Milestone PHARMACEUTICALS

Corporate Overview

July 2021

Joseph Oliveto

President & CEO

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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 possibility that data will support FDA approval, (iii) the potential market size and the rate and degree of market acceptance of 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, and (iv) the sufficiency of Milestone's capital resources. 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 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 etripamil for PSVT, 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, 2020, under the caption "Risk Factors." 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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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 through mid-2023

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

PSVT & AFib-RVR Populations in the US

	PSVT	Atrial Fibrillation
Total Patients (2016)	**2 Million[4]**	**5 Million[1]** (expected to grow to 7-12M by 2030[1,3])
Discharged ED Visits & Hospital Admissions (2016)[2]	**145 Thousand**	**785 Thousand**
Target Market Addressable (Patient Population)	**0.8 – 1.2 Million[6]**	**2 Million[5]**

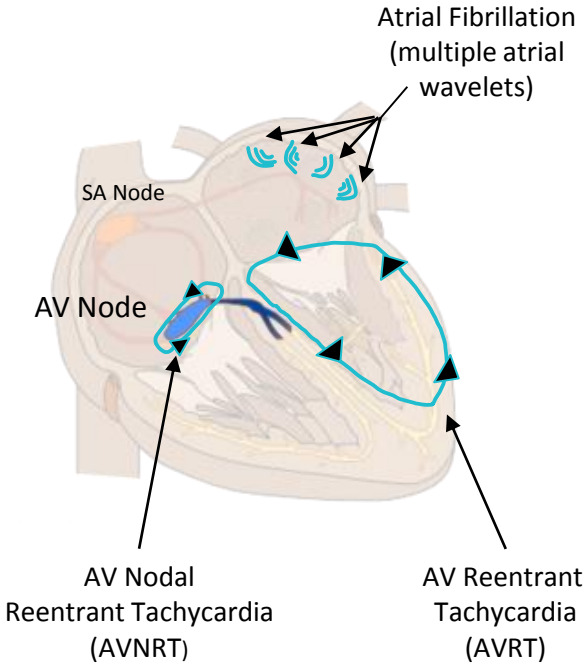
Source(s): 1. Khavjou, et al., Projections of Cardiovascular Disease Prevalence and Costs: 2015–2035, American Heart Association, November 2016. 2. HCUP ED & Admissions Data (2016), accessed January 2021. 3. Colilla S, et al., Am J Card. 2013 112:1142–1147. 4. Sacks, N.C., et al., 23rd World Congress on Heart Disease (Boston 2018). 5. 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. 6. 40-65% of PSVT patients have >1 episodes of PSVT requiring an ED visit, or having episodes lasting >10 minutes, or are on chronic prophylaxis for PSVT. Estimates based on internal market research and longitudinal analysis of claims data.

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
150 - 250 bpm	110 - 175 bpm
Episode frequency and duration is highly variable	

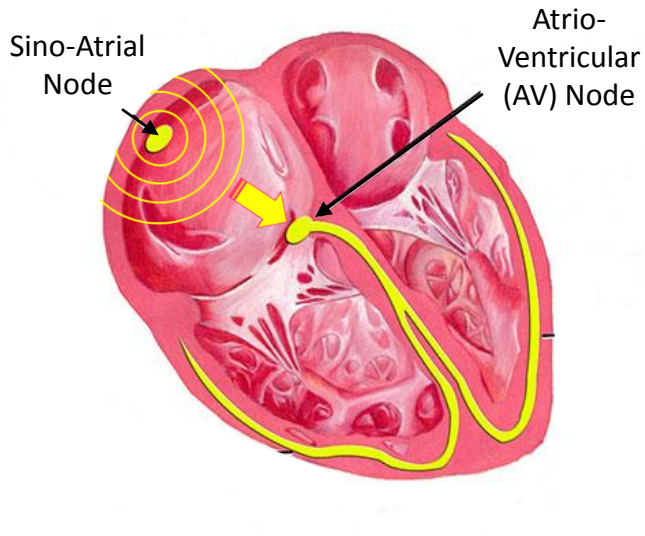
Common Symptoms Include	
	Heart palpitations / Chest pressure or pain
	Shortness of breath / Fatigue
	Light-headedness / Anxiety



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

Role of Intravenous L-Type Calcium Channel Blockers



IV CCBs like verapamil or diltiazem slow conduction over the AV node…

for PSVT

…to break the tachycardia and return the heart to sinus rhythm

for AFib-RVR

…to reduce the ventricular rate while still in AFib

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

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

Issues 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

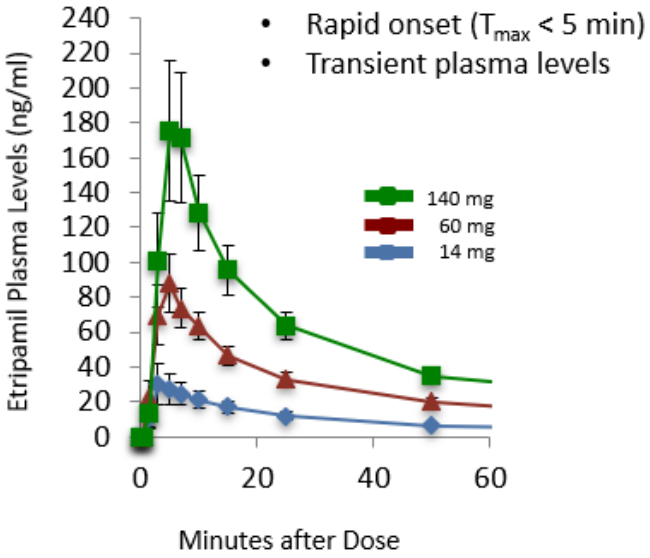
- Reduces ED visits / hospital admissions
- Less need for chronic medications
- Alternative or bridge to ablation procedure

