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**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

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**FORM 8-K**

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**CURRENT REPORT  
Pursuant to Section 13 or 15(d) of the  
Securities Exchange Act of 1934**

Date of Report (Date of earliest event reported):  
**June 2, 2021**

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**MILESTONE PHARMACEUTICALS INC.**

(Exact name of registrant as specified in its charter)

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**Québec**  
(state or other jurisdiction of incorporation)

**001-38899**  
(Commission File Number)

**Not applicable**  
(I.R.S. Employer Identification No.)

**1111 Dr. Frederik-Philips  
Boulevard, Suite 420  
Montréal, Québec CA**  
(Address of principal executive offices)

**H4M 2X6**  
(Zip Code)

Registrant's telephone number, including area code: **(514) 336-0444**

(Former name or former address, if changed since last report.)

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Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

**Title of each class**  
Common Shares

**Trading Symbol(s)**  
MIST

**Name of each exchange on which registered**  
The Nasdaq Stock Market LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

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**Item 8.01. Other Events.**

On June 2, 2021, Milestone Pharmaceuticals, Inc. (the "Company") updated its corporate presentation that it intends to use in connection with presentations at conferences and meetings. The full text of the Company's corporate presentation is filed as Exhibit 99.1 hereto and incorporated herein by reference.

**Item 9.01. Financial Statements and Exhibits.**

(d) Exhibits.

<b>Exhibit No.</b>	<b>Description</b>
<a href="#">99.1</a>	<a href="#">Corporate Presentation dated June 2, 2021</a>

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**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

**MILESTONE PHARMACEUTICALS INC.**

By: /s/ Amit Hasija  
Amit Hasija  
Chief Financial Officer

Dated: June 2, 2021

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**Milestone**  
PHARMACEUTICALS

## Corporate Overview

June 2021

**Joseph Oliveto**  
President & CEO





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 to 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.

This Presentation contains trademarks, trade names and service marks of other companies, which are the property of their respective owners. Certain information contained in this Presentation and statements made orally during this Presentation relate to or is based on studies, publications, surveys and other data obtained from third-party sources and Milestone’s own internal estimates and research. While Milestone believes these third-party studies, publications, surveys and other data to be reliable as of the date of the Presentation, it has not independently verified, and makes no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources. In addition, no independent source has evaluated the reasonableness or accuracy of Milestone’s internal estimates or research and no reliance should be made on any information or statements made in this Presentation relating to or based on such internal estimates and research.



## 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



	PSVT	Atrial Fibrillation
 <b>Total Patients (2016)</b>	<b>2 Million<sup>4</sup></b>	<b>5 Million<sup>1</sup></b> (expected to grow to 7-12M by 2030 <sup>1-3</sup> )
 <b>Discharged ED Visits &amp; Hospital Admissions (2016)<sup>2</sup></b>	<b>145 Thousand</b>	<b>785 Thousand</b>
 <b>Target Market Addressable (Patient Population)</b>	<b>0.8 – 1.2 Million<sup>6</sup></b>	<b>2 Million<sup>5</sup></b>

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.

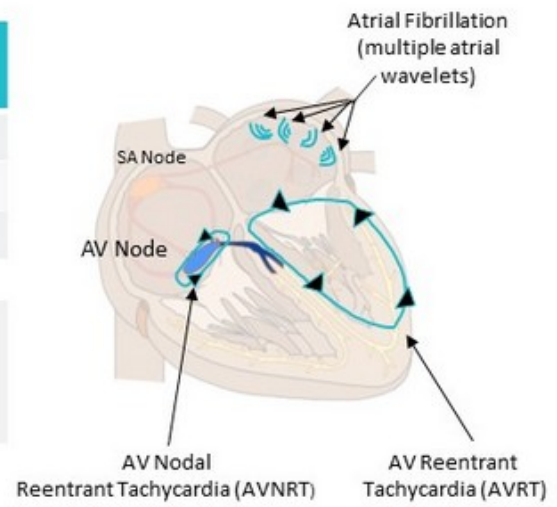
# Supraventricular Tachycardias with a Common Patient Burden



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	

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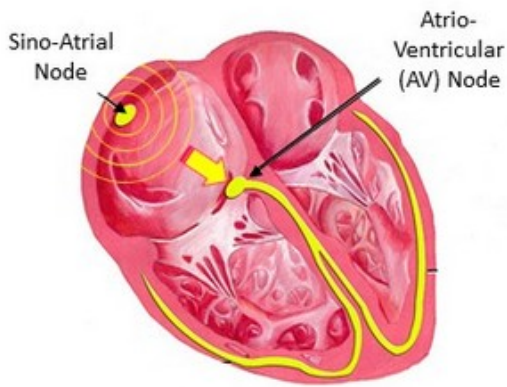


PSVT = Paroxysmal Supraventricular Tachycardia; AFib-RVR = Atrial Fibrillation with Rapid Ventricular Rate

Sources: adapted from [https://en.ecgpedia.org/index.php?title=Supraventricular\\_Rhythms](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



