DIAPIN Therapeutics

Developing Novel Transformative Therapies for Cardiovascular and Metabolic Diseases

Non-confidential Presentation - June 26

Cardiovascular Disease is the Leading Cause of Death[1]

1 death every 1.6 seconds[1]

1 in 3, ~20M global deaths per year[1],

Most deaths are **preventable**[2]

Est. Costs by 2030[2]

1 Trillion

- Risks of heart disease and stroke increase with age, diabetes, obesity, high blood pressure, stress, pregnancy complications, infection, smoking, alcohol, sedentary lifestyle, dyslipidemia, poor diet, PCOS, pollution[1,2,3]

For the many personally affected

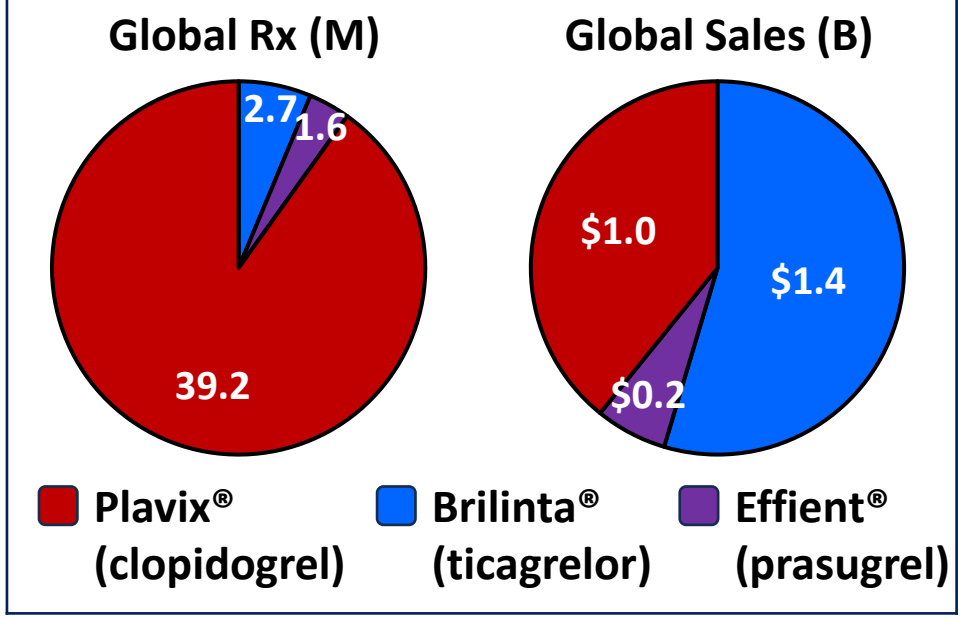
and for everyone – **CHANGE IS NEEDED**

1. WHO, July 2025, *Cardiovascular Diseases (CVDs).* 2. World Heart Federation, infographic 2021. 3. Centers for Disease Control Heart Disease Risk Factors

Market Landscape - Established Standard of Care

- Cardiovascular disease leading cause of death with >32M heart attacks and strokes every year[1]
- The AHA Guidelines - dual antiplatelet therapy (aspirin + P2Y12 inhibitor) to reduce risk of future heart attack, stroke and coronary stent thrombosis[2]

P2Y12 Inhibitors Annual Sales and Rx[3]



- Clopidogrel leads market with ~90% utilization
- Ticagrelor leads in revenue due to branded pricing
- Current treatments DO NOT work for everyone
- Significant black box safety concerns and side effects.

New Best-in-Class antiplatelet must be safer and more effective!

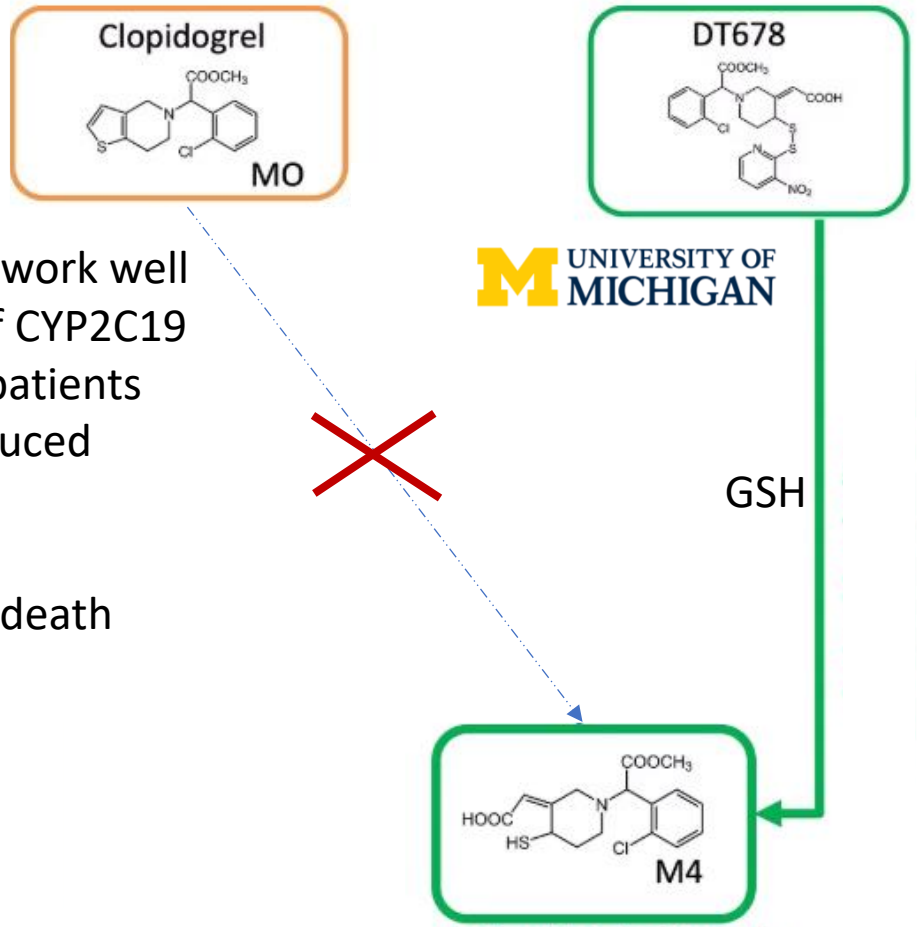
1. WHO, 2025, *Cardiovascular Diseases (CVDs)*., 2. 2025 ACC/AHA Guidelines on Dual Antiplatelet Therapy (2025), *Circulation*, 151: 13., 3. Global Data Forecasted for 2023.

Introducing New Antiplatelet Drug DT678

Novel Prodrug Synthesized Using an AI Designed Enzyme

Clopidogrel does **NOT** work well in patients with loss of CYP2C19 function = **25-60%** of patients or in patients with reduced metabolic function

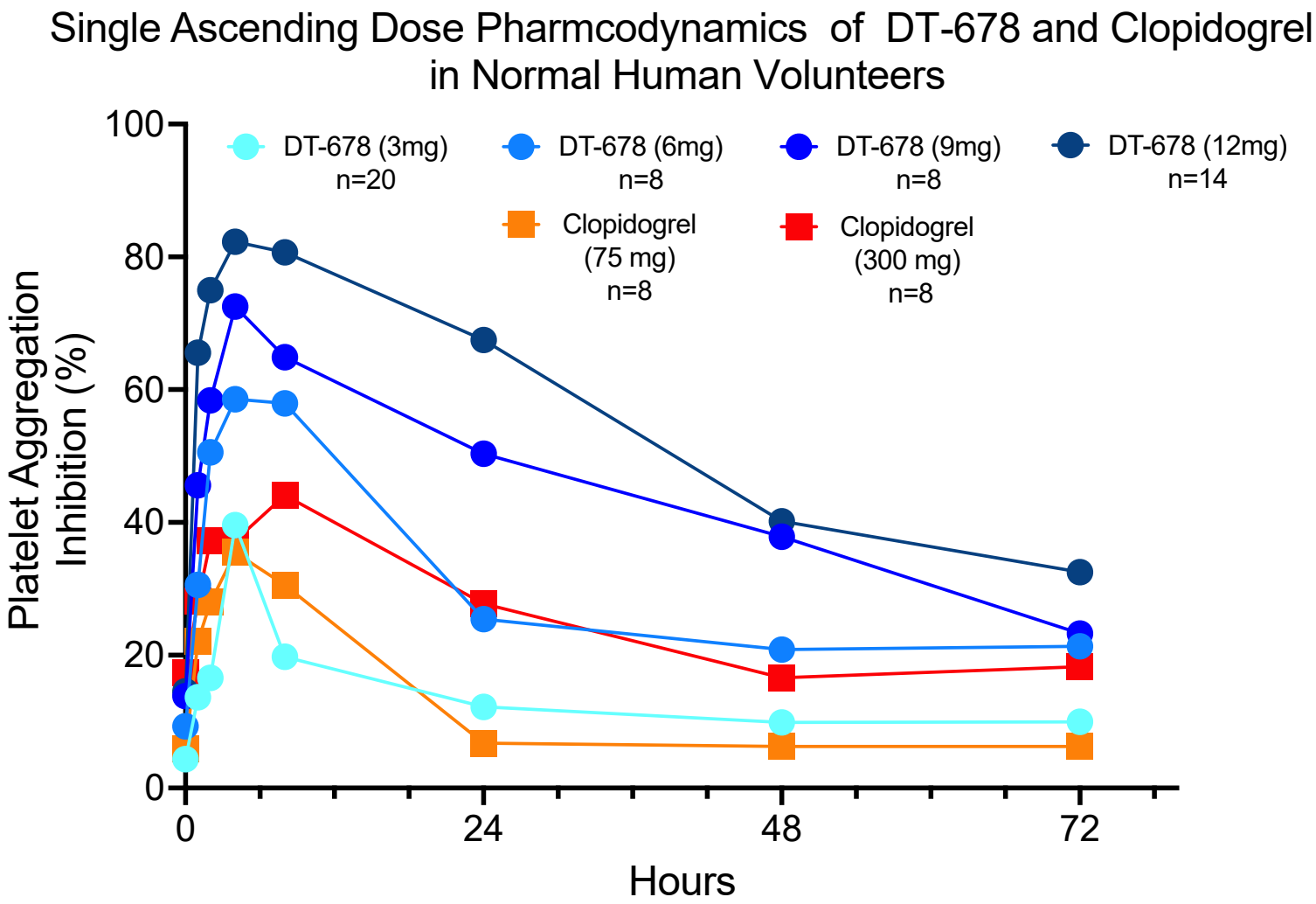
= heart attack, stroke, death



- **Works well for ALL Patients** regardless of CYP/metabolic function
- **Generates same active metabolite M4 –** basis of 505b2 NDA pathway – endorsed by FDA
- **Quick, efficient, safer with no drug interactions**
- **Safe profile in Ph1, Phase 2 in progress**
- **Clear path to NDA, approval, market differentiation & revenue**

