REDEMPLO® (plozasiran) FDA Approval Conference Call

November 18, 2025

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REDEMPLO® FDA Approval Conference Call
November 2025

Welcome and Introductions

Vince Anzalone, CFA
Vice President, Finance and IR

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This presentation contains forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. Any statements contained in this release except for historical information may be deemed to be forward-looking statements. Without limiting the generality of the foregoing, words such as “may,” “will,” “expect,” “believe,” “anticipate,” “hope,” “intend,” “plan,” “project,” “could,” “estimate,” “continue,” “target,” “forecast” or “continue” or the negative of these words or other variations thereof or comparable terminology are intended to identify such forward-looking statements. In addition, any statements that refer to projections of our future financial performance, trends in our business, expectations for our product pipeline, products or product candidates, including anticipated regulatory submissions and clinical program results, prospects or benefits of our collaborations with other companies, or other characterizations of future events or circumstances are forward-looking statements. These forward-looking statements include, but are not limited to, statements about the cost-savings and other benefits of our pricing program for REDEMPLO (plozasiran); our beliefs and expectations regarding the impacts of REDEMPLO on patient health and the health care system; our beliefs and expectations regarding the anticipated launch of REDEMPLO and pricing, value, or expected timing for availability of REDEMPLO; our beliefs and expectations regarding the Rely On REDEMPLO patient support program; the initiation, timing, progress and results of our preclinical studies and clinical trials, and our research and development programs; our expectations regarding the potential benefits of the partnership, licensing and/or collaboration arrangements and other strategic arrangements and transactions we have entered into or may enter into in the future; our beliefs and expectations regarding milestone, royalty or other payments that could be due to or from third parties under existing agreements; and our estimates regarding future revenues, research and development expenses, capital requirements and payments to third parties. These statements are based upon our current expectations and speak only as of the date hereof. Actual results or outcomes may differ materially and adversely from those expressed in any forward-looking statements as a result of numerous factors and uncertainties the safety and efficacy of our products and product candidates, pricing and reimbursement decisions related to our products, demand for our products, decisions of regulatory authorities and the timing thereof, the duration and impact of regulatory delays in our clinical programs, our ability to finance our operations, the likelihood and timing of the receipt of future milestone and licensing fees, the future success of our scientific studies, our ability to successfully develop and commercialize drug candidates, the timing for starting and completing clinical trials, rapid technological change in our markets, the enforcement of our intellectual property rights, and the other risks and uncertainties described in our most recent Annual Report on Form 10-K, subsequent Quarterly Reports on Form 10-Q and other documents filed with the Securities and Exchange Commission from time to time. We assume no obligation to update or revise forward-looking statements to reflect new events or circumstances.

Agenda

Topic	Presenter
Introductions and Agenda	Vince Anzalone, CFA
REDEMPLO® - Arrowhead's First FDA Approval	Chris Anzalone, Ph.D.
Disease Background and Label	James Hamilton, M.D., MBA
PALISADE Phase 3 Clinical Data	Bruce Given, M.D.
U.S. Commercial Launch Plan	Andy Davis, MBA
Key Takeaways and Arrowhead Looking Forward	Chris Anzalone, Ph.D.
Q&A	Panel

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REDEMPLO® - Arrowhead's First FDA Approval

Chris Anzalone, Ph.D.
President and CEO

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REDEMPLO® Now FDA-Approved

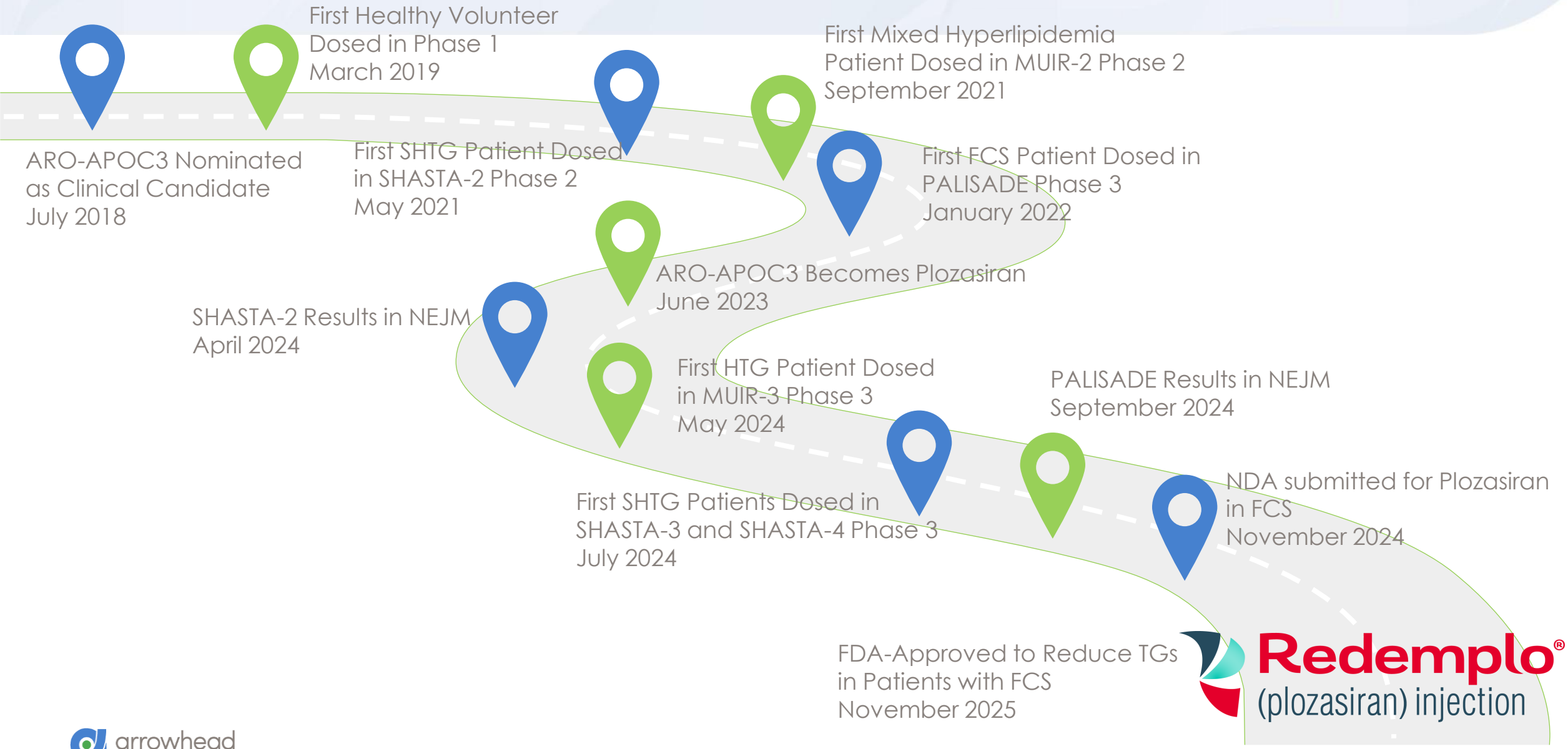
Redemplo®
(plozasiran) injection

- REDEMPLO is the first and only siRNA/RNAi-based medicine FDA-approved to reduce triglycerides in adults with familial chylomicronemia syndrome (FCS)
- First FDA-approved medicine utilizing Arrowhead's proprietary Targeted RNAi Molecule (TRiM™) platform

REDEMPLO Positioned as Promising New Medicine for FCS

- **Dramatic reductions** in triglycerides in patients with **genetically confirmed and clinically defined FCS**
- **Reduced** numerical incidence of **acute pancreatitis**
- **Convenient** dosing once **every three months** with at home **self-administration**
- **Strong label** with no contraindications, warnings or precautions
- Commercial team ready to **launch today**

ARO-APOC3 to Plozasiran to REDEMPLO - Path to First Approval



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Each AP Event Associated With Significant Healthcare Burden

Challenges around Diagnosis[1]

- **~5** physicians typically seen before diagnosis[2]
- **~50%** of patients are misdiagnosed[2]
- Distributed treatment teams[3]
  - Endocrinologists
  - Lipidologists
  - Cardiologists
  - Pancreatologists
  - Primary care
  - Dietitians

Human Cost

- Acute pancreatitis is always a serious medical condition and **can be fatal**
- Acute pancreatitis events make subsequent events **more likely and more severe**
- FCS patients can experience **severe brain fog and recurrent abdominal pain**
  - Compromised quality of life
  - Lost productivity

Economic Cost of Acute Pancreatitis[2,4]

- **>$60,000** in estimated medical costs **per episode** of acute pancreatitis for patients with FCS[5,*,†,**]
- **93%** of episodes involved an inpatient stay, at an average of **10 days spent in an inpatient setting**[5]

*Based on a 2013 study that used the Thomson MarketScan US Commercial Claims and Encounters and Medicare Supplemental Database to identify chylomicronemia (including FCS and non-FCS) cases between 2000 and 2009.[5]

†One-hundred and four episodes of acute pancreatitis were identified, with an average of 3 outpatient visits per episode. Average total medical costs were $31,820 per episode of acute pancreatitis, with inpatient stays accounting for $30,408.[5]

** Company estimates of current costs

References: 1. Stroes E et al. *Atherosclerosis Supplements*. 2017;23:1-7. **2.** Davidson M et al. *J Clin Lipidology*. 2018;12(4):898-907. **3.** Falko JM. *Endocr Pract*. 2018;24(8):756-763. **4.** Gaudet D et al. *Lipids Health Dis*. 2020;19(1):120. doi: 10.1186/s12944-020-01302-x. **5.** Gaudet D et al. *J Med Econ*. 2013;16(5):657–666.

