



DIAPIN Therapeutics

**Developing Novel Transformative Therapies for
Cardiovascular and Metabolic Diseases**

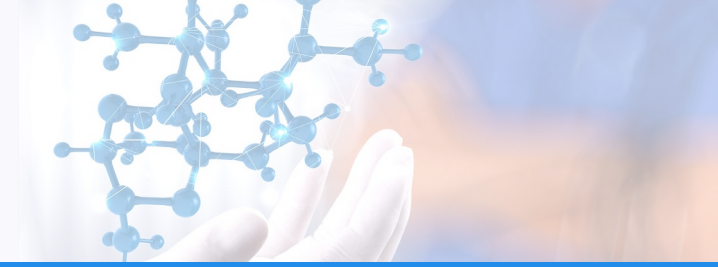


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www.diapin.com



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Diapin Therapeutics, Inc.



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Cardiovascular Disease is the Leading Cause of Death¹

1 death every 1.6 seconds¹
1 in 3, ~20M global deaths per year¹,

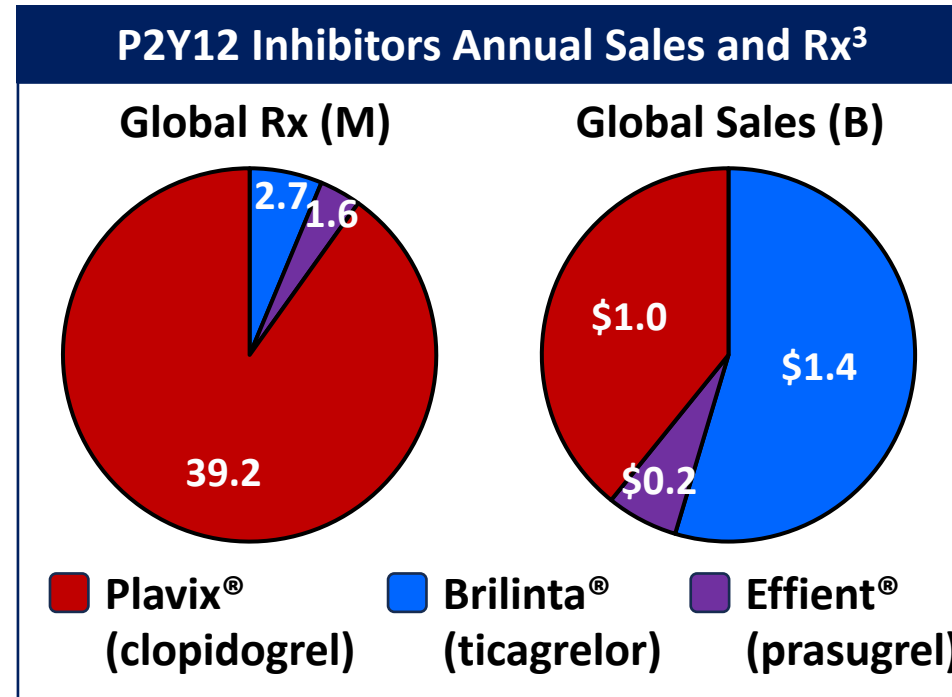
Est. Costs by 2030²
1 Trillion

Most deaths are **preventable**²

Market Landscape - Established Standard of Care



- **>32M heart** attacks and strokes every year¹
- The AHA Guidelines - dual antiplatelet therapy (aspirin + P2Y12 inhibitor) to reduce risk of future heart attack, stroke and coronary stent thrombosis²



- 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!

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.

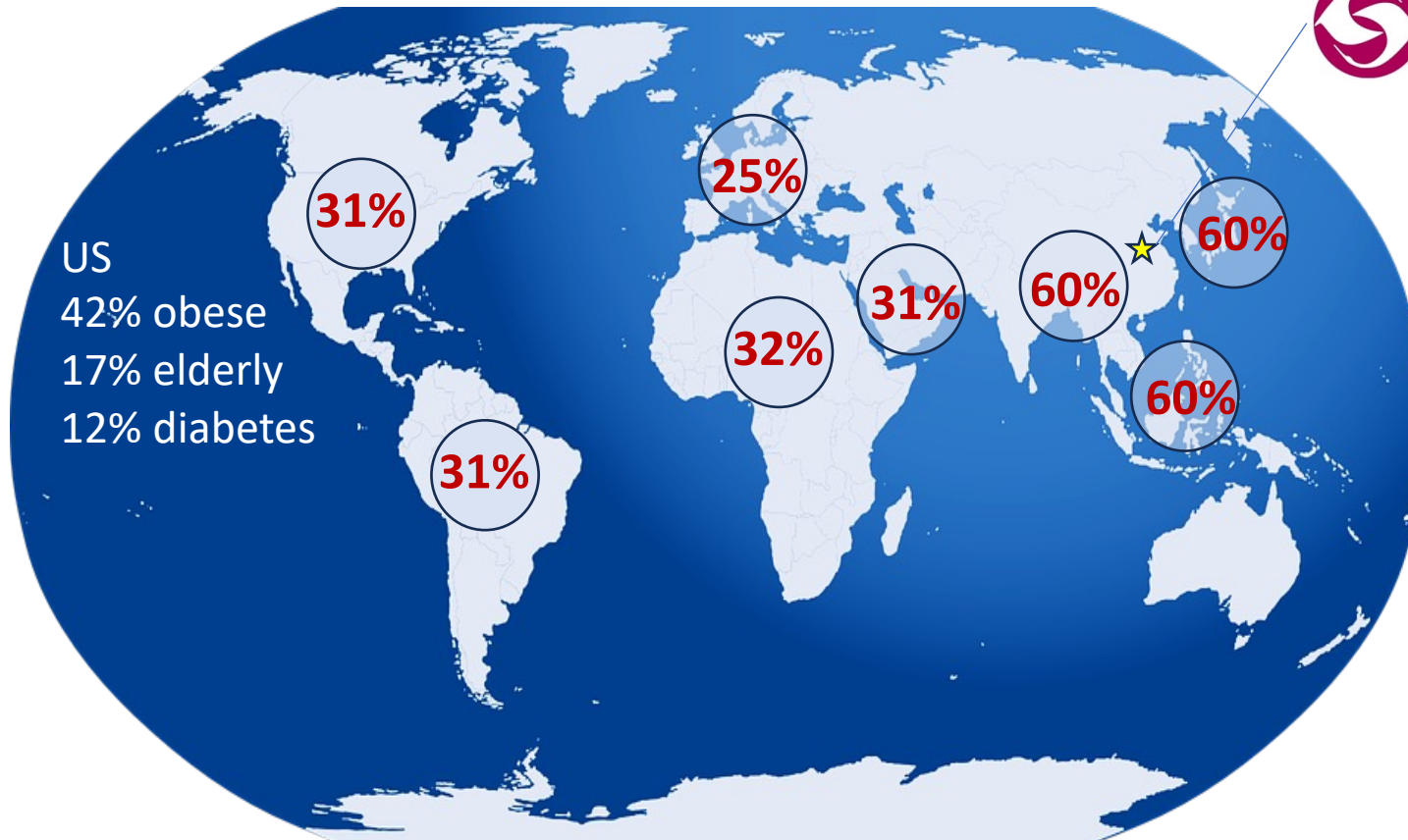
- Effectiveness of Plavix depends on conversion to an active metabolite by the cytochrome P450 (CYP) system, principally CYP2C19. (5.1, 12.3)
- Tests are available to identify patients who are CYP2C19 poor metabolizers. (12.5)
- Consider use of another platelet P2Y12 inhibitor in patients identified 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 CYP2C19¹ LoF Mutations



% IM and PMs

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

Reduced clopidogrel efficacy in **diabetics³, obese⁴ & elderly patients⁵** with lower CYP2C19 function.⁶

Beijing SL collaboration.
Phase 2 in progress.