Phase 1 Results

3mg of DT678 is Equivalent to 75mg of Clopidogrel



- **DT678 is 25X more effective, 3mg has similar antiplatelet effects to 75mg clopidogrel**
- **DT678 has dose proportional Pharmacodynamic antiplatelet effects - clinical biomarker**
- **6 & 9m chronic toxicology studies complete**
- **Phase 2 in progress**

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DT678 Advantages

Improved safety, efficacy, faster onset, less bleeding and more flexibility

Risk	DT678[1,2]	Clopidogrel[3]	Ticagrelor[4]	Prasugrel[5]	Cangrelor[6]
Reduced Safety Warnings	✓	X	X	X	X
Reduced Bleeding Risk	✓	X	X	X	X
Improved efficacy	✓	X	✓	✓	✓
Fast Onset	✓	X	X	X	✓
Reduced Side effects	✓	X	X	X	X
No Drug-Drug interactions	✓	X	X	✓	✓

1. Zhang, H et al., 2014, *Thromb Haemost*., 112(6):1304-11., 2. Lauver, DA et al., 2019, *Pharmacol Res Perspect.,* 25;7(4):e00509., 3. FDA, 2016, Plavix® (clopidogrel) product label., 4. FDA, 2016, Brilinta® (ticagrelor) product label., 5. FDA, 2012, Effient® (prasugrel) product label., 6. FDA, 2019, Kengreal® (cangrelor) product label.

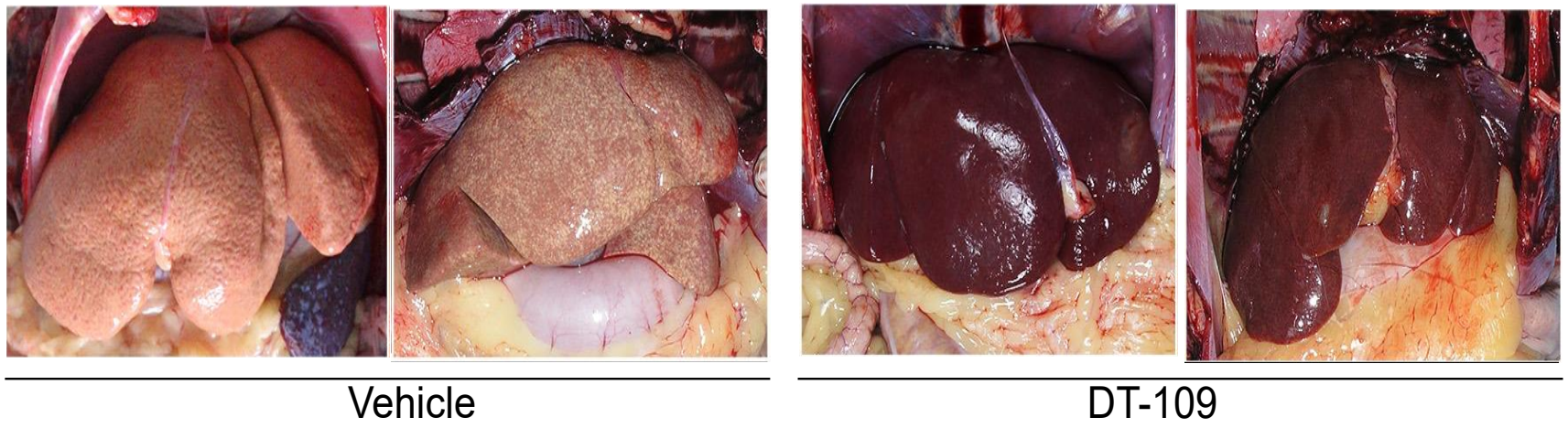
Diapin Pipeline

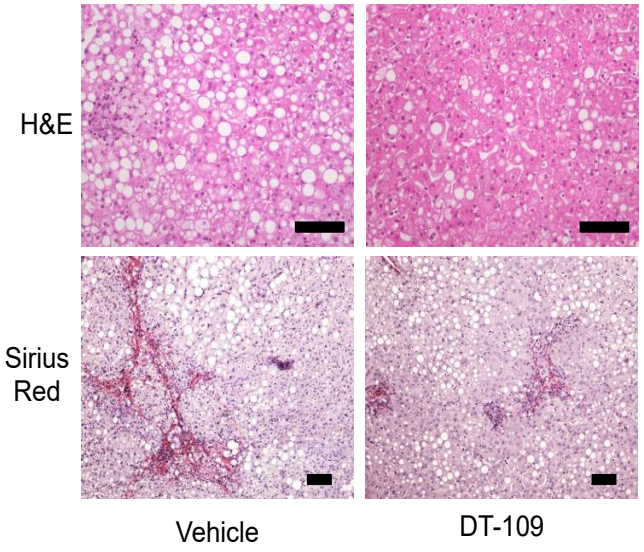
2 Cardiovascular and Metabolic Disease Treatment Innovations

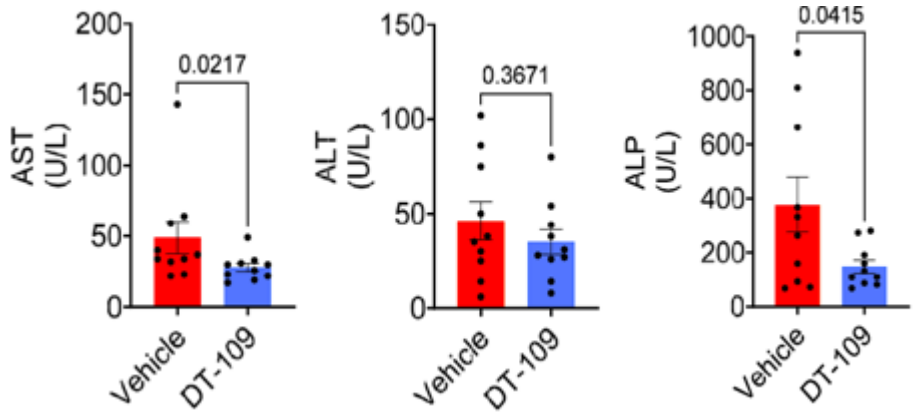
	INDICATION	PRECLINICAL	CANDIDATE SELECTION	IND-ENABLING	PHASE I	PHASE II	PHASE III
DT678 (antiplatelet)	ACS/Myocardial Infarction						
	Stroke						
	Peripheral Artery Disease						
DT-109 (tripeptide)	Metabolic Steatohepatitis						
	Primary Biliary Cholangitis						
	Atherosclerosis - CVD						
	Type 2 Diabetes						
	Familial Hypercholesterolemia						
	Undisclosed Indication						

DT109 MASH efficacy in Non-Human Primates

Reduction in Liver Fat, Fibrosis, Scarring and Liver Enzymes after 5m



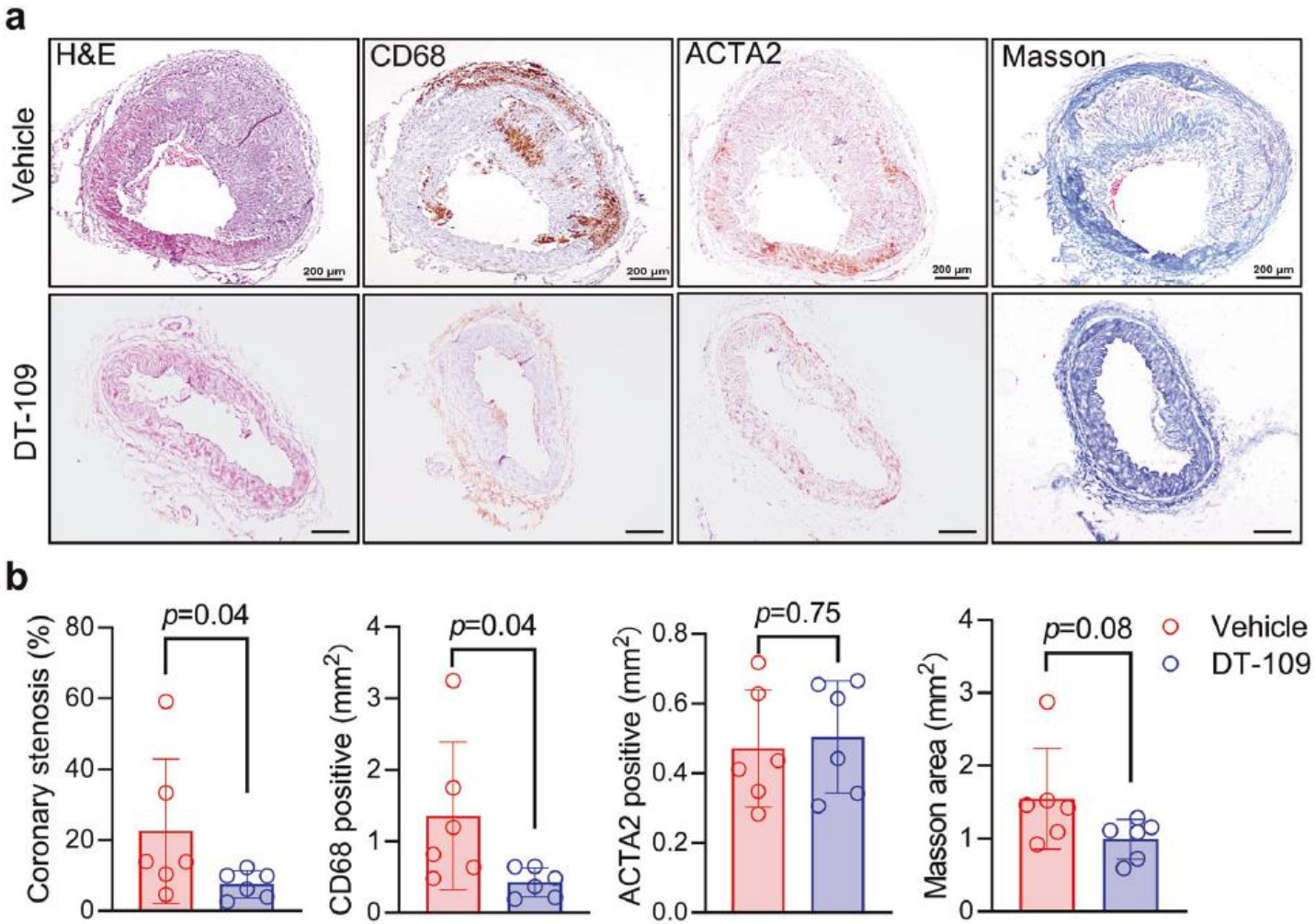




- **DT109 significantly decreased overall Liver Fat**
- **DT109 reduced liver fat content, fibrosis and scarring**
- **DT109 reduced liver enzymes: AST, ALT and ALP**

Qu P, Rom O, Li K, et al. *Cell Metab*. 2023;35(5)

DT109 Attenuates Atherosclerosis and Vascular Calcification in NHPs



- DT109 caused a significant reduction in coronary stenosis and macrophage infiltration.
- These results demonstrate that DT109 significantly reduced coronary atherosclerosis.

