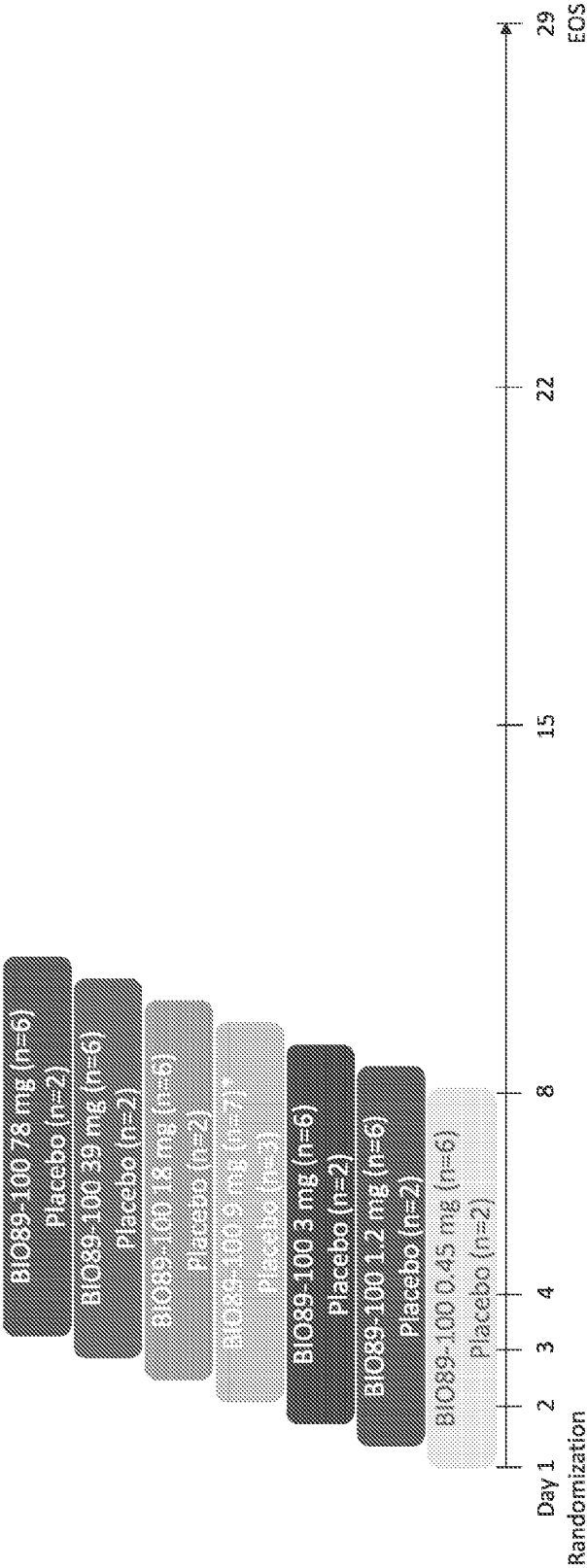


FIG. 1



*Cohort 5 = 2-person cohort at the same dose level (9 mg) as Cohort 4

FIG. 2

g p

Mean (SD) or %	Pooled BID89-100 (n=43)	Placebo (n=15)
Age (years)	39.3 (10.0)	39.4 (9.3)
Male (%)	86%	87%
White (%)	67%	53%
Hispanic/Latino (%)	44%	40%
Weight (kg)	79.9 (11.1)	83.0 (14.9)
BMI (kg/m ²)	26.5 (3.1)	27.3 (3.0)

FIG. 3

Parameter Mean (SD)	Pooled BI089-100 (n=43)	Placebo (n=15)
Triglycerides (mg/dL)	92.1 (33.9)	99.3 (42.0)
Total Cholesterol (mg/dL)	182.2 (28.8)	197.5 (31.8)
HDL (mg/dL)	46.6 (9.2)	50.8 (12.3)
LDL (mg/dL)	122.2 (26.9)	129.6 (26.6)
Glucose (mg/dL)	87.8 (7.3)	89.3 (6.1)
Insulin (uIU/mL)	7.3 (3.1)	7.3 (2.9)
ALT (U/L)	21.0 (7.9)	22.3 (5.7)
AST (U/L)	20.3 (4.5)	19.5 (4.0)
GGT (U/L)	25.2 (10.7)	25.4 (8.7)

FIG. 4: Safety Summary: BIO89-100 Was Well-Tolerated

System Organ Class		Placebo		BIO89-100						Pooled	
Preferred Term	(N=15)	0.45 mg (N=6)	1.2 mg (N=6)	3 mg (N=6)	9.1 mg (N=7)	16.2 mg (N=6)	35 mg (N=5)	75 mg (N=6)	BIO89-100 (N=43)		
n (%)											
ANY	3 (20.0)	0	0	0	1 (14.3)	3 (50.0)	6 (100)	3 (50.0)	13 (30.2)		
Injection site induration	1 (6.7)	0	0	0	1 (14.3)	0	5 (83.3)	1 (16.7)	7 (16.3)		
Injection site erythema	1 (6.7)	0	0	0	0	0	3 (50.0)	2 (33.3)	5 (11.6)		
Injection site pain	0	0	0	0	0	0	2 (33.3)	0	2 (4.7)		
Headache	1 (6.7)	0	0	0	0	2 (33.3)	0	0	2 (4.7)		

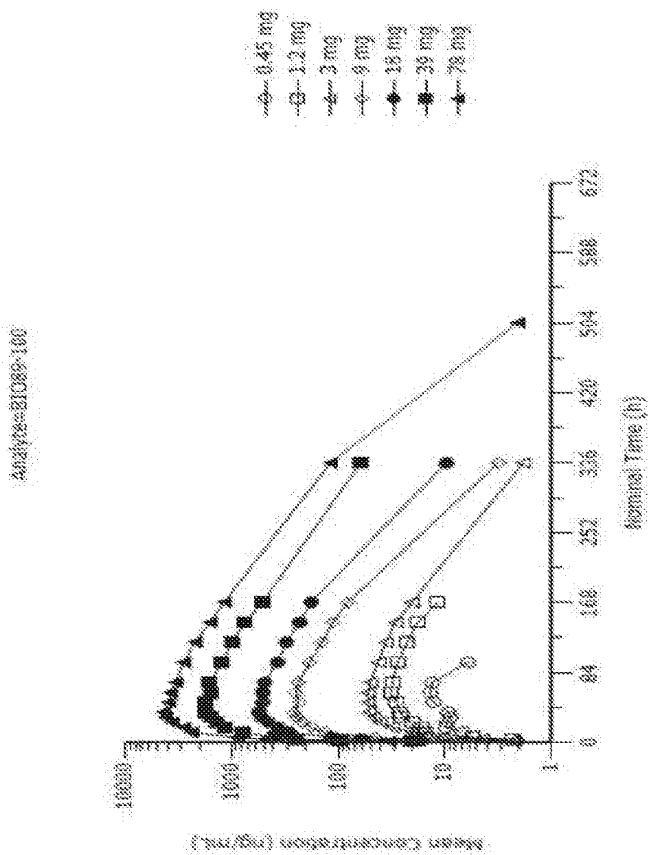


FIG 5B

Dose (mg/k g)	T _{ma} x (h)	C _{max} (ng/m L)	AUC _{inf} (ng·h/m L)	T _{1/2} (h)
0.45	39	16.7	4920	202
1.2	60	33.1	5750	112
3	60	57.7	9050	96.9
9	48	294	38500	59.2
18	36	593	78200	54.4
39	54	1940	24700	54.9
78	36	4500	541000	53.4

Data shown as mean values except median for T_{max}
CV% for AUC_{inf} ranges from 17.88 to 43.18%

FIG 5A

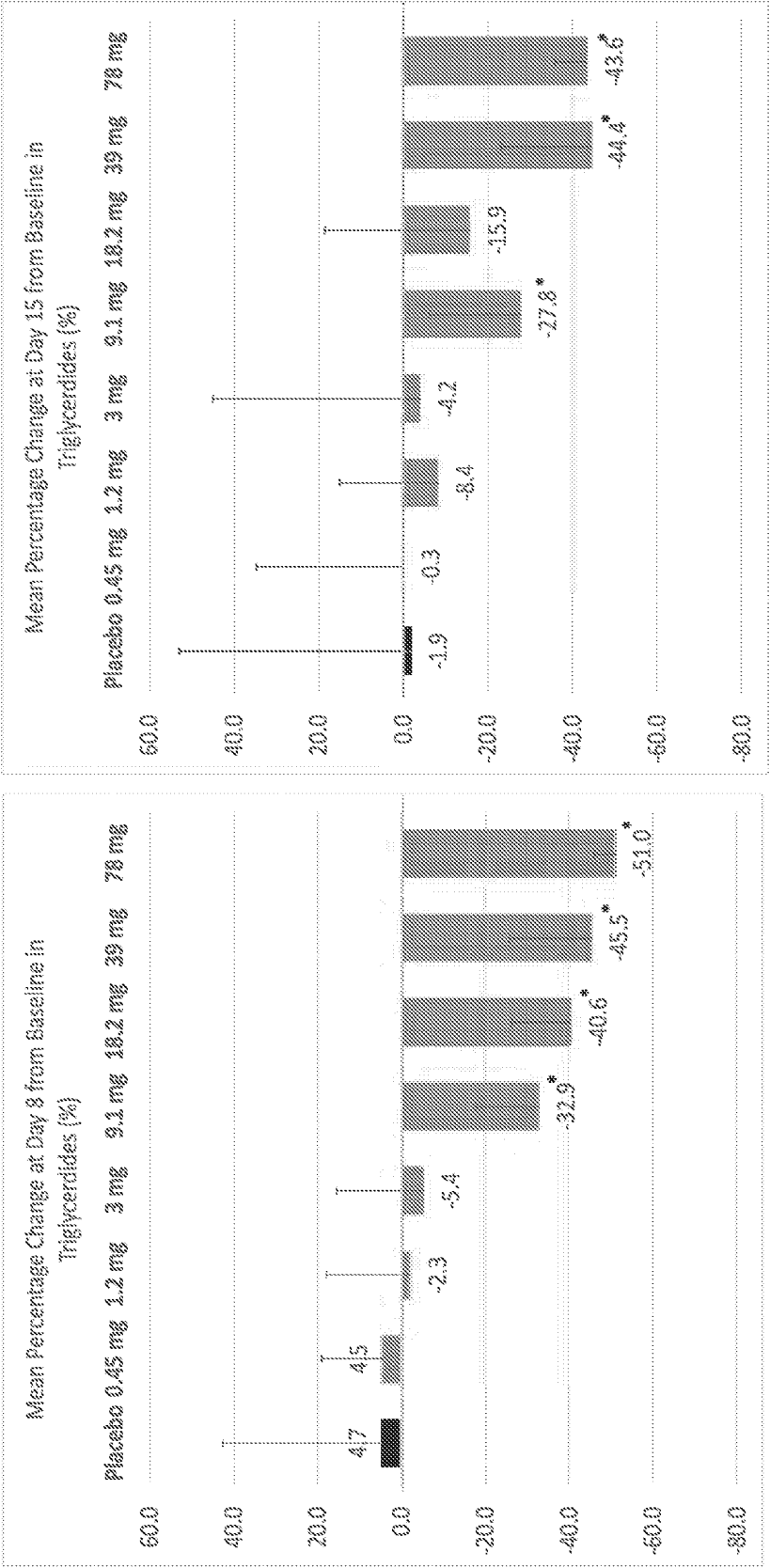
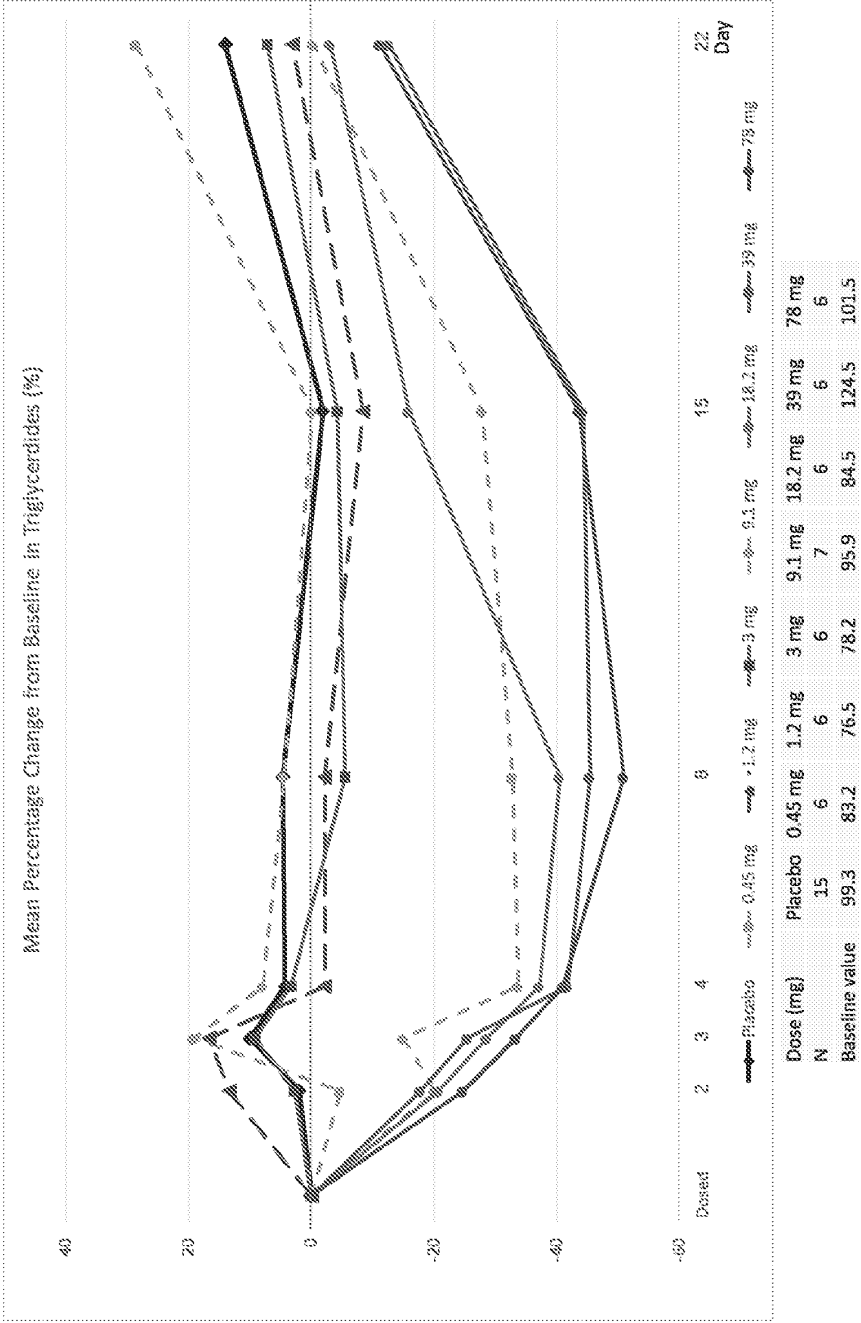


FIG. 6A

Dose (mg)	Placebo	0.45 mg	1.2 mg	3 mg	9.1 mg	18.2 mg	39 mg	78 mg
N	15	6	6	6	7	6	6	6
Baseline value	99.3	83.2	76.5	78.2	95.9	84.5	124.5	101.5

* 95% CI exclude 0 mg/dL
Error bars represent the SD

FIG. 7



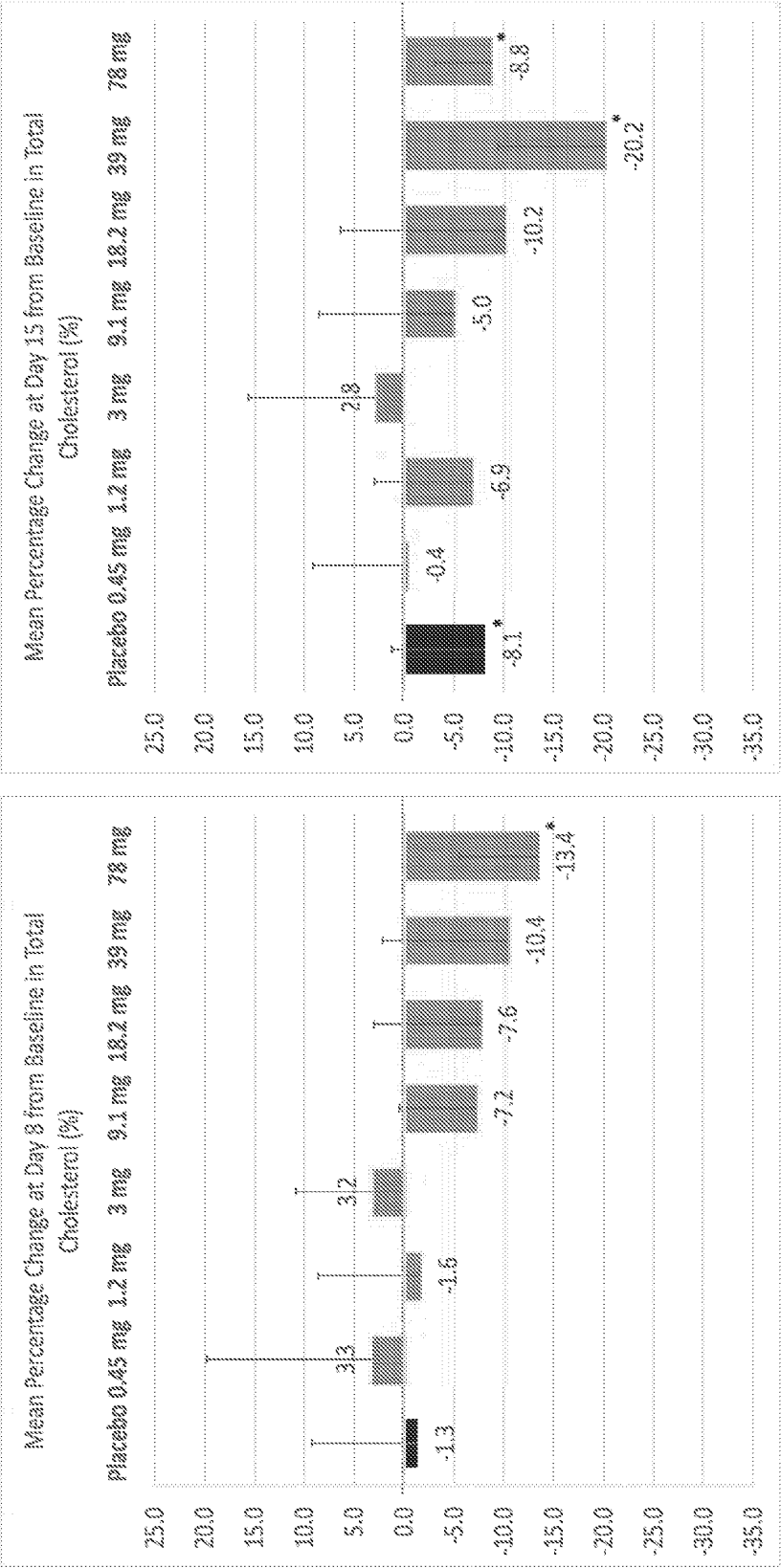
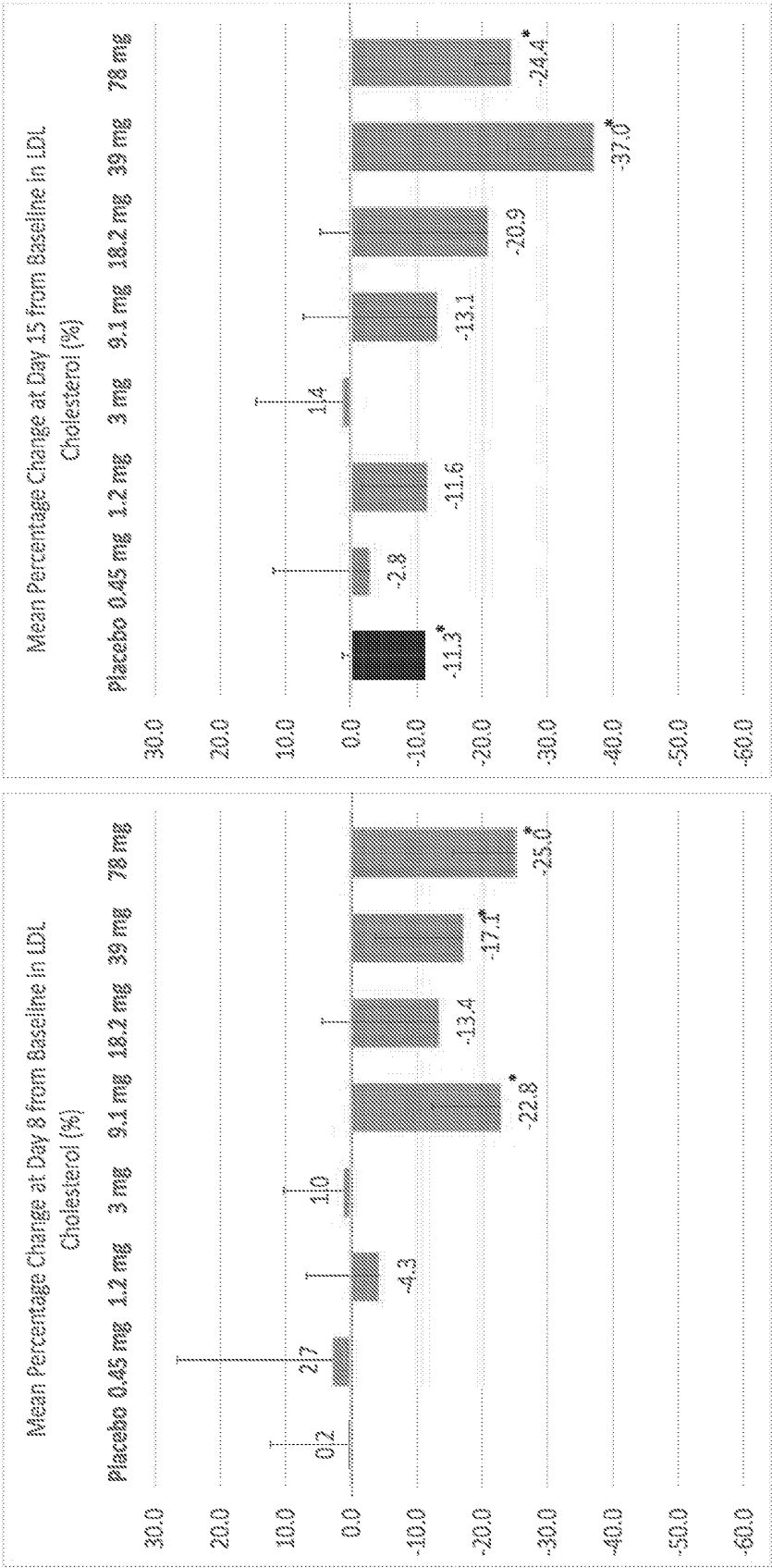


FIG. 8A

Dose (mg)	Placebo	0.45 mg	1.2 mg	3 mg	9.1 mg	18.2 mg	39 mg	78 mg
N	15	6	6	6	7	6	6	6
Baseline	197.5	152.5	178.8	185.8	184.9	185	203.3	184.3

FIG. 8B



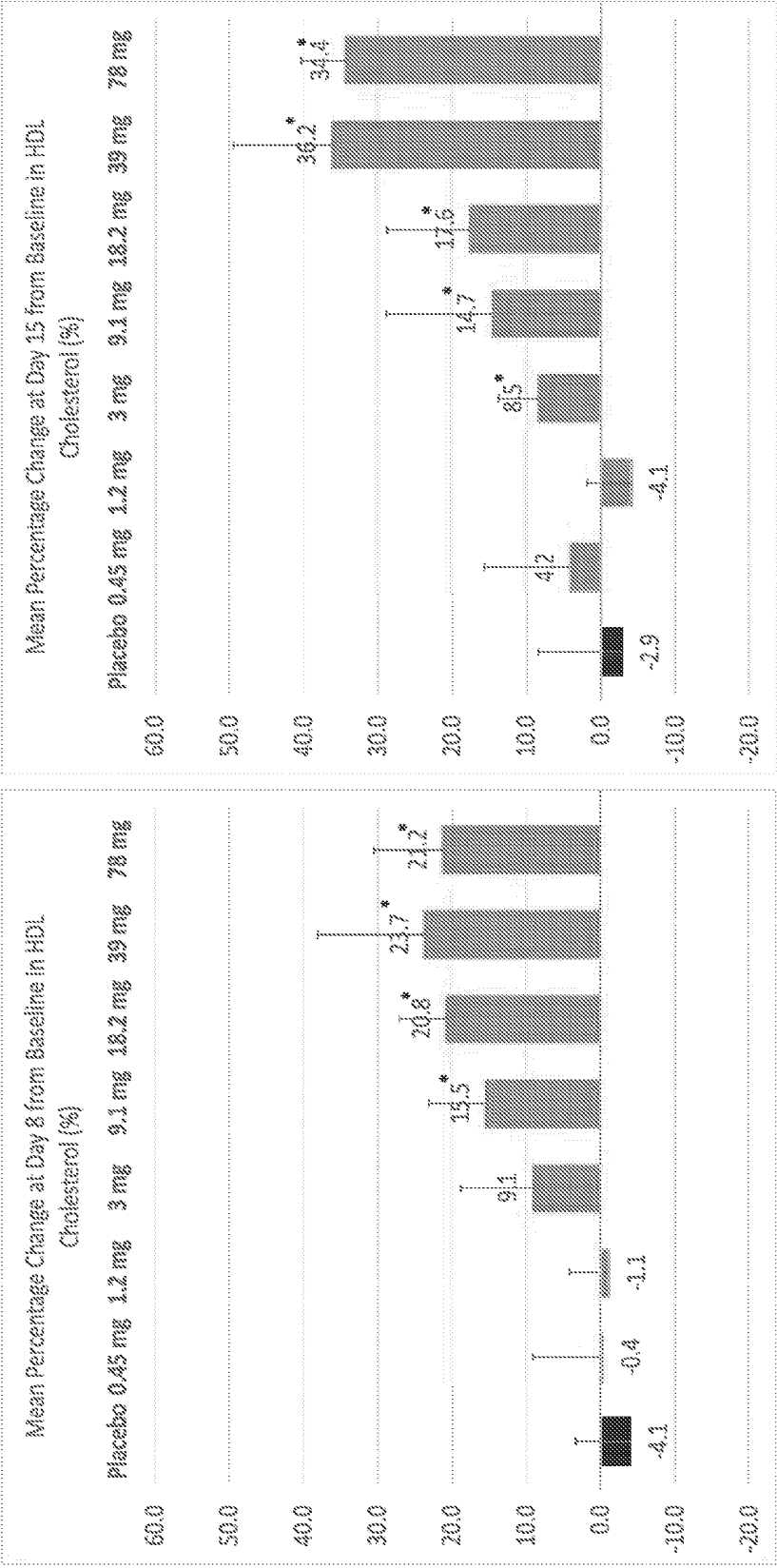


FIG. 10A

Dose (mg)	Placebo	0.45 mg	1.2 mg	3 mg	9.1 mg	18.2 mg	39 mg	78 mg
N	15	6	6	6	7	6	6	6
BL	50.8	44.5	50	48.5	51	44.8	44.2	42.7

FIG. 10B * 95% CI exclude 0 mg/dL
Error bars represent the SD

FIG. 11

Parameter (mean)	89blo Overall	BMS	Akero
Study Population	Healthy Volunteers	Healthy obese	Type 2 diabetics
Age (yr)	39.3	40.4	53.3
Weight (kg)	80.7	101.9	--
BMI (kg/m ²)	26.7	33.6	--
Fasting glucose (mg/dL)	88.2	--	--
ALT (U/L)	21.3	--	--
Triglycerides (mg/dL)	94.0	--	--
HgA1c (%)	--	--	> 6.5%

BMS: Charles et al. AASLD 2016
Akero: AMG 876 20100015 Clinical Study Report Synopsis

FIG. 12

	BIO89-100				BMS ^Δ		Akero [*]
	Max % change (Day 8 or Day 15) [*] SAD Healthy Volunteer				Day 14 % change MAD Healthy Obese		% change SAD Type 2 diabetics
	9.1 mg	18.2 mg	39 mg	78 mg	10 mg QD	21 mg QW	
TRIG	-33%	-41%	-45%	-51%	-35%	-25%	"up to -50%"
LDL	-23%	-21%	-37%	-25%	-25%	-20%	"up to -40%" ← 210 mg dose
HDL	16%	21%	36%	34%	-8%	-9%	"up to 50%"

Note: separate studies, not head-to-head comparison
* * % change is calculated based on baseline mean and change from baseline mean; max % change is the max between D8 or D15 & Charles et al. AASLD 2016; BMS data read from figure so not precise.
Δ AMG 876 20100015 Clinical Study Report Synopsis; data stated as "compared to placebo"

FIG. 13

	BIO89-100			BM5A		Akero [^]
	Max % change (Day 8 or Day 15)* SAD Healthy Volunteer			Day 14 % change MAD Healthy Obese	% change SAD Type 2 diabetics	
	9.1 mg	18.2 mg	39 mg	78 mg	10 mg QD	21 mg QW
TRIG	-33%	-41%	-45%	-51%	-35%	-25%
LDL	-23%	-21%	-37%	-25%	-25%	-20%
HDL	16%	21%	36%	34%	-8%	-9%

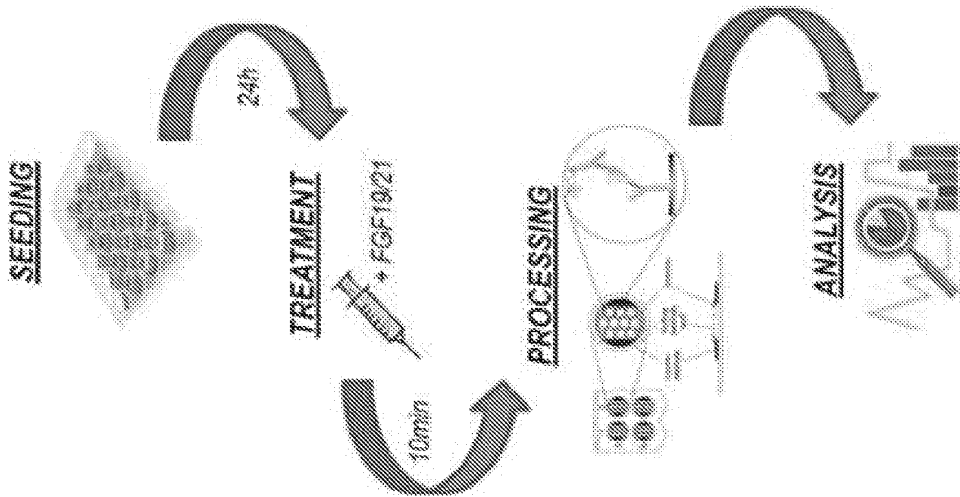
Note: separate studies, not head-to-head comparison
* * % change is calculated based on baseline mean and change from baseline mean; max % change is the max between D8 or D15 & Charles et al. AASLD 2016; BMS data read from figure so not precise.
[^] AMG 876 20100015 Clinical Study Report Synopsis; Akero S-1; data stated as "compared to placebo"

FIG. 14

	BIO89-100*				Madrigal#		Viking^		Intercept^
	Max % chg (D8 or D15)				% chg at D14 **		% chg at D14		% chg at W12
	SAD				MAD		MAD		Phase 2 72W
	Healthy Volunteers				Healthy with LDL > 110		Healthy with ↑ cholesterol		NASH patients
	9.1 mg	18.2 mg	39 mg	78 mg	80mg	100mg	5mg	10mg	25mg
TRIG	-33%	-41%	-45%	-51%	-60%	-44%	-10%	-30%	-6%
LDL	-23%	-21%	-37%	-25%	-28%	-22%	-32%	-45%	21%
HDL	16%	21%	36%	34%	no apparent change; data not presented		"no meaningful trends"		-9%

Note: separate studies, not head-to-head comparison
* % change is calculated based on baseline mean and change from baseline mean; max % change is the max between D8 or D15
Taub et al; Atherosclerosis 2013; Madrigal corporate deck Sept 2017
^FLINT study; Neuschwander-Tetri et al; Lancet 2015; read from figures
** placebo subtracted

FIG. 15



	pERK				
	FGF21 (nM)	Repl1	Repl2	Mean	StDev
FGF21	3000	881	854	867.5	19.1
	600	806	866	836.0	42.4
	120	892	845	868.5	33.2
	24	674	645	659.5	20.5
	4.8	689	686	687.5	2.1
	0.96	701	765	733.0	45.3
	0.192	598	647	622.5	34.5
	0.0384	668	602	635.0	46.7
	0.00768	629	635	632.0	4.2
	0.00154	697	598	647.5	70.0
	0.00031	587	557	572.0	21.2
	0.00006	885	648	766.5	167.6
	vehicle	752	701	726.5	36.1

	pERK				
	BIO89-100 (nM)	Repl1	Repl2	Mean	StDev
BIO89-100	3000	874	997	935.5	66.2
	600	846	907	876.5	33.6
	120	689	837	763.0	88.8
	24	674	884	779.0	123.0
	4.8	598	795	696.5	120.3
	0.96	663	803	733.0	111.4
	0.192	678	667	672.5	37.1
	0.0384	701	694	697.5	19.7
	0.00768	732	804	768.0	84.8
	0.00154	688	709	698.5	53.3
	0.00031	602	664	633.0	68.1
	0.00006	597	689	643.0	48.2
	vehicle	602	667	634.5	42.9

FIG. 16A

FIG. 16B

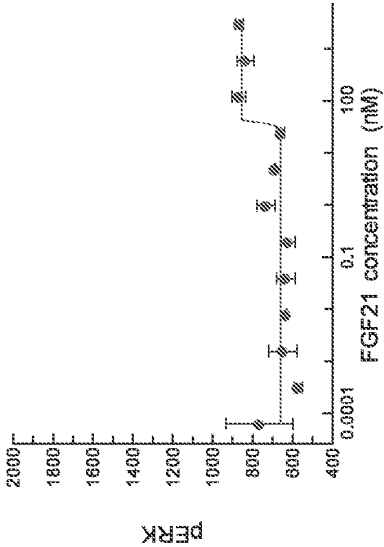
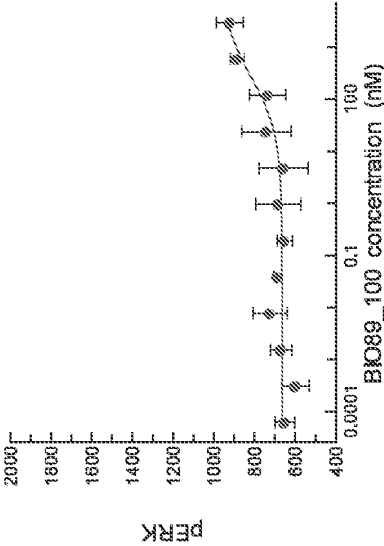


