Cadrenal Therapeutics, Inc.

NASDAQ: CVKD

January 2024

Cautionary Statement Concerning 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, 2022 filed with the Securities and Exchange Commission on March 30, 2023. 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.

Corporate Overview

Late-stage Drug with Orphan Drug and Fast Track Designations

- **Developing tecarfarin, a late-stage novel oral and reversible anticoagulant (blood thinner) to prevent heart attacks, strokes and deaths due to blood clots in patients with certain conditions where Vitamin K Antagonists (e.g. warfarin) have failed to achieve sufficiently reliable anticoagulation and DOACs (Eliquis-class drugs) have not shown benefit. These areas include the following orphan diseases:**
  - End Stage Kidney Disease (ESKD) with Atrial Fibrillation (AFib)
  - Left Ventricular Assist Devices (LVADs)
  - Antiphospholipid Syndrome (APS)
- **Tecarfarin, a novel VKA, was specifically designed to metabolize via an alternate pathway than warfarin – a metabolic pathway that is abundant and essentially insaturable, providing a much more reliable pharmacokinetic profile than warfarin.**
  - Orphan drug and Fast Track designations for ESKD with AFib providing for 7-year marketing exclusivity following FDA approval
  - One pivotal Phase III trial remaining for ESKD with AFib; pursuing development for patients with LVADs and/or APS
  - Tecarfarin has been evaluated in 11 clinical trials in 1,003 subjects and has generally been well-tolerated in adult subjects with a variety of medical conditions, including patients with chronic kidney disease (CKD)
  - Approximately $90 million invested in clinical and regulatory work to date
- **U.S. market potential estimated in excess of $2 billion combined for the three targeted orphan indications.**

Significant Unmet Need & Market Opportunity for Tecarfarin

Tecarfarin is targeted for indications where warfarin FAILS to achieve sufficiently stable anticoagulation and DOACs (Eliquis-class drugs) have clinically not shown benefit.

1 High Level of Unmet Need

- There is a lack of approved anticoagulation therapies for certain conditions requiring chronic anticoagulation, including ESKD with AFib, LVADs and APS
- DOACs (e.g., Xarelto and Eliquis) are not FDA-approved for use with ESKD patients who also have AFib
- DOACs are contraindicated for LVAD and APS
- Physicians are frustrated with warfarin outcomes and are hesitant to prescribe DOACs absent positive clinical benefit
- Estimated 130,000 ESKD + AFib patients in the U.S. with no indicated therapy

2 Proven Mechanism of Action

- Tecarfarin is a VKA with a well-understood mechanism of action
- Phase 2/3 clinical data supports that tecarfarin is an effective anticoagulant
- Tecarfarin provides stable anticoagulation with >72% time in therapeutic range (TTR) overall and across key subgroups
- Tecarfarin is a reversible anticoagulant

3 Improved Safety Profile (Less Bleeding)

- Tecarfarin's retrometabolic design provides for more stable anticoagulation than warfarin, thereby decreasing the risk of stroke and bleeding
- Unlike warfarin, tecarfarin is metabolized by esterases, escaping metabolism by the cytochrome P450 (CYP450) system and thereby avoiding CYP450-mediated drug-drug or drug-food interactions as well as genetic variations
- CKD did not adversely affect the metabolism of tecarfarin as it did with warfarin in a head-to-head Phase 1 PK trial
- Extensive safety data from 11 clinical trials in over 1,000 subjects

Significant Unmet Need & Market Opportunity for Tecarfarin (cont.)

Tecarfarin is targeted for indications where warfarin FAILS to achieve sufficiently stable anticoagulation and DOACs (Eliquis-class drugs) are not widely prescribed for certain conditions.

4 Clear Regulatory Pathway with No Development Competition

- Tecarfarin was granted Orphan Drug Designation and Fast Track Approval by FDA for ESKD + AFib, providing 7-year marketing exclusivity, and clarity regarding the pathway to approval
- Based on FDA guidance, the basis of approval will be the results of a single pivotal Phase 3 placebo-controlled trial of tecarfarin in ESKD + AFib (N=492)
- The newest class of anticoagulants (Factor XIs) are in development but not being pursued for these certain orphan diseases

5 Strong Adoption and Premium Pricing of Tecarfarin Projected

- Despite ongoing off-label usage of DOACs, KOLs expect strong adoption of tecarfarin
- Conversion to tecarfarin expected to be highest in the uncontrolled and untreated patient segments
- Given the gap in effective options for these patient populations, payers expect access and coverage for tecarfarin
- Marketed drugs for certain rare CV conditions command significant price premiums that value the tecarfarin addressable market at over $2 billion annually combined in the U.S.

6 Other Orphan Drug Indications

- LVADs and APS offer additional and alternative clinical trials/paths to commercialization or lifecycle management opportunities
- Potential additional FDA Orphan Drug designations are under evaluation

ANTICOAGULATION CHALLENGES

Orphan Diseases Lack Effective Anticoagulation

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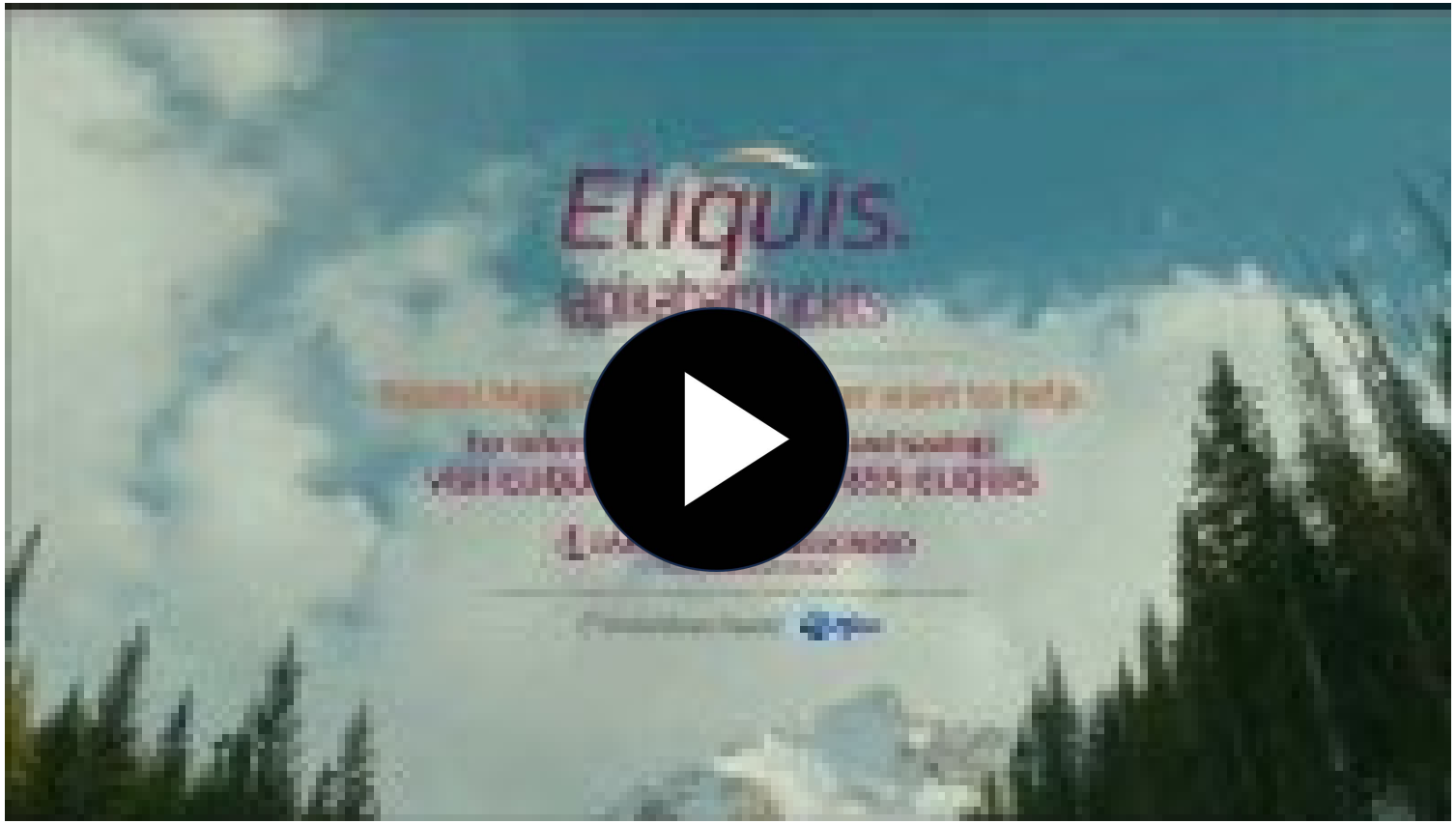
The Problem: Certain Orphan Diseases Lack Effective Anticoagulation

Physicians are frustrated with warfarin outcomes and are hesitant to prescribe DOACs more broadly given the negative evidence in clinical trials.

