



# Commercial Investor Event: Preparation for Potential Launch of **CARDAMYST™** (etripamil) Nasal Spray

Joe Oliveto, President & CEO

Lorenz Muller, CCO



Investigational Product. Not approved  
for commercial use in any jurisdiction.

## Disclaimer

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This presentation discusses our intended promotional launch strategy for CARDAMYST™ (etripamil) nasal spray, which has not yet been approved for commercial use in any jurisdiction. Our new drug application (“NDA”) remains under review by the U.S. Food and Drug Administration (“FDA”) with a Prescription Drug User Fee Act (“PDUFA”) date of March 27, 2025. Any plans described herein remain subject to FDA approval of the NDA.

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- 01  Introduction and Overview
- 02  The Problem
- 03  Our Innovation
- 04  The Opportunity
- 05  Commercial Strategy and Execution

# Our Mission



We are a patient-centric biopharmaceutical company intending to bring etripamil nasal spray to patients living with paroxysmal supraventricular tachycardia (PSVT) and atrial fibrillation with rapid rate (AFib-RVR)



# 2025 – A Potentially Transformative Year for Milestone



## PSVT

- Potential approval of CARDAMYST, PDUFA March 27, 2025
- Promotional launch of CARDAMYST, expected mid-2025

## AFib-RVR

- Planned Phase 3 study start for etripamil in second indication
- AFib-RVR represents larger potential target population than PSVT

## Finances & Other

- \$75M payment expected upon approval from royalty financing
- Expected to fund operations into mid-2026, combined with current cash
- Commercial launch of CARDAMYST is first priority
- Patent estate potentially extended to 2042\*

\*Feb 2025 – US Patent Office issued notice of allowance for patent covering repeat dose regimen

Key: PDUFA = Prescription Drug User Fee Act /

# Our Vision for Commercial Success of CARDAMYST



## GOAL

**Patients**  
Empowerment



Easy to use

**Prescribers**  
Provides a solution



Easy to prescribe

**Payers**  
Efficiency



Limit need to manage

Plan to Leverage Experience in PSVT to Launch Confidently

Key: PSVT = Paroxysmal Supraventricular Tachycardia

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Commercial Strategy and Execution

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Commercial Strategy and Execution

# PSVT Puts a Significant Burden on Patients



**Paroxysmal Supraventricular Tachycardia** is a common symptomatic arrhythmia (abnormal heart rhythm) characterized by attacks of very rapid heart rate



Donnette from Huntsville AL

## Disease Characteristics

- Chronic condition with symptomatic attacks
- Incidence and duration unpredictable
- Often anxiety-provoking
- 50% of patients are under 65
- 65% of patients are women
- Mostly managed by cardiologists

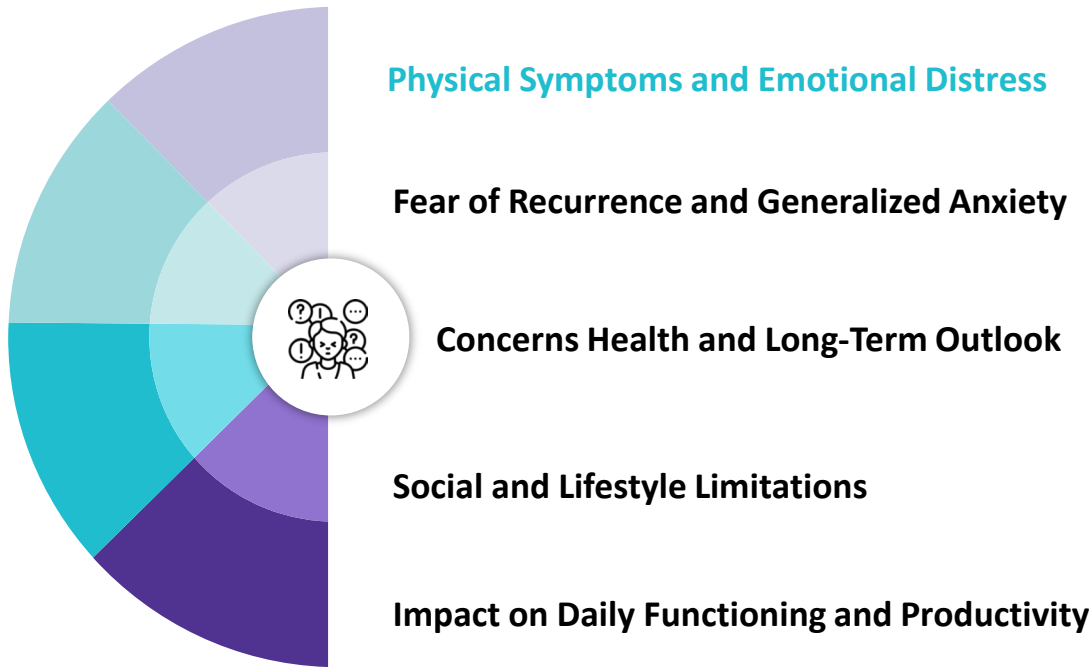
## Patient impact

- Discomfort during attacks, symptoms
- Anxiety between attacks, unpredictability
- Per year >650,000 claims seeking treatment
  - ~100,000 ablations
  - >140,000 ED visits
  - >40,000 hospitalizations

