Milestone PHARMACEUTICALS

Company Overview

June 6, 2024

Forward Looking Statement

The Presentation contains forward-looking statements within the meaning of the safe harbor provisions of the Private Securities Litigation Reform Act of 1995, as amended. Words such as ‘‘aim,’’ ‘‘anticipate,’’ ‘‘assume,’’ ‘‘believe,’’ ‘‘contemplate,’’ ‘‘continue,’’ ‘‘could,’’ ‘‘design,’’ ‘‘due,’’ ‘‘estimate,’’ ‘‘expect,’’ ‘‘goal,’’ ‘‘intend,’’ ‘‘may,’’ ‘‘objective,’’ ‘‘plan,’’ ‘‘predict,’’ ‘‘positioned,’’ ‘‘potential,’’ ‘‘project,’’ ‘‘seek,’’ ‘‘should,’’ ‘‘target,’’ ‘‘will,’’ ‘‘would’’ (as well as other words or expressions referencing future events, conditions or circumstances) are intended to identify forward-looking statements. These forward- looking statements are based on Milestone's expectations and assumptions as of the date of this Presentation. Each of these forward-looking statements involves risks and uncertainties. Actual results may differ materially from these forward-looking statements. Forward-looking statements contained in this Presentation include statements regarding (i) the design, progress, timing, scope and results of the etripamil clinical trials in PSVT and AFib-RVR, (ii) the potential efficacy, safety and tolerability of CARDAMYST for PSVT and etripamil for AFib-RVR, (iii) the potential of CARDAMYST to deliver a new PSVT therapeutic option to market, (iv) plans relating to commercializing CARDAMYST, if approved, including the geographic areas of focus and sales strategy, (v) the potential market size and the rate and degree of market acceptance of CARDAMYST (etripamil) and any future product candidates and the implementation of Milestone's business model and strategic plans for its business, etripamil and any future product candidates (vi) Milestone’s expected cash runway and (vii) potential royalty payments. Important factors that could cause actual results to differ materially from those in the forward-looking statements include, but are not limited to, the risks inherent in biopharmaceutical product development and clinical trials, including the lengthy and uncertain regulatory approval process, uncertainties as to whether our NDA filing for CARDAMYST will be approved by the FDA, uncertainties related to the timing of initiation, enrollment, completion and evaluation of clinical trials, including the RAPID and ReVeRA trials, and whether the clinical trials will validate the safety and efficacy of CARDAMYST for PSVT, etripamil for AFib-RVR or other indications, among others, as well as risks related to pandemics and public health emergencies, including those related to COVID-19, and risks related the sufficiency of our capital resources and our ability to raise additional capital. These and other risks are set forth in Milestone's filings with the U.S. Securities and Exchange Commission, including in its annual report on Form 10-K for the year ended December 31, 2023, under the caption "Risk Factors”, as such discussion may be updated in future filings we make with the SEC. Except as required by law, Milestone assumes no obligation to update any forward- looking statements contained herein to reflect any change in expectations, even as new information becomes available.

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CARDAMYST™ (etripamil) nasal spray is an investigational new drug, which is not approved for commercial distribution in the United States.

Milestone Pharmaceuticals:
Aspiring to Give Patients Control over Common Heart Conditions

Empowering Patients
Self-Treat Common Arrhythmias

- CARDAMYST™ (etripamil) nasal spray: investigational novel calcium channel blocker
- Fast-acting, well-tolerated, portable, on-demand
- Shift from Emergency Department to patient self-management

PSVT
Commercial Launch Preparation

- NDA accepted May 2024, PDUFA action date Mar 2025
- Successful Phase 3 -Published in *The Lancet*
- Experienced leadership driving commercialization

AFib-RVR
Market Expansion Opportunity

- End of Phase 2 Meeting expected mid-2024
- FDA Phase 3 study guidance – 1Q 2024
- Positive Phase 2 ReVeRA Study – AHA Presentation and published in *Circulation AE* – Nov 2023

PSVT = Paroxysmal Supraventricular Tachycardia; AFib-RVR = Atrial Fibrillation with Rapid Ventricular Rate; NDA = New Drug Application; AHA – American Heart Association.
Citations: Stambler B et al, *The Lancet* (2023); Camm AJ et al, *Circulation: Arrhythmia & Electrophysiology* (2023)

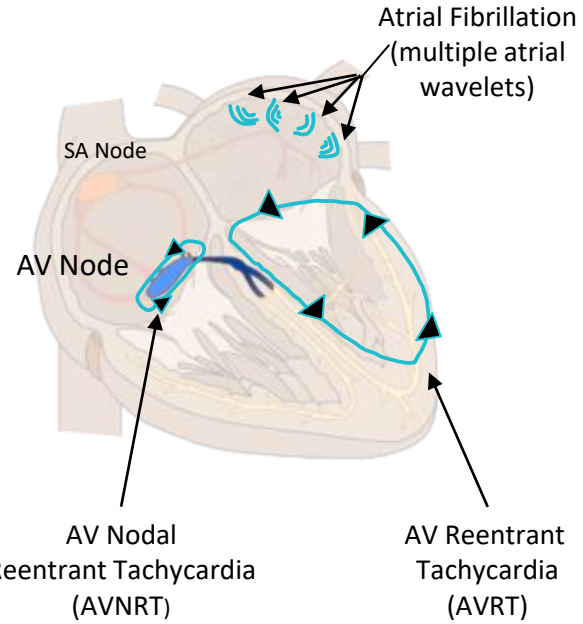
Atrial Arrhythmias with a Common Patient Burden & Cardiac Target

BURDEN: Patients with PSVT & AFib-RVR report marked, often-disabling symptoms

TARGET: PSVT & AFib-RVR Rely on AV Nodal Properties

PSVT (AVNRT and AVRT)	AFib-RVR (a subset of AFib)
Regular rapid heart rate	Irregular rapid heart rate
Commonly 150 - 250 bpm	Commonly 100 - 175 bpm
Episode frequency and duration is highly variable; occurring without warning	

Common Symptoms Include		
	Heart palpitations	Chest pressure or pain
	Shortness of breath	Fatigue
	Light-headedness	Anxiety / Loss-of-control



PSVT = Paroxysmal Supraventricular Tachycardia; AFib-RVR = Atrial Fibrillation with Rapid Ventricular Rate
Sources: adapted from https://en.ecgpedia.org/index.php?title=Supraventricular_Rhythms, accessed 2/2021

Current Treatment of Acute Attacks in the Emergency Department are Burdensome and Costly

For many patients, physicians and payers:

- Time-consuming, disruptive
- Often results in a hospital admission
- Expensive use of healthcare system resources

Need for simple, fast-acting treatment, reduce trips to ED and calls to physicians

ED = Emergency Department

PSVT and AFib-RVR Populations in the US

	PSVT	Atrial Fibrillation
Total Patients (2030)	2.6 Million[3]	10 Million[1]
Discharged ED Visits & Hospital Admissions (2016)[2]	145 Thousand	785 Thousand
Target Addressable Market (2030) Patient Population	**1.0-1.6 Million[5]**	**~3-4 Million[4]**

Source(s): **1.** Colilla et al., Am. J. Cardiol. 2013, 112(8), 1142-1147; Miyasaka et al., Circulation, 2006, 114, 119-125. American Heart Association **2**. HCUP ED & Admissions Data (2016), accessed January 2021. **3.** Rehorn et al. Journal of Cardiovascular Electrophysiology. 2021 Aug; 32(8): 2199-2206. doi: 10.1111/jce.15109. Epub 2021 Jun 14. 2018 prevalence of 2M anticipated to grow at a CAGR of ~2% **4.** Quantitative Survey conducted by Triangle Insights, May 2021, N=250 Clinical Cardiologists, Interventional Cardiologists, and Electrophysiologists. **5.** Estimate of TAM (~40%-60% of prevalence) based on internal PSVT patient market research (BluePrint Research Group, n=247) and longitudinal analysis of claims data.