Jia L, Qu P, Zhao Y, et al. *Signal Transduct Target Ther*. 2025;10(1):122

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Funding Status – Seed Stage Raising 7.5M

Pharma with CVMD portfolios

NOVARTIS, sanofi, BAYER, Lilly, AstraZeneca, AMGEN, Johnson&Johnson, VIATRIS, novo nordisk, CORXEL, Pfizer, Cipla, MERCK, Boehringer Ingelheim

~1bn Comparable Exits

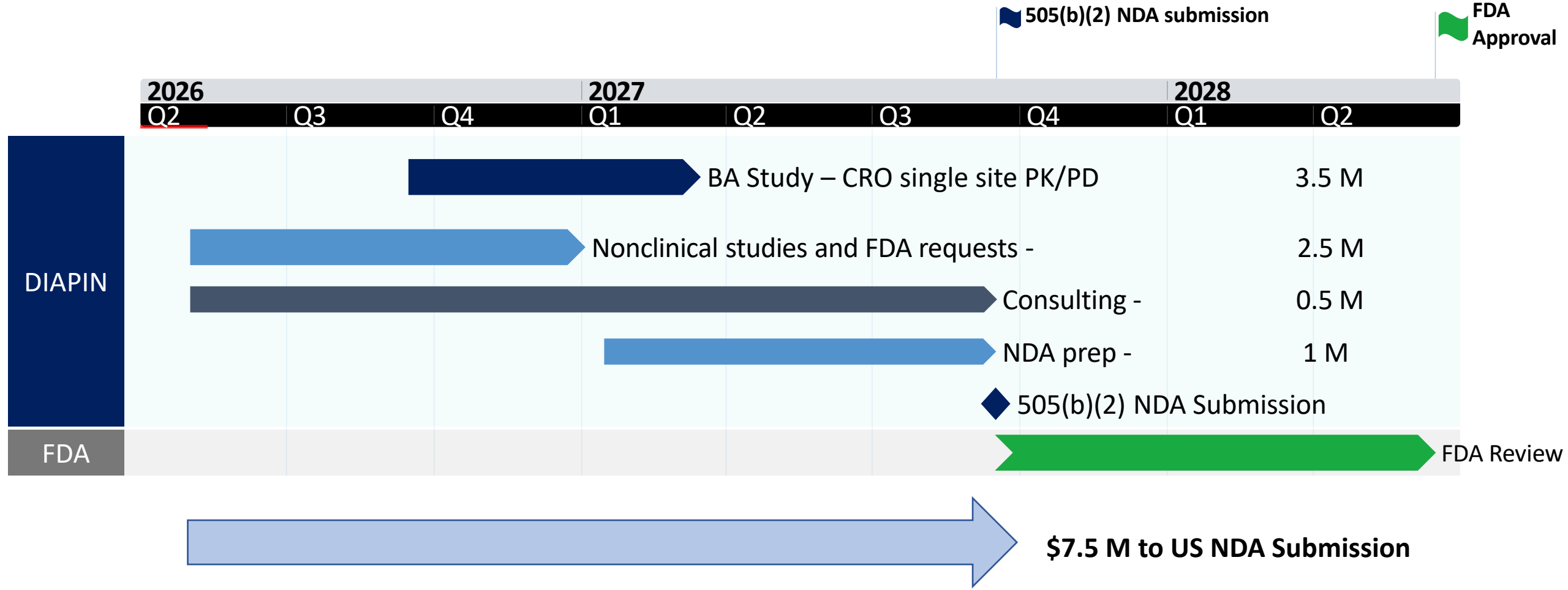
Exit at NDA submission to Biotech or Pharma partner

EXIT

Multiple Exit opportunities: strategic partner, out-licensing, acquisition, IPO

EXIT Revenue generating		NDA approved, Launch DT678
EXIT Series A		Prepare for NDA approval, Launch, IPO
EXIT $7.5M	Seed Round 7.5 Million **3 million committed**	Bioavailability Study, Response to FDA Requests, file NDA
$6M	Phase 1s Completed (China) IND filed (US &China) in Ph2	✓ Grants, Beijing SL, Founders, and Investors

DT678 Use of 7.5 Million Seed Round



Timeline contingent on funding

Diapin Therapeutics Team

Successful Track Record and Exits Through NDA and Commercialization

Jessica Reed, Ph.D.
CEO, Board Member
Millendo, MMS, Pfizer, Parke-Davis

Charles Bisgaier, Ph.D.
Chairman of the Board
Former Pfizer Research Fellow
Founder and investor of 10+ corporations

Eugene Chen, M.D., Ph.D.
Founder, Board Member
Prof of Medicine, Univ of Michigan
Director for Adv Models for Translational Sciences

Mingo Xu, M.D., Ph.D.
Board Member and GM of Beijing SL Pharmaceutical

Michael Iannuzzi, MD, MBA
CMO,
CUNY School of Medicine

Sara Melton
Business Development,
Sales & Marketing Advisor

Paul Jeffrey
Commercialization Advisor
Former Pfizer VP
Early Commercial Development

University of Michigan · Pfizer · Esperion Therapeutics · ProNAi · MMS Holdings Inc. · imagine PHARMA · Parke-Davis People Who Care · HYGIEIA · Gemphire Therapeutics · BIOSAVITA · MILLENDO THERAPEUTICS · GeneToBe The Rare Disease Company

Lipitor atorvastatin calcium tablets · NEXLETOL (bempedoic acid) tablets · Aricept donepezil HCl tablet 23 mg · BANZEL (rufinamide) · AcipHex rabeprazole sodium · VIZIMPRO DACOMITINIB

Lopid 600 (Gemfibrozil Tablets, USP) · d-Nav by HYGIEIA A BETTER WAY TO USE INSULIN · Byetta exenatide injection · Fycompa (perampanel) tablets · Onfi (clobazam) Tablets · Osphena (ospemifene) tablets 60 mg · Dalvance (dalbavancin) for injection

Diapin Scientific Advisory Team

Best-in-class and Diverse Medical Team Guiding Development

Dr. Dan Eitzman, MD

Professor of Internal Medicine

University of Michigan Medical School

Dr. Charles Burant, MD, PhD

Dr. Robert C. and Veronica Atkins Professor of Metabolism

University of Michigan School of Public Health

Dr. George King, MD

Chief Scientific Officer at Joslin Diabetes Center & Professor of Medicine

Harvard School of Medicine

Dr. Arun J. Sanyal, MD

Chief of Division of Gastroenterology, Hepatology & Nutrition & Professor of Medicine

Virginia Commonwealth University

Dr. Shamir Mehta, MD

Douglas A. Holder Endowed Chair and Professor of Medicine

McMaster University

Summary and Thanks

Raising seed round of $7.5 million to File US NDA for DT678

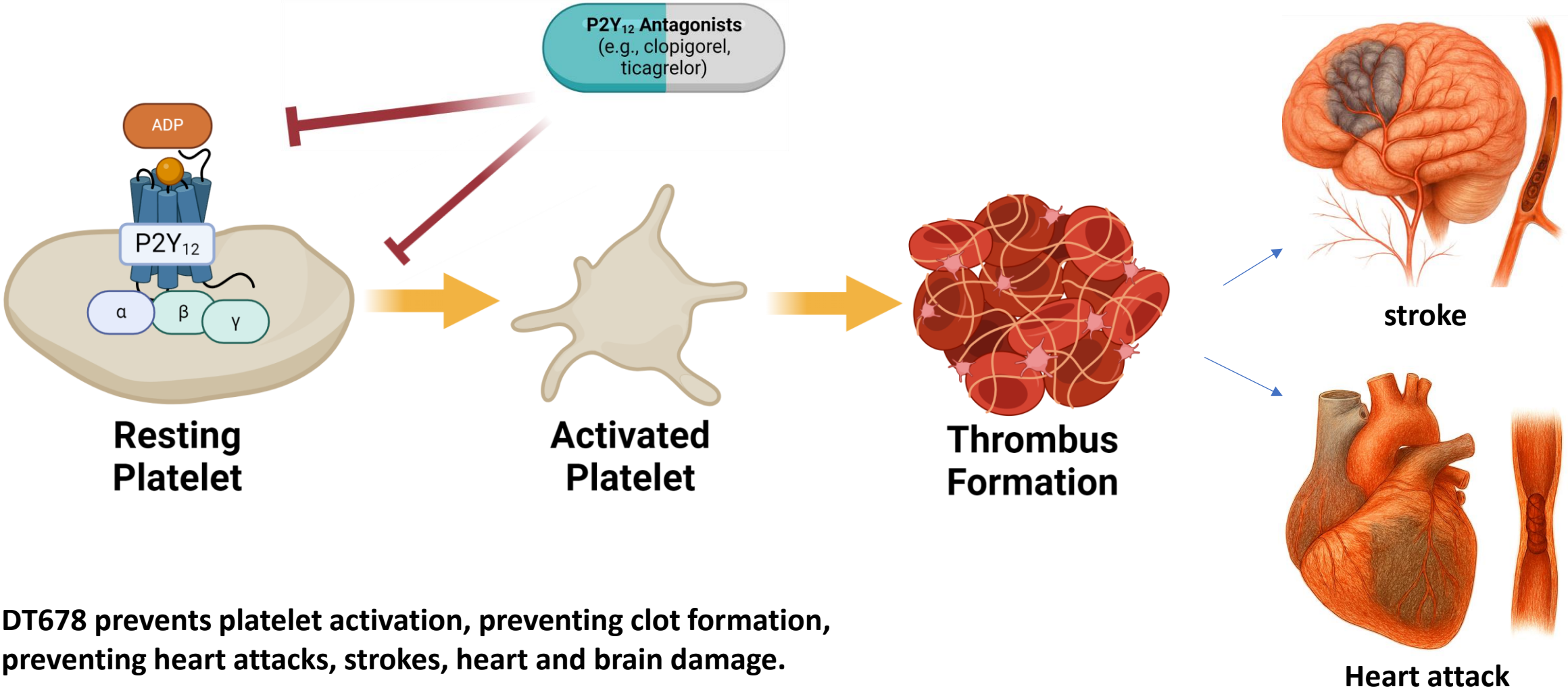
For more information please contact: jreed@diapin.com

