Milestone PHARMACEUTICALS

Corporate Overview

March 24, 2022

Joseph Oliveto

Chief Executive Officer

Disclaimers

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Milestone (Nasdaq: MIST) - Corporate Highlights

Phase 3 Cardiovascular Company

Targeting Large Areas of Unmet Need

- PSVT
- AFib-RVR
- Additional pipeline opportunities

Paradigm-Changing Approach

- Etripamil: novel calcium channel blocker (IP protection until 2036)
- Shift from the ED to patient self-management

Recent Events Position for Future Success

- First Phase 3 study findings and FDA guidance in PSVT
- Next Pivotal Phase 3 efficacy result in PSVT expected by 2H 2022
- Financial runway expected into 2H 2023

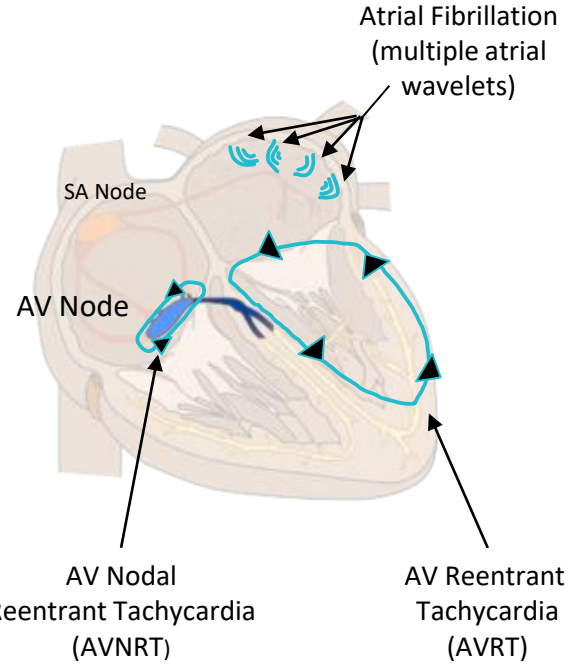
PSVT = Paroxysmal Supraventricular Tachycardia; AFib-RVR = Atrial Fibrillation with Rapid Ventricular Rate; ED = Emergency Department

Atrial Arrhythmias with a Common Patient Burden

Patients with PSVT and AFib-RVR report feeling a loss of control

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	

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



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 Standard of Care for PSVT & AFib-RVR

		PSVT	AFib-RVR
Chronic / preventive		• Chronic oral BBs and CCBs • Reduce number of episodes	• Chronic oral therapies (rate, rhythm, anti-coagulation) • Break-through episodes of RVR in chronic rate/rhythm control patients
		• Catheter ablation • ~80k/yr patients opt for ablation • >90% reported success rate	• Catheter ablation • ~100k patients/yr opt for ablation • ~50-80% reported success rate
Acute		• IV adenosine or DC cardioversion • ~150K ED visits/hospital per year • Many patients wait out episodes	• IV CCBs or DC cardioversion • ~785K ED visits/hospital per year • Many patients wait out episodes

PSVT = Paroxysmal Supraventricular Tachycardia; AFib-RVR = Atrial Fibrillation with Rapid Ventricular Rate; IV = Intravenous; CCBs = Calcium Channel Blockers; DC = Direct Current

Sources: Internal estimates based on market research and longitudinal analysis of Truven/Marketscan and Medicare claims data; Page RL et al, 2015 ACC/AHA/HRS guideline for the management of adult patients with supraventricular tachycardia: executive summary: a report of the ACC/AHA Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. Circulation. 2016;133:e471–e505

Potential Paradigm-Changing Treatment to Empower Patient Control of their Condition

Drawbacks with the current standard of care in the Emergency Department (ED)

- Time consuming
- Anxiety provoking
- Costly
- Often results in a hospital admission
- Experienced by patients as a loss of control

Intervention used by the patient whenever & wherever an episode occurs

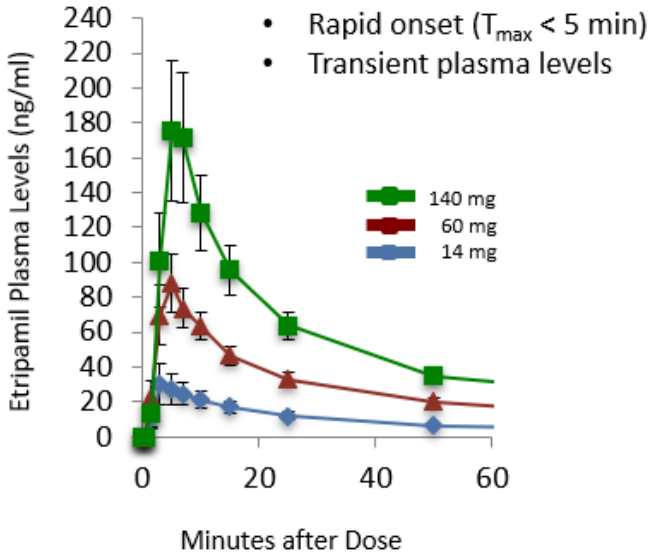
- Reduces ED visits / hospital admissions
- Less need for chronic medications
- Alternative or bridge to ablation procedure

Etripamil Nasal Spray is Designed to be Fast, Convenient, and Empowering

Prospectively designed to treat common tachycardias outside the Emergency Department (ED)

	Etripamil
Class	Novel CCB
Potency (IC_{50})	11 nM
Metabolism	Rapid: Esterase-mediated

- Clinically-validated mechanism
  - Calcium channel blockers (CCBs) prolong refractoriness and slow conduction over the AV node
- Rapid onset of action
- Convenient patient self-administered nasal spray
- Short duration of action



AV = Atrio-ventricular; nM = nanomolar

Error bars indicate standard error of the mean

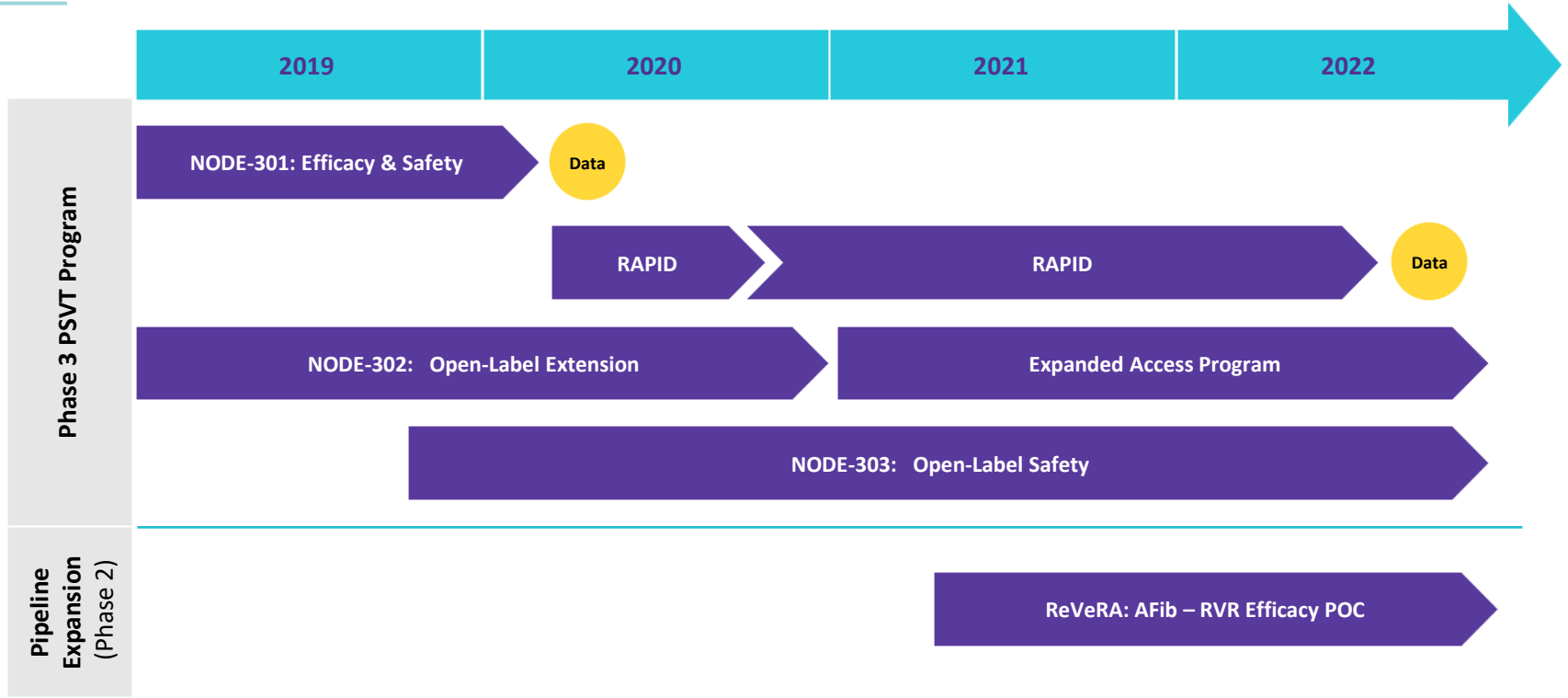
Clinical Program Overview for Etripamil

Clinical development programs designed to support NDA filing in PSVT, while concurrently building safety database and running Phase 2 ReVeRA to support AFib-RVR program

NODE-1 PSVT	ReVeRA AFib-RVR	NODE-301 PSVT	RAPID PSVT	NODE-303/302 PSVT
Phase 2	**Phase 2**	**Phase 3**	**Phase 3**	**Phase 3**
Efficacy	Efficacy POC	Efficacy	Efficacy	Safety
Published	Enrolling	Complete	Enrolling	Enrolling/ Complete
Electrophysiology Lab	Emergency Department	At home	At Home	At Home
N= 104 1:1 randomized	N=50 1:1 randomized	N=419 2:1 randomized	N~500 1:1 randomized	N ~1000 Open label