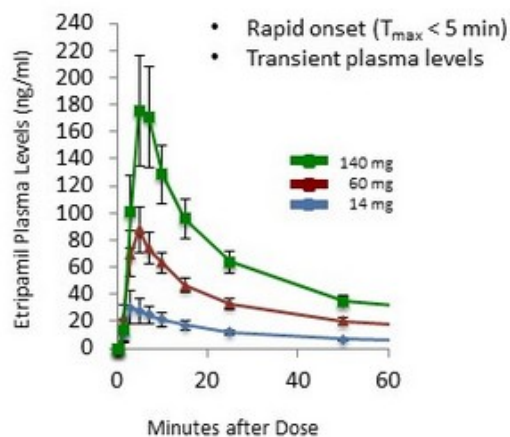
Prospectively designed to treat common tachycardias outside the Emergency Department (ED)



Etripamil	
Class	Novel CCB
Potency (IC <sub>50</sub> )	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

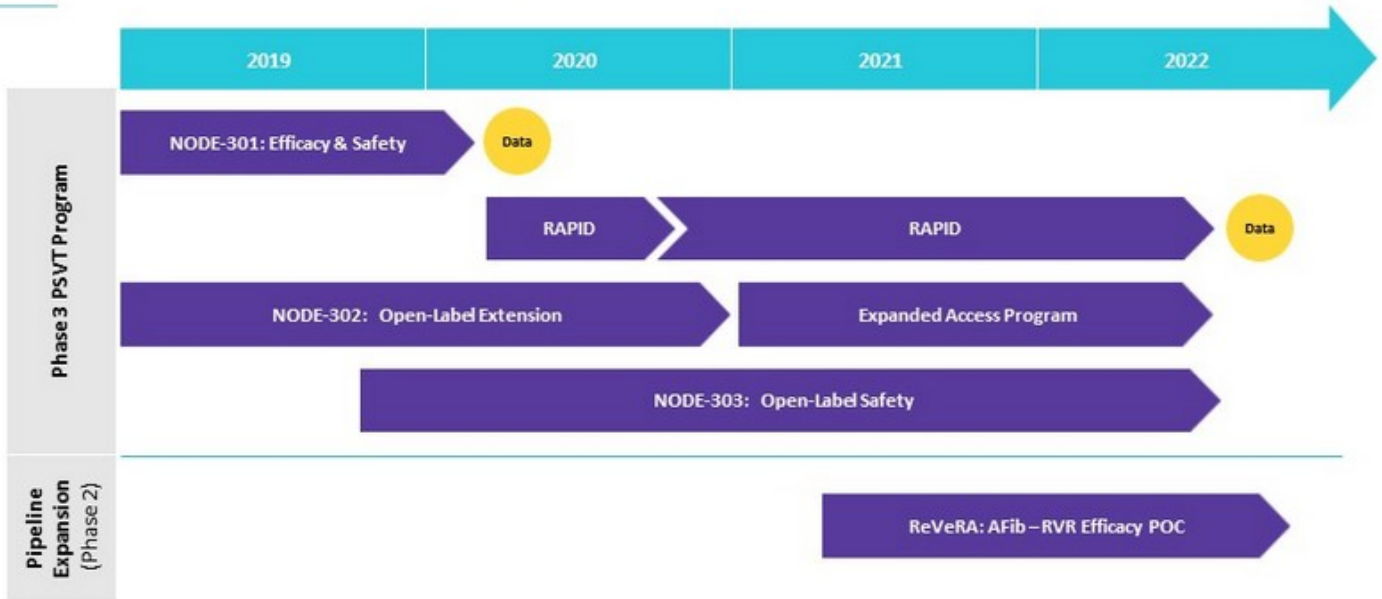


Phase 3 program designed to support NDA filing in PSVT while concurrently building safety database and running Phase 2 ReVeRA to support AFib-RVR program

<b>NODE-1</b> PSVT	<b>ReVeRA</b> AFib-RVR	<b>NODE-301</b> PSVT	<b>RAPID</b> PSVT	<b>NODE-303/302</b> PSVT
<b>Phase 2</b>	<b>Phase 2</b>	<b>Phase 3</b>	<b>Phase 3</b>	<b>Phase 3</b>
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

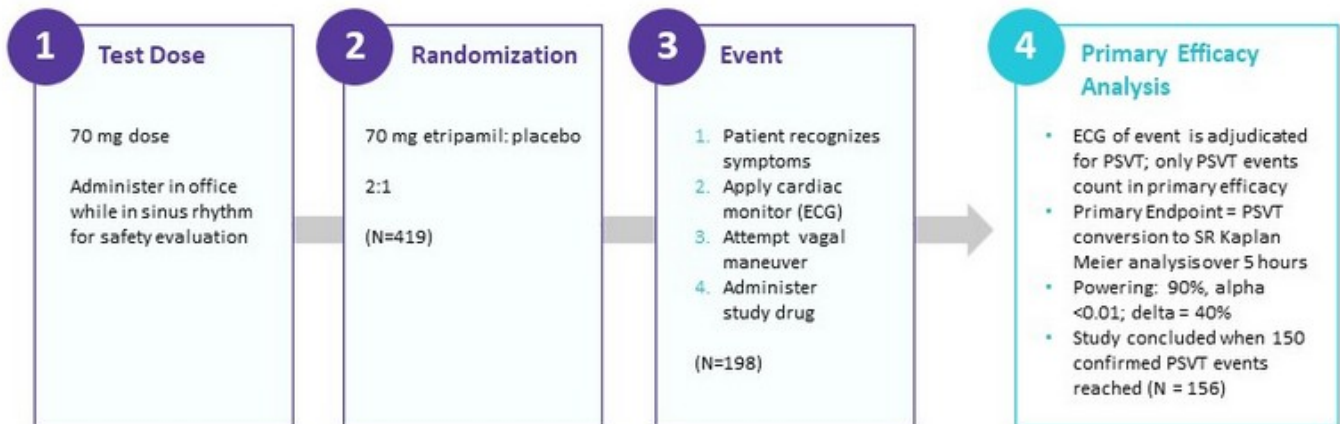


AFib-RVR = Atrial Fibrillation with Rapid Ventricular Rate; POC = Proof of Concept

