Milestone PHARMACEUTICALS

Company Overview

公司概述

November 29, 2023

2023年11月29日

Lorenz Muller

Chief Commercial Officer / 首席商务官

Forward Looking Statement / 前瞻性声明

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.

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

Milestone Pharmaceuticals:
Aspiring to Give Patients Control over Common Heart Conditions / 希望患者控制常见的心脏疾病

Empowering Patients
Self-Treat Common Arrhythmias / 让患者能够自我治疗常见心律失常

- Etripamil Nasal Spray: novel calcium channel blocker / Etripamil鼻腔喷雾剂：新型钙通道阻滞剂
- Fast-acting, well-tolerated, portable, on-demand / 见效快、耐受性好、便携、按需使用
- Shift from Emergency Department to patient self-management /从急诊科转向患者自我管理

PSVT
Commercial Launch Preparation / 商业启动准备

- NDA filed – Oct 2023 / 申请NDA – 2023年10月
- Successful Phase 3 / 三期成功
- Published in *The Lancet* / 发表在《柳叶刀》
- Experienced leadership driving commercialization / 经验丰富的领导团队驱动商业化

AFib-RVR
Market Expansion Opportunity / 市场扩张机会

- Positive Phase 2 Study - ReVeRA / 积极的二期研究 - ReVeRA
- AHA Featured Science Presentation – Nov. 2023 / AHA特色科学研究专场报告 – 2023年11月
- FDA guidance outlines path to sNDA / FDA指导规划sNDA路径

PSVT = Paroxysmal Supraventricular Tachycardia; AFib-RVR = Atrial Fibrillation with Rapid Ventricular Rate; NDA = New Drug Application; sNDA = supplemental NDA / PSVT = 阵发性室上性心动过速；AFib-RVR = 房颤伴快速心室率；NDA = 新药申请；sNDA = 补充 NDA

PSVT & Atrial Fibrillation with Rapid Ventricular Rate are Sizable and Underserved Markets in the US / PSVT 和房颤伴快速心室率在美国的市场相当大但尚未得到充分服务

	PSVT	Atrial Fibrillation / 房颤
Total Patients(2030) / 患者总数(2030)	2.6 Million[3] / 260万[3]	10 Million[1] / 1000万[1]
Discharged ED Visits & Hospital Admissions (2016)[2] / 出院急诊室就诊人次和入院人次(2016)[2]	145 Thousand / 14.5万	785 Thousand / 78.5万
Target Addressable Market (2030) Patient Population / 目标市场患者人数 **(2030)**	**1.0-1.6 Million[5] / 100万-160万[5]**	**~3-4 Million / 约300-400万[4]**

Source(s): / 来源：**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. / HCUP ED & 入院数据(2016)，2021年1月获得。 **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. / Triangle Insights 于 2021 年 5 月进行了定量调查，调查对象包括 250 名临床心脏病医师、介入心脏病医师和电生理医师。 **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. / 根据 PSVT 患者内部市场调研（BluePrint Research Group，n=247）和理赔数据纵向分析得出的 TAM 估计值（约为患病率的 40%-60%）。

PSVT and AFib-RVR Cause Markedly Symptomatic Attacks That Disrupt Patients' Lives / PSVT 和AFib-RVR引起症状明显的发作，扰乱患者的生活

Symptoms include… / 症状包括…

- Heart palpitations / 心悸
- Chest pressure or pain / 胸压或疼痛
- Shortness of breath / 呼吸困难
- Fatigue / 疲倦
- Light-headedness / 头晕
- Anxiety / 焦虑

Many patients feel anxious and powerless / 许多患者感到焦虑和无力

PSVT = Paroxysmal Supraventricular Tachycardia; AFib-RVR = Atrial Fibrillation with Rapid Ventricular Rate / PSVT = 阵发性室上性心动过速；AFib-RVR = 房颤伴快速心室率

Current Treatment of Acute Attacks in the Emergency Department are Burdensome and Costly /目前急诊科对急性发作的治疗既繁重又昂贵

For many patients, physicians and payers: / 对于许多患者、医生和付款人来说：

- Time-consuming, disruptive / 费时、颠覆性的
- Often results in a hospital admission / 经常导致住院
- Expensive use of healthcare system resources / 医疗保健系统资源的昂贵使用

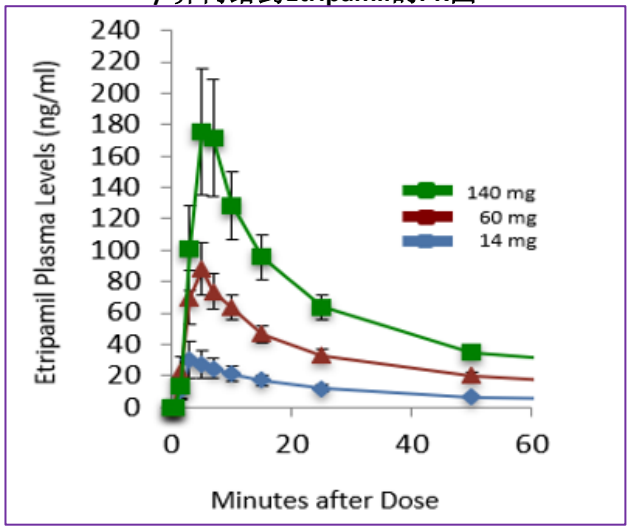
Need for simple, fast-acting treatment, reduce trips to ED and calls to physicians / 需要简单、见效快的治疗方法，减少去急诊室的次数和给医生打电话的次数

ED = Emergency Department / 急诊科

Etripamil Nasal Spray: A Novel CCB Designed to be Fast, Convenient, and Patient-Empowering / Etripamil鼻腔喷雾剂： 快速、方便、赋能患者的新型CCB

- Developed to rapidly terminate episodes of PSVT and acutely slow rate in AFib-RVR / 开发用于快速终止 PSVT 发作和AFib-RVR 急性心率减慢
- Designed for patient self-administration where and whenever the episodes occur / 专为患者随时随地自行用药而设计
- Novel, investigational, L-type calcium channel blocker /正在研究的创新L型钙通道阻滞剂
- Formulated as intranasal spray with: / 配制为鼻内喷雾剂：
  - Rapid onset of action (T_{max} ≤ 7 min) / 快速起效(T_{max} ≤ 7分钟)
  - Eliminated from blood in a few hours /几小时内从血液中清除
- Patent Protection until 2036 / 专利保护期至2036年

