GenVara

BIOPHARMA

THE APPLICATION OF GENETIC VARIATION FOR CARDIOVASCULAR DISEASE

Developing A Genetically Targeted Therapy Treating Atrial Fibrillation in Patients with Heart Failure

Investment Highlights

De-risked Short-Term Opportunity to FDA Approval for Novel Cardiovascular Therapy

GENCARO™ oral therapy for genetically defined patients with heart failure & atrial fibrillation

- Billon dollar opportunity in large growing market
- IP protection through 2044

De-risked phase 3 clinical trial with FDA guidance in place

- Two completed pharmacogenetic trials inform Phase 3 design
- One small (350 patient) phase 3 trial to FDA approval

$65M funds 3 years of company operations and phase 3 trial costs to FDA submission

High value exit potential due to biopharma demand for market-ready CV products

Proven leadership team with multiple exits

Strong Genvara Leadership Team

Extensive Cardiovascular Drug Development Experience with Multiple Exits

Michael Bristow, MD, PhD: Chairman, CSMO

Tom Keuer, MS: President & CEO

Jeff Dekker: Chief Financial Officer

Richard Clark: Chief Business Officer

Sharon Perry: VP Regulatory Affairs & Quality

Ian Carroll, PhD: VP Data Information Systems

Cardiovascular Disease

Leading Cause Of US Death And Morbidity

Atrial Fibrillation (AF) & Heart Failure (HF) Are Major Contributors

Heart Failure (HF)

- Heart can't pump enough blood to meet the body's needs
- Classified by left ventricular ejection fraction (LVEF):
  - LVEF < 40% ➔HFrEF (LVEF ≤ 35% ➔ "HFlrEF")
  - 40% ≥ LVEF < 50% ➔ HFmrEF
  - LVEF ≥ 50%➔ HFpEF (LVEF 40%-54% ➔ "HFmprEF")
- Upon diagnosis the overall five-year survival rate is only 50%
- Currently 6.7M HF patients in U.S. (60M worldwide)

Atrial Fibrillation (AF)

- Heart upper chambers (atria) beat chaotically and dyssynchronous with lower chambers
- Causes blood disruption leading to a rapid heart rate, fatigue and dizziness
- Increases stroke risk and causes heart failure

- **Both AF & HF prevalence growing**
- **One condition worsens and/or triggers onset of the other**
- **Approx 45% of patients with HF have concomitant AF**

A Significant Unmet Need Exists For Targeted Solutions

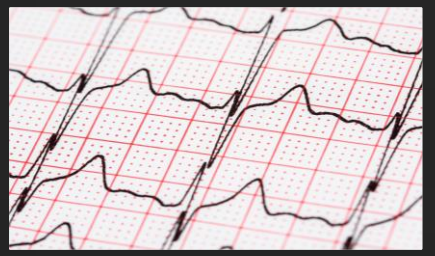
That Improve Heart Failure Outcomes and Treat Atrial Fibrillation

01.

Beta Blockers (β-Blockers)

- Foundational mortality reducing therapy in HFrEF
- Not approved or effective in HFmrEF and HFpEF, which represents 60% of HF
- Manage rapid heart rate in AF with or without heart failure
- However, standard β-Blockers do NOT have a significant anti-arrhythmic effect, i.e. do not convert AF to sinus rhythm

02.



Antiarrhythmic Drug Therapies

- Treat the AF rhythm
- But are NOT durably effective
- In heart failure are NOT safe and/or may worsen LV function and symptoms

03.

Ablation (procedure)

- Effective for atrial fibrillation in heart failure
- Expensive, invasive with high failure rate often requiring repeat procedures
- Not as effective for more serious HF (Class III and IV)