POC = Proof of Concept; AFib-RVR = Atrial Fibrillation with Rapid Ventricular Rate; PSVT = Paroxysmal Supraventricular Tachycardia

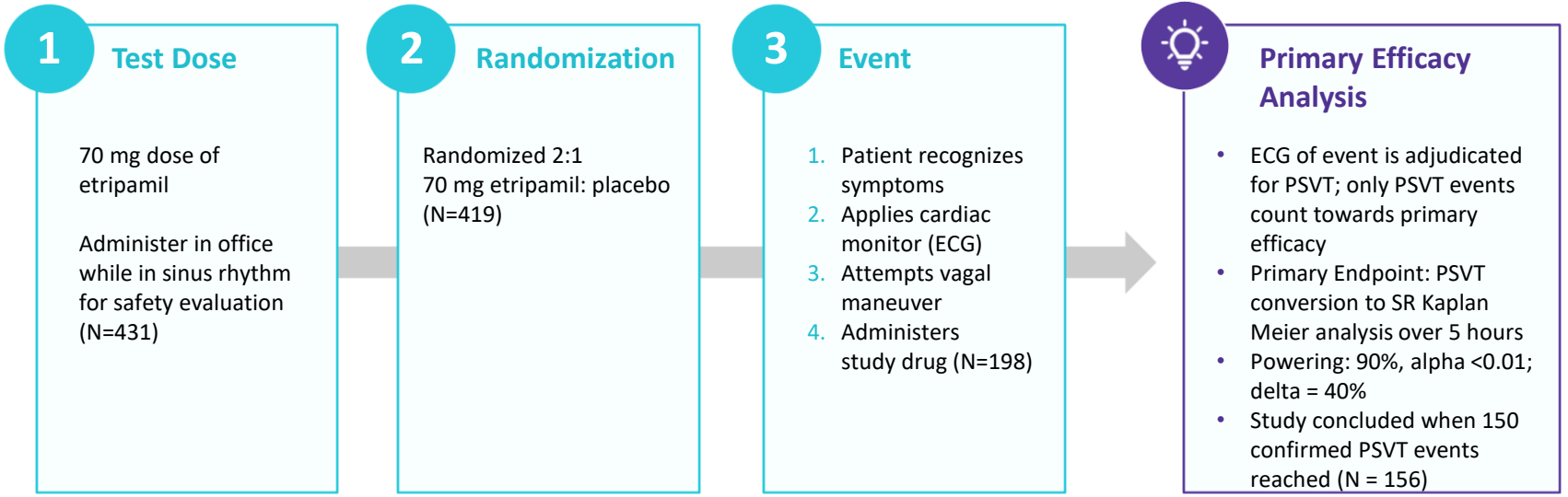
Development Plan for Etripamil



AFib-RVR = Atrial Fibrillation with Rapid Ventricular Rate; POC = Proof of Concept

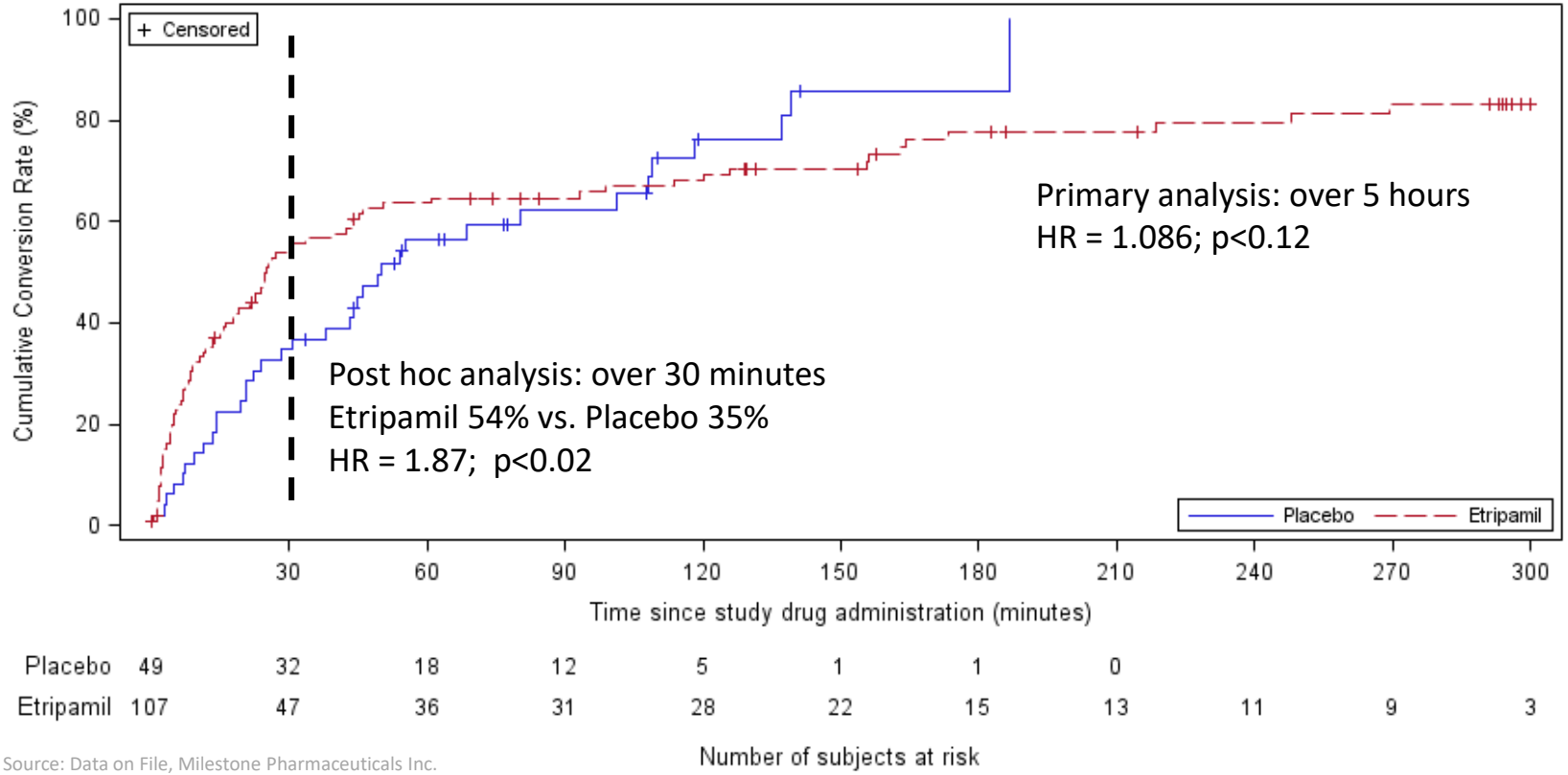
NODE-301 Study Design

NODE-301 patients taking etripamil had no serious adverse events



SR = Sinus Rhythm; ECG = Electrocardiogram; PSVT = Paroxysmal Supraventricular Tachycardia

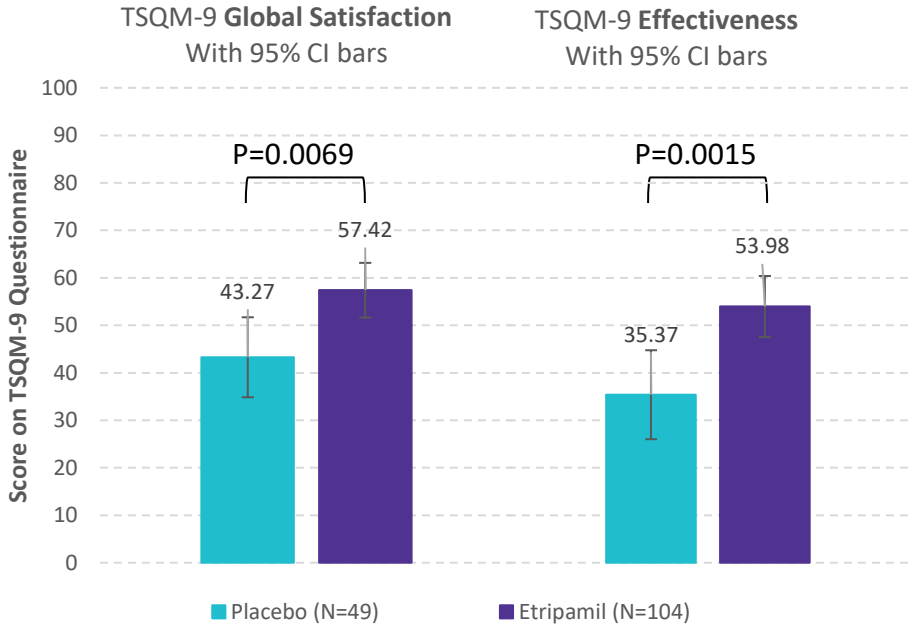
NODE-301 Kaplan-Meier Plot of Conversion to Sinus Rhythm

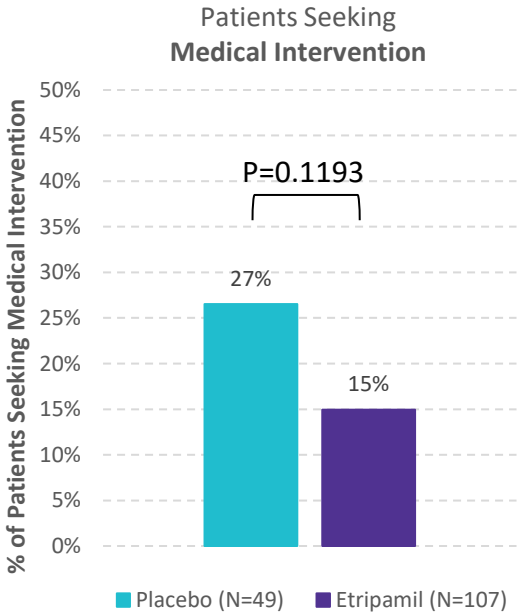


Source: Data on File, Milestone Pharmaceuticals Inc.

