UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 8-K

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

Date of Report (Date of earliest event reported):
March 7, 2023

MILESTONE PHARMACEUTICALS INC.
(Exact name of registrant as specified in its charter)

Québec	**001-38899**	**Not applicable**
(state or other jurisdiction of incorporation)	(Commission File Number)	(I.R.S. Employer Identification No.)

1111 Dr. Frederik-Philips Boulevard, Suite 420 Montréal, Québec CA	**H4M 2X6**
(Address of principal executive offices)	(Zip Code)

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

Not applicable
(Former name or former address, if changed since last report.)

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	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Shares	MIST	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. ☒

Item 7.01. Other Events.

On March 7, 2023, in connection with the Cowen Annual Health Care Conference, the Company provided an updated corporate presentation that may be used in connection with presentations at conferences and investor meetings. The full text of the Company's corporate presentation is filed as Exhibit 99.1 hereto, and incorporated herein by reference, and may also be accessed through the "Investors & Media" section of the Company's website at www.milestonepharma.com.

The Company intends to use its website as a means of disclosing material non-public information and for complying with its disclosure obligations under Regulation FD. Such disclosures will be included on its website in the "Investors & Media" sections. Accordingly, investors should monitor such portions of its website, in addition to following press releases, SEC filings and public conference calls and webcasts.

The information furnished under this Item 7.01, including Exhibit 99.1, shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, or the Exchange Act, or subject to the liabilities of that section or Sections 11 and 12(a)(2) of the Securities Act of 1933, or the Securities Act. The information in this Item 7.01, including Exhibit 99.1, shall not be deemed incorporated by reference into any other filing with the U.S. Securities Exchange Commission, or the SEC, made by the Company, whether made before or after the date hereof, regardless of any general incorporation language in such filing.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Corporate Presentation dated March 7, 2023.
104	Cover Page Interactive Data File--the cover page XBRL tags are embedded within the Inline XBRL document

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: March 7, 2023

Exhibit 99.1


Milestone™
PHARMACEUTICALS
Corporate Overview
March 2023

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 etripamil, (iii) the potential of etripamil to deliver a clinically meaningful benefit to patients with PSVT in the home-setting environment and to empower patients to take control of their condition as well as provide value to the healthcare system, (iv) the possibility that data could fulfill the efficacy requirement for an NDA submission with the FDA for etripamil, (v) plans relating to commercializing etripamil, if approved, including the geographic areas of focus and sales strategy and (vi) 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. 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, 2021, 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.

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 sources 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.

Etripamil is an investigational new drug, which is not approved for commercial distribution in the United States.

Recent Progress on PSVT & AFib-RVR Programs for Etripamil

1. **Positive FDA feedback** – PSVT NDA filing package proposal considered acceptable
2. **Completed last two Phase 3 PSVT trials** – RAPID-Extension & NODE-303
3. **On target for NDA filing for PSVT** - Q3, 2023
4. **Initial data of etripamil in AFib-RVR coming soon** - Q2, 2023

PSVT and AFib-RVR Cause Markedly Symptomatic Attacks That Disrupt Patients' Lives

Symptoms include…

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

Many patients feel anxious and powerless

Paroxysmal Supraventricular Tachycardia (PSVT) and Atrial Fibrillation with Rapid Ventricular Response (AFib-RVR)

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

Etripamil Nasal Spray is a Novel L-type Investigational Calcium Channel Blocker Designed to Treat 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

Milestone Pharma - Targeting Vast Unmet Need for Patient Management of Common Heart Conditions

Targeting Common Arrhythmias

- PSVT
- AFib-RVR
- High burden on patients *and* on the healthcare system

Empowering Patients to Treat Themselves

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

Positioned for **Success**

- Positive Phase 3 results in PSVT
- NDA submission Q3 2023
- AFib-RVR program expands market – Initial data Q2 2023
- Experienced leadership driving commercialization

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

Standard of Care is Inadequate – Most Patients Experience Events Despite Preventative Options

	Chronic / Preventive	Acute
PSVT	• Oral Beta Blockers and Calcium Channel Blockers (CCB) to reduce episodes • Catheter ablation	• Vagal maneuver & "Pill in Pocket" (oral CCB or BB, off-label) have poor efficacy • **IV adenosine, IV CCB or DC cardioversion - requires ED or hospital visits**
AFib-RVR	• Oral Therapies for rate or rhythm control • Catheter ablation	• Oral drugs for rate or rhythm control – however do not prevent breakthrough AFib • **IV CCB or DC cardioversion - requires ED or hospital visits**

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

PSVT & Atrial Fibrillation with Rapid Ventricular Rate are Sizable and Underserved Markets 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 Adressable (2030) Patient Population)	**1.0-1.6 Million[5]**	**AFib-RVR ~3-4 Million[4]**

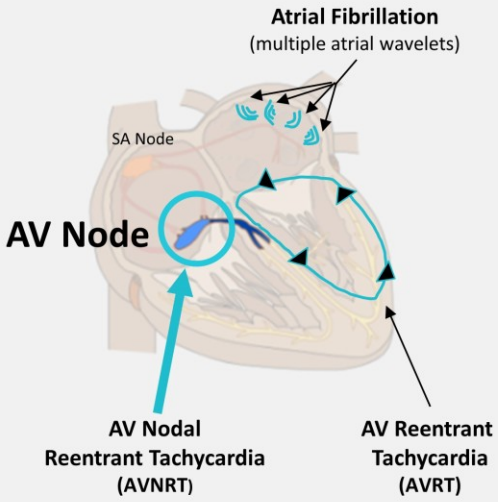
Source(s): **1.** Colilla et al., Am. J. Cardiol. 2013, 112(8), 1142-1147; Miyasaka et al., Circulation, 2006, 114, 119-125. American Heart Association **2**. HCUP ED & Admissions Data (2016), accessed January 2021. **3.** Rehorn et al. Journal of Cardiovascular Electrophysiology. 2021 Aug; 32(8): 2199-2206. 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 on internal PSVT patient market research (BluePrint Research Group, n=247) and longitudinal analysis of claims data.

Intravenous Calcium Channel Blockers Are Proven Effective for PSVT and AFib-RVR

Intravenous Calcium Channel Blockers (CCB)

- Slows conduction signal from the atria to the ventricles over the AV Node
- PSVT: breaks the circuit, returning heart to normal rhythm
- AFib-RVR: slows heart rate and reduces symptoms while remaining in Atrial Fibrillation

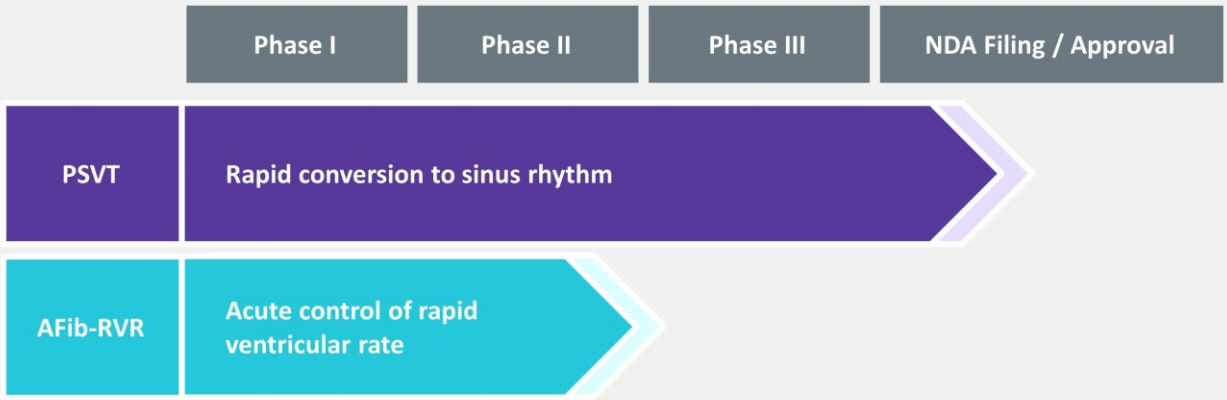
Etripamil Nasal Spray is an investigational novel CCB



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

Etripamil Clinical Pipeline Advancement

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



Comprehensive Data Supports FDA New Drug Application for Rapid Conversion of PSVT 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 ~450

- >1,600 Patient Exposures to Etripamil ≥ 70 mg
- Positive Phase 3 pivotal RAPID trial anchors NDA submission (2023)

NDA = New Drug Application
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 70 mg regimen or placebo during a PSVT event outside the medical setting

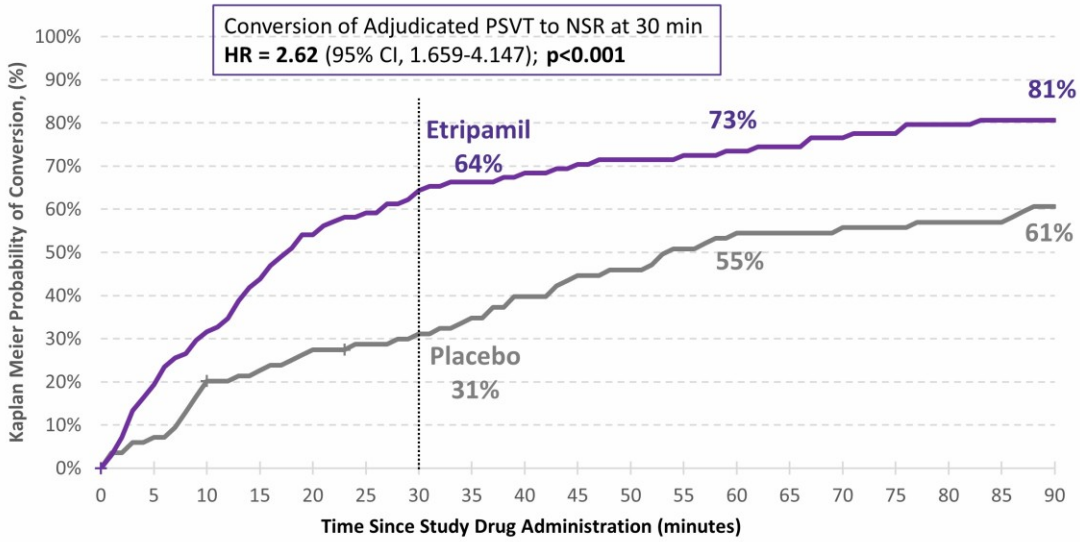
Repeat-dose regimen – if symptoms not resolved in 10 minutes, second dose administered