PK Plot of Intranasally Administered Etripamil / 鼻内给药Etripamil的PK图

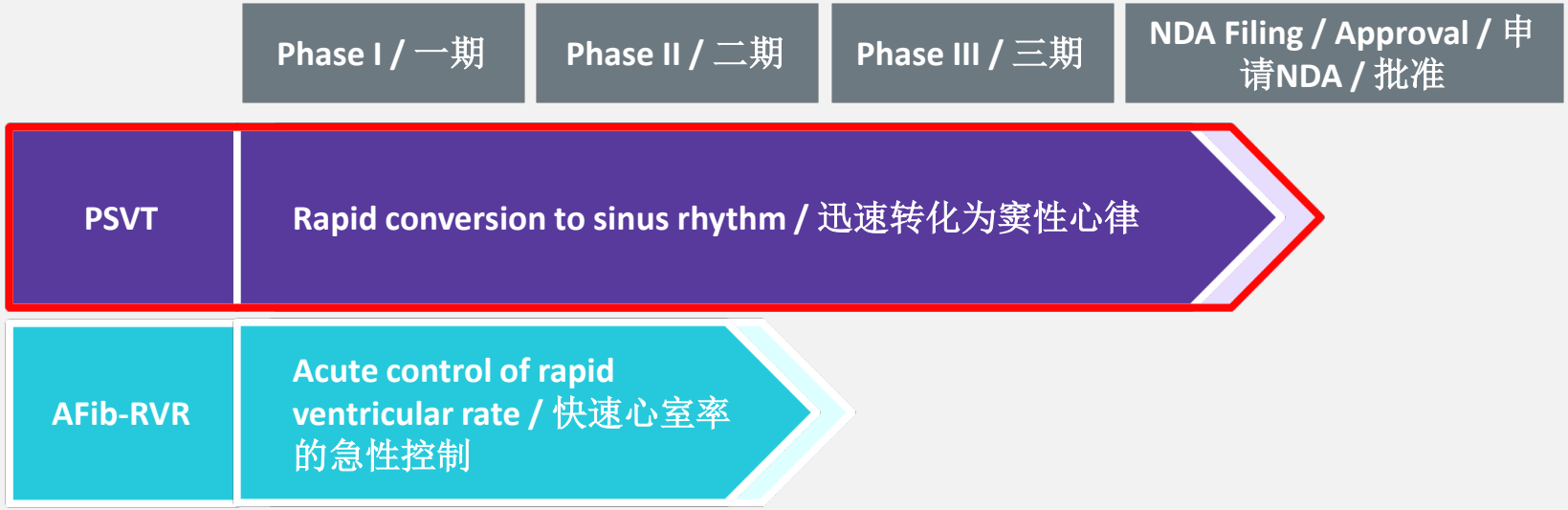


PSVT= paroxysmal supraventricular tachycardia. CCB=calcium channel blocker PK = pharmacokinetic. Error bars = standard error (SE) of the mean. / PSVT=阵发性室上性心动过速； CCB=钙通道阻滞剂； PK=药代动力学。误差条 = 平均值的标准误差 (SE)

Sources: / 来源： 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.

Clinical Pipeline Advancement for Etripamil / Etripamil的临床管线推进

Pharmacology of L-type calcium channel blockers drives broad clinical utility / L 型钙通道阻滞剂的药理作用推动广泛的临床应用



PSVT = Paroxysmal Supraventricular Tachycardia; AFib-RVR = Atrial Fibrillation with Rapid Ventricular Rate; NDA = New Drug Application / PSVT = 阵发性室上性心动过速； AFib-RVR = 房颤伴快速心室率； NDA = 新药申请

Comprehensive Data Supports FDA New Drug Application for Rapid Conversion of SVT Episodes to Sinus Rhythm in Adults / 全面数据支持FDA关于将成人SVT发作快速转为窦性心律的新药申请

NODE-1 / 节点-1	NODE-301 / 节点-301	NODE-302 / 节点-302 (Ext. of NODE-301 / 节点-301的延伸)	RAPID	NODE-303 / 节点-303
Phase 2 / 二期	**Phase 3 / 三期**	**Phase 3 / 三期**	**Phase 3 / 三期**	**Phase 3 / 三期**
Efficacy / 有效性 (dose finding /剂量发现)	Efficacy / 有效性	Safety & Efficacy / 安全性与有效性 (Repeat Episodes / 重复事件)	Efficacy / 有效性	Safety / 安全性 (Repeat EpisodesEpisodes / 重复事件)
N = 64	N = 431	N = 169	N=706	N ~450

- >1,600 Patient Exposures to Etripamil ≥ 70 mg / 1600多名患者服用Etripamil超过70毫克
- Positive Phase 3 pivotal RAPID trial anchors NDA submission (2023) / 积极的三期关键RAPID试验支持NDA提交(2023)

NDA = New Drug Application; SVT = Supraventricular Tachycardia / NDA=新药申请；SVT=房上性心动过速
NB: NODE-301 and RAPID studies also collected Safety information / NB： 节点301和RAPID研究也手机安全性信息
Source: Milestone Pharmaceuticals Data on File / 来源： Milestone Pharmaceuticals存储的数据

Positive Phase 3 RAPID Trial in Patients with PSVT / 在PSVT患者进行三期RAPID试验获得积极结果

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 / 随机、双盲、安慰剂对照试验招募了 706 名患者，让他们在医疗环境之外发生 PSVT 事件时自行服用 Etripamil 70 毫克方案或安慰剂

Repeat-dose regimen – if symptoms not resolved in 10 minutes, second dose administered / 重复给药方案 - 如果症状在 10 分钟内未缓解，则进行第二次给药

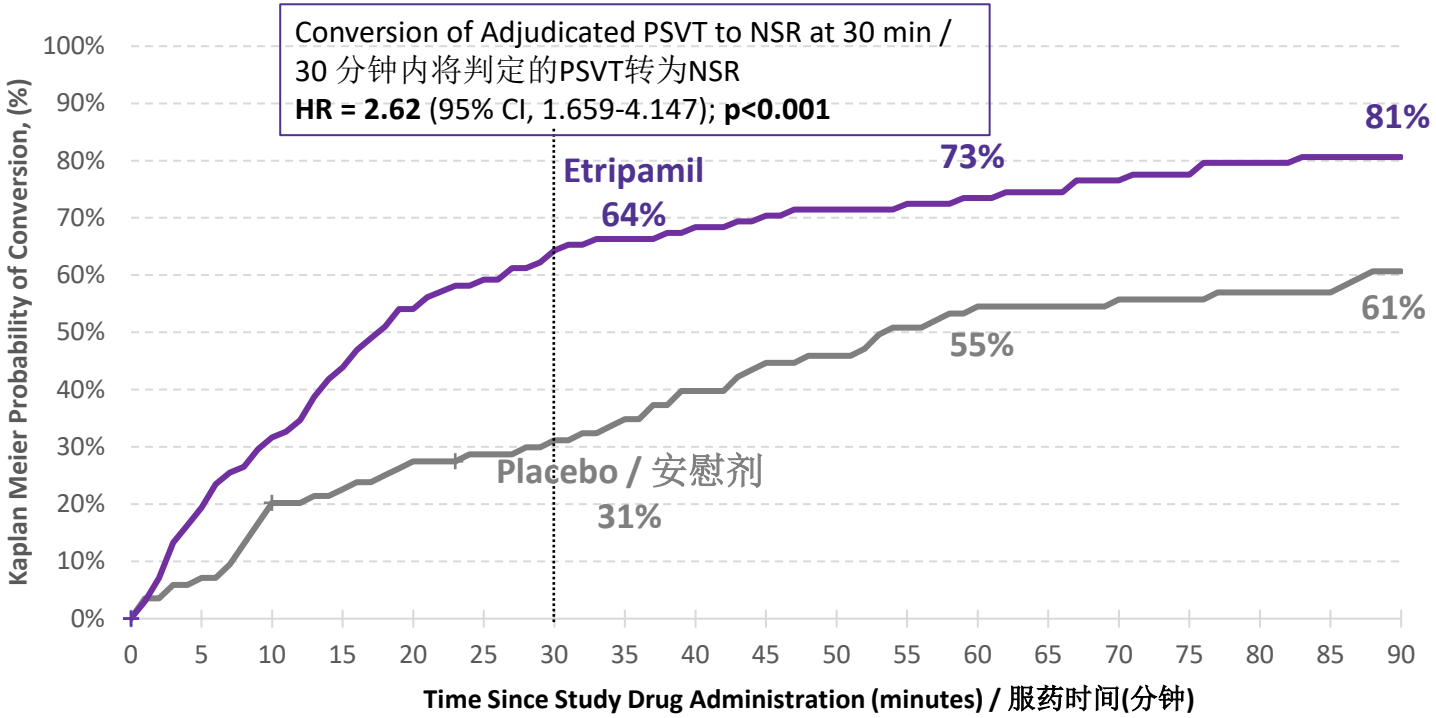
- Achieved primary endpoint - statistical significance / 取得主要终点 – 统计学意义
  (HR = 2.62; 95% CI 1.66, 4.15; p<0.001)
- Need for additional medical interventions or emergency department care ~40% lower for etripamil patients compared to placebo / 与安慰剂相比，etripamil患者需要额外医疗干预或急诊室护理的比例降低了 ~40%。
- Favorable safety and tolerability consistent with prior studies – the most common AEs localized to nasal administration site / 良好的安全性和耐受性与之前的研究结果一致 - 最常见的 AE 均发生在鼻腔给药部位

