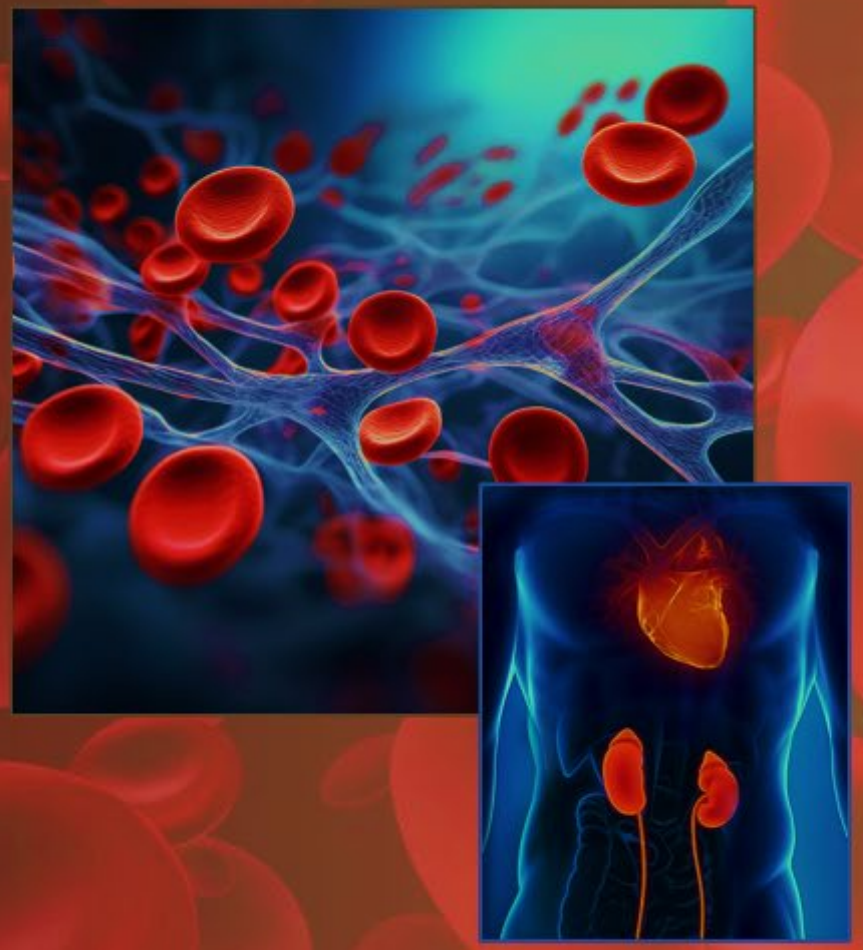
CADRENAL THERAPEUTICS

Bridging Critical Gaps in Anticoagulation Therapeutics



Cadrenal Therapeutics, Inc.

Nasdaq: CVKD

September 2025

Forward-looking Statements

This document contains forward-looking statements. In addition, from time to time, we or our representatives may make forward-looking statements orally or in writing. We base these forward-looking statements on our expectations and projections about future events, which we derive from the information currently available to us. Such forward-looking statements relate to future events or our future performance, including: our financial performance and projections; our growth in revenue and earnings; and our business prospects and opportunities. You can identify forward-looking statements by those that are not historical in nature, particularly those that use terminology such as “may,” “should,” “expects,” “anticipates,” “contemplates,” “estimates,” “believes,” “plans,” “projected,” “predicts,” “potential,” or “hopes” or the negative of these or similar terms.

In evaluating these forward-looking statements, you should consider various factors, including: our ability to successfully develop and commercialize product candidates, our ability to raise capital when needed, and the competitive environment of our business. These and other factors may cause our actual results to differ materially from any forward-looking statement, including those risk factors disclosed in our Annual Report on Form 10-K for the year ended December 31, 2024, filed with the Securities and Exchange Commission on March 13, 2025, and our Quarterly Reports for the periods ended March 31, 2025, and June 30, 2025. Forward-looking statements are only predictions. The forward-looking events discussed in this document and other statements made from time to time by us or our representatives may not occur, and actual events and results may differ materially and are subject to risks, uncertainties, and assumptions about us. We are not obligated to publicly update or revise any forward-looking statement, whether as a result of uncertainties and assumptions, the forward-looking events discussed in this document, and other statements made from time to time by us or our representatives might not occur.

Cadrenal Therapeutics – Overview

Problem	• Treatment gaps exist in the growing $38 billion global anticoagulant market • Too little anticoagulation → Thrombosis (clotting); Too much anticoagulation → Bleeding
Solutions	• Bridge gaps by developing novel and differentiated blood thinners • **Tecarfarin**: an oral Vitamin K antagonist with a proven MoA – same as warfarin • **Frunexian:** a parenteral (intravenous) FXIa inhibitor
Differentiation	• Develop drugs that improve anticoagulation predictability and control • **Tecarfarin** – Completely different – *and desirable* - metabolic pathway than warfarin • **Frunexian** – Only parenteral FXIa with *fast-on / fast-off* profile for acute care use
Market Opportunity	• Focus on orphan and high-risk CV populations • **$2B+** peak annual revenue potential from portfolio*
Development Plans	• **Tecarfarin: ESKD+AF** – Plan to initiate Ph2 study (FPI 1Q26) in ESKD patients transitioning to dialysis • **Frunexian** – Advance CMC in preparation for Phase 2 commencing late 2026 • **Tecarfarin: LVAD** – Plan to initiate Ph2 study (FPI 2H26) in LVAD patients

