

Figure 1. Flow of Patients Through the Trial

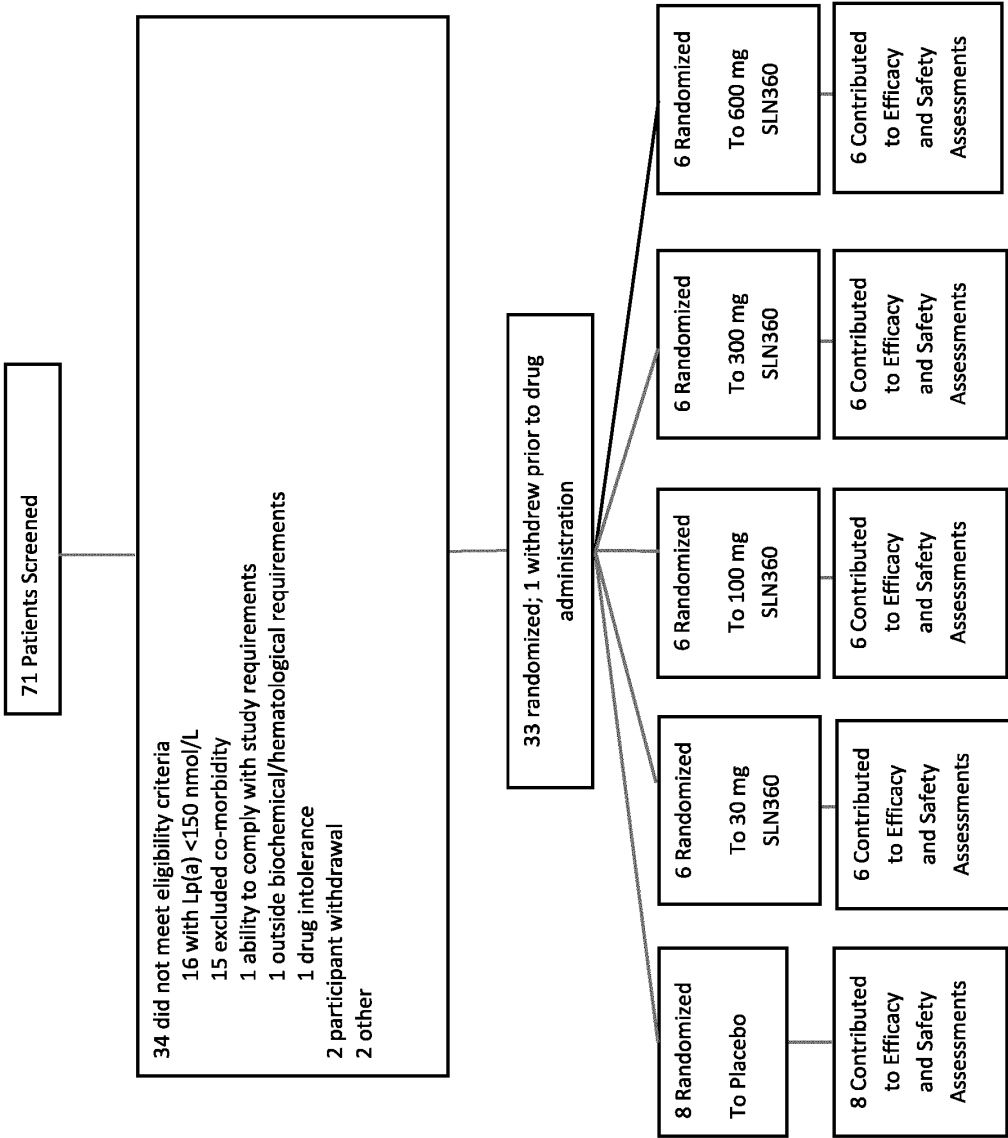


Figure 2a. Lipoprotein(a) Concentrations from Baseline to 150 Days After Administration

