Milestone PHARMACEUTICALS

Joseph Oliveto

Chief Executive Officer

June 2019

Disclaimers

This Presentation contains forward-looking statements within the meaning of the safe harbor provisions of the Private Securities Litigation Reform Act of 1995, as amended. In some cases, you can identify forward-looking statements by terminology such as ‘‘aim,’’ ‘‘anticipate,’’ ‘‘assume,’’ ‘‘believe,’’ ‘‘contemplate,’’ ‘‘continue,’’ ‘‘could,’’ ‘‘design,’’ ‘‘due,’’ ‘‘estimate,’’ ‘‘expect,’’ ‘‘goal,’’ ‘‘intend,’’ ‘‘may,’’ ‘‘objective,’’ ‘‘plan,’’ ‘‘predict,’’ ‘‘positioned,’’ ‘‘potential,’’ ‘‘seek,’’ ‘‘should,’’ ‘‘target,’’ ‘‘will,’’ ‘‘would’’ and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements about the initiation, timing, progress and results of our current and future clinical trials of etripamil, including our Phase 3 clinical trials of etripamil for the treatment of paroxysmal supraventricular tachycardia (“PSVT”), and of our research and development programs; our plans to develop and commercialize etripamil and any future product candidates; the expected benefits of using etripamil to treat PSVT; our expectations regarding the potential market size and the rate and degree of market acceptance of etripamil and any future product candidates and the implementation of our business model and strategic plans for our business, etripamil and any future product candidates. Such forward-looking statements are subject to inherent uncertainties, risks and assumptions that are difficult to predict. Factors that could cause actual results to differ include, but are not limited to, our dependence on the success of our Phase 3 clinical trials of etripamil for PSVT, 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 and completion of clinical trials, and whether the clinical trials will validate the safety and efficacy of etripamil for PSVT or other indications, among others. These and other risks and uncertainties are described more fully in the section titled “Risk Factors” in the final prospectus dated May 8, 2019 filed with the Securities and Exchange Commission pursuant to Rule 424(b) on May 9, 2019. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We undertake no obligation to update or revise any forward-looking statements, whether as a result of new information, the occurrence of certain events or otherwise.

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 the Company’s own internal estimates and research. While the Company 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 the Company’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.

Milestone - Corporate Highlights

- Phase 3 Cardiovascular Company with data read out in 1H, 2020
- PSVT is a robust market represented by ~2M patients in US
- Paradigm-changing approach enabling patient self-management
- Potentially first new drug therapy in PSVT in > 25 years
- New Chemical Entity with proprietary IP protection until 2036
- Pipeline opportunities beyond the lead indication
- Initial Public Offering, May 13, 2019 – approx. $88M net proceeds