GENCARO™ - First Pharmacogenetic Targeted Treatment

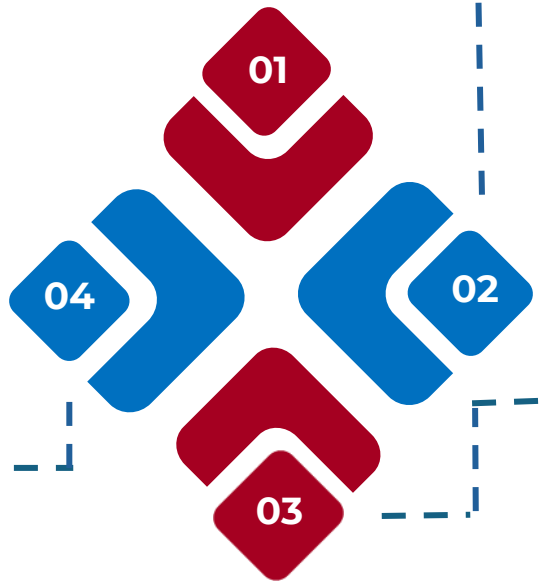
For Heart Failure Patients with Atrial Fibrillation

Phase 3-enabled CV Asset
High Return Feasible

- **Small Phase 3 Label- Enabling Trial |** Near-term commercial @ low cost
- **Strong Phase 2 Insights and FDA Interactions |** Technically de-risked
- **Large % of HF & High AF Incidence |** Large patient #'s in mature markets
- **New IP through 2044 |** Long commercial runway

Unique Label
Supports Differentiation

- **AF in HF |** The only one!
- **Superiority against the Standard of Care |** Guideline inclusion expected



High Unmet Need
New Therapy Needed

- **Few Good Drug Therapy Options |** No directly competitive drugs
- **Generic Beta Blockers Off-Label |** Manageable payer landscape

Innovative & Leading-Edge
Enthusiasm & Plausibility

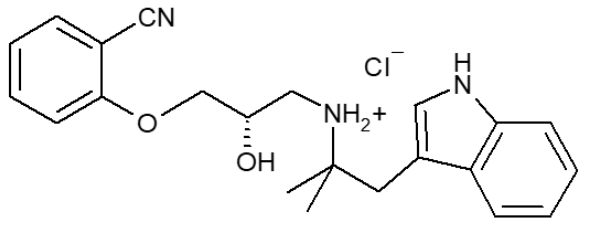
- **Genetically Targeted |** High precision medicine interest
- **Unique Mechanism of Action |** Provides both rhythm and rate therapy
- **AF Burden Substudy |** Device based Leading edge of the field

GENCARO™ Provides Unique And Proven Cardiac Benefits

With Differentiated Mechanism of Action in Genotyped Patient Population

Genotype Specific Responses

- **Disease modifying:** Works by reversing structural and electrical remodeling of heart
- **Approx 65% of HF & AF population with responsive genotype**
- **Only Beta Blocker with these properties**



Differentiated Mechanisms of Action Uniquely Cardioprotective

- **Sympatholysis:** Lowers norepinephrine (modestly) – more potent inhibition of β1 adrenergic receptor (β1 -AR) pathway
- **Inverse Agonism** – Inactivates constituitivley active β1-ARs – more protective of heart
- **Internalization of normally non-internalizing β1 and β2-AR haplotype variants -** Leads to cardioprotective signaling

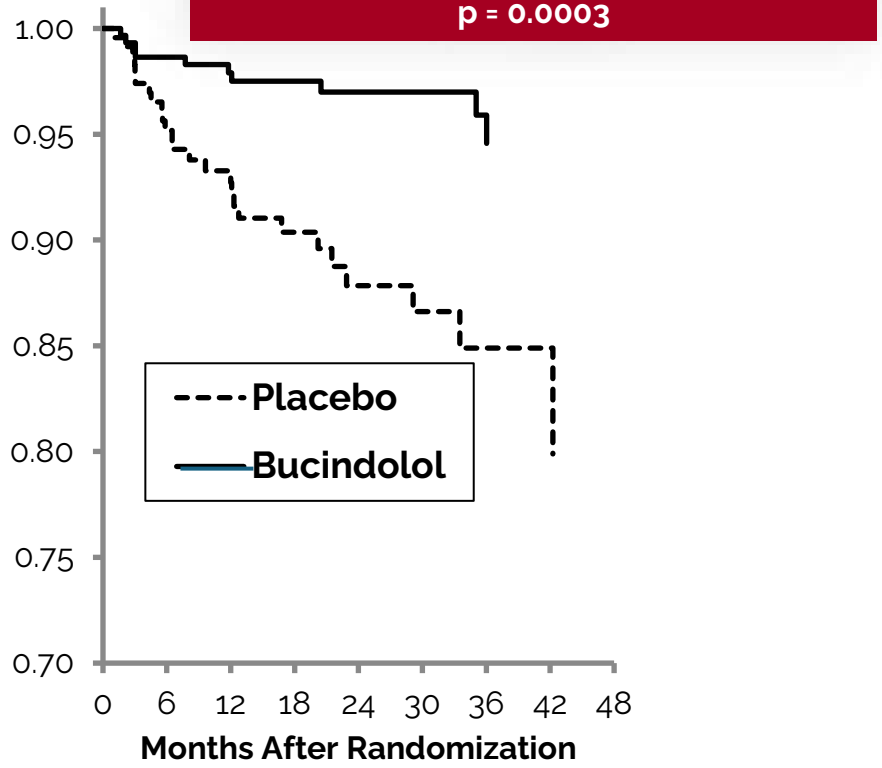
Extensive Clinical Data Two Pharmacogenetic (PGt) Trials