Visit our webpage for investors: https://www.diapin.com/investors

- ☑ Projected global sales >$20 Bn
- ☑ FDA endorsed 505b2 pathway
- ☑ Defined market differentiation
- ☑ Defined use of proceeds to NDA
- ☑ Robust IP portfolio
- ☑ Best-in-class

Appendix

Mechanism of Action $P2Y_{12}$ Antagonists

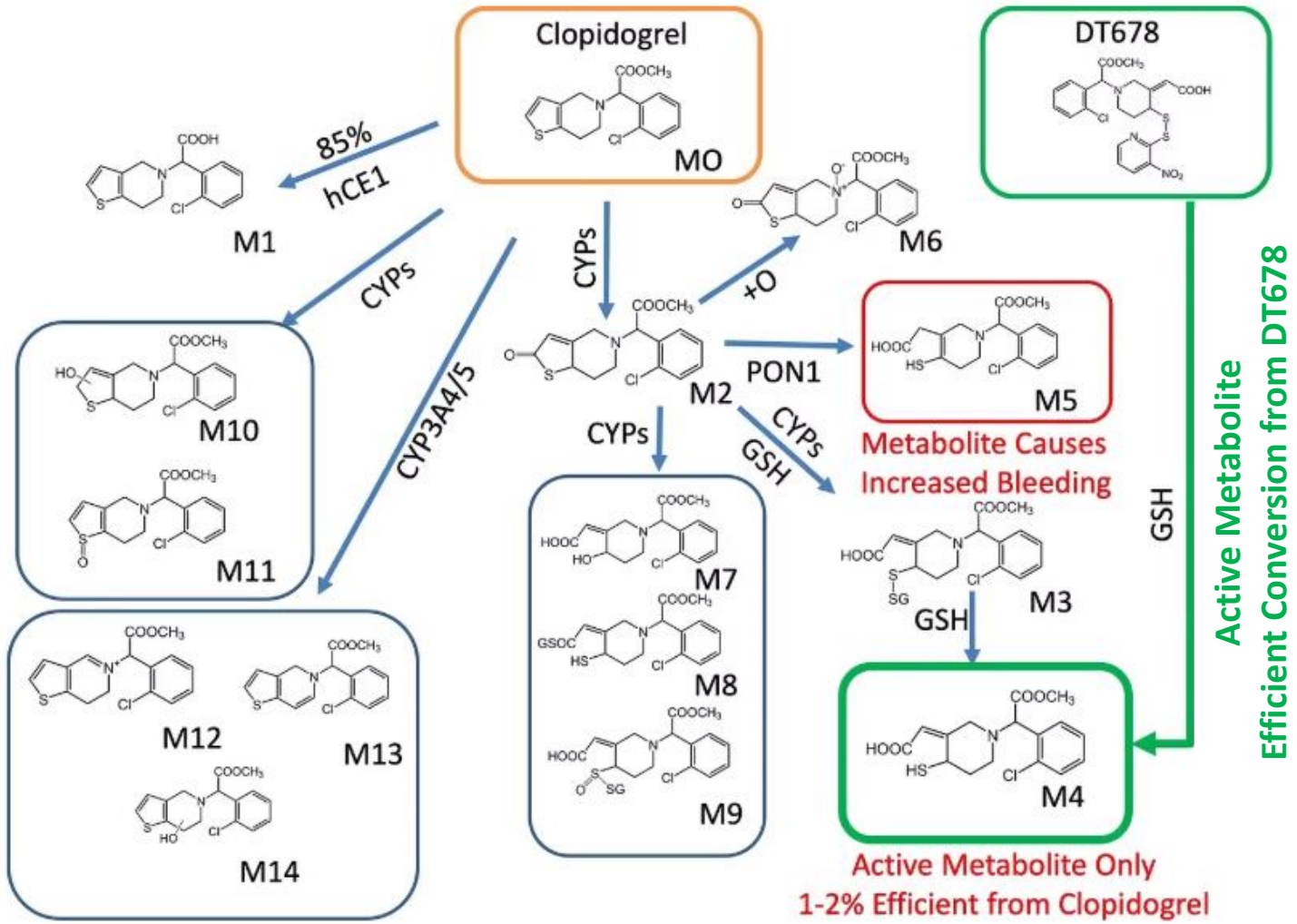


DT678 prevents platelet activation, preventing clot formation, preventing heart attacks, strokes, heart and brain damage.

Introducing DT678

Novel Prodrug Synthesized Using an AI Designed Enzyme

UNIVERSITY OF MICHIGAN



- DT678 is synthesized using an AI designed CYP enzyme[1]
- DT678 is converted to M4, independently of hepatic cytochrome P450 (CYP) enzymes including CYP2C19[4,5]
- Clopidogrel is a prodrug metabolized by CYP2C19 to its active metabolite, M4[2]
- ~1-2% of M4 is formed from clopidogrel, while M4 is formed efficiently from DT678
- Clopidogrel generates many metabolites including M5 which is known to cause increased bleeding risk[1,3,6]

1. Zhu, Y. et al., 2018, *Nature Communications* (2018) 9:3952., 2. Pereillo, J. M. et al., 2002, *Drug Metab. Dispos.* 30, 1288–1295. 3. Li, G. et al., 2016, *Int. J. Clin. Exp. Med*. 9, 15607–15620., 4. Zhang, J. et al, 2016, *J Pharmacol Exp Ther.*, 359:11–17., 5. Zhang, J. et al, 2013, *Mol Pharmacol.*, 83:848–856., 6. Kuszynski DS, Lauver DA., 2022, *Purinergic Signal*, 18(3): 253–265.

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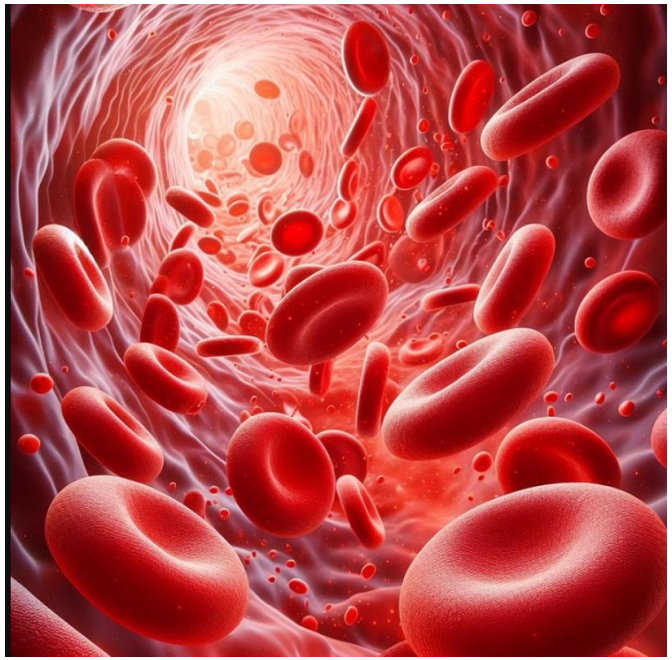
Overview of Diapin Therapeutics DT678

Leading the way to a potential new best-in-class antiplatelet



OVERVIEW	A novel prodrug with a clear regulatory path to NDA via 505(b)(2) with extended IP protection and clear market differentiation.
UNMET NEED	Antiplatelets, P2Y12s: Increased bleeding risk, diminished effect in many patients, slow onset of action and negative side effects
LEAD ASSET	Oral & IV administered P2Y12 inhibitor, unique metabolism, potential for improved efficacy & safety, Ph1 complete, in Ph2.
ASK	$7.5 mill Seed round for US trial, FDA requests & NDA submission. Approval & launch in 2028, short path to revenue generation.
TEAM	Experienced team to develop a safer more effective drug with a multi-billion market opportunity and significant potential for ROI.

Plavix® (clopidogrel) – FDA BLACK BOX WARNING!

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use PLAVIX safely and effectively. See full prescribing information for PLAVIX.

PLAVIX (clopidogrel bisulfate) tablets, for oral use
Initial U.S. Approval: 1997

WARNING: DIMINISHED ANTIPLATELET EFFECT IN PATIENTS WITH TWO LOSS-OF-FUNCTION ALLELES OF THE CYP2C19 GENE

See full prescribing information for complete boxed warning.

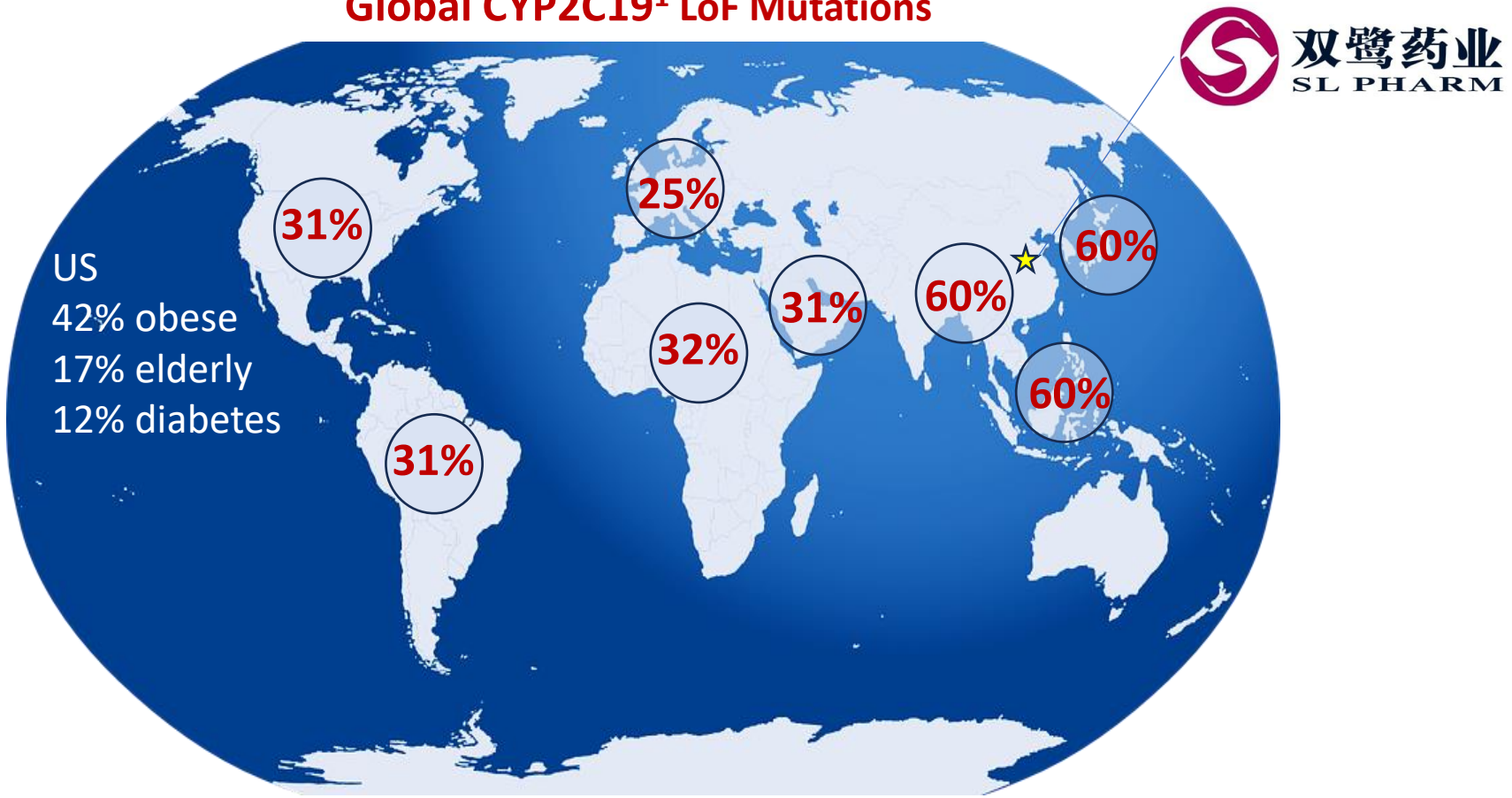
- **Effectiveness of Plavix depends on conversion to an active metabolite by the cytochrome P450 (CYP) system, principally CYP2C19. (5.1, 12.3)**
- **Tests are available to identify patients who are CYP2C19 poor metabolizers. (12.5)**
- **Consider use of another platelet P2Y12 inhibitor in patients identified as CYP2C19 poor metabolizers. (5.1)**