CARDAMYST is a Novel L-type Investigational Calcium Channel Blocker Designed to Treat Episodes Quickly

Fast onset of action
(T_{max} ≤ 7 min)

Patient
self-administered

Small enough to
fit in your pocket

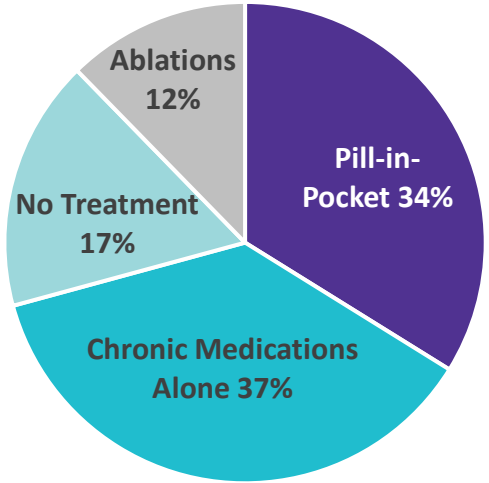
Empowering patients to treat symptomatic attacks

Current US PSVT Market

Total annual US healthcare expenditures of ~$3B

- Prevalence ~2M patients diagnosed with PSVT
- ~650K patients treated per year
  - ~300K newly diagnosed per year
  - >150K ED/hospital visits per year
  - ~80K ablations per year

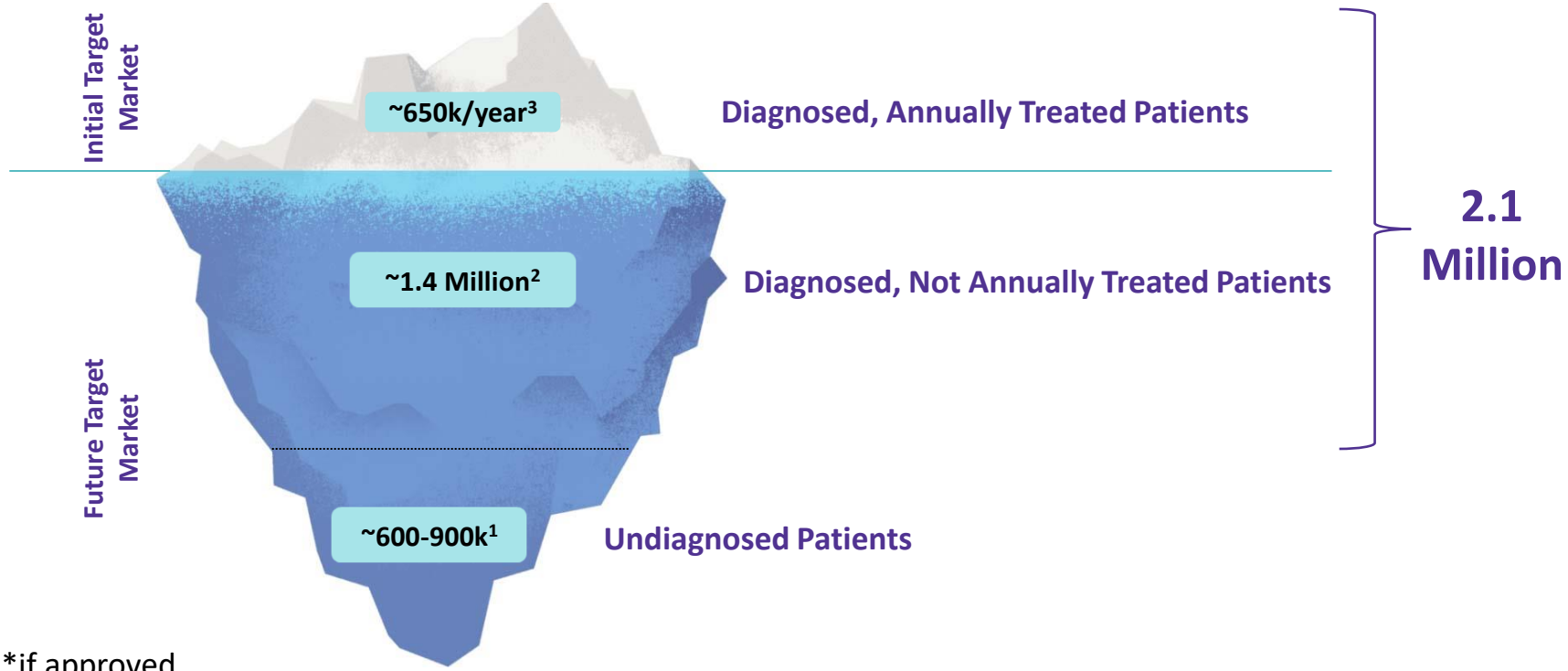
Current Management



PSVT = Paroxysmal Supraventricular Tachycardia; ED = Emergency Department

Source: (1) Sacks, N.C. et al; Prevalence of Paroxysmal Supraventricular Tachycardia (PSVT) in the US in Patients Under 65 Years of Age; Abstract and Oral Presentation at the International Academy of Cardiology Annual Scientific Sessions 2018, 23rd World Congress on Heart Disease; Precision Xtract, Boston, MA, USA; and data-on-file from IBM Marketscan® Commercial Research Database (<65y) and the Medicare Limited Dataset (≥65y), with demographic, enrollment and claims data for commercially insured (Truven) and Medicare covered patients using PSVT code 427.0 or I47.1 for up to a 9-year interval between 2008 and 2016 inclusive; (2) Quantitative market research conducted by Triangle Insights Group (n=250 cardiologists), June-September 2020

Core PSVT Market is Addressable *Now**, with Large Potential for Expansion



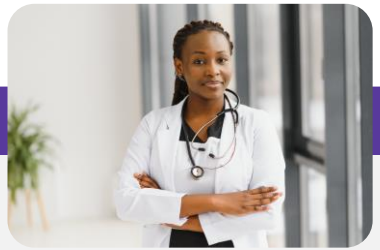
*if approved

Sources: 1) assumes annual incidence rate for PSVT of ~300k from longitudinal claims analysis and the average time to diagnosis (currently 2-3 years) can be reduced to <6 months 2) Calculated as the difference between PSVT prevalence of 2.1M and annual treatment rate of ~650k from Truven MarketScan data, 2008-2016 analyzed by Precision Xtract, 2019 3) Estimated number of unique patients with annual claims for PSVT from Truven MarketScan data, 2008-2016 analyzed by Precision Xtract, 2019.

CARDAMYST Has Substantial Potential Value for Stakeholder Groups If Approved

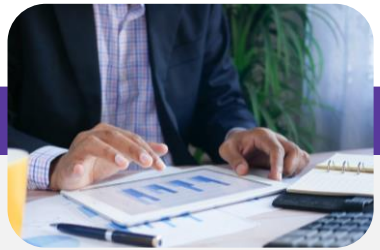
Patients - Empowerment

- Fast, reliable self-administration
- Less disruption, reliance on the Emergency Department
- Less fear over when the next event will occur



Physicians – Dependable Tool

- Designed for patient self-management
- Frees up physician time and office resources
- Trusted CCB mechanism



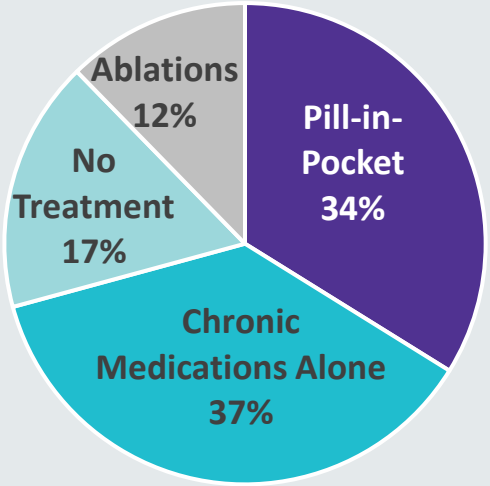
Payers – More Efficient Use of Resources