Primary: Conversion of Adjudicated PSVT to Normal Sinus Rhythm (NSR) at 30 min / 主要指标：30 分钟内将判定的PSVT转为正常窦性心律 (NSR)

HR = Hazard Ratio; CI = Confidence Interval / HR = 危险比； CI = 置信区间
Source: Milestone Pharmaceuticals Data on File / 来源： Milestone Pharmaceuticals存储的数据

Data Indicates Fast Conversion to Normal Sinus Rhythm (NSR) / 数据显示快速转为正常窦性心律 (NSR)

RAPID Study / RAPID 研究



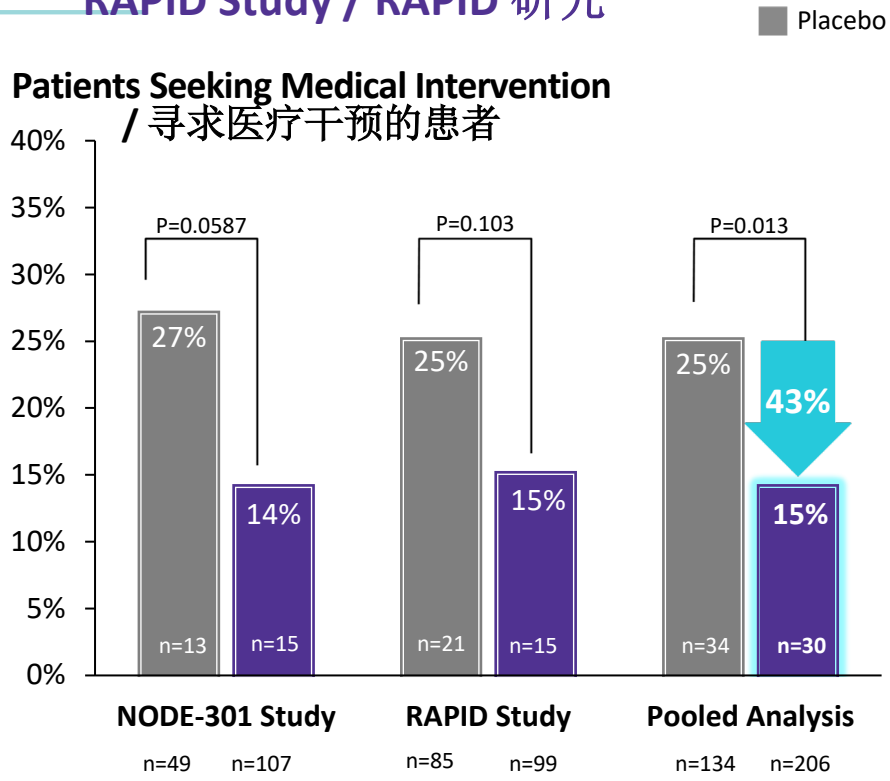
Number of Subjects at Risk / 处于危险中的受试者数量																				
Placebo	85	78	67	64	60	58	56	53	49	45	44	40	37	37	36	36	35	35	32
Etripamil	99	79	67	55	45	40	35	33	31	29	28	27	26	25	23	22	20	19	19

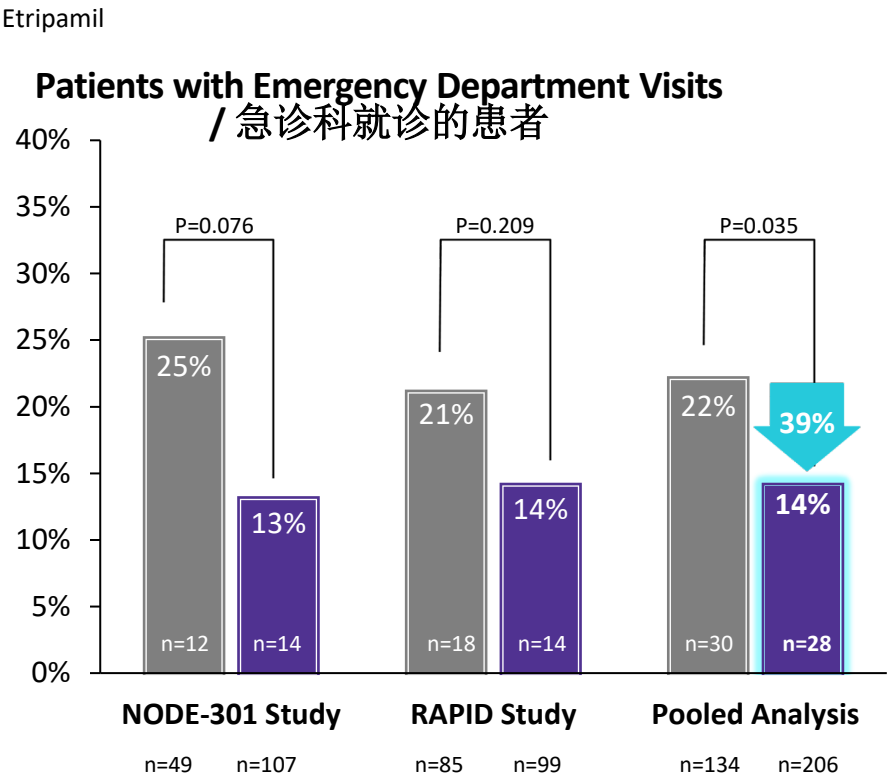
Source: Milestone Pharmaceuticals Data on File

HR = Hazard Ratio; CI = Confidence Interval / HR = 危险比； CI = 置信区间

Fewer Medical Interventions and Emergency Department Visits / 减少医疗干预和急诊就诊次数

RAPID Study / RAPID 研究





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. / RAPID 统计分析计划中预先规定了数据的汇总和分析。 对每个研究数据集和汇总数据集采用卡方检验进行统计分析

