Milestone PHARMACEUTICALS

Corporate Overview – October 2019

Joseph Oliveto

Chief Executive Officer

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Milestone - Corporate Highlights

- Phase 3 Cardiovascular Company with data read out anticipated 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
- $95M Initial Public Offering - May 13, 2019
- Cash and equivalents of $145.8M (June 30, 2019) – expected runway into Q3, 2021

PSVT = Paroxysmal Supraventricular Tachycardia

Management Team

Joseph Oliveto
Chief Executive Officer

CHELSEA THERAPEUTICS · Lundbeck · Roche · pappas VENTURES

Amit Hasija
Chief Financial Officer

Fulcrum Therapeutics · SANOFI · Goldman Sachs · CREDIT SUISSE · MERCK

Francis Plat, MD
Chief Medical Officer

MERCK · NOVARTIS · Daiichi-Sankyo · Bristol-Myers Squibb

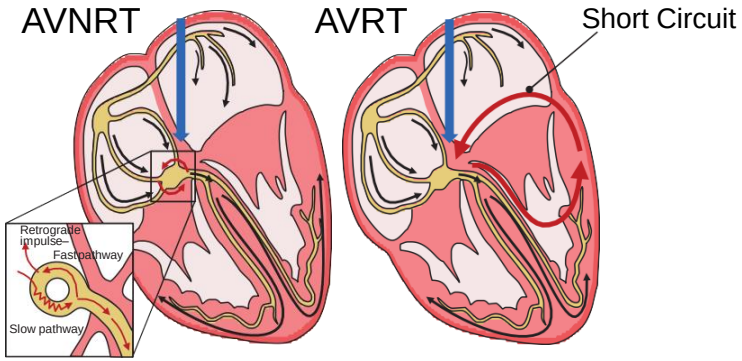
Lorenz Muller
Chief Commercial Officer

exact sciences · Daiichi-Sankyo · CVT CV Therapeutics · MERCK

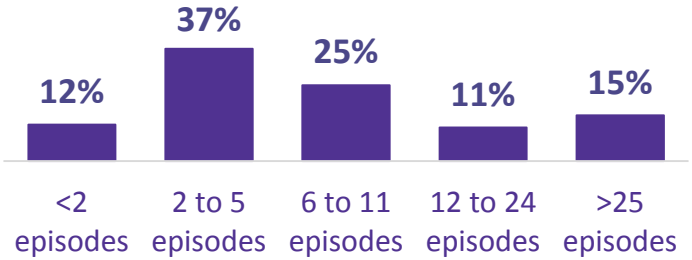
Philippe Douville, PhD
Chief Scientific Officer / Founder

