

Welcome to R&D Day

June 11, 2025



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A detailed microscopic image of several red blood cells, showing their characteristic biconcave shape and internal structure. The cells are in various stages of focus, with some in sharp detail and others blurred in the background.

Today's Agenda

Date: June 11, 2025

Corporate Update: Michael Davidson, MD, CEO, NewAmsterdam

- Alzheimer's Update
 - PREVAIL Update
 - Why is PREVAIL Derisked
-

Science Update: John Kastelein, MD, PhD, FESC, CSO, NewAmsterdam

- What we saw in BROADWAY (Subgroup Analysis)
 - Pooled/Updated MACE data
 - Particles Driving MACE
 - Lp(a) Driving MACE
 - Diabetes
-

Commercial Update: BJ Jones, CCO, NewAmsterdam

- Market Opportunity
 - Differentiated Product
 - HCP Preference
 - Commercial Launch
-

Closing: Michael Davidson, MD, CEO, NewAmsterdam

Q&A

Previous 18 Months Were a Time of Groundwork, Goals and Growth



Completed and announced results for BROOKLYN, BROADWAY, and TANDEM Phase 3 studies



Building world-class commercial and MSL functions



Doubled in size (~100) with new hires and offices in Amsterdam, NL, Miami, FL, and Philadelphia metro area



Secured funding to support US Commercial launch, if approved, with cash at 1Q25 of ~\$810M

2024



Composition of matter IP Granted



Announced topline results for BROOKLYN Phase 3 trial



Announced topline results for TANDEM Phase 3 trial



Announced topline results for BROADWAY Phase 3 trial



Published BROADWAY in NEJM



Published TANDEM in The Lancet



Announced Alzheimer's topline



Full AD data to be presented at AAIC



EMA submission

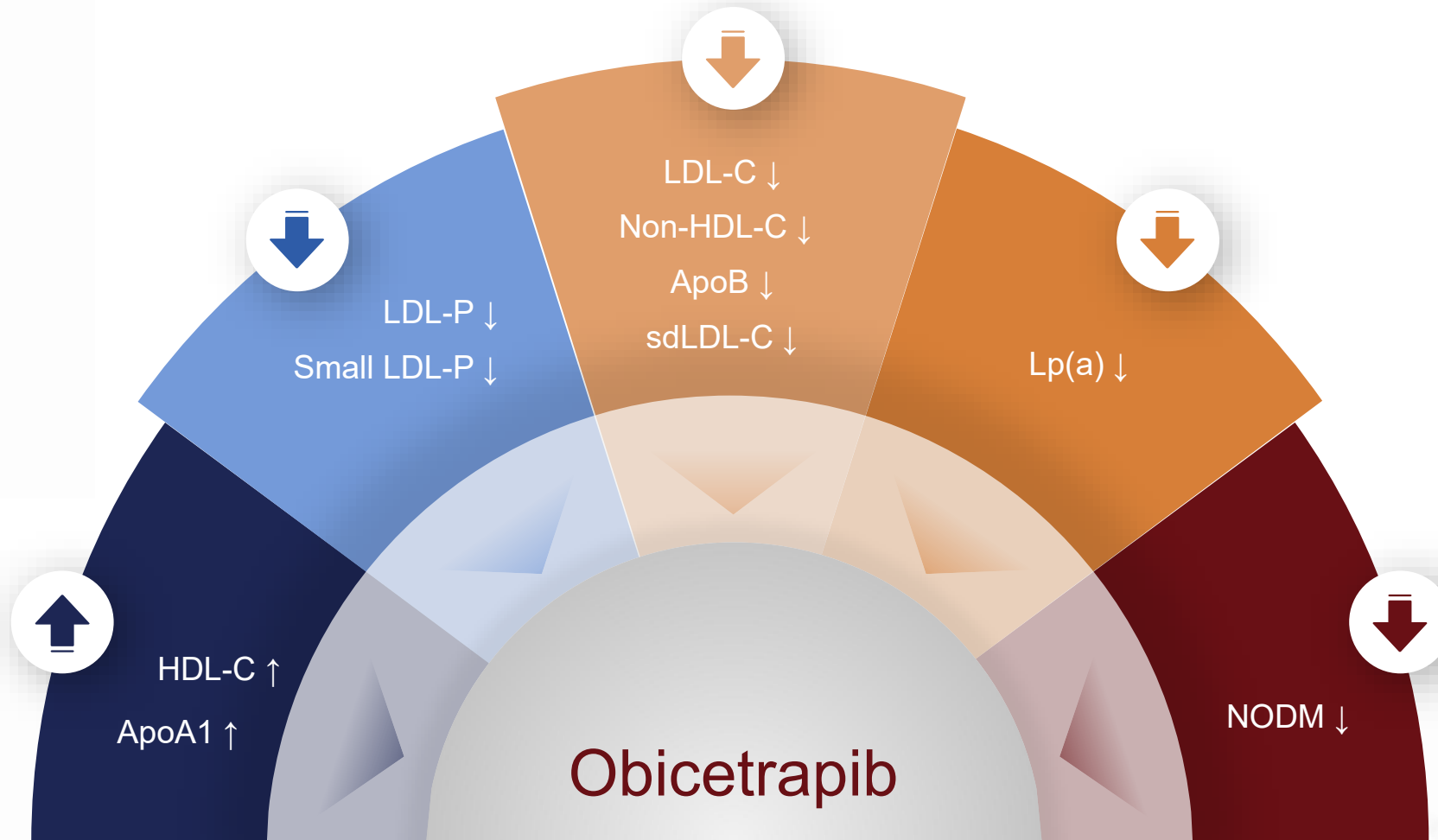


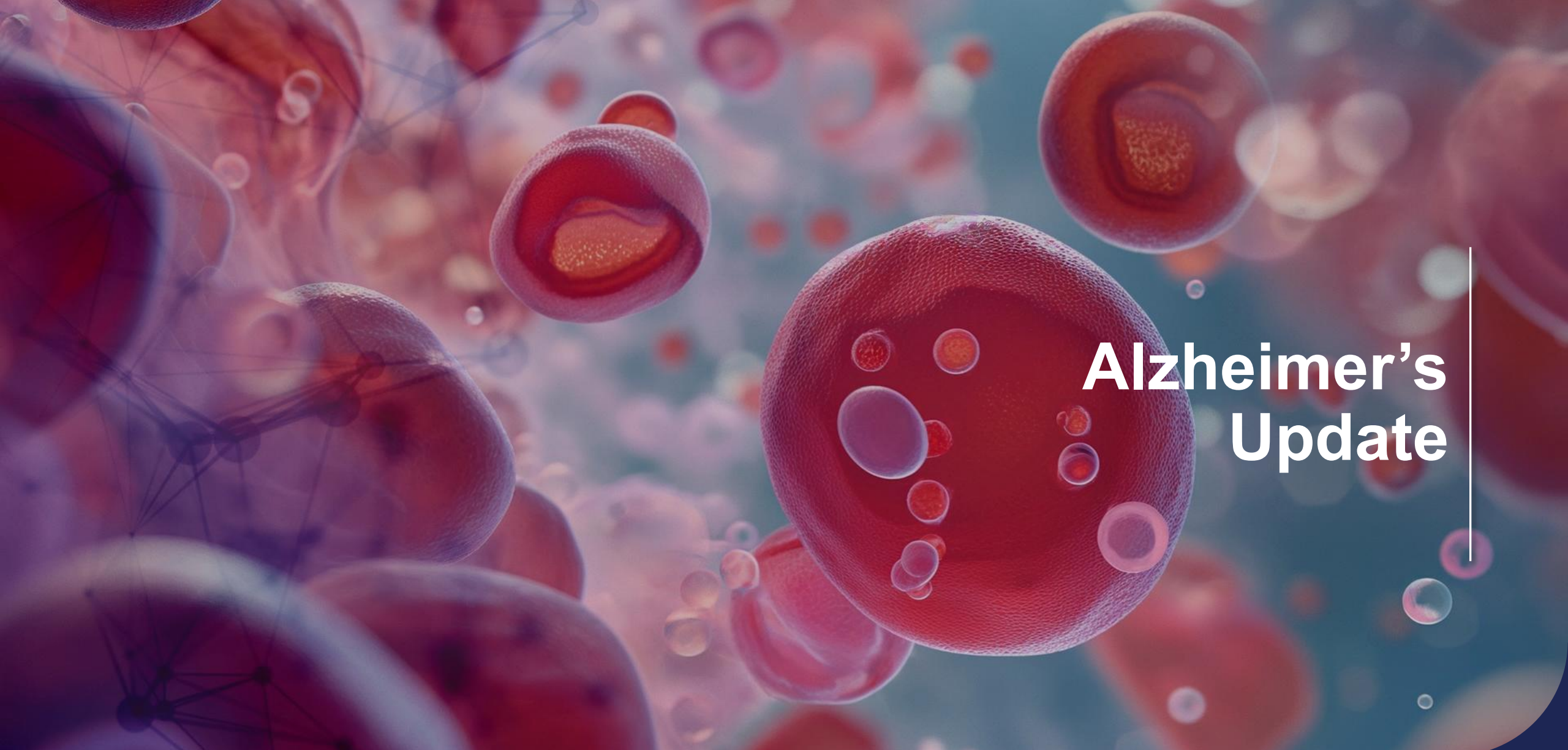
Completion of VINCENT Phase 2 trial

1H 2025

2H 2025

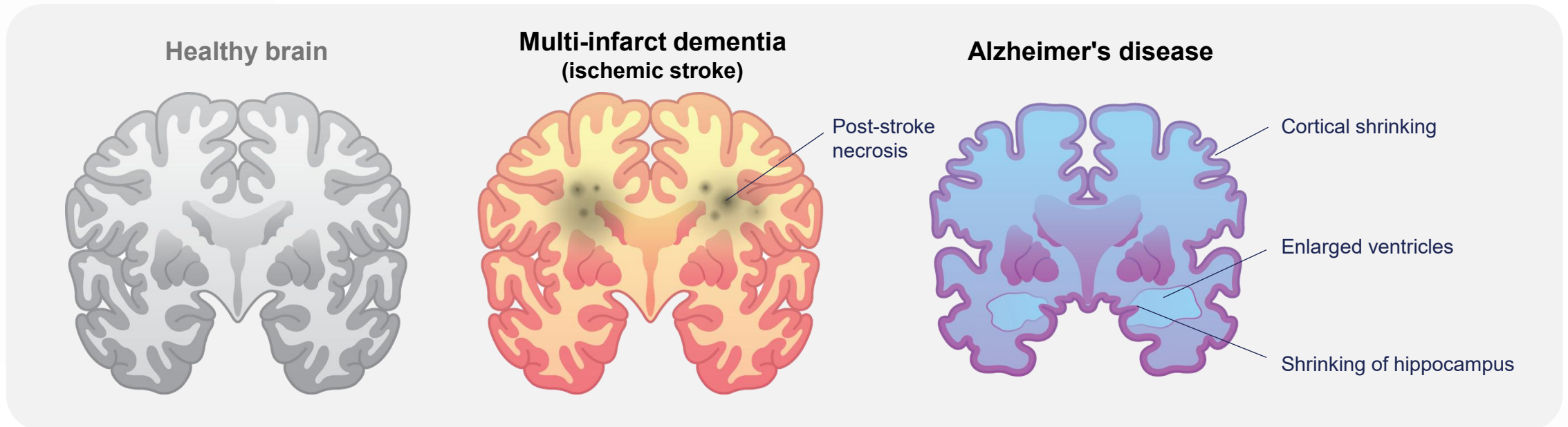
Obicetrapib Observed to Impact Multiple Factors Associated with Cardiometabolic Disease