	Warfarin	DOACs (Pradaxa, Xarelto, Eliquis and Savaysa)
ESKD+AFib 	⊖ Higher risk of bleeding in dialysis patients with Afib compared to DOACs ⊖ Multiple dose adjustments to keep patients within International Normalized Ratio (INR) range ⊖ Drug interaction in patients with multiple comorbidities	⊖ Limited head-to-head evidence; existing data fails to demonstrate benefit in thromboembolism and stroke risk ⊖ Not included in ESKD treatment guidelines ⊖ Ambiguity in dosing recommendations
LVAD 	⊖ High frequency (“inevitability”) of thrombotic events despite warfarin therapy ⊖ Patients require multiple dose adjustments to maintain within the appropriate INR range	⊖ Cost and time of reversal compared to vitamin K is not acceptable for patients at high risk of bleeding or intervention ⊖ LVAD patients excluded from studies ⊖ DOACs are not guideline recommended therapy for patients with LVAD

Eliquis 2023 Commercial

Eliquis highlights in its own commercial that you should not take for certain conditions.

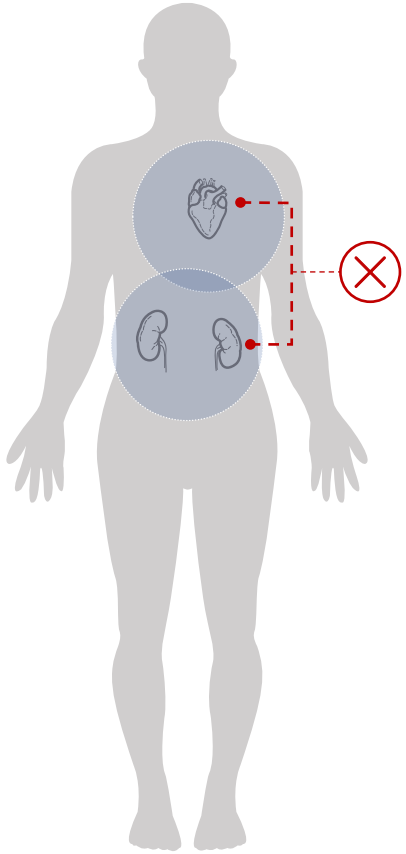


"Don't take ELIQUIS if you have an artificial heart valve…"

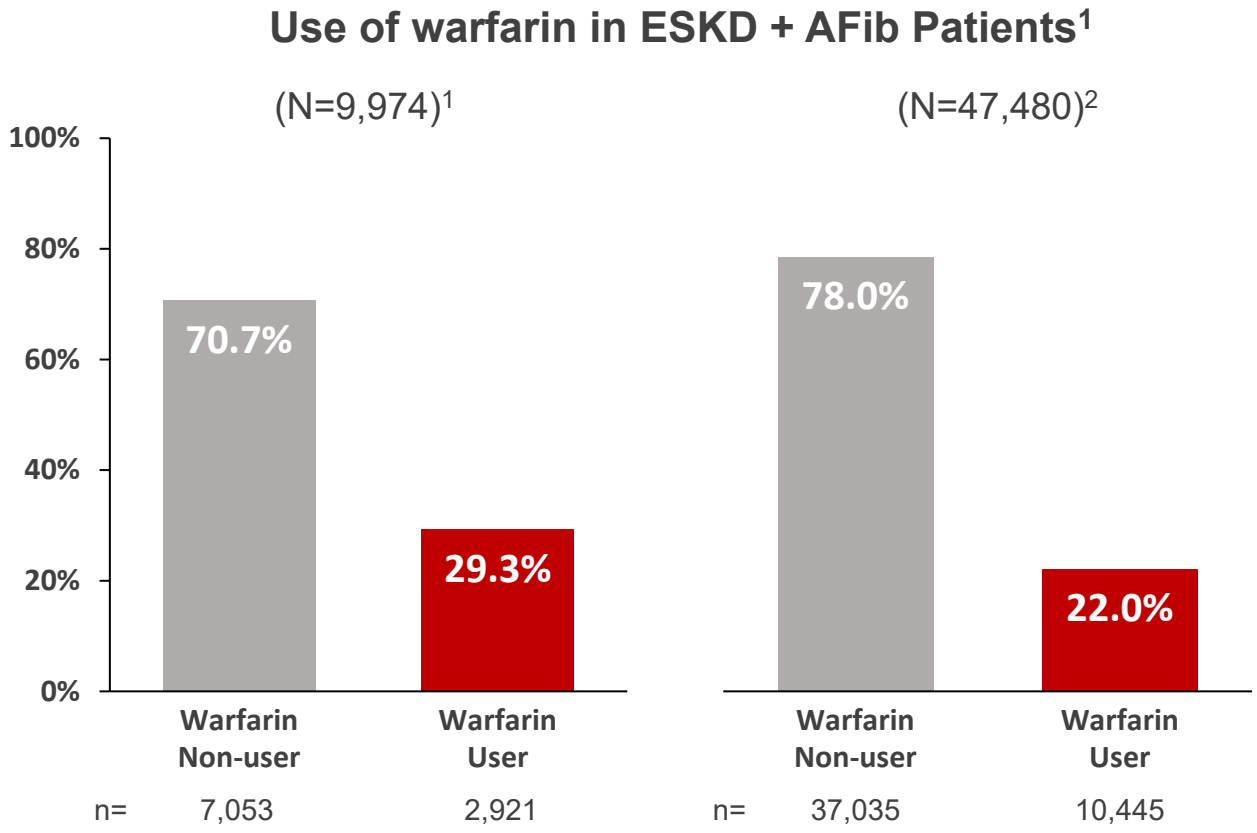
ELIQUIS is not for patients who have antiphospholipid syndrome (APS).

Significant Underserved Patient Populations

Despite the significantly increased risk of stroke in ESKD patients with AFib, most patients are not anticoagulated due to the lack of evidence of benefit



Most patients with ESKD + AFib <u>are not prescribed</u> ANY anticoagulation to reduce their risk of stroke



1. Yoon CY, Noh J, Jhee JH, et al. Warfarin Use in Patients With Atrial Fibrillation Undergoing Hemodialysis: A Nationwide Population-Based Study. *Stroke*. 2017;48(9):2472-2479. doi:10.1161/STROKEAHA.117.017114
2. Randhawa MS, Vishwanath R, Rai MP, et al. Association Between Use of Warfarin for Atrial Fibrillation and Outcomes Among Patients With End-Stage Renal Disease: A Systematic Review and Meta-analysis. *JAMA Netw Open*. 2020;3(4):e202175. doi:10.1001/jamanetworkopen.2020.2175

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HOW TECARFARIN ADRESSESES ANTICOAGULTION CHALLENGES

Tecarfarin’s Improved Metabolic Pathway

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Tecarfarin Looks to Solve Warfarin's Major Problems

Tecarfarin provides a more stable anticoagulation than warfarin due to its metabolism, thereby decreasing the risk of stroke and bleeding.