GENZON BioSciences · Algene Biotechnologies

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

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

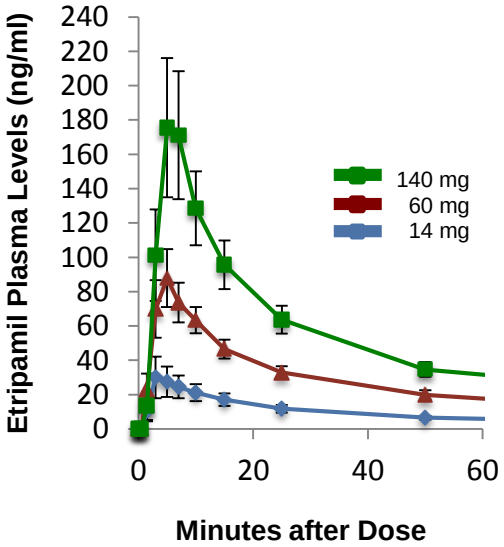
Etripamil

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**

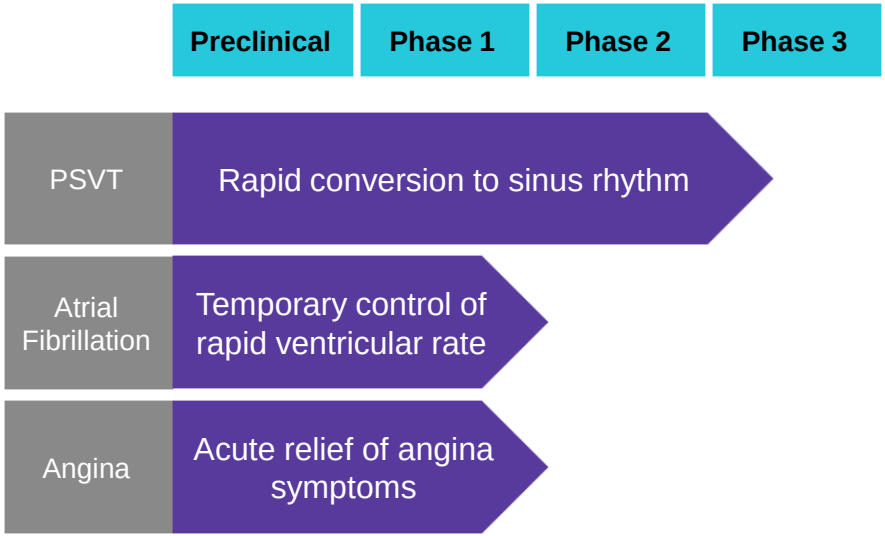


Error bars indicate standard error of the mean

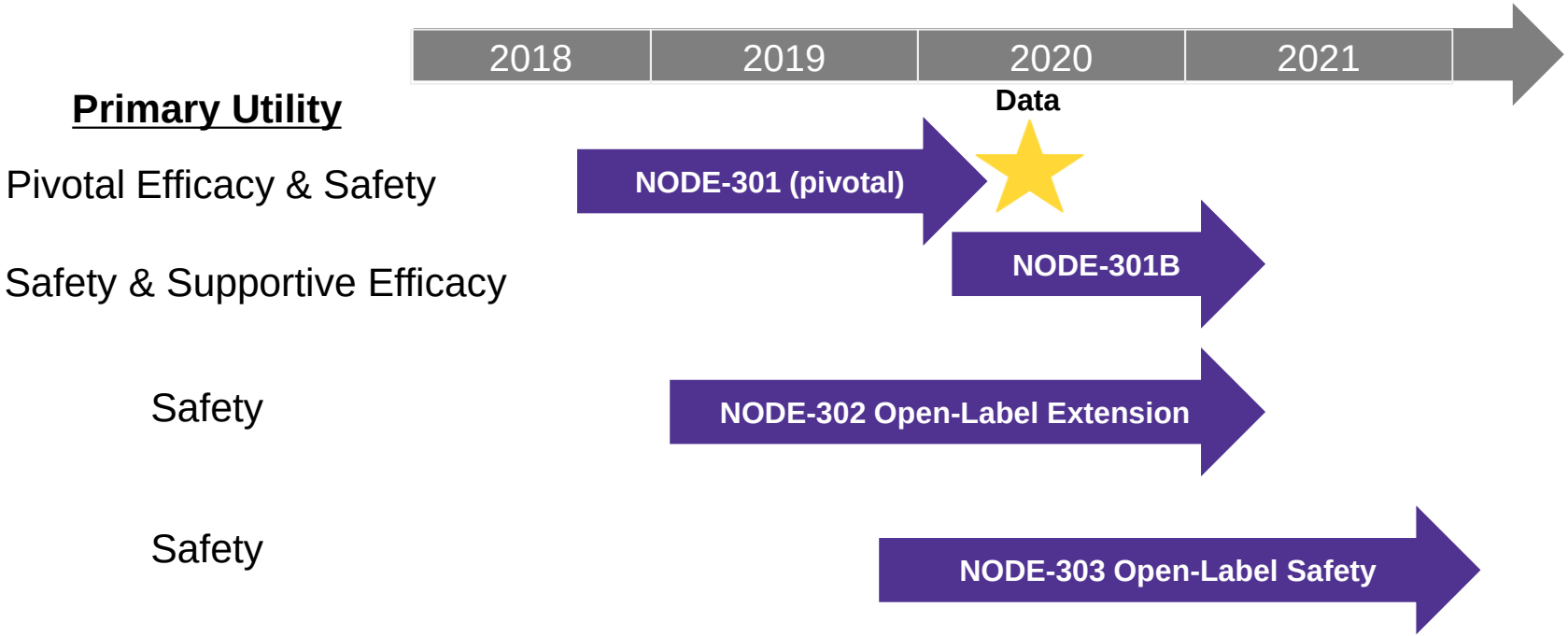
AV = Atrio-ventricular

Etripamil Clinical Pipeline