Alzheimer's Update

CETPi Bears Therapeutic Potential for Both Multi-infarct Dementia and Alzheimer's Disease

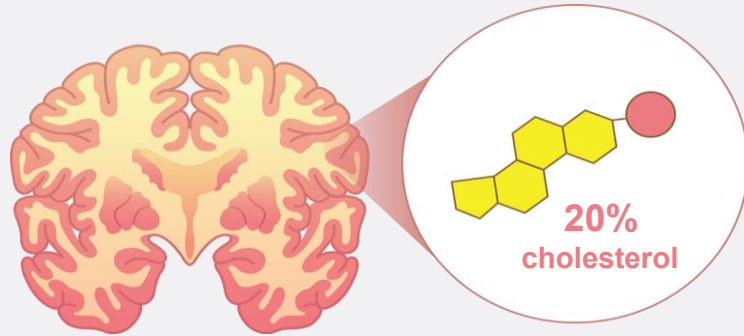


There is emerging evidence of a vascular component in multi-infarct dementia, **implying that LDL-lowering would help reduce atherosclerosis in the brain** ⁽¹⁾

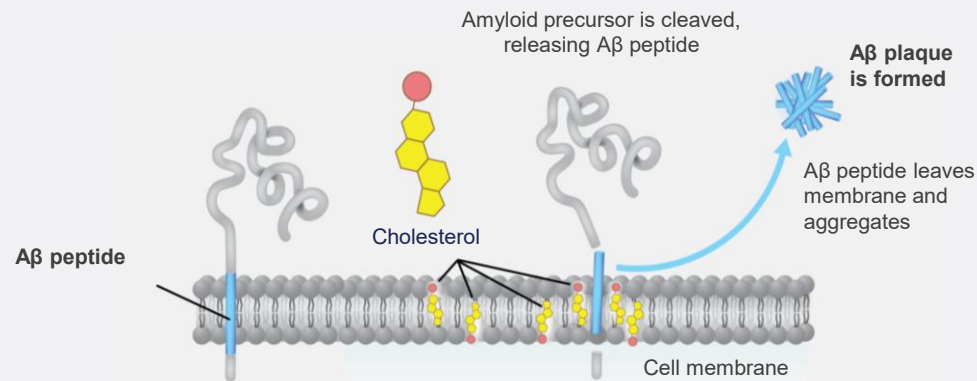
Alzheimer's disease results in the **generalized degeneration of the brain**, with over 50M people affected WW and an economic burden of >\$1 trillion ⁽²⁾

Elevated Cholesterol Levels in the Brain Precede Formation of Amyloid-Beta (A β) Plaques

The brain is the most cholesterol-rich organ; it contains only 2% body mass but has 20% of the body's cholesterol



A β plaque formation inside AD brain cells



During early development, oligodendrocytes synthesize large quantities of cholesterol for myelination

In adults, when myelination is complete, glial cells and, to a lesser extent, neurons account for the steady-state production of cholesterol

The brain uses a unique mechanism for cholesterol recycling and redistribution

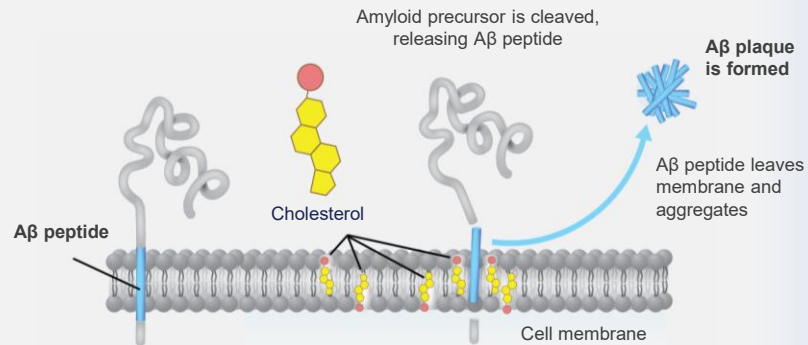
- Involves an ApoE-mediated lipoprotein pathway unique to the CNS whereby cholesterol is turned over
- Excess oxysterols are ultimately delivered to the liver for secretion into the bile

Cholesterol itself does not exit the brain but instead is converted to a metabolite, 24S-hydroxycholesterol

- 24S-hydroxycholesterol is a proxy for excess cholesterol that will be measured in our phase 2a clinical trial

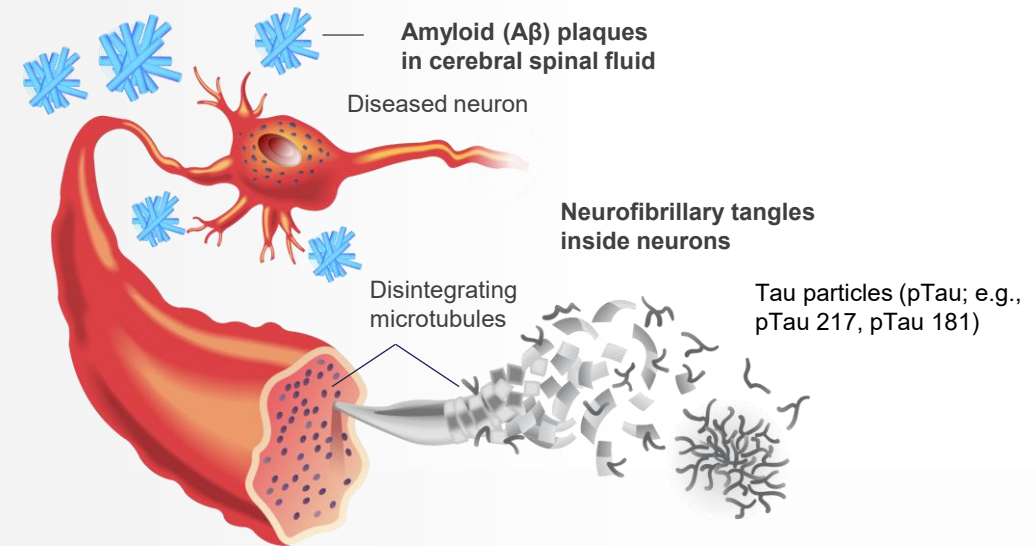
Amyloid Beta (A β) and Tau Proteins Play Significant Roles in the Development and Progression of Alzheimer's Disease

A β plaque formation inside AD brain cells



Cholesterol in membranes facilitates aggregation of A β peptides into amyloid plaques; improved clearance of cholesterol, therefore, may preempt progression of AD

AD is characterized by:



These significant issues in AD are caused by cholesterol dysregulation

A β plaques formation

Neurofibrillary tangle formation

Myelination issues

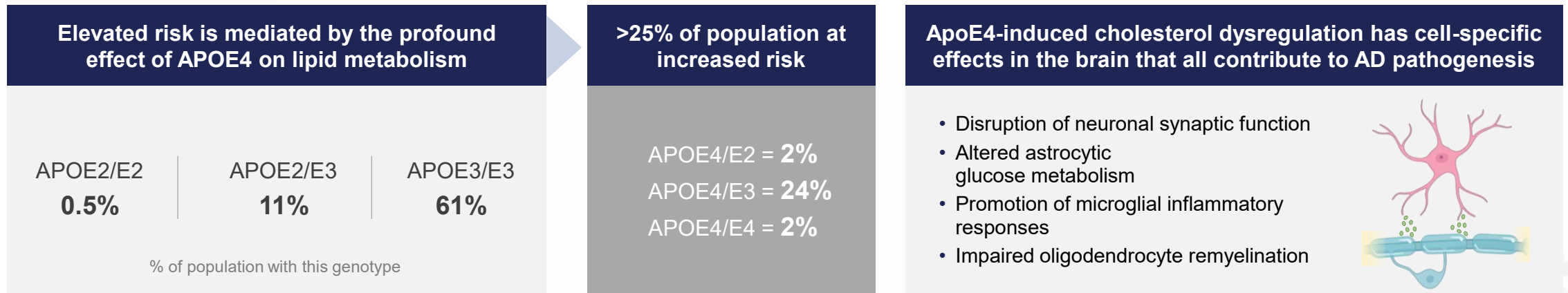
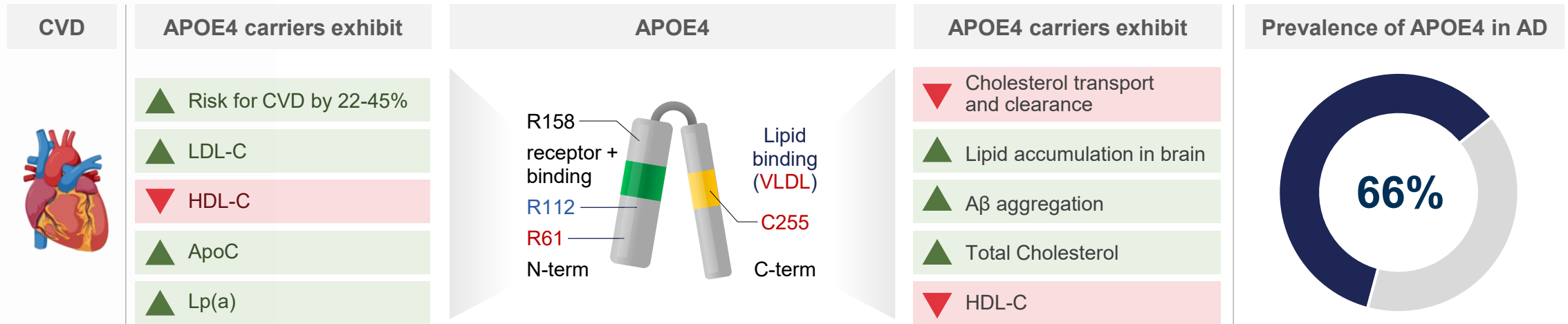
Oxidative stress

Bioenergetic issues

Inflammation issues

BBB integrity

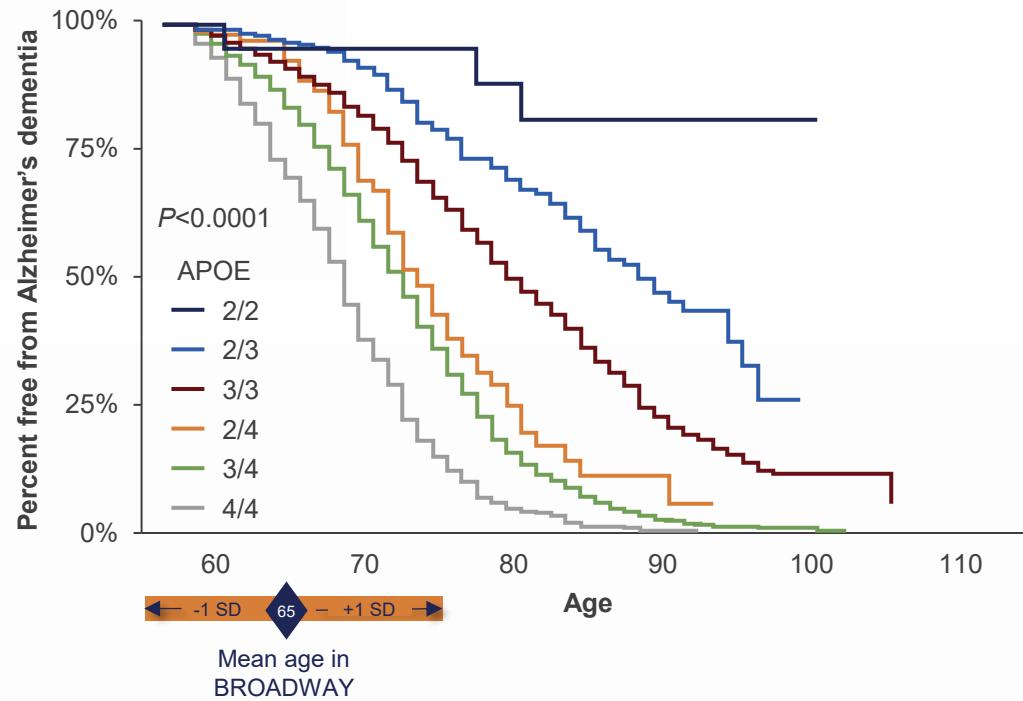
ApoE4 is a Risk Factor for Both CVD and Alzheimer's Disease¹⁻⁵