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The FCS Lived Experience

Meet Scott, Living with FCS

- Diagnosed after **23 years of symptoms** and **25 persistent pancreatitis attacks**.
- Symptoms began in childhood. In his 20s, noticed **eruptive xanthomas** and **stomach pains** with **no known cause**. His TGs were tested, and numbers were "through the roof," although no action taken.
- First acute **pancreatitis episode at 30**, launching a **decade of medical crises**.
- Triglycerides hit 24,000 mg/dL during a hospitalization, still with no diagnosis.
- In one year, he spent **2 weeks every 8 weeks in the ICU,** missing life at home with family and work, unable to maintain existing career.
- Doctors repeatedly accused him of alcoholism, placing blame on him, providing **no answers** to what was happening in his body.
- **Discovered FCS and subsequent diagnosis** through relentless self-advocacy and online research, taking information to his doctor for discussion and confirmation.
- For every Scott, there are countless others whose symptoms are overlooked and diagnoses delayed. **Arrowhead's mission is to bring them answers and potential relief sooner.**

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One-REDEMPLO Pricing Model: Consistent Pricing Across Indications

We are committed to sustainable innovation and rational pricing
- Different patients should not pay different prices for this medicine based on their disease

One-REDEMPLO is a pricing model that sets a single consistent product price for multiple potential indications

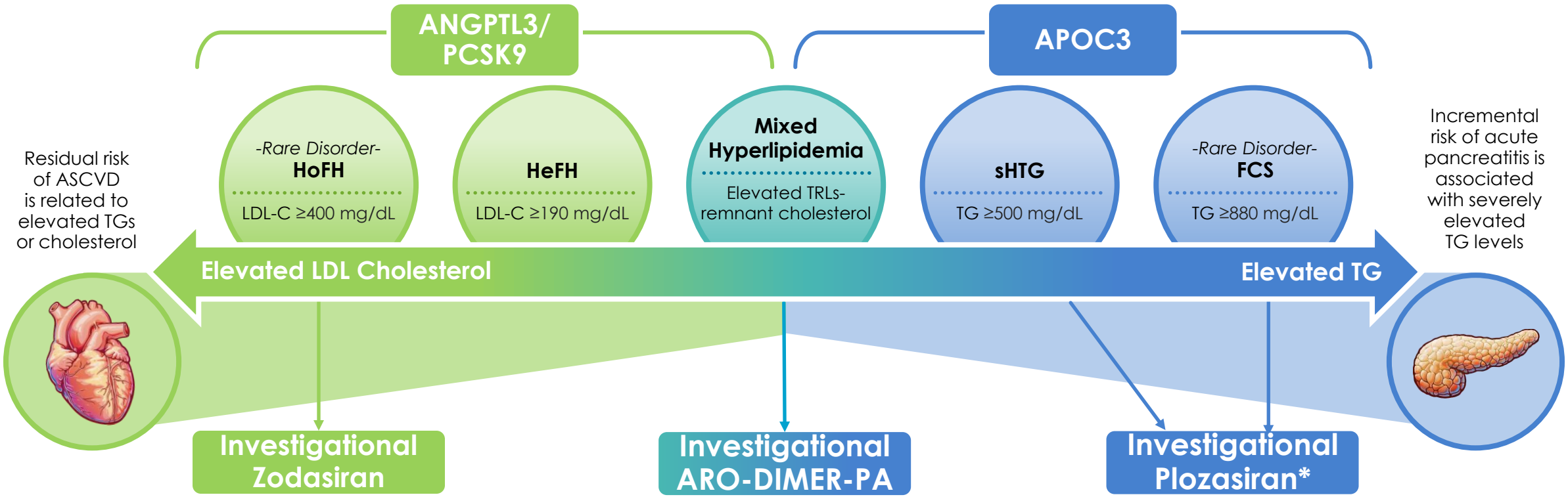
One-REDEMPLO price is based on value for severe patients within the broader SHTG market: pending successful Phase 3 studies and subsequent regulatory review and approval

One-REDEMPLO price is reflective of the long-term value to patients, providers, and the health system: we have time to work with payors to demonstrate this while SHASTA-3 and SHASTA-4 are ongoing

REDEMPLO is launched with $60,000 WAC price and is intended to maintain price throughout the long lifecycle of the product

Arrowhead Also Active Across TG/LDL and ASCVD/AP Spectrum

Lipid Disorders, Including FCS, sHTG, Mixed Hyperlipidemia, and HoFH, Are Characterized by a Spectrum of **Elevated Levels of TGs and/or Cholesterol**[1-12]



ASCVD, atherosclerotic cardiovascular disease; **FCS**, familial chylomicronemia syndrome; **HeFH**, heterozygous familial hypercholesterolemia; **HoFH**, homozygous familial hypercholesterolemia; **LDL-C**, low-density lipoprotein cholesterol; **sHTG**, severe hypertriglyceridemia; **TG**, triglyceride; **TRL**, triglyceride-rich lipoprotein.

*REDEMPLO (plozasiran) is FDA-approved to reduce TGs in FCS in the U.S., investigational plozasiran has not been reviewed or approved to treat FCS outside the U.S. or sHTG in any countries

1. Malick WA, et al. *J Am Coll Cardiol*. 2023;81(16):1646-1658. 2. Larouche M, et al. *Curr Atheroscler Rep*. 2023;25(12):1101-1111. 3. Nordestgaard BG, et al. *Lancet*. 2014;384(9943):626-635. 4. Mach F, et al. *Eur Heart J*. 2020;41(1):111-188. 5. Lloyd-Jones DM, et al. *J Am Coll Cardiol*. 2022;80(14):1366-1418. 6. McGowan MP, et al. *J Am Heart Assoc*. 2019;8(24):e013225. 7. Yang Z, et al. *Front Cardiovasc Med*. 2022;9:913977. 8. Romandini A, et al. *Pharmaceuticals* (Basel). 2023;16(2):176. 9. Virani SS, et al. *J Am Coll Cardiol*. 2021;78(9):960-993. 10. Gaudet D, et al. *N Engl J Med*. 2014;371(23):2200-2206. 11. Berberich AJ, et al. *Endocr Rev*. 2022;43(4):611-653.

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Disease Background and Label

James Hamilton, M.D., MBA
Chief Medical Officer and Head of R&D

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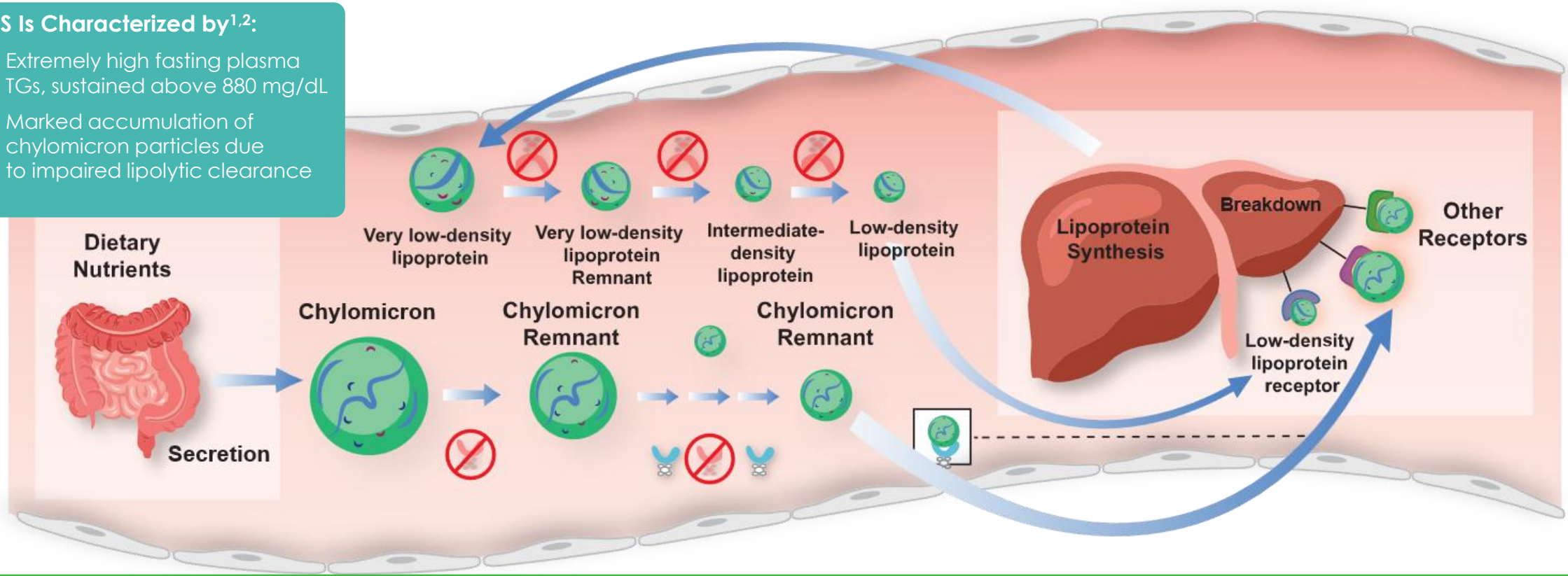
Genetic/Clinical FCS Caused by Inability to Break Down Chylomicrons

Overview of TG Metabolism in Patients With FCS[3]

FCS Is Characterized by[1,2]:

- Extremely high fasting plasma TGs, sustained above 880 mg/dL
- Marked accumulation of chylomicron particles due to impaired lipolytic clearance



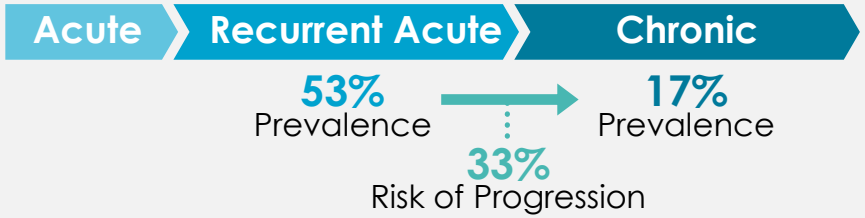
The buildup of chylomicrons causes significant risks[2] - the most severe being acute pancreatitis and its life-threatening sequelae

References: 1. Gaudet D et al. *N Engl J Med*. 2014;371(23):2200-2206. **2.** Shamsudeen I, Hegele RA. *Expert Rev Clin Pharmacol*. 2022;15(4):395-405. **3.** Mszar R et al. *J Clin Med*. 2023;12(4):1382.

Patients With FCS Have Multiple Clinical Manifestations, the Most Serious of Which Is Acute Pancreatitis

Acute Pancreatitis Is the Most Serious, Severe, and Potentially Fatal Complication of FCS, Which Affects ≥50% of Patients[1]

The Pancreatitis Disease Continuum[2]

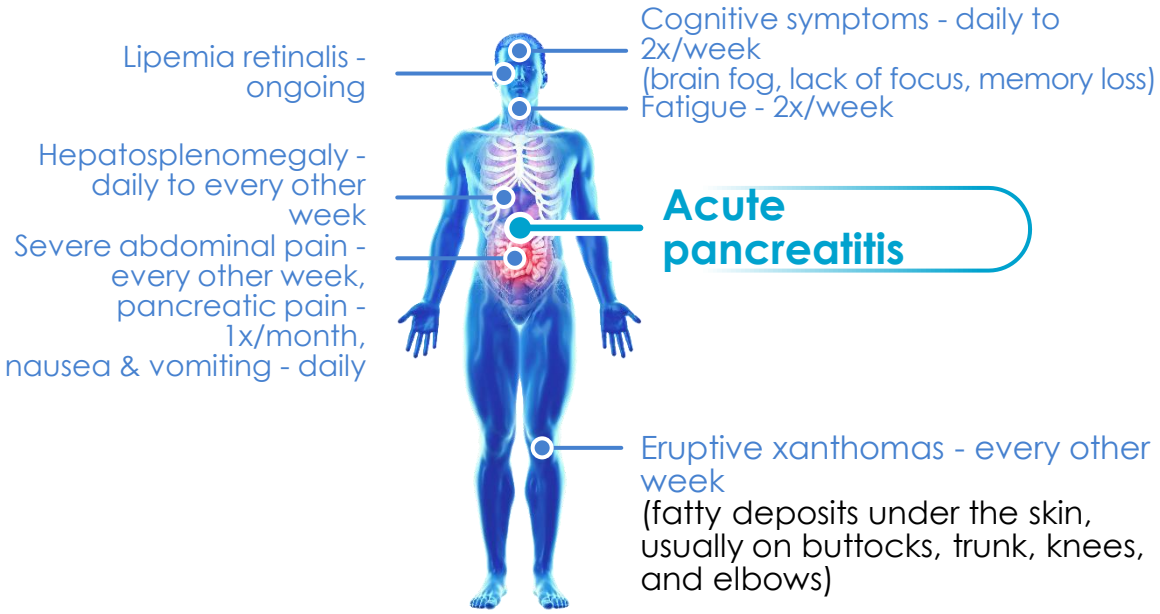


~5%–6% **Overall mortality rate** for TG-induced acute pancreatitis in patients with FCS[3]