FIG. 16C

FIG. 16D



FGF21	pERK				
	FGF21 (nM)	Repl1	Repl2	Mean	StDev
	3000	4457	4236	4351.5	163.3
	600	4098	4468	4283.0	261.6
	120	3256	4198	3727.0	666.1
	24	3774	3875	3824.5	71.4
	4.8	2845	2275	2560.0	403.1
	0.96	1854	1664	1759.0	134.4
	0.192	1272	1057	1164.5	152.0
	0.0384	978	702	840.0	195.2
BIO89-100	pERK				
	BIO89-100 (nM)	Repl1	Repl2	Mean	StDev
	3000	5534	5013	5191.3	296.8
	600	5024	5667	5385.7	328.9
	120	4989	4426	4577.3	360.7
	24	5015	4780	4858.0	136.0
	4.8	4468	4165	4097	4243.3
	0.96	4071	3350	4136	3835.7
	0.192	2650	2499	3021	2723.3
	0.0384	2049	2106	1866	2007.0
vehicle	pERK				
		Repl1	Repl2	Mean	StDev
		804	507	506	605.7
		836	547	884	755.7
		778	776	800	784.7
		830	709	569	702.7
					130.6

FIG. 17A

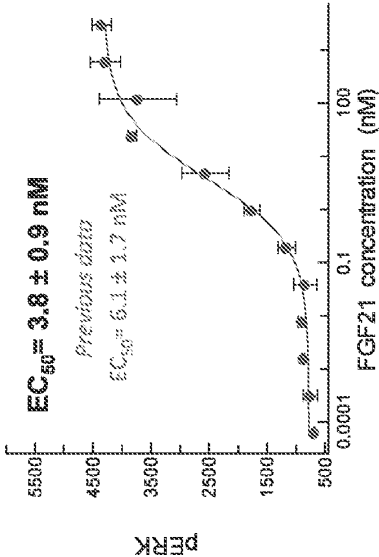


FIG. 17B

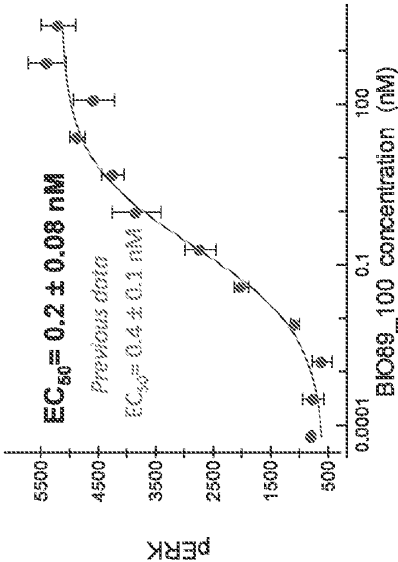


FIG 17C

FIG. 17D

FGF21	pERK				
	FGF21 (nM)	Repl1	Repl2	Mean	StDev
	3000	2278	2178	2228.0	70.7
	600	2331	2236	2283.5	67.2
	120	2045	2336	2190.5	205.8
	24	1823	1975	1899.0	107.5
	4.8	1458	1356	1407.0	72.1
	0.96	1098	1165	1131.5	47.4
	0.192	805	875	840.0	49.5
	0.0384	853	802	827.5	36.1
	0.00768	884	678	781.0	145.7
	0.00154	578	771	674.5	136.5
	0.00031	669	582	625.5	61.5
BIO89-100	pERK				
	BIO89-100 (nM)	Repl1	Repl2	Mean	StDev
	3000	2669	2463	2563.0	103.1
	600	2576	2600	2548.3	69.7
	120	2325	2600	2359.0	225.9
	24	2310	2339	2288.3	64.3
	4.8	1983	2042	2064.7	95.0
	0.96	1502	1658	1603	1587.7
	0.192	935	1146	1021	1034.0
	0.0384	1124	1035	1155	1104.7
	0.00768	988	1102	882	990.7
	0.00154	678	887	836	797.0
	0.00031	884	801	774	819.7
	0.00006	755	772	687	738.0
	vehicle	706	698	768	724.0

FIG. 18A

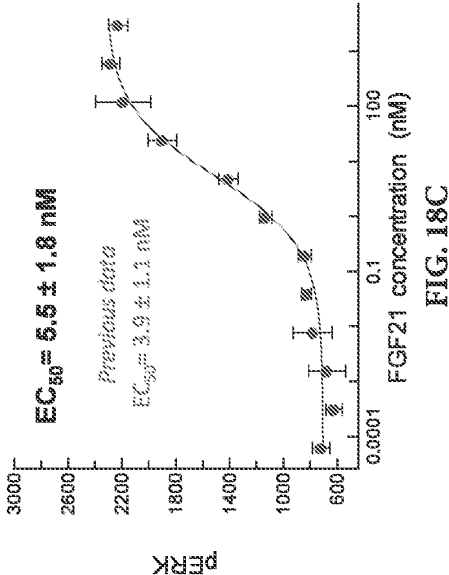


FIG. 18B

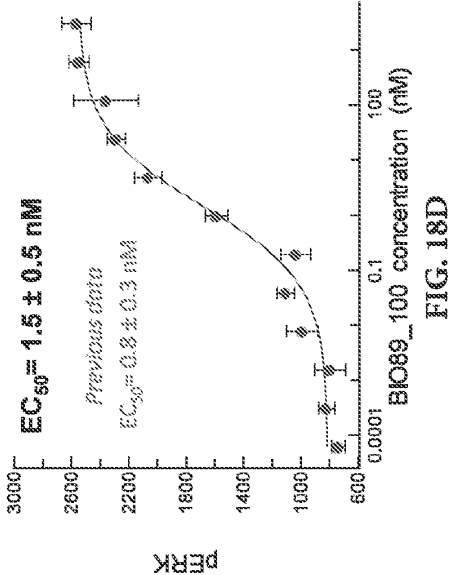


FIG. 18C

FIG. 18D

FGF21	pERK					
	FGF21 (nM)	Rep11	Rep12	Mean	StdDev	
	3000	886	1271	1078.5	272.2	
	600	1008	1013	1010.5	3.5	
	120	1135	924	1029.5	149.2	
	24	954	810	882.0	101.8	
	4.8	678	807	742.5	91.2	
	0.96	667	997	832.0	233.3	
	0.192	647	700	673.5	37.5	
	0.0384	625	657	641.0	22.6	
BIO89-100	pERK					
	BIO89-100 (nM)	Rep11	Rep12	Mean	StdDev	
	3000	678	1078	885.3	200.4	
	600	1006	1021	963.0	86.1	
	120	1423	1001	1090.3	298.2	
	24	998	867	906	923.7	67.3
	4.8	899	904	953	918.7	29.8
	0.96	806	758	669	744.3	69.5
	0.192	978	801	630	803.0	174.0
	0.0384	754	599	974	775.7	189.4
BIO89-100	pERK					
	BIO89-100 (nM)	Rep11	Rep12	Mean	StdDev	
	3000	678	1078	885.3	200.4	
	600	1006	1021	963.0	86.1	
	120	1423	1001	1090.3	298.2	
	24	998	867	906	923.7	67.3
	4.8	899	904	953	918.7	29.8
	0.96	806	758	669	744.3	69.5
	0.192	978	801	630	803.0	174.0
	0.0384	754	599	974	775.7	189.4

FIG. 20A

FIG. 20B

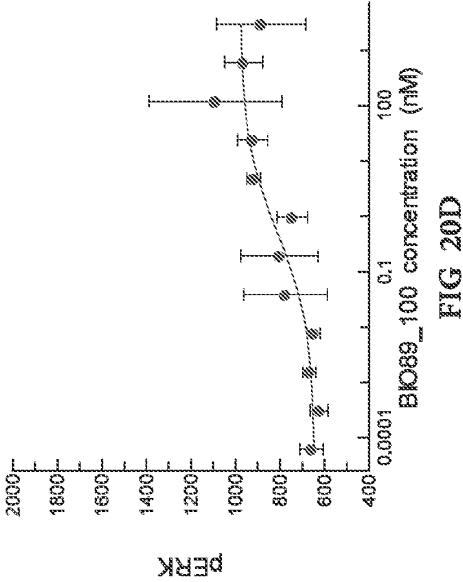
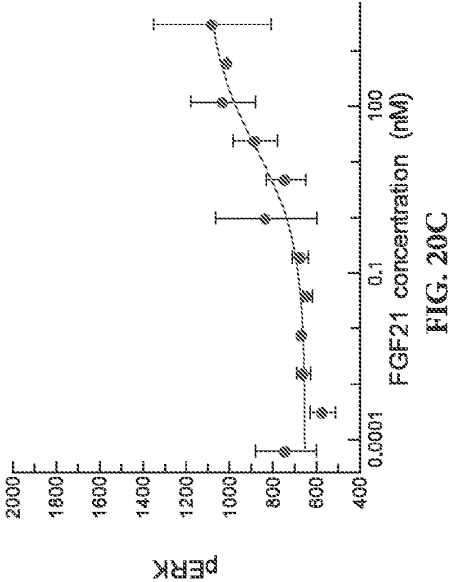


FIG. 20C

FIG. 20D

FIG. 21

Cells	FGF21		BIO89_100	
	EC ₅₀ (nM)		EC ₅₀ (nM)	
	Mean ± StDev		Mean ± StDev	
	Emax (pERK)		Emax (pERK)	
KLB	nd	726	nd	1089
KLB/FGFR1	4,5 ± 1	4277	0,3 ± 0,07	4966
KLB/FGFR2	4,5 ± 0,9	2058	1,1 ± 0,4	2471
KLB/FGFR3	1,8 ± 0,3	2214	1,2 ± 0,4	2770
KLB/FGFR4	nd	969	nd	995

pERK						
FGF19 (nM)	Repl1	Repl2	Repl3	Mean	StdDev	
3000	901	982	991	958.0	49.6	
600	884	924	903	903.7	20.0	
120	874	861	808	847.7	35.0	
24	841	866	852	853.0	12.5	
4.8	808	765	735	769.3	36.7	
0.96	769	784	850	801.0	43.1	
0.192	782	763	721	755.3	31.2	
0.0384	686	654	696	678.7	21.9	
0.00768	604	522	696	604.0	82.0	
0.00154	548	593	633	591.3	42.5	
0.00031	622	673	535	610.0	69.8	
0.00006	657	623	578	619.3	39.6	
vehicle	633	627	501	587.0	74.5	

FIG. 22A

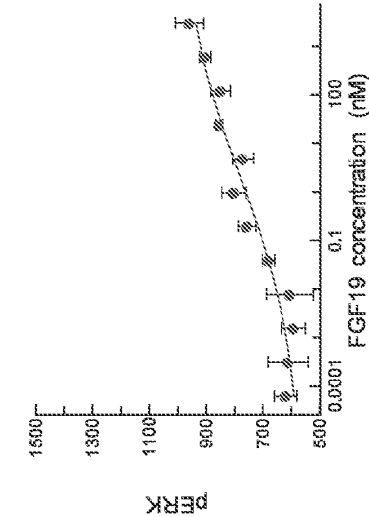
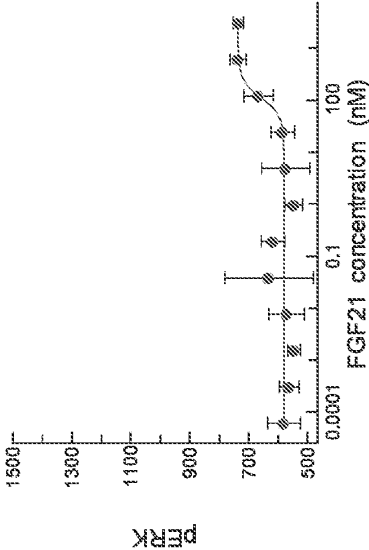


FIG. 22C

pERK						
FGF21 (nM)	Repl1	Repl2	Repl3	Mean	StdDev	
3000	721	730	755	735.3	17.6	
600	735	764	708	735.7	28.0	
120	701	688	609	666.0	49.8	
24	624	586	543	584.3	40.5	
4.8	548	509	666	574.3	81.7	
0.96	542	518	579	546.3	30.7	
0.192	660	611	582	617.7	39.4	
0.0384	525	566	802	631.0	149.5	
0.00768	632	512	568	570.7	60.0	
0.00154	526	547	565	546.0	19.5	
0.00031	556	598	533	562.3	33.0	
0.00006	519	603	622	581.3	54.8	
vehicle	633	627	501	587.0	74.5	

FIG. 22B



pERK Functional Assay in KLB/FGFR1 expressing cells-

FGF19	pERK				
	FGF19 (nM)	Repl1	Repl2	Repl3	Mean StDev
	3000	10034	10002	10831	10289.0 469.7
	600	9884	10332	10147	10121.0 225.1
	120	6541	9551	9531	8541.0 1732.1
	24	6573	6431	6307	6437.0 133.1
	4.8	3573	3415	3307	3431.7 133.8
	0.96	1576	1554	1698	1609.3 77.6
	0.192	1446	1498	1532	1492.0 43.3
	0.0384	798	801	732	777.0 39.0
	0.00768	549	667	598	604.7 59.3
	0.00154	665	687	556	636.0 70.1
	0.00031	637	746	539	640.7 103.5
	0.00006	674	725	648	682.7 39.7
	vehicle	632	661	588	627.0 36.8

FGF19

FIG. 23A

FGF21	pERK				
	FGF21 (nM)	Repl1	Repl2	Repl3	Mean StDev
	3000	4223	4229	3994	4148.7 134.0
	600	4286	3947	4166	4133.0 171.9
	120	3844	3668	3948	3820.0 141.5
	24	3317	3086	2997	3133.3 165.2
	4.8	2501	2188	2384	2357.7 158.2
	0.96	1555	1368	1429	1450.7 95.4
	0.192	1338	1376	1509	1407.7 89.8
	0.0384	760	658	501	639.7 130.5
	0.00768	779	901	632	770.7 134.7
	0.00154	602	548	632	594.0 42.6
	0.00031	668	613	499	593.3 86.2
	0.00006	426	638	754	605.0 166.3
	vehicle	632	661	588	627.0 36.8

FGF21

FIG. 23B

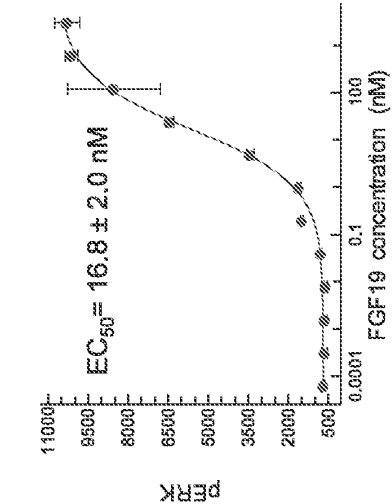


FIG. 23C

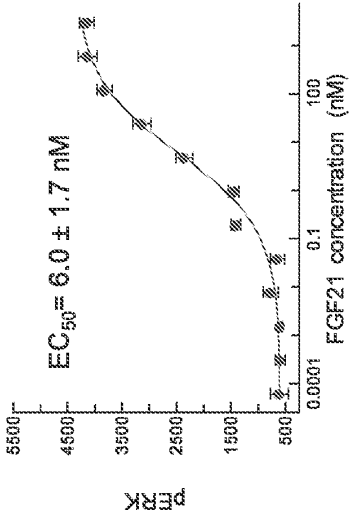


FIG. 23D

Previous data on FGF21
EC₅₀ = 4.2 ± 2.0 nM

	pERK					
	FGF21 (nM)	Rep11	Rep12	Rep13	Mean	StDev
FGF21	3000	2015	1998	1972	1995.0	21.7
	600	1823	1887	1942	1884.0	59.6
	120	2016	1980	1893	1963.0	63.2
	24	1872	1886	1903	1887.0	15.5
	4.8	1354	1276	1183	1271.0	85.6
	0.96	1034	1157	999	1063.3	83.0
	0.192	701	772	803	758.7	52.3
	0.0384	713	732	787	744.0	38.4
	0.00768	602	598	587	595.7	7.8
	0.00154	678	634	553	621.7	63.4
	0.00031	812	645	684	713.7	87.4
	0.00006	772	668	780	740.0	62.5
	vehicle	635	603	499	579.0	71.1

FIG. 24B

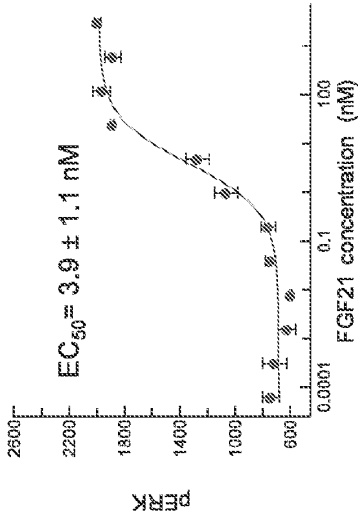


FIG. 24D

Previous data on FGF21
EC₅₀ = 5.3 ± 0.8 nM

	pERK					
	FGF19 (nM)	Rep11	Rep12	Rep13	Mean	StDev
FGF19	3000	1045	1091	1103	1079.7	30.6
	600	972	1131	869	990.7	132.0
	120	1032	998	922	984.0	56.3
	24	852	759	710	773.7	72.1
	4.8	772	723	676	723.7	48.0
	0.96	719	655	623	665.7	48.9
	0.192	690	595	639	641.3	47.5
	0.0384	680	625	596	633.7	42.7
	0.00768	670	658	597	641.7	39.1
	0.00154	721	701	661	694.3	30.6
	0.00031	670	668	605	647.7	37.0
	0.00006	792	774	772	779.3	11.0
	vehicle	635	603	499	579.0	71.1

FIG. 24A

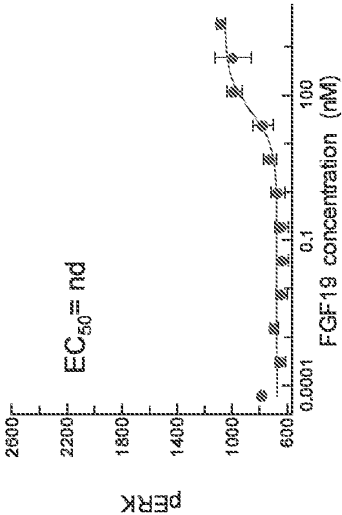


FIG. 24C

FGF21	pERK					
	FGF21 (nM)	Repl1	Repl2	Repl3	Mean	StDev
	3000	1987	1899	2135	2007.0	119.3
	600	2215	2036	1786	2012.3	215.5
	120	1956	2017	2001	1991.3	31.6
	24	1875	1965	1799	1879.7	83.1
	4.8	1688	1880	1729	1755.7	101.1
	0.96	1244	1320	1201	1255.0	60.3
	0.192	901	879	900	893.3	12.4
	0.0384	852	846	803	833.7	26.7
	0.00768	785	800	601	728.7	110.8
	0.00154	658	678	645	660.3	16.6
	0.00031	663	663	801	709.0	79.7
	0.00006	605	578	701	628.0	64.6
	vehicle	645	599	669	637.7	35.6

FIG. 25B

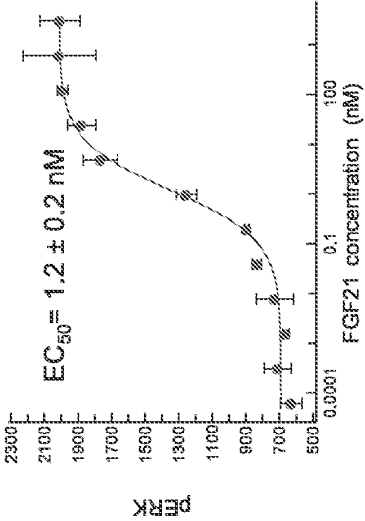


FIG. 25D

Previous data on FGF21
EC₅₀ = 2.4 ± 0.6 nM

FGF19	pERK					
	FGF19 (nM)	Repl1	Repl2	Repl3	Mean	StDev
	3000	2215	2236	2665	2320.0	254.0
	600	2324	2245	2455	2341.3	106.1
	120	2217	2046	2354	2205.7	154.3
	24	2218	1983	2001	2067.3	130.8
	4.8	1747	1755	1802	1768.0	29.7
	0.96	1554	1401	1378	1444.3	95.7
	0.192	1226	1337	1201	1254.7	72.4
	0.0384	997	875	883	918.3	68.2
	0.00768	775	702	687	721.3	47.1
	0.00154	686	557	663	635.3	68.8
	0.00031	662	682	631	658.3	25.7
	0.00006	643	603	547	597.7	48.2
	vehicle	645	599	669	637.7	35.6

FIG. 25A

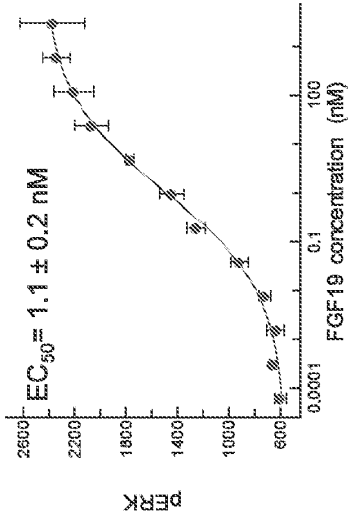


FIG. 25C

pERK						
FGF21 (nM)	Repl1	Repl2	Repl3	Mean	StdDev	
3000	1011	1078	900	996.3	89.9	
600	957	1021	865	947.7	78.4	
120	996	1001	847	948.0	87.5	
24	885	867	906	886.0	19.5	
4.8	1032	904	953	963.0	64.6	
0.96	801	758	689	742.7	67.3	
0.192	689	801	630	706.7	86.9	
0.0384	547	599	674	606.7	63.8	
0.00768	563	683	635	660.3	24.1	
0.00154	598	641	667	635.3	34.8	
0.00031	673	623	583	626.3	45.1	
0.00006	644	667	705	672.0	30.8	
vehicle	549	677	657	627.7	68.9	

FIG. 26B

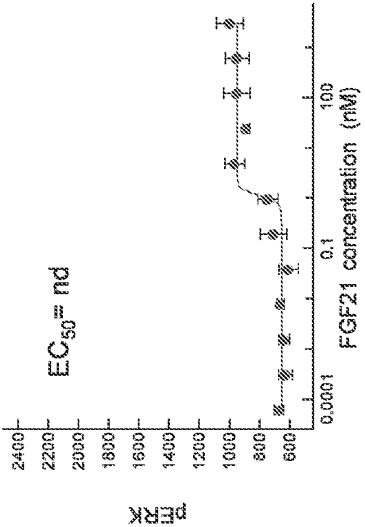


FIG. 26D

pERK						
FGF19 (nM)	Repl1	Repl2	Repl3	Mean	StdDev	
3000	15132	16477	14428	15345.7	1041.1	
600	14655	13305	17889	15283.0	2355.6	
120	15647	15477	12607	14577.0	1708.2	
24	12547	13366	15423	13778.7	1481.7	
4.8	9412	9932	9441	9595.0	292.2	
0.96	8042	8982	6024	7682.7	1511.4	
0.192	2542	2216	2331	2363.0	165.3	
0.0384	1125	1205	1337	1222.3	107.1	
0.00768	874	401	504	593.0	248.7	
0.00154	665	665	998	776.0	192.3	
0.00031	942	701	663	768.7	151.3	
0.00006	695	649	709	684.3	31.4	
vehicle	549	677	657	627.7	68.9	

FIG. 26A

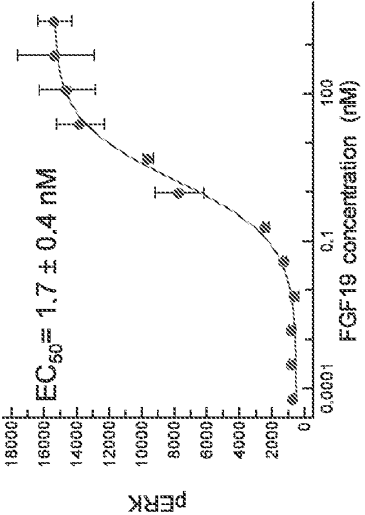


FIG. 26C

	pERK						pERK						pERK					
	EGF (nM)	Rep1	Rep2	Rep3	Mean	StDev	FGF21 (nM)	Rep1	Rep2	Rep3	Mean	StDev	FGF21 (nM)	Rep1	Rep2	Rep3	Mean	StDev
EGF	3000	1464	1250	1346	1353.3	57.7	3000	602	577	559	579.3	11.1	3000	482	501	491.5	6.7	
	600	1320	1248	1359	1309.0	55.6	600	623	596	559	592.7	20.5	600	542	510	526.0	11.3	
	120	1122	1138	1140	1133.3	3.4	120	502	511	490	501.0	10.5	120	410	408	409.0	0.7	
	24	1312	932	1348	1197.3	210.6	24	493	489	451	477.7	19.5	24	472	417	444.5	19.4	
	4.8	705	570	660	645.0	48.2	4.8	406	457	458	440.3	9.9	4.8	444	435	439.5	3.2	
	0.96	570	671	636	625.7	23.8	0.96	438	423	422	427.7	3.0	0.96	396	375	385.5	7.4	
FGF21	0.192	504	521	501	508.7	10.1	0.192	402	486	459	449.0	19.1	0.192	454	351	402.5	36.4	
	0.0384	468	491	373	444.0	59.4	0.0384	441	434	427	434.0	4.0	0.0384	416	466	441.0	17.7	
	0.00768	400	385	373	386.0	7.2	0.00768	409	488	409	435.3	40.2	0.00768	332	303	317.5	10.3	
	0.001536	506	456	581	514.3	62.5	0.001536	353	443	412	402.7	21.1	0.001536	380	365	372.5	5.3	
	0.0003072	424	582	437	481.0	74.3	0.0003072	425	406	443	424.7	18.5	0.0003072	331	321	326.0	3.5	
	0.00006	247	331	313	297.0	17.0	0.00006	412	381	431	408.0	25.0	0.00006	415	334	374.5	28.6	
	vehicle	-	433	441	437.0	4.0	vehicle	-	433	441	437.0	4.0	vehicle	433	441	437.0	2.8	

FIG. 27A

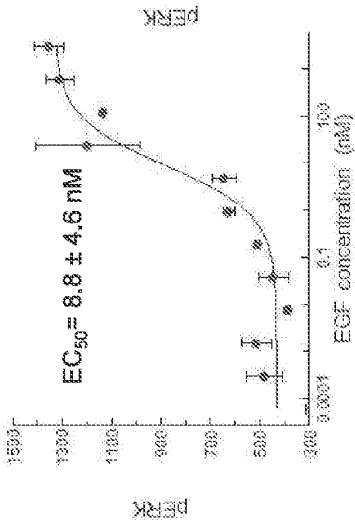


FIG. 27B

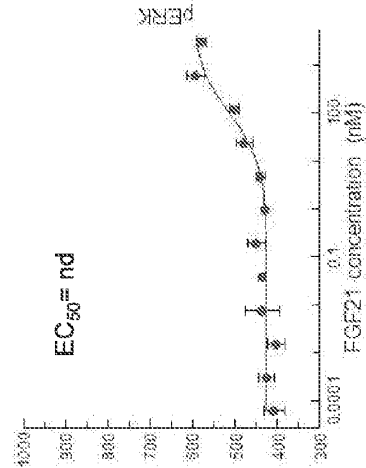


FIG. 27C

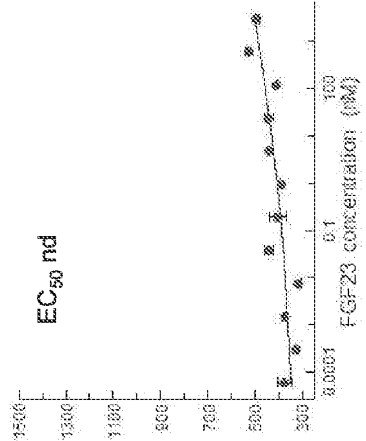


FIG. 27D

FIG. 27E

FIG. 27F

EGF						FGF21						FGF23					
PERK						PERK						PERK					
EGF (nM)	Rep11	Rep12	Rep13	Mean	StDev	FGF21 (nM)	Rep11	Rep12	Rep13	Mean	StDev	FGF23 (nM)	Rep11	Rep12	Mean	StDev	
3000	2230	2342	2300	2290.7	27.3	3000	3856	3412	4033	3767.0	311.6	3000	1331	655	993.0	239.0	
600	2554	2065	2530	2379.7	233.0	600	3624	4034	4974	4210.7	499.6	600	1266	1222	1244.0	15.6	
120	1861	1971	2433	2088.3	240.1	120	4892	4060	3702	4218.0	264.4	120	1370	1120	1245.0	88.4	
24	1987	2013	1804	1934.7	105.6	24	2812	3234	3690	3245.3	260.1	24	896	818	857.0	27.6	
4.8	1360	1150	1254	1254.7	60.2	4.8	2454	2175	2226	2285.3	54.7	4.8	1082	1078	1080.0	1.4	
0.96	1098	1080	1044	1074.0	19.3	0.96	1630	1566	1370	1522.0	102.8	0.96	1098	1074	1086.0	8.5	
0.192	910	801	805	838.7	20.7	0.192	1590	1708	1172	1490.0	269.6	0.192	942	1123	1032.5	64.0	
0.0384	630	692	976	766.0	147.3	0.0384	560	468	614	547.3	73.1	0.0384	864	896	880.0	11.3	
0.00768	858	840	864	854.0	12.1	0.00768	706	672	516	631.3	80.9	0.00768	742	950	846.0	73.5	
0.001536	734	706	392	610.7	161.0	0.001536	604	600	590	598.0	5.3	0.001536	670	642	656.0	9.9	
0.0003072	766	850	808	808.0	24.2	0.0003072	722	588	622	644.0	28.2	0.0003072	846	654	750.0	67.9	
0.00005	570	858	578	668.7	142.9	0.00006	494	390	664	516.0	137.1	0.00006	632	948	790.0	111.7	
vehicle	816	588	688	697.3	60.6	vehicle	614	846	836	765.3	44.0	vehicle	620	888	754.0	94.8	

FIG. 28A

FIG. 28B

FIG. 28C

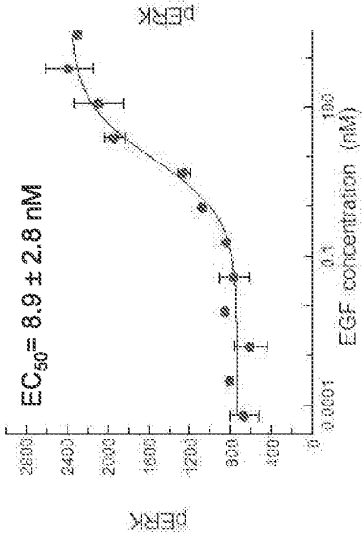


FIG. 28D

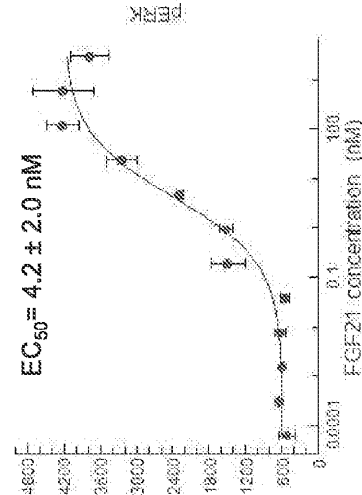


FIG. 28E

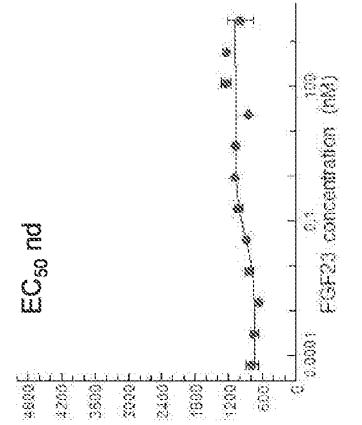


FIG. 28F

EGF						FGF21						FGF23					
PERK						PERK						PERK					
EGF (nM)	Rep1	Rep2	Rep3	Mean	StDev	FGF21 (nM)	Rep1	Rep2	Rep3	Mean	StDev	FGF23 (nM)	Rep1	Rep2	Mean	StDev	
3000	2394	2123	2008	2175.0	85.5	3000	1928	1880	1771	1859.7	58.0	3000	918	1003	960.5	30.1	
600	2542	2411	2781	2578.0	185.3	600	1866	1748	2030	1881.3	141.1	600	686	530	608.0	55.2	
120	2101	2301	2315	2239.0	40.4	120	1766	1944	2094	1934.7	89.4	120	898	688	793.0	74.2	
24	1992	1667	1456	1705.0	134.1	24	1996	1644	2324	1988.0	340.0	24	498	490	494.0	2.8	
4.8	1454	1182	1271	1285.7	52.4	4.8	1375	986	1453	1254.7	234.4	4.8	548	706	627.0	55.9	
0.96	1210	1234	1524	1322.7	148.6	0.96	856	998	1045	966.3	39.6	0.96	846	590	718.0	90.5	
0.192	842	874	866	860.7	6.7	0.192	742	644	724	703.3	41.5	0.192	526	530	528.0	1.4	
0.0384	775	776	819	790.0	21.9	0.0384	802	880	766	816.0	57.1	0.0384	552	566	559.0	4.9	
0.00768	532	599	766	632.3	88.4	0.00768	806	631	776	737.7	75.1	0.00768	568	558	563.0	3.5	
0.001536	543	689	711	647.7	32.2	0.001536	734	771	899	801.3	66.9	0.001536	476	590	533.0	40.3	
0.0003072	944	599	811	784.7	115.5	0.0003072	701	760	667	709.3	45.6	0.0003072	646	626	636.0	7.1	
0.00005	880	782	877	846.3	48.5	0.00005	546	773	870	729.7	71.9	0.00005	614	554	584.0	21.2	
vehicle	665	655	721	680.3	33.3	vehicle	702	699	601	667.3	50.0	vehicle	466	406	436.0	21.2	

FIG. 29A

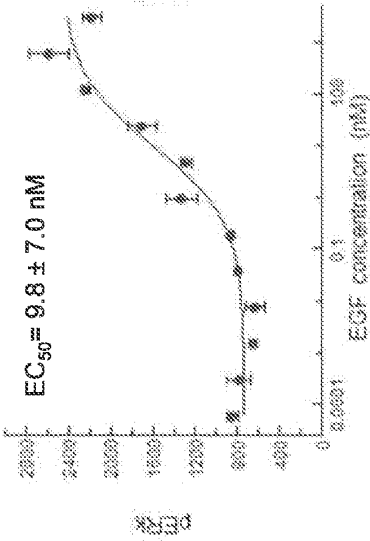


FIG. 29D

FIG. 29B

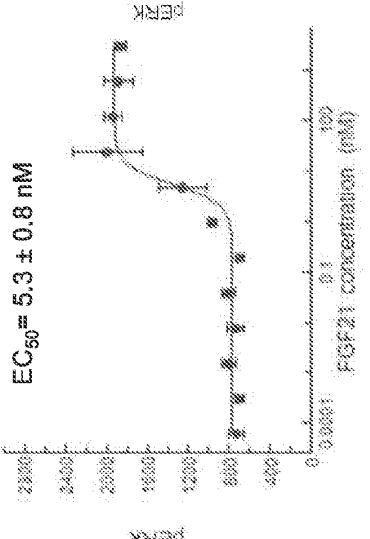


FIG. 29E

FIG. 29C

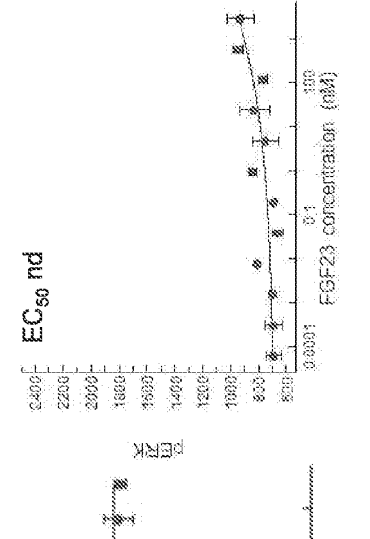


FIG. 29F

PERK						
EGF (nM)	Rep11	Rep12	Rep13	Mean	StDev	
3000	2731	2099	2322	2217.3	111.6	E
600	2011	2183	2210	2134.7	38.2	
120	2550	2435	2591	2525.3	78.3	
24	1811	1788	1891	1830.0	51.8	
4.8	1432	1401	1392	1408.3	8.2	
0.96	1109	1022	1022	1051.0	16.7	G
0.192	861	1012	804	892.3	104.4	
0.0384	701	990	783	824.7	109.5	
0.00768	771	671	772	738.0	51.4	
0.001536	563	810	671	681.3	77.4	
0.0003072	801	735	677	737.7	34.3	F
0.00006	694	621	551	622.0	40.7	
vehicle	667	788	580	678.3	104.1	

