Corporate Overview

April 2025

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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, 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	Common Shares Outstanding	Market Capitalization	Cash and Investments[1]
$12.34	~126m	~$1.55bn	~$1.4bn
(4/14/25)	(12/31/24)		(proforma 12/31/24 including Sarepta payments received)

Analyst Coverage

B. RILEY · BERNSTEIN SOCIETE GENERALE GROUP · CANTOR · CHARDAN · citi · Goldman Sachs · H.C. WAINWRIGHT & CO. · Jefferies · LEERINK PARTNERS · Morgan Stanley · PIPER SANDLER · RBC Capital Markets · TD Cowen a division of TD Securities · UBS · ZACKS

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

Breaking the Mold of Medicine with RNA Interference

Arrowhead Pharmaceuticals is an **RNAi therapeutics platform company** with a **broad pipeline** of **wholly owned and partnered** product candidates on pace for its **first commercial launch in 2025**.

Commercial Launch Planned in 2025

- **Plozasiran** for familial chylomicronemia syndrome US FDA **PDUFA date 11/18/25**
- Additional regulatory submissions planned for 2025
- Commercial leadership, sales and marketing, market access, and medical science liaisons from medical affairs are in place

Broad Pipeline

- **16 clinical stage programs** (8 wholly-owned; 8 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 tissue types

Financial Resources

- **Strong balance sheet** with **funding into 2028** to push candidates to commercialization
- **Additional non-dilutive capital expected** from Sarepta, Amgen, Takeda, GSK, and Royalty Pharma as milestones are achieved
- Potential for **additional** product and/or platform **deals**

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Review of Key Terms for Transformative 2025 Sarepta Deal

Financial Terms

$500 million	upfront payment
$325 million	in stock at $27.25/share
$250 million	paid in $50m annual installments over 5 years
$300 million	in near-term payments, associated with ARO-DM1 enrollment (potential in 2025)
$110-410m	Development milestones per program
$500-700m	Sales milestones per program
>$11bn	Total potential value

Tiered royalties to **low double-digits**

Programs

Clinical

- ARO-DUX4 – FSHD
- ARO-DM1 – DM1
- ARO-MMP7 – IPF
- ARO-ATXN2 – SCA2

Preclinical

- ARO-HTT – Huntingtons
- ARO-ATXN1 – SCA1
- ARO-ATXN3 – SCA3
- ARO-ATXN2 – SCA2

Discovery

Up to 6 new CNS or muscle targets. Sarepta responsible for clinical development and commercialization

Drug Manufacturing

Arrowhead manufactures clinical drug supply for all programs, and commercial drug product for 4 current clinical programs

Deal Closed February 2025
Sets ARWR on Potential Long-term Path to Profitability

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Arrowhead's Growth Drivers in 2025 and Beyond

Arrowhead's first **commercial launch of plozasiran** in familial chylomicronemia planned for Q4 2025 (PDUFA 11/18/25)

Phase 3 studies of plozasiran in **severe hypertriglyceridemia (potential $2-3 billion opportunity)** on pace to enable second launch in 2027

Commercial focus on cardiometabolic pipeline

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**

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Primary Focus Over the Next 2 – 3 Years

Plozasiran
Zodasiran

Obesity

CNS

Value Support

- ARO-CFB and ARO-C3
- ARO-PNPLA3
- ARO-RAGE and new pulmonary targets
- New discovery programs
- Partnered programs

  HBV HSD Olpasiran DUX4 DM1 Fazirsiran ATXN2 HTT MMP7

Supporting Areas Provide Redundancy and Additional Runway Potential via Partnerships

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Arrowhead Technology and Clinical Pipeline

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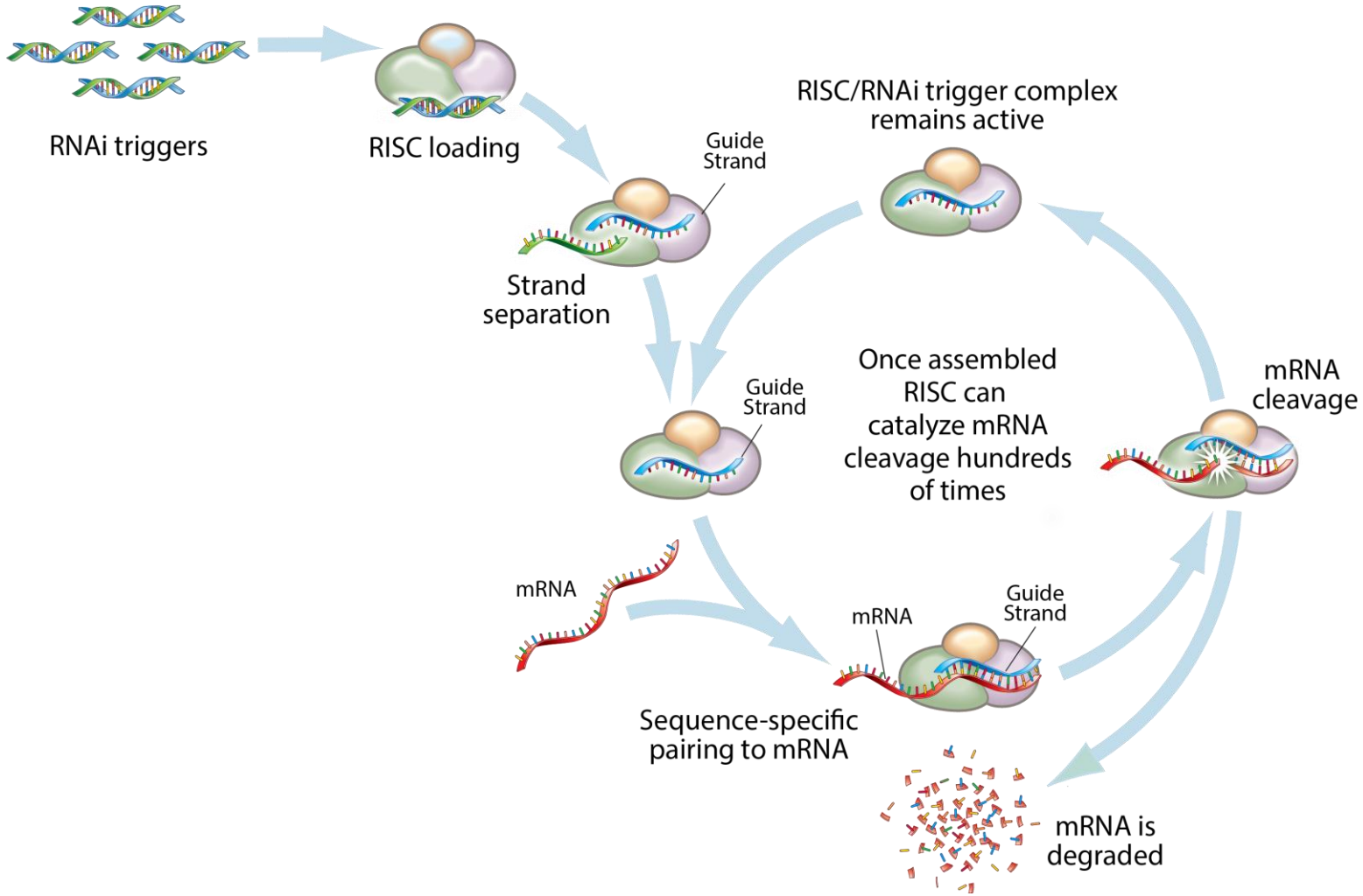
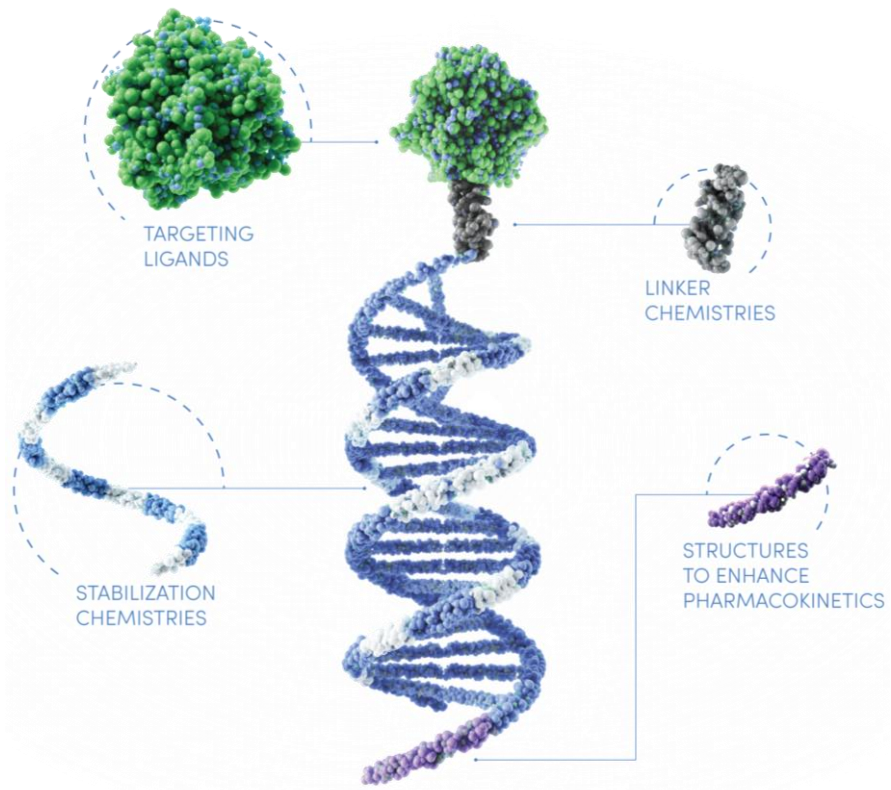
RNA Interference (RNAi) Pathway