30% The **mortality rate** in patients with FCS **in cases of pancreatic necrosis** following an infected pancreatic abscess or persistent multiple organ failure[3]

≥500 mg/dL Patients with **high TG levels** during the early phase of acute pancreatitis are at an **increased risk of multisystem or persistent organ failure[4]**

Clinical Signs and Symptoms of FCS[3,5-7,*]



Acute Pancreatitis Is Associated With Frequent Hospitalizations, Intensive Care, Plasmapheresis Therapy, and Surgeries That Significantly Impact Daily Living and Quality of Life[1,8-10]

References: 1. Gaudet D et al. *Lipids Health Dis*. 2020;19(1):120. doi: 10.1186/s12944-020-01302-x. **2.** Machicado JD, Yadav D. *Dig Dis Sci*. 2017;62(7):1683-1691. **3.** Davidson M et al. *J Clin Lipidology*. 2018;12(4):898-907. **4.** Sue LY et al. *Pancreas*. 2017;46(7):874-879. **5.** Brunzell JD, Bierman EL. *Med Clin North Am*. 1982;66(2):455-468. **6.** Shamsudeen I, Hegele RA. *Expert Rev Clin Pharmacol*. 2022;15(4):395-405. **7.** Wang P et al. *J Clin Imaging Sci*. 2020;10(64):1-3. **8.** Davidson D et al. *J Patient Reported Outcomes*. 2021;5(1):72. doi: 10.1186/s41687-021-00347-5. **9.** Gaudet D et al. *J Clin Lipidology*. 2016;10(3):680-681. **10.** Krauß LU et al. *Dig Dis*. 2023;41(4):647-655.

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Professional Guidelines Recommend Reducing TG Levels to <500 mg/dL to Lower the Risk of Acute Pancreatitis

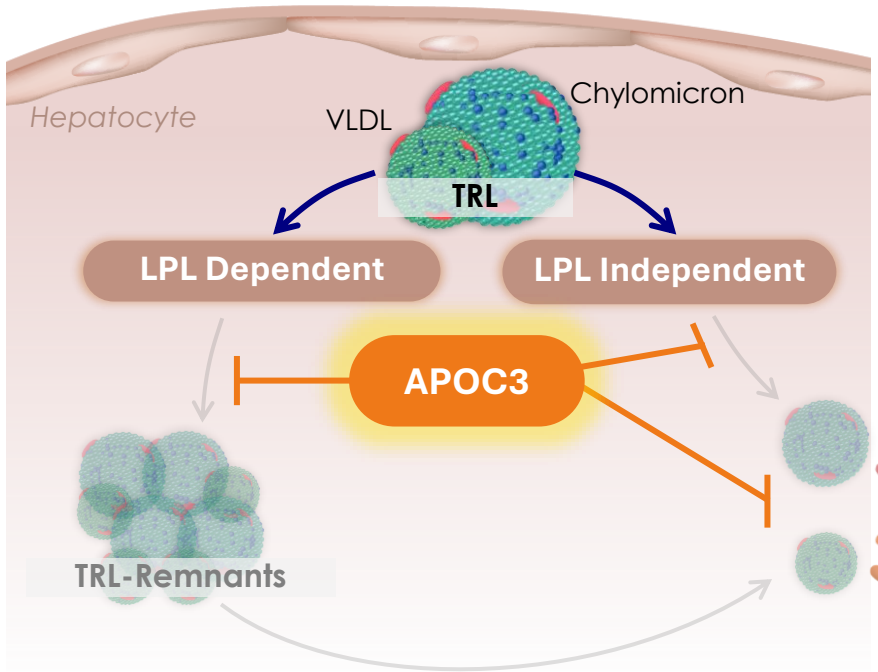
Guideline(s)	Recommendations
American Association of Clinical Endocrinologists (AACE) **American College of Endocrinology** (ACE)	**To reduce the risk of acute pancreatitis**, a fibrate, prescription-grade omega-3 fatty acid, and/or niacin should be given to all patients with severe hypertriglyceridemia (>500 mg/dL), **with the goal of reducing TGs to well below 500 mg/dL**[1]
American College of Cardiology (ACC)* **American Heart Association** (AHA)* **National Lipid Association** (NLA)	**To prevent acute pancreatitis,** it is reasonable to **reduce TGs whenever levels exceed 500 mg/dL**[2] When the TG concentration is very high (≥500 mg/dL, and especially if ≥1000 mg/dL), **reducing the concentration to <500 mg/dL to prevent pancreatitis becomes the primary goal of therapy**[3]

*The following organizations also contributed to these guidelines: American Association of Cardiovascular and Pulmonary Rehabilitation (AACVPR), American Academy of Physician Associates (AAPA), Association of Black Cardiologists (ABC), American College of Preventive Medicine (ACPM), American Diabetes Association (ADA), American Geriatrics Society (AGS), American Pharmacists Association (APhA), American Society for Preventive Cardiology (ASPC), National Lipid Association (NLA), and Preventive Cardiovascular Nurses Association (PCNA).

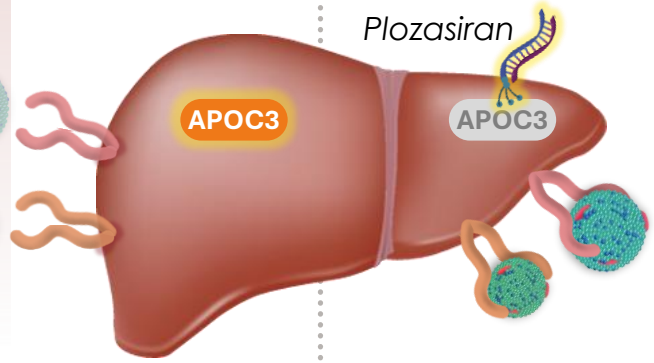
References: 1. Handelsman Y et al. *Endocr Pract*. 2020;26(10):1196-1224. **2.** Grundy SM et al. *Circulation*. 2019;139(25):e1082-e1143.

REDEMPLO Mechanism of Action
Targeting APOC3, a Key Regulator of TG and TRL Metabolism

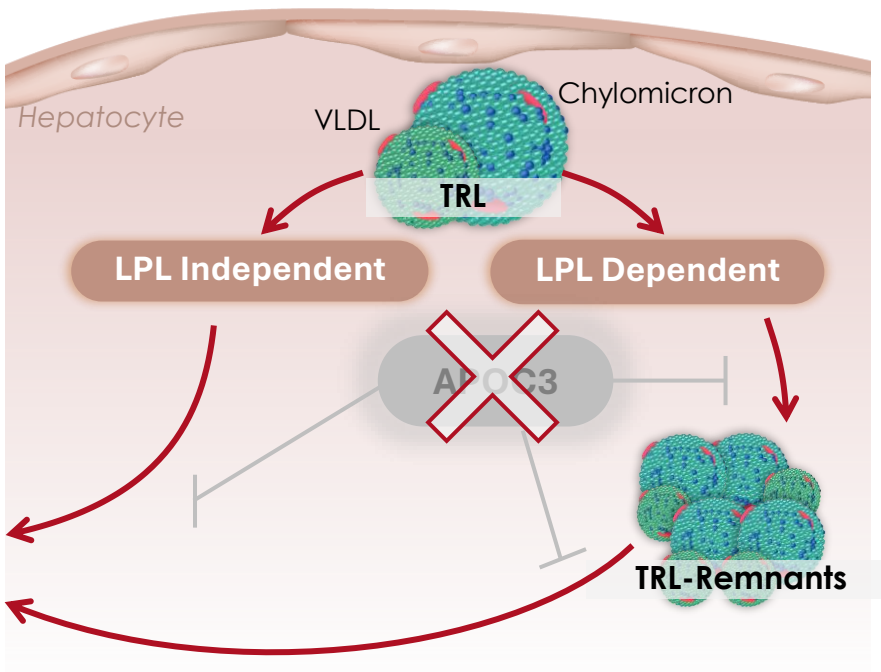
CHYLOMICRONEMIA[1,2]



APOC3 inhibits LPL and delays clearance of TRL-remnants by preventing uptake by liver receptors, increasing plasma TGs



REDEMPLO (plozasiran)[2]



Silencing APOC3 enhances TG lipolysis and TRL-remnant clearance by hepatic receptors, reducing plasma TGs

APOC3, apolipoprotein C3; **HL**, hepatic lipase; **LPL**, lipoprotein lipase; **TG**, triglycerides; **TRL**, triglyceride rich lipoproteins; **VLDL**, very low-density lipoprotein. **1.** Van Zwol W et al. *J Clin Med*. 2019; 8:1085. **2.** Ballantyne CM, et al. *New Engl J Med*. 2024; Published online: May 28, 2024. DOI: 10.1056/NEJMoa2404143.

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REDEMPLO Label – Indication Statement and Dosing

----------INDICATIONS AND USAGE----------

REDEMPLO is an apolipoprotein C-III *(apoC-III)*-directed small interfering ribonucleic acid (siRNA) indicated as an adjunct to diet to reduce triglycerides in adults with familial chylomicronemia syndrome (FCS). (1)

----------DOSAGE AND ADMINISTRATION----------

- The recommended dosage of REDEMPLO is 25 mg injected subcutaneously once every 3 months. (2.1)
- Inject REDEMPLO subcutaneously into the front of the thigh or abdomen. The outer area of the upper arm can be used as an injection site if a healthcare provider or caregiver administers the injection. (2.2)

----------DOSAGE FORMS AND STRENGTHS----------

Injection: 25 mg/0.5 mL solution in a single-dose pre-filled syringe. (3)

REDEMPLO Label – No Contraindications, Warnings or Precautions, and Acceptable Adverse Event Profile

----------CONTRAINDICATIONS----------

None. (4)

----------ADVERSE REACTIONS----------

Most common adverse reactions in REDEMPLO treated patients (incidence ≥10% of patients treated with REDEMPLO and >5% more frequently than with placebo) are hyperglycemia, headache, nausea, and injection site reaction. (6.1)

REDEMPLO Label – Clinical Efficacy

14 CLINICAL STUDIES

Table 2: Baseline (BL) and Percent Changes from Baseline in Lipid/Lipoprotein Parameters in Patients with FCS at Month 10 in Trial 1

Parameter (mg/dL)	REDEMPLO 25 mg N=26		Placebo (pooled) N=25		REDEMPLO 25 mg vs. Placebo
	BL	% change at Month 10	BL	% change at Month 10	Treatment Difference % change (95% CI) at Month 10
Triglycerides[b]	2008	-80	2053	-17	-59[a] (-90, -28)
Non-HDL-C[c]	279	-39	268	4	-42 (-67, -18)
LDL-C[c]	24	112	28	20	92 (4, 180)
Total ApoB[c]	72	27	79	12	15 (-16, 46)
ApoB-48[c]	10	-61	11	45	-106 (-180, -33)

Abbreviations: ApoB = apolipoprotein B; CI= confidence interval; BL = baseline; FCS=familial chylomicronemia syndrome; non-HDL-C = non high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol.
[a] Reached statistical significance (p value < 0.0001).
[b] Median; Hodges-Lehmann method was used to estimate the median difference (location shift) and its corresponding 95% confidence interval for percent changes. Missing data were imputed using washout imputation.
[c] Mean; Analysis of covariance (ANCOVA) model was used to estimate the mean difference and its corresponding 95% confidence interval for percent changes. Missing data were imputed using washout imputation.