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

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

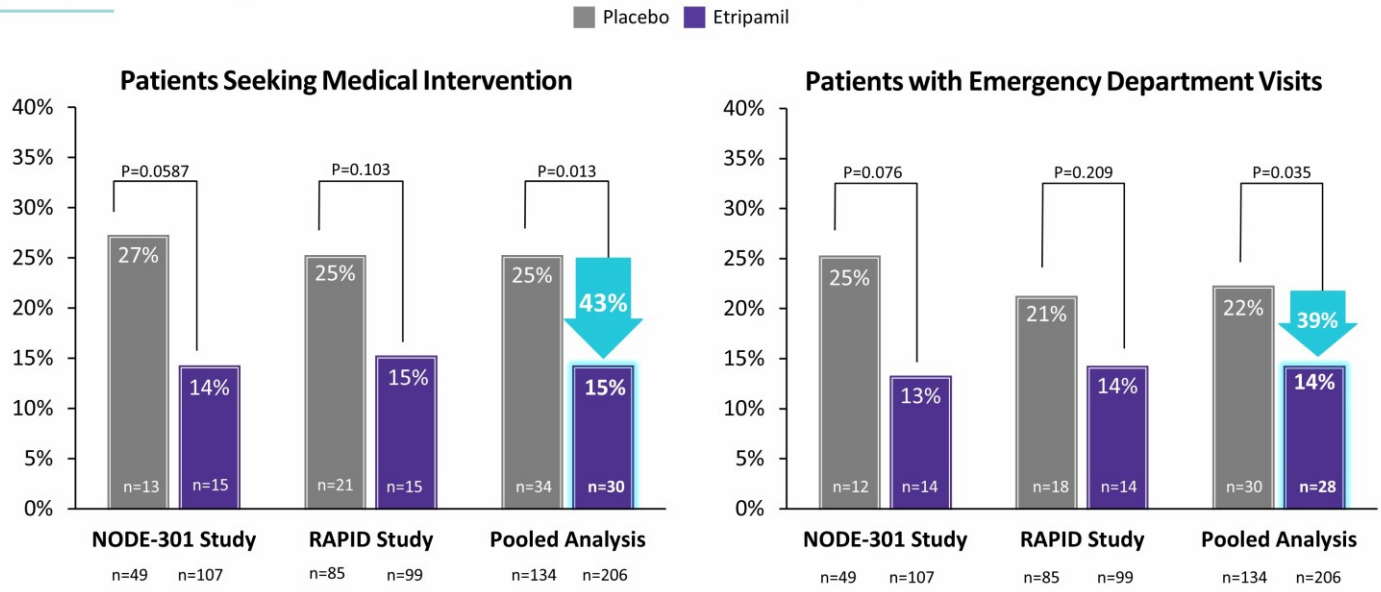
HR = Hazard Ratio; CI = Confidence Interval
Source: Milestone Pharmaceuticals Data on File

Data Indicates 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

Fewer Medical Interventions and Emergency Department Visits
RAPID Study



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.

Etripamil Well-Tolerated with a Favorable Safety Profile
RAPID Study – Safety Events

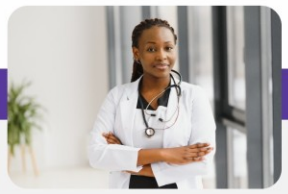
Subject-reported AEs,[1] n (%)	Placebo[2] N=120	Etripamil[2] N=135
Nasal discomfort	6 (5.0)	31 (23.0)
Nasal congestion	1 (0.8)	17 (12.6)
Rhinorrhea	3 (2.5)	12 (8.9)
Epistaxis	2 (1.7)	8 (5.9)[3]
Syncope	0.0	0.0
Loss of Consciousness	0.0	0.0
Pre-Syncope	0.0	0.0
Dizziness	0.0	1 (0.7)[4]
Subjects with Events 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 – up to 24 hours following drug administration. Source: Milestone Pharmaceuticals Data on File.

Etripamil Has Substantial Potential Value for Stakeholder Groups If Approved

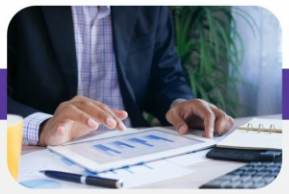
Patients - Empowerment

- 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



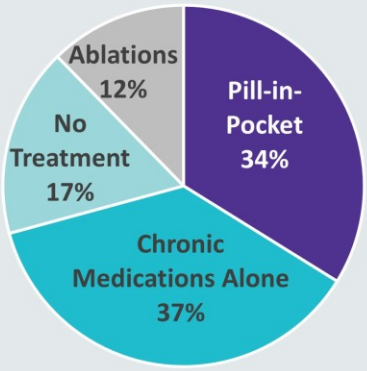
Payers – More Efficient Use of Resources

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

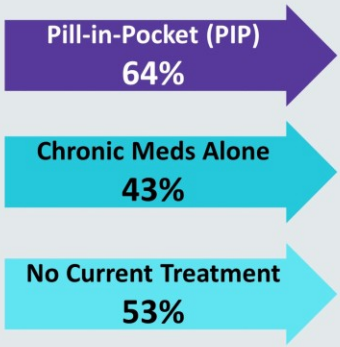
Sources: Internal market research, PSVT = Paroxysmal Supraventricular Tachycardia, ED = Emergency Department

Cardiologist Expect to Prescribe Etripamil to the Majority of Unablated PSVT Patients

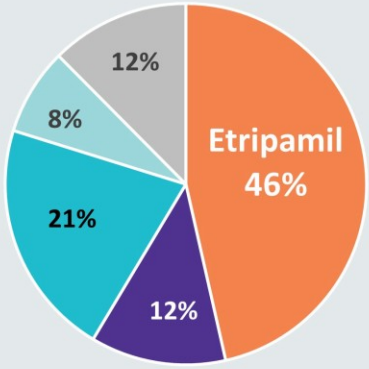
Current PSVT Management



Cardiologists Stated Adoption of Etripamil per Segment



Impact of Cardiologist Adoption of Etripamil



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

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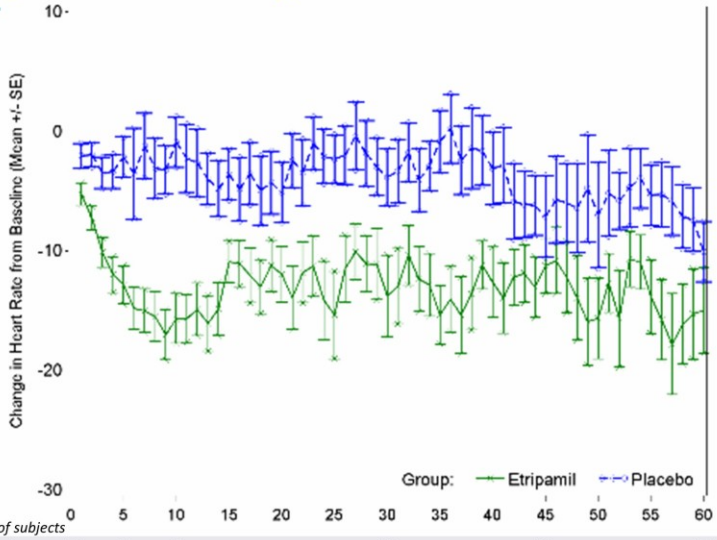
Effect of Etripamil on Heart Rate (HR) while in SVT (NODE-301 Study)



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.

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

1 Patient presents to ED with episode of AFib-RVR

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

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

2 Dosing & Assessment

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

3 Efficacy Analysis

Primary: Maximum reduction in VR within 60 min

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

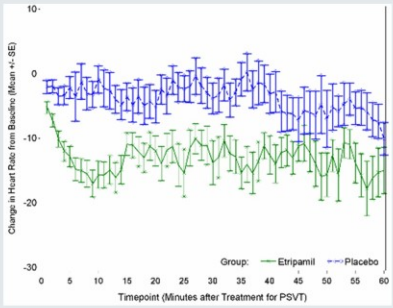
- **Time to** VR reduction
- **Duration** of VR reductions
  - <100 bpm, ≥ 10% reduction, ≥ 20% reduction
- Patient satisfaction with treatment (TSQM-9)

AFib-RVR = Atrial Fibrillation with Rapid Ventricular Rate; TSQM-9, Treatment Satisfaction Questionnaire for Medication; ED = Emergency Department

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

Potential Effect of Etripamil on Heart Rate on Patients in AFib-RVR

PSVT Patients HR Reduction NODE-301



Afib-RVR In PSVT Program

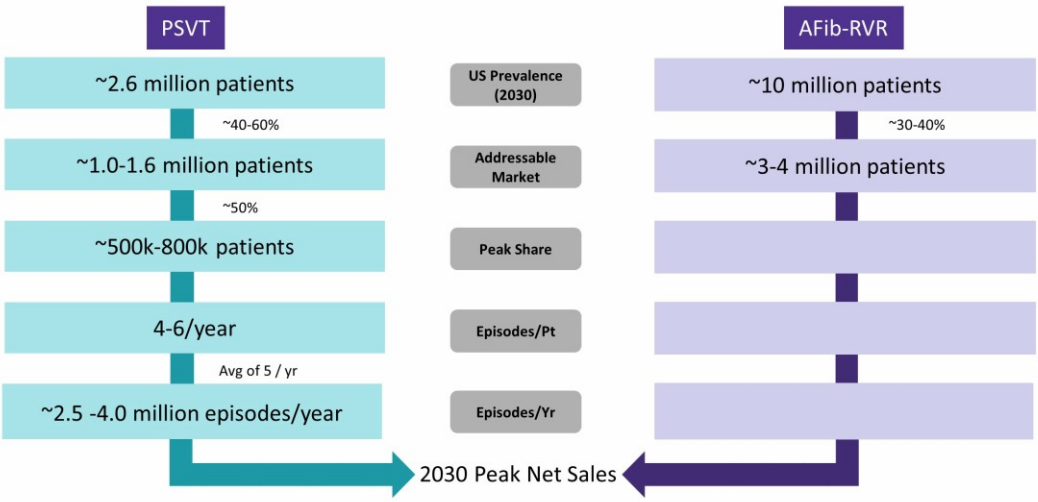
Medical Conference Q2' 2023

AFib-RVR in REVERA (interim)

Public Release Q2' 2023

Utilizing Proof of Concept Data to Design Pivotal AFib-RVR Study

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

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

Finances – as of September 30, 2022

- Cash, cash equivalents and short-term investments of $77.2M
  - $80.7M Proforma for Ji-Xing Milestone Payment (1)
- Cash funds operations through 2023
- Equity - 42.8M in shares and pre-funded warrants outstanding
  - 34.3M common shares
  - 8.5M pre-funded warrants (2)

