Milestone PHARMACEUTICALS

RAPID Top Line Results Conference Call

October 17, 2022

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Call Participants

Prepared Remarks

- Joseph Oliveto, President and Chief Executive Officer
- David Bharucha, MD, PhD, Chief Medical Officer
- Lorenz Muller, Chief Commercial Officer

Additional Q&A Participants

- Amit Hasija, Chief Financial Officer
- Jeff Nelson, Chief Operating Officer
- Francis Plat, MD, Chief Scientific Officer

Agenda

- RAPID Top Line Data
- Initial Readthrough to Commercial Opportunity
- Regulatory Next Steps
- Q&A

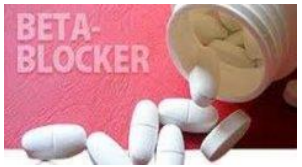
PSVT–Substantial Disease Burden

PSVT

- **Heart rates commonly 150 - 250 beats per min**
- **Episode frequency and duration unpredictable**
- **Symptoms:**
  - ✓ Palpitations
  - ✓ Shortness of breath
  - ✓ Chest pressure or pain
  - ✓ Sweating
  - ✓ Lightheadedness or fainting
  - ✓ Fatigue
  - ✓ Anxiety

Current Standards of Care

Preventive



- Chronic oral BBs and CCBs
- Goal to reduce frequency of episodes

- Catheter ablation (~10% of patients)
- Perceived risk of procedure limits patient receptivity

Acute

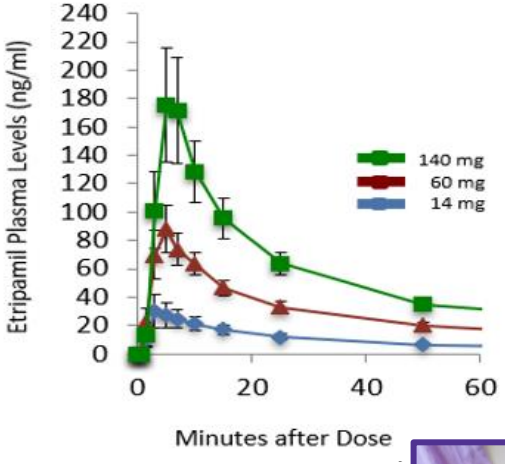
- Vagal maneuvers
- IV medications (adenosine, CCBs) or electrical cardioversion
- At-home, patient-administered treatments limited to off-label use of Pill-in-Pocket BBs and CCBs

PSVT = Paroxysmal Supraventricular Tachycardia; BBs = Beta Blockers; CCBs = Calcium Channel Blockers; IV = Intravenous

Sources: 1. Internal estimates based on market research; 2. Page RL et al, 2015 ACC/AHA/HRS guideline for the management of adult patients with supraventricular tachycardia; Circulation. 2016;133:e471–e505; 3. https://en.ecgpedia.org/index.php?title=Supraventricular_Rhythms, accessed 2/2021

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

- Clinically-validated mechanism
  - CCBs prolong refractoriness and slow conduction over the AV node, terminating most PSVTs
- Formulated for intranasal self-administration with rapid onset of action
- Designed to be rapidly inactivated by ubiquitous human blood esterase enzymes
- Patent protection until 2036