Key: ED = Emergency Department

Citations: Internal market research and longitudinal analysis of Truven/Marketscan and Medicare claims data; IQVIA Pharmedics Plus 2019 Commercial claims for patients <65yo and Medicare LDS 5% for patients >65yo (ICD: I47.1); Healthcare Utilization Project (HCUP) 2019, <https://hcup-us.ahrq.gov/databases.jsp>; accessed 11/2024; <https://youtu.be/oqwNSC-Jkaw>

# Majority of Patients with PSVT have Anxiety and Reduced QoL Both During and Between Episodes



**>80%**  
of all patients with PSVT  
report some level of  
anxiety, with the majority  
having moderate or  
severe symptoms

Key: QoL = Quality of Life  
Citations: Internal Market Research

# Many Current Treatments in the Market are Inconvenient, Intrusive, and/or Ineffective



## Chronic / Preventive

### Oral BBs and CCBs

- reduce episodes
- only somewhat effective
- require daily administration
- unwanted side effects

### Catheter ablation

- often curative
- risks associated with invasive procedure
- only elected by ~15% patients (mostly young)

## Acute

### “Pill in Pocket” = off label oral CCB or BB, or Vagal maneuver

- poor efficacy
- “do no harm”

### ED, Urgent Care Visit or Hospitalization

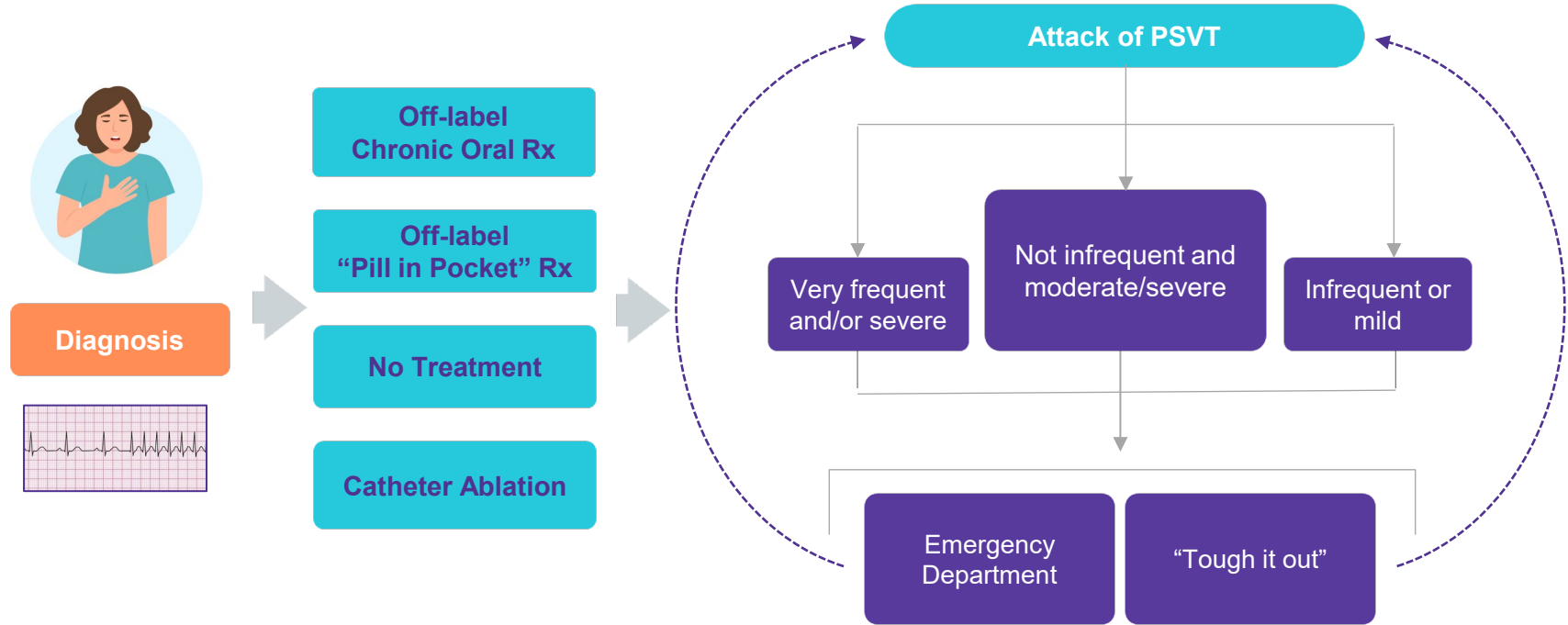
- IV adenosine, IV CCB or DC cardioversion
- time consuming
- costly
- stressful

## Most Patients Experience Attacks Despite Preventive Options

Key: BB = Beta Blocker; CCB = Calcium Channel Blocker

Citations: 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. Circulation. 2016;133:e471–e505

# Underappreciated Journey of a Patient with PSVT: Drawn-out Diagnoses & Difficult, Limited Treatment Options



Key: Rx = prescription

# PSVT Drives Significant Costs for the Healthcare System



**>\$5B** Total annual US spending for patients with PSVT<sup>1</sup>

Costs post-diagnosis are primarily driven by<sup>2</sup>:



Inpatient services



Diagnostic testing



Ablation procedures

**>140K** Emergency department visits per year due to PSVT<sup>1</sup>

~25%

patients who present to ED  
are hospitalized<sup>3</sup>

\$2.5k

average cost of  
ED visit<sup>4,5</sup>

\$15k

average cost of  
hospitalization<sup>4,6,7</sup>

Citations: 1. Milestone Pharmaceuticals. Data on file. 2. Chew DS, et al. *Am Heart J*. 2021;233:132-140. 3. Murman DH, et al. *Acad Emerg Med*. 2007;14(6):578-581. 4. Sacks NC et al. *Am J Cardiol*. 2020 Jan 15;125(2):215-221. 5. Jiang S et al. *J Manag Care Spec Pharm*. 2022 Nov;28(11):1321-1330. 6. Deshmukh A et al. *Heart Rhythm O2*. 2022 7. Data on file (HCUP NIS 2019 and CMS hospitalization payments, 2021)

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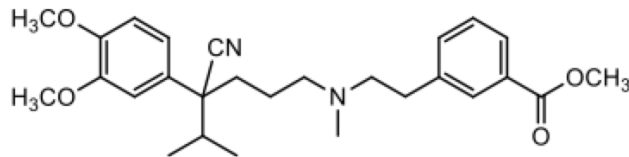
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Commercial Strategy and Execution

# CARDAMYST is a Novel Investigational CCB Designed to Treat Episodes of PSVT Safely and Quickly



NCE

Short-acting CCB

MOA very well understood and trusted

- 1 Convenient patient self-administered nasal spray
- 2 Portable, on demand
- 3 Fast onset of action, well tolerated

**Empowering patients to treat symptomatic attacks**

Key: NCE = New Chemical Entity; CCB = Calcium Channel Blocker; MOA = Mechanism of Action

# CARDAMYST Would Put Patients in Control of Their PSVT



## Efficacy

Fast onset delivers quick relief from symptoms of PSVT

## Safety

Safety and tolerability supports confident use at home

## Convenience

On-demand use reduces reliance on healthcare system

## Cost

Cost effective compared with an ED visit/hospitalization



**Rapid & Reliable Relief**  
Provide meaningful relief from episode symptoms and duration

**Patient Empowerment**  
Empower in disease management & avoid unneeded healthcare visits

**Quiet Mind**  
Reduce worry between episodes with versatile on-demand treatment

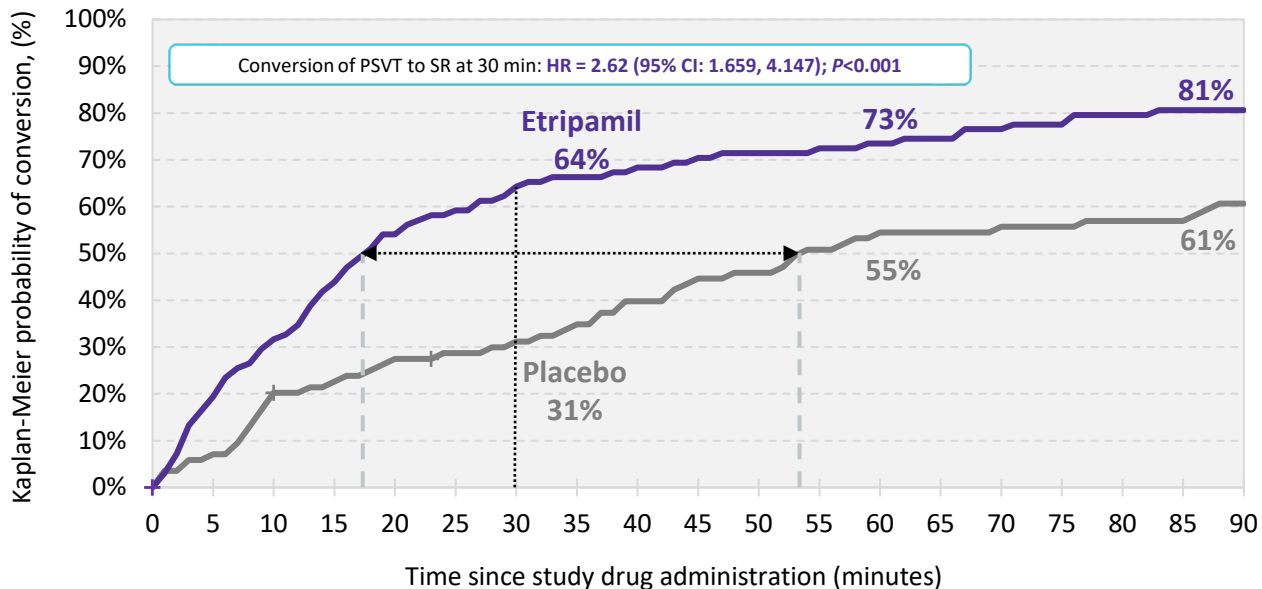
**Active Living**  
Allow a return to normal rhythm

*Investigational Product. Not approved for commercial use in any jurisdiction*

Sources: Internal market research,

# Fast Relief to More Patients

## Efficacy Data from RAPID



### 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

Key: CI = confidence interval; HR = hazard ratio; SR = sinus rhythm  
 1. Stambler BS, et al. *Lancet*. 2023;402(10396):118-128.