Median percent change in TG from baseline (Figure 1) and median absolute TG values (Figure 2) over time demonstrated a consistent lowering effect during the 12-month treatment period.

Figure 1: Median Percent Change from Baseline in Fasting Triglycerides Over Time in Trial 1

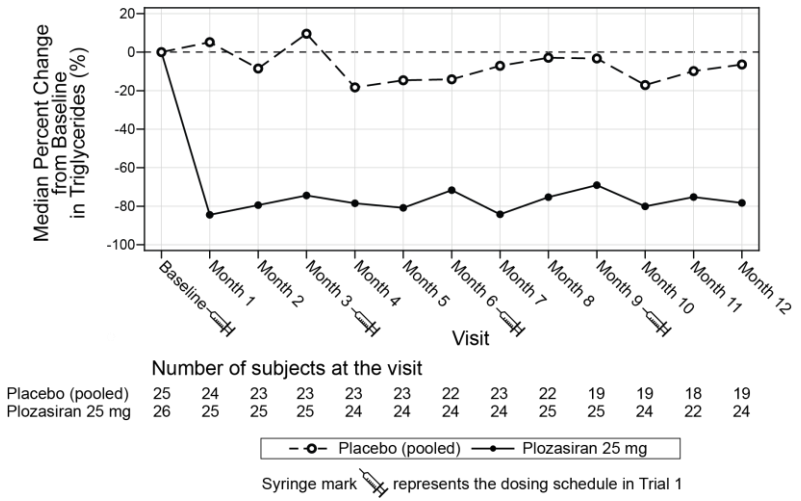
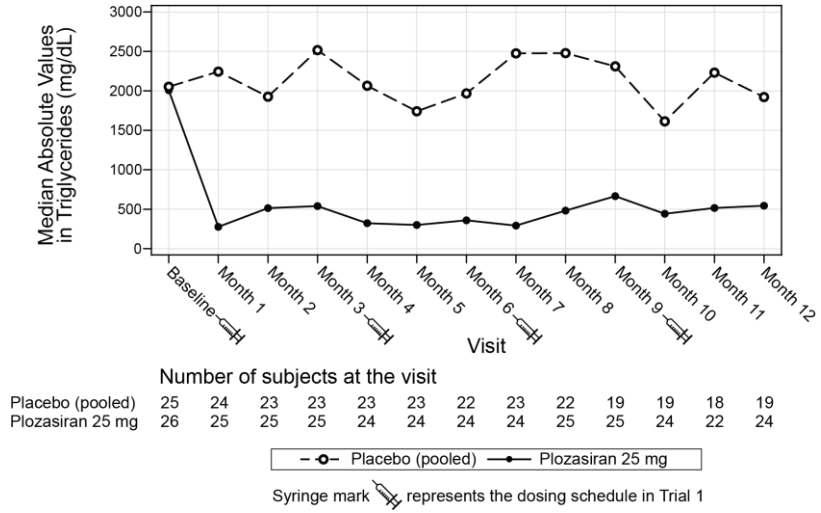


Figure 1: Median Absolute Fasting Triglyceride Levels (mg/dL) in Trial 1



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PALISADE Phase 3 Clinical Data

Bruce Given, M.D.
Chief Medical Scientist

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PALISADE Phase 3 Study Enrolled Patients with FCS Defined Clinically or Genetically Confirmed

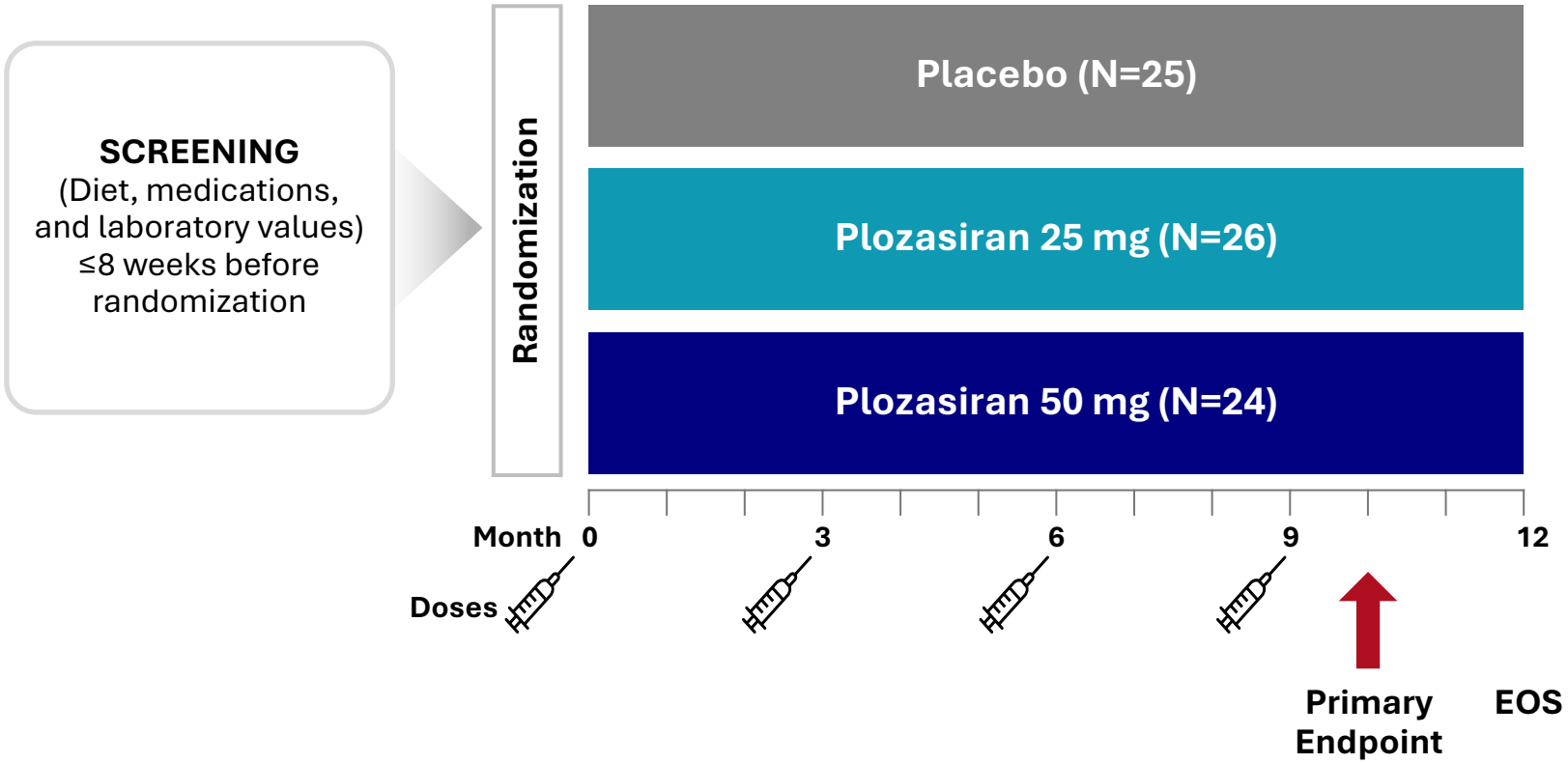
Criteria included history of multiple TG measurements above 1000 mg/dL (at least 880 mg/dL at screening), despite standard of care; plus at least one of the following:

1. Prior genetic testing diagnostic of FCS* OR
2. Recurrent episodes of acute pancreatitis§ OR
3. Recurrent hospitalizations for severe abdominal pain without other explainable cause OR
4. History of childhood pancreatitis OR
5. Family history of HTG-induced acute pancreatitis

Genetic testing was done on all patients not previously tested for FCS variants

*Supportive genetic testing includes but is not limited to homozygous, compound heterozygous, or double heterozygote for loss-of-function or otherwise inactivating mutations in genes affecting lipoprotein lipase activity including LPL, APOC2, APOA5, GPIHBP1, GPD1, or LMF1; or evidence of low LPL activity (<20% of normal) based on source-verifiable documentation; § not caused by alcohol or cholelithiasis. FCS, familial chylomicronemia syndrome; HTG, hypertriglyceridemia; TG, triglycerides.

PALISADE: Randomized Placebo-Controlled Phase 3 Study of Plozasiran in Patients with FCS



Primary Endpoint:

- Placebo-adjusted median percent change in triglycerides at Month 10

Multiplicity-controlled key secondary endpoints:

1. Percent change from baseline at Months 10 and 12 (averaged) in fasting triglycerides
2. Percent change from baseline at Month 10 in fasting APOC3
3. Percent change from baseline at Month 12 in fasting APOC3
4. Incidence of positively adjudicated events of acute pancreatitis during the randomized period

APOC3, apolipoprotein C3; FCS, familial chylomicronemia syndrome; EOS, end of study.

PALISADE Baseline Characteristics

Characteristic	Pooled Placebo (N=25)	Plozasiran 25 mg (N=26)	Plozasiran 50 mg (N=24)
Mean (SD) age, years	47 (14)	48 (14)	43 (11)
Female, n (%)	11 (44)	14 (54)	13 (54)
Male, n (%)	14 (56)	12 (46)	11 (46)
White, n (%)	19 (76)	19 (73)	17 (71)
Mean (SD) BMI, kg/m^2	25 (4)	26 (4)	25 (5)
Median (Q1, Q3) APOC3, mg/dL	39 (29, 50)	39 (27, 44)	30 (18, 37)
Mean (SD) APOC3, mg/dL	40 (18)	39 (17)	33 (20)
Median (Q1, Q3) triglyceride, mg/dL	2053 (1435, 2755)	2008 (1204, 3361)	1902 (1434, 2948)
Mean (SD) triglyceride, mg/dL	2272 (1141)	2350 (1375)	2492 (1523)
Receiving statins n (%)	11 (44)	11 (42)	12 (50)
Fibrates, n (%)	16 (64)	19 (73)	15 (63)
Omega-3 fatty acids, n (%)	6 (24)	9 (35)	7 (29)
Diabetes or pre-diabetes, n (%)	11 (44)	10 (39)	7 (29)
Genetic confirmation of FCS, n (%)	14 (56)	14 (54)	16 (67)
Previous episode of pancreatitis, n (%)	22 (88)	23 (89)	22 (92)

Data are reported as mean (±SD) unless otherwise noted. Note: Diabetic patients are defined as having HbA1c ≥6.5% or fasting glucose ≥126 mg/dL or with medical history of 'diabetes' or receiving diabetic medications at baseline. *% = 100 x n/N', N' is the number of diabetic or prediabetic patients at baseline.

APOC3, apolipoprotein C3; BMI, body mass index; FCS, familial chylomicronemia syndrome; N, number; Q, quartile; SD, standard deviation; W, week.