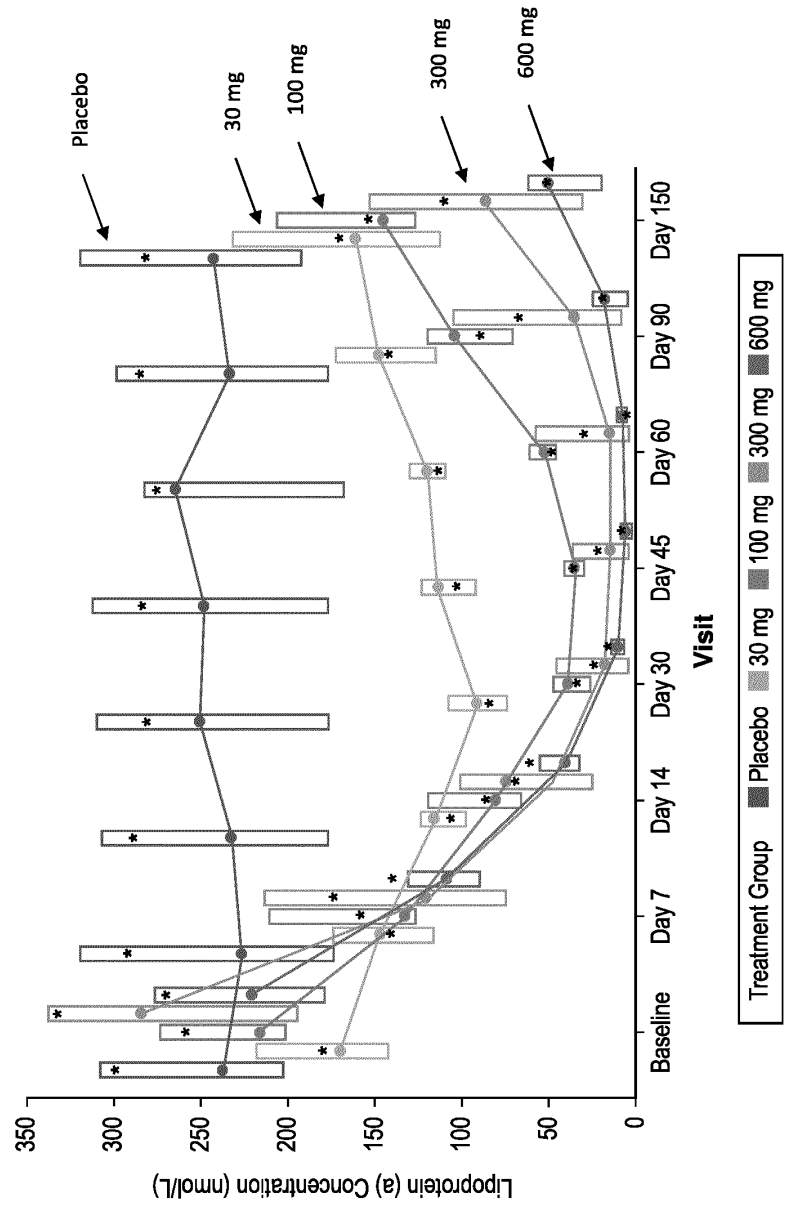


Figure 2b. Percent Change in Lipoprotein(a) Concentration from Baseline to 150 Days after Administration

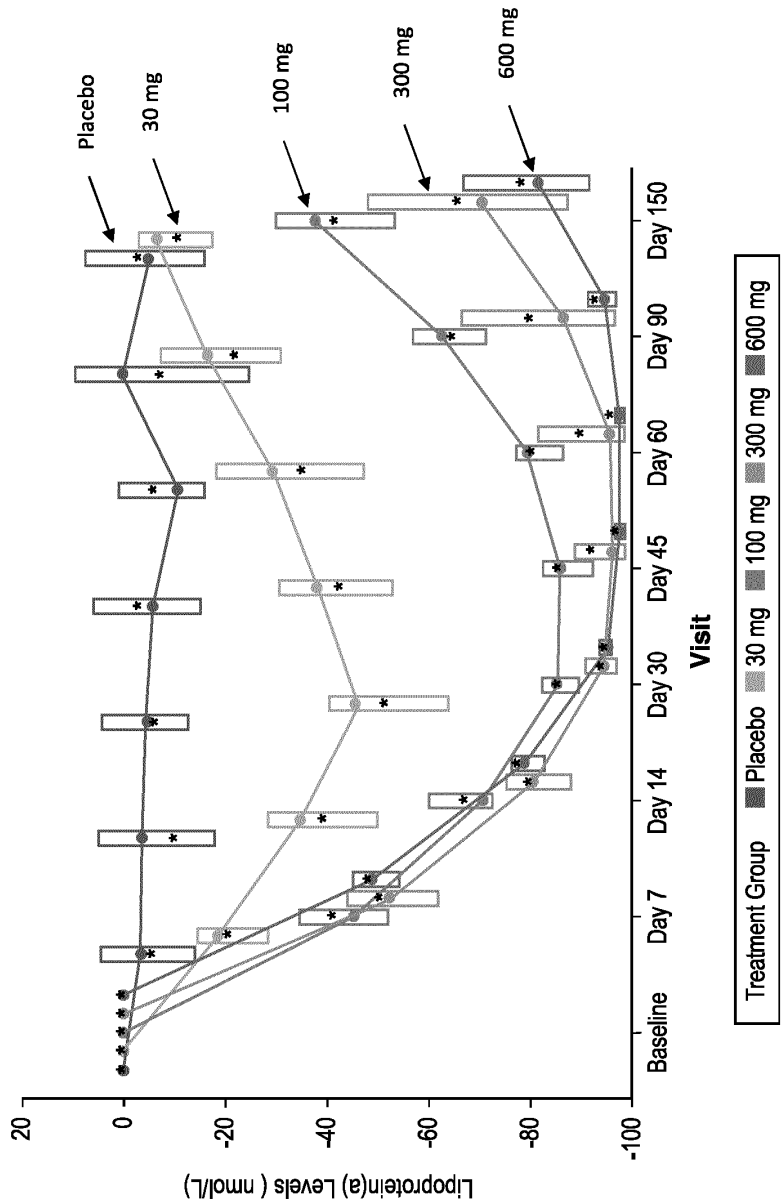


Figure 3a. Mean and 95% CIs for Percent Change in Low-Density Lipoprotein Cholesterol Concentrations from Baseline to 150 Days