NODE-301 Key Secondary Endpoints

Key secondary endpoints from NODE-301 support benefit of etripamil to patients and payers





NODE-301 Safety Analysis

Randomized Treatment Emergent Adverse Events (RTEAE)	Etripamil N=138 (%)	Placebo N=60 (%)
Subjects with any RTEAE	53 (38.4)	12 (20.0)
Maximum severity of RTEAE		
Mild	45 (32.6)	10 (16.7)
Moderate	8 (5.8)	3 (3.3)
Severe	0 (0.0)	0 (0.0)
Most Common Adverse Events (>5%)		
Nasal discomfort	27 (19.6)	4 (6.7)
Nasal congestion	11 (8.0)	2 (3.3)
Epistaxis	9 (6.5)	0 (0.0)
Rhinorrhea	8 (5.8)	1 (1.7)
Throat irritation	7 (5.1)	1 (1.7)

RTEAE timing: up to 24 hours following double-blind study drug administration

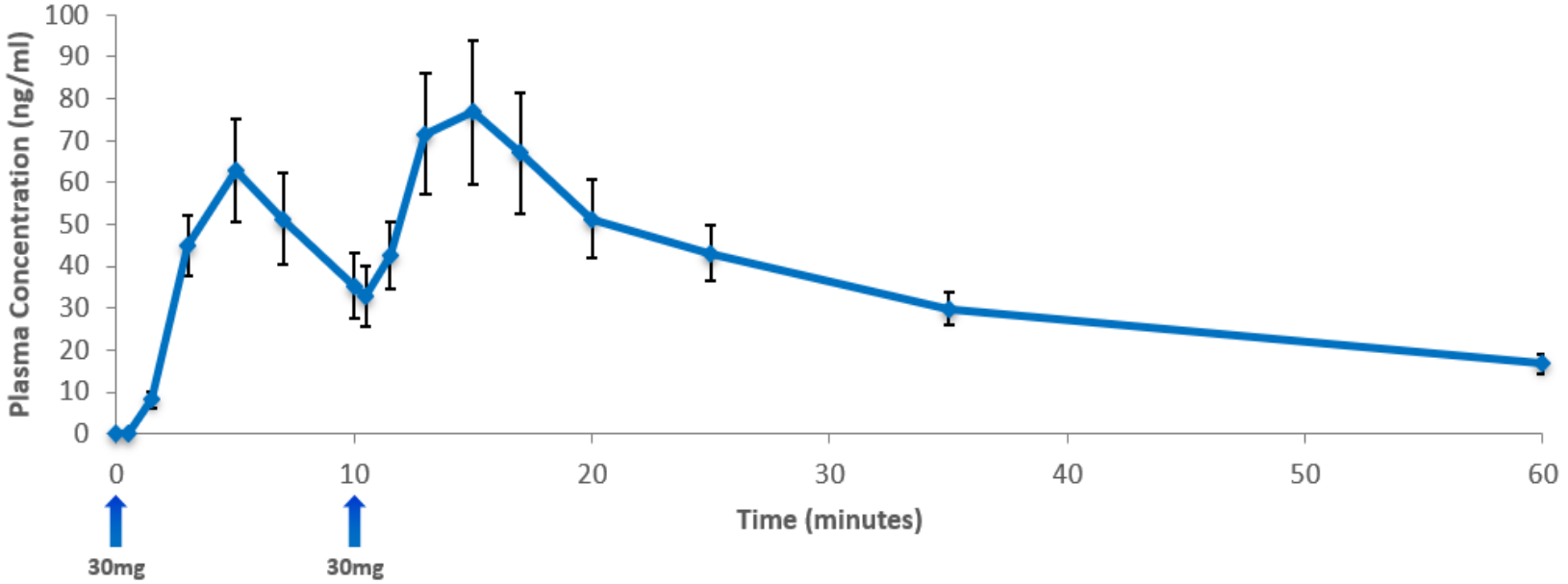
Source: Data on File, Milestone Pharmaceuticals Inc.

FDA Guidance Following NODE-301 Data

- NODE-301 post hoc analysis plus one additional study (RAPID) together can be used to potentially fulfill the efficacy requirement for an NDA filing for etripamil in PSVT
  - Primary analysis of 30-minute observation window
  - RAPID Study target p-value of $p < 0.05$
- Evaluation of higher exposures to improve efficacy and clinical meaningfulness
- RAPID to utilize a 70 mg repeat dosing regimen
  - Patients who still have symptoms 10 min after their drug administration will take a second dose of study drug
  - Pool the single dose with the repeat dose administrations to maintain power and compare etripamil to placebo

PK of Etripamil 30 mg Repeat Administration at T=10 min
(Study MSP-2017-1096)

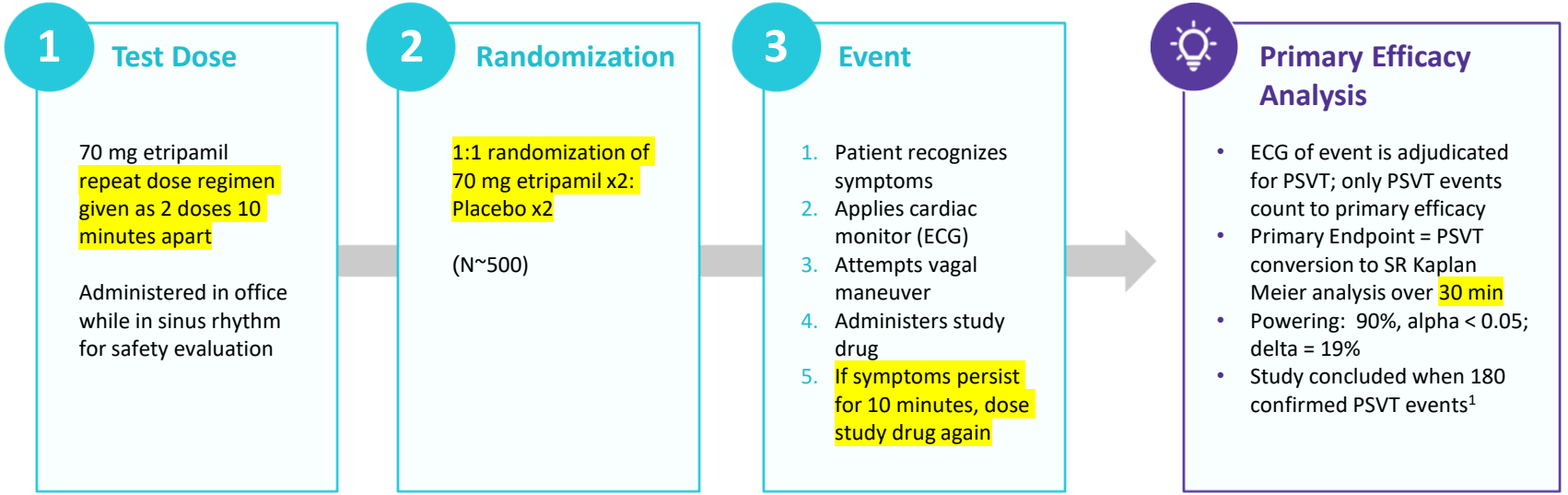
Repeat administration increases both Cmax and AUC



N=7, Error bars are standard error

Source: Data on File, Milestone Pharmaceuticals Inc.

RAPID Study Design



[1] includes ~30 events expected to be treated with the single dose double-blind study drug administration from NODE-301 patients who experienced an event prior to the RAPID study being available

ReVeRA – Proof of Concept for AFib with Rapid Ventricular Rate

PSVT - Lead Indication in Phase 3 Registration Studies;
AFib-RVR - Second Indication in Phase 2 POC Study

NODE-1 PSVT	ReVeRA AFib-RVR	NODE-301 PSVT	RAPID PSVT	NODE-303/302 PSVT
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SR = Sinus Rhythm; ECG = Electrocardiogram; PSVT = Paroxysmal Supraventricular Tachycardia; AFib-RVR = Atrial Fibrillation with Rapid Ventricular Rate; POC = Proof of Concept

The ReVeRA Trial

Reduction of **Ve**ntricular **R**ate in Patients with **A**trial Fibrillation

1 Patient presents to ED with episode of AFib-RVR

Inclusion:
- Atrial Fibrillation ≥ 1 hour
- Ventricular Rate ≥ 110 bpm

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

2 Dosing & Assessment

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

Efficacy Analysis

- Primary: Maximum reduction in ventricular rate within 60 min
  - N=50: 90% powered to detect 20 bpm difference in max reduction, α=0.05;
- Time from drug administration to lowest ventricular rate
- Time to and duration of ventricular rate reductions
  - <100 bpm, ≥ 10% reduction, ≥ 20% reduction
- Patient satisfaction with treatment (TSQM-9)

CHADs 0 = No Heart Failure/No Hypertension/Age < 65/No Diabetes/No History of Stroke or TIA/No Coronary ischemic disease; OAC = Oral Anti-coagulant; AFib-RVR = Atrial Fibrillation with Rapid Ventricular Rate; TSQM-9, Treatment Satisfaction Questionnaire for Medication; ED = Emergency Department

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Commercial Opportunity

Etripamil – Addressing Market Needs in PSVT and AFib-RVR

Potential for high receptivity to etripamil across stakeholders

Future with Etripamil – a Potentially Better Treatment Option

Patients

- Self-management of acute episodes
- Reduces ED visits/hospital admissions

Physicians (Cards, EPs, PCPs)

- Better risk/benefit profile
- Expected to have significant adoption in unablated patients

Payers

- Reduction in ED/hospital admissions
- Improvement in patient satisfaction

Cards = Cardiologists, EPs = Electrophysiologists, PCPs = Primary Care Providers, PSVT = Paroxysmal Supraventricular Tachycardia, ED = Emergency Department