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



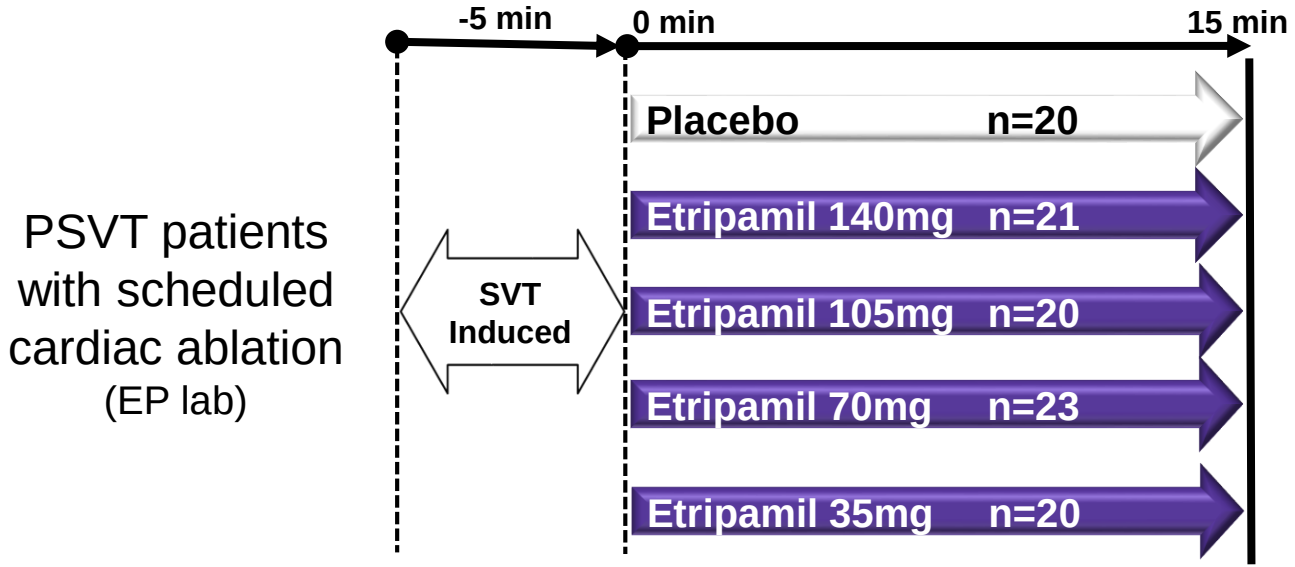
Etripamil PSVT Phase 3 Development Plan



PSVT = Paroxysmal Supraventricular Tachycardia

Phase 2a/b Study Design

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

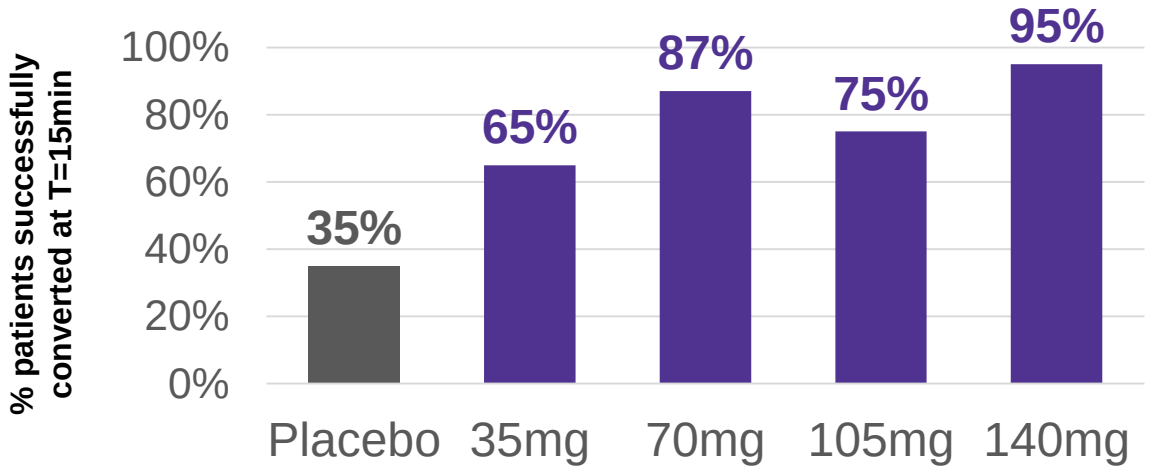


Endpoint: conversion to sinus rhythm within 15 minutes
>80% power to show a 50% absolute difference vs. placebo