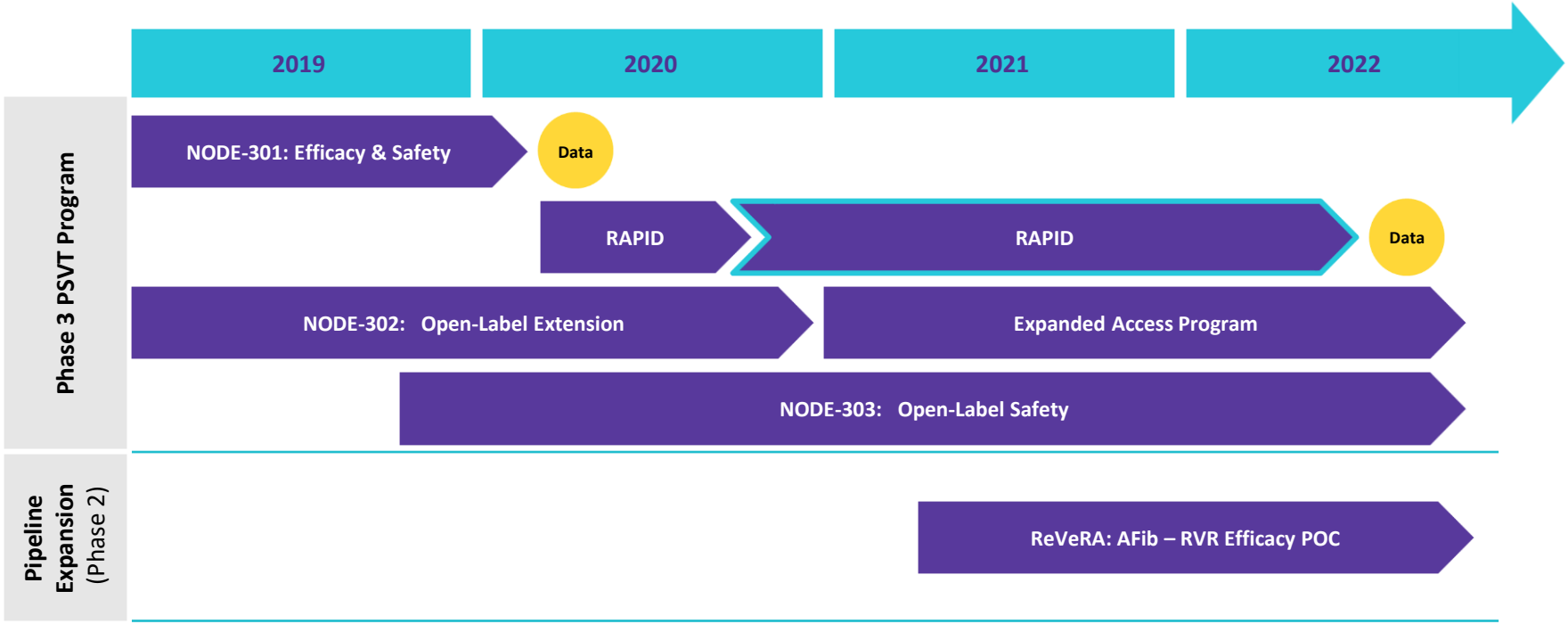


AV=atrioventricular

RAPID Top Line Data Overview

1. **Achieved primary efficacy endpoint**
   - Patients who self-administered etripamil demonstrated statistically significant and clinically meaningful PSVT conversion rates over the first 30 minutes compared to placebo
   - Etripamil 64% vs. placebo 31%; (hazard ratio [HR] = 2.62; 95% CI 1.66, 4.15; p<0.001)
2. **Favorable safety and tolerability data consistent with those observed in prior trials**
3. **Analyses of pooled data from RAPID and NODE-301 studies show statistically significant reduction in medical interventions and visits to the emergency department**

