



EAS 94th Congress

24-27 May 2026 | Athens, Greece



Liver-Targeted ANGPTL3 Silencing with AZD1705 Lowers Atherogenic Lipoproteins: Preclinical Validation and Phase 1 Results

Helena Edlund¹, Xiao-Rong Peng¹, Erik Ryberg¹, Peter Gennemark¹, Macarena P. Quintana-Hayashi¹, Alexis Hofherr¹, Víctor López Juan¹, Yongling Xiao², Delia Florica, Eva Hurt-Camejo¹, Michael McCarthy³, Niklas Bergh¹

¹AstraZeneca, Gothenburg, Sweden; ²AstraZeneca, Mississauga, Canada; ³AstraZeneca Gaithersburg, Maryland, USA



EAS
European
Atherosclerosis
Society

eas-congress.com/2026



Disclosure Slide

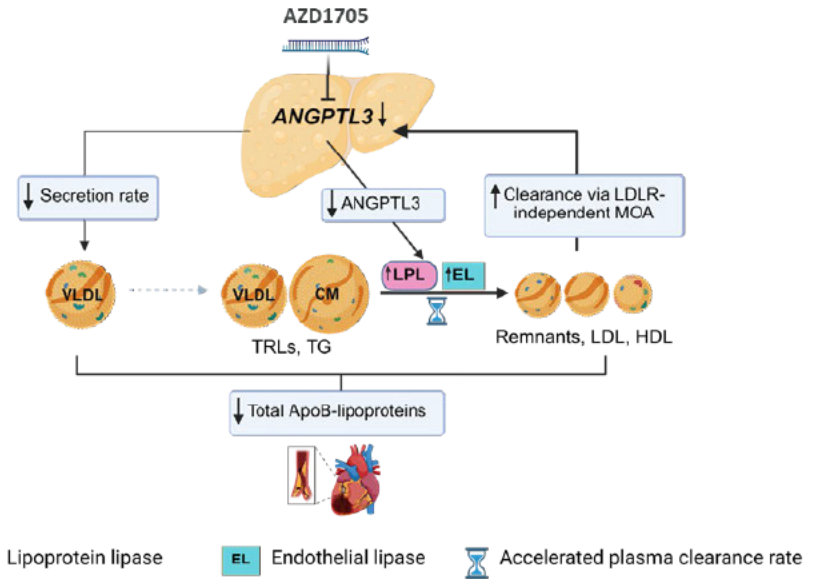
☐	No, nothing to disclose
☒	Yes, please specify:

<i>Company Name</i>	<i>Honoraria/ Expenses</i>	<i>Consulting/ Advisory Board</i>	<i>Funded Research</i>	<i>Royalties/ Patent</i>	<i>Stock Options</i>	<i>Ownership/ Equity Position</i>	<i>Employee</i>	<i>Other (please specify)</i>
AstraZeneca, Gothenburg, Sweden			X				X	



AZD1705 is a GalNAc-conjugated ANGPTL3 siRNA that reduces ApoB-lipoproteins independent of LDLR for treatment of mixed dyslipidemia with ASCVD

- **Dyslipidaemia** is a major risk factor for cardiovascular disease (CVD)
- **ANGPTL3** is a hepatocyte expressed regulator of lipid and lipoprotein metabolism with multiple potential modes of action, including inhibition of lipoprotein lipase (LPL) and endothelial lipase (EL)
- **ANGPTL3** loss-of-function variants are associated with lower lipid levels and reduced risk of atherosclerotic cardiovascular disease



Apo=apolipoprotein; VLDL=very-low-density lipoprotein; CM=chylomicron; LDL=low-density lipoprotein; HDL=high-density lipoprotein; TG=triglycerides; LDLR=LDL-receptor; MOA=mechanism of action

ATVB (2021), 41:1753-1759; Cell report Medicine (2025), 6:102152; J. Lipid Res. (2020) 61:1271-1286; N Engl J Med. 2017;377(3):211-21

ANGPTL3 siRNA reduced circulating ANGPTL3 protein and dyslipidemia in obese ZSF1 rats