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

Phase 2 Primary Endpoint

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

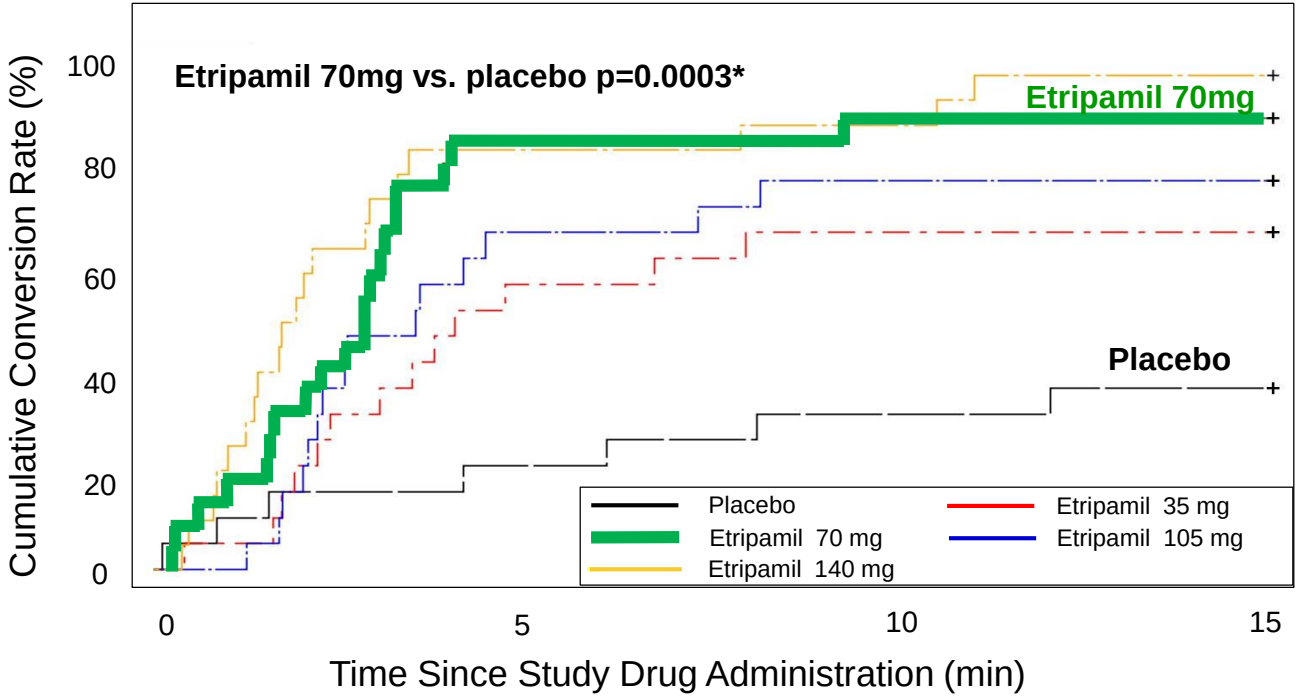


# patients converted at 15 min	7/20	13/20	20/23	15/20	20/21
p-value		0.1128	0.0006	0.0248	<.0001

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 2 Time to Conversion

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

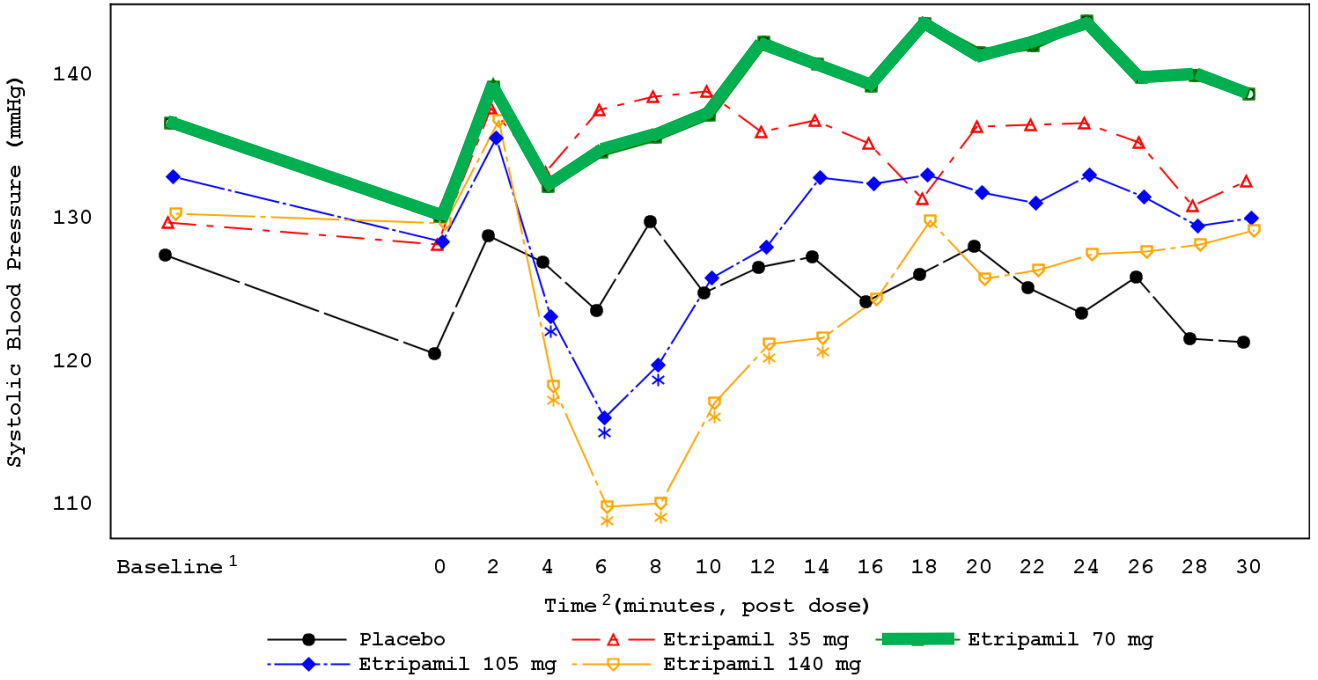


*Hazard Ratio and 95% Confidence Intervals etripamil 70mg vs. placebo; 4.99 (2.09, 11.93)