PERK						
FGF21 (nM)	Rep11	Rep12	Rep13	Mean	StDev	
3000	1838	2521	2088	2149.0	234.4	FGF21
600	2281	2133	2219	2211.0	47.5	
120	2311	2012	2192	2171.7	98.6	
24	2109	2067	1921	2032.3	76.3	
4.8	1677	1896	1621	1728.0	133.3	
0.96	1191	1033	1088	1104.0	37.2	FGF23
0.192	920	901	1161	994.0	131.7	
0.0384	810	811	991	870.7	91.7	
0.00768	689	701	718	702.7	9.4	
0.001536	666	691	661	672.7	15.1	
0.0003072	781	711	504	665.3	108.8	PERK
0.00006	788	842	801	810.3	21.5	
vehicle	667	788	580	678.3	104.1	

PERK						
FGF23 (nM)	Rep11	Rep12	Rep13	Mean	StDev	
3000	1066	788		927.0	98.3	FGF23
600	899	991		945.0	32.5	
120	719	810		764.5	32.2	
24	981	677		829.0	107.5	
4.8	877	620		748.5	90.9	
0.96	801	881		841.0	28.3	PERK
0.192	671	705		688.0	12.0	
0.0384	609	712		660.5	35.4	
0.00768	817	800		808.5	6.0	
0.001536	721	671		696.0	17.7	
0.0003072	781	604		692.5	62.6	vehicle
0.00006	622	763		692.5	49.9	
vehicle	667	788		727.5	42.8	

FIG. 30A

FIG. 30B

FIG. 30C

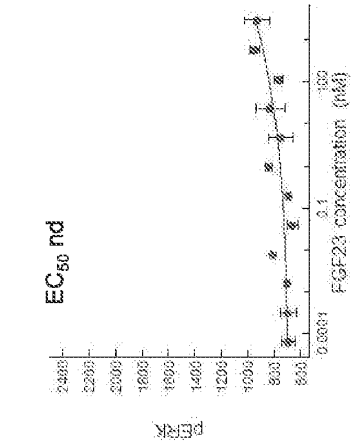
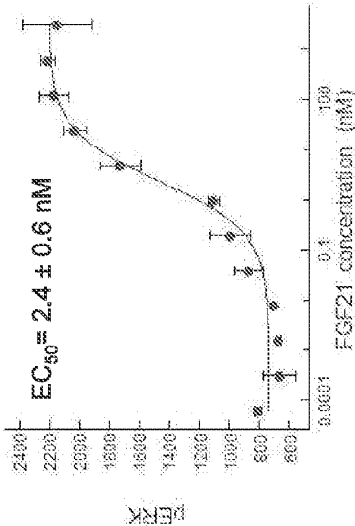
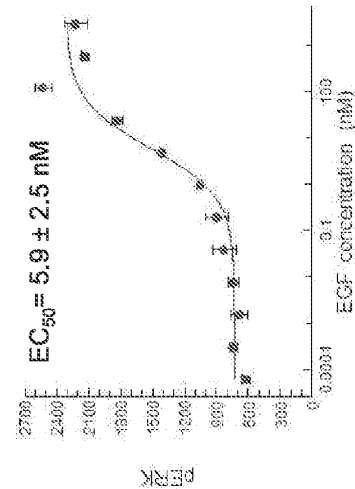


FIG. 30D

FIG. 30E

FIG. 30F

	pERK						pERK					
	EGF (nM)	Rep11	Rep12	Rep13	Mean	StDev	FGF23 (nM)	Rep11	Rep12	Rep13	Mean	StDev
EGF	3000	2230	2005	2310	2181.7	153.1	3000	984	982	901	955.7	41.3
	600	1998	2213	2011	2074.0	103.4	600	898	787	881	855.3	48.6
	120	2217	1992	1779	1996.0	124.1	120	1012	698	905	871.7	111.1
	24	1887	1690	1762	1779.7	47.5	24	910	978	698	862.0	140.7
	4.8	1332	1298	1521	1383.7	112.5	4.8	1001	1011	850	954.0	81.6
	0.96	981	1182	1090	1084.3	54.8	0.96	756	740	671	722.3	35.8
	0.192	801	778	871	816.7	46.7	0.192	655	510	799	654.7	144.5
	0.0384	771	607	584	654.0	35.7	0.0384	658	560	504	574.0	37.0
	0.00768	770	701	771	747.3	35.6	0.00768	600	604	550	584.7	27.4
	0.001536	599	599	581	593.0	9.2	0.001536	544	532	512	529.3	10.9
FGF21	0.0003072	671	501	501	557.7	32.7	0.0003072	491	499	566	518.7	34.4
	0.00006	550	669	685	628.0	22.6	0.00006	533	601	601	578.3	13.1
	vehicle	501	558	601	553.3	26.3	vehicle	501	558	601	553.3	26.3
FGF23												
FGF23												
FGF23												
FGF23												

FIG. 31A

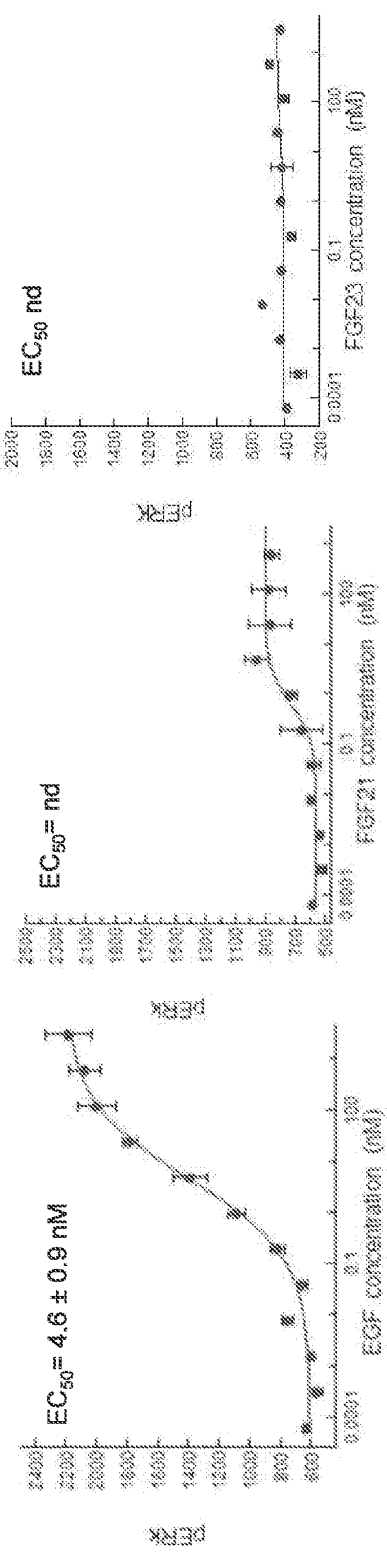
FIG. 31B

FIG. 31C

FIG. 31D

FIG. 31E

FIG. 31F



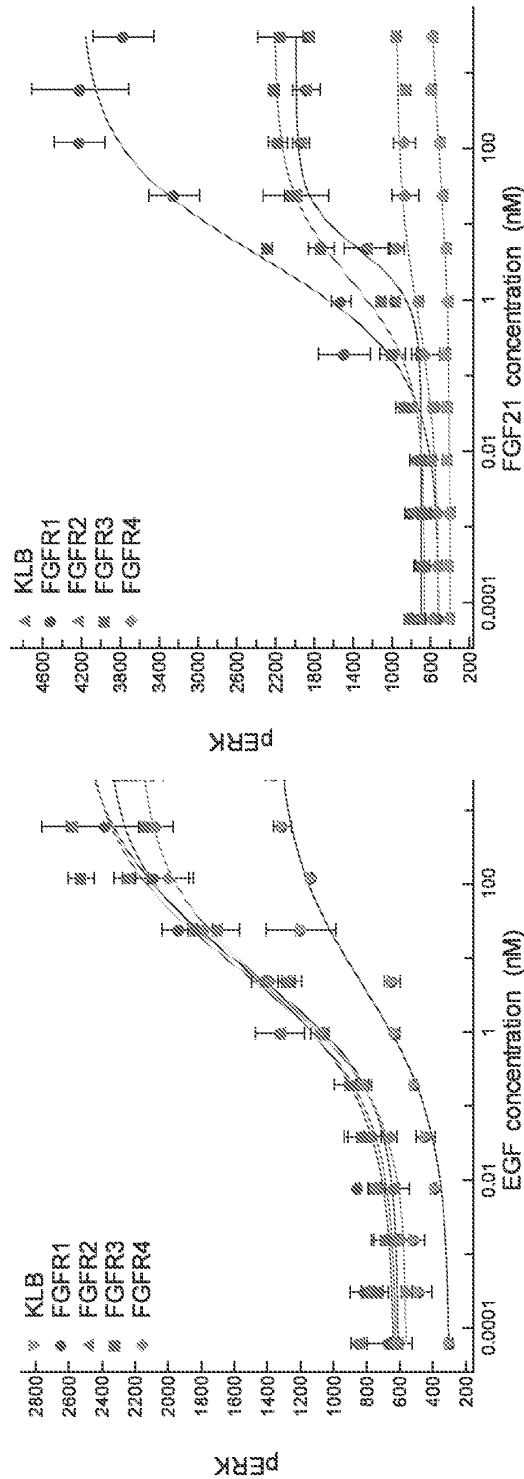


FIG. 32B

FIG. 32A

Receptor	FGF21		EGF	
	EC ₅₀ (nM) Mean ± sd	E _{max} (pERK)	EC ₅₀ (nM)	E _{max} (pERK)
KLB	nd	*602.1	8.8	1331
FGFR1	4.2 ± 2.0	4192	8.9	2364
FGFR2	5.3 ± 0.8	1923	9.8	2461
FGFR3	2.4 ± 0.6	2203	5.9	2307
FGFR4	nd	*901	4.6	2198

*Low E_{max} less than 2-fold of basal level

FIG. 32C

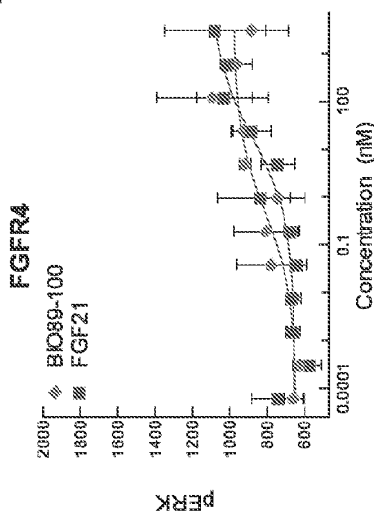
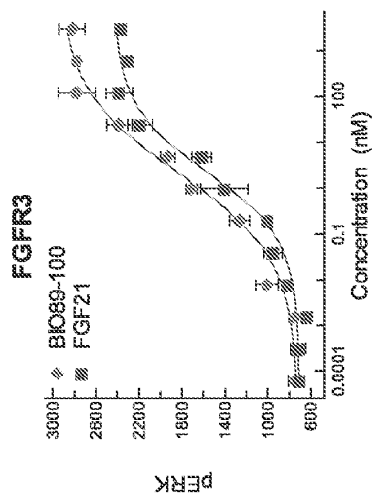
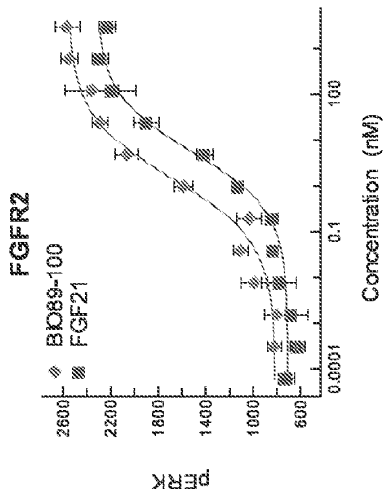
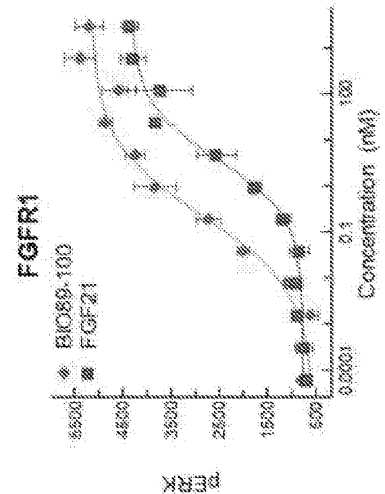
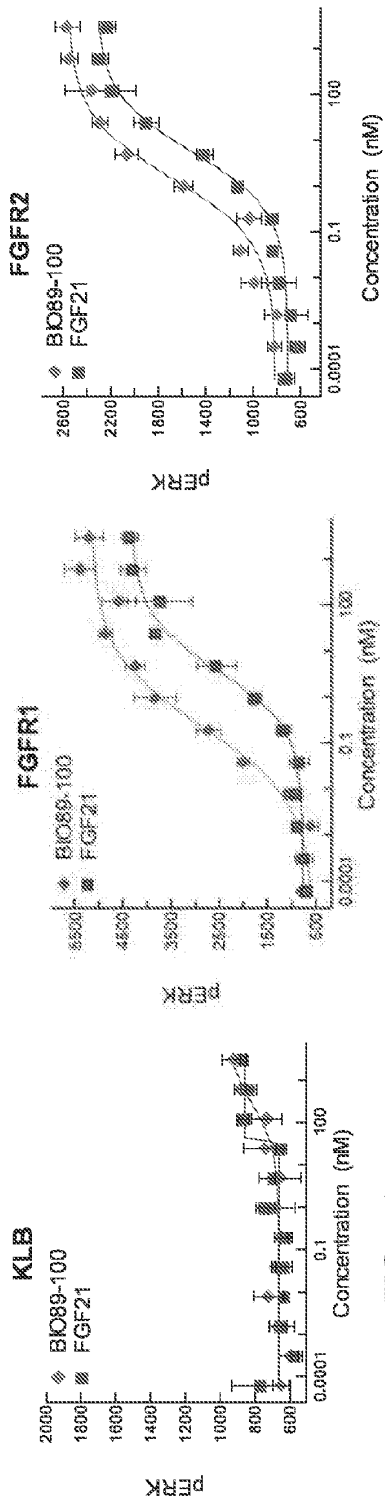
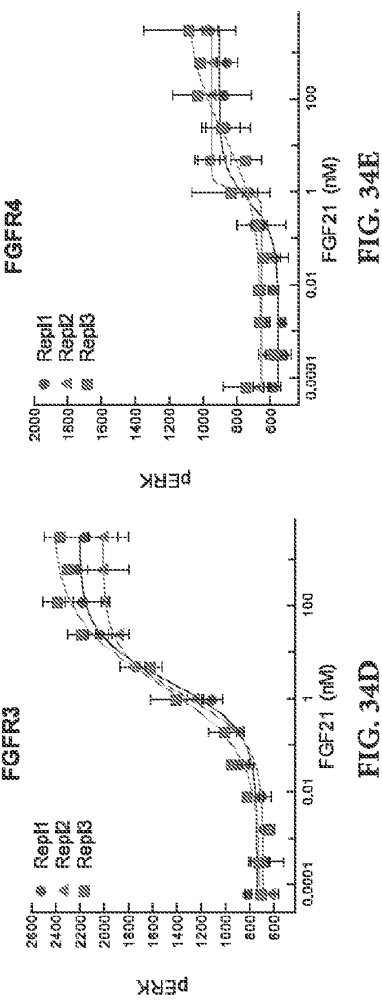
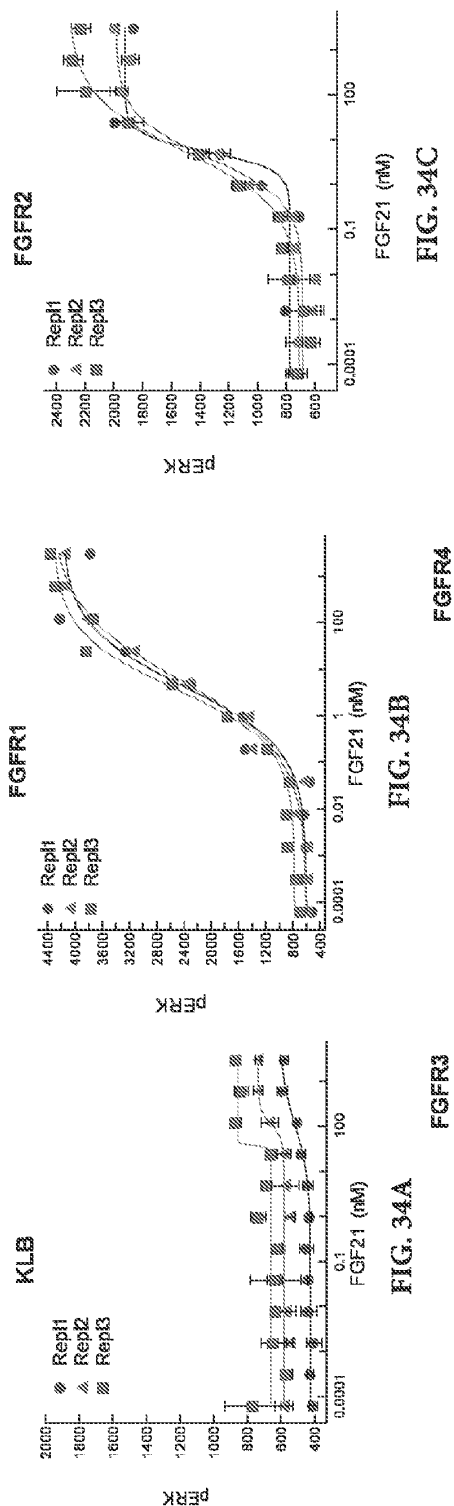


FIG. 33D

FIG. 33E

Receptor	FGF21		BIO89-100	
	EC ₅₀ (nM) Mean ± StDev	E _{max} (pERK)	EC ₅₀ (nM) Mean ± StDev	E _{max} (pERK)
KLB	nd	857	nd	968
FGFR1	3,8 ± 0,9	4313	0,2 ± 0,1	5145
FGFR2	5,5 ± 1,8	2316	1,5 ± 0,5	2553
FGFR3	2,2 ± 0,8	2426	2,1 ± 0,7	2942
FGFR4	nd	1106	nd	980

FIG. 33F



Receptor	FGF21 (Exp1)			FGF21 (Exp2)			FGF21 (Exp3)		
	EC ₅₀ (nM)	Mean ± StDev	E _{max} (pERK)	EC ₅₀ (nM)	Mean ± StDev	E _{max} (pERK)	EC ₅₀ (nM)	Mean ± StDev	E _{max} (pERK)
KLB	nd	nd	602	nd	nd	737	nd	nd	857
FGFR1	4,2 ± 1,9		4192	6,0 ± 1,7		4355	3,8 ± 0,9		4313
FGFR2	5,3 ± 0,8		1923	3,9 ± 1,1		1987	5,5 ± 1,8		2316
FGFR3	2,3 ± 0,6		2203	1,2 ± 0,2		2010	2,2 ± 0,8		2426
FGFR4	0,6 ± 0,3		901	nd		948	nd		1106

FIG. 34F

FGF21 (nM)	KLB		FGFR1		FGFR2		FGFR3		FGFR4	
	Mean	StDev	Mean	StDev	Mean	StDev	Mean	StDev	Mean	StDev
3000	727.4	144.2	4089.1	296.8	2027.6	186.3	2172.8	178.9	1010.2	62.6
600	721.4	122.3	4208.9	75.0	2016.3	231.4	2173.8	146.4	937.8	78.0
120	678.5	184.1	3921.7	260.8	2029.4	140.2	2181.3	195.0	949.7	78.9
24	573.8	91.4	3401.1	371.0	1924.7	55.2	2033.0	153.7	876.7	12.9
4.8	567.4	123.7	2401.0	142.4	1310.9	83.6	1702.4	79.3	886.5	124.8
0.96	569.0	153.9	1577.2	161.4	1053.7	83.0	1254.0	149.5	765.7	58.3
0.192	563.1	98.8	1354.1	169.2	767.3	68.7	962.9	60.4	678.3	26.3
0.0384	586.7	114.9	675.7	149.6	795.8	45.3	884.3	58.6	607.2	33.5
0.00768	546.0	100.6	765.2	131.7	704.8	96.9	749.4	59.9	637.0	45.4
0.001536	532.1	123.0	686.5	156.8	699.2	97.3	656.3	18.7	607.7	68.9
0.0003072	519.7	82.4	662.8	80.5	682.8	49.7	697.4	28.2	571.8	53.8
0.00006	585.3	179.3	602.2	84.3	729.6	10.5	713.6	91.7	663.8	81.6
vehicle	583.5	144.8	703.8	70.4	642.9	55.9	665.2	23.8	592.7	37.4

FIG. 35A

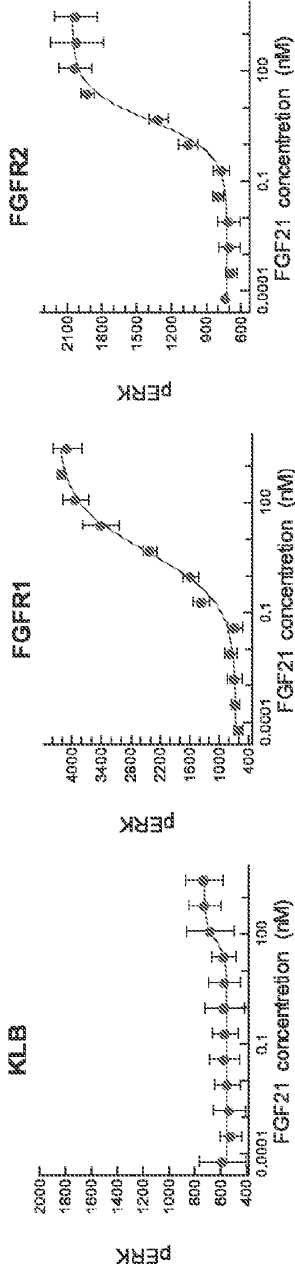


FIG. 35B

FIG. 35C

FIG. 35D

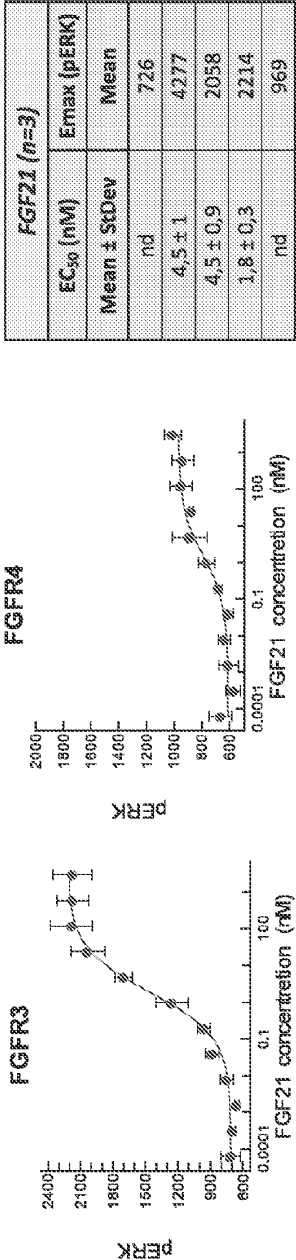
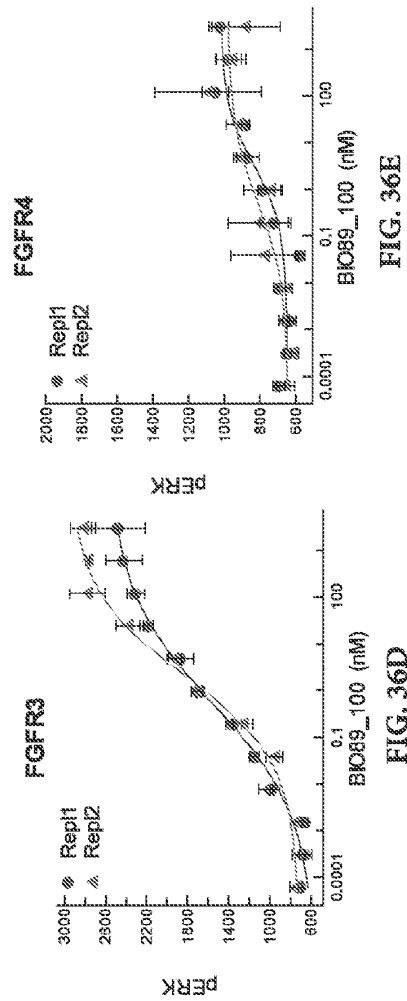
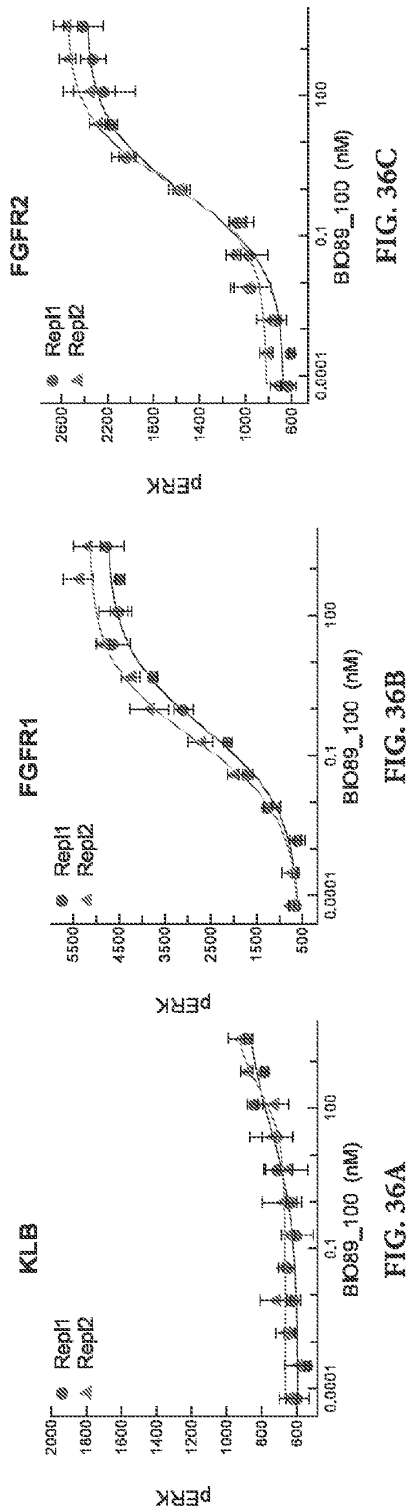


FIG. 35E

FIG. 35F

FIG. 35G

FGF21 (n=3)		
EC ₅₀ (nM)	Emax (pERK)	
Mean ± StDev	Mean	
nd	726	
4.5 ± 1	4277	
4.5 ± 0.9	2058	
1.8 ± 0.3	2214	
nd	969	



Receptor	BIO89_100 (Exp1)		BIO89_100 (Exp2)	
	EC ₅₀ (nM) Mean ± StDev	E _{max} (pERK)	EC ₅₀ (nM) Mean ± StDev	E _{max} (pERK)
KLB	nd	899	nd	968
FGFR1	0,4 ± 0,1	4765	0,2 ± 0,1	5145
FGFR2	0,8 ± 0,3	2386	1,5 ± 0,5	2553
FGFR3	0,5 ± 0,2	2569	2,1 ± 0,7	2942
FGFR4	nd	1020	nd	980

FIG. 36F

BIO89_100 (nM)	KLB		FGFR1		FGFR2		FGFR3		FGFR4	
	Mean	StDev	Mean	StDev	Mean	StDev	Mean	StDev	Mean	StDev
3000	898.2	30.4	4974.3	53.4	2486.2	47.4	2646.2	95.5	954.3	107.3
600	833.5	9.7	4929.2	163.0	2435.7	28.6	2597.3	111.8	969.7	11.8
120	785.3	30.8	4535.5	122.0	2292.8	30.2	2542.3	62.1	1070.9	157.4
24	724.8	25.9	4741.8	170.0	2223.7	14.7	2282.2	48.7	902.3	30.6
4.8	680.5	27.7	3992.3	84.3	2045.7	15.1	1897.7	40.6	894.5	25.2
0.96	657.2	57.7	3460.2	149.2	1572.2	3.4	1705.7	8.0	765.0	24.9
0.192	623.5	36.9	2422.8	126.2	1049.7	25.0	1307.3	12.8	762.3	68.0
0.0384	666.3	7.9	1850.3	12.2	1031.0	61.5	1051.7	29.8	675.3	115.2
0.00768	670.8	32.4	1163.2	0.1	971.5	46.1	994.3	63.0	669.7	3.3
0.001536	653.5	14.3	603.3	79.8	756.5	23.9	700.3	20.7	651.3	4.3
0.0003072	567.5	37.0	705.3	92.1	709.7	21.8	686.2	0.2	634.5	14.6
0.00006	623.7	12.1	707.0	31.2	679.3	10.2	722.2	26.1	676.0	12.6
vehicle	618.8	22.4	664.8	66.4	651.5	23.2	672.5	18.4	646.8	20.7

FIG. 37A

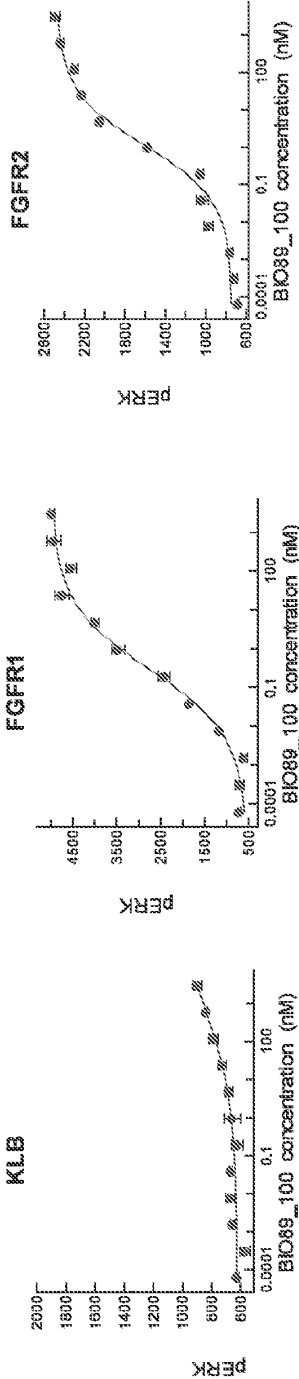


FIG. 37B

FIG. 37C

FIG. 37D

BIO89_100 (n=2)		
EC ₅₀ (nM)	E _{max} (pERK)	
Mean ± StDev	Mean	
nd	1089	
0.3 ± 0.07	4966	
1.1 ± 0.4	2471	
1.2 ± 0.4	2770	
nd	995	

FIG. 37E

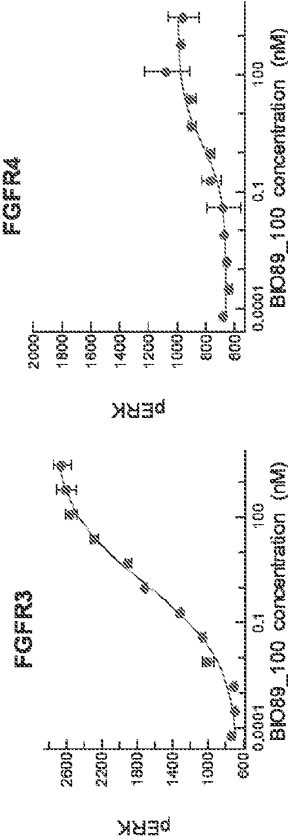


FIG. 37F

FIG. 37G

FIG. 38A

Phase 1b/2a NASH Trial Design

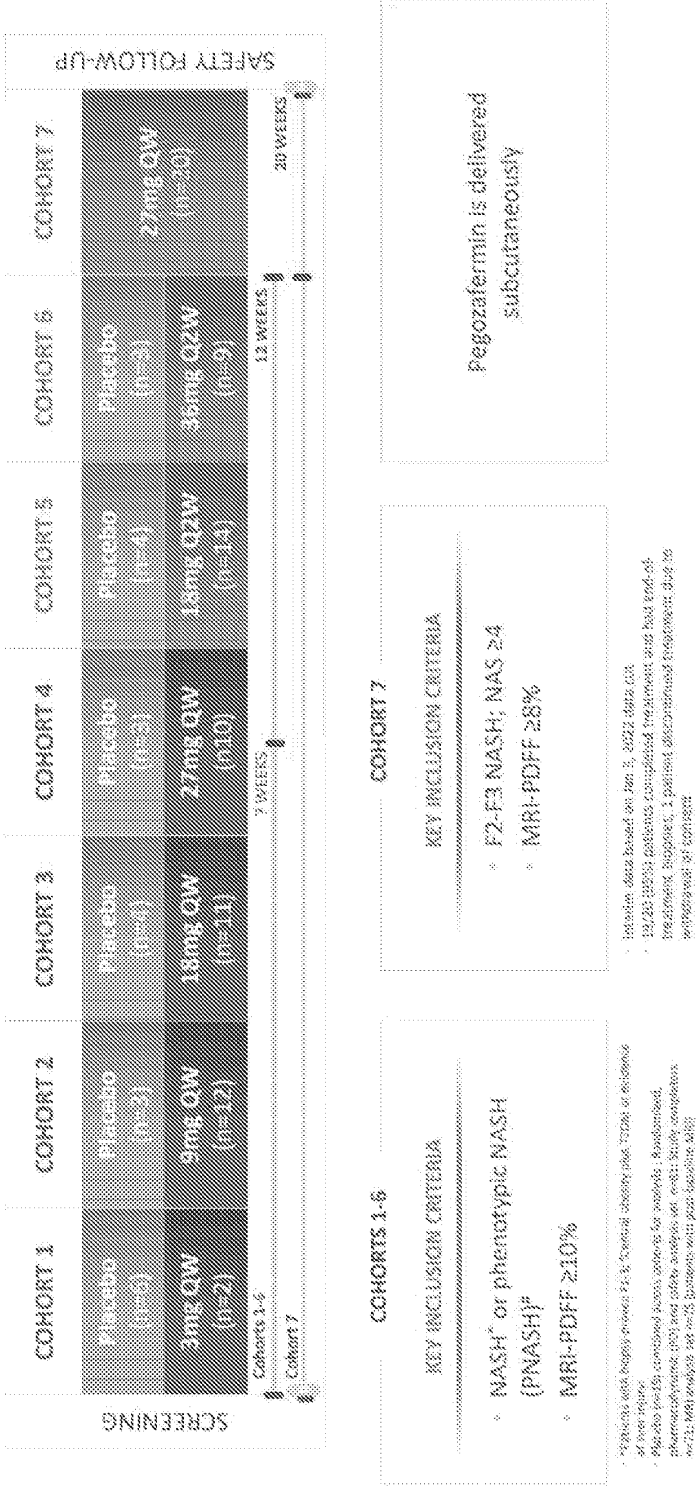


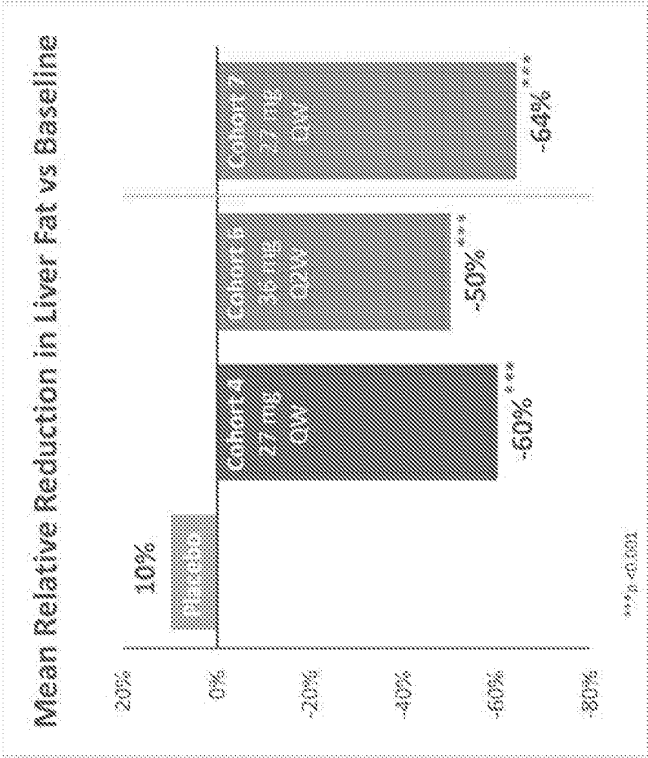
FIG 38B

Baseline Characteristics

Parameter (Mean or %)	Cohorts 1-6 (n=71)	Cohort 7 (n=20)
Age (years)	51.9	58.4
Female	61.7%	75.0%
Weight (kg)	93.6	104.6
BMI (kg/m ²)	34.6	37.0
Type 2 Diabetes	45.7%	85.0%
% F2 / % F3	NA	35% / 65%
NAS	NA	5.3
MRI-PDFF (%)	21.3	21.1
ALT (U/L)	41.5	47.1
AST (U/L)	31.0	36.1
Pro-C3 (ng/ml)	11.9	19.3
VCTE (kPa)	7.3	14.3
Triglycerides (mg/dL)	174.3	170.0