Advantages of RNAi

- Nobel Prize winning discovery
- Natural, efficient, and catalytic process
- Selective silencing of disease associated genes
- Potential to address previously "undruggable" targets
- High specificity
- Rapid path from idea to clinical candidate
- Positive record of clinical safety and tolerability

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

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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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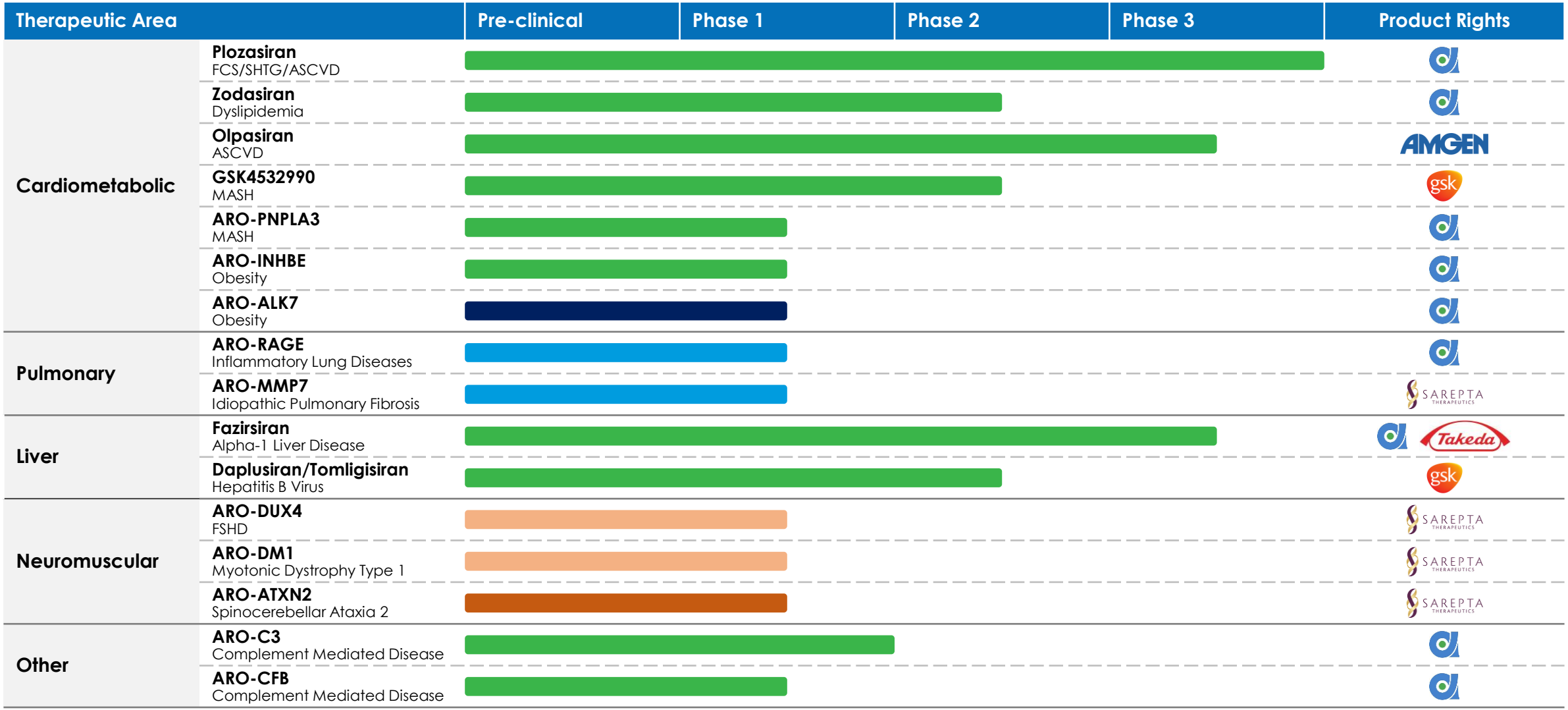
Robust Clinical Pipeline & Near-term Commercial Opportunities



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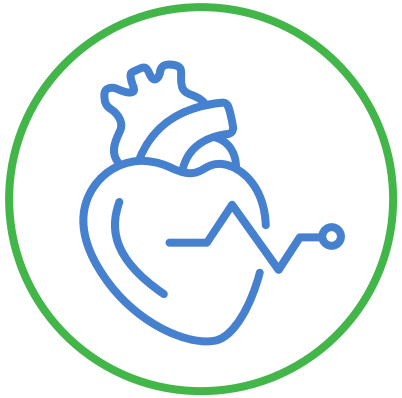