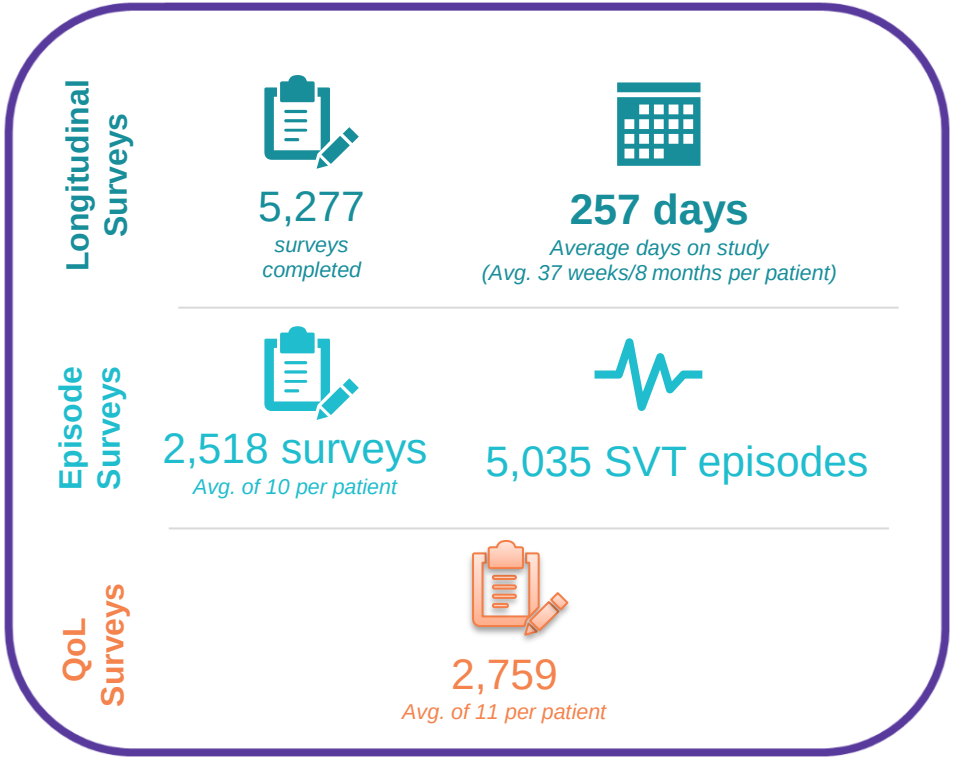
Sources: Internal market research

New Data Enhances Understanding of Burden of PSVT

Analysis of Prospective Patient Reported Outcomes Longitudinal Data

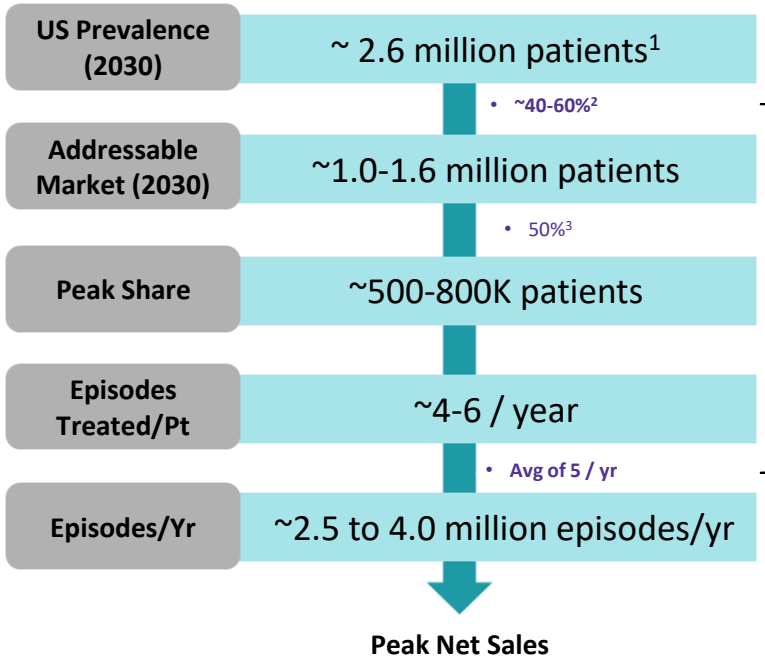
247 US & UK patients

- **Phase 1: Baseline Survey** *(medical and SVT episode history)*
- **Phase 2: Longitudinal Weekly Surveys** *(episode survey if experienced an episode, QoL survey if not)*



Source(s): PSVT patient market research, 2019 (BluePrint Research Group, n=247, n=198 US & n=49 UK)

Peak US Market Opportunity for Etripamil 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

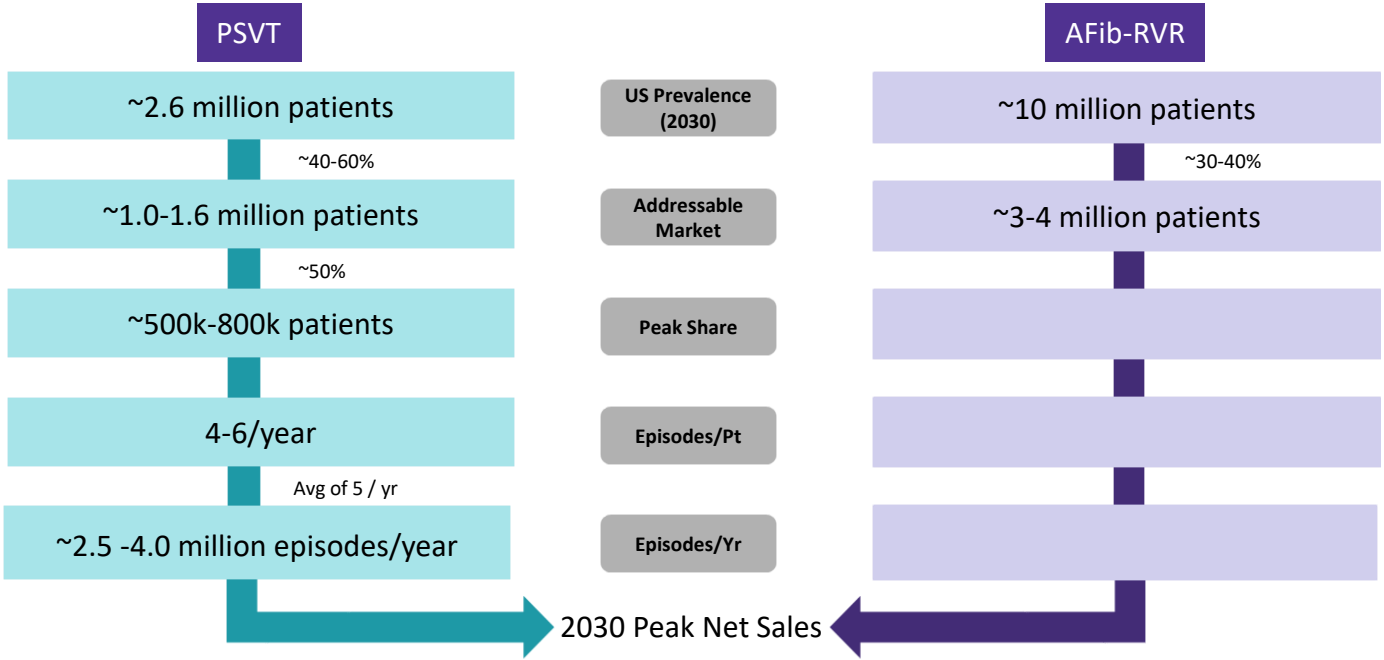
35% last at least 30 minutes

*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).

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

Market research suggests a TAM of 4+ million patients across both PSVT and AFib-RVR indications



AF – RVR = Atrial Fibrillation with Rapid Ventricular Rate; TAM = Target Addressable Market; Internal estimates based on market and outcomes research, Milestone Pharmaceuticals

Sources: Internal estimates based on market research, Milestone Pharmaceuticals Inc.

Finances – as of December 31, 2021

- Cash, cash equivalents and short-term investments of $114.1M
- Cash funds operations past guidance for top-line data and into 2nd half of 2023
- Equity - 42.2M in shares and pre-funded warrants outstanding
  - 29.9M common shares
  - 12.3M pre-funded warrants

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Thank you

Management Team

Joseph Oliveto
Chief Executive Officer

Amit Hasija
Chief Financial Officer

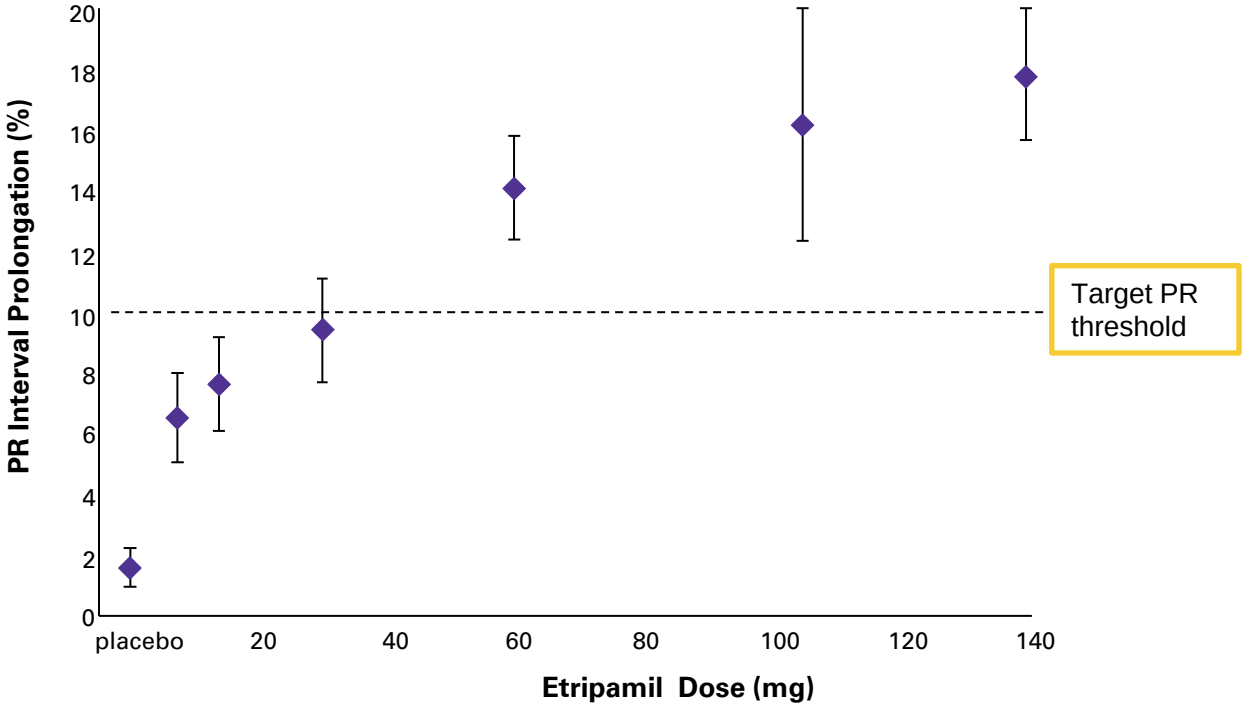
David Bharucha, MD, PhD
Chief Medical Officer