- **Plavix (clopidogrel) is metabolized to its active metabolite in the liver via CYP enzymes including CYP2C19**
- **Alternatives to Plavix – not as safe, higher incidence of bleeding and worse side effect profile**
- **Why Now? 1h Point of Care test FDA approved to rapidly identify CYP2C19 mutations.**

Global Opportunity for Improved Antiplatelet Safety

Patients with Reduced CYP2C19 Function Through Genetics, Diabetes, Obesity & Age.

Global CYP2C19[1] LoF Mutations



Patients with CYP2C19 LoF mutations have increased risk of major adverse cardiovascular events if treated with clopidogrel[2]

% IM and PMs

- **25-32%** Africa, Americas, Europe, Middle East
- **60%** Asia, India, Pacific Island Nations

Reduced clopidogrel efficacy in diabetics[3], obese[4] & elderly patients[5] with lower CYP2C19 function.[6]

Beijing SL collaboration. Phase 2 in progress.

1. Klein MD, 2019, *Arter, Thromb, & Vasc Biol*, 39:4., 2. Beitelshees AL, et. al, 2022, *JAHA*, 11(4):e024159.
3. Shahim B. et al, 2023, *JAHA*, 12(1): e026482. 4. Puccini M. Cardiovasc Drug Ther 2023 Aug;37(4):833-837.
5. Abudahab S, Pharmacogenomics 2024, 25(1) 41–54 , 6. Tomlinson B et al, 2023, Exp Opin on Drug Met & Tox, 19:12, 867-870.

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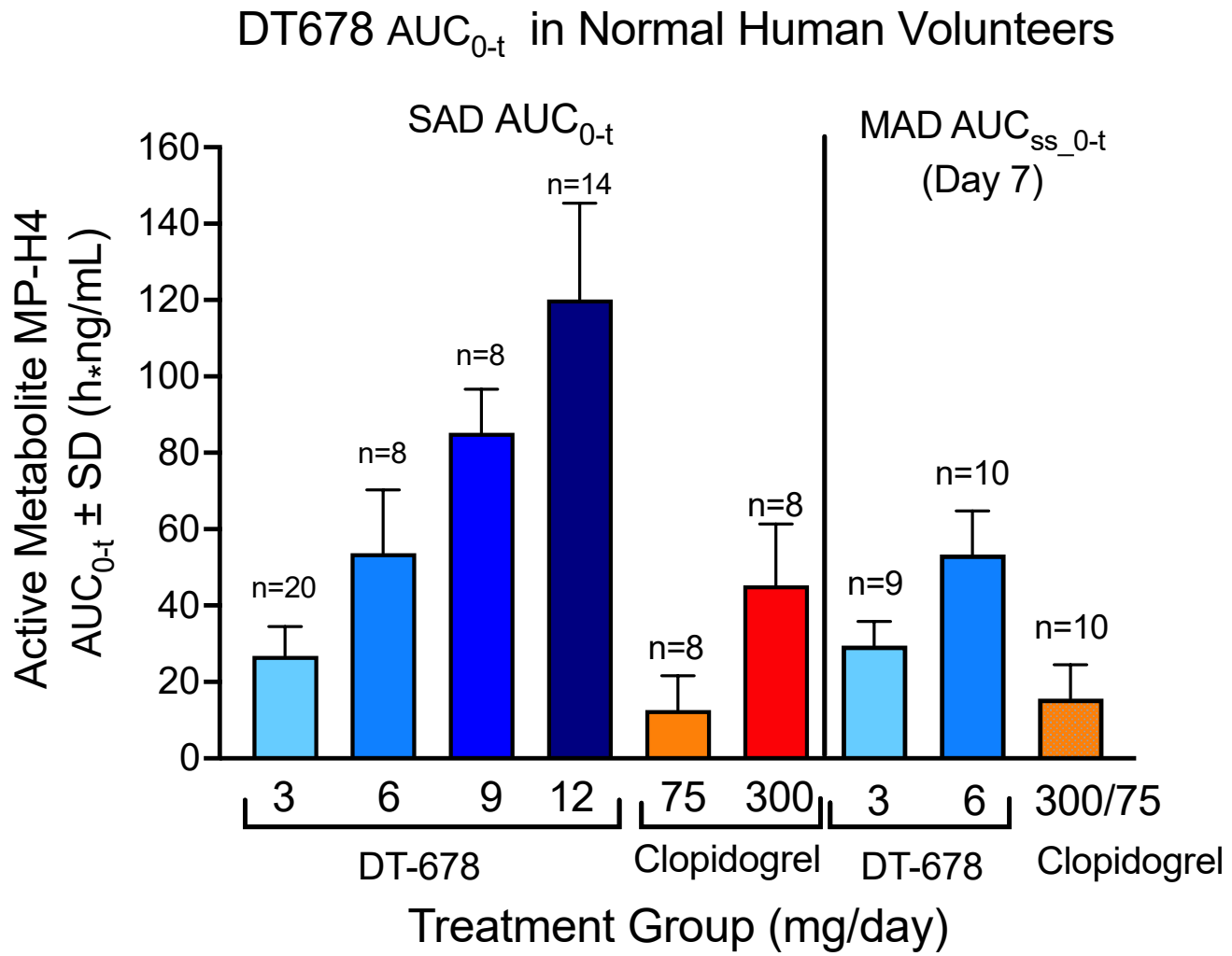
Phase 1 SAD/MAD Study Results

3mg of DT678 Results in Similar AUC_{0-t} as Clopidogrel 75mg



- **IND filed in China and US.**
- **DT678 has nonclinical neuro and cardio protective benefits versus clopidogrel.**
- **DT678 has linear dose proportional PK**
- **The active metabolite is generated efficiently from 3mg DT678 with similar AUC to clopidogrel 75mg at day 1 and day 7**
- **DT678 has a favorable safety profile (Ph1 SAD, MAD, FE, and DDI completed in China)**

Phase I Data
MP-H4 is same as M4

DT678 Clinical Development Plan

Defined Path to NDA Submission and Approval

FDA Endorsed the 505b2 submission pathway:

- FDA agreed to the 505(b)(2)[1] approach and comparative bioavailability (BA) study, endorsing the strategy to bring DT678 to market efficiently
- FDA has agreed that no additional efficacy studies are required if BA study successful
- FDA agreed that if DT678 is not metabolized via CYP2C19 the clopidogrel black box label would not apply

Equivalence:

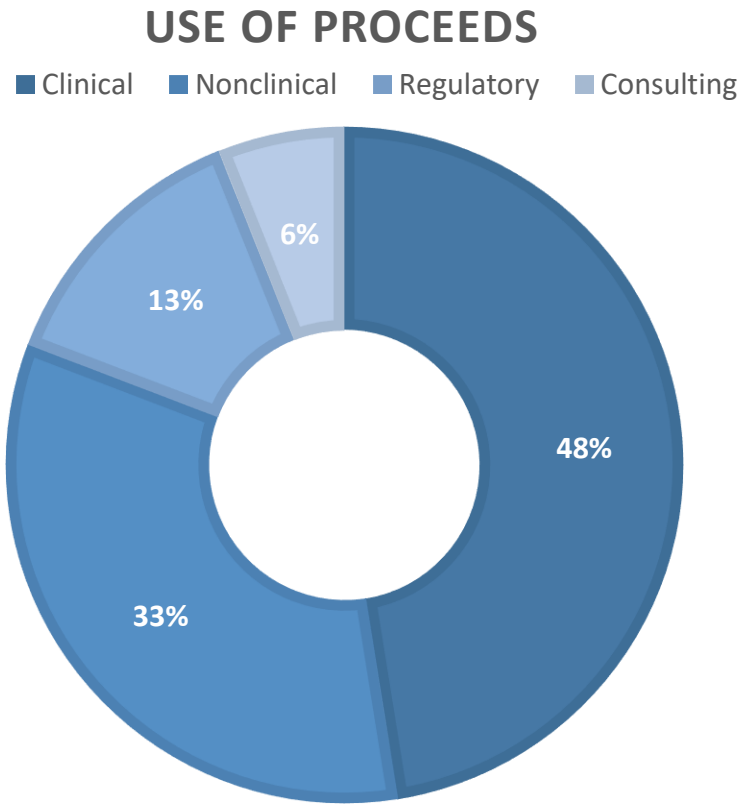
- DT678 is a novel prodrug where the active metabolite (M4) is identical to clopidogrel
- DT678 shows dose equivalence to clopidogrel in pharmacokinetic (PK) and pharmacodynamic (PD) studies

Superiority:

- DT678 has shown multiple benefits versus clopidogrel and other P2Y12 inhibitors
  - Greater potency, fewer metabolites and off target effects (e.g. bleeding)
  - no CYP2C19 or CES-1 patient variability, linear and predictable PK and PD, no dyspnea, once a day dosing, potential for reduced bleeding, faster onset with cardio and neuroprotection.