- **Phase 3 HF 3,500 patient BEST trial,** placebo controlled with 1040 patient PGt substudy
  - Favorable safety profile and PGt enhancement of efficacy
  - PGt substudy: 74% reduction in AF onset in LVEF ≤ 35%
- **Phase 2 GENETIC-AF Trial with active comparator (Toprol-XL)**
  - 46% reduction in AF recurrence with LVEF ≤ 55% (58% reduction in LVEF 40-55%)
  - 55% reduction in AF burden demonstrated in substudy

GENCARO™ Proven Effective for AF Reduction in HF

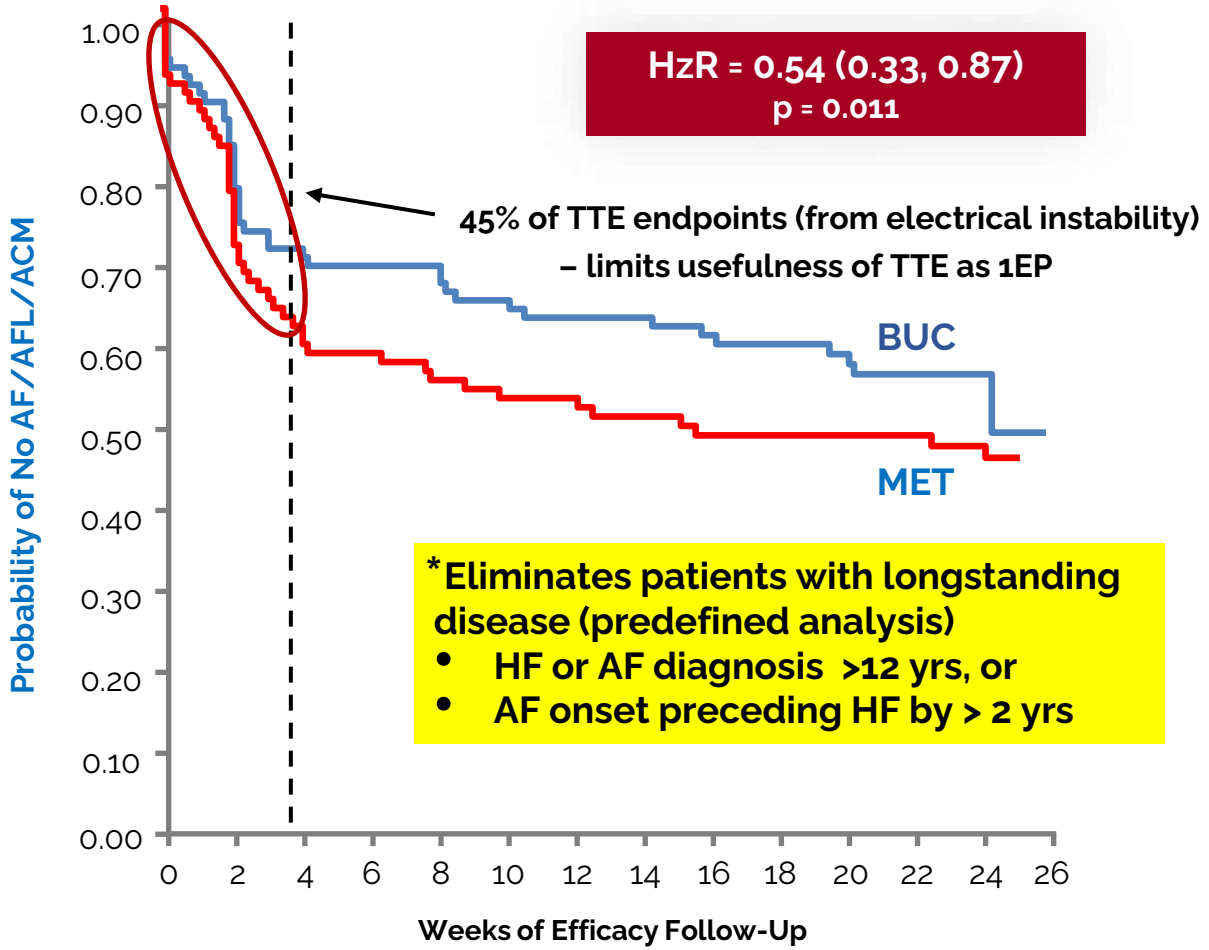
Two Clinical Trials Demonstrate Benefit of Pharmacogenetic Targeting