EAS
94th Congress

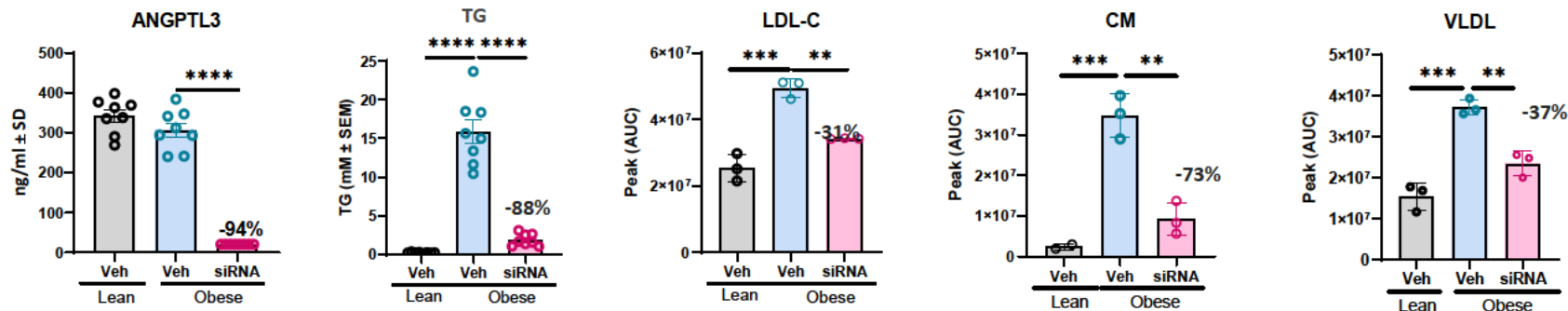
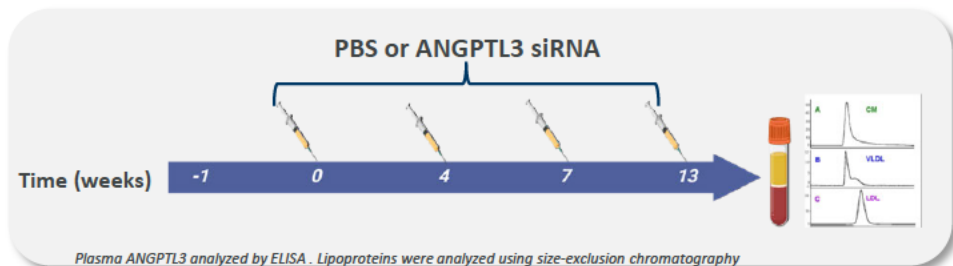
24-27 May 2026 | Athens, Greece



Lean and obese ZSF1 rats

Treatment groups:

- Vehicle (PBS, n=8)
- ANGPTL3 siRNA (n=8, 4 mg/kg q3w)



One-way ANOVA multiple comparisons. Mean ± SEM. * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$; **** $P < 0.0001$

Obese ZSF1 rat: Compound heterozygous, carrying two mutant leptin receptor alleles ($Lepr^{fa}$ and $Lepr^{cr}$)

TG=triglycerides; LDL-C=low-density lipoprotein cholesterol; CM=chylomicron; VLDL=very-low-density lipoprotein; PBS=phosphate-buffered saline