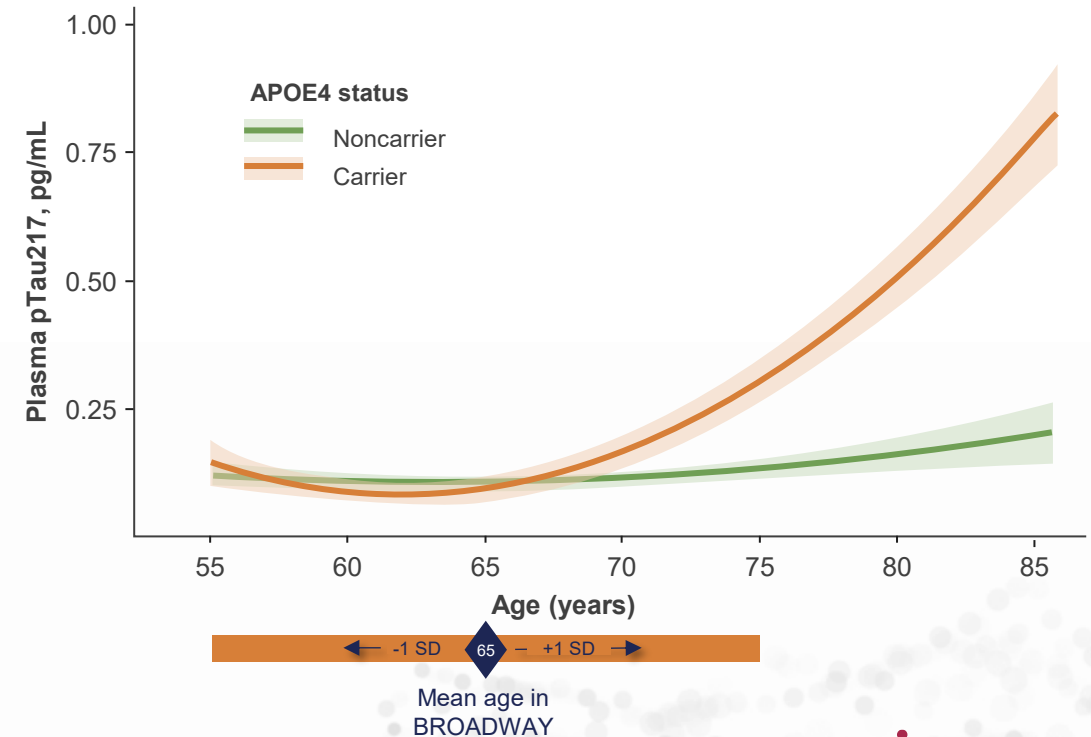
ApoE4 is the Strongest Genetic Risk Factor for Sporadic AD,¹ With a Close Link to Increased pTau 217 Levels

Each copy of ApoE4 is associated with increased risk for AD. Therapies are needed that can slow down or prevent disease progression, particularly in ApoE4 carriers¹

Increased risk of Alzheimer's dementia for ApoE4 carriers and earlier in life¹



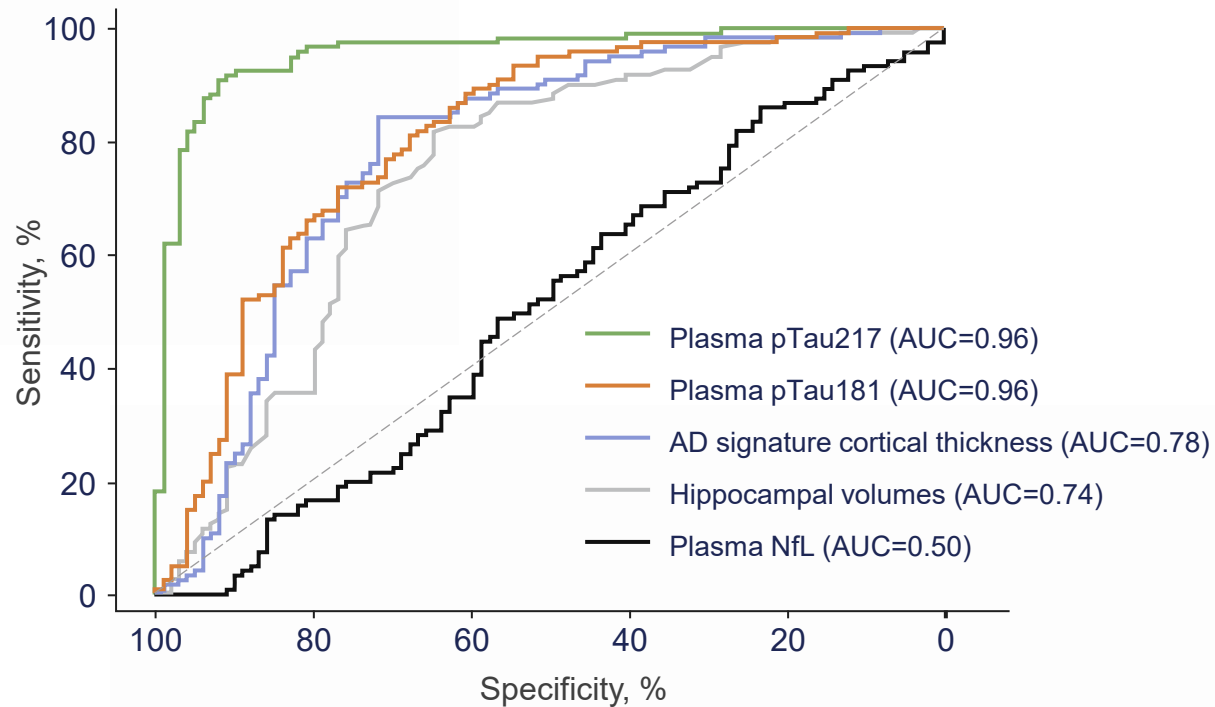
Plasma pTau217 levels by age according ApoE4 status



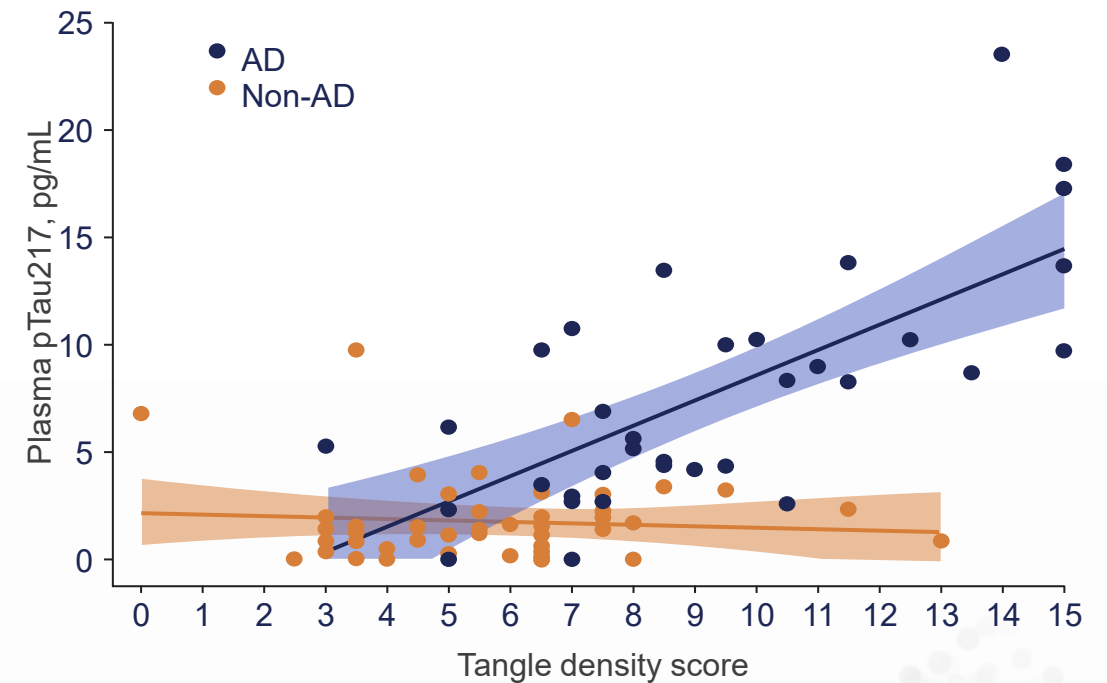
AAD, Alzheimer's disease; APOE, apolipoprotein E. 1. Reiman EM et al. Nat Commun. 2020;11(1):667. 2. Reiman EM et al. Nat Commun. 2020;11(supplementary information):667. 2. Longitudinal trajectory of plasma pTau217 in cognitively unimpaired subjects according to APOE4 status. Interaction plot derived from linear mixed models of plasma pTau217 in healthy controls. Estimates come from the interaction effects of the best model for plasma pTau217. Predicted plasma pTau217 values are shown on the y-axis. The x-axis represents age in years. Colored lines are regression lines of APOE ϵ 4 carriers (blue) and noncarriers (teal), and the shaded area represents 95% CI. Age-related longitudinal trajectory was higher in APOE ϵ 4 carriers.

Plasma pTau217 is a Strong Predictor of AD Pathology

pTau217 as a biomarker to assess AD progression



pTau217 correlates with PET tangle density



Recent News Further Validates pTau217 Levels Predict Presence of Amyloid Plaques in the Brain



FDA clears first blood test to reliably predict Alzheimer's disease

"The ability to diagnose Alzheimer's earlier with a simple blood test, like we do for cholesterol, is a game changer, allowing more patients to receive treatment options that have the potential to significantly slow or even prevent the disease," Fillit said.



FDA greenlights first blood test to help diagnose Alzheimer's disease in the US

It works by measuring two proteins in blood plasma: pTau217 and beta-amyloid 1-42. A ratio of those proteins tends to correlate with the occurrence or absence of amyloid plaques in the brain, which are among the hallmarks of Alzheimer's disease. The test does not measure amyloid directly but can signal its presence.

STAT

FDA clears first blood test for diagnosing Alzheimer's

The test from Japan-based Fujirebio Diagnostics could help patients get treatment faster

The newly cleared test from Fujirebio measures two proteins, pTau217 and beta-amyloid 1-42, found in human plasma, a component of blood. A numerical ratio of the levels of the two proteins is correlated to the presence or absence of amyloid plaques in the brain.