Francis Plat, MD
Chief Scientific Officer

Lorenz Muller
Chief Commercial Officer

Jeff Nelson
Chief Operating Officer

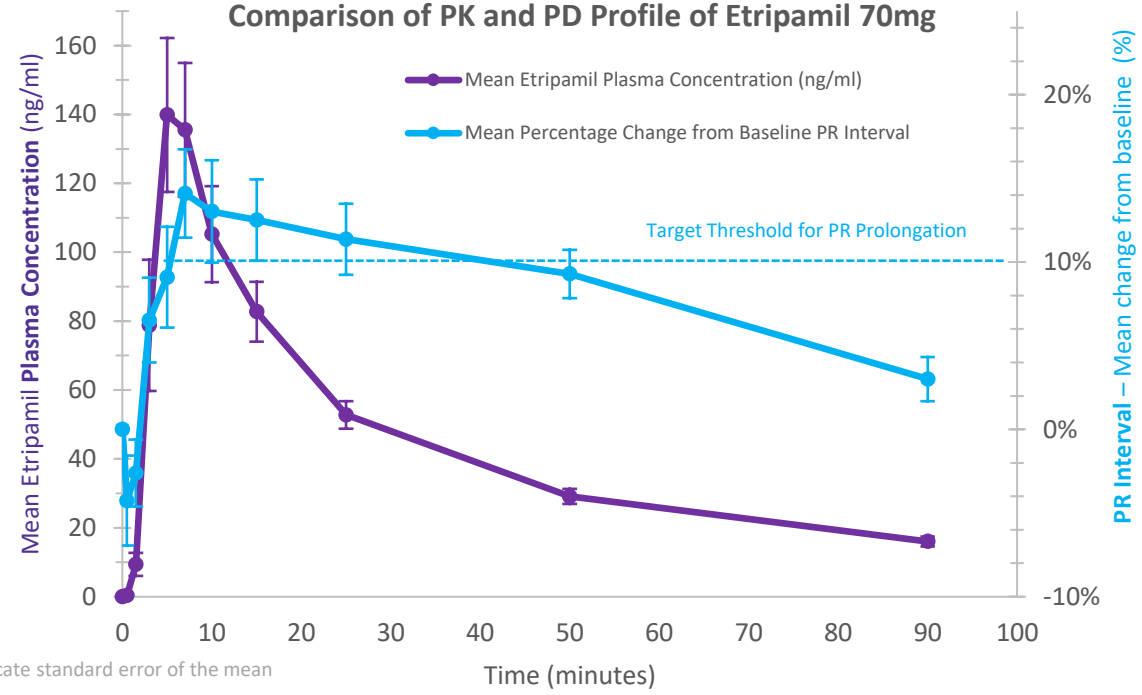
Etripamil Phase 1 Pharmacology
PR Prolongation Used to Select Doses for Phase 2



Error bars indicate standard error of the mean

Etripamil Nasal Spray Pharmacological Results (NODE-102)

Anticipated therapeutic effect within 45 minutes; peak within 10 minutes

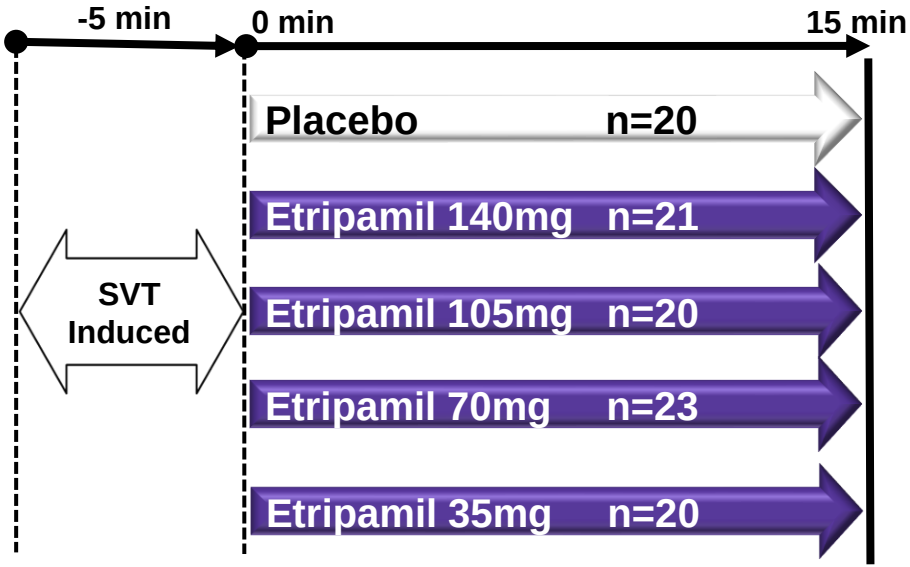


N=24; Error bars indicate standard error of the mean

Phase 2a/b Study Design (NODE-1)

Objectives: Demonstrate superiority of etripamil over placebo in terminating SVT and dose ranging trend analysis

PSVT patients with scheduled cardiac ablation (EP lab)

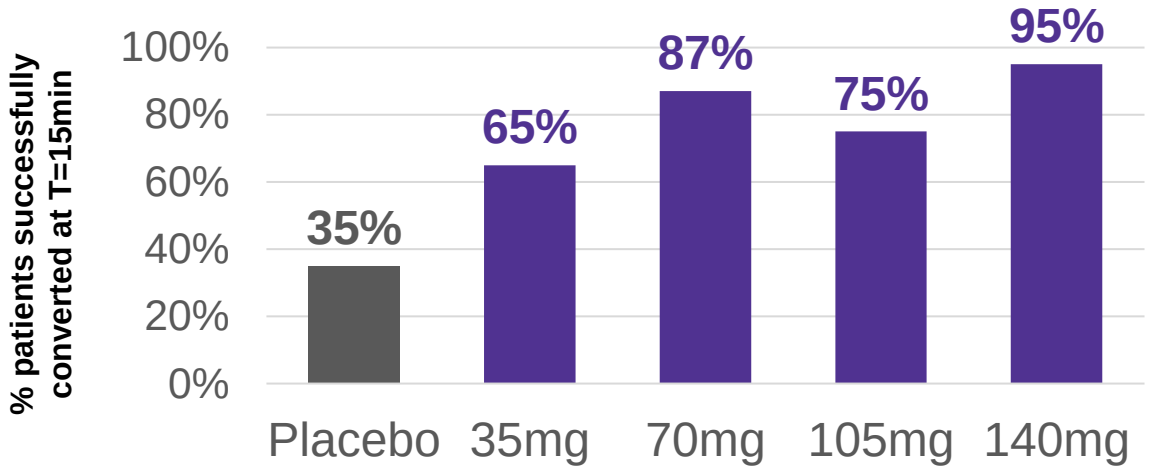


Endpoint: conversion to sinus rhythm within 15 minutes
>80% power to show a 50% absolute difference vs. placebo

EP = electrophysiology, SVT = supraventricular tachycardia, PSVT = Paroxysmal Supraventricular Tachycardia

Phase 2 Primary Endpoint

Etripamil three highest doses demonstrated 75-95% conversion rates which are statistically significant compared to placebo