Phase 1 Study Design

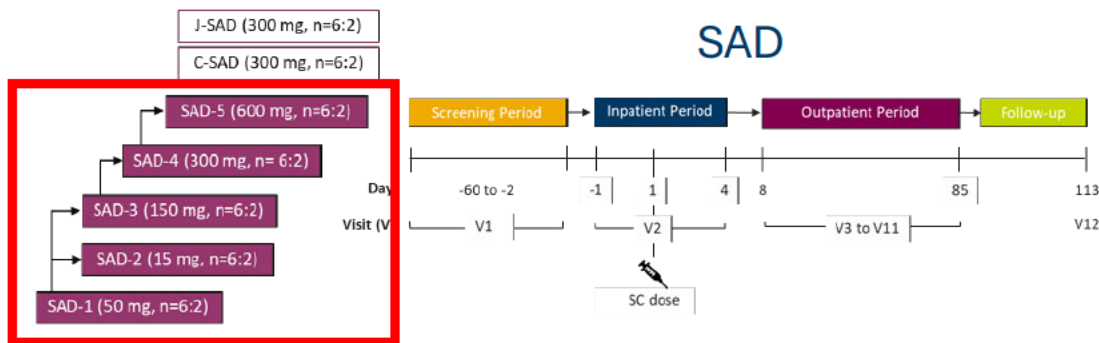


EAS
94th Congress

24-27 May 2026 | Athens, Greece

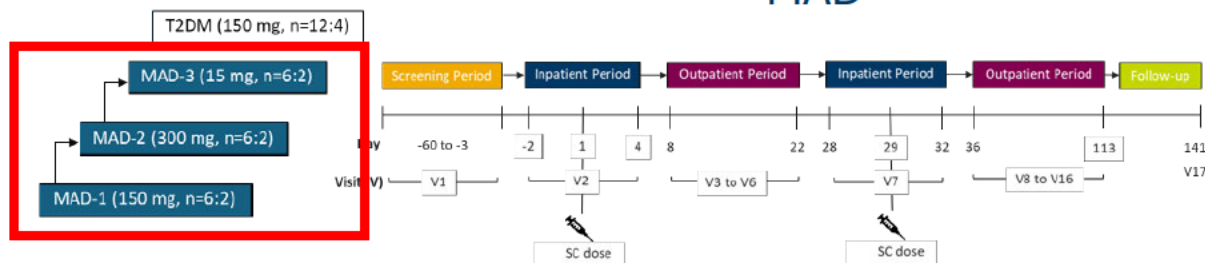
Key Inclusion criteria:

- LDL-C ≥ 70 mg/dl (1.81mmol/L) and < 190 mg/dL (4.91 mmol/L)
- Fasting serum TGs ≥ 150 mg/dl (1.69 mmol/L) and ≤ 500 mg/dl (5.64 mmol/L)
- Statins: SAD, Statins excluded; MAD, May or may not be receiving moderate- or high-intensity statin therapy (stable dose for ≥ 3 months)



Key Endpoints:

- Safety and tolerability of AZD1705
- Effect on plasma ANGPTL3 protein levels
- Effect on levels of LDL-C, ApoB and TG



Baseline Characteristics



EAS
94th Congress

24-27 May 2026 | Athens, Greece

	SAD						MAD			
	PBO (n=10)	15 mg (n=6)	50 mg (n=6)	150 mg (n=6)	300 mg (n=6)	600 mg (n=6)	PBO (n=6)	15 mg (n=6)	150 mg (n=6)	300 mg (n=6)
Age (yrs)	44 (23-57)	42 (30-56)	46.5 (32-55)	35 (31-56)	43 (19-60)	36.5 (28-56)	53 (30-63)	53 (42-65)	51 (38-64)	56.5 (53-62)
Sex (males)	8 (80%)	5 (83.3%)	4 (66.7%)	6 (100%)	6 (100%)	5 (83.3%)	3 (50%)	4 (66.7%)	3 (50%)	3 (50%)
BMI (kg/m²)	28 (25.3-30.7)	29.6 (26-33)	30 (24-35)	29.4 (22-36)	27 (23-33)	26.4 (19-32)	31.5 (25.7-35)	29.5 (24-35)	28.9 (27.1-31.7)	29.8 (25-34)
Statin user	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	4 (66.7%)	3 (50%)	6 (100%)	2 (33.3%)
ANGPTL3 (µg/L)	89.9 (77-120)	79.4 (67-86)	108 (87-126)	91.1 (78-121)	82.9 (74-112)	106.3 (86-175)	159.5 (113-277)	104 (53-168)	106.1 (73-200)	218.6 (111-277)
ApoB (mg/dL)	104 (73-127)	94 (81-149)	127.5 (87-158)	108 (70-139)	113.5 (61-130)	119.5 (96-137)	92.5 (79-122)	84 (50-105)	80 (71-118)	119.5 (81-167)
LDL-C (mg/dL)	127.5 (88-157)	117 (97-171)	149.5 (102-209)	126.5 (107-173)	135.5 (80-163)	145.5 (115-181)	96.5 (88-170)	101.5 (64-117)	93.5 (67-106)	137.5 (88-220)
Non-HDL-C (mg/dL)	149 (111-190)	136 (119-217)	186 (120-230)	159.5 (114-226)	161 (90-190)	176 (128-203)	133 (116-202)	126.5 (85-156)	122 (95-153)	183.5 (119-326)
HDL-C (mg/dL)	37.5 (30-67)	41.5 (34-59)	46.5 (28-61)	40.5 (34-60)	46.5 (35-67)	40.5 (33-74)	40 (28-70)	45 (33-50)	51 (24-76)	44 (41-58)
TG (mg/dL)	128 (77-182)	124.5 (64-282)	141.5 (114-219)	136.5 (55-223)	108 (62-184)	108.5 (92-204)	121.5 (73-342)	201.5 (81-255)	146 (110-248)	216.5 (170-346)
Remnant Chol (mg/dL)	24.5 (11-34)	22 (14-62)	26.5 (18-47)	29.5 (7-53)	17.5 (10-45)	20 (10-43)	25 (22-54)	30 (21-39)	28.5 (22-47)	46.5 (31-106)