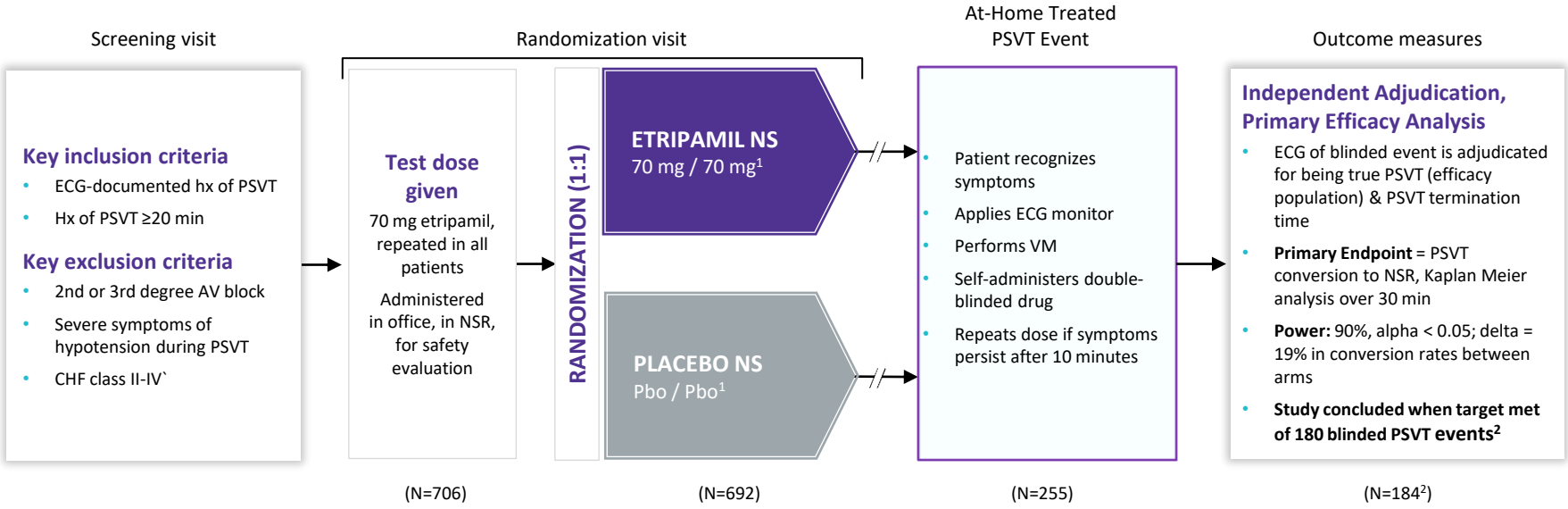
Development Plan for Etripamil



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

RAPID Phase 3 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



ECG=electrocardiogram; Hx=history; CHF=congestive heart failure; NSR=normal sinus rhythm; VM=vagal maneuver; NS=nasal spray

1. Repeat dose of study drug self-administered if PSVT episode does not resolve within 10 minutes after first dose. 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 and had database lock; all blinds maintained

Of the patients in the RAPID Study who had the repeat dose regimen available to them, 66% who took etripamil and 79% who took placebo went on to take a repeat dose of study drug

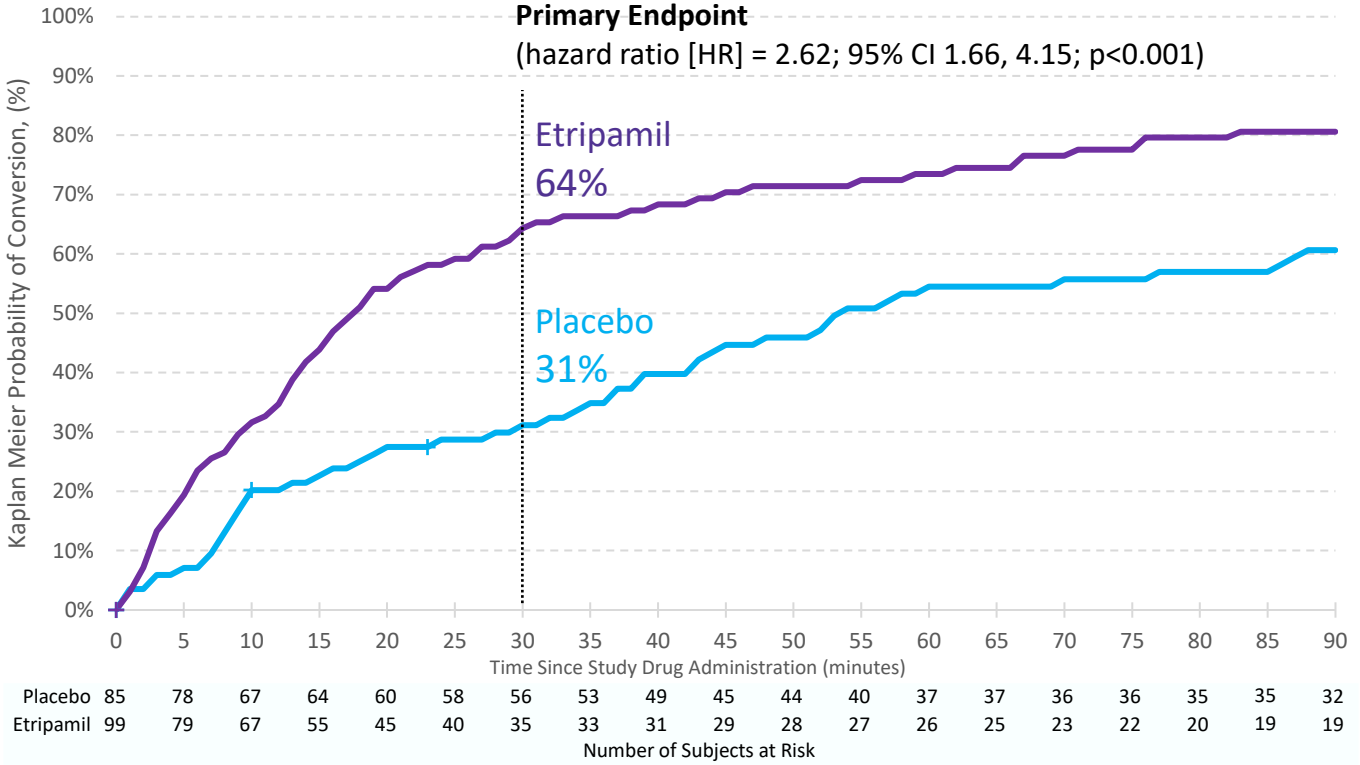
RAPID Patient Demographics & Baseline Characteristics