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) slow conduction over the AV node
- Rapid onset of action
- Convenient patient self-administered nasal spray
- Short duration of action



AV = Atrio-ventricular

Error bars indicate standard error of the mean

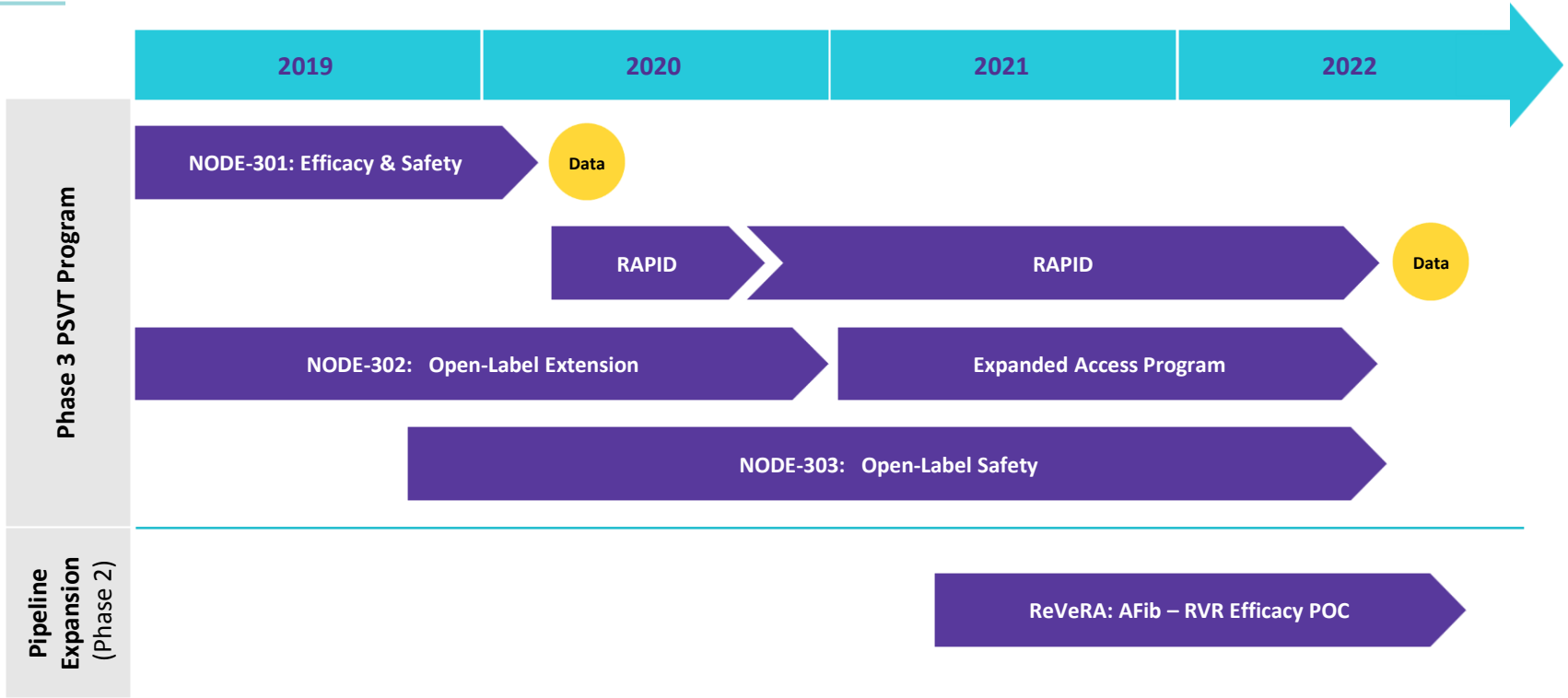
Clinical Program for Etripamil Enrolling Phase 2, Phase 3, and Safety

Phase 3 program 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 on drug had no serious adverse events

1 Test Dose

70 mg dose of etripamil

Administer in office while in sinus rhythm for safety evaluation

(N=431)

2 Randomization

70 mg etripamil: placebo

2:1

(N=419)