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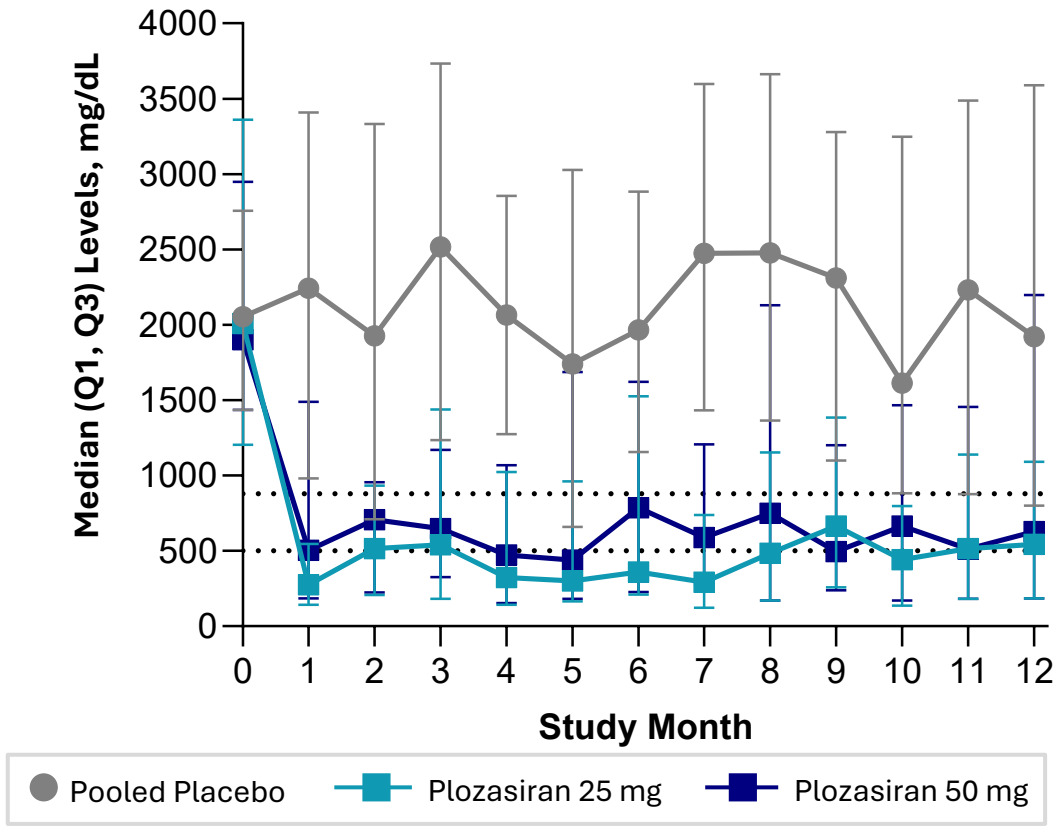
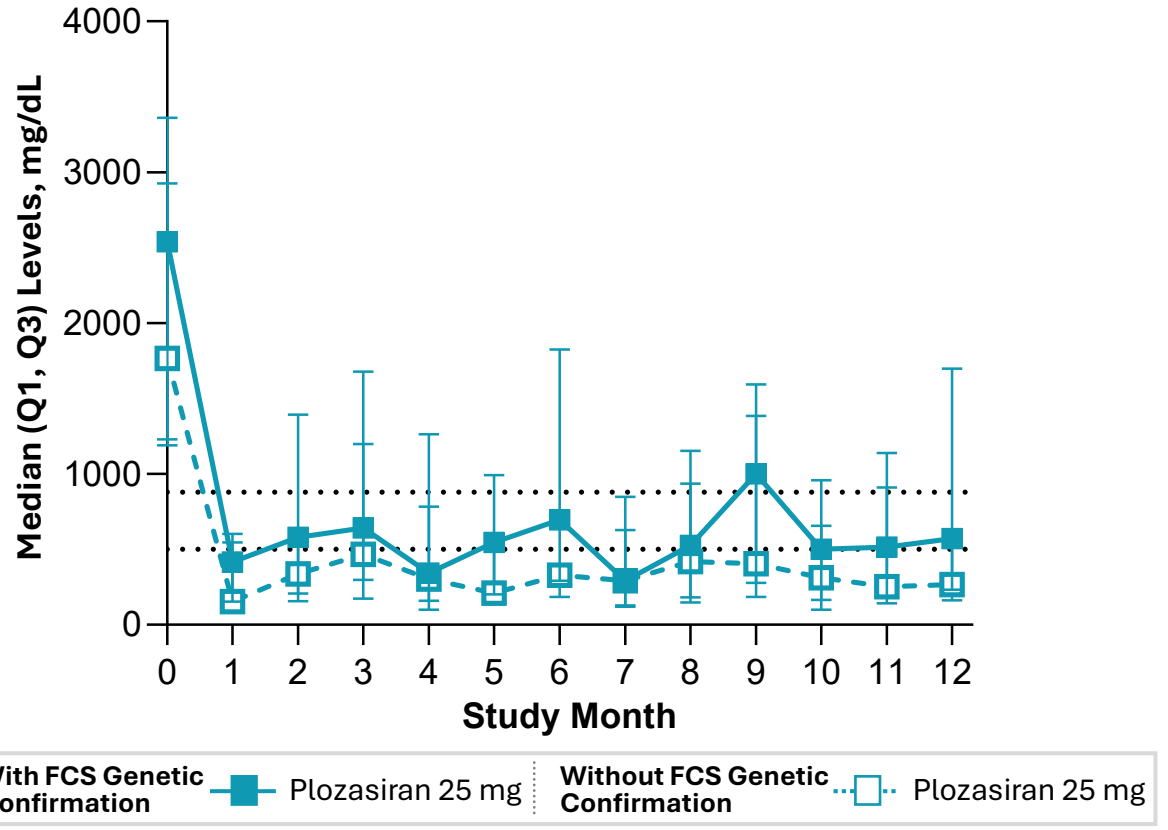
In PALISADE Median TGs Reduced 80% from Baseline at 1 month to Below Guideline Directed AP Risk Thresholds





75% of patients reached TGs < 880 mg/dL & 50% reached < 500 mg/dL at 10 months
The effects were similar between genetic and non-genetic FCS[1]

AP, acute pancreatitis; Q1, 1st quartile; Q3, 3rd quartile; SEM, standard error of mean; TG, triglycerides.

1. Circulation 2025 Mar 11;151(10):733-736. doi:10.1161/CIRCULATIONAHA.124.072860. Epub 2024 Nov 16., and Presented at AHA Scientific Sessions 2024

Between group differences are not statistically significant through all time points.

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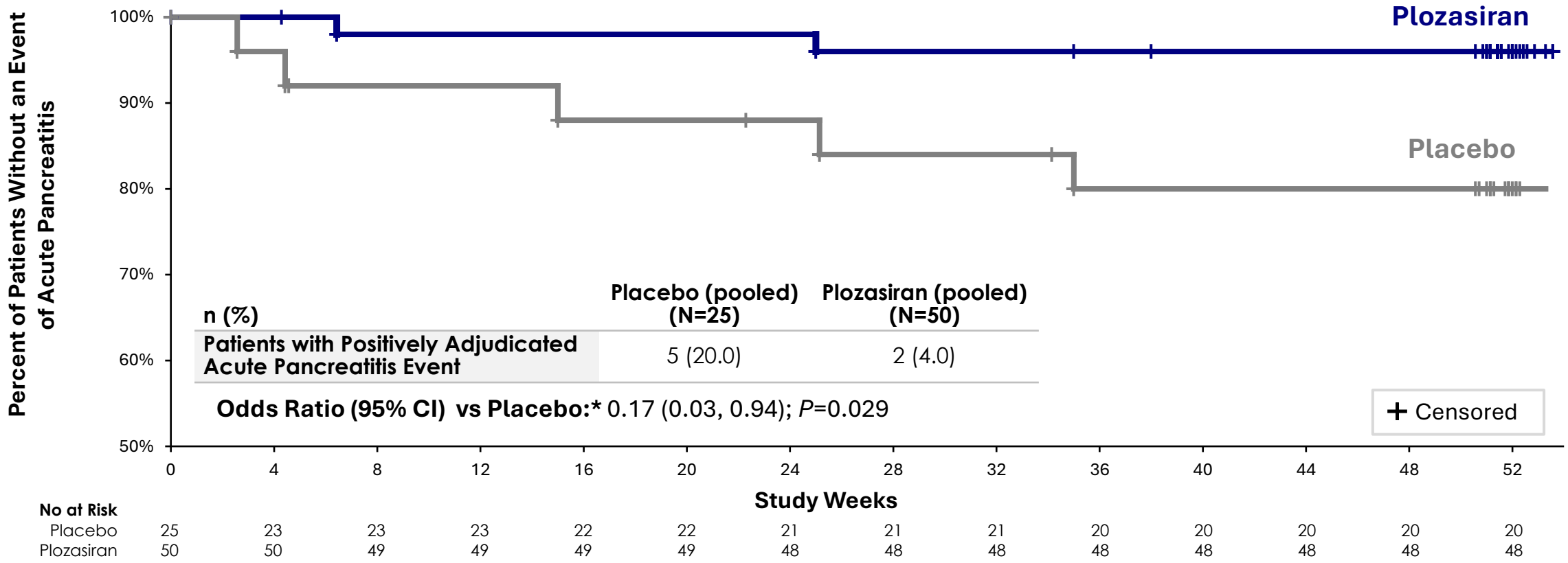
Plozasiran Significantly[1] Reduced the Incidence of AP† in the Phase 3 PALISADE Study*

This is based on a prespecified analysis of the PALISADE study in which 25 mg plozasiran and 50 mg plozasiran were pooled. 50 mg plozasiran has not been reviewed or approved to treat any disease.

Time to First Pancreatitis Event



n (%)	Placebo (pooled) (N=25)	Plozasiran (pooled) (N=50)
Patients with Positively Adjudicated Acute Pancreatitis Event	5 (20.0)	2 (4.0)

Odds Ratio (95% CI) vs Placebo:* 0.17 (0.03, 0.94); *P*=0.029

1. In prespecified pooled analysis of 25 mg plozasiran group and 50 mg plozasiran group (50 mg plozasiran has not been reviewed or approved to treat any disease.*Odds ratio, 95% CI, and P-value were based on CMH test stratified by baseline TG category. 7 incident cases occurred in 5 of 25 (20%) participants receiving placebo and 2 incident cases occurred in 2 of 50 (4%) participants in the plozasiran-treated group. † 4 patients with AP events were FCS genotype negative
CI=confidence interval; CMH=Cochran-Mantel-Haenszel; TG=triglyceride.