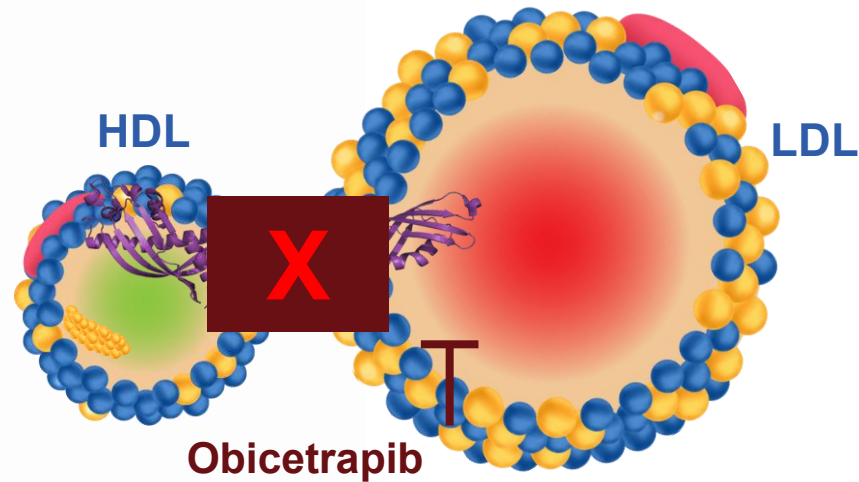
FDA clears 1st blood test to help diagnose Alzheimer's disease

The test is for older Americans already exhibiting signs of Alzheimer's.

By [Youri Benadjaoud](#)
May 16, 2025, 4:51 PM



Obicetrapib is a Potent CETP Inhibitor Currently Being Studied for its Potential to Delay or Prevent AD in ApoE4 Carriers



RATIONALE

Obicetrapib offers a mechanistically distinct approach that targets upstream lipid dysregulation vs downstream pathology

Unlike anti-amyloid therapies, obicetrapib addresses upstream lipid dysregulation, oxidation, and inflammation that may drive AD pathogenesis

Phase 3 studies have shown the lipid-modifying ability of obicetrapib in >3000 patients with a favorable safety profile

Key observations from a proof-of-concept study in 13 ApoE4 carriers with MCI and biomarker-proven AD:

- Significant reductions in plasma and CSF levels of 24S- and 27-hydroxycholesterol
- Increased levels of lipophilic antioxidants and carotenoids, in both plasma and CSF
- Stabilization of key AD biomarkers, suggesting potential disease-modifying effects

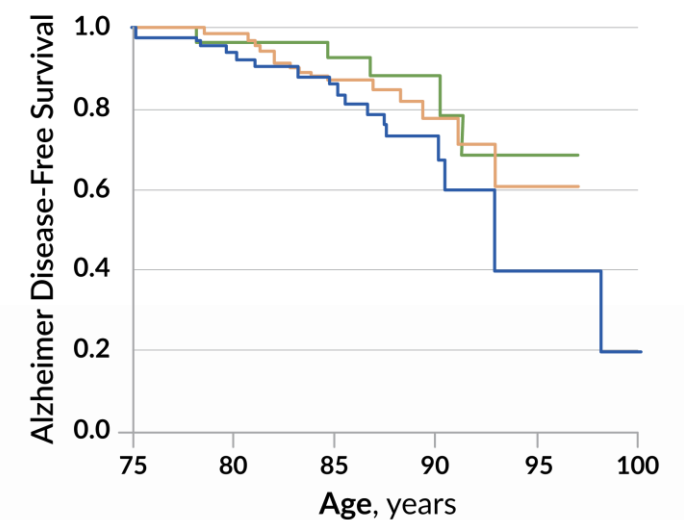
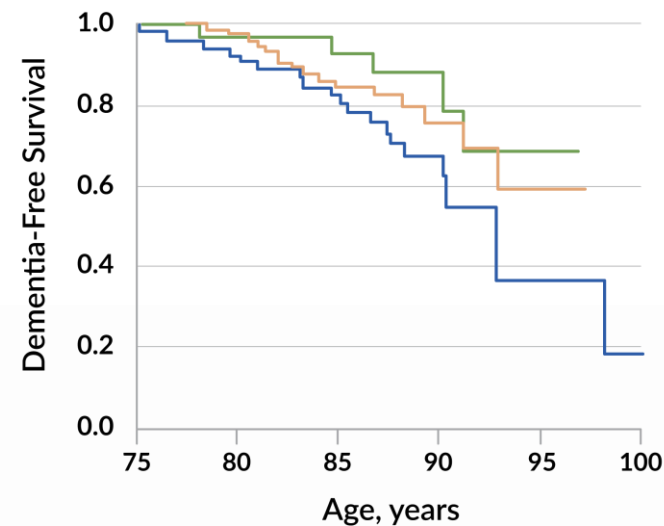
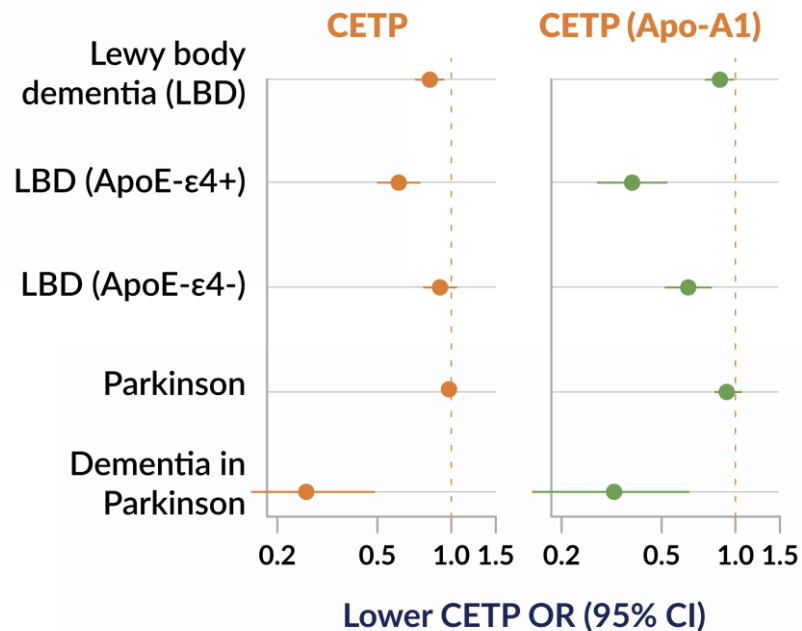
CETP Loss-of-Function (LoF) Genotype May be Associated with Slower Memory Decline and Lower AD Risk



CETP's potential involvement in CNS cholesterol homeostasis is supported by genomic data



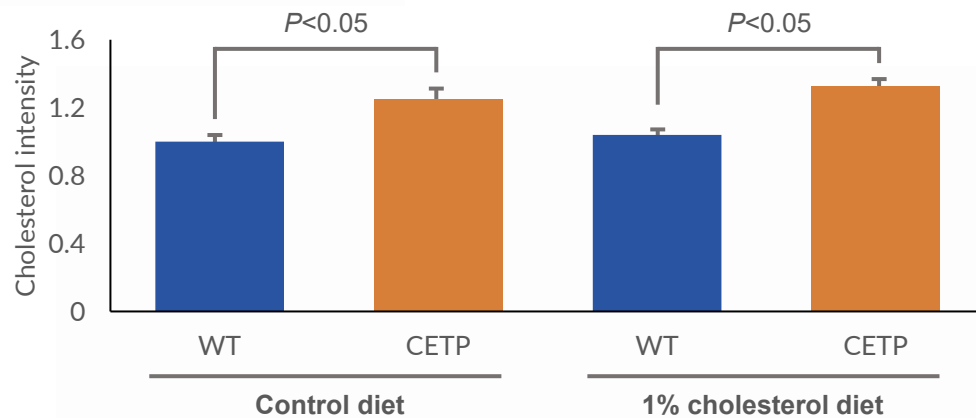
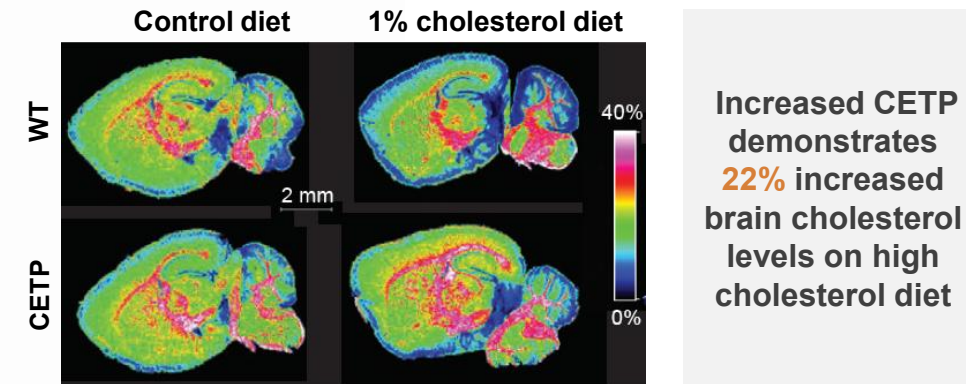
CETP LoF may be associated with lower CETP activity & a corresponding increase in HDL levels



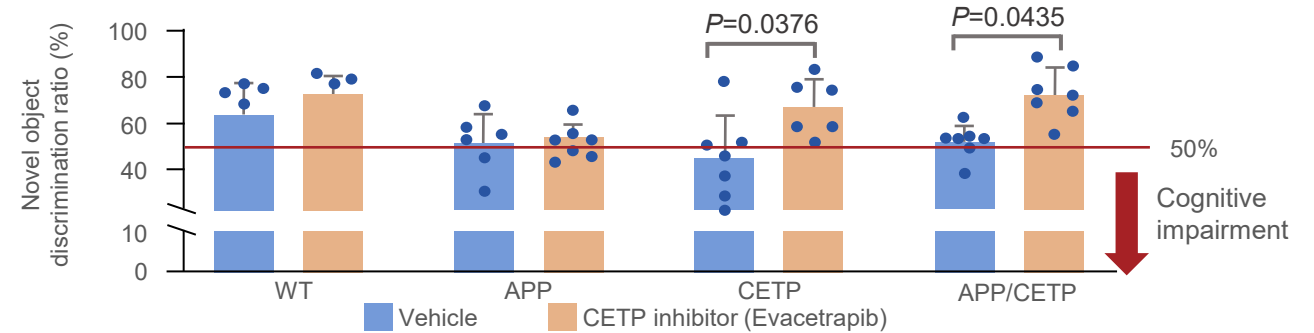
— 2 LoF CETP genes — 1 LoF CETP gene — Normal CETP

CETP Knock-in Mice Have Increased Brain Cholesterol Levels and CETPi Observed to Rescue Cognition in Preclinical Models of CETP-induced AD¹⁻³

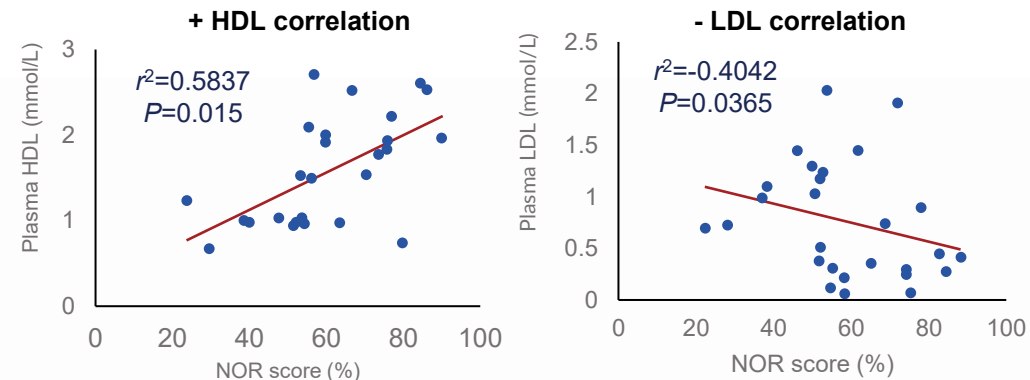
CETP transgenic mice have lower plasma HDL-C levels and increased brain cholesterol levels¹



CETP inhibition with evacetrapib led to cognitive improvement^{2,3}



Plasma Lipoproteins Were Correlated With NOR Score



Positive correlation observed between NOR score and HDL quantification in CETP and APP/CETP-expressing female mice

Negative correlation observed between NOR score and LDL quantification in CETP and APP/CETP-expressing female mice

A separate study demonstrated that **CETP inhibitors** can enter the brain⁴

AD, Alzheimer's disease; APP, amyloid precursor protein; CETP, cholesterol ester transfer protein; CETPi, CETP inhibitor; HDL, high-density lipoprotein;

HDL-C, high-density lipoprotein cholesterol; LDL, low-density lipoprotein; NOR, novel object recognition; WT, wild-type.