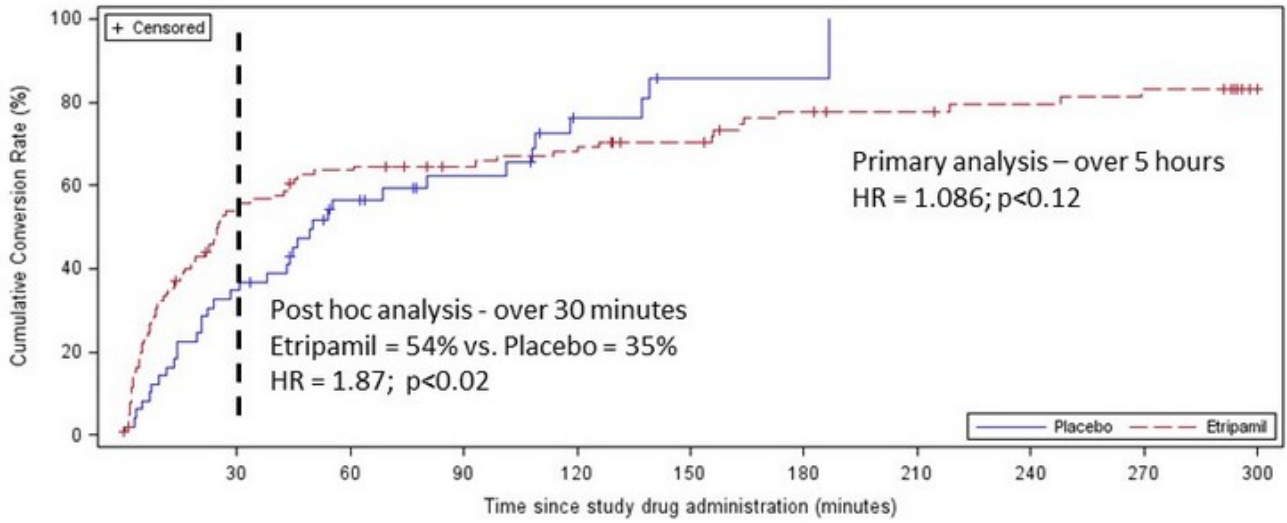
# NODE-301 Study Design



NODE-301 patients on drug had no serious adverse events



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



		30	60	90	120	150	180	210	240	270	300
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.



Randomized Treatment Emergent Adverse Events (RTEAE)	Etripamil N=138 (%)	Placebo N=60 (%)
<b>Subjects with any RTEAE</b>	53 (38.4)	12 (20.0)
<b>Maximum severity of RTEAE</b>		
Mild	45 (32.6)	10 (16.7)
Moderate	8 (5.8)	3 (3.3)
Severe	0 (0.0)	0 (0.0)
<b>Most Common Adverse Events (&gt;5%)</b>		
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

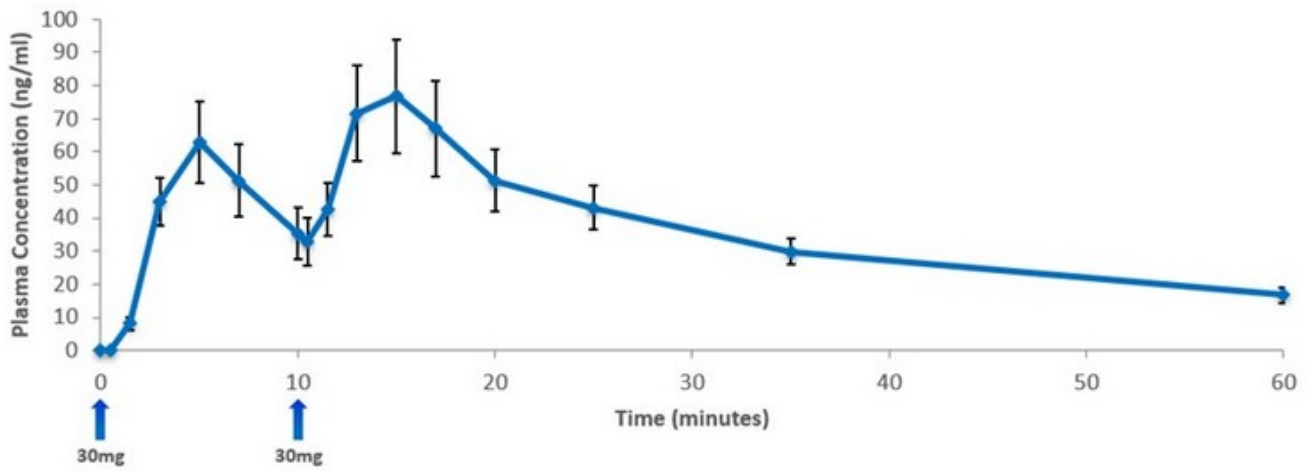
Source: Data on File, Milestone Pharmaceuticals Inc.