ADRβ1 Arg389Arg, BEST DNA substudy
N = 441



(Aleong et al, JACC Heart Fail; 1:338-44, 2013)

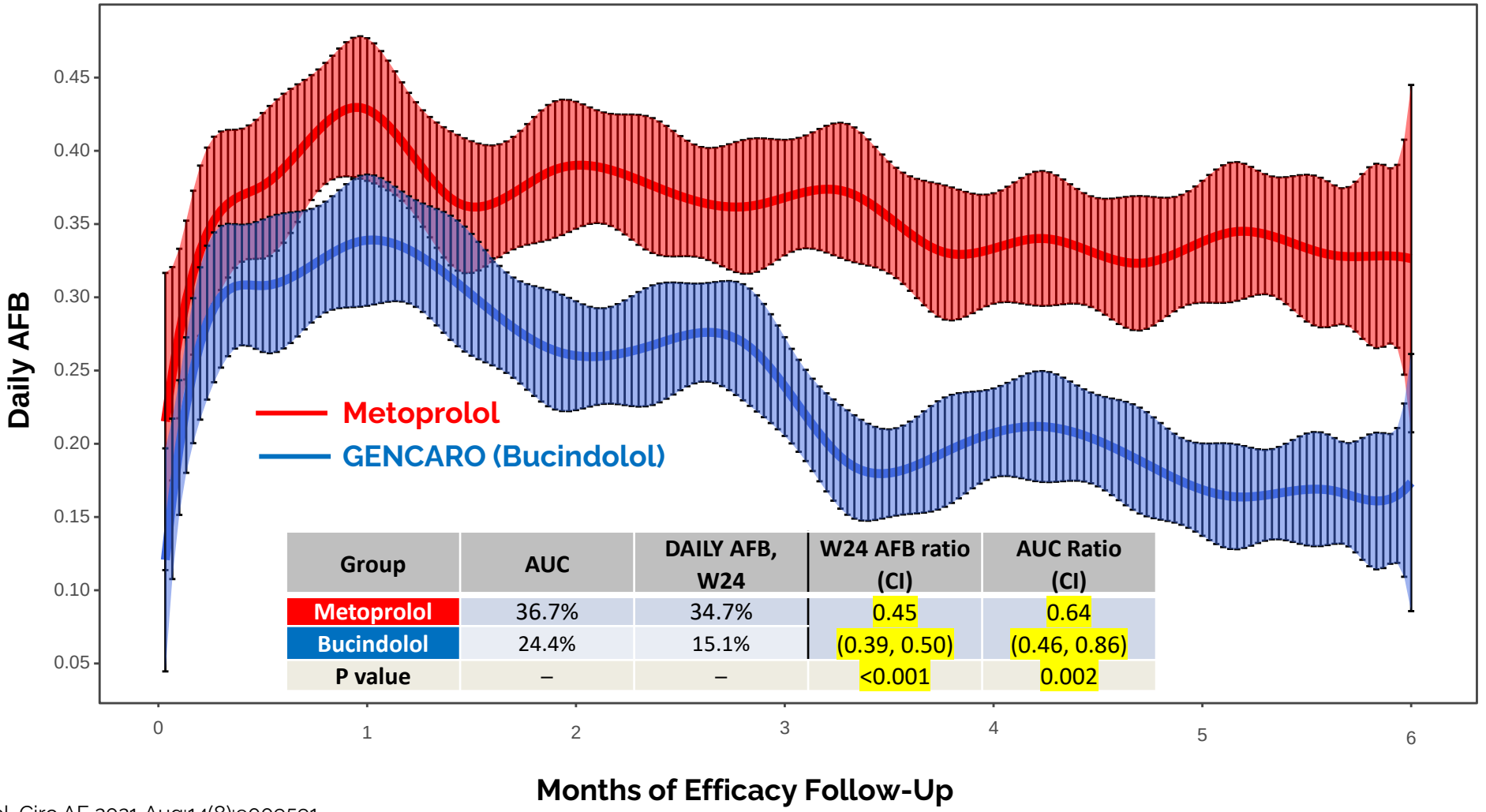
GENETIC-AF Precision Phenotyping Cohort*
N = 196