Warfarin

CHALLENGING TO CONTROL

despite nearly 70 years of experience

Metabolism via the cytochrome P450 pathway

Significant variability in PK due to genetic variants and competition with other drugs

MAJOR PROBLEM

for patients with certain orphan diseases

Variable/Unreliable anticoagulation

in patients at high risk for thrombotic events

Tecarfarin

SPECIFICALLY DESIGNED

to solve the warfarin metabolism problem

Metabolized via an alternate pathway that is abundant and essentially insaturable

Reliable, stable PK profile

STABLE ANTICOAGULATION

with proven mechanism of action

including patients with certain orphan diseases

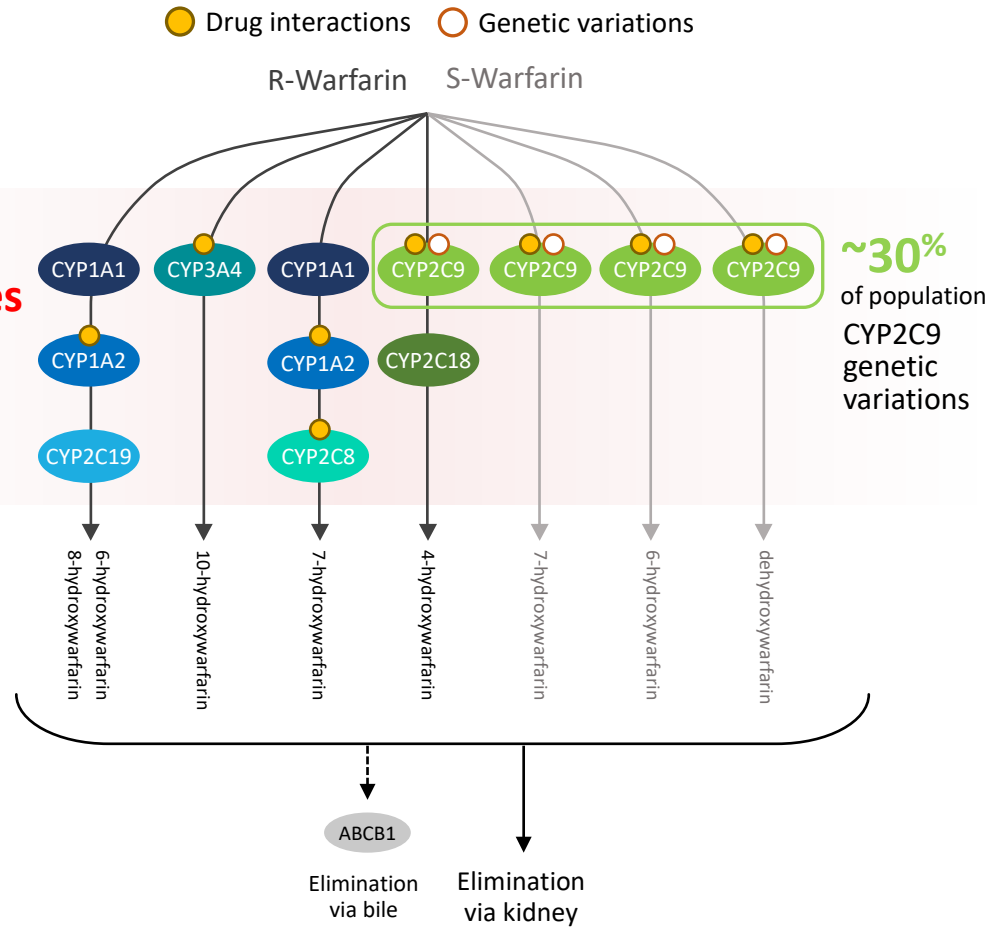
Tecarfarin's Metabolic Advantage

Tecarfarin is metabolized via an alternate pathway that is abundant and essentially insaturable, thereby avoiding the bottleneck in the CYP450 pathway where warfarin in metabolized.

Warfarin

CYP450

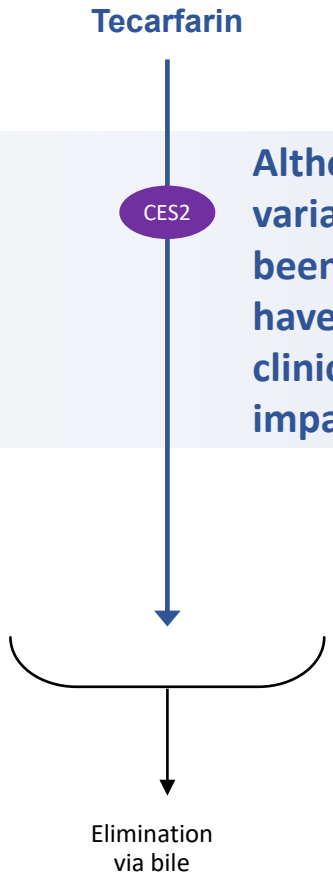
7 Different CYP450 Isoenzymes involved in Warfarin Metabolism!



~30% of population CYP2C9 genetic variations

Tecarfarin

Human CarboxylEsterase 2 (CES2)



Although genetic variation in CES2 has been identified there have been no reports of clinically significant impact

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CLINICAL DATA

11 Human Clinical Trials With More Than 1,000 Patients Support Safety and Efficacy of Tecarfarin

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Tecarfarin Demonstrates TTR Above Anticoagulation Control Threshold

Phase 2/3 trial shows Tecarfarin provides stable anticoagulation with >72% TTR overall and across key subgroups

Phase 2/3 Trial completed (N=607)

- Tecarfarin vs. well-controlled warfarin trial
- Randomized, double-blind trial designed to compare the quality of anticoagulation
- Average Time in Therapeutic Range (TTR) as measured by the International Normalized Ratio (INR)
- Dosing managed by a centralized dose control center

Key Tecarfarin Findings

Tecarfarin Demonstrated

TTR >72%

overall and across key subgroups

Demonstrated trends suggesting **improved TTR control** in key subgroups expected to do poorly with warfarin

Demonstrated **similar major bleeding** as warfarin and **no thrombotic events**

TTR of 70% or greater is generally accepted as the goal for stable anticoagulation with a VKA

In real world use of warfarin, TTR averages approximately 40-59%

Source: EmbraceAC Review by Whitlock et al., 2016

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TTR Decreases with CKD Severity for AFib Patients on Warfarin

AFib Patients with ESKD on Warfarin are Poorly Controlled with TTR of 42-51%, compared to the TTR goal of 70% or greater

- Time in Therapeutic Range (TTR)[1,2,5]
  - Well-established FDA metric used to evaluate anticoagulation control (safety and efficacy)
  - Higher TTR levels correlate directly with improved clinical outcomes including rates of death, bleeding, myocardial infarction, stroke, and systemic embolism
- TTR predictive of clinical outcomes
  - Stage 4 and 5 CKD with AFib: Similar TTR cutoffs predictive of mortality and cardiovascular outcomes[3,4]
- Overall TTR for AFib Patients with ESKD on warfarin is 42-51%[6]
- Only 21% of ESKD patients on dialysis using warfarin achieve TTR ≥60%[6]