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

Etripamil 70 mg showed no drop in blood pressure



[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

Phase 2a/b Clinical Conclusions

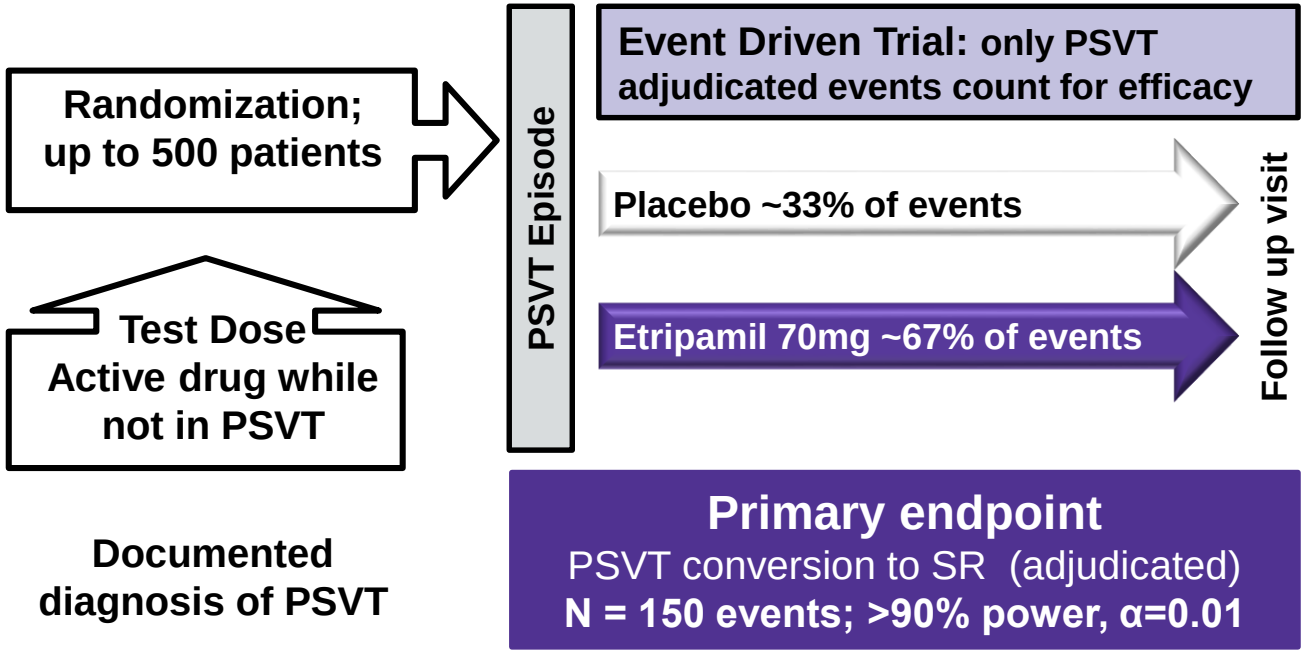
- Etripamil at 70, 105 and 140 mg is significantly better than placebo in terminating PSVT
- Median time to conversion <3 min with etripamil 70mg
- 70 mg dose showed no mean blood pressure (BP) drop
- Most frequent side effect was nasal irritation or nasal congestion; however these were transient
- Etripamil 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 Provided a Clear Regulatory Path for Etripamil in PSVT

NODE-301

Single pivotal efficacy study to support NDA submission

- Once target of 150 adjudicated events reached, collection of blinded data from patients who have not experienced an event to continue as separate dataset called "**NODE-301B**"