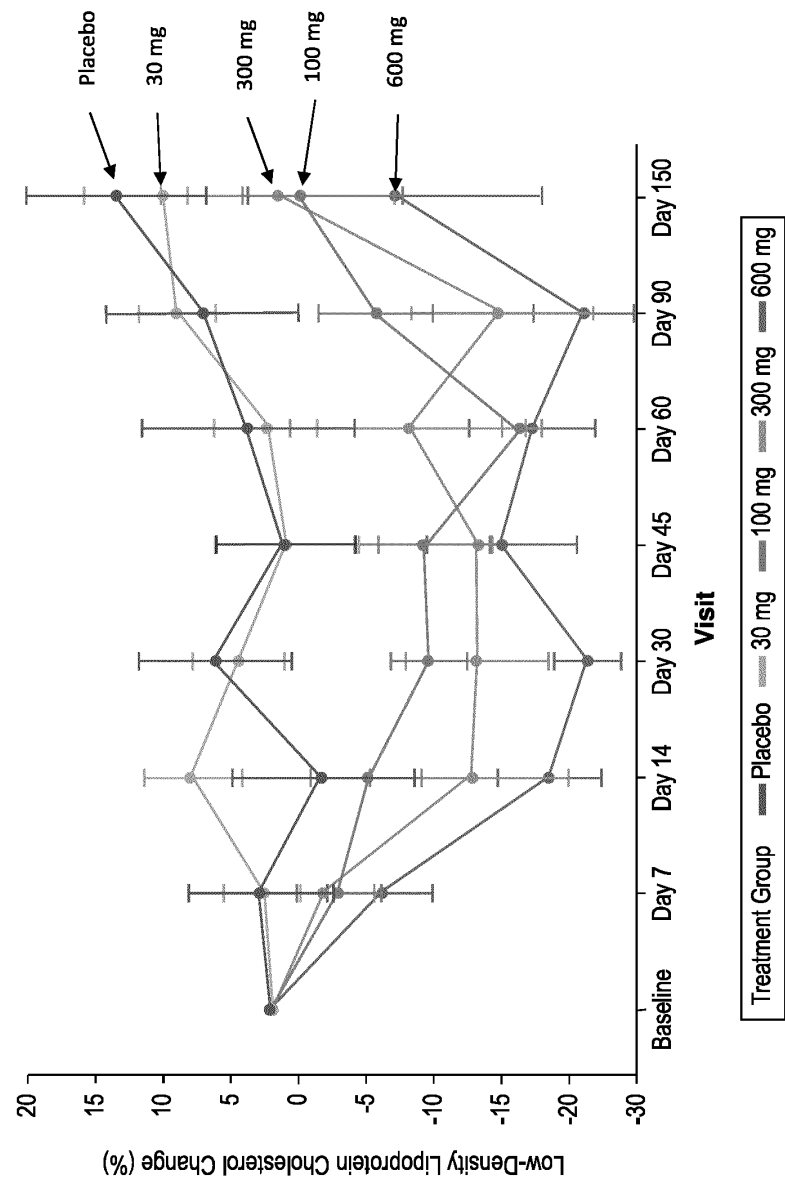


Figure 3b. Mean and 95% CIs for Percent Change in Apolipoprotein B Concentrations from Baseline to 150 Days