(1) Ji Xing Milestone Payment of $3.5M due upon Successful Completion of RAPID trial. RAPID trial top-line results 10/17/2022
(2) 3,809,523 pre-funded warrants exercised in October

Milestone Pharma - Targeting Vast Unmet Need for Patient Management of Common Heart Conditions

Targeting Common Arrhythmias

- PSVT
- AFib-RVR
- High burden on patients *and* on the healthcare system

Empowering Patients to Treat Themselves

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

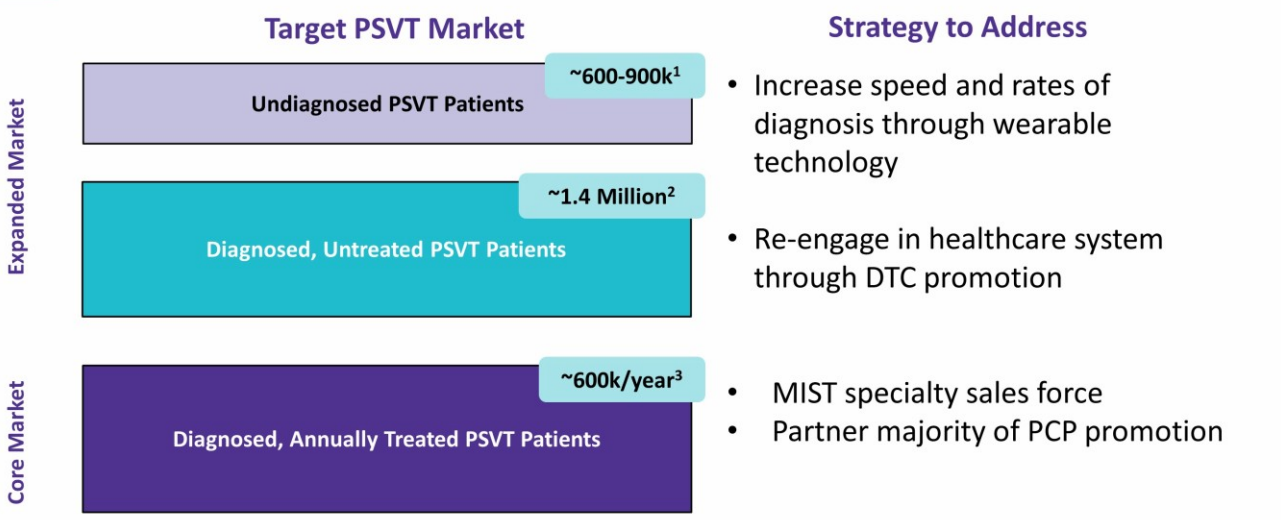
Positioned for **Success**

- Positive Phase 3 results in PSVT
- NDA submission Q3 2023
- AFib-RVR program expands market – Initial data Q2 2023
- Experienced leadership driving commercialization

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

Appendix

Core PSVT Market Addressable Now, if approved, 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.

Management of Patients with PSVT and Call Point Targeting

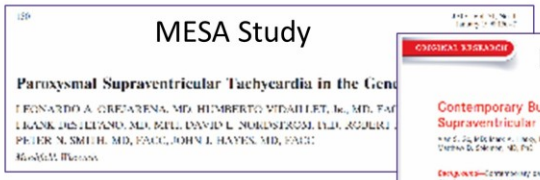
Majority of patients with PSVT managed by CV specialists, leading to commercial efficiencies

		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*			

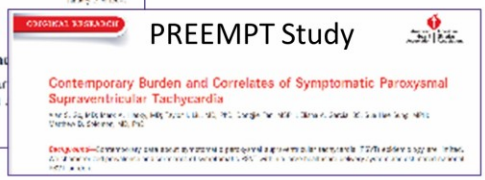
- Targeted sales force to reach majority of available opportunity
- Significant overlap with most common CV portfolio call points

Source: Internal market research

Published Disease Data Likely Under-Reports Burden of PSVT


MESA Study

Paroxysmal Supraventricular Tachycardia in the Gen


PREEMPT Study

Contemporary Burden and Correlates of Symptomatic Paroxysmal Supraventricular Tachycardia

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.

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

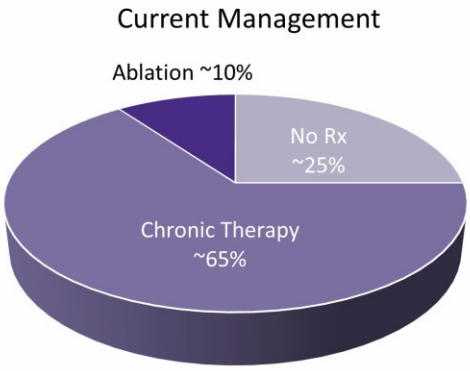
Prevalent PSVT Patients

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.

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



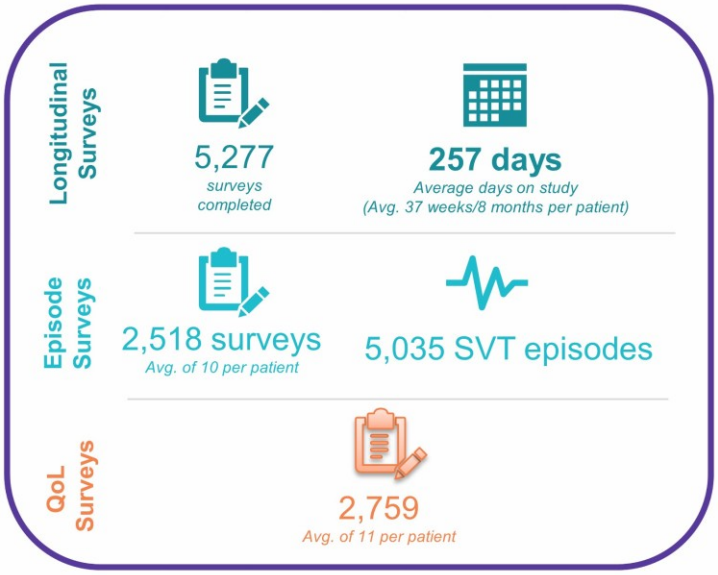
Source: Sacks, N.C. et al; Prevalence of Paroxysmal Supraventricular Tachycardia (PSVT) in the US in Patients Under 65 Years of Age; Abstract and Oral Presentation at the International Academy of Cardiology Annual Scientific Sessions 2018, 23rd World Congress on Heart Disease; Precision Xtract, Boston, 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.

New Data Enhances Understanding of Burden of PSVT

Analysis of Prospective Patient Reported Outcomes Longitudinal Data

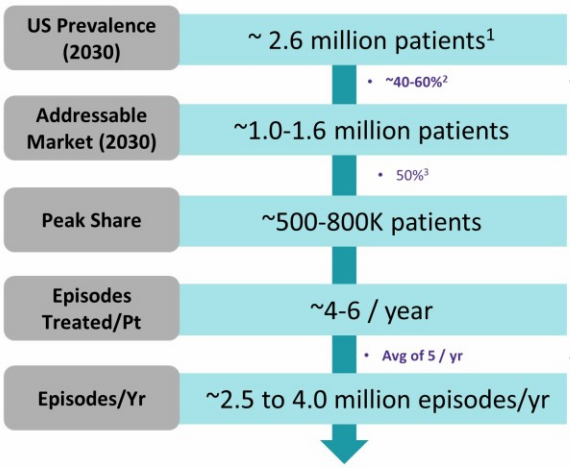
247 US & UK patients

- **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).

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).

RAPID Demographics & Baseline Characteristics (Safety Population)

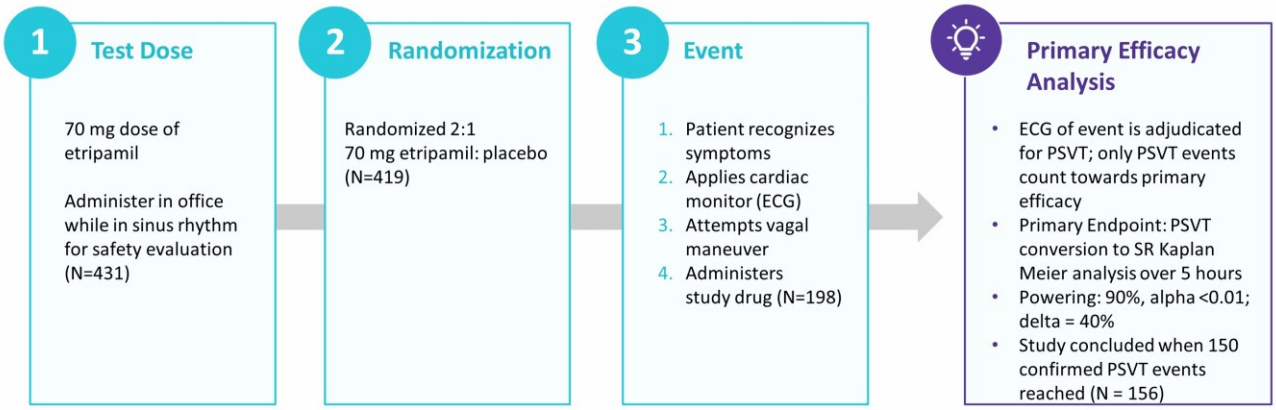
	Placebo (N=120)	Etripamil (N=135)	Overall (N=255)
Age, years			
Mean (SD)	**56.2** (12.0)	**52.4** (14.0)	**54.2** (13.2)
Median (range)	**58.0** (21, 78)	**52.0** (19, 82)	**55.0** (19, 82)
Sex, female, n (%)	**88** (73.3)	**93** (68.9)	**181** (71.0)
Race, n (%)			
American Indian or Alaska native	**0**	**1** (0.7)	**1** (0.4)
Asian	**4** (3.3)	**2** (1.5)	**6** (2.4)
Black or African American	**3** (2.5)	**4** (3.0)	**7** (2.7)
White	**110** (91.7)	**126** (93.3)	**236** (92.5)
Other	**3** (2.5)	**2** (1.5)	**5** (2.0)
PSVT confirmation duration, years			
Mean (SD)	**1.7** (3.8)	**2.2** (5.3)	**2.0** (4.7)
Median (range)	**0.5** (0.0, 32.2)	**0.3** (-0.7, 30.7)	**0.4** (-0.7, 32.2)
PSVT episodes in past year			
Mean (SD)	**10.8** (22.9)	**6.3** (13.9)	**8.4** (18.8)
Median (range)	**5.0** (0.0, 200.0)	**3.0** (0.0, 150.0)	**4.0** (0.0, 200.0)
Lifetime emergency department visits for PSVT			
Mean (SD)	**3.9** (11.2)	**4.6** (15.5)	**4.3** (13.6)
Median (range)	**2.0** (0.0, 120.0)	**2.0** (0.0, 160.0)	**2.0** (0.0, 160.0)
Concomitant medications, n (%)			
Beta blocker or calcium channel blocker	**80** (66.7)	**86** (63.7)	**166** (65.1)
Beta blocker only	**40** (33.3)	**45** (33.3)	**85** (33.3)
Calcium channel blocker only	**29** (24.2)	**30** (22.2)	**59** (23.1)
Beta blocker and calcium channel blocker	**11** (9.2)	**11** (8.1)	**22** (8.6)