Recent Acquisition

Recent Developments

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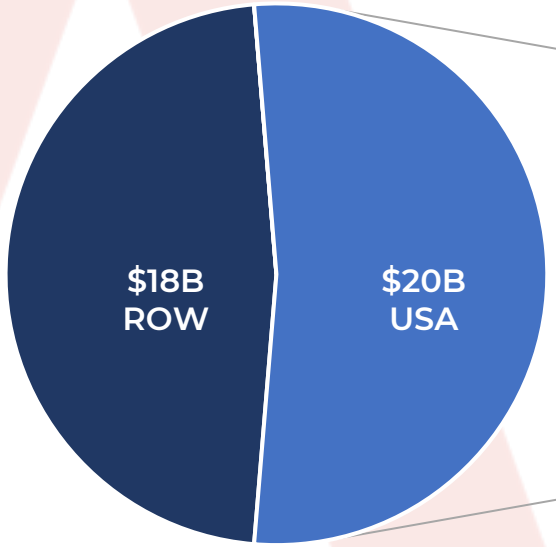
CKD: Chronic kidney disease
LVAD: Left ventricular assist device
***Based on management's analysis of market research and external data

A Multi-Billion-Dollar U.S. Opportunity

Addressing gaps in the $2B orphan and high-risk cardiovascular segment

$38B Global OAC Market Value ($Billions)



$20B
U.S. Market

$2B	Orphan & High-Risk CV Conditions
$6B	Venous Thromboembolism
$12B	Atrial Fibrillation

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- **145K** ESKD+AFib patients → No clinically proven OAC
- **15K** LVAD patients → No FDA-approved OAC
- **500K** MHV patients → DOACs contra-indicated
- Acute care in complex clinical settings

FDA **Tecarfarin has Orphan Drug and Fast-Track Designations**

- **ESKD+AFib:** ODD and Fast-Track Designations
- **LVAD:** ODD

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Based on management's analysis of market research and external data

Evolution of Anticoagulant Therapy

Including limitations and gaps of available treatments

Oral

Warfarin Limitations & Gaps
- Bleeding
- Monitoring/Adjustment
- Metabolism
- DDIs
- Dietary issues

DOAC Limitations & Gaps
- Bleeding
- No monitoring
- Not adjusted
- Reversibility
- Failure in MHV
- Continued role for VKAs

1941 Dicoumarol

1954 Warfarin **(Coumadin)**

2010 Dabigatran (***Pradaxa***)

2011 Rivaroxaban **(*Xarelto*)**

2012 Apixaban **(*Eliquis*)**

1939 Heparin

Heparin Limitations & Gaps
- Bleeding
- Infusion/Adjustment
- HIT/HITTS
- Thrombocytopenia
- Platelet activation
- Protamine reversal

1985 LMWH

1990 Argatroban

2000 Bivalirudin

New Agent Limitations & Gaps
- Bleeding
- No monitoring
- Not adjusted
- Lack of reversibility

Parenteral

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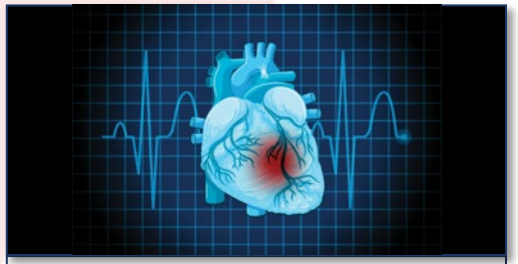
Poorly Controlled Anticoagulation – A Two-Edged Sword



Clotting events result in adverse outcomes, with substantial costs

MI
Stroke
VTE
Vascular occlusion
Death

Purpose

Prevent **pathological** clot formation

Therapeutic range

Too little

Consequences of POOR control

Too much

Greater Risk of Thrombosis (Clotting)

Greater Risk of Bleeding

Bleeding events lead to worse outcomes, require additional healthcare resources, and come with significant costs

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Tecarfarin - Addressing Treatment Gaps with Warfarin

	Warfarin	Tecarfarin
MoA	• VKA; Hepatic CYP450 metabolism	• VKA; Esterase metabolism
Target Considerations	• Genetic variability in enzyme levels	• Widely distributed, not restricted to the liver • No variability due to CYP2C9 polymorphisms
DDIs	• Frequent drug interactions	• Avoids common drug interactions
Safety	• Frequent monitoring and adjustment • Poor hepatic and renal function	• Fewer dose adjustments • Levels not affected by renal impairment • Potential for less bleeding

More reliable anticoagulation addressing specific issues in key at-risk populations

- End-stage Kidney Disease + Atrial Fibrillation
- Advanced heart failure and an implanted LVAD

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Tecarfarin - Metabolic Advantage

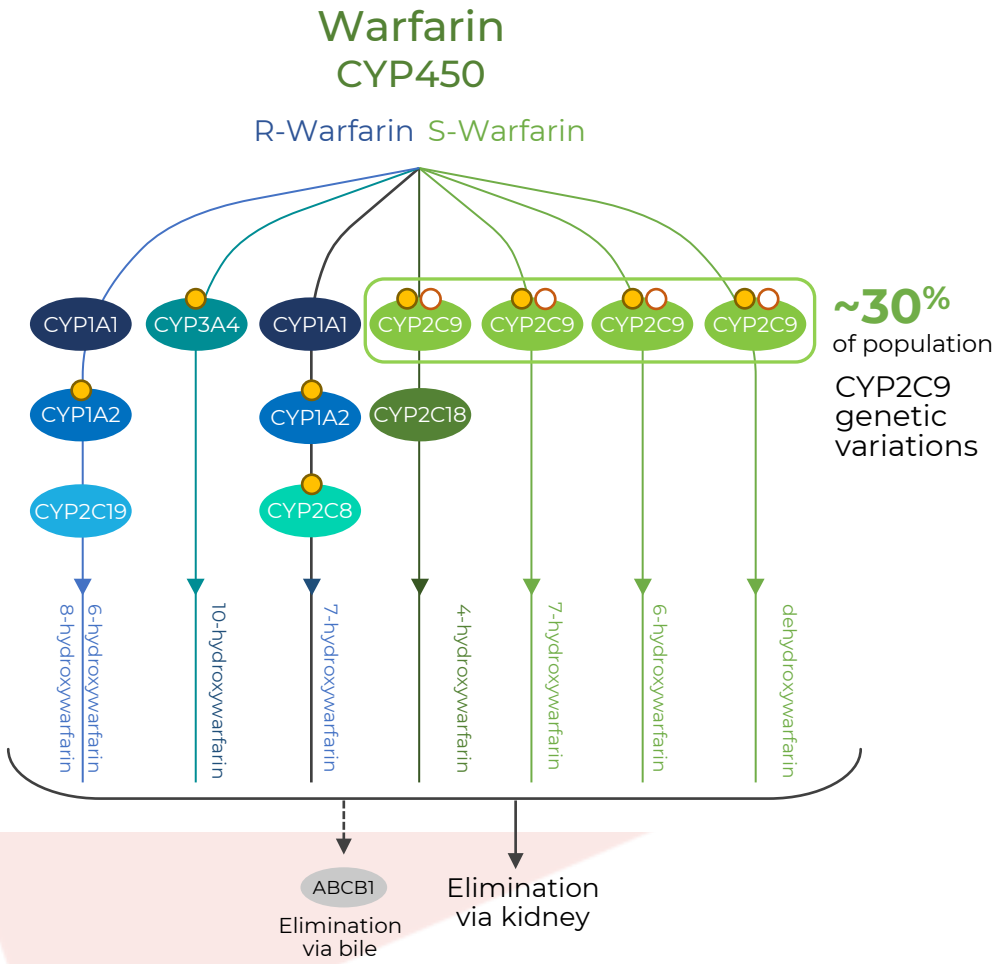
Metabolized via an alternate pathway - abundant and essentially insatiable