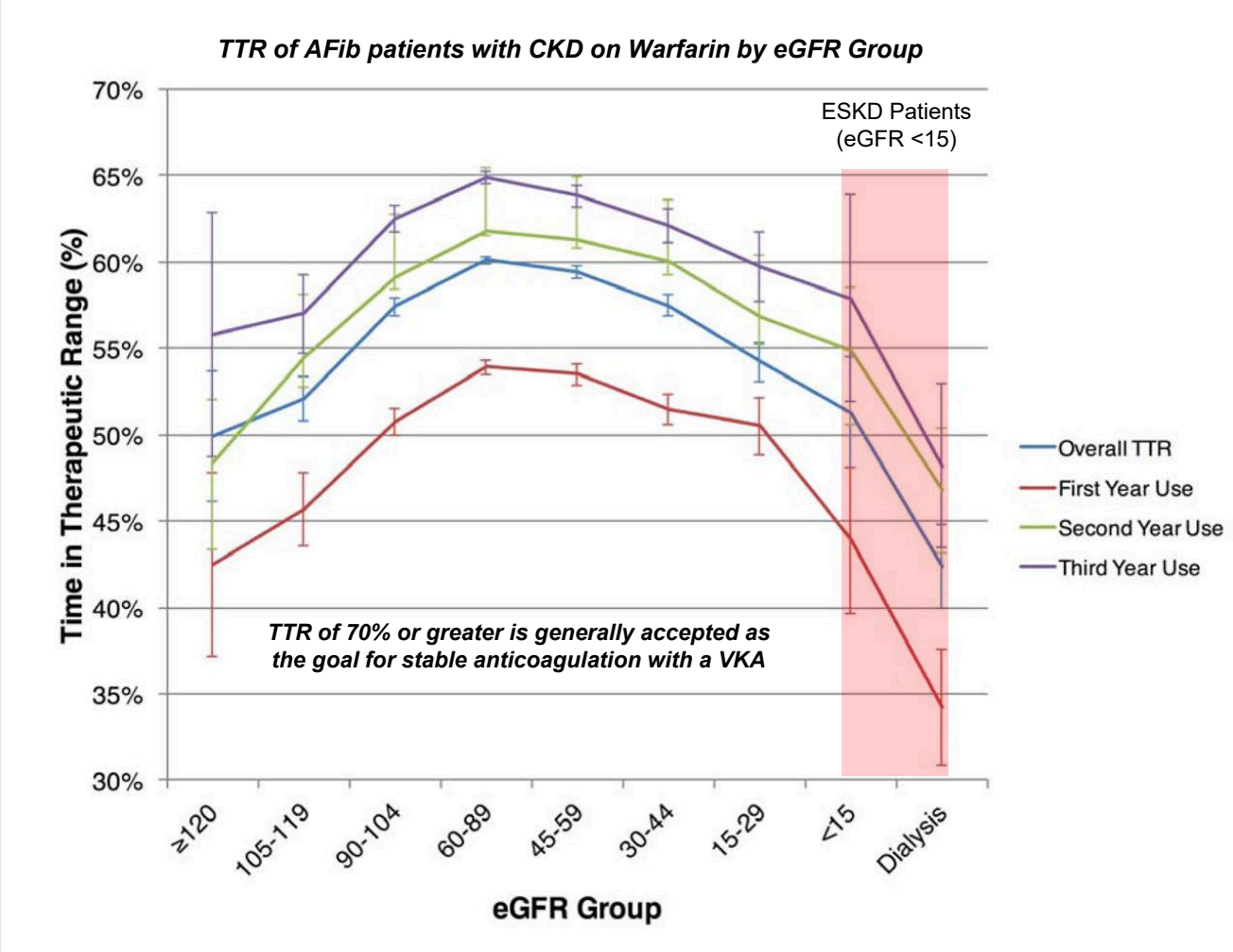


Figure 2. Warfarin Utilization and Anticoagulation Control in Patients with Atrial Fibrillation and Chronic Kidney Disease[6]

1) White et al. 2007; 2) Currie et al. 2006; 3) Szumer et al., 2017; 4) Inoue et al., 2018; 5) Jones et al. 2005 6) Yang et al. Heart (2017 June)

Phase 2/3 Trial Shows Tecarfarin is Well-Tolerated for Stroke and Thrombus Prevention, with Fewer Hemorrhagic Events

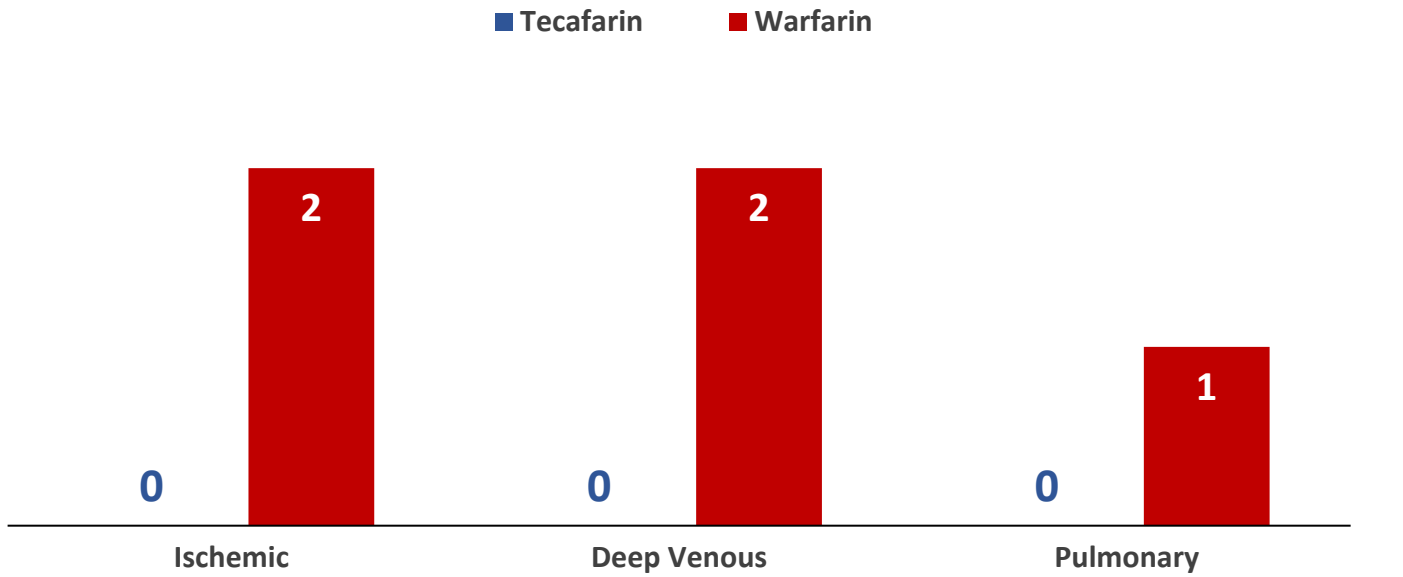
Tecarfarin had fewer thrombotic events compared to warfarin

Randomized, double-blind clinical trial

N=607
Patients with indications for chronic anticoagulation

Tecarfarin (n = 304)

Warfarin (n = 303)



Tecarfarin-treated subjects experienced numerically fewer major hemorrhages than the warfarin-treated patients and had numerically fewer thrombotic events

Whitlock RP, Fordyce CB, Midei MG, et al. A randomised, double blind comparison of tecarfarin, a novel vitamin K antagonist, with warfarin. The EmbraceAC Trial. *Thromb Haemost.* 2016;116(2):241-250. doi:10.1160/TH15-11-0910

Tecarfarin Phase 1 PK Trial in Stage 4 CKD Patients Provides Evidence that CKD Does Not Alter Tecarfarin Exposure While Warfarin Exposure is Increased

Summary Table

% change between Stage 4 CKD patients vs healthy subjects matched for each drug using a randomized crossover design (n=23)

	Tecarfarin (% change)	(S)-Warfarin (% change)
AUC	+15%	+44%
C_{max}	+6%	+7%
$t_{1/2}$	-8%	+19%

Result Highlights

Tecarfarin	Warfarin
Elimination from the body was not affected by severe kidney dysfunction	**Exposure increased 44% in Stage 4 CKD patients**
Half-life and the amount of drug in the body were similar in Stage 4 CKD patients and healthy subjects	**Plasma concentration and half-life increased in Stage 4 CKD patients**

Tecarfarin may lead to dosing that is more predictable than warfarin in CKD patients who require anticoagulation therapy