1. Oestereich F et al. *J Lipid Res.* 2022;63(9):100260. 2. Phénix J et al. *Alzheimer's Dement.* 2021;17(suppl3):e051134. 3. Phénix J et al. Poster presented at: Alzheimer's Association International Conference; July 26-30, 2021; Denver, USA. 4. Phénix J et al. *Front Pharmacol.* 2023;14:1171937.

Obicetrapib on Top of Max Tolerated Lipid-Modifying Therapy: Alzheimer's Biomarker Sub-study

Objective: To evaluate the effect of obicetrapib on biomarkers related to Alzheimer's Disease compared to placebo over 12-months

Study design: Randomized, double-blind, placebo-controlled

Main Inclusion Criteria:

Have a fasting serum LDL-C at Screening (Visit 1) as follows:

- Have a fasting serum LDL-C ≥ 55 mg/dL (≥ 1.4 mmol/L) to <100 mg/dL (<2.6 mmol/L) OR non-HDL-C ≥ 85 mg/dL (≥ 2.2 mmol/L) to <130 mg/dL (<3.4 mmol/L) with at least 1 risk enhancer

OR

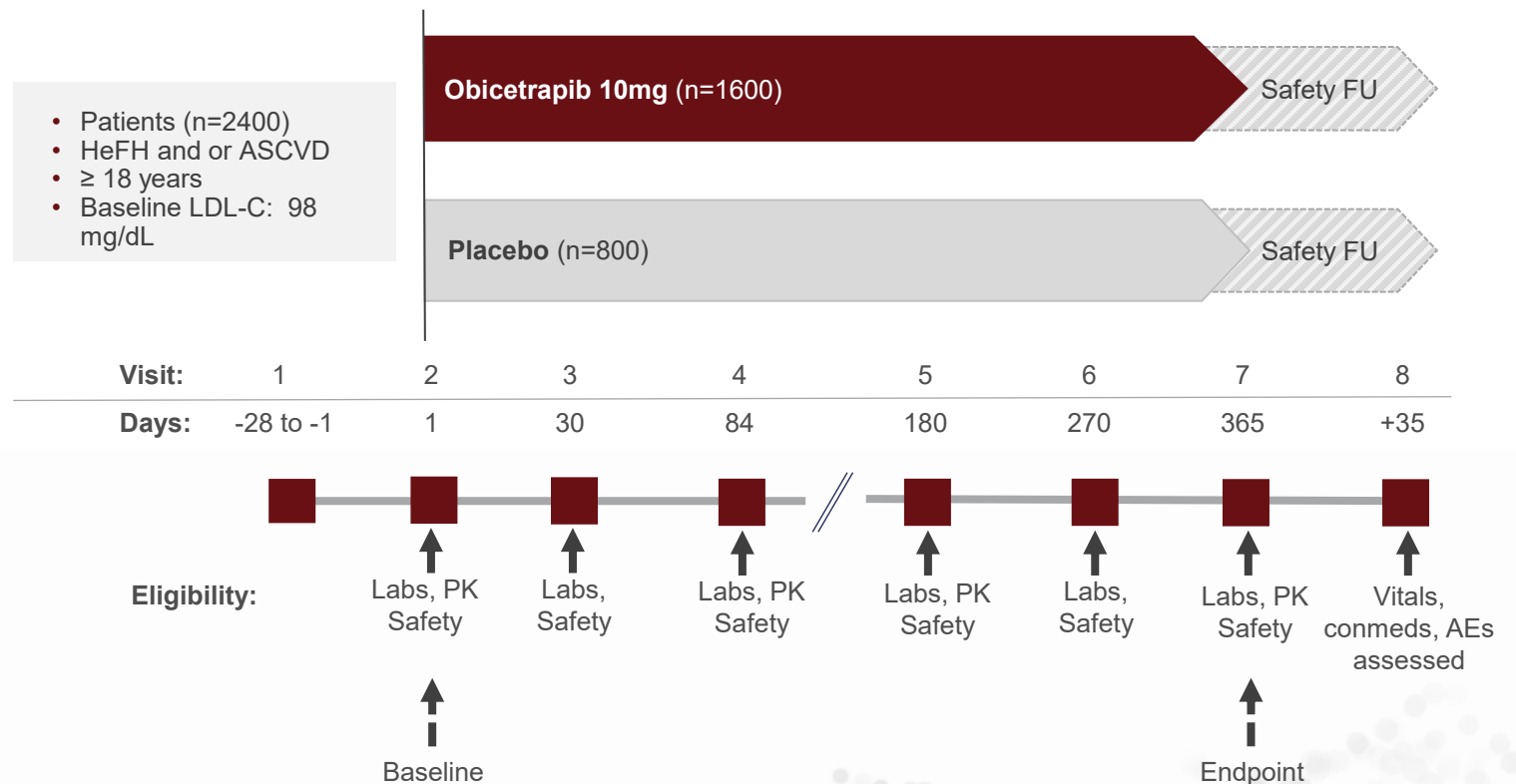
- Have a fasting serum LDL-C ≥ 100 mg/dL (≥ 2.6 mmol/L) OR non-HDL-C ≥ 130 mg/dL (≥ 3.4 mmol/L).

Main Exclusion Criteria:

- CV disease < 3 months
- HoFH
- Uncontrolled hypertension

Biomarker Endpoints:

- p-tau217 (primary outcome measure)
- Ratio of A β 42 to A β 40 (A β 42/A β 40)
- GFAP
- NFL
- p-tau181



What's Next for Obicetrapib and Alzheimer's Disease?

Full data to be presented as an oral presentation in a Developing Topics session

At the 2025 Alzheimer's Association International Conference

ALZHEIMER'S ASSOCIATION

AAIC>25

**Alzheimer's Association International Conference
July 27-31, 2025 | Toronto, Canada, and Online**

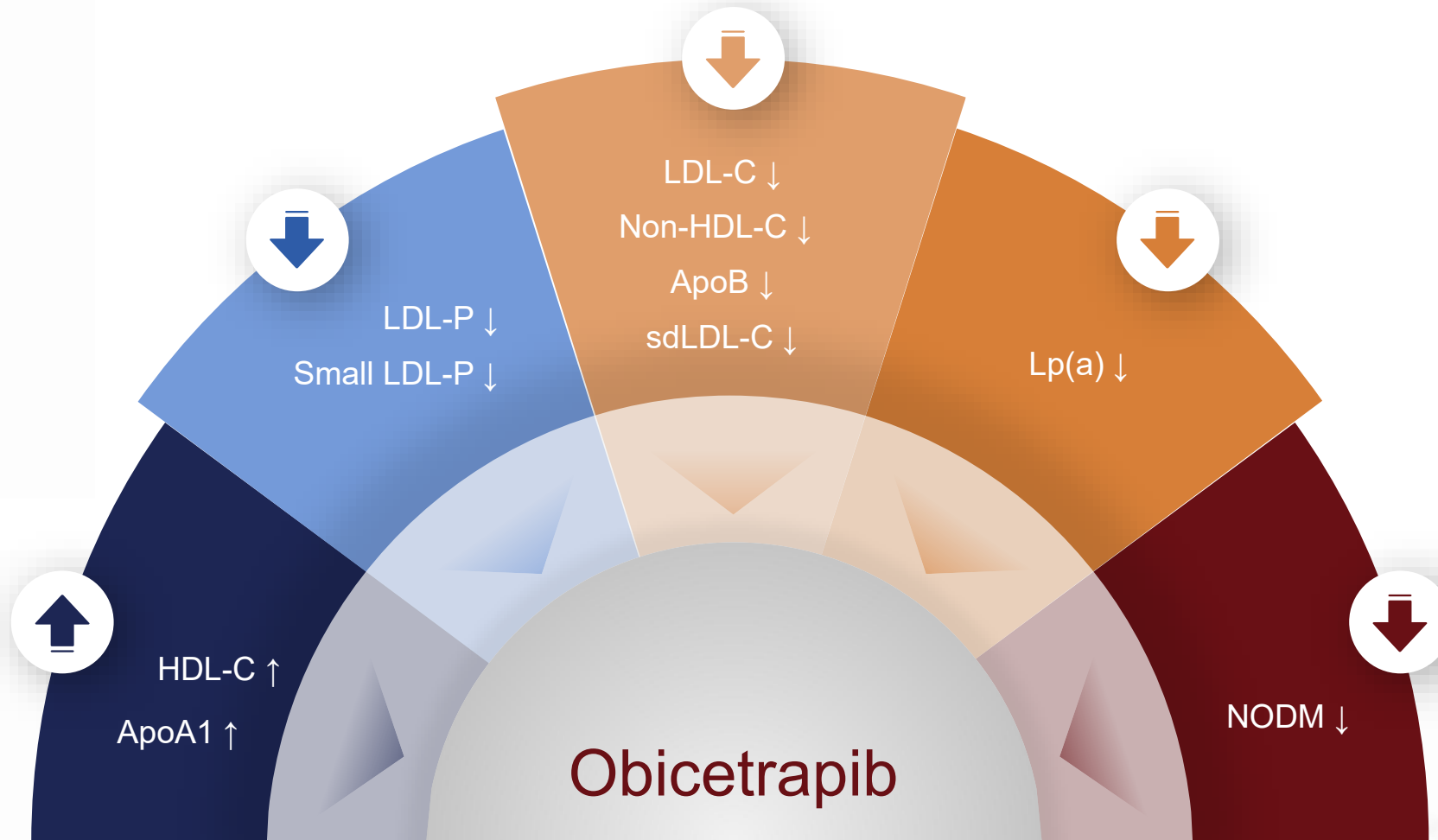
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“Today's report from NewAmsterdam is incredibly promising and points to a future of powerful combination therapies that address the key aspects of the disease from a variety of angles, and the distinct possibility of effective prevention strategies.”