Avoids CYP450 bottlenecks of warfarin

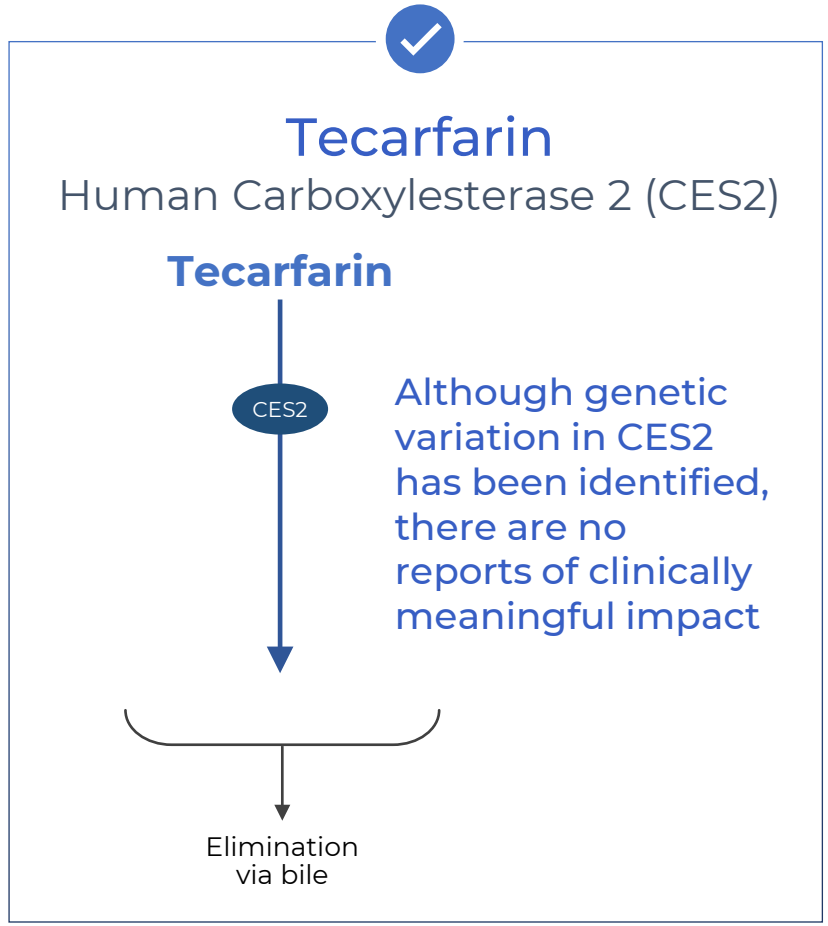
Drug interactions

Genetic variations

7 Different CYP450 Isoenzymes involved in Warfarin Metabolism!



~30% of population CYP2C9 genetic variations



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Developing Novel Drugs that Bridge Gaps in Anticoagulant Rx

Tecarfarin
A novel VKA

- Addresses important limitations of warfarin
  - Predictable metabolism, fewer interactions
- Suitable for patients with complex medication regimens
- Positive safety and efficacy data
- Consistent anticoagulation control
- Levels not affected in patients with poor kidney function
- Fills critical gaps unaddressed by DOACs

Frunexian
Acute parenteral FXIa inhibitor

- Potent (> 95%) XIa inhibition
- Effective blockade of contact activation
- Predictable PK/PD
- Parenteral administration
- Rapid onset, short half-life
- Phase 2 ready

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Pipeline and Current Programs

	Program	Target Indications	Regulatory Strategy/Status	Development Phase: Discovery	Preclinical	Phase I	Phase II	Phase III
11 clinical studies > 1,000 pts treated	**Tecarfarin** (VKA - Oral)	End-stage Kidney Disease (ESKD) with AFib	• FDA Orphan Drug Designation Granted • FDA Fast Track Designation granted • Phase 2/3 ready				★	
		Left Ventricular Assist Devices (LVADs)	• FDA Orphan Drug Designation Granted • Collaboration with Abbott • Phase 2/3 ready					
2 Phase 1 studies 80 pts treated	**Frunexian** (FXIa – IV)	Complex Cardiac Surgery	• Phase 2 ready					

