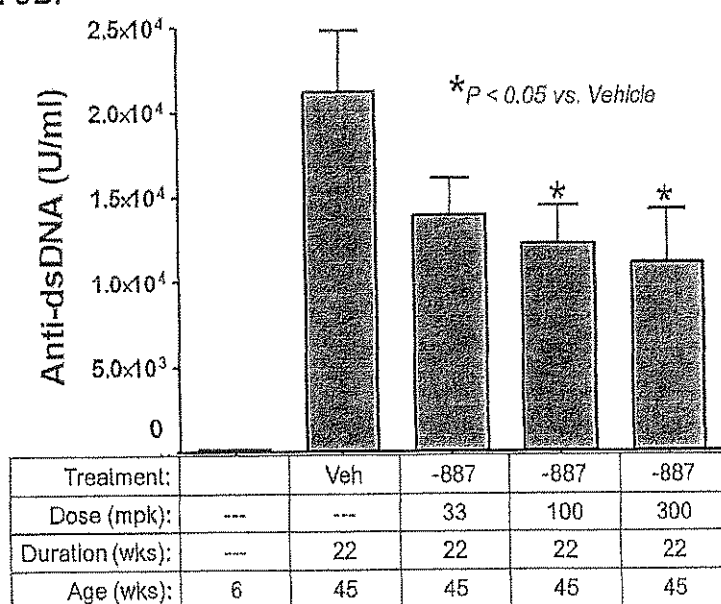


FIGURE 3

FIG. 3C.

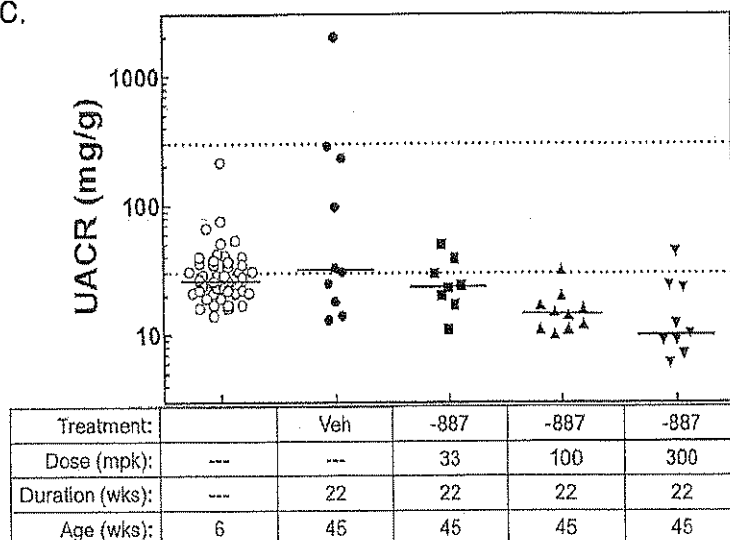


FIG. 3D.

Treatment:	Vehicle	ER-892887		
Dose (mpk):		33	100	300
Mortality (# deaths/total group #):	1/12	0/11	1/12	2/12
Dosing duration at death (days):	54		85	17, 53

FIG. 3E.

Glomerulonephritis (GN) Evaluation in NZB/W – Experiment #1				
	Vehicle	ER-892887		
Dose:	---	33mpk	100mpk	300mpk
Total Mice Examined:	10	12	10	9
GN Score:				
0/1+	4	8	9	5
2+	1	4	1	4
3+	1	0	0	0
4+	4	0	0	0
Percent combined incidence of Grade 3 and 4	50%	0%	0%	0%
Grade 0/1: within normal limits; Grade 2: MILD; Grade 3: MODERATE; Grade 4: MARKED				

FIGURE 4

FIG. 4A.

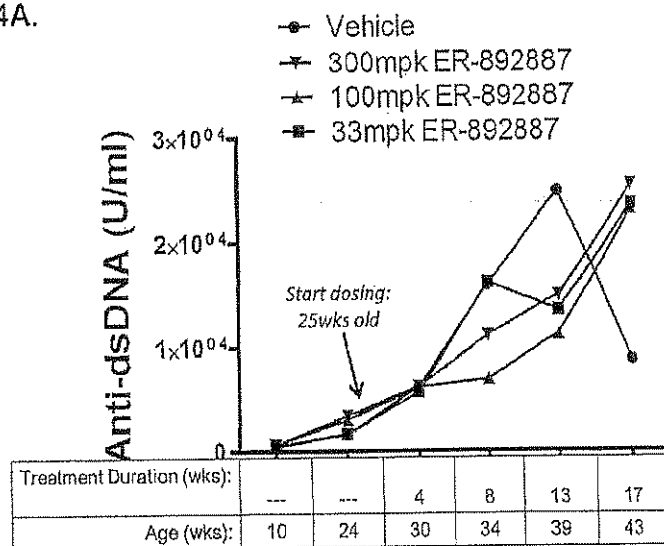


FIG. 4B.

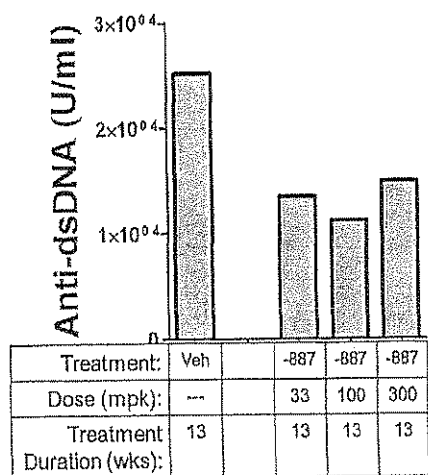


FIGURE 4

FIG. 4C.

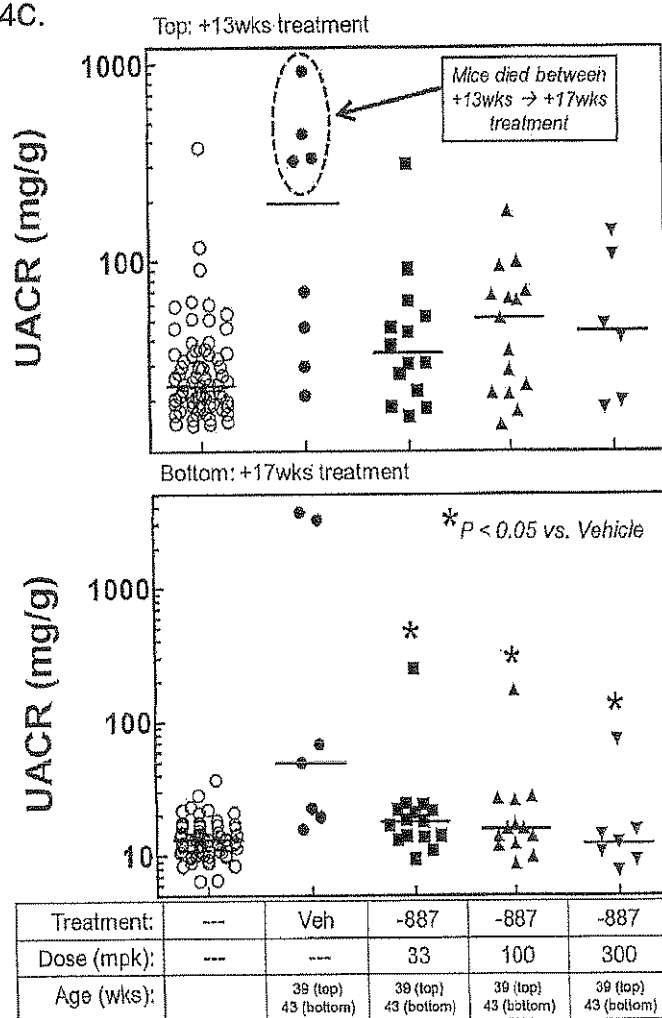


FIGURE 4

FIG. 4D.

NZB-8: Blood Urea Nitrogen (BUN)
(+13wks treatment)

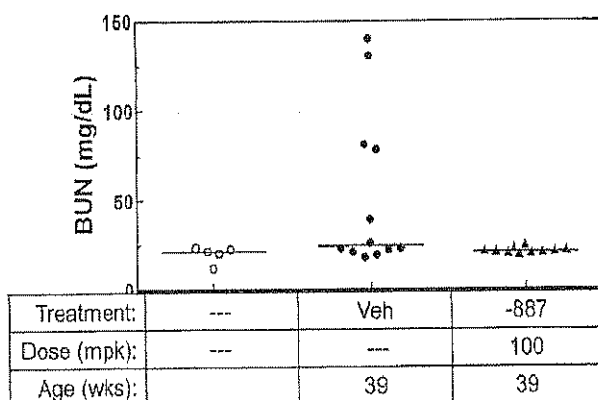


FIG. 4E.

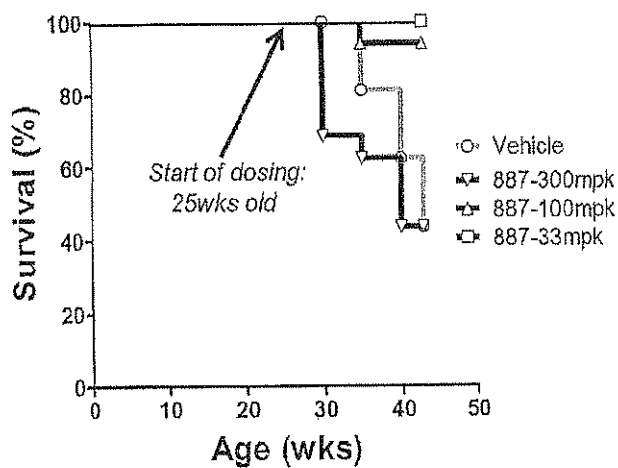


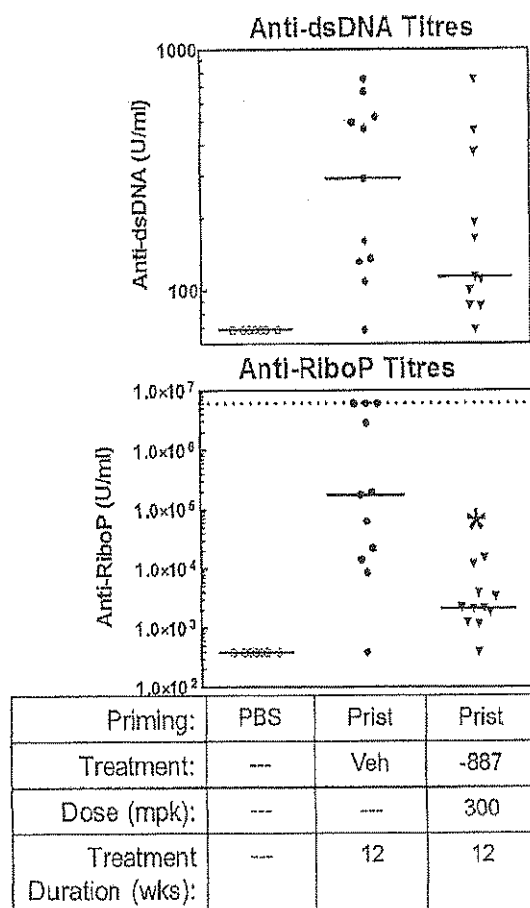
FIGURE 4

FIG. 4F.

Treatment:	Vehicle	ER-892887		
Dose (mpk):		33	100	300
Mortality: (# deaths/total group #)	9/16	0/16	1/16	9/16
Dosing duration at death (days):	67, 67, 82, 84, 98, 102, 104, 104, 113		63	8, 19, 25, 26, 29, 60, 92, 92, 96

FIGURE 5

FIG. 5A.



* $P < 0.05$ vs. Vehicle

FIGURE 5

FIG. 5B.

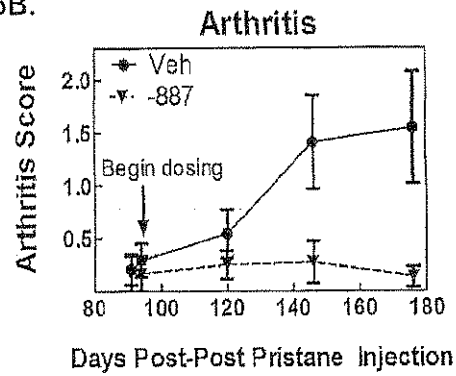


FIG. 5C.

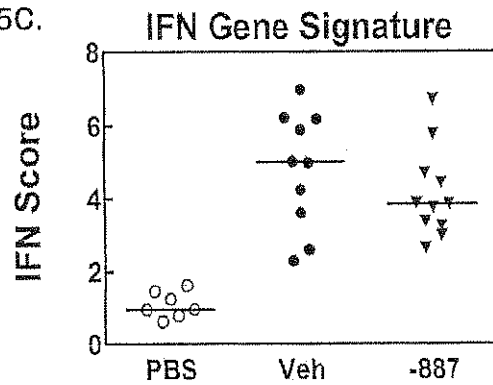


FIGURE 5

FIG. 5D.

Gene #:	Gene Name:
1	<i>Mx1</i> *
2	<i>Ifi44</i> *
3	<i>Irf7</i>
4	<i>Ifit1</i>
5	<i>Isg15</i>
6	<i>Usp18</i>
7	<i>Ifi204</i>
8	<i>Oas3</i>
9	<i>Fcgr1</i>
10	<i>Oasl2</i>
11	<i>Xaf1</i>
12	<i>Mmp8</i>
13	<i>Ifi202b</i>
14	<i>Mmp9</i>
15	<i>Fpr1</i>
16	<i>C3</i>
17	<i>Ms4a6c</i>
18	<i>Stat1</i>
19	<i>Epstl1</i>
20	<i>Ifi35</i>
21	<i>Bst2</i>
Twenty-one (21) genes significantly upregulated between Vehicle + Pristane vs. PBS control	
*Significantly reduced by ER-892887 (2 genes)	

FIGURE 6

FIG. 6A.

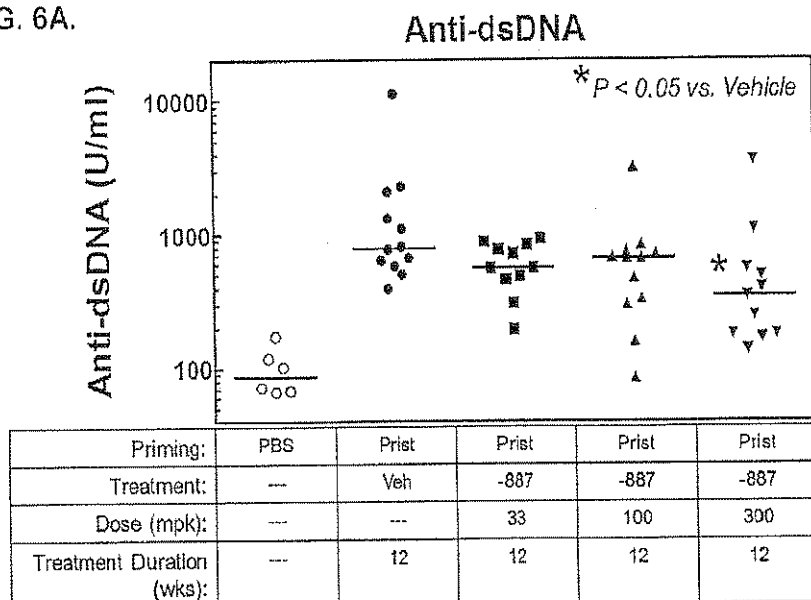


FIG. 6B.

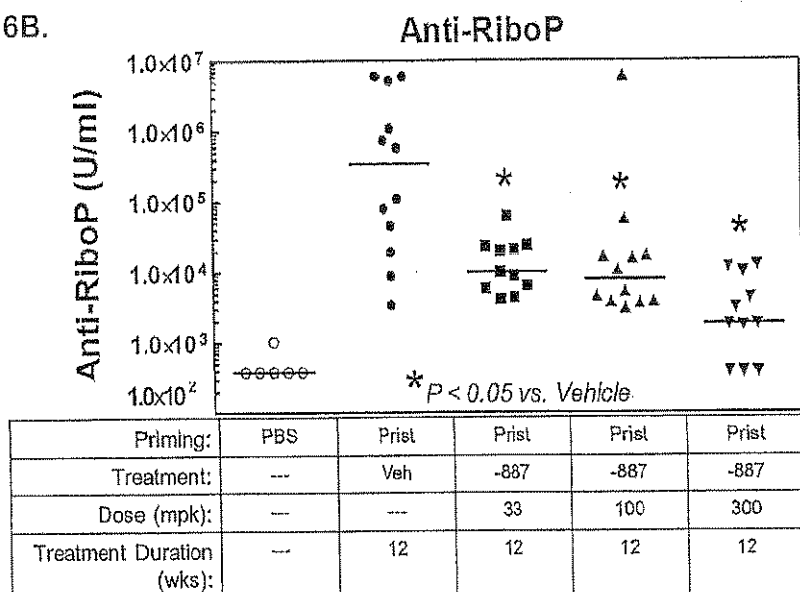


FIGURE 6

FIG. 6C.

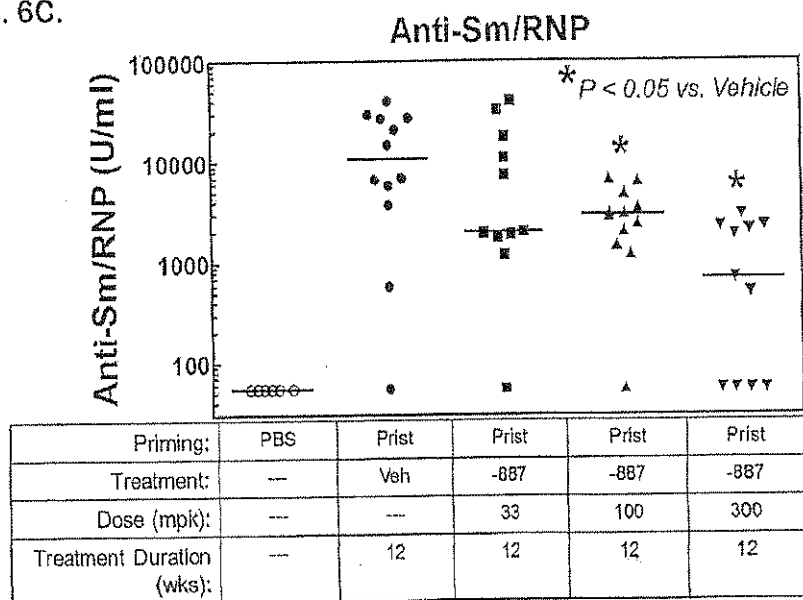


FIGURE 6

FIG. 6D.

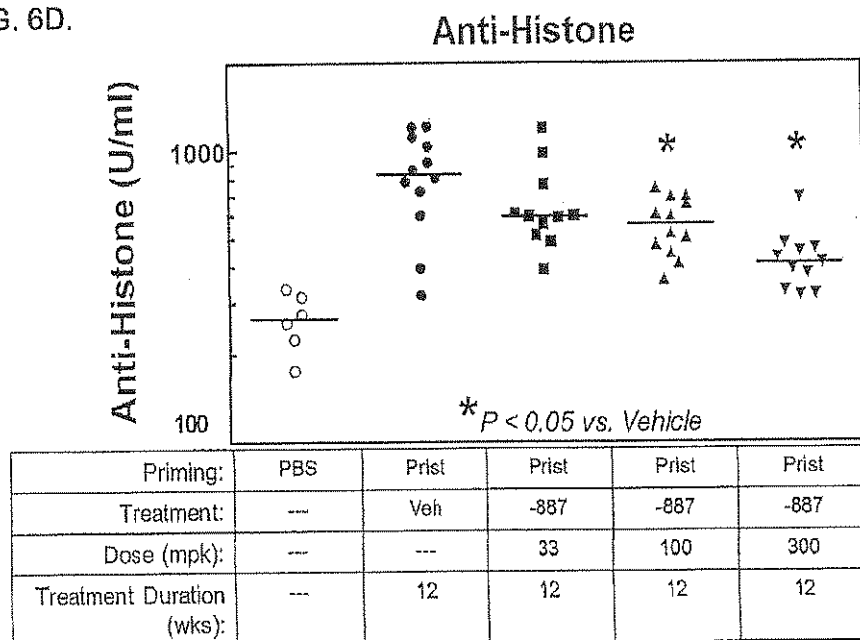


FIG. 6E.

Treatment:	Vehicle	ER-892887		
Dose (mpk):		33	100	300
Mortality: (# deaths/total group #)	0/12	1/12	0/12	1/12
Dosing duration at death (days):		1		51

FIGURE 6

FIG. 6F.

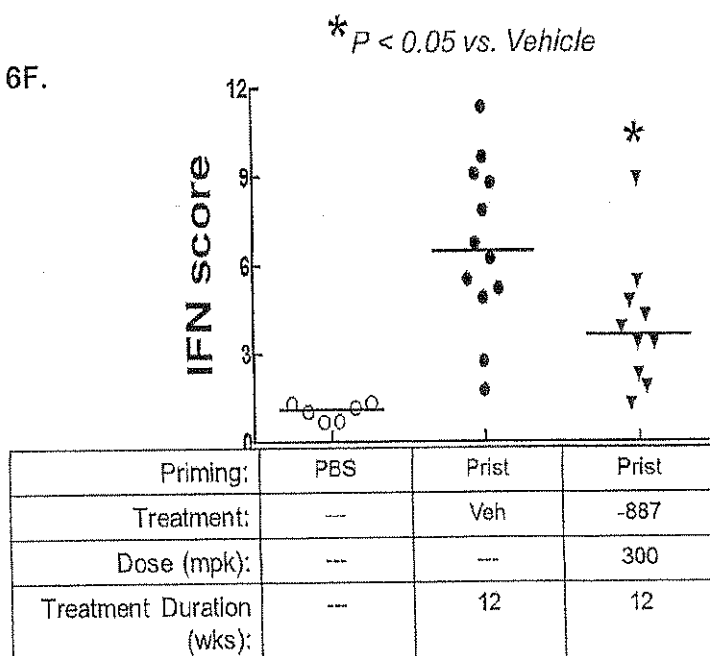


FIGURE 6

FIG. 6G.

Gene #:	Gene Name:
1	Bst2 *
2	Herc6 *
3	Ifi204 *
4	Ifi44 *
5	Irf7
6	Ifi2712a
7	Oas3
8	Oasl2
9	Usp18
10	Mmp8
11	Fcgr1
12	Ifit3
13	Isg15
14	Xaf1
15	Ifit1
16	Ifih1
17	Tnfsf13b
18	Cmpk2
19	Ms4a6c
20	Ccr2
21	Fpr1
22	Mmp9
Twenty-one (22) genes significantly upregulated between Vehicle + Pristane vs. PBS control	
*Significantly reduced by ER-892887 (4 genes)	

FIGURE 7

FIG. 7A.

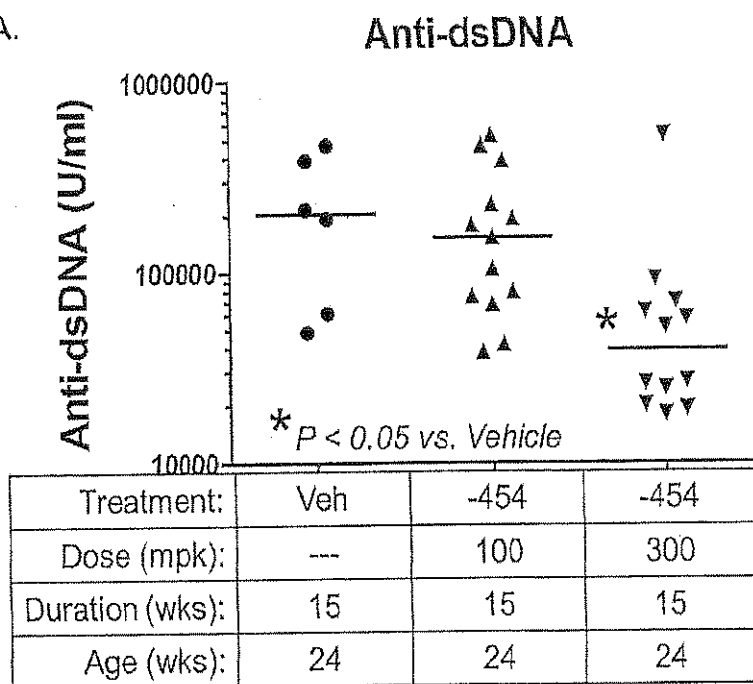


FIGURE 7

FIG. 7B.