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

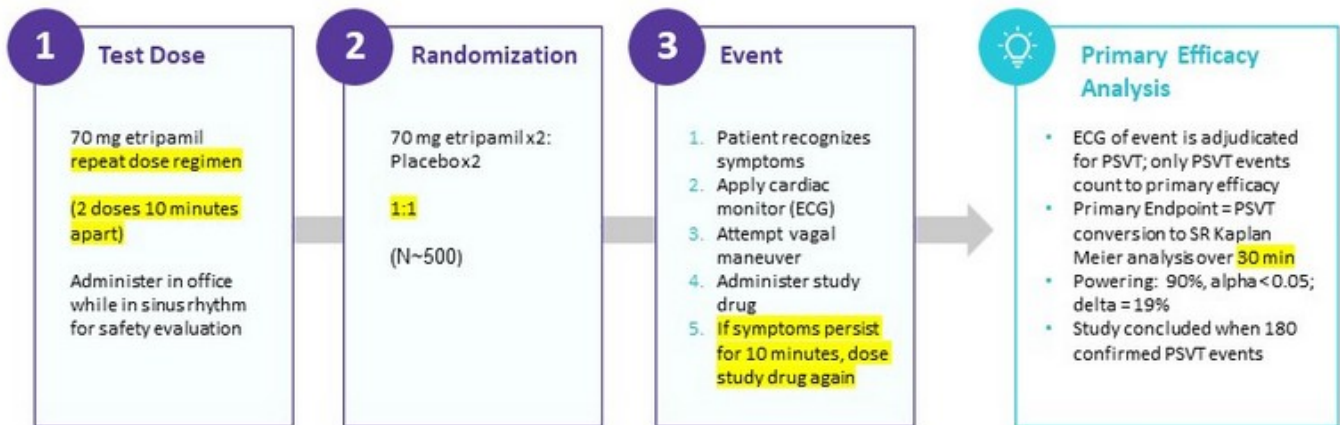


Repeat administration increases both C<sub>max</sub> and AUC



N=7, Error bars are standard error

Source: Data on File, Milestone Pharmaceuticals Inc.



<sup>1</sup> 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



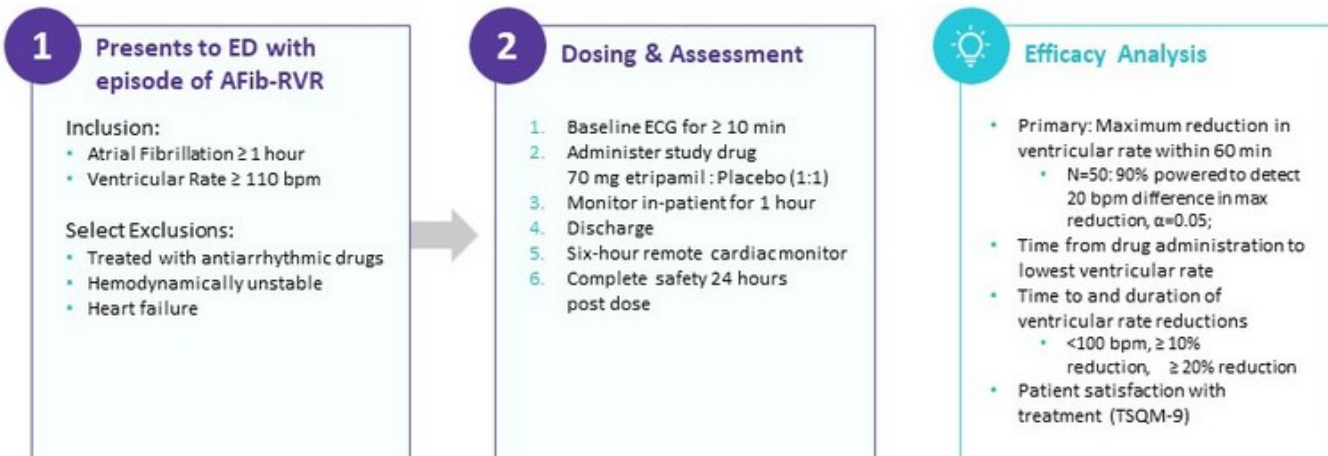
Phase 3 program designed to support NDA filing in PSVT, while concurrently building safety database and running Phase 2 ReVeRA to support AFib-RVR program