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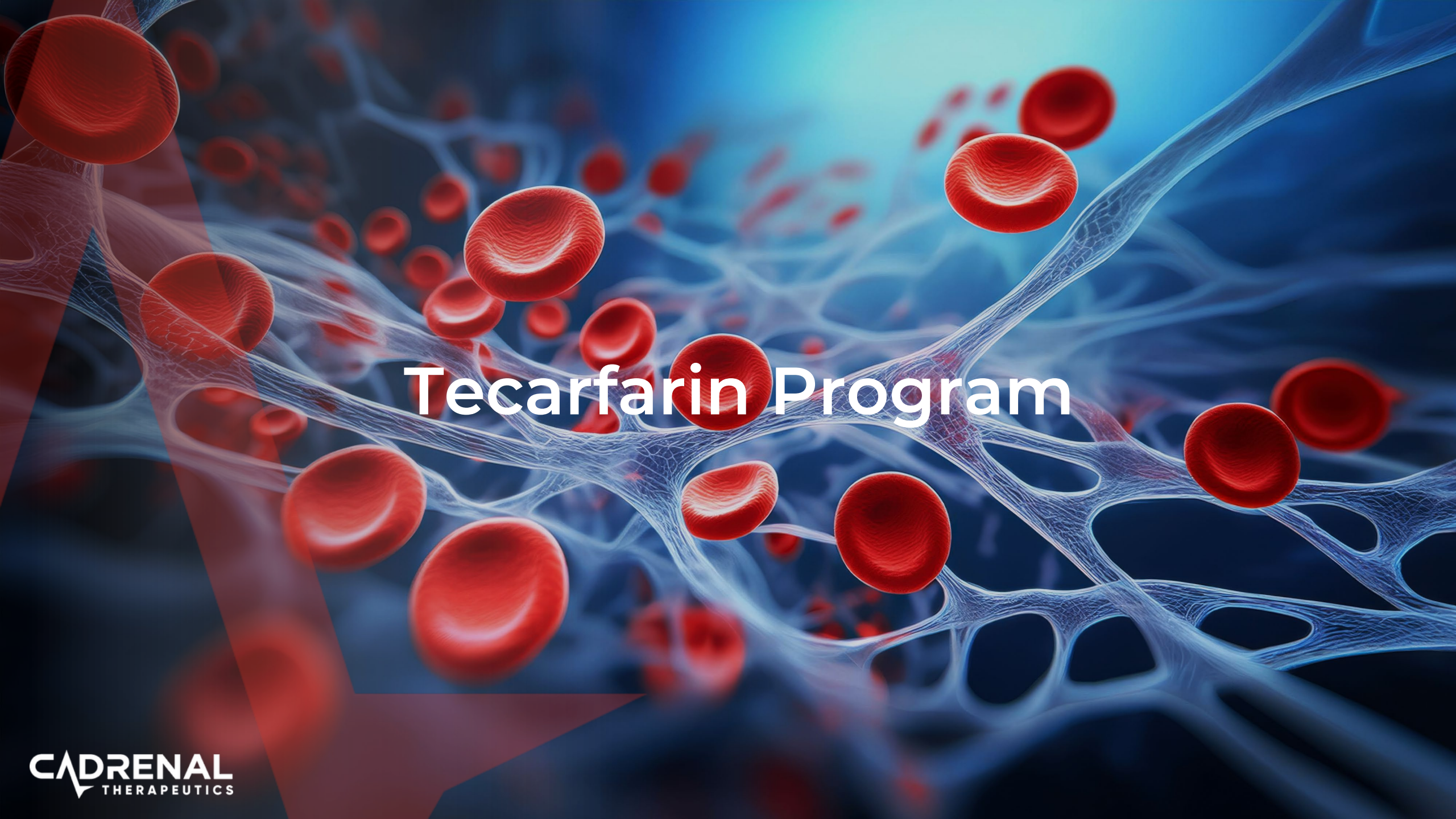

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EMBRACE-AC Phase 2/3 Study

Tecarfarin vs. Warfarin in Patients Requiring Chronic Anticoagulation

Trial Design

- Multi-center, randomized, double-blind - Tecarfarin vs. warfarin
- 607 patients with indications for chronic anticoagulation.
- Dosing of all study drugs centrally managed.
    - **Primary endpoint** - % time INR in the therapeutic range - TTR (interpolated)
    - **Secondary Endpoint** – % observed INR measurements in the therapeutic range

Efficacy

- A stable tecarfarin dose attained in 94.5 % of tecarfarin patients
- The mean % TTR with tecarfarin numerically, but not significantly, higher than with optimally managed warfarin
    - 72.3% tecarfarin vs 71.5% warfarin
- Nearly all subgroups favored tecarfarin for both % TTR and % observed INR values
- Additional impact of concomitant CYP2C9 inducers/inhibitors and CYP2C9 genotype

Safety

- Tecarfarin well tolerated
    - Only 1.6% of the tecarfarin subjects had major bleeding
    - **No** thrombotic events.

Tecarfarin more effective than optimally managed warfarin in certain sub-groups

- Well-tolerated
- Low incidence of major bleeding
- No thrombotic events

Opportunity to **improve** reliability in situations requiring tighter control

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Whitlock RP *et al.* ***Thromb Haemost*** 2016; 116(02): 241-250
DOI: 10.1160/TH15-11-0910

Tecarfarin Maintains Consistent Exposure in Stage 4 CKD Trial

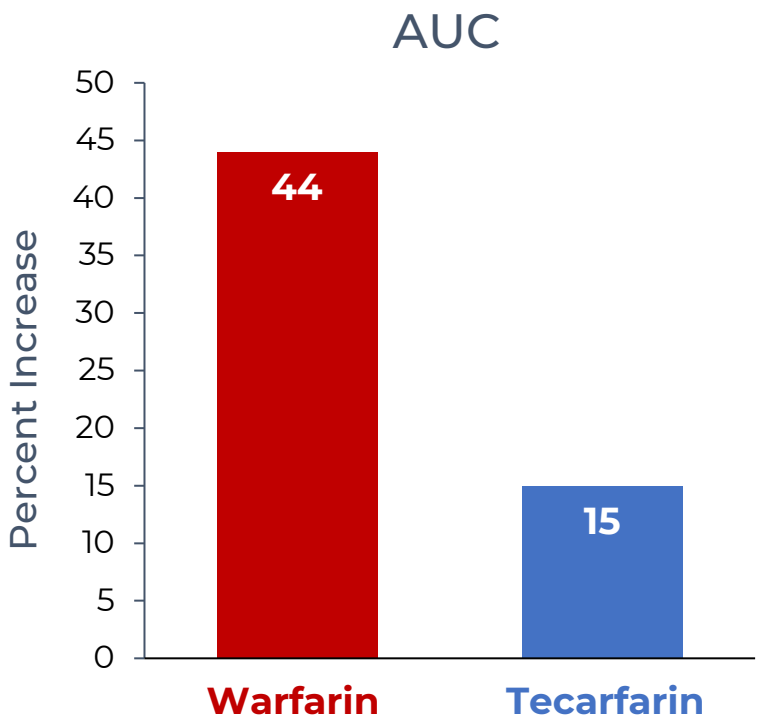
Tecarfarin exposure remains stable while **warfarin** levels significantly increase