Plozasiran Overview

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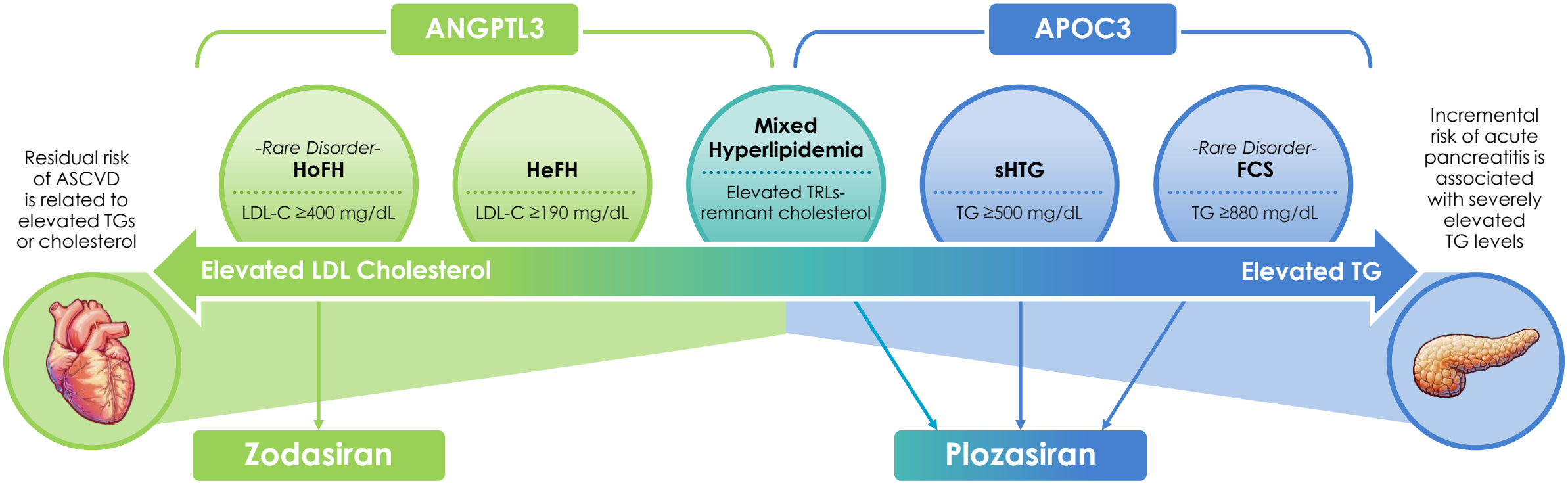
Plozasiran Being Developed Across the Triglyceride Spectrum Zodasiran Development Focused on HoFH

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.

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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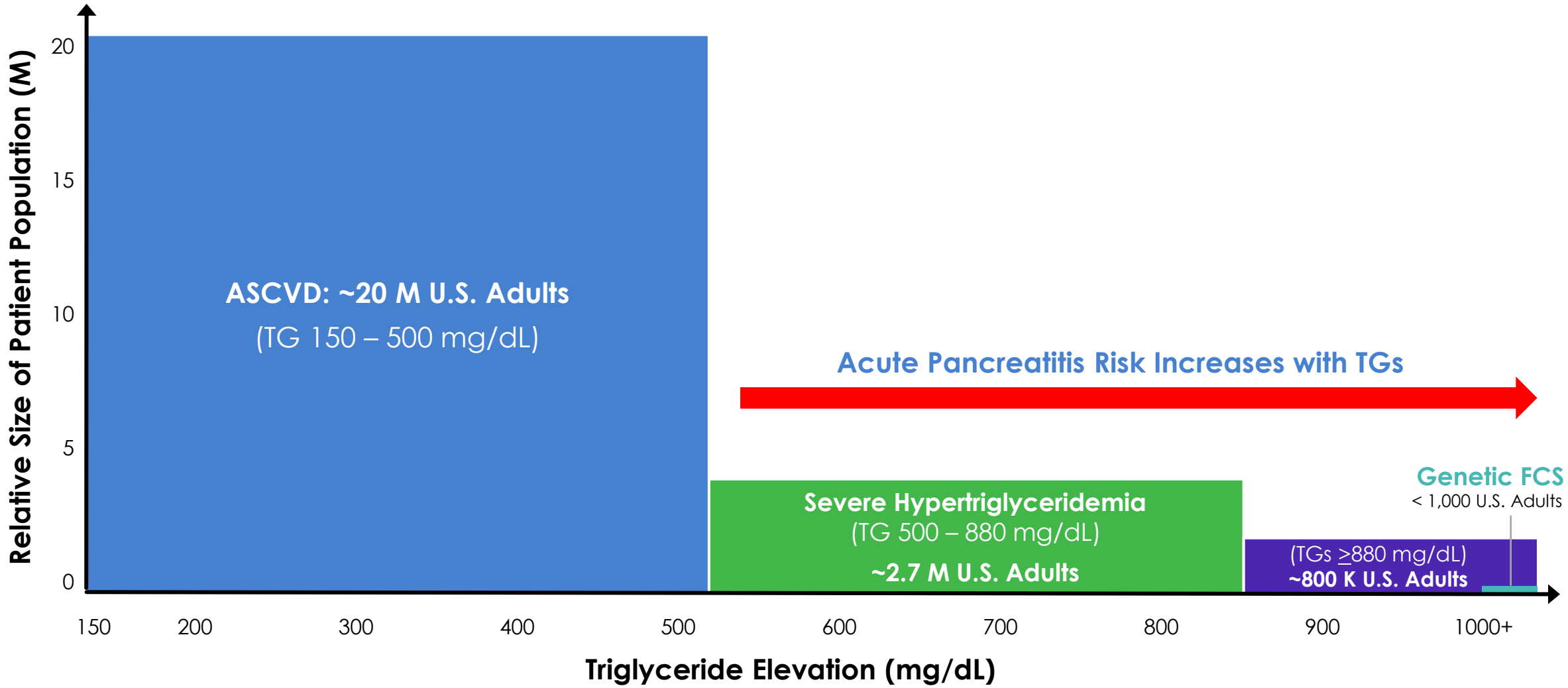
Large Unmet Need in Multiple Elevated Triglyceride Populations



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Comprehensive SUMMIT Clinical Program Across Populations

SUMMIT PROGRAM

Familial Chylomicronemia Syndrome (FCS)	PALISADE	In adults with **FCS and TG ≥880 mg/dL (N=75)**, the primary endpoint was to evaluate change in TG levels at Month 10*	Study Completed	Phase 3
Severe Hypertriglyceridemia (SHTG)	SHASTA-2	In adults with **TG ≥500 mg/dL (N=226)**, the primary endpoint was to evaluate change in TG levels at Month 6[1]*	Study Completed	Phase 2
	SHASTA-3	In adults with **TG ≥500 mg/dL (N=405)**, the primary endpoint is to evaluate change in TG levels at Month 12*[†]	Currently Enrolling	Phase 3
	SHASTA-4	In adults with **TG ≥500 mg/dL (N=300)**, the primary endpoint is to evaluate change in TG levels at Month 12*	Currently Enrolling	Phase 3
	SHASTA-5	In adults with **TG >880 mg/dL and a history of >2 acute pancreatitis events (N=140)**, the primary endpoint will be to evaluate the time to first occurrence of positively adjudicated acute pancreatitis event*	Coming Soon	Phase 3
Mixed Hyperlipidemia	MUIR	In adults with **TG 150-499 mg/dL and non-HDL-C ≥100 mg/dL or LDL-C ≥70 mg/dL (N=353)**, the primary endpoint was to evaluate change in TG levels at Month 6[2]*	Study Completed	Phase 2
	MUIR-3	In adults with **TG 150-499 mg/dL (N=1328)**, the primary endpoint is to evaluate change in TG levels at Month 12	Currently Enrolling	Phase 3
	CAPITAN	In adults with e**levated levels of TRLs and residual risk of primary or secondary ASCVD events**, the primary endpoint will be to evaluate the time to first occurrence of any component of clinical composite endpoint of CV death, nonfatal MI, nonfatal stroke, coronary revascularization, and major adverse limb events	Coming Soon	Phase 3

*Open-label extension period or study is available for patients who participate in the clinical trial program. †A subset of patients enrolled in SHASTA-3 will undergo serial MRI-PDFF in a substudy to assess change in LFC.