*Eliminates patients with longstanding disease (predefined analysis)
- HF or AF diagnosis >12 yrs, or
- AF onset preceding HF by > 2 yrs

GENETIC-AF Trial - AF Reduction Demonstrated vs. Toprol XL

Continuous Monitoring in AF Burden (AFB) Substudy

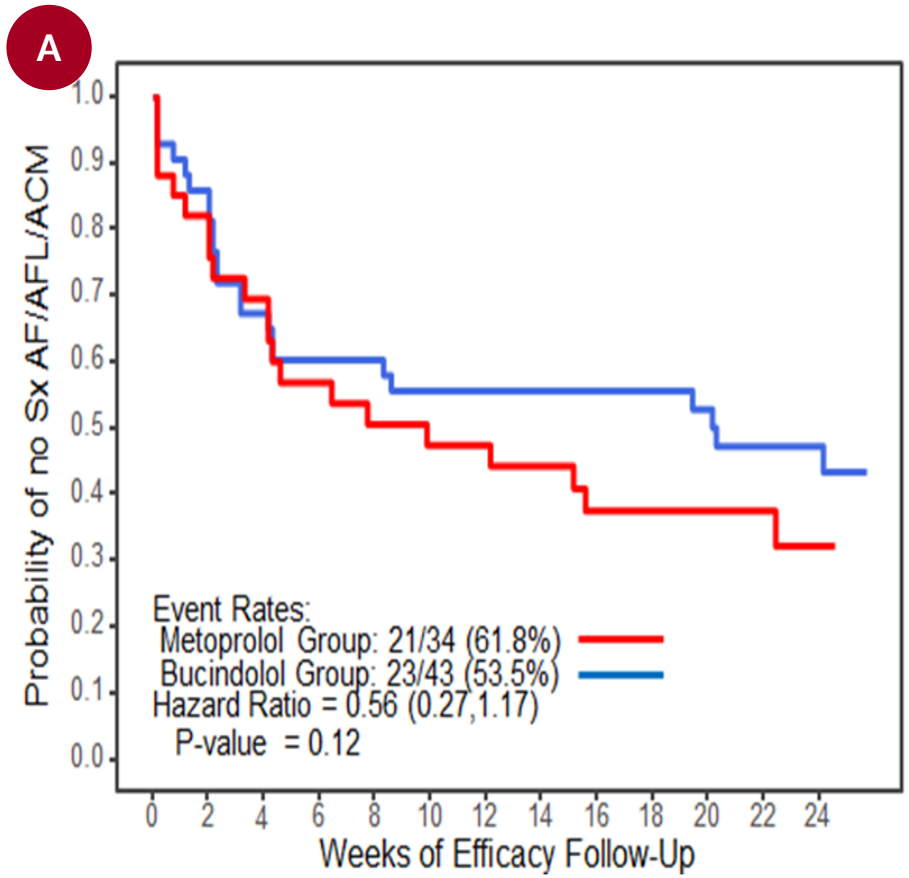


Group	AUC	DAILY AFB, W24	W24 AFB ratio (CI)	AUC Ratio (CI)
Metoprolol	36.7%	34.7%	0.45	0.64
Bucindolol	24.4%	15.1%	(0.39, 0.50)	(0.46, 0.86)
P value	–	–	<0.001	0.002