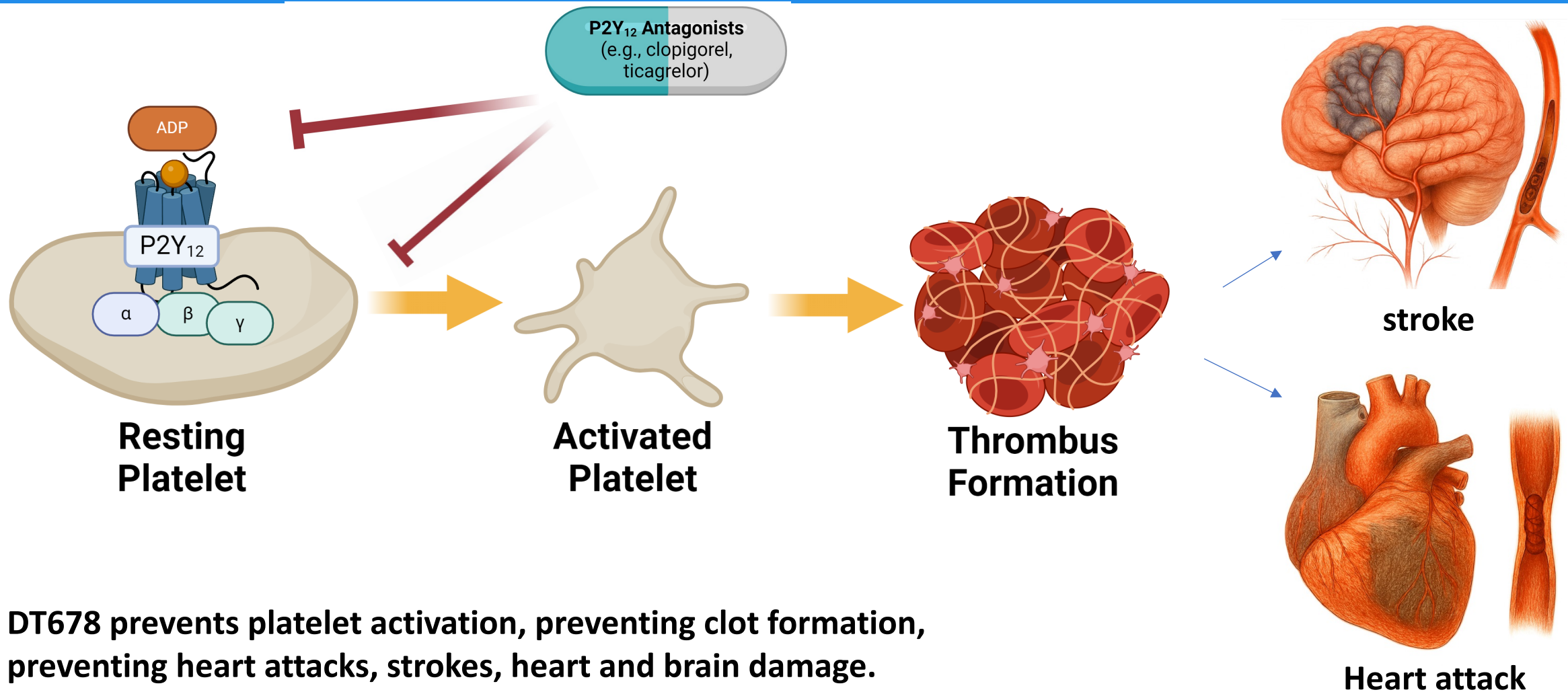
Patients with CYP2C19 LoF mutations have increased risk of major adverse cardiovascular events if treated with clopidogrel²

1. Klein MD, 2019, *Arter, Thromb, & Vasc Biol*, 39:4., 2. Beitelshes AL, et. al, 2022, *JAHA*, 11(4):e024159.

6 3. Shahim B. et al, 2023, *JAHA*, 12(1): e026482. 4. Puccini M. *Cardiovasc Drug Ther* 2023 Aug;37(4):833-837.

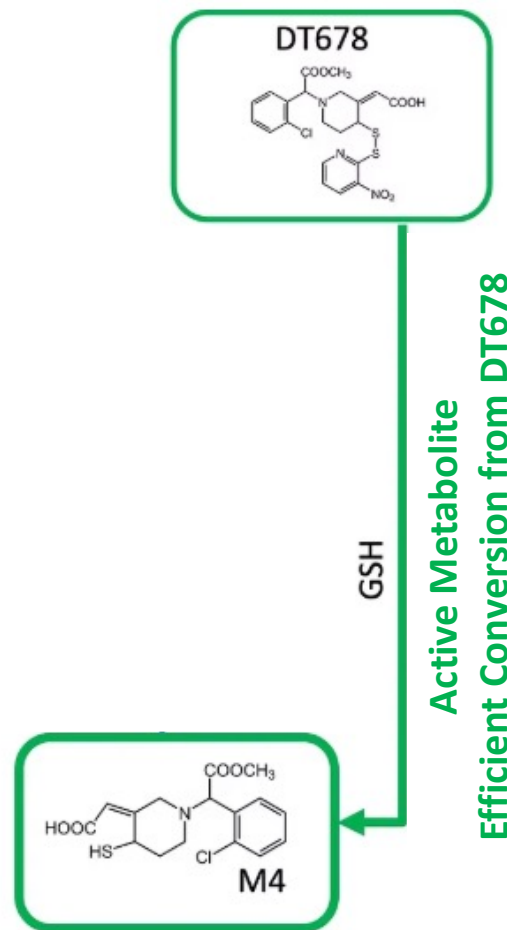
5. Abudahab S, *Pharmacogenomics* 2024, 25(1) 41-54 , 6. Tomlinson B et al, 2023, *Exp Opin on Drug Met & Tox*, 19:12, 867-870.

Mechanism of Action P2Y₁₂ Antagonists



Introducing DT678

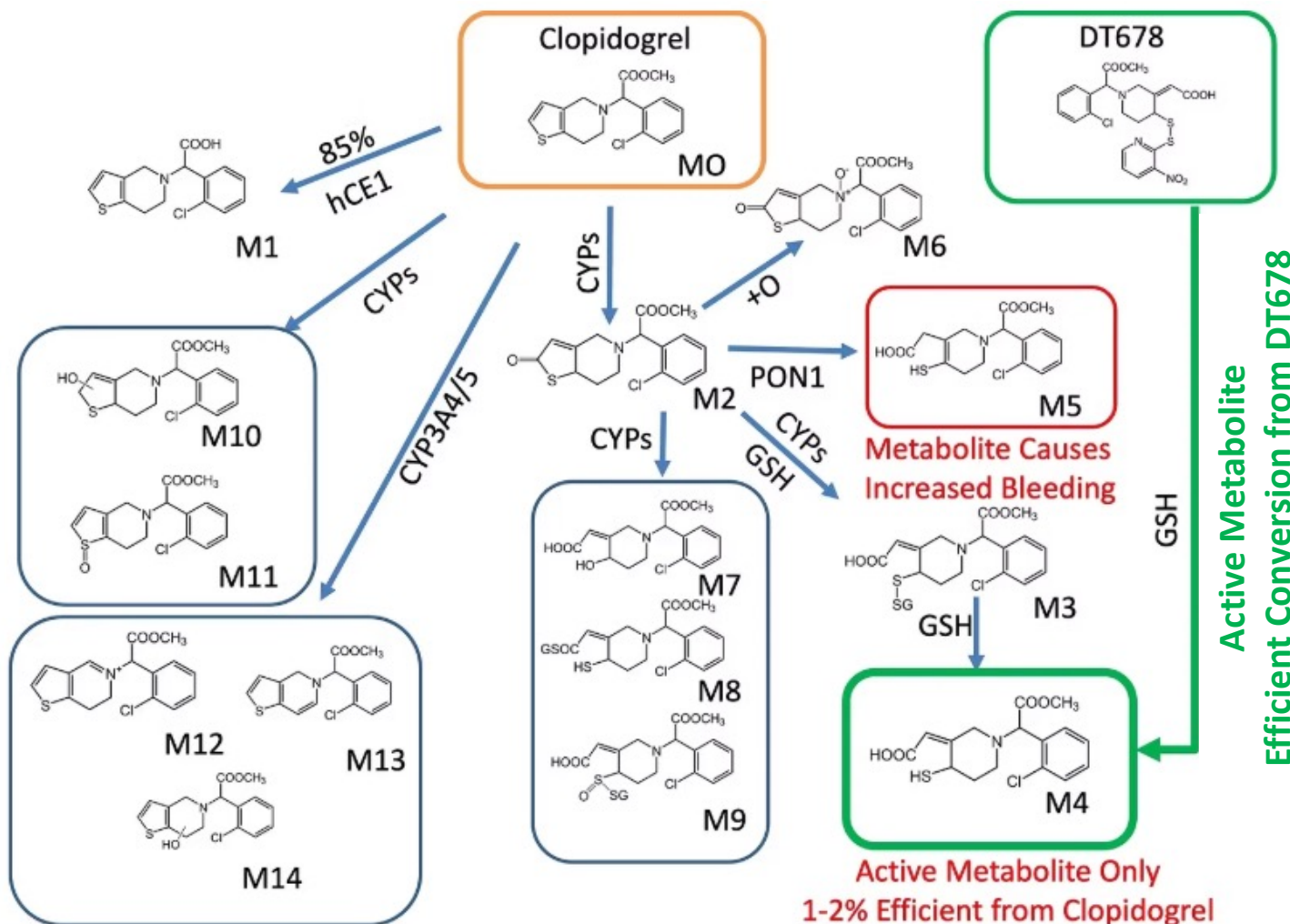
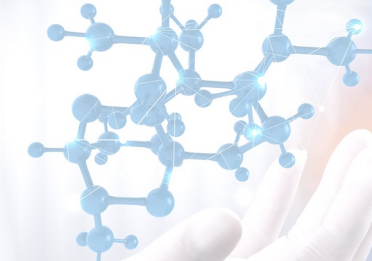
Novel Prodrug Synthesized Using an AI Designed Enzyme



