



Corporate Overview

December 2025

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, entering into new collaborations and achieving existing projected milestones, rapid technological changes in our markets, demand for our future products, legislative, regulatory and competitive developments and general economic conditions. Our Annual Report on Form 10-K, recent and forthcoming Quarterly Reports on Form 10-Q, recent Current Reports on Forms 8-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.

Financial Highlights

NASDAQ Global Select – Symbol ARWR

Stock
Price

\$56.25

(12/1/25)

Common Shares
Outstanding

~136m

(9/30/25)

Market
Capitalization

~\$7.65bn

Cash and
Investments¹

~\$920m

(9/30/25 does not include \$200m Sarepta milestone and \$200m Novartis upfront payment)

Analyst Coverage

B | RILEY

BERNSTEIN
SOCIETE GENERALE GROUP

CANTOR


CHARDAN

citi

**Goldman
Sachs**

 **H.C. WAINWRIGHT & CO.**

Jefferies

LEERINK
PARTNERS

Morgan Stanley

PIPER | SANDLER



**Capital
Markets**



TD Cowen
a division of TD Securities



ZACKS

1. Refer to 10Q and 10K filings for additional information about capital structure, including debt

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

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

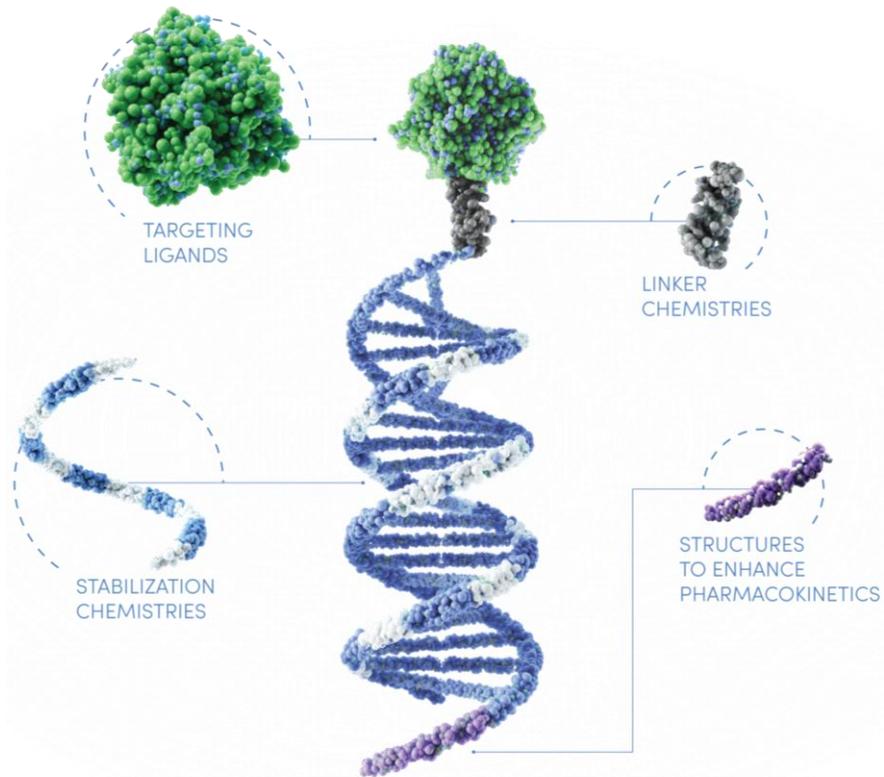


Robust pipeline and productive discovery engine provide opportunities for additional **capital inflows from business development**



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

Arrowhead's Targeted RNAi Molecule (TRiM™) Platform: The Broadest and Most Versatile in the Field



**Optimized Delivery of siRNA to
Multiple Cell Types**

TRiM™ also has rules and algorithms to optimize trigger sequence and modification patterns

Activity

Characterized by depth & duration of effect

- Ability to unlock previously undruggable targets

Specificity

To maximize activity and innate stability with the potential for reduced off-target effects

Versatility

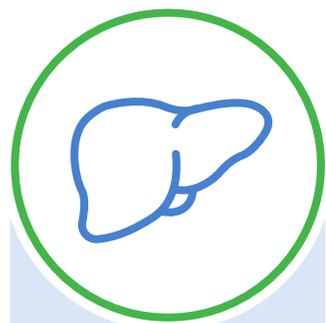
In structure and design offers multiple routes of administration and access to multiple tissues

- Facilitates rapid drug development and speed to patients

Simplicity

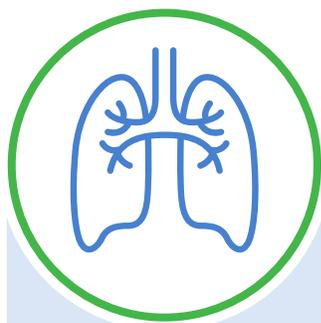
In design translates to relatively lower costs, and production at scale

TRiM™ Platform Enables Delivery to Seven Cell Types



Liver

Strong
clinical
validation



Lung

Deep lung
clinical
validation
(RAGE)