Note: Values are median (range) or n (%)

BMI=body mass index; Apo=apolipoprotein; LDL-C=low-density lipoprotein cholesterol; HDL-C=high-density lipoprotein cholesterol; TG=triglycerides; Chol=cholesterol; SAD=single ascending dose; MAD=multiple ascending dose

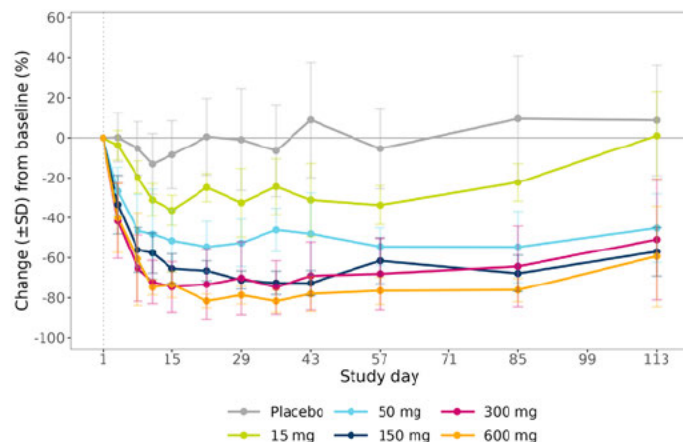
AZD1705 demonstrates dose-dependent prolonged reduction in ANGPTL3 protein levels



EAS
94th Congress

24-27 May 2026 | Athens, Greece

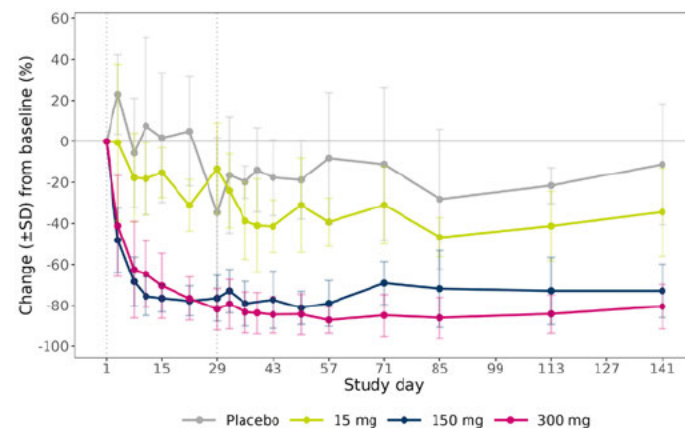
SAD



ANGPTL3 difference vs Placebo (%) at Day 85

	Placebo (n=10)	15 mg (n=6)	50 mg (n=6)	150 mg (n=6)	300 mg (n=6)	600 mg (n=5)
Difference (%)		-27.1%	-67.5%	-79.2%	-79.6%	-75.0%
P-value		0.606	0.119	0.063	0.066	0.081

MAD



ANGPTL3 difference vs Placebo (%) at Day 113

	Placebo (n=6)	15 mg (n=6)	150 mg (n=6)	300 mg (n=6)
Difference (%)		-22.6%	-54.9%	-58.8%
P-value		0.285	0.009	0.006

SAD=single ascending dose; MAD=multiple ascending dose

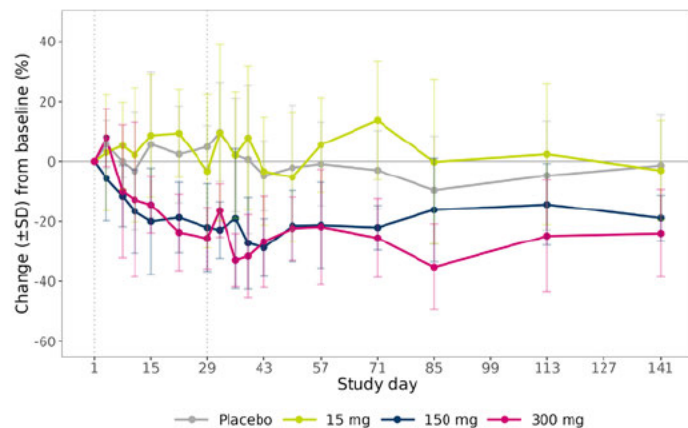
In MAD, AZD1705 resulted in dose-dependent reductions in ApoB and LDL-C