NODE-303

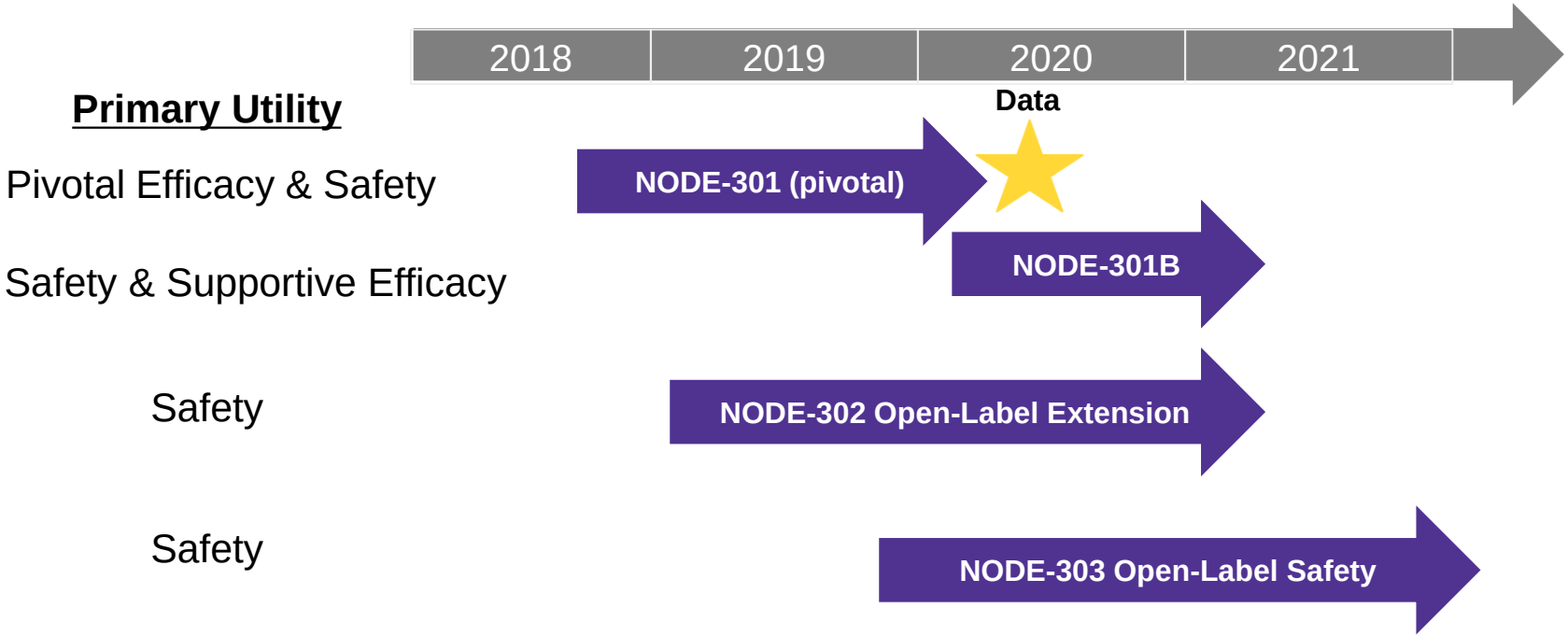
Open-label global safety trial

- Removed the in-office safety test dose that is currently required in the NODE-301 study

Population and Safety Database

- Program enrolling broad patient population including elderly and those on concomitant medications (e.g. calcium channel blockers and beta blockers)
- Total NDA safety data set of ≤ 1,500 unique patient events