### More Converted



**>2x** patients converted to SR within 30 minutes of taking CARDAMYST vs doing nothing

### Faster Conversion



**>3x** faster conversion of PSVT to SR with CARDAMYST vs doing nothing

### Fewer ED Visits



**~40%** reduction in ED use for CARDAMYST vs doing nothing

# Well-Tolerated with a Favorable Safety Profile

## Safety Data from RAPID



Subject-reported AEs from the RAPID Study, <sup>1</sup> n (%)	Placebo <sup>2</sup> n=120	Etripamil <sup>2</sup> 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) <sup>3</sup>

**Adverse Events were predominantly mediated by the route of administration**  
**No syncope, pre-syncope, or 2<sup>nd</sup>/3<sup>rd</sup> degree AV block**

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 eight rated as mild, two of eight rated as moderate, zero needing intervention.

Key: AV = Atrioventricular

Citations: American Heart Association Scientific Sessions, Late-Breaking Clinical Trial Presentation, November 2022; and The Lancet (2023).

# Our Vision for Commercial Success of CARDAMYST



## Patients Empowerment



Fast, reliable self-administration  
Less disruption, reliance on ED  
Less fear over when the next event will occur

## Prescribers Provides a solution



Trusted CCB mechanism  
Evidence-based new tool  
Frees up HCP time and office resources

## Payers Efficiency



Novel and cost-effective treatment  
Potential to reduce ED visits/hospital admissions

### Goal

Easy to use

Easy to prescribe

Limit need to manage

Key: HCP = Healthcare Provider  
Citations: Internal market research

# Payers Recognize the Value of CARDAMYST to Fill an Unmet Need for Cardiology HCPs



## Unmet Need

Payers report they will defer to cardiologists to interpret clinical unmet need



Given rational pricing, not expected to be “budget-impacting” enough to warrant active management



Minimal market competition less likely to drive large rebate pressure



See potential for efficacy endpoints to translate into reductions in healthcare resource utilization

Citations: Internal Market Research

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Commercial Strategy and Execution

# 2M+ Patients Cost the Healthcare System at Least \$5 Billion Annually

140,000 – 525,000 Emergency  
Department Visits per Year<sup>3</sup>

40,000 – 120,000 In-patient  
Admissions per Year<sup>3</sup>

**~2M+**  
Patients  
Diagnosed with  
PSVT<sup>1</sup>

~100,000 Ablations  
Performed per Year<sup>2</sup>

650,000 to 1M Patients  
Treated per Year<sup>2</sup>

Key: PSVT = Paroxysmal Supraventricular Tachycardia

Citations: 1. Rehorn M, et al. *J Cardiovasc Electrophysiol*. 2021 Aug;32(8):2199-2206. 2. IQVIA Pharmetrics Plus 2019 Commercial claims for patients <65yo and Medicare LDS 5% for patients >65yo (ICD: I47.1) 3. Healthcare Utilization Project (HCUP) 2019, <https://hcup-us.ahrq.gov/databases.jsp>; accessed 11/2024; range reflects ED visits/IP admissions with PSVT as primary diagnosis code to ED visits/IP admissions with PSVT in any diagnostic position.

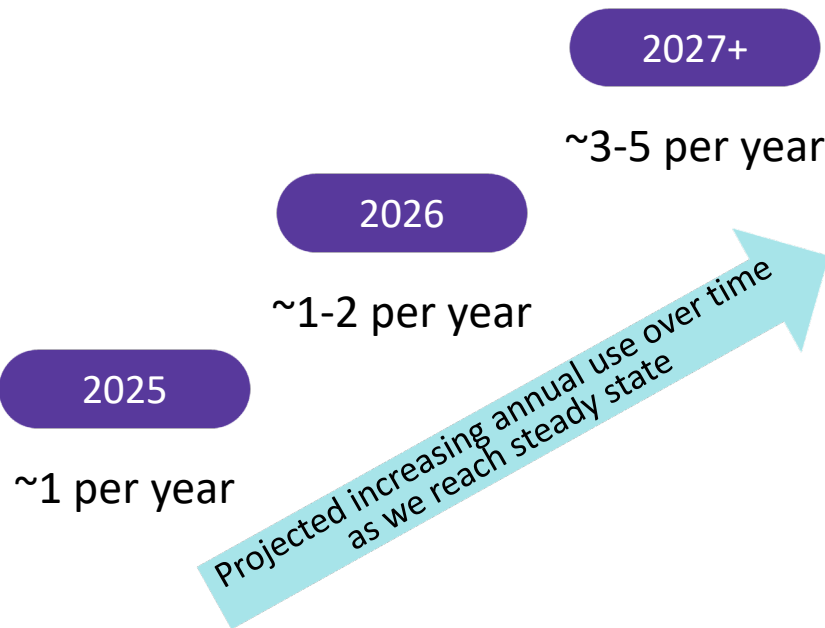
# Most Patients with a Diagnosis of PSVT Over Time Could Use CARDAMYST Multiple Times per Year