Milestone PHARMACEUTICALS

Phase 3 PSVT Program – Other than RAPID

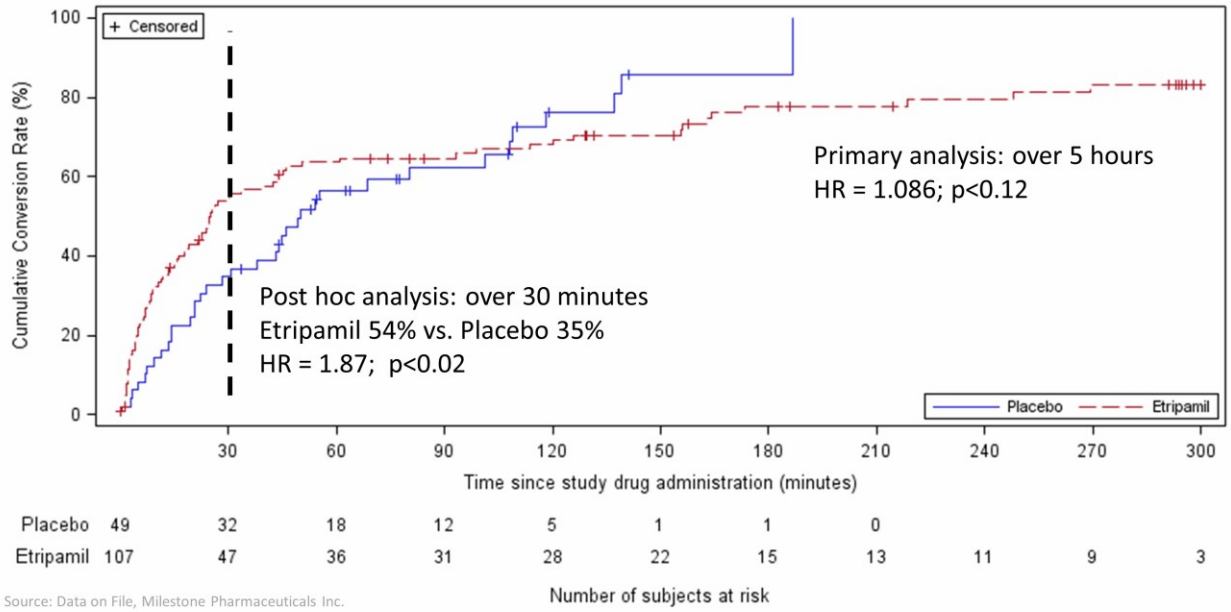
- NODE-301
- NODE-302

NODE-301 Study Design



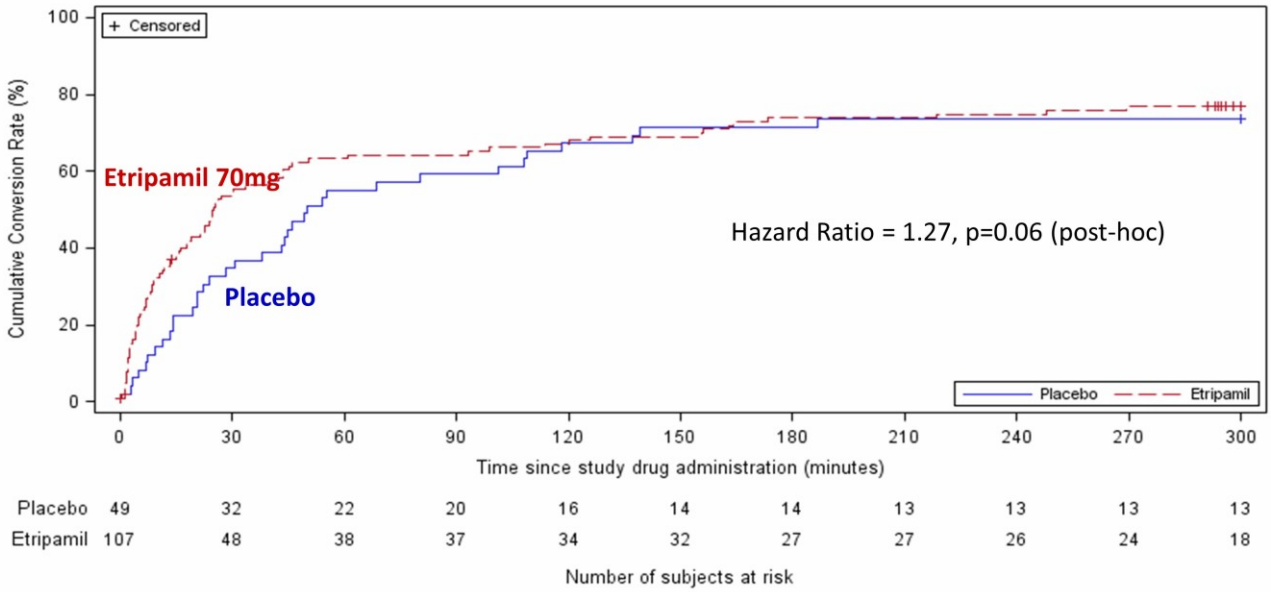
SR = Sinus Rhythm; ECG = Electrocardiogram; PSVT = paroxysmal supraventricular tachycardia

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



Source: Data on File, Milestone Pharmaceuticals Inc.

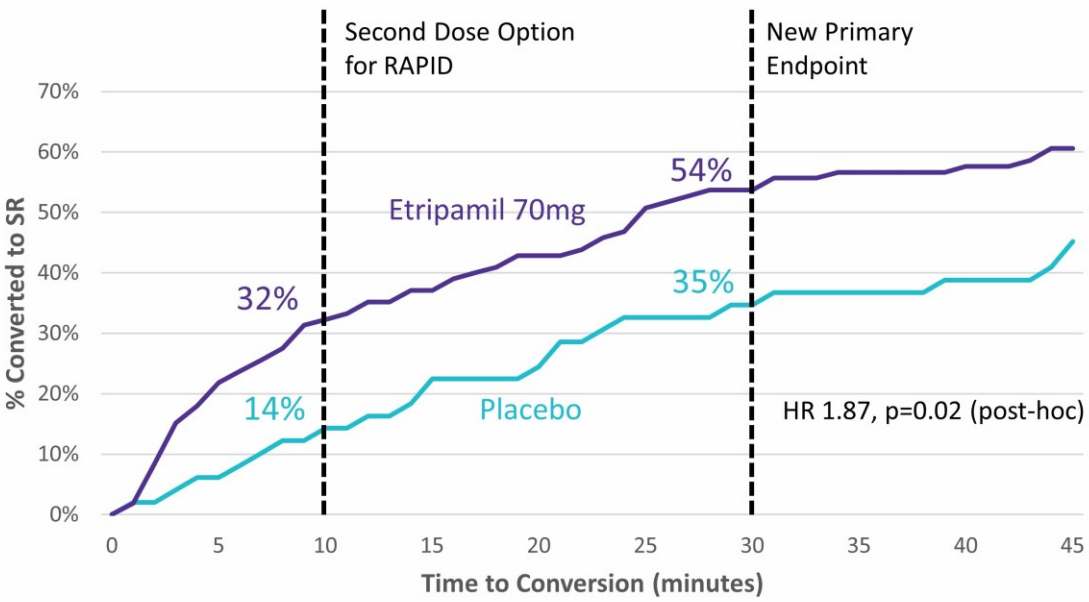
NODE-301 Conversion up to Hour 5 with Medical Intervention Patients Analyzed as Treatment Failures at 5 hours (post-hoc)



Number of subjects at risk											
Placebo	49	32	22	20	16	14	14	13	13	13	13
Etripamil	107	48	38	37	34	32	27	27	26	24	18

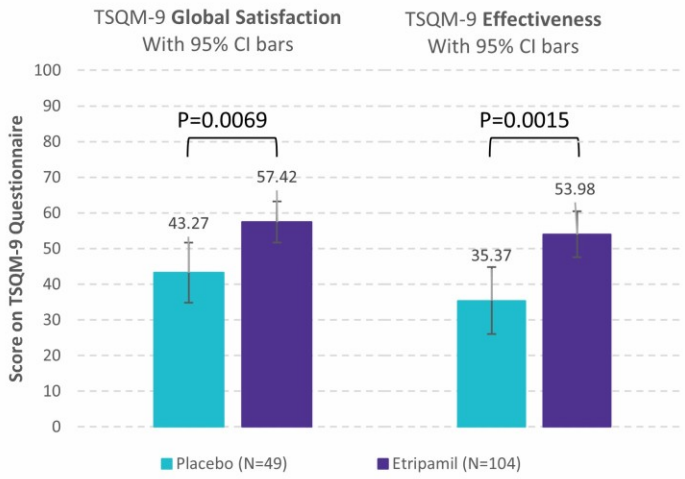
Subjects who convert following medical assistance are censored at 5 hours. Subjects who present missing data from time t to the end are censored at the time of last available data. Subjects who do not convert or are not censored before 5 hours are censored at 5 hours

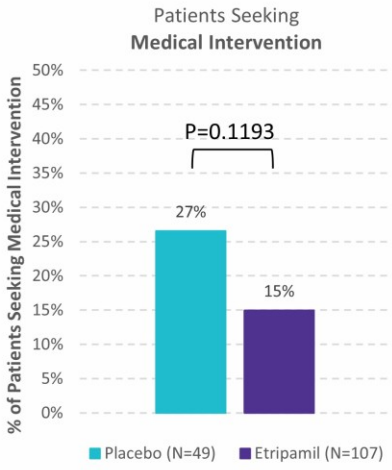
NODE-301 Efficacy – Time to Conversion over 45 Minutes



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.

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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.