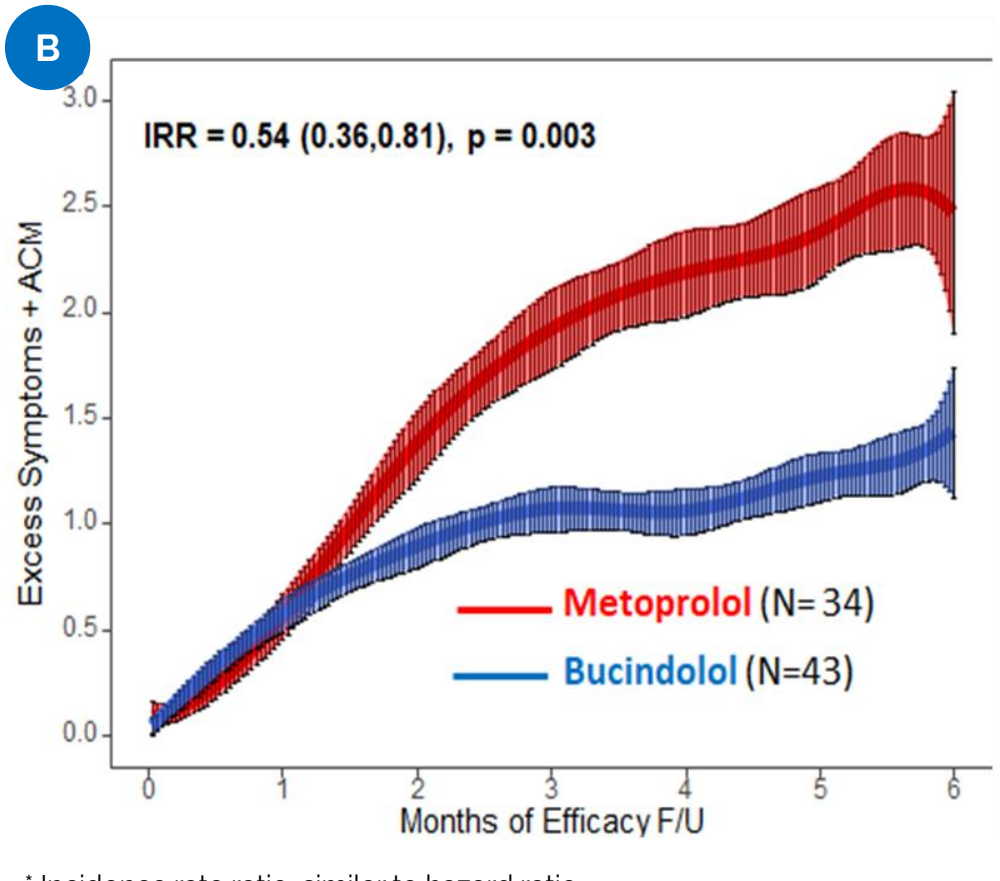
Piccini JP et al. Circ AE 2021 Aug;14(8):e009591.