- Novel and cost-effective treatment
- Reduction in ED/hospital admissions

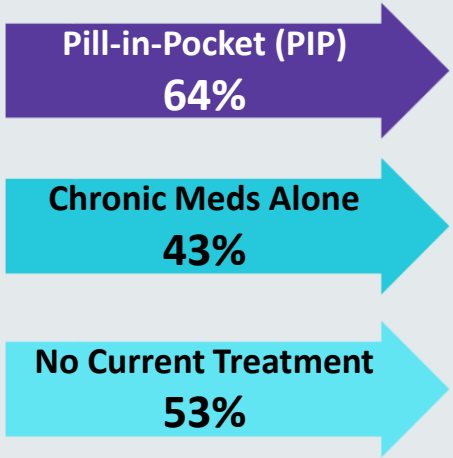
Sources: Internal market research, PSVT = Paroxysmal Supraventricular Tachycardia, CCB = Calcium Channel Blocker, ED = Emergency Department

Cardiologists Expect to Prescribe CARDAMYST to the Majority of Unablated Patients with PSVT

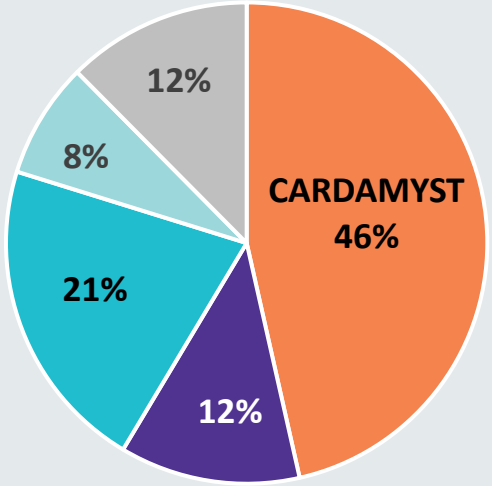
Current PSVT Management



Cardiologists' Stated Adoption of CARDAMYST per Segment



Impact of Cardiologist Adoption of CARDAMYST



Source: Quantitative market research conducted by Triangle Insights Group (n=250 cardiologists), June-September 2020; Estimated number of unique patients with annual claims for PSVT from Truven MarketScan data, 2008-2016 analyzed by Precision Xtract, 2019

Management of Patients with PSVT and Call Point Targeting

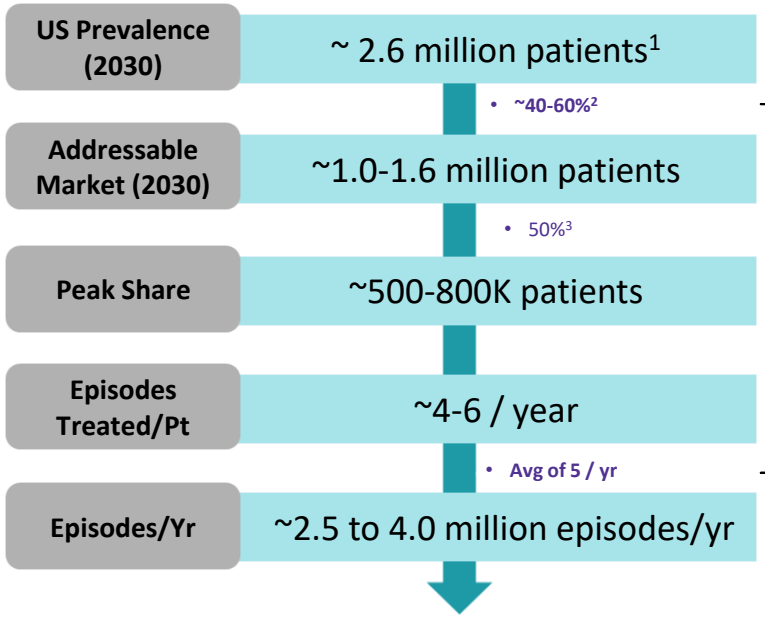
		Clinical Cardiologists	Primary Care Physicians	Electro-physiologists
% of patients managed		~60%	~30%	~10%
Long-term Use	*Add to or Replace Chronic Medications*	Primary Target		
Medium-term Use	*Defer Ablation*			Secondary Target
Short-term Use	*Bridge to Ablation*			

- Targeted sales force to reach majority of available opportunity
- Significant overlap with most common CV portfolio call points

Majority of patients with PSVT managed by CV specialists, leading to commercial efficiencies

Source: Internal market research

Peak US Market Opportunity for CARDAMYST in PSVT



Patients with PSVT

~60% with multiple 10+ minute moderate/severe* episodes per year

~45% Experience an average duration ≥30 min / episode

Episodes of PSVT

12-15 median annual episode frequency

60% last at least 10 minutes

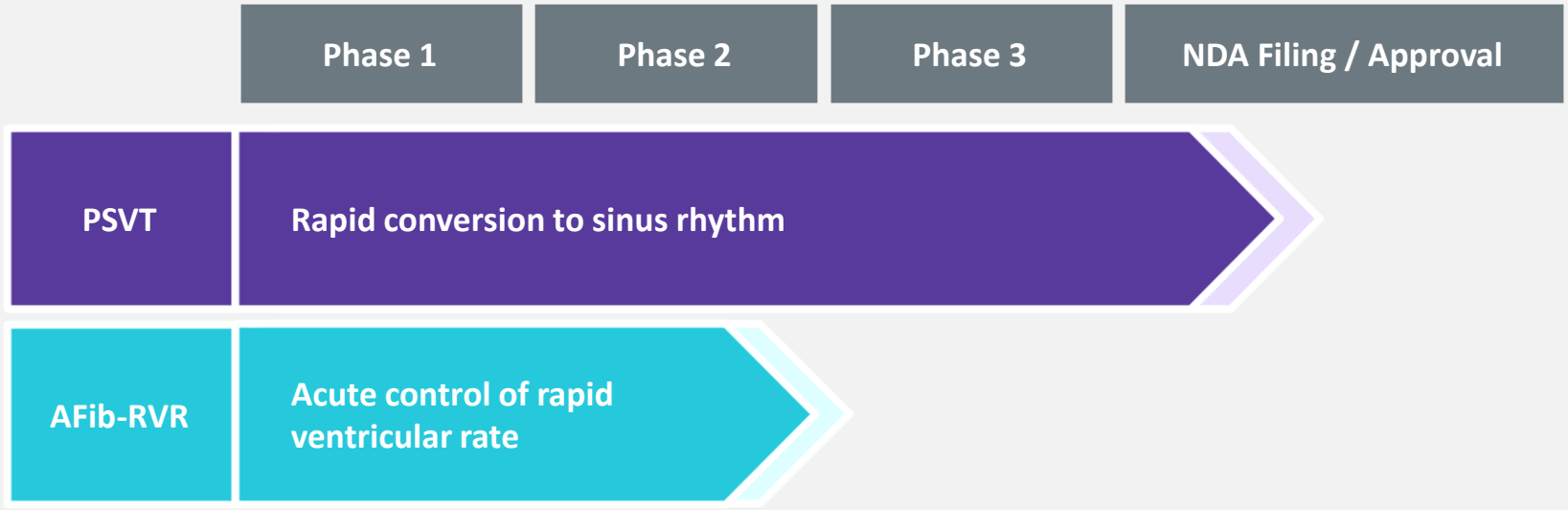
35% last at least 30 minutes

*Patient stated severity of SVT episode (mild, moderate, or severe)

Sources: Internal estimates based on market and outcomes research, Milestone Pharmaceuticals. **1.** Rehorn et al. Journal of Cardiovascular Electrophysiology. 2021 Aug; 32(8): 2199-2206. doi: 10.1111/jce.15109. Epub 2021 Jun 14. **2.** 2019 market research with patients conducted by BluePrint Research Group (n=247) . **3.** 2020 market research with HCPs conducted by Triangle Insights Group, 2020 (n=250).