ASCVD, atherosclerotic cardiovascular disease; CV, cardiovascular; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LFC, liver fat content; MI, myocardial infarction; MRI-PDFF, magnetic resonance imaging proton density fat fraction; TG, triglyceride; TRL, triglyceride-rich lipoprotein.

1. Gaudet D, et al. *JAMA Cardiol*. 2024:e240959. doi:10.1001/jamacardio.2024.0959 2. Ballantyne CM, et al. *N Engl J Med*. 2024. doi:10.1056/NEJMoa2404143

For more information or to refer a patient, please reach out to cardiomet@arrowheadpharma.com.
For additional information, please visit the Arrowhead Pharmaceuticals website. https://arrowheadpharma.com/science-and-innovation/clinical-trials/

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2024 Publications Demonstrate Competitive Profile

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Plozasiran for Managing Persistent Chylomicronemia and Pancreatitis Risk

Gerald F. Watts, D.Sc., M.D., Ph.D., Robert S. Rosenson, M.D., Robert A. Hegele, M.D., Ira J. Goldberg, M.D., Antonio Gallo, M.D., Ph.D., Ann Mertens, M.D., Ph.D., Alexis Baass, M.D., Rong Zhou, Ph.D., Ma'an Muhsin, M.D., Jennifer Hellawell, M.D., Nicholas J. Leeper, M.D., and Daniel Gaudet, M.D., Ph.D., for the PALISADE Study Group*

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Plozasiran, an RNA Interference Agent Targeting APOC3, for Mixed Hyperlipidemia

Christie M. Ballantyne, M.D., Szilard Vasas, M.D., Masoud Azizad, M.D., Peter Clifton, M.B., B.S., Ph.D., Robert S. Rosenson, M.D., Ting Chang, Ph.D., Stacey Melquist, Ph.D., Rong Zhou, Ph.D., Ma'an Mushin, M.D., Nicholas J. Leeper, M.D., Jennifer Hellawell, M.D., and Daniel Gaudet, M.D., Ph.D.

JAMA Cardiology

Research

JAMA Cardiology | Original Investigation

Plozasiran (ARO-APOC3) for Severe Hypertriglyceridemia
The SHASTA-2 Randomized Clinical Trial

Daniel Gaudet, MD, PhD; Denes Pall, MD, PhD; Gerald F. Watts, DSc, PhD, MD; Stephen J. Nicholls, MBBS, PhD; Robert S. Rosenson, MD; Karen Modesto, MD; Javier San Martin, MD; Jennifer Hellawell, MD; Christie M. Ballantyne, MD

NEJM Evidence

ORIGINAL ARTICLE

RNA Interference Therapy Targeting Apolipoprotein C-III in Hypertriglyceridemia

Daniel Gaudet, M.D., Ph.D.,[1] Peter Clifton, M.B.B.S., Ph.D.,[2] David Sullivan, M.B.B.S.,[3] John Baker, M.D.,[4] Christian Schwabe, M.D.,[5] Susan Thackwray, M.B., B.Ch.,[6] Russell Scott, M.B.Ch.B., Ph.D.,[7] James Hamilton, M.D.,[8] Bruce Given, M.D.,[8] Stacey Melquist, Ph.D.,[8] Rong Zhou, Ph.D.,[8] Ting Chang, Ph.D.,[8] Javier San Martin, M.D.,[8] Gerald F. Watts, D.Sc., Ph.D., D.M.,[9,10] Ira J. Goldberg, M.D.,[11] Joshua W. Knowles, M.D., Ph.D.,[12] Robert A. Hegele, M.D.,[13] and Christie M. Ballantyne, M.D.[14]

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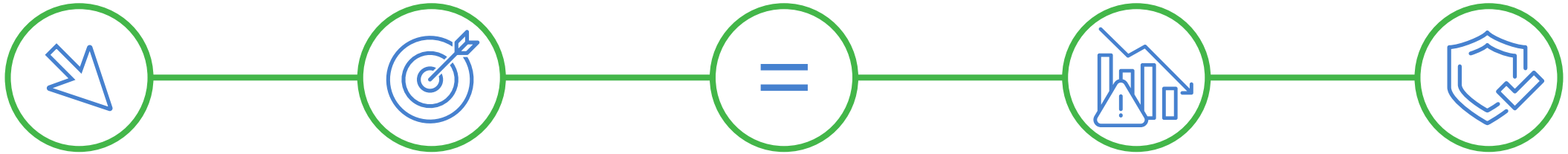
The Value Proposition for Plozasiran in FCS is Now Clear



TG Reduction

- **Deep:** reduction of 80% as early as month one[1]
- **Durable:** maintained throughout the treatment period

Goal Attainment

- Over 2/3 of plozasiran-treated patients reached levels **less than 880 mg/dL** and nearly 1/2 **less than 500 mg/dL**[2]

Consistent Effect

- Consistent TG reductions in patients with **genetically confirmed and clinically diagnosed FCS**

Risk Reduction

- **Statistically significant** reduction in risk of developing acute pancreatitis[3]

Attractive Profile

- **Favorable safety** and tolerability to date
- **Convenient dosing** every three-months

Delivering on What is Important to Patients, Physicians, and Payers

1. Compared to baseline. 2. At month 10. 3. In a pre-planned pooled analysis of active cohorts

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Our Commercialization Efforts Are on Track

	Key Launch Readiness Activities	
Medical	Medical Education and Communication strategy developed and field medical deployed and conducting scientific exchange	✓
Commercial Strategy	Marketing and Market Access strategy developed, leadership in place and executing on key go-to-market activities	✓
Patient Services	Patient hub provider selected and service offerings in development	✓
Regulatory	NDA for plozasiran for familial chylomicronemia syndrome accepted (11/18/25 PDUFA date) - Additional 2025 regulatory submissions planned	✓
Commercial Field Force	Field leadership in place, go-to-market model decided, and field force hiring plans established to enable Q4 2025 launch	○
Launch	Patient, provider, and payer Day 1 readiness	○

Obesity Overview

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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

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Two Initial Shots on Goal

ARO-INHBE

ARO-ALK7

- Substantial weight loss in animal models
- High quality weight loss
  - Fat loss, lean muscle mass retention
- No decrease in food intake
- Durable effects
  - Expected quarterly SC dosing: ARO-INHBE
  - Potentially less frequent: ARO-ALK7
- Genetic validation
- In combination with tirzepatide:
  - Sub-therapeutic dose of Tirzepatide
  - High quality weight loss
- **ARO-INHBE in patients now**
- **ARO-ALK7 in patients in Q2 2025**

