



# Arrowhead Pharmaceuticals

## JP Morgan Healthcare Conference

January 8, 2024



## Safe Harbor Statement

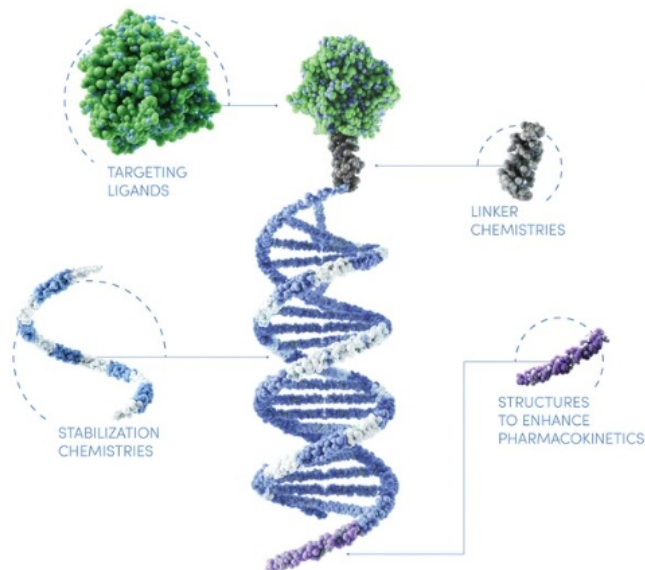
This presentation contains forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. These statements are based upon our current expectations and speak only as of the date hereof. Our actual results may differ materially and 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.

## Market Highlights

### ARWR – NASDAQ Global Select

Stock Price (1/5/24)	\$35.60
Common Shares Outstanding (including recent financing)	~123m
Market Cap (1/5/24)	~\$4.4b
Cash and Investments (9/30/23)	~\$404m
1/5/24 Financing Gross Proceeds	~\$450m

















# RNAi Company with Broad Applications



We created a modular, structurally simple system to:

1. Address multiple cell types
  - Go where disease is
2. Provide platform continuity/confidence
  - Enhanced expectation of success for new candidates
  - Lessons from prior candidates inform future candidates
  - **Potential for more candidates becoming approved drugs than industry average**
3. Move rapidly from idea to the clinic

# Clinical Pipeline

Therapeutic Area		Pre-clinical	Phase 1	Phase 2	Phase 3	Product Rights
Cardiometabolic	Plozasiran (ARO-APOC3) Hypertriglyceridemia					
	Zodasiran (ARO-ANG3) Dyslipidemia					
	Olpasiran CVD					AMGEN
	GSK4532990 NASH					
	ARO-PNPLA3 NASH					
Pulmonary	ARO-RAGE Inflammatory					
	ARO-MUC5AC Muco-Obstructive					
	ARO-MMP7 IPF					
Liver	Fazirsiran Alpha-1 Liver Disease					 
	JNJ-3989 HBV					
Neuromuscular	ARO-SOD1 ALS					
	ARO-DUX4 FSHD					
	ARO-DM1 DM1					
Other	HZN-457 Gout					
	ARO-C3 Complement Mediated Disease					
	ARO-CF8 Complement Mediated Disease					