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

# The ReVeRA Trial



## Reduction of Ventricular Rate in Patients with Atrial Fibrillation

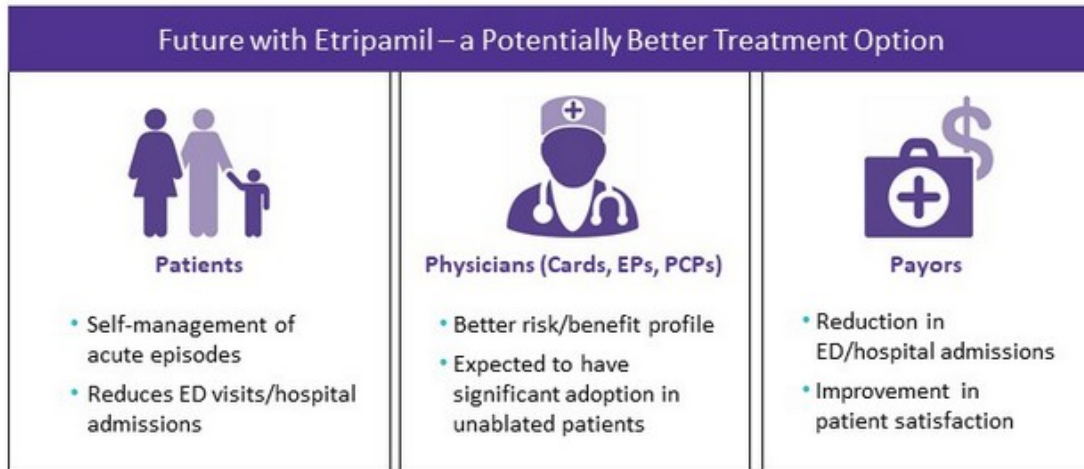


CHADs 0 = No Heart Failure/No Hypertension/Age  $< 65$ /No Diabetes/No History of Stroke or TIA/No Coronary ischemic disease; OAC, oral anti-coagulant; RVR, Rapid Ventricular Rate; TSQM-9, Treatment Satisfaction Questionnaire for Medication; ED = Emergency Department

## **Commercial Opportunity**



Potential for high receptivity to etripamil across stakeholders



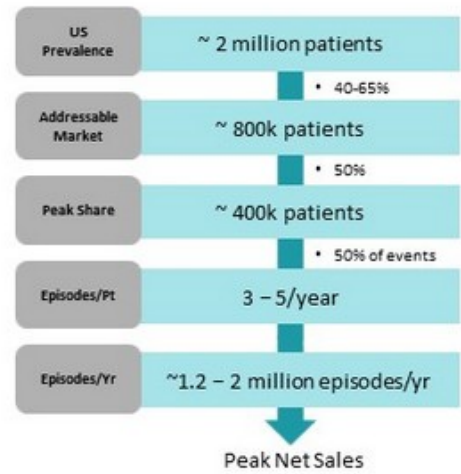
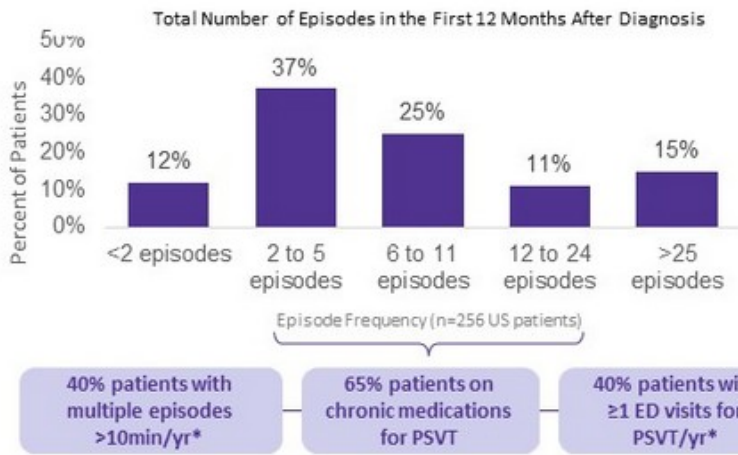
Cards = Cardiologists, EPs = Electrophysiologists, PCPs = Primary Care Providers, SVT = Supraventricular Tachycardia, ED = Emergency Department

Sources: Internal market research

# Projected US Market for Etripamil in PSVT



Market research suggests utilization of 1-2 million doses of etripamil in peak year for PSVT

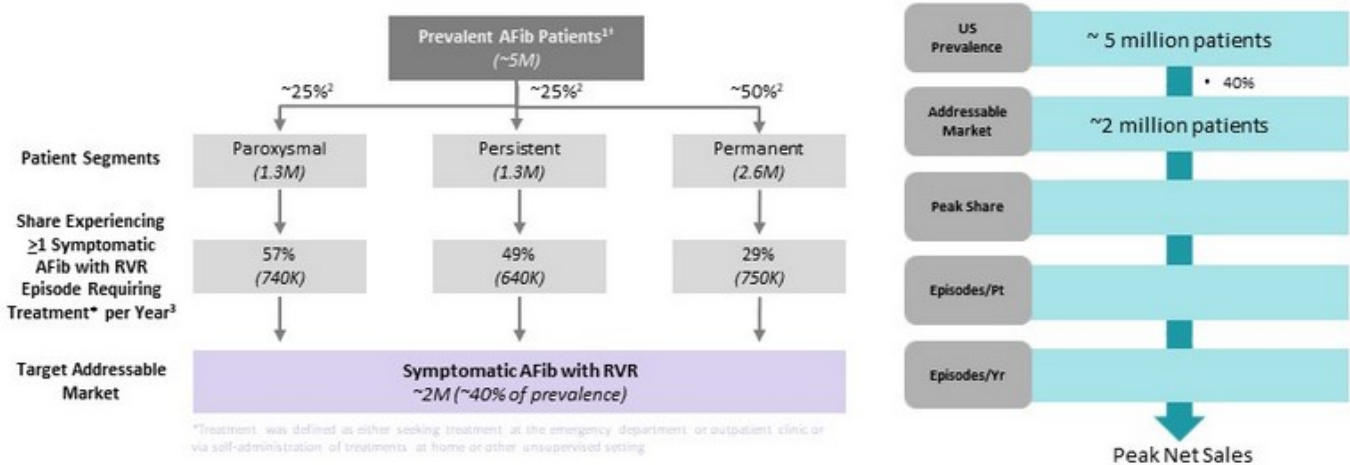


TAM = Target Addressable Market  
 \*Estimates are for patients in year after initial diagnosis; rates drop by 13-29% in years following their initial diagnosis  
 Sources: Internal estimates based on market research, Milestone Pharmaceuticals Inc.