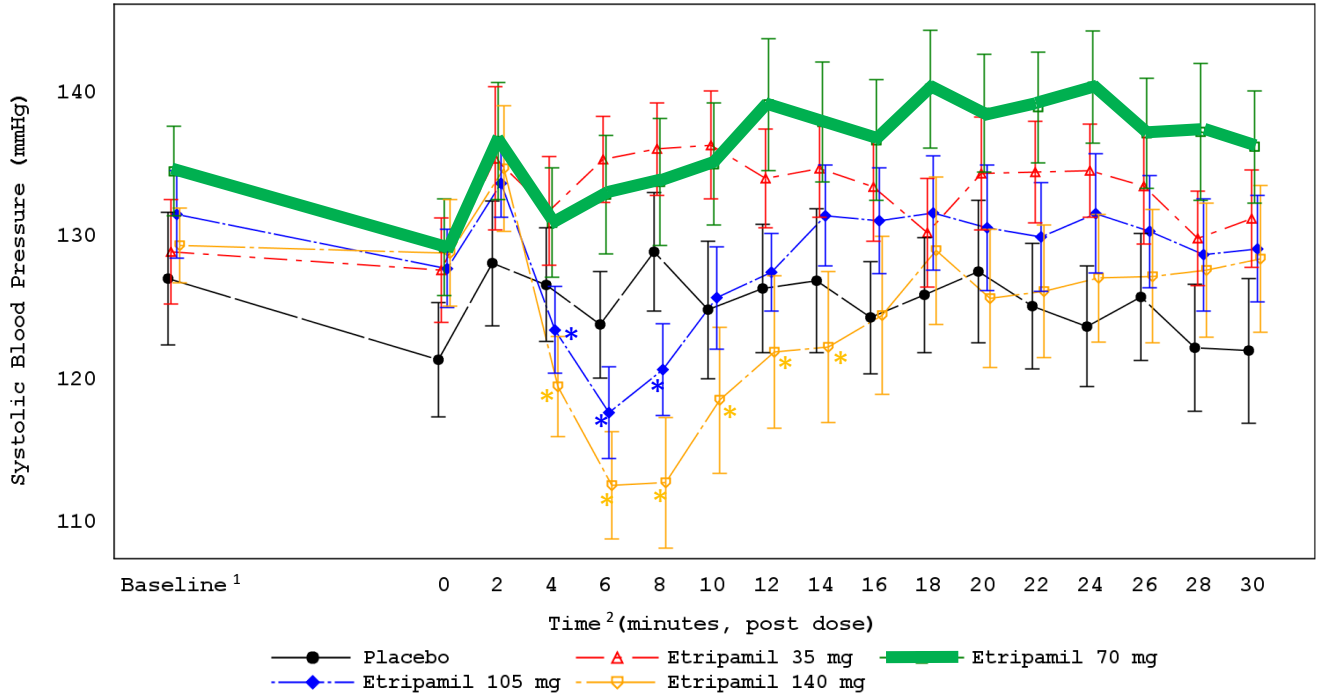


# patients converted at 15 min	7/20	13/20	20/23	15/20	20/21
p-value		0.1128	0.0006	0.0248	<.0001

Source: Stambler, B.S. et al.; Etripamil Nasal Spray for Rapid Conversion of Supraventricular Tachycardia to Sinus Rhythm; J Am Coll Cardiol. 2018;72(5):489–97

Phase 2 Mean Systolic Blood Pressure Effects

70 mg of etripamil showed no decrease in blood pressure; higher doses transient decreases

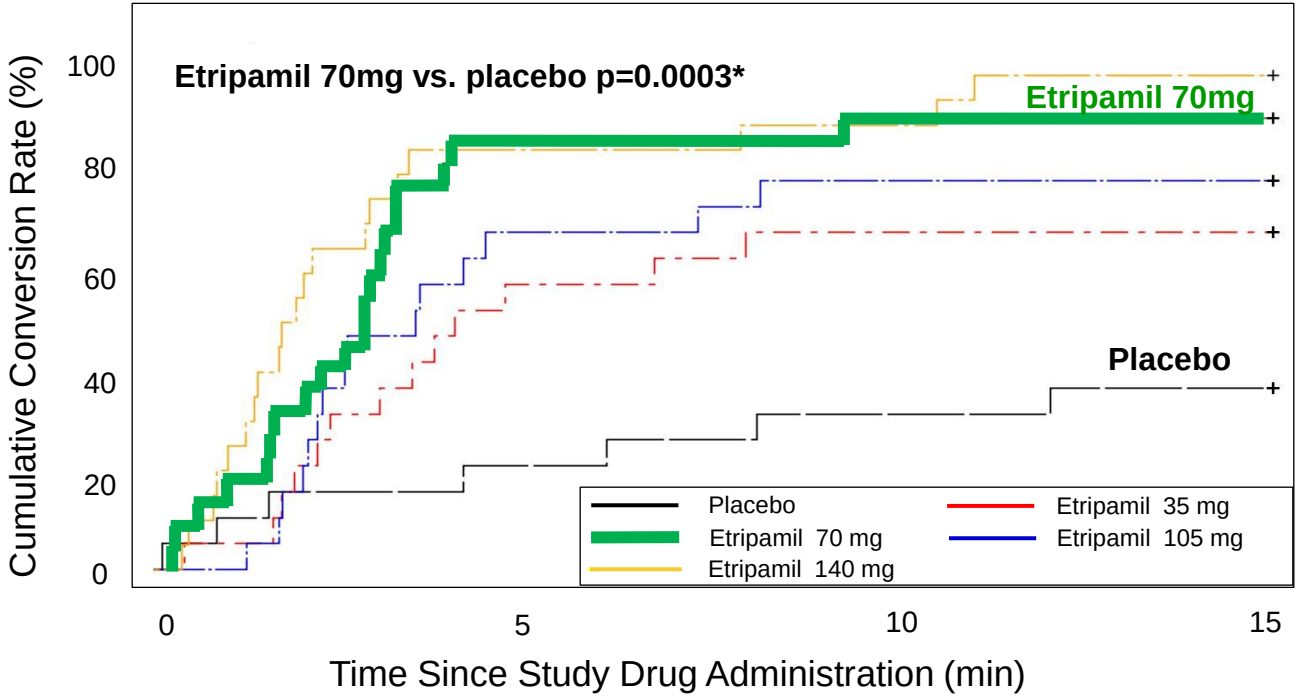


[1] Baseline is defined as the average of the 20-min and 10-min pre-dose measurements. [2] Time 0 is defined as the average of the measurements during supraventricular tachycardia between 5 and 0 min before study drug administration. *p < 0.05 versus baseline.

Source: Stambler, B.S. et al.; Etripamil Nasal Spray for Rapid Conversion of Supraventricular Tachycardia to Sinus Rhythm; J Am Coll Cardiol. 2018;72(5):489–97

Phase 2 Time to Conversion

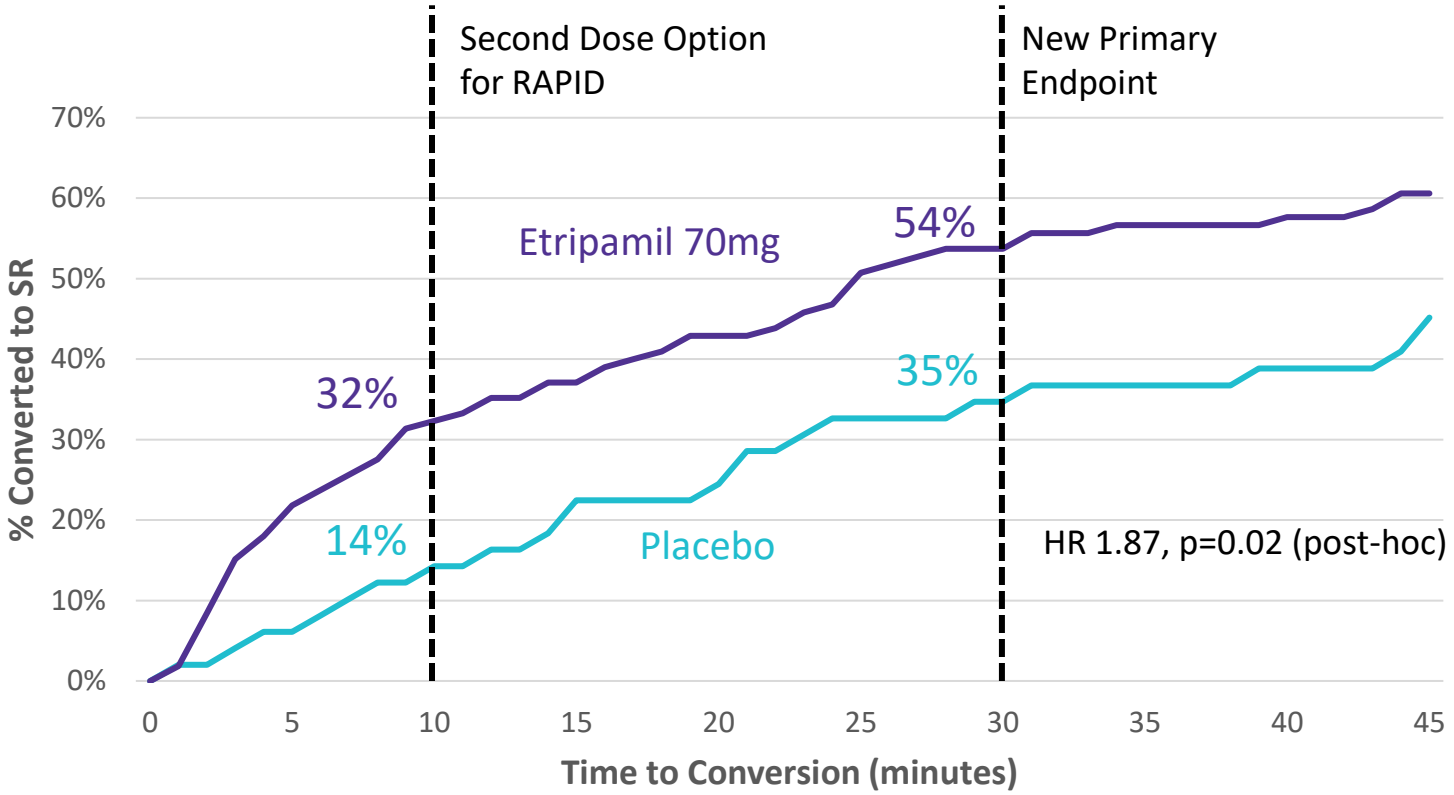
70mg etripamil dose showed rapid time to conversion (median < 3 min)