- DT678 is synthesized using an AI designed CYP enzyme¹
- DT678 is converted to M4, independently of hepatic cytochrome P450 (CYP) enzymes including CYP2C19^{4,5}

Introducing DT678

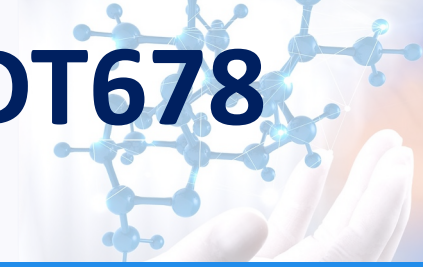
Novel Prodrug Synthesized Using an AI Designed Enzyme



- DT678 is synthesized using an AI designed CYP enzyme¹
- 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, M4²
- ~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}

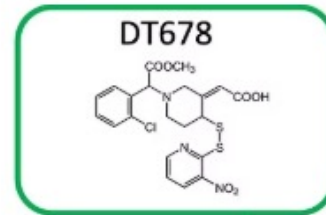
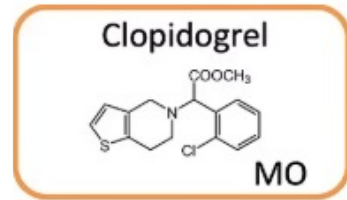
Introducing New Antiplatelet Drug DT678

Novel Prodrug Synthesized Using an AI Designed Enzyme

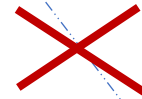


Clopidogrel does **NOT** work well in patients with loss of CYP2C19 function = **25-60%** of patients or in patients with reduced metabolic function

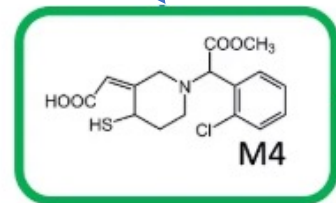
= heart attack, stroke, death



M UNIVERSITY OF MICHIGAN



GSH

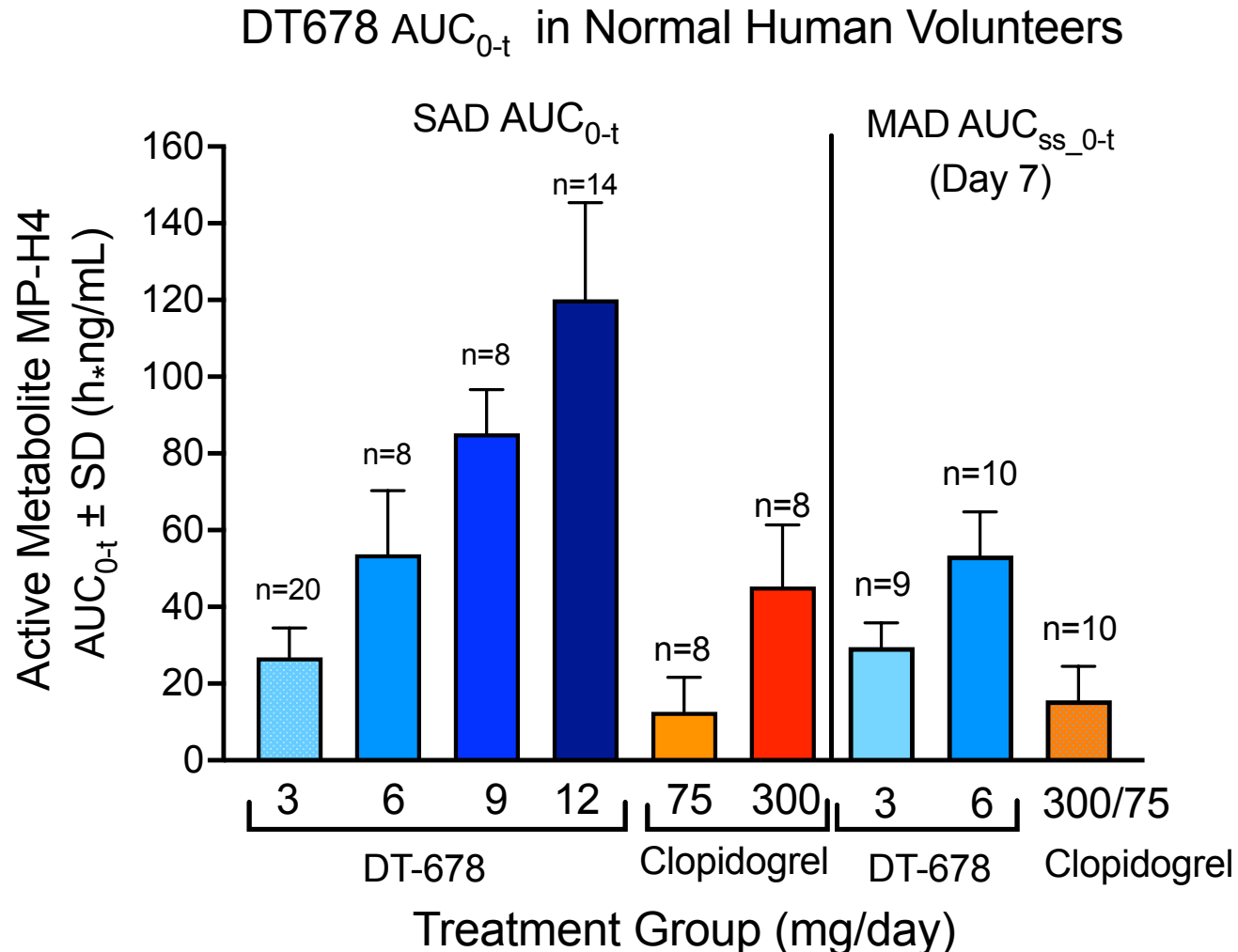
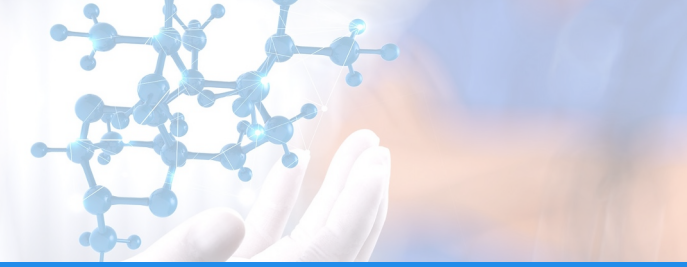


Active Metabolite
Efficient Conversion from DT678

- 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 SAD/MAD Study Results

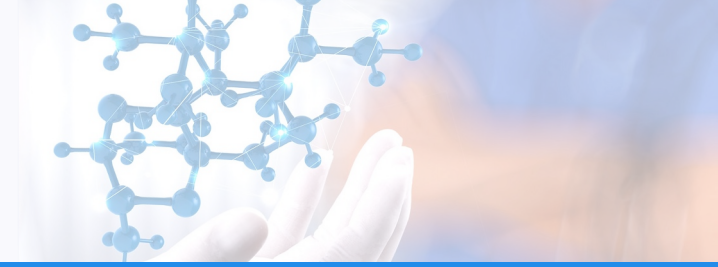
3mg of DT678 Results in Similar AUC_{0-t} as Clopidogrel 75mg