1. U.S. Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research (CDER)., 1999, *Applications Covered by Section 505(b)(2)*.

Use of Proceeds -7.5 Million to File DT678 NDA

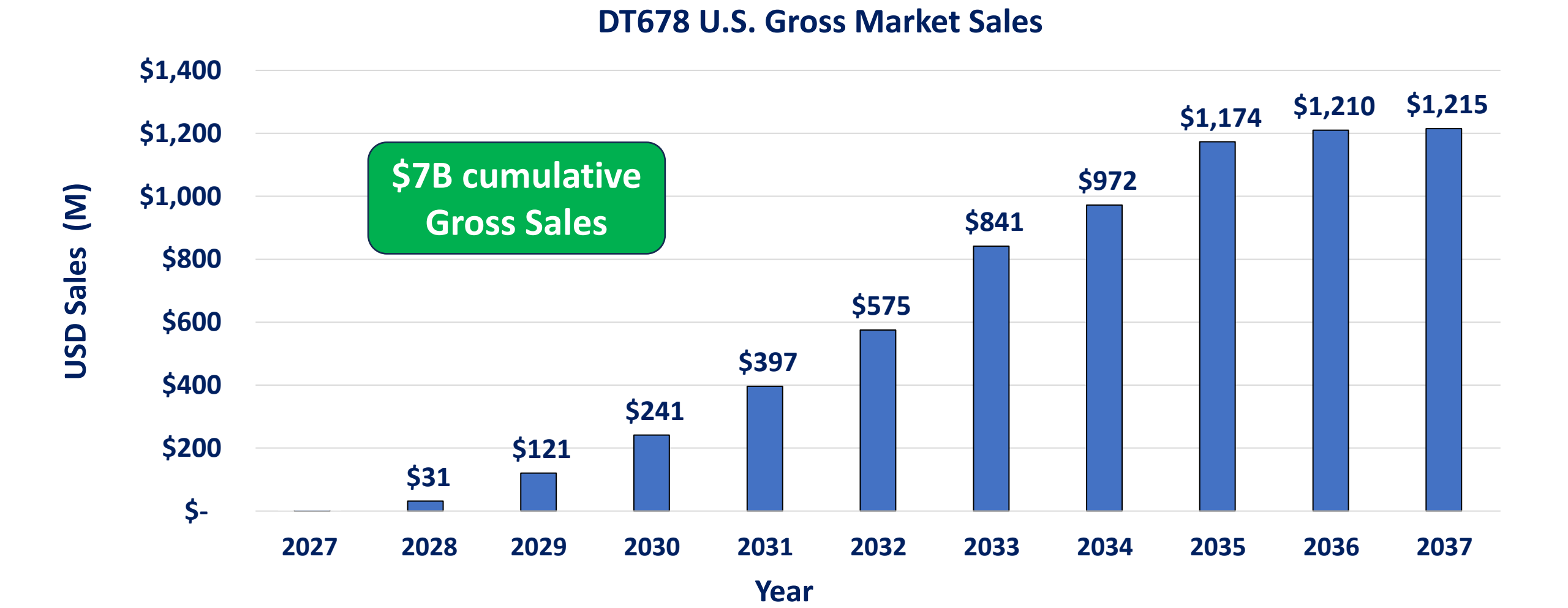


Planned Use of 7.5 Million

- **3.5 million - Clinical Study - CRO single site PK/PD study (48%)**
- **2.5 million – Nonclinical studies and FDA requests (33%)**
- **1 million – NDA regulatory filing (13%)**
- **0.5 million – Consulting, Clinical, PK/PD, Nonclinical, Regulatory (6%)**

DT678 US Forecast Aligned to Brilinta

Peaked at 10% Market Share in the U.S. by 2023



Assumed $495 per month per patient
IMS, GlobalData and Annual Reports

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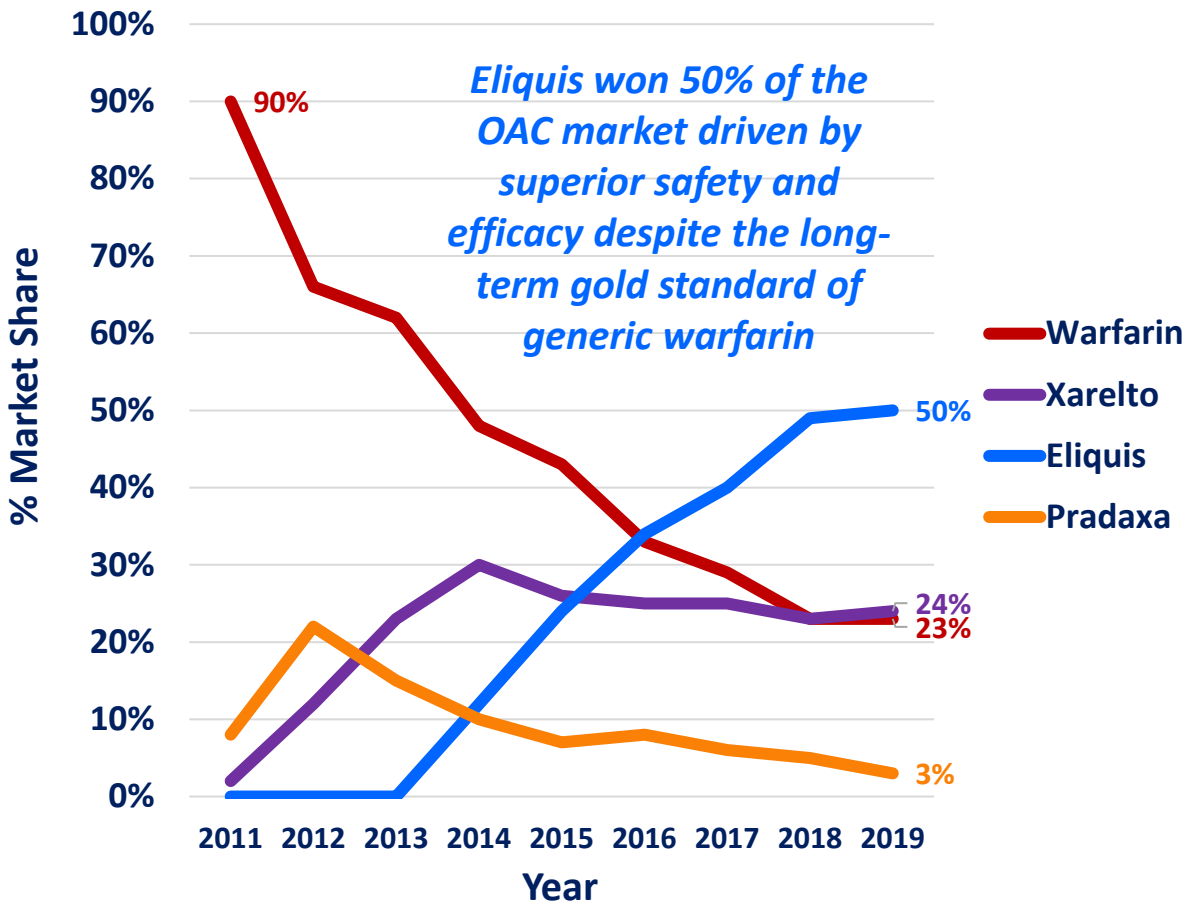
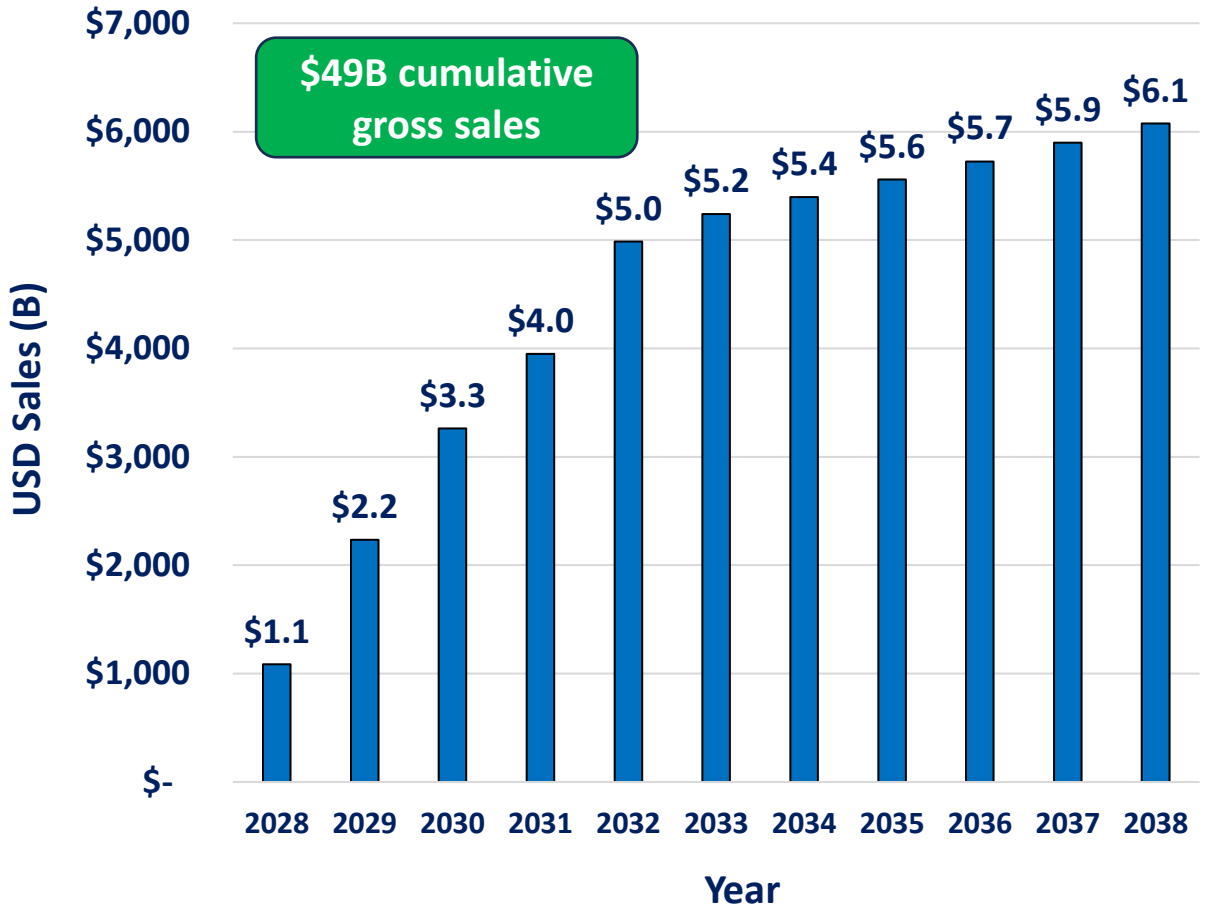
DT678 US Forecast Aligned to Eliquis