Potential for Additional Obesity Targets in Adipose and CNS

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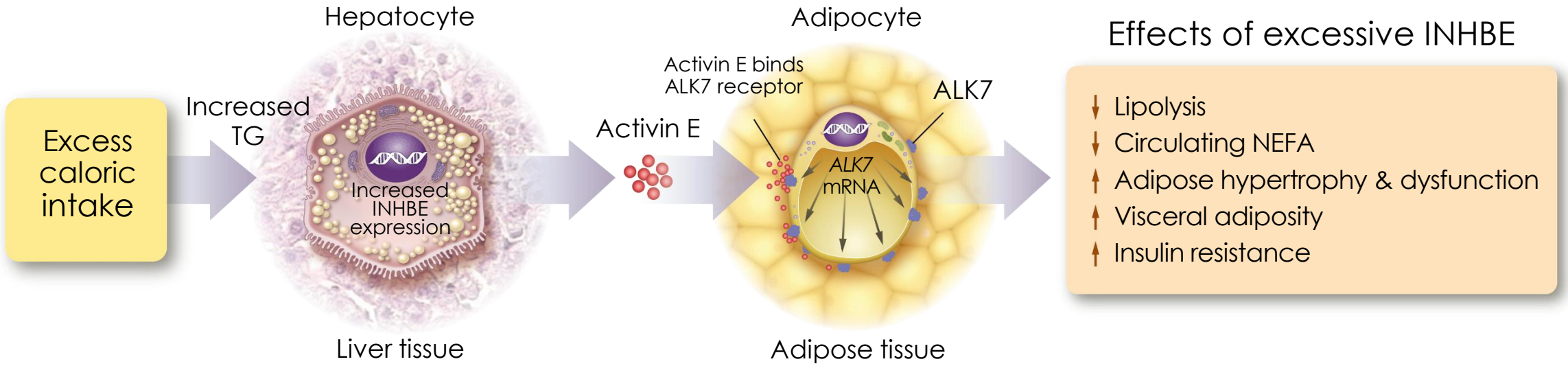
INHBE/ALK7 Pathway Regulates Energy Homeostasis in Adipose Tissue



Inhibin subunit beta E (*INHBE*) is primarily expressed in hepatocytes

Activin E (dimeric *INHBE* protein) is potent hepatokine secreted by the liver

ALK7 is a TGF-b receptor superfamily member preferentially expressed on adipocytes

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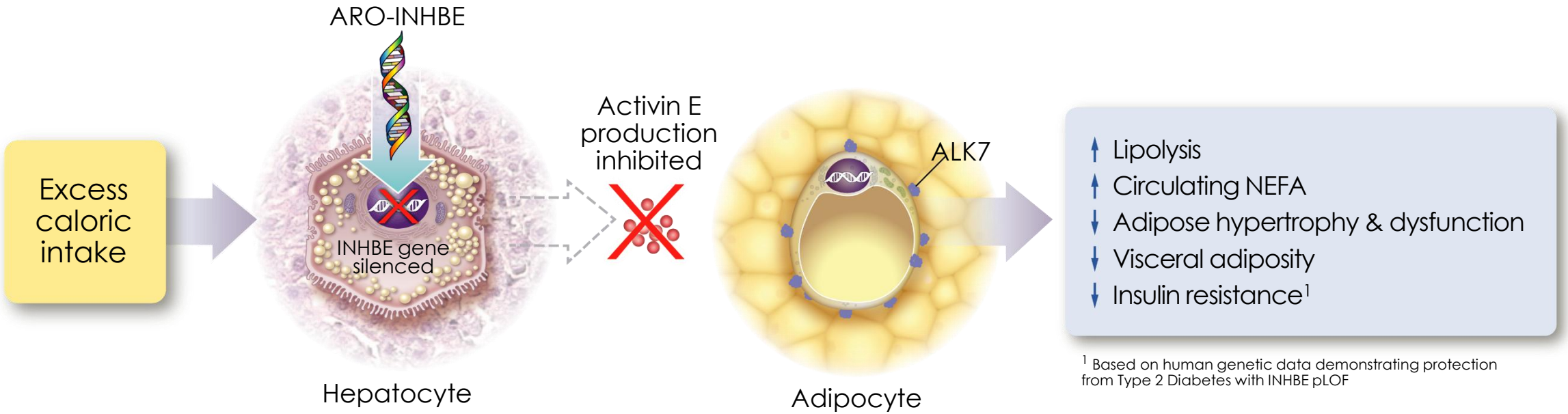
Silencing Hepatic *INHBE* May Inhibit Maladaptive Activin E – ALK7 Signaling and Improve Adipose Dysfunction in Obesity



[1] Based on human genetic data demonstrating protection from Type 2 Diabetes with INHBE pLOF

*Based on human genetic data demonstrating protection from Type 2 Diabetes with *INHBE* pLOF.

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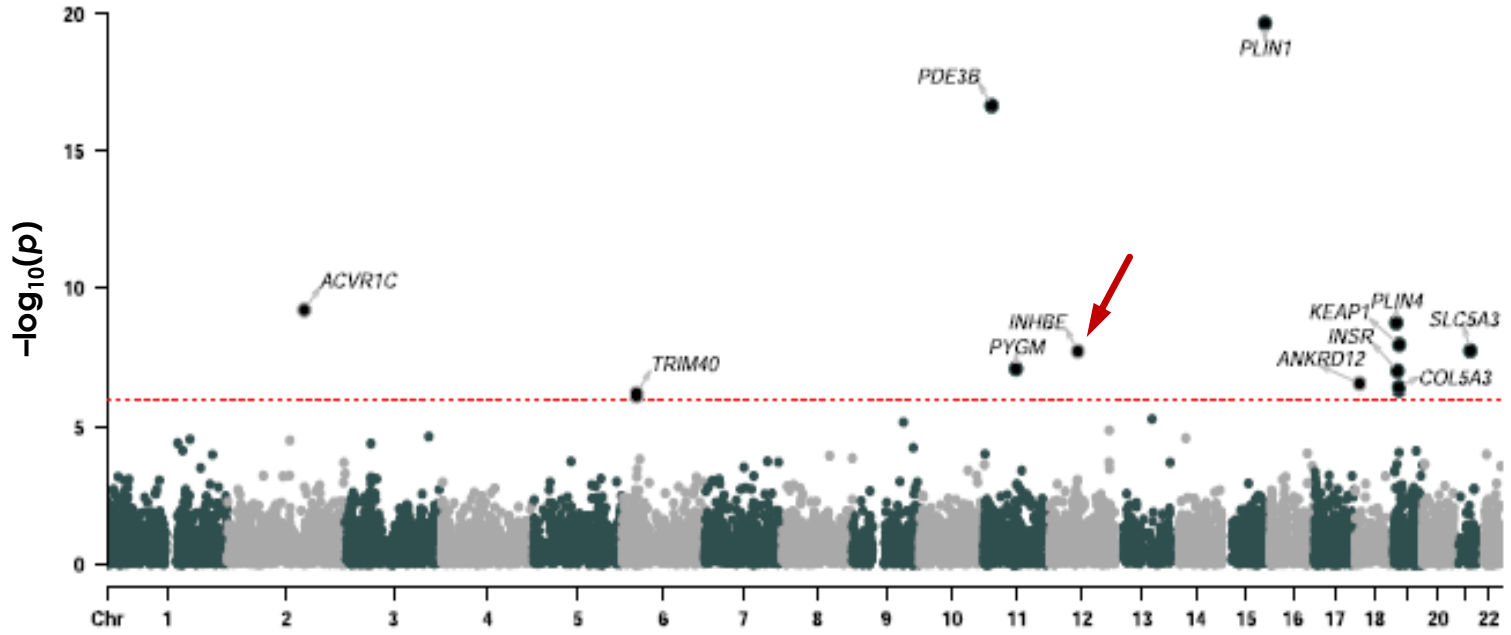
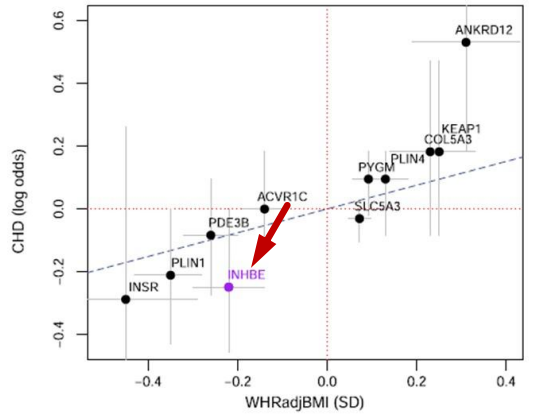
pLOF Variants of INHBE Are Associated with Reduced Abdominal Fat and Lower Risk of Coronary Heart Disease and Type 2 Diabetes