Etripamil Well-Tolerated with a Favorable Safety Profile / Etripamil耐受性和安全性好

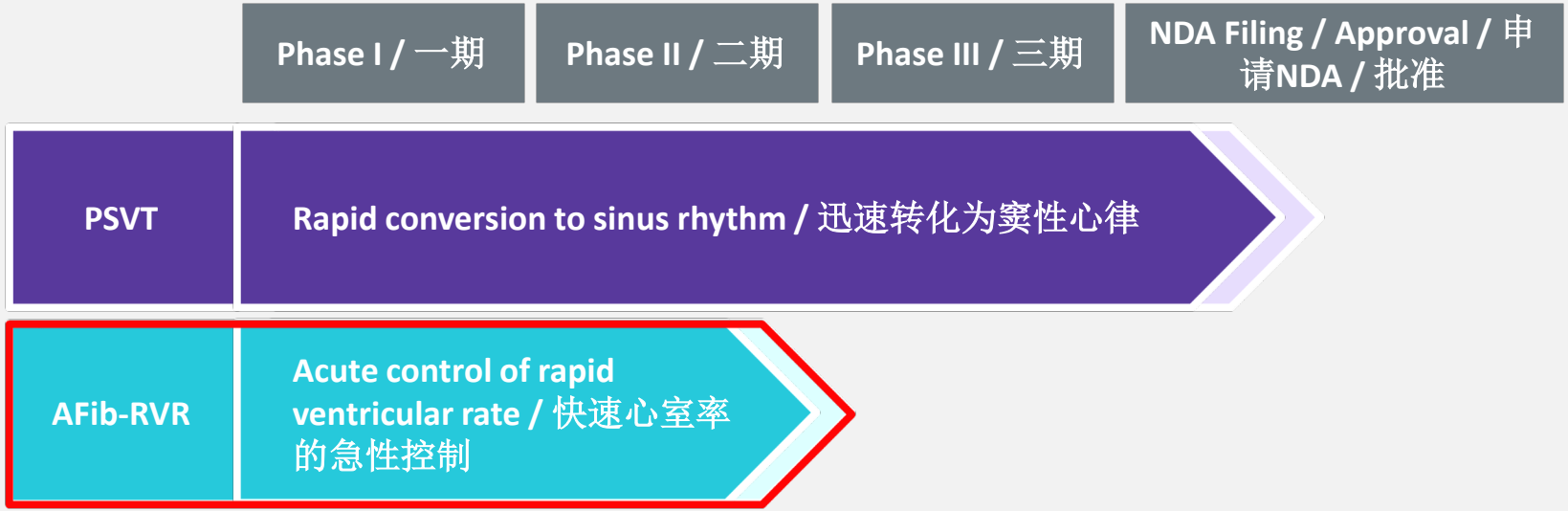
RAPID Study – Safety Events / RAPID研究 – 安全事件

Subject-reported AEs,[1] n (%) / 受试者报告不良事件，n (%)	Placebo[2] / 安慰剂[2] N=120	Etripamil[2] N=135
Nasal discomfort / 鼻部不适	6 (5.0)	31 (23.0)
Nasal congestion / 鼻腔阻塞	1 (0.8)	17 (12.6)
Rhinorrhea / 鼻液溢	3 (2.5)	12 (8.9)
Epistaxis / 鼻出血	2 (1.7)	8 (5.9)[3]
Syncope /晕厥	0.0	0.0
Loss of Consciousness / 失去意识	0.0	0.0
Pre-Syncope / 昏厥前	0.0	0.0
Dizziness / 头晕	0.0	1 (0.7)[4]
Subjects with Events from Independent ECG Reading,[5] n (%) / 有独立心电图读数事件的受试者，n (%)	**Placebo[6] / 安慰剂[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. / [1]随机治疗期间发生的不良事件，那些>5%的不良事件或那些被特别追踪为可能代表血压降低的不良事件。[2]安全人数。[3]8 个中有 6 个被评为轻度，8 个中有 2 个被评为中度，0 个需要干预。[4]被评为轻微。[5]心脏电生理专家评审委员会 [6]具有可评估的 5 小时动态心电图数据的安全人群。AE 时间--用药后 24 小时内。 来源： Milestone Pharmaceuticals存储的数据

Clinical Pipeline Advancement for Etripamil / Etripamil的临床管线推进

Pharmacology of L-type calcium channel blockers drives broad clinical utility / L 型钙通道阻滞剂的药理作用推动广泛的临床应用



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ReVeRA - Phase 2 Proof of Concept Trial of Etripamil in AFib-RVR in the Emergency Department Setting / Etripamil治疗AFib-RVR - 在急诊科环境中的二期概念验证试验

1 Patient presents to ED with episode of AFib-RVR /患者因AFib-RVR发作来到急诊室

2 Dosing & Assessment / 剂量与评估

3 Efficacy Analysis / 有效性分析

Inclusion: / 包括：

- Atrial Fibrillation ≥ 1 hour / 房颤≥1个小时
- Ventricular Rate (VR) ≥ 110 bpm / 心室率(VR) ≥ 110 bpm

Select Exclusions: / 选择排除：

- Treated with antiarrhythmic drugs / 用抗心律失常药物治疗
- Hemodynamically unstable / 血液流动不稳定
- Heart failure / 心力衰竭

1. Baseline ECG for ≥ 10 min /基线心电图 ≥ 10 分钟
2. Administer double blind study drug
   70 mg etripamil : Placebo (1:1) / 实行双盲研究， etripamil 70毫克：安慰剂(1:1)
3. Monitor in-patient for 1 hour / 监测住院病人1个小时
4. Six-hour remote cardiac monitor /6个小时远程心脏监护
5. Complete safety 24 hours post dose / 服药后24小时完全安全

Primary: Maximum reduction in VR within 60 min / 主要终点：在60分钟内最大程度减少VR

N=50: 90% powered to detect 20 bpm difference in max reduction, α=0.05 / 90% 的受试者能检测到最大减幅相差 20 bpm， α=0.05

- **Time to** VR reduction / VR减少的时间
- **Duration** of VR reductions / VR减少的持续时间
  - <100 bpm, ≥ 10% reduction, ≥ 20% reduction / <100 bpm, ≥ 10%减少， ≥ 20%减少
- Patient satisfaction with treatment (TSQM-9) / 患者满意治疗(TSQM-9)

AFib-RVR = Atrial Fibrillation with Rapid Ventricular Rate; TSQM-9, Treatment Satisfaction Questionnaire for Medication; ED = Emergency Department / AFib-RVR = 房颤伴快速心室率；TSQM-9，用药治疗满意度问卷；ED=急诊科

Assessing Ventricular Rate Reduction with Etripamil – How Much; How Fast; How Long /评估Etripamil降低心室率的程度、速度和时间

ReVeRA Primary Endpoint – Maximum Reduction in VR (60 min) / ReVeRA主要终点 – VR最大程度降低（60分钟）

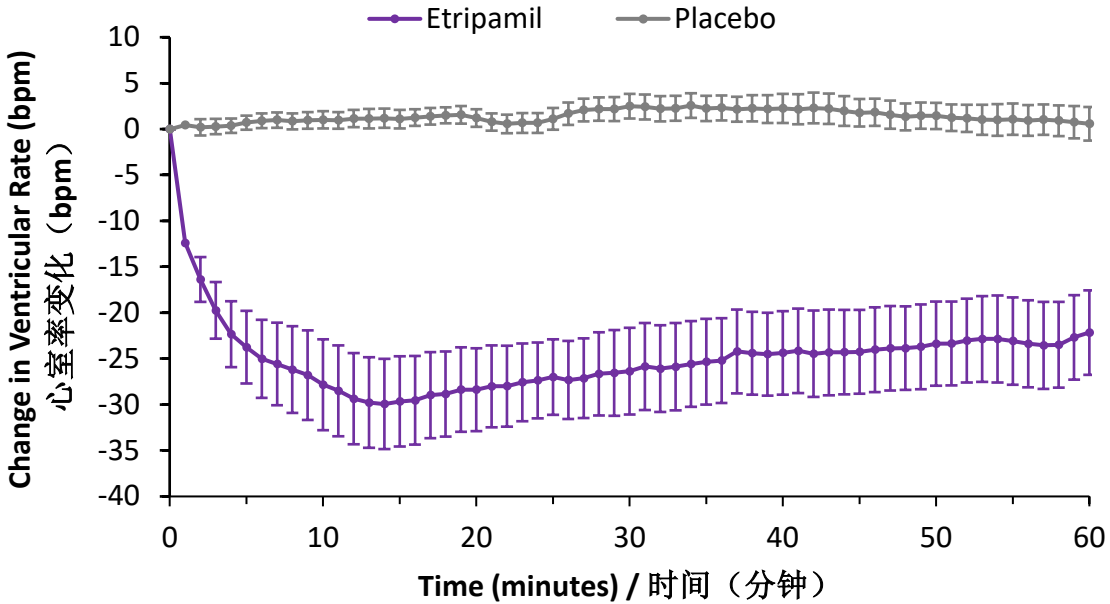
Primary Endpoint achieved with high degree of statistical significance / 达到主要终点，并具有高度统计学意义