PSVT = Paroxysmal Supraventricular Tachycardia

Management Team

Joseph Oliveto
Chief Executive Officer

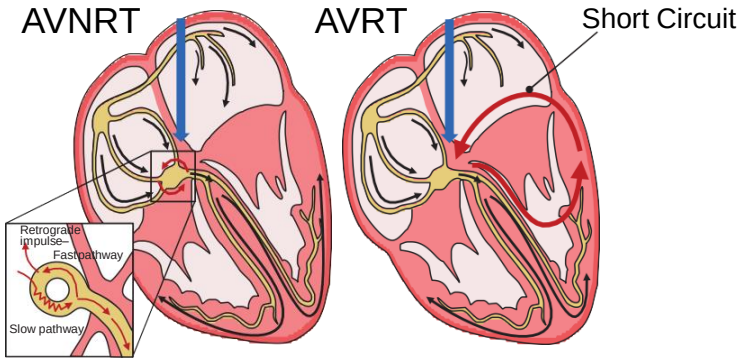
Francis Plat, MD
Chief Medical Officer

Lorenz Muller
Chief Commercial Officer

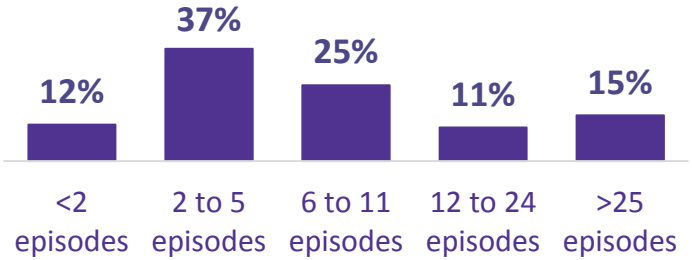
Philippe Douville, PhD
Chief Scientific Officer / Founder

Timothy Maness, CPA, CGMA
Vice President, Finance

Paroxysmal Supraventricular Tachycardia (PSVT)



PSVT episode frequency (per yr.)



- PSVT is a rapid heart rate condition that starts and stops without warning
- Heart rates >200 bpm are not uncommon
- Symptoms include
  - ✓ palpitations
  - ✓ sweating
  - ✓ chest pressure or pain, shortness of breath
  - ✓ sudden onset of fatigue
  - ✓ lightheadedness or dizziness
  - ✓ fainting or anxiety

AVNRT = Atrioventricular Nodal Re-entrant Tachycardia AVRT = Atrioventricular Re-entrant Tachycardia bpm = beats per minute

Sources: Internal estimates based on market research

Current Standard of Care for PSVT

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

Chronic / preventive

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

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

Acute

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

PSVT = Paroxysmal Supraventricular Tachycardia DC = Direct Current ED = Emergency Department

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

A Paradigm-Changing Approach

Opportunity to develop the first approved treatment to be used by patients whenever and wherever an episode of PSVT occurs

Non-invasive → Convenient → Empowering

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

PSVT = Paroxysmal Supraventricular Tachycardia

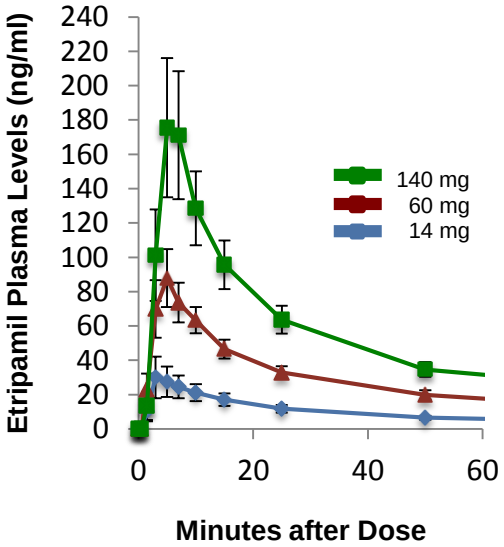
Etripamil

A paradigm-changing approach for treating PSVT

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

- **Clinically-validated mechanism**
  - Etripamil, Calcium Channel Blockers (CCBs), terminate PSVT through AV node modulation
- **Rapid onset of action**
- **Convenient patient self-administered nasal spray**
- **Short half-life**