Peaked at 50% Market Share in the U.S. by 2023

NOAC Market Share Trends US

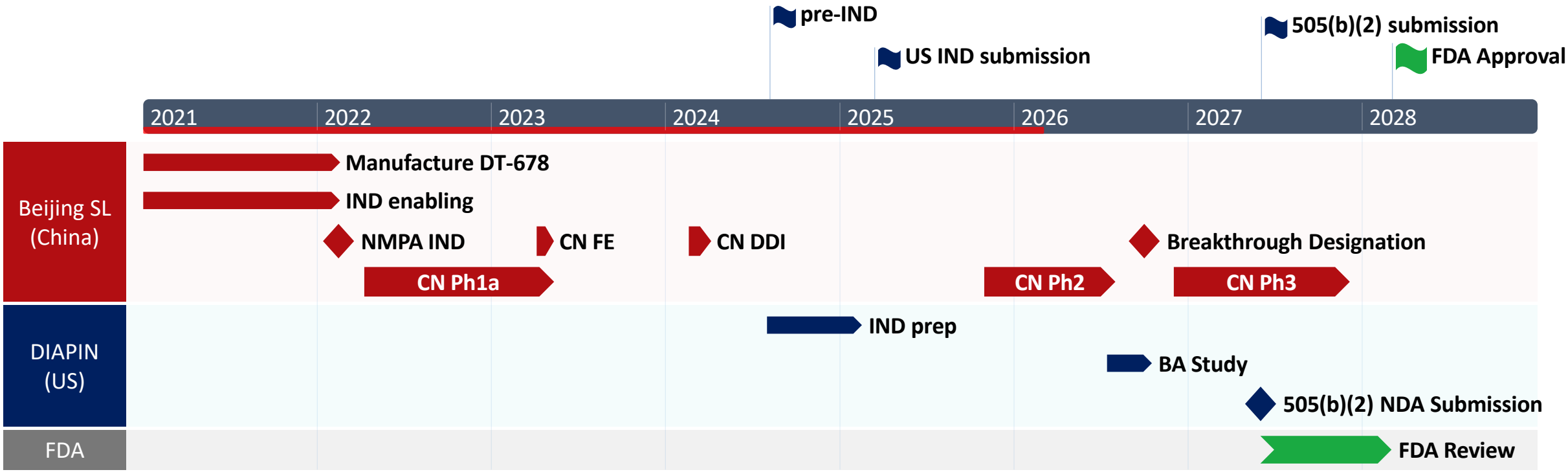


DT678 US Sales based on Eliquis Analog



Assumed $495 per month per patient
IMS, GlobalData and Annual Reports

DT678 NDA Approval Timeline*



Key Milestones:

- Start of US BA study
- Completion of Phase 2 study in China
- Completion of US BA study
- File 505(b)(2) NDA submission

$7.5 Million to US NDA submission

* Timeline contingent on funding

DT678 Intellectual Property Portfolio

Anticipating long-term patent protection through 2042 – DT678

NDA/EMA approval

TBD

2033

Composition of matter US-9718778 (61/750,633)

2035

Methods of use US-20170334853 (62/155,231)

2038

Methods of manufacture 62/624,494

2042

Additional patents anticipated

Issued or Validated Patent

Pending Patent

Intellectual Property Portfolio as of January 2025

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Opinions from Anti-Platelet Experts

"DT678 has sharpened the knife on clopidogrel with more potent sustained rapid onset. Efficacy with less bleeding is the holy grail"

McMaster University

"DT678 is a faster and safer clopidogrel. You achieved maximal anti-thrombotic activity in about 30 minutes, with IV option"

Icahn School of Medicine at Mount Sinai

"DT678 could be safer for HIV patients because retroviral agents reduce activity of ticagrelor and increase the activity of clopidogrel"

Cleveland Clinic Heart and Vascular Institute

"DT678 is a better version of prasugrel that is metabolized within one step. IV and oral is appealing"

HARVARD MEDICAL SCHOOL

DT678 Advantages

Less bleeds, better efficacy, faster onset and more flexibility

Risk	Property	DT-678[1,2]	Clopidogrel[3]	Ticagrelor[4]	Prasugrel[5]	Cangrelor[6]
Safety Concerns	No M5 metabolite to cause bleeds	✓	✗	✓	✗	✓
	Loading dose may not be required	✓	✗	✗	✗	✗
	Low dyspnea adverse event	✓	✓	✗	✓	✓
Diminished Efficacy	No dose adjustment	✓	✗	✗	✗	✗
	No interactions with CYP targeted drugs	✓	✗	✗	✗	✓
	No diminished efficacy for CYP2C19 PMs	✓	✗	✓	✓	✓
Onset of Action	Rapid onset of action (<5 min)	✓	✗	✗	✗	✓
	Ability to reverse receptor blockade*	✗	✗	✓	✗	✓
	Rapid offset of Action (<1 hour)	✗	✗	✗	✗	✓
Flexibility in Administration	IV and Oral dosages available	✓	✗	✗	✗	✗
	QD dosing to optimize compliance	✓	✓	✗	✓	✗
	Broad indication in ACS, MI and stroke	✓	✓	✓	✗	✗

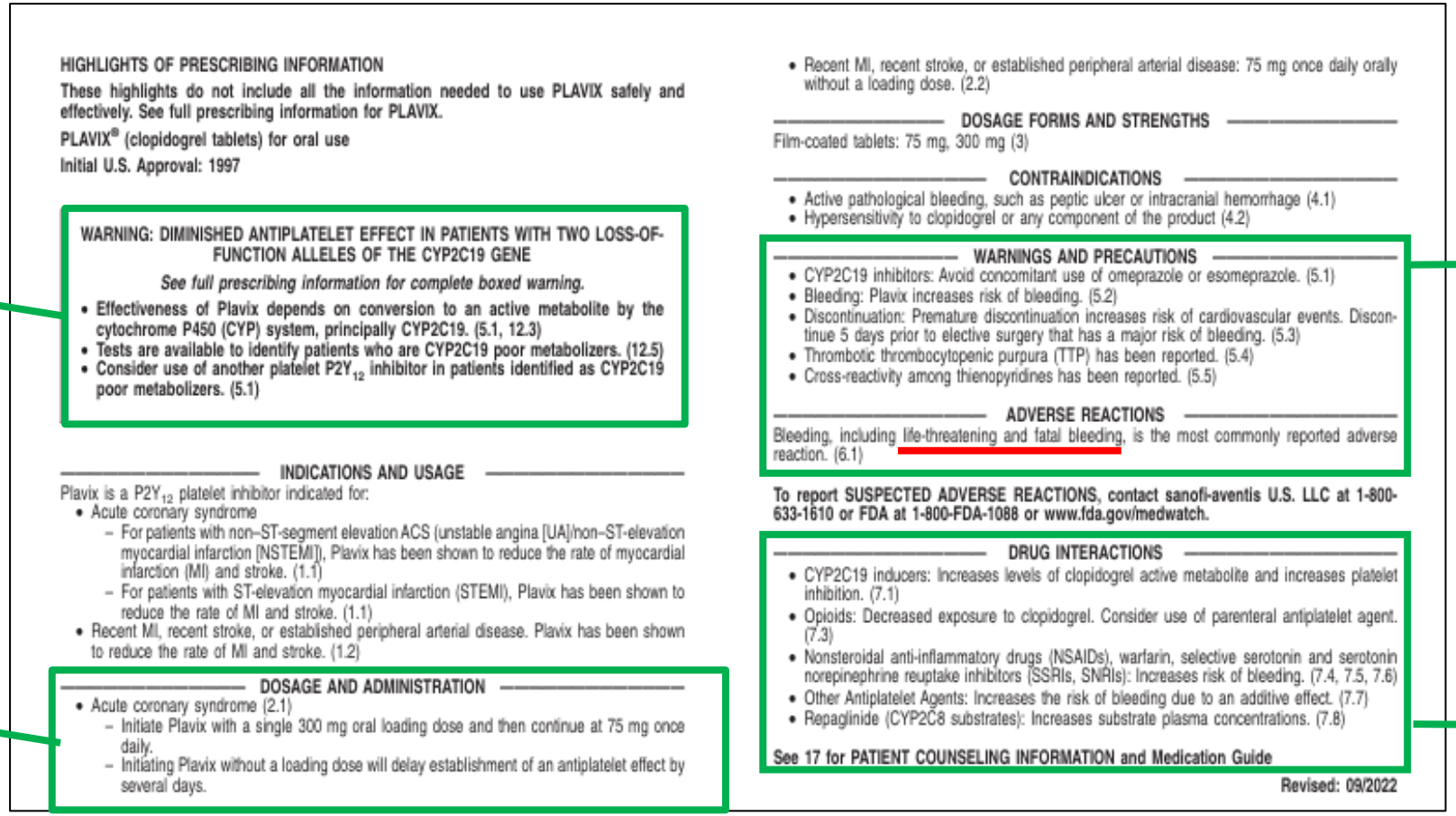
1. Zhang, H et al., 2014, *Thromb Haemost*., 112(6):1304-11., 2. Lauver, DA et al., 2019, *Pharmacol Res Perspect.,* 25;7(4):e00509., 3. FDA, 2016, Plavix® (clopidogrel) product label., 4. FDA, 2016, Brilinta® (ticagrelor) product label., 5. FDA, 2012, Effient® (prasugrel) product label., 6. FDA, 2019, Kengreal® (cangrelor) product label. PMs = poor metabolizers. *reversal via transfusion – most cost effective

DT678 Label Differences versus Plavix

Target Patients with CYP2C19 LOF, Obesity, Diabetes, Age & Bleeding Risk

Removal of black box warning

May not require loading dose



HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use PLAVIX safely and effectively. See full prescribing information for PLAVIX.

PLAVIX® (clopidogrel tablets) for oral use

Initial U.S. Approval: 1997

WARNING: DIMINISHED ANTIPLATELET EFFECT IN PATIENTS WITH TWO LOSS-OF-FUNCTION ALLELES OF THE CYP2C19 GENE

See full prescribing information for complete boxed warning.