*Presented at AHA Scientific Sessions 2024

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Summary of Safety and Tolerability from PALISADE Phase 3

	Pooled Placebo (N=25)	Plozasiran	
		25 mg (N=26)	50 mg (N=24)
Adverse Reactions[1]			
Hyperglycemia	2 (8)	5 (19)	5 (21)
Headache	2 (8)	3 (12)	5 (21)
Nausea	2 (8)	4 (15)	3 (13)
Injection site reactions	2 (4)	4 (15)	1 (4)
Severe TEAEs	5 (20)	3 (12)	3 (13)
Serious TEAEs	7 (28)	5 (19)	2 (8)
Deaths	0 (0)	0 (0)	0 (0)
Premature discontinuations[2]			
Any Reason	6 (24)	3 (12)	2 (8)
Adverse Event	0 (0)	2 (8)	1 (4)
HbA1c, mean % (SD)			
Baseline	6.1 (1.33)	5.7 (0.90)	5.59 (1.15)
Month 12	6.2 (1.17)	5.98 (1.00)	5.83 (1.56)
Platelet count, 10^9/liter, mean (SD)			
Baseline	217.9 (80.5)	204.4 (70.4)	192.9 (50.7)
Mean change from baseline at Month 10	25.9 (38.2)	28.7 (61.2)	-4.4 (48.2)
Mean change from baseline at Month 12	8.6 (47.5)	-4.3 (40.8)	-8.7 (50.8)

- A greater proportion of placebo-treated patients experienced SAEs
- Fewer premature discontinuations from blinded therapy with plozasiran
- No effect on platelet counts
- No deaths

[1] Adverse Reactions noted in the US Package Insert
[2] Premature discontinuation from blinded therapy
HbA1c, glycosylated hemoglobin; SD, standard deviation; SAE, serious adverse event; TEAE, treatment emergent adverse event. Hyperglycemia and injection site reactions are a composite of associated adverse event terms

REDEMPLO® FDA Approval Conference Call
November 2025

U.S. Commercial Launch Plan

Andy Davis, MBA
Senior Vice President, Global Cardiometabolic Franchise

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The Genetically Confirmed and Clinically Diagnosed FCS Population Is Estimated to be 6,500 People In The U.S.

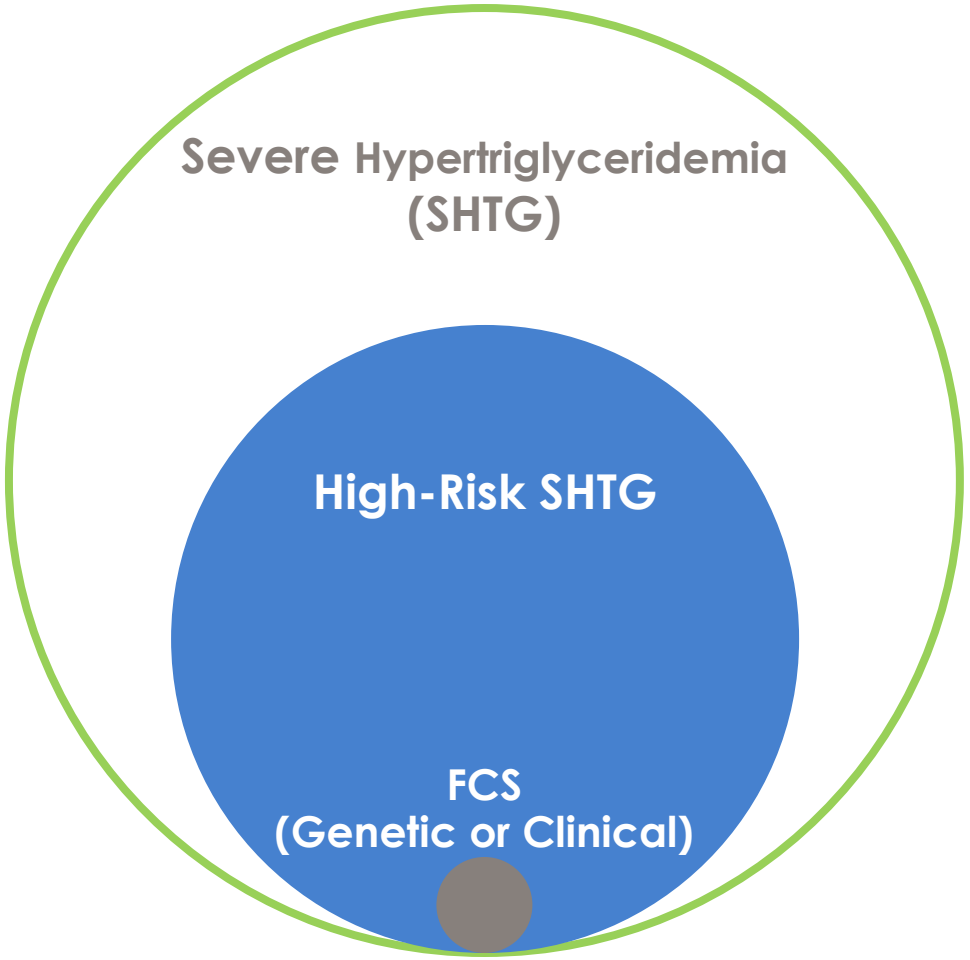

Figure Not to Scale

SHTG

- TGs ≥ 500 mg/dL
- > 3 million people
- Elevated Risk of AP

High-Risk SHTG

- TGs ≥ 880 mg/dL or ≥ 500 mg/dL With Prior AP History
- ~ 1 million people
- High Risk of AP

FCS (Genetic or Clinical)

- Persistently Elevated TGs ≥ 880 mg/dL
- Prevalent Prior History of AP
- ~ 6500 people
- Extremely High Risk of AP

Source: Nemeth, Journal of Clinical Medicine 2022; Rabacchi, Atherosclerosis 2015; Company Estimates

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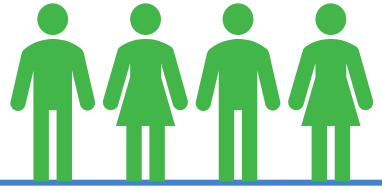
FCS Prescriber Base by Specialty



~6,500 FCS patients in the U.S.

HCPs Identified
Across 4 Specialties Who Primarily Treat FCS Patients

- **LIPIDOLOGISTS**
- **ENDOCRINOLOGISTS**
- **PREVENTIVE CARDIOLOGISTS**
- **INTERNAL MEDICINE/OTHER**

The REDEMPLO GO LO Campaign Features Key Messages That Support Quality Use of Medicine

PALISADE was a randomized, placebo-controlled, double-blind trial in adult patients with FCS maintained on a low-fat diet (≤20 grams of fat per day); N=75. The primary endpoint evaluated the median percent change from baseline in fasting triglyceride levels at Month 10.[1]

*Median fasting triglycerides at baseline were 2008 mg/dL for Redemplo (n=26) and 2053 mg/dL for placebo (n=25). The difference between Redemplo and the placebo group in median percent change in triglyceride levels from baseline to Month 10 was -58.7% (95% CI: -89.6, -27.9; *P*<0.0001).[1]

†Over the 12-month treatment period, the numerical incidence of acute pancreatitis in patients treated with Redemplo was lower compared with placebo: 2 (8%) vs 5 (20%), respectively.[1]

AP, acute pancreatitis; CI, confidence interval.

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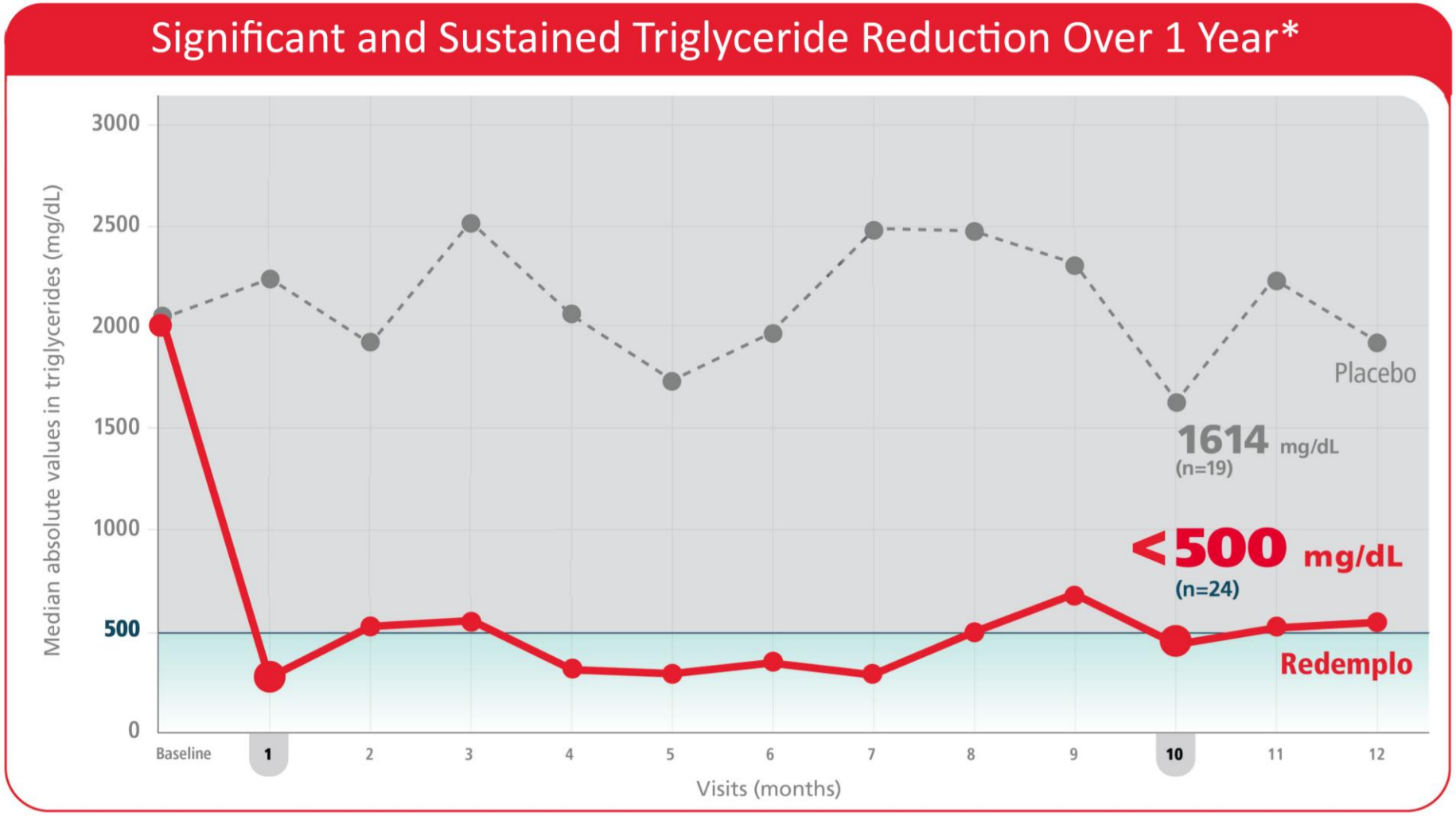
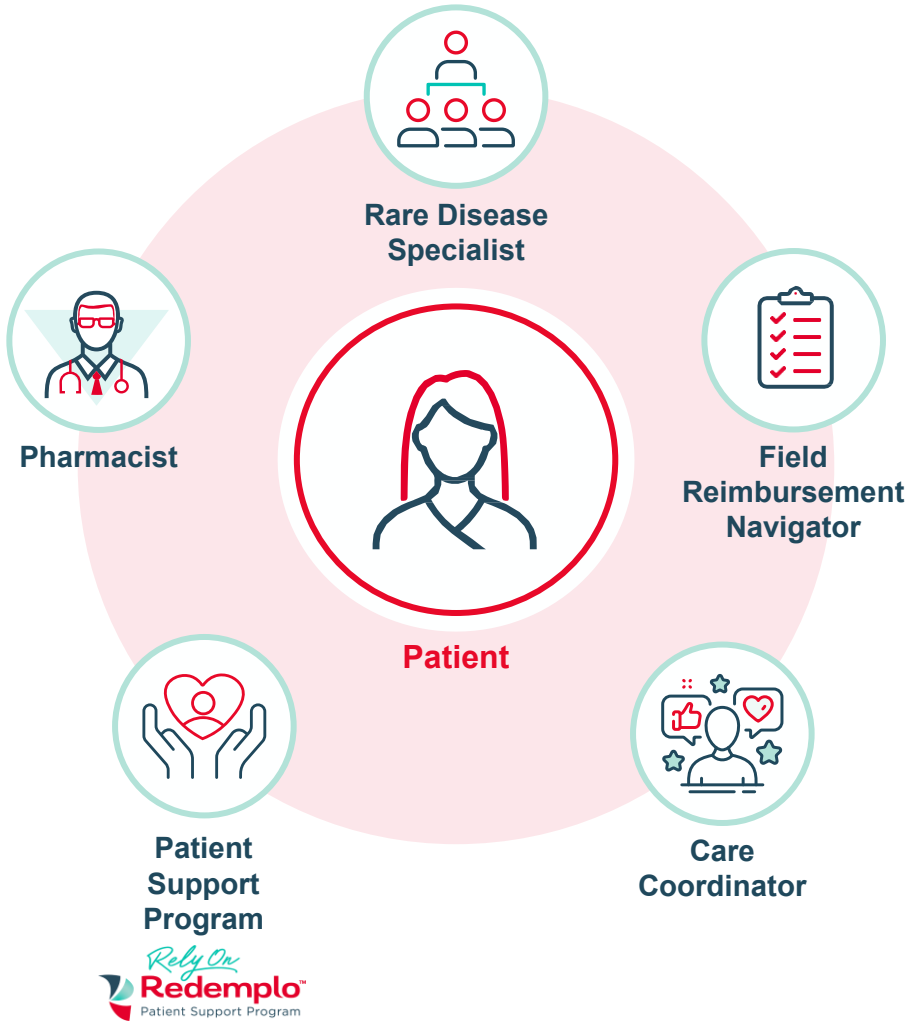
In PALISADE, REDEMPLO Delivered Sustained TG Reductions Median Level Below 500 mg/dL at Multiple Timepoints