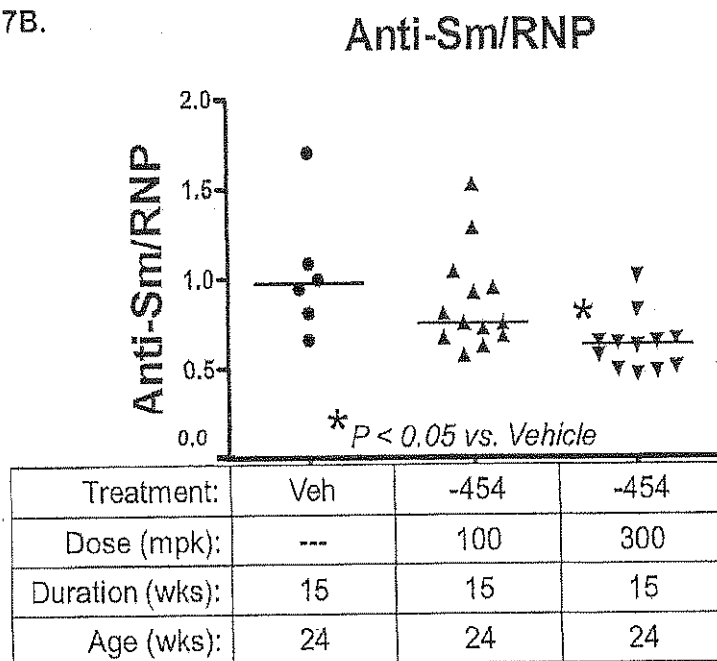


FIGURE 7

FIG. 7C.

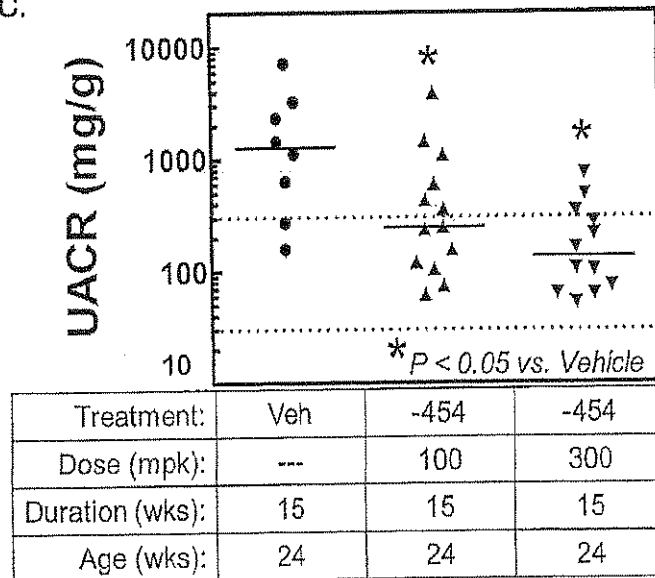


FIG. 7D.

Glomerulonephritis (GN) Evaluation in BXSB-Yaa Strain				
		Vehicle	ER-885454 (100mpk)	ER-885454 (300mpk)
Total Mice Examined:		6	12	13
	GN Score:			
	0/1	2	11	10
	2	1	1	3
	3	2	0	0
	4	1	0	0
Percent combined incidence of <u>Grade 3 and 4</u>		50%	0%	0%
Grade 0/1: within normal limits; Grade 2: MILD; Grade 3: MODERATE; Grade 4: MARKED				

FIGURE 8

FIG. 8A.

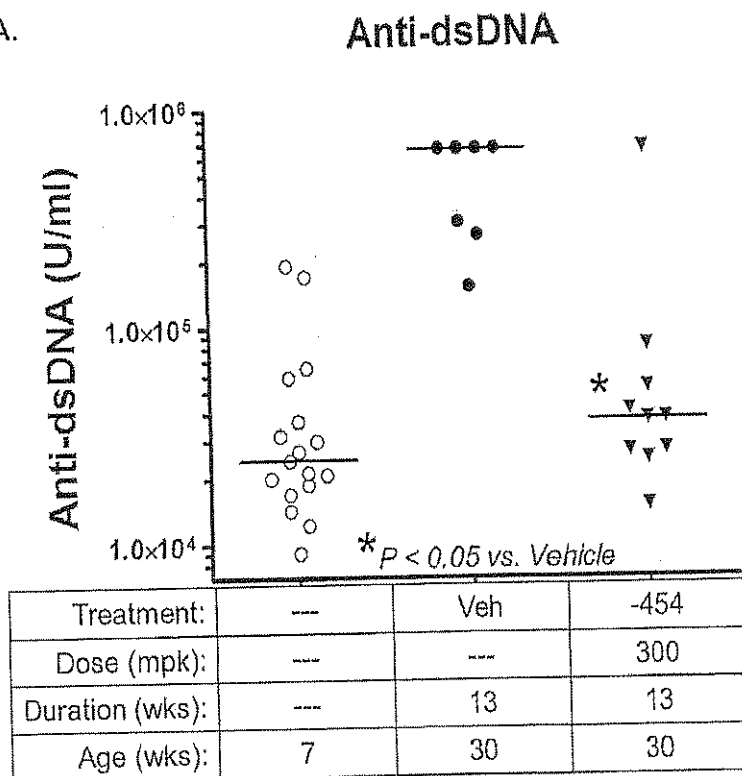


FIGURE 8

FIG. 8B.

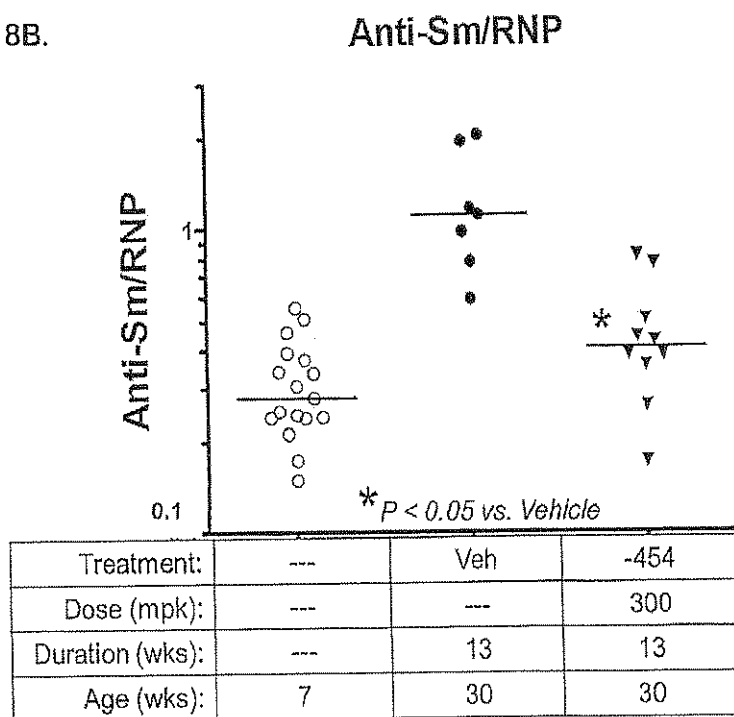
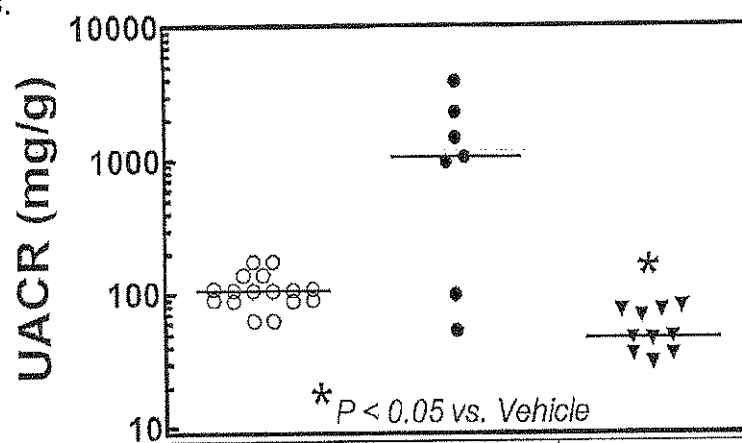


FIGURE 8

FIG. 8C.



Treatment:	---	Veh	-454
Dose (mpk):	---	---	300
Duration (wks):	---	12	12
Age (wks):	8	29	29

FIGURE 8

FIG. 8D.

Glomerulonephritis (GN) Evaluation in BXSB-Yaa Strain			
		Vehicle	ER-885454 (300mpk)
Total Mice Examined:		7	10
	GN Score:		
	0/1	2	10
	2	0	0
	3	3	0
	4	2	0
Percent combined incidence of <u>Grade 3 and 4</u>		71%	0%
Grade 0/1: within normal limits; Grade 2: MILD; Grade 3: MODERATE; Grade 4: MARKED			

FIGURE 9

FIG. 9A.

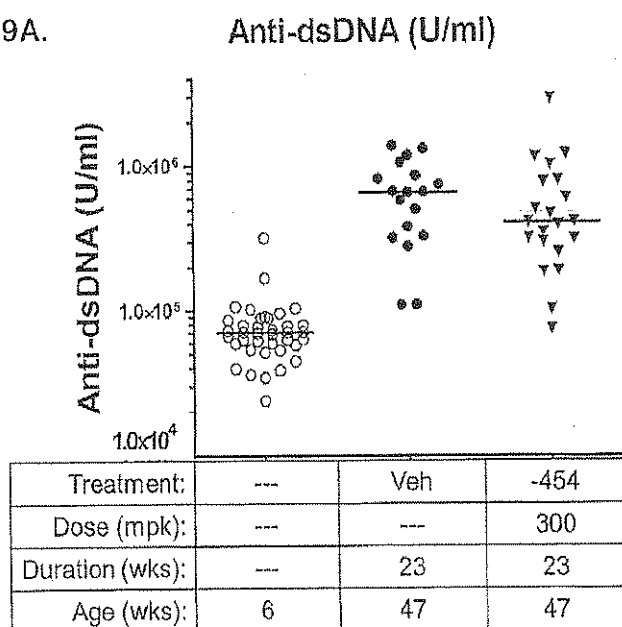


FIGURE 9

FIG. 9B.

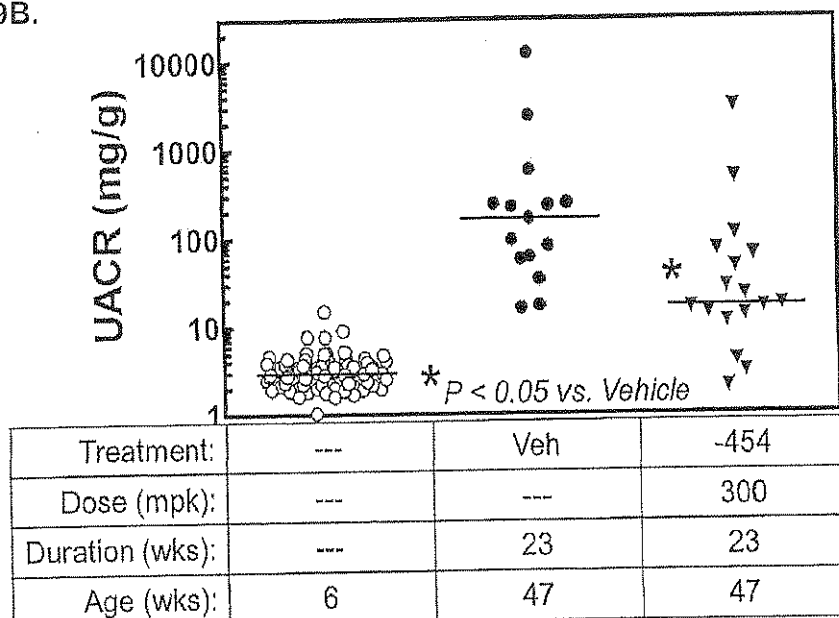
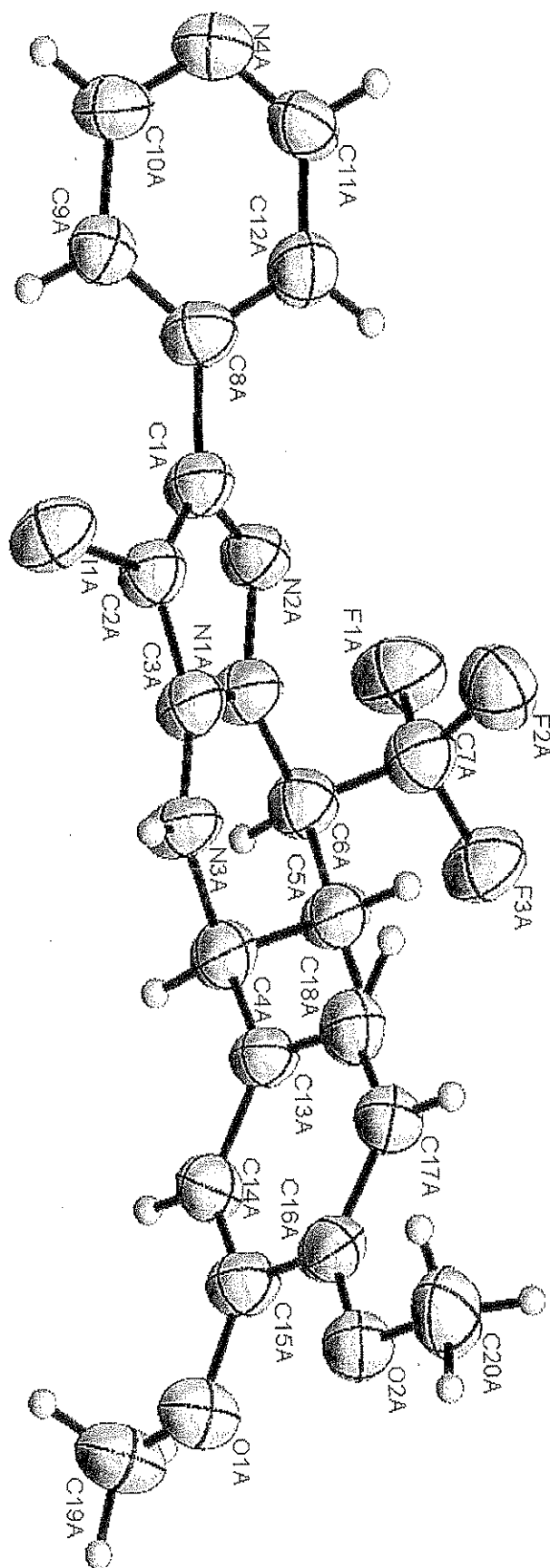
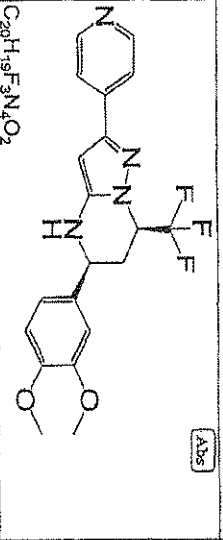
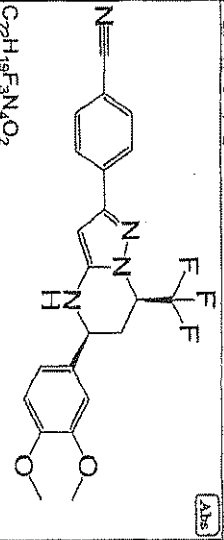
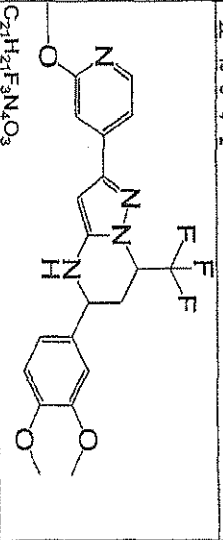
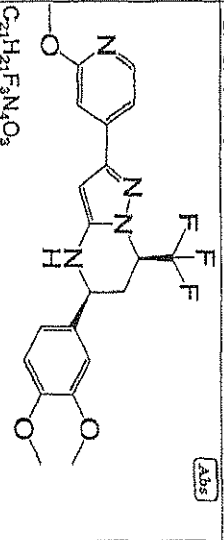
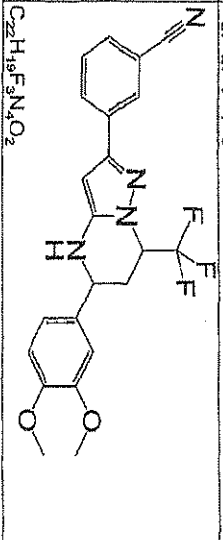


FIG. 9C.

Glomerulonephritis (GN) Evaluation in NZBxNZW Strain			
		Vehicle	ER-885454 (300mpk)
Total Mice Examined:		17	21
GN Score:	0	12/17	21
	1	4/17	0
	2	0	0
	3	1/17	0
	4	0	0
Percent combined incidence of <u>Grade 3 and 4</u>		6%	0%
Grade 0/1: within normal limits; Grade 2: MILD; Grade 3: MODERATE; Grade 4: MARKED			

FIGURE 10



ER-Number	Structure	Chemical Name	HEK/ TLR7 IC50 (μ M)	HEK/ TLR9 IC50 (μ M)	¹ H NMR	MS
ER-885454		(5S,7R)-5-(3,4-dimethoxyphenyl)-2-(pyridin-4-yl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine	0.050	> 10	¹ H NMR (400 MHz, CHLOROFORM-d) δ ppm 2.29 - 2.46 (m, 2 H) 2.47 - 2.60 (m, 2 H) 3.91 (s, 3 H) 3.93 (s, 3 H) 4.36 (s, 1 H) 4.45 (d, J=9.96 Hz, 1 H) 4.93 (dt, J=11.28, 5.79 Hz, 2 H) 5.85 (s, 1 H) 6.85 - 6.93 (m, 1 H) 6.93 - 7.04 (m, 2 H) 7.59 - 7.70 (m, 2 H) 8.56 - 8.66 (m, 2 H)	405.2
ER-885690		4-((5S,7R)-5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)benzonitrile	0.050	> 10	see ER-885484	
ER-886434		5-(3,4-dimethoxyphenyl)-2-(2-methoxypyridin-4-yl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine	0.090	> 10	¹ H NMR (400 MHz, CHLOROFORM-d) δ ppm 2.36 - 2.47 (m, 1 H) 2.54 (d, J=6.14 Hz, 1 H) 3.94 (s, 3 H) 3.96 (s, 3 H) 4.00 (s, 3 H) 4.34 (s, 1 H) 4.47 (dd, J=11.73, 2.08 Hz, 1 H) 4.89 - 5.01 (m, 1 H) 5.84 (s, 1 H) 6.89 - 6.95 (m, 1 H) 6.99 - 7.04 (m, 2 H) 7.09 - 7.13 (m, 1 H) 7.35 (dd, J=5.36, 1.39 Hz, 1 H) 8.20 (dd, J=5.36, 0.51 Hz, 1 H)	435.6
ER-886622		(5S,7R)-5-(3,4-dimethoxyphenyl)-2-(2-methoxypyridin-4-yl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine	0.020	> 10	see ER-886434	
ER-887238		3-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)benzonitrile	0.070	> 10		

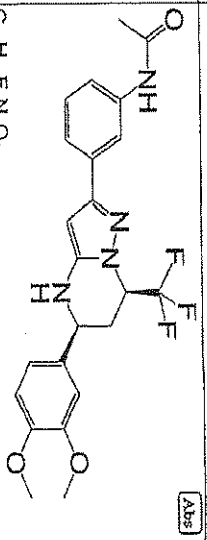
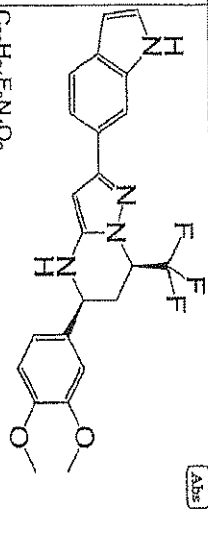
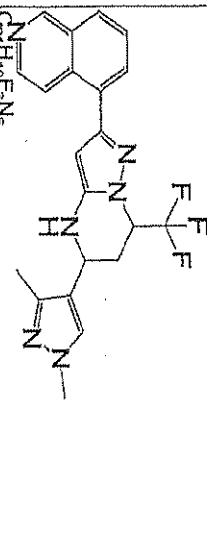
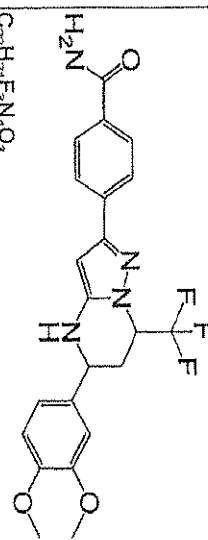
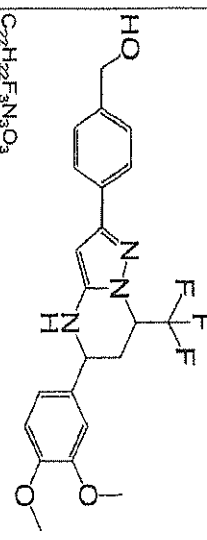
ER-Number	Structure	Chemical Name	HEK/ TLR7 IC50 (μ M)	HEK/ TLR9 IC50 (μ M)	¹ H NMR	MS
ER-887734		N-(3-((5S,7R)-5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenyl)acetamide	0.100	> 10		461.3
ER-887738		(5S,7R)-5-(3,4-dimethoxyphenyl)-2-(1H-indol-6-yl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine	0.090	> 10		443
ER-889862		5-(5-(1,3-dimethyl-1H-pyrazol-4-yl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)isoquinoline	0.040	> 10		413
ER-889871		4-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)benzamide	0.020	> 10		447.5
ER-889674		(4-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenyl)methanol	0.060	> 10		434

FIG. 11C

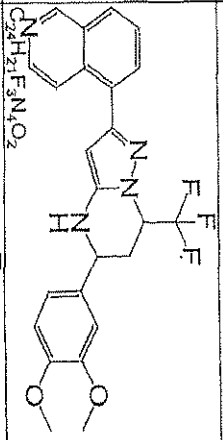
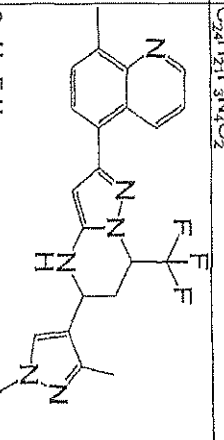
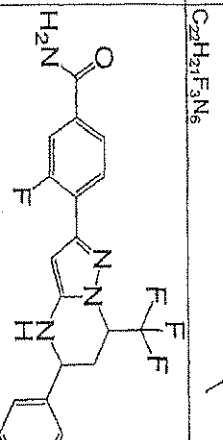
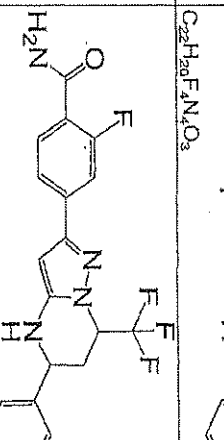
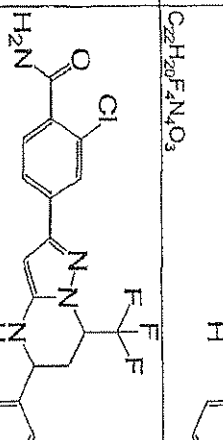
ER-Number	Structure	Chemical Name	HEK/ TLR7 IC50 (μ M)	HEK/ TLR9 IC50 (μ M)	¹ H NMR	MS
ER-889925		5-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)isquinoline	0.030	> 10		455.1
ER-890007		5-(5-(1,3-dimethyl-1H-pyrazol-4-yl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-8-methylquinoline	0.050	> 10		427
ER-890017		4-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-3-fluorobenzamide	0.070	> 10	see ER-892892	465
ER-890019		4-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-2-fluorobenzamide	0.020	> 10		465
ER-890020		2-chloro-4-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)benzamide	0.030	> 10		481