- **Effectiveness of Plavix depends on conversion to an active metabolite by the cytochrome P450 (CYP) system, principally CYP2C19. (5.1, 12.3)**
- **Tests are available to identify patients who are CYP2C19 poor metabolizers. (12.5)**
- **Consider use of another platelet $P2Y_{12}$ inhibitor in patients identified as CYP2C19 poor metabolizers. (5.1)**

INDICATIONS AND USAGE

Plavix is a $P2Y_{12}$ platelet inhibitor indicated for:

- Acute coronary syndrome
  - For patients with non–ST-segment elevation ACS (unstable angina [UA]/non–ST-elevation myocardial infarction [NSTEMI]), Plavix has been shown to reduce the rate of myocardial infarction (MI) and stroke. (1.1)
  - For patients with ST-elevation myocardial infarction (STEMI), Plavix has been shown to reduce the rate of MI and stroke. (1.1)
- Recent MI, recent stroke, or established peripheral arterial disease. Plavix has been shown to reduce the rate of MI and stroke. (1.2)

DOSAGE AND ADMINISTRATION

- Acute coronary syndrome (2.1)
  - Initiate Plavix with a single 300 mg oral loading dose and then continue at 75 mg once daily.
  - Initiating Plavix without a loading dose will delay establishment of an antiplatelet effect by several days.
- Recent MI, recent stroke, or established peripheral arterial disease: 75 mg once daily orally without a loading dose. (2.2)

DOSAGE FORMS AND STRENGTHS

Film-coated tablets: 75 mg, 300 mg (3)

CONTRAINDICATIONS

- Active pathological bleeding, such as peptic ulcer or intracranial hemorrhage (4.1)
- Hypersensitivity to clopidogrel or any component of the product (4.2)

WARNINGS AND PRECAUTIONS

- CYP2C19 inhibitors: Avoid concomitant use of omeprazole or esomeprazole. (5.1)
- Bleeding: Plavix increases risk of bleeding. (5.2)
- Discontinuation: Premature discontinuation increases risk of cardiovascular events. Discontinue 5 days prior to elective surgery that has a major risk of bleeding. (5.3)
- Thrombotic thrombocytopenic purpura (TTP) has been reported. (5.4)
- Cross-reactivity among thienopyridines has been reported. (5.5)

ADVERSE REACTIONS

Bleeding, including life-threatening and fatal bleeding, is the most commonly reported adverse reaction. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact sanofi-aventis U.S. LLC at 1-800-633-1610 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- CYP2C19 inducers: Increases levels of clopidogrel active metabolite and increases platelet inhibition. (7.1)
- Opioids: Decreased exposure to clopidogrel. Consider use of parenteral antiplatelet agent. (7.3)
- Nonsteroidal anti-inflammatory drugs (NSAIDs), warfarin, selective serotonin and serotonin norepinephrine reuptake inhibitors (SSRIs, SNRIs): Increases risk of bleeding. (7.4, 7.5, 7.6)
- Other Antiplatelet Agents: Increases the risk of bleeding due to an additive effect. (7.7)
- Repaglinide (CYP2C8 substrates): Increases substrate plasma concentrations. (7.8)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide

Revised: 09/2022

No interaction with CYP2C19 inhibitors

DT678 Label Differences versus Brillinta

Target Patients with intercranial / bleeding risk, bradycardia and DDIs

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use BRILINTA safely and effectively. See full prescribing information for BRILINTA.

BRILINTA® (ticagrelor) tablets, for oral use
Initial U.S. Approval: 2011

WARNING: (A) BLEEDING RISK, and (B) ASPIRIN DOSE AND BRILINTA EFFECTIVENESS
See full prescribing information for complete boxed warning.
BLEEDING RISK
- **BRILINTA, like other antiplatelet agents, can cause significant, sometimes fatal bleeding. (5.1, 6.1)**
- **Do not use BRILINTA in patients with active pathological bleeding or a history of intracranial hemorrhage. (4.1, 4.2)**
- **Do not start BRILINTA in patients undergoing urgent coronary artery bypass graft surgery (CABG). (5.1, 6.1)**
- **If possible, manage bleeding without discontinuing BRILINTA. Stopping BRILINTA increases the risk of subsequent cardiovascular events. (5.4)**

ASPIRIN DOSE AND BRILINTA EFFECTIVENESS
- **Maintenance doses of aspirin above 100 mg reduce the effectiveness of BRILINTA and should be avoided. (2.1, 5.2, 14.1)**

---------- RECENT MAJOR CHANGES ----------
Warnings and Precautions, Bradyarrhythmias (5.5) 09/2016

---------- INDICATIONS AND USAGE ----------
BRILINTA is a $P2Y_{12}$ platelet inhibitor indicated to reduce the rate of cardiovascular death, myocardial infarction, and stroke in patients with acute coronary syndrome (ACS) or a history of myocardial infarction (MI). For at

---------- DOSAGE AND ADMINISTRATION ----------
Initiate treatment with 180 mg oral loading dose following an ACS event. Continue treatment with 90 mg twice daily during the first year after an ACS event. After one year, administer 60 mg twice daily. (2.1)
Use BRILINTA with a daily maintenance dose of aspirin of 75-100 mg. (2.1, 5.2)

---------- DOSAGE FORMS AND STRENGTHS ----------
- 60 mg and 90 mg tablets (3)

---------- CONTRAINDICATIONS ----------
- History of intracranial hemorrhage (4.1)
- Active pathological bleeding (4.2)
- Hypersensitivity to ticagrelor or any component of the product (4.3)

---------- WARNINGS AND PRECAUTIONS ----------
- Dyspnea was reported more frequently with BRILINTA than with control agents in clinical trials. Dyspnea resulting from BRILINTA is self-limiting. (5.3)
- Severe Hepatic Impairment: Likely increase in exposure to ticagrelor. (5.6)

---------- ADVERSE REACTIONS ----------
Most common adverse reactions are bleeding 12% and dyspnea 14%. (5.1, 5.3, 6.1)
To report SUSPECTED ADVERSE REACTIONS, contact AstraZeneca at 1-800-236-9933 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

---------- DRUG INTERACTIONS ----------
- Avoid use with strong CYP3A inhibitors or CYP3A inducers. (7.1, 7.2)
- Patients receiving more than 40 mg per day of simvastatin or lovastatin may be at increased risk of statin-related adverse effects. (7.4)
- Monitor digoxin levels with initiation of or any change in BRILINTA. (7.5)

Risk of intercranial bleeding

Risk of Bradycardia

1x daily, reduced dosing errors

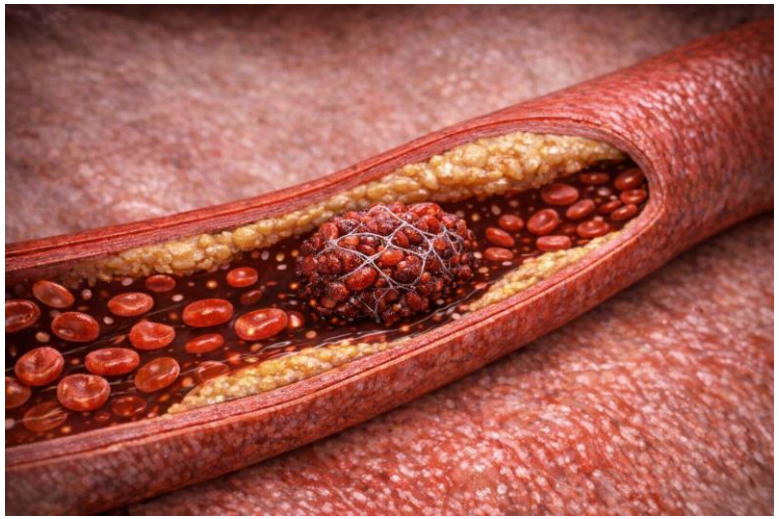
Contraindicated in patients with intercranial bleeding and pathological bleeding

Dyspnea and hepatic impairment Side effects

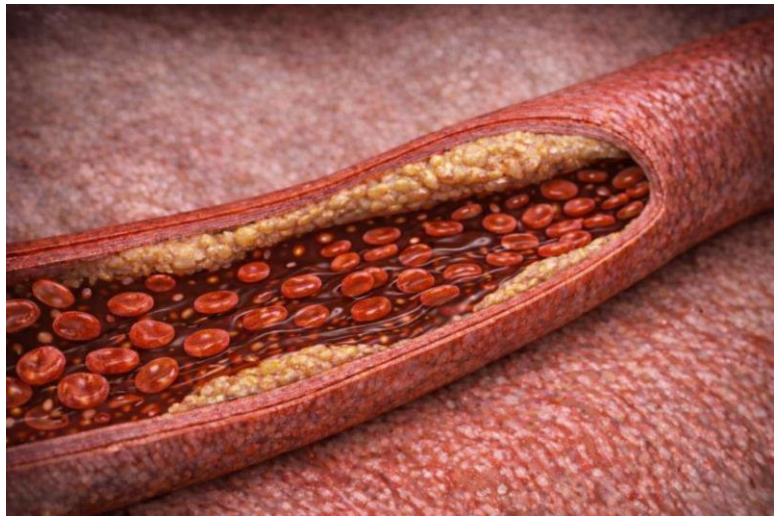
CYP3A4 and Drug-Drug interactions

DT678 Prevents Clot Formation
DT109 Reduces Atherosclerosis and Inflammation

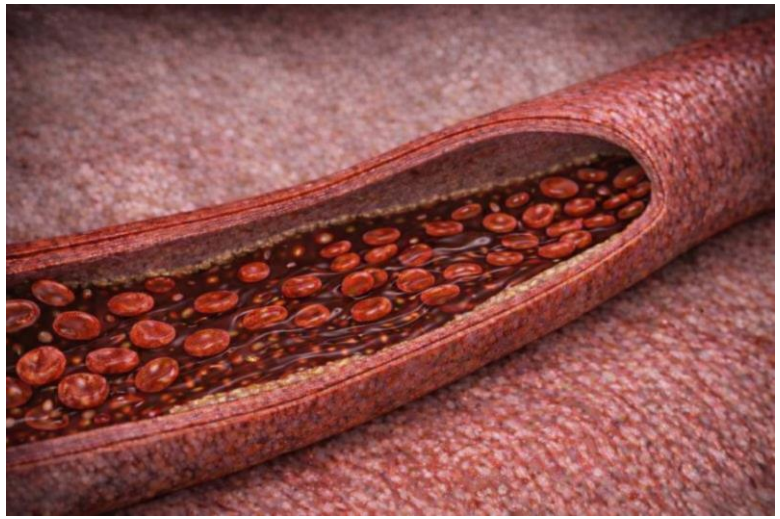
Artery blocked with atherosclerosis + clot



Artery with atherosclerosis



Artery with reduced atherosclerosis



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DT678 prevents clot formation Preventing artery blockages, heart attacks, strokes, heart and brain damage

DT109 reverses atherosclerosis preventing artery narrowing, stenosis, reduced blood flow and heart and brain damage

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