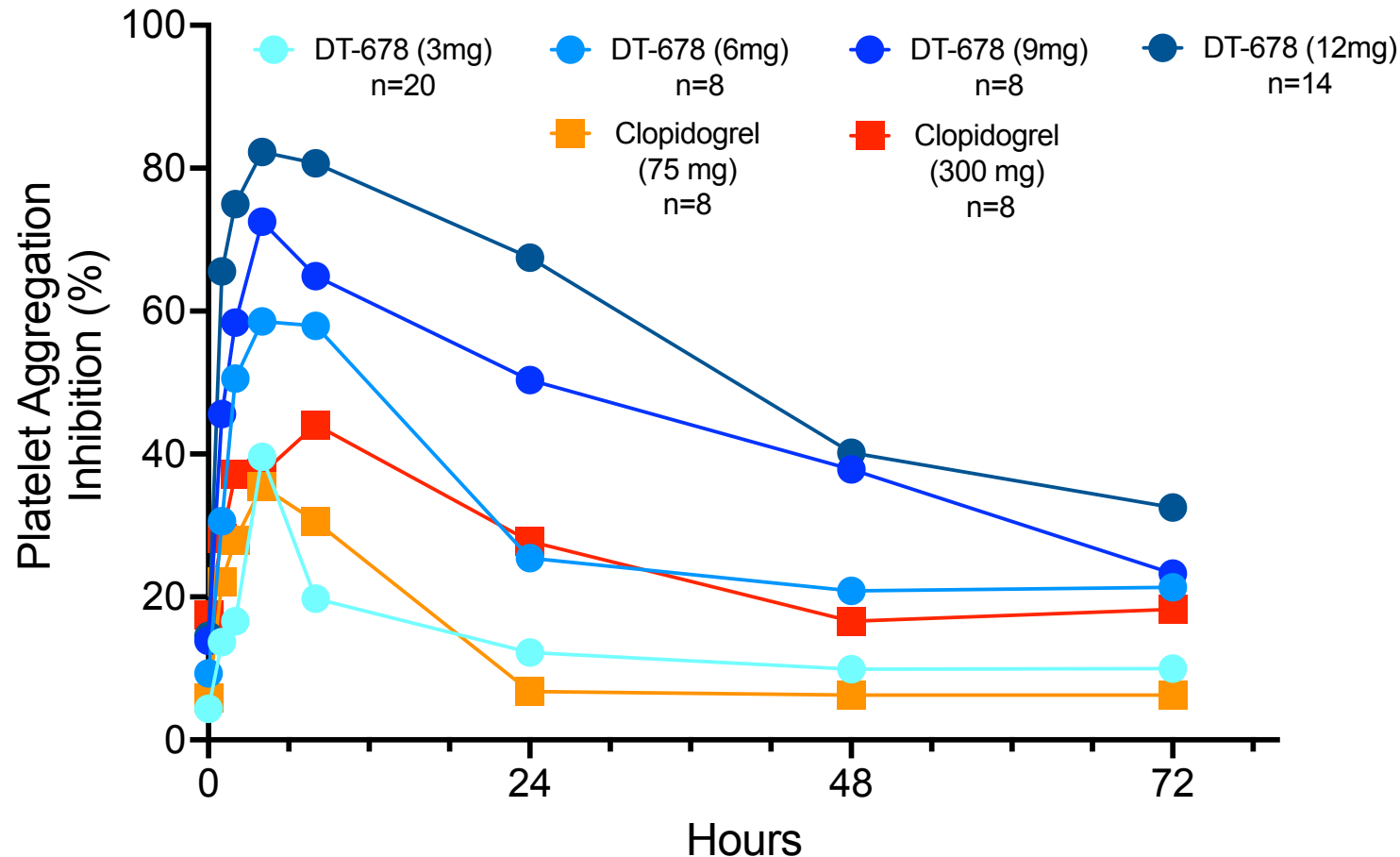
- IND filed in China and US.
- DT678 has nonclinical neuro and cardio protective benefits versus clopidogrel.
- DT678 has linear dose proportional PK
- The active metabolite is generated efficiently from 3mg DT678 with similar AUC to clopidogrel 75mg at day 1 and day 7
- DT678 has a favorable safety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

Phase 1 Results

3mg of DT678 is Equivalent to 75mg of Clopidogrel



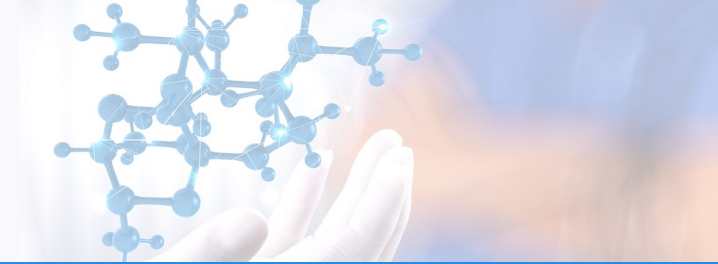
Single Ascending Dose Pharmacodynamics of DT-678 and Clopidogrel in Normal Human Volunteers



- 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

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.

DT678 Advantages

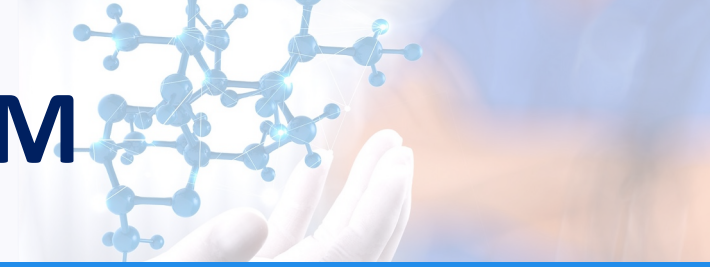
Improved safety, efficacy, faster onset, less bleeding and more flexibility



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	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.

Funding Status – Seed Stage Raising 7.5M



Pharma with CVMD portfolios



EXIT

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

~1bn Comparable Exits

Exit at NDA submission
to Biotech or Pharma
partner

Seed Round 7.5 Million
3 million committed

\$7.5M

EXIT

Series A

EXIT

Revenue
generating

NDA approved,
Launch DT678

EXIT

Phase 1s Completed (China)
IND filed (US & China) in Ph2

\$6M

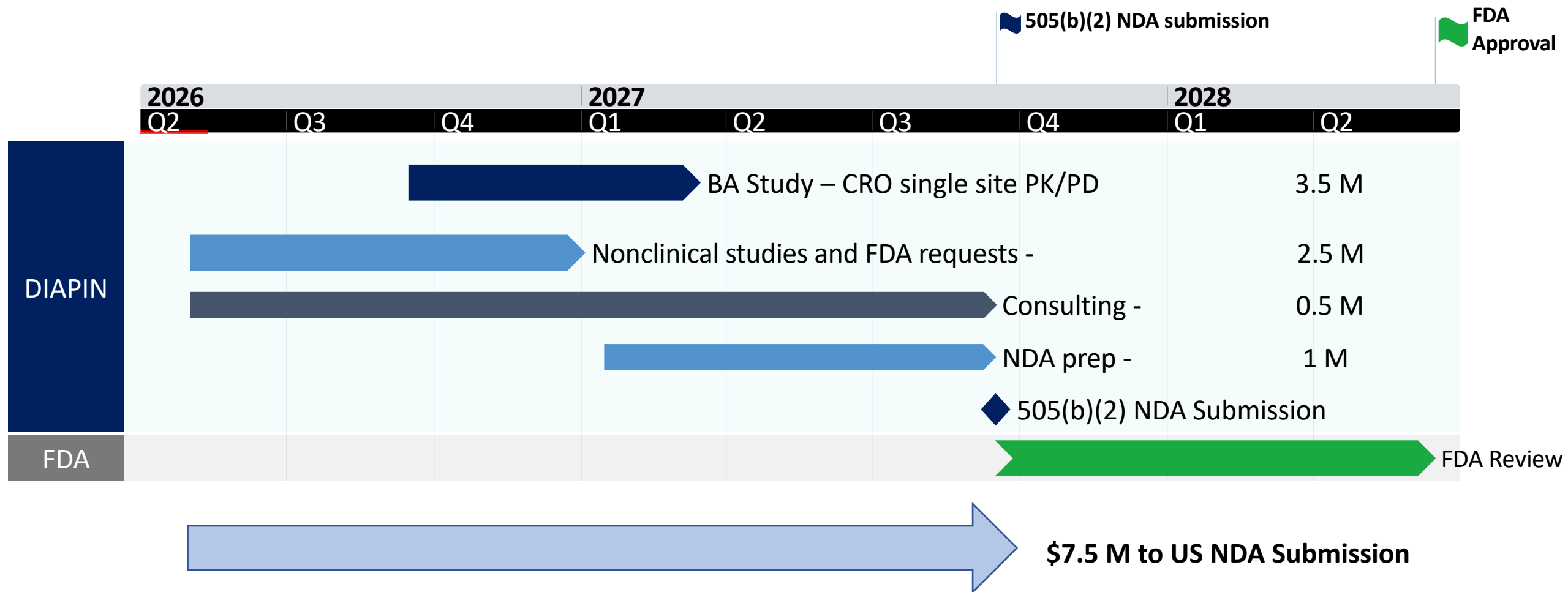


Grants, Beijing SL, Founders, and Investors

Bioavailability Study, Response to FDA Requests, file NDA

Prepare for NDA approval, Launch, IPO

DT678 Use of 7.5 Million Seed Round



Diapin Therapeutics Team

Successful Track Record and Exits Through NDA and Commercialization



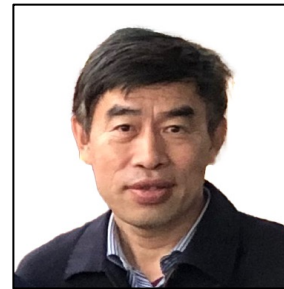
Jessica Reed, Ph.D.
CEO, Board Member
Millendo, MMS, Pfizer,
Parke-Davis