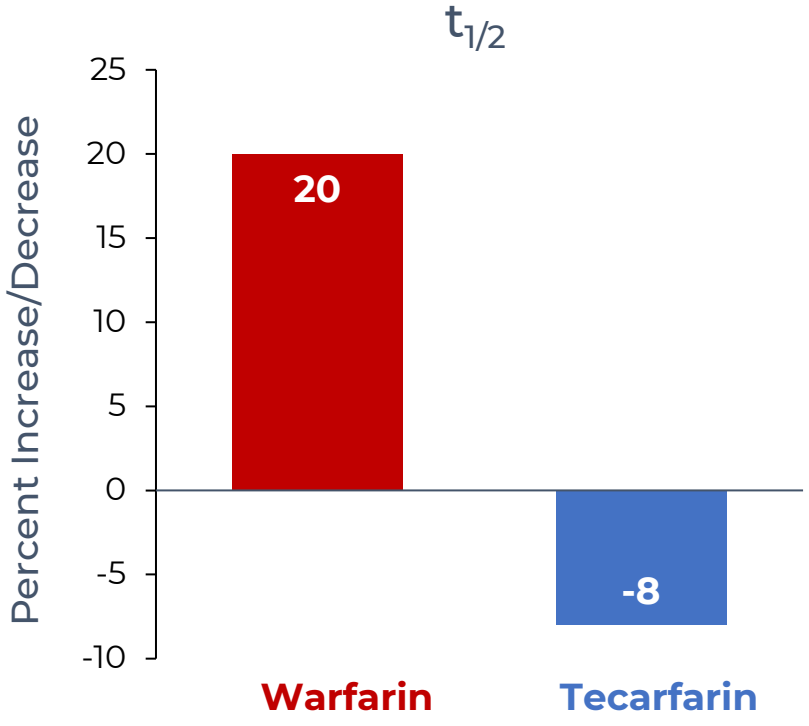
Higher levels + longer half life = Higher **bleeding** risk

Percent Increase in Drug Exposure for CKD Subjects vs Healthy Subjects

Warfarin vs **Tecarfarin**

(n =23)





Albrecht D *et al*. ***Thromb Haemost.*** 2017;117(11):2026-2033. doi:10.1160/TH16-10-0815

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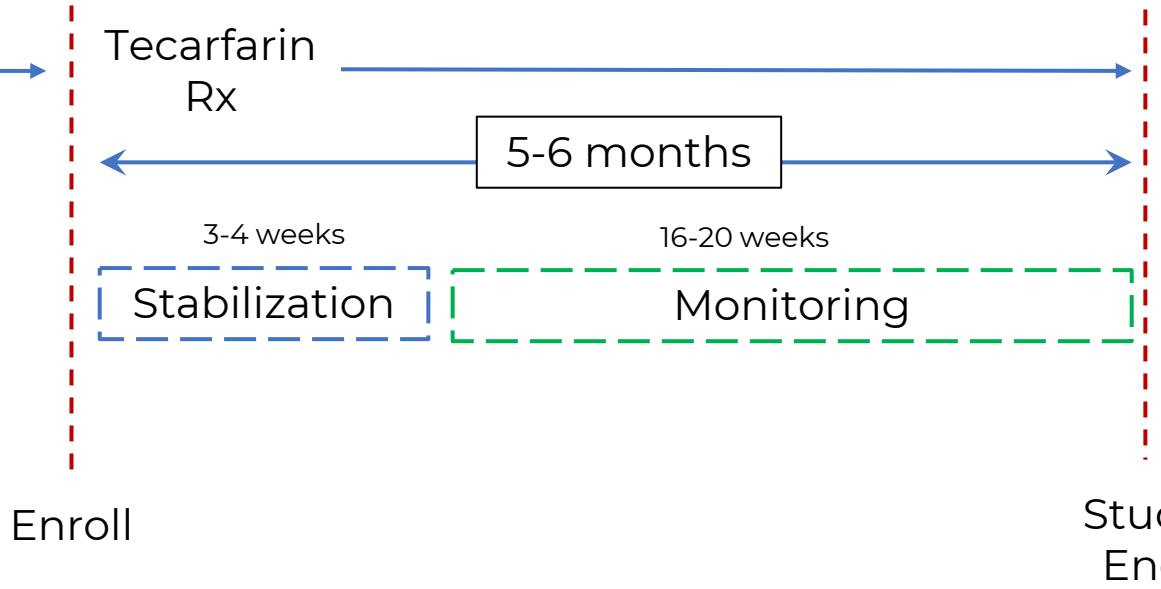
Tecarfarin Anticoagulation During Transition to Dialysis Phase 2 Study

Patients transitioning to dialysis with indications for anticoagulant Rx (including AFib)

n = 25-30

Maintenance
Plus
Urgent/Acute



Primary endpoint
Safety

Secondary Endpoints
TTR after stabilization
Time to stabilize
% time high
% time low
Bleeding events
Dose adjustments
Thrombotic events

Est. Cost $3.5M

- Single arm
- Open label, not randomized
- 2 Strata – maintenance, urgent/acute
- 4-5 clinical centers (US)

De-risk planned future registration study → **Optimize coagulation and study management** → **Fewer patients, less time and cost, higher probability of success**