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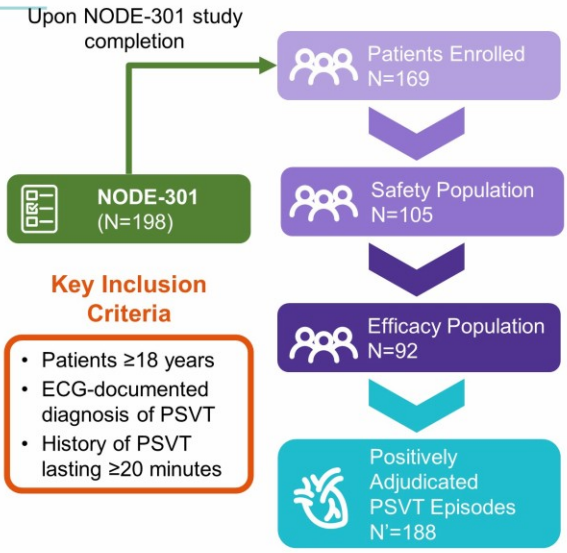
Nasal discomfort	27 (19.6)	4 (6.7)
Nasal congestion	11 (8.0)	2 (3.3)
Epistaxis	9 (6.5)	0 (0.0)
Rhinorrhea	8 (5.8)	1 (1.7)
Throat irritation	7 (5.1)	1 (1.7)
Headache	4 (2.9)	0 (0.0)
Sneezing	3 (2.2)	0 (0.0)
Atrioventricular (AV) block first degree	2 (1.4)	0 (0.0)
Dysgeusia	2 (1.4)	1 (1.7)
Sinus congestion	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-302 Study Design: Single-arm, Open-label Extension Study From NODE-301



Study Procedures

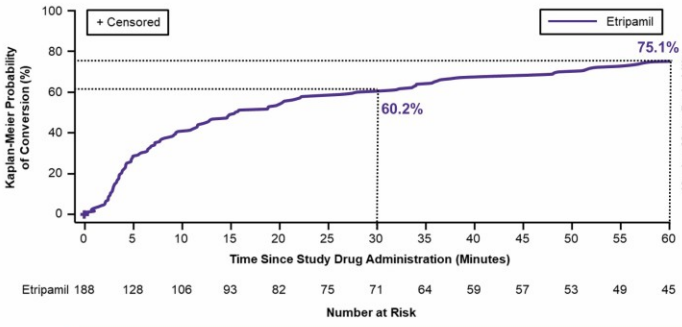
1. Patient perceived PSVT episode
2. Patient applied CMS
3. Patient performed trained VM
4. If episode persisted, patient self-administered etripamil 70 mg intranasally
5. CMS ECG monitoring continued for 5 hours
6. An independent adjudication committee used the complete CMS ECG recordings to confirm PSVT and conversion to sinus rhythm

- Patients continued in the study for up to 11 treated episodes
- Median time in the study: 223 days[a] (range: 1−584)

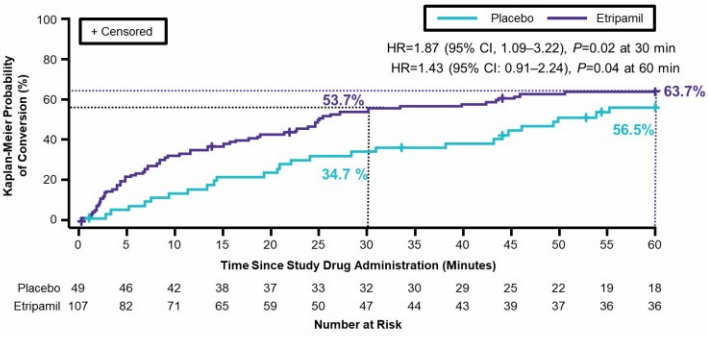
CMS = cardiac monitoring system. ECG = electrocardiogram. PSVT = paroxysmal supraventricular tachycardia. VM = vagal maneuver.
Positively Adjudicated = independently confirmed to be PSVT by ECG review by blinded adjudicator. [a]Includes patients with 0 episodes.
Source: Ip, JE et al; Etripamil Nasal Spray Is Effective and Safe for Conversion of Repeated Spontaneous Episodes of Paroxysmal Supraventricular Tachycardia During Long-term Follow-up: Results From the NODE-302 Study; Heart Rhythm Society 2022 Congress Late Breaking Clinical Trials Presentation, Apr 29-May 1, 2022

Conversion of Adjudicated PSVT to Sinus Rhythm at 30 and 60 Minutes – NODE-302 and NODE-301

NODE-302 at 30 and 60 Minutes (all episodes)



NODE-301 at 30 and 60 Minutes: Post Hoc



NODE-302	NODE-301
Open-label	Randomized, double-blind, placebo-controlled
Medical interventions censored at end of observation period (5 hr)	Medical interventions censored at time of intervention

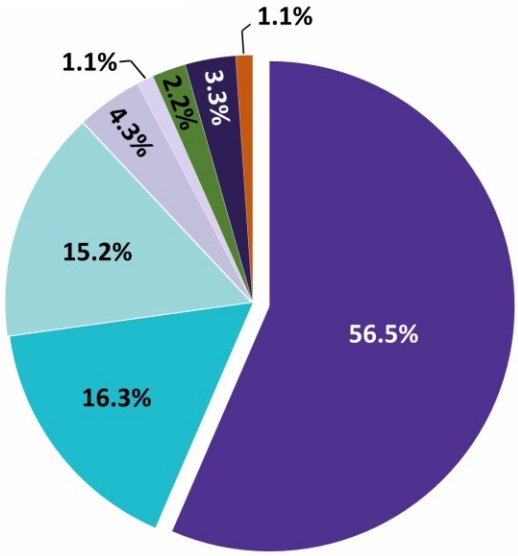
CI = confidence interval; HR = hazard ratio; PSVT = paroxysmal supraventricular tachycardia

Source: Ip, JE et al; Etripamil Nasal Spray Is Effective and Safe for Conversion of Repeated Spontaneous Episodes of Paroxysmal Supraventricular Tachycardia During Long-term Follow-up: Results From the NODE-302 Study; Heart Rhythm Society 2022 Congress Late Breaking Clinical Trials Presentation, Apr 29-May 1, 2022

NODE-302: Number of Positively Adjudicated PSVT Episodes Per Patient Treated With Etripamil

- 52/92 patients (56.5%) used etripamil for 1 episode
- 40/92 patients (43.5%) used etripamil for 2 or more episodes

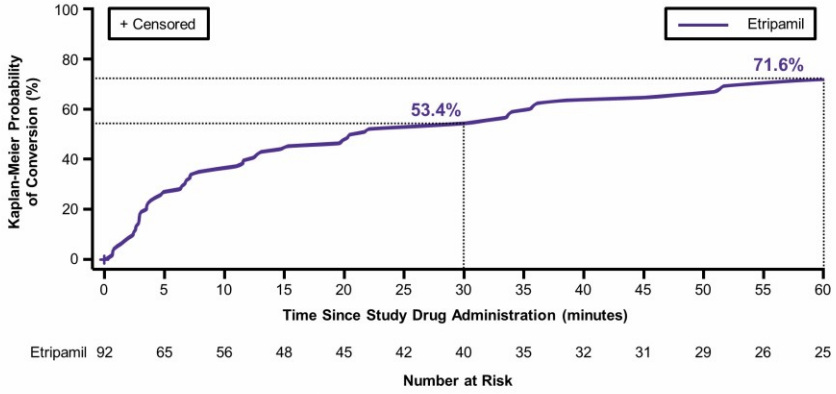
# of Episodes per patient	# of Patients
1	n=52
2	n=15
3	n=14
4	n=4
5	n=1
6	n=2
7	n=3
10	n=1



PSVT = paroxysmal supraventricular tachycardia. Positively Adjudicated = independently confirmed to be PSVT by ECG review by blinded adjudicator.

Source: Ip, JE et al; Etripamil Nasal Spray Is Effective and Safe for Conversion of Repeated Spontaneous Episodes of Paroxysmal Supraventricular Tachycardia During Long-term Follow-up: Results From the NODE-302 Study; Heart Rhythm Society 2022 Congress Late Breaking Clinical Trials Presentation, Apr 29-May 1, 2022

NODE-302: Conversion of Adjudicated PSVT to Sinus Rhythm – 1st Episode

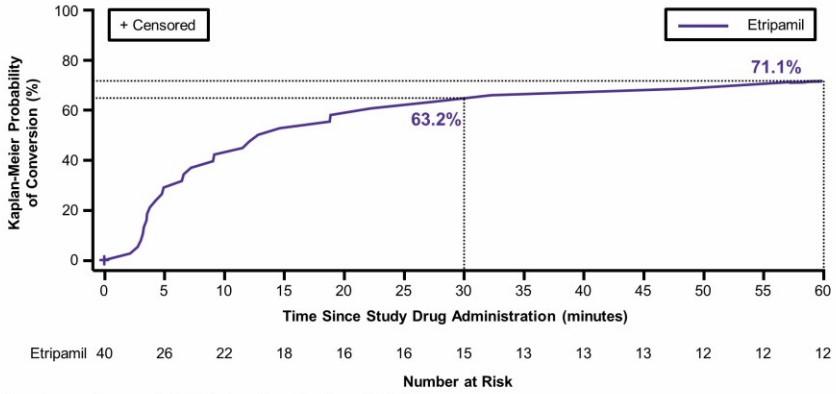


- Data are from 1st confirmed PSVT episode (n=92)[a]
- Median time from NODE-302 enrollment to 1st treated episode: 46.5 days (range: 3–518)[b]
- Kaplan-Meier estimate for conversion by 30 minutes: 53.4%[a]
- Median time to conversion: 21.1 minutes (95% CI, 11.6–35.5)

[a]n=4 were censored at time=0 due to conversion before drug administration. [b]Excludes patients with 0 episodes.
PSVT = paroxysmal supraventricular tachycardia

Source: Ip, JE et al; Etripamil Nasal Spray Is Effective and Safe for Conversion of Repeated Spontaneous Episodes of Paroxysmal Supraventricular Tachycardia During Long-term Follow-up: Results From the NODE-302 Study; Heart Rhythm Society 2022 Congress Late Breaking Clinical Trials Presentation, Apr 29-May 1, 2022

NODE-302: Conversion of Adjudicated PSVT to Sinus Rhythm – 2nd Episode



- Data are from 2nd confirmed PSVT episode (n=40)[a]
- Median time from NODE-302 enrollment to 2nd treated episode: 93.5 days (range: 18–290)[b]
- Kaplan-Meier estimate for conversion by 30 minutes: 63.2%[a]
- Median time to conversion: 13.7 minutes (95% CI, 6.6–32.3)