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FIG. 39A



Cohort 4 and Cohort 6: Mean Analysis: SGLT Inhibitor LS Means: p values vs placebo. Data from week 13.
Cohort 7: SGLT Analysis: SGLT p value for change from baseline based on 10-fold analysis; Data from week 20

FIG. 39B

	≥30% Relative Reduction in Liver Fat	≥50% Relative Reduction in Liver Fat
Cohort 4	86%	71%
Cohort 6	88%	50%
Cohort 7	100%	78%

FIG. 40A

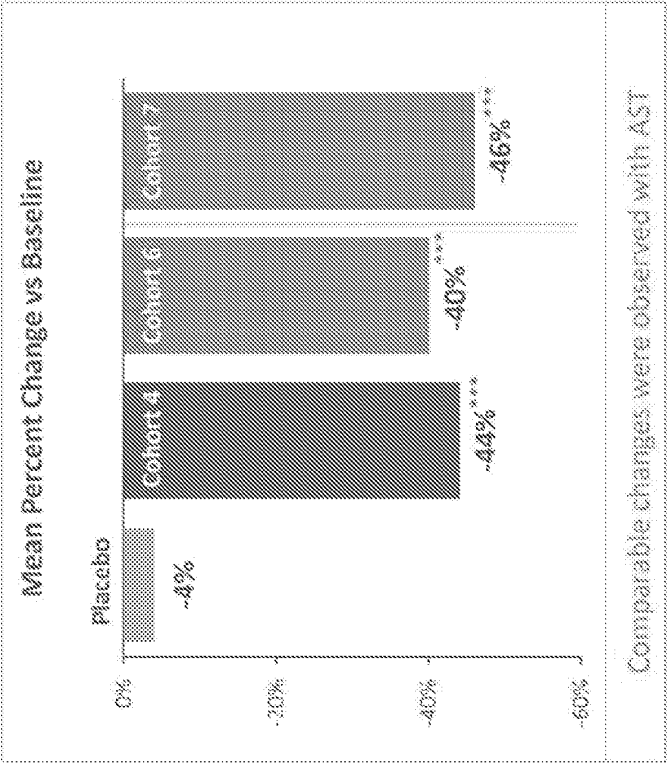


FIG. 40B

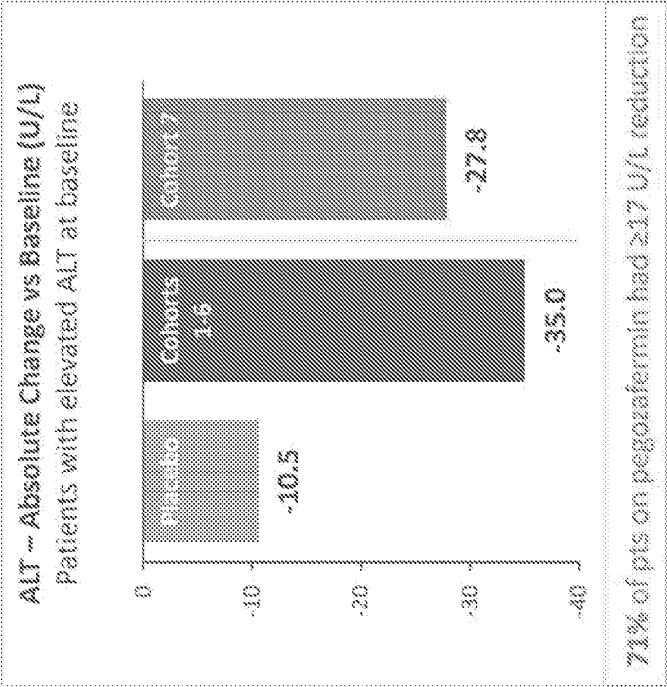


FIG. 41A

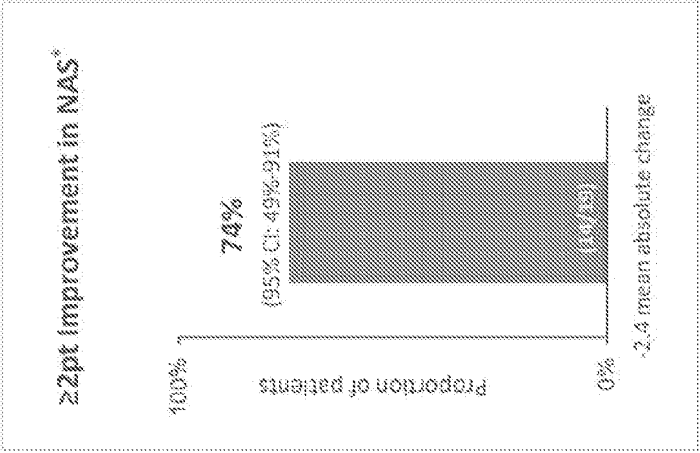
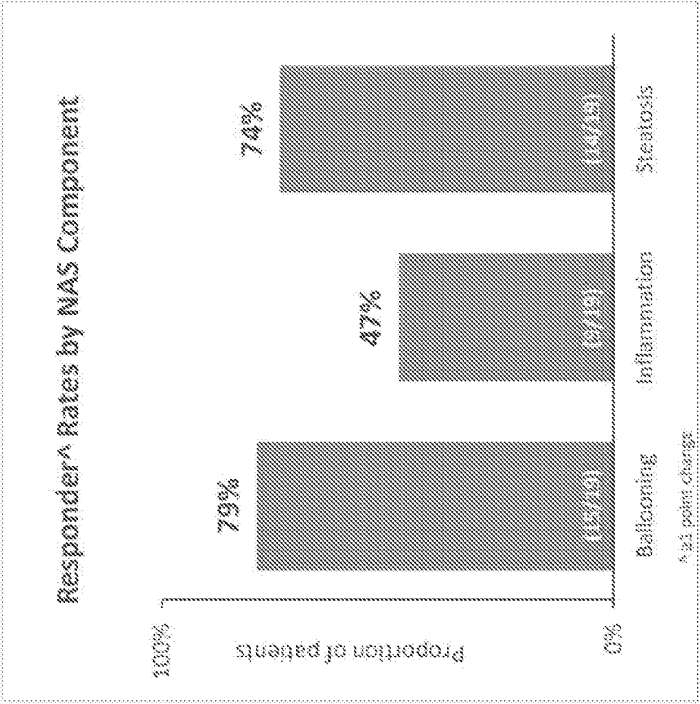


FIG. 41B



* with ≥2 point improvement in ballooning or inflammation

FIG. 42

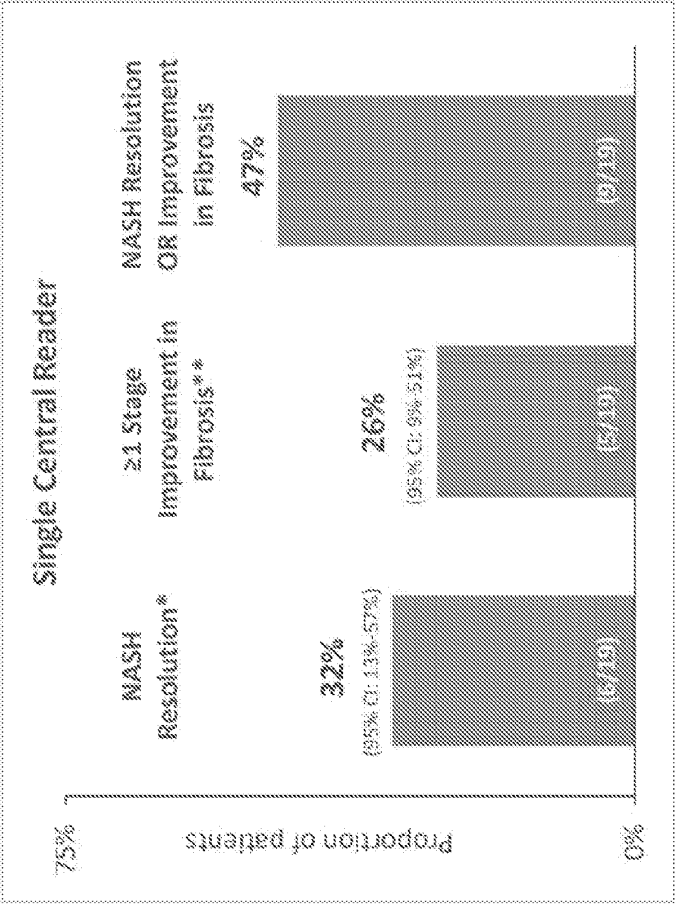


FIG. 43A

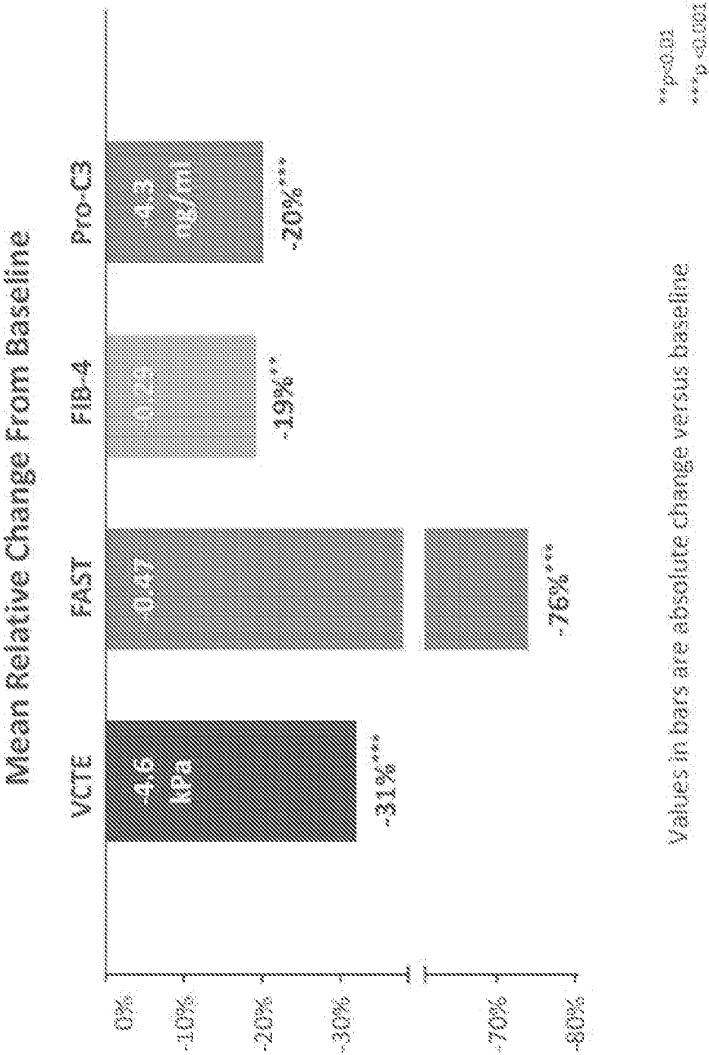


FIG. 43B

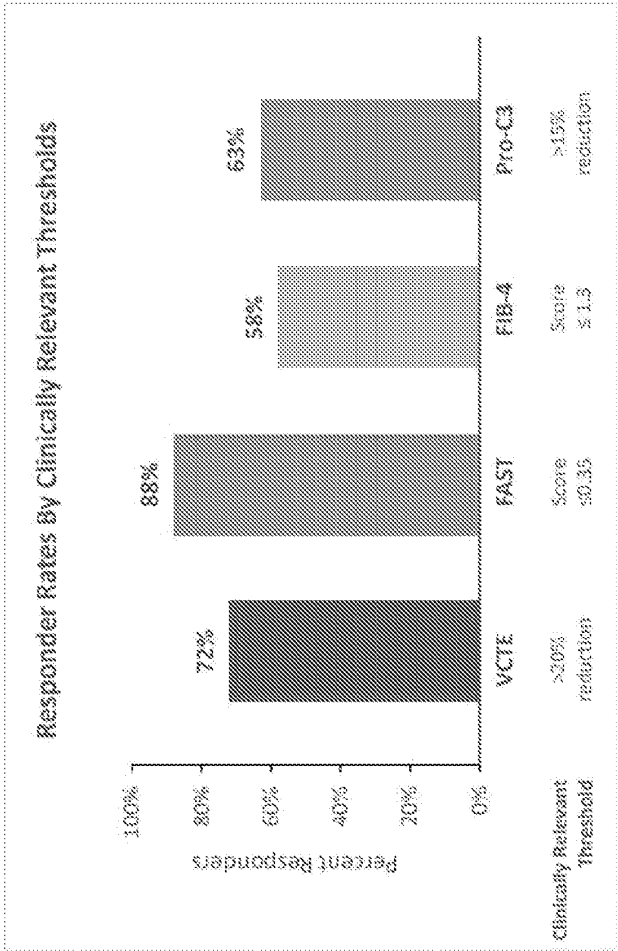


FIG. 44A

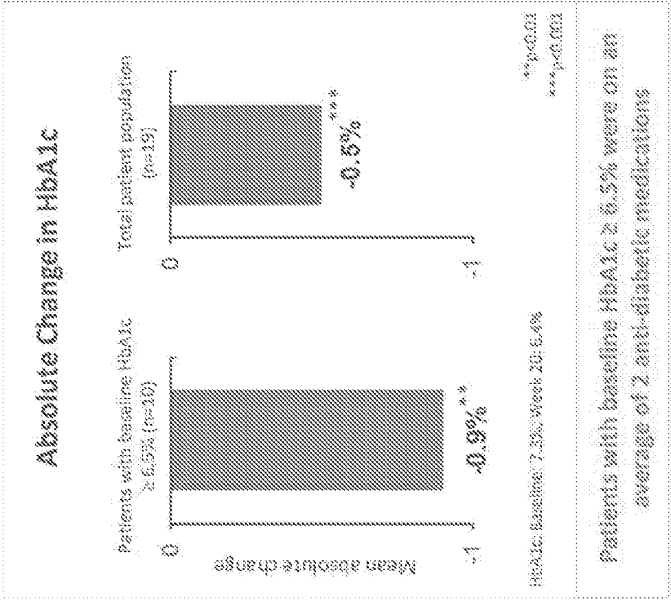


FIG. 44B

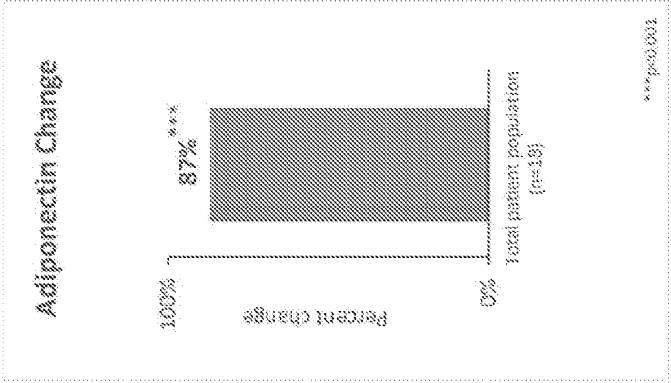
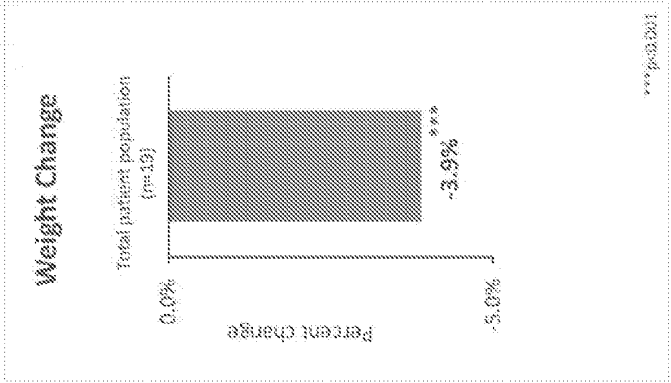


FIG. 44C



p value for change from baseline based on MANOVA analysis; all data are from cohort 1

FIG. 45

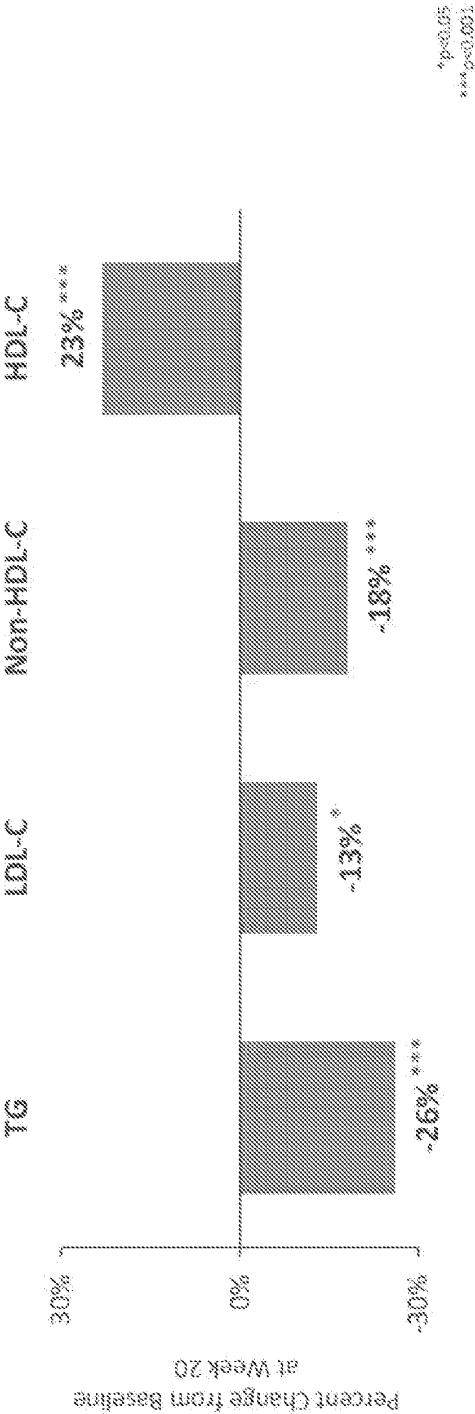


FIG. 47

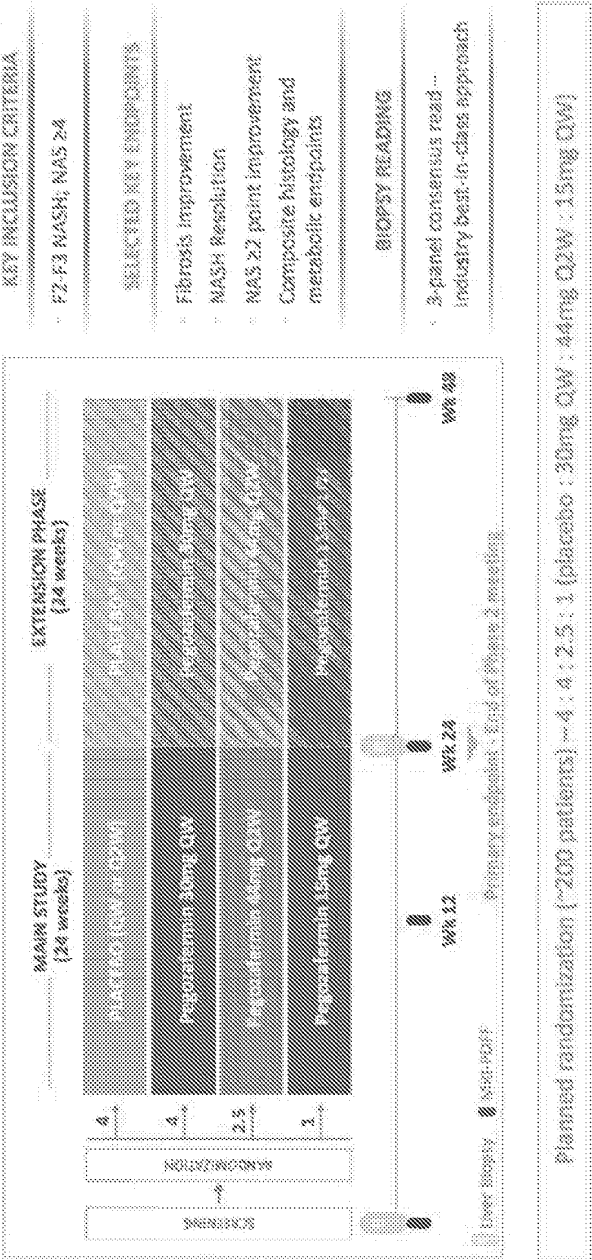


FIG. 48

per week.

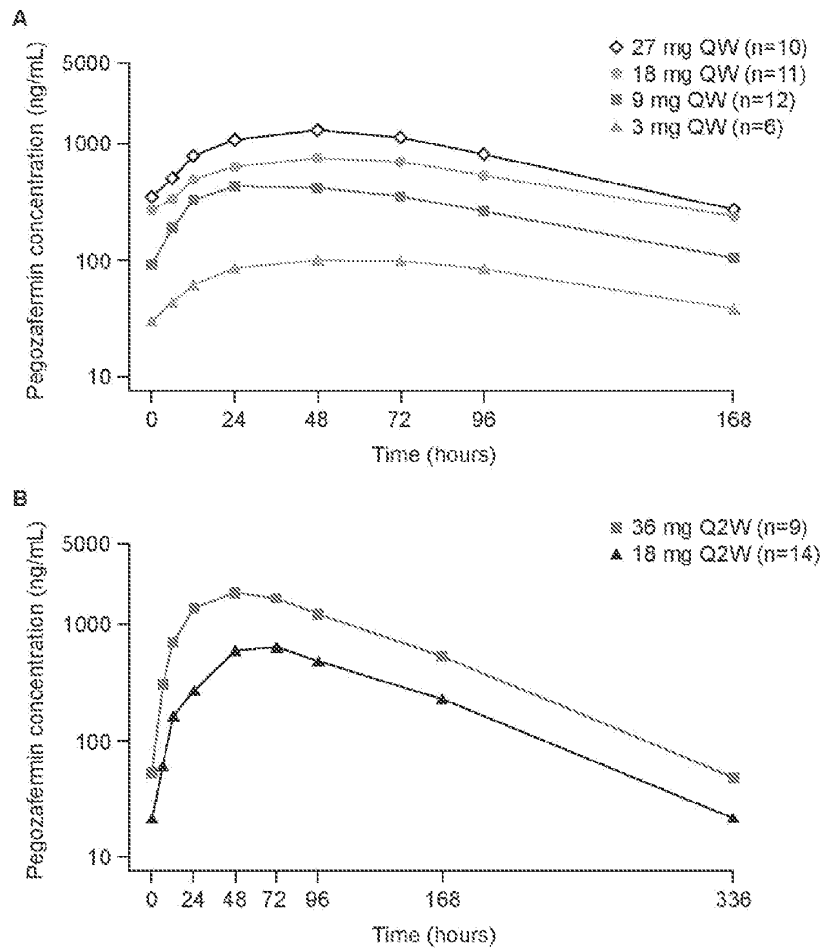


FIG. 49

every week.

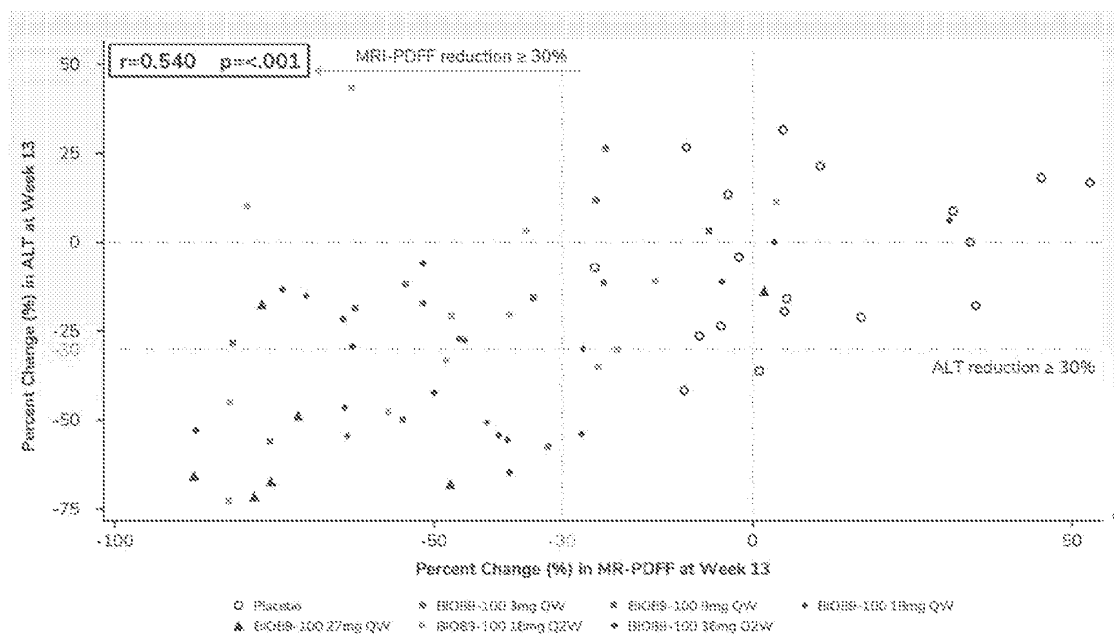


FIG. 50

	Placebo (n=18)	Pegozafermin						
		3 mg QW (n=5)	9 mg QW (n=11)	18 mg QW (n=10)	27 mg QW (n=7)	18 mg Q2W (n=13)	36 mg Q2W (n=8)	Pooled (n=54)
≥30% relative reduction from baseline at week 13								
n (%)	0 (0·0)	3 (60·0)	9 (81·8)	6 (60·0)	6 (85·7)	9 (69·2)	7 (87·5)	40 (74·1)
95% CI ^a	..	(22·6, 88·5)	(51·8, 95·0)	(30·9, 83·5)	(47·9, 97·5)	(42·0, 87·5)	(52·2, 97·8)	(54·8, 83·9)
p value ^b	..	0·0056	<0·0001	0·0006	<0·0001	<0·0001	<0·0001	<0·0001
≥50% relative reduction from baseline at week 13								
n (%)	0 (0·0)	1 (20·0)	6 (54·5)	5 (50·0)	5 (71·4)	5 (38·5)	4 (50·0)	26 (48·1)
95% CI ^a	..	(-1·10, 63·2)	(27·7, 79·0)	(23·3, 76·7)	(35·3, 92·0)	(16·7, 64·8)	(21·1, 78·9)	(28·8, 61·2)
p value ^b	..	0·22	0·0010	0·0026	0·0004	0·0076	0·0047	0·0001

CI=confidence interval. MRI=magnetic resonance imaging. MRI-PDFF=magnetic resonance imaging proton-density fat fraction.
PD=pharmacodynamic. Q2W=once every 2 weeks. QW=once per week.

^aScore (Miettinen–Nurminen) 95% CI.

^bp value versus placebo from Fisher's exact test.

FIG. 51

Amendment No. (Date of Approval (reference: MOD0063302 1)	Key Details of the Amendment
Amendment No. 1.0, 29 June 2019	- Objectives/endpoints relating to PD assessments were modified in Section 1.1 Synopsis and the Section 3 Objectives and Endpoints. - Cohort 3 (18 mg weekly) was added in Section 1.1 Synopsis, Section 4 Study Design, Section 6.1 Study Intervention Administered, and as a global change. - Sample size was updated in the Section 1.1 Synopsis, Section 4 Study Design, and Section 9.2 Sample Size Determination. - Stratification by biopsy-confirmed NASH with fibrosis status of F1, F2, and F3 in the 18 mg QW and 18 mg Q2W cohorts was added in the Section 1.1 Synopsis, Section 4 Study Design, and Section 6.4 Measures to Minimize Bias: Randomisation. - Clarification that endogenous FGF21 levels were to be collected at Baseline for all subjects and were to be repeated only in ADA-positive subjects at 3-5 months after EOS for potential analysis in Section 1.2 Synopsis, Section 1.3 SOA, Section 2 Study Design, and Section 8.6.1 Immunogenicity Assessments. - Each domicile period was shortened to a 2 overnight stay in Section 1.2 SOA. Prior errors and formatting were corrected. - Emerging data from the SAD study and recent publications were included in Section 2.2.3 Background and Section 2.3.1 Risk Assessment. - Repeat screening measurements were added and the eligibility criterion for ALT/AST was refined in Section 5.2 Exclusion Criteria. - Section 6.7.1 on monitoring suspected DILI was revised. - Text related to secondary objectives on selected markers in Section 9.1 Statistical Hypotheses was revised. - Formatting, style, typos, and glossary, were updated, and consistency was checked to align across protocol sections as global changes.
Administrative Letter #1, 19 July 2019	The glucose drink given to subjects was amended from a 75-gram, 7.5 oz. size to a 75-gram, 10 oz size.

Amendment No. (Date of Approval (reference: MOD0063302 1)	Key Details of the Amendment
Administrative Letter #2, 19 July 2019	The SOA was changed to include an “X” for IGF-1 on Day 50 for Cohorts 5 and 6.
Amendment No. 2, 09 February 2020	- Follow-up procedures for subjects who tested positive for neutralizing antibodies to BIO89-100 were clarified in Section 2.3.1.1 Potential Risk: Immunogenicity and Section 8.6.1 Immunogenicity Assessments. - Neutralizing immunogenicity was added to ADA objectives/endpoints and corresponding analysis in Section 1.1 Synopsis, Section 3 Objectives and Endpoints and Section 9.4.3 Immunogenicity Analyses. - Optional percutaneous liver biopsy, a clarified definition of T2DM and central obesity, and a revision of pregnancy and contraception inclusion criterion number 5 were added to Section 5.1 Inclusion Criteria. - Section 5.2 Exclusion Criteria were clarified. - The use of CYP3A during the study was clarified in Section 6.6 Concomitant Therapy. - Sampling collection procedures for urine drug tests on Day -1 were clarified, and tests previously missing were added to Appendix 2 Clinical Laboratory Tests. - The definition of women who were not of childbearing potential (NCBP) was clarified and pregnancy was clarified as a mandatory criterion for permanent discontinuation of study intervention in Appendix 4 Contraception Guidance and Section 7.2 Subject Discontinuation/Withdrawal from Study. - Section 1.2 SOA and corresponding footnotes were updated to align with changes in the protocol. - Editorial, consistency, and formatting changes were made as global changes.
Administrative Letter #3, 19 March 2020	- Contraceptive requirements for presumptive fertile male subjects who were partnered with women who were NCBP, either post-menopausal or through sterilization or other surgical procedures, were clarified as follows: - Men were to confirm that their partners were determined to be sterile or post-menopausal based on medical judgment; this could be confirmed either by statement or medical records, if presented by the subject. - Men were not required to use other contraceptives when sexually active with a sterile or post-menopausal partner.

Amendment No. (Date of Approval (reference: MOD0063302 1)	Key Details of the Amendment
	○ Men who were sexually active with fertile women needed to confirm that they would use 2 forms of contraceptives as per protocol.
Amendment No. 3.0, 25 March 2020	• Actions were added to address the potential disruptions to the study due to the COVID-19 pandemic in Section 1.1 Synopsis and Section 4 Study Design. • Fibroscan assessments were added to Day 50 and Day 92/ET study visits in Section 1.2 SOA and Section 8.6.2 Pharmacodynamics. • Fibroscan CAP score and Fibroscan VCTE score were added as exploratory endpoints in Section 3 Objectives and Endpoints. • Inclusion criterion #7 (Section 5.1, Appendix 4) was clarified to state that male subjects who were sexually active with female partners who were not of a childbearing potential (postmenopausal or surgically sterile) were to confirm that their partner had been medically confirmed to be sterile. • Exclusion criterion #2 (Section 5.2) was clarified to exclude subjects with clinically significant infectious disorders, including subjects who tested positive for COVID-19, even if they were asymptomatic. • Exclusion criterion #10 (Section 5.2) was clarified to state that subjects with stage 4 fibrosis based on VCTE or FIB-4 but who had a liver biopsy within 12 months of screening and reported fibrosis stage of F0-F3 were to be considered eligible based on the liver biopsy result. • Exclusion criterion #18 (Section 5.2) was clarified to state that presumptive fertile, sexually active male subjects whose female partner was pregnant were excluded. • Clarification that IP could be administered by a home health care worker on a case-by-case basis if circumstances related to the COVID-19 pandemic precluded dosing at the study site was added to Section 6.2 Administration Instruction and Section 6.3 Preparation/Handling/Storage/Accountability. • The procedure for visit adjustment in case of dosing outside of window was clarified in Section 6.5 Study Intervention Compliance. • Clarification that the COVID-19 vaccine was allowed, if available, and that COVID-19 treatment was to be discussed with the Medical Monitor on a case-by-case basis was added to Section 6.6.1 Prohibited Medications/Therapies. • Stopping Rules and Dose Modifications (Section 6.7) were clarified to add that the Sponsor could suspend or terminate the study in the event of external circumstances that did not enable the study to be properly conducted including potential circumstances related to the COVID-19 pandemic.