Human Genome-wide Association Study

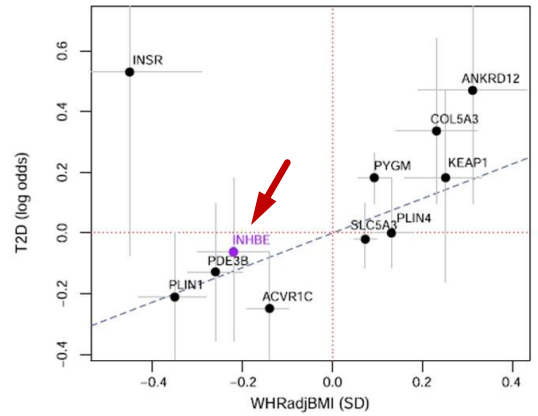
Waist-to-Hip Ratio Adjusted for BMI



CHD Risk



T2D Risk



Nature Communications. (2022)13:4319. https://doi.org/10.1038/s41467-022-31757-8. www.nature.com/naturecommunications.

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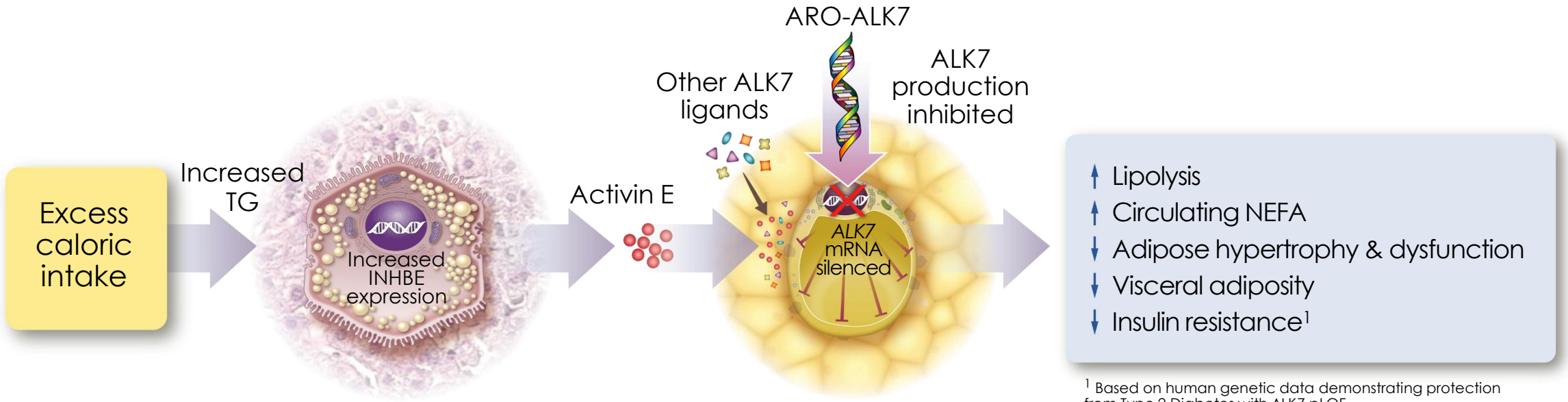
Activin Receptor-like Kinase 7 (ALK7, *ACVR1C*) is a Genetically Validated Adipose Target



[1] Based on human genetic data demonstrating protection from Type 2 Diabetes with ALK7 pLOF

- ALK7 is a TGF-β receptor superfamily member preferentially expressed on adipocytes
- Ligands may include: GDF3, GDF11, ActB, ActE, ActAB, ActC, Nodal
- ALK7 signaling suppresses lipolysis, increasing adipocyte size and lipid content

Emdin et al, *Diabetes* 2019; 68(1):226-234. DOI: 10.2337/DB18-0857

pLOF *ALK7* Variants Are Associated with Lower Risks of Obesity and Type 2 Diabetes

Table 2—Association of variants in *ACVR1C* with WHRadjBMI and with type 2 diabetes

Variant	Minor allele frequency (%)	WHRadjBMI β (95% CI)	WHRadjBMI *P* value	Type 2 diabetes OR (95% CI)	Type 2 diabetes *P* value
Asn150His	1.1	−0.089 (−0.11, −0.067)	3.4×10^{-17}	0.88 (0.83, 0.94)	8.7×10^{-5}
Ile195Thr	0.2	−0.15 (−0.09, 0.19)	1.0×10^{-9}	0.79 (0.67, 0.93)	0.005
Ile482Val	7.2	−0.019 (−0.01, −0.027)	1.6×10^{-5}	0.95 (0.93, 0.97)	4.8×10^{-6}
rs72927479	5.1	−0.035 (−0.045, −0.025)	2.6×10^{-12}	0.93 (0.89, 0.97)	6.0×10^{-4}

Estimates for WHRadjBMI were derived through linear regression analysis in UK Biobank. Estimates for type 2 diabetes were derived through meta-analysis of UK Biobank and the DIAGRAM ExTexT2D Consortium.