	Placebo Randomized Dose[1] N=85	Etripamil Randomized Dose[1] N=99
Age, Years		
Mean (SD)	56.7 (10)	50.8 (14)
Median (range)	57 (27 - 78)	50 (19 - 77)
Sex, Female, n (%)	62 (72.9)	69 (69.7)
Race, n (%)		
American Indian or Alaska Native	0	1 (1.0)
Asian	2 (2.4)	0
Black or African American	2 (2.4)	3 (3.0)
White	78 (91.8)	93 (93.9)
Other	3 (3.5)	2 (2.0)

1. Efficacy Population

Source: Milestone Pharmaceuticals Data on File

RAPID Efficacy



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

Source: Milestone Pharmaceuticals Data on File

RAPID Secondary Endpoints

Reduction in Medical Interventions and ED visits in RAPID and NODE 301 Statistically Significant when Combined

	Relative Reduction	p value
Medical Interventions	43%	0.013
Emergency Department Visits	39%	0.035

Reductions in Medical Interventions and Emergency Department visits were not statistically significant in the RAPID study alone

Source: Milestone Pharmaceuticals Data on File

RAPID Safety Analysis

	Placebo Randomized Dose[1] N=120	**Etripamil Randomized Dose[1]** N=135
Subjects with any RTEAE, n (%)	20 (16.7)	68 (50.4)
Maximum severity of any RTEAE, n (%) of 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)

1. Safety Population

TEAE timing – up to 24 hours following drug administration. TEAE = treatment-emergent adverse event; RTEAE = randomized TEAE; SAE = serious adverse event; AE = adverse event

Source: Milestone Pharmaceuticals Data on File

RAPID Safety – Selected Adverse Events

Subjects with RTEAE, Incidence >5%, n (%)	Placebo Randomized Dose[4] N=120	Etripamil Randomized Dose[4] 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)
Selected Adverse Events,[3] n (%)	**Placebo Randomized Dose[4] N=120**	**Etripamil Randomized Dose[4] N=135**
Syncope or Loss of Consciousness or Pre-Syncope	0.0	0.0
Dizziness	0.0	1 (0.7)
First Degree AV Block[1]	0.0	1 (0.7)
Second-Degree AV Block or Third-Degree AV Block	0.0	0.0
Bradyarrhythmia	1 (0.8)	0.0
Atrial Fibrillation	1 (0.8)	0.0
Atrial Tachycardia or Atrial Flutter	0.0	0.0
Ventricular Tachycardia[2]	0.0	3 (2.2)

1. Newly prolonged PR. 2. All cases are non-sustained tachycardia. 3. Preferred Terms listed on same row were separately reported. 4. Safety Population TEAE timing – up to 24 hours following drug administration.