FIG. 11D

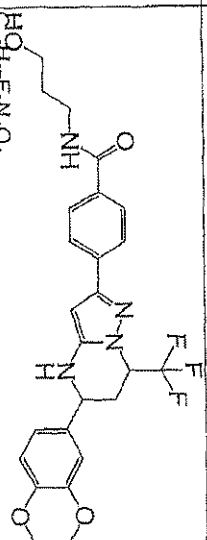
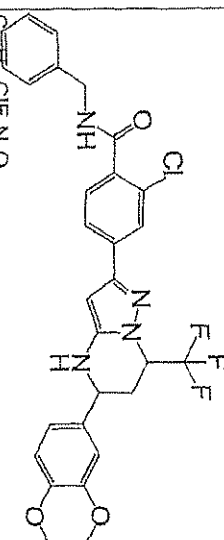
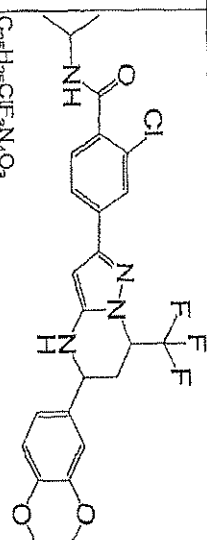
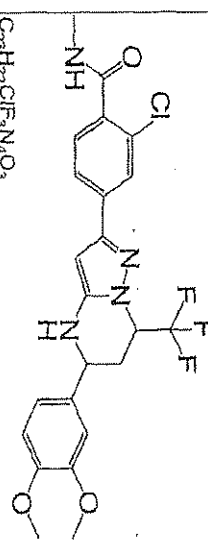
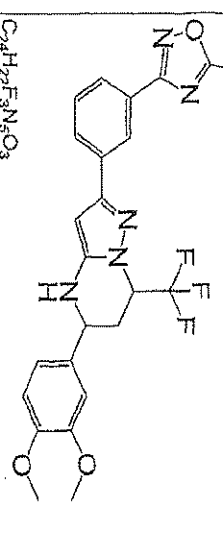
ER-Number	Structure	Chemical Name	HEK/ TLR7 IC50 (μ M)	HEK/ TLR9 IC50 (μ M)	¹ H NMR	MS
ER-890024		4-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-N-(3-hydroxypropyl)benzamide	0.050	> 10	see ER-892893	505
ER-890027		N-benzyl-2-chloro-4-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)benzamide	0.030	> 10		571
ER-890028		2-chloro-4-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-N-isopropylbenzamide	0.030	> 10		523
ER-890029		2-chloro-4-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-N-methylbenzamide	0.030	> 10	see ER-892899	495
ER-890035		3-(3-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenyl)-5-methyl-1,2,4-oxadiazole	0.002	> 10		486

FIG. 11E

ER-Number	Structure	Chemical Name	HEK/ TLR7 IC50 (μ M)	HEK/ TLR9 IC50 (μ M)	¹ H NMR	MS
ER-890043		5-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-1H-benzotriazole-2(3H)-one	0.010	> 10		460
ER-890044		4-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenyl)piperazine-1-yl)methanone	0.005	> 10	¹ H NMR (400 MHz, METHANOL-d ₄) δ ppm 2.23 (dt, J=13.30, 11.35 Hz, 1 H) 2.54 (ddd, J=13.38, 6.28, 2.46 Hz, 1 H) 2.82 (br. s., 2 H) 2.90 (br. s., 2 H) 3.66 - 3.79 (m, 1 H) 3.85 (s, 3 H) 3.88 (s, 3 H) 4.46 (dd, J=11.70, 2.30 Hz, 1 H) 5.01 - 5.16 (m, 1 H) 5.86 (s, 1 H) 6.99 (d, J=8.33 Hz, 1 H) 7.06 (dd, J=8.33, 1.92 Hz, 1 H) 7.12 (d, J=1.92 Hz, 1 H) 7.39 - 7.49 (m, 2 H) 7.80 - 7.90 (m, 2 H)	516.6
ER-890050		2-(3-(1H-pyrazol-1-yl)phenyl)-5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine	0.005	> 10		470
ER-890978		2-(2-chloropyridin-4-yl)-5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine	0.040	> 10	¹ H NMR (400 MHz, METHANOL-d ₄) δ ppm 2.23 (dt, J=13.32, 11.42 Hz, 1 H) 2.53 (ddd, J=13.36, 6.04, 2.31 Hz, 1 H) 3.84 (s, 3 H) 3.87 (s, 4 H) 4.47 (dd, J=11.60, 2.21 Hz, 1 H) 5.07 - 5.17 (m, 1 H) 5.96 (s, 1 H) 6.96 - 7.00 (m, 1 H) 7.03 - 7.07 (m, 1 H) 7.10 (d, J=1.87 Hz, 1 H) 7.70 (dd, J=5.25, 1.41 Hz, 1 H) 7.75 - 7.80 (m, 1 H) 8.33 (dd, J=5.25, 0.55 Hz, 1 H)	439.5
ER-891029		5-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-N-methylpicolinamide	0.050	> 10		462

FIG. 11F

ER-Number	Structure	Chemical Name	HEK/ TLR7 IC50 (μ M)	HEK/ TLR9 IC50 (μ M)	¹ H NMR	MS
ER-891043		5-(3,4-dimethoxyphenyl)-2-(1,7-dimethyl-1H-indazol-5-yl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine	0.004	> 10		472
ER-891044		5-(3,4-dimethoxyphenyl)-2-(1,4-dimethyl-1H-indazol-5-yl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine	0.010	> 10		472
ER-891047		5-(3,4-dimethoxyphenyl)-2-(1,6-dimethyl-1H-indazol-5-yl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine	0.008	> 10		472
ER-891058		N-cyclopropyl-4-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-2-fluorobenzamide	0.050	> 10		505
ER-892887		(4-((5S,7R)-5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenyl)(piperazin-1-yl)methanone	0.006	6.02	¹ H NMR (400 MHz, METHANOL-d ₄) δ ppm 1.15 (d, J=6.15 Hz, 1 H) 2.23 (dt, J=13.27, 11.34 Hz, 1 H) 2.54 (ddd, J=13.38, 6.28, 2.49 Hz, 1 H) 3.85 (s, 3 H) 3.87 (s, 4 H) 4.46 (dd, J=11.57, 2.16 Hz, 1 H) 5.09 (dd, J=10.93, 6.06 Hz, 1 H) 5.88 (s, 1 H) 6.96-7.01 (m, 1 H) 7.03-7.08 (m, 1 H) 7.11 (d, J=1.94 Hz, 1 H) 7.47-7.56 (m, 2 H) 7.81-7.95 (m, 2 H)	516.6

FIG. 11G

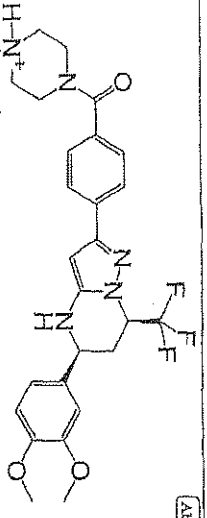
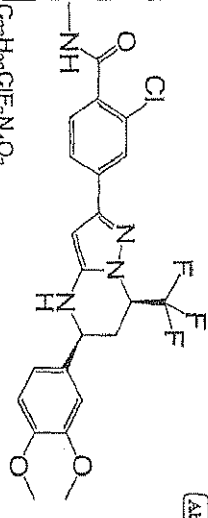
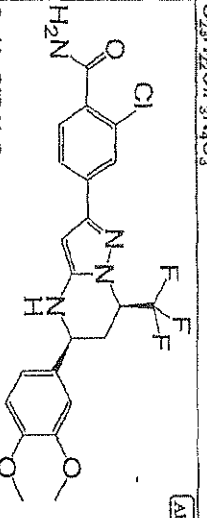
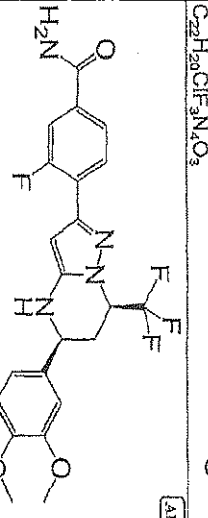
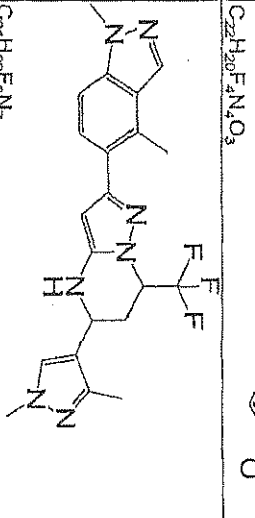
ER-Number	Structure	Chemical Name	HEK/ TLR7 IC50 (μ M)	HEK/ TLR9 IC50 (μ M)	¹ H NMR	MS
ER-892887		4-((5S,7R)-5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-y]benzoyl) piperazin-1-ium chloride	0.010	> 10	see ER-890044	516.6
ER-892889		2-chloro-4-((5S,7R)-5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-y]benzoyl)-N-methylbenzamide	0.020	> 10	¹ H NMR (400 MHz, METHANOL-d ₄) δ ppm 2.23 (dt, J=13.29, 11.38 Hz, 1 H) 2.53 (ddd, J=13.34, 6.19, 2.44 Hz, 1 H) 2.86 - 2.96 (m, 3 H) 3.84 (s, 3 H) 3.87 (s, 3 H) 4.45 (dd, J=11.62, 2.23 Hz, 1 H) 5.03 - 5.16 (m, 1 H) 5.86 (s, 1 H) 6.98 (d, J=8.28 Hz, 1 H) 7.05 (dd, J=8.34, 1.93 Hz, 1 H) 7.11 (d, J=1.91 Hz, 1 H) 7.46 (d, J=7.97 Hz, 1 H) 7.72 (dd, J=7.97, 1.56 Hz, 1 H) 7.83 (d, J=1.45 Hz, 1 H)	496
ER-892890		2-chloro-4-((5S,7R)-5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-y]benzoyl)-N-methylbenzamide	0.040	> 10	¹ H NMR (400 MHz, METHANOL-d ₄) δ ppm 2.20 - 2.29 (m, 1 H) 2.50 - 2.58 (m, 1 H) 3.83 - 3.86 (m, 3 H) 3.86 - 3.90 (m, 3 H) 4.46 (dd, J=11.65, 2.12 Hz, 1 H) 5.10 - 5.14 (m, 1 H) 5.87 (s, 1 H) 6.99 (d, J=8.28 Hz, 1 H) 7.06 (dd, J=8.32, 2.02 Hz, 1 H) 7.11 (d, J=1.91 Hz, 1 H) 7.51 - 7.55 (m, 1 H) 7.70 - 7.75 (m, 1 H) 7.84 (d, J=1.49 Hz, 1 H)	482.2
ER-892892		4-((5S,7R)-5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-y]benzoyl)-N-methylbenzamide	0.040	> 10	¹ H NMR (400 MHz, METHANOL-d ₄) δ ppm 2.20 (dt, J=13.26, 11.41 Hz, 1 H) 2.50 (ddd, J=13.36, 6.20, 2.45 Hz, 1 H) 3.27 (dt, J=3.31, 1.64 Hz, 1 H) 3.80 (s, 4 H) 3.83 (s, 5 H) 4.42 (dd, J=11.57, 2.20 Hz, 1 H) 5.02 - 5.12 (m, 1 H) 5.92 (d, J=4.21 Hz, 1 H) 6.94 (d, J=8.35 Hz, 1 H) 7.02 (dd, J=8.39, 1.90 Hz, 1 H) 7.08 (d, J=1.98 Hz, 1 H) 7.58 - 7.72 (m, 2 H) 8.00 (t, J=7.84 Hz, 1 H)	465.5
ER-892900		2-((1,4-dimethyl-1H-indazol-5-yl)-5-(1,3-dimethyl-1H-pyrazol-4-yl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-y]benzoyl)-N-methylbenzamide	0.100	> 10		430.1

FIG. 11H

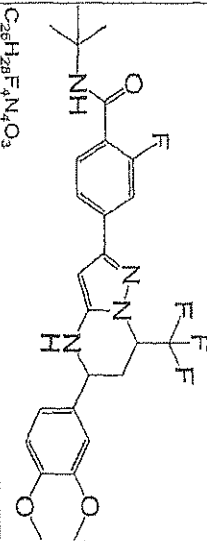
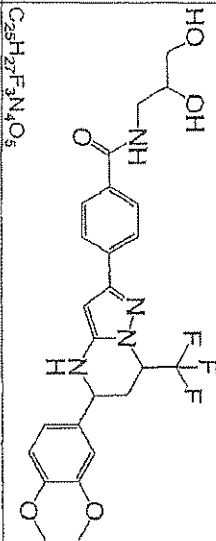
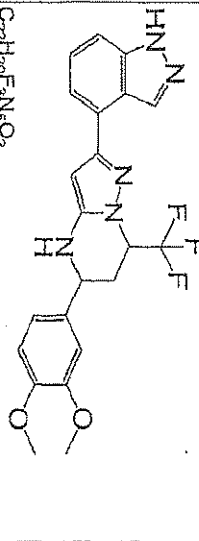
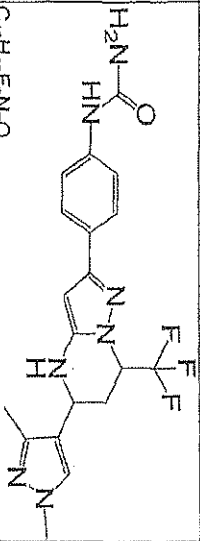
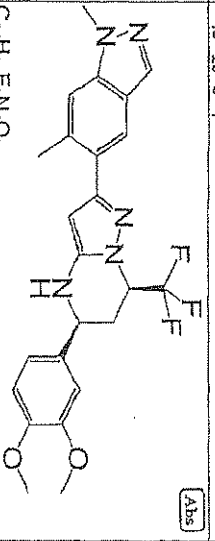
ER-Number	Structure	Chemical Name	HEK/ TLR7/IC50 (μ M)	HEK/ TLR9/IC50 (μ M)	¹ H NMR	MS
ER-892908		N-(tert-butyl)-4-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-2-fluorobenzamide	0.050	> 10		521
ER-892930		N-(2,3-dihydroxypropyl)-4-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)benzamide	0.030	> 10		
ER-892931		5-(3,4-dimethoxyphenyl)-2-(1H-indazol-4-yl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine	0.040	> 10		444
ER-893888		1-(4-(5-(1,3-dimethyl-1H-pyrazol-4-yl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenyl)urea	0.020	> 10	¹ H NMR (400 MHz, METHANOL-d ₄) δ ppm 2.24 (dt, J=13.17, 11.38 Hz, 2H) 2.48 - 2.55 (m, 1H) 2.56 (s, 4H) 3.84 (s, 3H) 3.87 (s, 3H) 4.05 (s, 3H) 4.47 (dd, J=11.58, 2.08 Hz, 1H) 5.02 - 5.16 (m, 1H) 5.62 (s, 1H) 6.98 (d, J=8.28 Hz, 1H) 7.03 - 7.10 (m, 1H) 7.12 (d, J=1.87 Hz, 1H) 7.41 (s, 1H) 7.78 (s, 1H) 7.91 - 7.99 (m, 1H)	
ER-893961		(5S,7R)-5-(3,4-dimethoxyphenyl)-2-(1,5-dimethyl-1H-indazol-5-yl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine	0.040	> 10		472.5

FIG. 11 I

ER-Number	Structure	Chemical Name	HEK/ TLR7 IC50 (μ M)	HEK/ TLR9 IC50 (μ M)	¹ H NMR	MS
ER-893969		5-((5S,7R)-5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-1H-benzotriazole-2(3H)-one	0.020	> 10	¹ H NMR (400 MHz, METHANOL-d4) δ ppm 2.15 - 2.28 (m, 1H) 2.47 - 2.56 (m, 1H) 3.04 (s, 3H) 3.87 (s, 3H) 4.44 (dd, J=1.62, 2.12 Hz, 1H) 5.04 (dd, J=1.37, 5.46 Hz, 1H) 5.77 (s, 1H) 6.95 - 7.01 (m, 1H) 7.02 - 7.08 (m, 1H) 7.09 - 7.14 (m, 1H) 7.40 - 7.49 (m, 1H) 7.52 - 7.60 (m, 2H) 7.60 - 7.70 (m, 2H)	460.5
ER-893972		(5S,7R)-5-(3,4-dimethoxyphenyl)-2-(1,4-dimethyl-1H-indazol-5-yl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine	0.010	> 10	¹ H NMR (400 MHz, METHANOL-d4) δ ppm 2.21 (dt, J=13.06, 11.42 Hz, 1H) 2.47 - 2.55 (m, 1H) 2.65 (s, 3H) 3.78 - 3.82 (overlapping signals, 5H) 3.83 (s, 4H) 3.87 - 3.91 (m, 1H) 4.03 (s, 3H) 4.45 (dd, J=1.63, 2.22 Hz, 1H) 5.07 (m, J=4.70 Hz, 1H) 5.61 (s, 1H) 6.95 (d, J=8.35 Hz, 1H) 7.04 (dd, J=8.37, 1.81 Hz, 1H) 7.10 (d, J=1.98 Hz, 1H) 7.35 (d, J=8.61 Hz, 1H) 7.52 (d, J=8.68 Hz, 1H) 8.06 (d, J=0.88 Hz, 1H)	472.3
ER-893987		(5R,7S)-2-(1,4-dimethyl-1H-indazol-5-yl)-5-(1,3-dimethyl-1H-pyrazol-4-yl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine	0.090	> 10	δ 2.05, (m, 1H), 2.14, (s, 3H), 2.36, (m, 1H), 2.62, (s, 3H), 3.70, (s, 3H), 3.97, (s, 3H), 4.38, (m, 1H), 5.22, (m, 1H), 5.51, (s, 1H), 6.44, (s, 1H), 7.38, (d, 1H), 7.49, (d, 1H), 7.63, (s, 1H), 8.08, (s, 1H)	
ER-893990		(5S,7R)-5-(1,3-dimethyl-1H-pyrazol-4-yl)-2-(2-methyl-2H-indazol-5-yl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine	0.080	> 10	δ 2.03, (m, 1H), 2.11, (s, 3H), 2.33, (m, 1H), 3.69, (s, 3H), 4.09, (s, 3H), 4.33, (m, 1H), 5.19, (m, 1H), 5.67, (s, 1H), 6.48, (s, 1H), 7.50, (d, 1H), 7.62, (d, 1H), 7.65, (s, 1H), 7.91, (s, 1H), 8.26, (s, 1H)	
ER-894462		(4-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenyl)(3-hydroxyazetidin-1-yl)methanone	0.060	> 10		503

FIG. 11J

ER-Number	Structure	Chemical Name	HEK/ TLR7 IC50 (μ M)	HEK/ TLR9 IC50 (μ M)	¹ H NMR	MS
ER-894463		4-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-N-benzamide hydrochloride	0.050	6.09		
ER-894464		(3-aminopyrrolidin-1-yl)(4-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenyl)methanone hydrochloride	0.006	> 10	¹ H NMR (400 MHz, METHANOL-d4) δ ppm 1.82 (dd, 1 H) 2.17 - 2.32 (m, 2 H) 2.54 (dd, 1 H) 3.38 (m, 1 H) 3.47 - 3.50 (m, 1 H) 3.60 - 3.74 (m, 2 H) 3.74 - 3.83 (m, 1 H) 3.85 (m, 3 H) 3.87 (m, 3 H) 4.46 (d, 1 H) 5.00 - 5.14 (m, 1 H) 6.91 - 7.02 (m, 2 H) 7.02 - 7.16 (m, 2 H) 7.57 (t, 2 H) 7.84 (d, 2 H)	516.6
ER-894465		(4-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenyl)(3-hydroxypyrrolidin-1-yl)methanone	0.009	> 10	¹ H NMR (400 MHz, METHANOL-d4) δ ppm 1.89 - 2.16 (m, overlapping signals, 3 H) 2.23 (dt, 1 H) 2.52 (dd, 1 H) 3.39 (d, 1 H) 3.46 - 3.62 (m, 1 H) 3.62 - 3.81 (m, 2 H) 3.84 (s, 3 H) 3.87 (s, 3 H) 4.28 - 4.54 (m, 2 H) 4.98 - 5.17 (m, 1 H) 6.91 - 7.20 (m, 4 H) 7.48 - 7.65 (m, 2 H) 7.77 - 7.94 (m, 2 H)	518.6
ER-894466		(4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenyl)(piperazin-1-yl)methanone	0.010	10.00	¹ H NMR (400 MHz, METHANOL-d4) δ ppm 2.21 - 2.37 (m, 1 H) 2.89 - 2.92 (m, 4 H) 2.99 - 3.02 (m, overlapping signals, 1 H) 3.46 - 3.50 (m, 2 H) 3.67 - 3.75 (m, 2 H) 3.85 (s, 3 H) 3.87 (s, 3 H) 4.47 (dd, 1 H) 4.65 - 4.80 (m, 1 H) 6.49 (d, 6.63 (t, 1 H) 7.05 (m, 4 H) 7.36 - 7.49 (m, 2 H) 7.79 - 7.89 (m, 2 H)	498.6
ER-894595		1-(4-((5S,7R)-5-(1,3-dimethyl-1H-pyrazol-4-yl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenyl)urea	0.060	> 10	¹ H NMR (400 MHz, METHANOL-d4) δ ppm 2.04 (m, 1 H) 2.12 (s, 3 H) 2.36 (m, 1 H) 3.69 (s, 3 H) 4.35 (m, 1 H) 5.24 (m, 1 H) 5.56 (s, 1 H) 5.79 (s, 2 H) 6.44 (s, 1 H) 7.31 (d, 2 H) 7.49 (d, 2 H) 7.65 (s, 1 H) 8.52 (s, 1 H)	

FIG. 11K

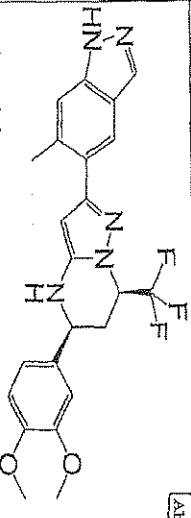
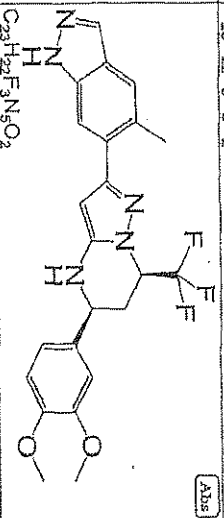
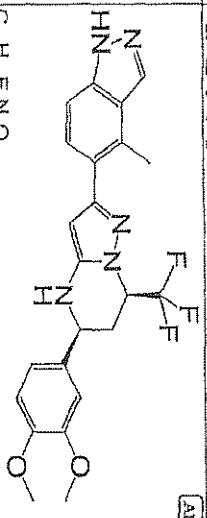
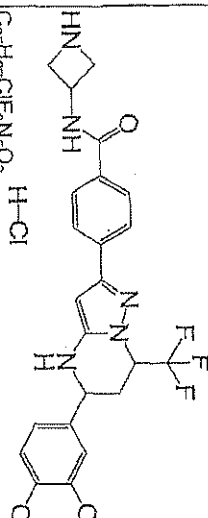
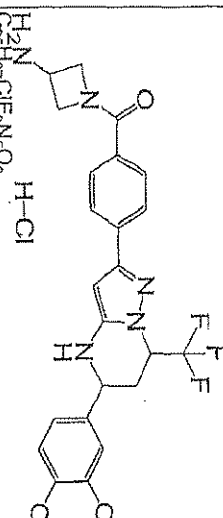
ER-Number	Structure	Chemical Name	HEK/ TLR7 IC50 (µM)	HEK/ TLR9 IC50 (µM)	¹ H NMR	MS
ER-894646		(5S, 7R)-5-(3,4-dimethoxyphenyl)-2-(6-methyl-1H-indazol-5-yl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine	0.030	> 10	¹ H NMR (400 MHz, CHLOROFORM-d) δ ppm 2.33 - 2.45 (m, 1 H) 2.50 (m, 1 H) 2.56 (s, 3 H, overlapping signals) 3.91 (s, 3 H) 3.93 (s, 3 H) 4.34 (s, 1 H) 4.41 - 4.50 (m, 1 H) 4.94 (dt, J=11.27, 5.77 Hz, 1 H) 5.63 (s, 1 H) 6.89 (d, J=8.20 Hz, 1 H) 6.96 - 7.06 (m, 2 H) 7.30 (s, 1 H) 7.85 (s, 1 H) 8.01 (s, 1 H)	458.3
ER-894647		(5S, 7R)-5-(3,4-dimethoxyphenyl)-2-(5-methyl-1H-indazol-6-yl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine	0.050	> 10	¹ H NMR (400 MHz, CHLOROFORM-d) δ ppm 2.36 - 2.49 (m, 1 H) 2.49 - 2.55 (m, 1 H) 2.55 (s, 3 H, overlapping signals) 3.91 (s, 3 H) 3.93 (s, 3 H) 4.32 (s, 1 H) 4.48 (d, J=9.92 Hz, 1 H) 4.95 (dt, J=11.37, 5.76 Hz, 1 H) 5.67 (s, 1 H) 6.85 - 6.94 (m, 1 H) 6.95 - 7.05 (m, 2 H) 7.59 (s, 1 H) 7.63 - 7.68 (m, 2 H)	
ER-894680		(5S, 7R)-5-(3,4-dimethoxyphenyl)-2-(4-methyl-1H-indazol-5-yl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine	0.040	> 10	¹ H NMR (400 MHz, METHANOL-d4) δ ppm 2.18 - 2.29 (m, 2 H) 2.47 - 2.55 (m, 1 H) 2.66 (s, 2 H) 3.81 (s, 3 H) 3.84 (s, 3 H) 4.45 (dd, J=11.55, 2.18 Hz, 1 H) 5.61 (s, 1 H) 6.89 - 6.98 (m, 2 H) 7.01 - 7.06 (m, 1 H) 7.10 (d, J=1.94 Hz, 1 H) 7.34 (d, J=8.64 Hz, 1 H) 7.48 (d, J=8.64 Hz, 1 H) 8.05 - 8.15 (m, 1 H)	458.6
ER-895077		N-(azetidin-3-yl)-4-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)benzamide hydrochloride	0.050	> 10	¹ H NMR (400 MHz, METHANOL-d4) δ ppm 2.12 - 2.33 (m, 1 H) 2.54 (dd, 1 H) 2.95-3.12 (m, 1H) 3.85 (s, 3H) 3.86 - 3.92 (m, 3 H) 3.92 - 4.00 (m, 2 H) 4.00 - 4.08 (m, 2 H) 4.46 (d, 2 H) 5.04 - 5.15 (m, 1 H) 6.94 - 7.17 (m, 4 H) 7.78 - 7.91 (m, 4 H)	502.5
ER-895078		(3-aminazetidin-1-yl)-4-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenylmethanone hydrochloride	0.020	> 10		502