3 Event

1. Patient recognizes symptoms
2. Apply cardiac monitor (ECG)
3. Attempt vagal maneuver
4. Administer study drug

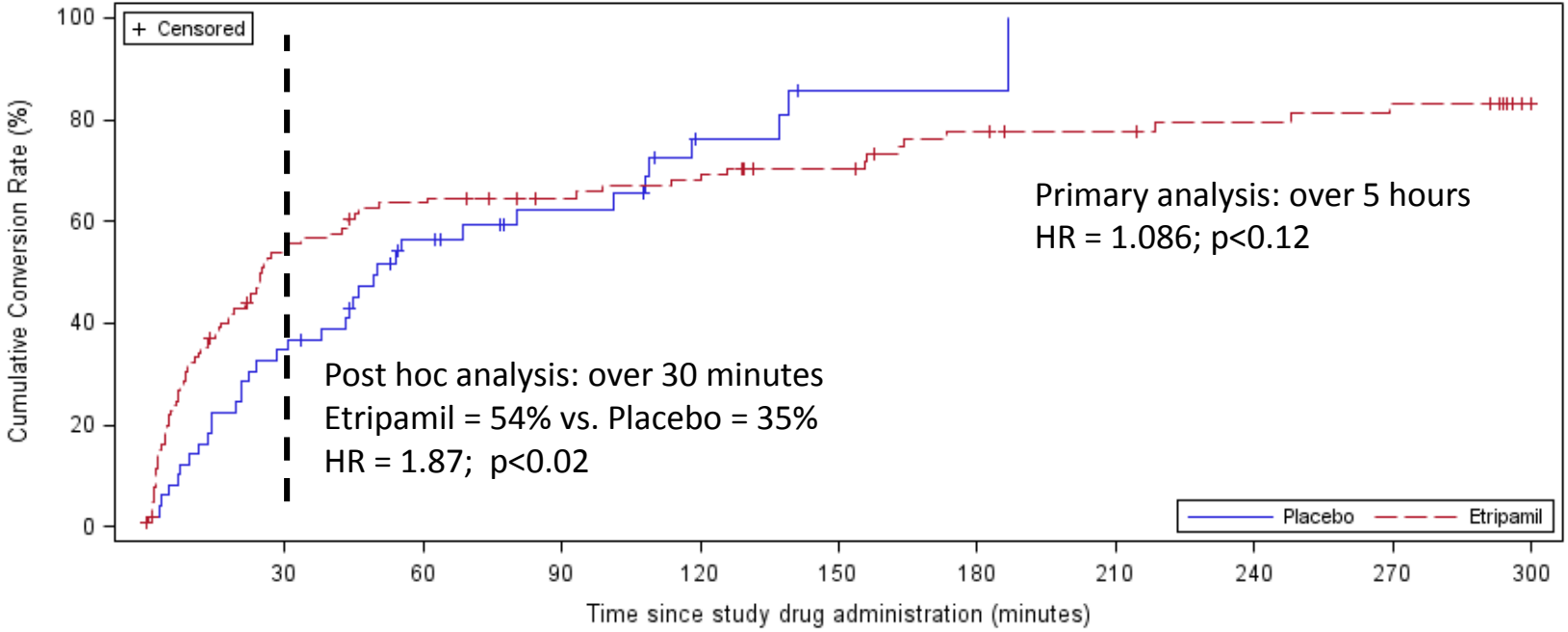
(N=198)

Primary Efficacy Analysis

- ECG of event is adjudicated for PSVT; only PSVT events count in primary efficacy
- Primary Endpoint = PSVT conversion to SR Kaplan Meier analysis over 5 hours
- Powering: 90%, alpha <0.01; delta = 40%
- Study concluded when 150 confirmed PSVT events reached (N = 156)

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

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



Placebo	49	32	18	12	5	1	1	0			
Etripamil	107	47	36	31	28	22	15	13	11	9	3

Number of subjects at risk

Source: Data on File, Milestone Pharmaceuticals Inc.

NODE-301 Safety Analysis

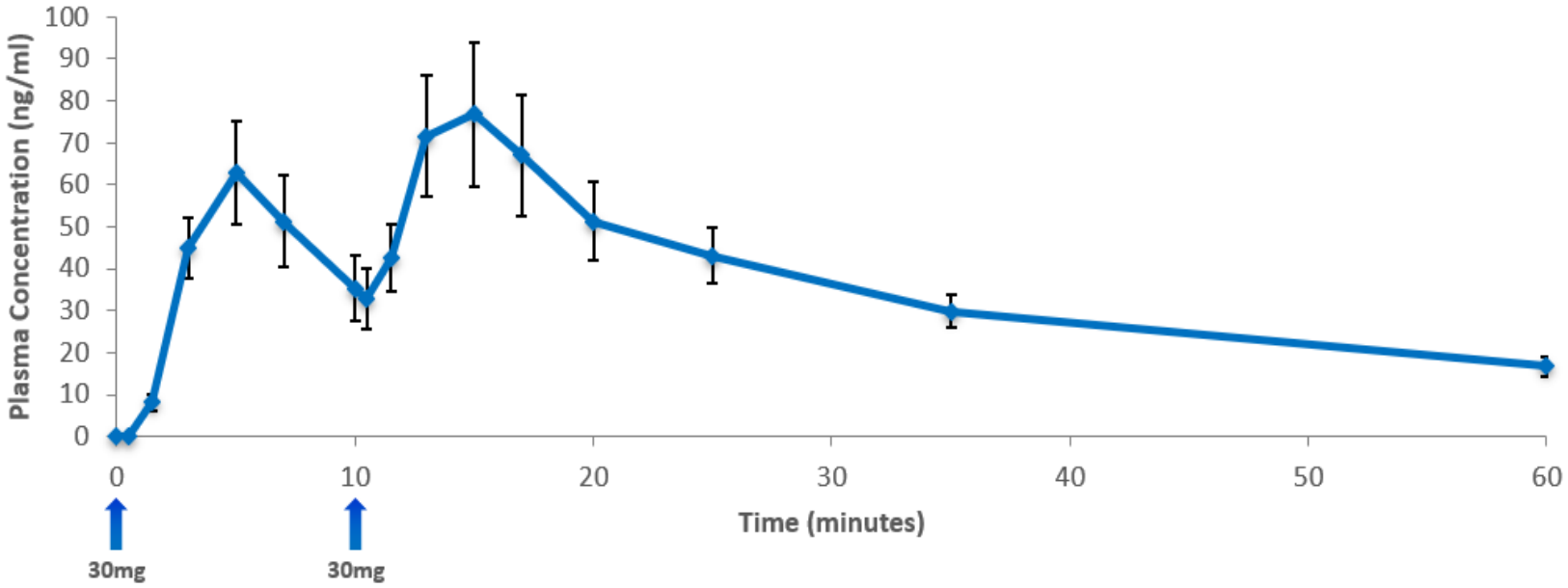
Randomized Treatment Emergent Adverse Events (RTEAE)	Etripamil N=138 (%)	Placebo N=60 (%)
Subjects with any RTEAE	53 (38.4)	12 (20.0)
Maximum severity of RTEAE		
Mild	45 (32.6)	10 (16.7)
Moderate	8 (5.8)	3 (3.3)
Severe	0 (0.0)	0 (0.0)
Most Common Adverse Events (>5%)		
Nasal discomfort	27 (19.6)	4 (6.7)
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.