# Verticals

## Cardiometabolic

### Plozasiran (APOC3)

- FCS: P3 complete Q2
- sHTG: P3 start Q1

### Zincirasiliran (ANG3)

- HoFH: P3 start Q1
- ASCVD: CVOT Q2

### Adipose targets

- Target-rich
- Good silencing
  - >90% KD
  - >6 mo duration
- In clinic 2024

## Pulmonary

### ARO-RAGE

- Asthma
- P2 expected 2024

### ARO-MMP7

- IPF
- P2 expected 2024

### ARO-MUC5AC

- COPD/Asthma
- P2 expected 2024

### New Targets

- Potent 2024 CTA

## CNS

### Still early, but...

- Target-rich
- New CTAs in 2024
- Systemic delivery
  - Possible 2025

## Partner Targets

### ARO-PNPLA3

### ARO-C3

### ARO-DUX4

### ARO-DM1

### ARO-CFB?

## Partnered

### Olpasiran

- Amgen: LP(a), P3

### Fazirsiran

- Takeda: AAT,

### GSK4532990

- GSK: HSD, P2

### JNJ3989

- GSK: HBV, P2

# Multiprong Approach to Capital





## A Different kind of Biotech Company

### **Arrowhead has a broad value proposition**

1. Validated technology
2. Real scarcity
  - Just 2 companies drive RNAi innovation
3. Leaders in expanding the reach of RNAi
  - Going where unmet medical need is
4. Large pipeline
  - Many opportunities to create value
  - Failure in a single program is not catastrophic
  - Ample opportunities for non-dilutive capital via partnering



## Wholly-owned Drug Candidates



# Cardiometabolic Vertical



# Staged Commercial Approach: Plozasiran

## FCS

### US Population

- <1k genetic FCS in US
- 70-100k with TGs >880mg/dl and history of pancreatitis

### Status

- P3 complete Q2 2024
- NDA planned ~EOY 2024
- **Planned launch next year**

## Sever Hypertriglyceridemia (SHTG)

### US Population

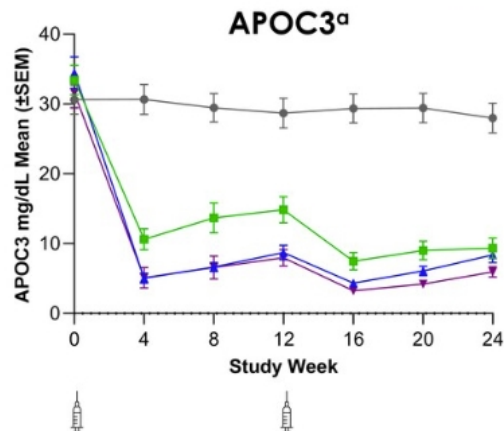
- 3-4m with TGs >500mg/dl in US
  - ~1m with TGs >880mg/dl

### Status

- P3 launch 1H 2024
- Expected length of treatment: 1 year
- Expected approvable endpoint: lowering TGs

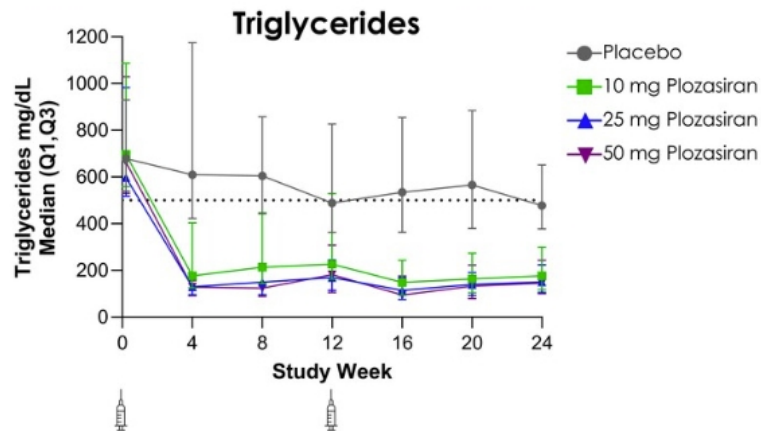
**We believe Plozasiran has blockbuster potential**

# Plozasiran: Encouraging P2 data in patients with SHTG



Least Squares Mean\* % Change from Baseline at Week 24

-2%	-69%	-73%	-79%
	p<0.0001	p<0.0001	p<0.0001



Least Squares Mean\* % Change from Baseline at Week 24

-17%	-66%	-70%	-74%
	p<0.0001	p<0.0001	p<0.0001

# Staged Commercial Approach: Zodasiran

## HoFH

### US Population

- ~1,000
- PCSK9 inhibitors do little for true HoFH

### Status

- P3 launch 1H 2024
- Expected P3 length of treatment: 1 yr
- Expected approvable endpoint: lowering LDL-c
  - We've seen 48% reduction in this pop