[a]n=2 were censored at time=0 due to conversion before drug administration. [b]Excludes patients with 0 and 1 episodes.
PSVT = paroxysmal supraventricular tachycardia
Source: Ip, JE et al; Etripamil Nasal Spray Is Effective and Safe for Conversion of Repeated Spontaneous Episodes of Paroxysmal Supraventricular Tachycardia During Long-term Follow-up: Results From the NODE-302 Study; Heart Rhythm Society 2022 Congress Late Breaking Clinical Trials Presentation, Apr 29-May 1, 2022

NODE-302 Consistency of Conversion at 30 Minutes between the 1st and 2nd Adjudicated PSVT Episodes

	No Conversion on 1st Episode	Conversion on 1st Episode
No conversion on 2nd episode	9	5
Conversion on 2nd episode	5	21

- 75% of patients (30/40) had a consistent response between the 1st and 2nd episode (Chi-square=8.09; *P*=0.0045)
- 21/26 patients (81%) who converted on their 1st episode also successfully converted during their 2nd episode

PSVT = paroxysmal supraventricular tachycardia

Source: Ip, JE et al; Etripamil Nasal Spray Is Effective and Safe for Conversion of Repeated Spontaneous Episodes of Paroxysmal Supraventricular Tachycardia During Long-term Follow-up: Results From the NODE-302 Study; Heart Rhythm Society 2022 Congress Late Breaking Clinical Trials Presentation, Apr 29-May 1, 2022

NODE-302: Additional Medical Intervention

- 13% of patients and 8.5% of positively adjudicated PSVT episodes required additional medical intervention
- Additional medical interventions included:
  - Intravenous adenosine (n=12)
  - Physician-initiated vagal maneuver (n=2)
  - Orally self-administered rescue medication (pill in the pocket, n=2)

PSVT = paroxysmal supraventricular tachycardia. Positively Adjudicated = independently confirmed to be PSVT by ECG review by blinded adjudicator.

Source: Ip, JE et al; Etripamil Nasal Spray Is Effective and Safe for Conversion of Repeated Spontaneous Episodes of Paroxysmal Supraventricular Tachycardia During Long-term Follow-up: Results From the NODE-302 Study; Heart Rhythm Society 2022 Congress Late Breaking Clinical Trials Presentation, Apr 29-May 1, 2022

NODE-302: Most Frequent Etripamil-related TEAEs

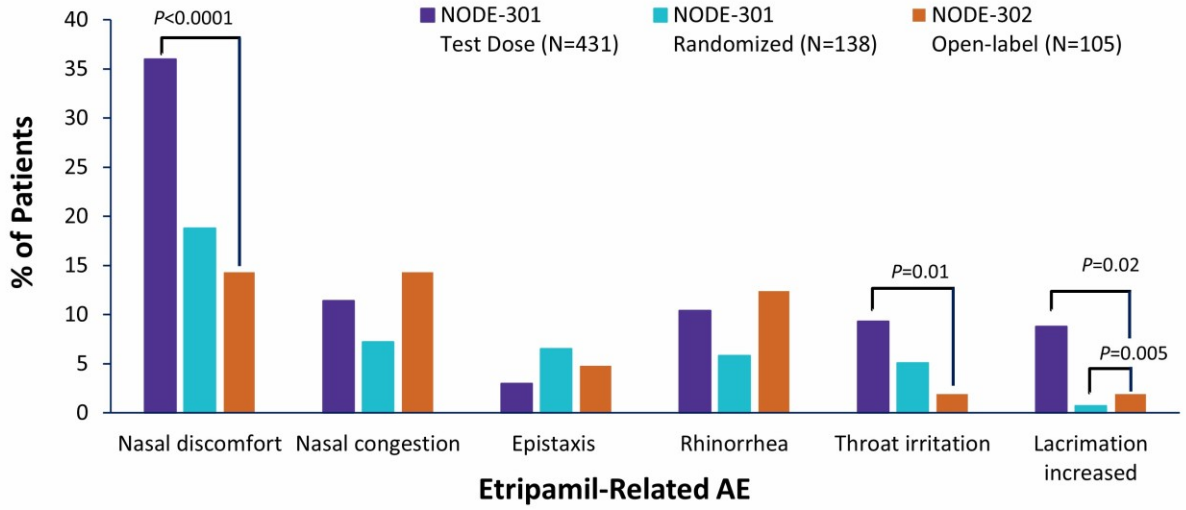
Etripamil-related TEAEs Occurring in >1%,[a] n (%)	Safety Population (N=105)
Patients with any TEAE	34 (32.4)
TEAEs by preferred term	
Nasal discomfort	15 (14.3)
Nasal congestion	15 (14.3)
Rhinorrhea	13 (12.4)
Epistaxis	5 (4.8)
Sneezing	4 (3.8)
Cough	2 (1.9)
Throat irritation	2 (1.9)
Headache	2 (1.9)
Lacrimation increased	2 (1.9)

- Majority of TEAEs were nasal/local, mild, and brief
- No reported cases of syncope or symptoms of hypotension
- No episodes of AV block or pauses after PSVT conversion with etripamil

[a]Etripamil-related TEAEs are defined as AEs with a start date occurring 0 to 24 hours after etripamil dose that were considered related to etripamil by investigator; patients could have more than one TEAE.
AE = adverse event; AV = atrioventricular; PSVT = paroxysmal supraventricular tachycardia; TEAE = treatment-emergent adverse event

Source: Ip, JE et al; Etripamil Nasal Spray Is Effective and Safe for Conversion of Repeated Spontaneous Episodes of Paroxysmal Supraventricular Tachycardia During Long-term Follow-up: Results From the NODE-302 Study; Heart Rhythm Society 2022 Congress Late Breaking Clinical Trials Presentation, Apr 29-May 1, 2022

Comparison of Etripamil-Related AEs with Repeat Dosing – NODE-301 and NODE-302



Assessed using the Cochran–Mantel–Haenszel test.
AE = adverse event. Etripamil-related AEs were defined as having a start date of 0 to 24 h after drug dose. AEs were assessed from separate but linked trials as labeled.

Source: Ip, JE et al; Etripamil Nasal Spray Is Effective and Safe for Conversion of Repeated Spontaneous Episodes of Paroxysmal Supraventricular Tachycardia During Long-term Follow-up: Results From the NODE-302 Study; Heart Rhythm Society 2022 Congress Late Breaking Clinical Trials Presentation, Apr 29-May 1, 2022

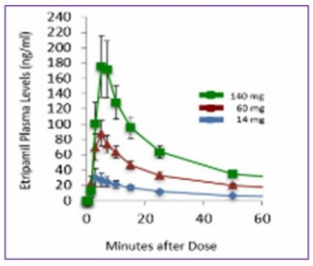
Milestone
PHARMACEUTICALS

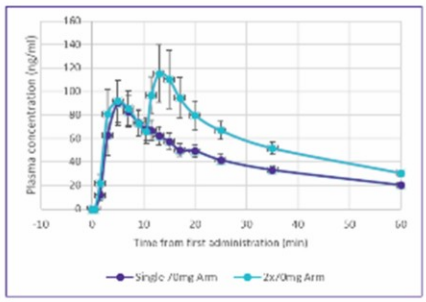
Phase 2 and Phase 1 Clinical Studies

Etripamil Nasal Spray: A Novel CCB Designed to be Fast, Portable, and Patient-Empowering

- Developed to rapidly terminate episodes of PSVT
- Designed for patient self-administration where and whenever the episodes occur
- Novel, investigational, L-type calcium channel blocker
- Formulated as intranasal spray with:
  - Rapid onset of action (T_{max} ≤ 7 min)
  - Short-lasting duration: eliminated from blood within a few hours
- Patent Protection until 2036

PK Plots of Intranasally Administered Etripamil (single and repeat dosing)

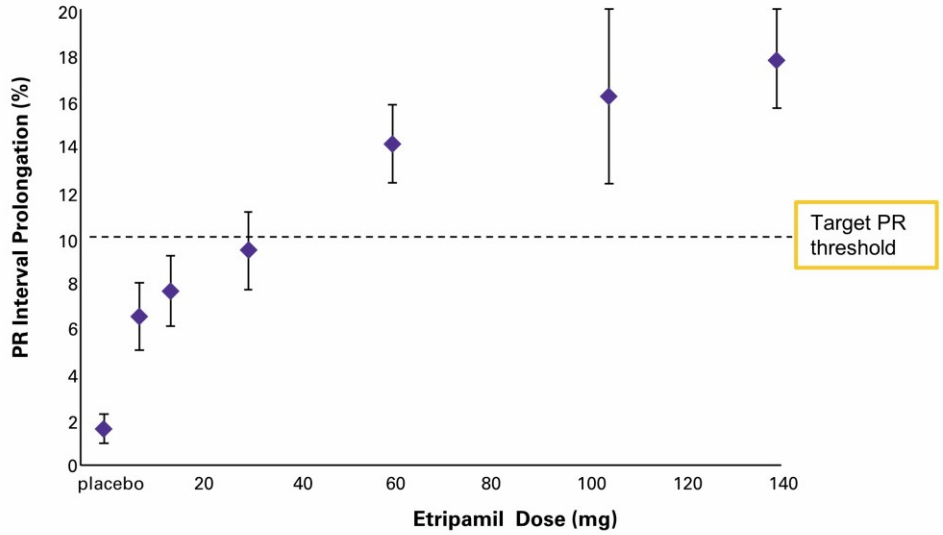




PSVT= paroxysmal supraventricular tachycardia. CCB=calcium channel blocker
PK = pharmacokinetic. Error bars = standard error (SE) of the mean.

Sources: Stambler BS, et al., J Am Coll Cardiol. 2018; Wight D, et al. J Am Coll Cardiol. 2022 Mar, 79 (9_Supplement); Ip Ip JE, et al. manuscript in preparation. ; NODE-PK-101, -103, data on file.