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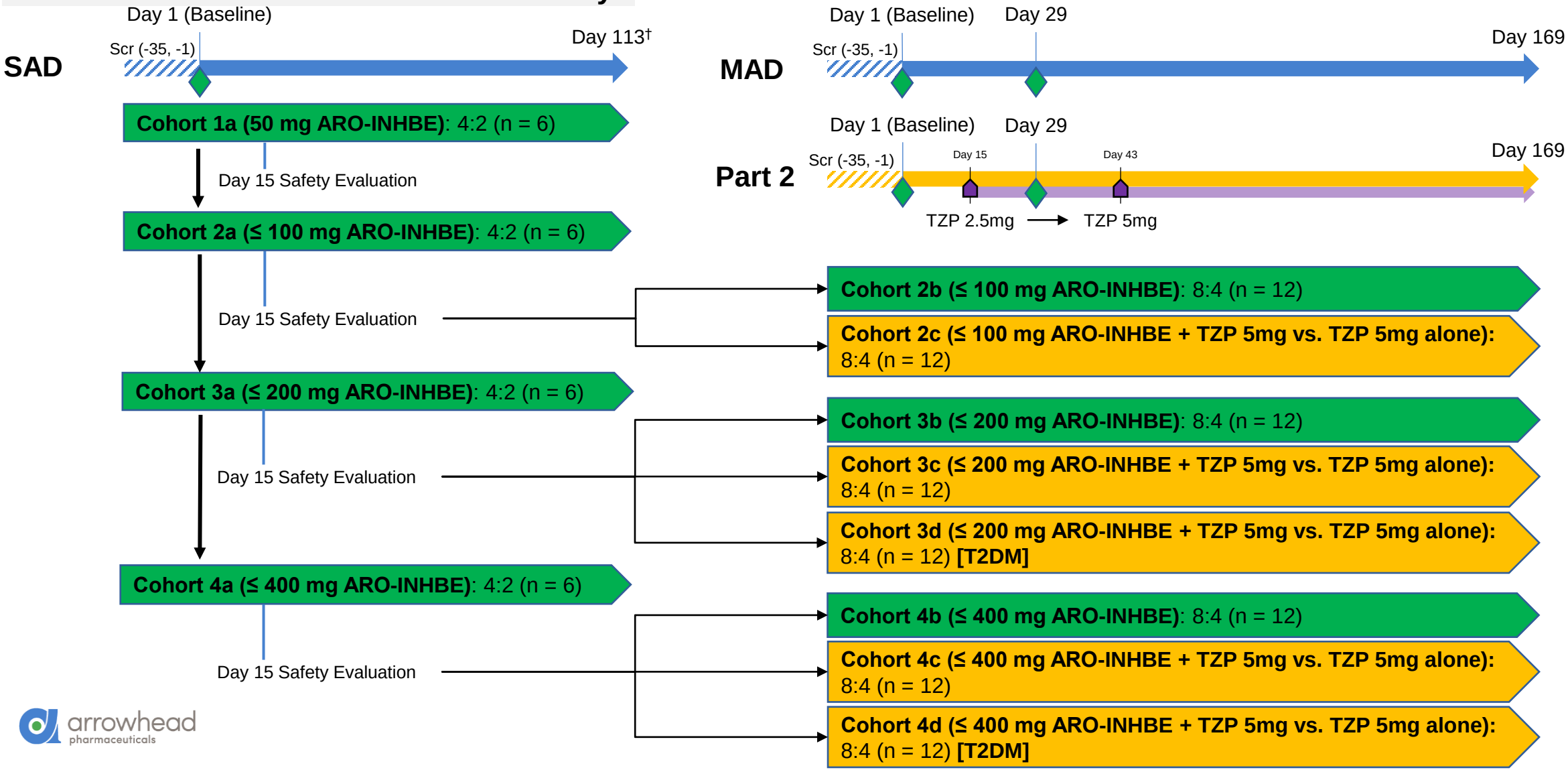
ARO-INHBE Integrated Study Design (Part 1A/1B/2)

ARO-INHBE
Tirzepatide

Part 1A SAD: Adult Volunteers with Obesity

Part 1B MAD: Adult Volunteers with Obesity without T2DM
Part 2: Combination Treatment Patients Obesity with/without T2DM



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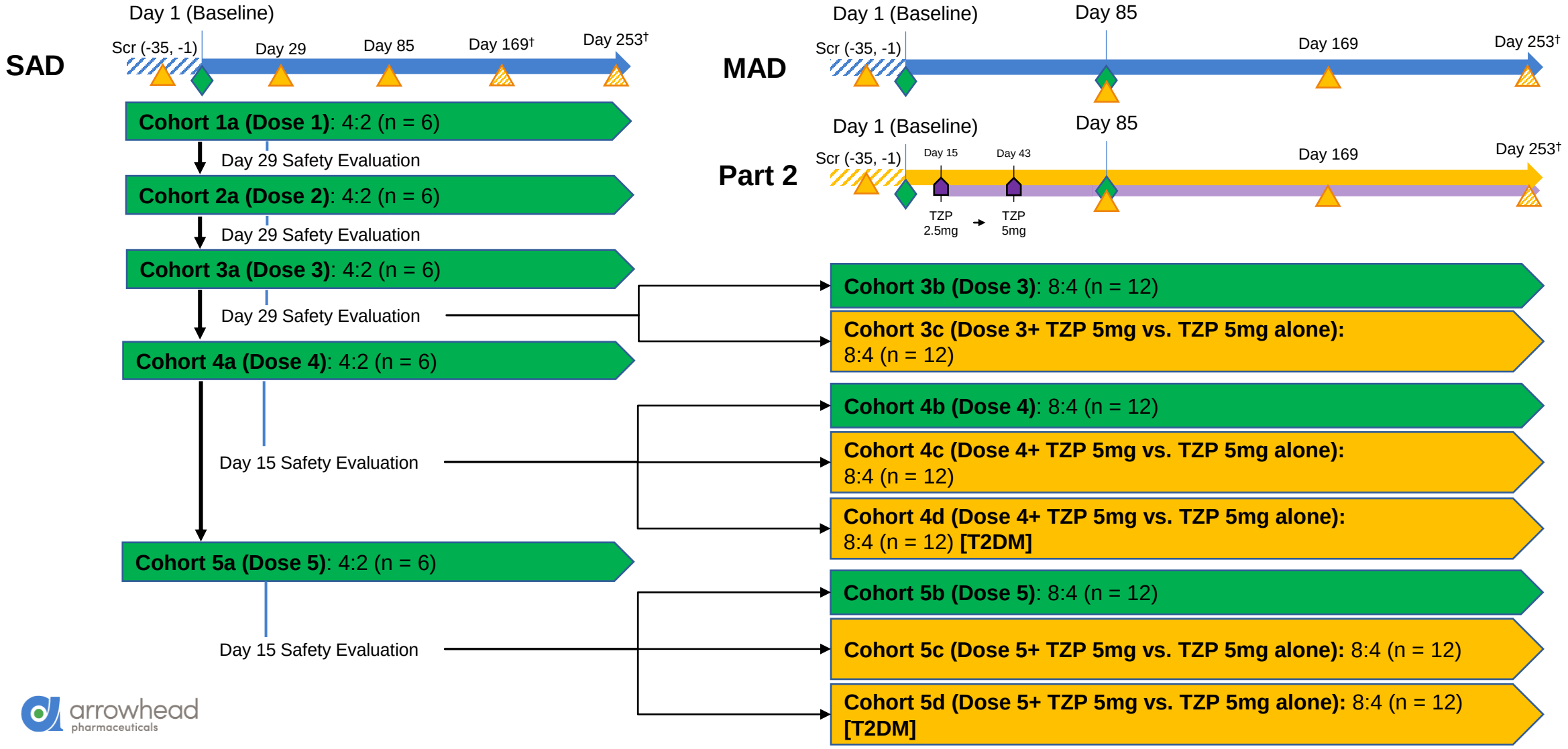
ARO-ALK7 Integrated Study Design (Part 1A/1B/2)