FIG. 11L

ER-Number	Structure	Chemical Name	HEK1 TLR7 IC50 (μ M)	HEK1 TLR9 IC50 (μ M)	¹ H NMR	MS
ER-895080		(4-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenyl)(2,6-diazaspiro[3.4]nonan-2-yl)methanone 2,2,2-trifluoroacetate	0.050	> 10	¹ H NMR (400 MHz, METHANOL-d ₄) δ ppm 1.77 - 1.97 (m, 1 H) 2.06 - 2.18 (m, 1 H) 2.18 - 2.31 (m, 1 H) 2.89 (d, 2 H) 2.96 - 3.09 (m, 2 H) 3.11 - 3.21 (m, 2 H) 3.85 (s, 3 H) 3.87 (s, 3 H) 4.14 (br. s., 2 H) 4.37 (br. s., 2 H) 4.46 (d, 1 H) 6.90 - 7.17 (m, 4 H) 7.59 - 7.76 (m, 2 H) 7.80 - 7.90 (m, 2 H)	542.6
ER-895081		N-(6-aminospiro[3.3]heptan-2-yl)-4-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)benzamide 2,2,2-trifluoroacetate	0.050	> 10		556
ER-895082		(4-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenyl)(2,7-diazaspiro[4.4]nonan-2-yl)methanone 2,2,2-trifluoroacetate	0.070	> 10	¹ H NMR (400 MHz, METHANOL-d ₄) δ ppm 1.94 - 2.19 (m, 3 H) 2.21 - 2.26 (m, overlapping signals, 1 H) 2.54 (ddd, 1 H) 3.06 - 3.19 (m, 2 H) 3.24 (d, 1 H) 3.39 (t, 1 H) 3.59 (d, 1 H) 3.62 - 3.78 (m, overlapping signals, 4 H) 3.85 (s, 3 H) 3.87 (s, 3 H) 4.46 (dd, 1 H) 5.00 - 5.15 (m, 1 H) 6.93 - 7.15 (m, 4 H) 7.51 - 7.65 (m, 2 H) 7.79 - 7.91 (m, 2 H)	556.6
ER-895083		(4-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenyl)(3-(methoxymethylamino)methyl)azetidin-1-yl)methanone 2,2,2-trifluoroacetate	0.070	> 10	¹ H NMR (400 MHz, METHANOL-d ₄) δ ppm 1.23 - 1.38 (m, 1 H) 2.17 - 2.33 (m, 1 H) 2.37 - 2.46 (m, 2 H) 2.53 (ddd, 1 H) 2.77 (q, 1 H) 2.82 - 2.92 (m, 3 H) 3.84 (s, 3 H) 3.87 (m, 3 H) 4.10 (dd, 1 H) 4.28 (t, 1 H) 4.42 - 4.54 (m, 2 H) 5.00 - 5.14 (m, 1 H) 6.96 - 7.20 (m, 4 H) 7.61 - 7.73 (m, 2 H) 7.76 - 7.91 (m, 2 H)	530.6

FIG. 11M

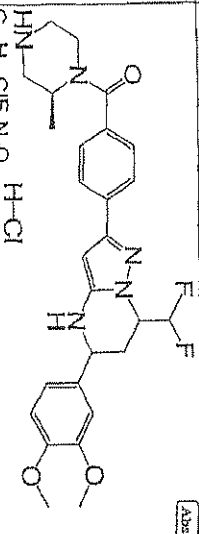
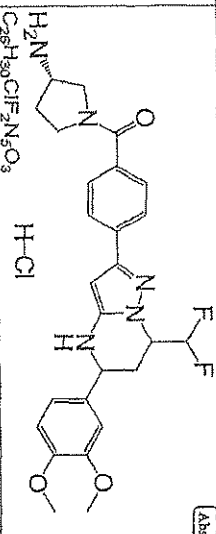
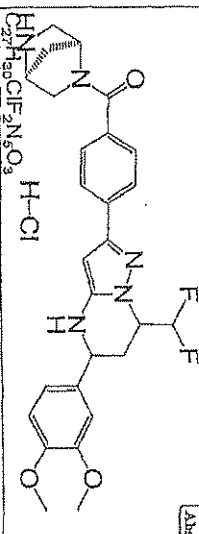
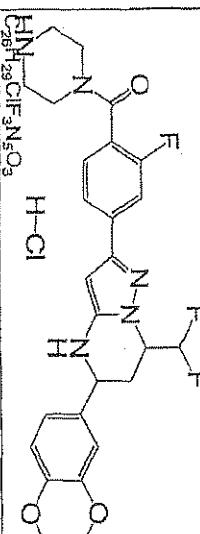
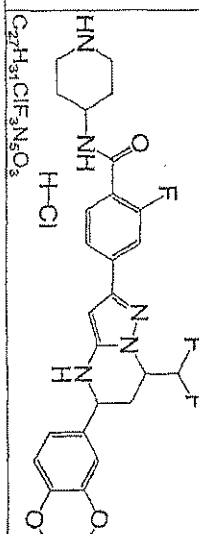
ER-Number	Structure	Chemical Name	HEK/ TLR7 IC50 (μ M)	HEK/ TLR9 IC50 (μ M)	¹ H NMR	MS
ER-895088		(4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)methanone hydrochloride	0.020	8.99	¹ H NMR (400 MHz, METHANOL-d ₄) δ ppm 1.18 - 1.30 (m, 1H) 1.36 (d, 3H) 2.21 - 2.41 (m, 2H) 2.63 - 2.77 (m, 2H) 2.84 (m, 2H) 2.93 (dd, 2H) 3.85 (s, 3H) 3.87 (s, 3H) 4.47 (dd, 1H) 5.93 - 7.02 (m, 1H) 7.02 - 7.18 (m, 2H) 7.41 (d, 2H) 7.76 - 7.89 (m, 4H)	512.7
ER-895089		((S)-3-aminopyrrolidin-1-yl)(4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)methanone hydrochloride	0.020	7.73		498
ER-895090		(1S,4S)-2,5-diazabicyclo[2.2.1]heptan-2-yl(4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)methanone hydrochloride	0.010	4.57	¹ H NMR (400 MHz, METHANOL-d ₄) δ ppm 2.20 - 2.40 (m, 1H) 2.98 - 3.09 (m, 7H) 3.10 - 3.20 (m, 1H) 4.47 (m, 1H) 3.61 - 3.73 (m, 1H) 3.85 (s, 3H) 3.87 (s, 3H) 4.38 - 4.52 (m, 2H) 5.93 - 7.02 (m, 1H) 7.02 - 7.17 (m, 2H) 7.48 - 7.62 (m, 2H) 7.77 - 7.90 (m, 2H)	510.6
ER-895091		(4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)methanone hydrochloride	0.080	8.40		516
ER-895092		4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-2-fluoro-N-(piperidin-4-yl)benzamide hydrochloride	0.010	4.34		530

FIG. 11N

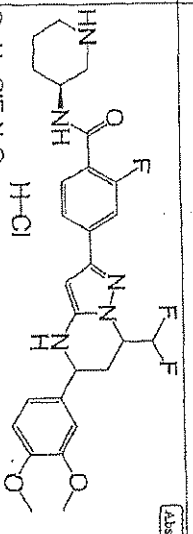
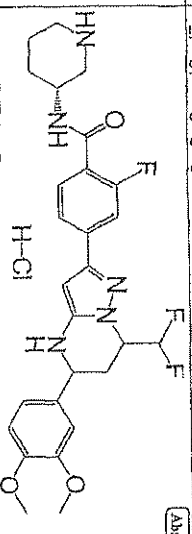
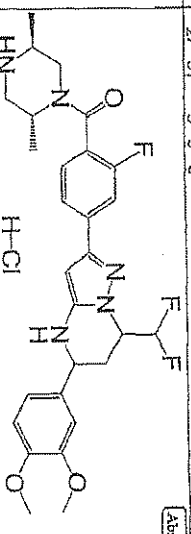
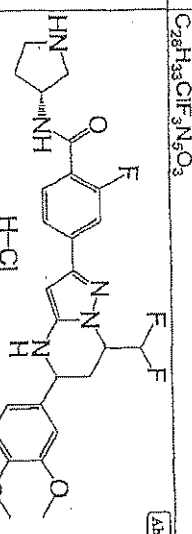
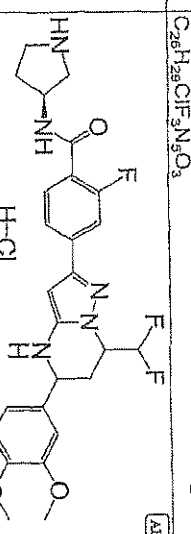
ER-Number	Structure	Chemical Name	HEK/ TLR7 IC50 (μ M)	HEK/ TLR9 IC50 (μ M)	¹ H NMR	MS
ER-895093		4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-2-fluoro-N-((S)-piperidin-3-yl)benzamide hydrochloride	0.040	10.00		530
ER-895094		4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-2-fluoro-N-((R)-piperidin-3-yl)benzamide hydrochloride	0.030	8.46		530
ER-895096		4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-2-fluoro-N-((2R,5S)-2,5-fluorophenyl)((2R,5S)-2,5-dimethylpiperazin-1-yl)methanone hydrochloride	0.030	9.35	¹ H NMR (400 MHz, METHANOL-d ₄) δ ppm 1.12 - 1.38 (br. m, 6 H) 2.31 (m, 2 H) 2.59 (m, 1 H) 2.74 (m, 1 H) 2.94 (m, 1 H) 3.12 (m, 1 H) 3.22 (m, 2 H) 3.83 (s, 3 H) 3.86 (s, 3 H) 4.46 (d, 1 H) 4.74 (m, 1 H) 6.62 (t, 1 H) 6.95 - 7.11 (m, 4 H) 7.32 - 7.38 (m, 1 H) 7.53 - 7.67 (m, 2 H)	544
ER-895097		4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-2-fluoro-N-((R)-pyrrolidin-3-yl)benzamide hydrochloride	0.050	4.27		516
ER-895098		4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-2-fluoro-N-((S)-pyrrolidin-3-yl)benzamide hydrochloride	0.020	4.03	¹ H NMR (400 MHz, METHANOL-d ₄) δ ppm 1.76 - 1.96 (m, 1 H) 2.12 - 2.39 (m, 2 H) 3.34 (br. s., 2 H) 3.53 - 3.81 (m, overlapping signals, 2 H) 3.85 (s, 3 H) 3.87 (s, 3 H) 3.93 (br. s., 1 H) 4.47 (dd, 1 H) 4.63 - 4.83 (m, 1 H) 6.63 (t, 1 H) 6.92 - 7.02 (m, 1 H) 7.02 - 7.18 (m, 3 H) 7.51 - 7.65 (m, 2 H) 7.74 - 7.90 (m, 2 H)	498.6

FIG. 110

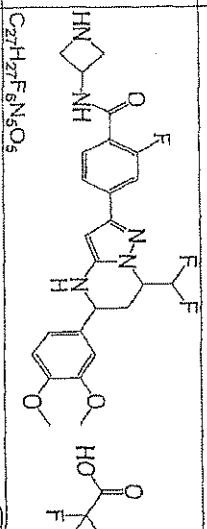
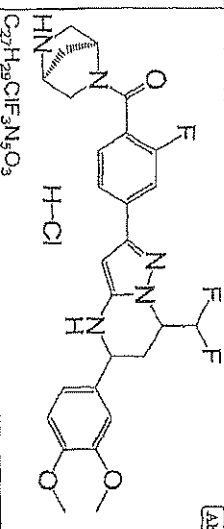
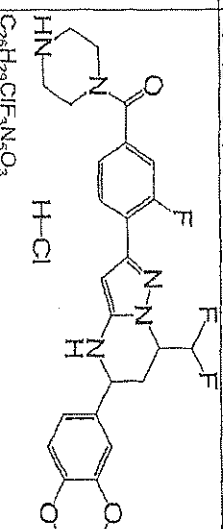
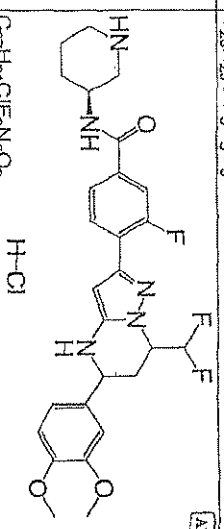
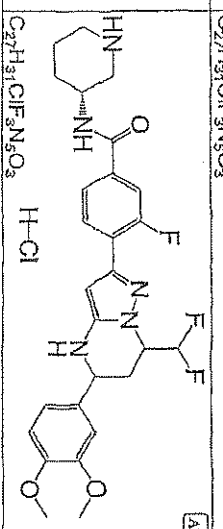
ER-Number	Structure	Chemical Name	HEK/ TLR7 IC50 (μ M)	HEK/ TLR9 IC50 (μ M)	¹ H NMR	MS
ER-895099		N-(4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-2-fluorobenzamide 2,2,2-trifluoroacetate	0.030	4.48	¹ H NMR (400 MHz, METHANOL-d ₄) δ ppm 2.31 (m, 2 H) 3.83 (s, 3 H) 3.86 (s, 3 H) 3.93 (m, 3 H) 4.04 (m, 2 H) 4.46 (d, 1 H) 4.72 (m, 1 H) 6.63 (t, 1 H) 6.93 - 7.12 (m, 4 H) 7.53 - 7.68 (m, 2 H) 7.74 (t, 1 H)	502
ER-895101		(1S,4S)-2,5-diazabicyclo[2.2.1]heptan-2-yl(4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-2-fluorophenyl)methanone hydrochloride	0.030	10.00	¹ H NMR (400 MHz, METHANOL-d ₄) δ ppm 1.80 (dd, 2 H) 2.20 - 2.39 (m, 2 H) 2.91 (m, 1 H) 3.04 (m, 1 H) 3.23 (m, 1 H) 3.47 (m, 1 H) 3.61 (m, 1 H) 3.77 (m, 1 H) 3.83 (s, 3 H) 3.86 (s, 3 H) 4.46 (d, 1 H) 4.72 (m, 1 H) 6.63 (t, 1 H) 6.95 - 7.12 (m, 4 H) 7.39 - 7.49 (m, 2 H) 7.55 - 7.69 (m, 1 H)	528
ER-895102		(4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-3-fluorophenyl)piperazin-1-yl)methanone hydrochloride	0.080	10.00		516
ER-895104		4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-3-fluoro-N-((S)-piperidin-3-yl)benzamide hydrochloride	0.090	10.00		530
ER-895105		4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-3-fluoro-N-((R)-piperidin-3-yl)benzamide hydrochloride	0.080	10.00		530

FIG. 11P

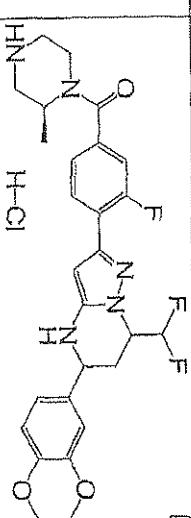
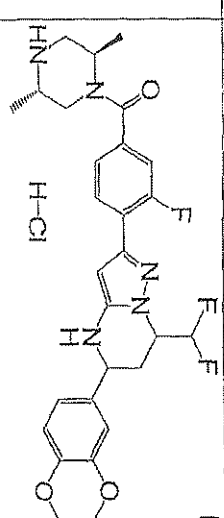
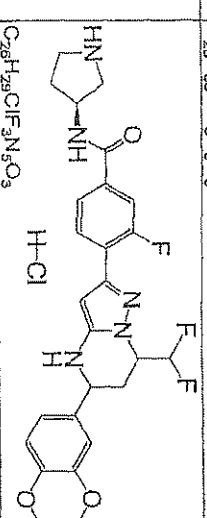
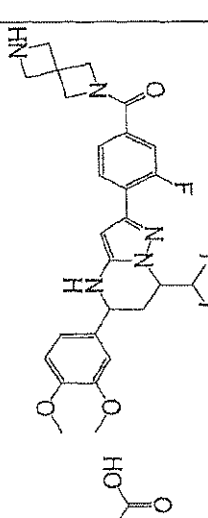
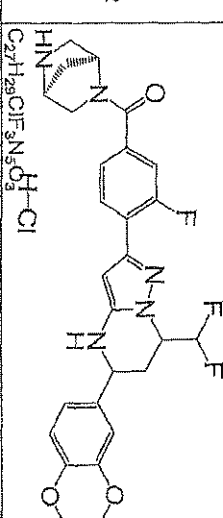
ER-Number	Structure	Chemical Name	HEK/ TLR7 IC50 (μ M)	HEK/ TLR9 IC50 (μ M)	¹ H NMR	MS
ER-895106	 <chem>C27H31ClF3N5O3</chem>	(4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-3-fluorophenyl)((S)-2-methylpiperazin-1-yl)methanone hydrochloride	0.060	10.00		530
ER-895107	 <chem>C28H33ClF3N5O3</chem>	(4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-3-fluorophenyl)((2R,5S)-2,5-dimethylpiperazin-1-yl)methanone hydrochloride	0.020	10.00		544
ER-895109	 <chem>C28H29ClF3N5O3</chem>	4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-3-fluoro-N-((S)-pyrrolidin-3-yl)benzamide hydrochloride	0.100	10.00		516
ER-895111	 <chem>C29H29F6N5O5</chem>	(4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-3-fluorophenyl)((2,6-diazaspiro[3.3]heptan-2-yl)methanone 2,2,2-trifluoroacetate	0.090	10.00		528
ER-895112	 <chem>C27H29ClF3N5O3</chem>	(1S,4S)-2,5-diazabicyclo[2.2.1]heptan-2-yl((4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-3-fluorophenyl)methanone hydrochloride	0.050	10.00		528

FIG. 11Q

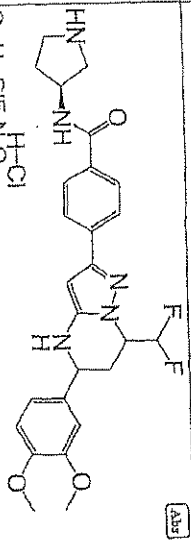
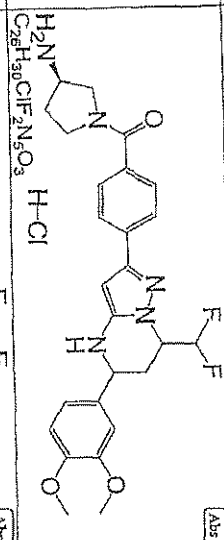
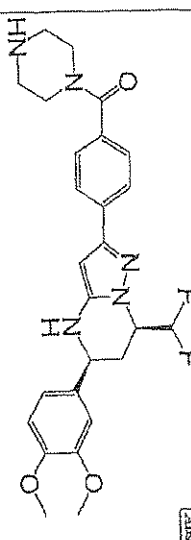
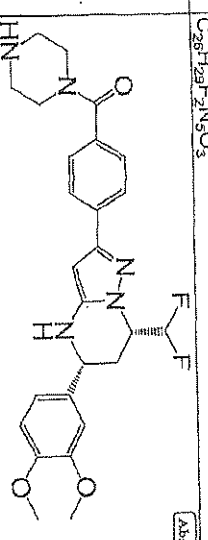
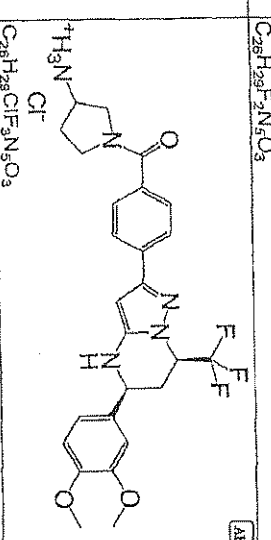
ER-Number	Structure	Chemical Name	HEK/ TLR7 IC50 (μ M)	HEK/ TLR9 IC50 (μ M)	¹ H NMR	MS
ER-895115		4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-N-(S)-pyrrolidin-3-yl)benzamide hydrochloride	0.050	10.00	¹ H NMR (400 MHz, METHANOL-d ₄) δ ppm 2.15 - 2.24 (m, 1 H) 2.27 (d, 1 H) 2.29 - 2.46 (m, 1 H) 3.11 - 3.25 (m, 3 H) 3.33 - 3.43 (m, 1 H) 3.43 - 3.65 (m, 2 H) 3.85 (s, 3 H) 3.87 (s, 3 H) 4.42 - 4.53 (m, 1 H) 4.55 - 4.66 (m, 1 H) 6.63 (s, 1 H) 6.90 - 7.18 (m, 4 H) 7.79 - 7.93 (m, 2H) 8.53 (s, 1 H)	498.6
ER-895116		((R)-3-aminopyrrolidin-1-yl)(4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenyl)methanone hydrochloride	0.030	10.00	¹ H NMR (400 MHz, METHANOL-d ₄) δ ppm 1.67 - 1.92 (m, 1 H) 2.07 - 2.17 (m, 1 H) 2.17 - 2.42 (m, 1 H) 3.40 (dd, 1 H) 3.44 - 3.59 (m, 1 H) 3.62 - 3.75 (m, 2 H) 3.75 - 3.82 (m, 1 H) 3.85 (s, 3 H) 3.87 (s, 3 H) 4.47 (dd, 1 H) 4.62 - 4.80 (m, 1H) 6.63 (t, 1 H) 6.94 - 7.02 (m, 1 H) 7.02 - 7.18 (m, 3 H) 7.57 (t, 2 H) 7.79 - 7.89 (m, 2 H)	498.7
ER-895302		(4-((5S,7R)-7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenyl)(piperazin-1-yl)methanone	0.020	10.00		
ER-895303		(4-((5R,7S)-7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenyl)(piperazin-1-yl)methanone	0.030	6.39		
ER-895396		1-(4-((5S,7R)-5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)benzoyl)pyrrolidin-3-aminium chloride	0.020	> 10		