Clinical Pipeline Advancement for Etripamil

Pharmacology of L-type calcium channel blockers drives broad clinical utility



PSVT = Paroxysmal Supraventricular Tachycardia; AFib-RVR = Atrial Fibrillation with Rapid Ventricular Rate; NDA = New Drug Application

Comprehensive Data Supports FDA New Drug Application for Rapid Conversion of SVT Episodes to Sinus Rhythm in Adults

NODE-1	NODE-301	NODE-302 (Ext. of NODE-301)	RAPID	NODE-303
Phase 2	**Phase 3**	**Phase 3**	**Phase 3**	**Phase 3**
Efficacy (dose finding)	Efficacy	Safety & Efficacy (Repeat Episodes)	Efficacy	Safety (Repeat Episodes)
N = 64	N = 431	N = 169	N=706	N = 503

- >1,600 Patient Exposures to Etripamil ≥ 70 mg
- Positive Phase 3 pivotal RAPID trial anchors NDA submission

NDA = New Drug Application; SVT = Supraventricular Tachycardia
NB: NODE-301 and RAPID studies also collected Safety information
Source: Milestone Pharmaceuticals Data on File

Positive Phase 3 RAPID Trial in Patients with PSVT

Randomized, double-blind, placebo-controlled trial enrolled 706 patients to self-administer etripamil NS 70 mg regimen or placebo NS during a PSVT event outside the medical setting

Repeat-dose regimen – if symptoms not resolved in 10 minutes, second dose administered

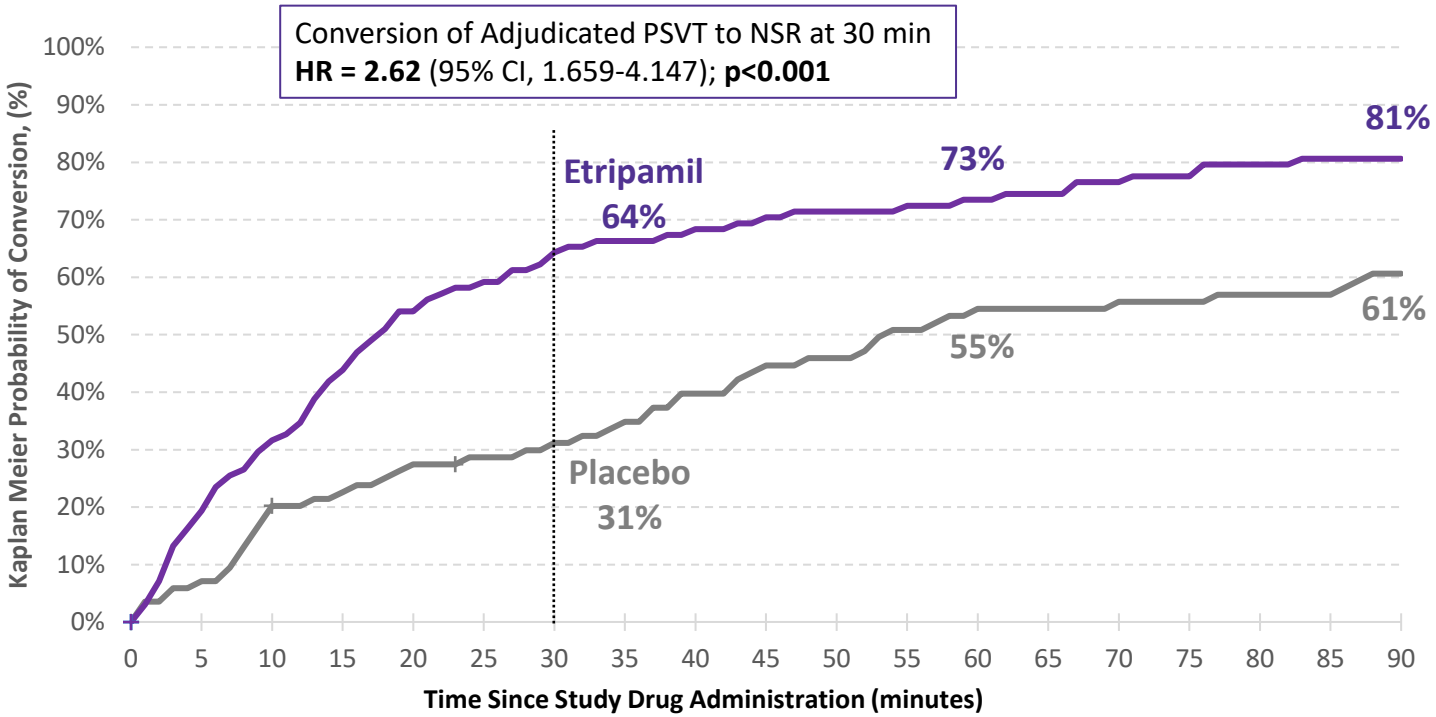
- Achieved primary endpoint - statistical significance (HR = 2.62; 95% CI 1.66, 4.15; p<0.001)
- Median time to conversion 17.2 min with etripamil vs. 53.5 min with placebo
- Need for additional medical interventions or emergency department care ~40% lower for etripamil patients compared to placebo
- Favorable safety and tolerability consistent with prior studies – the most common AEs localized to nasal administration site

Primary: Conversion of Adjudicated PSVT to Normal Sinus Rhythm (NSR) at 30 min

NS= nasal spray; HR = Hazard Ratio; CI = Confidence Interval. Median Time To Conversion data: 17.2 min (95% CI 13.4, 26.5) with etripamil nasal spray regimen vs. 53.5 min (95% CI 38.7, 87.3) with placebo. Source: American Heart Association Scientific Sessions, Late-Breaking Clinical Trial Presentation, November 2022; *Am Heart J (2022)*; and *The Lancet (2023).*

Data Indicate Fast Conversion to Normal Sinus Rhythm (NSR)