- **Rapid onset (T_{max} < 5 min)**
- **Transient plasma levels**

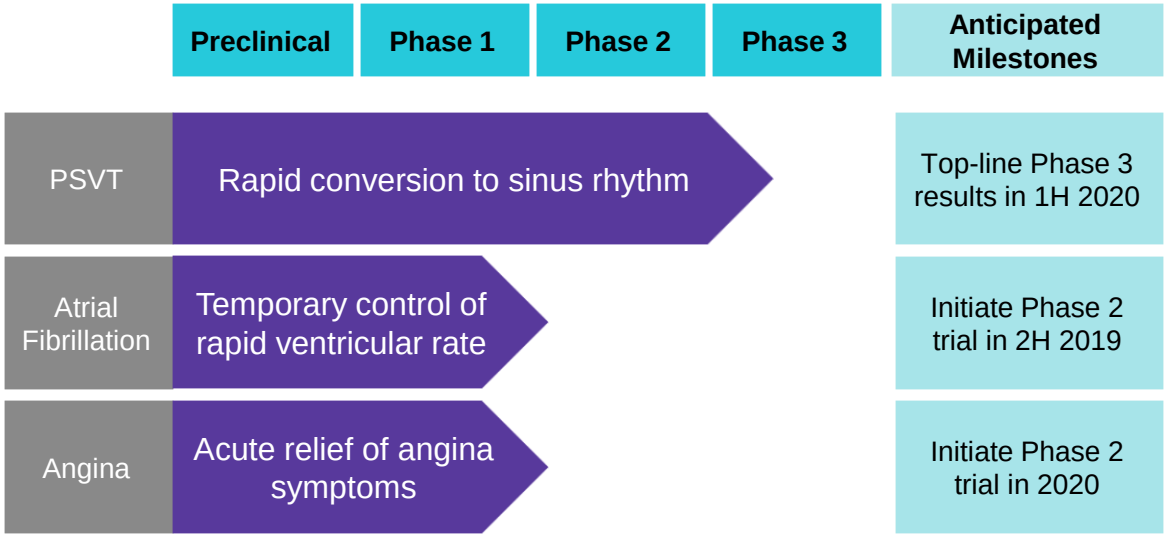


Error bars indicate standard error of the mean

AV = Atrio-ventricular

Etripamil Clinical Pipeline

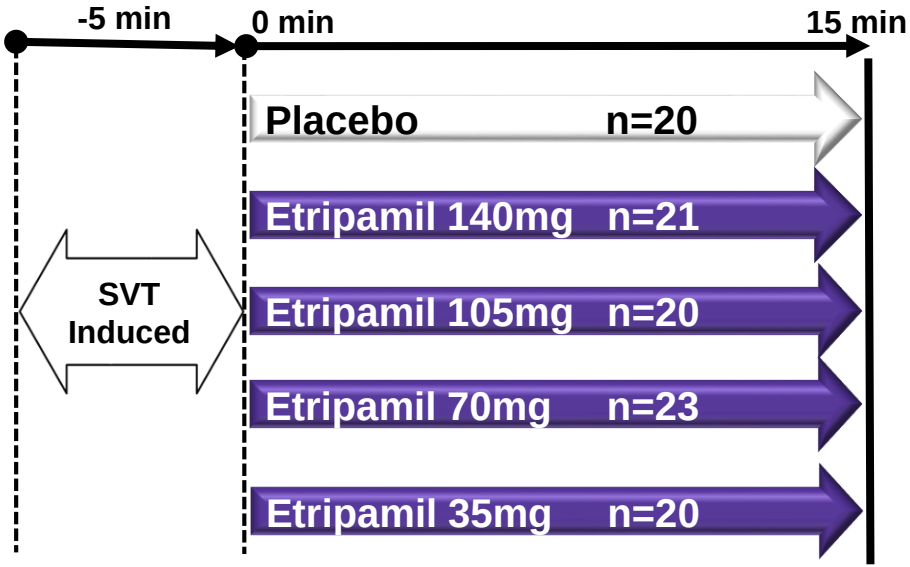
Pharmacology of L-type calcium channel blockers drives broad clinical utility



Phase 2a/b Study Design

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

PSVT patients with scheduled cardiac ablation (EP lab)