EAS
94th Congress

24-27 May 2026 | Athens, Greece

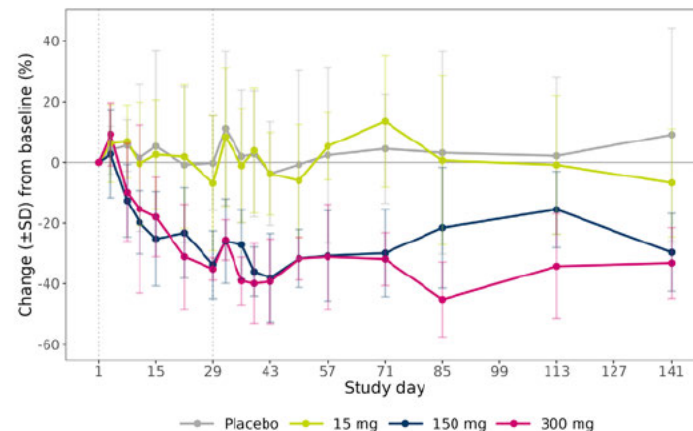
ApoB



ApoB difference vs Placebo (%) at Day 113

	Placebo (n=6)	15 mg (n=6)	150 mg (n=6)	300 mg (n=6)
Difference (%)		-0.2%	-12.7%	-13.9%
P-value		0.996	0.779	0.769

LDL-C



LDL-C difference vs Placebo (%) at Day 113

	Placebo (n=6)	15 mg (n=6)	150 mg (n=6)	300 mg (n=6)
Difference (%)		-11.1%	-25.0%	-35.3%
P-value		0.836	0.676	0.517

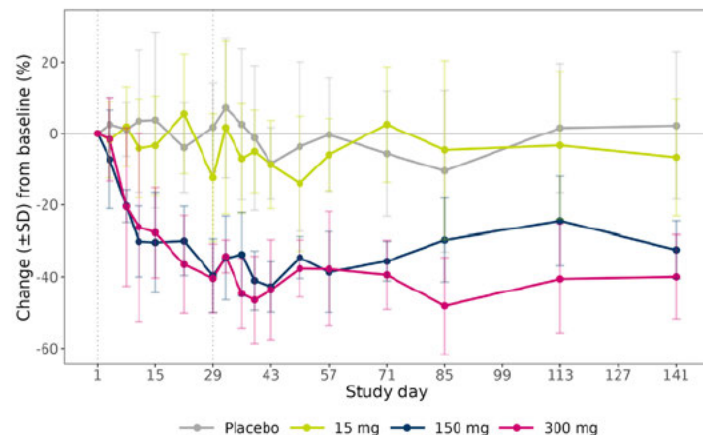
In MAD, AZD1705 resulted in dose-dependent reductions in non-HDL-C and HDL-C



EAS
94th Congress

24-27 May 2026 | Athens, Greece

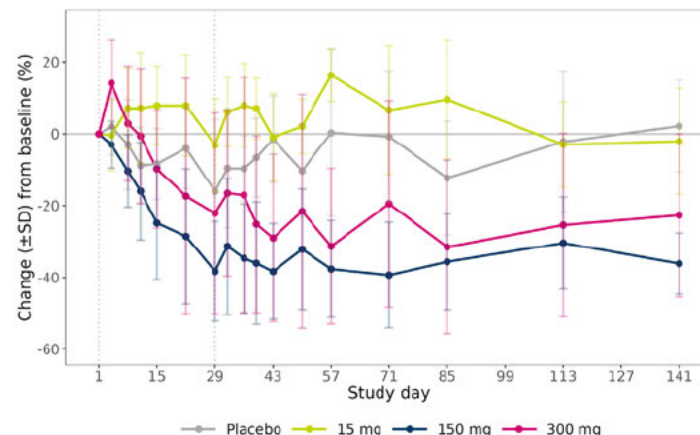
Non-HDL-C



Non-HDL-C difference vs Placebo (%) at Day 113

	Placebo (n=6)	15 mg (n=6)	150 mg (n=6)	300 mg (n=6)
Difference (%)		-11.0%	-27.8%	-35.6%
P-value		0.750	0.465	0.300