## Broad ASCVD Population (Primary and Secondary Prevention)

### US Population

- >10m

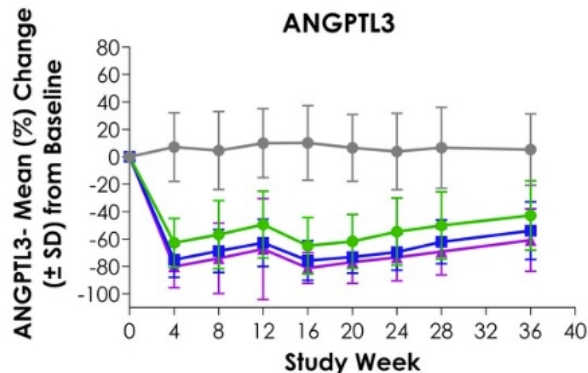
### Status

- P3 CVOT launch 1H 2024
  - either Zodasiran or Plozasiran

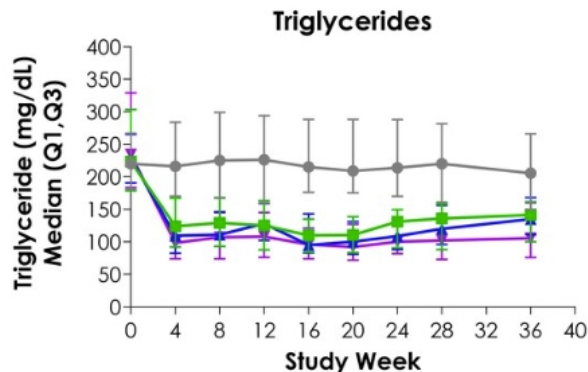
**We believe Zodasiran has blockbuster potential**

# Zodasiran: Encouraging P2 data

● Placebo ● 50 mg ARO-ANG3 ■ 100 mg ARO-ANG3 ▲ 200 mg ARO-ANG3



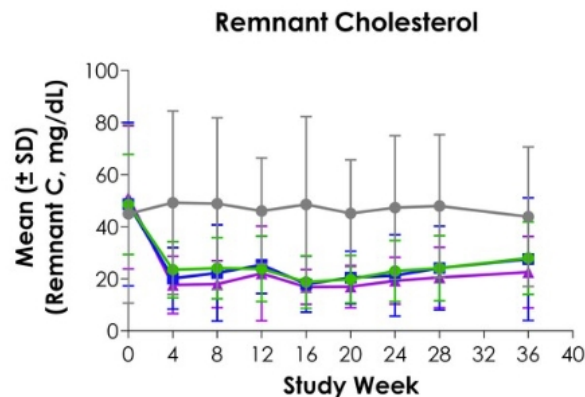
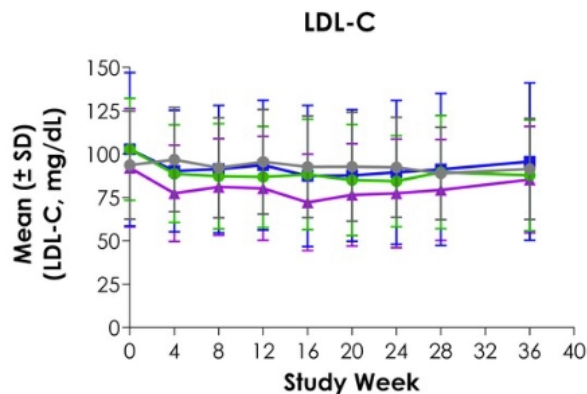
ANGPTL3 Difference vs Placebo (%) at Week 24			
Placebo (N=51)	50 mg (N=51)	100 mg (N=51)	200 mg (N=51)
---	-54.3**	-69.8**	-73.7**



Triglyceride Difference vs Placebo (%) at Week 24			
Placebo (N=51)	50 mg (N=51)	100 mg (N=51)	200 mg (N=51)
---	-51.2**	-56.6**	-63.1**