# Projected US Market for Etripamil in AFib-RVR



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



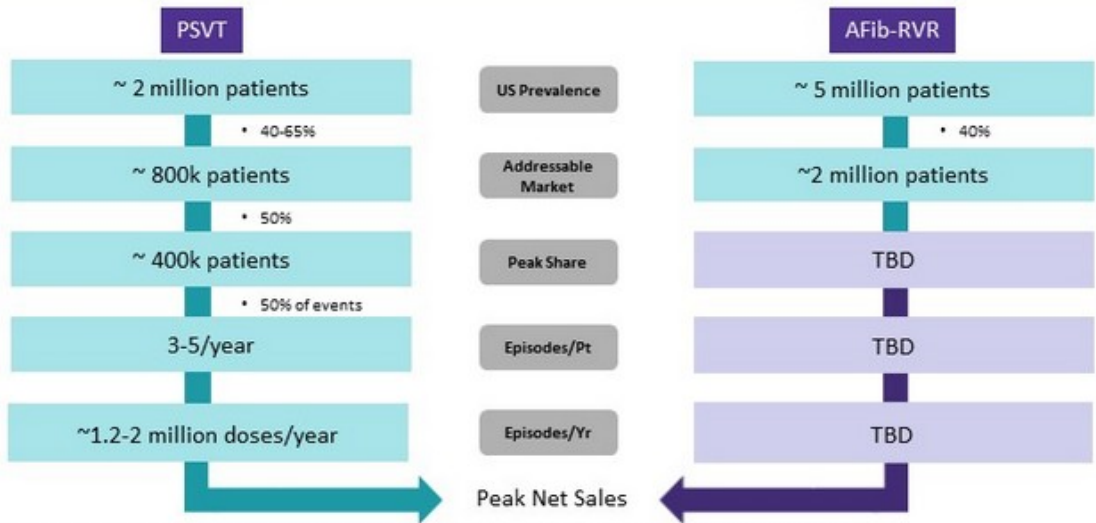
1. Colilla et al., Am. J. Cardiol. 2013, 112(8), 1142-1147; 2. Zoni-Berisso et al., Clin. Epidemiol., 2014, 6, 213-220; Benjamin et al., Circulation, 2019, 139, e56-e528; Go et al., JAMA, 2001, 285(18), 2370-2375; Turakhia et al., PLOS ONE, 2018, 13(4), e0195088; Komej et al., Circ. Res., 2020, 127, 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 = 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.



### Proforma cash \$149.9M<sup>2</sup>

- \$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<sup>3</sup> 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<sup>3</sup>

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.

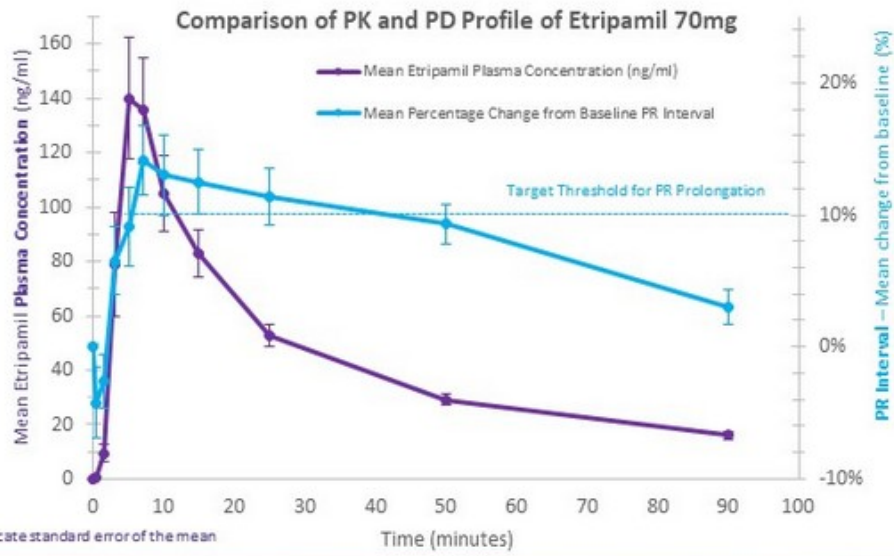
**Thank you**

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# Etripamil Nasal Spray Pharmacological Results (NODE-102)