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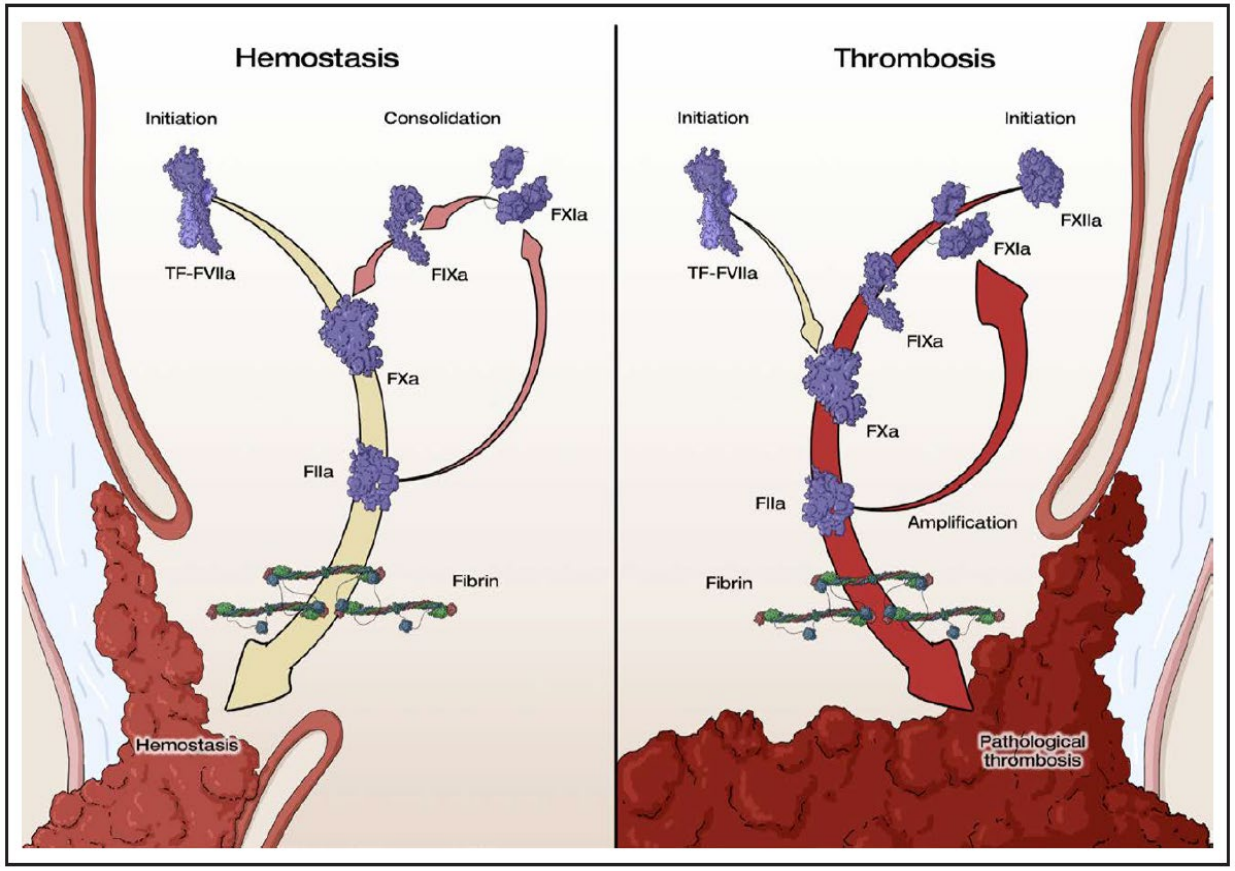
Addressing Additional Treatment Gaps with Factor XIa Inhibition

Hemostasis (preventing bleeding in response to an injury)

Thrombosis (pathological thrombus formation)

Factor XIa inhibition presents an opportunity to **prevent thrombosis *without* increasing the risk of bleeding**



In hemostasis FXI plays a minor role

In pathological thrombosis FXI plays a fundamental role

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Greco A *et al* ***Circulation.*** 2023;147:897–913.
DOI: 10.1161/CIRCULATIONAHA.122.062353

Frunexian : First & Only IV for Acute Care Periprocedural Usage

	Asset	MoA	Half-Life	Indications
Acute	**Frunexian** *Cadrenal*	Small molecule (IV)	Short (minutes)	• Complex Cardiac Surgery (CABG) (Ph 2)
Chronic	**Milvexian** *BMS/JNJ*	Small-molecule (Oral)	Moderate (hours)	• Acute Coronary Syndrome (Ph 3) • Atrial Fibrillation (Ph 3) • Secondary Stroke Prevention (Ph 3)
	Asundexian *Bayer*	Small-molecule (Oral)	Moderate (hours)	• Secondary Stroke Prevention (Ph 3) • Note: Afib trial (OCEANIC) terminated
	SHR2285 *Hengrui Pharm.*	Small-molecule (Oral)	Moderate (hours)	• VTE Prevention in Total Knee Replacement (Ph 2)
	Abelacimab *NVS*	Antibody (SC / IV)	Long (days)	• Atrial Fibrillation (Ph 3) • Cancer Associated VTE (Ph 3)
	Osocimab *Bayer*	Antibody (IV)	Long (days)	• Thrombosis Prevention in TKR (Ph 2) • Chronic Kidney Disease (Ph 2)
	Xisomab 3G3 *Bayer*	Antibody (IV)	Moderate (hours)	• Cancer Associated Thrombosis (Ph 3) • Chronic Hemodialysis in ESKD (Ph 2)
	Mk-2060 *Merck*	Antibody (IV)	N/A	• Vascular access graft patency in ESKD (Ph 2)
	Fesomersen *Ionis*	Antisense Oligonucleotide (SC)	Long (days)	• ESKD (Ph 2)

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FXIa Inhibitors In the News

- $4B+ in recent strategic investments in next generation FXI inhibitors
- Major investments in CV programs and FXI assets led by big pharma
- Leading life science funds pursuing FXI inhibitors
- **Validates frunexian FXI acquisition and strategy to bridge therapeutic gaps in $38B global anticoagulation market**