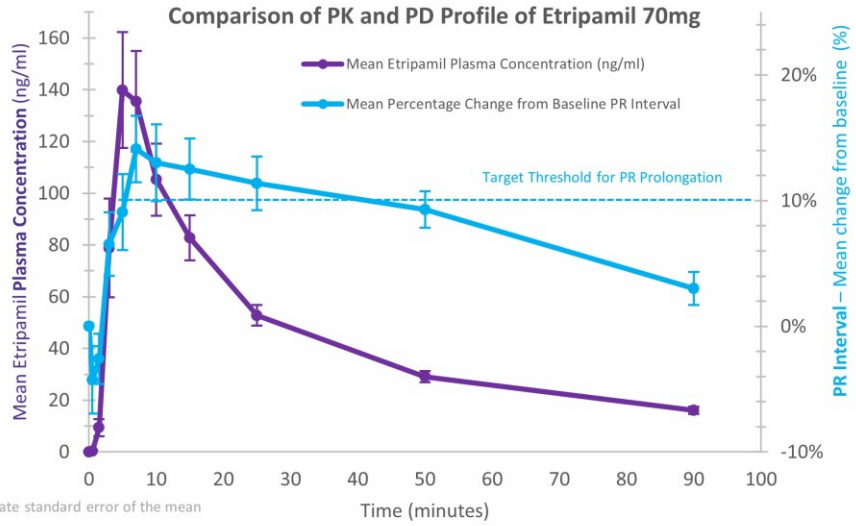
Etripamil Phase 1 Pharmacology
PR Prolongation Used to Select Doses for Phase 2



Error bars indicate standard error of the mean

Etripamil Nasal Spray Pharmacological Results (NODE-102)

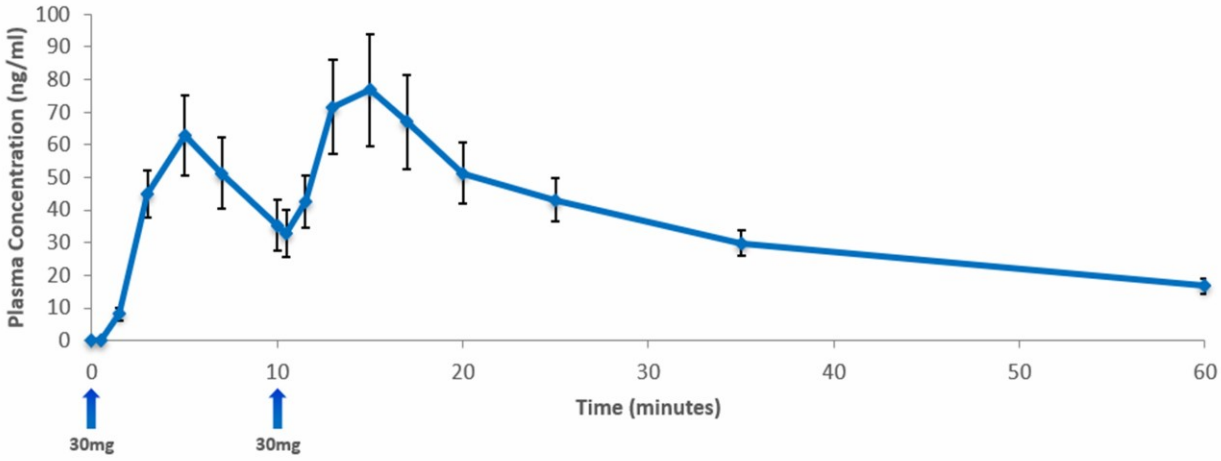
Anticipated therapeutic effect within 45 minutes; peak within 10 minutes



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

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

Repeat administration increases both Cmax and AUC

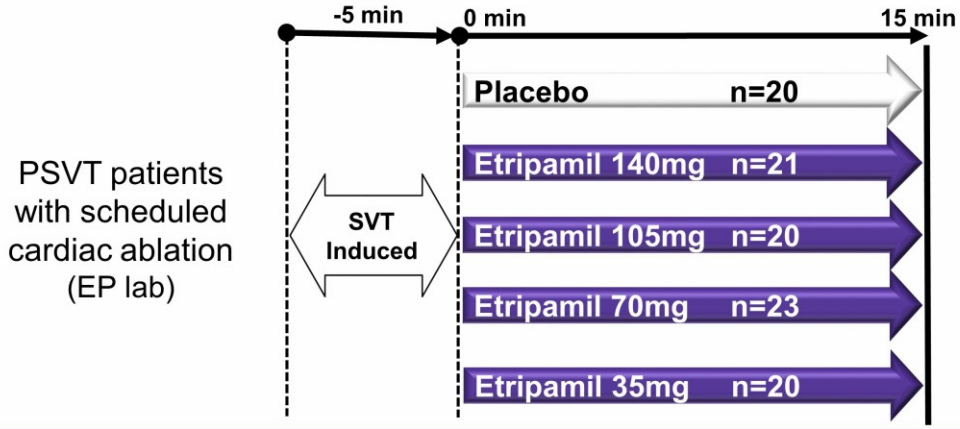


N=7, Error bars are standard error

Source: Data on File, Milestone Pharmaceuticals Inc.

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

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

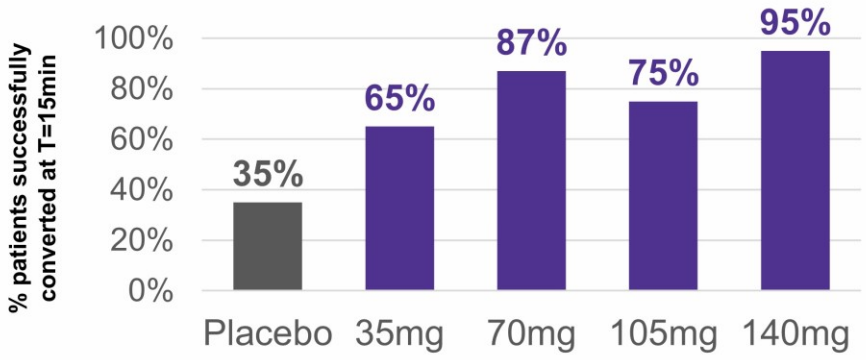


Endpoint: conversion to sinus rhythm within 15 minutes
>80% power to show a 50% absolute difference vs. placebo

EP = electrophysiology. SVT = supraventricular tachycardia, PSVT = paroxysmal supraventricular tachycardia

Phase 2 Primary Endpoint

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

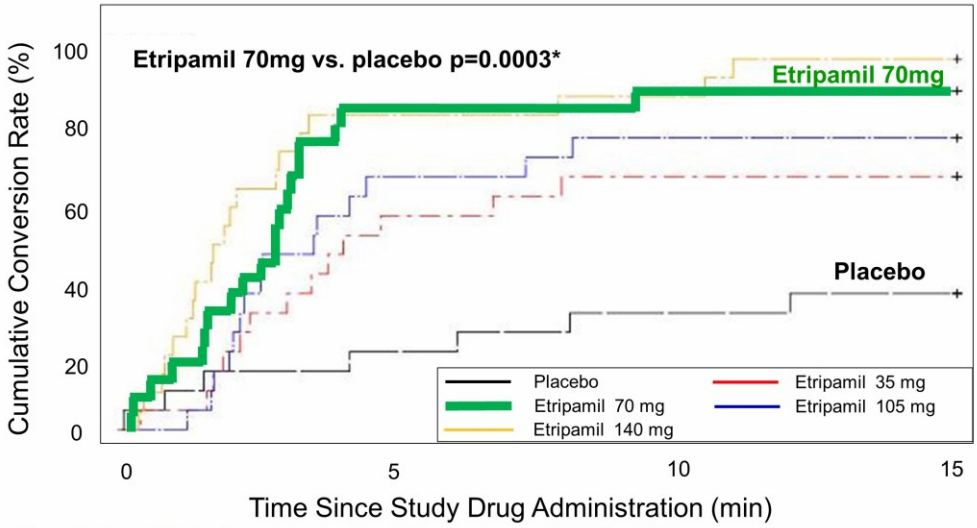


# patients converted at 15 min	7/20	13/20	20/23	15/20	20/21
p-value		0.1128	0.0006	0.0248	<.0001

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 Time to Conversion

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

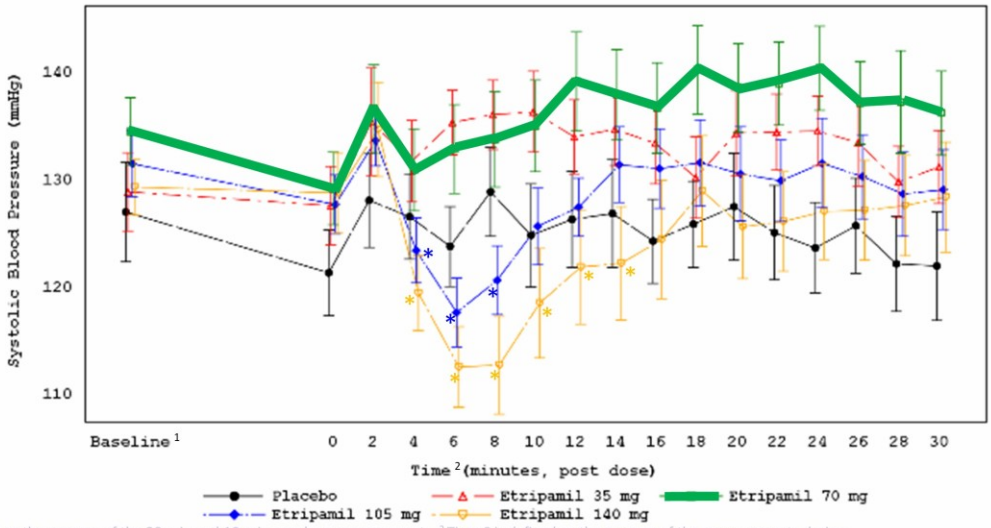


*Hazard Ratio and 95% Confidence Intervals etripamil 70mg vs. placebo; 4.99 (2.09, 11.93)

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

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.