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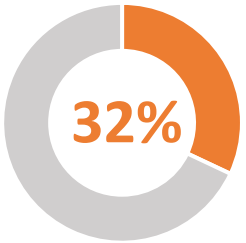
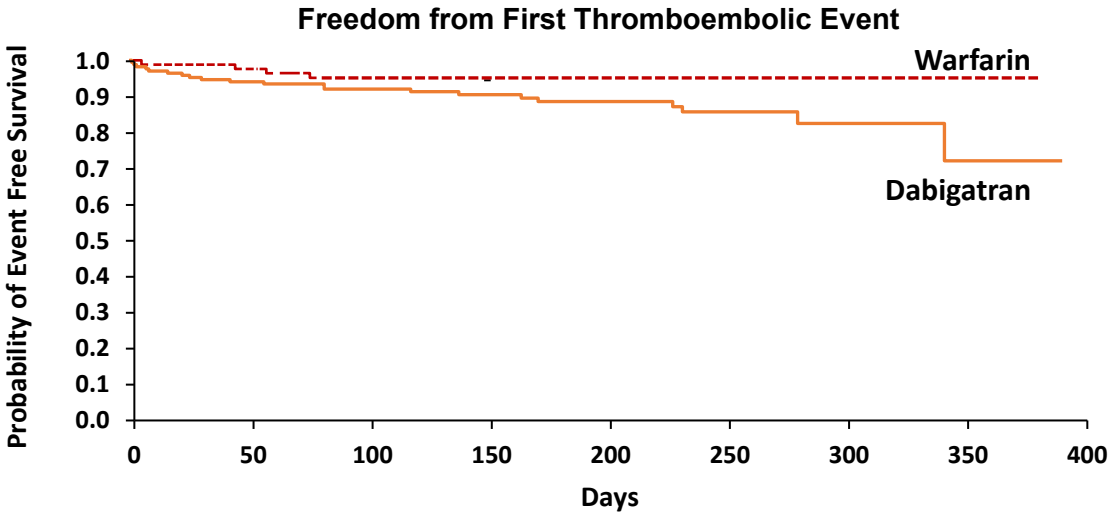
Dabigatran Versus Warfarin in Patients with Mechanical Heart Valves
EXCESS RISK AND NO BENEFIT

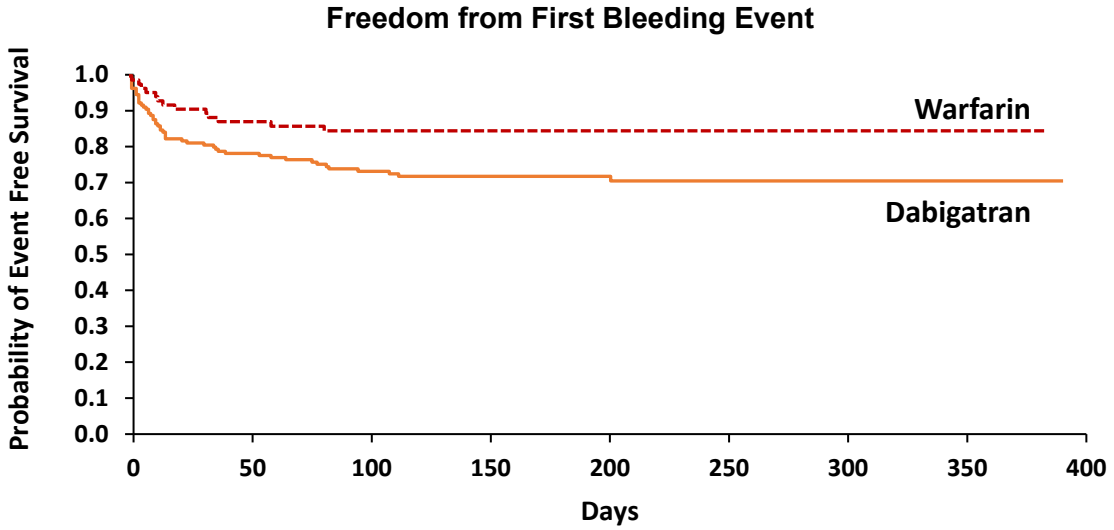
Trial terminated prematurely
due to an excess of thromboembolic and bleeding events among patients in the **dabigatran group**

	Dabigatran N=168 N (%)	Warfarin N=84 n (%)
Ischemic or unspecified stroke	9 (5.4)	0
Major bleeding	7 (4.2)	2 (2%)



Dose adjustment or discontinuation of dabigatran
(as-treated analysis)





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Eikelboom, JW. et al. *New England Journal of Medicine.* 2013. DOI: 10.1056/NEJMoa1300615

APS Patients Randomized to DOACs Have Increased Arterial Thrombosis Risk

TRIAL SITES

RAPS	UK	(N = 116)
TRAPS	Italy	(N = 120)
Ordi-Ros, et al.	Spain	(N = 190)
ASTRO-APS	US	(N = 48)

Patients with Thrombotic APS
N = 474

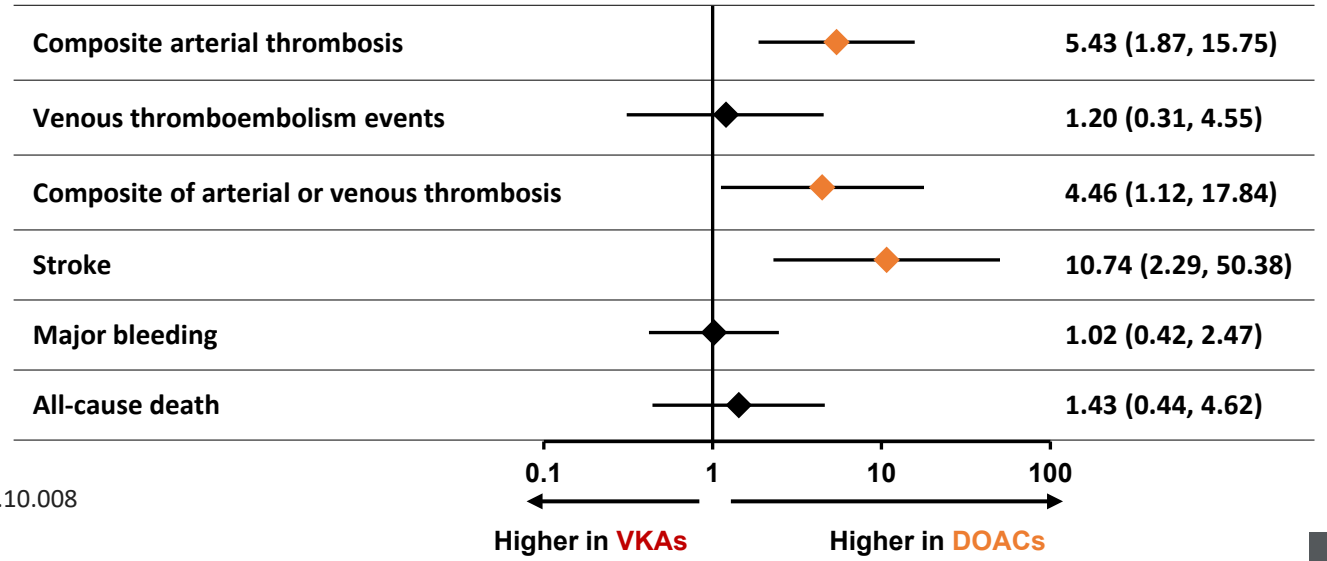
R

- Vitamin K Antagonists (VKAs)
- Direct Oral Anticoagulants (DOACs)

RESULTS

Use of DOACs compared with VKAs was associated with:

- Increased odds of arterial thrombotic events, especially stroke
- No change in the odds of VTE or major bleeding
- Results were consistent within subgroups



Khairani CD, Bejjani A, Piazza G, et al. *J Am Coll Cardiol*. 2023;81(1):16-30. doi:10.1016/j.jacc.2022.10.008

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PIPELINE & COMMERCIAL OPPORTUNITY