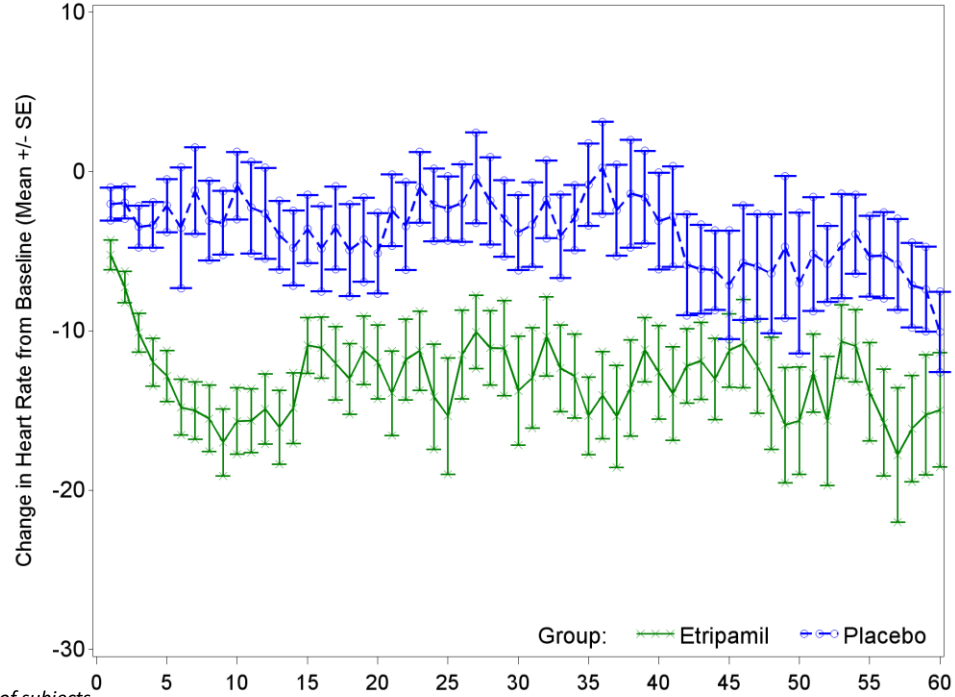
*Hazard Ratio and 95% Confidence Intervals etripamil 70mg vs. placebo; 4.99 (2.09, 11.93)

Source: Stambler, B.S. et al.; Etripamil Nasal Spray for Rapid Conversion of Supraventricular Tachycardia to Sinus Rhythm; J Am Coll Cardiol. 2018;72(5):489–97

NODE-301 Efficacy– Time to Conversion over 45 Minutes



Effect of Etripamil on Heart Rate (HR) while in SVT (NODE-301 Study)



Number of subjects

Placebo	48	41	41	28	20	17
Etripamil	102	69	60	41	31	30

- Improvement in HR observed within first minute, with maximum difference at 10 minutes
- Differences were statistically significant through 40 minutes
- Reduction in heart rate in etripamil group sustained for 1 hour
- Some patients reported symptom relief even though they had not converted to sinus rhythm

Source: Ip, JE et al; "Etripamil Nasal Spray Reduces Heart Rate in Patients With Paroxysmal Supraventricular Tachycardia Prior to Conversion to Sinus Rhythm"; Poster presentation at AHA Scientific Sessions, November 14, 2021.

NODE-301 Safety Analysis

Randomized Treatment Emergent Adverse Events (RTEAE)	Etripamil N=138	Placebo N=60
Subjects with any RTEAE	53 (38.4)	12 (20.0)
Maximum severity of RTEAE		
Mild	45 (32.6)	10 (16.7)
Moderate	8 (5.8)	3 (3.3)
Severe	0 (0.0)	0 (0.0)
Subjects with any Serious Adverse Event (SAE)	0 (0.0)	1 (1.7)
Subjects with any SAE related to study drug	0 (0.0)	0 (0.0)
Subjects with any AE leading to death	0 (0.0)	0 (0.0)
Subjects with AE leading to study drug discontinued	0 (0.0)	0 (0.0)

RTEAE timing – up to 24 hours following double-blind study drug administration

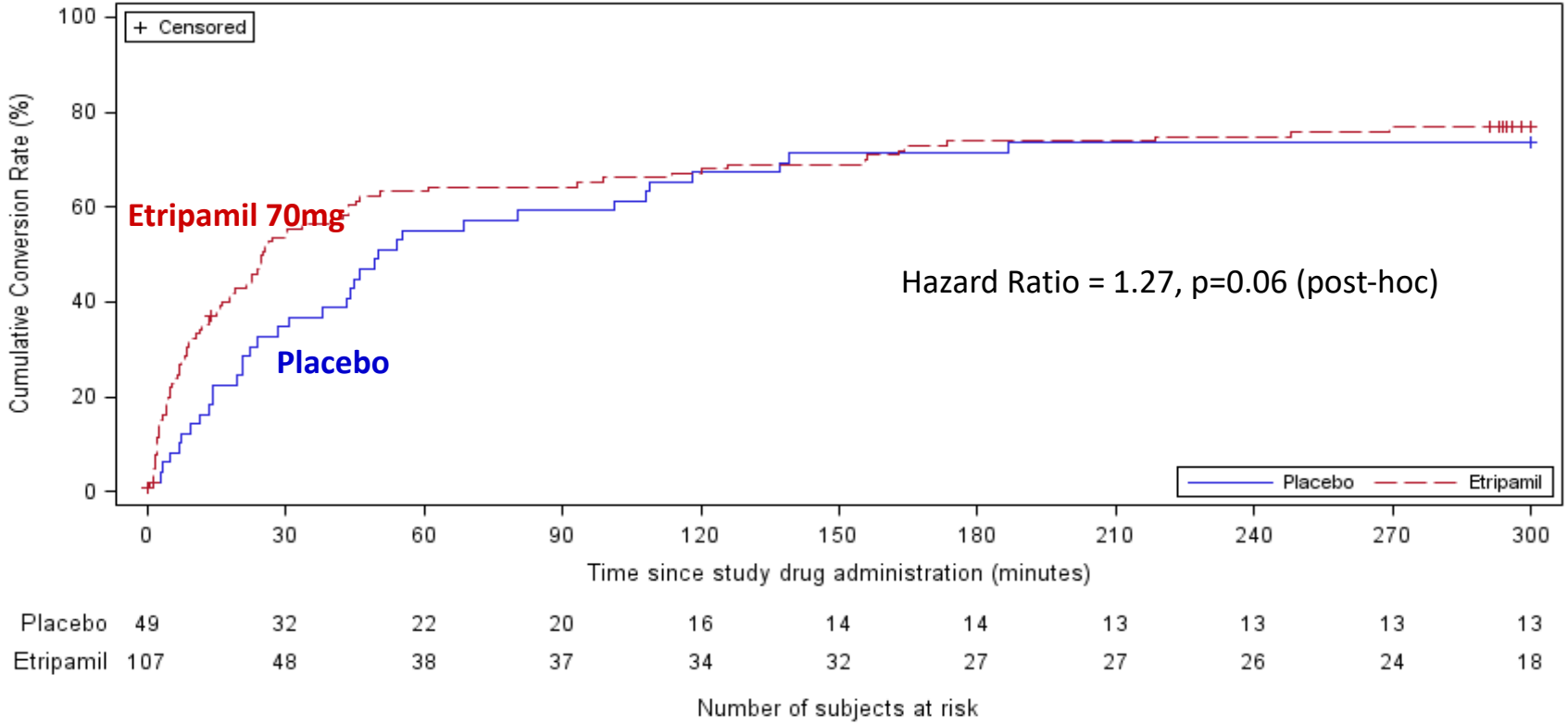
Source: Data on File, Milestone Pharmaceuticals Inc.

NODE-301 Safety Analysis

Randomized Treatment Emergent Adverse Events	Etripamil (N=138)	Placebo (N=60)
Nasal discomfort	27 (19.6)	4 (6.7)
Nasal congestion	11 (8.0)	2 (3.3)
Epistaxis	9 (6.5)	0 (0.0)
Rhinorrhea	8 (5.8)	1 (1.7)
Throat irritation	7 (5.1)	1 (1.7)
Headache	4 (2.9)	0 (0.0)
Sneezing	3 (2.2)	0 (0.0)
Atrioventricular (AV) block first degree	2 (1.4)	0 (0.0)
Dysgeusia	2 (1.4)	1 (1.7)
Sinus congestion	1 (0.7)	2 (3.3)
Rhinalgia	1 (0.7)	1 (1.7)
Ventricular tachycardia	1 (0.7)	1 (1.7)
Lacrimation increased	1 (0.7)	1 (1.7)
Burning sensation	1 (0.7)	0 (0.0)
Presyncope	1 (0.7)	0 (0.0)
Migraine	1 (0.7)	0 (0.0)

Stambler, BS et al; Etripamil Nasal Spray for Acute Termination of Spontaneous Episodes of PSVT (NODE-301); Heart Rhythm Society Late Breaking Clinical Trails Randomized Trials D-LBCT01; Presented Online May 8, 2020

NODE-301 Conversion up to Hour 5 with Medical Intervention Patients Analyzed as Treatment Failures at 5 hours (post-hoc)



Subjects who convert following medical assistance are censored at 5 hours. Subjects who present missing data from time t to the end are censored at the time of last available data. Subjects who do not convert or are not censored before 5 hours are censored at 5 hours

PSVT & Atrial Fibrillation Populations in the US

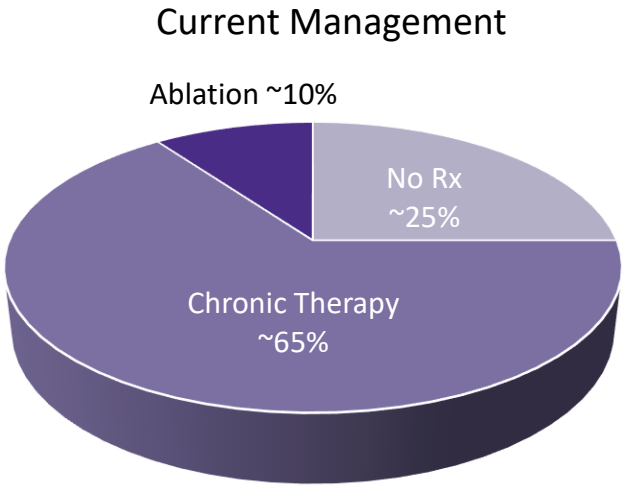
	PSVT	Atrial Fibrillation
Total Patients (2030)	**2.6 Million[3]**	**10 Million[1]**
Discharged ED Visits & Hospital Admissions (2016)[2]	**145 Thousand**	**785 Thousand**
Target Market Addressable (2030) (Patient Population)	**1.0-1.6 Million[5]**	**~3-4 Million[4]**

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.** 30%-40% of AF patients have >1 symptomatic episode per year of AF with RVR requiring treatment, Triangle Insights Group Market Research, N=25, January 2021. **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.