RAPID Study

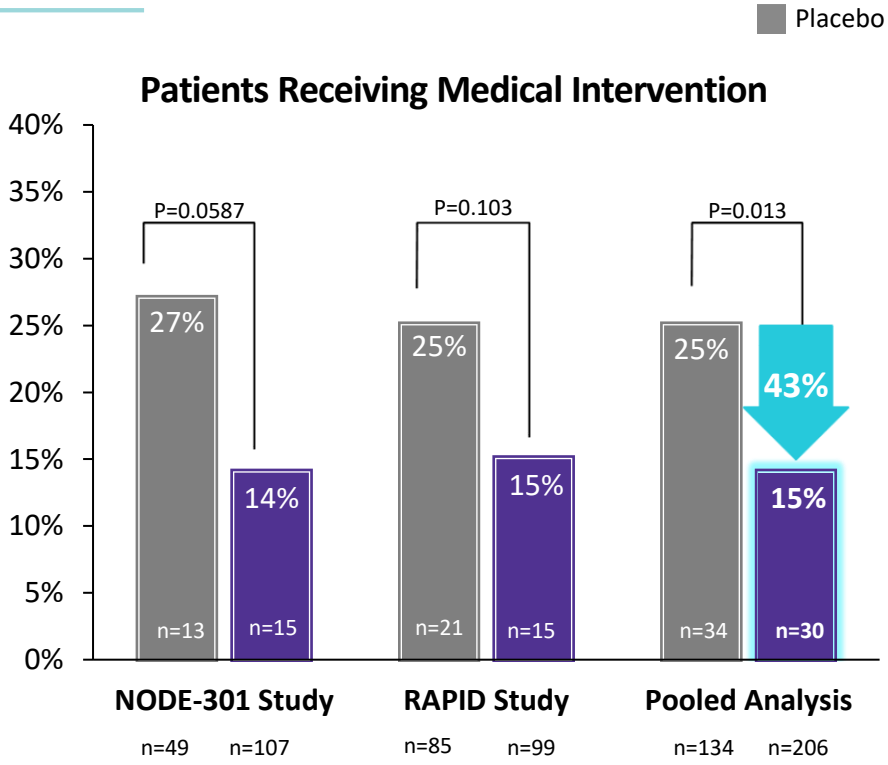


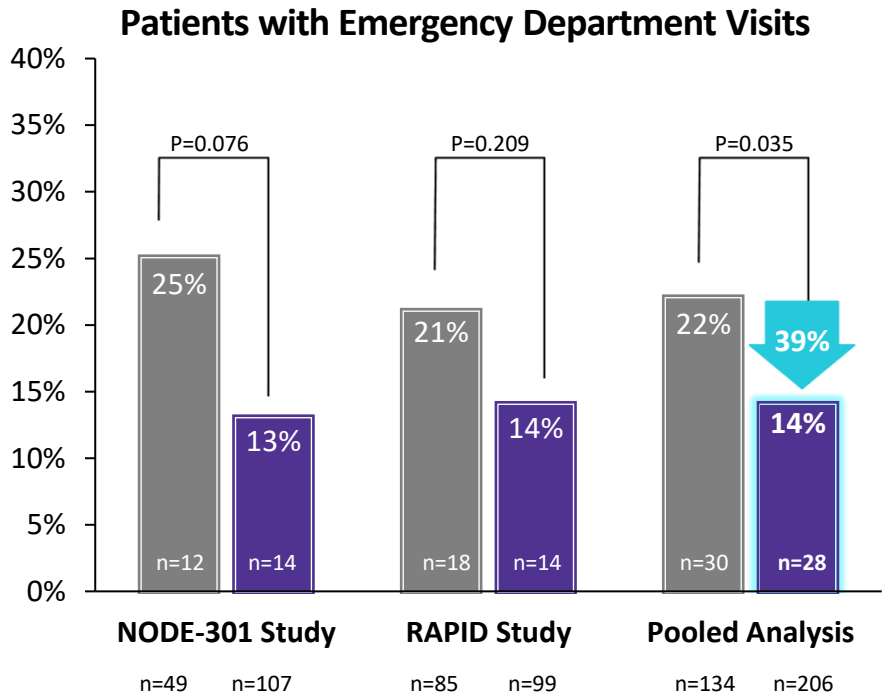
Number of Subjects at Risk																			
Placebo	85	78	67	64	60	58	56	53	49	45	44	40	37	37	36	36	35	35	32
Etripamil	99	79	67	55	45	40	35	33	31	29	28	27	26	25	23	22	20	19	19

HR = Hazard Ratio; CI = Confidence Interval. Source: American Heart Association Scientific Sessions, Late-Breaking Clinical Trial Presentation, November 2022; and *The Lancet (2023).*

Fewer Medical Interventions and Emergency Department Visits

RAPID & NODE-301 Studies





Pooling of data and analyses were prespecified in RAPID statistical analysis plan. Statistical analyses performed by Chi-square test for each study data set and pooled data set. Sources: American Heart Association Scientific Sessions, Late-Breaking Clinical Trial Presentation (Nov. 2022); International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Presentation (May 2023)

CARDAMYST Well-Tolerated with a Favorable Safety Profile

RAPID Study – Safety Events

Subject-reported AEs,[1] n (%)	Placebo[2] N=120	Etripamil[2] N=135
Nasal discomfort	6 (5.0)	31 (23.0)
Nasal congestion	1 (0.8)	17 (12.6)
Rhinorrhea	3 (2.5)	12 (8.9)
Epistaxis	2 (1.7)	8 (5.9)[3]
Syncope	0.0	0.0
Loss of Consciousness	0.0	0.0
Pre-Syncope	0.0	0.0
Dizziness	0.0	1 (0.7)[4]
Subjects with Events from Independent ECG Reading,[5] n (%)	**Placebo[6] N=116**	**Etripamil[6] N=128**
2nd Degree AV Block - Mobitz I AV Block	0	0
2nd Degree AV Block - Mobitz II AV Block	0	0
3rd Degree AV Block	0	0

[1] Randomized-period treatment-emergent adverse events, those ≥5% or those specifically tracked as potentially representing lowered blood pressure. [2] Safety Population. [3] Six of 8 rated as mild, 2 of 8 rated as moderate, 0 needing intervention. [4] Rated as mild. [5]Expert cardiac electrophysiologist adjudication committee. [6]Safety population with evaluable 5-hr. ambulatory ECG data. AE timing – within 24 hours following drug administration. Source: American Heart Association Scientific Sessions, Late-Breaking Clinical Trial Presentation, November 2022; and *The Lancet (2023).*

PSVT & AFib-RVR Populations in the US

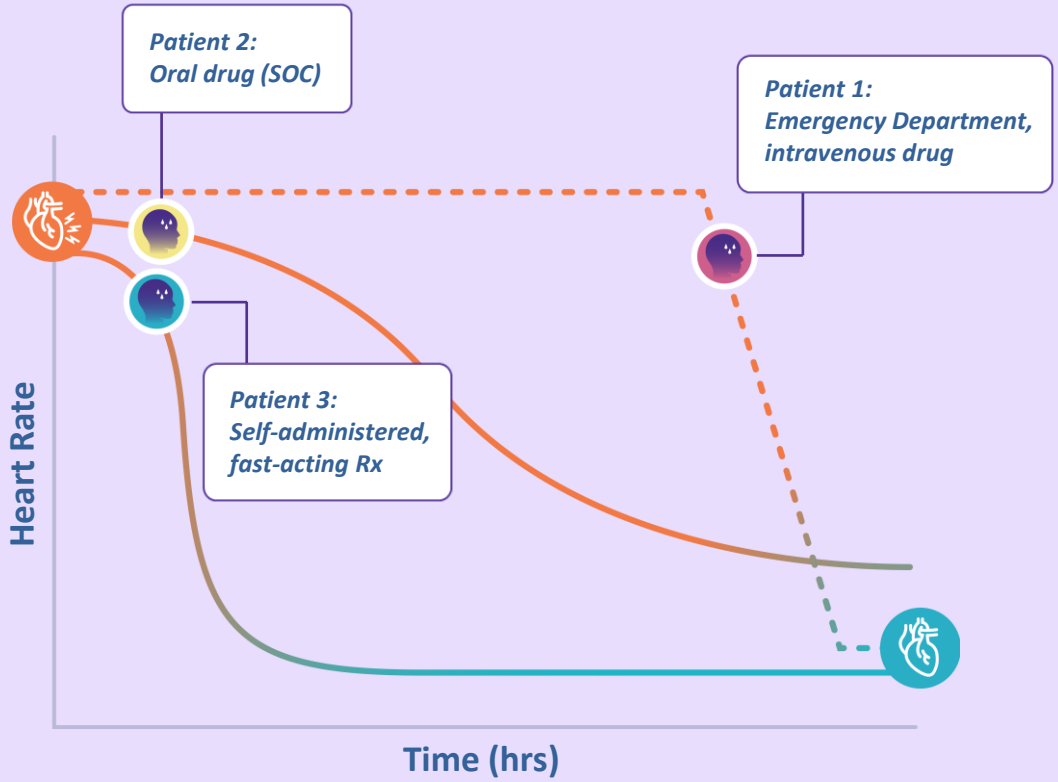
	PSVT	Atrial Fibrillation
Total Patients (2030)	2.6 Million[3]	**10 Million[1]**
Discharged ED Visits & Hospital Admissions (2016)[2]	145 Thousand	**785 Thousand**
Target Addressable Market (2030) Patient Population	**1.0-1.6 Million[5]**	**AFib-RVR ~3-4 Million[4]**

Source(s): **1.** Colilla et al., Am. J. Cardiol. 2013, 112(8), 1142-1147; Miyasaka et al., Circulation, 2006, 114, 119-125. American Heart Association **2**. HCUP ED & Admissions Data (2016), accessed January 2021. **3.** Rehorn et al. Journal of Cardiovascular Electrophysiology. 2021 Aug; 32(8): 2199-2206. doi: 10.1111/jce.15109. Epub 2021 Jun 14. 2018 prevalence of 2M anticipated to grow at a CAGR of ~2% **4.** Quantitative Survey conducted by Triangle Insights, May 2021, N=250 Clinical Cardiologists, Interventional Cardiologists, and Electrophysiologists. **5.** Estimate of TAM (~40%-60% of prevalence) based 2019 market research with patients conducted by BluePrint Research Group, (n=247)

AFib-RVR – Acute Treatment Scenarios

Acute AFib-RVR Attack

- Heart palpitations
- Chest pressure or pain
- Shortness of breath
- Fatigue
- Light-headedness
- Anxiety



Potential Use Cases of Etripamil for AFib-RVR

1. Acute, stand-alone, portable treatment for rate control and symptom control
2. Acute treatment as a bridge (“precursor”) to the delayed effects of oral rate-control or anti-arrhythmic drug administration
3. Use peri-ablation
4. Non-invasive administration opens options for potential treatment without an IV line in emergency-department or ambulance setting