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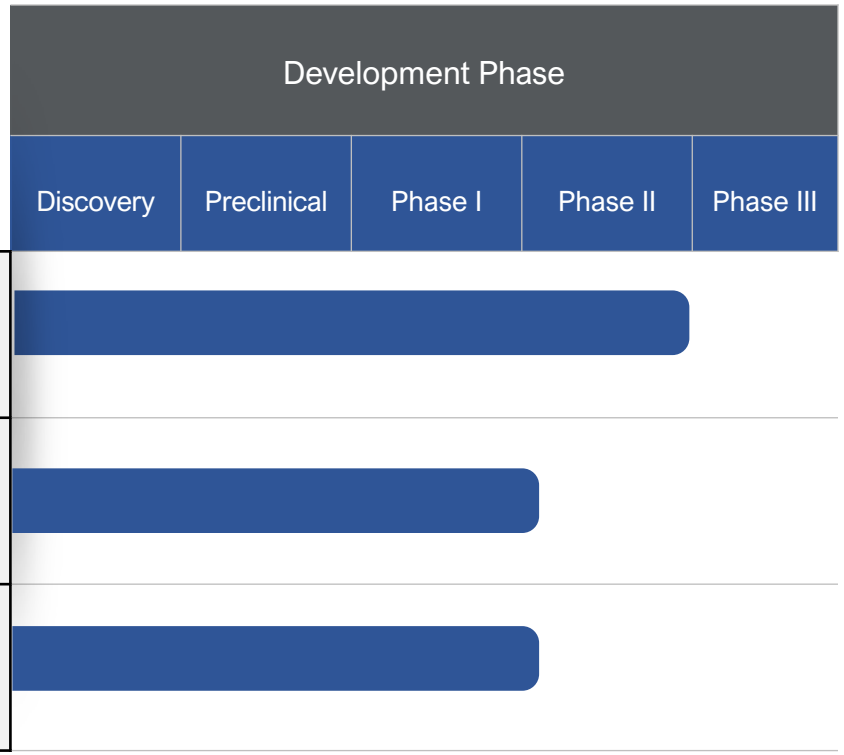
Tecarfarin Clinical Development Pipeline

Late-stage drug with orphan drug and Fast Track designations

Program	Prioritized Target Indications	Regulatory Strategy/Status
Tecarfarin	End Stage Kidney Disease with AFib	FDA Orphan Drug Designation Granted FDA Fast Track Designation Granted EMA Orphan Drug Application In Process
	Left Ventricular Assist Devices (LVADs)	FDA Orphan Drug application pending review, developing trial protocol
	Antiphospholipid Syndrome (APS)	FDA Orphan Drug application pending review, developing trial protocol



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Premium Pay for High Value Cardiovascular Orphan Drugs

Track record of recent transactions for orphan drugs in cardiovascular space

CAMZYOS → Bristol Myers Squibb™

Developed by MyoKardia and the company was subsequently acquired by BMS for $13 billion

FDA DESIGNATIONS	**Orphan Drug, Priority Review**
EXPEDITED APPROVAL	Based on a 251-patient study called EXPLORER, in which patients randomized to take the drug had significantly better peak oxygen consumption and improved on a widely used measurement of heart failure when compared to those who got a placebo.
PRICE	$89,500 a year ($245/day) – *one of the most expensive CV drugs*
NOTABLY	The approval came with a warning for the risk of heart failure and an FDA-mandated plan to manage that risk.

FoldRx → Pfizer

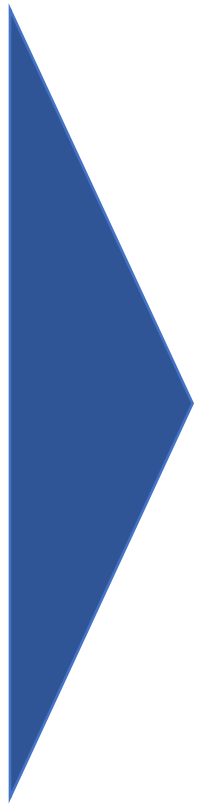
Developed by FoldRx with $88 million in private financing, before FoldRx was subsequently acquired by Pfizer

FDA DESIGNATIONS	**Orphan Drug, Fast Track, Priority Review & Breakthrough Therapy**
EXPEDITED APPROVAL	Based on ATTR-ACT trial (Transthyretin Amyloidosis Cardiomyopathy Clinical Trial) - randomized 441 patients to tafamidis or placebo for 30 months
PRICE	$225,000 a year ($616/day) - *the most expensive CV drug*
YEAR 2 SALES FOLLOWING LAUNCH	$1.3 billion collectively for Vyndaqel® and Vyndamax®

Attractive Addressable Market Opportunities for Rare Medical Conditions

U.S. market potential estimated in excess of $2 billion for three targeted rare medical condition indications

- **End Stage Kidney Disease with AFib**
- **+**
- **Left Ventricular Assist Devices**
- **+**
- **Antiphospholipid Syndrome**



Approximately

>$2 Billion

Combined Peak Annual Market Potential*
(if approved by the FDA)

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*Based on management's market analysis studies and expected adoption rates.

MANAGEMENT, BOARD & SCIENTIFIC ADVISORY BOARD

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Leadership Team

Quang Pham CEO & Founder, Chairman	espero BIOPHARMA; D+R LATHIAN HEALTHCARE MULTICHANNEL MARKETING; Genentech
Douglas Losordo, MD Chief Medical Officer	LONGEVERON; KBP BIOSCIENCES; caladrius BIOSCIENCES; NYU Langone MEDICAL CENTER; Northwestern University
Matthew Szot, CPA Chief Financial Officer	S&W SEED COMPANY; SENESTECH; INVO bioscience Life Begins Within; RIPCURL; KPMG
John R. Murphy Director	O'Reilly AUTO PARTS; SUMMIT Materials; APRIA
Steven Zelenkofske, DO Director	AstraZeneca; sanofi aventis; Boston Scientific; NOVARTIS; SwanBio THERAPEUTICS; ACHILLION; RegadoBiosciences
Glynn Wilson, PhD Director	JUPITER WELLNESS; SB SmithKline Beecham; TAPIMMUNE
Robert Lisicki Director	ARENA PHARMACEUTICALS; INCARDA Therapeutics, Inc.; REGENERON; Daiichi-Sankyo; AMGEN

Scientific Advisory Board (SAB)

Christopher Granger, MD	○ Professor of Medicine in the Division of Cardiology at Duke University ○ Member, Duke Clinical Research Institute (DCRI)	Duke University
Sean Pokorney, MD, MBA	○ Electrophysiologist and Assistant Professor of Medicine	Duke University
Eloine M. Hylek, MD, MPH	○ Professor of Medicine, Boston University School of Medicine ○ Director of the Thrombosis and Anticoagulation Service at Boston Medical Center (BMC)	Boston 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	Harvard Medical School Beth Israel Lahey Health Beth Israel Deaconess Medical Center Baim Institute for Clinical Research
Wolfgang C. Winkelmayer, MD, MPH	○ Chief, Section of Nephrology, Professor of Medicine, Baylor University ○ Director, Selzman Institute for Kidney Health	Baylor University
Richard Whitlock, MD	○ Cardiac Surgeon and Professor of Surgery, McMaster University Medical Center ○ Investigator, Population Health Research Institute	McMaster University
A. Michael Lincoff, MD	○ Vice Chairman, Dept. of Cardiovascular Medicine, Cleveland Clinic ○ Director of Clinical Research, Lerner Research Institute	Cleveland Clinic

FINANCIALS & HIGHLIGHTS

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Financial Summary

Cap Table (as of 11/9/23)

Cash (at 11/9/23)	$9 million
Debt	NONE
Common Shares Outstanding (excluding pre-funded warrants)	13,022,754
Pre-Funded Warrants	2,985,715
As Adjusted – Common Shares Outstanding	16,008,469
Warrants – Investors (avg. $1.75)	4,285,715
Warrants - Underwriter & Placement Agt. Warrants (avg. $2.68)	389,071
Stock Options Outstanding (avg. $0.86)	1,175,000

Q3 2023 Financial Results

Operating Expenses (excluding non-cash items)	$989,000

Market Capitalization

As of 11/9/23	$7 million

Insider Ownership (Common Stock)

Insider Ownership as Percent of Shares Outstanding	47%

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Why Tecarfarin Now?

Tecarfarin is targeted for indications where warfarin FAILS to achieve sufficiently stable anticoagulation and DOACs (Eliquis-class drugs) have clinically not shown benefit.