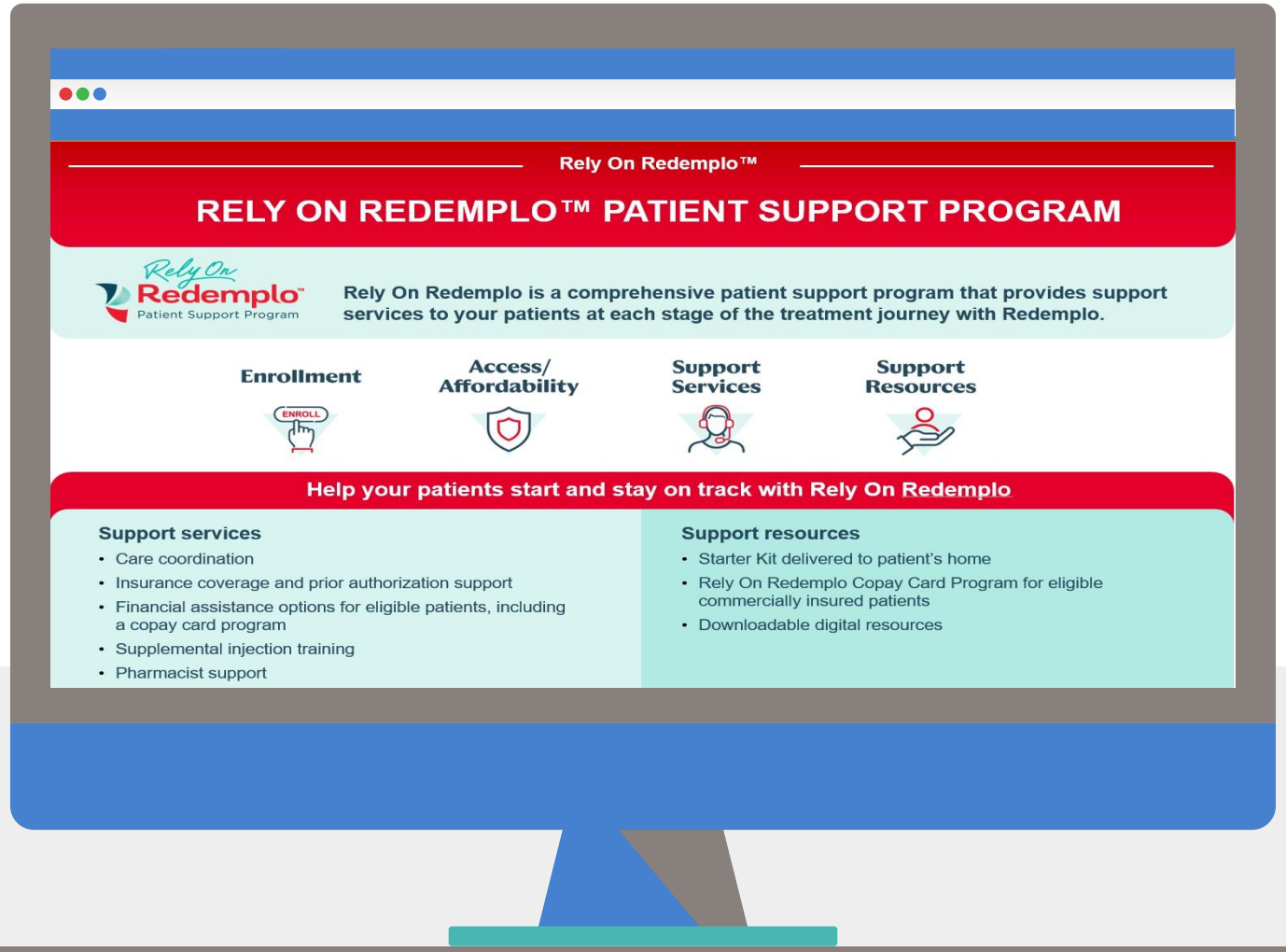


*Median fasting triglycerides at baseline were 2008 mg/dL for Redemplo (n=26) and 2053 mg/dL for placebo (n=25).[1]
CI, confidence interval.

The Patient And HCP Support Ecosystem Is Now Ready To Deliver High Quality Service



Rely On REDEMPLO Patient Support Program



Feedback From Physicians, Payers, Patients, And Caregivers Has Been Very Encouraging

There is high unmet need for FCS patients, so a product with such impressive efficacy cannot come soon enough.
– Endocrinologist

I'm impressed by the results showing similar TG reductions from baseline in study participants with genetically and clinically confirmed FCS
– Cardiologist

It's remarkable how many patients reach triglyceride levels below 500 mg/dL.
– Lipidologist

Plozasiran has been on our radar and we are looking forward to its approval for the unmet need in FCS.
– Payer

I'd be motivated to get on this treatment to get my triglycerides down and regain a lot of moments with my kids I missed because I wasn't feeling well.
– FCS Patient

This new therapy is going to propel us into a new life that we've never had access to before. We're not standing still; we're not looking back. We're returning our lifestyle to some normalcy.
– Caregiver

Source: Market Research, Discussion Notes

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REDEMPLO® FDA Approval Conference Call
November 2025

Key Takeaways and Arrowhead Looking Forward

Chris Anzalone, Ph.D.
President and CEO

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REDEMPLO Positioned as Promising New Medicine for FCS

- **Dramatic reductions** in triglycerides in patients with **genetically confirmed and clinically defined FCS**
- **Reduced** numerical incidence of **acute pancreatitis**
- **Convenient** dosing once **every three months** with at home **self-administration**
- **Strong label** with no contraindications, warnings or precautions
- Innovative, consistent, **One-REDEMPLO** price model across indications
- Commercial team ready to **launch today**

Bringing RNA Interference to Patients

Arrowhead Pharmaceuticals is a **RNAi therapeutics platform company** with a **broad pipeline** of **wholly owned and partnered** candidates and achieved its **first commercial launch in 2025**

First Commercial Launch in 2025

- **REDEMPLO®** (plozasiran) **approved by US FDA** as an adjunct to diet to reduce triglycerides in adults with familial chylomicronemia syndrome (FCS)
- Additional regulatory review/approvals anticipated in 2026
- Potential **Multi-billion-dollar** opportunity across future indications

Broad Pipeline

- **19 clinical stage programs** (10 wholly-owned; 9 partnered)
- Mix of **early, mid, and late-stage** candidates targeting **rare and high prevalence diseases**
- Growing pipeline with **2-3 new clinical programs planned per year**

Proprietary Platform

- **Targeted RNAi Molecules** platform (**TRiM™**) designed for **deep and durable gene silencing**
- **Fulfilling the promise** of bringing RNAi therapeutics to diseases **outside of the liver**
- Potential to be **best-in-class** across several tissue types

Financial Resources

- **Additional non-dilutive capital expected** from Sarepta, Amgen, Takeda, GSK, Novartis, and Royalty Pharma as milestones are achieved
- **Strong balance sheet** with **funding into fiscal 2028** to push candidates to commercialization

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TRiM™ Platform Enables Delivery to Seven Cell Types

Liver	Lung	Skeletal Muscle	CNS	Adipose	Ocular	Cardio-myocyte
Strong clinical validation	Deep lung clinical validation (RAGE)	Early clinical stage	Early clinical stage	Early clinical stage	Preclinical Stage	Preclinical Stage