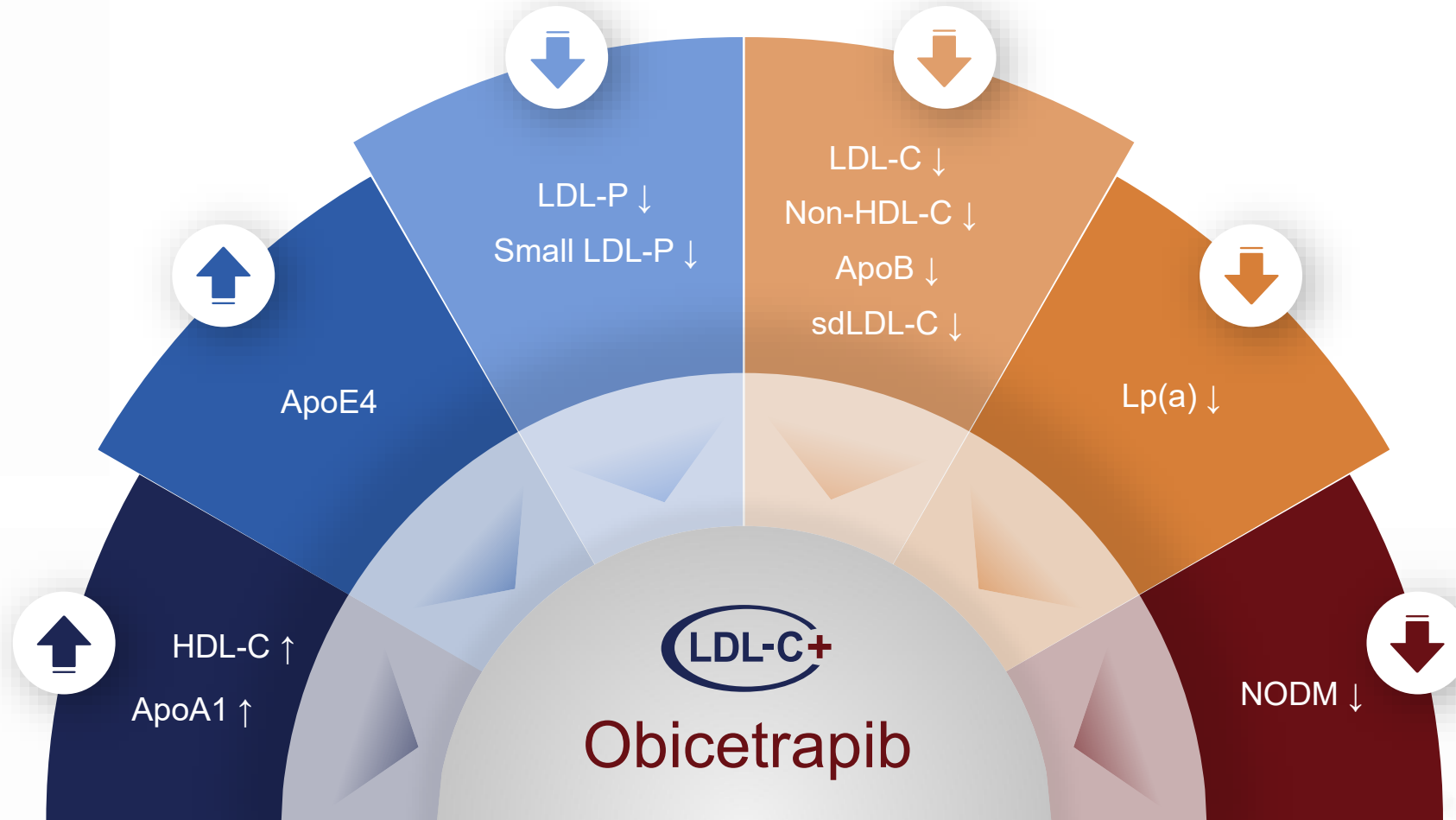
“Reducing the progression of Alzheimer's biomarkers suggests the potential to significantly alter the course of the disease, certainly in the studied population.”

- Alzheimer's Association

Obicetrapib Observed to Impact Multiple Factors Associated with Cardiometabolic Disease



The Future of Hyperlipidemia Treatment Goes Beyond LDL-C





PREVAIL Update

BROADWAY and TANDEM Publications Outline Obicetrapib's Potential Impact on LDL-C and Beyond



The NEW ENGLAND
JOURNAL of MEDICINE

THE NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Safety and Efficacy of Obicetrapib in Patients at High Cardiovascular Risk

S.J. Nicholls,¹ A.J. Nelson,² M. Dittmarsch,² J.J.P. Kastelein,^{2,3} C.M. Ballantyne,^{4,5} K.K. Ray,⁶ A.M. Navar,⁷ S.E. Nissen,⁸ M. Harada-Shiba,⁹ D.L. Curcio,² A. Neild,² D. Kling,² A. Hsieh,² J. Butters,² B.A. Ference,¹⁰ U. Laufs,¹¹ M. Banach,¹² R. Mehran,¹³ A.L. Catapano,¹⁴ Y. Huo,¹⁵ M. Szarek,^{13,16,17} V. Balinskaite,¹⁸ and M.H. Davidson,² for the BROADWAY Investigators*

ABSTRACT

BACKGROUND Obicetrapib is a highly selective cholesteryl ester transfer protein inhibitor that reduces low-density lipoprotein (LDL) cholesterol levels. The efficacy and safety of obicetrapib have not been fully characterized among patients at high risk for cardiovascular events.

METHODS We conducted a multinational, randomized, placebo-controlled trial involving patients with heterozygous familial hypercholesterolemia or a history of atherosclerotic cardiovascular disease who were receiving maximum tolerated doses of lipid-lowering therapy. Patients with an LDL cholesterol level of 100 mg per deciliter or higher or a non-high-density lipoprotein (HDL) cholesterol level of 130 mg per deciliter or higher, as well as those with an LDL cholesterol level of 55 to 100 mg per deciliter or a non-HDL cholesterol level of 85 to 130 mg per deciliter and at least one additional cardiovascular risk factor, were eligible for inclusion. The patients were randomly assigned in a 2:1 ratio to receive either 10 mg of obicetrapib once daily or matching placebo for 365 days. The primary end point was the percent change in the LDL cholesterol level from baseline to day 84.

RESULTS A total of 2530 patients underwent randomization; 1686 patients were assigned to receive obicetrapib and 844 to receive placebo. The mean age of the patients was 65 years, 34% were women, and the mean baseline LDL cholesterol level was 98 mg per deciliter. The least-squares mean percent change from baseline to day 84 in the LDL cholesterol level was -29.9% (95% confidence interval [CI], -32.1 to -27.8) in the obicetrapib group, as compared with 2.7% (95% CI, -0.4 to 5.8) in the placebo group, for a between-group difference of -32.6 percentage points (95% CI, -35.8 to -29.5; $P < 0.0001$). The incidence of adverse events appeared to be similar in the two groups.

CONCLUSIONS Among patients with atherosclerotic cardiovascular disease or heterozygous familial hypercholesterolemia who were receiving maximum tolerated doses of lipid-lowering therapy and were at high risk for cardiovascular events, obicetrapib reduced LDL cholesterol levels by 29.9%. (Funded by NewAmsterdam Pharma; BROADWAY ClinicalTrials.gov number, NCT05142722.)

THE LANCET

Fixed-dose combination of obicetrapib and ezetimibe for LDL cholesterol reduction (TANDEM): a phase 3, randomised, double-blind, placebo-controlled trial

Ashish Sarma,¹ Danielle Brennan,² Kirstyn Hayden,³ Amanda Stronczek,⁴ Anne C Goldberg,⁵ Erin D Micho,⁶ Darren K McGuire,⁷ Denise Mason,⁸ Grace Tessek,⁹ Stephen J Nicholls,¹⁰ Douglas Kling,¹¹ Annie L Neild,¹² John Kastelein,¹³ Michael Davidson,¹⁴ Marc Dittmarsch,¹⁵ Steven E Nissen

Summary **Background** Reducing LDL cholesterol prevents atherosclerotic cardiovascular disease (ASCVD) events. The aim of this study was to evaluate the LDL cholesterol-lowering efficacy of a fixed-dose combination (FDC) of obicetrapib, a CETP inhibitor, and ezetimibe.

Methods This randomised, double-blind trial across 48 US sites including hospitals, private and group practices, and independent research centres included participants at least 18 years old with pre-existing or high risk for ASCVD or heterozygous familial hypercholesterolaemia with LDL cholesterol concentrations of 1.8 mmol/L (70 mg/dL) or greater despite maximally tolerated lipid-lowering therapy excluding ezetimibe, or having statin intolerance. Participants were randomly assigned (1:1:1) to obicetrapib 10 mg plus ezetimibe 10 mg FDC, obicetrapib 10 mg monotherapy, ezetimibe 10 mg monotherapy, or placebo administered daily for 84 days. The co-primary endpoints in the intention-to-treat population were the percent LDL cholesterol changes in the FDC group compared with placebo, ezetimibe monotherapy, and obicetrapib monotherapy, and the placebo-adjusted change in the obicetrapib monotherapy group. The trial was prospectively registered (NCT06095597) and is completed.

Findings Between March 4 and July 3, 2024, 407 participants were randomly assigned. The median age was 65.0 years (IQR 62.0–73.0) and 177 (43%) were female. Mean baseline LDL cholesterol was 2.4 mmol/L (2.5 mmol/L, 2.6 mmol/L, and 2.5 mmol/L in the placebo (n=102), ezetimibe monotherapy (n=101), obicetrapib monotherapy (n=102), and FDC groups (n=102), respectively. At day 84, percent differences in LDL cholesterol reduction with the FDC were -48.6% (95% CI -58.3 to -38.9) versus placebo, -27.9% (-37.5 to -18.4) versus ezetimibe, and -16.8% (-26.4 to -7.1) versus obicetrapib. Obicetrapib monotherapy decreased LDL cholesterol by 31.9% (22.1 to 41.6) versus placebo. Adverse event rates were similar in the FDC (52 [51%] of 102), obicetrapib (55 [54%] of 102), and ezetimibe (54 [53%] of 101) groups and lowest with placebo (38 [37%] of 102). Serious adverse event rates were generally similar across FDC (three [3%] of 102), obicetrapib (six [6%] of 102), ezetimibe (seven [7%] of 101), and placebo (four [4%] of 102) groups. Deaths occurred in one [1%] of 102 participants with FDC, one [1%] of 102 with obicetrapib, one [1%] of 101 with ezetimibe, and none with placebo.

Interpretation Combination therapy of obicetrapib and ezetimibe significantly reduced LDL cholesterol. This oral, single-pill therapy could improve LDL cholesterol management in patients with pre-existing or high risk for ASCVD.

Funding NewAmsterdam Pharma.

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Introduction

Treatment of elevated LDL cholesterol concentrations is a primary strategy for risk reduction in individuals with pre-existing or high risk for atherosclerotic cardiovascular disease (ASCVD).¹ Clinical trials of several classes of LDL cholesterol-lowering drugs have shown consistent reductions in major adverse cardiovascular events.^{2,3} A large meta-analysis of statin drug trials demonstrated a 22% reduction in cardiovascular events for each 1 mmol/L (38.7 mg/dL) reduction in LDL cholesterol concentration.⁴ Despite the availability of multiple classes of drugs that lower LDL cholesterol, including treatment with high-intensity statins, many patients with ASCVD

do not achieve target concentrations of LDL cholesterol.⁵ Barriers to the effective control of LDL cholesterol after the use of maximally tolerated statin therapy include the limited use of non-statin therapies, particularly limited access to injectable medications, and possibly patient fears about injectable medications.^{6,7} Accordingly, there is an unmet medical need for effective orally administered LDL cholesterol-lowering therapies.

Pharmacological inhibition of the cholesteryl ester transfer protein (CETP) has been associated with inconsistent reductions in LDL cholesterol in previous trials.^{8–10} Obicetrapib is an orally administered, selective CETP inhibitor that significantly reduced LDL cholesterol

www.thelancet.com Published online May 7, 2025; [https://doi.org/10.1016/S0140-6736\(25\)00731-4](https://doi.org/10.1016/S0140-6736(25)00731-4)



“We already have other effective LDL-C and ApoB lowering non-statins, so I am particularly impressed with the impact on small LDL-P, Lp(a) and NODM which is unique to obicetrapib.”

