18th Global Cardiovascular Clinical Trialists Forum

Arrowhead perspective on HTG clinical trials

December 3rd, 2021

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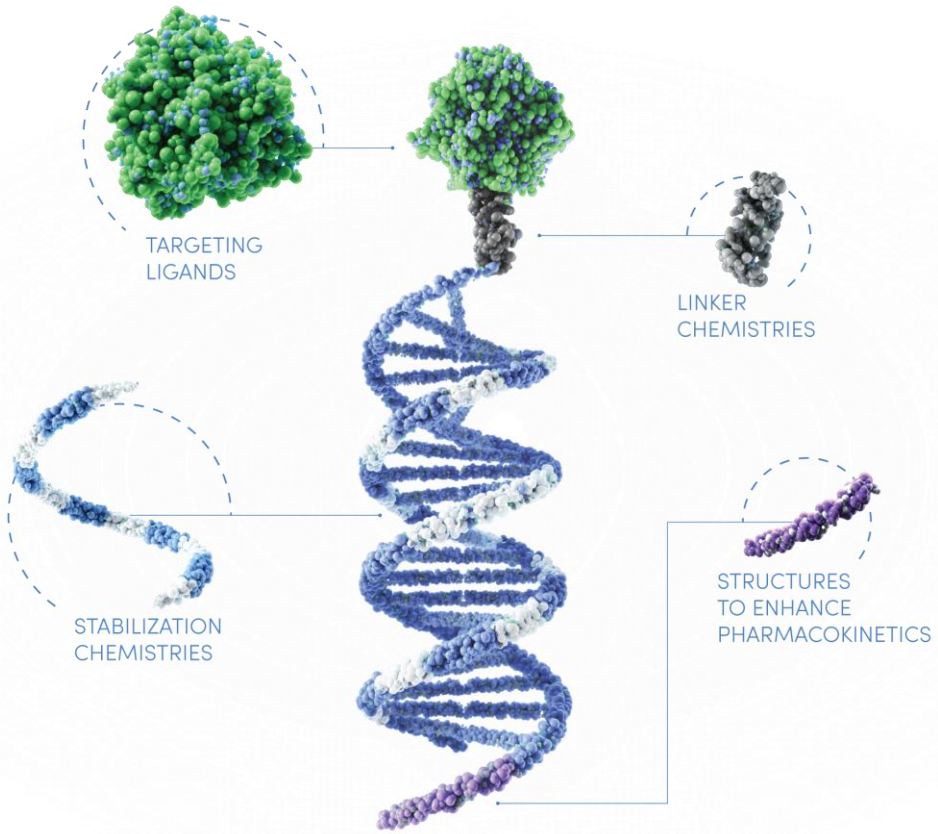
Safe Harbor Statement

This presentation contains forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. These statements are based upon our current expectations and speak only as of the date hereof. Our actual results may differ materially and adversely from those expressed in any forward-looking statements as a result of various factors and uncertainties, including, without limitation, our developmental stage and limited operating history, our ability to successfully and timely develop products, enter into collaborations and achieve other projected milestones, rapid technological change in our markets, demand for our future products, legislative, regulatory and competitive developments and general economic conditions. Our Annual Report on Form 10-K and other SEC filings discuss some of the important risk factors that may affect our ability to achieve the anticipated results, as well as our business, results of operations and financial condition. Readers are cautioned not to place undue reliance on these forward-looking statements. Additionally, Arrowhead disclaims any intent to update these forward-looking statements to reflect subsequent developments.

TRiM™ Platform: Targeted RNAi Molecule



TRiM™ has rules and algorithms to optimize trigger sequence

- Limit cross reactivity with off target genes and disallow miRNA homology
- Maximize activity
- Maximize innate stability
- Rational use and placement of modifying chemistries
- Unique RNAi chemistry insights and expertise

Pipeline: Two molecules targeting TGs

THERAPEUTIC AREA		PRE-CLINICAL	PHASE 1	PHASE 2	PHASE 3	Product Rights
Cardiometabolic	**ARO-APOC3** FCS, sHTG					Arrowhead
	ARO-ANG3 Dyslipidemia					Arrowhead
	Olpasiran CVD					Amgen
Pulmonary	**ARO-ENAC** Cystic fibrosis					Arrowhead
	ARO-Lung2 COPD					Arrowhead
Liver	**ARO-HSD** NASH					Arrowhead
	ARO-AAT AATD					Arrowhead / Takeda
	JNJ-3989 HBV					Janssen
	ARO-XDH Gout					Horizon
	ARO-C3 PNH, others					Arrowhead
Oncology	**ARO-HIF2** RCC					Arrowhead
Muscular Dystrophy	**ARO-DUX4** FSHD					Arrowhead
Undisclosed	**JNJ1**					Janssen
	JNJ2					Janssen
	JNJ3					Janssen