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



Diapin Scientific Advisory Team

Best-in-class and Diverse Medical Team Guiding Development



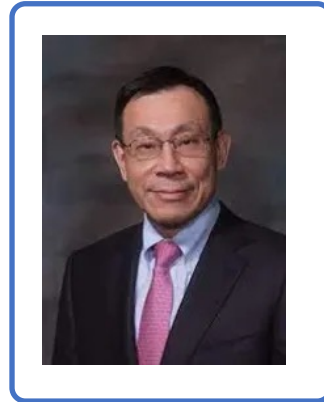
Dr. Dan Eitzman, MD

Professor of Internal
Medicine
University of Michigan
Medical School



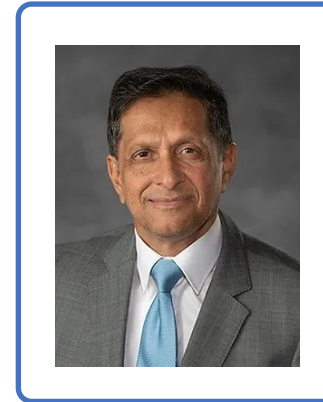
Dr. Charles Burant, MD, PhD

Dr. Robert C. and Veronica
Atkins Professor of
Metabolism
University of Michigan
School of Public Health



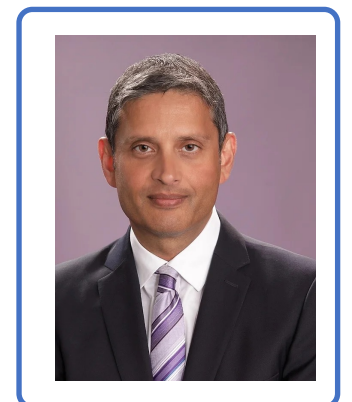
Dr. George King, MD

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



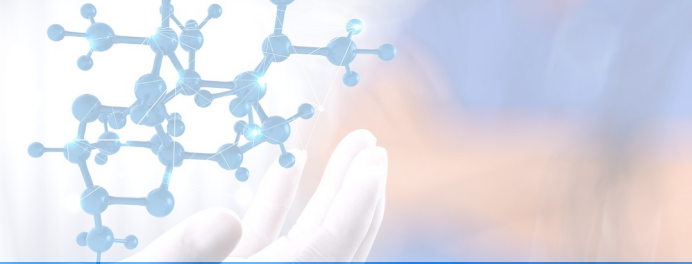
Dr. Shamir Mehta, MD

Douglas A. Holder Endowed
Chair and Professor of Medicine
McMaster University



Diapin Pipeline

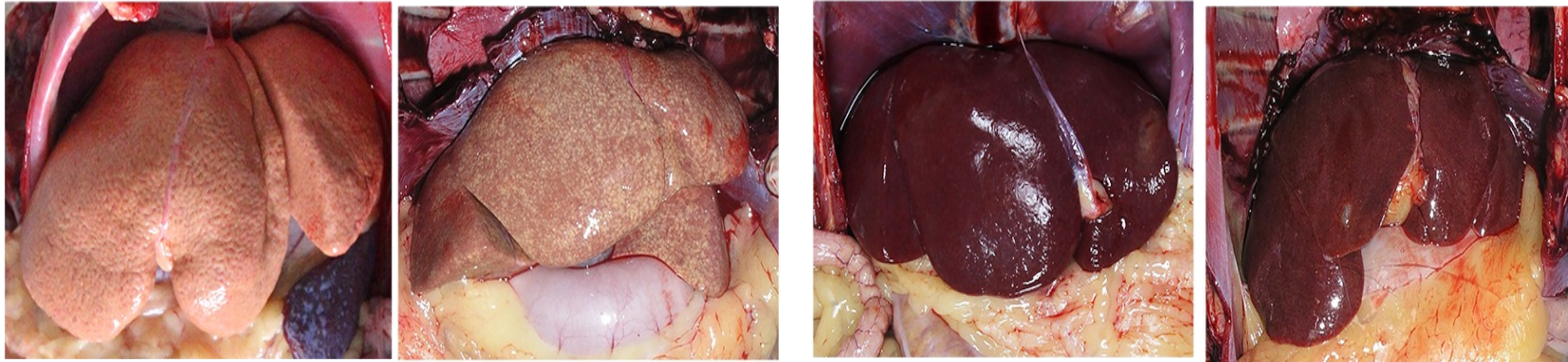
Cardiovascular and Metabolic Disease Treatment Innovation



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

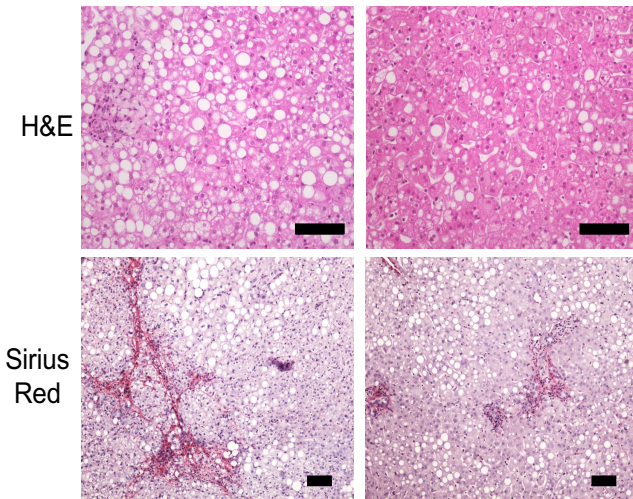
DT109 MASH efficacy in Non-Human Primates