## Projected use of CARDAMYST:

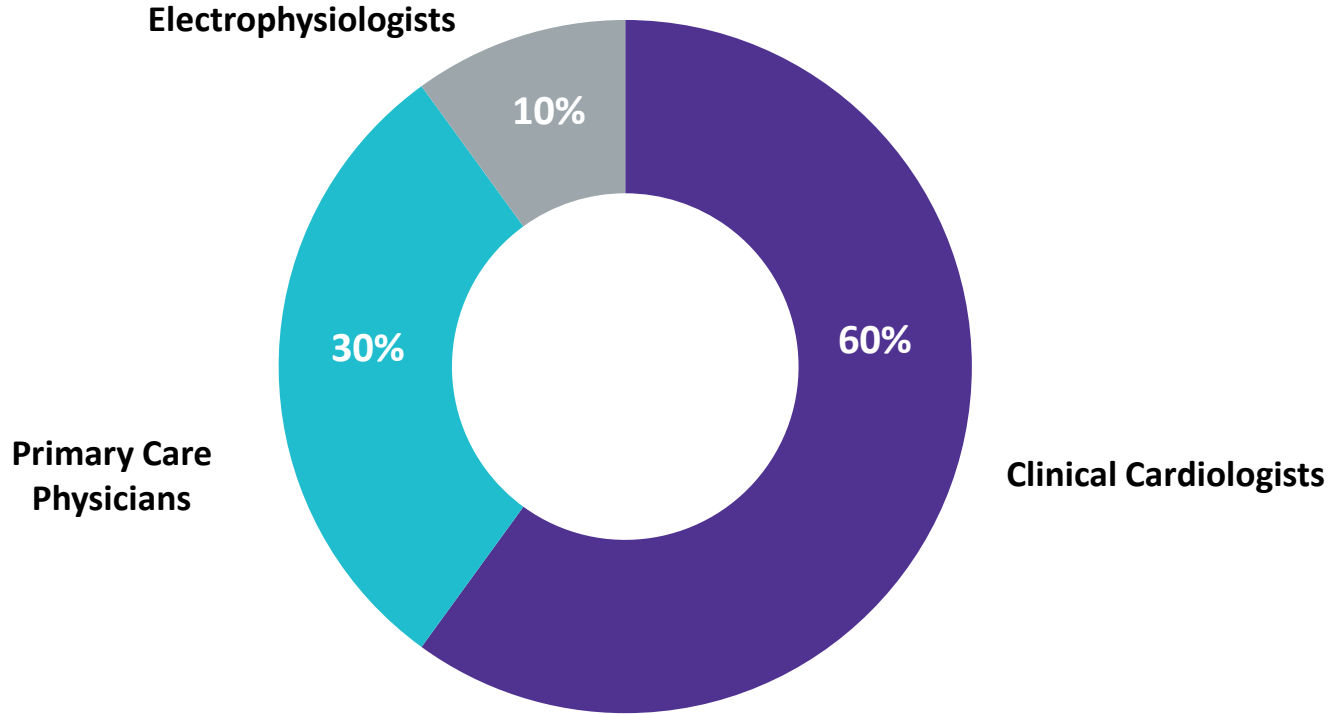
3-5 times per year

Source	Reported Frequency of use of CARDAMYST/yr
Randomized Clinical Studies <sup>1</sup>	3-9
Open Label Studies <sup>2</sup>	2-4
Observational Study <sup>3</sup>	4-6
Market Research <sup>4</sup>	3-4