Tissue Targets: Liver, Lung, Tumor, Muscle

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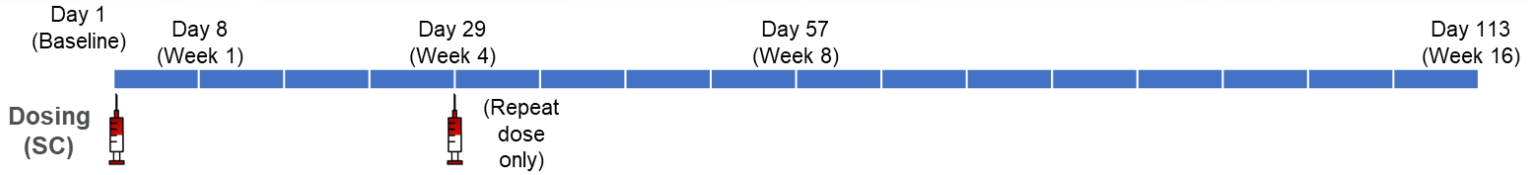
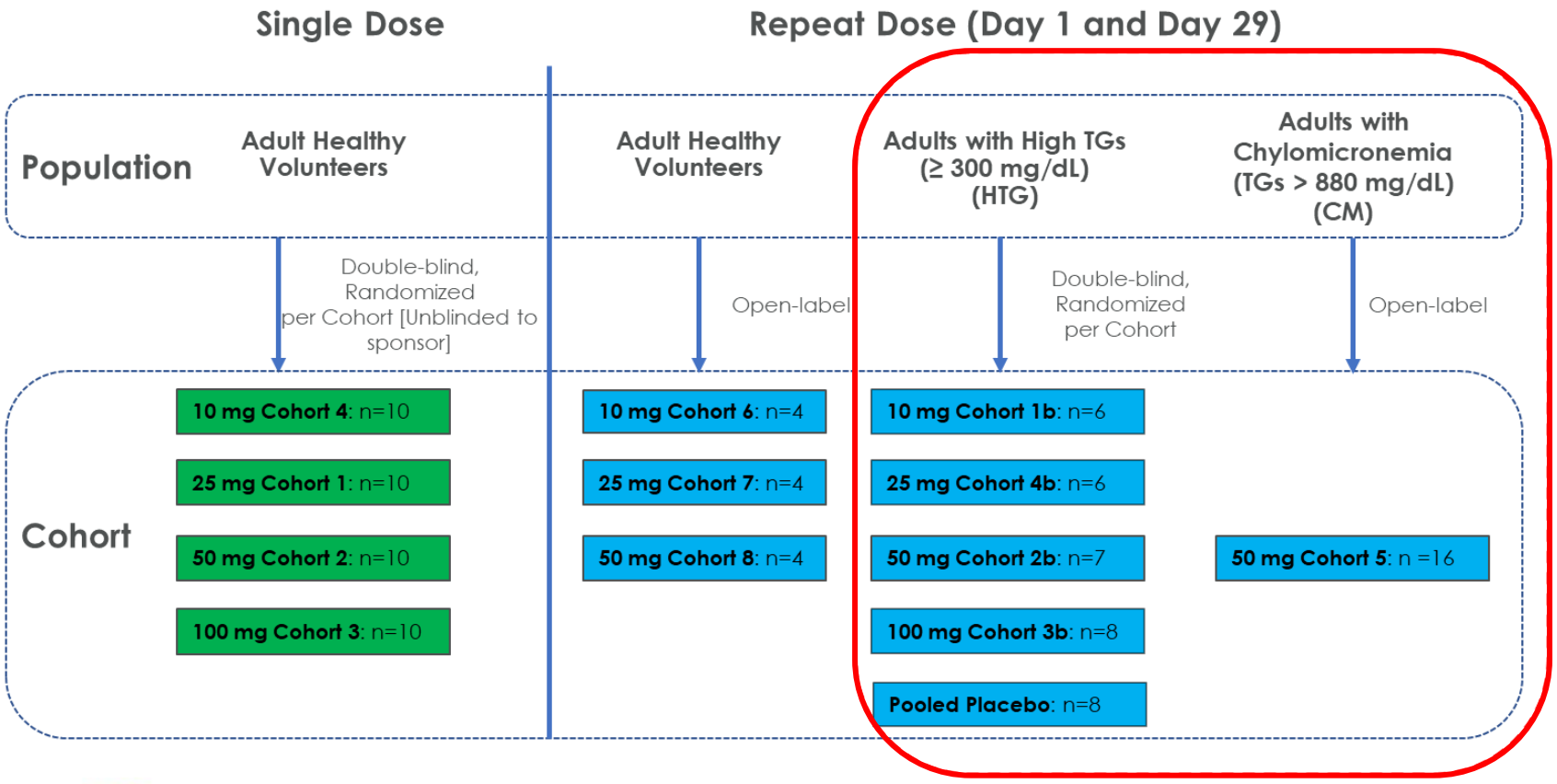
Phase 1/2a study to evaluate the effect of ARO-APOC3 in patients with hypertriglyceridemia (HTG) or chylomicronemia (CM)