FIG. 11R

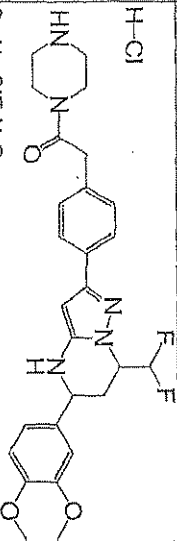
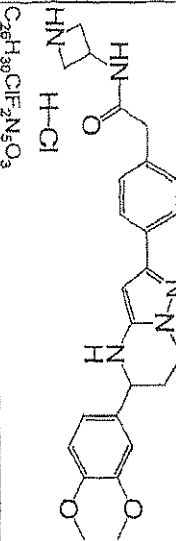
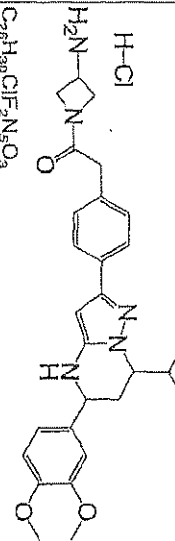
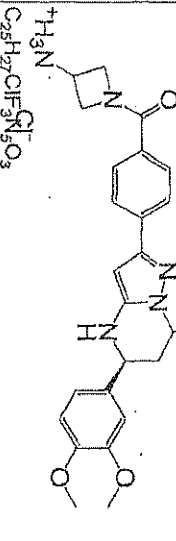
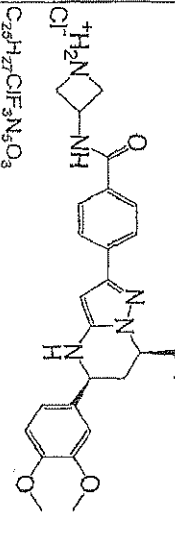
ER-Number	Structure	Chemical Name	HEK1 TLR7 IC50 (μ M)	HEK1 TLR9 IC50 (μ M)	¹ H NMR	MS
ER-895436		2-(4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenyl)-1-(piperazin-1-yl)ethanone hydrochloride	0.020	10.00	(DMSO-d6) δ 2.03, (m, 1H), 2.18, (m, 1H), 2.98, (m, 4H), 3.52, (s, 2H), 3.65, (m, 4H), 3.68, (s, 3H), 3.72, (s, 3H), 4.21, (m, 1H), 4.75, (m, 1H), 5.66, (s, 1H), 6.62, (s, 1H), 6.64, (br t, 1H), 6.92, (dd, 2H), 7.00, (s, 1H), 7.18, (d, 2H), 7.62, (d, 2H), 8.97, (s, 1H)	
ER-895437		N-(azetidin-3-yl)-2-(4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenyl)acetamide hydrochloride	0.080	10.00	(DMSO-d6) δ 2.03, (m, 1H), 2.18, (m, 1H), 3.40, (s, 2H), 3.68, (s, 3H), 3.72, (s, 3H), 4.01 (m, 5H), 4.40, (m, 1H), 4.75, (m, 1H), 5.65, (s, 1H), 6.62, (s, 1H), 6.64, (br t, 1H), 6.92, (m, 2H), 7.00, (s, 1H), 7.18, (d, 2H), 7.62, (d, 2H), 8.22, (br s, 1H), 8.32, (br s, 1H)	
ER-895438		1-(3-aminoazetidin-1-yl)-2-(4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenyl)ethanone hydrochloride	0.070	10.00	(DMSO-d6) δ 2.03, (m, 1H), 2.18, (m, 1H), 3.40, (s, 2H), 3.68, (s, 3H), 3.72, (s, 3H), 3.86, (m, 2H), 4.03, (m, 2H), 3.91, (m, 1H), 4.40, (m, 1H), 4.75, (m, 1H), 5.65, (s, 1H), 6.62, (s, 1H), 6.64, (br t, 1H), 6.92, (m, 2H), 7.00, (s, 1H), 7.18, (d, 2H), 7.62, (d, 2H), 8.84, (d, 2H)	
ER-895486		1-(4-((5S,7R)-5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)benzoyl)azetidin-3-aminium chloride	0.030	> 10	NMR for racemate reported	
ER-895498		3-(4-((5S,7R)-5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)benzamido)azetidin-1-ium chloride	0.020	> 10		

FIG. 11S

ER-Number	Structure	Chemical Name	HEK/ TLR7 IC50 (μ M)	HEK/ TLR9 IC50 (μ M)	¹ H NMR	MS
ER-695548		4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-y]phenyl)-2,5-dimethylpiperazin-1-ylmethanone hydrochloride	0.008	10.00		
ER-895550		4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-y]phenyl)-2,5-dimethylpiperazin-1-ylmethanone hydrochloride	0.030	5.97		
ER-895577		4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-y]phenyl)-2,5-dimethylpiperazin-1-ylmethanone hydrochloride	0.020	7.82		
ER-895676		(R)-3-(4-((3S,7R)-5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-y]phenyl)-2-yl)benzamide hydrochloride	0.030	7.20	NMR for racemate reported	
ER-895678		(S)-3-(4-((3S,7R)-5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-y]phenyl)-2-yl)benzamide hydrochloride	0.020	8.60	NMR for racemate preferable	

FIG. 11T

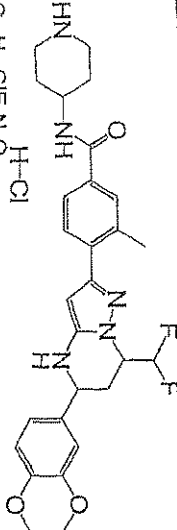
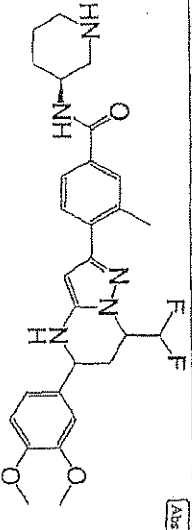
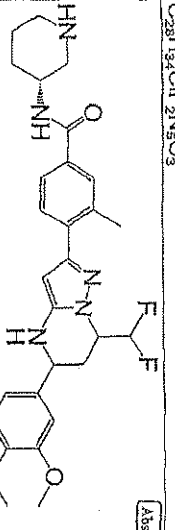
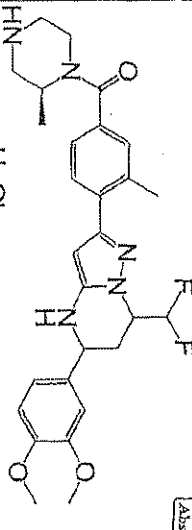
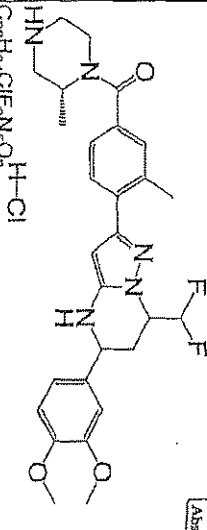
ER-Number	Structure	Chemical Name	HEK/ TLR7 IC50 (μ M)	HEK/ TLR9 IC50 (μ M)	¹ H NMR	MS
ER-895718		4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-3-methyl-N-(piperidin-4-yl)benzamide hydrochloride	0.040	10.00		526
ER-895719		4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-3-methyl-N-((S)-piperidin-3-yl)benzamide hydrochloride	0.030	5.24		526
ER-895720		4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-3-methyl-N-((R)-piperidin-3-yl)benzamide hydrochloride	0.030	4.96		526
ER-895721		4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-3-methylpiperazin-1-yl)methanone hydrochloride	0.050	10.00		526
ER-895722		4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-3-methylpiperazin-1-yl)methanone hydrochloride	0.070	10.00		526

FIG. 11U

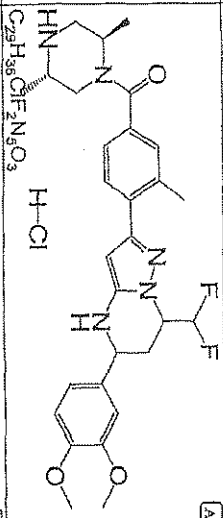
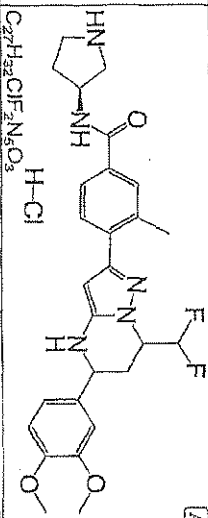
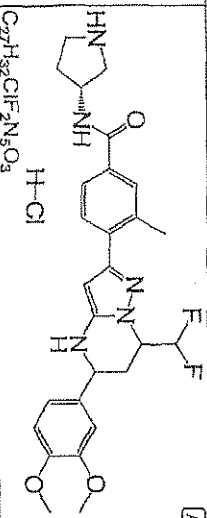
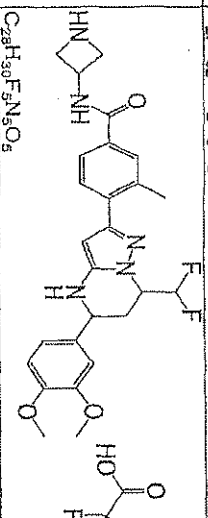
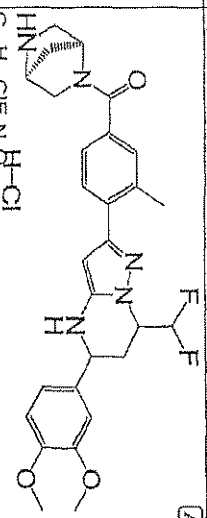
ER-Number	Structure	Chemical Name	HEK/ TLR7 IC50 (μ M)	HEK/ TLR9 IC50 (μ M)	¹ H NMR	MS
ER-895723		(4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-3-methylphenyl)((2R,5S)-2,5-dimethylpiperazin-1-yl)methanone hydrochloride	0.030	10.00		540
ER-895725		4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-3-methyl-N-((S)-pyrrolidin-3-yl)benzamide hydrochloride	0.030	2.91		512
ER-895726		4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-3-methyl-N-((R)-pyrrolidin-3-yl)benzamide hydrochloride	0.030	1.29		512
ER-895727		N-(azetidin-3-yl)-4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-3-methylbenzamide 2,2,2-trifluoroacetate	0.030	5.50		498
ER-895729		(1S,4S)-2,5-diazabicyclo[2.2.1]heptan-2-yl(4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-3-methylphenyl)methanone hydrochloride	0.040	10.00		524

FIG. 11V

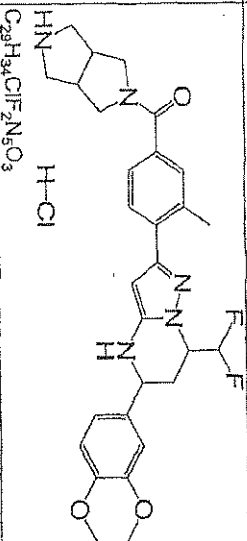
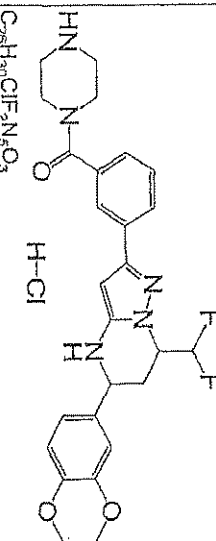
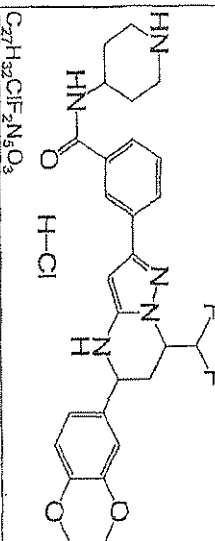
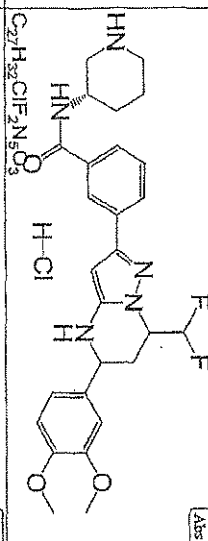
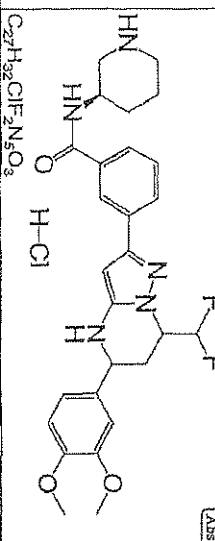
ER-Number	Structure	Chemical Name	HEK/ TLR7 IC50 (μ M)	HEK/ TLR9 IC50 (μ M)	¹ H NMR	MS
ER-895730		(4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-3-methylphenyl)(hexahydropyrazolo[3,4-c]pyrrol-2(1H)-yl)methanone hydrochloride	0.020	8.54	¹ H NMR (400 MHz, METHANOL-d ₄) δ ppm 2.46 (s, 3 H) 2.57 (m, 1 H) 2.72 (m, 1 H) 2.87 (m, 3 H) 2.99 (m, 2 H) 3.08 (m, 2 H) 3.54 (m, 2 H) 3.71 (m, 2 H) 3.81 (s, 3 H) 3.84 (s, 3 H) 4.45 (d, 1 H) 4.70 (m, 1 H) 5.54 (t, 1 H) 6.95 (d, 1 H) 7.03 (d, 1 H) 7.09 (s, 1 H) 7.35 (m, 2 H) 7.52 (d, 1 H)	538
ER-895731		(3-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenyl)(piperazin-1-yl)methanone hydrochloride	0.060	10.00	¹ H NMR (400 MHz, METHANOL-d ₄) δ ppm 2.31 (m, 2 H) 2.79 (br. m., 4 H) 3.46 (br. m., 4 H) 3.83 (s, 3 H) 3.86 (s, 3 H) 4.46 (d, 1 H) 4.72 (br. m., 1 H) 6.61 (t, 1 H) 6.96 - 7.11 (m, 4 H) 7.32 (d, 1 H) 7.47 (t, 1 H) 7.75 - 7.85 (m, 2 H)	498
ER-895732		3-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-N-(piperidin-4-yl)benzamide hydrochloride	0.020	10.00	¹ H NMR (400 MHz, METHANOL-d ₄) δ ppm 1.51 - 1.66 (m, 2 H) 1.98 (d, 2 H) 2.23 - 2.40 (m, 2 H) 2.69 - 2.80 (m, 2 H) 3.13 (d, 2 H) 3.83 (s, 3 H) 3.86 (s, 3 H) 4.47 (d, 1 H) 4.72 (br. m., 1 H) 6.63 (t, 1 H) 6.94 - 7.11 (m, 4 H) 7.46 (t, 1 H) 7.73 (d, 1 H) 7.89 (d, 1 H) 8.17 (s, 1 H)	512
ER-895733		3-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-N-((S)-piperidin-3-yl)benzamide hydrochloride	0.010	10.00		512
ER-895734		3-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-N-((R)-piperidin-3-yl)benzamide hydrochloride	0.009	10.00		512

FIG. 11W

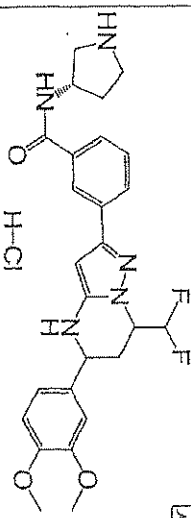
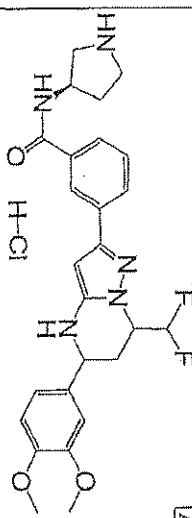
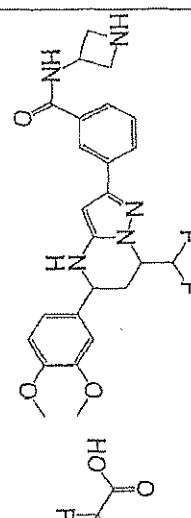
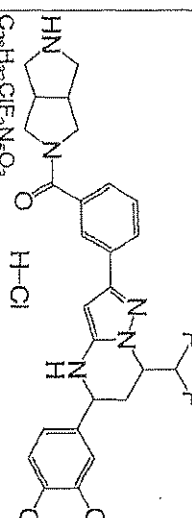
ER-Number	Structure	Chemical Name	HEK/ TLR7 IC50 (μ M)	HEK/ TLR9 IC50 (μ M)	¹ H NMR	MS
ER-895739		3-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-N-((S)-pyrrolidin-3-yl)benzamide hydrochloride	0.010	0.31		498
ER-895740		3-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-N-((R)-pyrrolidin-3-yl)benzamide hydrochloride	0.020	1.38		498
ER-895741		N-(azetidin-3-yl)-3-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)benzamide 2,2,2-trifluoroacetate	0.070	7.95		484
ER-895744		(3-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenyl)(hexahydopyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone hydrochloride	0.040	0.15	¹ H NMR (400 MHz, METHANOL-d ₄) δ ppm 2.20 - 2.44 (m, 1 H) 2.70 (br. s., 1) 2.83 (d, 1 H) 2.95 (br. s., 1 H) 3.03 - 3.14 (m, 1 H) 3.18 (dd, 1 H) 3.33 - 3.36 (m, 1 H) 3.41 (d, 1 H) 3.60 (d, 1 H) 3.70 - 3.81 (m, 1 H) 3.85 (s, 3 H) 3.87 (s, 3 H) 4.47 (dd, 1 H) 4.66 - 4.80 (m, 1 H) 6.63 (t, 1 H) 6.92 - 7.02 (m, 1 H) 7.02 - 7.17 (m, 3 H) 7.49 - 7.61 (m, 2 H) 7.76 - 7.89 (m, 2 H)	524.7

FIG. 11X

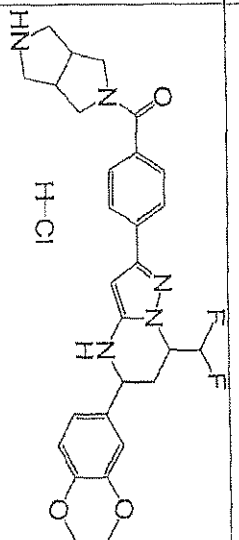
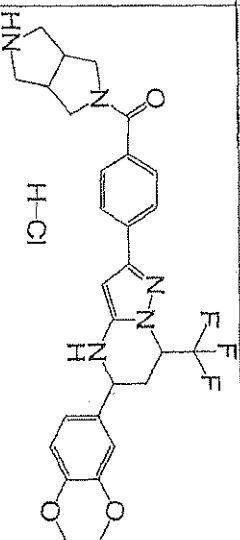
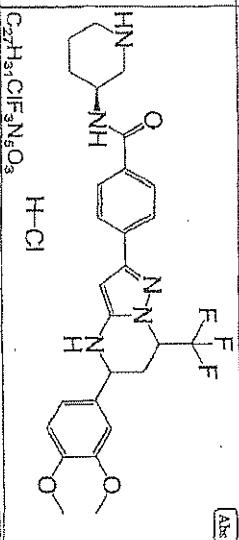
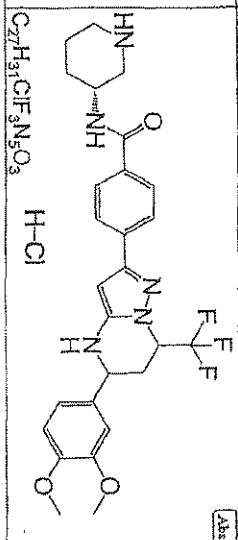
ER-Number	Structure	Chemical Name	HEK/ TLR7 IC50 (μ M)	HEK/ TLR9 IC50 (μ M)	¹ H NMR	MS
ER-895745		(4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenyl)(hexahydroxy-3,4-cipryl-2(1H)-yl)methanone hydrochloride	0.080	3.86		524
ER-895746		(4-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenyl)(hexahydroxy-3,4-cipryl-2(1H)-yl)methanone hydrochloride	0.020	3.51		542
ER-895748		4-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-N-(S)-piperidin-3-yl)benzamide hydrochloride	0.030	> 10	¹ H NMR (400 MHz, METHANOL-d ₄) δ ppm 1.57 - 1.72 (m, 2 H) 1.77 - 1.89 (m, 1 H) 2.04 (d, 1 H) 2.23 (dt, 1 H) 2.48 - 2.71 (m, 3 H) 3.00 (d, 1 H) 3.21 (dd, 1 H) 3.84 (s, 3 H) 3.87 (m, 3 H) 3.99 - 4.13 (m, 1 H) 4.46 (dd, 1 H) 5.02 - 5.16 (m, 1 H) 6.91 - 7.16 (m, 4 H) 7.78 - 7.92 (m, 4 H)	530.7
ER-895749		4-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-N-(R)-piperidin-3-yl)benzamide hydrochloride	0.030	> 10	¹ H NMR (400 MHz, METHANOL-d ₄) δ ppm 1.56 - 1.71 (m, 2 H) 1.82 (d, 1 H) 2.05 (br. s, 1 H) 2.23 (dt, 1 H) 2.54 (dd, 1 H) 2.58 - 2.70 (m, 2 H) 3.00 (d, 1 H) 3.21 (dd, 1 H) 3.85 (s, 3 H) 3.87 (s, 3 H) 4.01 - 4.11 (m, 1 H) 4.46 (dd, 1 H) 5.03 - 5.14 (m, 1 H) 6.99 (d, 1 H) 7.06 (dd, 1 H) 7.12 (d, 2 H) 7.79 - 7.90 (m, 4 H)	530.6

FIG. 11Y

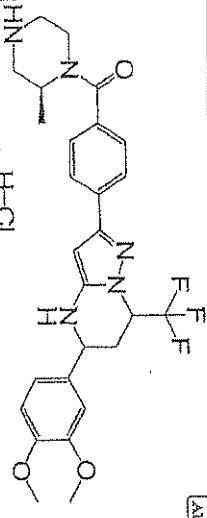
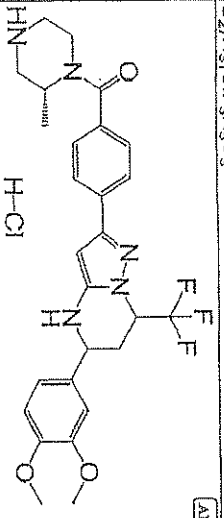
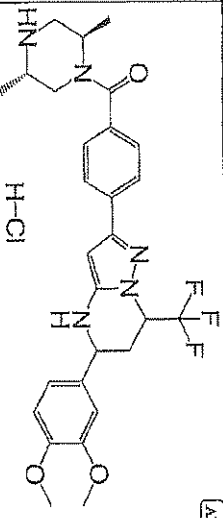
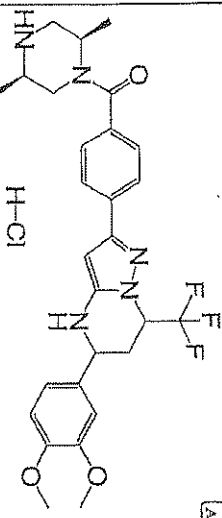
ER-Number	Structure	Chemical Name	HEK/ TLR7 IC50 (μ M)	HEK/ TLR9 IC50 (μ M)	¹ H NMR	MS
ER-895750		(4-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenyl)((S)-2-methylpiperazin-1-yl)methanone hydrochloride	0.040	> 10		530
ER-895751		(4-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenyl)((R)-2-methylpiperazin-1-yl)methanone hydrochloride	0.030	> 10	¹ H NMR (400 MHz, METHANOL-d ₄) δ ppm 2.12 - 2.31 (m, 2H) 2.54 (ddd, 2 H) 2.63 - 2.78 (m, 2 H) 2.78 - 2.88 (m, 2 H) 2.94 (dd, 2 H) 3.85 (s, 3 H) 3.87 (s, 3 H) 4.46 (dd, 1 H) 5.09 (dt, 1 H) 6.90 - 7.02 (m, 1 H) 7.02 - 7.16 (m, 3 H) 7.42 (d, 2 H) 7.85 (d, 4 H)	530.7
ER-895752		(4-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenyl)((2R,5S)-2,5-dimethylpiperazin-1-yl)methanone hydrochloride	0.009	> 10	¹ H NMR (400 MHz, METHANOL-d ₄) δ ppm 1.20 (m, 3H) 1.35 (d, 3 H) 2.09 - 2.31 (m, 1 H) 2.45 - 2.62 (m, 2 H) 2.94 (m, 1H) 3.15 (br. s., 1 H) 3.22 (dd, 1 H) 3.43 (dd, 1 H) 3.85 (s, 3 H) 3.87 (s, 3 H) 4.46 (dd, 1 H) 5.09 (dt, 1 H) 6.92 - 7.02 (m, 2 H) 7.02 - 7.16 (m, 2 H) 7.40 (d, 2 H) 7.85 (d, 2 H)	544.6
ER-895753		(4-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenyl)((2R,5R)-2,5-dimethylpiperazin-1-yl)methanone hydrochloride	0.070	> 10	¹ H NMR (400 MHz, METHANOL-d ₄) δ ppm 1.00 (br. s., 1 H) 1.09 - 1.26 (m, 4 H) 1.26 - 1.42 (m, 3 H) 2.23 (dt, 1 H) 2.54 (ddd, 1 H) 2.95 (br. s., 1 H) 3.20 (m, 1H) 3.24 (dd, 1H) 3.39 - 3.51 (m, 1 H) 3.85 (s, 3 H) 3.87 (m, 3 H) 4.46 (dd, 1 H) 4.99 - 5.17 (m, 1 H) 6.93 - 7.02 (m, 1 H) 7.02 - 7.18 (m, 3 H) 7.40 (d, 2 H) 7.85 (d, 2 H)	544.6