AFib-RVR = atrial fibrillation with rapid ventricular rate, Rx = treatment, IV = intravenous

A drug that is rapidly acting and self-administered outside of a medical setting would have characteristics that would help an unmet need

ReVeRA - Phase 2 Proof of Concept Trial of Etripamil in AFib-RVR in the Emergency Department Setting

1 Patient presents to ED with episode of AFib-RVR

2 Dosing & Assessment

3 Efficacy Analysis

Key Inclusion:
- Atrial Fibrillation ≥ 1 hour
- Ventricular Rate (VR) ≥ 110 bpm
- Paroxysmal, persistent, or permanent

Select Exclusion:
- Treated with antiarrhythmic drugs
- Hemodynamically unstable
- Heart failure

1. Baseline ECG for ≥ 10 min
2. Administer double blind study drug 70 mg etripamil : Placebo (1:1)
3. Monitor in-patient for 1 hour
4. Six-hour remote cardiac monitor
5. Complete safety 24 hours post dose

Primary: Maximum reduction in VR within 60 min

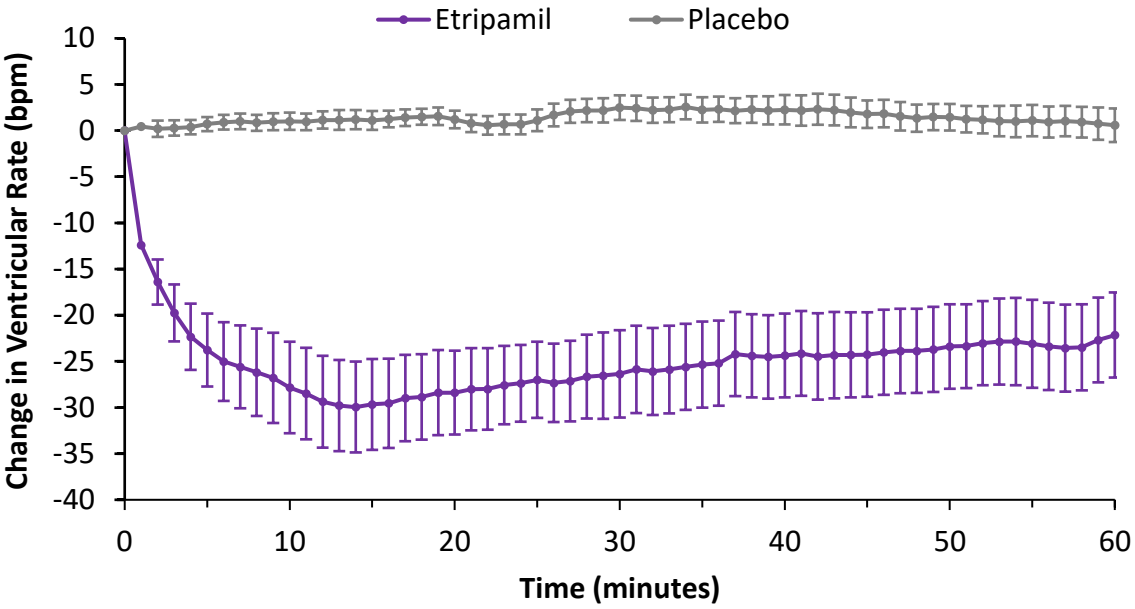
N=50: 90% powered to detect 20 bpm difference in max reduction, α=0.05

- **Time to** VR reduction
- **Duration** of VR reductions
  - <100 bpm, ≥ 10% reduction, ≥ 20% reduction
- Patient satisfaction with treatment (TSQM-9)

AFib-RVR = Atrial Fibrillation with Rapid Ventricular Rate; TSQM-9, Treatment Satisfaction Questionnaire for Medication; ED = Emergency Department.
Source: American Heart Association Scientific Sessions, Featured Science Presentation, Nov. 2023; and *Circulation: Arrhythmia & EP* (Nov. 2023)

Assessing Ventricular Rate Reduction with Etripamil – How Much; How Fast; How Long

ReVeRA – Substantial & Rapid Reduction in VR with Etripamil



PRIMARY ENDPOINT: Maximum Reduction in VR from Baseline	Placebo NS, N=25[1]	Etripamil NS (70 mg) N=24[1]
Mean, bpm	-5.06	-34.97
Difference in means, bpm	--	-29.91
p-value[2]	**--**	**<0.0001**

NS = Nasal Spray; VR = ventricular rate; bpm = beats per minute

Note: Data plotted on time course are not those directly used for calculation of Primary Endpoint (by pre-specified plan). X-axis: of plot: time following drug administration; Y-axis: 5-min moving average, bpm ±SEM. [1] Efficacy Population (all randomized patients receiving study drug remaining in atrial fibrillation with adequately diagnostic ECG recordings for at least 60 min post drug)
[2] By ANCOVA. Source: American Heart Association Scientific Sessions, Featured Science Presentation, Nov. 2023; and *Circulation: Arrhythmia & EP* (Nov. 2023)

ReVeRA Study: TSQM-9 PRO[1] Assessment & Results

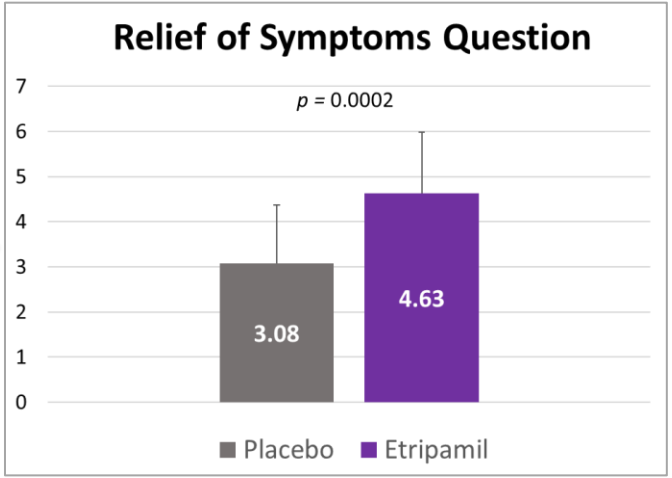
ReVeRA Data Show Significant Improvement in Patient-Reported Relief of Symptoms

- TSQM-9 PRO[1] includes an Effectiveness Domain
- Domain includes three questions, each answered on 7-point anchored scale

1	2	3	4	5	6	7
Extremely Dissatisfied	Very Dissatisfied	Dissatisfied	Somewhat Satisfied	Satisfied	Very Satisfied	Extremely Satisfied

- The domain score is calculated from its three question scores
  - Domain score is on a 0 to 100-point scale
  - Domain score of 50/100 corresponds to a 4/7 = "Somewhat Satisfied"

	Placebo[2] N=25	Etripamil[2] N=24	p value[3]
Effectiveness Domain Scores, mean (SD)	**36.67 (21.64)**	**62.69 (21.59)**	**p<0.0001**



Delta = 1.55 units on Relief of Symptoms

[1] Treatment Satisfaction Questionnaire for Medication-9, a validated Patient-Reported Outcome tool. [2] Efficacy Population (all randomized patients receiving study drug remaining in atrial fibrillation with adequately diagnostic ECG recordings for at least 60 min post drug). [3] From t-test. Source: American Heart Association Scientific Sessions, Featured Science Presentation, Nov. 2023; and *Circulation: Arrhythmia & EP* (Nov. 2023)