**Skeletal
Muscle**

Early
clinical
stage



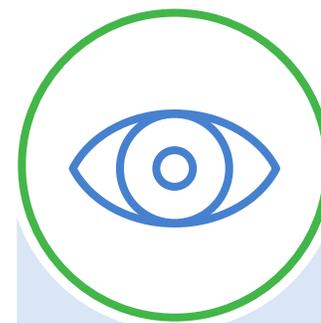
CNS

Early
clinical
stage



Adipose

Early
clinical
stage



Ocular

Preclinical
Stage



**Cardio-
myocyte**

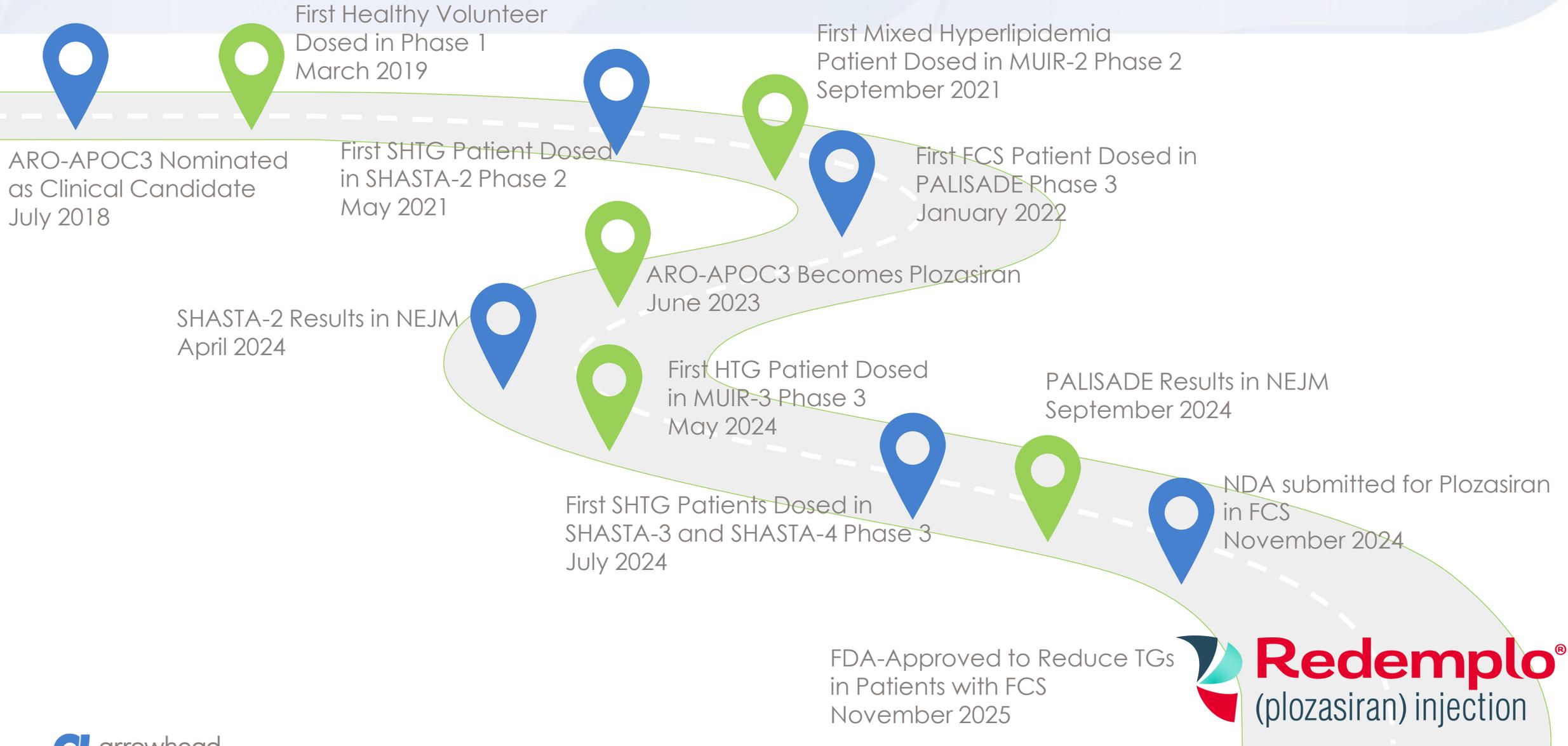
Preclinical
Stage

Arrowhead is Fulfilling the Promise of Bringing RNAi Throughout the Body

REDEMPLO[®] (plozasiran) Arrowhead's First FDA Approval



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



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 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 $\geq 10\%$ of patients treated with REDEMPLO and $>5\%$ more frequently than with placebo) are hyperglycemia, headache, nausea, and injection site reaction. (6.1)

REDEMPLO Positioned as Promising New Medicine for FCS

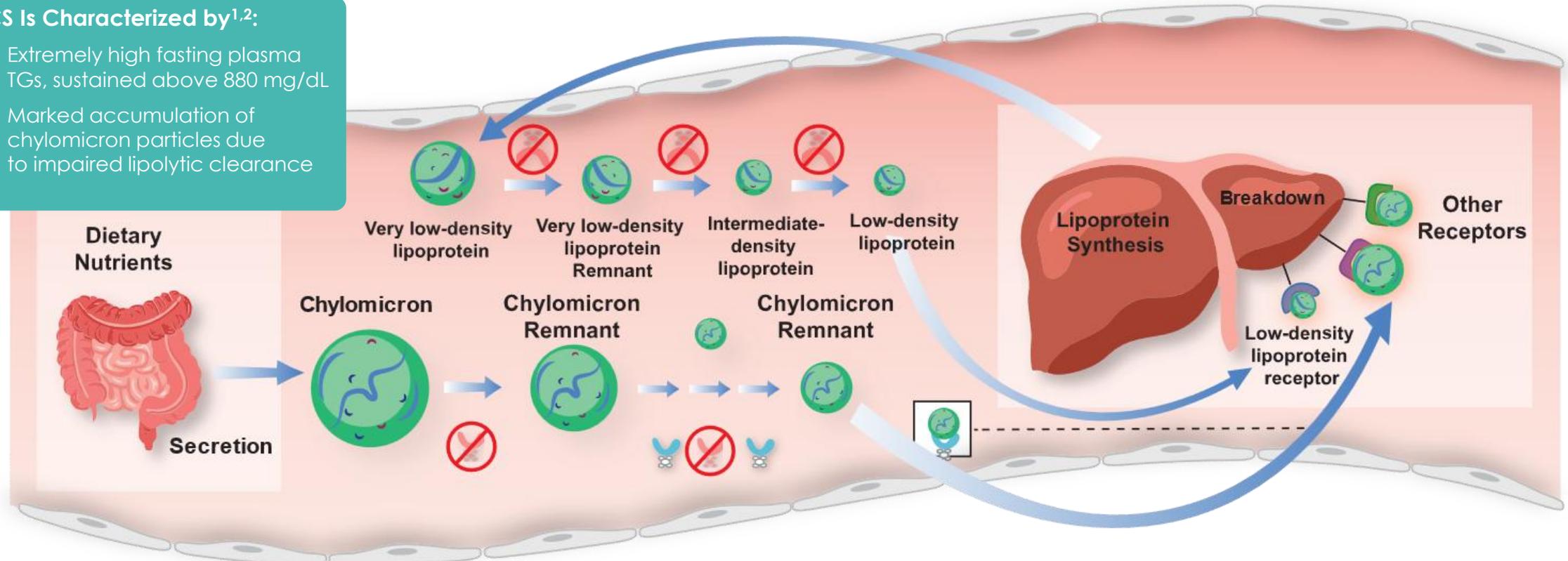
-  **Dramatic reductions** in triglycerides in patients with **genetically confirmed and clinically defined FCS**
-  **Reduced** numerical incidence of **acute pancreatitis**
-  **Convenient** dosing once **every three months** with at home **self-administration**
-  **Strong label** with no contraindications, warnings or precautions
-  Innovative, consistent, **One-REDEMPLO** price model across indications
-  Commercial team ready to **launch on Day 1**