FIG. 11Z

ER-Number	Structure	Chemical Name	HEK/ TLR7 IC50 (μ M)	HEK/ TLR9 IC50 (μ M)	¹ H NMR	MS
ER-8956754		(1S,4S)-2,5-diazabicyclo[2.1]heptan-2-yl(4-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenyl)methanone hydrochloride	0.020	5.95		528
ER-895755		(4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-3-methylphenyl)(piperazin-1-yl)methanone hydrochloride	0.040	10.00		512
ER-895809		5-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-N-((S)-pyrrolidin-3-yl)picolinamide hydrochloride	0.030	3.83		517.5
ER-895810		5-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-N-((R)-pyrrolidin-3-yl)picolinamide hydrochloride	0.030	2.83		517.5

FIG. 11AA

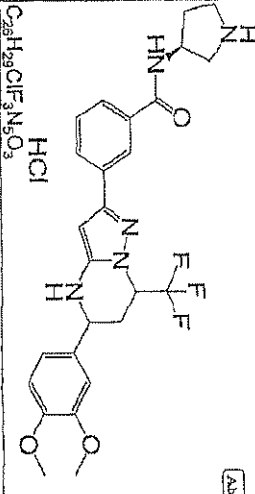
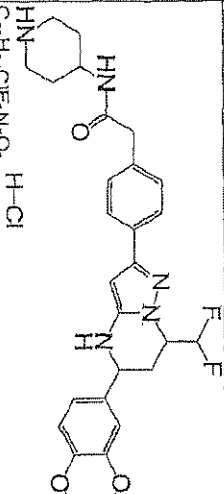
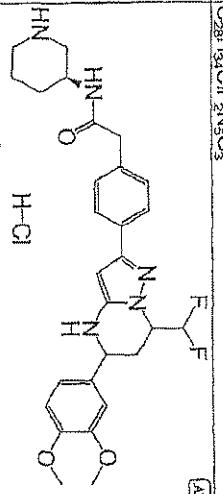
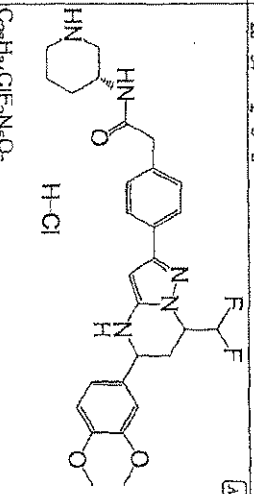
ER-Number	Structure	Chemical Name	HEK/ TLR7 IC50 (μ M)	HEK/ TLR9 IC50 (μ M)	¹ H NMR	MS
ER-895811		3-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-N-((S)-pyrrolidin-3-yl)benzamide hydrochloride	0.040	5.31	¹ H NMR (400 MHz, DMSO-d ₆) δ ppm: 2.04 (m, 1H), 2.12 (dd, 1H), 2.20-2.33 (m, 1H), 2.44 (m, 1H), 3.17-3.27 (m, 2H), 3.33-3.43 (m, 2H), 3.76 and 3.79 (2s, 6H), 4.46 (d, 1H), 4.53 (m, 1H), 5.27-5.28 (m, 1H), 5.84 (s, 1H), 6.82 (s, 1H), 6.96-7.01 (m, 2H), 7.08 (s, 1H), 7.49 (t, 1H), 7.79 (d, 1H), 7.89 (d, 1H), 8.17 (s, 1H), 8.81 (s, 1H).	516.5
ER-896059		2-(4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenyl)-N-(piperidin-4-yl)acetamide hydrochloride	0.090	0.19		526
ER-896060		2-(4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenyl)-N-((S)-piperidin-3-yl)acetamide hydrochloride	0.030	10.00		526
ER-896061		2-(4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenyl)-N-((R)-piperidin-3-yl)acetamide hydrochloride	0.030	9.41		526

FIG. 11BB

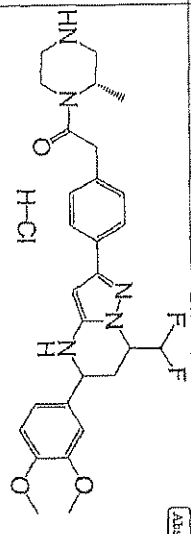
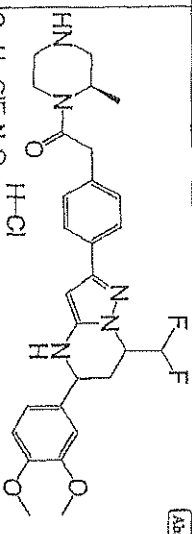
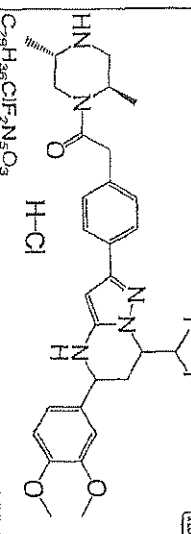
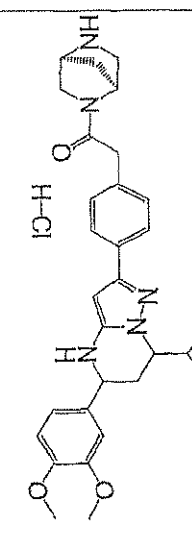
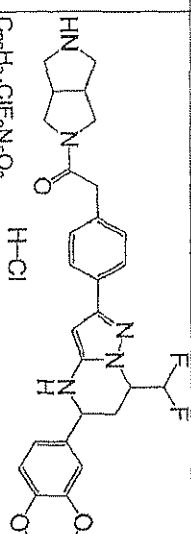
ER-Number	Structure	Chemical Name	HEK/ TLR7 IC50 (μ M)	HEK/ TLR9 IC50 (μ M)	¹ H NMR	MS
ER-896062		2-(4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenyl)-1-((S)-2-methylpiperazin-1-yl)ethanone hydrochloride	0.030	6.93		526
ER-896063		2-(4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenyl)-1-((R)-2-methylpiperazin-1-yl)ethanone hydrochloride	0.070	9.62		526
ER-896064		2-(4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenyl)-1-((2R,5S)-2,5-dimethylpiperazin-1-yl)ethanone hydrochloride	0.060	6.95		540
ER-896067		1-((1S,4S)-2,5-diazabicyclo[2.2.1]heptan-2-yl)-2-(4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenyl)ethanone hydrochloride	0.040	9.64		524
ER-896068		2-(4-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenyl)-1-((hexahydroindolo[3,4-c]pyrrolo-2(1H)-yl)ethanone hydrochloride	0.040	7.80		538

FIG. 11CC

ER-Number	Structure	Chemical Name	HEK/ TLR7 IC50 (μ M)	HEK/ TLR9 IC50 (μ M)	¹ H NMR	MS
ER-896071		N-(azetidin-3-ylmethyl)-3-(7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)benzamide 2,2,2-trifluoroacetate	0.090	10.00		498
ER-896072		5-(3,4-dimethoxyphenyl)-2-(3-(piperazin-1-ylmethyl)phenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine dihydrochloride	0.090	> 10		
ER-896073		5-(3,4-dimethoxyphenyl)-2-(4-(4-methylpiperazin-1-yl)methyl)phenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine dihydrochloride	0.050	8.64		
ER-896133		(5-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)piperazin-1-yl)methanone dihydrochloride	0.020	> 10	¹ H NMR (400 MHz, Methanol-d ₄) δ ppm: 2.25 (dd, 1H), 2.53-2.58 (m, 1H), 3.35 (m, 4H), 3.85 and 3.88 (2s, 6H), 3.91-4.03 (m, 4H), 4.49 (dd, 1H), 5.11-5.17 (m, 1H), 6.99 (d, 1H), 7.00 (s, 1H), 7.06 (dd, 1H), 7.11 (d, 1H), 7.81 (d, 1H), 8.33 (dd, 1H), 9.01 (d, 1H).	517.5
ER-896134		5-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-N-(piperidin-4-yl)picolinamide dihydrochloride	0.020	> 10	¹ H NMR (400 MHz, Methanol-d ₄) δ ppm: 1.57-1.63 (m, 2H), 1.89-2.03 (m, 2H), 2.23 (dd, 1H), 2.56-2.58 (m, 1H), 2.74 (t, 2H), 3.12 (d, 2H), 3.85 and 3.88 (2s, 6H), 4.03-4.07 (m, 1H), 4.48 (d, 1H), 5.10-5.16 (m, 1H), 6.00 (s, 1H), 7.00 (d, 1H), 7.08 (dd, 1H), 7.11 (d, 1H), 8.10 (d, 1H), 8.27 (d, 1H), 9.03 (s, 1H).	531.5

57/80
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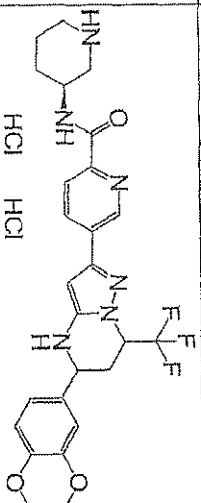
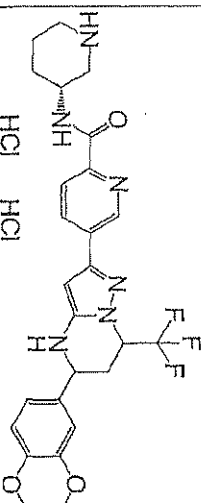
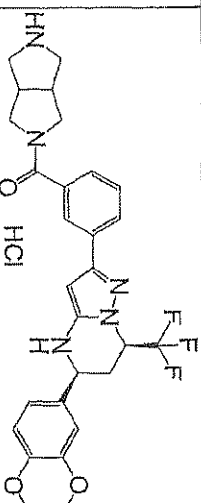
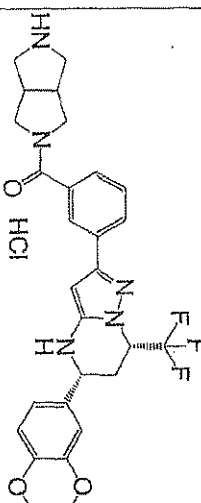
ER-Number	Structure	Chemical Name	HEK/TLR7 IC50 (μM)	HEK/TLR9 IC50 (μM)	¹ H NMR	M/S
ER-896135		5-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-N-(S)-pipecidin-3-yl)picolinamide dihydrochloride	0.030	7.94	¹ H NMR (400 MHz, Methanol-d ₄) δ ppm: 1.84-1.89 (m, 2H), 2.08-2.10 (m, 2H), 2.24 (dd, 1H), 2.52-2.57 (m, 1H), 3.01-3.13 (m, 2H), 3.34-3.50 (m, 2H), 3.85 and 3.87 (2s, 6H), 4.30 (m, 1H), 4.48 (d, 1H), 5.10-5.16 (m, 1H), 5.94 (s, 1H), 6.99 (d, 1H), 7.06 (dd, 1H), 7.11 (d, 1H), 8.11 (d, 1H), 8.27 (d, 1H), 9.03 (s, 1H).	531.5
ER-896136		5-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-N-(R)-piperidin-3-yl)picolinamide dihydrochloride	0.030	6.38	¹ H NMR (400 MHz, Methanol-d ₄) δ ppm: 1.84-1.89 (m, 2H), 2.08-2.10 (m, 2H), 2.24 (dd, 1H), 2.52-2.57 (m, 1H), 3.01-3.14 (m, 2H), 3.34-3.52 (m, 2H), 3.85 and 3.88 (2s, 6H), 4.28-4.31 (m, 1H), 4.48 (d, 1H), 5.10-5.15 (m, 1H), 5.96 (s, 1H), 6.99 (d, 1H), 7.06 (dd, 1H), 7.11 (d, 1H), 8.11 (d, 1H), 8.27 (d, 1H), 9.03 (s, 1H).	531.5
ER-896386		(3-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenyl)(hexahydropyrimol[3,4-c]pyrrol-2(1H)-yl)methanone hydrochloride	0.030	0.36	¹ H NMR (400 MHz, DMSO-d ₆) δ ppm: 1.23-1.28 (m, 2H), 2.07-2.16 (dd, 1H), 2.42-2.46 (m, 1H), 3.00-4.00 (m, 8H), 3.76 and 3.79 (2s, 6H), 4.45 (dd, 1H), 5.24-5.30 (m, 1H), 5.81 (s, 1H), 6.81 (s, 1H), 6.96-7.01 (m, 2H), 7.07 (d, 1H), 7.41-7.47 (m, 2H), 7.79-7.82 (m, 2H).	542.4
ER-896387		(3-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenyl)(hexahydropyrimol[3,4-c]pyrrol-2(1H)-yl)methanone hydrochloride	0.080	0.39	¹ H NMR (400 MHz, DMSO-d ₆) δ ppm: 1.23-1.28 (m, 2H), 2.07-2.16 (dd, 1H), 2.42-2.46 (m, 1H), 3.00-4.00 (m, 8H), 3.76 and 3.79 (2s, 6H), 4.45 (dd, 1H), 5.24-5.30 (m, 1H), 5.81 (s, 1H), 6.81 (s, 1H), 6.96-7.01 (m, 2H), 7.07 (d, 1H), 7.41-7.47 (m, 2H), 7.79-7.82 (m, 2H).	542.4

FIG. 11EE

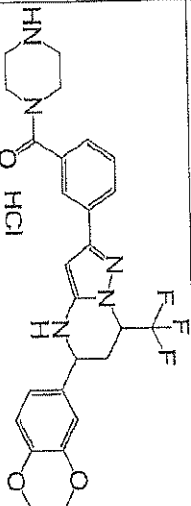
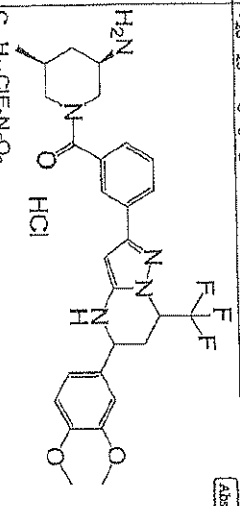
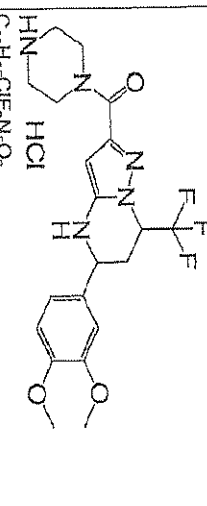
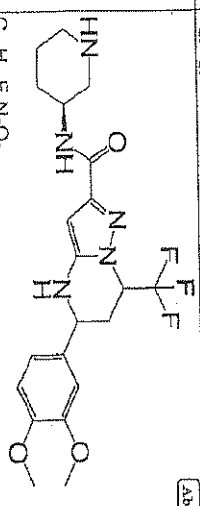
ER-Number	Structure	Chemical Name	HEK/ TLR7 IC50 (μ M)	HEK/ TLR9 IC50 (μ M)	¹ H NMR	MS
ER-896388		(3-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenyl)piperazin-1-ylmethanone hydrochloride	0.030	> 10		515.2
ER-896389		((3R,5S)-3-amino-5-methylpiperidin-1-yl)(3-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenyl)methanone hydrochloride	0.090	13.37		544.4
ER-896452		(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)(piperazin-1-yl)methanone hydrochloride	0.185	10.00	¹ H NMR (400 MHz, DMSO-d ₆) δ ppm: 2.10 (dd, 1H), 2.42-2.47 (m, 1H), 3.15-3.23 (m, 4H), 3.57-3.86 (m, 2H), 3.76 and 3.78 (2s, 6H), 4.12-4.26 (m, 2H), 4.45 (d, 1H), 5.26-5.33 (m, 1H), 5.66 (s, 1H), 6.91 (s, 1H), 6.97 (s, 2H), 7.05 (s, 1H), 7.05 (s, 1H), 9.13 (br, 2H).	440.3
ER-896453		5-(3,4-dimethoxyphenyl)-N-((S)-piperidin-3-yl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine-2-carboxamide	0.224	10.00	¹ H NMR (400 MHz, DMSO-d ₆) δ ppm: 1.62-1.71 (m, 2H), 1.84-1.87 (m, 2H), 2.11 (dd, 1H), 2.42-2.47 (m, 1H), 2.72 (m, 1H), 2.89-2.91 (m, 1H), 3.17-3.22 (m, 1H), 3.75 and 3.78 (2s, 6H), 4.14-4.16 (m, 1H), 4.40 (dd, 1H), 5.29 (m, 1H), 5.74 (s, 1H), 6.68 (s, 1H), 6.97 (s, 2H), 7.05 (s, 1H), 7.86 (t, 1H), 8.84 (br, 1H), 9.05 (br, 2H).	454.3

FIG. 11FF

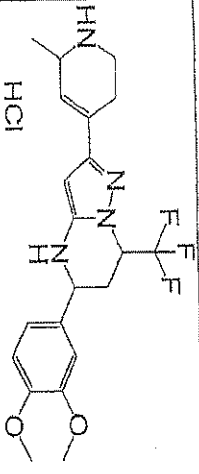
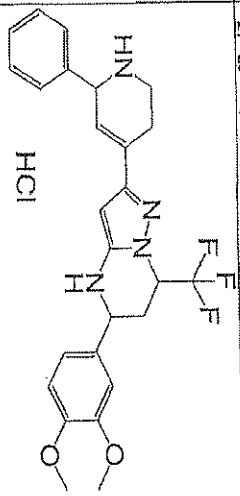
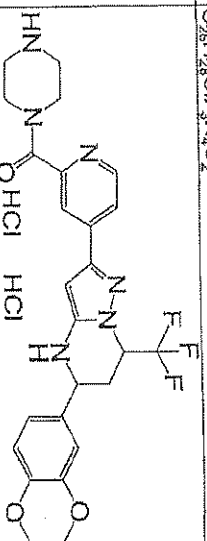
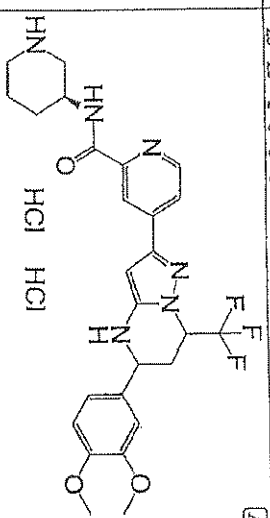
ER-Number	Structure	Chemical Name	HEK/ TLR7 IC50 (μ M)	HEK/ TLR9 IC50 (μ M)	¹ H NMR	MS
ER-896993		5-(3,4-dimethoxyphenyl)-2-(6-methyl-1,2,3,6-tetrahydropyridin-4-yl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine hydrochloride	0.065	10.00		
ER-896997		5-(3,4-dimethoxyphenyl)-2-(6-phenyl-1,2,3,6-tetrahydropyridin-4-yl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine hydrochloride	0.130	7.60		
ER-897034		(4-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)piperidin-1-yl)methanone dihydrochloride	0.110	> 10	¹ H NMR (400 MHz, Methanol-d ₄) δ ppm: 2.25 (dd, 1H), 2.53-2.58 (m, 1H), 3.31 (m, 4H), 3.85 and 3.87 (2s, 6H), 3.80-4.20 (m, 4H), 4.49 (dd, 1H), 5.14-5.20 (m, 1H), 6.99 (d, 1H), 7.05 (d, 1H), 7.10 (s, 1H), 8.02 (d, 1H), 8.19 (s, 1H), 8.66 (d, 1H).	517.4
ER-897036		4-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-N-(S)-piperidin-3-yl)picolinamide dihydrochloride	0.010	5.06	¹ H NMR (400 MHz, Methanol-d ₄) δ ppm: 1.83-1.90 (m, 2H), 2.09-2.12 (m, 2H), 2.25 (dd, 1H), 2.53-2.59 (m, 1H), 3.01-3.12 (m, 2H), 3.30-3.54 (m, 2H), 3.85 and 3.88 (2s, 6H), 4.31-4.36 (m, 1H), 4.50 (d, 1H), 5.14-5.20 (m, 1H), 6.99 (d, 1H), 7.06 (dd, 1H), 7.11 (d, 1H), 8.05 (d, 1H), 8.58 (s, 1H), 8.67 (d, 1H).	531.4

FIG. 11GG

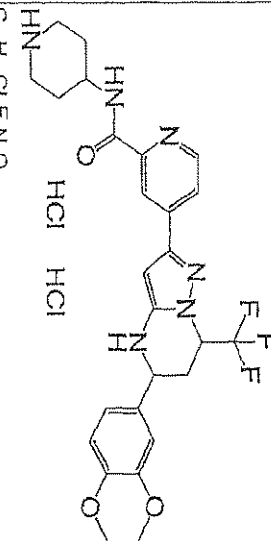
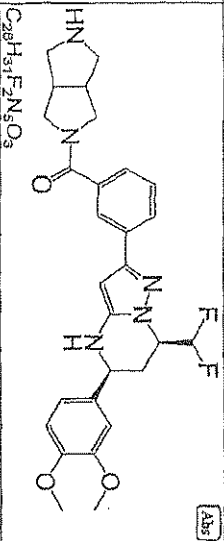
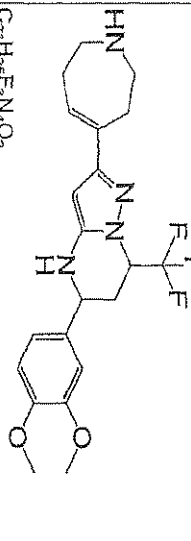
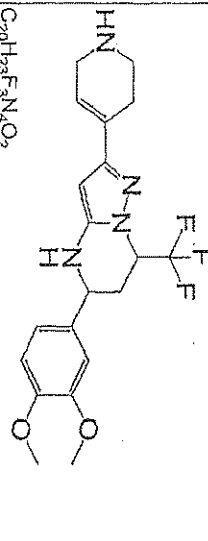
ER-Number	Structure	Chemical Name	HEK/TLR7 IC50 (μM)	HEK/TLR9 IC50 (μM)	¹ H NMR	MS
ER-897037		4-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-N-(piperidin-4-yl)picolinamide dihydrochloride	0.010	6.17	¹ H NMR (400 MHz, Methanol-d ₄) δ ppm: 1.90-2.00 (m, 2H), 2.21-2.30 (m, 3H), 2.53-2.59 (m, 1H), 3.13-3.21 (m, 2H), 3.49-3.52 (m, 2H), 3.85 and 3.87 (2s, 6H), 4.21-4.27 (m, 1H), 4.50 (d, 1H), 5.15-5.21 (m, 1H), 6.99 (d, 1H), 7.06 (dd, 1H), 7.11 (d, 1H), 8.10 (d, 1H), 8.62 (s, 1H), 8.67 (d, 1H).	531.5
ER-897077		(3-((5S,7R)-7-(difluoromethyl)-5-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)phenyl)(hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone	0.090	> 10		
ER-897090		5-(3,4-dimethoxyphenyl)-2-(2,3,6,7-tetrahydro-1H-azepin-4-yl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine	0.030	10.00	NMR of each isomer available	423.06
ER-897097		5-(3,4-dimethoxyphenyl)-2-(1,2,3,6-tetrahydropyridin-4-yl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine	0.058	10.00	NMR of each isomer available	409.08