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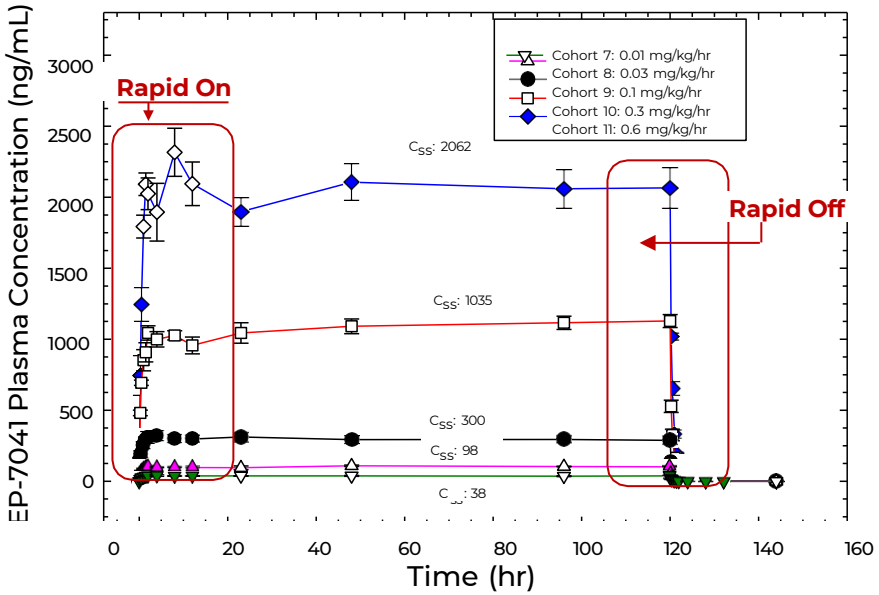
Frunexian Phase I Data – Well-Tolerated with Attractive PK/PD

Two completed Phase I SAD/MAD studies in healthy volunteers

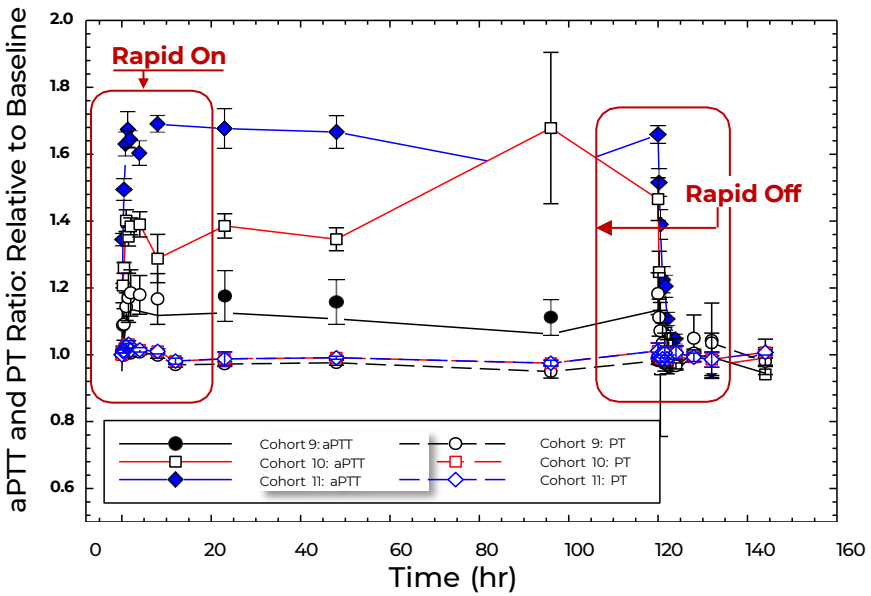
- Well-tolerated at doses up to 2.25 mg/kg/h
- No SAEs

- Both PK and PD (aPTT) dose-related and predictable in both studies
- Steady-state plasma levels of the drug rapidly achieved and rapidly decreased at cessation
- Therapeutic inhibition (aPTT) rapidly achieved without affecting the extrinsic pathway (PT) even at maximal doses
- With continuous infusions steady-state inhibition maintained
- Consistent, reliable, dose-dependent inhibition of plasma FXIa activity