PRIMARY ENDPOINT: Maximum Reduction in VR from Baseline / 主要终点：最大限度从基线降低VR	**Placebo NS,[1]** N=25	**Etripamil NS, 70 mg,[1]** N=24
Baseline Ventricular Rate (SD) / 基线心室率(SD)	135.54 (13.93)	130.33 (15.28)
Mean / 平均值 (95% CI), bpm	-5.06 (-7.44, -2.67)	-34.97 (-45.13, -24.87)
Difference in means / 平均值的差额 (95% CI), bpm	--	**-29.91** (-40.31, -19.52)
p-value[2]	**--**	**<0.0001**

[1] Efficacy Population (all randomized patients receiving study drug remaining in atrial fibrillation with adequately diagnostic ECG recordings for at least 60 min post drug). Maximum VR reductions determined based on 5-min moving average of VR. [2] By ANCOVA. bpm ±SEM. bpm = beats per minute. CI = confidence interval. SD = standard deviation. VR = ventricular rate. / [1]疗效人群（所有接受研究药物的随机患者，在用药后至少 60 分钟内仍处于心房颤动状态，且心电图记录具有充分诊断性）。 根据 VR 的 5 分钟移动平均值确定最大 VR 减少量。 [2] By ANCOVA. bpm ±SEM。bpm = 每分钟心跳次数。CI = 置信区间。 SD = 标准偏差。VR = 心室率。

ReVeRA – Mean VR Change from Baseline (60 min) / VR从基线变化的平均值（60分钟）[1]

ReVeRA Data Show Substantial & Rapid Reduction in VR for the Etripamil Group / ReVeRA数据显示， Etripamil组的VR大幅且快速降低



PRIMARY ENDPOINT: Maximum Reduction in VR from Baseline / 主要终点：VR从基线降低最大值	Placebo NS, N=25[1]	Etripamil NS, 70 mg, N=24[1]
Mean / 平均值 (95% CI), bpm	-5.06 (-7.44, -2.67)	-34.97 (-45.13, -24.87)
Difference in means / 平均值差额 (95% CI), bpm	--	-29.91 (-40.31, -19.52)
p-value[2]	--	**<0.0001**

Note: Data plotted on time course are not those directly used for calculation of Primary Endpoint (by pre-specified plan). X-axis: of plot: time following drug administration; Y-axis: 5-min moving average, bpm ±SEM. [1] Efficacy Population (all randomized patients receiving study drug remaining in atrial fibrillation with adequately diagnostic ECG recordings for at least 60 min post drug). [2] By ANCOVA. Bpm = beats per minute. CI = confidence interval. SEM = standard error of the mean, VR = ventricular rate. / 注：绘制的时间进程数据并非直接用于计算主要终点的数据（根据预先指定的计划）。图中 X 轴：给药后的时间；Y 轴：5 分钟移动平均值，bpm ±SEM。 1 疗效人群（所有接受研究药物的随机患者在用药后至少 60 分钟内仍处于心房颤动状态，且心电图记录具有充分诊断性）。2 协方差分析。Bpm = 每分钟心跳次数。CI = 置信区间。SEM = 平均值标准误差，VR = 心室率。

ReVeRA Study: TSQM-9 PRO[1] Assessment & Results / ReVeRA研究： TSQM-9 PRO[1] 评估与结果

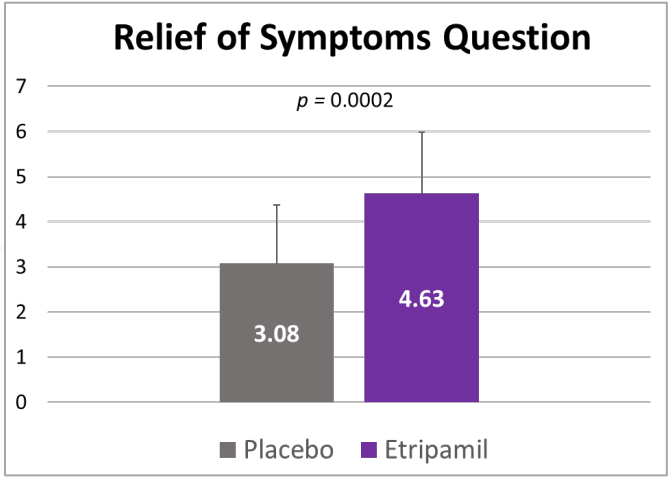
ReVeRA Data Show Significant Improvement in Patient-Reported Relief of Symptoms / ReVeRA 数据表明显著改善患者报告的症状缓解

- TSQM-9 PRO[1] includes an Effectiveness Domain / TSQM-9 PRO[1]包括有效性域
- Domain includes three questions, each answered on 7-point anchored scale /域包括三个问题，每个问题按 7 点锚定量表回答

1	2	3	4	5	6	7
Extremely Dissatisfied 极度不满意	Very Dissatisfied / 非常不满意	Dissatisfied / 不满意	Somewhat Satisfied / 基本满意	Satisfied / 满意	Very Satisfied / 非常满意	Extremely Satisfied / 极度满意

- The domain score is calculated from its three question scores / 域分数是根据三个问题的分数计算出来的
  - Domain score is on a 0 to 100-point scale / 域分数为0到100分
  - Domain score of 50/100 corresponds to a 4/7 = “Somewhat Satisfied” / 域得分 50/100 相当于 4/7 =“基本满意"

	Placebo[2] N=25	Etripamil[2] N=24	p value[3]
Effectiveness Domain Scores, mean (SD) /有效性域得分，平均值(SD)	**36.67 (21.64)**	**62.69 (21.59)**	**p<0.0001**



Delta = 1.55 units on Relief of Symptoms / Delta = 1.55 单位 症状的缓解

[1] Treatment Satisfaction Questionnaire for Medication-9, a validated Patient-Reported Outcome tool. [2] Efficacy Population (all randomized patients receiving study drug remaining in atrial fibrillation with adequately diagnostic ECG recordings for at least 60 min post drug). [3] From t-test / [1]药物治疗满意度问卷-9，这是一个经过验证的患者报告结果工具。[2]疗效人群（所有随机接受研究药物的患者，在用药后至少 60 分钟内仍处于心房颤动状态，且心电图记录具有充分诊断性）。[3]来自T测试

ReVeRA Study - Most Common Adverse Events (≥5% Frequency) / ReVeRA研究 – 最常见的不良事件（ ≥5%频率）