Amendment No. (Date of Approval (reference: MOD0063302 1)	Key Details of the Amendment
	• Study Assessments and Procedures (Section 8) were clarified to indicate that any situation at the site level with potential impact on subject safety or study conduct, including situations related to COVID-19 infection or control measures, should have been discussed with the Sponsor immediately upon occurrence or awareness to determine potential impact on study subject(s) or study conduct. • Statistical Analyses (Section 9.4) were clarified to state that subjects with dose interruptions impacted by the COVID-19 pandemic were to be noted in the listings, and that subgroups including and excluding subjects with dose interruptions due to the COVID-19 pandemic may have been considered for efficacy and safety analyses if appropriate. • Clarification that some or all monitoring activities (Section 10.6.1 Data Quality Assurance) may be halted or performed remotely due to the COVID-19 pandemic, and in such a case details of the changes made to the monitoring strategy would be described in the Monitoring Plan. • The glossary was updated.

FIG. 52

Methods section	Supporting text
Randomisation and masking	The randomisation ratios were as follows: 3:1 (pegozafermin:placebo) for cohorts 1 (n=8), 4 (n=12) and 6 (n=12), 4:1 for cohort 2 (n=15), and a 7:2 split into 3:1 and 4:1 for cohorts 3 (n=18) and 5 (n=18). Cohorts 3 and 5 were stratified by BC-NASH with fibrosis status of F1, F2, and F3 (Yes/No) to minimise bias (Amendment No. 1.0, 29 June 2019) (supplementary table 2). Block sizes were as follows: 4 for cohorts 1, 4 and 6, 5 for cohort 2, and 9 split into 4 and 5 for cohorts 3 and 5.
Procedures	Patient discontinuation or withdrawal was allowed for the following reasons: investigator decision, adverse event (AE) or intercurrent illness, non-compliance with protocol requirements, subject withdrawal of consent, pregnancy, sponsor termination or suspension of the study, or lost to follow-up As a result of the COVID-19 pandemic, the study protocol was amended to allow interruption in dosing and study procedures for up to 4 weeks due to COVID-related circumstances, and to define COVID-related circumstances for the analyses (Amendment No. 3.0, 25 March 2020) (supplementary table 2).

FIG. 53

	Screening period				Treatment period													Follow-up period					
	1	2	3	4	5	6	7	8	9	10	11	12	13	14-20	21	22	23						
Study visit																							
Study day	-59 to -8	-7 to -3	-1	1	2	3	4	5	6	7	8	15	22	28	29	30	31	32	33	36, 43, 50, 57, 64, 71, 78	85	92 ET ^a	113 LTOS
Informed consent	X																						
Medical history/demographics	X																						
Percutaneous liver biopsy (optional) ^b	X																						
Prior medications	X																						
Inclusion and exclusion criteria	X		X																				
Complete physical exam ^c	X															X						X	X
Symptom-directed physical exam ^d			X	B	P			B	B	B				B					B	B			
Body weight ^f	X			B				B	B	B				B					B	B			
Waist and hip measurements	X			B										B					H D50			X	X
Fibroscan ^l	X																		D50			X	
12-lead ECG (single) ^g	X			B	X			B	B	B				B		X				B	X	X	
Urine drug screen and alcohol breath test	X		X ^h																				
Clinical laboratory tests ⁱ	X	X		B	X			B	B	B				B		X			B at D36, D50, and D71	B	X	X	X
Cortisol (24-h urine collection) ^j	X																		D50		X		
Urinalysis	X						X								X				B at D50		X	X	X
HbA _{1c}	X						X												B at D50		X	X	X
Serology ^k	X																						
TSH	X																						
Pregnancy test in WOCBP only ^l	X(S)							B	B	B				B					B	B	X	X	X
Vital signs ^m	X		X	X	P	X	X	X	X	X				X	P	X	X	X	X	X	X	X	X
Columbia Suicide Severity Rating Scale			X																D50		X		
Randomisation			X																				
Study intervention administration ⁿ			X				X	X	X	X				X					X	X			
PK blood collection ^o			X	X	X	X	X	B	B	B				X	X	X	X		B at D36, D50, D57, and D71	B	X	X	X

	Screening period				Treatment period														Follow-up period				
	1	2	3	4	5	6	7	8	9	10	11	12	13	14-20	21	22	23						
Study visit																							
Study day	-59 to -8	-7 to -3	-1	1	2	3	4	5	6	7	8	15	22	28	29	30	31	32	33	36, 43, 50, 57, 64, 71, 78	85	92/ET ^a	113/EOS
PD and biomarker blood sampling																							
IGF1, total			B					B	B						B at D50		X						
Adiponectin			B					B							B at D50		X						
CK18, ELF panel, and PRO-C3			B												B at D50		X						PRO-C3 only
Free fatty acid			B					B							B at D50		X						X
OGTT ^b			X														X						
Insulin (not part of OGTT)			B					B							B at D50								X
HOMA-IR calculation			X												B at D50		X						X
MRI-PDFF, visceral fat, and subcutaneous fat ^c	X														D50		X						
Plasma sample for potential future bone biomarkers analysis ^d			X												B at D50		X						X
Pharmacogenomic (DNA) blood sampling			X																				
Exploratory biomarker analysis ^e			X												B at D50		X						X
Immunogenicity ^f			B						B						B at D50		X ^g						X
Endogenous FGF21 ^h			B																				
Adverse event monitoring ^a	X	X	X														X					X	X
Concomitant medication	X	X	X														X					X	X
Domiciled ^a			X	X																			

All outpatient visits were to have a study window of ± 1 day. The dosing days for the cohorts are indicated in pink.

ADA=anti-drug antibody; ALT=alanine aminotransferase; AST=aspartate aminotransferase; B=pre-dose; CK18=cytokeratin 18; CTX=carboxy-terminal collagen crosslinks; D=day; ECG=electrocardiogram; ELF=enhanced liver fibrosis; EOS=end of study; ET=early termination; FGF21=fibroblast growth factor 21; FSH=follicle stimulating hormone; HbA_{1c}=glycated haemoglobin; HOMA-IR= homeostatic model assessment of insulin resistance; IGF1=insulin-like growth factor 1; MRI=magnetic resonance imaging; MRI-PDFF=magnetic resonance imaging proton-density fat fraction; OGTT=oral glucose tolerance test; P=pre-discharge; P1NP=N-terminal propeptide of type I collagen; PD=pharmacodynamic; PK=pharmacokinetic; PRO-C3=N-terminal propeptide of type III collagen; S=serum; TSH=thyroid stimulating hormone; WOCBP=women of childbearing potential.

^aFor any participant who withdrew before completion of the study, an ET visit was conducted, if possible, with the same assessments as the D92 visit.

^bOptional liver biopsy may have been performed for participants who did not have a medical contraindication for a liver biopsy and did not have a liver biopsy in the 24 months before screening. For participants who underwent a previous liver biopsy >24 months before screening who would not have qualified for the study based on results of the initial biopsy, there should have been sound clinical basis to expect different findings in a repeat biopsy based on medical judgement. Any biopsy needed to be approved in advance by the sponsor and only after the participant had met all other inclusion and exclusion criteria.

- ^cComplete physical exam done at screening included recording height, weight, and calculating body mass index.
- ^dSymptom-directed physical exam was done pre-dose and pre-discharge from the phase 1 unit on domiciled dosing visits (first and fifth doses), and pre-dose on ambulatory dosing visits. Additional physical examinations were performed if clinically indicated.
- ^eOn domiciled and ambulatory visits, body weight was measured pre-dose.
- ^fFibroscan (Echosens, Waltham, MA, USA) was performed during screening, before MRI for all participants.
- ^g12-lead safety ECGs were recorded as single bedside measurements; on domiciled dosing visits (first and fifth doses), ECGs were measured pre-dose and 24 h post dose. On ambulatory dosing visits, ECG was measured pre-dose. Additional ECGs were conducted if clinically indicated.
- ^hOn D-1, urine drug screen could have been done at a local laboratory. However, a sample should also have been collected for central laboratory evaluation.
- ⁱClinical laboratory tests included biochemistry, hematology, coagulation, and TSH for determination of postmenopausal status; on domiciled dosing visits (first and fifth doses), clinical laboratory samples were collected pre-dose and 24 h post dose; on ambulatory visits, clinical laboratory samples were collected pre-dose and 24 h post dose. For all participants, ALT and AST samples were collected twice during the screening period (≥ 2 weeks apart), with the second assessment collected at D-7 to D-3. A third sample, if required, was collected via an unscheduled visit.
- ^jAmbulatory 24-h urine collection for cortisol was done within 14 days from baseline, on D50 and D92/ET. It was recommended that participants collect urine for the 24 h before the D-7 to D-3 visit and bring the container with them to this visit. Alternatively, urine could have been collected for the 24 h before the randomisation visit (D-1) and brought to the site on D-1 (the result was not required for eligibility confirmation). For D50 and D92/ET, the participant started collection 24 h before coming into the clinic and brought the sample to the visit.
- ^kSerology tests included hepatitis B surface antigen, hepatitis C virus, and HIV 1 and 2 antibodies.
- ^lThe serum urine pregnancy test was conducted at screening; at all other time points, a urine pregnancy test was done to guide clinical decisions to dose on dosing days. Before the first dosing, the baseline urine pregnancy test was performed on D-1 to allow for randomisation on that day. If the urine test was positive, a confirmatory serum pregnancy test was conducted.
- ^mVital signs included supine blood pressure, pulse, body temperature, and respiratory rate. Vital signs were measured pre-dose (before scheduled blood draws and study intervention administration), 1, 12, and 24 h post dose, and pre-discharge on domiciled dosing visits (first and fifth doses). On dosing ambulatory visits, vital signs were measured pre-dose (before scheduled blood draws and study intervention administration) and pre-discharge. On non-dosing visits, vital signs were measured before scheduled blood draws. Starting from randomisation, blood pressure and pulse were measured in duplicate; the first measurement was taken up to 15 min before the indicated time point. Additional vital signs measurements may have been done if clinically indicated. Participants were in a supine or semi-erect/seated position and resting for ≥ 5 min before measurements.
- ⁿStudy intervention was administered subcutaneously to the abdomen region by qualified study personnel.
- ^oAdditional blood samples for PK analysis may have been collected if clinically indicated (eg, in the case of a serious adverse event).
- ^pBlood samples for the OGTT were collected under fasting conditions (10 h) at the following time points: 0 (just before ingesting glucose), 30, 60, 90, 120, and 180 min. On D92/ET, the insulin was captured from the OGTT.
- ^qAt screening, MRI-PDFF was done within 35 days of baseline (D1). On D50 and D92, MRI-PDFF was done within ± 2 days of the planned visit date. If outside the window, MRI-PDFF was performed as close to the target day as possible and protocol deviation was recorded.
- ^rSamples for CTX and PINP were obtained at the designated time points for storage and potential future analysis. The D42 sample was obtained pre-dose.
- ^sSamples for RNA as well as plasma and serum samples were collected for potential future exploratory assessments to increase understanding of pegozafermin biological activity and identify potential existing and/or emerging biomarkers.
- ^tParticipants who tested positive for neutralising antibodies to pegozafermin at the EOS visit (or at the ET visit if withdrawn from study) were asked to return for additional follow-up testing. This testing occurred approximately every 3 months starting from when the site was notified of the positive result until: (1) neutralising antibodies were no longer detectable; or (2) the participant had been followed up for a period of ≥ 1 year (± 4 weeks). More frequent testing (eg, every month) or testing for a longer period may have been requested in the event of safety-related concerns. Follow-up testing was not required if it was established that the participant did not receive pegozafermin. All follow-up results, both positive and negative, were to be communicated to the sites. A blood sample for

ADA assessment was also to be collected upon observation of any severe hypersensitivity reaction (eg, anaphylaxis). Participants who tested positive for binding, non-neutralising antibodies and had clinical sequelae that were considered potentially related to an anti-pegzofermin antibody response may also have been asked to return for additional follow-up testing.

^uInmunogenicity sample on D92/E1 was only collected for participants who terminated early from the study.

^vBaseline samples of endogenous FGF21 were analysed; sample(s) were also obtained from neutralising ADA+ participants with additional follow-up visit(s) for potential future analysis.

^wThe sites may have taken non-personally identifying photographs of potential injection-site reactions (optional).

^xParticipants in cohorts 1 to 4 were to be domiciled at the clinic from 1 day before dosing until 24 h after the first and fifth doses. Other study visits were ambulatory. On D8, 15, and 22 (ambulatory dosing visits), participants remained at the site for observation for ≥ 2 h after dosing.

FIG. 54

		Screening period			Treatment period																Follow-up period				
Study visit		1	2	3			4	5	6	7	8	9	10			11	12	13,14	15	16	17–19 ^a	20	21		
Study day		–59 to –6	–7 to –3	–1	1	2	3	4	5	6	7	8	15	22	28	29	30	31	32	33,36	43	50	57,71,85	92/ET ^b	113/EOS
Informed consent		X																							
Medical history/demographics		X																							
Percutaneous liver biopsy (optional) ^c		X																							
Prior medications		X																							
Inclusion and exclusion criteria		X		X																					
Complete physical exam ^d		X														X									
Symptom-directed physical exam ^e				X	B	P					X	B	X		B								X	X	
Body weight ^f		X			B					X	B	X		B		B									
Waist and hip measurements		X			B										B						X		X		
Fibroscan ^g		X																			X		X		
12-lead ECG (single) ^h		X			B	X				X	B			B		B	X					B (D85)	X	X	
Urine drug screen and alcohol breath test		X		X ⁱ																					
Clinical laboratory tests ^j		X	X		B	X				X	B	X		B	X						X	B (D71, D85)	X	X	
Cortisol (24-h urine collection) ^k		X																			X		X		
Urinalysis		X		X											X						X		X	X	
HbA _{1c}		X		X																	X		X	X	
Serology ^l		X																							
TSH		X																							
Pregnancy test in WOCBP only ^m	X (S)		X									B										B	X	X	
Vital signs ⁿ	X		X	X	P	X	X	X	X	X	X	X	X	X	X	P	X	X	X	X	X	X	X	X	
Columbia Suicide Severity Rating Scale			X																		X		X		
Randomisation			X																						
Study intervention administration ^o				X							X				X							X			
PK blood collection ^p					X	X	X	X	X	X	X	B	X	X	X	X	X	X	X	X	X	B (D57, D71, D85)	X	X	

	Screening period			Treatment period																Follow-up period		
	1	2		3	4	5	6	7	8	9	10	11	12	13, 14	15	16	17–19 ^a	20	21			
	–59 to –8	–7 to –3	–1	1	2	3	4	5	6	7	8	9	10	11	12	13, 14	15	16	17–19 ^a	20	21	
Study visit																						
Study day																						
PD and biomarker blood sampling																						
IGF1, total				B						X	B		B						X			
Adiponectin				B						X			B					X	X			
CK18, ELF panel, and PRO-C3				B									B					X		PRO-C3 only		
Free fatty acid				B						X			B					X	X	X		
OGTT ^b			X																			
Insulin (not part of OGTT)				B						X			B					X		X		
HOMA-IR calculation				X														X	X	X		
MRI-PDFF, visceral fat, and subcutaneous fat ^c	X																	X				
Plasma sample for potential future bone biomarkers analysis ^d			X															X	X	X		
Pharmacogenomic (DNA) blood sampling			X																			
Exploratory biomarker analysis ^e			X																			
Immunogenicity ^h				B						B			B					X	X	X		
Endogenous FGF21 ^h				B																		
Adverse event monitoring ^a	X	X	X															n	X	X		
Concomitant medication	X	X	X																X	X		
Domiciled ^g			X	X	X								X	X	X							

All outpatient visits were to have a study window of ± 1 day. The dosing days for the cohorts are indicated in pink.

ADA=anti-drug antibody. ALT=alanine aminotransferase. AST=aspartate aminotransferase. B=pre-dose. CK18=cytokeratin 18. CTX=carboxy-terminal collagen crosslinks. D=day. ECG=electrocardiogram. ELF=enhanced liver fibrosis. EOS=end of study. ET=early termination. FGF21=fibroblast growth factor 21.

FSH=follicle stimulating hormone. HbA_{1c}=glycated haemoglobin. HOMA-IR= homeostatic model assessment of insulin resistance. IGF1=insulin-like growth factor 1. MRI=magnetic resonance imaging. MRI-PDFF=magnetic resonance imaging proton-density fat fraction. OGTT=oral glucose tolerance test. P=pre-discharge. PINP=N-terminal propeptide of type I collagen. PD=pharmacodynamic. PK=pharmacokinetic. PRO-C3=N-terminal propeptide of type III collagen. S=serum; TSH=thyroid stimulating hormone. WOCBP=women of childbearing potential.

^aBetween visits 17 and 19, on D64 and D78, participants were contacted by phone to inquire about adverse events and concomitant medications.

^bFor any participant who withdrew before completion of the study, an ET visit was conducted, if possible, with the same assessments as the D92 visit.

^cOptional liver biopsy may have been performed for participants who did not have a medical contraindication for a liver biopsy and did not have a liver biopsy in the 24 months before screening. For participants who underwent a previous liver biopsy >24 months before screening who would not have qualified for the study based on results of the initial biopsy, there should have been a sound clinical basis to expect different findings in a repeat biopsy based on medical judgement.

Any biopsy needed to be approved in advance by the sponsor and only after the participant had met all other inclusion and exclusion criteria.

^aComplete physical exam done at screening included recording height, weight, and calculating body mass index.

^eSymptom-directed physical exam was done pre-dose and pre-discharge from the phase 1 unit on domiciled dosing visits (first and third dose), and pre-dose on ambulatory dosing visits. Additional physical examinations were also performed if clinically indicated.

^fOn domiciled and ambulatory visits, body weight was measured pre-dose.

^gFibroscan (Echosens, Waltham, MA, USA) was performed during screening, before MRI for all participants.

^h12-lead safety ECGs were recorded as single bedside measurements. On domiciled dosing visits (first and third doses), ECGs were measured pre-dose and 24 h post dose; on ambulatory dosing visits, ECG was measured pre-dose. Additional ECGs were conducted if clinically indicated.

ⁱOn D-1, urine drug screen could have been done at a local laboratory, however, a sample should also have been collected for central laboratory evaluation.

^jClinical laboratory tests included biochemistry, haematology, coagulation, and FSH for determination of postmenopausal status; on domiciled dosing visits (first and third doses), clinical laboratory samples were collected pre-dose and 24 h post dose; on ambulatory visits, clinical laboratory samples were collected pre-dose. For all participants, ALT and AST samples were collected twice during the screening period (≥ 2 weeks apart), with the second assessment to be collected at D-7 to D-3. A third sample, if required, was collected via an unscheduled visit.

^kAmbulatory 24-h urine collection for cortisol was done within 14 days from baseline, on D50 and D92/ET. It was recommended that participants collected urine for the 24 h before the D-7 to D-3 visit and brought the container with them to this visit. Alternatively, urine could have been collected for the 24 h before the randomisation visit (D-1) and brought to the site on D-1 (the result was not required for eligibility confirmation). For D50 and D92/ET, the participant started collection 24 h before coming into the clinic and brought the sample to the visit.

^lSerology tests included hepatitis B surface antigen, hepatitis C virus, and HIV 1 and 2 antibodies.

^mThe serum urine pregnancy test was conducted at screening; at all other time points, a urine pregnancy test was done to guide clinical decisions to dose on dosing days. Before the first dosing, the baseline urine pregnancy test was performed on D-1 to allow for randomisation on that day. If the urine test was positive, a confirmatory serum pregnancy test was conducted.

ⁿVital signs included supine blood pressure, pulse, body temperature, and respiratory rate. Vital signs were measured pre-dose (before scheduled blood draws and study intervention administration), 1, 12, and 24 h post dose, and pre-discharge on domiciled dosing visits (first and third doses). On dosing ambulatory visits, vital signs were measured pre-dose (before scheduled blood draws and study intervention administration) and pre-discharge. On non-dosing visits, vital signs were measured before scheduled blood draws. Starting from randomisation, blood pressure and pulse were measured in duplicate; the first measurement was taken up to 15 min before the indicated time point. Additional vital signs measurements may have been done if clinically indicated. Participants were in a supine or semi-erect/seated position and resting for ≥ 5 min before measurements.

^oStudy intervention was administered subcutaneously to the abdomen region by qualified study personnel.

^pAdditional blood samples for PK analysis may have been collected if clinically indicated (eg, in the case of a serious adverse event).

^qBlood samples for the OGTT were collected under fasting conditions (10 h) at the following time points: 0 (just before ingesting glucose), 30, 60, 90, 120, and 180 min. On D92/ET the insulin was captured from the OGTT.

^rAt screening, MRI-PDFF was done within 35 days of baseline (D1). On D50 and D92, MRI-PDFF was done within ± 2 days of the planned visit date. If outside the window, MRI-PDFF was performed as close to the target day as possible and protocol deviation was recorded.

^sSamples for CTX and PINP were obtained at the designated time points for storage and potential future analysis. The D42 sample was obtained pre-dose.

^tSamples for RNA as well as plasma and serum samples were collected for potential future exploratory assessments to increase understanding of pegozafermin biological activity and identify potential existing and/or emerging biomarkers.

^uParticipants who tested positive for neutralising antibodies to pegozafermin at the EOS visit (or at the ET visit if withdrawn from study) were asked to return for additional follow-up testing. This testing occurred approximately every 3 months starting from when the site was notified of the positive result until: (1) neutralising antibodies were no longer detectable; or (2) the participant had been followed up for a period of ≥ 1 year (± 4 weeks). More frequent testing (eg, every month) or testing for a longer period may have been requested in the event of safety-related concerns. Follow-up testing was not required if it was established

that the participant did not receive pegozafermin. All follow-up results, both positive and negative, were to be communicated to the sites. A blood sample for ADA assessment was also to be collected upon observation of any severe hypersensitivity reaction (eg. anaphylaxis). Participants who tested positive for binding, non-neutralising antibodies and had clinical sequelae that were considered potentially related to an anti-pegzozafermin antibody response may also have been asked to return for additional follow-up testing.

^vImmunogenicity sample on D92/ET was only to be collected for participants who terminated early from the study.

^wBaseline samples of endogenous FGF21 were analysed; sample(s) were also obtained from neutralising ADA+ participants with additional follow-up visit(s) for potential future analysis.

^xThe sites may have taken non-personally identifying photographs of potential injection-site reactions (optional).

^yParticipants in cohorts 5 and 6 were domiciled at the clinic from 1 day before dosing until 24 h after the first dose and 24 h after the third dose; other study visits were ambulatory. On the D15 ambulatory dosing visit, participants remained at the study site for observation for ≥ 2 h after dosing.

FIG. 55

	Placebo (n=10)	Pegzofermin						Pooled (n=62)
		3 mg QW (n=6)	9 mg QW (n=12)	18 mg QW (n=11)	27 mg QW (n=10)	18 mg Q3W (n=14)	36 mg Q3W (n=9)	
Screened ^a	..	..	..	..	..	..	..	275
Randomised ^b	19	6	12	11	10	14	9	81
Safety ^c	19	6	12	11	10	14	9	81
Pharmacokinetics ^d	0	6	12	11	10	14	9	62
Pharmacodynamics ^e	19	6	12	11	10	14	9	81
Pharmacodynamics—MRI ^f	18	6	11	10	8	14	8	75

MRI=magnetic resonance imaging. PD=pharmacodynamic. PK=pharmacokinetic. Q2W=once every 2 weeks. QW=once per week.

^aAll individuals who signed informed consent and underwent screening.

^bAll randomised participants who received at least one dose of study drug. One participant was planned for placebo treatment, but actually received pegzofermin 3 mg QW.

^cAll screened analysis set participants who were assigned a randomisation number in the study. The safety analysis set row was summarised based on planned treatment.

^dAll participants in the safety analysis set who received at least one dose of study drug and had at least one on-study PK measurement.

^eAll participants in the safety analysis set who had measurable post-baseline PD data.

^fAll participants in the safety analysis set who had measurable post-baseline MRI assessments.

FIG. 56

	Placebo (n=18)	Pegzoalfermin					
		3 mg QW (N=6)	9 mg QW (N=11)	18 mg QW (N=10)	27 mg QW (N=8)	18 mg Q2W (N=14)	36 mg Q2W (N=8)
MRI-PDFF hepatic fat fraction, %							
Change from baseline to day 92							
n, unstructured	18	5	11	10	7	13	8
LS mean (SE)	1.42 (1.42)	-7.50 (2.56)	-10.04 (1.81)	-7.50 (1.91)	-13.51 (2.19)	-9.00 (1.63)	-9.68 (2.12)
90% CI of LS mean	(-0.94, 3.79)	(-11.76, -3.24)	(-13.07, -7.02)	(-10.68, -4.31)	(-17.16, -9.86)	(-11.72, -6.27)	(-13.22, -6.13)
95% CI of LS mean	(-1.40, 4.25)	(-12.60, -2.40)	(-13.66, -6.42)	(-11.30, -3.69)	(-17.87, -9.14)	(-12.25, -5.74)	(-13.92, -5.43)
p value ^a	0.3182	0.0045	<0.0001	0.0002	<0.0001	<0.0001	<0.0001
LS mean difference compared with placebo ^b	..	-8.93 (2.92)	-11.47 (2.30)	-8.92 (2.37)	-14.93 (2.61)	-10.42 (2.16)	-11.10 (2.55)
90% CI of LS mean difference	..	(-13.80, -4.05)	(-15.30, -7.63)	(-12.88, -4.96)	(-19.28, -10.59)	(-14.03, -6.82)	(-15.36, -6.84)
95% CI of LS mean difference	..	(-14.76, -3.09)	(-16.06, -6.87)	(-13.66, -4.18)	(-20.13, -9.73)	(-14.74, -6.11)	(-16.20, -6.00)
p value ^c	..	0.0032	<0.0001	0.0004	<0.0001	<0.0001	<0.0001
Percent change from baseline to day 92							
n, unstructured	18	5	11	10	7	13	8
LS mean (SE)	9.77 (6.04)	-36.94 (11.01)	-49.62 (7.73)	-36.11 (8.14)	-60.39 (9.40)	-43.19 (6.99)	-50.39 (9.07)
90% CI of LS mean	(-0.32, 19.86)	(-55.30, -18.59)	(-62.52, -36.71)	(-49.69, -22.52)	(-76.06, -44.73)	(-54.85, -31.54)	(-65.53, -35.26)
95% CI of LS mean	(-2.30, 21.84)	(-58.90, -14.99)	(-65.06, -34.17)	(-52.37, -19.85)	(-79.14, -41.65)	(-57.14, -29.25)	(-68.51, -32.28)
p value ^a	0.1108	0.0013	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
LS mean difference compared with placebo ^b	..	-46.72 (12.56)	-59.39 (9.82)	-45.88 (10.14)	-70.16 (11.17)	-52.96 (9.24)	-60.16 (10.90)
90% CI of LS mean difference	..	(-67.66, -25.77)	(-75.77, -43.01)	(-62.80, -28.96)	(-88.80, -51.53)	(-68.38, -37.55)	(-78.35, -41.98)
95% CI of LS mean difference	..	(-71.77, -21.66)	(-78.99, -39.78)	(-66.13, -25.63)	(-92.46, -47.87)	(-71.41, -34.52)	(-81.93, -38.40)
p value ^c	..	0.0004	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

Mixed-model repeated measures (MMRM) analysis was used to analyse the change from baseline and the percent change from baseline in MRI parameters. The model included baseline as a covariate, and treatment group, visit and the interaction between treatment group and visit as factors.
CI=confidence interval. LS=least-squares. MRI=magnetic resonance imaging. MRI-PDFF=magnetic resonance imaging proton-density fat fraction.
PD=pharmacodynamic. Q2W=once every 2 weeks. QW=once per week. SE=standard error.
^ap value of the within-group treatment difference.
^bThe difference between treatment and placebo.
^cp value of the between-group and placebo treatment difference.

FIG. 57

	Placebo (n=18)	Pegzofermin					
		3 mg QW (N=6)	9 mg QW (N=11)	18 mg QW (N=10)	27 mg QW (N=8)	18 mg Q2W (N=14)	36 mg Q2W (N=8)
Liver volume, L							
Change from baseline to day 92							
n, unstructured	17	5	11	10	7	12	8
LS mean (SE)	0.01 (0.05)	-0.29 (0.09)	-0.19 (0.06)	-0.10 (0.07)	-0.33 (0.08)	-0.22 (0.06)	-0.24 (0.08)
90% CI of LS mean	(-0.08, 0.09)	(-0.44, -0.14)	(-0.30, -0.08)	(-0.21, 0.01)	(-0.46, -0.20)	(-0.32, -0.12)	(-0.37, -0.12)
95% CI of LS mean	(-0.10, 0.11)	(-0.47, -0.11)	(-0.32, -0.06)	(-0.23, 0.03)	(-0.48, -0.17)	(-0.34, -0.10)	(-0.40, -0.09)
p value ^a	0.8948	0.0024	0.0041	0.1346	<0.0001	0.0005	0.0020
LS mean difference compared with placebo ^b	..	-0.29 (0.10)	-0.20 (0.08)	-0.11 (0.08)	-0.33 (0.09)	-0.22 (0.08)	-0.25 (0.09)
90% CI of LS mean difference	..	(-0.47, -0.12)	(-0.33, -0.06)	(-0.25, 0.03)	(-0.49, -0.18)	(-0.35, -0.09)	(-0.40, -0.10)
95% CI of LS mean difference	..	(-0.50, -0.09)	(-0.36, -0.03)	(-0.28, 0.06)	(-0.52, -0.15)	(-0.38, -0.07)	(-0.43, -0.07)
p value ^c	..	0.0064	0.0191	0.2040	0.0007	0.0055	0.0079
Percent change from baseline to day 92							
n, unstructured	17	5	11	10	7	12	8
LS mean (SE)	1.19 (2.32)	-15.32 (4.12)	-8.85 (2.89)	-5.66 (3.03)	-15.18 (3.53)	-10.71 (2.68)	-10.84 (3.42)
90% CI of LS mean	(-2.69, 5.07)	(-22.19, -8.44)	(-13.68, -4.03)	(-10.71, -0.60)	(-21.07, -9.28)	(-15.17, -6.25)	(-16.55, -5.12)
95% CI of LS mean	(-3.45, 5.83)	(-23.55, -7.09)	(-14.63, -3.07)	(-11.71, 0.39)	(-22.23, -8.13)	(-16.05, -5.37)	(-17.67, -4.00)
p value ^a	0.6101	0.0004	0.0032	0.0663	<0.0001	0.0002	0.0024
LS mean difference compared with placebo ^b	..	-16.51 (4.73)	-10.04 (3.71)	-6.85 (3.81)	-16.37 (4.23)	-11.90 (3.54)	-12.03 (4.14)
90% CI of LS mean difference	..	(-24.40, -8.62)	(-16.23, -3.86)	(-13.22, -0.48)	(-23.43, -9.31)	(-17.81, -5.99)	(-18.94, -5.11)
95% CI of LS mean difference	..	(-25.95, -7.06)	(-17.45, -2.64)	(-14.47, 0.78)	(-24.82, -7.92)	(-18.97, -4.83)	(-20.30, -3.75)
p value ^c	..	0.0009	0.0087	0.0775	0.0003	0.0013	0.0051

Mixed-model repeated measures (MMRM) analysis was used to analyse the change from baseline and the percent change from baseline in MRI parameters. The model included baseline as a covariate, and treatment group, visit and the interaction between treatment group and visit as factors.

CI=confidence interval. LS=least-squares. MRI=magnetic resonance imaging. Q2W=once every 2 weeks. QW=once per week. SE=standard error.

^ap value of the within-group treatment difference.

^bThe difference between treatment and placebo.

^cp value of the between-group and placebo treatment difference.

FIG. 58

	Placebo (n=19)	Pegzofermin					
		3 mg QW (N=6)	9 mg QW (N=12)	18 mg QW (N=11)	27 mg QW (N=10)	18 mg Q2W (N=14)	36 mg Q2W (N=9)
ALT, U/L							
Change from baseline to day 92							
n, unstructured	18	4	11	10	7	13	7
LS mean (SE)	-3.4 (3.4)	-10.4 (6.3)	-9.9 (4.3)	-10.9 (4.5)	-30.0 (5.3)	-9.6 (3.9)	-22.4 (5.1)
90% CI of LS mean	(-9.1, 2.2)	(-21.0, 0.1)	(-17.0, -2.8)	(-18.5, -3.3)	(-38.9, -21.2)	(-16.1, -3.0)	(-30.9, -13.9)
95% CI of LS mean	(-10.2, 3.3)	(-23.1, 2.2)	(-18.4, -1.3)	(-20.0, -1.8)	(-40.7, -19.4)	(-17.4, -1.7)	(-32.6, -12.2)
p value ^a	0.3118	0.1038	0.0241	0.0200	<0.0001	0.0175	<0.0001
LS mean difference compared with placebo ^b	..	-7.0 (7.2)	-6.4 (5.4)	-7.4 (5.6)	-26.6 (6.3)	-6.1 (5.2)	-18.9 (6.1)
90% CI of LS mean difference	..	(-19.0, 5.0)	(-15.5, 2.7)	(-16.9, 2.0)	(-37.1, -16.0)	(-14.8, 2.5)	(-29.2, -8.7)
95% CI of LS mean difference	..	(-21.3, 7.4)	(-17.3, 4.5)	(-18.8, 3.9)	(-39.2, -13.9)	(-16.5, 4.2)	(-31.2, -6.7)
p value ^c	..	0.3337	0.2412	0.1937	<0.0001	0.2402	0.0030
Percent change from baseline to day 92							
n, unstructured	18	4	11	10	7	13	7
LS mean (SE)	-4.18 (5.47)	-16.87 (10.62)	-26.65 (6.99)	-26.73 (7.40)	-43.69 (8.55)	-18.83 (6.38)	-39.84 (8.42)
90% CI of LS mean	(-13.32, 4.96)	(-34.57, 0.83)	(-38.32, -14.97)	(-39.09, -14.37)	(-57.95, -29.44)	(-29.48, -8.17)	(-53.88, -25.79)
95% CI of LS mean	(-15.12, 6.76)	(-38.05, 4.30)	(-40.62, -12.68)	(-41.53, -11.93)	(-60.75, -26.64)	(-31.59, -6.07)	(-56.65, -23.03)
p value ^a	0.4479	0.1165	0.0003	0.0006	<0.0001	0.0045	<0.0001
LS mean difference compared with placebo ^b	..	-12.69 (11.96)	-22.47 (8.86)	-22.55 (9.19)	-39.51 (10.19)	-14.65 (8.40)	-35.66 (10.07)
90% CI of LS mean difference	..	(-32.63, 7.24)	(-37.25, -7.68)	(-37.90, -7.20)	(-56.51, -22.52)	(-28.68, -0.62)	(-52.45, -18.86)
95% CI of LS mean difference	..	(-36.54, 11.16)	(-40.17, -4.77)	(-40.93, -4.17)	(-59.85, -19.17)	(-31.44, 2.15)	(-55.76, -15.55)
p value ^c	..	0.2922	0.0137	0.0171	0.0002	0.0863	0.0007

Mixed-model repeated measures (MMRM) analysis was used to analyse the change from baseline and the percent change from baseline in liver parameters. The model included baseline as a covariate, and treatment group, visit and the interaction between treatment group and visit as factors.

AL.T=alanine aminotransferase. CI=confidence interval. LS=least-squares. MRI=magnetic resonance imaging. Q2W=once every 2 weeks. QW=once per week.