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 Test Dose

70 mg etripamil repeat dose regimen

(2 doses 10 minutes apart)

Administer in office while in sinus rhythm for safety evaluation

2 Randomization

70 mg etripamil x2: Placebo x2

1:1

(N~500)

3 Event

1. Patient recognizes symptoms
2. Apply cardiac monitor (ECG)
3. Attempt vagal maneuver
4. Administer study drug
5. If symptoms persist for 10 minutes, dose study drug again

Primary Efficacy Analysis

- ECG of event is adjudicated for PSVT; only PSVT events count to primary efficacy
- Primary Endpoint = PSVT conversion to SR Kaplan Meier analysis over 30 min
- Powering: 90%, alpha < 0.05; delta = 19%
- Study concluded when 180 confirmed PSVT events[1]

[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

Clinical Program for Etripamil Enrolling Phase 2, Phase 3, and Safety

Phase 3 program designed to support NDA filing in PSVT, while concurrently building safety database and running Phase 2 ReVeRA to support AFib-RVR program

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N= 104 1:1 randomized	**N=50** 1:1 randomized	**N=419** 2:1 randomized	**N~500** 1:1 randomized	**N ~1000** Open label

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 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
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

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

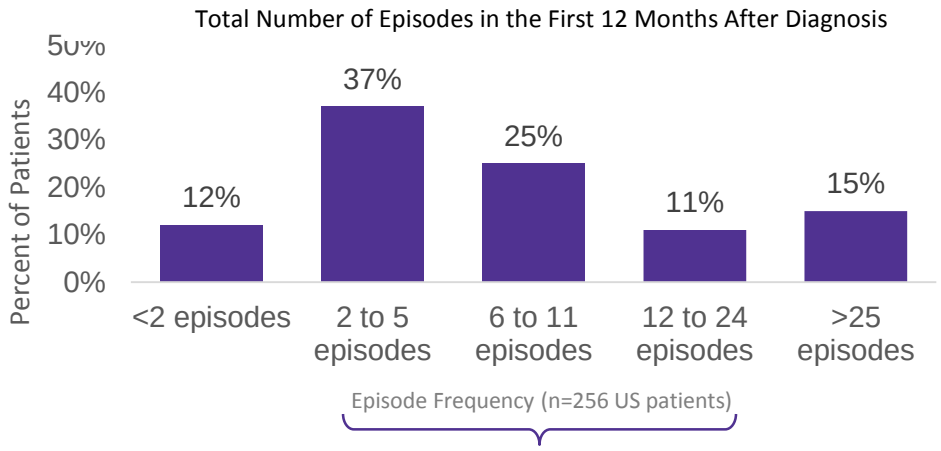
- Reduction in ED/hospital admissions
- Improvement in patient satisfaction

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

Sources: Internal market research

Projected US Market for Etripamil in PSVT

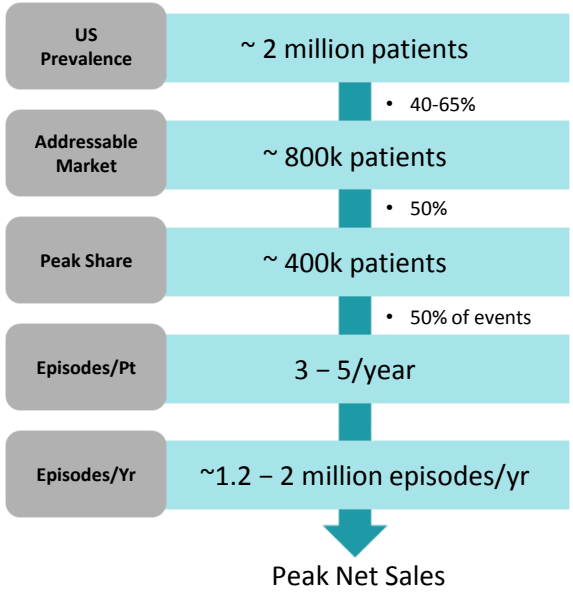
Market research suggests treatment of 1-2 million episodes of SVT with etripamil in peak year