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



Vehicle

DT-109

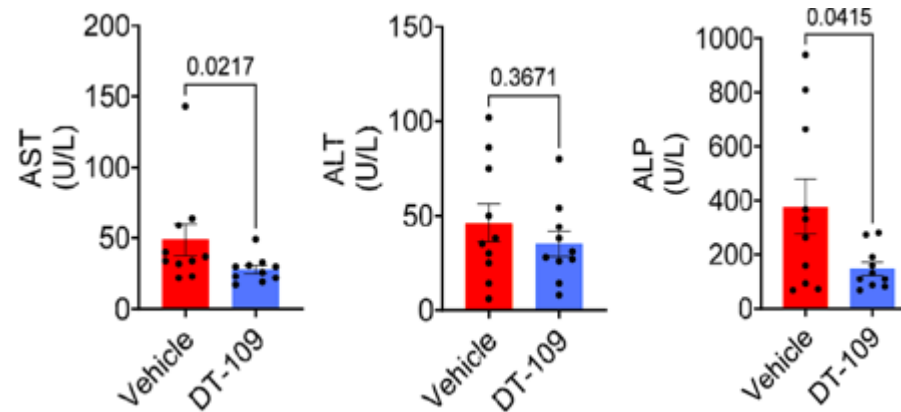


H&E

Sirius
Red

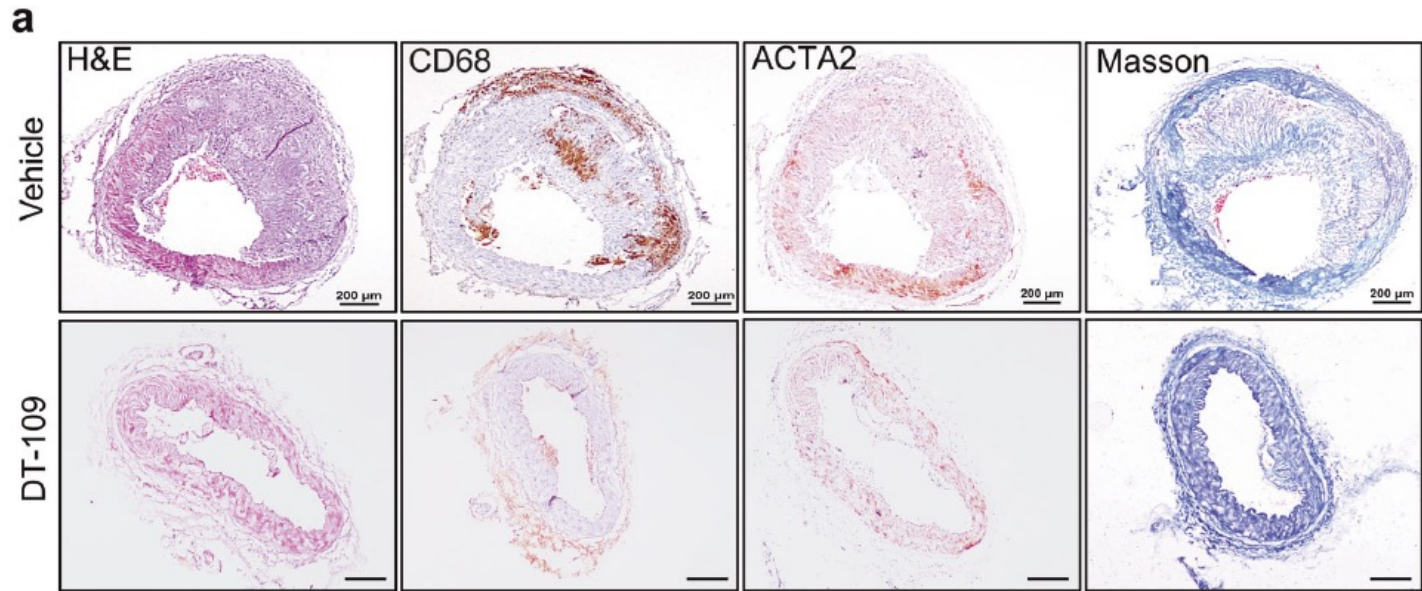
Vehicle

DT-109

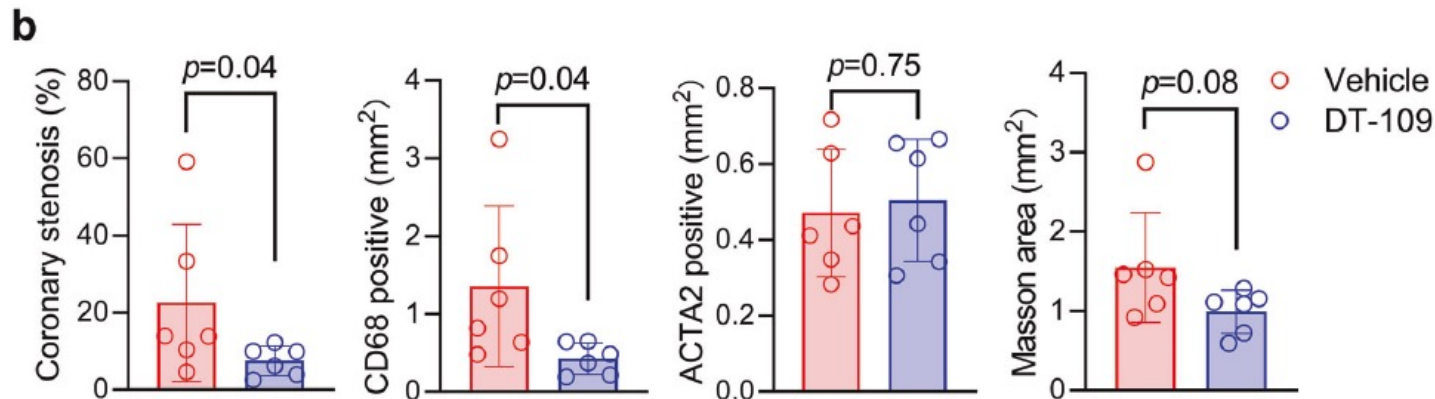


- DT109 significantly decreased overall Liver Fat
- DT109 reduced liver fat content, fibrosis and scarring
- DT109 reduced liver enzymes: AST, ALT and ALP

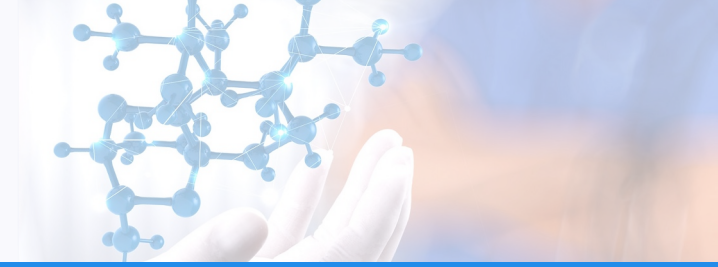
DT109 Attenuates Atherosclerosis and Vascular Calcification in NHPs



- DT109 caused a significant reduction in coronary stenosis and macrophage infiltration.
- These results demonstrate that DT109 significantly inhibited coronary atherosclerosis in addition to aortic lesions.



Invest in Diapin and Help Save Lives



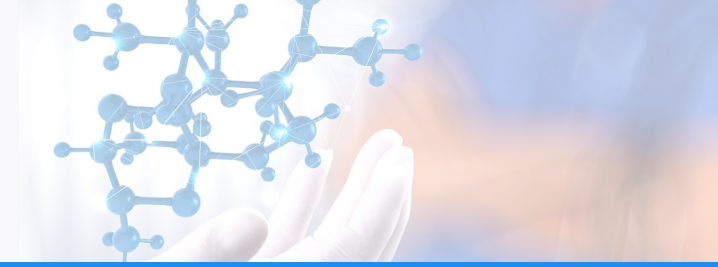
Raising seed round of \$7.5 million to File DT678 US New Drug Application