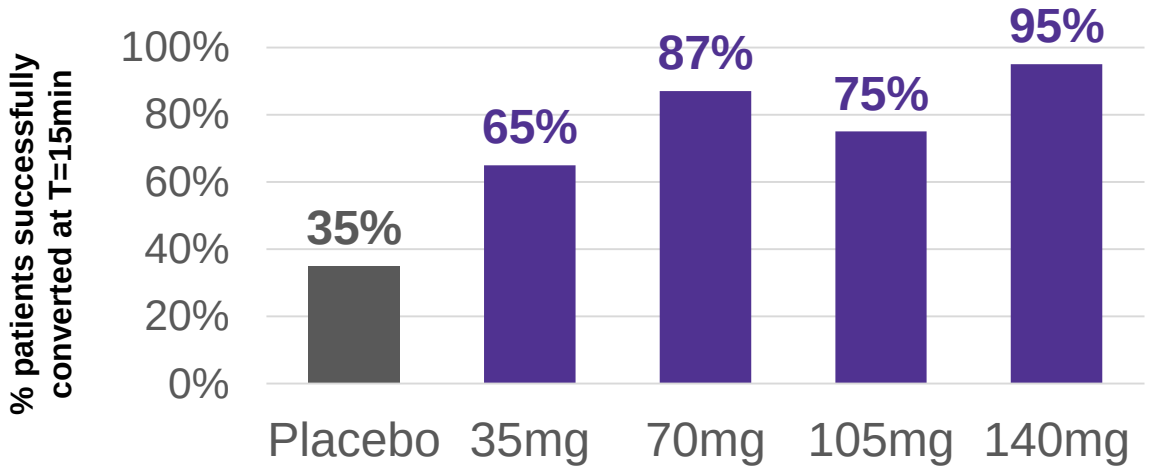


Endpoint: conversion to sinus rhythm within 15 minutes
>80% power to show a 50% absolute difference vs. placebo

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

Phase 2 Primary Endpoint

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



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

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

Phase 2a/b Clinical Conclusions

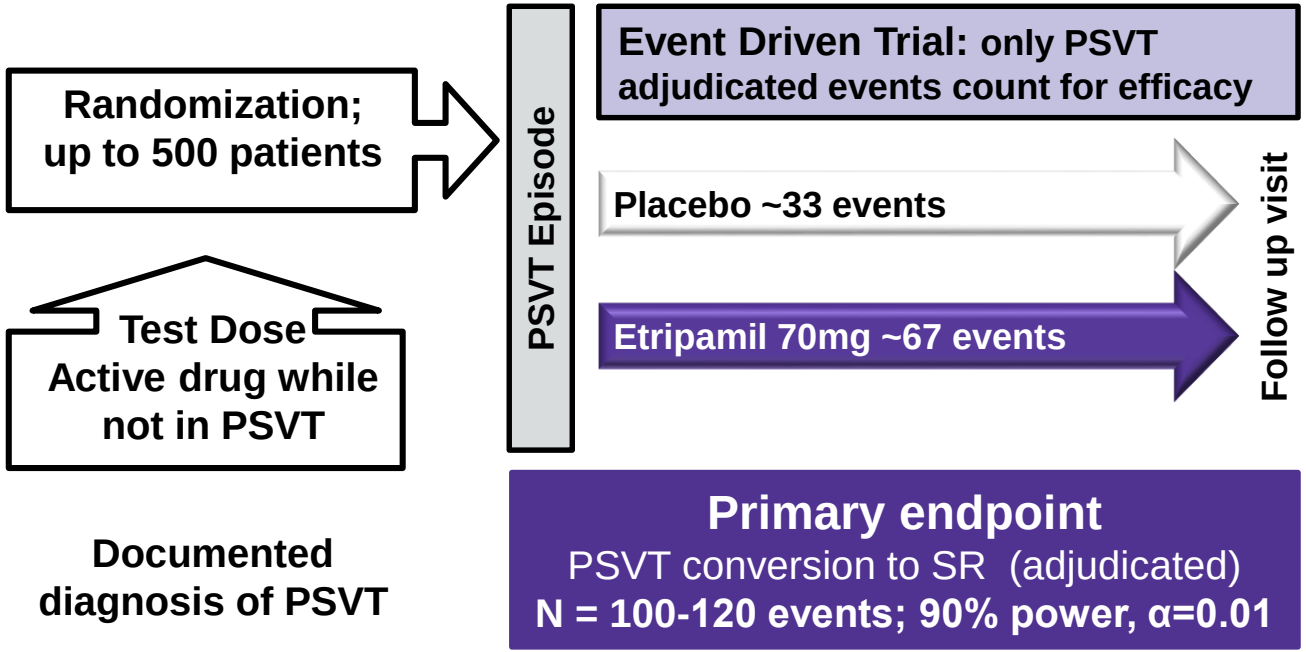
- Etripamil at 70, 105 and 140 mg is significantly better than placebo in terminating PSVT
- Median time to conversion <3 min with etripamil 70mg
- 70 mg dose showed no mean blood pressure (BP) drop
- Most frequent side effect was nasal irritation or nasal congestion; however these were transient
- Etripamil 70 mg demonstrated the best efficacy/safety profile to take into Phase 3