– Cardiologist, Massachusetts

“Obicetrapib could be the future of LDL-C lowering and could potentially replace PCSK9i mAb given the beneficial effects demonstrated on other lipoproteins beyond just LDL-C and ApoB reduction.”

– Cardiologist, Ohio

“The magnitude of Lp(a) reduction in BROOKLYN, BROADWAY and TANDEM could get patients with very high Lp(a) levels into the ‘normal’ range.” This is a huge advantage for obicetrapib that other existing LD-C lowering agents cannot achieve.”

– Cardiologist, Pennsylvania

“If the MACE benefit in PREVAIL follows the early MACE benefit shown in BROADWAY, there is no doubt obicetrapib could be positioned ahead of all other non-statins given the exceptional tolerability and oral route.”

– Internal Medicine, Ohio

PREVAIL Designed to Apply Lessons Learned from Previous CVOTs to Reduce Risk and Demonstrate Obicetrapib's Full Benefit



Greater LDL-C lowering activity anticipated
Targeting higher baseline LDL-C patients



Higher *absolute* LDL-C reduction expected to lead to greater MACE benefit



Longer duration of follow up
Targeting higher-risk patient population



Maximizes opportunity for MACE reduction



Differentiated secondary endpoints



Potentially enhanced commercial profile vs. other LDL-C lowering agents

BROADWAY Designed to be a Predictor of PREVAIL

BROADWAY

1° endpoint – week 12

N = 2532

Obicetrapib 10 mg (2:1 randomization)

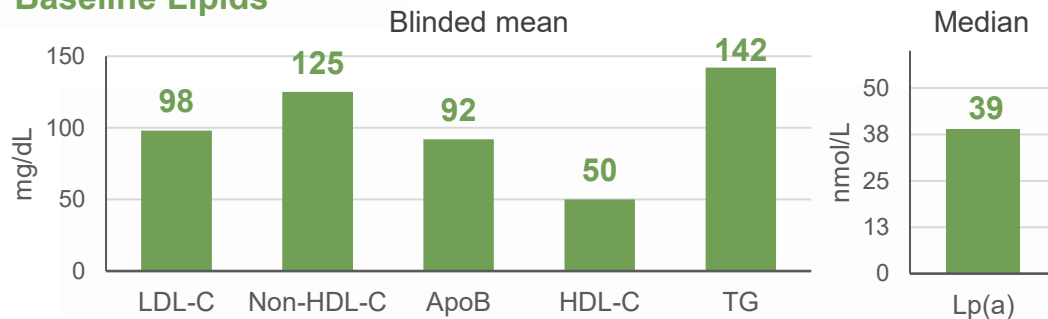
Placebo

13-months

Key Inclusion Criteria

- ASCVD or HeFH
- LDL-C ≥ 55 mg/dL w/risk factors, or
- LDL-C ≥ 100 mg/dL
- Maximally tolerated lipid lowering therapy

Baseline Lipids



Baseline Lipid Modifying Therapy

- Any statin: 91%
- High intensity statin: 65%
- Ezetimibe: 26%
- PCSK9i: 4%
- SGLT2i: 11%
- GLP-1: 6%

PREVAIL

LDL-C endpoint

N = 9541

Obicetrapib 10 mg (1:1 randomization)

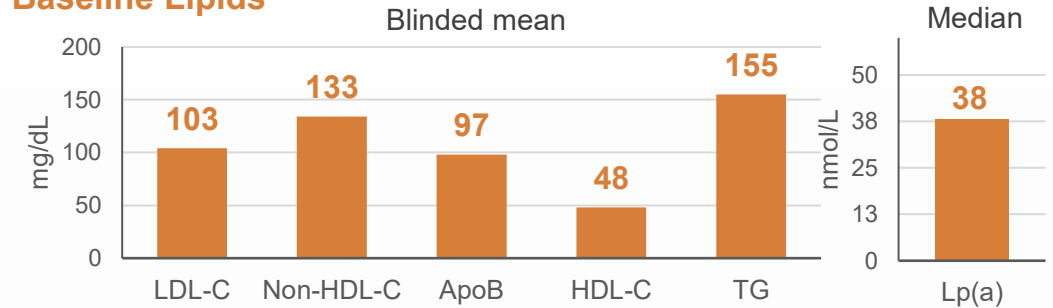
Placebo

54-months

Key Inclusion Criteria

- ASCVD
- LDL-C ≥ 55 mg/dL w/risk factors, or
- LDL-C ≥ 100 mg/dL
- Maximally tolerated lipid lowering therapy

Baseline Lipids



Baseline Lipid Modifying Therapy

- Any statin: >90%
- High intensity statin: 70%
- Ezetimibe: 23%
- PCSK9i: 2%
- SGLT2i: 14%
- GLP-1: 6%

Similar Patient Demographics Between BROADWAY and PREVAIL

BROADWAY

	Placebo N=844	Obicetrapib 10 mg N=1686
Mean Age (years)	65.3	65.4
<65 years	360 (42.7)	706 (41.9)
65 to 74 years	352 (41.7)	683 (40.5)
75+ years	132 (15.6)	297 (17.6)
Sex (F) n (%)	280 (33.2)	573 (34.0)
Region n (%)		
North America	313 (37.1)	591 (35.1)
Eastern Europe	282 (33.4)	580 (34.4)
Western Europe	104 (12.3)	213 (12.6)
Asia	145 (17.2)	302 (17.9)
Other ¹	--	--
Race n (%)		
White	647 (76.7)	1241 (73.6)
Asian	150 (17.8)	312 (18.5)
African American	39 (4.6)	112 (6.6)
Other	8 (1.0)	21 (1.3)

PREVAIL

All N=9541
65.0
4266 (44.7)
3732 (39.1)
1543 (16.2)
2952 (30.9)
3573 (37.4)
2232 (23.4)
2108 (22.1)
1315 (13.8)
313 (3.3)
7986 (83.7)
1044 (10.9)
397 (4.2)
114 (1.1)

Similar Patient Demographics Between BROADWAY and PREVAIL (Cont'd)

BROADWAY

	Placebo N=844	Obicetrapib 10 mg N=1686
Height (cm)	170.1	169.9
Weight (kg)	86.3	85.2
BMI (mean)	29.7	29.4
< 25 kg/m ²	162 (19.2)	352 (20.9)
25 - 30 kg/m ²	334 (39.6)	657 (39.0)
> 30 kg/m ²	346 (41.0)	676 (40.1)
Missing		
Diabetes n (%)	336 (39.8)	624 (37.0)
HeFH	143 (16.9)	284 (16.8)
Statin n (%)	782 (93.0)	1533 (91.0)
High Intensity	581 (68.8)	1152 (68.3)
Low or Moderate Intensity	201 (23.8)	381 (22.6)
None	62 (7.3)	153 (9.1)
Ezetimibe n (%)	220 (26.1)	453 (26.9)
PCSK9i n (%)	33 (3.9)	62 (3.7)
GLP1 n (%)	48 (5.7)	111 (6.6)
SGLT2 n (%)	92 (10.9)	188 (11.2)

PREVAIL

All N=9541
169.9
86.3
29.8
1573 (16.5)
3906 (40.9)
4042 (42.4)
20 (0.2)
3607 (37.8)
N/A
70%
22%
8%
2150 (22.5)
187 (2.0)
540 (5.7)
1360 (14.2)

PREVAIL Selection of 4-Point MACE

General concepts for using a composite endpoint for regulatory filing:

- Composite endpoints are used to aggregate events with a similar etiology in a way to increase the power of the study to be able to detect a statistically significant difference for the treatment under investigation. However, the composite endpoint must meet certain criteria:
 - The individual components of the composite endpoint should host clinically meaningful endpoints for the disease under investigation (in this case, atherosclerotic disease)
 - Individual components are expected to react similarly to the therapy under investigation, which means the expected relative risk reduction for each component is expected to be the same.
 - The individual components of the 4-point MACE endpoint – CHD death, non-fatal MI, fatal and non-fatal ischemic stroke, coronary revascularization – have proven to consistently show similar relative risk reduction for each component in previously conducted LDL-C lowering trials irrespective of the MOA for the treatment under investigation

3-Point MACE

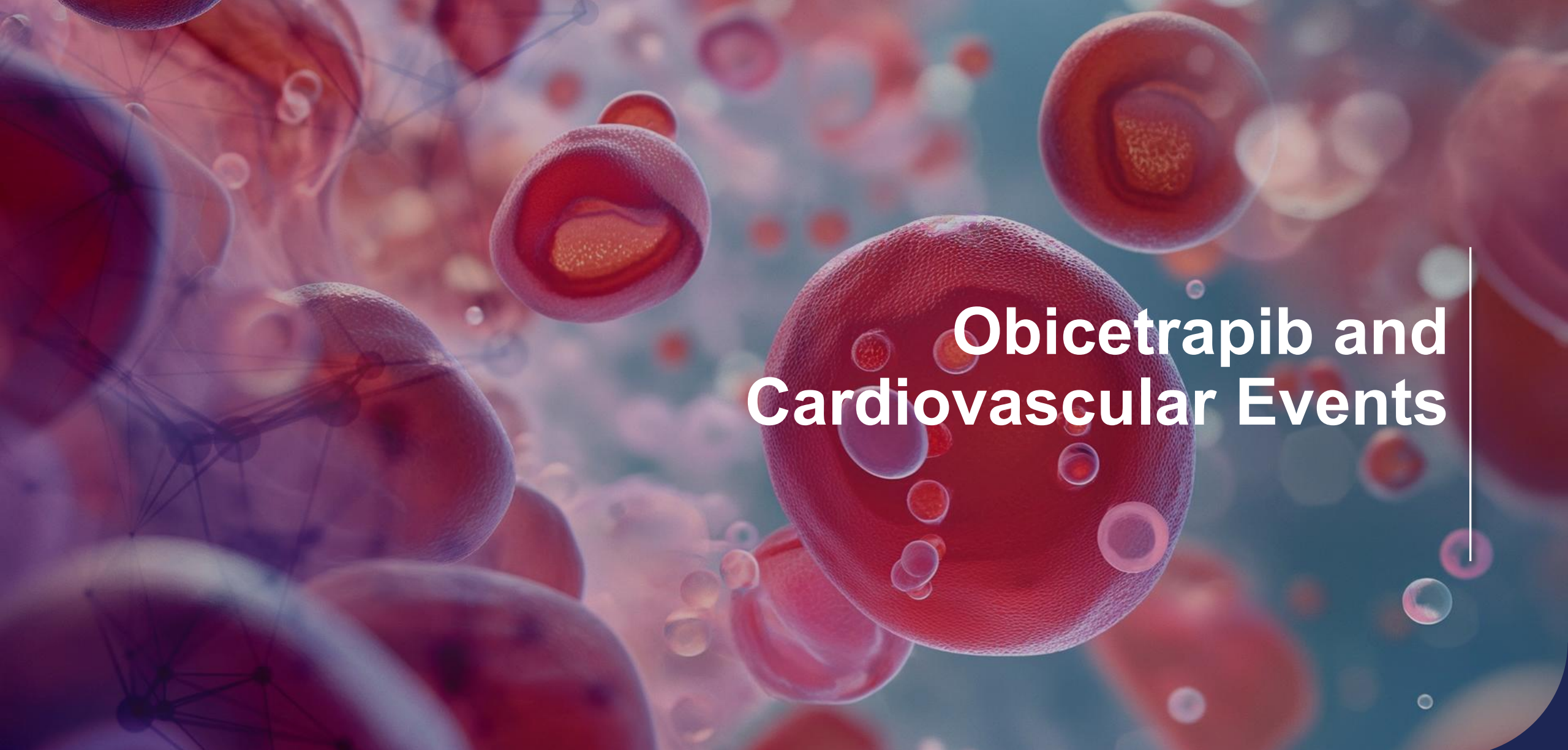
(CHD death, non-fatal MI, coronary revascularization)