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

For more information contact: Jessica Reed, CEO. jreed@diapin.com

<https://www.diapin.com/investors>





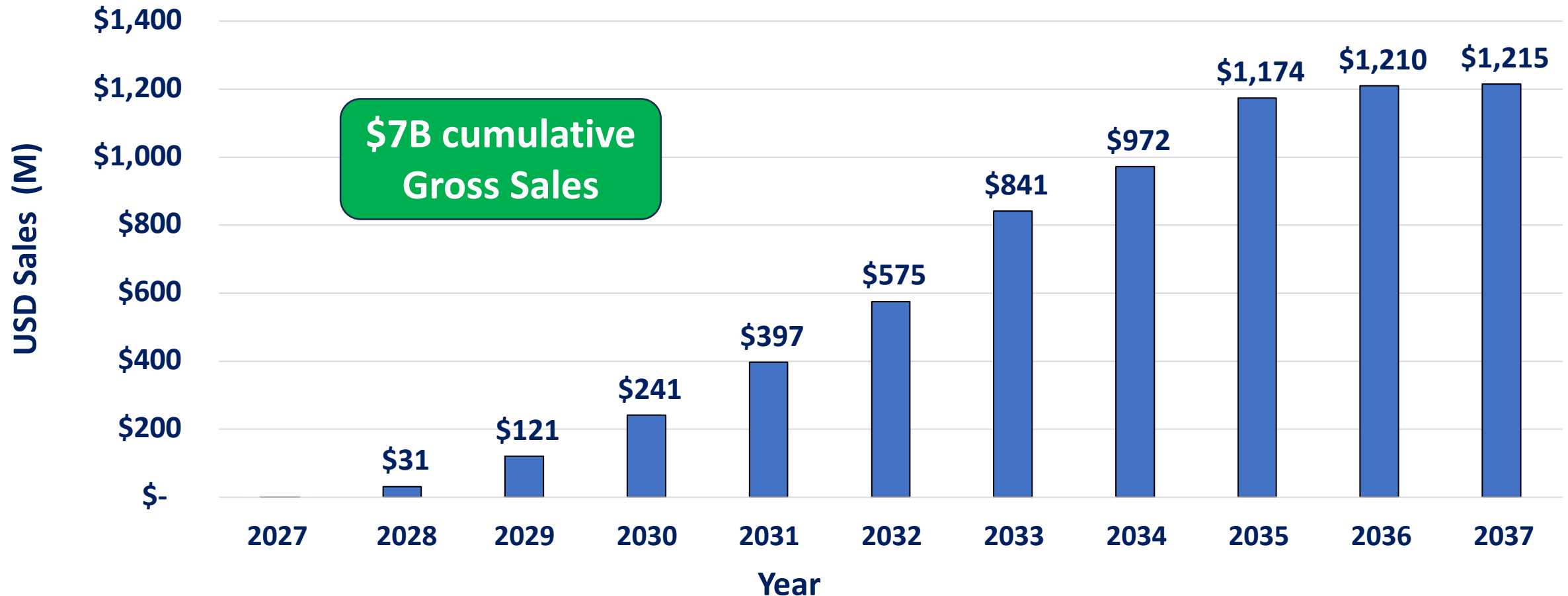
Appendix

DT678 US Forecast Aligned to Brilinta

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



DT678 U.S. Gross Market Sales

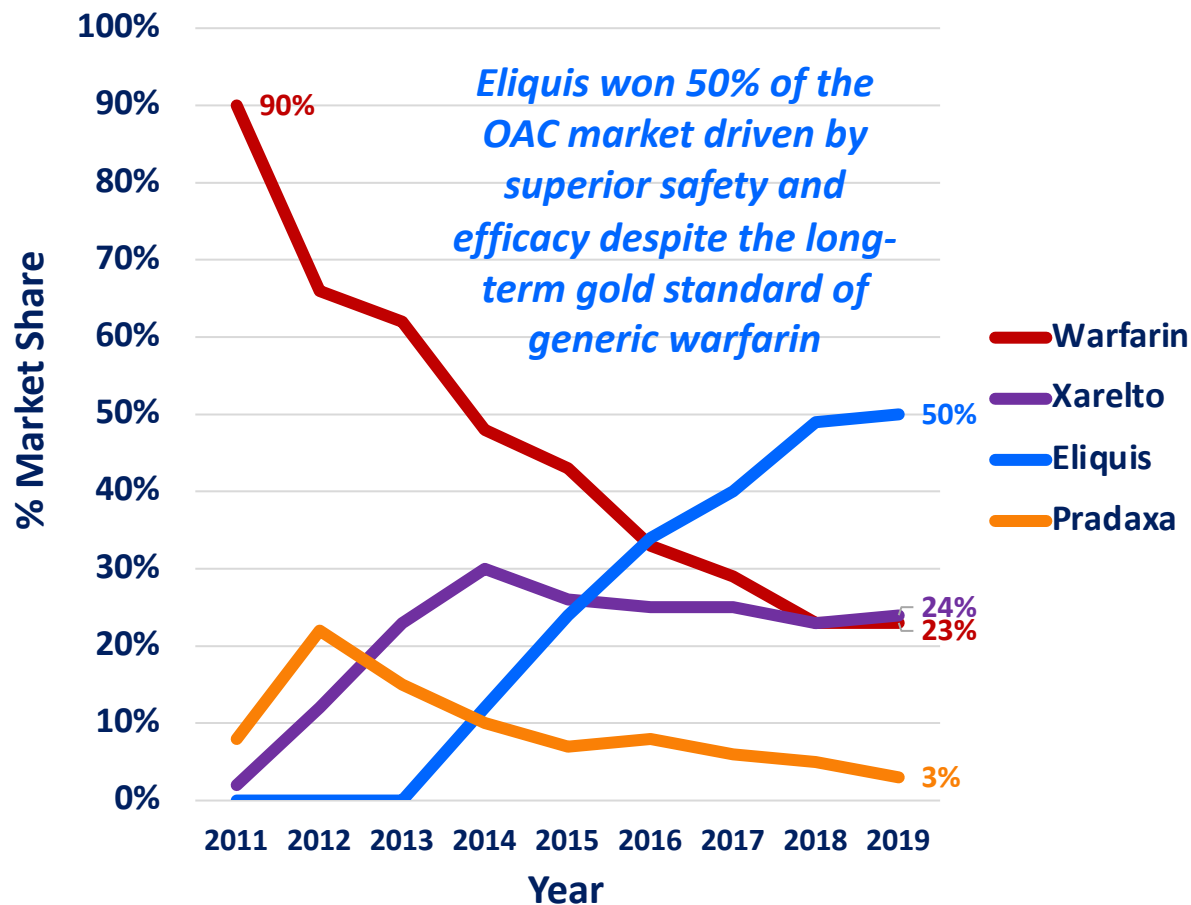


DT678 US Forecast Aligned to Eliquis

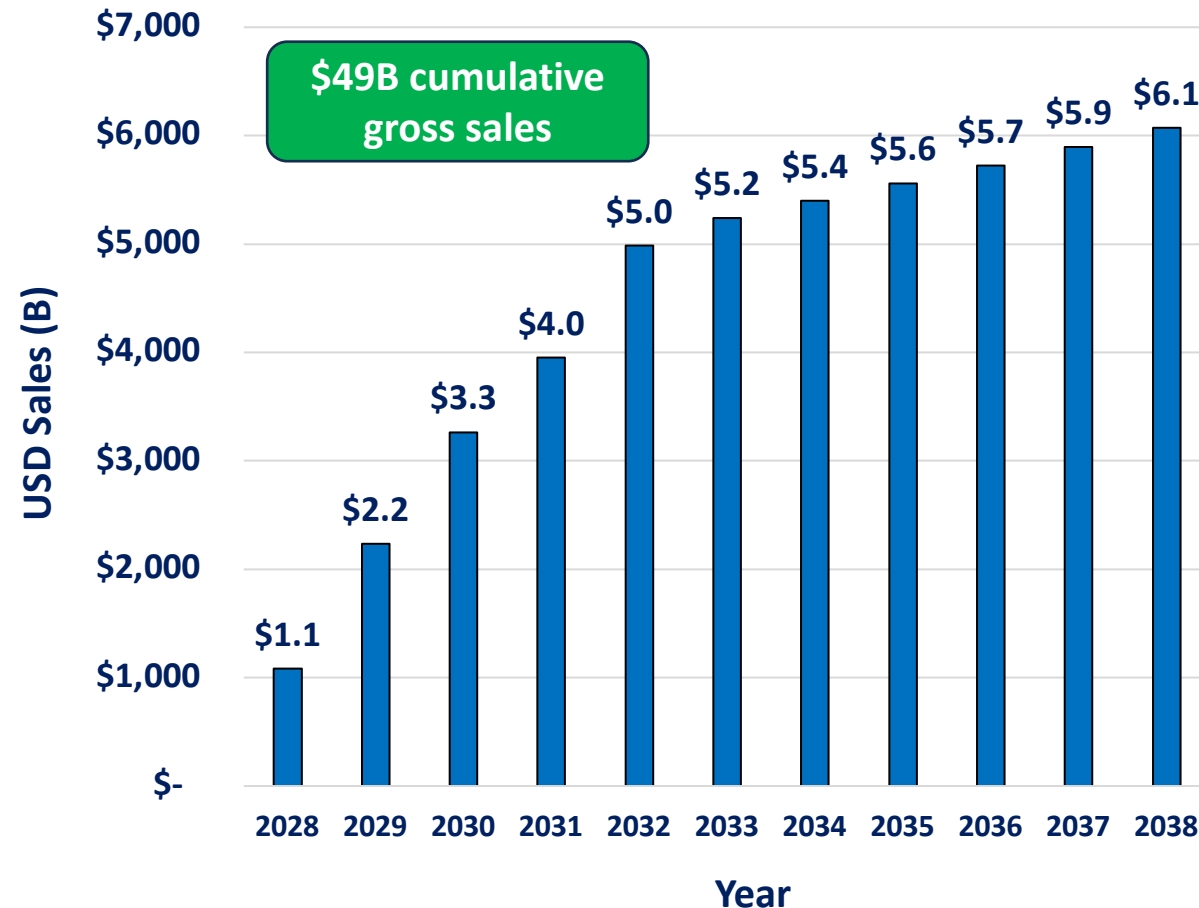
Peaked at 50% Market Share in the U.S. by 2023