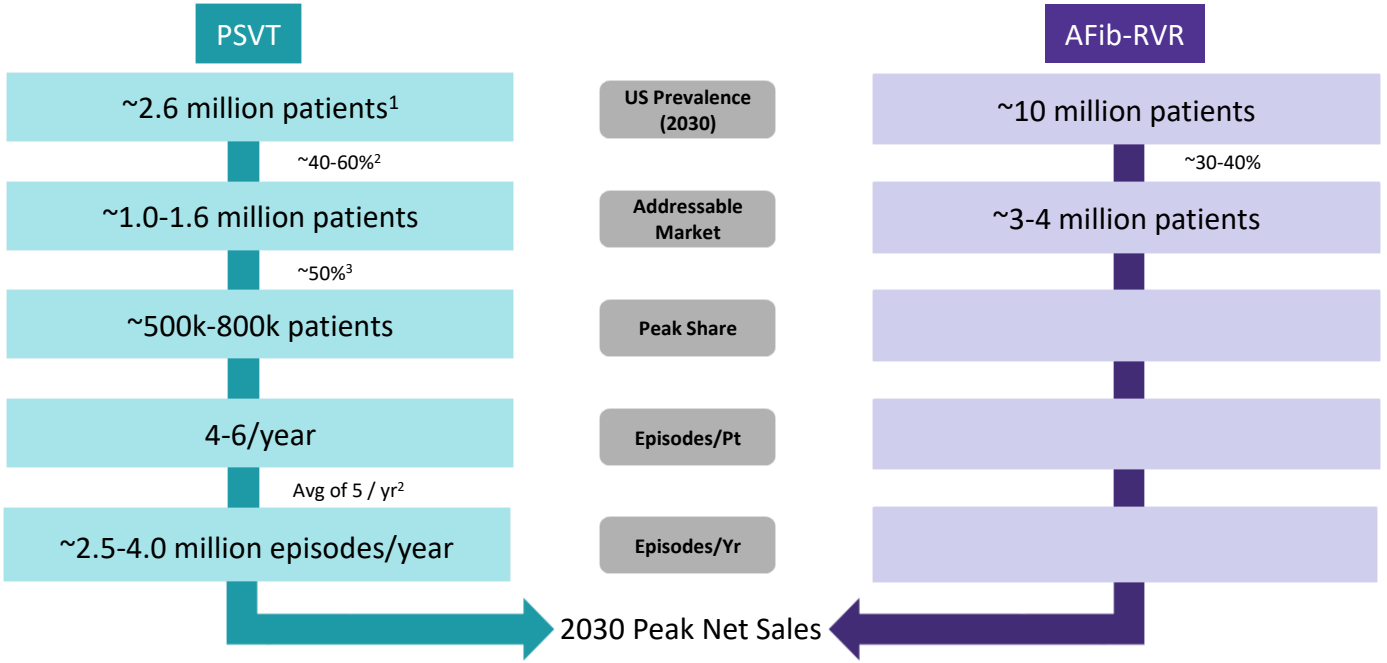
Proposed Phase 3 Registrational Study in AFib-RVR

- Key Inclusion Criterion: history of symptomatic episodes of AFib-RVR
- Patients self-administer drug at-home for perceived episodes of AFib-RVR
  - Same clinical trial and etripamil NS treatment approach as used in PSVT program
- Dose: etripamil NS 70 mg (same as proposed indication in PSVT); repeat-dose regimen
- Primary endpoint = maximum reduction in VR, same as ReVeRA; etripamil vs placebo
- Key Secondary endpoint = symptom relief, via PRO
- Objectives:
  - Show $p < 0.05$ for Primary and Key Secondary endpoints in ITT population; no alpha-spend
  - Show meaningful PRO-based change in Target population (eg, 1-point change on 7-point scale)
- Estimated study size: N ≈ 150-200 total events, based on[1]: 90% power, $p < 0.05$

AFib-RVR = atrial fibrillation with rapid ventricular rate; ITT = intention to treat; PSVT = paroxysmal supraventricular tachycardia; TSQM = Treatment Satisfaction Questionnaire for Medication PRO; PRO = patient reported outcome

[1] Sizing assumptions also include PRO delta of 1.2 points, standard deviation = 1.6, Target/ITT population ratio of 0.70

Peak US Market Opportunity for CARDAMYST in PSVT and AFib-RVR



AF – RVR = Atrial Fibrillation with Rapid Ventricular Rate; TAM = Target Addressable Market

Market Research Suggests a TAM of 4+ Million Patients across both PSVT and AFib-RVR Indications

Sources: **1.** Rehorn et al. Journal of Cardiovascular Electrophysiology. 2021 Aug; 32(8): 2199-2206. doi: 10.1111/jce.15109. ; **2.** 2019 market research with patients conducted by BluePrint Research Group, (n=247); **3.** 2020 market research with healthcare providers conducted by Triangle Insights Group, (n=250)

Financials as of March 31, 2024

- Pro-forma cash and short-term investments of $89.5M
  - Funds operations into 2026
- Synthetic Royalty Financing of $75M available upon approval(1)
- Launch funded for 4+ quarters, if etripamil approved mid-2025
- Pro-Forma Equity: 66.2M in shares & prefunded warrants
  - 53.3M common shares
  - 12.9M pre-funded warrants

(1) In March 2023, Milestone announced a $125.0M strategic with RTW Investments. The financings consists of $50.0M in convertible notes issued in March 2023, and a commitment $75.0M in non-dilutive royalty funding if etripamil is approved by the FDA.

Milestone Pharmaceuticals:
Aspiring to Give Patients Control over Common Heart Conditions

Empowering Patients
Self-Treat Common Arrhythmias

- CARDAMYST: investigational novel calcium channel blocker
- Fast-acting, well-tolerated, portable, on-demand
- Shift from Emergency Department to patient self-management

PSVT
Commercial Launch Preparation

- NDA accepted May 2024, PDUFA action date Mar 2025
- Successful Phase 3 -Published in *The Lancet*
- Experienced leadership driving commercialization

AFib-RVR
Market Expansion Opportunity

- End of Phase 2 Meeting expected mid-2024
- FDA Phase 3 study guidance – 1Q 2024
- Positive Phase 2 ReVeRA Study – AHA Presentation and published in *Circulation AE* – Nov 2023

PSVT = Paroxysmal Supraventricular Tachycardia; AFib-RVR = Atrial Fibrillation with Rapid Ventricular Rate; NDA = New Drug Application; RTF = Refusal to File; AHA – American Heart Association.
Citations: Stambler B et al, *The Lancet* (2023); Camm AJ et al, *Circulation: Arrhythmia & Electrophysiology* (2023)

Milestone PHARMACEUTICALS

Thank you

Strategic Financing with RTW
Funds launch and commercialization of CARDAMYST in PSVT

$50M
Convertible Notes

- 6-year term
- Initial Conversion Price $5.23/share
  - 50% premium to 30-day VWAP[1]
- 6% coupon
  - Payable quarterly, or at our option payable in kind (PIK) for first 3 years

$75M
Synthetic Royalty

- Funded if FDA approves etripamil in PSVT
- Non-dilutive synthetic royalty
- 7% Royalty[2] <$500M[3]
- 4% Royalty $500-$800M
- 1% Royalty >$800M

[1] VWAP – Volume Weighted Average Price as of 3/27/23 [2] Rate can increase by 2.5% if certain annual net sales thresholds are not met [3] Annual net product sales of etripamil in the United States

NDA Resubmitted for CARDAMYST in PSVT

- NDA Resubmission – March 2024
  - Expect standard NDA review period following resubmission
  - Resubmission included:
    - Supplementary datasets using a slightly different method to define "treatment-emergent AEs”
    - ECG datafiles in additional formats to better enable FDA analyses
- Type A meeting with FDA – February 2024
  - Timing of adverse events in question had minimal impact on the overall characterization of the safety profile of CARDAMYST
  - Confirmation of Milestone’s approach to address RTF
- Refusal to File Notice – December 2023
  - FDA requested clarification about the times recorded for some AEs in the Phase 3 clinical trials

PSVT = Paroxysmal Supraventricular Tachycardia; NDA = New Drug Application; RTF = Refusal to File; ECG = electrocardiogram; AEs = adverse events

Comprehensive Data Supports FDA New Drug Application for Rapid Conversion of SVT Episodes to Sinus Rhythm in Adults

	NODE-303
	Phase 3
(	Safety (Repeat Episodes)
	N=503

Presented at The American College of Cardiology Annual Meeting and Published in *The Journal of The American College of Cardiology* April 8, 2024

Following slides from ACC presentation

- >1
- Po ssion

NDA = New Drug Application; SVT = Supraventricular Tachycardia
NB: NODE-301 and RAPID studies also collected Safety information
Source: Milestone Pharmaceuticals Data on File