ARO-ALK7 Tirzepatide Adipose Aspiration

Part 1A SAD: Adult Volunteers with Obesity without T2DM

Part 1B MAD: Adult Volunteers with Obesity without T2DM
Part 2: Combination Treatment Patients Obesity with/without T2DM



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Key Endpoints

1° Safety

2° Pharmacokinetics

Exploratory

- **Serum Activin E** (ARO-INHBE only)
- **Adipose Expression of ALK7** (ARO-ALK7 only)
- Weight change (kg/%)
- Waist circumference
- Body adiposity, adipose distribution, fat mass vs lean mass (MRI)
- Liver fat content (MRI-PDFF)
- Fasting lipids and fat metabolism parameters
- Glycemic control parameters

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CNS Overview

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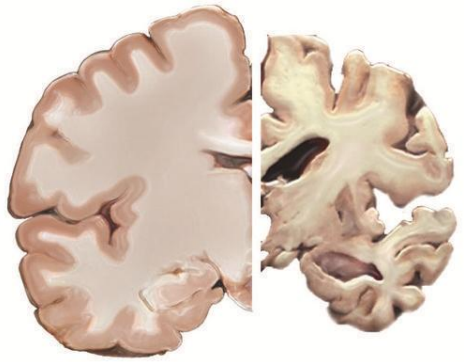
Neurodegenerative Diseases Are an Enormous Burden Uniquely Addressable by RNA Therapeutics

Over **50 million** neurodegeneration patients worldwide[1] and few disease modifying therapies

Healthy Brain



Diseased Brain

- 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)

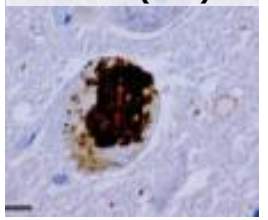
Tauopathies
- Alzheimer's disease (AD)
- Fronto-temporal dementia (FTD)
- Progressive Supranuclear Palsy
- Corticobasal Degeneration

Amyloidoses
- Alzheimer's disease (AD)
- Prion diseases

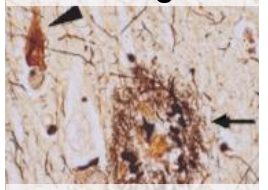
Synucleinopathies
- Parkinson's disease (PD)
- Lewy body dementia
- Multiple system atrophy

Expansion Repeat Disorders
- Huntington's disease (HD)
- Spinocerebellar ataxias (SCA)

SOD1 (ALS)

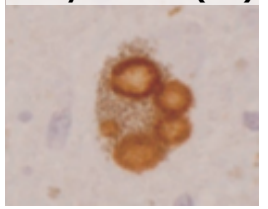


Tau tangles

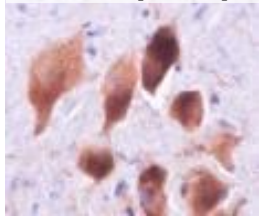


Amyloid plaques

Lewy bodies (PD)



ATXN2 (SCA2)



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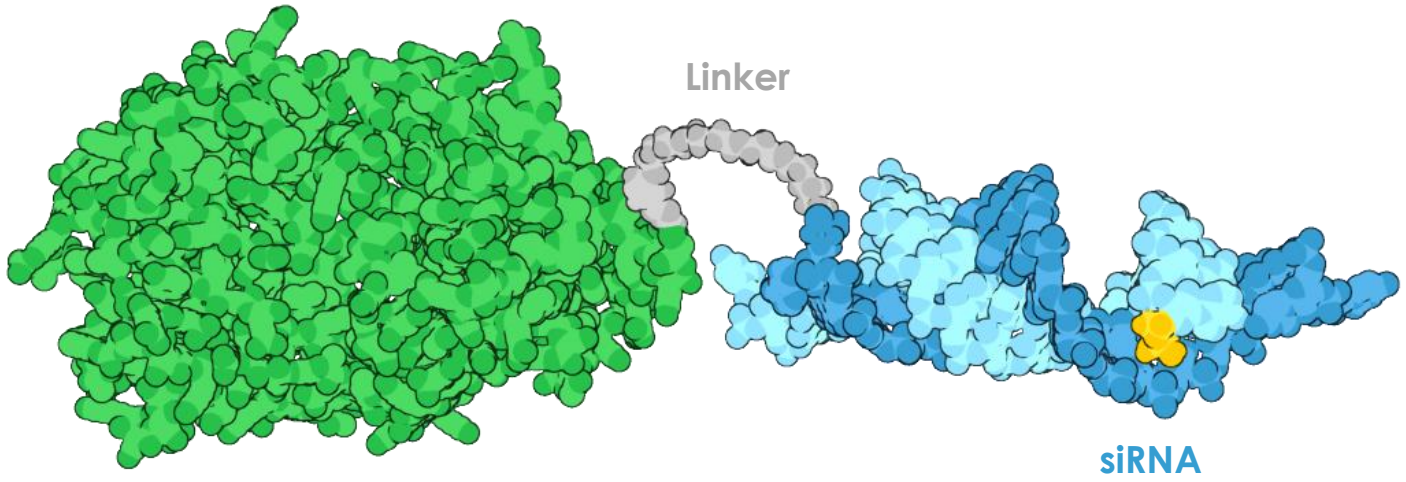
Next Gen. CNS-TRiM™ Platform via Subcutaneous Administration



Systemic Delivery to CNS Potentially Disruptive

We Have Developed an Optimized Systemic Delivery Platform for CNS

- **Ligand-driven** delivery via noninvasive BBB penetration and cellular uptake in brain tissue
- **Effective** and durable reduction in expression levels of therapeutically-relevant gene targets in preclinical studies
- **Convenient** dosing via subcutaneous (SC) administration with potential for monthly to quarterly dosing
- **Favorable** safety profile in rodent and NHP >10x margin over efficacious dose

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First Programs for Alzheimer's, Parkinson's, and Huntington's

ARO-MAPT

ARO-HTT

ARO-SCN

- Well-validated targets
- Deep KD in animal models
- Deep brain distribution in preclinical studies
- Subcutaneous administration
- **ARO-MAPT and ARO-HTT in clinic this year**
- **ARO-SCN in clinic in Q1 2026**

Opportunities for Many Future Targets

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Catalyst Calendar

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Robust 2025 Catalyst Calendar

	Q1	Q2	Q3	Q4
Plozasiran		SHASTA-5 start (acute AP study)	SHASTA-3/4 and MUIR-3 full enrollment	FCS launch (pending review/approval)
	Addl reg submissions and publications			
Zodasiran		HoFH Phase 3 start		
ARO-INHBE				Phase 1/2 Part 1 data
ARO-ALK7		Phase 1/2 start		
Fazirsiran	Phase 3 REDWOOD full enrollment			
ARO-DUX4				Possible data
ARO-DM1				Achieve SRPT milestones Possible data
ARO-MMP7				Phase 1/2 data
ARO-CFB and ARO-C3			Data in 2H	
CNS				ARO-MAPT CTA ARO-HTT CTA

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Thank You!

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