Arrowhead is Fulfilling the Promise of Bringing RNAi Throughout the Body

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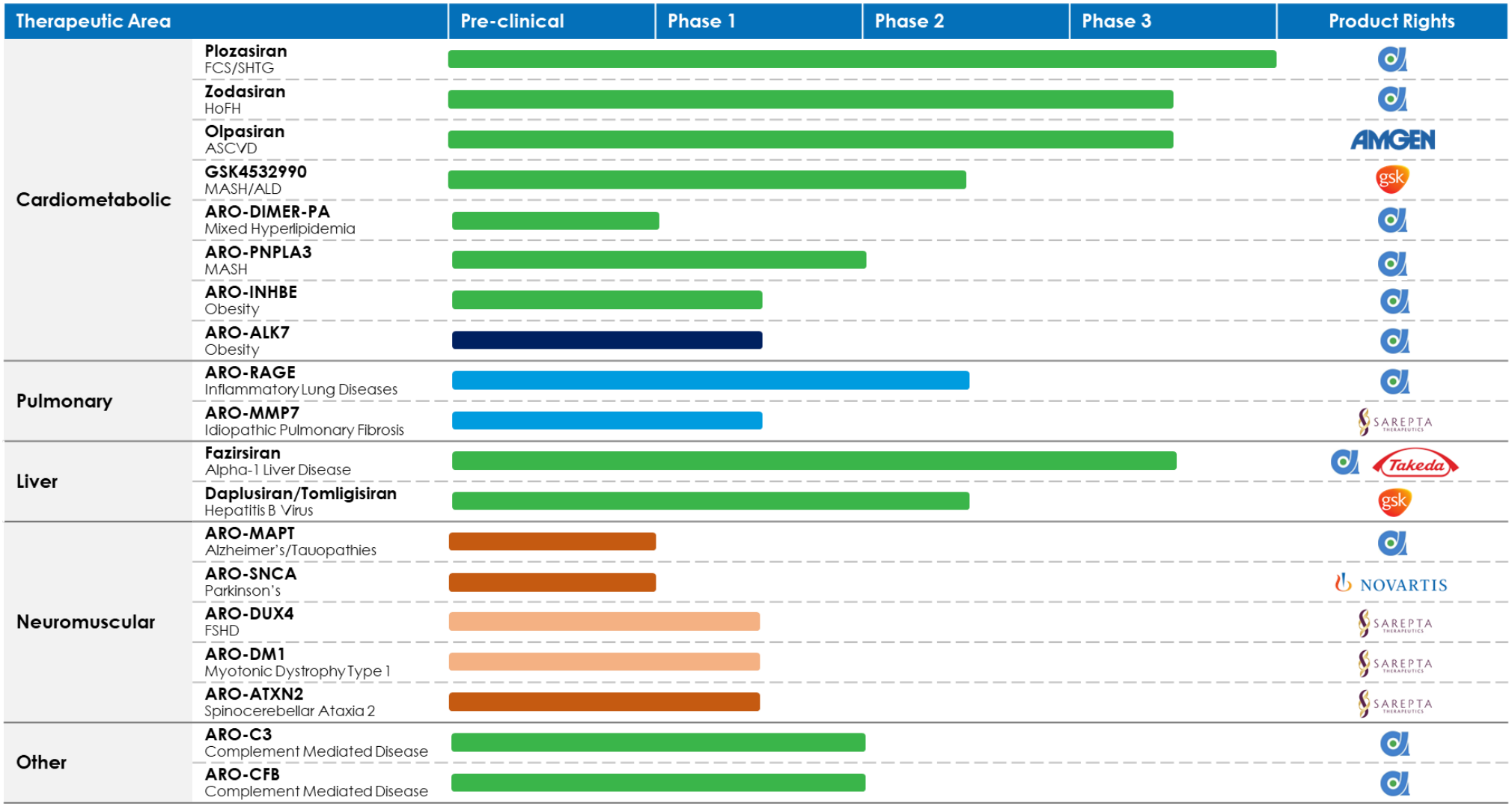
Robust Pipeline with Multiple Mid- and Late-Stage Opportunities



*Sanofi holds product rights to plozasiran and ARO-DIMER-PA in Greater China only

Arrowhead's Growth Drivers in 2026 and Beyond

Arrowhead's first **commercial sales of REDEMPLO** in familial chylomicronemia

Phase 3 studies of plozasiran in **severe hypertriglyceridemia (potential multi-billion-dollar opportunity)** on pace to readout in Q3 2026

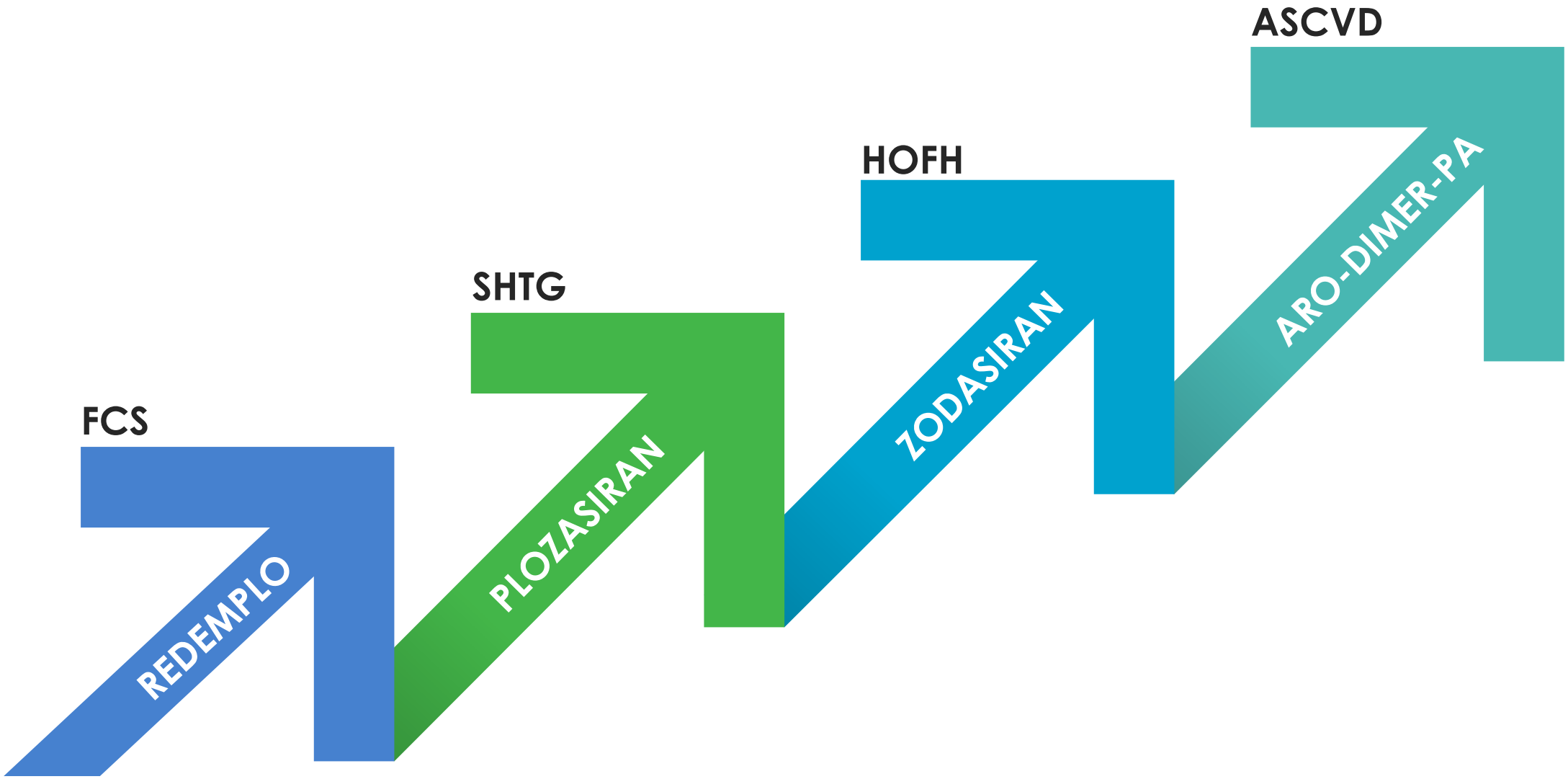
ARO-DIMER-PA targeting PCSK9 and APOC3 first clinical **readout in 2H 2026**

Emerging potential high value **obesity and CNS pipelines** including systemic delivery across blood brain barrier

Robust pipeline and productive discovery engine provide opportunities for additional **capital inflows from business development**

Funded into 2028, potentially through **multiple independent and partner launches**

And We Anticipate Additional Cardiometabolic Launches



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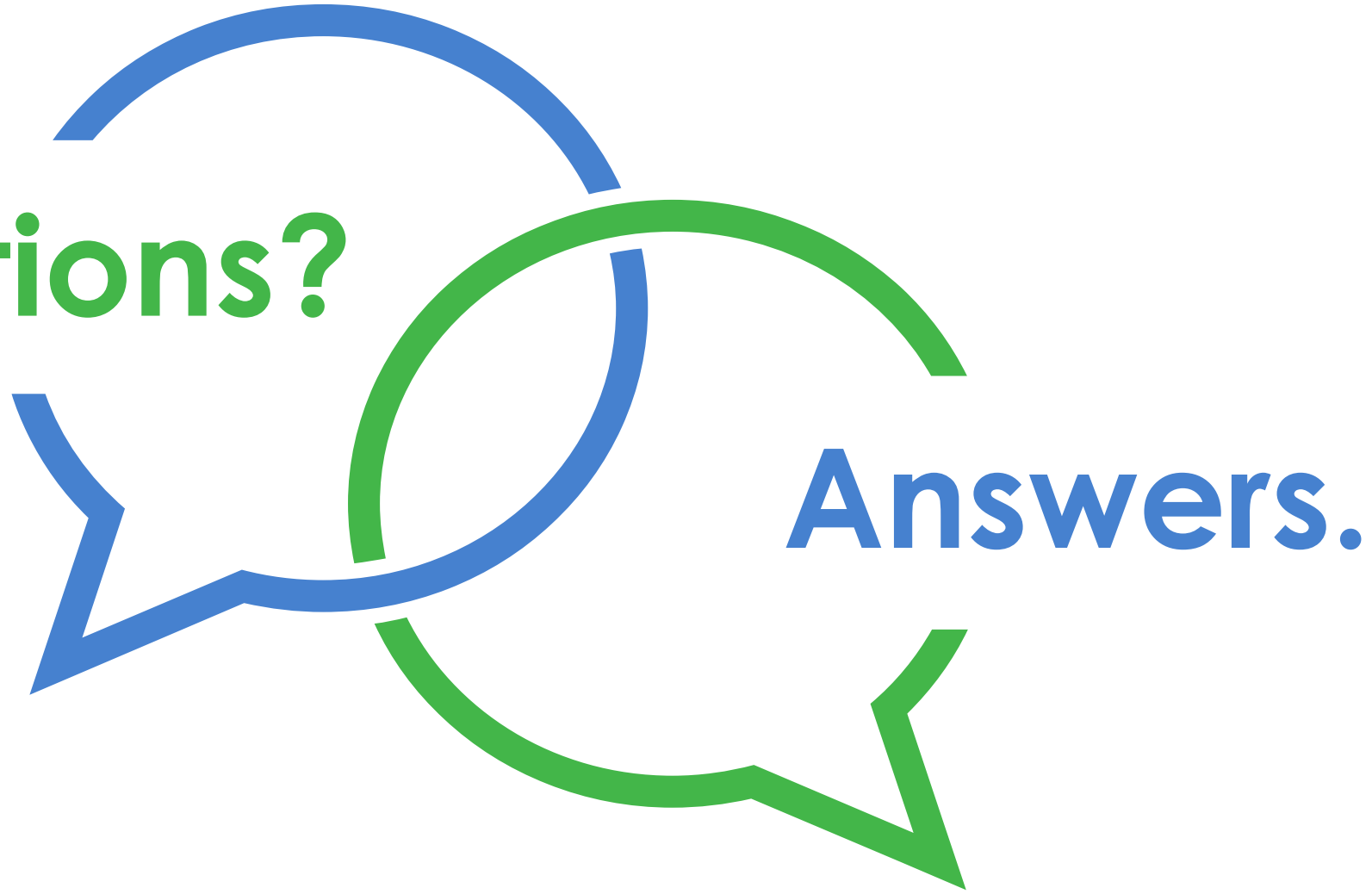
Questions?



Answers.