SE=standard error.

^ap value of the within-group treatment difference.

^bThe difference between treatment and placebo.

^cp value of the between-group and placebo treatment difference.

FIG. 59

ALT, U/L	Placebo (n=6)	Pooled pegzofermin (N=22)
Change from baseline to day 92		
n, unstructured	5	17
LS mean (SE)	-10.3 (9.9)	-34.6 (5.1)
90% CI of LS mean	(-27.5, 6.9)	(-43.3, -25.8)
95% CI of LS mean	(-31.1, 10.6)	(-45.1, -24.0)
p value ^a	0.3140	<0.0001
LS mean difference compared with placebo ^b	..	-24.3 (11.1)
90% CI of LS mean difference	..	(-43.6, -5.0)
95% CI of LS mean difference	..	(-47.6, -0.9)
p value ^c	..	0.0426
Percent change from baseline to day 92		
n, unstructured	5	17
LS mean (SE)	-10.08 (12.37)	-47.20 (6.42)
90% CI of LS mean	(-31.35, 11.19)	(-58.22, -36.19)
95% CI of LS mean	(-35.79, 15.62)	(-60.50, -33.90)
p value ^a	0.4240	<0.0001
LS mean difference compared with placebo ^b	..	-37.12 (13.94)
90% CI of LS mean difference	..	(-61.08, -13.16)
95% CI of LS mean difference	..	(-66.07, -8.17)
p value ^c	..	0.0144

Mixed-model repeated measures (MMRM) analysis was used to analyse the change from baseline and the percent change from baseline in liver parameters. The model included baseline as a covariate, and treatment group, visit and the interaction between treatment group and visit as factors.
ALT=alanine aminotransferase. CI=confidence interval. LS=least-squares. SE=standard error.

^ap value of the within group treatment difference.

^bThe difference between treatment and placebo.

^cp value of the between group and placebo treatment difference.

FIG. 60

	Placebo (n=19)	Pegzofermin					
		3 mg QW (N=6)	9 mg QW (N=12)	18 mg QW (N=11)	27 mg QW (N=10)	18 mg Q2W (N=14)	36 mg Q2W (N=9)
AST, U/L							
Change from baseline to day 92							
n, unstructured	18	4	11	10	7	13	7
LS mean (SE)	-5.2 (2.0)	-13.4 (3.8)	-8.9 (2.5)	-6.1 (2.7)	-14.5 (3.2)	-6.3 (2.3)	-14.1 (3.0)
90% CI of LS mean	(-8.5, -1.9)	(-19.7, -7.1)	(-13.2, -4.7)	(-10.6, -1.6)	(-19.8, -9.2)	(-10.2, -2.4)	(-19.1, -9.0)
95% CI of LS mean	(-9.2, -1.2)	(-21.0, -5.8)	(-14.0, -3.8)	(-11.5, -0.7)	(-20.8, -8.2)	(-10.9, -1.6)	(-20.1, -8.0)
p value ^a	0.0117	0.0008	0.0008	0.0265	<0.0001	0.0089	<0.0001
LS mean difference compared with placebo ^b	..	-8.2 (4.3)	-3.7 (3.2)	-0.9 (3.3)	-9.3 (3.8)	-1.1 (3.1)	-8.9 (3.6)
90% CI of LS mean difference	..	(-15.4, -1.0)	(-9.1, 1.7)	(-6.5, 4.7)	(-15.6, -3.0)	(-6.2, 4.0)	(-15.0, -2.8)
95% CI of LS mean difference	..	(-16.8, 0.4)	(-10.2, 2.7)	(-7.6, 5.8)	(16.8, -1.8)	(-7.2, 5.0)	(-16.2, -1.6)
p value ^c	..	0.0604	0.2519	0.7880	0.0158	0.7221	0.0179
Percent change from baseline to day 92							
n, unstructured	18	4	11	10	7	13	7
LS mean (SE)	-4.40 (4.85)	-29.36 (9.47)	-19.90 (6.15)	-15.10 (6.52)	-37.88 (7.52)	-11.41 (5.63)	-25.32 (7.43)
90% CI of LS mean	(-12.52, 3.72)	(-45.17, -13.56)	(-30.19, -9.60)	(-26.02, -4.18)	(-50.45, -25.32)	(-20.84, -1.98)	(-37.73, -12.91)
95% CI of LS mean	(-14.13, 5.33)	(-48.28, -10.45)	(-32.23, -7.56)	(-28.19, -2.02)	(-52.93, -22.84)	(-22.70, -0.11)	(-40.18, -10.46)
p value ^a	0.3682	0.0029	0.0021	0.0246	<0.0001	0.0478	0.0012
LS mean difference compared with placebo ^b	..	-24.96 (10.64)	-15.49 (7.82)	-10.70 (8.12)	-33.48 (8.97)	-7.01 (7.43)	-20.92 (8.89)
90% CI of LS mean difference	..	(-42.74, -7.19)	(-28.58, -2.41)	(-24.30, 2.91)	(-48.47, -18.49)	(-19.44, 5.43)	(-35.77, -6.07)
95% CI of LS mean difference	..	(-46.24, -3.69)	(-31.17, 0.19)	(-27.00, 5.60)	(-51.43, -15.54)	(-21.91, 7.89)	(-38.70, -3.13)
p value ^c	..	0.0222	0.0527	0.1936	0.0004	0.3498	0.0220

Mixed-model repeated measures (MMRM) analysis was used to analyse the change from baseline and the percent change from baseline in liver parameters. The model included baseline as a covariate, and treatment group, visit and the interaction between treatment group and visit as factors.

AST=aspartate aminotransferase. CI=confidence interval. LS=least-squares. SE=standard error. Q2W=once every 2 weeks. QW=once per week.

^ap value of the within-group treatment difference.

^bThe difference between treatment and placebo.

^cp value of the between-group and placebo treatment difference.

FIG. 61

	Placebo (n=19)	Pegzofermin					
		3 mg QW (N=6)	9 mg QW (N=12)	18 mg QW (N=11)	27 mg QW (N=10)	18 mg Q2W (N=14)	36 mg Q2W (N=9)
PRO-C3, ng/mL							
Change from baseline to day 92							
n, unstructured	18	4	11	10	7	13	7
LS mean (SE)	-0.29 (0.78)	-2.96 (1.63)	-2.03 (1.01)	0.06 (1.05)	-3.84 (1.25)	-1.56 (0.92)	-2.43 (1.25)
90% CI of LS mean	(-1.60, 1.02)	(-5.68, -0.24)	(-3.71, -0.36)	(-1.69, 1.81)	(-5.93, -1.75)	(-3.09, -0.03)	(-4.52, -0.34)
95% CI of LS mean	(-1.85, 1.28)	(-6.21, 0.30)	(-4.04, -0.03)	(-2.03, 2.16)	(-6.34, -1.34)	(-3.39, 0.27)	(-4.93, 0.07)
p value ^a	0.7149	0.0741	0.0472	0.9532	0.0032	0.0931	0.0565
LS mean difference compared with placebo ^b	..	-2.67 (1.81)	-1.75 (1.27)	0.35 (1.31)	-3.55 (1.48)	-1.27 (1.21)	-2.14 (1.48)
90% CI of LS mean difference	..	(-5.69, 0.35)	(-3.86, 0.37)	(-1.84, 2.53)	(-6.03, -1.08)	(-3.29, 0.74)	(-4.62, 0.33)
95% CI of LS mean difference	..	(-6.28, 0.94)	(-4.28, 0.79)	(-2.27, 2.96)	(-6.52, -0.59)	(-3.68, 1.14)	(-5.11, 0.82)
p value ^c	..	0.1446	0.1736	0.7904	0.0196	0.2948	0.1531
Percent change from baseline to day 92							
n, unstructured	18	4	11	10	7	13	7
LS mean (SE)	3.26 (7.02)	-19.71 (14.53)	-18.79 (9.02)	1.08 (9.38)	-22.67 (11.20)	-11.18 (8.19)	-12.76 (11.22)
90% CI of LS mean	(-8.45, 14.97)	(-43.93, 4.52)	(-33.84, -3.73)	(-14.58, 16.75)	(-46.35, -8.99)	(-24.86, 2.49)	(-31.47, 5.95)
95% CI of LS mean	(-10.75, 17.28)	(-48.70, 9.28)	(-36.81, -0.77)	(-17.67, 19.83)	(-50.02, -5.32)	(-27.55, 5.18)	(-35.15, 9.63)
p value ^a	0.6436	0.1794	0.0412	0.9085	0.0160	0.1771	0.2595
LS mean difference compared with placebo ^b	..	-22.97 (16.14)	-22.05 (11.38)	-2.18 (11.72)	-30.93 (13.26)	-14.44 (10.79)	-16.02 (13.29)
90% CI of LS mean difference	..	(-49.88, 3.94)	(-41.04, -3.06)	(-21.74, 17.38)	(-53.06, -8.81)	(-32.45, 3.56)	(-38.18, 6.14)
95% CI of LS mean difference	..	(-55.17, 9.23)	(-44.78, 0.68)	(-25.59, 21.23)	(-57.41, -4.46)	(-36.00, 7.11)	(-42.54, 10.50)
p value ^c	..	0.1592	0.0570	0.8531	0.0227	0.1854	0.2321

Mixed-model repeated measures (MMRM) analysis was used to analyse the change from baseline and the percent change from baseline in liver parameters. The model included baseline as a covariate, and treatment group, visit and the interaction between treatment group and visit as factors.

CI=confidence interval. LS=least-squares. PRO-C3=λ-terminal propeptide of type III collagen. SE=standard error. Q2W=once every 2 weeks. QW=once per week.

^ap value of the within-group treatment difference.
^bThe difference between treatment and placebo.
^cp value of the between-group and placebo treatment difference.

FIG. 62

	Placebo (n=19)	Pegzofermin					
		3 mg QW (N=6)	9 mg QW (N=12)	18 mg QW (N=11)	27 mg QW (N=10)	18 mg Q2W (N=14)	36 mg Q2W (N=9)
Triglycerides, mg/dL							
Change from baseline to day 92							
n, unstructured	17	5	11	10	7	9	7
LS mean (SE)	-14.1 (13.7)	-42.8 (25.4)	-50.8 (17.2)	-22.8 (18.1)	-47.5 (21.5)	-58.7 (18.9)	-53.1 (21.6)
90% CI of LS mean	(-37.2, 9.0)	(-85.5, -0.2)	(-79.7, -22.0)	(-53.2, 7.6)	(-83.6, -11.4)	(-90.4, -27.0)	(-89.2, -16.9)
95% CI of LS mean	(-41.8, 13.6)	(-94.0, 8.3)	(-85.4, -16.2)	(-59.3, 13.7)	(-90.8, -4.2)	(-96.6, -20.7)	(-96.4, -9.7)
p value ^a	0.3116	0.0986	0.0050	0.2141	0.0322	0.0031	0.0175
LS mean difference compared with placebo ^b	..	-28.8 (28.9)	-36.7 (22.0)	-8.7 (22.7)	-33.4 (25.5)	-44.6 (23.4)	-39.0 (25.6)
90% CI of LS mean difference	..	(-77.3, 19.7)	(-73.7, 0.2)	(-46.9, 29.5)	(-76.3, 9.4)	(-83.8, -5.4)	(-81.9, 3.9)
95% CI of LS mean difference	..	(-86.9, 29.4)	(-81.1, 7.6)	(-54.6, 37.1)	(-84.8, 17.9)	(-91.6, 2.3)	(-90.5, 12.5)
p value ^c	..	0.3247	0.1020	0.7026	0.1967	0.0621	0.1340
Percent change from baseline to day 92							
n, unstructured	17	5	11	10	7	9	7
LS mean (SE)	-2.21 (6.23)	-22.74 (11.53)	-23.95 (7.74)	-17.71 (8.20)	-27.63 (9.66)	-28.49 (8.62)	-20.71 (9.74)
90% CI of LS mean	(-12.62, 8.21)	(-42.00, -3.47)	(-36.89, -11.01)	(-31.41, -4.01)	(-43.78, -11.49)	(-42.88, -14.11)	(-36.98, -4.44)
95% CI of LS mean	(-14.68, 10.27)	(-45.80, 0.33)	(-39.45, -8.45)	(-34.12, -1.30)	(-46.96, -8.30)	(-45.71, -11.28)	(-40.19, -1.23)
p value ^a	0.7246	0.0532	0.0030	0.0349	0.0058	0.0016	0.0375
LS mean difference compared with placebo ^b	..	-20.53 (13.10)	-21.74 (9.94)	-15.50 (10.30)	-25.43 (11.50)	-26.29 (10.63)	-18.50 (11.57)
90% CI of LS mean difference	..	(-42.43, 1.36)	(-38.36, -5.13)	(-32.72, 1.72)	(-44.64, -6.22)	(-44.04, -8.54)	(-37.83, 0.82)
95% CI of LS mean difference	..	(-46.75, 5.68)	(-41.64, -1.85)	(-36.13, 5.12)	(-48.43, -2.43)	(-47.54, -5.04)	(-41.64, 4.63)
p value ^c	..	0.1224	0.0327	0.1379	0.0308	0.0162	0.1149

Mixed-model repeated measures (MMRM) analysis was used to analyse the change from baseline and the percent change from baseline in lipid parameters. The model included baseline as a covariate, and treatment group, visit and the interaction between treatment group and visit as factors.

CI=confidence interval. LS=least-squares. SE=standard error. Q2W=once every 2 weeks. QW=once per week.

^ap value of the within-group treatment difference.

^bThe difference between-treatment and placebo.

^cp value of the between-group and placebo treatment difference.

FIG. 63

	Placebo (n=19)	Pegzofermin					
		3 mg QW (N=6)	9 mg QW (N=12)	18 mg QW (N=11)	27 mg QW (N=10)	18 mg Q2W (N=14)	36 mg Q2W (N=9)
LDL-C, mg/dL							
Change from baseline to day 92							
n, unstructured	17	5	11	10	7	10	7
LS mean (SE)	-0.9 (4.4)	-11.5 (7.9)	-20.7 (5.6)	-2.8 (5.8)	-19.9 (6.8)	-7.4 (5.4)	-7.8 (6.6)
90% CI of LS mean	(-8.1, 6.4)	(-24.7, 1.7)	(-30.1, -11.3)	(-12.4, 6.9)	(-31.1, -8.6)	(-16.3, 1.6)	(-18.8, 3.2)
95% CI of LS mean	(-9.6, 7.8)	(-27.2, 4.2)	(-31.9, -9.4)	(-14.3, 8.8)	(-33.3, -6.4)	(-18.1, 3.4)	(-21.0, 5.4)
p value ^a	0.8450	0.1494	0.0005	0.6355	0.0045	0.1752	0.2423
LS mean difference compared with placebo ^b	..	-10.6 (9.0)	-19.8 (7.2)	-1.9 (7.2)	-19.0 (8.0)	-6.5 (6.9)	-6.9 (7.9)
90% CI of LS mean difference	..	(-25.7, 4.4)	(-31.7, -7.9)	(-14.0, 10.2)	(-32.4, -5.6)	(-18.0, 5.0)	(-20.1, 6.3)
95% CI of LS mean difference	..	(-28.6, 7.3)	(-34.1, -5.6)	(-16.4, 12.6)	(-35.0, -3.0)	(-20.3, 7.3)	(-22.7, 8.9)
p value ^c	..	0.2410	0.0072	0.7939	0.0209	0.3501	0.3840
Percent change from baseline to day 92							
n, unstructured	17	5	11	10	7	10	7
LS mean (SE)	1.15 (4.08)	-6.17 (7.38)	-13.45 (5.29)	2.59 (5.41)	-16.46 (6.34)	-5.02 (5.06)	-4.11 (6.20)
90% CI of LS mean	(-5.66, 7.97)	(-18.48, 6.15)	(-22.27, -4.62)	(-6.45, 11.62)	(-27.04, -5.89)	(-13.45, 3.40)	(-14.45, 6.23)
95% CI of LS mean	(-7.00, 9.31)	(-20.90, 8.57)	(-24.01, -2.89)	(-8.23, 13.41)	(-29.12, -3.81)	(-15.10, 5.06)	(-16.49, 8.26)
p value ^a	0.7786	0.4066	0.0134	0.6340	0.0116	0.3239	0.5094
LS mean difference compared with placebo ^b	..	-7.32 (8.43)	-14.60 (6.71)	1.44 (6.78)	-17.62 (7.54)	-6.18 (6.49)	-5.27 (7.43)
90% CI of LS mean difference	..	(-21.37, 6.74)	(-25.79, -3.41)	(-9.88, 12.75)	(-30.19, -5.05)	(-17.00, 4.65)	(-17.65, 7.12)
95% CI of LS mean difference	..	(-24.14, 9.50)	(-27.99, -1.21)	(-12.11, 14.98)	(-32.66, -2.57)	(-19.13, 6.78)	(-20.09, 9.56)
p value ^c	..	0.3882	0.0330	0.8328	0.0224	0.3447	0.4807

Mixed-model repeated measures (MMRM) analysis was used to analyse the change from baseline and the percent change from baseline in lipid parameters. The model included baseline as a covariate, and treatment group, visit and the interaction between treatment group and visit as factors.

CI=confidence interval. LDL-C=low-density lipoprotein cholesterol. LS=least-squares. SE=standard error. Q2W=once every 2 weeks. QW=once per week.

^ap value of the within-group treatment difference.

^bThe difference between treatment and placebo.

^cp value of the between-group and placebo treatment difference.

FIG. 64

	Placebo (n=19)	Pegzofermin					
		3 mg QW (N=6)	9 mg QW (N=12)	18 mg QW (N=11)	27 mg QW (N=10)	18 mg Q2W (N=14)	36 mg Q2W (N=9)
HDL-C, mg/dL							
Change from baseline to day 92							
n, unstructured	17	5	11	10	7	10	7
LS mean (SE)	0.7 (1.4)	6.7 (2.5)	5.5 (1.7)	3.6 (1.8)	1.3 (2.1)	8.8 (1.7)	5.2 (2.1)
90% CI of LS mean	(-1.6, 3.0)	(2.6, 10.9)	(2.6, 8.3)	(0.5, 6.6)	(-2.2, 4.7)	(6.0, 11.7)	(1.7, 8.7)
95% CI of LS mean	(-2.0, 3.5)	(1.7, 11.7)	(2.0, 8.9)	(-0.1, 7.2)	(-2.8, 5.4)	(5.4, 12.3)	(1.0, 9.4)
p value ^a	0.6030	0.0092	0.0023	0.0558	0.5410	<0.0001	0.0155
LS mean difference compared with placebo ^b	..	6.0 (2.9)	4.8 (2.2)	2.9 (2.3)	0.5 (2.5)	8.1 (2.2)	4.5 (2.5)
90% CI of LS mean difference	..	(1.2, 10.8)	(1.1, 8.4)	(-1.0, 6.7)	(-3.6, 4.7)	(4.4, 11.8)	(0.3, 8.6)
95% CI of LS mean difference	..	(0.3, 11.7)	(0.4, 9.1)	(-1.8, 7.5)	(-4.4, 5.5)	(3.7, 12.5)	(-0.5, 9.5)
p value ^c	..	0.0401	0.0347	0.2196	0.8278	0.0005	0.0793
Percent change from baseline to day 92							
n, unstructured	17	5	11	10	7	10	7
LS mean (SE)	1.96 (2.97)	18.17 (5.43)	11.19 (3.68)	9.20 (3.92)	2.90 (4.50)	20.10 (3.76)	9.79 (4.53)
90% CI of LS mean	(-3.01, 6.92)	(9.12, 27.23)	(5.03, 17.34)	(2.65, 15.75)	(-4.60, 10.41)	(13.83, 26.38)	(2.22, 17.36)
95% CI of LS mean	(-3.99, 7.90)	(7.33, 29.02)	(3.81, 18.56)	(1.36, 17.05)	(-6.08, 11.89)	(12.60, 27.61)	(0.73, 18.85)
p value ^a	0.5124	0.0014	0.0036	0.0223	0.5206	<0.0001	0.0346
LS mean difference compared with placebo ^b	..	16.22 (6.20)	9.23 (4.73)	7.24 (4.93)	0.95 (5.39)	18.15 (4.79)	7.84 (5.43)
90% CI of LS mean difference	..	(5.86, 26.57)	(1.33, 17.13)	(-1.00, 15.49)	(-8.05, 9.94)	(10.16, 26.14)	(-1.23, 16.90)
95% CI of LS mean difference	..	(3.82, 28.61)	(-0.23, 18.69)	(-2.63, 17.12)	(-9.82, 11.71)	(8.58, 27.71)	(-3.01, 18.68)
p value ^c	..	0.0112	0.0557	0.1473	0.8612	0.0003	0.1538

Mixed-model repeated measures (MMRM) analysis was used to analyse the change from baseline and the percent change from baseline in lipid parameters. The model included baseline as a covariate, and treatment group, visit and the interaction between treatment group and visit as factors.

CI=confidence interval. HDL-C=high-density lipoprotein cholesterol. LS=least-squares. PD=pharmacodynamic. SE=standard error. Q2W=once every 2 weeks. QW=once per week.

^ap value of the within-group treatment difference.

^bThe difference between treatment and placebo.

^cp value of the between-group and placebo treatment difference.

FIG. 65

	Placebo (n=19)	Pegzofermin					
		3 mg QW (N=6)	9 mg QW (N=12)	18 mg QW (N=11)	27 mg QW (N=10)	18 mg Q2W (N=14)	36 mg Q2W (N=9)
Non-HDL-C, mg/dL							
Change from baseline to day 92							
n, unstructured	17	5	11	10	7	10	7
LS mean (SE)	-1.3 (4.8)	-12.8 (8.8)	-24.1 (6.2)	-7.3 (6.4)	-25.8 (7.4)	-12.6 (5.9)	-12.8 (7.3)
90% CI of LS mean	(-9.3, 6.7)	(-27.3, 1.8)	(-34.5, -13.7)	(-18.0, 3.4)	(-38.2, -13.3)	(-22.5, -2.7)	(-25.0, -0.7)
95% CI of LS mean	(-10.9, 8.3)	(-30.2, 4.7)	(-36.5, -11.6)	(-20.1, 5.5)	(-40.6, -10.9)	(-24.4, -0.8)	(-27.4, 1.7)
p value ^a	0.7849	0.1493	0.0002	0.2577	0.0009	0.0368	0.0830
LS mean difference compared with placebo ^b	..	-11.4 (10.0)	-22.8 (7.9)	-6.0 (8.0)	-24.4 (8.9)	-11.3 (7.6)	-11.5 (8.8)
90% CI of LS mean difference	..	(-28.0, 5.2)	(-35.9, -9.6)	(-19.4, 7.4)	(-39.2, -9.7)	(-24.0, 1.4)	(-26.1, 3.1)
95% CI of LS mean difference	..	(-31.3, 8.4)	(-38.5, -7.0)	(-22.0, 10.0)	(-42.1, -6.8)	(-26.5, 3.9)	(-29.0, 5.9)
p value ^c	..	0.2546	0.0053	0.4571	0.0074	0.1423	0.1922
Percent change from baseline to day 92							
n, unstructured	17	5	11	10	7	10	7
LS mean (SE)	1.18 (3.56)	-6.31 (6.45)	-13.87 (4.61)	-1.92 (4.74)	-16.32 (5.51)	-7.75 (4.38)	-6.34 (5.39)
90% CI of LS mean	(-4.75, 7.12)	(-17.08, 4.45)	(-21.56, -6.19)	(-9.84, 5.99)	(-25.51, -7.13)	(-15.06, -0.44)	(-15.33, 2.66)
95% CI of LS mean	(-5.92, 8.29)	(-19.19, 6.57)	(-23.07, -4.67)	(-11.40, 7.55)	(-27.32, -5.33)	(-16.49, 0.99)	(-17.10, 4.43)
p value ^a	0.7403	0.3313	0.0037	0.6862	0.0042	0.0815	0.2442
LS mean difference compared with placebo ^b	..	-7.50 (7.35)	-15.06 (5.85)	-3.11 (5.93)	-17.51 (6.54)	-8.93 (5.63)	-7.52 (6.47)
90% CI of LS mean difference	..	(-19.76, 4.76)	(-24.82, -5.30)	(-13.01, 6.80)	(-28.43, -6.58)	(-18.32, 0.46)	(-18.31, 3.27)
95% CI of LS mean difference	..	(-22.17, 7.18)	(-26.74, -3.37)	(-14.96, 8.75)	(-30.58, -4.43)	(-20.17, 2.30)	(-20.44, 5.40)
p value ^c		0.3114	0.0123	0.6022	0.0095	0.1173	0.2491

Mixed-model repeated measures (MMRM) analysis was used to analyse the change from baseline and the percent change from baseline in lipid parameters. The model included baseline as a covariate, and treatment group, visit and the interaction between treatment group and visit as factors.

CI=confidence interval. HDL-C=high-density lipoprotein cholesterol. LS=least-squares. SE=standard error. Q2W=once every 2 weeks. QW=once per week.

^ap value of the within-group treatment difference.

^bThe difference between treatment and placebo.

^cp value of the between-group and placebo treatment difference.

FIG. 66

	Placebo (n=19)	Pegzofermin					
	3 mg QW (N=6)	9 mg QW (N=12)	18 mg QW (N=11)	27 mg QW (N=10)	18 mg Q2W (N=14)	36 mg Q2W (N=9)	
HOMA-IR							
Change from baseline to day 92							
n, unstructured	11	3	6	7	11	5	
LS mean (SE)	0.40 (6.07)	1.55 (3.24)	1.43 (2.47)	-4.23 (2.23)	-0.88 (1.80)	-5.81 (2.66)	
90% CI of LS mean	(-10.14, 10.94)	(-3.96, 7.07)	(-2.85, 5.72)	(-8.09, -0.38)	(-4.00, 2.24)	(-10.39, -1.22)	
95% CI of LS mean	(-12.38, 13.17)	(-5.09, 8.20)	(-3.76, 6.63)	(-8.90, 0.43)	(-4.66, 2.90)	(-11.35, -0.27)	
p value ^a	0.9486	0.6357	0.5688	0.0728	0.6314	0.0409	
LS mean difference compared with placebo ^b	..	-0.24 (6.31)	0.80 (3.03)	-4.87 (2.84)	-1.51 (2.51)	-6.44 (3.21)	
90% CI of LS mean difference	..	(-11.18, 10.71)	(-5.25, 7.18)	(-4.44, 6.04)	(-5.84, 2.81)	(-11.96, -0.92)	
95% CI of LS mean difference	..	(-13.50, 13.03)	(-6.64, 8.47)	(-5.55, 7.15)	(-6.74, 3.71)	(-13.11, 0.23)	
p value ^c	..	0.9703	0.8047	0.7948	0.5522	0.0576	
Percent change from baseline to day 92							
n, unstructured	11	3	6	7	11	5	
LS mean (SE)	-0.09 (15.72)	7.40 (30.62)	37.07 (20.87)	-41.42 (19.48)	-4.57 (15.57)	-41.11 (23.39)	
90% CI of LS mean	(-26.62, 26.44)	(-44.25, 59.06)	(1.79, 72.35)	(-74.33, -8.51)	(-30.88, 21.74)	(-80.62, -1.61)	
95% CI of LS mean	(-31.96, 31.78)	(-54.64, 69.44)	(-5.33, 79.47)	(-80.96, -1.87)	(-36.18, 27.04)	(-88.58, 6.35)	
p value ^a	0.9953	0.8103	0.0846	0.0406	0.7709	0.0874	
LS mean difference compared with placebo ^b	..	7.49 (34.21)	37.16 (26.13)	-41.33 (25.06)	-4.48 (22.01)	-41.02 (28.40)	
90% CI of LS mean difference	..	(-80.00, 100.92)	(-50.25, 65.24)	(-83.65, 1.00)	(-41.65, 32.70)	(-88.96, 6.92)	
95% CI of LS mean difference	..	(-98.24, 119.17)	(-61.87, 76.85)	(-15.89, 90.21)	(-82.17, 9.52)	(-98.61, 16.57)	
p value ^c	..	0.8462	0.8279	0.1638	0.1079	0.1573	

Mixed-model repeated measures (MMRM) analysis was used to analyse the change from baseline and the percent change from baseline in metabolic parameters. The model included baseline as a covariate, and treatment group, visit and the interaction between treatment group and visit as factors.

CI=confidence interval. HOMA-IR= homeostatic model assessment of insulin resistance. LS=least-squares. SE=standard error. Q2W=once every 2 weeks.

QW=once per week.

^ap value of the within-group treatment difference.

^bThe difference between treatment and placebo.

^cp value of the between-group and placebo treatment difference.

FIG. 67

	Placebo (n=19)	Pegzofermin					
	3 mg QW (N=6)	9 mg QW (N=12)	18 mg QW (N=11)	27 mg QW (N=10)	18 mg Q2W (N=14)	36 mg Q2W (N=9)	
Glucose, mg/dL							
Change from baseline to day 92							
n, unstructured	17	2	10	10	7	7	
LS mean (SE)	10.0 (9.2)	51.0 (20.1)	12.7 (11.6)	-7.5 (12.2)	-9.7 (14.2)	5.9 (13.6)	
90% CI of LS mean	(-5.6, 25.5)	(17.4, 84.5)	(-6.7, 32.2)	(-28.1, 13.0)	(-33.5, 14.1)	(-16.9, 28.7)	
95% CI of LS mean	(-8.7, 28.6)	(10.8, 91.1)	(-10.6, 36.0)	(-32.2, 17.1)	(-38.2, 18.9)	(-21.4, 33.2)	
p value ^a	0.2866	0.0137	0.2774	0.5396	0.4992	0.6657	
LS mean difference compared with placebo ^b	..	41.0 (22.1)	2.8 (14.8)	-17.5 (15.3)	-19.6 (17.0)	-4.1 (16.5)	
90% CI of LS mean difference	..	(4.1, 77.8)	(-22.1, 27.6)	(-43.2, 8.2)	(-48.1, 8.9)	(-31.7, 23.6)	
95% CI of LS mean difference	..	(-3.1, 85.1)	(-27.0, 32.6)	(-48.4, 13.3)	(-53.8, 14.6)	(-37.2, 29.1)	
p value ^c	..	0.0680	0.8532	0.2585	0.2537	0.8063	
Percent change from baseline to day 92							
N, unstructured	17	2	10	10	7	7	
LS mean (SE)	7.94 (5.53)	38.90 (12.78)	11.92 (6.97)	-3.77 (7.27)	-7.18 (8.48)	3.80 (8.21)	
90% CI of LS mean	(-1.33, 17.20)	(17.62, 60.18)	(0.25, 23.58)	(-15.97, 8.44)	(-21.39, 7.03)	(-9.93, 17.53)	
95% CI of LS mean	(-3.17, 19.04)	(13.45, 64.35)	(-2.06, 25.90)	(-18.40, 10.87)	(-24.21, 9.84)	(-12.65, 20.25)	
p value ^a	0.1574	0.0032	0.0930	0.6070	0.4010	0.6454	
LS mean difference compared with placebo ^b	..	30.96 (13.88)	3.98 (8.87)	-11.70 (9.13)	-15.12 (10.16)	-4.14 (9.93)	
90% CI of LS mean difference	..	(7.84, 54.08)	(-10.89, 18.85)	(-27.02, 3.61)	(-32.14, 1.90)	(-20.76, 12.48)	
95% CI of LS mean difference	..	(3.31, 58.62)	(-13.84, 21.80)	(-30.06, 6.65)	(-35.51, 5.27)	(-24.05, 15.77)	
p value ^c	..	0.0287	0.6556	0.2059	0.1428	0.6783	

Mixed-model repeated measures (MMRM) analysis was used to analyse the change from baseline and the percent change from baseline in metabolic parameters. The model included baseline as a covariate, and treatment group, visit and the interaction between treatment group and visit as factors.

CI=confidence interval. LS=least-squares. SE=standard error. Q2W=once every 2 weeks. QW=once per week.

^ap value of the within-group treatment difference.

^bThe difference between treatment and placebo.

^cp value of the between-group and placebo treatment difference.

FIG. 68

	Placebo (n=19)	Pegzafertin					
		3 mg QW (N=6)	9 mg QW (N=12)	18 mg QW (N=11)	27 mg QW (N=10)	18 mg Q2W (N=14)	36 mg Q2W (N=9)
HbA1c (%)							
Change from baseline to day 92							
n, unstructured	18	5	11	10	7	13	7
LS mean (SE)	0.01 (0.16)	0.58 (0.29)	0.08 (0.20)	0.06 (0.22)	-0.26 (0.25)	-0.08 (0.19)	0.54 (0.25)
90% CI of LS mean	(-0.26, 0.29)	(0.10, 1.07)	(-0.26, 0.42)	(-0.30, 0.42)	(-0.67, 0.16)	(-0.39, 0.23)	(0.12, 0.95)
95% CI of LS mean	(-0.32, 0.34)	(0.00, 1.17)	(-0.33, 0.49)	(-0.37, 0.49)	(-0.75, 0.24)	(-0.46, 0.30)	(0.04, 1.03)
p value ^a	0.9339	0.0501	0.6945	0.7688	0.3046	0.6707	0.0343
LS mean difference compared with placebo ^b	..	0.57 (0.33)	0.07 (0.26)	0.05 (0.28)	-0.27 (0.30)	-0.09 (0.26)	0.53 (0.30)
90% CI of LS mean difference	..	(0.02, 1.12)	(-0.37, 0.50)	(-0.41, 0.51)	(-0.77, 0.23)	(-0.52, 0.33)	(0.02, 1.02)
95% CI of LS mean difference	..	(-0.09, 1.23)	(-0.45, 0.59)	(-0.50, 0.60)	(-0.87, 0.33)	(-0.61, 0.42)	(-0.08, 1.12)
p value ^c	..	0.0880	0.7979	0.8566	0.3711	0.7149	0.0875
Percent change from baseline to day 92							
n, unstructured	18	5	11	10	7	13	7
LS mean (SE)	0.61 (2.28)	7.36 (4.05)	1.80 (2.84)	3.05 (2.99)	-3.66 (3.42)	-1.85 (2.60)	6.89 (3.43)
90% CI of LS mean	(-3.19, 4.41)	(0.61, 14.11)	(-2.93, 6.54)	(-1.95, 8.04)	(-9.36, 2.05)	(-6.19, 2.49)	(1.17, 12.62)
95% CI of LS mean	(-3.94, 5.16)	(-0.72, 15.44)	(-3.86, 7.47)	(-2.93, 9.02)	(-10.48, 3.17)	(-7.05, 3.34)	(0.05, 13.74)
p value ^a	0.7890	0.0734	0.5270	0.3125	0.2893	0.4792	0.0485
LS mean difference compared with placebo ^b	..	6.75 (4.57)	1.19 (3.61)	2.43 (3.81)	-4.27 (4.14)	-2.47 (3.54)	6.28 (4.16)
90% CI of LS mean difference	..	(-0.87, 14.36)	(-4.84, 7.22)	(-3.93, 8.79)	(-11.17, 2.63)	(-8.37, 3.44)	(-0.66, 13.22)
95% CI of LS mean difference	..	(-2.36, 15.86)	(-6.03, 8.41)	(-5.18, 10.04)	(-12.52, 3.99)	(-9.53, 4.60)	(-2.02, 14.59)
p value ^c	..	0.1440	0.7425	0.5255	0.3059	0.4888	0.1357

Mixed-model repeated measures (MMRM) analysis was used to analyse the change from baseline and the percent change from baseline in metabolic parameters. The model included baseline as a covariate, and treatment group, visit and the interaction between treatment group and visit as factors.