- **Unmet Need –** Certain medical conditions exist requiring chronic anticoagulation where warfarin has been unreliable, and DOACs (Eliquis-class drugs) are not FDA-approved.
- **Development Landscape** – The newest class of anticoagulants (Factor XIs) are still in development and are not being pursued for these rare medical conditions. One Factor XI has already been abandoned
- **Proven Mechanism of Action –** Tecarfarin is a VKA with a well-understood mechanism of action; clinical data supports that tecarfarin is an effective anticoagulant
- **Improved Safety Profile** – Tecarfarin is metabolized via a different metabolic pathway than warfarin – thus providing more stable anticoagulation than warfarin, thereby decreasing the risk of stroke and bleeding
- **Regulatory Pathway** – Tecarfarin was granted Orphan Drug Designation and Fast Track Approval by FDA for ESKD + AFib, providing 7-year marketing exclusivity, clarity regarding the pathway to approval
- **Large Commercial Opportunity** -- Marketed drugs for certain rare CV diseases command significant price premiums that value the tecarfarin addressable market at over $2B, subject to FDA approval

Contact Us

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APPENDIX

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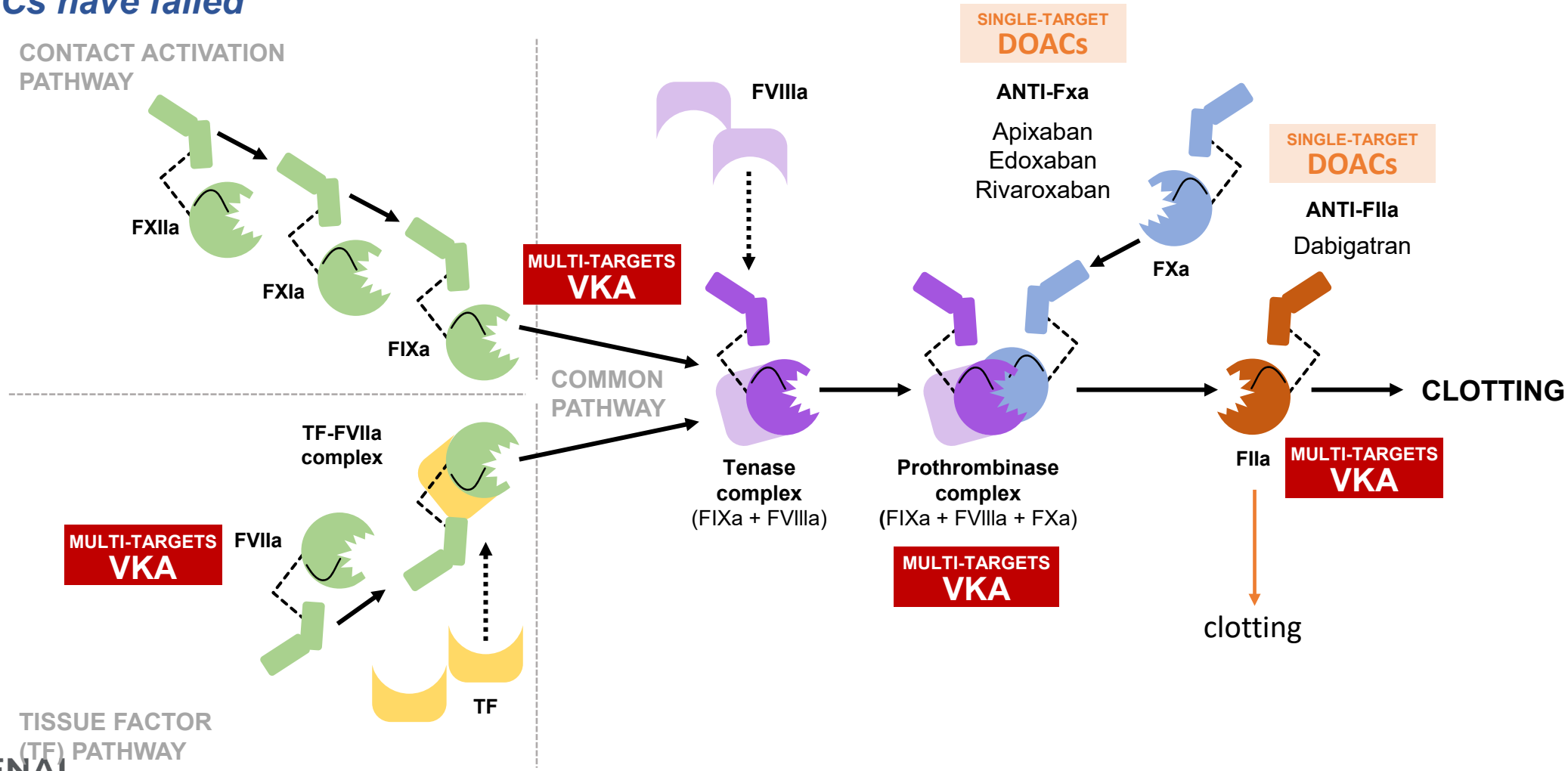
Vitamin K Antagonism Inhibits Multiple Factors (II, VII, IX, X, Proteins C & S) in the Clotting Cascade vs. Single Targets of Newer Agents

Proven mechanism of action resulting in clinically meaningful anticoagulation in certain conditions where DOACs have failed



Warfarin Metabolism via CYP450 is Complicated by Known Competitors, Inhibitors and Inducers and the Established Impact of Genetic Variants

Enzymes	Substrates	Inhibitors	Inducers
CYP 3A4	amlodipine, simvastatin, **warfarin**, amiodarone, sildenafil, midazolam, fluoxetine, haloperidol, codeine, oxycodone, methadone, fentanyl	ciprofloxacin, ketoconazole, ritonavir, methylprednisone, imatinib, tamoxifen, cimetidine, grapefruit juice	simvastatin, efavirenz, pentobarbital, carbamazepine, phenobarbital, phenytoin, valproic acid, caffeine
CYP IA2	alosetron, caffeine, duloxetine, melatonin, ramelteon, tacrine, tizanidine	ciprofloxacin, enoxacin, fluvoxamine, oral contraceptives, phenylpropanolamine	montelukast, phenytoin, smoking components of cigarettes
CYP 2C8	repaglinide, paclitaxel, methadone	gemfibrozil, fluvoxamine, ketoconazole, trimethoprim	rifampin
CYP 2C9	celecoxib, **warfarin**, phenytoin	amiodarone, fluconazole, miconazole, oxandrolone, capecitabine, etravirine, fluvastatin, metronidazole, Sulfinpyrazone, tigecycline	carbamazepine, rifampin, aprepitant, bosentan, phenobarbital, St. John's wort
CYP 2D6	lidocaine, metoprolol, haloperidol, fluoxetine, amitriptyline, metoclopramide, codeine, oxycosone, tramadol	amiodarone, chlorpromazine, citalopram, bupropion	rifampin, dexamethasone

Tecarfarin was specifically designed to avoid metabolism via the CYP450 Pathway, thus improving safety and efficacy over warfarin

CADRENAL THERAPEUTICS

Tecarfarin is Metabolized via the Human Carboxyl Esterase 2 Pathway (CES2) Provides More Effective, Safe, and More Consistent Anti-coagulation

Enzymes	Substrates	Inhibitors	Inducers
CYP 3A4	amlodipine, simvastatin, warfarin, amiodarone, sildenafil, midazolam, fluoxetine, haloperidol, codeine, oxycodone, methadone, fentanyl	ciprofloxacin, ketoconazole, ritonavir, methylprednisone, imatinib, tamoxifen, cimetidine, grapefruit juice	simvastatin, efavirenz, pentobarbital, carbamazepine, phenobarbital, phenytoin, valproic acid, caffeine
CYP IA2	alosetron, caffeine, duloxetine, melatonin, ramelteon, tacrine, tizanidine	ciprofloxacin, enoxacin, fluvoxamine, oral contraceptives, phenylpropanolamine	montelukast, phenytoin, smoking components of cigarettes
CYP 2C8	repaglinide, paclitaxel, methadone	gemfibrozil, fluvoxamine, ketoconazole, trimethoprim	rifampin
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CYP 2D6	lidocaine, metoprolol, haloperidol, fluoxetine, amitriptyline, metoclopramide, codeine, oxycosone, tramadol	amiodarone, chlorpromazine, citalopram, bupropion	rifampin, dexamethasone

