SUPPLEMENTAL MATERIAL

Study Safety:

The safety of alirocumab and its effects on blood lipids have been previously reported for men and women receiving repeated subcutaneous doses as high as 150 mg every 2 weeks (q2w) and 300 mg every four weeks.[1, 2] Each subject received a physical examination, ECG, and collection of blood and urine for laboratory safety assessments during the study in-patient visits. The subjects returned about 10 weeks after the last study dose, when systemic exposure to alirocumab was negligible, for final safety assessments.

There were no deaths and no serious adverse events in the study. There were no treatment discontinuations due to an adverse event in the study. In the safety population (N=20) there were 15 subjects with any treatment-emergent adverse event (TEAE), and 1 subject with a severe TEAE. The most frequent TEAEs by Primary System Organ Class and Preferred Term were Infections and infestations with 7 subjects (Nasopharyngitis [6] , Gingivitis [1]), General disorders and administration site conditions with 4 (Injection site reaction [3], Infusion site bruising [1], Vessel puncture site bruise [1]), and Nervous system disorders with 3 (Headache [3], Dizziness [1]). For vital signs, electrocardiograms, and laboratory parameters, there were no potentially clinically significant abnormalities that were associated with an adverse event.

Anti-drug antibody (ADA) samples from a total of 18 subjects who were dosed with 150 mg alirocumab q2w were analyzed in this study. Three samples from 3 subjects had a

positive response in the ADA assay. Two subjects had a treatment emergent ADA response. One subject was positive at Day 1 with a titer of 30, but had no positive ADA response in the post-dose samples.

Methods:

Hepatic Lipase (HL) and Lipoprotein Lipase (LpL) Activity Measurements: Fasting plasma was collected 15 minutes following an intravenous heparin injection (60 U/kg body weight) at the end of each treatment period for measurement of LpL and HL concentration and activity. Post heparin plasma (PHP) total lipase activities were assayed in triplicate using radiolabeled TG emulsion as a substrate.[3, 4] Results were expressed as µmol of FA released per ml per hr. The contribution of HL was determined by including 1 M NaCl in the assay; the activity of HL was subtracted from the total lipase activity to estimate LpL.

Post Prandial Lipemia: Participants were admitted to the Irving Institute for Clinical and Translational Research Inpatient Unit after a 12 hour overnight fast, and blood was obtained. Immediately after, a high fat liquid meal providing 1237 Kcal per $2m^2$ body surface area from 75% fat (40% saturated, 20% mono-unsaturated, 15% poly-unsaturated), 10% protein, and 15% carbohydrate, was administered within 10 minutes. Blood samples were obtained at 1, 2, 3, and 5 and 8 hours after the formula was consumed. The data are presented as area under the curve above baseline (IAUC) of plasma TG and apoB48 concentrations.[5]