NODE-303 Phase 3 Study Design

Real-world design:
- No test dose
- No exclusion of Atrial Fibrillation or Atrial Flutter history
- Multiple episodes (up to four)

Screening visit

Key inclusion criteria
- Patients ≥18 years old
- Documented PSVT
- Episodes lasting ≥20 min

Key exclusion criteria
- Evidence of ventricular pre-excitation
- 2nd- or 3rd-degree AV block
- History of severe symptoms of hypotension or syncope during PSVT

Treatment period

Treated PSVT episode
- Patient recognizes symptoms
- Applies cardiac monitor (ECG)
- Attempts VM
- Administers etripamil 70 mg intranasally
- If symptoms persist for 10 min, dose etripamil 70 mg again[a]
- Keep cardiac monitor for at least 1 hr

Follow-up visit
Additional study drug dispensed

Additional PSVT episodes (up to 4 in total) and follow-up visits

End of study

Final visit
Study completion, discontinuation, or after 4th episode

Outcome measures

Safety assessments
- AEs
- SAEs
- Arrhythmias and conduction disorders detected on ECG

Efficacy assessments
- Termination of PSVT
- Frequency of additional medical interventions
- Patient-reported outcomes

[a]Approximately 21 months after the study started, the protocol was amended to allow a repeat 70-mg dose to be self-administered if symptoms persisted 10 minutes following the first dose. If the symptoms of PSVT have not resolved within 20 minutes after study drug administration, the patient may seek appropriate medical care as needed. AE = adverse event. AF = atrial fibrillation. AFL = atrial flutter. AV = atrioventricular. ECG = electrocardiography. PSVT = paroxysmal supraventricular tachycardia. SAE = serious adverse event. SR = sinus rhythm. VM = vagal maneuver.

Most Common (≥5%) Treatment-Emergent Adverse Events Within 24 h After Etripamil Administration (Safety Population)

TEAE 24 h	Single Dose (70 mg) (*N*=428)		Optional Repeat Dose (2 × 70 mg) (*N*=75)		Total Safety Population (*N*=503)	
System organ class Preferred term	Events, *n*	Patients, *n* (%)	Events, *n*	Patients, *n* (%)	Events, *n*	Patients, *n* (%)
Any TEAE 24 h	652	228 (53.3)	124	41 (54.7)	776	269 (53.5)
Gastrointestinal disorders	24	21 (4.9)	5	5 (6.7)	29	26 (5.2)
Nausea	5	5 (1.2)	4	4 (5.3)	9	9 (1.8)
Nervous system disorders	65	42 (9.8)	5	4 (5.3)	70	46 (9.1)
Headache	32	23 (5.4)	4	3 (4.0)	36	26 (5.2)
Respiratory, thoracic, and mediastinal disorders	485	198 (46.3)	97	39 (52.0)	582	237 (47.1)
Nasal discomfort	189	126 (29.4)	43	26 (34.7)	232	152 (30.2)
Nasal congestion	80	59 (13.8)	13	11 (14.7)	93	70 (13.9)
Rhinorrhea	76	54 (12.6)	18	12 (16.0)	94	66 (13.1)
Epistaxis	39	33 (7.7)	6	4 (5.3)	45	37 (7.4)

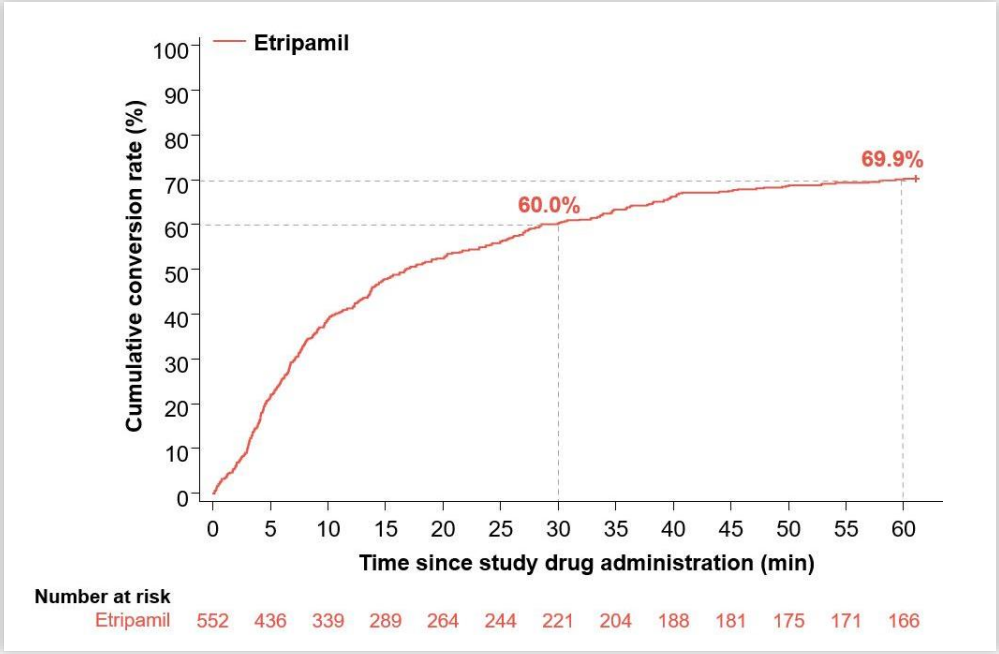
Data are presented for TEAEs 24 h that occurred in ≥5% of patients (by preferred term) in the total safety population. Within each system organ class and within each preferred term, patients with more than one event are counted once only. A TEAE 24 h was defined as an AE starting or worsening within 24 hours after study drug administration, or an AE that started within 12 hours prior to study drug administration. AE = adverse event. TEAE = treatment-emergent adverse event.

TEAEs of Special Interest (Safety Population)

	Single Dose (70 mg) (*N*=428)		Repeat Dose (2 × 70 mg) (*N*=75)		Total Safety Population (*N*=503)	
System Organ Class Preferred Term	**Events, *n***	**Patients, *n* (%)**	**No. of Events**	***n* (%)**	**No. of Events**	***n* (%)**
Any AEs	20	15 (3.5)	3	3 (4.0)	23	18 (3.6)
Cardiac disorders	6	3 (0.7)	3	3 (4.0)	9	6 (1.2)
Sinus arrest (≥3 seconds)	2	1 (0.2)	1	1 (1.3)	3	2 (0.4)
Atrioventricular block, first degree	1	1 (0.2)	1	1 (1.3)	2	2 (0.4)
Atrioventricular block, second degree	2	1 (0.2)	0	0	2	1 (0.2)
Atrioventricular block, third degree	0	0	0	0	0	0
Atrial flutter	0	0	1[a]	1 (1.3)	1	1 (0.2)
Atrial fibrillation	1[b]	1 (0.2)	0	0	1	1 (0.2)
Nervous system disorders	12	10 (2.3)	0	0	12	10 (2.0)
Dizziness	11[c]	9 (2.1)	0	0	11	9 (1.8)
Syncope	1[d]	1 (0.2)	0	0	1	1 (0.2)
Vascular disorders	2	2 (0.5)	0	0	2	2 (0.4)
Hypotension	2[e]	2 (0.5)	0	0	2	2 (0.4)

One transient third-degree heart block occurred after IV adenosine. [a]Moderate severity. [b]Not related to study drug. [c]Two events of dizziness were of moderate severity. [d]One event of syncope was severe. [e]One event of hypotension was mild and one event of hypotension was severe. AE = adverse event. IV = intravenous. TEAE = treatment-emergent adverse event.

Conversion of PSVT to SR: All Episodes (Efficacy Population) Secondary Efficacy Assessments



KM Estimate of PSVT Conversion to Sinus Rhythm	By 30 Minutes	By 60 Minutes
NODE-301	53.7	63.7
NODE-302	60.2	75.1
RAPID	64.3	73.5
NODE-303	**60**	**69.9**

Median time to conversion:
17.0 min (95% CI, 13.9–22.3)

CI = confidence interval. KM = Kaplan Meier. PSVT = paroxysmal supraventricular tachycardia. SR = sinus rhythm.