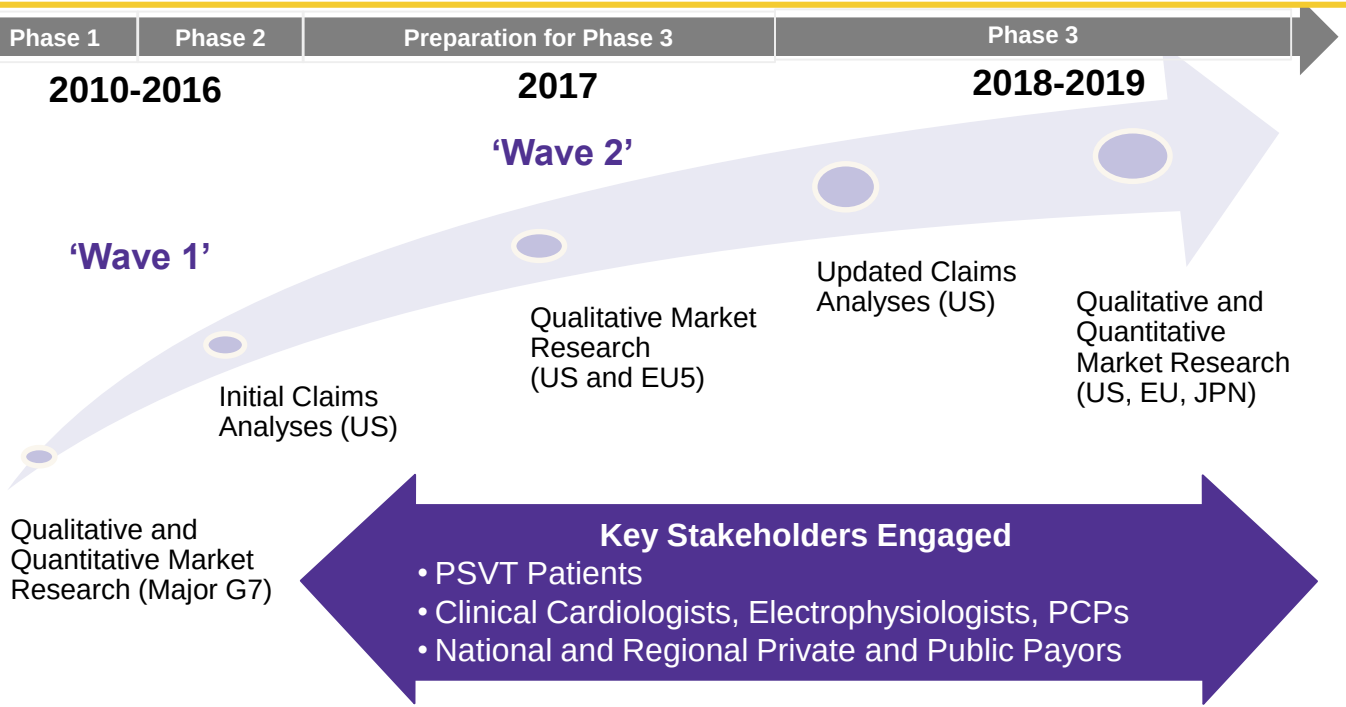
Etripamil PSVT Phase 3 Development Plan



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

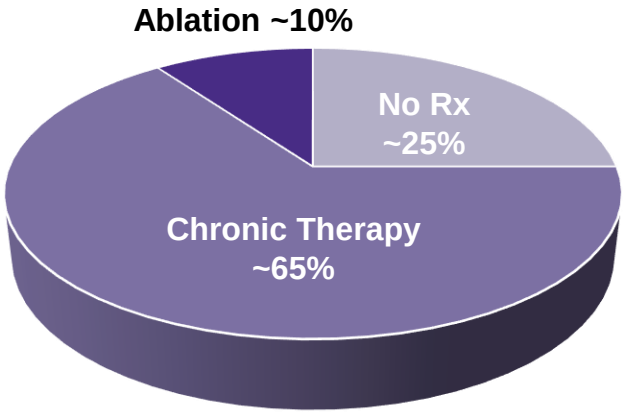
Sources: Internal estimates based on market research and longitudinal analysis of Truven/Marketscan and Medicare claims data

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

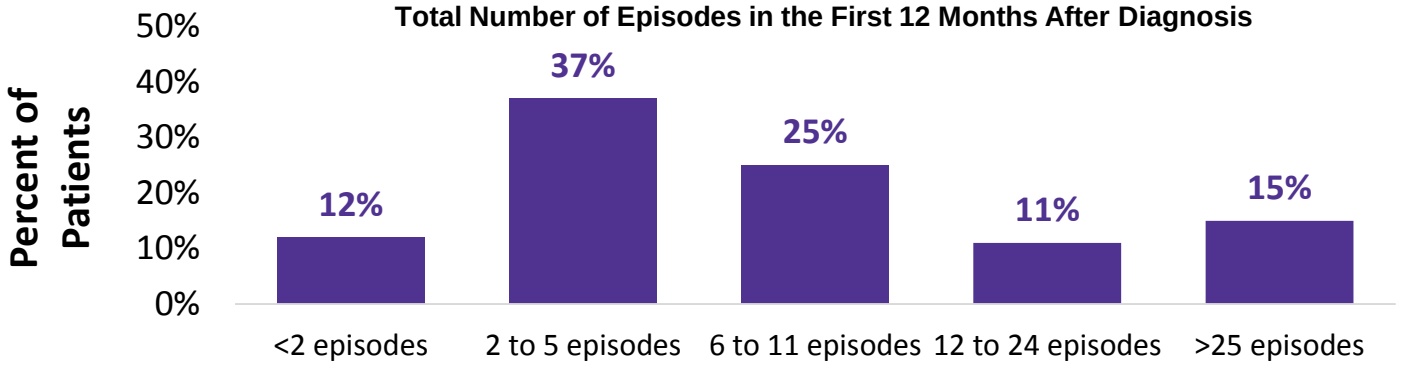
Current Management



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.

Target Addressable Market for PSVT

Market research suggests TAM for PSVT of >800k patients



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

65% patients on chronic medications for PSVT

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

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

Etripamil – Addressing Market Needs

Potential for high receptivity to the etripamil profile across stakeholders

Patients	Physicians (Cards, EPs, PCPs)	Payors
		
Future with Etripamil– a Better Treatment Option		
• Self-management of acute episodes • Less need for chronic medications • Avoidance of 50-75% of ED visits/hospital admissions	• Better risk/reward profile • Expected to have significant adoption in unablated patients • Alternative to ablation • Bridge to ablation	• Reduction in ED/hospital admissions • Deferral of ablation • Improvement in patient satisfaction

Cards = Cardiologists, EPs = Electrophysiologists, PCPs = Primary Care Physicians

Sources: Internal market research

PSVT Patient Management and Call Point Targeting

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

		Clinical Cardiologists	Primary Care Physicians	Electro-physiologists
% of PSVT patients managed		**~60%**	**~30%**	**~10%**
Long-term Use	*Add to or Replace Chronic Medications*	**Primary Target**		
Medium-term Use	*Defer Ablation*			**Secondary Target**
Short-term Use	*Bridge to Ablation*			