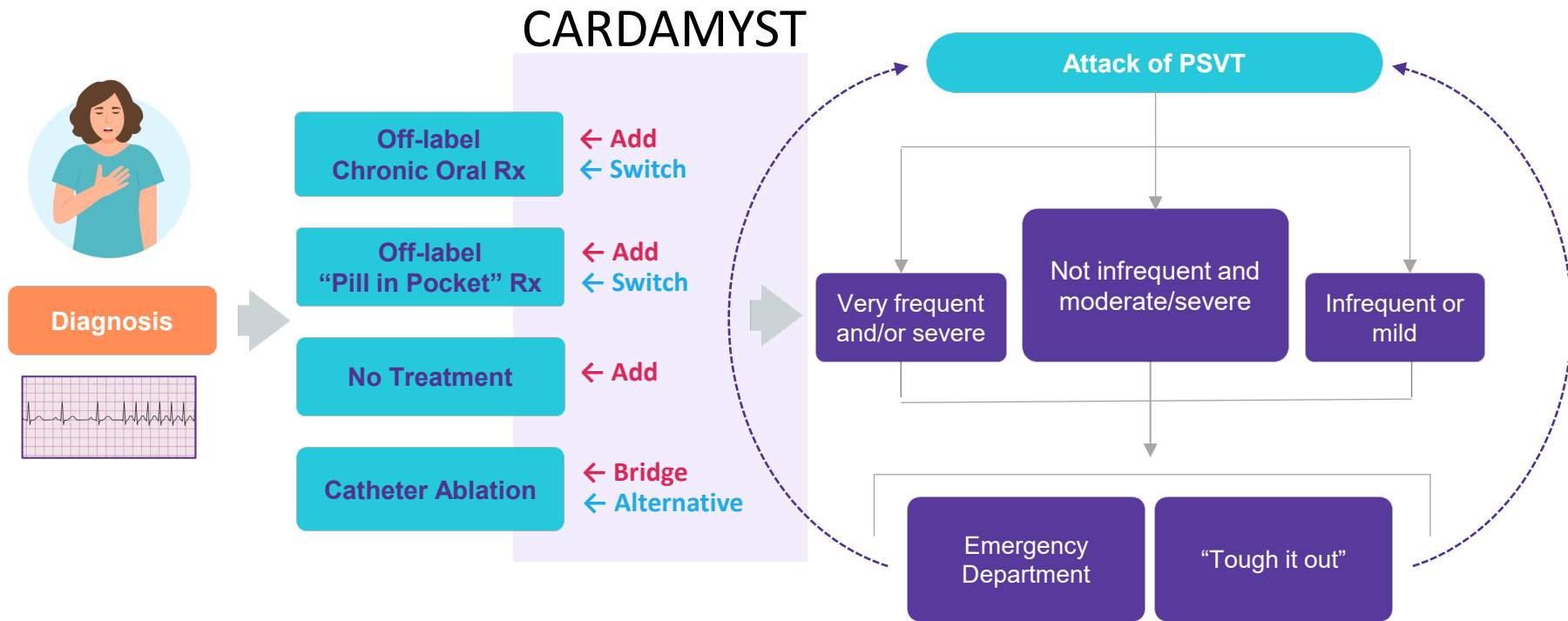
Citations: 1. Stambler BS, et al. Lancet 2023 Jul 8;402(10396):118-128.; Stambler BS, et al. CIRCEP. 2022 Dec;15(12):e010915. 2. Ip JE et al. JACC. 2024 May 21;83(20):2032-2034.; Ip JE et al. JAHA. 2023 Oct 3;12(19):e028227. 3. PSVT patient longitudinal study (n=247 US & UK), conducted by Blueprint Research Group, 2019-2020. 4. Quantitative market research (n=250 clinical cardiologists) conducted by Triangle Insights Group, 2020-2021.

# Patients with PSVT are Primarily Treated by Cardiologists in the Outpatient Setting



Citations: Internal Market Research

# Versatility of CARDAMYST Leads to Multiple Use Cases

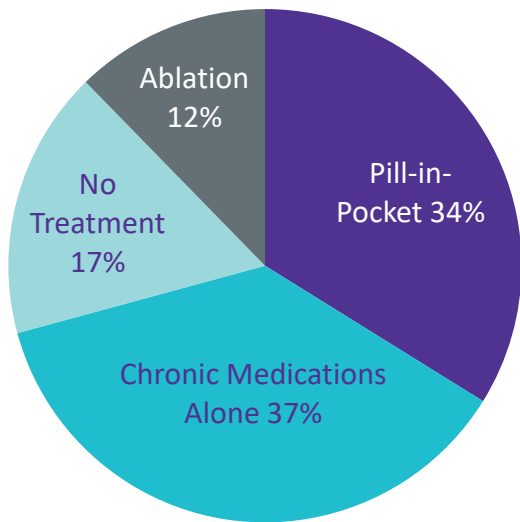


Citations: Internal Market Research

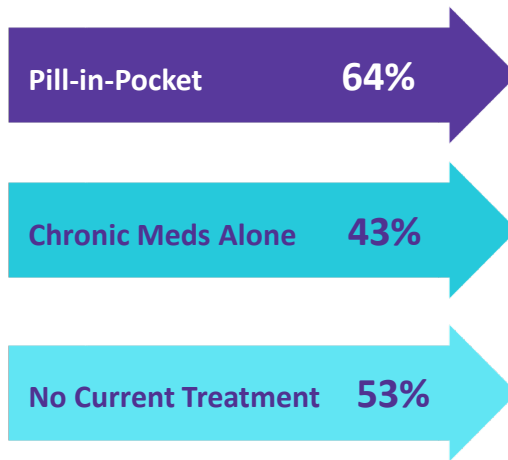
# Cardiologists Expect to Prescribe CARDAMYST to the Majority of Unablated Patients with PSVT



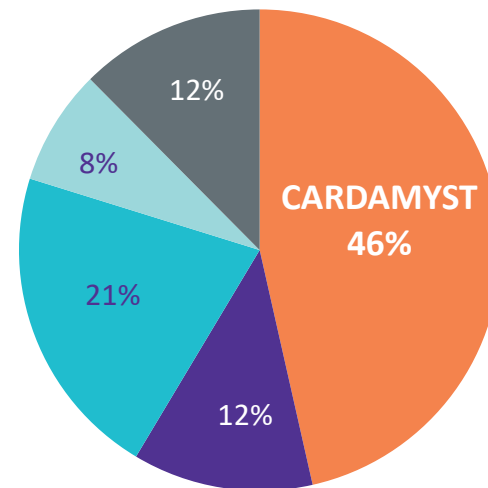
## Current Management of PSVT



## Cardiologists' Stated Adoption of CARDAMYST per Segment



## Impact of Expected Cardiologist Adoption of CARDAMYST



Citation: 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

# Electrophysiologists Have an Important Role to Play with CARDAMYST



- KOLs in arrhythmias respected for their input on P&T and guidelines
- Perform ~100,000 cardiac ablations annually in the U.S.
- Treat ~10% of patients with PSVT