CI=confidence interval. HbA_{1c}=glycated haemoglobin. LS=least-squares. SE=standard error. Q2W=once every 2 weeks. QW=once per week.

^ap value of the within-group treatment difference.

^bThe difference between treatment and placebo.

^cp value of the between-group and placebo treatment difference.

FIG. 69

	Placebo (n=19)	Pegzofermin					
		3 mg QW (N=6)	9 mg QW (N=12)	18 mg QW (N=11)	27 mg QW (N=10)	18 mg Q2W (N=14)	36 mg Q2W (N=9)
Change from baseline to day 85							
n, unstructured	18	5	11	10	7	13	8
LS mean (SE)	1.23 (0.83)	0.65 (1.45)	2.17 (1.03)	2.58 (1.11)	-0.54 (1.25)	2.35 (0.96)	3.18 (1.20)
90% CI of LS mean	(-0.16, 2.61)	(-1.77, 3.08)	(0.45, 3.89)	(0.72, 4.43)	(-2.63, 1.54)	(0.76, 3.95)	(1.17, 5.18)
95% CI of LS mean	(-0.43, 2.88)	(-2.25, 3.55)	(0.12, 4.23)	(0.35, 4.80)	(-3.03, 1.95)	(0.44, 4.26)	(0.78, 5.58)
p value [1]	0.1436	0.6548	0.0386	0.0238	0.6669	0.0165	0.0101
LS mean difference compared with placebo [2]	..	-0.57 (1.67)	0.95 (1.32)	1.35 (1.39)	-1.77 (1.50)	1.12 (1.27)	1.95 (1.46)
90% CI of LS mean difference	..	(-3.36, 2.21)	(-1.26, 3.15)	(-0.97, 3.66)	(-4.27, 0.73)	(-0.99, 3.24)	(-0.49, 4.39)
95% CI of LS mean difference	..	(-3.91, 2.76)	(-1.69, 3.58)	(-1.42, 4.12)	(-4.76, 1.22)	(-1.40, 3.65)	(-0.96, 4.87)
p value [3]	..	0.7322	0.4775	0.3354	0.2427	0.3783	0.1865
Percent change from baseline to day 85							
n, unstructured	18	5	11	10	7	13	8
LS mean (SE)	1.38 (0.59)	1.19 (1.06)	2.59 (0.74)	2.47 (0.79)	-0.80 (0.86)	2.11 (0.69)	2.64 (0.86)
90% CI of LS mean	(0.41, 2.36)	(-0.56, 2.93)	(1.36, 3.81)	(1.16, 3.79)	(-2.22, 0.62)	(0.97, 3.25)	(1.21, 4.06)
95% CI of LS mean	(0.22, 2.55)	(-0.90, 3.27)	(1.13, 4.04)	(0.91, 4.04)	(-2.50, 0.90)	(0.75, 3.47)	(0.94, 4.34)
p value [1]	0.0204	0.2636	0.0006	0.0022	0.3539	0.0026	0.0026
LS mean difference compared with placebo [2]	..	-0.20 (1.21)	1.20 (0.94)	1.09 (0.99)	-2.18 (1.04)	0.73 (0.90)	1.26 (1.04)
90% CI of LS mean difference	..	(-2.20, 1.81)	(-0.36, 2.77)	(-0.54, 2.73)	(-3.91, -0.46)	(-0.77, 2.23)	(-0.47, 2.98)
95% CI of LS mean difference	..	(-2.59, 2.20)	(-0.66, 3.07)	(-0.86, 3.04)	(-4.24, -0.12)	(-1.06, 2.52)	(-0.80, 3.32)
p value [3]	..	0.8718	0.2043	0.2710	0.0380	0.4223	0.2299

Mixed-model repeated measures (MMRM) analysis was used to analyse the change from baseline and the percent change from baseline in anthropomorphic parameters. The model included baseline as a covariate, and treatment group, visit and the interaction between treatment group and visit as factors.

CI=confidence interval. LS=least-squares. SE=standard error. Q2W=once every 2 weeks. QW=once per week.

^ap value of the within-group treatment difference.

^bThe difference between treatment and placebo.

^cp value of the between-group and placebo treatment difference.

FIG. 70

	Placebo (n=19)	Pegzofermin					
		3 mg QW (N=6)	9 mg QW (N=12)	18 mg QW (N=11)	27 mg QW (N=10)	18 mg Q2W (N=14)	36 mg Q2W (N=9)
Adiponectin, ug/mL							
Change from baseline to day 92							
n, unstructured	18	5	11	10	7	13	7
LS mean (SE)	-0.34 (0.43)	1.05 (0.79)	1.05 (0.79)	1.80 (0.58)	3.35 (0.66)	1.23 (0.50)	0.67 (0.66)
90% CI of LS mean	(-1.06, 0.38)	(-0.26, 2.36)	(0.20, 2.02)	(0.83, 2.77)	(2.25, 4.44)	(0.39, 2.06)	(-0.43, 1.77)
95% CI of LS mean	(-1.21, 0.52)	(-0.52, 2.62)	(0.02, 2.20)	(0.64, 2.95)	(2.03, 4.66)	(0.23, 2.22)	(-0.65, 1.99)
p value ^a	0.4323	0.1858	0.0466	0.0029	<0.0001	0.0169	0.3140
LS mean difference compared with placebo ^b	..	1.39 (0.90)	1.45 (0.70)	2.15 (0.72)	3.69 (0.79)	1.57 (0.66)	1.01 (0.79)
90% CI of LS mean difference	..	(-0.11, 2.89)	(0.29, 2.62)	(0.94, 3.35)	(2.37, 5.00)	(0.47, 2.67)	(-0.31, 2.33)
95% CI of LS mean difference	..	(-0.40, 3.19)	(0.06, 2.85)	(0.70, 3.59)	(2.11, 5.26)	(0.25, 2.89)	(-0.57, 2.59)
p value ^c	..	0.1258	0.0415	0.0044	<0.0001	0.0208	0.2045
Percent change from baseline to day 92							
n, unstructured	18	5	11	10	7	13	7
LS mean (SE)	-4.25 (7.80)	37.65 (14.48)	25.46 (9.88)	29.09 (10.47)	60.85 (12.00)	23.11 (9.07)	24.14 (12.10)
90% CI of LS mean	(-17.27, 8.77)	(13.51, 61.79)	(8.97, 41.94)	(11.62, 46.57)	(40.86, 80.85)	(7.98, 38.23)	(3.96, 44.31)
95% CI of LS mean	(-19.83, 11.33)	(8.76, 66.54)	(5.73, 45.19)	(8.18, 50.01)	(36.93, 84.77)	(5.01, 41.21)	(0.00, 48.28)
p value ^a	0.5877	0.0114	0.0122	0.0071	<0.0001	0.0131	0.0500
LS mean difference compared with placebo ^b	..	41.90 (16.47)	29.71 (12.59)	33.34 (13.05)	65.11 (14.31)	27.36 (11.96)	28.39 (14.40)
90% CI of LS mean difference	..	(14.44, 69.36)	(8.71, 50.71)	(11.56, 55.12)	(41.25, 88.96)	(7.41, 47.31)	(4.37, 52.50)
95% CI of LS mean difference	..	(9.04, 74.76)	(4.57, 54.84)	(7.27, 59.41)	(36.57, 93.65)	(3.48, 51.24)	(-0.35, 57.12)
p value ^c	..	0.0132	0.0213	0.0130	<0.0001	0.0254	0.0528

Mixed-model repeated measures (MMRM) analysis was used to analyse the change from baseline and the percent change from baseline in metabolic parameters. The model included baseline as a covariate, and treatment group, visit and the interaction between treatment group and visit as factors.

CI=confidence interval. LS=least-squares. SE=standard error. Q2W=once every 2 weeks. QW=once per week.

^ap value of the within group treatment difference.

^bThe difference between treatment and placebo.

^cp value of the between group and placebo treatment difference.

FIG. 71

	Placebo (n=19)	Pegzofermin					
		3 mg QW (N=6)	9 mg QW (N=12)	18 mg QW (N=11)	27 mg QW (N=10)	18 mg Q2W (N=14)	36 mg Q2W (N=9)
Change from baseline to day 92							
n, unstructured	16	5	7	10	6	9	7
LS mean (SE)	0.06 (0.05)	0.15 (0.08)	0.12 (0.07)	0.03 (0.06)	0.14 (0.07)	0.12 (0.06)	0.09 (0.07)
90% CI of LS mean	(-0.02, 0.14)	(0.01, 0.28)	(0.01, 0.24)	(-0.07, 0.13)	(0.02, 0.27)	(0.02, 0.22)	(-0.02, 0.21)
95% CI of LS mean	(-0.03, 0.15)	(-0.02, 0.31)	(-0.02, 0.26)	(-0.09, 0.15)	(-0.01, 0.29)	(0.00, 0.24)	(-0.05, 0.23)
p value ^a	0.2124	0.0817	0.0794	0.6257	0.0590	0.0474	0.1878
LS mean difference compared with placebo ^b	..	0.09 (0.09)	0.07 (0.08)	-0.03 (0.07)	0.08 (0.09)	0.06 (0.08)	0.03 (0.08)
90% CI of LS mean difference	..	(-0.07, 0.25)	(-0.07, 0.21)	(-0.15, 0.10)	(-0.06, 0.23)	(-0.06, 0.19)	(-0.11, 0.17)
95% CI of LS mean difference	..	(-0.10, 0.28)	(-0.10, 0.23)	(-0.18, 0.12)	(-0.09, 0.26)	(-0.09, 0.22)	(-0.13, 0.20)
p value ^c	..	0.3554	0.4343	0.6949	0.3390	0.4020	0.6883
Percent change from baseline to day 92							
N, unstructured	16	5	7	10	6	9	7
LS mean (SE)	20.91 (13.96)	28.70 (24.68)	50.20 (21.05)	27.08 (17.76)	51.58 (22.08)	43.85 (18.17)	56.12 (20.81)
90% CI of LS mean	(-2.45, 44.26)	(-12.56, 69.96)	(15.00, 85.40)	(-2.64, 56.81)	(14.70, 88.46)	(13.50, 74.21)	(21.36, 90.89)
95% CI of LS mean	(-7.06, 48.88)	(-20.71, 78.12)	(8.05, 92.36)	(-8.52, 62.69)	(7.43, 95.73)	(7.51, 80.20)	(14.50, 97.75)
p value ^a	0.1399	0.2497	0.0205	0.1331	0.0228	0.0189	0.0091
LS mean difference compared with placebo ^b	..	7.79 (28.29)	29.29 (25.33)	6.18 (22.63)	30.67 (26.07)	22.95 (22.91)	35.22 (25.13)
90% CI of LS mean difference	..	(-39.51, 55.10)	(-13.06, 71.64)	(-31.69, 44.04)	(-12.89, 74.24)	(-15.36, 61.25)	(-6.78, 77.21)
95% CI of LS mean difference	..	(-48.86, 64.45)	(-21.43, 80.02)	(-39.18, 51.53)	(-21.49, 82.84)	(-22.92, 68.81)	(-15.07, 85.50)
p value ^c	..	0.7840	0.2523	0.7860	0.2441	0.3208	0.1663

Mixed-model repeated measures (MMRM) analysis was used to analyse the change from baseline and the percent change from baseline in metabolic parameters. The model included baseline as a covariate, and treatment group, visit and the interaction between treatment group and visit as factors.

CI=confidence interval. FFA=free fatty acid. LS=least-squares. SE=standard error. Q2W=once every 2 weeks. QW=once per week.

^ap value of the within-group treatment difference.

^bThe difference between treatment and placebo.

^cp value of the between-group and placebo treatment difference.

FIG. 72

		Pegazaferrin					
Placebo (n=19)		3 mg QW (N=6)	9 mg QW (N=12)	18 mg QW (N=11)	27 mg QW (N=10)	18 mg Q2W (N=14)	36 mg Q2W (N=9)
Change from baseline to day 50							
n, unstructured	14	4	4	4	7	8	6
LS mean (SE)	-3.05 (2.58)	-2.84 (4.90)	0.24 (4.70)	-4.40 (4.72)	1.61 (3.68)	-6.13 (3.38)	-3.39 (4.00)
90% CI of LS mean	(-7.39, 1.29)	(-11.09, 5.41)	(-7.66, 8.14)	(-12.33, 3.53)	(-4.58, 7.80)	(-11.80, -0.45)	(-10.11, 3.33)
95% CI of LS mean	(-8.26, 2.16)	(-12.74, 7.06)	(-9.24, 9.72)	(-13.91, 5.11)	(-5.82, 9.03)	(-12.93, 0.68)	(-11.45, 4.68)
p value ^a	0.2440	0.5654	0.9598	0.3560	0.6643	0.0766	0.4013
LS mean difference compared with placebo ^b	..	0.21 (5.54)	3.29 (5.36)	-1.35 (5.38)	4.66 (4.50)	-3.08 (4.26)	-0.34 (4.76)
90% CI of LS mean difference	..	(-9.11, 9.52)	(-5.72, 12.29)	(-10.39, 7.68)	(-2.91, 12.22)	(-10.23, 4.07)	(-8.34, 7.66)
95% CI of LS mean difference	..	(-10.97, 11.39)	(-7.51, 14.09)	(-12.19, 9.49)	(-4.42, 13.73)	(-11.65, 5.50)	(-9.94, 9.26)
p value ^c	..	0.9702	0.5427	0.8027	0.3064	0.4735	0.9435
Percent change from baseline to day 50							
n, unstructured	14	4	4	4	7	8	6
LS mean (SE)	-15.82 (32.62)	-6.12 (61.71)	82.00 (59.79)	3.28 (60.01)	78.40 (46.41)	-25.96 (42.75)	-10.36 (50.33)
90% CI of LS mean	(-70.66, 39.01)	(-109.90, 97.66)	(-18.48, 182.47)	(-97.56, 104.13)	(0.39, 156.40)	(-97.79, 45.87)	(-95.00, 74.29)
95% CI of LS mean	(-81.61, 49.96)	(-130.63, 118.39)	(-38.52, 202.52)	(-117.68, 124.25)	(-15.18, 171.97)	(-112.11, 60.20)	(-111.91, 91.20)
p value ^a	0.6301	0.9215	0.1772	0.9566	0.0984	0.5469	0.8379
LS mean difference compared with placebo ^b	..	9.70 (69.79)	97.82 (68.09)	19.11 (68.29)	94.22 (56.74)	-10.13 (53.79)	5.47 (59.99)
90% CI of LS mean difference	..	(-107.65, 127.06)	(-16.60, 212.24)	(-95.66, 133.87)	(-1.16, 189.60)	(-100.52, 80.26)	(-95.40, 106.33)
95% CI of LS mean difference	..	(-131.09, 150.50)	(-39.43, 235.07)	(-118.55, 156.77)	(-20.19, 208.63)	(-118.55, 98.29)	(-115.55, 126.48)
p value ^c	..	0.8901	0.1579	0.7809	0.1041	0.8515	0.9278

Mixed-model repeated measures (MMRM) analysis was used to analyse the change from baseline and the percent change from baseline in metabolic parameters. The model included baseline as a covariate, and treatment group, visit and the interaction between treatment group and visit as factors.

Adipo-IR=adipose tissue insulin resistance which is derived from fasting insulin and free fatty acid. CI=confidence interval. LS=least-squares. PD=pharmacodynamic.

SE=standard error. Q2W=once every 2 weeks. QW=once per week.

^ap value of the within-group treatment difference.

^bThe difference between treatment and placebo.

^cp value of the between-group and placebo treatment difference.

FIG. 73

	Placebo (n=19)	Pegzofermin						Overall (N=81)
		3 mg QW (n=6)	9 mg QW (n=12)	18 mg QW (n=11)	27 mg QW (n=10)	18 mg Q2W (n=14)	36 mg Q2W (n=9)	
Site								
1101	4	4	2	0	2	0	0	12
1102	0	0	0	0	0	0	0	0
1103	2	0	0	4	0	6	0	12
1104	5	2	9	3	1	0	4	24
1105	2	0	0	1	0	1	0	4
1106	0	0	0	0	0	0	0	0
1107	0	0	1	1	2	1	1	6
1108	1	0	0	0	0	5	0	6
1109	0	0	0	0	0	0	0	0
1110	2	0	0	0	1	1	1	5
1111	2	0	0	0	4	0	3	9
1112	0	0	0	0	0	0	0	0
1113	1	0	0	1	0	0	0	2
1114	0	0	0	1	0	0	0	1

FIG. 74

	BC-NASH ^a (n=15)	PNASH ^b (n=66)	Overall (n=81)
Age, mean, years	50.6	52.2	51.9
Male, %	20.0	42.4	38.3
Weight, mean, kg	99.3	92.3	93.6
BMI, mean, kg/m ²	35.4	34.4	34.6
T2DM, %	26.7	50.0	45.7
MRI-PDFF, %	21.2	21.4	21.3
ALT, mean, U/L	42.9	41.1	41.5
ALT >ULN, %	26.7	36.4	34.6
AST, mean, U/L	34.9	30.0	31.0

ALT=alanine aminotransferase. AST=aspartate aminotransferase; BC-NASH=biopsy-confirmed non-alcoholic steatohepatitis. BMI=body mass index. MRI-PDFF=magnetic resonance imaging proton-density fat fraction. PNASH=phenotypic non-alcoholic steatohepatitis. T2DM=type 2 diabetes mellitus. ULN=upper limit of normal.

^aDefined as NASH Clinical Research Network fibrosis stage 1, 2, or 3 based on biopsy performed in the 24 months before screening, or PNASH if biopsy was not available.

^bDefined as: obesity (BMI >30 kg/m²) with either T2DM (fasting plasma glucose ≥126 mg/dL, plasma glucose in a 75 g oral glucose tolerance test ≥200 mg/dL, or glycated haemoglobin ≥6.5 %); obesity with evidence of liver injury (increased ALT [^c≥40 U/L in men or ≥30 U/L in women]; and/or FibroScan (EchoSens, Waltham, MA, USA) vibration-controlled transient elastography score ≥7 kPa.

^cULN=45 U/L.

FIG. 75

	MRI-PDFF responder (n=40)	MRI-PDFF non-responder (n=14)
Age, years		
Mean (SD)	52.83 (8.335)	47.54 (13.603)
Median (IQR)	53.15 (46.40, 58.45)	51 (2.40, 56.70)
Female, n (%)	26 (65.0)	7 (50.0)
Race, n (%)		
Black or African American	2 (5.0)	2 (14.3)
White	37 (92.5)	12 (85.7)
Other	1 (2.5)	0
Ethnicity, n (%)		
Hispanic or Latino	39 (97.5)	11 (78.6)
Not Hispanic of Latino	1 (2.5)	3 (21.4)
Weight, kg		
Mean (SD)	89.908 (17.868)	104.454 (18.345)
Median (IQR)	87.55 (80.175, 97.050)	104.7 (92.100, 119.100)
BMI, kg/m ²		
Mean (SD)	33.95 (4.905)	37.33 (6.274)
Median (IQR)	33.65 (30.45, 37.40)	38.05 (31.30, 43.30)
T2DM history		
No	24 (60.0)	10 (71.4)
Yes	16 (40.0)	4 (28.6)
ALT, U/L		
Mean (SD)	42.8 (30.60)	40.4 (23.63)
Median (IQR)	33.5 (23.0, 52.5)	32.5 (26.0, 46.0)
AST, U/L		
Mean (SD)	33.0 (25.72)	26.9 (12.41)
Median (IQR)	24.5 (19.5, 32.0)	23.5 (21.0, 29.0)
MRI-PDFF, %		
Mean (SD)	20.60 (8.715)	22.14 (6.763)
Median (IQR)	18.6 (13.70, 26.20)	20.15 (18.20, 27.60)
≥1/5 high-risk NAFLD criteria, ^a n (%)	37 (92.5)	13 (92.9)
≥2/5 high-risk NAFLD criteria, ^a n (%)	24 (60.0)	10 (71.4)

ALT=alanine aminotransferase. AST=aspartate aminotransferase. BMI=body mass index. IQR=interquartile range. MRI-PDFF=magnetic resonance imaging proton-density fat fraction. NAFLD=non-alcoholic fatty liver disease SD=standard deviation. T2DM=type 2 diabetes mellitus.

^aBaseline ALT >1×ULN; vibration-controlled transient elastography ≥7.0 kPa; enhanced liver fibrosis ≥7.7; PRO-C3 ≥14.71 ng/mL; and Fibrosis-4 index score >1.3.

FIG. 76

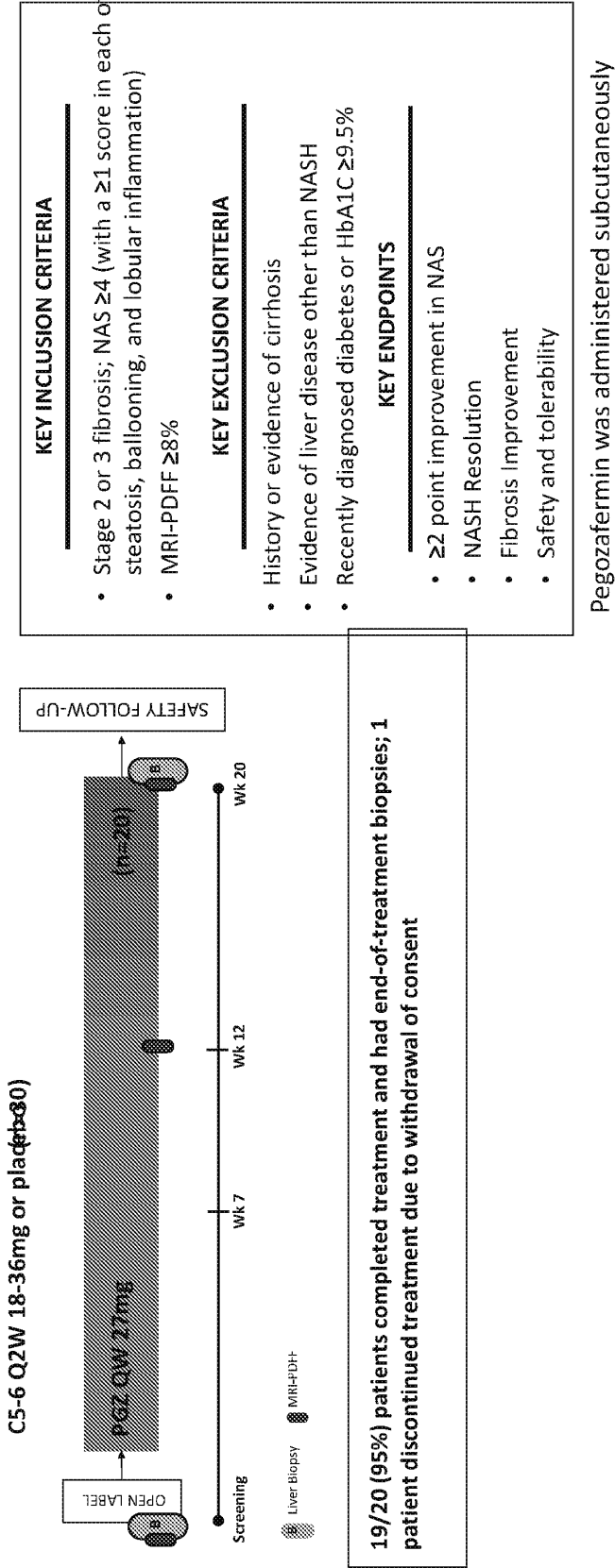


FIG. 77

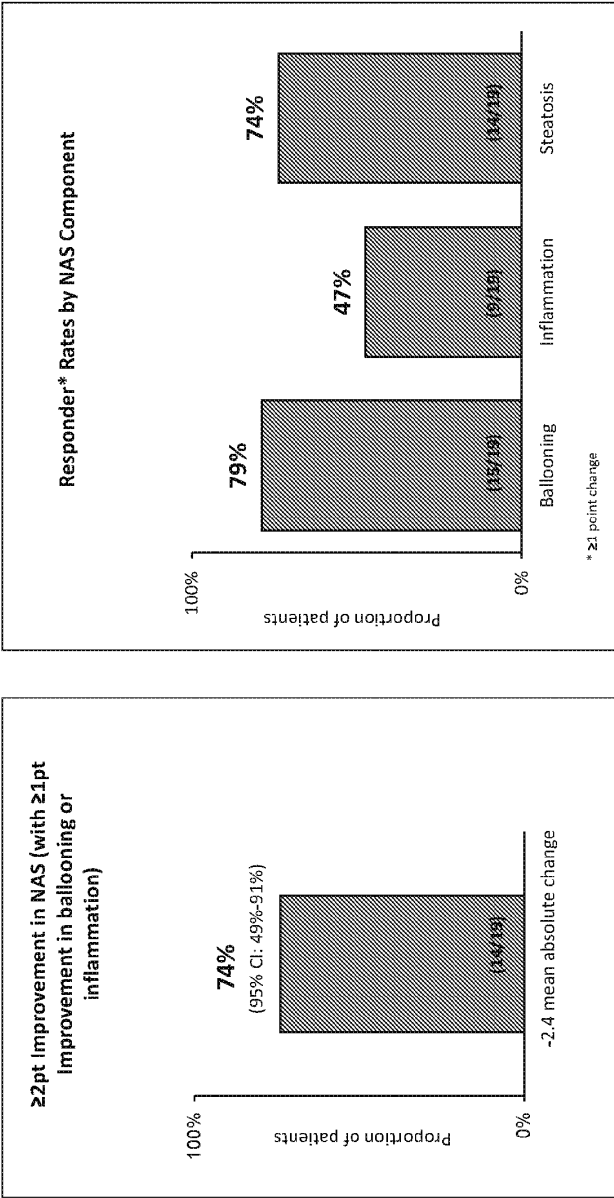


FIG. 78

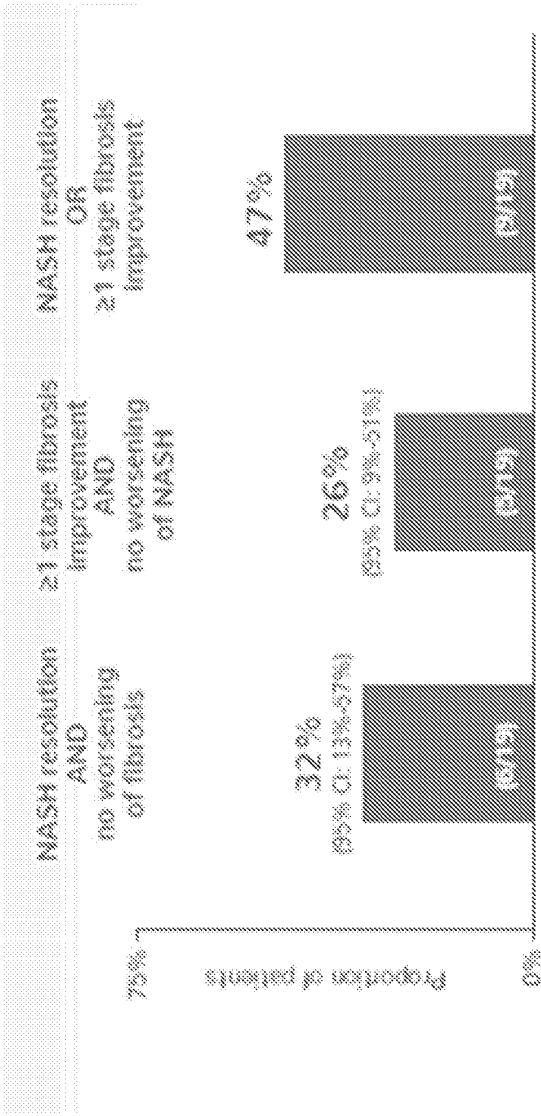


Figure 79

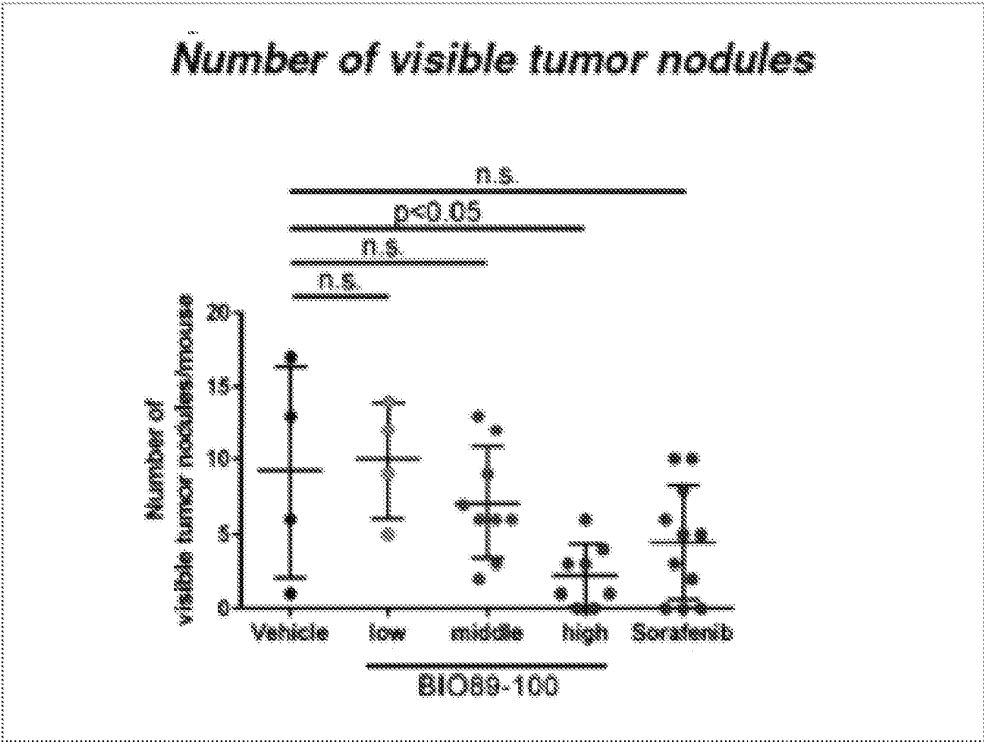
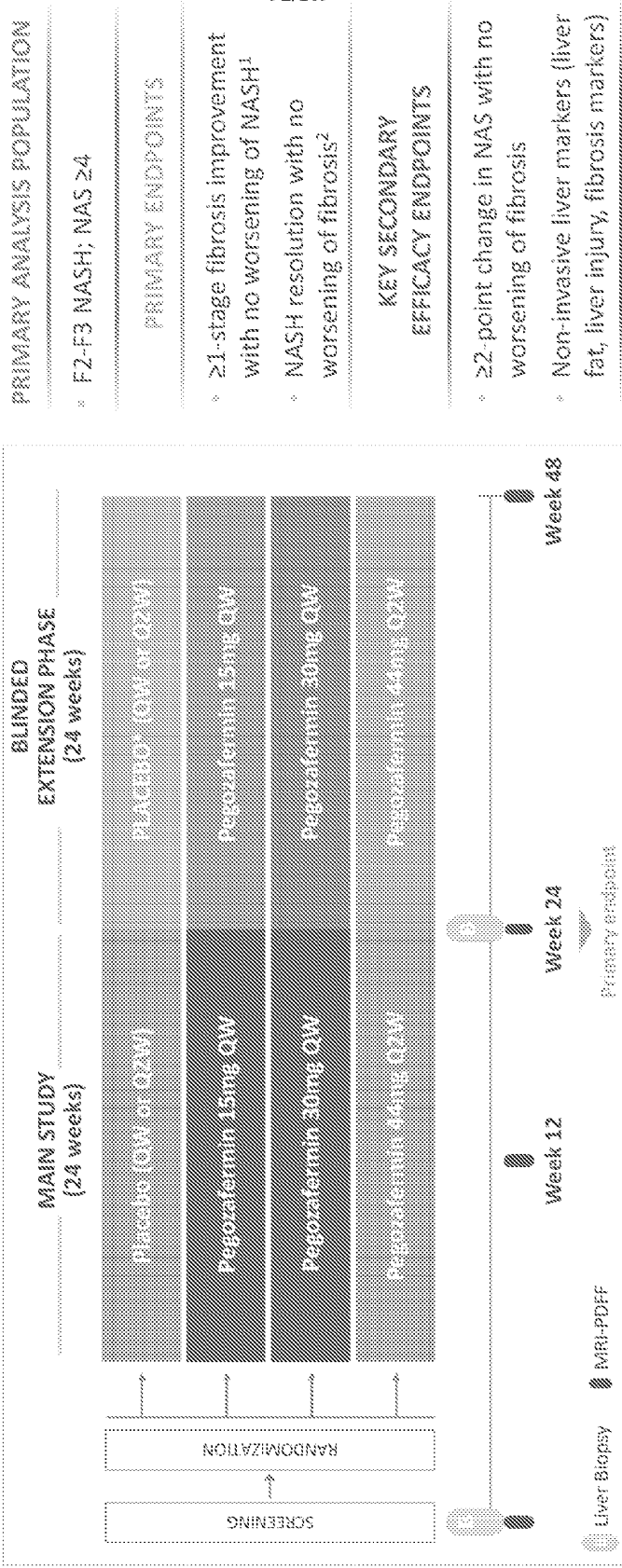


FIG. 80

ENLIVEN Trial Design



¹ Improvement in liver fibrosis by at least 1 stage and no worsening of steatohyperlipidemia defined as no increase in NAFL or ballooning, inflammation, or steatosis (FLS draft guidance).
² Resolution of steatohyperlipidemia is defined as absent fatty liver disease or treated or simple steatosis without steatohyperlipidemia, and a NAS score of 0-1 for inflammation, 0 for ballooning and any value for steatosis (FLS draft guidance).
³ Some placebo patients were re-randomized to the extension phase to receive pegzofermin.
NAS, NASH Activity Score; MRI-PDFF, Magnetic resonance imaging-estimated proton density fat fraction; QW, Every week; Q2W, Every 2 weeks.