40% patients with multiple episodes >10min/yr*

65% patients on chronic medications for PSVT

40% patients with ≥1 ED visits for PSVT/yr*

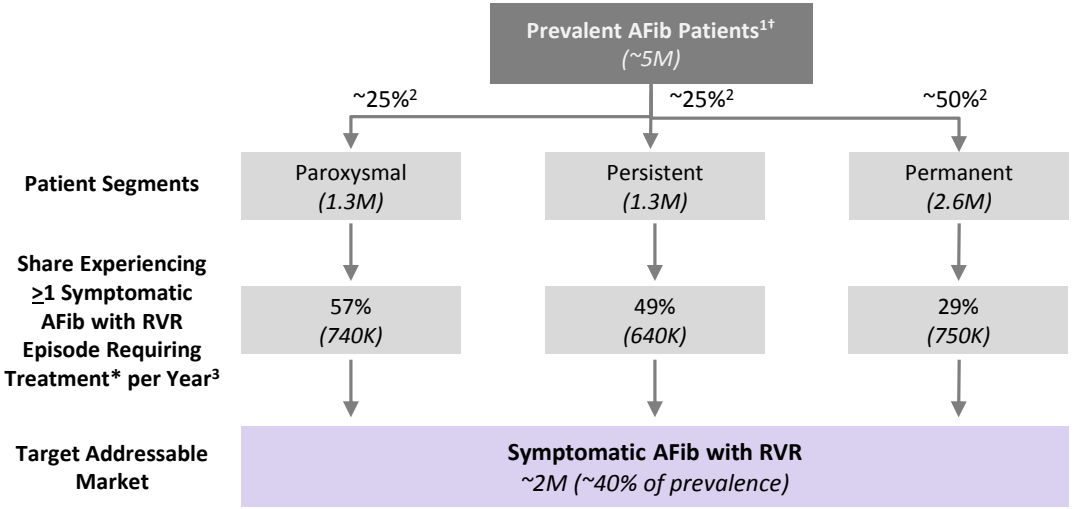


*Estimates are for patients in year after initial diagnosis; rates drop by 13-29% in years following their initial diagnosis

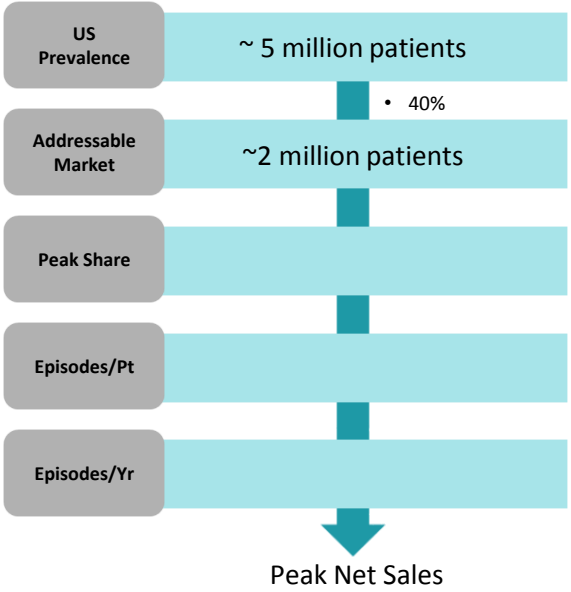
Sources: Internal estimates based on market research, Milestone Pharmaceuticals Inc.

Projected US Market for Etripamil in AFib-RVR

Market research suggests a target addressable market of ~ 2 million patients for AFib-RVR



*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



1. Colilla et al., Am. J. Cardiol. 2013, 112(8), 1142-1147; 2. Zoni-Berisso et al., Clin. Epidemiol., 2014, 6, 213-220; Benjamin et al., Circulation, 2019, 139, e56-e528; Go et al., JAMA, 2001, 285(18), 2370-2375; Turakhia et al., PLOS ONE, 2018, 13(4), e0195088; Kornej et al. Circ. Res., 2020, 127, 4-20; Miyasaka et al., Circulation, 2006, 114, 119-125; Naccarelli et al., Am. J. Cardiol., 2009, 104(11), 1534-1539; Williams et al., Am. J. Cardiol., 2017, 120(11), 1961-1965; Ball et al., Int. J. Cardiol., 2013, 5(1), 1807-1824; 3. Primary Research Interviews conducted by Triangle Insights, January-February 2021, Clinical Cardiologists (n=9), Interventional Cardiologists (n=6), and Electrophysiologists (n=10)

Projected US Market for Etripamil in Arrhythmias (PSVT and AFib-RVR)

Market research suggests a TAM of ~3 million patients in peak year

PSVT		AFib-RVR
~ 2 million patients	US Prevalence	~ 5 million patients
• 40-65%		• 40%
~ 800k patients	Addressable Market	~2 million patients
• 50%		
~ 400k patients	Peak Share	TBD
• 50% of events		
3-5/year	Episodes/Pt	TBD
~1.2-2 million doses/year	Episodes/Yr	TBD

Peak Net Sales

PSVT = Paroxysmal Supraventricular Tachycardia; AF – RVR = Atrial Fibrillation with Rapid Ventricular Rate; TAM = Target Addressable Market

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

Finances – as of March 31, 2021[1]

Proforma cash $149.9M[2]

- $129.9M in Cash as of March 31, 2021
- $20M in Equity and Upfront cash from Ji Xing deal