HDL-C



HDL-C difference vs Placebo (%) at Day 113

	Placebo (n=6)	15 mg (n=6)	150 mg (n=6)	300 mg (n=6)
Difference (%)		-4.8%	-28.7%	-23.0%
P-value		0.989	0.936	0.949

MAD= multiple ascending dose; HDL-C=high-density lipoprotein cholesterol;

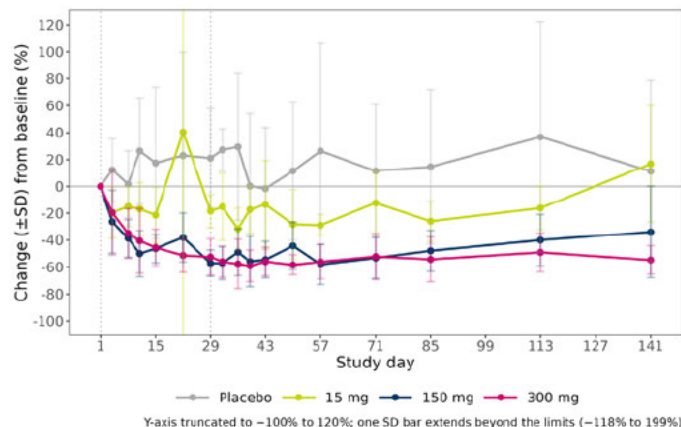
In MAD, AZD1705 resulted in dose-dependent reductions in TG and Remnant cholesterol



EAS
94th Congress

24-27 May 2026 | Athens, Greece

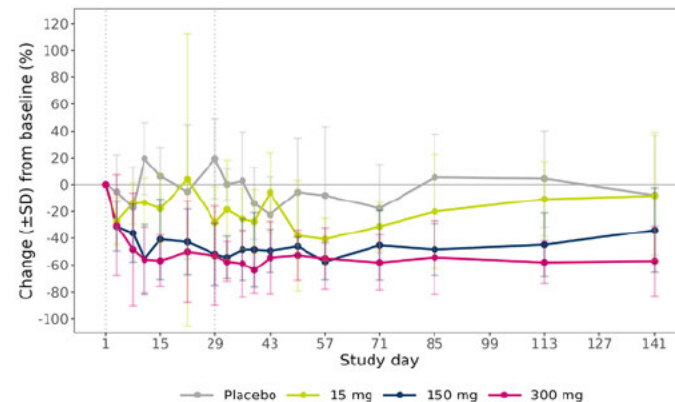
Triglycerides



TG difference vs Placebo (%) at Day 113

	Placebo (n=6)	15 mg (n=6)	150 mg (n=6)	300 mg (n=6)
Difference (%)		-50.2%	-75.3%	-78.4%
P-value		0.883	0.825	0.819

Remnant cholesterol



Remnant Chol difference vs Placebo (%) at Day 113

	Placebo (n=6)	15 mg (n=6)	150 mg (n=6)	300 mg (n=6)
Difference (%)		-11.3%	-46.3%	-45.9%
P-value		0.563	0.013	0.017

MAD= multiple ascending dose; TG=triglycerides; chol=cholesterol

AZD1705 demonstrated a favourable tolerability profile

- AZD1705 was well tolerated, with no safety concerns identified
- No serious adverse events (SAEs) related to the study drug or adverse events leading to discontinuation (DAEs) were reported
- Injection site reactions (ISRs) were the most common reported adverse events, and were generally mild, occasionally moderate, and reversible
- No clinically relevant changes in laboratory variables, vital signs, physical examination, or ECGs were observed



Conclusions

- AZD1705 data demonstrate favourable safety profile in subjects with mixed dyslipidaemia
- AZD1705 shows dose dependent and durable reduction in ANGPTL3 circulating protein levels and in atherogenic lipoproteins including LDL-C, Apo-B and non-HDL-C
- Reduction in atherogenic lipoproteins and TG and favourable safety support the potential of AZD1705 to treat residual ASCVD risk in patients with elevated atherogenic lipoproteins not at LDL-C goal.

*The authors would like to thank the patients and caregivers
who participated in this study*



Apo=apolipoprotein; LDL-C=low-density lipoprotein cholesterol; HDL-C=high-density lipoprotein cholesterol; TG=triglycerides;
ASCVD=atherosclerotic cardiovascular disease