FIG. 11HH

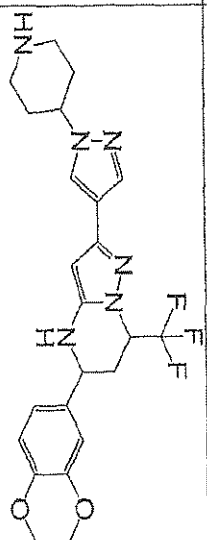
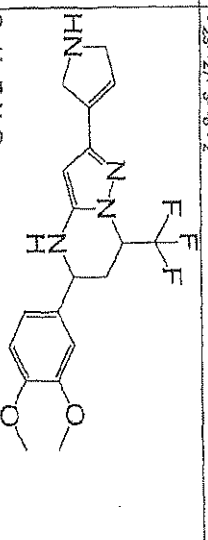
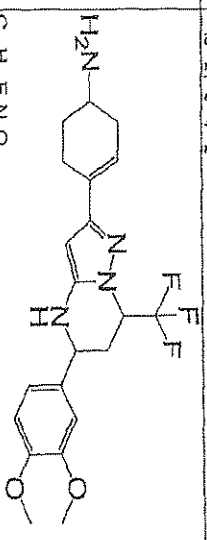
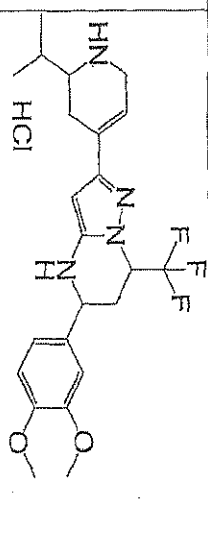
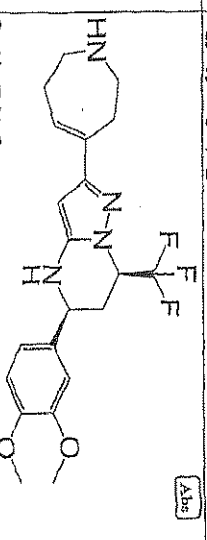
ER-Number	Structure	Chemical Name	HEK/ TLR7 IC50 (μ M)	HEK/ TLR9 IC50 (μ M)	¹ H NMR	MS
ER-897105		5-(3,4-dimethoxyphenyl)-2-(1-(piperidin-4-yl)-1H-pyrazol-4-yl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine	0.010	3.25	NMR of each isomer available	477.09
ER-897130		2-(2,5-dihydro-1H-pyrrol-3-yl)-5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine	0.059	10.00	¹ H NMR (400 MHz, METHANOL-d ₄) δ ppm 2.08 - 2.26 (m, 1 H) 2.50 (ddd, 1 H) 3.76 - 3.91 (m, 8 H) 4.00 (d, 2 H) 4.36 - 4.44 (m, 1 H) 4.94 - 5.05 (m, 1 H) 5.51 (s, 1 H) 6.16 (t, 1 H) 6.90 - 7.14 (m, 3 H).	395.03
ER-897142		4-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)cyclohex-3-enamine	0.009	10.00	NMR of each isomer available	423.06
ER-897178		5-(3,4-dimethoxyphenyl)-2-(2-isopropyl-1,2,3,6-tetrahydropyridin-4-yl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine hydrochloride	0.060	6.87		
ER-897212		(5S,7R)-5-(3,4-dimethoxyphenyl)-2-(2,3,6,7-tetrahydro-1H-azepin-4-yl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine	0.030	6.29	(400 MHz, METHANOL-d ₄) δ ppm 1.67 - 1.81 (m, 2 H) 2.07 - 2.19 (m, 1 H) 2.43 (ddd, 1 H) 2.71 - 2.80 (m, 2 H) 2.99 - 3.09 (m, 2 H) 3.40 (d, 2 H) 3.77 - 3.84 (m, 6 H) 4.26 - 4.38 (m, 1 H) 4.87 - 4.96 (m, 1 H) 5.50 (s, 1 H) 6.29 (t, 1 H) 6.86 - 7.08 (m, 3 H).	423.44

FIG. 11 II

ER-Number	Structure	Chemical Name	HEK/ TLR7 IC50 (μ M)	HEK/ TLR9 IC50 (μ M)	¹ H NMR	MS
ER-897214	 <small>(Abs)</small>	(5S,7R)-5-(3,4-dimethoxyphenyl)-2-(1-(piperidin-4-yl)-1H-pyrazol-4-yl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine	0.009	6.21	¹ H-NMR (400 MHz, METHANOL-d ₄) δ ppm 1.83 - 2.04 (m, 2 H) 2.05 - 2.29 (m, 3 H) 2.46 - 2.56 (m, 1 H) 2.67 - 2.82 (m, 2 H) 3.17 (d, 2 H) 3.82 - 3.95 (m, 6 H) 4.21 - 4.35 (m, 1 H) 4.36 - 4.50 (m, 1 H) 4.95 - 5.10 (m, 1 H) 5.59 - 5.71 (m, 1 H) 6.89 - 7.19 (m, 3 H) 7.70 - 7.85 (m, 1 H) 7.93 - 8.07 (m, 1 H),	477.44
ER-897215	 <small>(Abs)</small>	(5R,7S)-5-(3,4-dimethoxyphenyl)-2-(1-(piperidin-4-yl)-1H-pyrazol-4-yl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine	0.060	3.50	¹ H NMR (400 MHz, METHANOL-d ₄) δ ppm 1.82 - 2.04 (m, 2 H) 2.03 - 2.29 (m, 3 H) 2.40 - 2.58 (m, 1 H) 2.67 - 2.83 (m, 2 H) 3.17 (d, 2 H) 3.84 (s, 3 H) 3.86 (s, 3 H) 4.29 (ddd, 1 H) 4.41 (d, 1 H) 4.94 - 5.09 (m, 1 H) 5.60 - 5.68 (m, 1 H) 6.90 - 7.15 (m, 3 H) 7.70 - 7.81 (m, 1 H) 7.93 - 8.03 (m, 1 H)	477.44
ER-897269	 <small>(Abs)</small>	(5S,7R)-5-(3,4-dimethoxyphenyl)-2-(1,2,3,6-tetrahydropyridin-4-yl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine	0.030	> 10	¹ H-NMR (400 MHz, METHANOL-d ₄) δ ppm 2.04 - 2.20 (m, 1 H) 2.37 - 2.49 (m, 3 H) 2.89 - 3.02 (m, 2 H) 3.31 (s, 1 H) 3.35 - 3.43 (m, 2 H) 3.76 - 3.90 (m, 8 H) 4.26 - 4.38 (m, 1 H) 4.88 - 4.97 (m, 1 H) 5.50 (s, 1 H) 6.15 (br. s., 1 H) 6.86 - 7.11 (m, 1 H)	408.39
ER-897364	 <small>(Abs)</small>	4-((5S,7R)-5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)cyclohex-3-enamine	0.040	> 10	¹ H NMR (400 MHz, METHANOL-d ₄) δ ppm 1.29 (br. s., 1 H) 1.49 - 1.66 (m, 1 H) 1.92 - 2.08 (m, 2 H) 2.33 - 2.53 (m, 3 H) 2.62 (d, 1 H) 3.04 (br. s., 1 H) 3.82 - 3.88 (m, 6 H) 4.37 (d, 1 H) 4.92 - 5.00 (m, 1 H) 5.53 (d, 1 H) 6.13 (br. s., 1 H) 6.90 - 7.12 (m, 3 H),	424.44

FIG. 11JJ

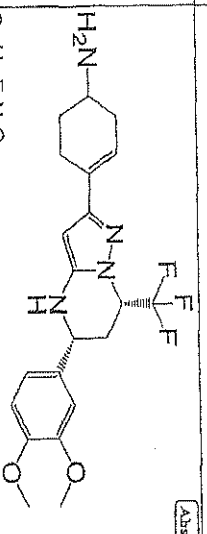
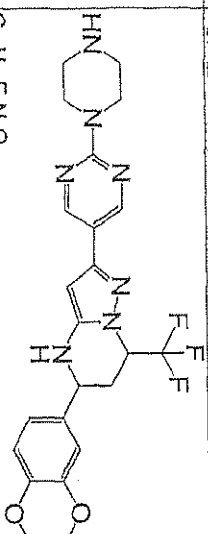
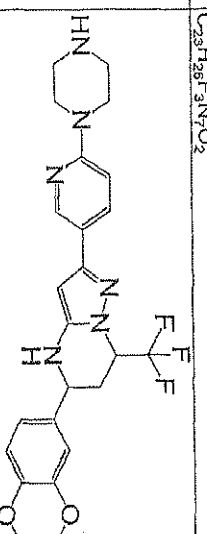
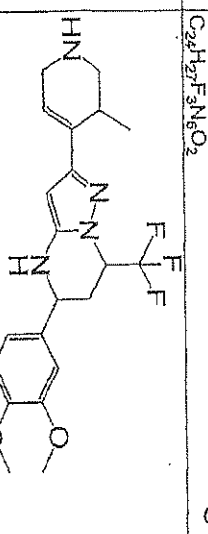
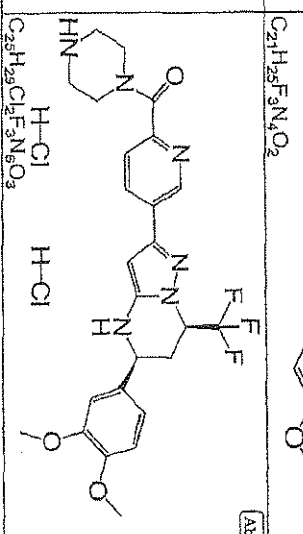
ER-Number	Structure	Chemical Name	HEK/ TLR7 IC50 (μ M)	HEK/ TLR9 IC50 (μ M)	¹ H NMR	MS
ER-897365		4-((5S,7R)-5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)cyclohex-3-enamine	0.040	> 10	¹ H NMR (400 MHz, METHANOL-d ₄) δ ppm 1.29 (br. s., 1 H) 1.48 - 1.64 (m, 1 H) 1.90 - 2.05 (m, 2 H) 2.33 - 2.53 (m, 3 H) 2.61 (d, 1 H) 3.02 (d, 1 H) 3.84 (d, 6 H) 4.36 (d, 1 H) 4.92 - 5.00 (m, 1 H) 5.49 - 5.55 (m, 1 H) 6.13 (br. s., 1 H) 6.92 - 7.12 (m, 3 H).	424.44
ER-897361		5-(3,4-dimethoxyphenyl)-2-(2-(piperazin-1-yl)pyrimidin-5-yl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine	0.030	4.73	NMR of each isomer available	490.07
ER-897405		5-(3,4-dimethoxyphenyl)-2-(6-(piperazin-1-yl)pyridin-3-yl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine	0.050	2.02	NMR of each isomer available	489.04
ER-897547		5-(3,4-dimethoxyphenyl)-2-(3-methyl-1,2,3,6-tetrahydropyridin-4-yl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine	0.070	8.78	¹ H NMR (400 MHz, METHANOL-d ₄) δ ppm 1.12 - 1.21 (m, 3 H) 2.08 - 2.27 (m, 1 H) 2.42 - 2.55 (m, 1 H) 2.68 - 2.86 (m, 2 H) 3.01 (dt, 1 H) 3.35 - 3.43 (m, 2 H) 3.84 (s, 3 H) 3.86 (s, 3 H) 4.39 (d, 1 H) 4.98 (dd, 1 H) 5.46 - 5.53 (m, 1 H) 6.04 - 6.15 (m, 1 H) 6.91 - 7.15 (m, 3 H).	423.1
ER-897560		(5-(3S,7R)-5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)piperidin-2-yl)methanone dihydrochloride	0.050	> 10	¹ H NMR (400 MHz, METHANOL-d ₄) δ ppm 2.25 (1 H), 2.32 (1 H), 2.56 (1 H), 3.38 (4 H), 3.56 (1 H), 3.86 (6 H), 3.99 (4 H), 4.50 (1 H), 5.15 (1 H), 7.05 (4 H), 7.85 (1 H), 8.40 (1H), 9.04 (1H)	518.52

FIG. 11KK

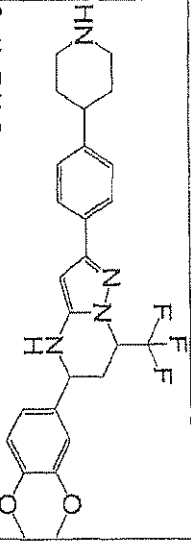
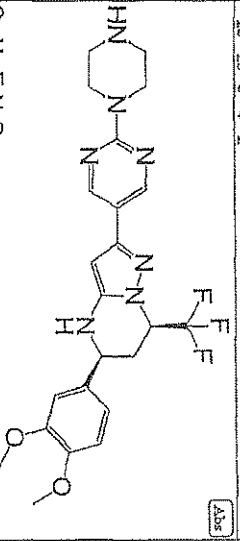
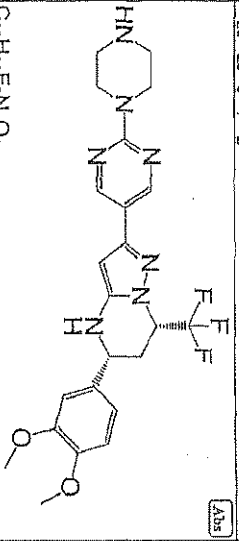
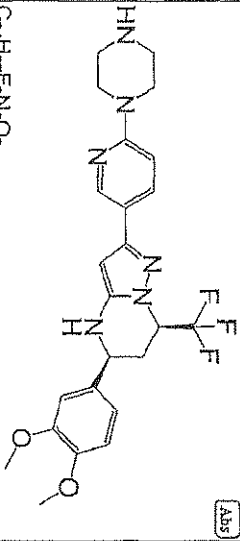
ER-Number	Structure	Chemical Name	HEK/ TLR7 IC50 (μ M)	HEK/ TLR9 IC50 (μ M)	¹ H NMR	MS
ER-897597		5-(3,4-dimethoxyphenyl)-2-(4-(piperidin-4-yl)phenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine	0.020	2.07	NMR of each isomer available	486.95
ER-897714		(5S,7R)-5-(3,4-dimethoxyphenyl)-2-(2-(piperazin-1-yl)pyrimidin-5-yl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine	0.020	2.20	¹ H-NMR (400 MHz, METHANOL-d ₄) δ ppm 2.13 - 2.29 (m, 1 H) 2.52 (ddd, 1 H) 2.82 - 2.95 (m, 4 H) 3.76 - 3.94 (m, 10 H) 4.37 - 4.48 (m, 1 H) 4.99 - 5.12 (m, 1 H) 5.74 (s, 1 H) 6.91 - 7.18 (m, 3 H) 8.56 - 8.73 (m, 2 H)	490.22
ER-897715		(5R,7S)-5-(3,4-dimethoxyphenyl)-2-(2-(piperazin-1-yl)pyrimidin-5-yl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine	0.070	2.41	¹ H NMR (400 MHz, METHANOL-d ₄) δ ppm 2.15 - 2.28 (m, 1 H) 2.44 - 2.59 (m, 1 H) 2.81 - 2.98 (m, 4 H) 3.74 - 4.06 (m, 10 H) 4.36 - 4.50 (m, 1 H) 5.05 (dt, 1 H) 5.74 (s, 1 H) 6.91 - 7.28 (m, 3 H) 8.65 (s, 2 H)	490.26
ER-897716		(5S,7R)-5-(3,4-dimethoxyphenyl)-2-(6-(piperazin-1-yl)pyridin-3-yl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine	0.008	4.47	¹ H NMR (400 MHz, METHANOL-d ₄) δ ppm 2.14 - 2.30 (m, 1 H) 2.52 (ddd, 1 H) 2.88 - 3.02 (m, 4 H) 3.50 - 3.59 (m, 4 H) 3.84 (s, 3 H) 3.87 (s, 3 H) 4.35 - 4.51 (m, 1 H) 4.95 - 5.13 (m, 1 H) 5.74 (s, 1 H) 6.85 (d, 1 H) 6.94 - 7.17 (m, 3 H) 7.92 (dd, 1 H) 8.45 (d, 1 H)	489.25

FIG. 11LL

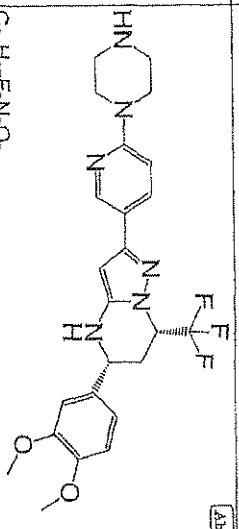
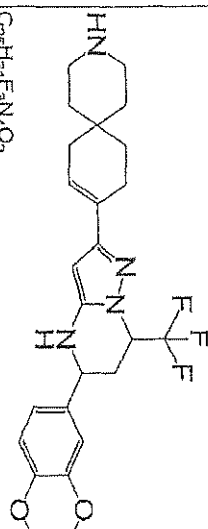
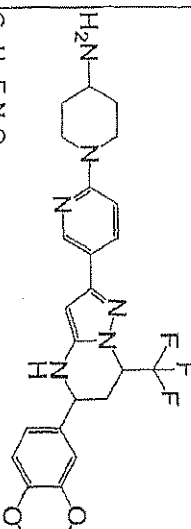
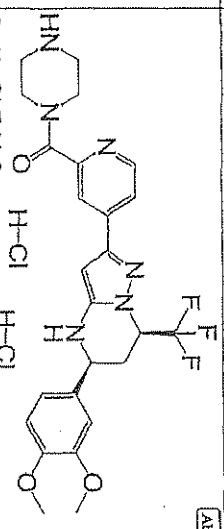
ER-Number	Structure	Chemical Name	HEK/ TLR7 IC50 (μ M)	HEK/ TLR9 IC50 (μ M)	¹ H NMR	MS
ER-897717		(5R,7S)-5-(3,4-dimethoxyphenyl)-2-(6-(piperazin-1-yl)pyridin-3-yl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine	0.070	0.87	¹ H NMR (400 MHz, METHANOL-d4) δ ppm 2.14 - 2.30 (m, 1 H) 2.52 (ddd, 1 H) 2.90 - 3.02 (m, 4 H) 3.49 - 3.61 (m, 4 H) 3.84 (s, 3 H) 3.87 (s, 3 H) 4.38 - 4.48 (m, 1 H) 4.97 - 5.11 (m, 1 H) 5.74 (s, 1 H) 6.86 (d, 1 H) 6.95 - 7.17 (m, 3 H) 7.93 (dd, 1 H) 8.45 (d, 1 H), 1 H),	489.29
ER-897728		5-(3,4-dimethoxyphenyl)-2-(3-azaspiro[5.5]undec-8-en-9-yl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine	0.010	5.46	NMR of each isomer available	477.13
ER-897765		1-(5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)piperidin-4-amine	0.080	2.13	¹ H NMR (400 MHz, METHANOL-d4) δ ppm 1.45 (qd, 2 H) 1.96 (d, 2 H) 2.14 - 2.30 (m, 1 H) 2.52 (ddd, 1 H) 2.86 - 3.10 (m, 3 H) 3.82 - 3.95 (m, 7 H) 4.29 - 4.47 (m, 3 H) 4.99 - 5.09 (m, 1 H) 5.73 (s, 1 H) 6.82 - 7.14 (m, 4 H) 7.90 (dd, 1 H) 8.43 (d, 1 H),	503.04
ER-897777		(4-((5S,7R)-5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)piperidin-2-yl)piperidin-2-yl)methanone dihydrochloride	0.100	10.00		

FIG. 11MM

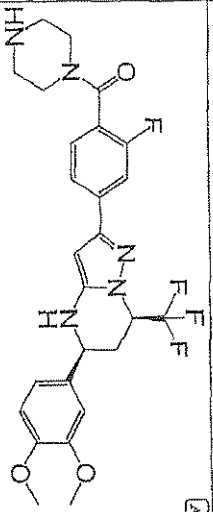
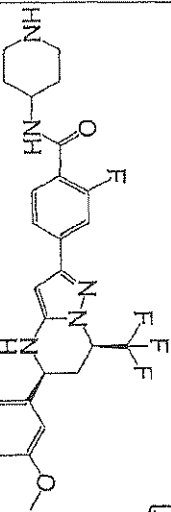
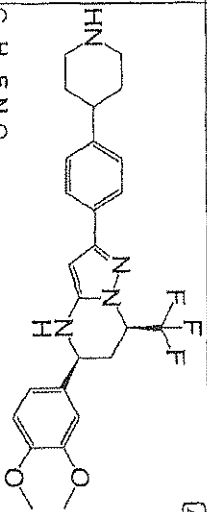
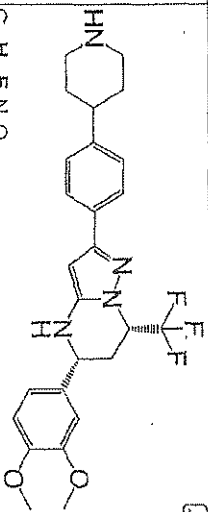
ER-Number	Structure	Chemical Name	HEK/ TLR7 IC50 (μ M)	HEK/ TLR9 IC50 (μ M)	¹ H NMR	MS
ER-897789		(4-((5S,7R)-5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-2-fluorophenyl)(piperazin-1-yl)methanone dihydrochloride	0.050	10.00		
ER-897791		4-((5S,7R)-5-(3,4-dimethoxyphenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-yl)-2-fluoro-N-(piperidin-4-yl)benzamide dihydrochloride	0.040	5.99		
ER-897814		(5S,7R)-5-(3,4-dimethoxyphenyl)-2-(4-(piperidin-4-yl)phenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine	0.030	1.37	¹ H NMR (400 MHz, METHANOL-d ₄) δ ppm 1.61 - 1.79 (m, 2 H) 1.81 - 1.95 (m, 2 H) 2.13 - 2.31 (m, 1 H) 2.53 (ddd, 1 H) 2.64 - 2.85 (m, 3 H) 3.18 (d, 2 H) 3.84 (s, 3 H) 3.87 (s, 3 H) 4.38 - 4.49 (m, 1 H) 5.00 - 5.11 (m, 1 H) 5.76 - 5.82 (m, 1 H) 6.94 - 7.14 (m, 3 H) 7.23 - 7.30 (m, 2 H) 7.63 - 7.72 (m, 2 H).	
ER-897815		(5R,7S)-5-(3,4-dimethoxyphenyl)-2-(4-(piperidin-4-yl)phenyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine	0.100	2.00	¹ H NMR (400 MHz, METHANOL-d ₄) δ ppm 1.63 - 1.77 (m, 2 H) 1.79 - 1.94 (m, 2 H) 2.09 - 2.31 (m, 1 H) 2.53 (ddd, 1 H) 2.63 - 2.84 (m, 3 H) 3.17 (d, 2 H) 3.84 (s, 3 H) 3.87 (s, 3 H) 4.38 - 4.49 (m, 1 H) 4.99 - 5.12 (m, 1 H) 5.79 (s, 1 H) 6.94 - 7.14 (m, 3 H) 7.26 (d, 2 H) 7.64 - 7.71 (m, 2 H).	

FIG. 11NN

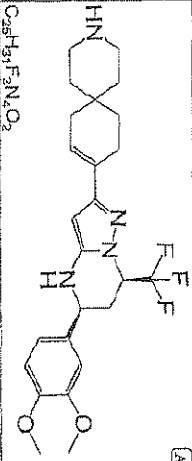
ER-Number	Structure	Chemical Name	HEK/ TLR7 IC50 (μ M)	HEK/ TLR9 IC50 (μ M)	¹ H NMR	MS
ER-897851	 $C_{25}H_{31}F_3N_4O_2$	(5S,7R)-5-(3,4-dimethoxyphenyl)-2-(3-azaspiro[5.5]undec-9-en-9-yl)-7-(trifluoromethyl)-1,5-alpyrimidine	0.041	8.63	¹ H NMR (400 MHz, METHANOL-d ₄) δ ppm 1.36 - 1.48 (m, 4 H) 1.52 - 1.65 (m, 2 H) 1.97 - 2.20 (m, 3 H) 2.27 - 2.51 (m, 3 H) 2.68 - 2.89 (m, 4 H) 3.74 - 3.84 (m, 6 H) 4.24 - 4.37 (m, 1 H) 4.90 (dd, 1 H) 5.44 - 5.50 (m, 1 H) 6.02 - 6.14 (m, 1 H) 6.86 - 7.09 (m, 3 H).	477.3

Figure 12

FIG. 12A.

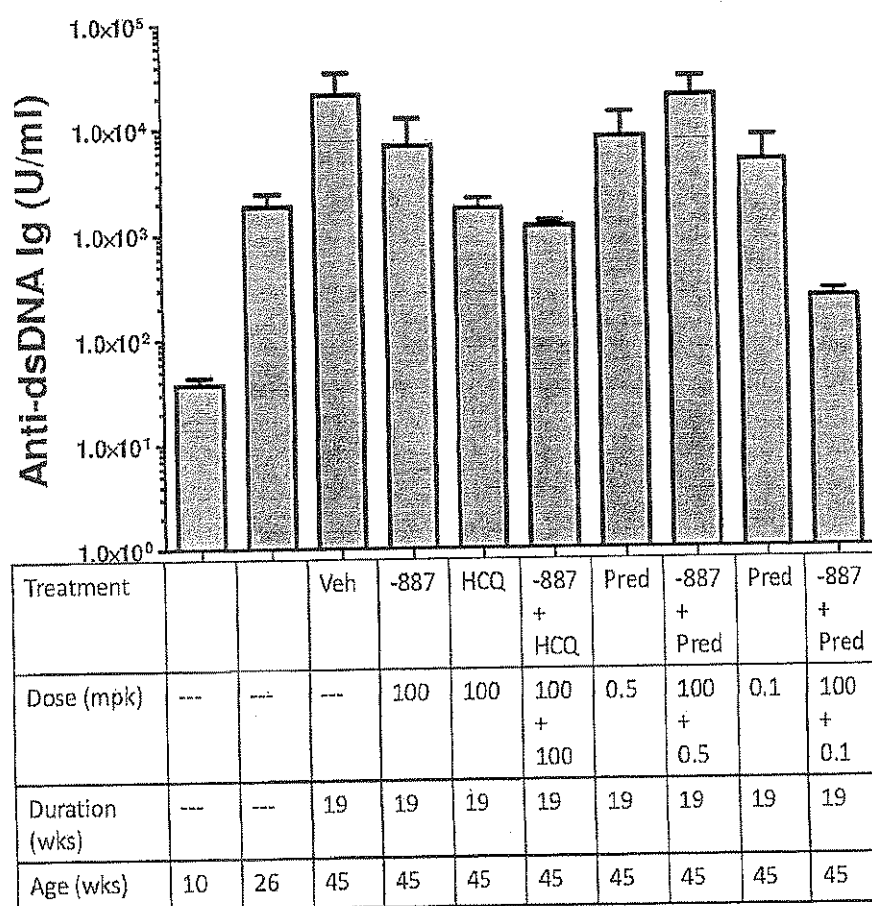


FIG. 12B.