Attractive PK for Critical Care Setting



PD Supportive of Clinically Effective Ranges




Development Plan &
Investment Highlights
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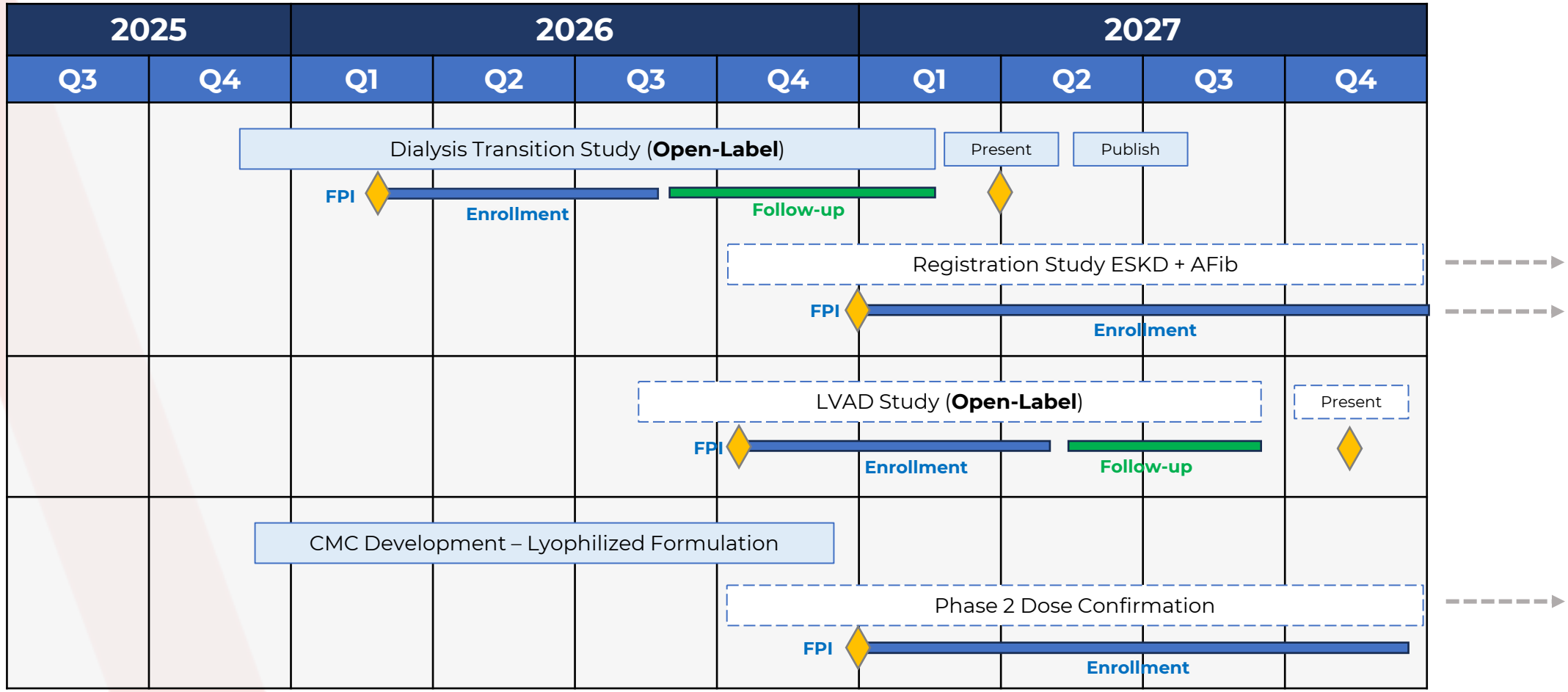
Near-Term Clinical Development Plans



Key Milestones

- FDA Interactions – Phase 2 and Registration studies
- Tecarfarin Phase 2 first patient in (FPI): ESKD+AFib (1Q26); LVAD (4Q26)
- Frunexian FPI: Complex cardiac surgery (1Q27)
- Ongoing data readouts (open label)

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Key Investment Highlights

An opportunity to invest ahead of value-inflecting events

Unmet Need	Differentiation	Path Forward	Opportunity
Tecarfarin			

• **Poor warfarin control**
  • Thrombosis
  • Bleeding
• **DOAC limitations**
• **Genetic variants** impacting warfarin metabolism
• **Drug-drug interactions** with warfarin
	• **Only** VKA in late-stage development worldwide
	• **Orphan designation** in ESKD+AFib and LVAD
	• **Not metabolized by CYP450**
	• **Not affected by renal impairment**;
		• **Extensive safety data** (N=1,000+ dosed)
		• **Phase 2 study** in patients transitioning to dialysis
		• **Abbott collaboration** for LVAD program
		• **Phase 2 study** in LVAD patients
			• **Targeted populations** where DOACs are contra-indicated, unapproved, or not recommended
			• **Continuing need for better VKA**
			• **Premium pricing**

Frunexian			
• **Only acute-care parenteral FXIa inhibitor** in development	• **Fast-on / fast-off** potent, dose-proportionate parenteral FXIa inhibition	• **Phase 2 dosing** in preparation for Phase 3 program in complex cardiac surgery	• **Treatment gaps** with unfractionated heparin

$2 Billion+
U.S. Market Opportunity

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Financials, Capitalization & Insider Alignment

Cap Table	
Cash (at 6/30/2025)	$5.6 million
Debt	NONE
Common Shares Outstanding (at 8/22/2025)	2,046,854
Warrants – Investors (avg. $17.82)	615,940
Stock Options Outstanding (avg. $17.48)	433,001

2025 Financial Results – Six Months Ended June 30	
Operating Expenses (excluding non-cash items)	$6.5 million
Cash used in operating activities	$7.7 million

Market Capitalization	
As of 8/22/2025	$26 million

Insider Ownership (Common Stock)	
Insider Ownership as Percent of Shares Outstanding	25%

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Experienced Leadership

Across clinical to commercial drug development

Quang X. Pham
CEO & Founder, Chairman

James Ferguson, MD, FACC, FAHA
Chief Medical Officer

Matthew Szot, CPA
Chief Financial Officer

Jeff Cole
Chief Operating Officer

John R. Murphy
Board Member

Steven Zelenkofske, DO
Board Member

Glynn Wilson, PhD
Board Member

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Scientific Advisors

Leaders in cardiovascular innovation

Wolfgang C. Winkelmayer, MD, MPH

Chief, Section of Nephrology,
Professor of Medicine, **Baylor University**

Director, **Selzman Institute for Kidney Health**

Richard Whitlock, MD

Cardiac Surgeon and Professor of Surgery,
McMaster

University Medical Center Investigator,
Population Health Research Institute

Christopher Granger, MD

Professor of Medicine in the Division of Cardiology,
Duke University

Member, Duke Clinical Research Institute (DCRI)

Elaine M. Hylek, MD, MPH

Professor of Medicine,
Boston University School of Medicine

Director of the Thrombosis and Anticoagulation
Service at **Boston Medical Center (BMC)**

Sean Pokorney, MD, MBA

Electrophysiologist and Assistant Professor of Medicine,
Duke University

C. Michael Gibson, MD

Professor of Medicine,
Harvard Medical School

Interventional Cardiologist,
Beth Israel Deaconess Medical Center

President & CEO,
Baim Institute for Clinical Research

Michael Lincoff, MD

Vice Chairman, Dept. of Cardiovascular Medicine,
Cleveland Clinic

Director of Clinical Research,
Lerner Research Institute

Mandeep, Mehra MD, MSc, FRCP

Medical Director of the
Brigham Heart and Vascular Center,
William Harvey Distinguished Chair in Advanced Cardiovascular Medicine

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