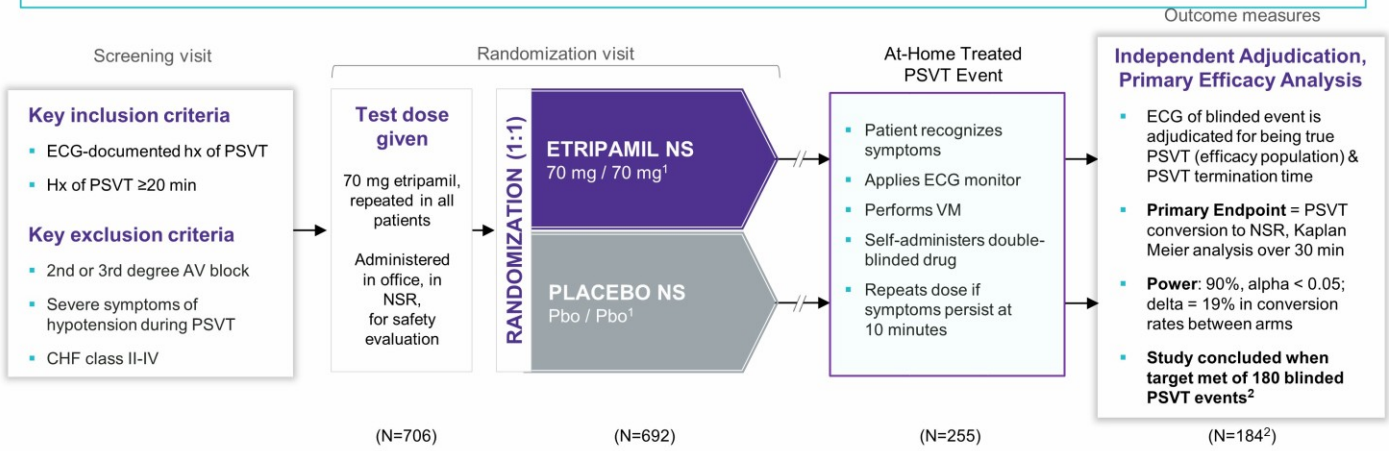
Source: Stambler, B.S. et al.; Etripamil Nasal Spray for Rapid Conversion of Supraventricular Tachycardia to Sinus Rhythm; J Am Coll Cardiol. 2018;72(5):489–97

Milestone
PHARMACEUTICALS

RAPID Detailed Slides

Phase 3 RAPID Clinical Study Design & Enrollment

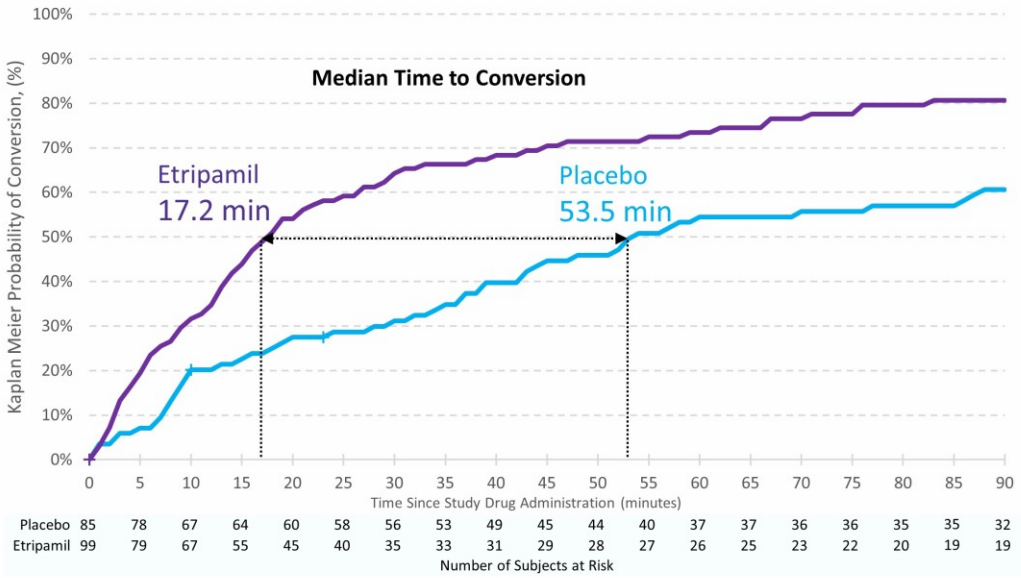
Objective: Evaluate the efficacy & safety of self-administered etripamil nasal spray in patients experiencing a PSVT episode in the at-home setting



[1] Repeat dose of study drug self-administered if PSVT episode does not resolve within 10 minutes after first dose. Of the patients in the RAPID Study who had the repeat dose regimen available to them, 66% of etripamil arm and 79% of placebo arm took a repeat dose of study drug. [2] Includes 29 events treated with one dose of double-blind study drug administration in NODE-301 Part 1, patients with events after that study met its target event goal & had database lock; all blinds maintained. Hx = history; CHF = congestive heart failure; NSR = normal sinus rhythm; VM = vagal maneuver; NS = nasal spray

Ref.: Stambler, BS et al. Rationale for & design of a multicenter placebo-control, phase 3 study to assess efficacy and safety of intranasal etripamil for the conversion of PSVT. *Amer Heart J* (2022).

RAPID Efficacy



"+" symbol on graph indicates censoring for signal loss (n=4 over 90 minutes)

Source: Milestone Pharmaceuticals Data on File

RAPID Safety – Direct ECG Reading[1]

	Placebo Randomized Dose[2] N=120	Etripamil Randomized Dose[2] N=135
Non-sustained ventricular tachycardia[3]	19 (16.4)	18 (14.1)
Sustained ventricular tachycardia (≥ 30 seconds)	1 (0.9)[4]	0
PSVT Recurrence	5 (4.3)	4 (3.1)
Atrial Fibrillation ≥30 seconds	4 (3.5)	1 (0.8)
Atrial Tachycardia ≥30 seconds	1 (0.9)	2 (1.6)
Prolonged PR, for duration of ≥30 seconds	1 (0.9)	2 (1.6)
Atrial Flutter ≥30 seconds	1 (0.9)	0
Sinus Bradycardia ≤40 bpm	1 (0.9)	0
PVC greater than 6 PVCs within 45 seconds	0	0
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] Independent cardiac-electrophysiologist adjudication committee evaluated all ECG recordings in the Safety Population. All adjudication performed blinded to treatment assignment.
[2] Safety Population, based on 5-hour ECG recordings beginning prior to double-blind drug dosing. [3] No dizziness reported in these patients. [4] Blinded-expert ECG readings were indeterminate between supraventricular tachycardia with a wide-QRS vs. ventricular tachycardia; for conservatism, rated as the latter. Of note, this tachycardia was present prior to administration of placebo.

RAPID Safety Analysis

	Placebo Randomized Dose[1] N=120	Etripamil Randomized Dose[1] N=135
Subjects with any Randomized-period TEAE, n (%)	20 (16.7)	68 (50.4)
Maximum severity of any RTEAE, n' (%) of subjects with any RTEAE		
Mild	15 (75.0%)	46 (67.6%)
Moderate	4 (20.0%)	21 (30.9%)
Severe	1 (5.0%)	1 (1.5%)
Subjects with SAE	1 (0.8)	0
Subjects with SAE related to study drug	0	0
Subjects with AE leading to death	0	0
Subjects with drug-related AE leading to study discontinuation	0	3 (2.2)[2]

[1] Safety Population. [2] Three events were: Frequent PVCs and couplets after PSVT termination; non-sustained VT after PSVT termination; allergic reaction, treated with oral Benadryl.

TEAE timing – up to 24 hours following drug administration. TEAE = treatment-emergent adverse event; RTEAE = randomized-period TEAE; SAE = serious adverse event; AE = adverse event; PVC = premature ventricular complex; PSVT = paroxysmal supraventricular tachycardia; VT = ventricular tachycardia.

Source: Milestone Pharmaceuticals Data on File

RAPID Safety – Adverse Events

Subjects with Randomized-period TEAE, Incidence >5%, n (%)	Placebo Randomized Dose[2] N=120	Etripamil Randomized Dose[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]
Subjects with Randomized-period TEAE,[1] n (%)	**Placebo Randomized Dose[2] N=120**	**Etripamil Randomized Dose[2] N=135**
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]

[1] Adverse events specifically acquired as adverse events of interest, as potentially representing lowered blood pressure. [2] Safety Population.
[3] Six of 8 rated as mild, 2 of 8 rated as moderate. [4] Rated as mild.
TEAE = treatment-emergent adverse event. TEAE timing – up to 24 hours following drug administration.

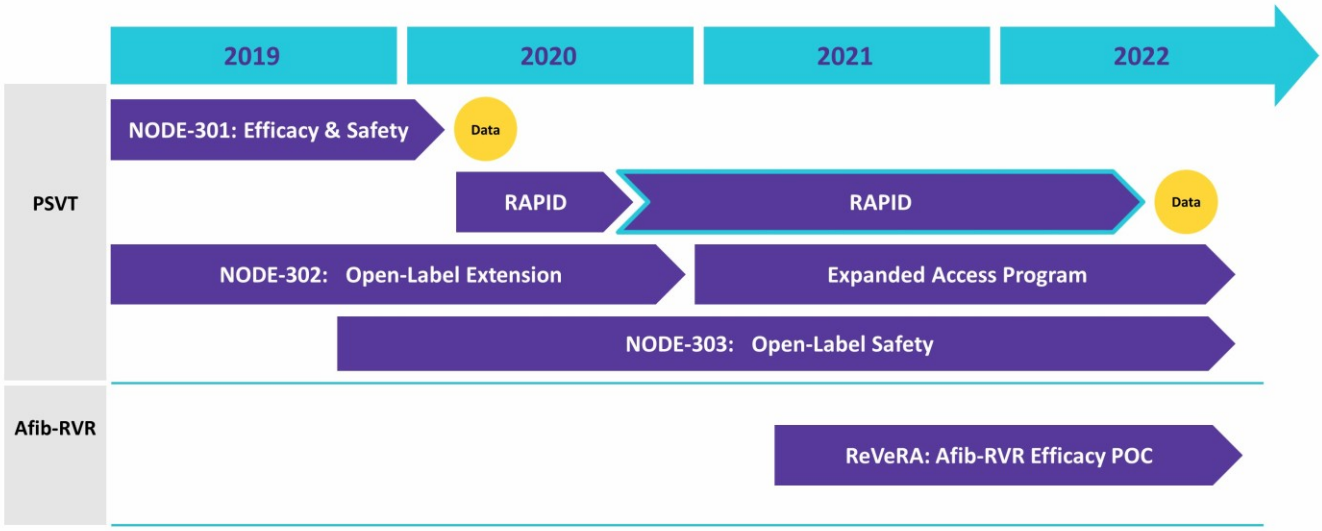
Source: Milestone Pharmaceuticals Data on File0

Conversion Rates from PSVT to Normal Rhythm (all studies)

R&D Phase, Study	Etripamil, 70 mg (% Conversion)	Placebo (% Conversion)	Hazard Ratio	p value	Statistical Analysis Notes
Phase 3 RAPID	64	31	2.62	<0.001	Kaplan Meier analysis through 30 min
Phase 3 NODE-301	54	35	1.87	<0.02	Kaplan Meier analysis through 30 min, post-hoc
Phase 3 NODE-302	60	–	–	–	Kaplan Meier analysis through 30 min
Phase 2 NODE-1	87	35	–	0.0006	Landmark analysis at 15 min

Source: Milestone Pharmaceuticals Data on File

Etripamil Development Program Per Study



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