NOAC Market Share Trends US

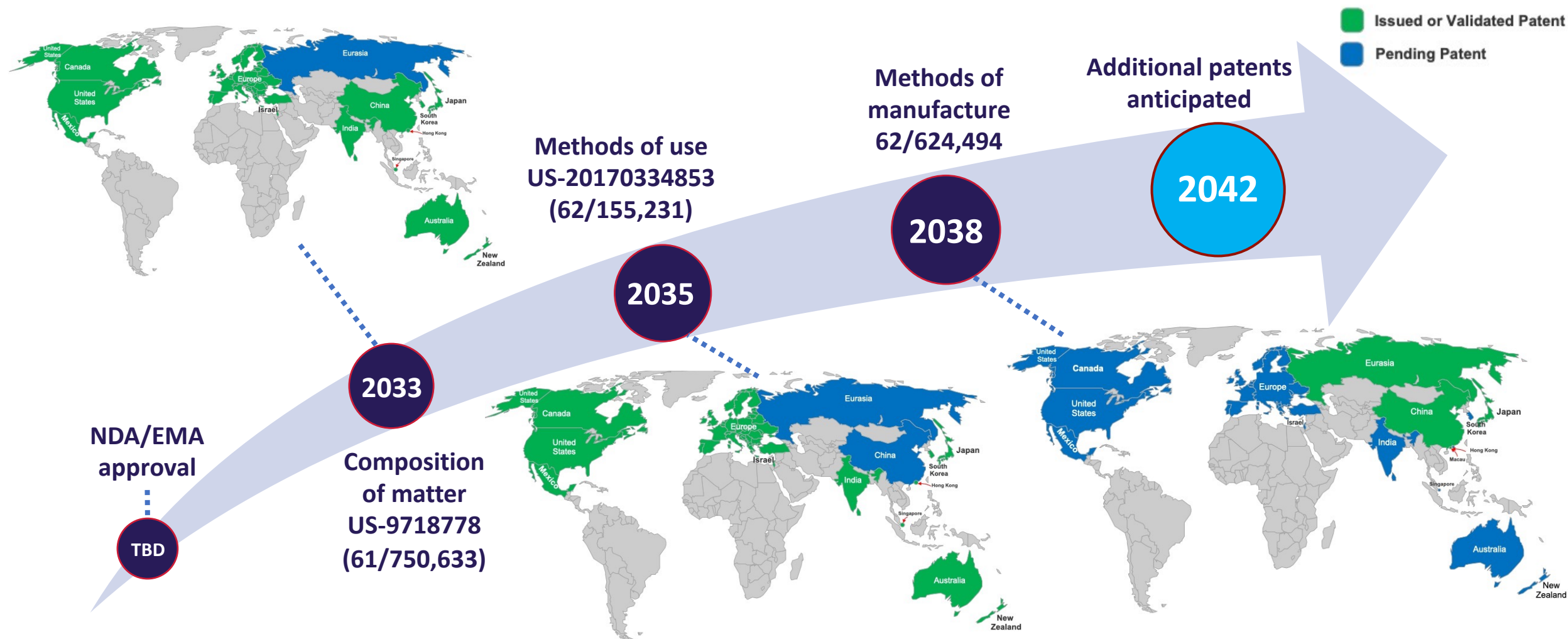


DT678 US Sales based on Eliquis Analog



DT678 Intellectual Property Portfolio

Anticipating long-term patent protection through 2042 – DT678



DT678 Label Differences versus Plavix

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

Removal of
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 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)

INDICATIONS AND USAGE

Plavix is a P2Y₁₂ 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

May not require
loading dose

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 P2Y₁₂ 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)

1x daily, reduced dosing errors

Contraindicated in patients with intercranial bleeding and pathological bleeding

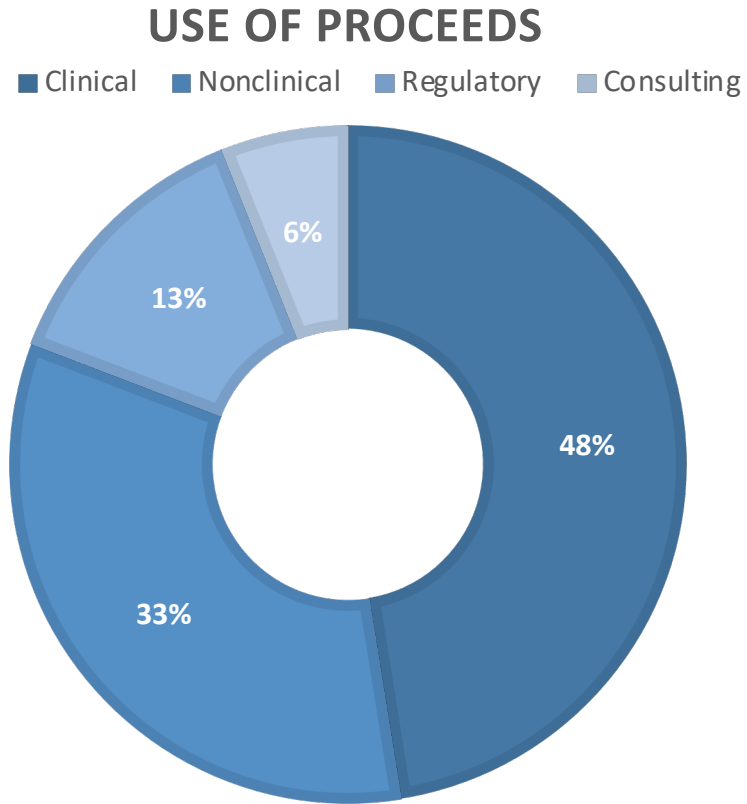
Dyspnea and hepatic impairment
Side effects

CYP3A4 and Drug-Drug interactions

Risk of intercranial bleeding

Risk of Bradycardia

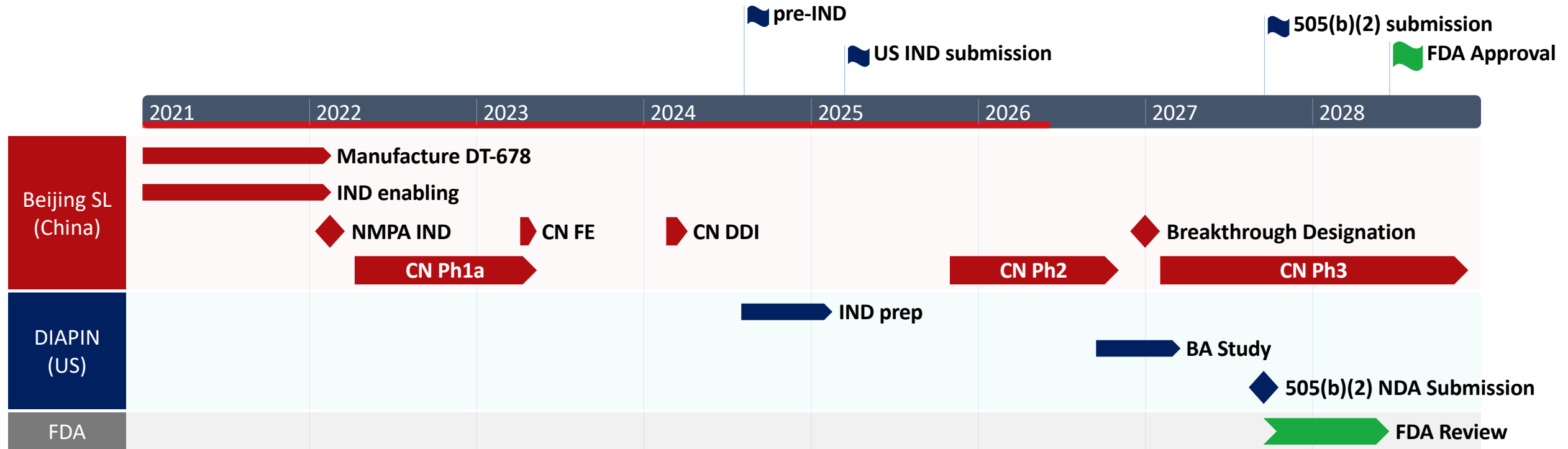
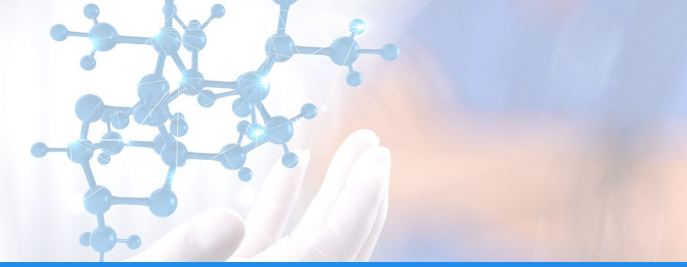
Use of Proceeds -7.5 Million to File DT678 NDA



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 NDA Approval Timeline*



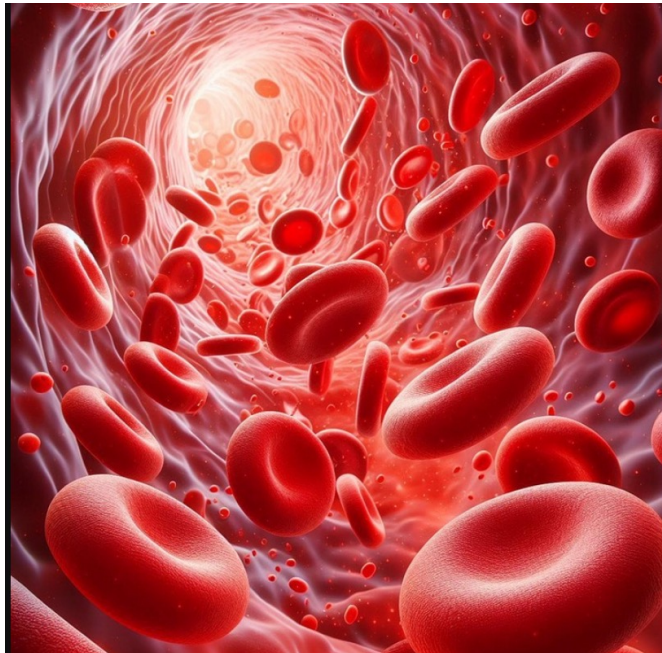
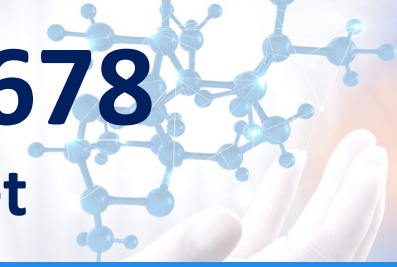
Key Milestones:

- 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

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

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 FDA requests, US trial & 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.