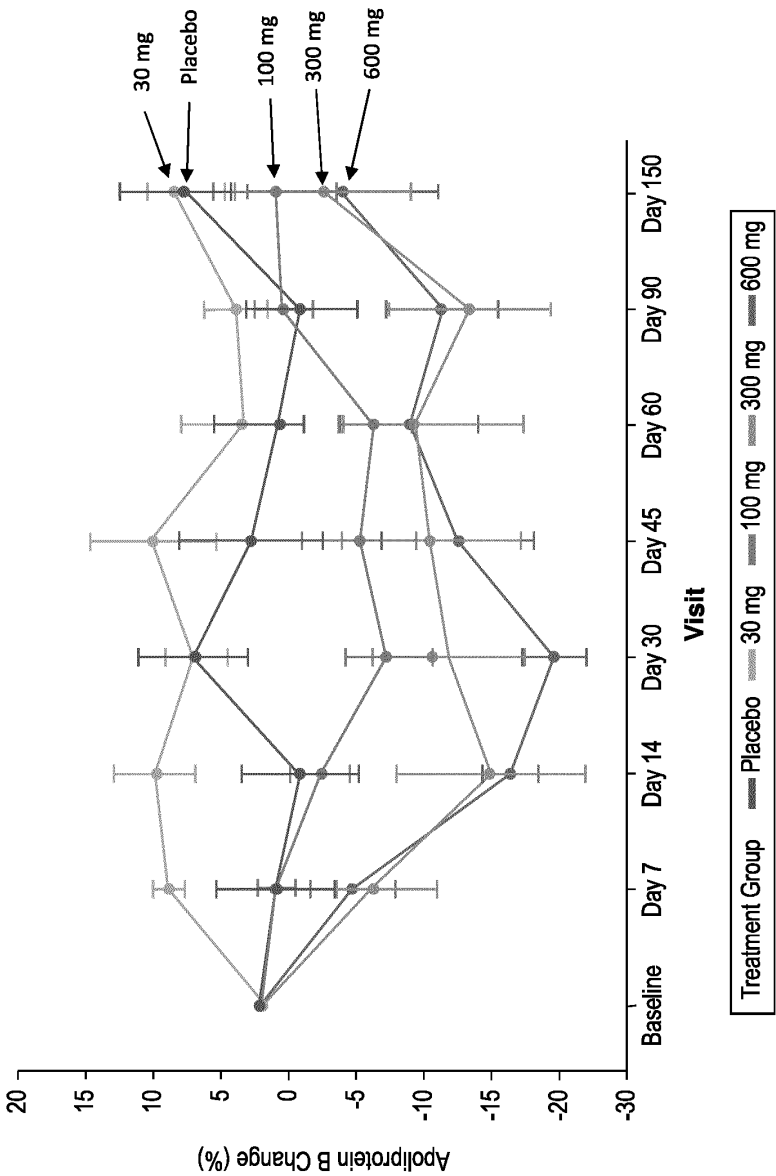


Figure 4

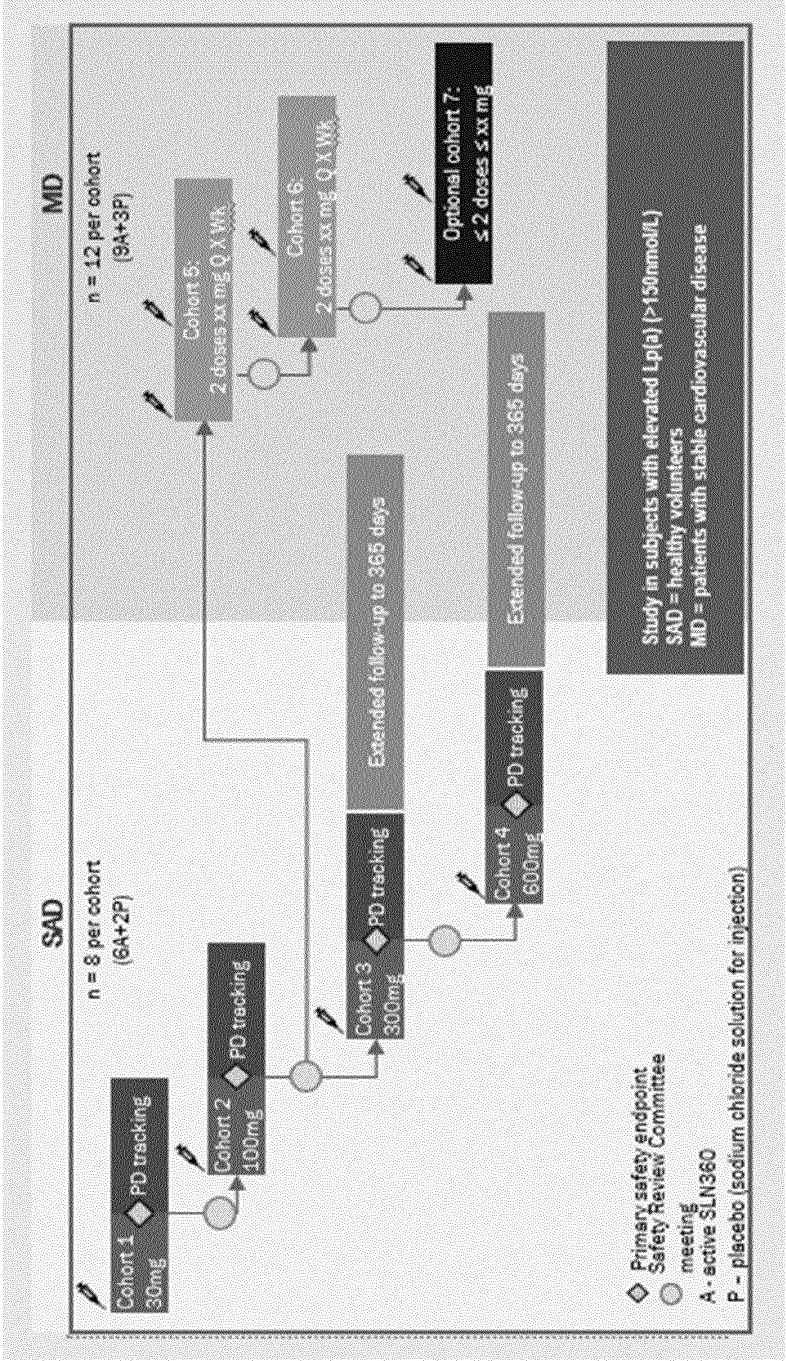
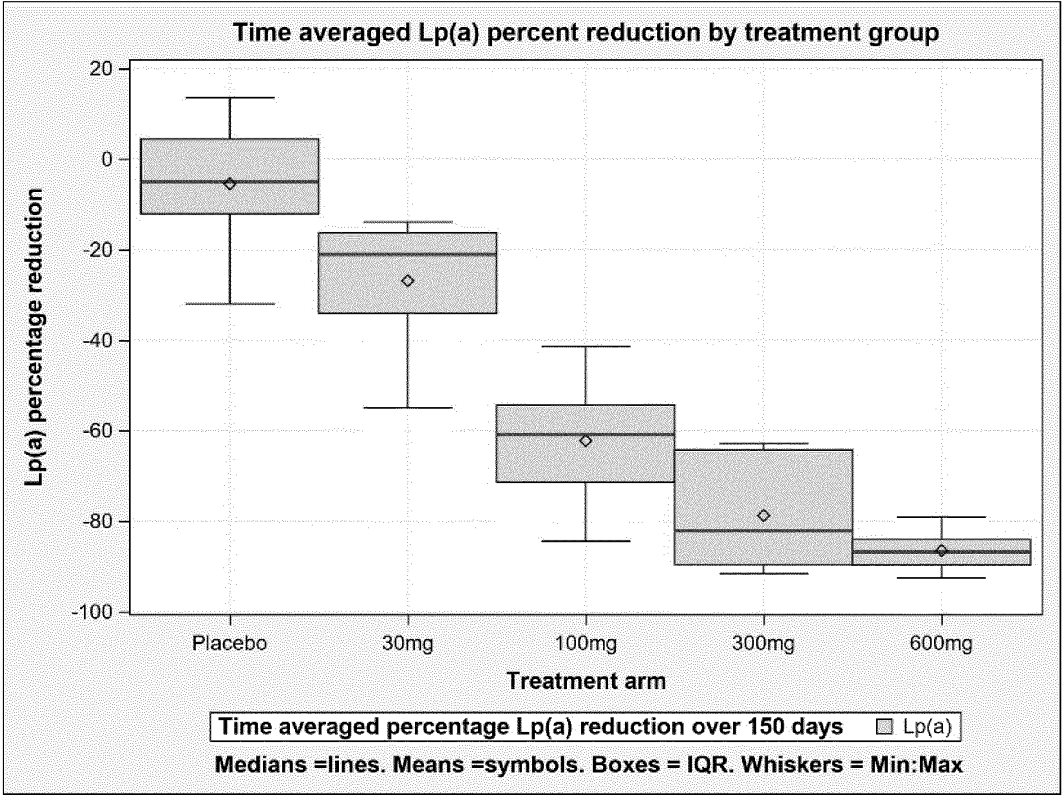