Cash funds operations past guidance for top-line data and into mid-2023

Equity - 42.1M[3] in shares and pre-funded warrants outstanding

- 29.8M common shares
- 11.4M pre-funded warrants
- 0.9M pre-funded warrants, in RTW private placement[3]

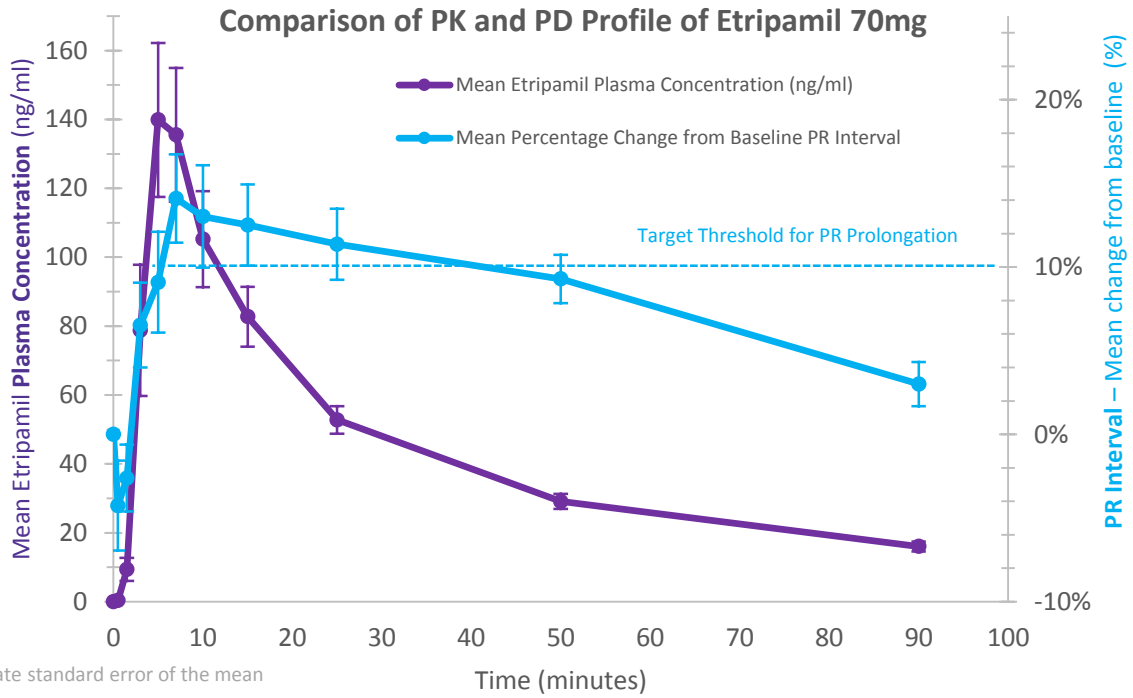
1) Adjusted to reflect financing events through May 17, 2021; 2) $129.9M as of March 31, 2021, plus $15.0M in upfront payments from Ji Xing Pharmaceuticals under license agreement and $5.0M in equity investment from RTW Investments, LP; 3) Includes pre-funded warrants to purchase 910,746 common shares issued to RTW Investments, LP.

Milestone PHARMACEUTICALS

Thank you

Etripamil Nasal Spray Pharmacological Results (NODE-102)

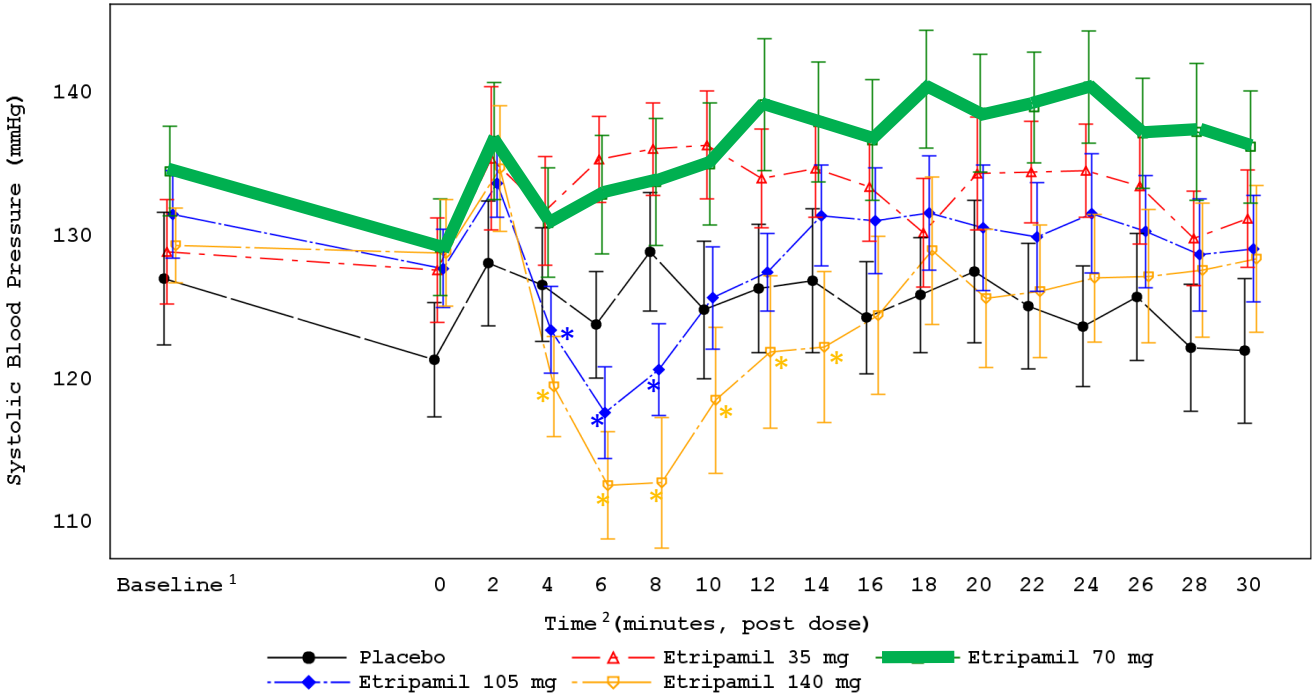
Anticipated therapeutic effect within 45 minutes; peak within 10 minutes