Patients with ≥1 of most common adverse events (≥5%)[1] 患者最常见不良事件≥1例(≥5%)[1]	Placebo / 安慰剂 (N= 29)[2]	Etripamil (N=27)[2]
Nasal Discomfort / 鼻部不适	11 (37.9%)	16 (59.3%)
Rhinorrhea / 鼻液溢	1 (3.4%)	9 (33.3%)
Increased Lacrimation / 流泪增加	5 (17.2%)	8 (29.6%)
Throat Irritation / 喉咙疼痛	--	5 (18.5%)
Dizziness / 头晕	3 (10.3%)	3 (11.1%)
Bradyarrhythmia / 心搏徐缓	--	2 (7.4%)[3]
Epistaxis /鼻出血	--	2 (7.4%)
Nasal Congestion / 鼻腔阻塞	1 (3.4%)	2 (7.4%)
Nasopharyngitis /鼻咽炎	--	2 (7.4%)
Nasal Congestion / 鼻腔阻塞	1 (3.4%)	2 (7.4%)
Oropharyngeal Pain /口咽痛	--	2 (7.4%)
Paresthesia /感觉异常	2 (6.9%)	1 (3.7%)
Intracardiac Thrombus / 心脏内血栓	2 (6.9%)	--

[1] Treatment-emergent adverse events, MeDRA terms. [2] Safety Population (all randomized patients receiving study drug). [3] Two patients each with 1 event of bradyarrhythmia. / [1] 治疗突发不良事件，MeDRA 术语。[2] 安全人群（所有接受研究药物的随机患者）。[3]两名患者各发生 1 例心搏徐缓。

ReVeRA Study - Summary of Serious Adverse Events / ReVeRA研究 – 严重不良事件总结

- One etripamil patient experienced 2 SAEs classified as related to study drug / 一名服用etripamil的患者发生了 2 例与研究药物有关的SAE
  - Transient severe bradycardia and syncope, assessed as due to hyper-vagotonia / 短暂性严重心动过缓和晕厥，被评估为迷走神经功能亢进所致
  - Occurred in a patient with a history of vagal events / 发生于有迷走神经事件史的患者
  - Fully resolved with placing the patient supine and without sequelae / 患者仰卧位完全解决，无后遗症
- Two placebo patients experienced 4 SAEs / 两名服用安慰剂患者发生了4例SAE
  - Patient-1: Intracardiac thrombus, peripheral artery occlusion / 患者1：心脏内血栓、外周动脉闭塞
  - Patient-2: Myocardial ischemia, atrial fibrillation / 患者2：心肌缺血、房颤

SAE = Serious Adverse Event. / SAE：严重不良事件

Proposed Phase 3 Registrational Study in AFib-RVR / 建议的AFib-RVR三期注册研究

- Key Inclusion Criterion: history of symptomatic episodes of AFib-RVR / 主要入选标准：有AFib-RVR症状的历史
- Patients self-administer drug at-home for perceived episodes of AFib-RVR / 患者感到AFib-RVR自行在家用药
- Dose: etripamil NS 70 mg (same as proposed indication in PSVT); repeat-dose regimen / 剂量： etripamil NS 70毫克（与PSVT的适应症建议的剂量相同）；重复用药
- Primary endpoint = maximum reduction in VR, same as ReVeRA; etripamil vs placebo / 主要终点 = 最大限度降低VR，与ReVeRA相同；etripamil vs 安慰剂
- Key Secondary endpoint = symptom relief, via PRO / 主要的次级终点 = 症状缓解，通过PRO
- Objectives: / 目标：
  - Show $p < 0.05$ for Primary and Key Secondary endpoints in ITT population; no alpha-spend / 在 ITT 群体中，主要终点和关键次要终点的 $p < 0.05$；无 alpha-spend
  - Show meaningful PRO-based change in Target population (eg, 1-point change on 7-point scale) / 在目标群体中PRO大幅变化（例如， 7分制中1分的变化）
- Estimated study size: N ≈ 150-200 total events, based on[1]: 90% power, $p < 0.05$ / 预期研究规模： N ≈ 150-200总事件，基于[1]：90% power, $p < 0.05$
- Timing / 时间
  - FDA Confirmation of Ph3 Protocol: 1Q 2024 / FDA批准三期方案：2024年第一季度
  - Study Start: Mid 2024 / 研究开始：2024年中期
  - Top-Line Data: Mid 2026 / 顶线数据：2016年中期

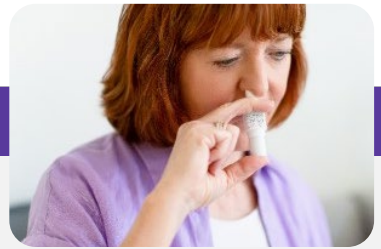
[1] Sizing assumptions also include PRO delta of 1.2 points, standard deviation = 1.6, Target/ITT population ratio of 0.70. AFib-RVR = atrial fibrillation with rapid ventricular rate; ITT = intention to treat; PSVT = paroxysmal supraventricular tachycardia; TSQM = Treatment Satisfaction Questionnaire for Medication PRO; PRO = patient reported outcome / 规模假设也包括1.2点PRO delta，标准差=1.6，目标/ITT群体比例为0.70。AFib-RVR = 房颤伴快速心室率；ITT =治疗意向；PSVT = 阵发性室上性心动过速；TSQM =用药治疗满意度问卷PRO；PRO = 患者报告结果

PSVT & Atrial Fibrillation with Rapid Ventricular Rate are Sizable and Underserved Markets in the US / PSVT 和房颤伴快速心室率在美国的市场相当大但尚未得到充分服务

	PSVT	Atrial Fibrillation
Total Patients (2030) / 患者总数 (2030)	2.6 Million[3] / 260万[3]	10 Million[1] / 1000万[1]
Discharged ED Visits & Hospital Admissions (2016)[2] **/** 出院急诊室就诊人次和入院人次(2016)[2]	145 Thousand / 14.5万	785 Thousand / 78.5万
Target Addressable Market (2030) Patient Population / 目标市场患者人数(2030)	**1.0-1.6 Million[5] / 100万-160万[5]**	**~3-4 Million / 约300-400万[4]**

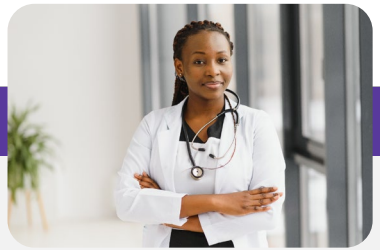
Source(s): / 来源：**1.** Colilla et al., Am. J. Cardiol. 2013, 112(8), 1142-1147; Miyasaka et al., Circulation, 2006, 114, 119-125. American Heart Association **2**. HCUP ED & Admissions Data (2016), accessed January 2021. / HCUP ED & 入院数据(2016)，2021年1月获得。 **3.** Rehorn et al. Journal of Cardiovascular 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. / Triangle Insights 于 2021 年 5 月进行了定量调查，调查对象包括 250 名临床心脏病医师、介入心脏病医师和电生理医师。 **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. / 根据 PSVT 患者内部市场调研（BluePrint Research Group，n=247）和理赔数据纵向分析得出的 TAM 估计值（约为患病率的 40%-60%）。

Etripamil Has Substantial Potential Value for Stakeholder Groups If Approved / 如果获批，Etripamil对利益相关群体具有巨大的潜在价值



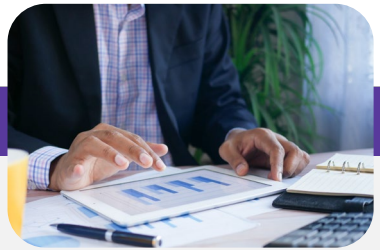
Patients - Empowerment / 患者 – 赋能

- Fast, reliable self-administration / 快速、可靠自行用药
- Less disruption, reliance on the Emergency Department / 更少的干扰、对急诊科的依赖
- Less fear over when the next event will occur / 下次事件发生时不会过度惊慌