Symptom Burden of AF (SxB_{AF}) - A Better Primary Endpoint

GENETIC-AF Precision Phenotyping Cohort, LVEF 40%-55%: Target Patient Population for Ph 3



Carroll, IA JACC Heart Fail, published online 11/24/24



* Incidence rate ratio, similar to hazard ratio

GENETIC-AF Endpoint Analysis:

Superior Efficacy Demonstrated vs. Toprol XL

Endpoint	GENETIC-AF Cohort	
Time to 1st AF/AFL/ACM (TTE) (Primary Endpoint)	1.01 (neutral)	(0.71, 1.42) p = 0.961 N = 267
Cumulative 24-week AF Burden (substudy)	0.64 (↓36%)	(0.46, 0.86) p = 0.002 N = 67
AF Burden at Week 24	0.45 (↓55%)	(0.39, 0.50) p < 0.001 N = 67
Symptom Burden of AF (SxB_{AF}): Target Ph3 Pts	0.54 (↓46%)	(0.36, 0.81) p = 0.003 N = 77
ECGs in Normal Sinus Rhythm	1.39 (↑39%)	(1.22, 1.58) p < 0.001 N = 257
AF Interventions (ECVs, Ablations, & Class 3 AA Drugs)	0.68 (↓32%)	(0.50, 0.91) p = 0.011 N = 257
Plasma NT-pro-BNP (HF Biomarker)	(↓2X)	P = 0.009 N = 257

Bradycardia prevalence (Buc. vs. met., VR< 60 bpm)	0.39 (↓61%)	(0.31, 0.49) P < 0.001 N = 256	Bradycardia AEs	11 (8.8%) Met, 1 (0.076%) Buc	P = 0.002

PRECISION-AF

Phase 3 Program Informed And De-risked By Phase 2 Clinical Results

- **Enriched Patient Population: PTP Cohort**
  - Eliminates non-responsive patients with longstanding AF
- **Improved Primary Endpoint: Symptom Burden of AF (SxB_{AF})**
  - Evaluates treatment effect over entire dosing period
  - Reviewed extensively with FDA and published
- **Focus on HF with LVEF ≥ 40%**
  - Highest efficacy demonstrated in Phase 2 ➔ Reduced trial size
  - Highest unmet medical need with greatest differentiation: No approved therapies
- **Incorporates PGt Targeting of Haplotypes**
  - Expansion of favorable patient population to 65%

PRECISION-AF

Cost Effective Pivotal Ph 3 Cardiovascular Trial with High Probability of Success

- **350 patients, 100 sites**
- **Estimated Trial Cost ~ $50M**
- **Timeline to Top Line data ~ 27 months from trial start**

- **Similar in Scope to Phase 2B GENETIC-AF**
  - Ensures efficient trial execution
- **Upside potential for HFlrEF labeling**
  - With a positive outcome

Significant Opportunity in Large Growing Market

Based on 2022 Syneos Primary Market Research Study on GENCARO™

Global AF & HF Genotype Positive Market

Total Addressable Market (TAM)

Assumes US Market Provides 50% of Global Market

U.S. AF & HF Genotype Positive Market

Serviceable Addressable Market (SAM)