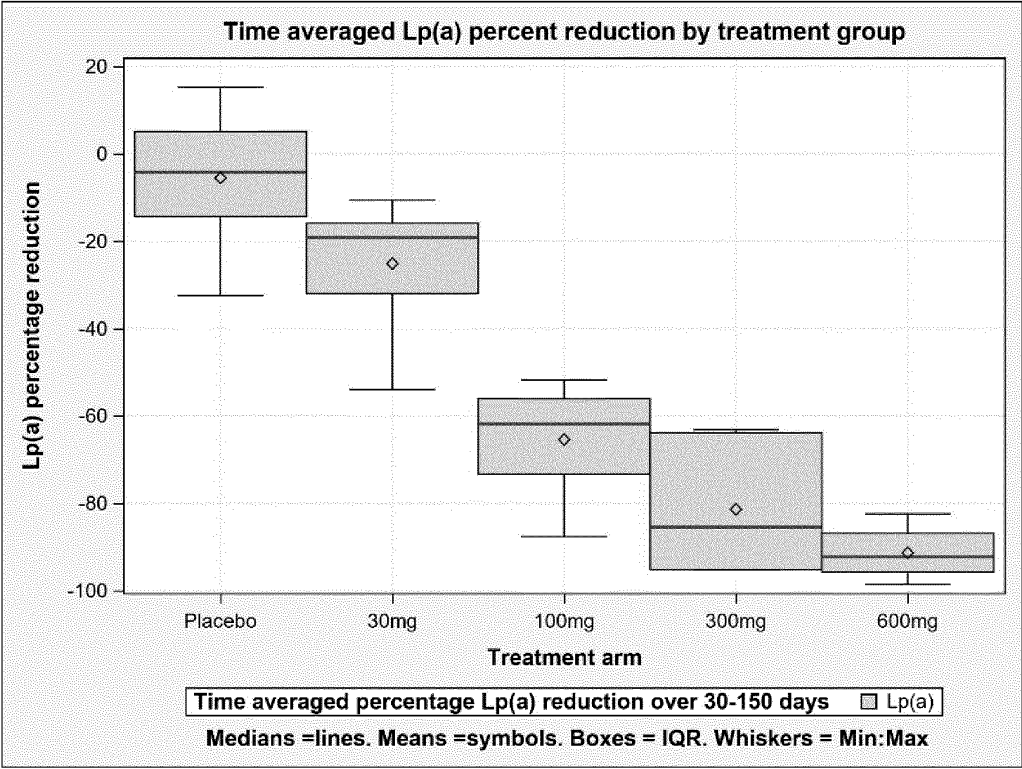
Figure 5. Time averaged Results Over 0-150 days



300 mg – 82% median reduction

600 mg – 87% median reduction

Figure 6. Time averaged Results Over 30-150 days



300 mg – 85% median reduction

600 mg – 92% median reduction

Table 1. Baseline Characteristics of Participants

	All Participants (n=32)	Placebo (n=8)	30 mg (n=6)	100 mg (n=6)	300 mg (n=6)	600 mg (n=6)
Age, mean (SD), y	49.6 (13.5)	52.9 (12.0)	45.5 (10.5)	46.3 (12.3)	58.7 (13.2)	43.7 (17.5)
Male (%)	15 (47)	2 (25)	4 (67)	4 (67)	2 (33)	3 (50)
Female of Childbearing Potential	1 (3)	1 (13)	0	0	0	0
BMI, mean (SD), kg/m ²	27 (3.9)	25 (4.0)	26 (3.3)	29 (3.7)	29 (4.0)	27 (3.8)
Race (%)						
White	20 (63)	6 (75)	1 (17)	5 (83)	3 (50)	5 (83)
Black	11 (34)	1 (13)	5 (83)	1 (17)	3 (50)	1 (17)
Asian	1 (3)	1 (13)	0	0	0	0
Relevant Medical Conditions (%)						
Hypertension	3 (9)	0	0	0	2 (33)	1 (17)
Diabetes	1 (3)	1 (13)	0	0	0	0
Lp(a), median (IQR), nmol/L	224 (188, 278)	238 (203, 308)	171 (142, 219)	217 (202, 274)	285 (195, 338)	231 (179, 276)
Total cholesterol, mean (SD), mg/dL	185 (44)	185 (54)	197 (47)	195 (47)	170 (19)	180 (51)
LDL-C, mean (SD), mg/dL	108 (42)	99 (48)	113 (38)	121 (46)	100 (25)	108 (54)

Table 1: Baseline Characteristics of Participants (Contd.)