Physicians – Dependable Tool / 医生 – 可靠的工具

- Designed for patient self-management / 设计为患者可自我管理
- Frees up physician time and office resources / 释放医生时间和办公室资源
- Trusted CCB mechanism / 可靠的CCB机制



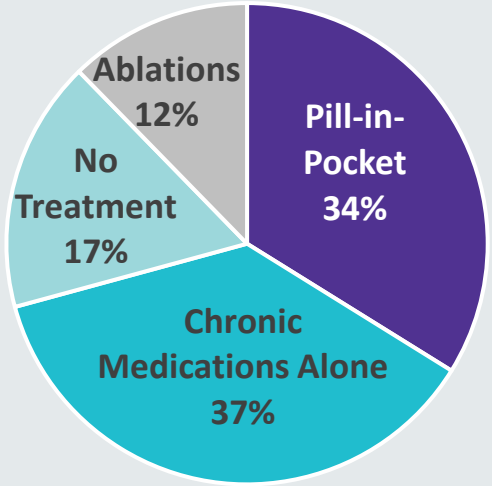
Payers – More Efficient Use of Resources / 支付者 – 更高效地使用资源

- Novel and cost-effective treatment / 新颖且成本效益好的治疗方法
- Reduction in ED/hospital admissions / 减少急诊科/入院

Sources: Internal market research, PSVT = Paroxysmal Supraventricular Tachycardia, ED = Emergency Department / 来源：内部市场研究， PSVT = 阵发性室上性心动过速，ED = 急诊科

Cardiologists Expect to Prescribe Etripamil to the Majority of Unablated Patients with PSVT / 心脏病科医生有望为大多数未经消融的PSVT患者开处方Etripamil

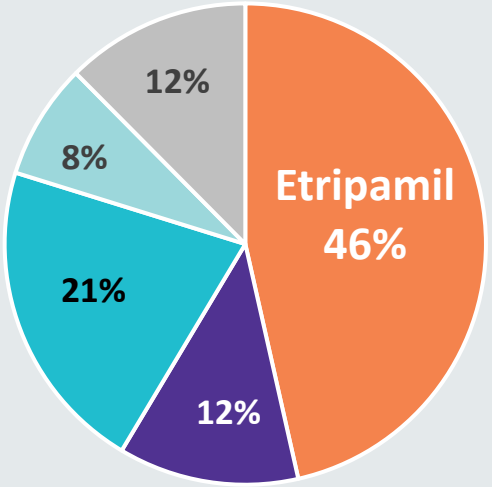
Current PSVT Management / 当前的PSVT管理



Cardiologists' Stated Adoption of Etripamil per Segment / 心脏病科医生建议每个部分采用Etripamil

- Pill-in-Pocket / 口袋药 (PIP) 64%
- Chronic Meds Alone /单独使用慢性药物 43%
- No Current Treatment / 当前无治疗 53%

Impact of Cardiologist Adoption of Etripamil / 心脏病科医生采用Etripamil的影响

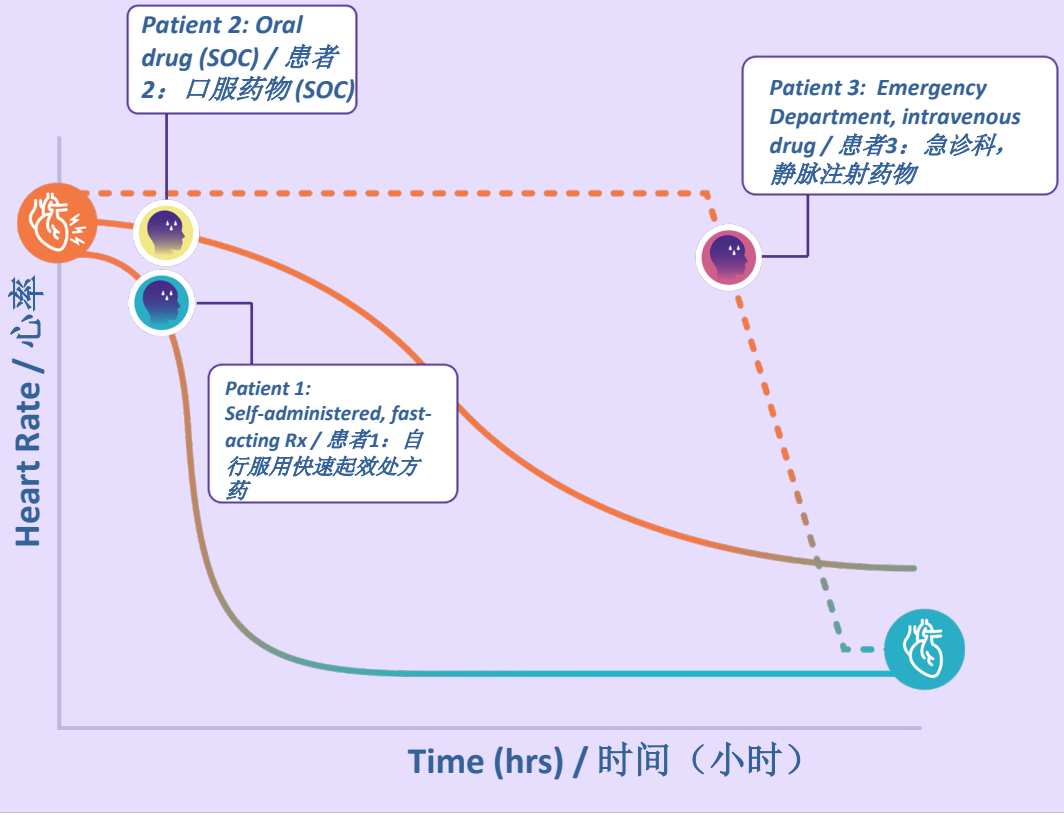


Source: Quantitative market research conducted by Triangle Insights Group (n=250 cardiologists), June-September 2020; Estimated number of unique patients with annual claims for PSVT from Truven MarketScan data, 2008-2016 analyzed by Precision Xtract, 2019 / 资料来源：Triangle Insights Group 开展的定量市场研究（n=250 名心脏病科医生），2020 年 6 月至 9 月；Precision Xtract 分析的 2008-2016 年 Truven MarketScan 数据显示的 PSVT 年度索赔患者估计人数，2019 年

AFib-RVR – Acute Treatment Scenarios / 急性治疗场景

Acute AFib-RVR Attack / 急性AFib-RVR发作

- Heart palpitations / 心悸
- Chest pressure or pain /胸压或疼痛
- Shortness of breath / 呼吸困难
- Fatigue / 疲倦
- Light-headedness / 头晕
- Anxiety / 焦虑