Source: Adapted from 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

Pivotal Phase 3 Study Design

NODE-301
Etripamil Clinical Research in PSVT

Objective: Superiority of etripamil over placebo in terminating PSVT events in the outpatient setting



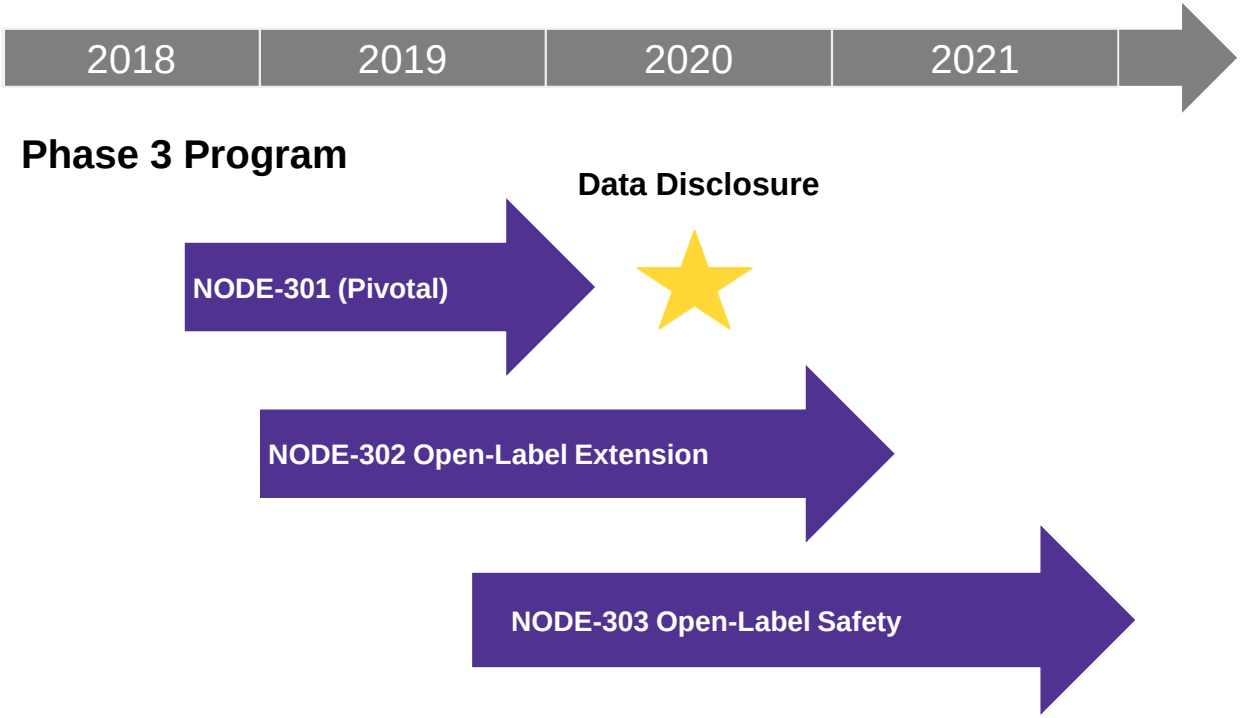
SR = Sinus Rhythm; PSVT = Paroxysmal Supraventricular Tachycardia; Study randomization scheme 2:1 etripamil : placebo