Genetic/Clinical FCS Caused by Inability to Break Down Chylomicrons

Overview of TG Metabolism in Patients With FCS³

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



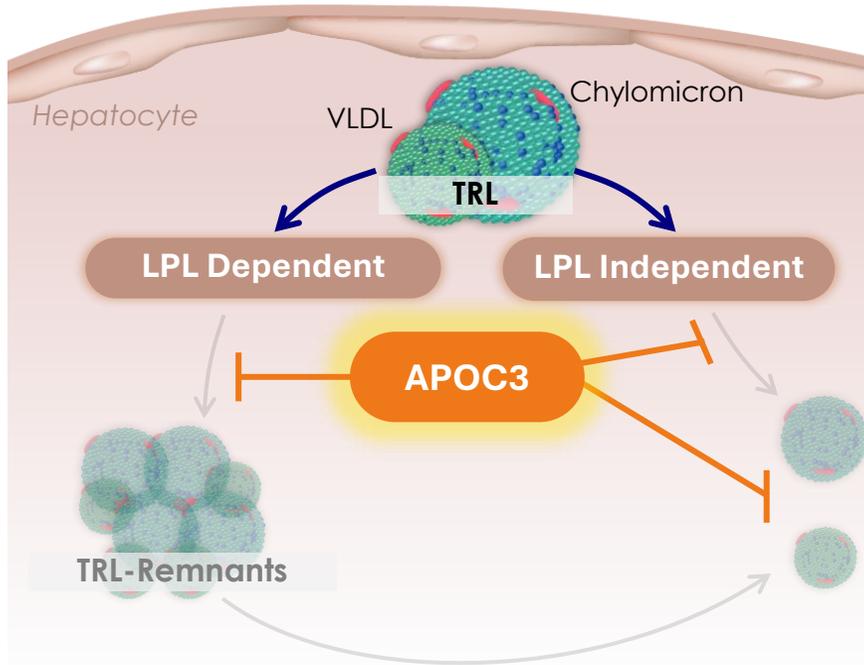
The buildup of chylomicrons causes significant risks² - the most severe being acute pancreatitis and its life-threatening sequelae

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.

REDEMPLO Mechanism of Action

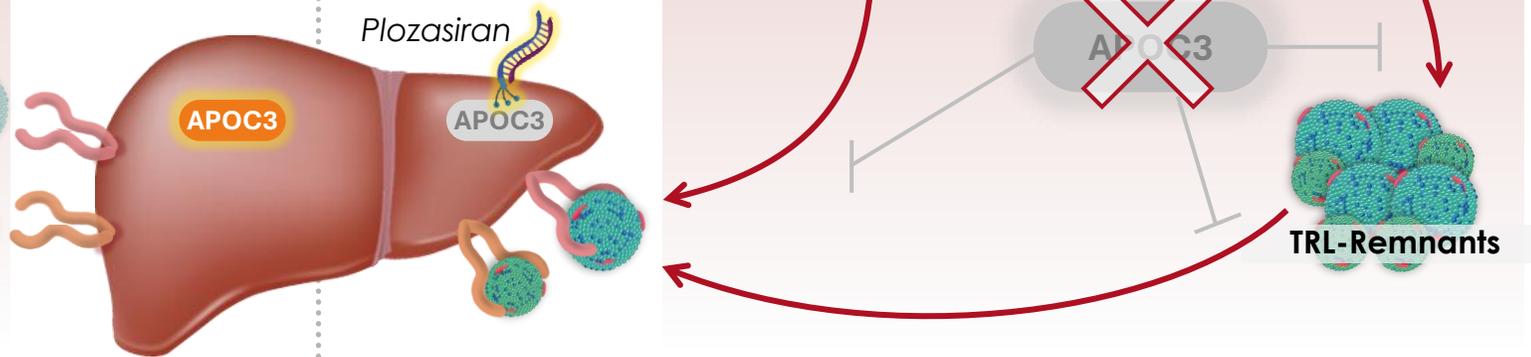
Targeting APOC3, a Key Regulator of TG and TRL Metabolism

CHYLOMICRONEMIA^{1,2}



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

REDEMPLO (plozasiran)²



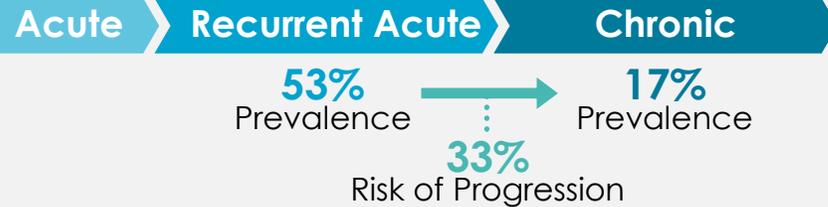
Silencing APOC3 enhances TG lipolysis and TRL-remnant clearance by hepatic receptors, reducing plasma TGs

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.