**EPs report willingness to use CARDAMYST in majority of cases<sup>1</sup>**

**Bridge to ablation  
between consultation  
and procedure (33%)**

**Alternative to ablation  
for patients hesitant  
about procedure (24%)**

Key: KOL = Key Opinion Leader; P&T = Pharmacy & Therapeutics; PSVT = Paroxysmal Supraventricular Tachycardia; AFib-RVR = Atrial Fibrillation with Rapid Ventricular Rate; EPs = Electrophysiologists  
Citations: Internal Market Research

# Accessible and Compelling Commercial Opportunity for CARDAMYST



## No anticipated branded competition

**100%** share of voice

Lower rebate pressure

## Low barrier to prescribing

Familiar and trusted MOA

Evidence-based

## Opportunity for early demand generation and quality coverage

~**650k** patients treated annually

~**50%** commercially-insured patients

Cost offsets driven by lower HRU

Key: MOA = Mechanism of Action; HRU = Healthcare Resource Utilization  
Citations: Internal Market Research and Longitudinal Analysis of Truven/Marketscan and Medicare claims data

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**Commercial Strategy and Execution**

# Fully Integrated and Experienced Launch Leadership Team



**Roshan Girglani**  
VP of Marketing



**Jeff Moore**  
VP of Sales



**Anita Holtz MSN, CRNP, CMD**  
VP Head of Medical Affairs



**John Jackimiec**  
VP of Market Access



**Joseph Oliveto**  
President and CEO



**Lorenz Muller**  
Chief Commercial Officer



**David Bharucha, MD PhD**  
Chief Medical Officer

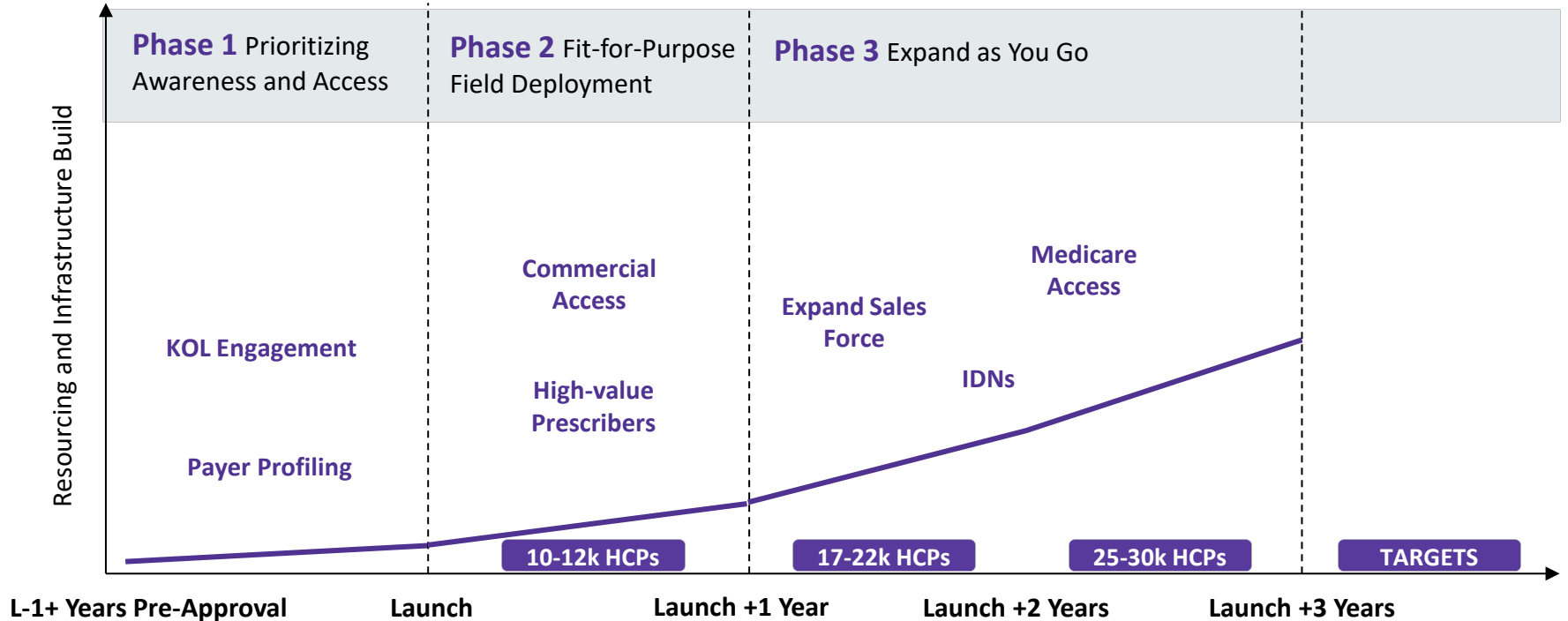


# Go-to-Market Model for CARDAMYST

## Balancing Need to Generate Demand with Managing Commercial Burn



### Planned Phased Commercial Launch Plan



Key: HCPs = Healthcare Providers

Citations: Adopted from Sandberg Orne, L. et al; "Empowering the Next-Generation Launch Model"; Trinity White Paper, June 2022. Data on File (Symphony Open Claims, Veeva Patient Compass, 2021-2024).