Study Endpoints

Safety (Primary):

- Incidence and frequency of adverse events

Key Pharmacodynamics (PD) and Lipid Parameters:

- Change from baseline over time in APOC3
- Change from baseline over time in the following key parameters: Triglyceride, HDL-C, non-HDL-C

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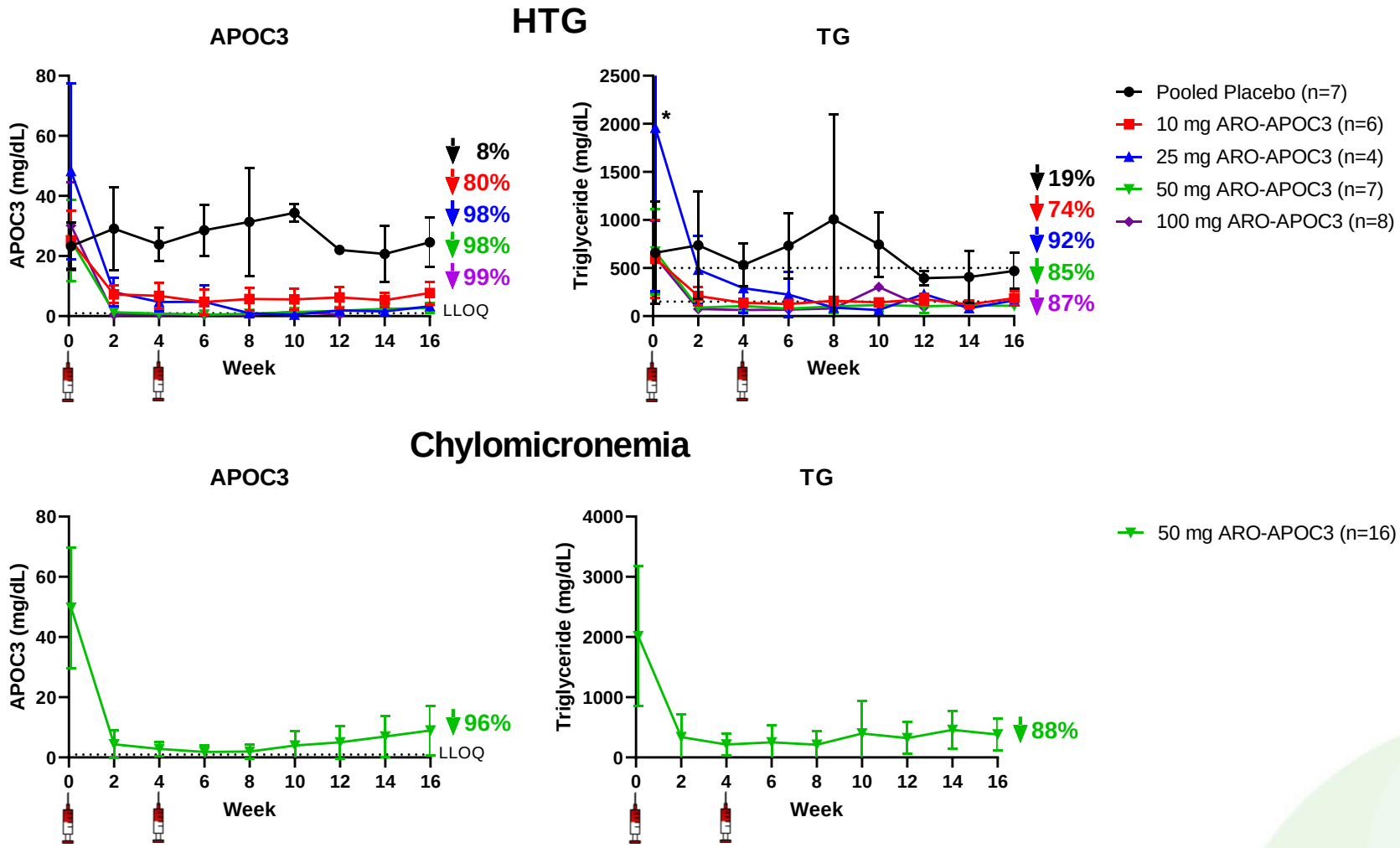
Data cut date: 31 Aug 2020