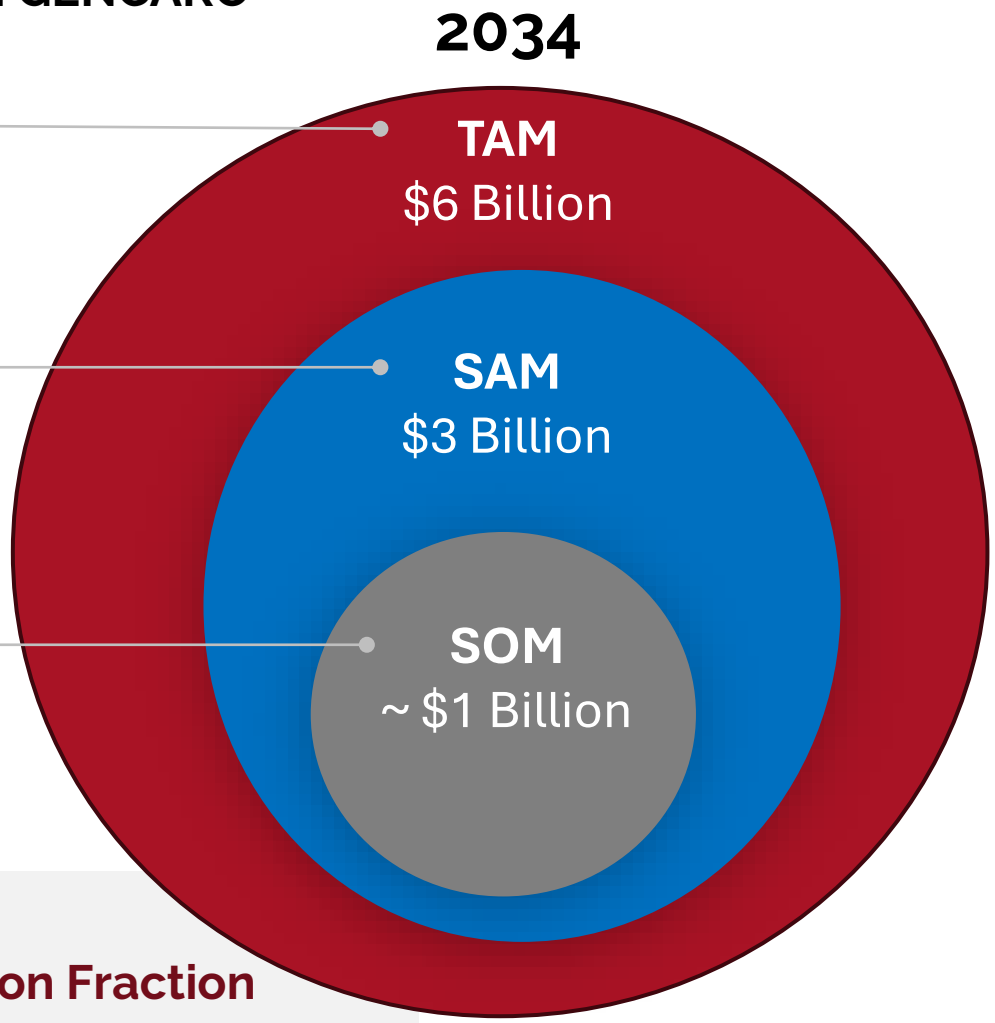
~ 600K+ Patients - Non-reduced Ejection Fraction HF, With AF, & 50% Genotype Positive @ ~$900 per month, 40% Gross to Net Discount

(Assumes current price aligned with Entresto today)

33% Penetration of U.S. Market

Serviceable Obtainable Market (SOM)

Syneos Primary Market Research Supports 50% Penetration



~7% Market CAGR

Upside with Genotype Expansion & HF Reduced Ejection Fraction

- HF Prevalence - Savarese et al. 2022. Cardiovasc. Res.
- Non-reduced HF - Roger et al. 2021. Circ. Res.
- AF Prevelance in HF - Goyal et al. 2018. Int. J. Cardiol

Comparables Support High Exit Potential Upon Positive Phase 3 Results

Cardiovascular Biopharma Focus Remains Significant

Bristol Myers Squibb / MYOKARDIA / CAMZYOS™ (mavacamten) 2.5, 5, 10, 15mg capsules	MERCK / ACCELERON PHARMA / WINREVAIR™ (sotatercept-csrk) for injection 45 mg, 60 mg	novo nordisk / Cardior	CHINOOK THERAPEUTICS / NOVARTIS
$13.1B October 2020	**$11.5 B** October 2021	**$1.1 B** March 2024	**$3.5 B** March 2024
Positive Phase 3 prior to FDA Approval for Hypertrophic Cardiomyopathy Therapy	Rare disease company Winrevair in phase 3 for Pulmonary Arterial Hypertension at time of acquisition Plus, one approved therapy for anemia in certain rare blood disorders	Phase 2 RNA based therapies in Heart Failure	Oral atrasentan to treat rare kidney disease in phase 3 and zigakibart

Roadmap To A Billion Dollar Market

$1.6 Million Founder Seed	$65 MILLION Series A Round Q3 2025-Q3 2028

2025		2026		2027		2028	
Q1-2	Q3-4	Q1-2	Q3-4	Q1-2	Q3-4	Q1-2	Q3-4

Team	Finalize Team
Clinical Trial Prep	Clinical Trial Prep
Clinical-Precision-AF(350 pts)	Clinical – Phase 3 PRECISION-AF (350 Pts) ★ Top line data
Clinical-Haplotype (75 pts)	Phase 2 Haplotype Trial, Grant-Funded
Business Development	Establish Corporate Partnership

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