Rigorous Biopsy Reading Method Designed to Identify Drug Effect

1864

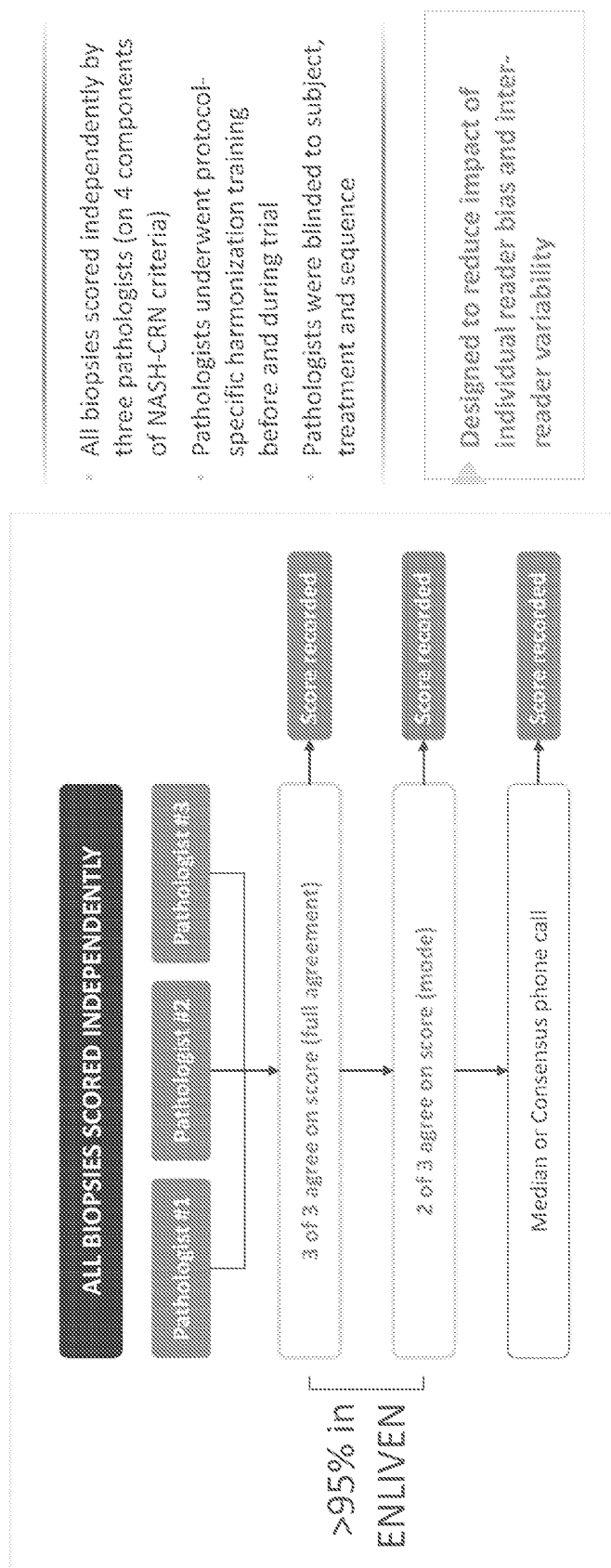
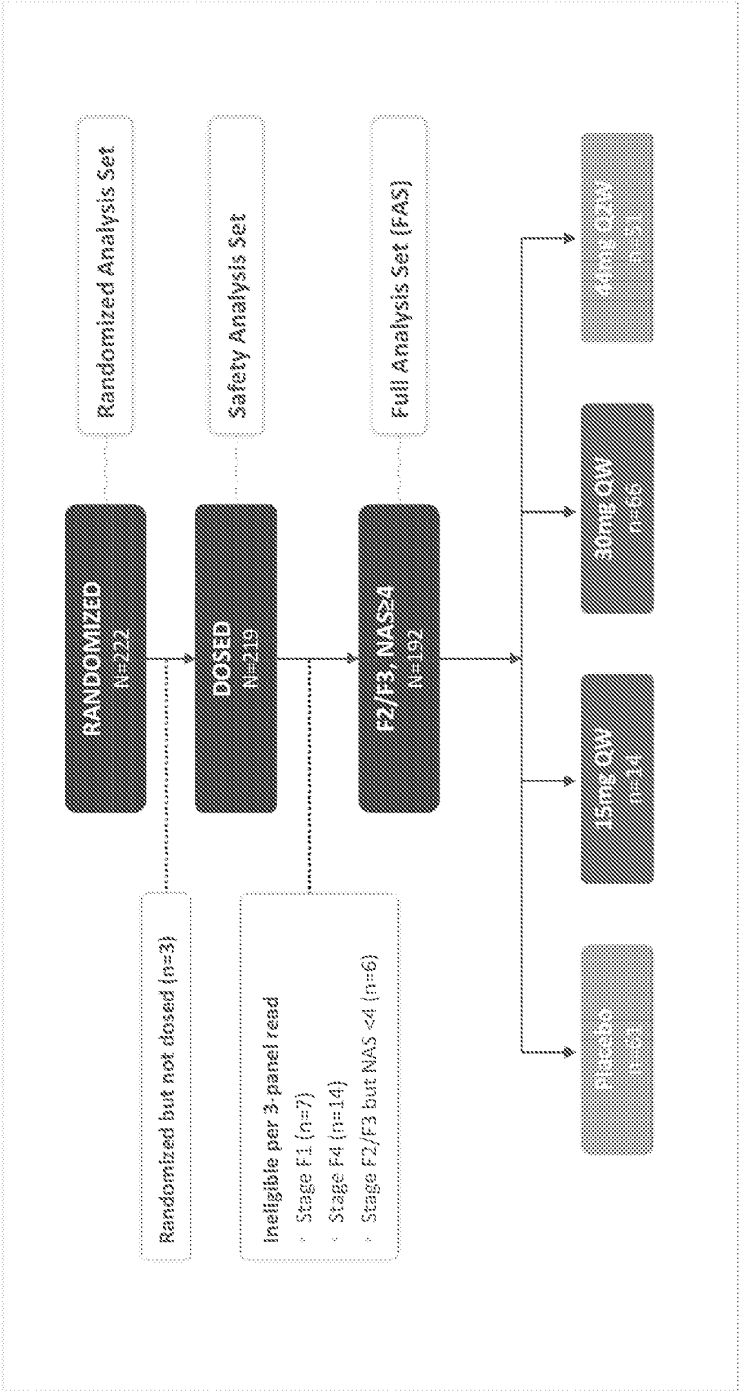


FIG. 82

Patient Disposition and Analysis Sets



Analysis Sets were prospectively defined
Completer Analysis Set = FAS subjects with biopsies at both baseline and Week 24 (n=164).
MRI-PDFF Analysis Set = all subjects in FAS with baseline and at least one post-baseline MRI-PDFF assessment (n=181).

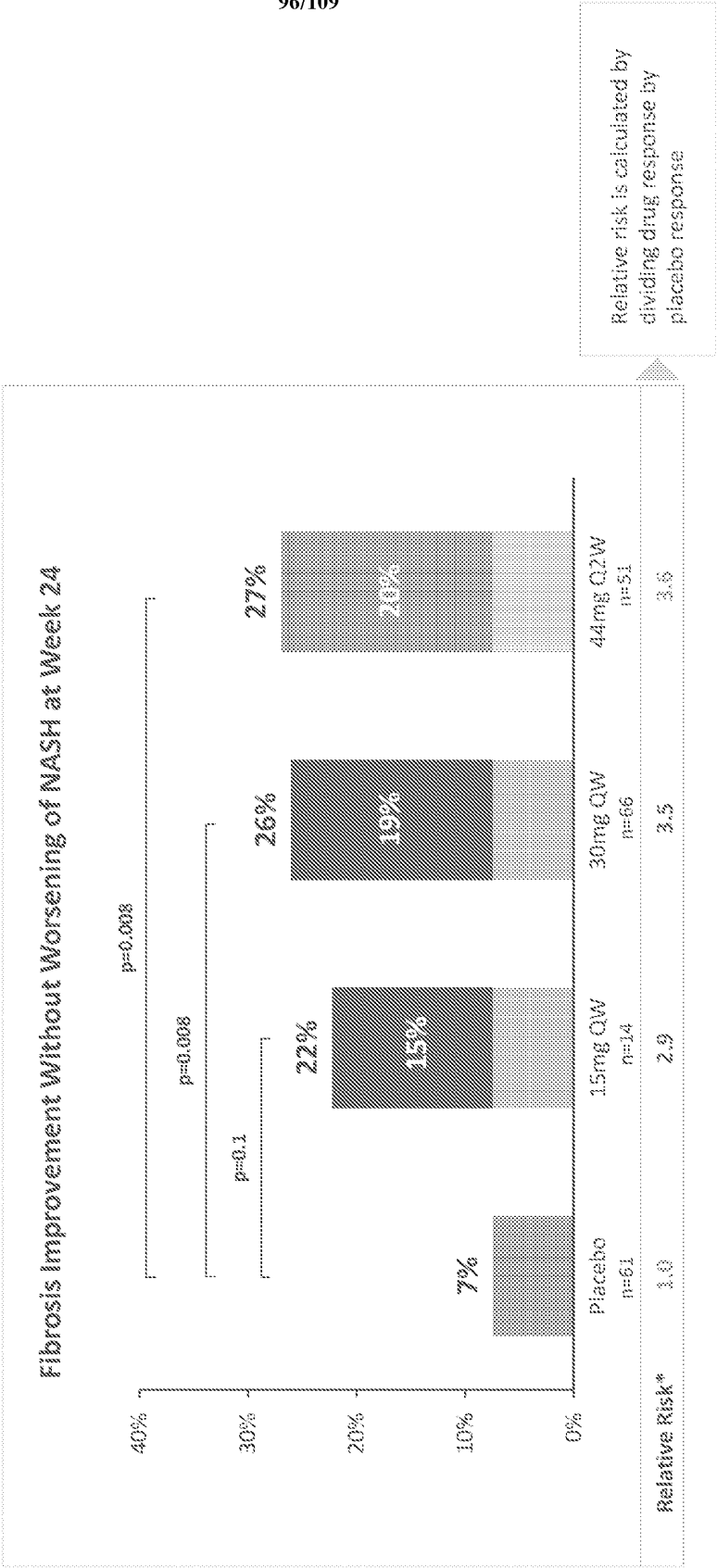
Baseline Characteristics Well Balanced Across Dose Groups FIG. 83

Parameter (Mean or %)	Placebo (n=71)	15mg QW (n=71)	30mg QW (n=73)	45mg QW (n=57)	Total (n=222)
Age (years)	56	55	55	55	56
Female	55%	43%	69%	65%	61%
BMI (kg/m ²)	38	38	35	36	37
Type 2 Diabetes	69%	86%	62%	61%	66%
Fibrosis Stage (% F3)	66%	43%	64%	53%	60%
NAFLD Activity Score	5.0	4.8	5.3	5.2	5.1
Liver Fat Content (MRI-PDFF)	16.7%	15.8%	16.7%	15.8%	16.4%
Liver Stiffness (VCTE, kPa)	14.1	11.2	12.5	13.2	13.0
PRO-C3 (ng/ml)	50	62	54	52	53
ALT (U/L)	50	61	60	56	56
AST (U/L)	41	48	47	42	44
HbA1c, overall population (%)	6.6	7.0	6.6	6.7	6.7
Triglycerides (mg/dL)	170	186	175	165	172

Source: Randomized Avelumab Set.
ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; MRI-PDFF, magnetic resonance proton density fat fraction; VCTE, vibration-controlled transient elastography; PRO-C3, procollagen type III C-peptide.

Pegzofermin Demonstrated Statistical Significance on Fibrosis Improvement with Weekly and Every-Two-Week Dosing

FIG. 84



Pre-Specified Additional Analyses Confirm Robustness of Primary Efficacy Results

Fibrosis Improvement Without Worsening of NASH at Week 24

	30mg QW	45mg Q2W
Completer Analysis Set (n=164)		
Effect Size (placebo-adjusted)	19%	20%
p-value	0.009	0.008
Intent-to-treat (ITT; missing data = non-responder); (n=152)		
Effect Size (placebo-adjusted)	15%	16%
p-value	0.019	0.015

FIG. 85

Descriptive Analysis Data of Cirrhotic (F4) Patients from ENLIVEN

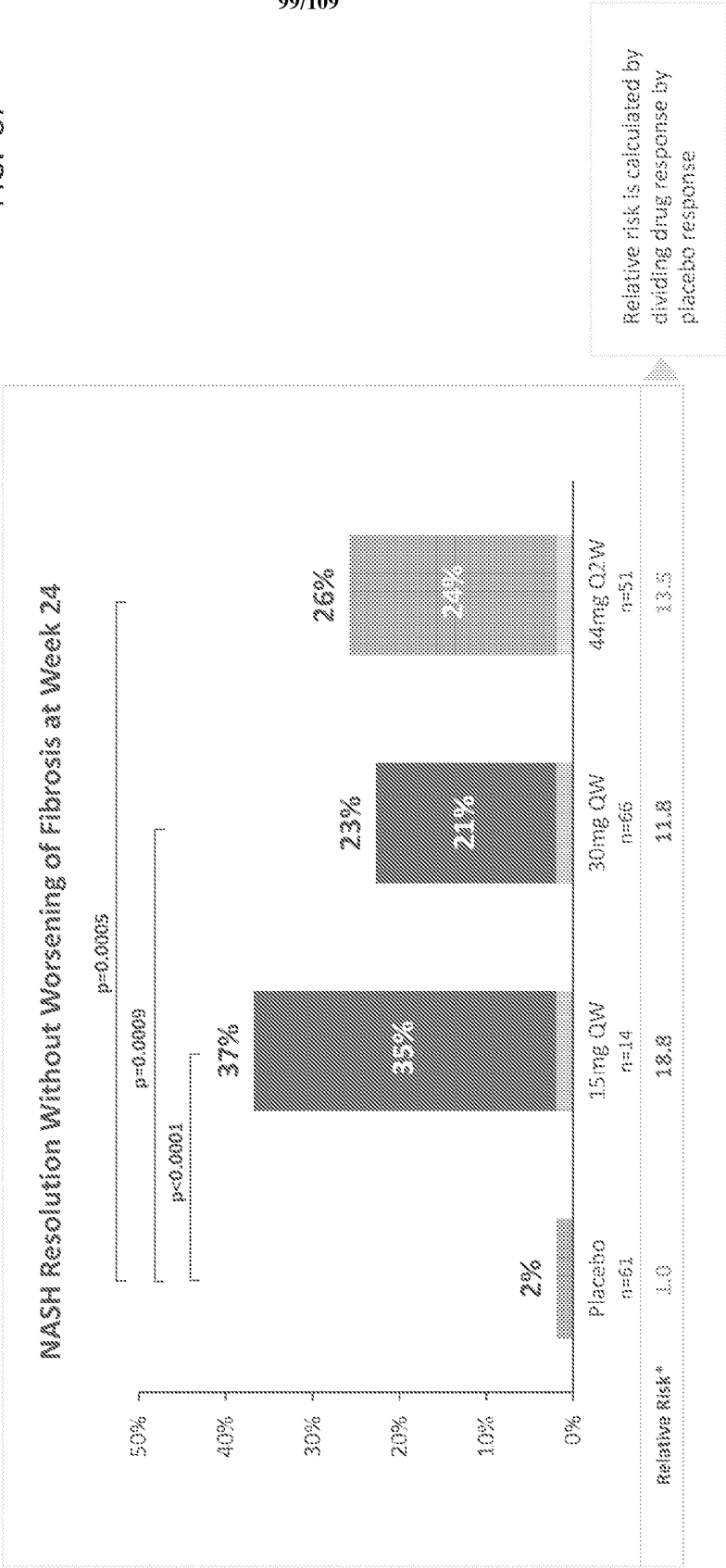
FIG. 86



¹Improvement in liver fibrosis by 21 stage and no worsening of steatohepatitis defined as no increase in NAs for ballooning, inflammation, or steatosis.

Pegzofermin Demonstrated Statistical Significance on NASH Resolution at All Doses

FIG. 87



Pre-Specified Additional Analyses Confirm Robustness of Primary Efficacy Results

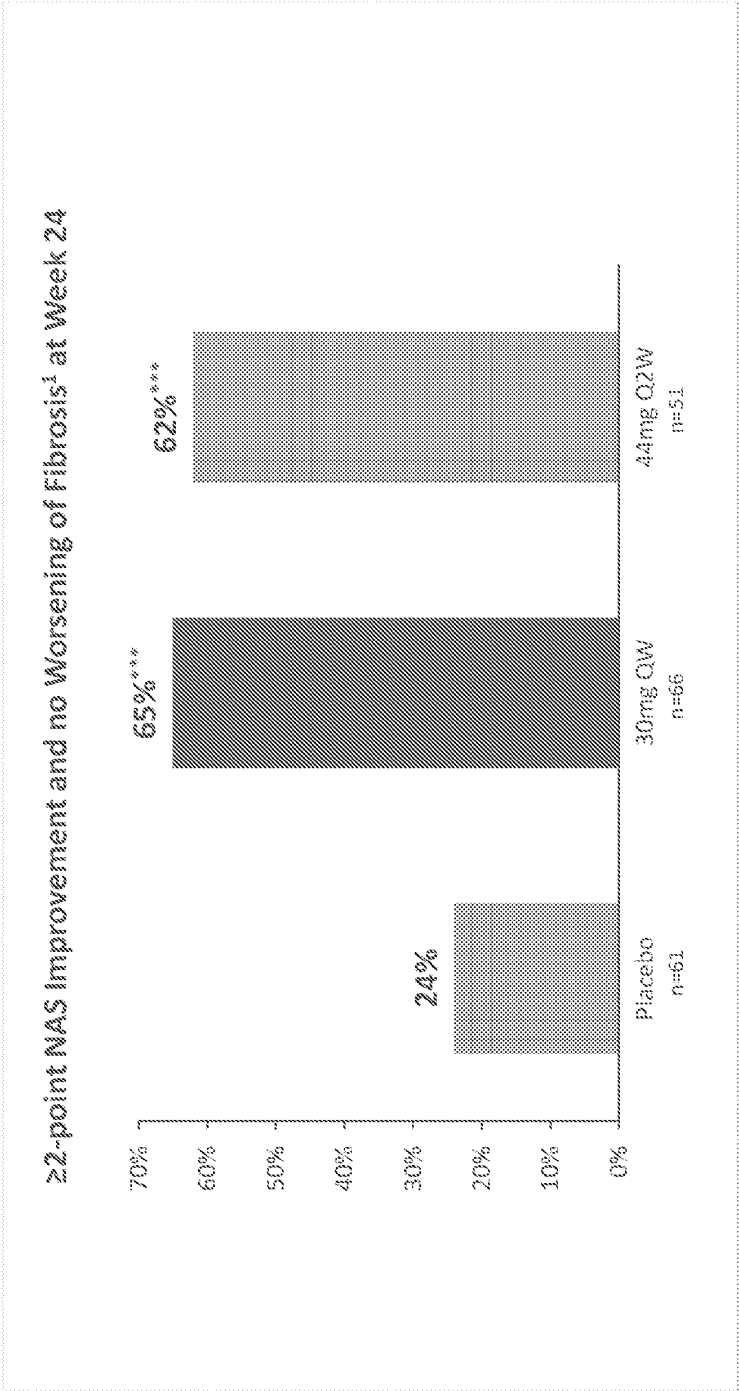
FIG. 88

NASH Resolution Without Worsening of Fibrosis at Week 24

	30mg QW	44mg Q2W
Completer Analysis Set (n=164)		
Effect Size (placebo-adjusted)	21%	24%
p-value	0.0009	0.0004
ITT (missing data = non-responder); (n=192)		
Effect Size (placebo-adjusted)	17%	20%
p-value	0.0019	0.0009

Pegzofermin Demonstrated Statistical Significance on ≥ 2 -point NAS Improvement

FIG. 89



Pegzofermin Demonstrated Robust Liver Fat Reduction with High Responder Rates by MRI-PDFF at Week 24

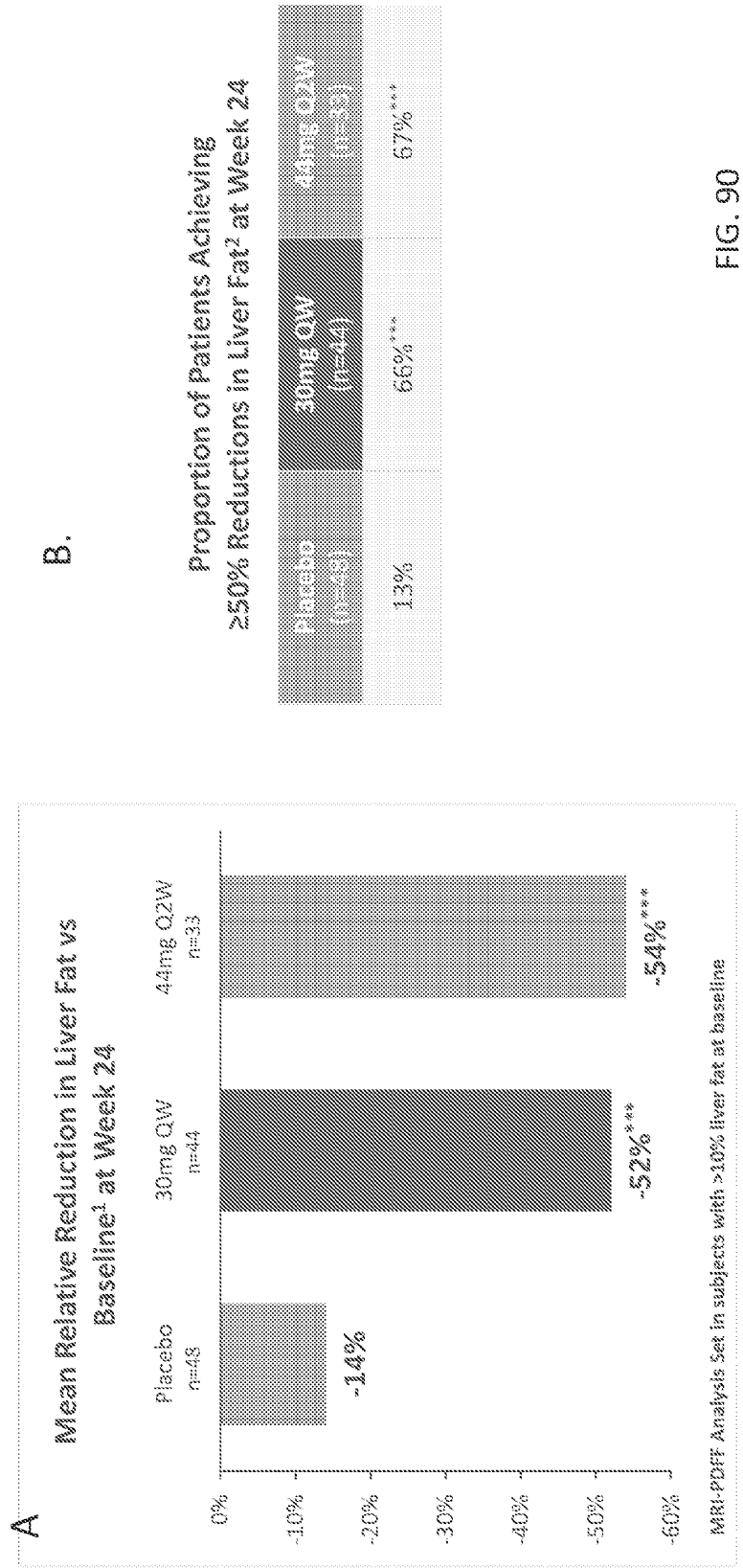
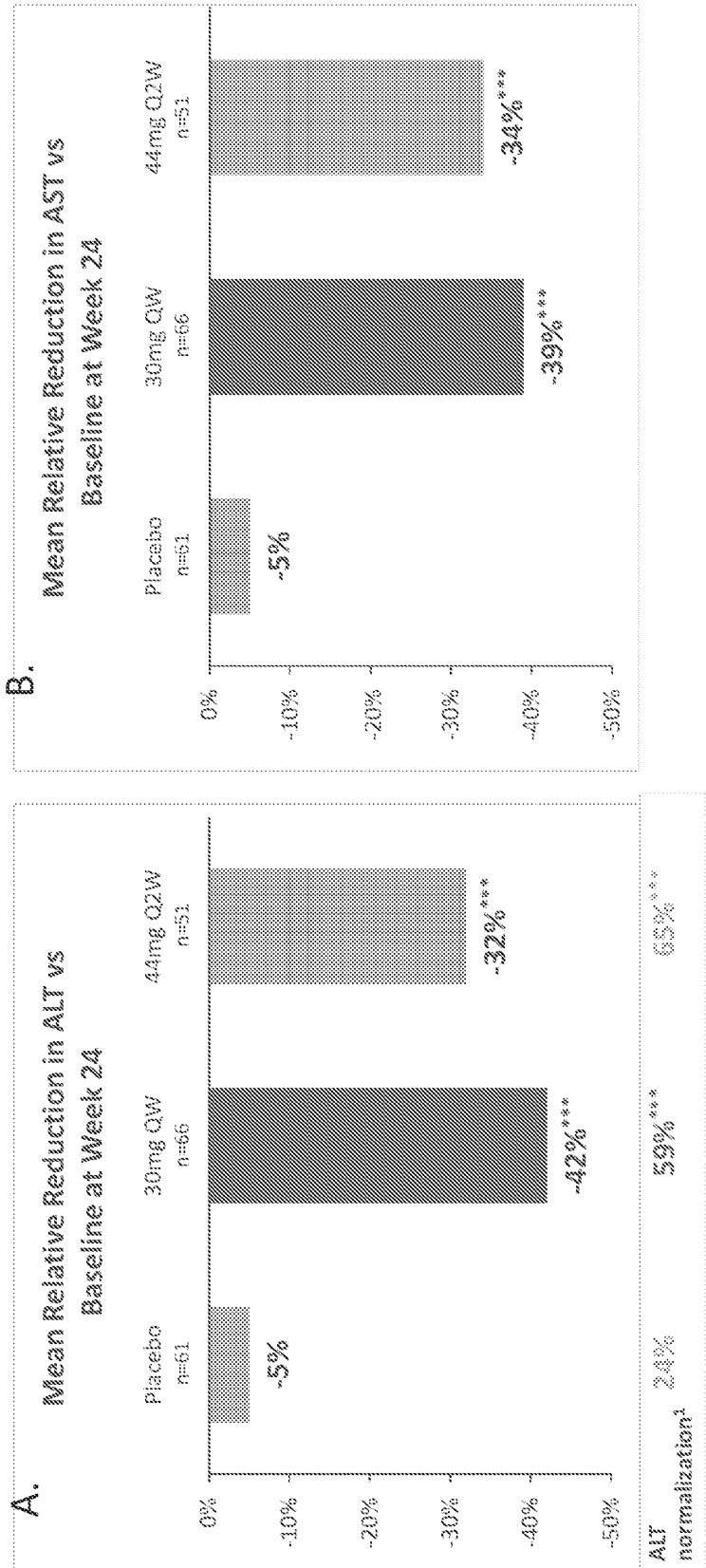
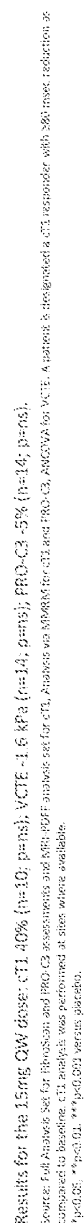


FIG. 90

Pegozafermin Demonstrated Significant Improvements in Markers of Liver Injury (ALT and AST)



W.G. 92



Pegzofermin Demonstrated Meaningful Reductions in HbA1c

Change in HbA1c from Baseline at Week 24

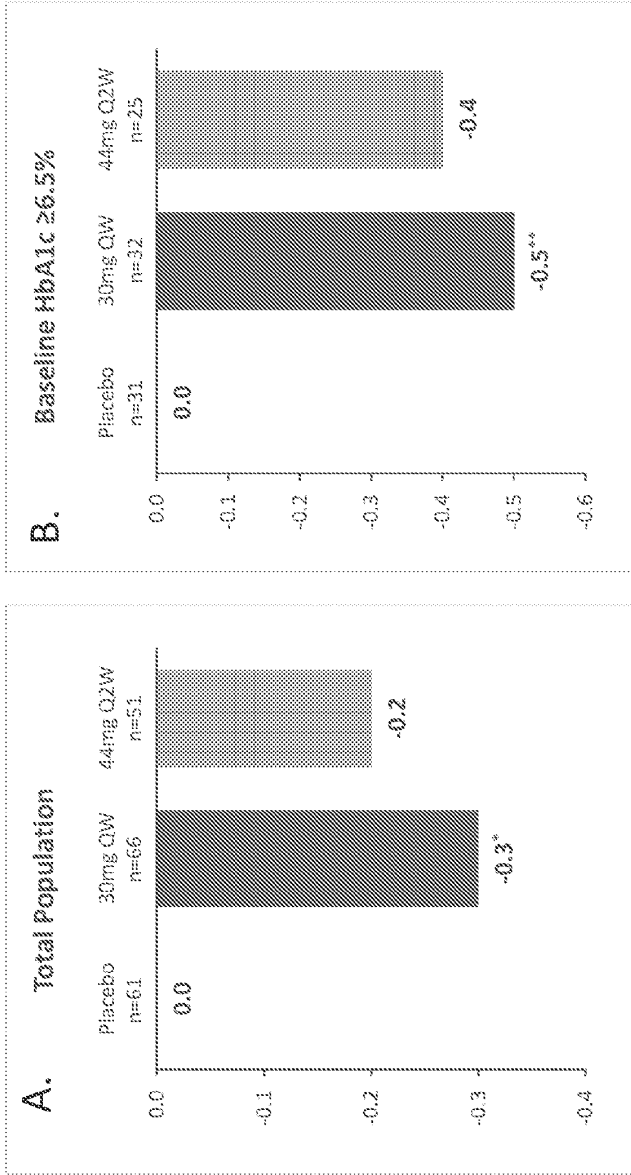


FIG. 93

Source: FIG 93 Analysis Set for either overall population or FAS with baseline HbA1c ≥6.5%. Analyses vs MP1963
*p<0.05, **p<0.01 versus placebo.

Pegozafermin Demonstrated Meaningful Changes in Serum Lipids

Percent Change in Serum Lipids from Baseline at Week 24

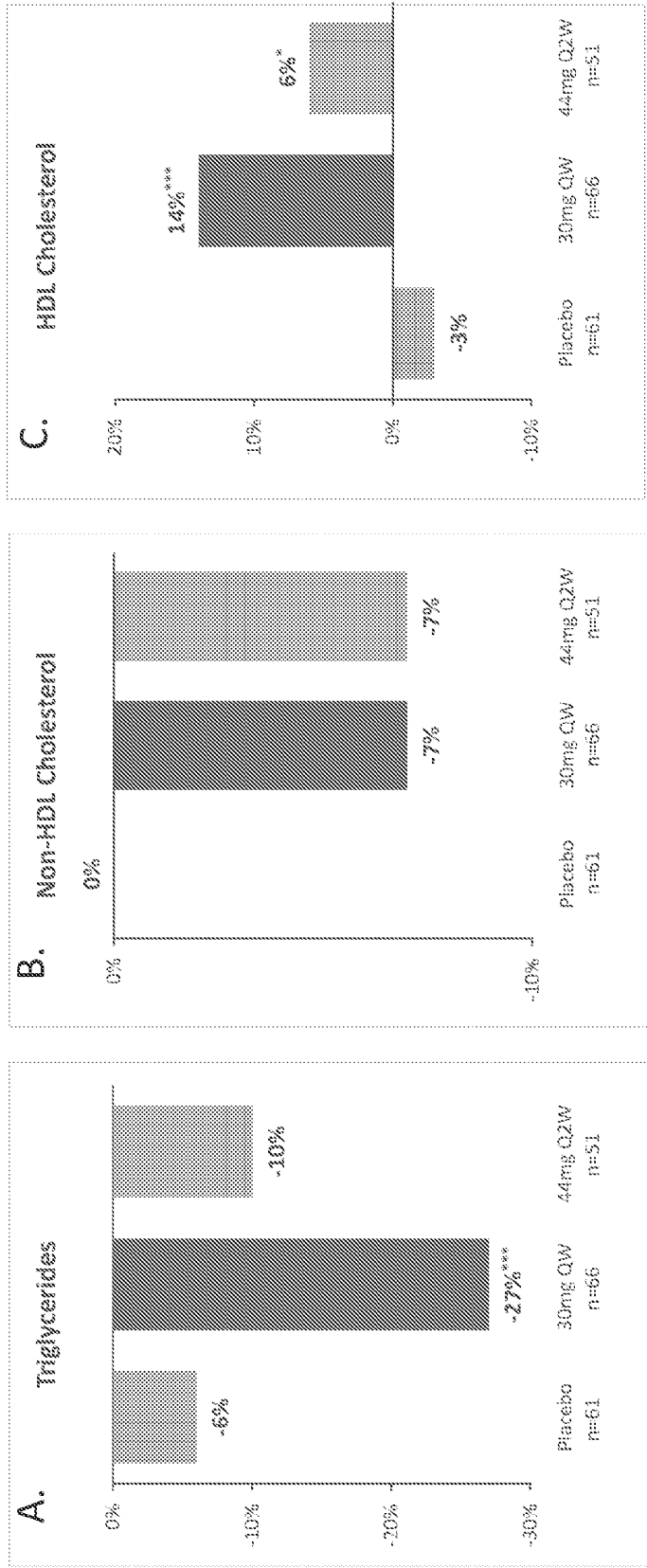


FIG. 94

Source: Full Analysis Set. Analysis via one-tailed t-test for triglycerides (reported as median) and paired t-test for HDL cholesterol. Subject is with missing week 24 triglycerides are excluded from the comparative analysis.
Non-HDL cholesterol and HDL cholesterol (reported as 1-tailed) with changes from baseline (absolute or %) as dependent variables.
*p<0.05, **p<0.01, ***p<0.001 versus placebo.

Pegzofermin Was Well Tolerated Across Doses

Low incidence of treatment-related TEAEs

Drug-related TEAEs in ≥10% of patients

Preferred Term	Placebo (n=59)	15mg QW (n=21)	30mg QW (n=72)	44mg Q2W (n=57)
Diarrhea	3%	24%	17%	9%
Nausea	1%	14%	21%	18%
Injection site erythema	3%	14%	14%	5%
Injection site rash	1%	0	10%	4%
Increased appetite	0	10%	13%	5%

Most TEAEs were grade 1 or 2. No tremor reported.

	Placebo	15mg QW	30mg QW	44mg Q2W
Drug-related AEs leading to discontinuation	0	5% ^a	6% ^b	2% ^c
Drug-related Serious Adverse Event (SAE)	0	0	0	2% ^c

Related discontinuations: ^a Diarrhea [15 mg QW]; ^b Diarrhea [30 mg QW]; Nausea [30 mg QW]; Diarrhea [30 mg QW]; ISR erythema [44 mg Q2W];
Unrelated discontinuations: Angina [placebo]; Colon CA [30 mg QW]; COVID-19 [30 mg QW];

FIG. 95

Source: Safety Analysis Set. AE table cutoff ≥10% for patients for placebo, 30mg QW and 44mg Q2W doses.

FIG. 96A

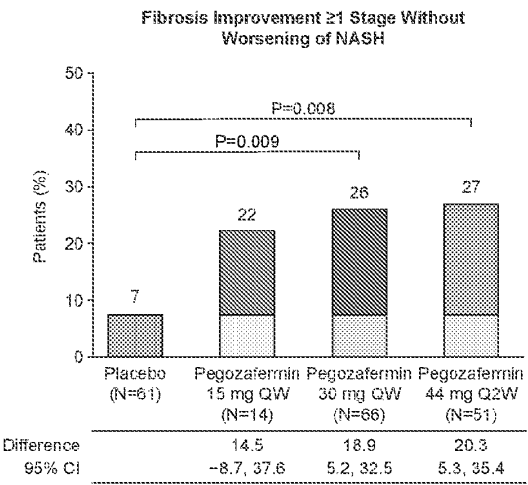


FIG. 96B

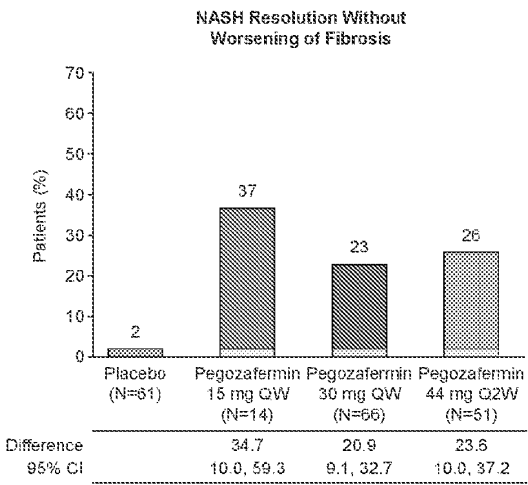


FIG. 97