Figure S1: Study Protocol

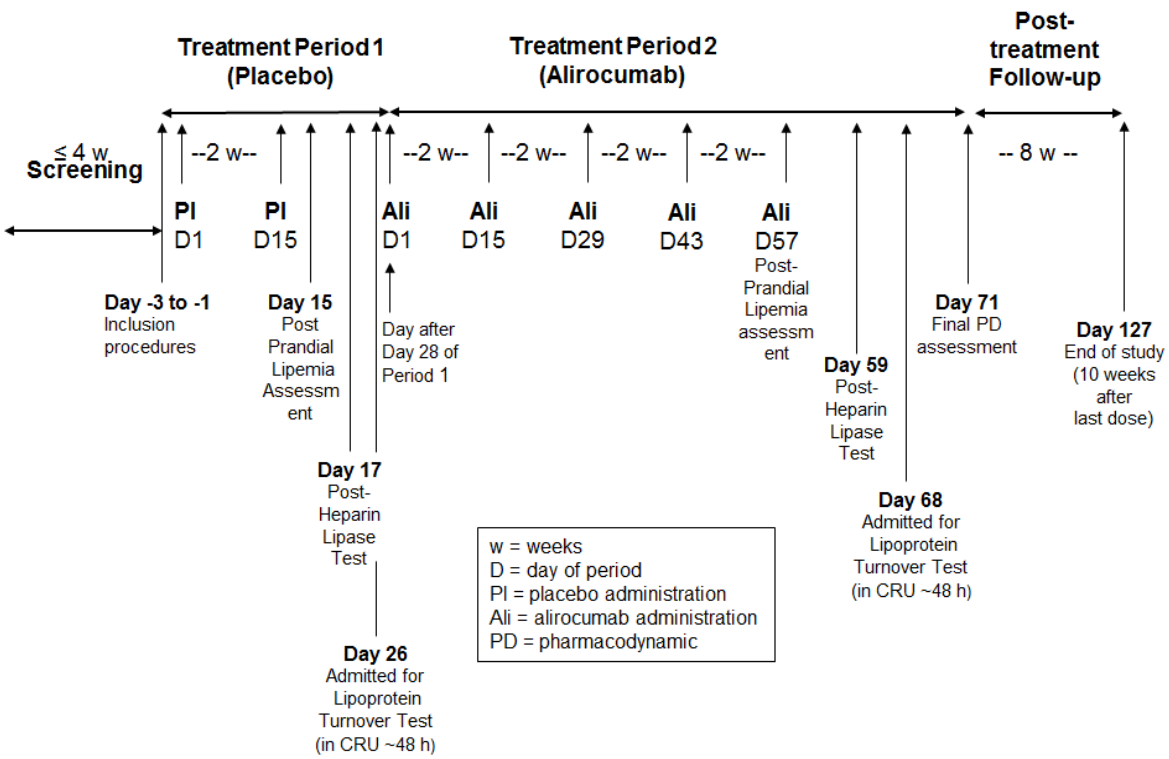

Figure S2: Patient flow through the study

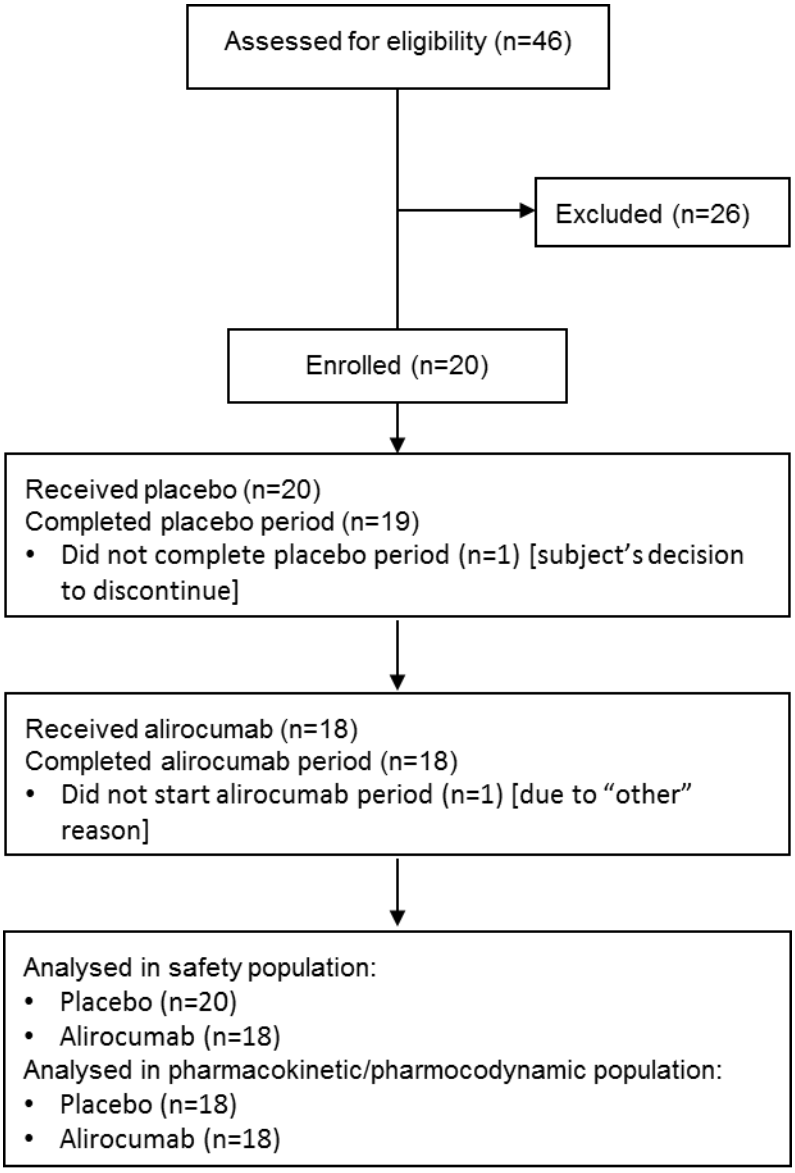

Table S1: Effect of Alirocumab on VLDL-, IDL-, and LDL-apoB particle number by ion mobility analysis.

Total Lipoprotein Particle Number (nmol/l)				
	Placebo	Alirocumab	% change (±SD)	p-value
LDL 180-233.3	1250.2	889.8	-28.4±16.4	<.0001
IDL 233.3-296.0	392.3	269.2	-31.6±18.2	<.0001
VLDL 296.0-547.0	97.6	61.7	-35.8±22.3	<.0001

Table S2: LDL particle number distribution

Lipoprotein particle number distribution			
LDL (size range-nm)	Placebo	Alirocumab	p-value
Large (224.6-233.30)	33.6±6.7%	27.3±5.4%	<.0001
Medium (214.1-224.6)	33.9±4.0%	30.5±2.2%	<.003
Small (204.9-214.1)	15.2±4.2%	18.2±3.4%	<.0001
Very small (180-205)	17.3±3.3%	24.0±3.7%	<.0001

References

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