Anticipated therapeutic effect within 45 minutes; peak within 10 minutes

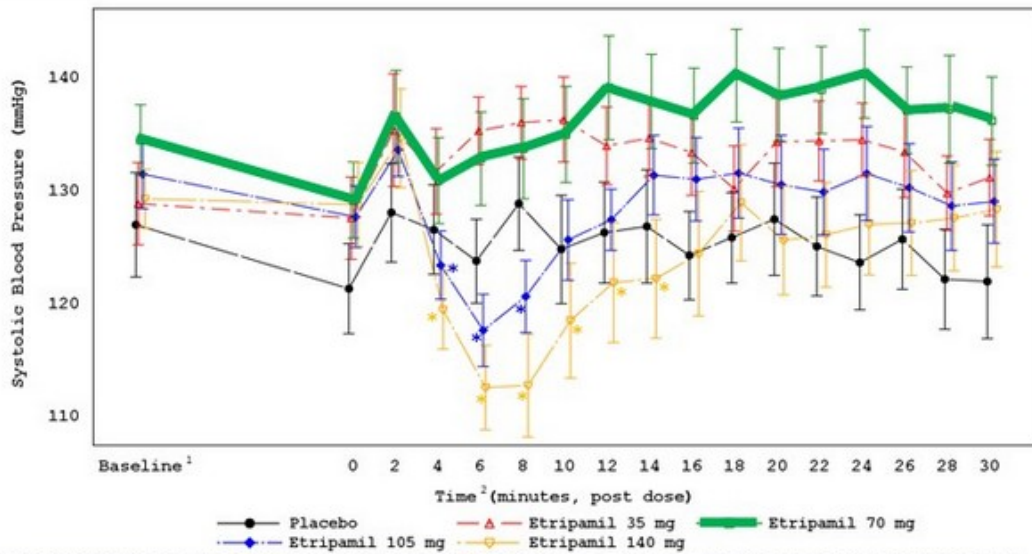


N=24; Error bars indicate standard error of the mean

## Phase 2 Mean Systolic Blood Pressure Effects



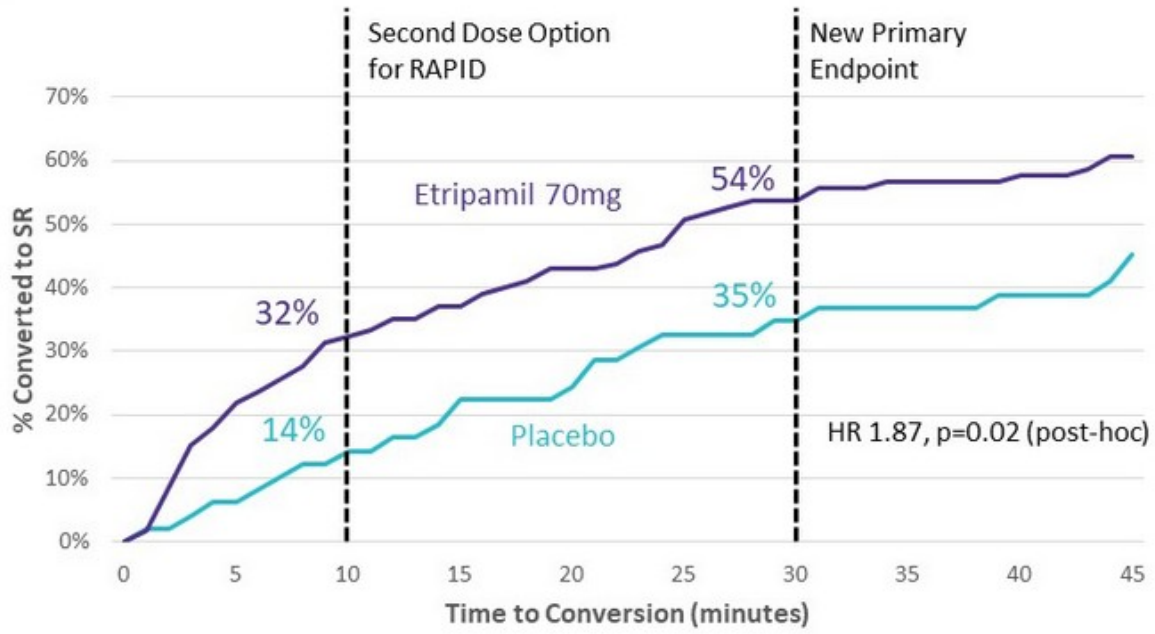
70 mg of etripamil showed no decrease in blood pressure; higher doses transient decreases



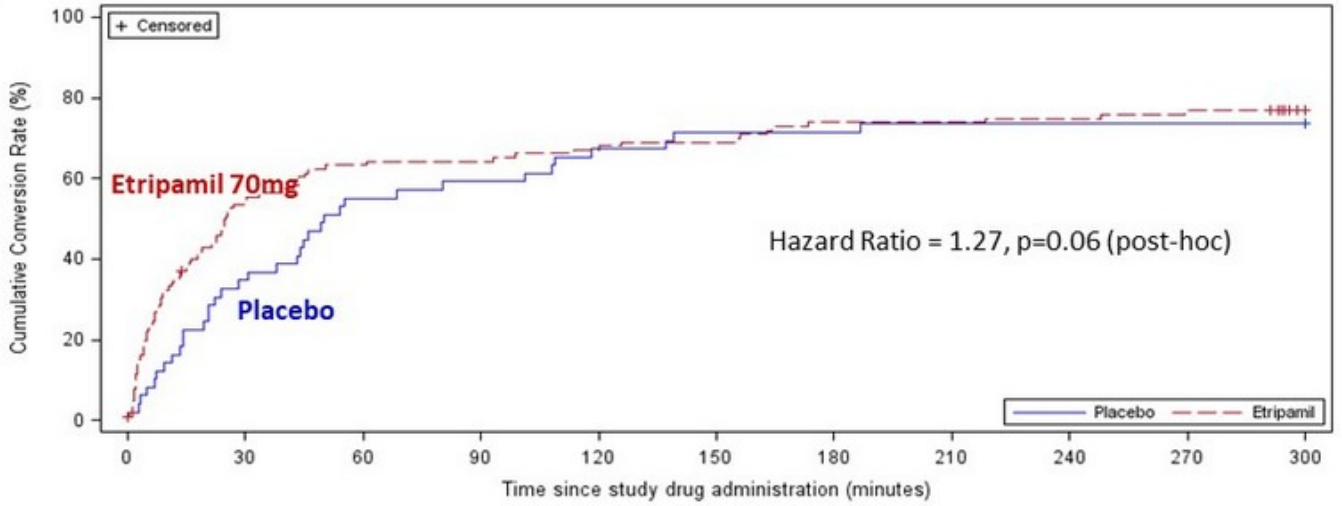
<sup>1</sup> Baseline is defined as the average of the 20-min and 10-min pre-dose measurements. <sup>2</sup> Time 0 is defined as the average of the measurements during supraventricular tachycardia between 5 and 0 min before study drug administration. \*p < 0.05 versus baseline.