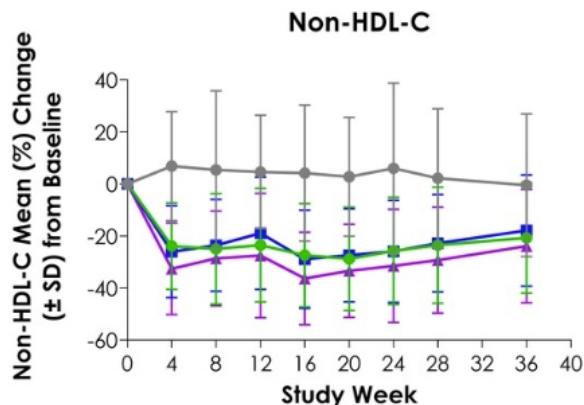
# Zodasiran: Encouraging P2 data

● Placebo ● 50 mg ARO-ANG3 ■ 100 mg ARO-ANG3 ▲ 200 mg ARO-ANG3

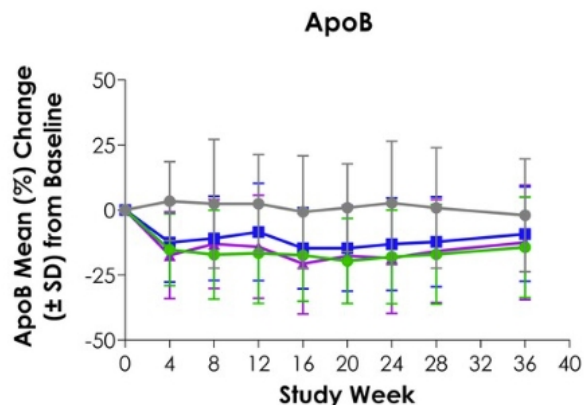


# Zodasiran: Encouraging P2 data

● Placebo ● 50 mg ARO-ANG3 ■ 100 mg ARO-ANG3 ▲ 200 mg ARO-ANG3



Non-HDL-C Difference vs Placebo (%) at Week 24			
Placebo (N=51)	50 mg (N=51)	100 mg (N=51)	200 mg (N=51)
---	-29.2**	-28.7**	-36.4**



ApoB Difference vs Placebo (%) at Week 24			
Placebo (N=51)	50 mg (N=51)	100 mg (N=51)	200 mg (N=51)
---	-18.7**	-15.2*	-21.9**



## Wholly-owned Drug Candidates

# Pulmonary Vertical

# Pulmonary Vertical

## ARO-RAGE

- Being developed for asthma
- P2 expected 2024
- Chronic tox data to move to P2
- Encouraging data in NHVs:
- After 2 doses of 92mg:
  - **~80% mean max KD in circulation**
  - **~90% max KD in circulation**
- After 2 doses of 184mg:
  - **~89% mean max KD in circulation**
  - **~96% max KD in circulation**
- Patient data has been similar
  - Complete data set in coming months

## ARO-MMP7

- Being developed for IPF
- P2 expected 2024
- Chronic tox data to move to P2
- Patient KD data in 2024

## ARO-MUC5AC

- Being developed for COPD/asthma
- P2 expected 2024
- Chronic tox has not started yet
- Patient KD data in 2024

**ARO-RAGE KD data and chronic tox from ARO-RAGE and ARO-MMP7 give us confidence in the pulmonary platform**

# Expectations Over the Next 12 Months

## Balance Sheet Strengthening

- Expect structured/product finance transaction over next few months
- Substantial business development opportunities

## Cardiometabolic

### Plozasiran

- Pivotal Phase 3 PALISADE study data (FCS)
- NDA filing and commercial buildout
- Phase 3 SHASTA-3 and SHASTA-4 initiation (SHTG)

### Zodasiran

- Phase 3 initiation: HoFH
- Phase 3 initiation: CVOT

## Pulmonary

### ARO-RAGE

- Additional KD data in asthma patients
- First evidence of FeNO reduction, a biomarker for the degree of IL-13 driven type 2 inflammation in the lung
- Phase 2 initiation

### ARO-MMP7 and ARO-MUC5AC

- Initial Phase 1 data in patients

## Platform and Pipeline Expansion

- Potential for initial data from muscular pipeline (ARO-DUX4, ARO-DM1)
- C3 data from different patient cohorts
- New CNS candidates in the clinic
- More data on CNS systemic delivery platform
- 1<sup>st</sup> adipose-targeted candidate in the clinic