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

Phase 2 Mean Systolic Blood Pressure Effects

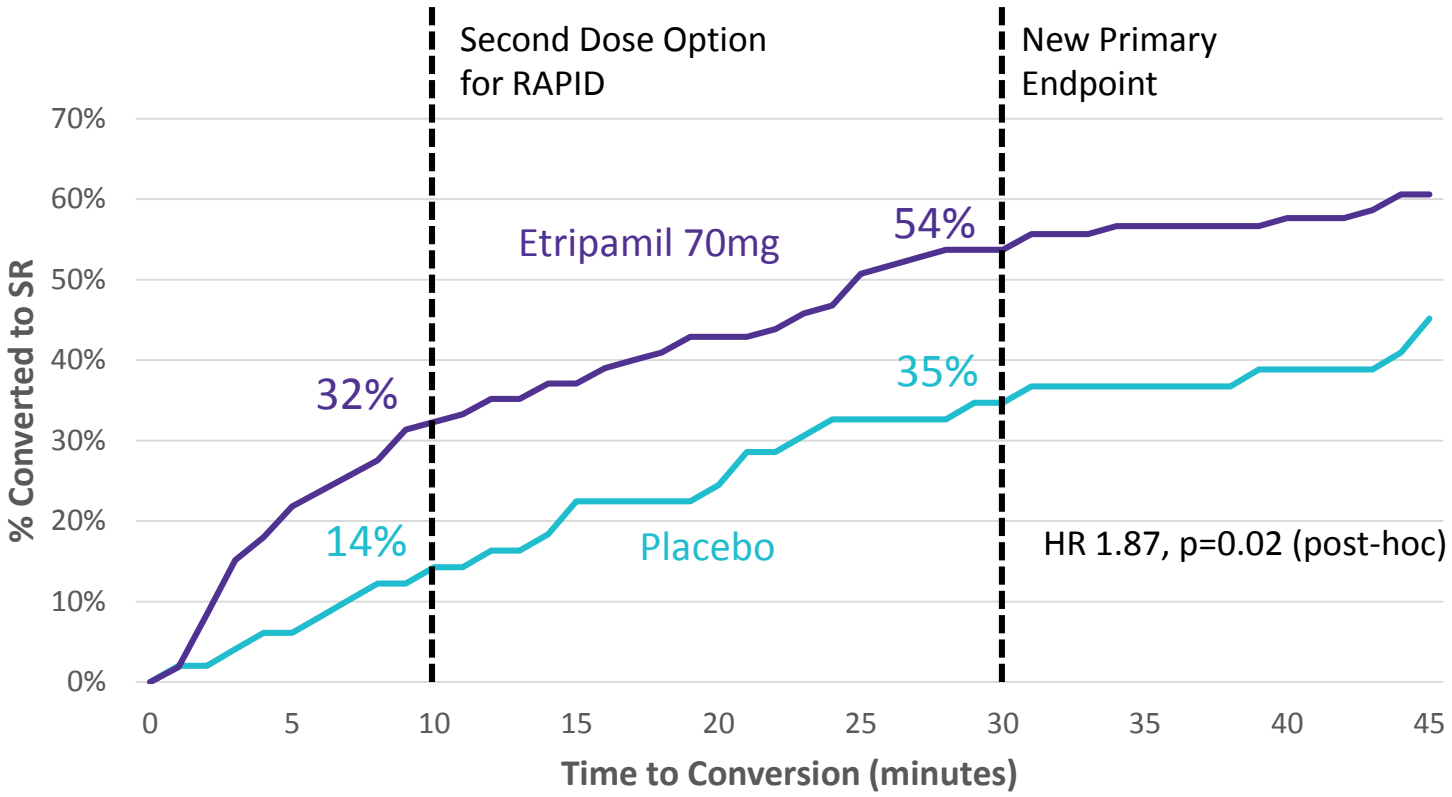
70 mg of etripamil showed no decrease in blood pressure; higher doses transient decreases