Current US PSVT Market

Total annual US healthcare expenditures of ~$3B

- Prevalence ~2M diagnosed PSVT patients
- ~300K newly diagnosed per year
- ~600K patients treated per year
- >150K ED/hospital visits per year
- ~80K ablations per year



Source: 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.

Current Standard of Care for PSVT

Current acute treatment options are invasive, inconvenient, anxiety-provoking and/or costly

Chronic / preventive

- Chronic oral medication with modest efficacy and unpleasant side effects
- 4-7 episodes/year despite preventive medications

- Catheter ablation
- ~80K ablations/year
- Only ~10% of patients opt for ablation

Acute

- IV adenosine or DC cardioversion in the ED
- >150K ED visits/hospital admissions per year
- Many patients endure episodes when they occur

DC = Direct Current

Sources: Internal estimates based on market research and longitudinal analysis of Truven/Marketscan and Medicare claims data; Page RL et al, 2015 ACC/AHA/HRS guideline for the management of adult patients with supraventricular tachycardia: executive summary: a report of the ACC/AHA Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. Circulation. 2016;133:e471–e505

Management of Patients with PSVT and Call Point Targeting

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

		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

Source: Internal market research

PRO Analyses Provide A Clearer Picture of Burden of PSVT than Market Research Alone

Unablated patients experience 5-6 episodes per year relevant for etripamil use

Episode Freq. for Patients <u>not</u> Receiving Catheter Ablation	**Market Research[1]** *(annual recall, n=250)*	**PRO Longitudinal Data[2]** *(weekly tracking, n=247)*
Annual Episode Freq	4-7 episodes / year	15 episodes/year*
% of patients with multiple 10+ min episodes / year	40%	68%
Annual Freq of Moderate-Severe 5+ min episodes	*N/A*	5-6 episodes / year*

Weekly tracking shows that patients are experiencing more episodes than previously thought – but that they tend to recall the moderate/severe episodes of longer duration (e.g., 5+ minutes)

*Patients on study at least 6 months were used to project annual episode frequency. Sample projections were weighted by stated episode frequency from an intake survey

Sources: Internal estimates based on market and outcomes research, Milestone Pharmaceuticals. 1. PSVT patient market research conducted by Triangle Insights Group, 2018 (n=250). 2. PSVT patient market research conducted by BluePrint Research Group, 2019 (n=247).

Core PSVT Market is Addressable Now, with Potential for Expansion

Target PSVT Market

Expanded Market

Undiagnosed PSVT Patients — ~600-900k[1]

Diagnosed, Untreated PSVT Patients — ~1.4 Million[2]

Core Market

Diagnosed, Annually Treated PSVT Patients — ~600k/year[3]

Strategy to Address

- Increase speed and rates of diagnosis through wearable technology
- Re-engage in healthcare system through DTC promotion
- MIST specialty sales force
- Partner majority of PCP promotion

Source: 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 2M and annual treatment rate of ~600k 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.

Estimating Prevalence, Incidence, and Annually Treated Patients Using Longitudinal Claims Data

- Analyzed commercial and Medicare claims data over a 9-year period, where patients were required to have 5 years of continuous enrollment
  - ✓ 1+ PSVT code required in the ED or inpatient setting (unique patients managed acutely)
  - ✓ 2+ PSVT codes required in the outpatient setting (additional unique patients managed chronically)

Age Group	Year 1	Year 2	Year 3	Year 4	Year 5	Total
Age < 65	271,024	196,653	169,988	155,966	145,485	939,116
Age 65+	377,493	220,596	209,358	188,925	166,286	1,162,658
All Ages	648,518	417,249	379,346	344,891	311,771	2,101,775

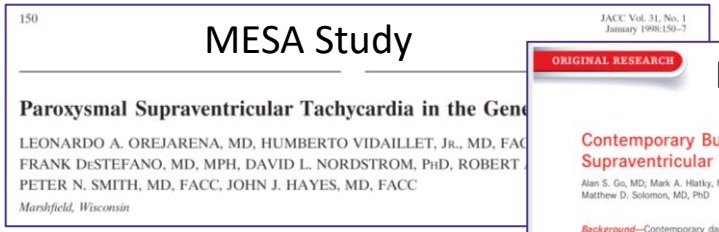
Annually Treated PSVT Patients

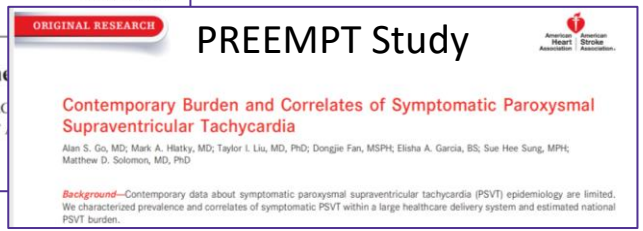
Incident PSVT Patients

Prevalent PSVT Patients

Source: 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.

Published Disease Data Likely Under-Reports Burden of PSVT





Strengths

- Provides important demographic and clinical characteristic data on patients with PSVT
- Positive Predictive Values from PREEMPT useful
- Less than 40% of incident cases in MESA would have been detected by PSVT ICD-9 Code 427.0

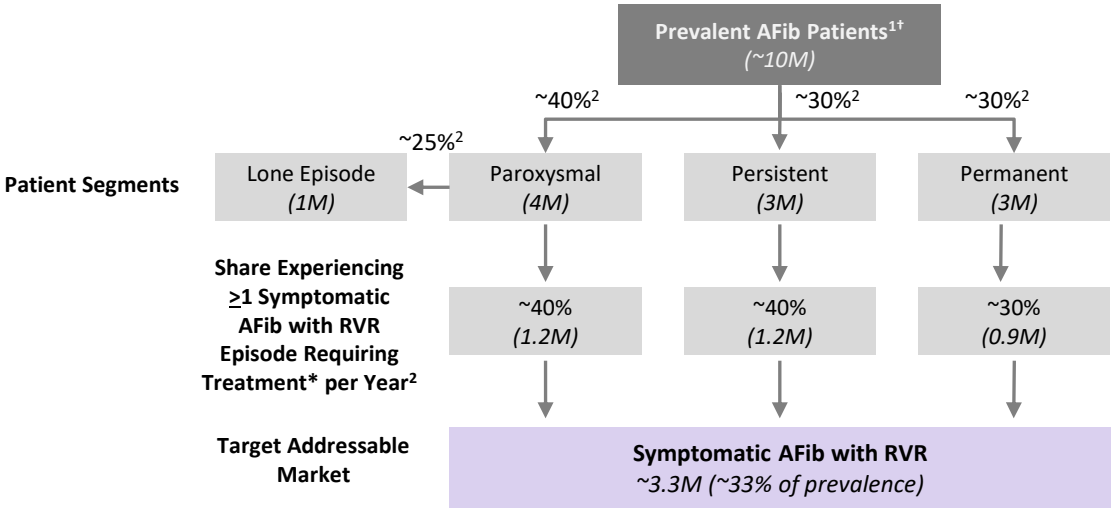
Weaknesses

- Data only from patients presenting to healthcare settings acutely, with the episode confirmed on ECG during the encounter
- PSVT episodes were only adjudicated during the first healthcare encounter with a PSVT or PSVT-related code in PREEMPT
- Non-representative, small, and non-contemporary population (MESA)

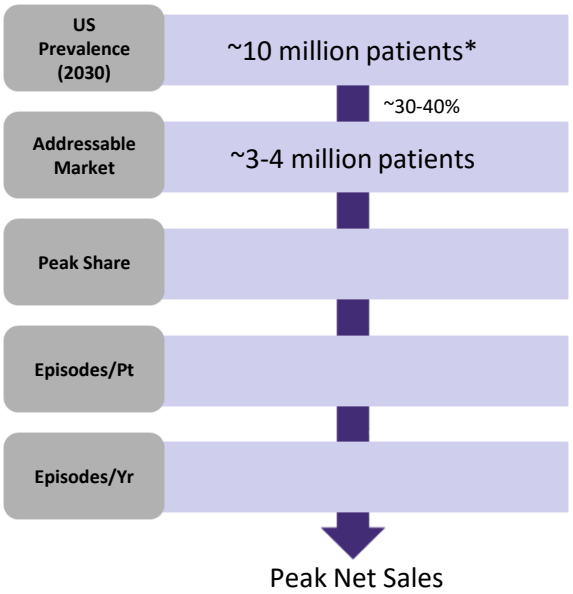
Source: Orejarena LA, Vidaillet H Jr, DeStefano F, Nordstrom DL, Vierkant RA, Smith, PN, Hayes JJ. Paroxysmal supraventricular tachycardia in the general population. J Am Coll Cardiol. 1998;31:150–157. Alan S. Go, MD; Mark A. Hlatky, MD; Taylor I. Liu, MD, PhD; Dongjie Fan, MSPH; Elisha A. Garcia, BS; Sue Hee Sung, MPH; Matthew D. Solomon, MD, PhD. Contemporary Burden and Correlates of Symptomatic Paroxysmal Supraventricular Tachycardia. J Am Heart Assoc. 2018;7:e008759. DOI: 10.1161/JAHA.118.008759.

Peak US Market Opportunity for Etripamil in AFib-RVR

Market research suggests a target addressable market of ~3-4 million patients for AFib-RVR by 2030



*Treatment was defined as either seeking treatment at the emergency department or outpatient clinic or via self-administration of treatments at home or other unsupervised setting



AFib-RVR = Atrial Fibrillation with Rapid Ventricular Rate
*Reflects the midpoint of published estimates (~8M to ~12M by 2025 or 2030)

1. Colilla et al., Am. J. Cardiol. 2013, 112(8), 1142-1147; Miyasaka et al., Circulation, 2006, 114, 119-125; Colilla et al., Am. J. Cardiol. 2013, 112(8), 1142-1147 ; American Heart Association **2**. HCUP ED & Admissions Data (2016), accessed January 2021. **2.** Quantitative Survey conducted by Triangle Insights, May 2021, N=250 Clinical Cardiologists, Interventional Cardiologists, and Electrophysiologists

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