Baseline characteristics of HTG and CM patient cohorts

	HTG (TG≥ 300 mg/dL)					Chylomicronemia
Mean (range) Fasting values	**Pooled Placebo n=8**	**10 mg ARO-APOC3 n = 6**	**25 mg ARO-APOC3 n = 6**	**50 mg ARO-APOC3 n = 7**	**100 mg ARO-APOC3 n = 8**	**50 mg ARO-APOC3 n=16 (all active)**
Age (years)	47.6 (30-68)	50.2 (40-55)	53.8 (36-62)	48.1 (19-64)	55.0 (36-70)	46.8 (20-65)
% Male	75	100	67	43	75	56
BMI (kg/m^2)	30.7 (21.8-39.5)	32.7 (25.3-39.2)	30.5 (25.8-34.7)	30.7 (20.1-40.0)	32.2 (27.3-36.3)	29.6 (20.3-35.3)
APOC3 (mg/dL)	23 (13-34)	25 (15-42)	45 (25-88)	25 (13-49)	30 (18-63)	50 (19-88)
Triglycerides (mg/dL)	618 (262-1746)	596 (318-1381)	1659 (459-3546)	671 (294-1593)	616 (283-1448)	2015 (344-4636)
VLDL-C (mg/dL)*	88 (40-200)	128 (62-372)	321 (94-645)	98 (51-253)	104 (61-162)	259 (58-542)
LDL-C (mg/dL) (direct assay)	80 (15-144)	87 (56-130)	87 (16-150)	76 (23-117)	95 (12-184)	25 (2-77)
HDL-C (mg/dL)	28 (16-38)	28 (12-38)	28 (18-38)	29 (22-44)	33 (18-64)	18 (10-36)
non-HDL-C (mg/dL)	168 (81-231)	213 (110-443)	347 (188-696)	210 (126-332)	204 (139-314)	302 (123-598)

* VLDL-C is not calculated when TG > 400 mg/dL

ARO-APOC3 results in substantial and sustained reduction of APOC3 and TG



Mean values +/- SD are plotted for each cohort ;% values are maximum mean reductions for each cohort (n>1 subject at a visit date)

Data cut date: 31 Aug 2020

Summary safety findings in HTG and CM patients

	HTG Cohorts (TG>300 mg/dL)					CM TG>880mg/dL	
TEAEs Reported in > 1 subject, AE Term (MedDRA Preferred Term)	**10 mg Cohort 1b n = 5**	**25 mg Cohort 4b n = 5**	**50 mg Cohort 2b n = 7**	**100 mg Cohort 3b n=8**	**Pooled Placebo N=8**	**50 mg Cohort 5 n=16**	**Total Active n = 41**
Injection site reaction – erythema, rash, discoloration, pain, bruising	0	2 (40%)	2 (28.5%)	2 (25%)	0	2 (12.5%)	8 (19.5%)
ALT, LFT, transaminase increased, Liver function test increased	0	1 (20%)	1 (14%)	2 (25%)	0	3 (19%)	7 (17%)
Headache	1 (20%)	2 (40%)	2 (28.5%)	1 (12.5%)	0	0	6 (15%)
Upper respiratory tract infection	0	1 (20%)	2 (28.5%)	0	0	1 (6%)	4 (10%)
Rash	0	0	0	2 (25%)	0	1 (6%)	3 (7%)
Abdominal distention	0	2 (40%)	0	0	0	0	2 (5%)
Diarrhea	1 (20%)	0	1 (14%)	0	0	0	2 (5%)
Hyperglycemia	0	1 (20%)	1 (14%)	0	0	0	2 (5%)
Paresthesia	1 (20%)	0	0	1 (12.5%)	0	0	2 (5%)

Safety data cutoff 11 Sep 2020

- **AEs at injection site were all mild**
- **ALT elevations were generally asymptomatic and transient, returning towards baseline by end of study**
  - Only two subjects had ALT >3X ULN at two sequential visits with return to pre-dose baseline by Day 113 (EOS).
  - The highest ALT was in a subject with a history of cholelithiasis and biliary colic. Baseline ALT of 22 U/L, elevation on Day 85 to 230 U/L with return to 36 U/L on Day 99 and 33 U/L at Day 113 (EOS) Subject subsequently underwent elective cholecystectomy
- **No clinically significant adverse changes in platelets, total bilirubin or creatinine**
- **No drug discontinuations**
- **1 SAE of pancreatitis**
  - Not related to ARO-APOC3
  - History of pancreatitis, type 2 diabetes mellitus and gall stones
  - MRCP/endoscopic ultrasound indicated pancreatolithiasis as probable cause

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ARO-APOC3 Late-Stage Development

Three Global Phase 2b, Phase 3 clinical trials are open for enrollment:

- AROAPOC3-2001: Phase 2b in sHTG (> 500 mg/dL at Screening)
- AROAPOC3-2002: Phase 2b in mixed dyslipidemia (elevated TG and LDL-C at baseline)
- AROAPOC3-2003: Phase 3 in familial chylomicronemia syndrome (FCS)

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