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 $\geq 50\%$ of Patients¹

The Pancreatitis Disease Continuum²

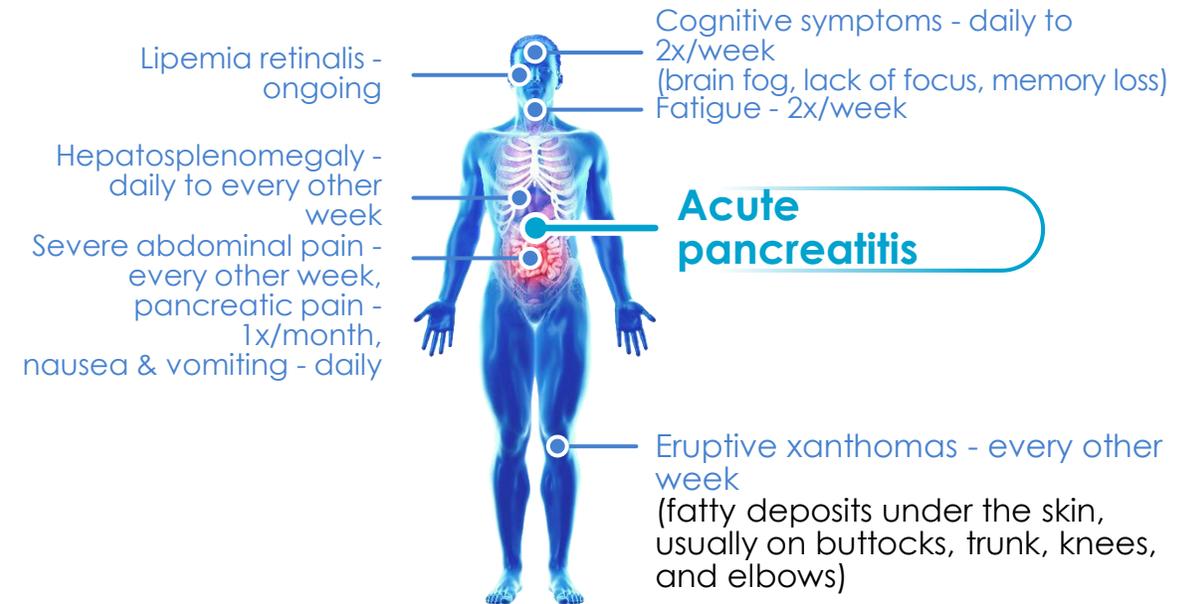


~5%–6% Overall mortality rate for TG-induced acute pancreatitis in patients with FCS³

30% The mortality rate in patients with FCS in cases of pancreatic necrosis following an infected pancreatic abscess or persistent multiple organ failure³

≥ 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 failure⁴

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.

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.**



Each AP Event Associated With Significant Healthcare Burden



Challenges around Diagnosis¹

- ~5 physicians typically seen before diagnosis²
- ~50% of patients are misdiagnosed²
- Distributed treatment teams³
 - 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.

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

REDEMPLO[®] (plozasiran) U.S. Commercial Launch Plan



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

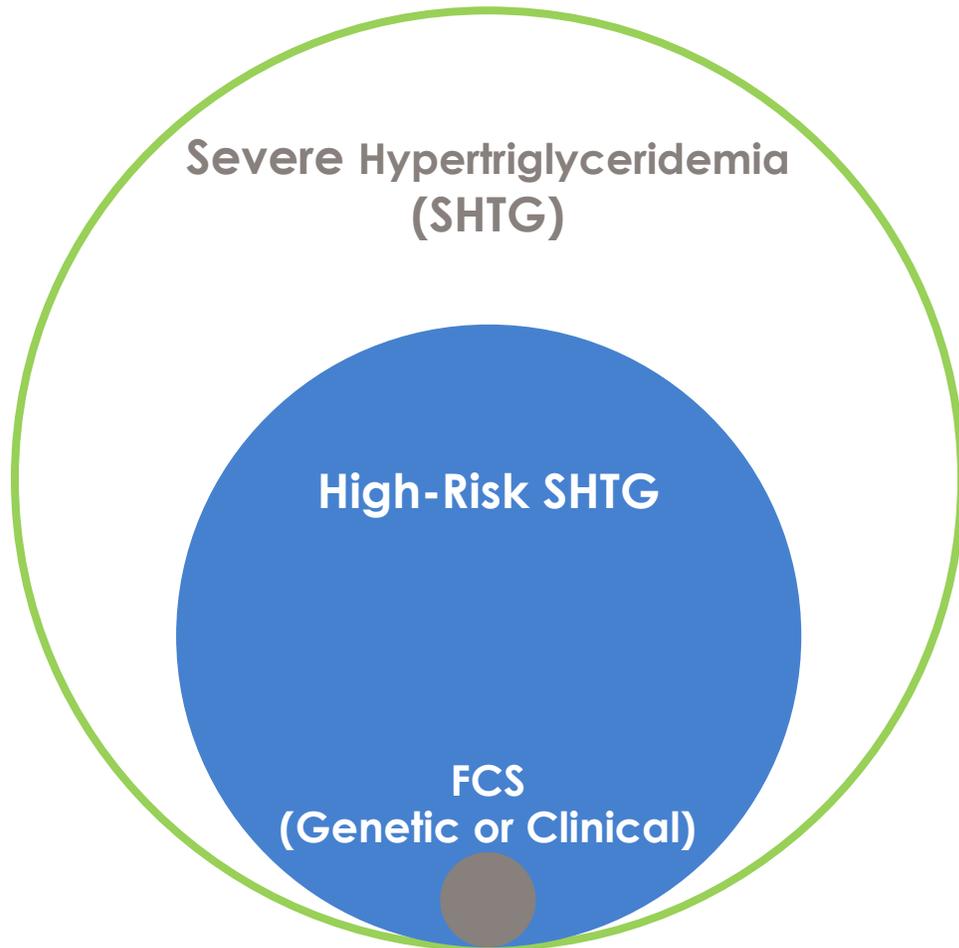


Figure Not to Scale

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

SHTG

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

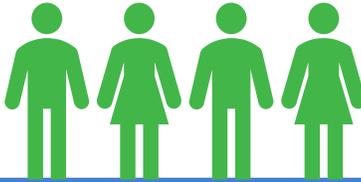
High-Risk SHTG

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

FCS (Genetic or Clinical)