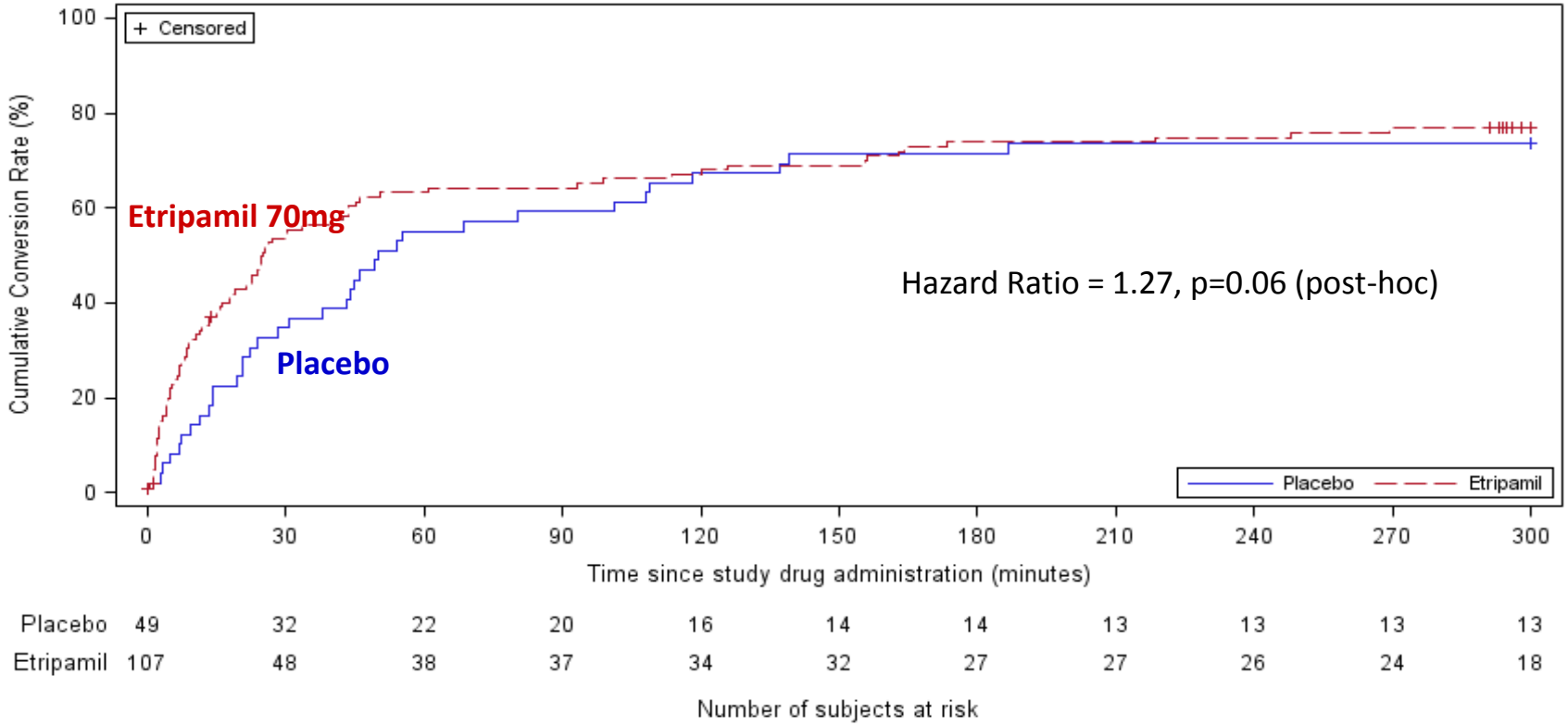
[1] Baseline is defined as the average of the 20-min and 10-min pre-dose measurements. [2] Time 0 is defined as the average of the measurements during supraventricular tachycardia between 5 and 0 min before study drug administration. *p < 0.05 versus baseline.

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

NODE-301 Efficacy– Time to Conversion over 45 Minutes



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 Patient Characteristics

- Age: teens to elderly
- Gender: majority are female
- Episode frequency and duration varies widely
  - Median 4-7 per year despite chronic medications
  - Almost 40% of patients have at least 2 episodes/year >10 min*
- Cardiovascular comorbidities in about half of patients
- 40% of patients have ≥ 1 ED visit per year*

Unmet Need

- Strongly negative experience associated with **adenosine in ED**
- Significant anxiety/fear of **ablation**
- Many patients indicate "**significant impact**" on QOL

*Estimates are for patients in year after initial diagnosis; rates drop by 13-29% in years following their initial diagnosis

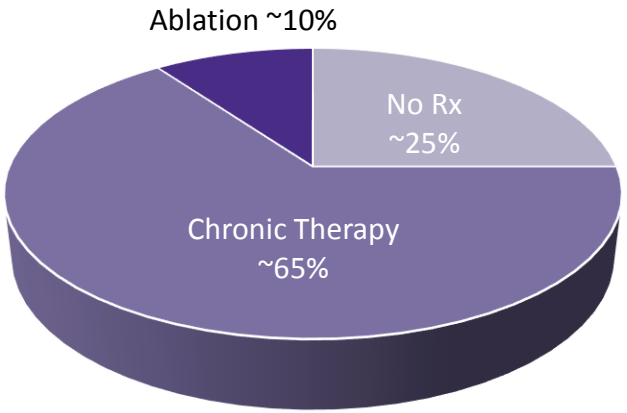
Sources: Internal estimates based on market research and longitudinal analysis of Truven/Marketscan and Medicare claims data

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

Current Management



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.

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.

PSVT Patient Management and Call Point Targeting

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

		Clinical Cardiologists	Primary Care Physicians	Electro-physiologists
% of PSVT 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

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.