CES2 Substrate Drugs

Antiplateletes/Anticoagulants
- Acetylsalicylic acid
- Prasugrel
- Dabigatran etexilate

Angiotensin receptor blockers
- Candesartan cilexetil
- Olmesartan medoxomil
- Azilsartan medoxomil

Antivitral agents
- Tenfovir disoproxil
- Adefovir dipivoxil
- Valacyclovir

CNS agents
- Cocaine
- Heroin
- 6-monoacetylmorphine

Immunosuppressive agents
- Methylprednisolone sodium succinate
- Deflazacort

Oncology agents
- Irinotecan
- Capecitabine

Anesthetic drug
- Procaine

Limited Substrates Identified

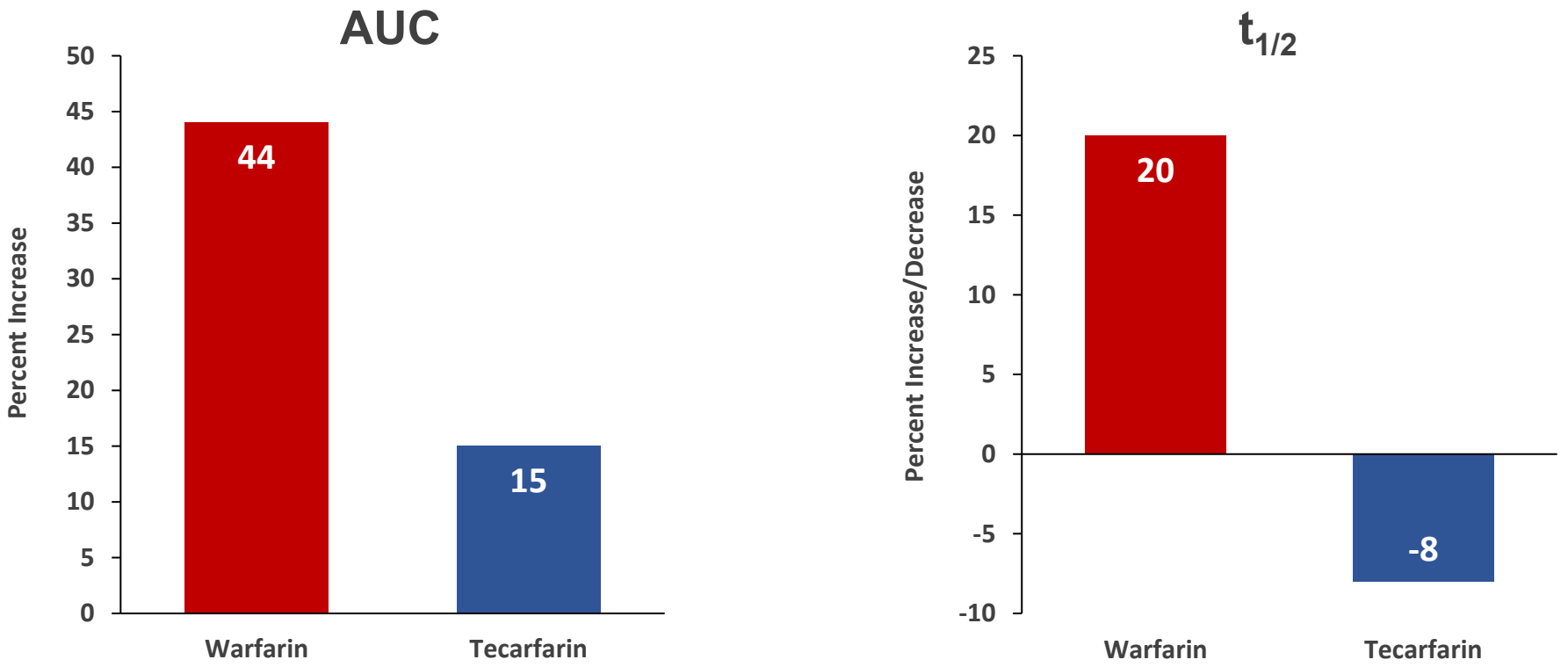
Genetic variation exists, but limited evidence of clinical impact

CADRENAL THERAPEUTICS

Kidney Failure Has a Significant Impact on Warfarin PK vs Tecarfarin

Tecarfarin metabolism not as impacted by kidney failure

Percent Increase in Exposure for Chronic Kidney Disease Subjects vs Healthy subjects for Warfarin and Tecarfarin (n =23)

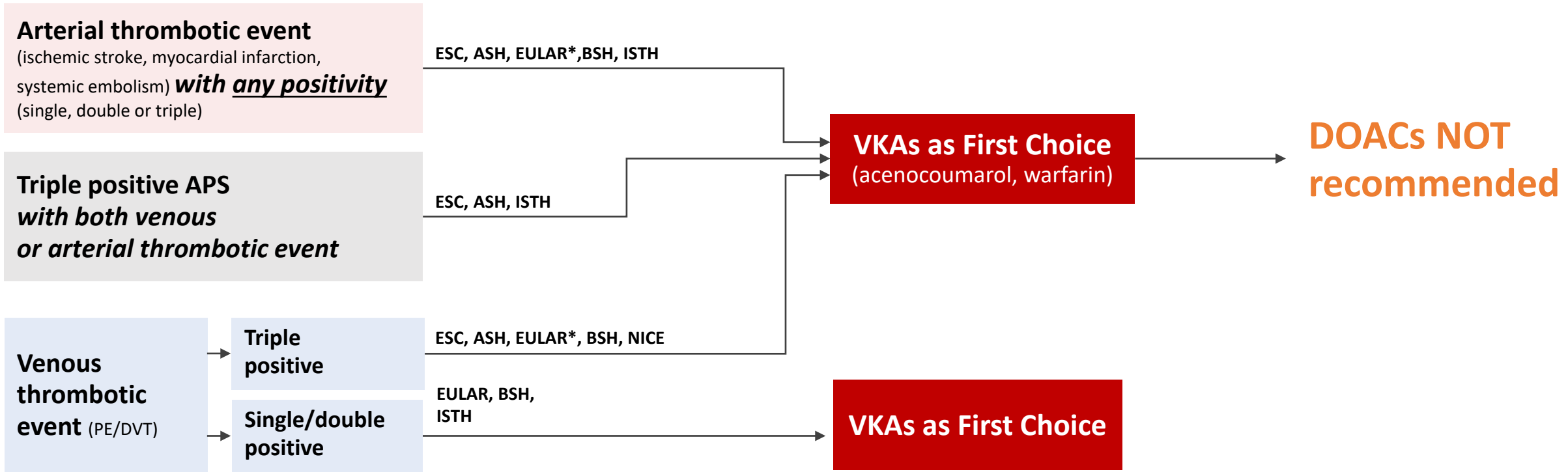


Albrecht D, Turakhia MP, Ries D, et al. Pharmacokinetics of Tecarfarin and Warfarin in Patients with Severe Chronic Kidney Disease. *Thromb Haemost.* 2017;117(11):2026-2033. doi:10.1160/TH16-10-0815

CARDIORENAL THERAPEUTICS

Summary of Guidelines Recommendations on Anticoagulant Treatment Prescription in Patients with Antiphospholipid Syndrome

PATIENTS WITH DEFINITE APS



* EULAR recommends to not use Rivaroxaban

ESC = European Society of Cardiology
ASH = American Society of Hematology
EULAR = European Alliance of Associations for Rheumatology
BSH = British Society for Haematology
ISH = International Society of Hematology

Pastori D et al. *Front. Cardiovasc. Med.* 2021. 8:715878. doi: 10.3389/fcvm.2021.715878

CARDIOVASCULAR THERAPEUTICS

Tecarfarin Phase 3 Trial Design for ESKD and AFib

Tecarfarin vs. Placebo in Patients with ESKD and AFib
Randomized, Double-Blind, Placebo-Controlled (no active control)