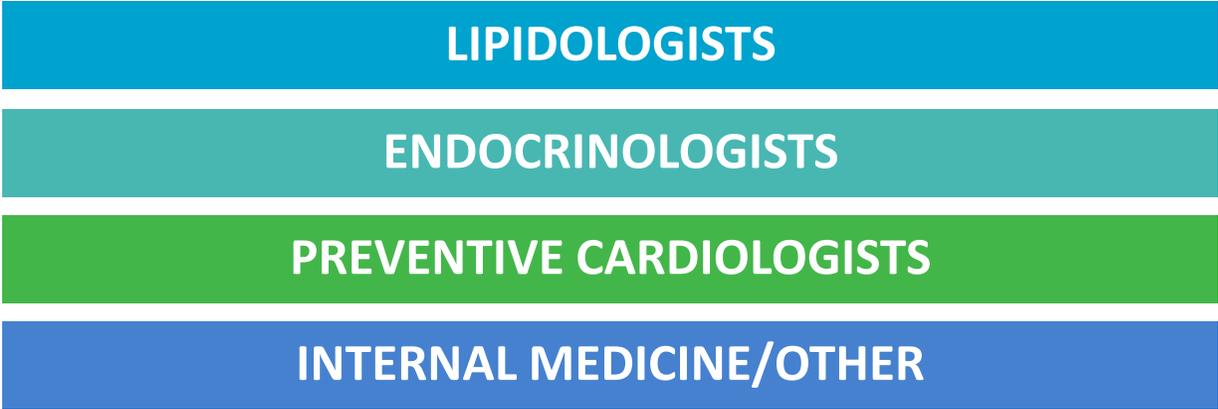
- Persistently Elevated TGs \geq 880 mg/dL
- Prevalent Prior History of AP
- ~ 6500 people
- Extremely High Risk of AP

FCS Prescriber Base by Specialty



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

**HCPs Identified
Across 4 Specialties Who Primarily Treat FCS Patients**



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

Redemplo[®]
(plozasiran) injection

For adult patients with Familial Chylomicronemia Syndrome (FCS),

**ON YOUR MARK,
GET SET,
LO**

**GO
LO**

Not actual patients.

80%

**Median Reduction
in Triglycerides^{1,*}**
from baseline



**Lowered Incidence of
Acute Pancreatitis^{1,*,†}**

**3
months**

**Convenient Dosing
Every 3 Months¹**
Self-administered

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.

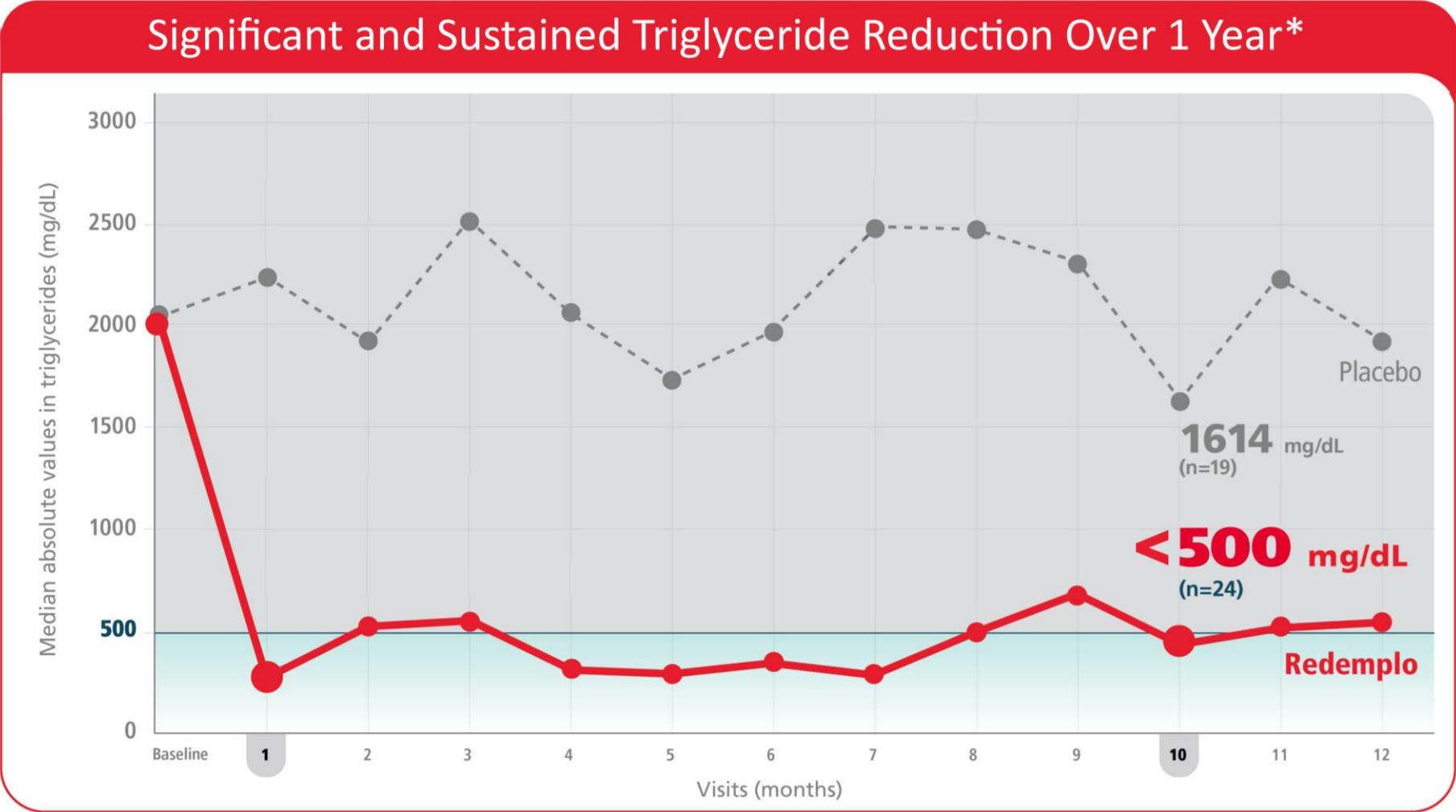
Professional Guidelines Recommend Reducing TG Levels to <500 mg/dL to Lower the Risk of Acute Pancreatitis