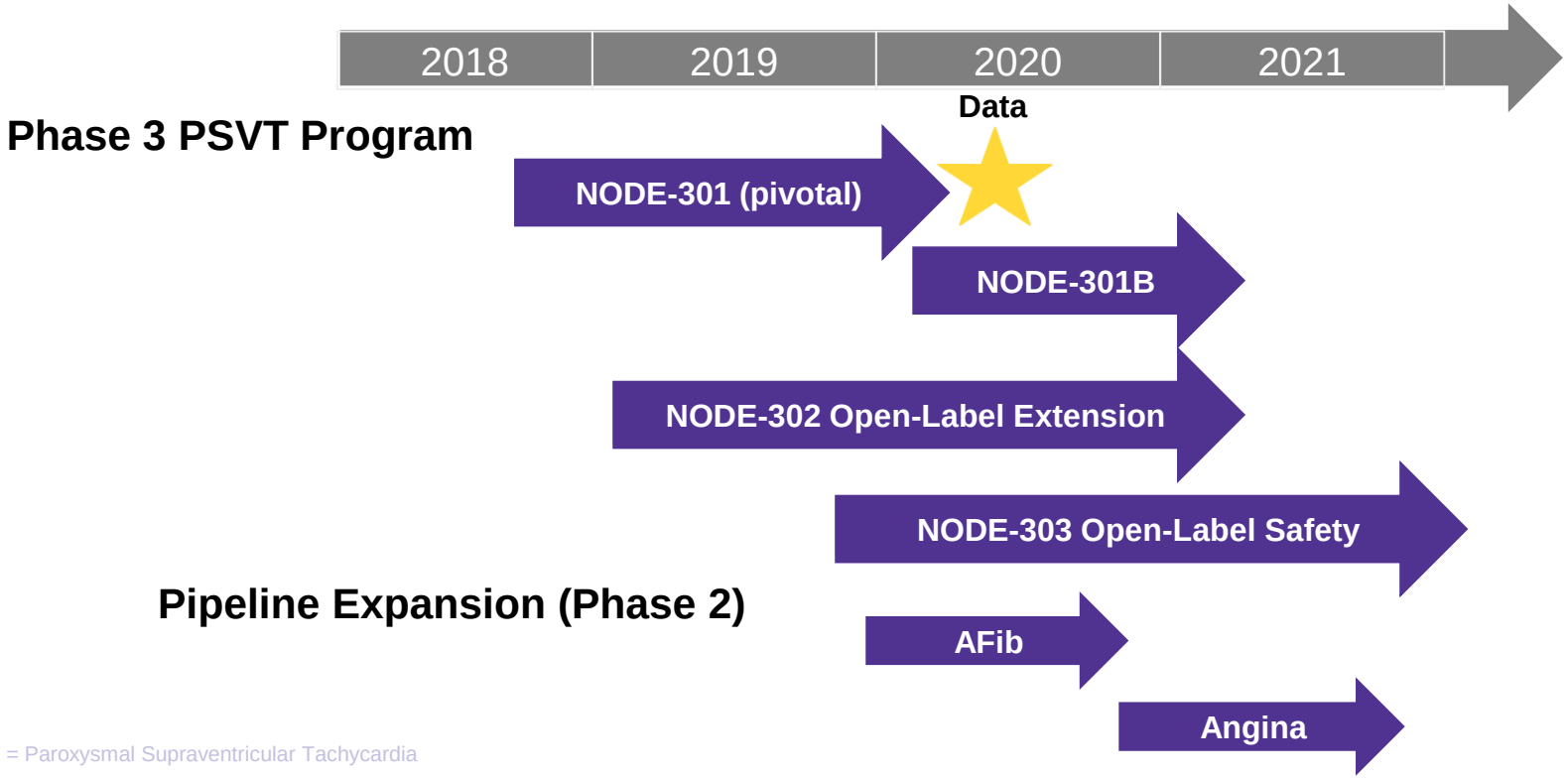
- Targeted sales force to reach majority of available opportunity
- Significant overlap with most common CV portfolio call points

Source: Internal market research

Finances

- Cash and equivalents of $145.8M (as of June 30, 2019)
  - IPO (May 2019) net proceeds of approx. $86M
- Runway expected into Q3, 2021
  - Phase 3 pivotal efficacy trial (NODE-301) top line data
  - Significant progression of Phase 3 safety study (NODE-303)
  - Continued PSVT market development via publications, patient education and Medical Affairs initiatives
  - Phase 2 endpoint in atrial fibrillation
- 24.5M shares outstanding

Etripamil Development Plan



PSVT = Paroxysmal Supraventricular Tachycardia

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 expected cash runway into 3Q, 2021, well beyond the anticipated date of Phase 3 efficacy results

PSVT = Paroxysmal Supraventricular Tachycardia

Milestone PHARMACEUTICALS

Thank you