FDA Guidance – End of Phase 2 Meeting

FDA provided a clear regulatory path for etripamil in PSVT

- NODE-301 protocol acceptable including design, dose, endpoint, statistical analysis, and sample size
- Inclusion of broad patient population
  - Including elderly and those on concomitant medications
- Single efficacy study acceptable for approval
- Total NDA safety data set of ≤ 1,500 unique patient events

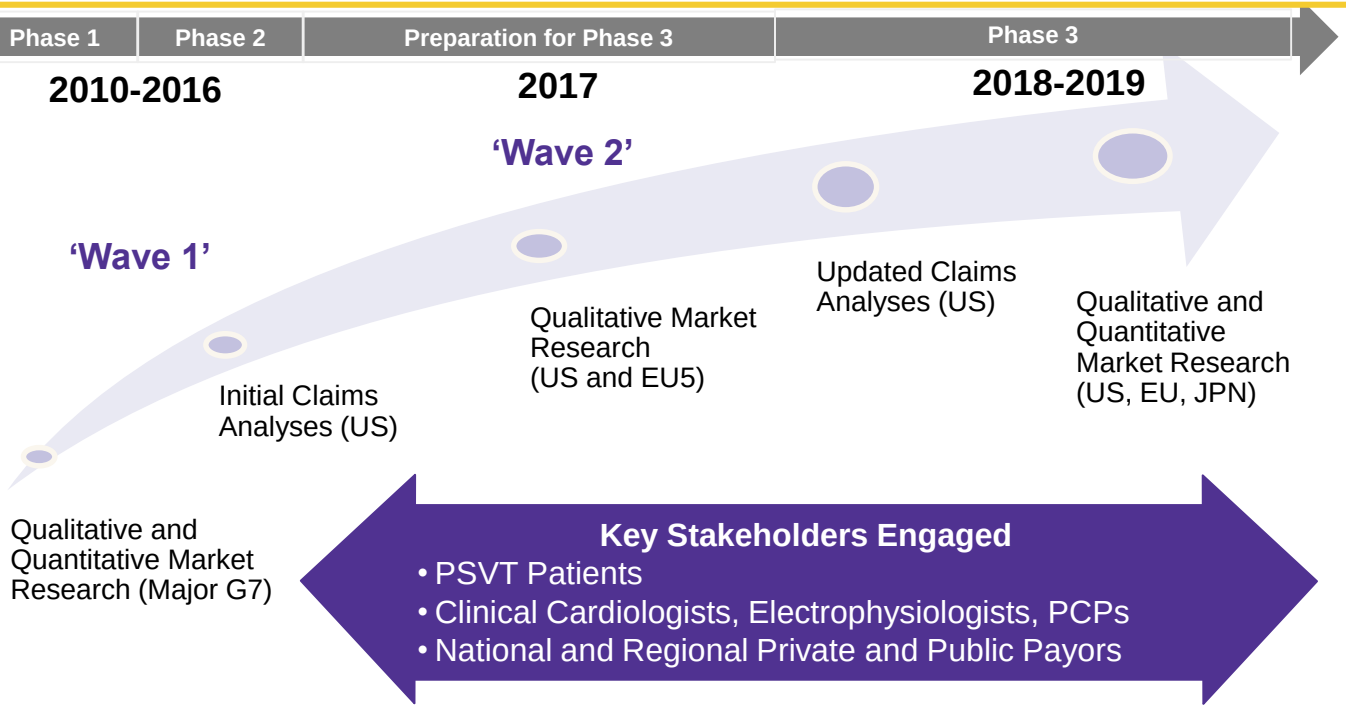
Etripamil PSVT Development Plan



PSVT = Paroxysmal Supraventricular Tachycardia

Milestone Knowledge Base for PSVT

Market research with extensive stakeholder interviews supplemented with multiple claims database analyses