Source: Milestone Pharmaceuticals Data on File

RAPID Top Line Conclusions

- Achieved primary endpoint with statistical significance and demonstrated clinical efficacy
- Favorable safety and tolerability data consistent with those observed in prior trials
- Patients who self-administered etripamil needed additional medical interventions or emergency department care less than those taking placebo

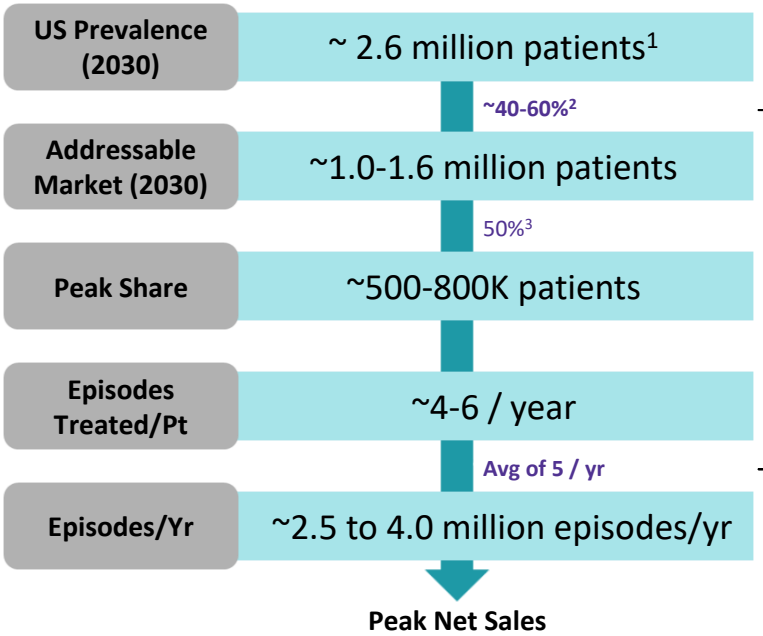
RAPID Impact on our Commercial Forecast for Etripamil

	Driver	Impact of RAPID Study Results
 Patients	• Faster conversion or symptom relief drive good experience which drives persistency • Avoiding need to go to ED is very attractive	⇧ patient positive experience and persistency
 Physicians	• Safety is primary driver for trial of etripamil • Efficacy of ≥50% conversion is bar given no other options • Avoiding ED use is very attractive	⇧ physician speed and depth of adoption
 Payers	• Reducing ED visits is valued • Limiting risk of overuse is important	⇧ payer value proposition

ED = emergency department

Sources: Internal estimates based on market research with providers, patients, and payers

RAPID Results Support 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).

Conversion Rates from PSVT to Normal Rhythm (all studies)

R&D Phase, Study	Etripamil (% Conversion)	Placebo (% Conversion)	Hazard Ratio	p value	Statistical Analysis Notes
Phase 3 RAPID	64	31	2.62	<0.001	Kaplan Meier analysis thru 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 thru 30 min
Phase 2 NODE-1	87	35	–	0.0006	Landmark analysis at 15 min

Source: Milestone Pharmaceuticals Data on File

Etripamil Clinical Safety Program to Support NDA Filing for PSVT

More than 1,600 Unique Patient Exposures to Etripamil ≥ 70 mg to Date

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)
Complete	Complete	Complete	Enrollment complete – extension thru 2022	Enrolling
N = 64	N = 431	N = 169	N=706	N ~450

NDA = New Drug Application

NB: NODE-301 and RAPID studies also collected Safety information

Source: Milestone Pharmaceuticals Data on File

Summary and Next Steps

1. **RAPID Conclusions**
   - RAPID achieved primary efficacy endpoint
   - Favorable safety and tolerability data consistent with those observed in prior trials
   - Pooled analysis with NODE-301 showed statistically significant reduction in ED utilization
2. **Commercial**
   - Safety and tolerability results – supports physician willingness to prescribe
   - Efficacy results – supports patient trial and persistency
   - Reduced Emergency Department utilization – supports value to the health care system
3. **NDA submission expected mid-2023 pending regulatory feedback**

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Questions?