Guideline(s)	Recommendations
 <p>American Association of Clinical Endocrinologists (AACE)</p>  <p>American College of Endocrinology (ACE)</p>	<p>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/dL¹</p>
 <p>American College of Cardiology (ACC)*</p>  <p>American Heart Association (AHA)*</p>  <p>National Lipid Association (NLA)</p>	<p>To prevent acute pancreatitis, it is reasonable to reduce TGs whenever levels exceed 500 mg/dL²</p> <p>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 therapy³</p>

*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).

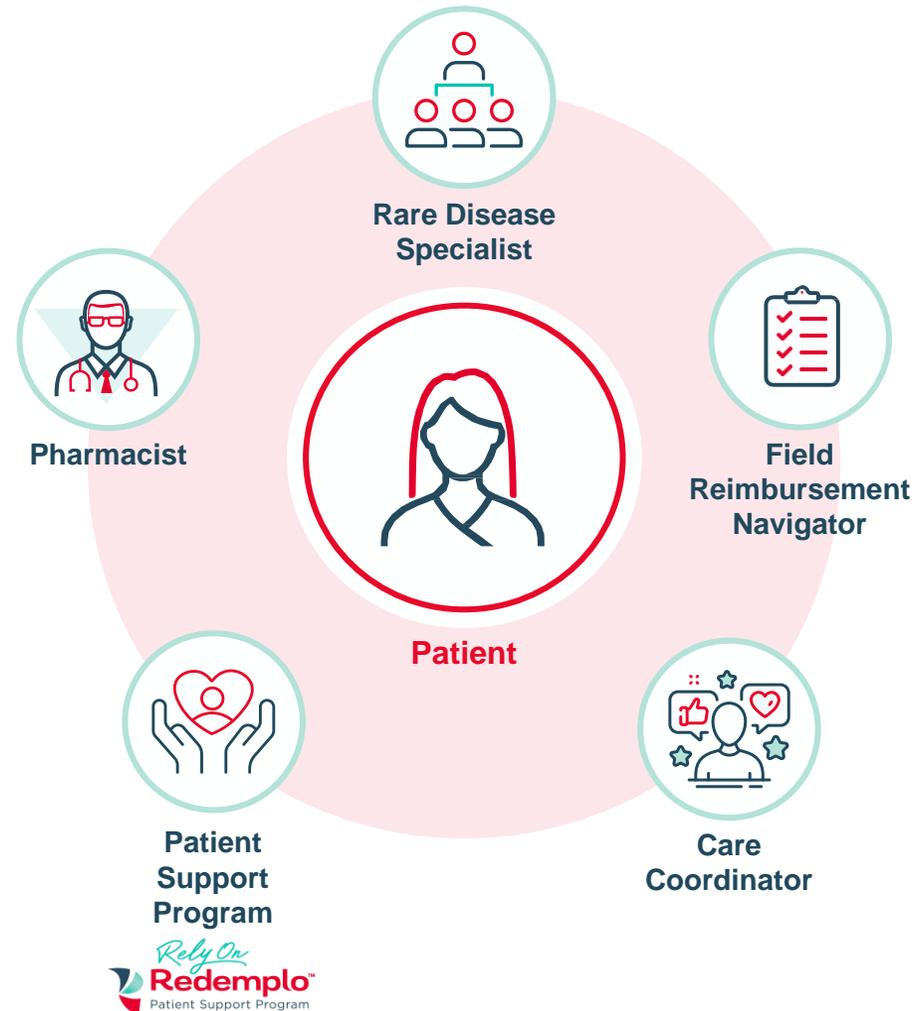
References: 1. Handelsman Y et al. *Endocr Pract.* 2020;26(10):1196-1224. 2. Grundy SM et al. *Circulation.* 2019;139(25):e1082-e1143.

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

Rely On Redemplo™

RELY ON REDEMPLO™ PATIENT SUPPORT PROGRAM

Rely On Redemplo™
Patient Support Program

Rely On Redemplo is a comprehensive patient support program that provides support services to your patients at each stage of the treatment journey with Redemplo.