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)



	0	30	60	90	120	150	180	210	240	270	300
Placebo	49	32	22	20	16	14	14	13	13	13	13
Etripamil	107	48	38	37	34	32	27	27	26	24	18

Number of subjects at risk

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  $\geq 1$  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

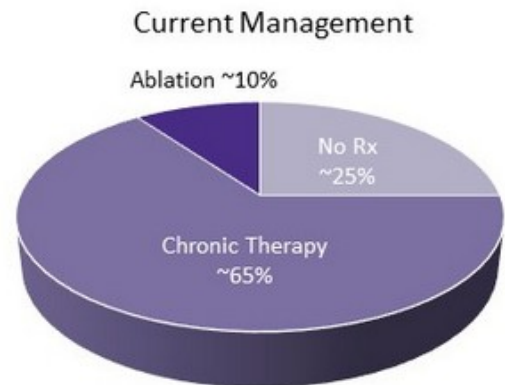
\*Estimates are for patients in year after initial diagnosis; rates drop by 13-29% in years following their initial diagnosis  
Sources: Internal estimates based on market research and longitudinal analysis of Truven/Marketscan and Medicare claims data





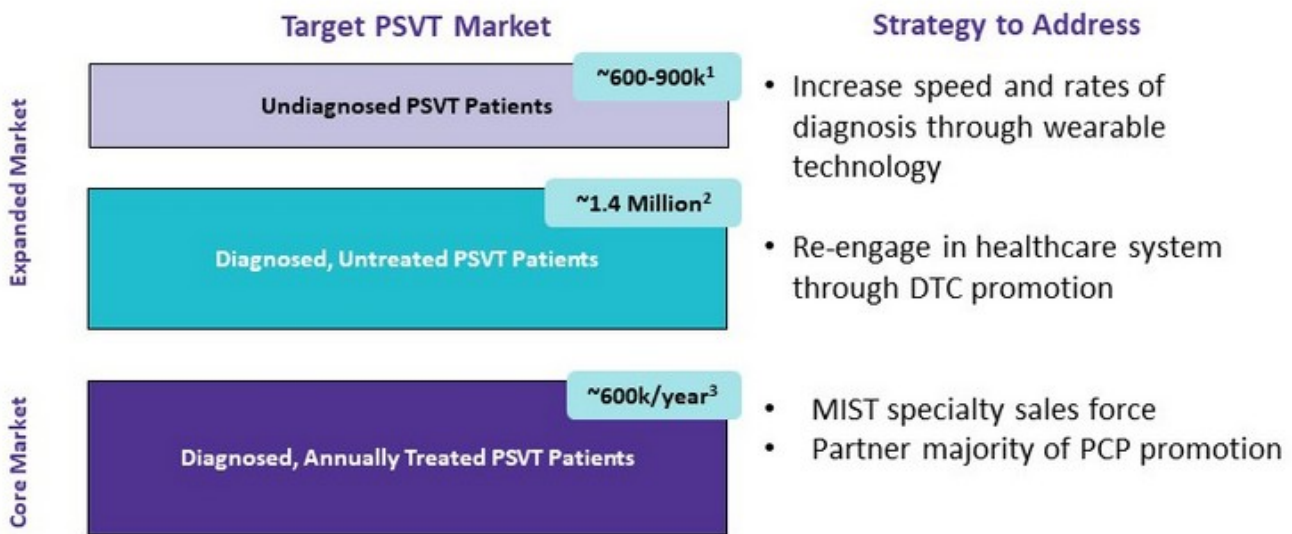
Total annual US healthcare expenditures of ~\$3B

- 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 5-year interval between 2008 and 2016 inclusive.

# Core PSVT Market is Addressable Now, with Potential for Expansion



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
<b>% of PSVT patients managed</b>		~60%	~30%	~10%
<b>Long-term Use</b>	<i>Add to or Replace Chronic Medications</i>	<b>Primary Target</b>		
<b>Medium-term Use</b>	<i>Defer Ablation</i>			<b>Secondary Target</b>
<b>Short-term Use</b>	<i>Bridge to Ablation</i>			

- 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