HDL-C, mean (SD), mg/dL	59 (16)	67 (20)	70 (14)	55 (14)	46 (9)	55 (9)
Triglycerides, median (IQR), mg/dL	74 (56, 122)	93 (59, 122)	55 (34, 71)	80 (63, 130)	85 (67, 179)	75 (42, 115)
Apolipoprotein B, mean (SD), mg/dL	85 (24)	81 (30)	83 (23)	94 (29)	89 (6)	81 (25)
Oxidized LDL, mean (SD), U/L	55 (18)	53 (22)	56 (18)	64 (24)	55 (7)	50 (15)
Relevant Concomitant Medications						
Statins (%)	13 (41)	5 (63)	0	2 (33)	3 (50)	3 (50)

SD= standard deviation. Lp(a)=lipoprotein(a). LDL-C = low density lipoprotein cholesterol HDL= High density lipoprotein cholesterol.

Table 2. Safety Assessments

	All Participants (n=32)	Placebo (n=8)	30 mg (n=6)	100 mg (n=6)	300 mg (n=6)	600 mg (n=6)
Treatment Emergent Adverse Events occurring in more than 3 participants, n (%)	30 (94)	6 (75)	6 (100)	6 (100)	6 (100)	6 (100)
Headache	9 (28)	1 (13)	2 (33)	1 (17)	0 (0)	5 (83)
Diarrhea	3 (9)	1 (13)	1 (17)	0 (0)	0 (0)	1 (17)
Arthralgia	3 (9)	0 (0)	1 (17)	0 (0)	1 (17)	1 (17)
Neutrophil count increased	3 (9)	0 (0)	0 (0)	0 (0)	0 (0)	3 (50)
C-reactive protein increased	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	4 (67)
Injection Site Adverse Events, n (%) [†]	23 (72)	1 (13)	5 (83)	6 (100)	5 (83)	6 (100)
Grade 1	18 (56)	1 (13)	5 (83)	6 (100)	4 (67)	2 (33)
Grade 2	5 (16)	0 (0)	0 (0)	0 (0)	1 (17)	4 (67)
Grade 3	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Table 2. Safety Assessments (Contd.)

Serious Adverse Events, n(%)	1 (3)	0 (0)	1 (17)	0 (0)	0 (0)	0 (0)
Liver Function Tests, n(%)						
ALT > 3x ULN	1 (3)*	0 (0)	1 (17)*	0 (0)	0 (0)	0 (0)
AST > 3x ULN	1 (3)*	0 (0)	1 (17)*	0 (0)	0 (0)	0 (0)
ALP >3x ULN	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Total bilirubin >2 ULN	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
QTc prolongation	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

† Graded using the Common Terminology Criteria for Adverse Events. *Elevations in ALT and AST to >3xULN occurred in the same participant at a single timepoint. ALT=Alanine Aminotransferase AST= Aspartate aminotransferase ALP= alkaline phosphatase ULN= upper limit of normal; QTc = Corrected QT interval

Table 3. Primary Efficacy Outcome: Change in Lipoprotein (a) Concentration over Time

Time from Baseline		Placebo (n=8)	30 mg (n=6)	100 mg (N=6)	300 mg (n=6)	600 mg (n=6)
		Median Baseline Lipoprotein(a) in nmol/L (IQR)				
		238 (203,308)	171 (142,219)	217 (202,274)	285 (195,338)	231 (179,276)
		Median Level and Change from Baseline in Lipoprotein(a) in nmol/L (IQR)				
24 hours	Value	259 (202,310)	183 (141,226)	204 (182,271)	269 (225,306)	218 (163,242)
	Absolute change	6 (-2,24)	12 (0,27)	-12 (-21,-3)	-22 (-38,-7)	-13 (-16,-2)
	Percent change	3 (-1,10)	6 (0,16)	-6 (-10,-1)	-8 (-11,-2)	-6 (-9,-1)
7 days	Value	227 (175,319)	149 (116,174)	133 (127,211)	121 (75,214)	115 (90,130)
	Absolute change	-12 (-33,13)	-38 (-61,-19)	-101 (-104,-69)	-145 (-182,-100)	-113 (-153,-90)
	Percent change	-3 (-14,5)	-18 (-28,-14)	-45 (-52,-34)	-52 (-62,-44)	-48 (-54,-45)
14 days	Value	233 (177,306)	116 (97,123)	81 (67,121)	48 (24,101)	42 (33,55)
	Absolute change	-14 (-52,11)	-71 (-103,-38)	-152 (-164,-140)	-235 (-261,-152)	-179 (-242,-149)
	Percent change	-3 (-18,5)	-35 (-50,-28)	-71 (-72,-60)	-81 (-88,-75)	-78 (-83,-76)
30 days	Value	251 (176,309)	92 (74,107)	40 (27,47)	18 (5,46)	10 (7,13)
	Absolute change	-10 (-45,10)	-89 (-119,-61)	-185 (-226,-163)	-268 (-292,-189)	-219 (-272,-172)
	Percent change	-4 (-12,5)	-46 (-64,-40)	-85 (-90,-82)	-95 (-97,-91)	-95 (-96,-94)

Table 3. Primary Efficacy Outcome: Change in Lipoprotein (a) Concentration over Time (Contd.)