- Enrollment**
- Access/Affordability**
- Support Services**
- Support Resources**

Help your patients start and stay on track with Rely On Redemplo

Support services	Support resources
<ul style="list-style-type: none">• Care coordination• Insurance coverage and prior authorization support• Financial assistance options for eligible patients, including a copay card program• Supplemental injection training• Pharmacist support	<ul style="list-style-type: none">• Starter Kit delivered to patient's home• Rely On Redemplo Copay Card Program for eligible commercially insured patients• Downloadable digital resources

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

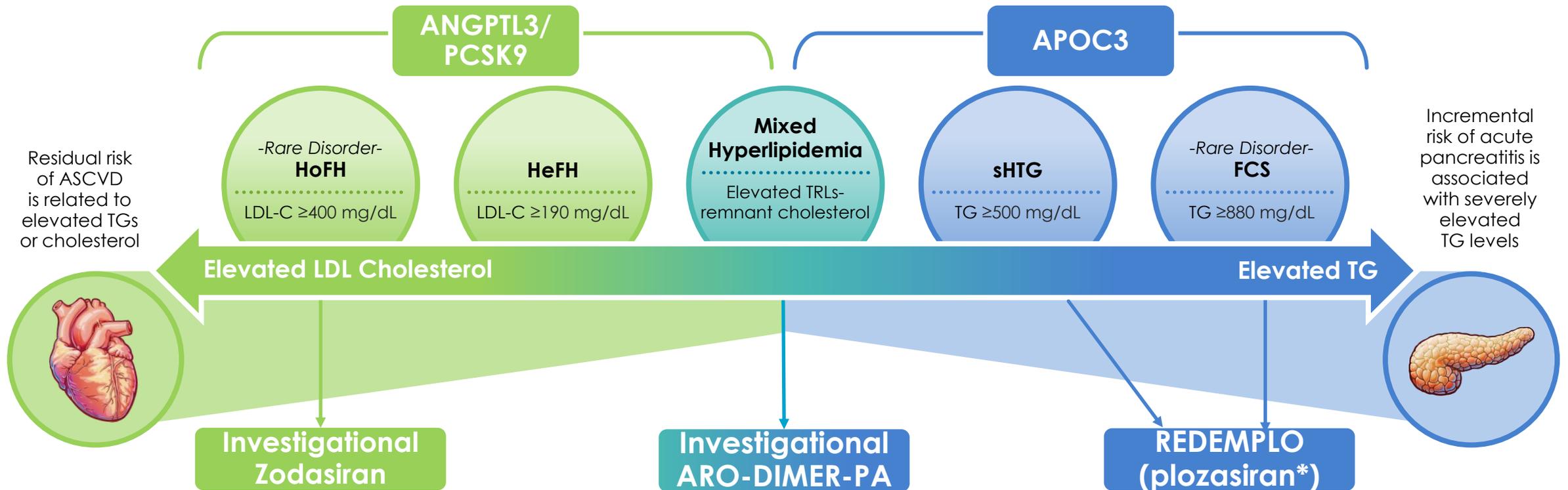


Expansion in Cardiometabolic



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

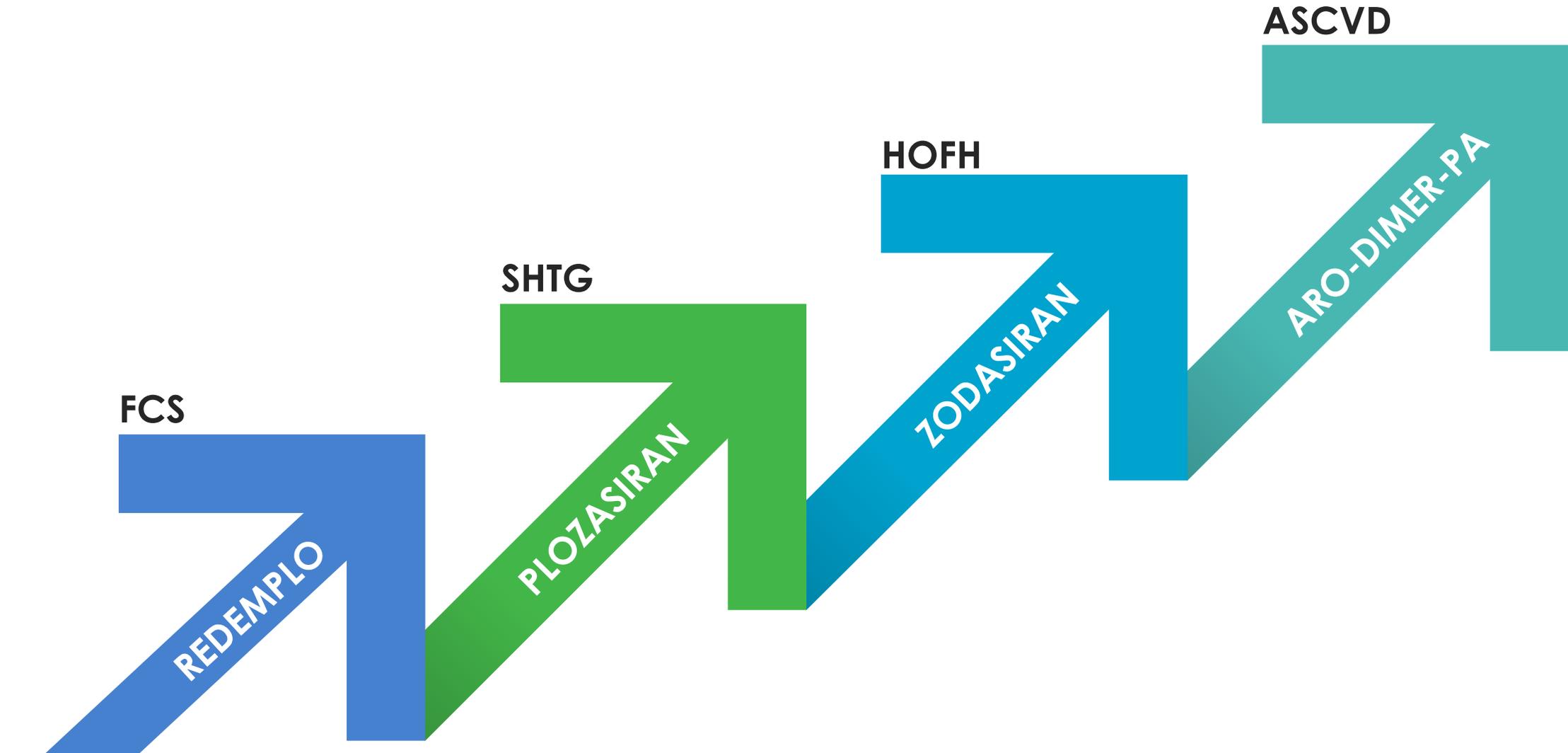


ASCVD, atherosclerotic cardiovascular disease; **FCS**, familial chylomicronemia syndrome; **HeFH**, heterozygous familial hypercholesterolemia; **HoFH**, homozygous familial hypercholesterolemia; **LDL-C**, low-density lipoprotein cholesterol; **sHTG**, severe hypertriglyceridemia; **TG**, triglyceride;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