PSVT Patient Characteristics

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

Unmet Need

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

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

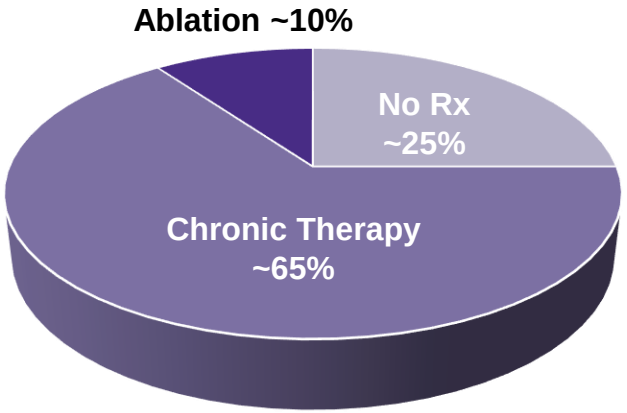
Sources: Internal estimates based on market research and longitudinal analysis of Truven/Marketscan and Medicare claims data

Current US PSVT Market

Total annual US healthcare expenditures of ~$3B

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

Current Management



Source: Sacks, N.C. et al; Prevalence of Paroxysmal Supraventricular Tachycardia (PSVT) in the US in Patients Under 65 Years of Age; Abstract and Oral Presentation at the International Academy of Cardiology Annual Scientific Sessions 2018, 23rd World Congress on Heart Disease; Precision Xtract, Boston, MA, USA; and data-on-file from Truven Health MarketScan Commercial research database and Medicare Limited Dataset, 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.

Potential Commercial Opportunity for Etripamil in PSVT

~2M diagnosed PSVT patients
(4 yr. prevalence)

800,000 TAM
(40% of 2M)

400,000
Etripamil patients
(50% of TAM)

Number of annual PSVT ablations	**80,000**
Ratio of etripamil-treated patients : ablation	x 3.5
Total expected etripamil patients/year	280,000
Etripamil expected doses/patient/year	x 3
Etripamil doses/year	840,000

TAM – Target Addressable Market

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

Finances

- Cash and equivalents of $71.2M (2019 Q1, unaudited)
- IPO (May 2019) net proceeds of $88M
- Runway into Q3, 2021 (existing cash + net IPO proceeds)
  - Phase 3 pivotal efficacy trial (Study 301) top line data
  - Initiation and significant progression of Phase 3 safety study (Study 303)
  - Continued PSVT market development via publications, patient education and Medical Affairs initiatives
  - Phase 2 endpoint in atrial fibrillation

Etripamil Development Plan

PSVT Program (Phase 3)

Data Disclosure

NODE-301 (Pivotal)

NODE-302 Open-Label Extension

NODE-303 Open Label Safety

Pipeline Expansion (Phase 2)

AFib

Angina

PSVT = Paroxysmal Supraventricular Tachycardia, Afib = Atrial Fibrillation

Milestone (Nasdaq: MIST) - Corporate Highlights

- Phase 3 Cardiovascular Company with pivotal efficacy data in 1H 2020
- PSVT is a robust market represented by ~2M patients in US
- Potentially first new drug therapy in PSVT in > 25 years
- Paradigm-changing approach enabling patient self-management & potential cost savings to the medical system
- Pipeline opportunities beyond the lead indication
- $95M IPO in May 2019 provides cash runway into 3Q, 2021, well beyond the Phase 3 efficacy results

PSVT = Paroxysmal Supraventricular Tachycardia

Milestone PHARMACEUTICALS

Thank you