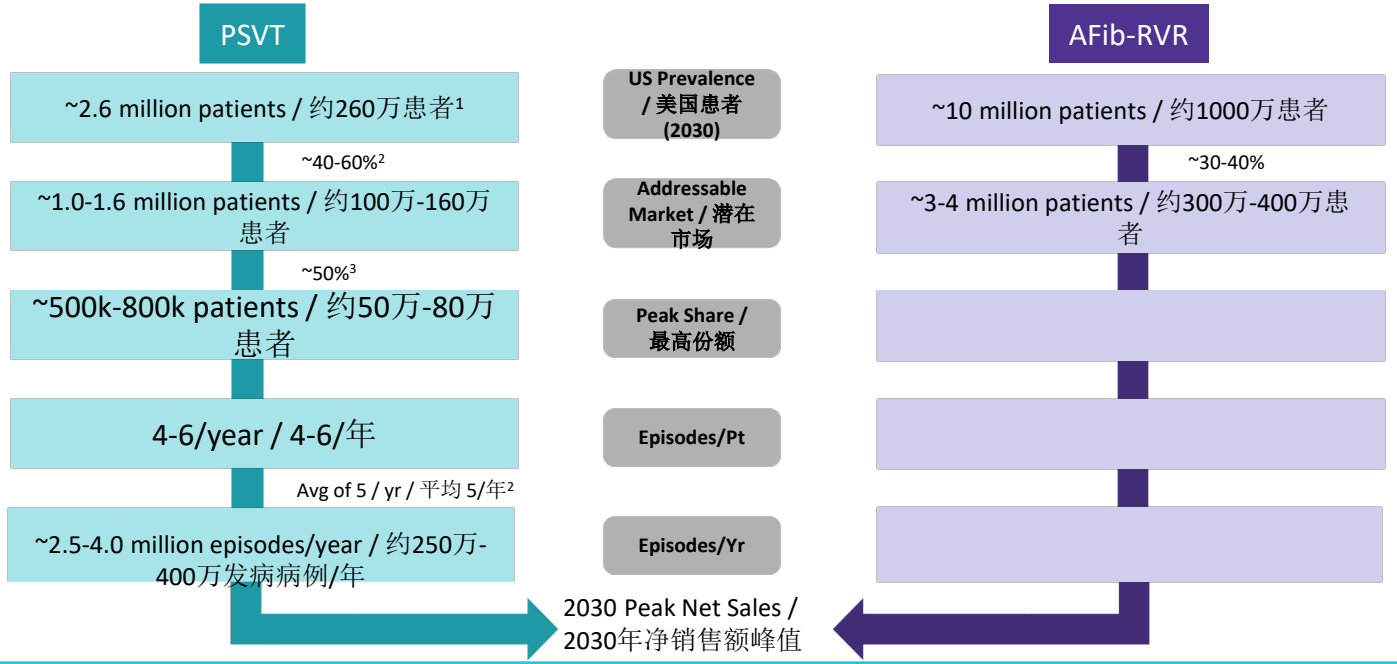
Potential Use Cases of Etripamil for AFib-RVR / Etripamil在AFib-RVR的潜在使用案例

1. Acute, stand-alone treatment for rate control and symptom control / 急性、独立治疗，用于控制心率和症状
2. Acute treatment as a bridge (“precursor”) to the delayed effects of oral rate-control or anti-arrhythmic drug administration / 作为口服控制心率或抗心律失常药物延迟效应的桥梁（“前奏”）的急性治疗
3. Use peri-ablation / 使用围消融方式
4. Non-invasive administration opens options for potential treatment without an IV line in emergency-department or ambulance setting / 无创用药为在急诊室或救护车环境中无需静脉注射管即可进行潜在治疗提供了选择

A drug that is rapidly acting and self-administered outside of a medical setting would have characteristics that would help an unmet need / 快速起效和在医疗环境外自行服用的药物具有有助于满足未满足需求的特点

AFib-RVR = atrial fibrillation with rapid ventricular rate, Rx = treatment, IV = intravenous / AFib-RVR =房颤伴快速心室率， Rx = 治疗，IV = 静脉

Peak US Market Opportunity for Etripamil in PSVT and AFib-RVR / Etripamil在治疗PSVT和AFib-RVR的美国市场峰值机会



Market Research Suggests a TAM of 4+ Million Patients across both PSVT and AFib-RVR Indications / 市场研究表明，PSVT 和AFib-RVR适应症的患者总人数超过 400 万

AF – RVR = Atrial Fibrillation with Rapid Ventricular Rate; TAM = Target Addressable Market / AFib-RVR =房颤伴快速心室率； TAM =目标市场

Sources: / 来源： **1.** Rehorn et al. Journal of Cardiovascular Electrophysiology. 2021 Aug; 32(8): 2199-2206. doi: 10.1111/jce.15109. ; **2.** 2019 market research with patients conducted by BluePrint Research Group, (n=247) / BluePrint Research Group进行的2019患者市场研究， (n=247) ; **3.** 2020 market research with healthcare providers conducted by Triangle Insights Group, (n=250) / Triangle Insights Group与医疗保健提供商进行的2020市场研究， (n=250)

Finances – as of September 30, 2023 / 财务状况 – 截止2023年9月30日

- Cash and short-term investments of $75.7M / 现金与短期投资为$7570万
- Synthetic Royalty Financing of $75M available upon approval (1) / 一旦获批，可用$7500万综合权利金融资 (1)
- Cash as of September 30, 2023 together with synthetic royalty financing expected to fund operations into mid-2025 / 截止2023年9月30日的现金与综合权利金融资预计可使用到2025年中期
- Equity - 43.1M in shares and pre-funded warrants outstanding(2) / 股权 –股票和预先筹资发行的未行权认股权证合计4310万股(2)
  - 33.5M common shares / 3350万普通股
  - 9.6M pre-funded warrants / 960万份预先筹资发行的认股权证

(1) In March 2023, Milestone announced a $125.0M strategic with RTW Investments. The financings consists of $50.0M in convertible notes issued in March 2023, and a commitment $75.0M in non-dilutive royalty funding if etripamil is approved by the FDA. / 2023 年 3 月，Milestone 公司宣布与 RTW Investments达成一项 $1.25亿的战略合作。此次融资包括 2023 年 3 月发行的 $5000万可转换债券，以及承诺在etripamil获得 FDA 批准后提供 $7500 万的非稀释性权利金。

(2) Common shares as of November 13, 2023. Pre-funded warrants as of September 30, 2023./ 截止2023年11月13日普通股。截止2023年9月30日预先筹资发行的认股权证

Milestone Pharmaceuticals:
Aspiring to Give Patients Control over Common Heart Conditions / 希望患者控制常见的心脏疾病

Empowering Patients
Self-Treat Common Arrhythmias / 让患者能够自我治疗常见心律失常

- Etripamil Nasal Spray: novel calcium channel blocker / Etripamil鼻腔喷雾剂：新型钙通道阻滞剂
- Fast-acting, well-tolerated, portable, on-demand / 见效快、耐受性好、便携、按需使用
- Shift from Emergency Department to patient self-management /从急诊科转向患者自我管理

PSVT
Commercial Launch Preparation / 商业启动准备

- NDA filed – Oct 2023 / 申请NDA – 2023年10月
- Successful Phase 3 / 三期成功
- Published in *The Lancet* / 发表在《柳叶刀》
- Experienced leadership driving commercialization / 经验丰富的领导团队驱动商业化

AFib-RVR
Market Expansion Opportunity / 市场扩张机会

- Positive Phase 2 Study - ReVeRA / 积极的二期研究 - ReVeRA
- AHA Featured Science Presentation – Nov. 2023 / AHA特色科学研究专场报告 – 2023年11月
- FDA guidance outlines path to sNDA / FDA指导规划sNDA路径

PSVT = Paroxysmal Supraventricular Tachycardia; AFib-RVR = Atrial Fibrillation with Rapid Ventricular Rate; NDA = New Drug Application; sNDA = supplemental NDA / PSVT = 阵发性室上性心动过速；AFib-RVR = 房颤伴快速心室率；NDA = 新药申请；sNDA = 补充 NDA

Milestone PHARMACEUTICALS

Questions?

问答环节