# Plans to Deliver Broad Quality Payer Coverage



**Payers**

**Coverage with Low  
Need to Control**

Net pricing below specialty tier  
Protection from overuse  
Commercial expected before  
Medicare



**Healthcare  
Providers**

**Not Onerous to  
Prescribe**

Limit need for paperwork  
or authorizations



**Patients**

**Accessible and  
Affordable**

Available via local pharmacy  
Reasonable out of pocket cost

Citations: Internal market research.

# Strong Value Proposition for CARDAMYST for Payers Can Lead to Broad Coverage without Onerous Restrictions for HCPs or Patients



## Commercial Coverage

**Goal:** Nominal access rebates with patient copay support provided to reduce out-of-pocket cost burden

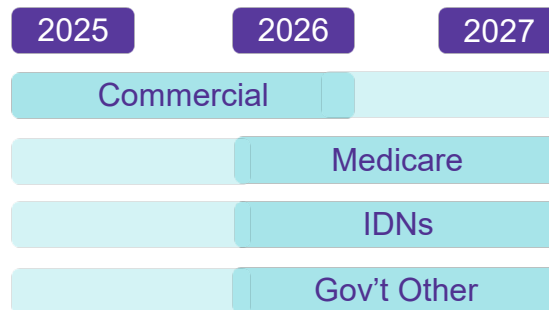
## Medicare Coverage

**Goal:** Rebate to specialty Tier threshold to avoid excessive patient out of pocket

## Utilization Management

- PA to label
- Reasonable quantity limits
- Specialty prescribing

## Priorities for Coverage



Key: U/M = Utilization Management; PA = Prior Authorization; I/E = Inclusion/ Exclusion; IDNs = Integrated Delivery Networks  
Citations: CRA Pricing Research 6/2022

# Key Elements of Launch Timeline for CARDAMYST



Key anticipated milestones for launch of CARDAMYST



Potential FDA approval expected March 27



Medical Information Center live



Patient support services live



Product available for order by pharmacies



Market Access reimbursement support live



Field Medical engaging with KOLs



Sales reps generating demand mid-2025

Key: FDA = Food and Drug Administration; KOLs = Key Opinion Leaders

# Priorities for Launching CARDAMYST



## Awareness and Demand Generation

Sales Leadership

Sales Force Territories

Sales Rep Hiring  following potential approval

Promotional Launch  mid-2025

## Access and HCP Experience

Distribution Contracts

Account Managers Profiling Payers

Fit-for-Purpose Reimbursement Support Programs

## Patient Experience and Affordability

Patient Support Services

Enable Contracting for Target Coverage

Copay Mitigation (Commercial)

# Factors Supporting Planned Launch Year Uptake of CARDAMYST



## Scripts Written

- Initial sales force covers 50% of potential
- Patients seeking treatment weekly
- HCP familiarity and evidence-based approach

## Scripts Filled

- Accessibility through retail distribution
- Fit-for-purpose HCP and patient support programs
- No anticipated branded competition
- Healthcare cost offsets

Citations: Internal Market Research

# Key Brand Performance Indicators for Planned Launch Year



## Strategic Objective:

Drive HCP Awareness  
& Adoption

- New to Brand Prescriptions (NBRx)
- Prescription Growth (week over week)

Establish & Maintain  
Broad, High-Quality  
Access & Affordability

- % Target Lives Covered (emphasis on commercial)
- % of Targets with “Acceptable” Coverage\*

\*Acceptable coverage includes, for example, absence of step edits and reasonable prior authorizations / quantity limits

# Anticipated Commercial Strategy

## Demonstrate Demand and Expand



**2024**

### FOUNDATION

- NDA submission & review
- Pubs & scientific presentations
- KOL engagement
- RWE generation and payer engagement
- Commercial leadership in place

**2025**

### POTENTIAL LAUNCH

- FDA approval
- Retail distribution
- Staged field force deployment
- Patient support services
- Focus on commercial coverage

**2026**

### EXPAND PROMOTION

- Expand field force
- Initiate patient activation
- Engage peer-to-peer promotion
- Expand access to government payers and IDNs

Key: NDA = New Drug Application; RWE = Real World Evidence

# Key Takeaways for Investment Thesis



- Milestone offers near-term commercial and mid-term clinical development catalysts to investors
- PSVT is a symptomatic and unpredictable condition without good patient-driven treatment options
- PSVT affects 2M+ Americans and costs the healthcare system over \$5B per year
- CARDAMYST, if approved, will be the first and only FDA-approved on-demand therapy for patients with PSVT
- Milestone is working to implement a cost-efficient launch strategy designed to:
  - drive near-term demand;
  - have a reasonable time to breakeven; and
  - offer substantial opportunities for growth and expansion

# Q&A



**Joseph Oliveto**  
President and CEO



**Amit Hasija**  
Chief Financial Officer,  
EVP Corporate Development



**Lorenz Muller**  
Chief Commercial Officer



**Guy Rousseau, PhD**  
SVP Regulatory Affairs &  
Quality Management



**David Bharucha, MD PhD**  
Chief Medical Officer



**Jeff Nelson**  
Chief Operating Officer



**Milestone**  
PHARMACEUTICALS

**Thank you**