And We Anticipate Additional Cardiometabolic Launches



Obesity Overview



Obesity Opportunities



Obesity increases risk of many diseases including diabetes, heart disease, stroke, and more and reducing fat mass may improve patient outcomes dramatically



This is not a market driven by aesthetics, rather by health outcomes and we believe payors agree



New therapies have made a big impact, but opportunities clearly exist for:

- Novel new mechanisms
- Therapies that better maintain lean mass and improve body composition
- Therapies that potentially reduce gastrointestinal adverse events



Genetics and biology support the Activin E ligand and ALK7 receptor pathway

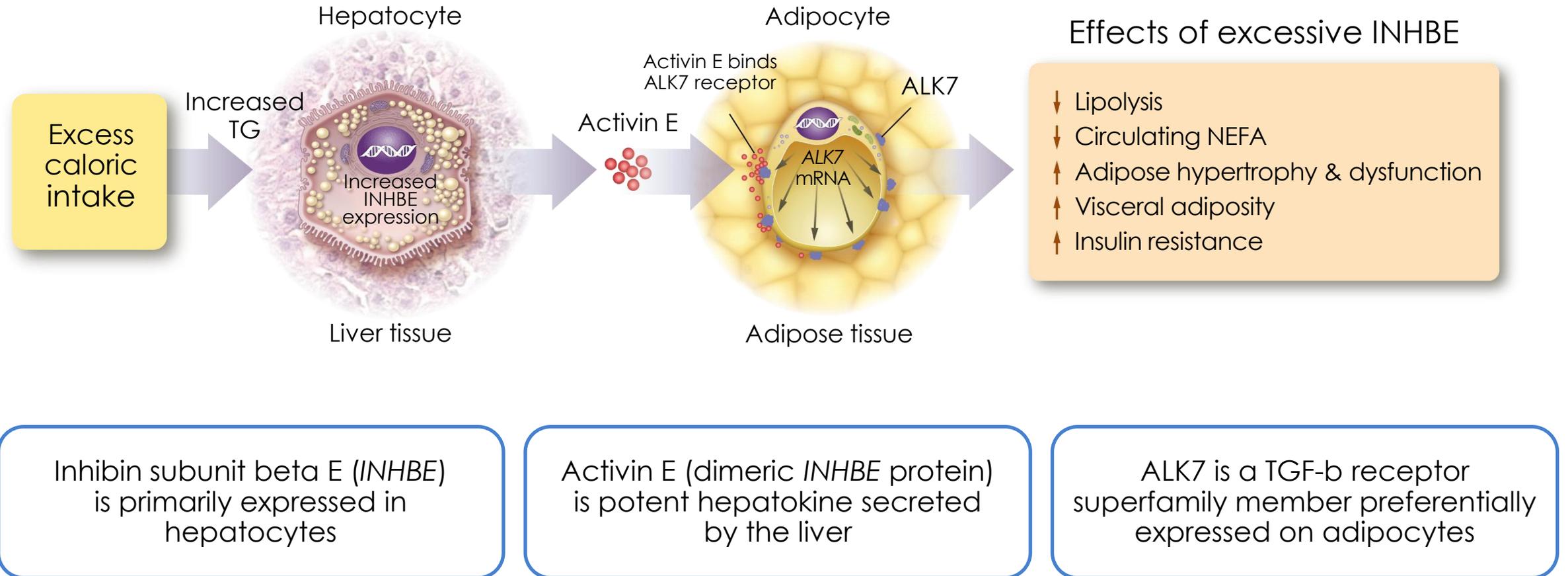


ARO-INHBE and ARO-ALK7 are highly active and show promising preclinical results



We believe we are first-in-class and potentially best-in-class with both targets

INHBE/ALK7 Pathway Regulates Energy Homeostasis in Adipose Tissue





CNS Overview

Neurodegenerative Diseases Are an Enormous Burden Uniquely Addressable by RNA Therapeutics



Over **50 million** neurodegeneration patients worldwide¹ and few disease modifying therapies



- Common feature is abnormal protein aggregation and neurotoxic gain of function: difficult mechanism to drug but RNAi approach knocks out disease-causing protein
- Recent progress in genetics and biomarker development are enabling clinical development in a broad range of neurodegenerative diseases, increasing probability of success

1. *Lancet Neurology* 2019, 18:459

TDP-43 Proteinopathies

- Amyotrophic Lateral Sclerosis (ALS)
- Fronto-temporal dementia (FTD)

Tauopathies

- Alzheimer's disease (AD)
- Fronto-temporal dementia (FTD)
- Progressive Supranuclear Palsy
- Corticobasal Degeneration

Amyloidoses

- Alzheimer's disease (AD)
- Prion diseases

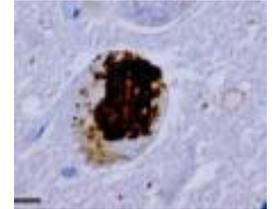
Synucleinopathies

- Parkinson's disease (PD)
- Lewy body dementia
- Multiple system atrophy

Expansion Repeat Disorders

- Huntington's disease (HD)
- Spinocerebellar ataxias (SCA)

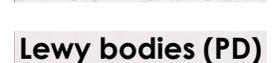
SOD1 (ALS)



Tau tangles



Amyloid plaques



Lewy bodies (PD)



ATXN2 (SCA2)



Thank You!