45 days	Value	248 (177,312)	114 (91,122)	35 (31,41)	15 (5,36)	6 (3,8)
	Absolute change	-17 (-39,11)	-75 (-107,-44)	-179 (-243,-163)	-265 (-286,-192)	-225 (-273,-175)
60 days	Percent change	-5 (-14,6)	-37 (-53,-30)	-86 (-92,-82)	-96 (-98,-89)	-97 (-99,-96)
	Value	265 (168,282)	120 (109,129)	52 (46,60)	14 (4,58)	6 (6,9)
	Absolute change	-20 (-61,3)	-54 (-96,-33)	-170 (-222,-156)	-254 (-267,-194)	-226 (-270,-174)
90 days	Percent change	-10 (-16,1)	-29 (-47,-18)	-79 (-86,-77)	-96 (-98,-82)	-98 (-98,-97)
	Value	234 (177,298)	147 (115,172)	104 (70,118)	35 (9,106)	17 (6,25)
	Absolute change	-11 (-58,23)	-26 (-73,-16)	-144 (-155,-131)	-199 (-248,-174)	-222 (-251,-174)
150 days	Percent change	1 (-24,10)	-16 (-30,-7)	-62 (-71,-57)	-87 (-96,-66)	-95 (-97,-91)
	Value	244 (192,319)	160 (112,231)	145 (127,206)	86 (31,153)	49 (21,61)
	Absolute change	-13 (-48,16)	-13 (-23,-4)	-75 (-121,-69)	-177 (-226,-78)	-173 (-222,-159)
	Percent change	-5 (-16,8)	-6 (-17,-3)	-37 (-53,-30)	-71 (-87,-48)	-81 (-92,-67)

Table 4. Effect of SLN360 on Total Cholesterol

Time from Baseline		Placebo (n=8)	30 mg (n=6)	100 mg (n=6)	300 mg (n=6)	600 mg (n=6)
		Mean Baseline Total Cholesterol in mg/dL (SD)				
		185 (54)	197 (47)	195 (47)	170 (19)	180 (51)
Mean Change from Baseline in Total Cholesterol in mg/dL (SD)						
7 days	Absolute change	-3 (16)	8 (9)	-4 (8)	-5 (13)	-14 (8)
	Percent change	-1 (10)	4 (4)	-2 (4)	-3 (8)	-8 (3)
14 days	Absolute change	-3 (19)	11 (16)	-6 (17)	-15 (22)	-27 (8)
	Percent change	-1 (12)	6 (8)	-2 (6)	-10 (14)	-16 (6)
30 days	Absolute change	10 (14)	6 (10)	-11 (17)	-14 (16)	-31 (12)
	Percent change	5 (8)	3 (6)	-4 (7)	-8 (10)	-18 (10)
45 days	Absolute change	1 (25)	6 (16)	-6 (11)	-13 (30)	-18 (15)

Table 4. Effect of SLN360 on Total Cholesterol (Contd.)

	Percent change	1 (15)	2 (8)	-2 (5)	-8 (17)	-10 (7)
60 days	Absolute change	0 (24)	8 (13)	-19 (19)	-4 (36)	-16 (14)
	Percent change	-1 (14)	4 (7)	-9 (10)	-4 (20)	-8 (5)
90 days	Absolute change	5 (22)	5 (14)	-6 (24)	-11 (27)	-28 (15)
	Percent change	3 (13)	2 (6)	-2 (12)	-7 (16)	-15 (6)
150 days	Absolute change	14 (23)	6 (26)	3 (24)	3 (28)	-14 (25)
	Percent change	10 (13)	4 (13)	3 (12)	1 (16)	-6 (14)

Table 5. Effect of SLN360 on Low-Density Lipoprotein Cholesterol

Time from Baseline		Placebo (n=8)	30 mg (n=6)	100 mg (n=6)	300 mg (n=6)	600 mg (n=6)
		Mean Baseline LDL Cholesterol in mg/dL (SD)				
		99 (48)	113 (38)	121 (46)	100 (25)	108 (54)
Mean Change from Baseline in LDL Cholesterol in mg/dL (SD)						
7 days	Absolute change	1 (17)	2 (8)	-6 (8)	-3 (10)	-13 (20)
	Percent change	1 (17)	1 (8)	-5 (8)	-4 (12)	-9 (11)
14 days	Absolute change	-3 (19)	7 (12)	-11 (17)	-15 (18)	-25 (17)
	Percent change	-4 (21)	7 (10)	-8 (10)	-16 (20)	-23 (10)
30 days	Absolute change	6 (17)	5 (10)	-18 (16)	-16 (13)	-30 (23)
	Percent change	5 (18)	3 (9)	-13 (8)	-17 (14)	-26 (7)
45 days	Absolute change	-2 (11)	1 (17)	-15 (20)	-16 (20)	-25 (26)

Table 5. Effect of SLN360 on Low-Density Lipoprotein Cholesterol (Contd.)