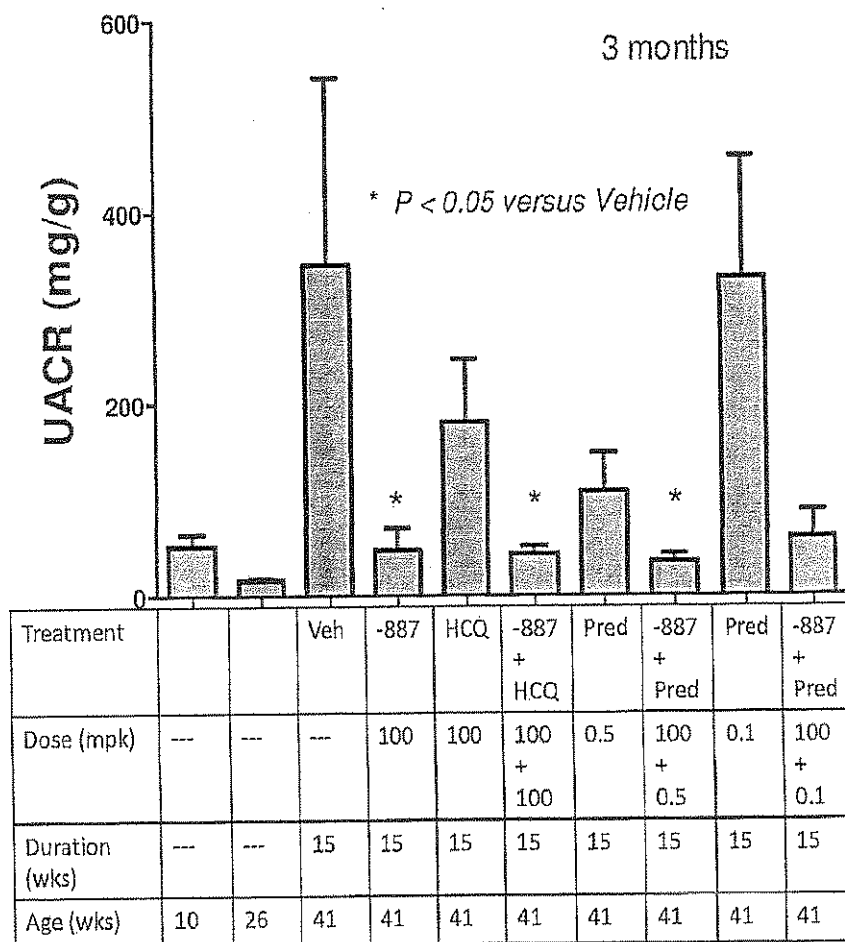


FIG. 12C.

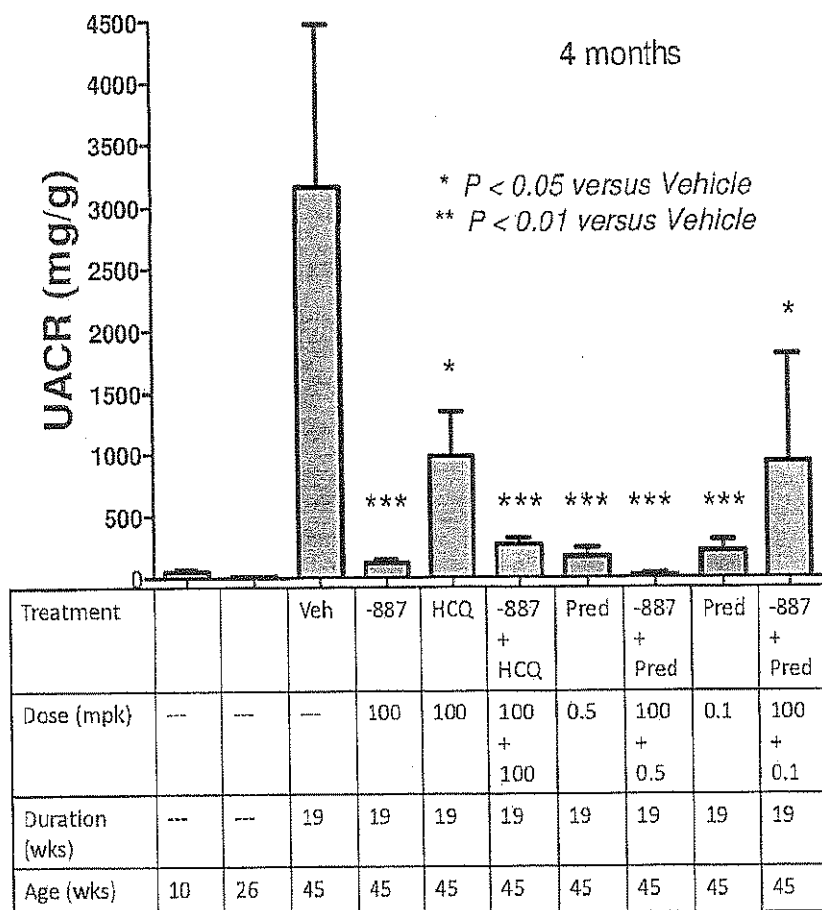


FIG. 12D.

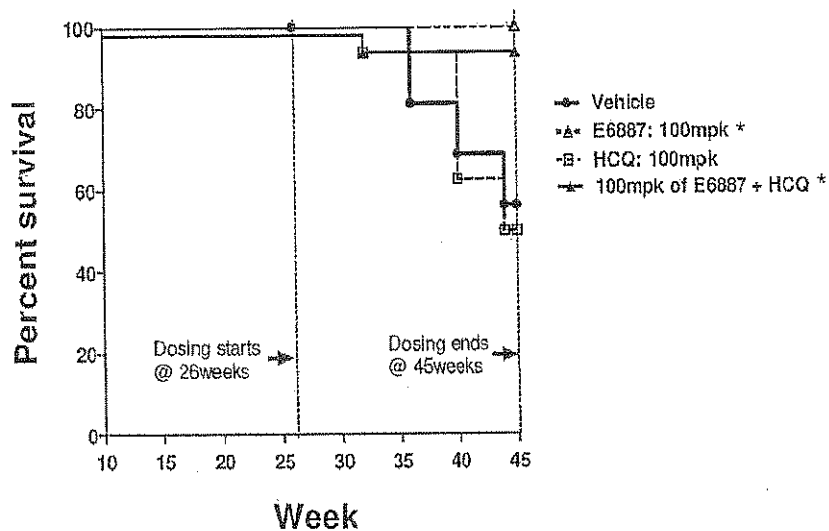


FIG. 12E.

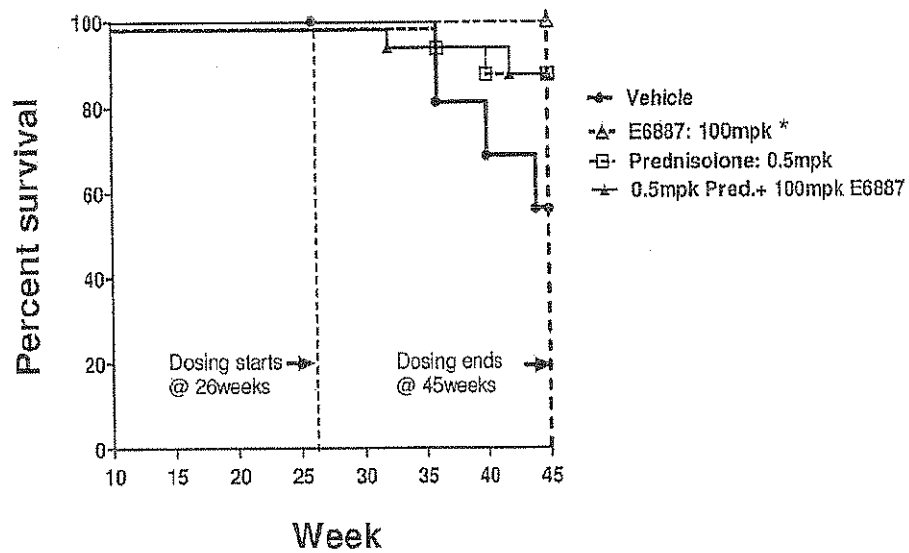


FIG. 12F.

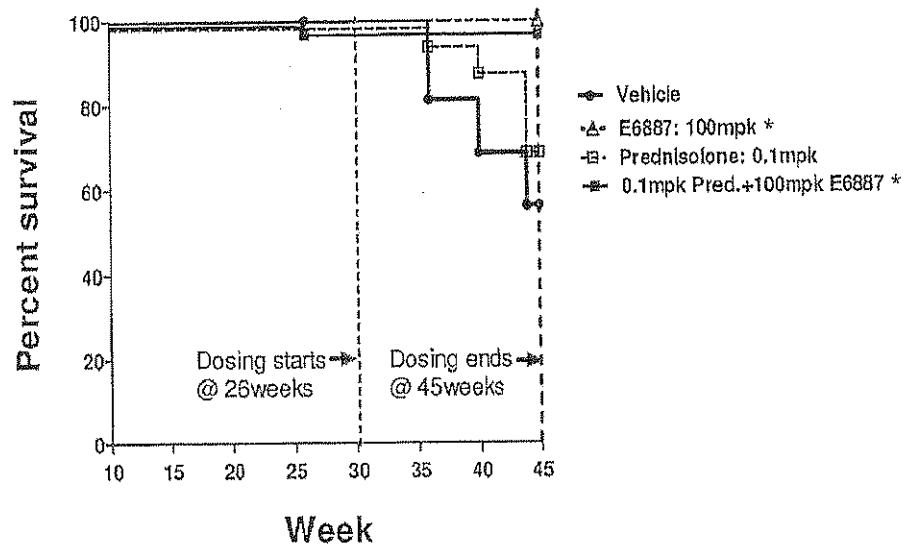


Figure 13

FIG. 13A.

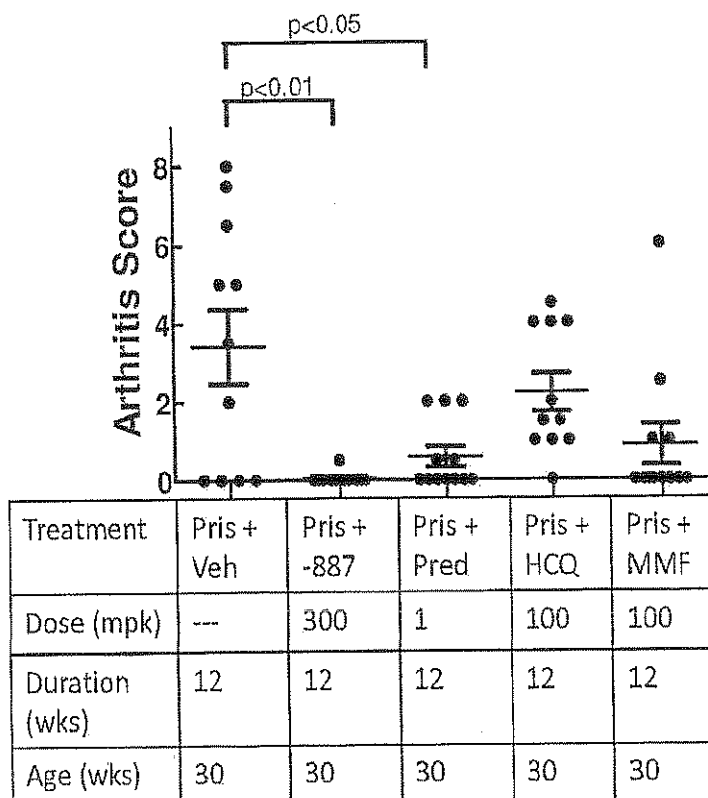


FIG. 13B.

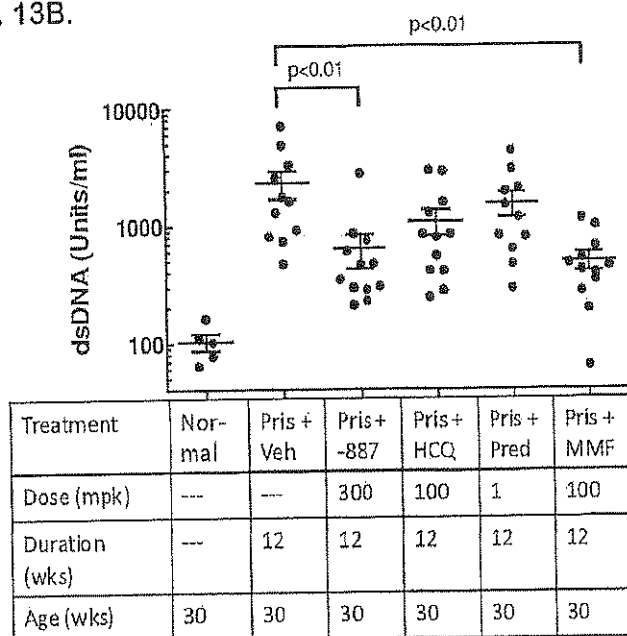
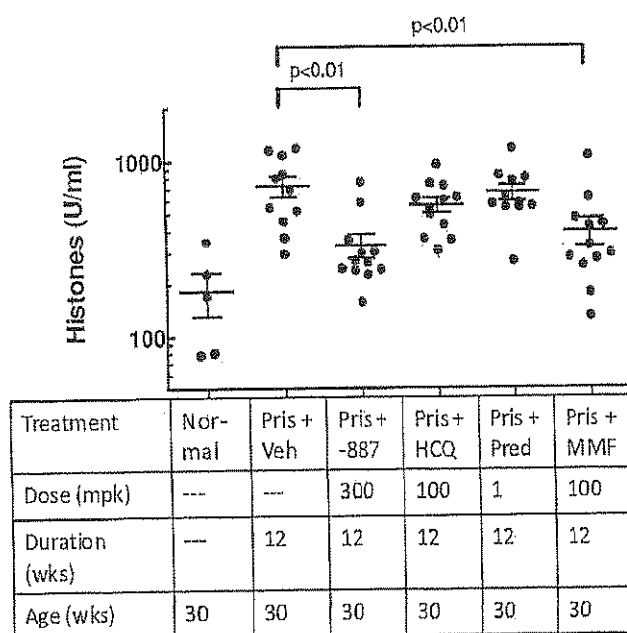


FIG. 13B. (continued)

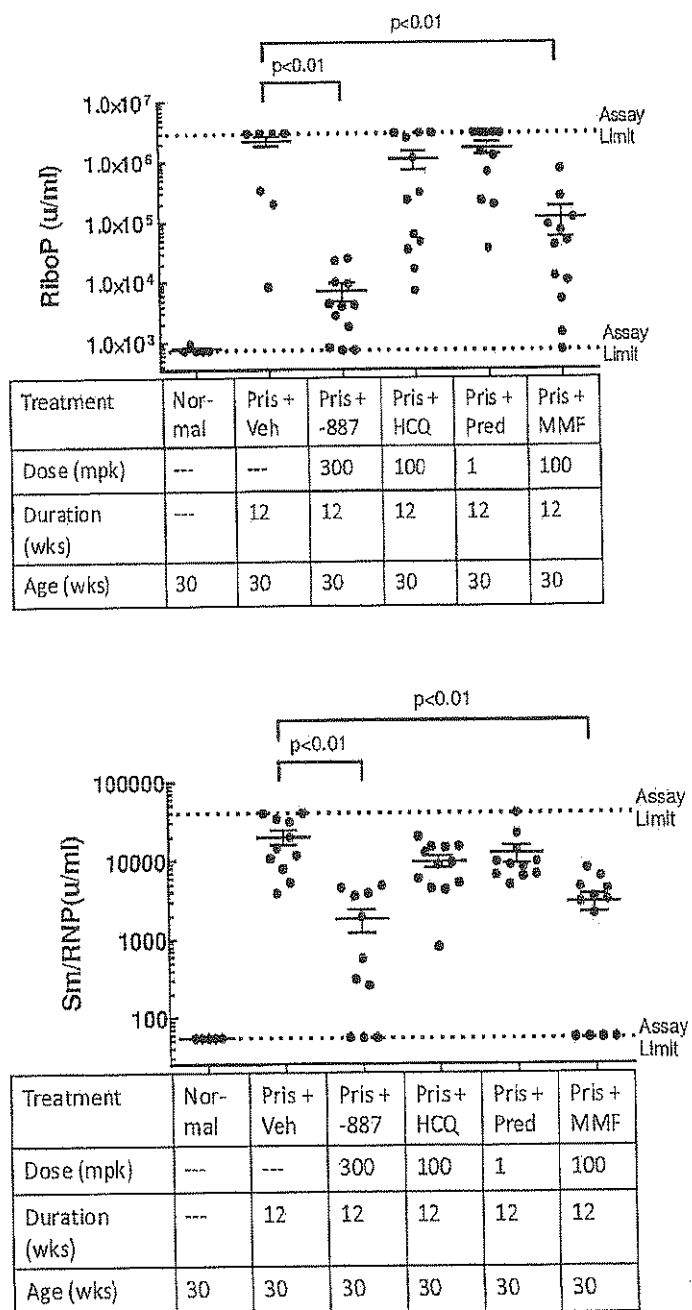


FIG. 13C.

Gene #:	Gene Name
1	Ccl2
2	Ifit1*
3	Ifit3
4	Ifi44*
5	Oasl2*
6	Isg15
7	Mmp8
8	Fcgr1*
9	Ifi2712a*
10	Oas3*
11	Usp18*
12	C1qa*
13	Irf7
14	Ddx60*
15	Cmpk2*
16	Xaf1
17	Fpr1
18	Ifi204*
19	Cxcl10
20	Siglec1*
21	Mx1*
22	Herc6*
23	Ms4a6c
24	Ifi202b
25	Il6
26	Cd40
27	Prf1
28	Cd38
29	Irf5
30	Lta
31	Il6ra
32	Trex1

FIG. 13C. (continued)

33	Ccl5
Thirty three (33) genes significantly upregulated between Pristane + Vehicle vs. uninduced PBS control ($P < 0.05$, at least 1.5 fold change)	
* Significantly reduced by ER-892887 vs. vehicle-treated pristane-induced mice (14 genes) ($P < 0.05$, at least 1.5 fold change)	

FIG. 13D.

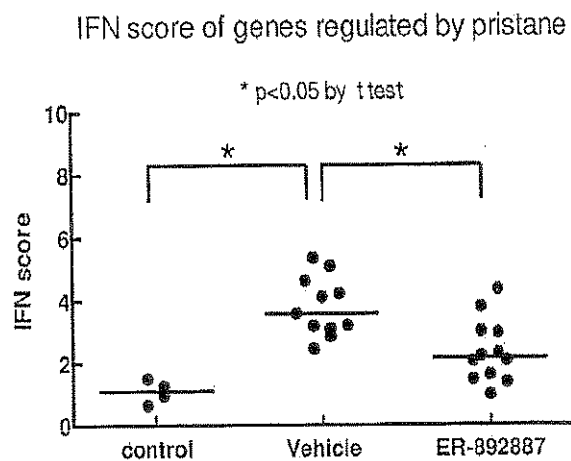


Figure 14

FIG. 14A.

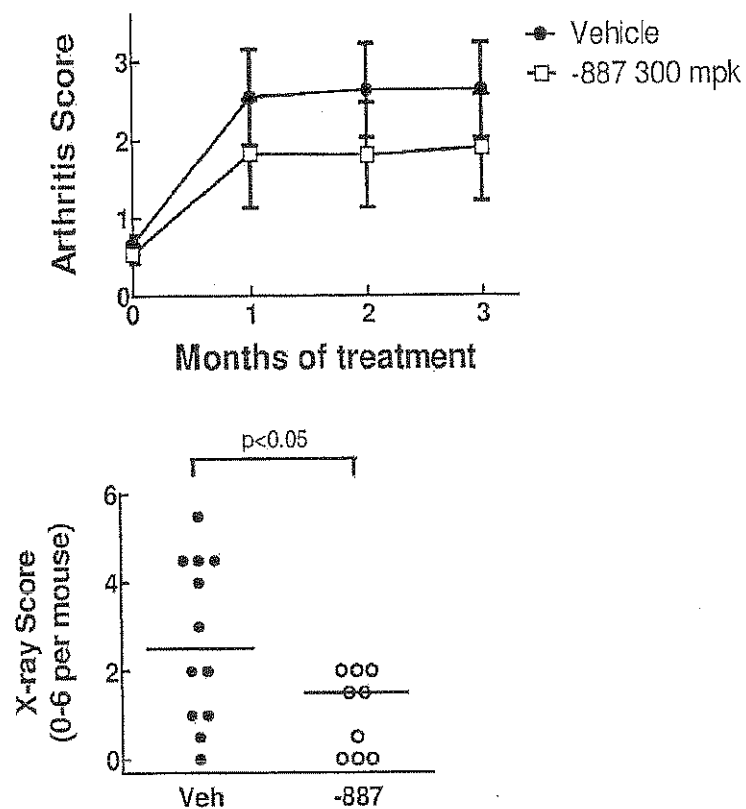


FIG. 14B.

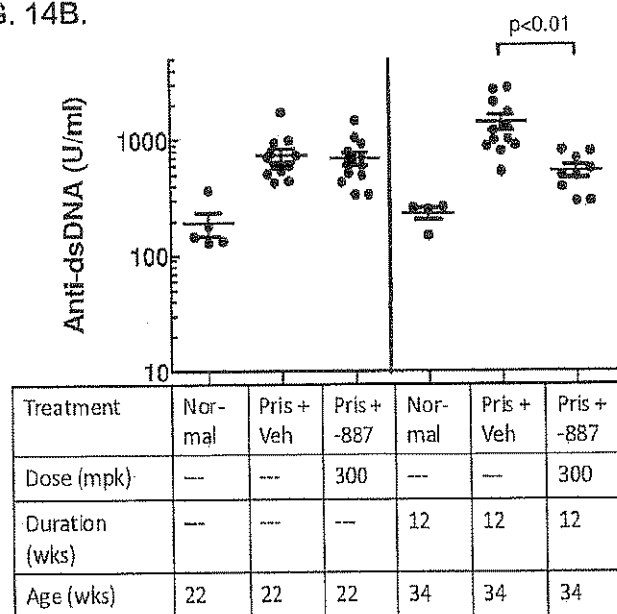
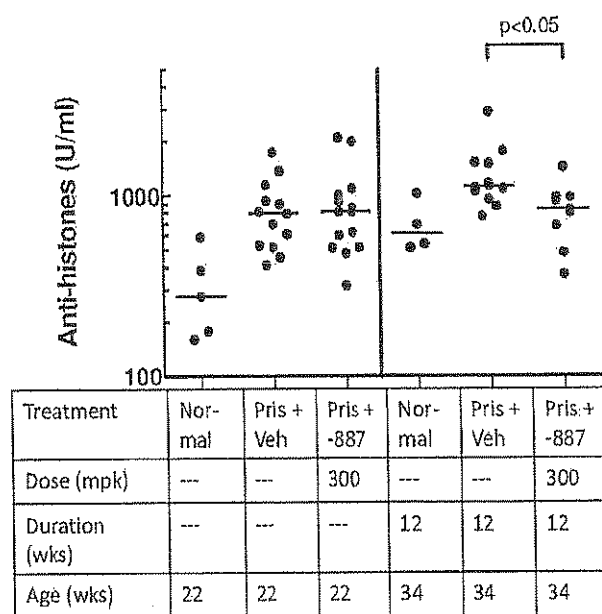


FIG. 14B. (continued)