	Percent change	-1 (16)	-1 (14)	-12 (14)	-17 (20)	-19 (15)
60 days	Absolute change	2 (23)	3 (11)	-25 (10)	-9 (24)	-28 (28)
	Percent change	2 (25)	0 (10)	-21 (4)	-11 (24)	-21 (13)
90 days	Absolute change	5 (24)	9 (8)	-12 (18)	-19 (17)	-32 (28)
	Percent change	6 (22)	8 (8)	-9 (12)	-19 (18)	-26 (10)
150 days	Absolute change	10 (20)	10 (17)	-6 (31)	-1 (21)	-19 (33)
	Percent change	13 (21)	9 (16)	-2 (22)	-1 (23)	-10 (29)

Table 6. Effect of SLN360 on Apolipoprotein(B)

Time from Baseline	Mean Baseline Apolipoprotein B in mg/dL (SD)					
	Placebo (n=8)	30 mg (n=6)	100 mg (n=6)	300 mg (n=6)	600 mg (n=6)	
	81 (30)	83 (23)	94 (29)	89 (6)	81 (25)	
Mean Change from Baseline in Apolipoprotein B in mg/dL (SD)						
7 days	Absolute change	-1 (14)	7 (4)	-1 (3)	-8 (11)	-7 (8)
	Percent change	-1 (14)	8 (4)	-1 (3)	-9 (13)	-7 (9)
14 days	Absolute change	-1 (13)	8 (8)	-4 (5)	-16 (16)	-17 (7)
	Percent change	-3 (14)	9 (8)	-5 (5)	-19 (19)	-20 (6)
30 days	Absolute change	6 (14)	4 (4)	-11 (9)	-14 (13)	-20 (8)
	Percent	6 (13)	5 (6)	-10 (9)	-15 (15)	-24 (6)

Table 6. Effect of SLN360 on Apolipoprotein(B) (Contd.)

	change						
45 days	Absolute change	0 (10)	9 (12)	-8 (10)	-12 (16)	-15 (14)	
	Percent change	1 (17)	9 (13)	-8 (11)	-14 (18)	-16 (16)	
60 days	Absolute change	-1 (15)	3 (9)	-9 (8)	-11 (19)	-13 (15)	
	Percent change	-1 (15)	2 (12)	-9 (7)	-12 (22)	-12 (14)	
90 days	Absolute change	-2 (11)	2 (4)	-2 (6)	-15 (14)	-14 (14)	
	Percent change	-3 (13)	2 (6)	-2 (6)	-17 (16)	-15 (11)	
150 days	Absolute change	5 (9)	6 (10)	-3 (16)	-5 (15)	-8 (15)	
	Percent change	6 (9)	7 (11)	-1 (12)	-5 (18)	-7 (19)	

Table 7. Effect of SLN360 on Oxidized LDL

Time from Baseline	Placebo (n=8)	30 mg (n=6)	100 mg (n=6)	300 mg (n=6)	600 mg (n=6)
	Mean Baseline Oxidized LDL in U/L* (SD)				
	53 (22)	56 (18)	64 (24)	55 (7)	50 (15)
Mean Change from Baseline in Oxidized LDL in U/L* (SD)					
7 days	Absolute change	-1 (8)	7 (7)	4 (5)	1 (11)
	Percent change	-1 (16)	10 (12)	6 (7)	2 (20)
14 days	Absolute change	-3 (7)	5 (6)	-0.5 (4)	-5 (10)
	Percent change	-7 (15)	9 (9)	-1 (7)	-8 (20)
30 days	Absolute change	4 (12)	3 (8)	-7 (10)	-4 (9)
	Percent change	6 (22)	6 (13)	-8 (15)	-8 (18)
					-20 (10)

Table 7. Effect of SLN360 on Oxidized LDL (Contd.)

45 days	Absolute change	-3 (11)	3 (8)	-2 (6)	-2 (12)	-7 (10)
	Percent change	-3 (18)	5 (15)	-4 (10)	-4 (22)	-11 (16)
60 days	Absolute change	-3 (9)	-0.5 (9)	-4 (10)	-1 (14)	-8 (8)
	Percent change	-5 (19)	-1 (15)	-4 (15)	-3 (26)	-14 (13)
90 days	Absolute change	-2 (6)	3 (7)	-1 (10)	-6 (8)	-9 (7)
	Percent change	-4 (13)	6 (12)	1 (15)	-11 (16)	-16 (8)
150 days	Absolute change	2 (5)	8 (8)	1 (10)	3 (13)	-4 (9)
	Percent change	4 (10)	19 (20)	6 (14)	5 (25)	-6 (19)

*Mercodia oxidized LDL ELISA, Mercodia AB, Sylveniusgatan 8A, SE-754 50 Uppsala, Sweden

Table 8. Pharmacokinetic Parameters

	30 mg (n=6)	100 mg (n=6)	300 mg (n=6)	600 mg (n=6)
C _{max} (ng/mL)	115.8 ± 32.6	265.7 ± 125.5	979.2 ± 386.6	3035.0 ± 1131.4
T _{max} (h)	3.6 ± 2.7	6.3 ± 2.9	7.0 ± 2.4	6.4 ± 3.0
AUC _(0-last) (h*ng/mL)	898.0 ± 219.4	3229.8 ± 809.9	13166.1 ± 4295.8	36719.9 ± 9530.9

C_{max} = maximum plasma concentration, T_{max} = Time (in hours) to reach peak plasma concentration, AUC_(0-last) = area under the concentration time curve to the last measurable concentration.