- Uncommon composite endpoint compared to previously conducted LDL-C lowering trials
- Regulatory agencies, including the FDA, will conduct an independent assessment for various composite CV endpoints which will include the composite of fatal and non-fatal stroke

4-Point MACE

(CHD death, non-fatal MI, fatal and non-fatal ischemic stroke, coronary revascularization)

- Commonly accepted composite
- Provides greater power to detect a robust statistically significant difference for the number of patients included in PREVAIL as in comparison to 3-point MACE this composite will generate more CV events



Obicetrapib and Cardiovascular Events

Exploratory Endpoint: Major Adverse Cardiovascular Events (MACE)

BROADWAY MACE Data⁽¹⁾

	Placebo N = 844	Obicetrapib N= 1686	Hazard Ratio	95% CI
All-cause mortality – no. (%)	12 (1.4)	19 (1.1)	0.83	(0.40-1.71)
Coronary heart death – no. (%)	5 (0.6)	8 (0.5)	0.80	(0.26-2.44)
First 4-point MACE – no. (%)	44 (5.2)	70 (4.2)	0.79	(0.54-1.15)

BROADWAY + BROOKLYN Pooled MACE Data ⁽¹⁾

	Placebo N = 962	Obicetrapib N= 1920	Hazard Ratio	95% CI
All-cause mortality – no. (%)	14 (1.5)	20 (1.0)	0.78	(0.39-1.58)
Coronary heart death – no. (%)	7 (0.7)	9 (0.5)	0.63	(0.24-1.70)
First 4-point MACE – no. (%)	49 (5.1)	75 (3.9)	0.75	(0.53-1.08)

4-point MACE: CHD death, Non-fatal myocardial infarction, non-fatal stroke, coronary revascularization

1. MACE was evaluated in BROADWAY as an exploratory endpoint. There may be limitations on the interpretation of MACE data derived from both BROOKLYN and BROADWAY studies given they were not designed to assess MACE as the primary and secondary endpoints.

Consistent Trend in MACE Across Multiple Components

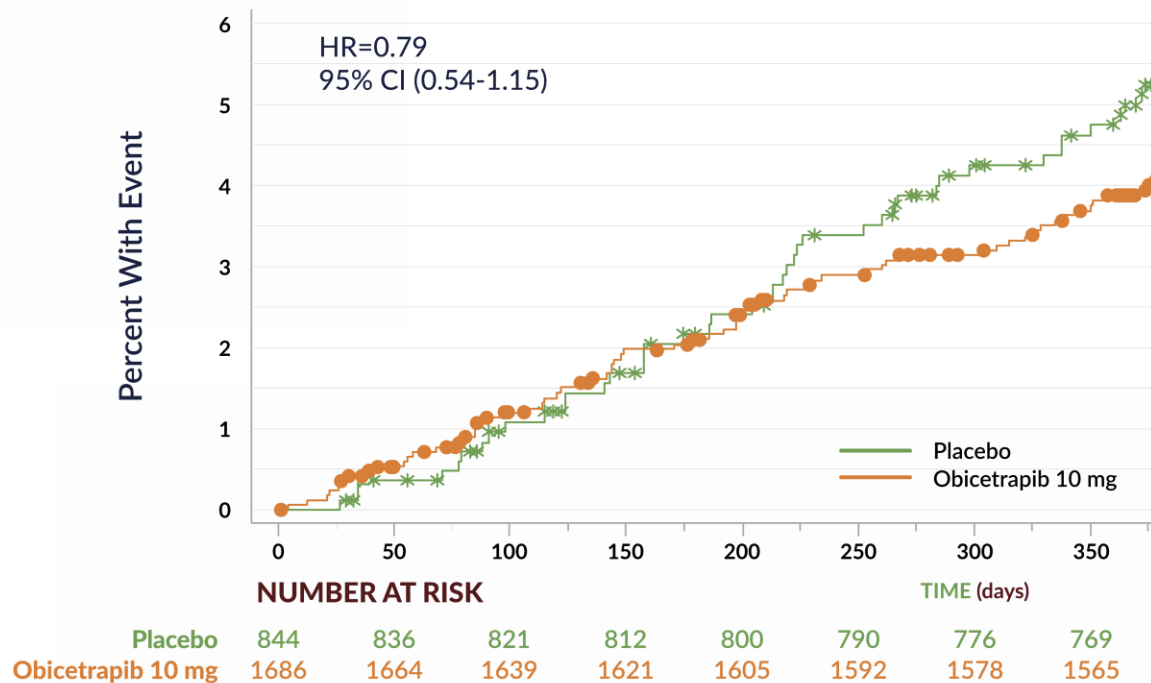
Pooled MACE Components

	BROADWAY		BROOKLYN		Pooled	
Cardiovascular events – no. (%)	Obicetrapib	Placebo	Obicetrapib	Placebo	Obicetrapib	Placebo
Death from CHD, nonfatal MI, stroke, or coronary revascularization	70 (4.2)	44 (5.2)	5 (2.1)	5 (4.2)	75 (3.9)	49 (5.1)
Death from CHD	5 (0.3)	4 (0.5)	1 (0.4)	2 (1.7)	6 (0.4)	6 (0.6)
Nonfatal MI	20 (1.2)	11 (1.3)	1 (0.4)	0 (0.0)	21 (1.1)	11 (1.1)
Stroke	14 (0.8)	5 (0.6)	1 (0.4)	0 (0.0)	15 (0.7)	5 (0.5)
Coronary revascularization	31 (1.8)	24 (2.8)	2 (0.9)	3 (2.5)	33 (1.7)	27 (2.8)

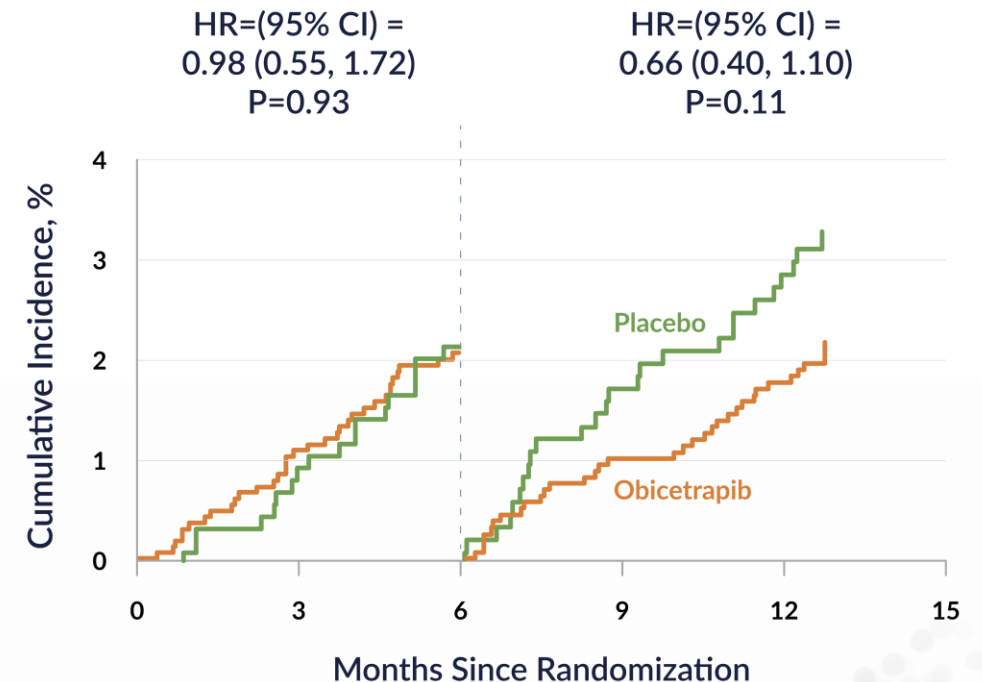
Kaplan-Meier Curve Separates at Day 200 Driven by Attenuation of Events in the Obicetrapib Arm



Kaplan Meier Curve



Landmark Analysis: Censored at 6 months



4-point MACE: CHD death, Non-fatal myocardial infarction, non-fatal stroke, coronary revascularization

Note: While not powered to detect a MACE benefit, we observed positive MACE data as part of our review of the exploratory endpoint. BROADWAY was not powered to measure MACE benefit and the MACE data presented below may not be predictive of the MACE data we observe in PREVAIL, which has been designed to measure MACE benefit.

Explaining BROADWAY's Observed 21% MACE Reduction

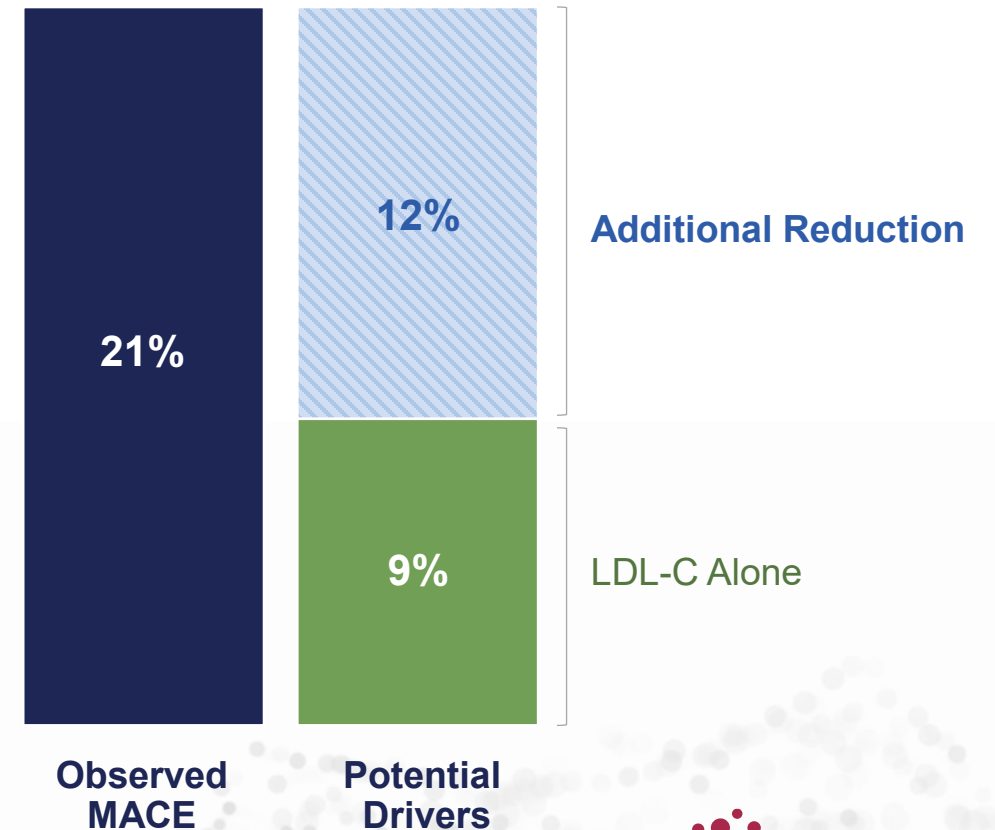


Based on the CTT line, the expectation for a 33% reduction in LDL-C from placebo would be a 9% MACE reduction, after 12 months

The observed reduction was 21% after 12 months

What is driving this greater than expected observed reduction?

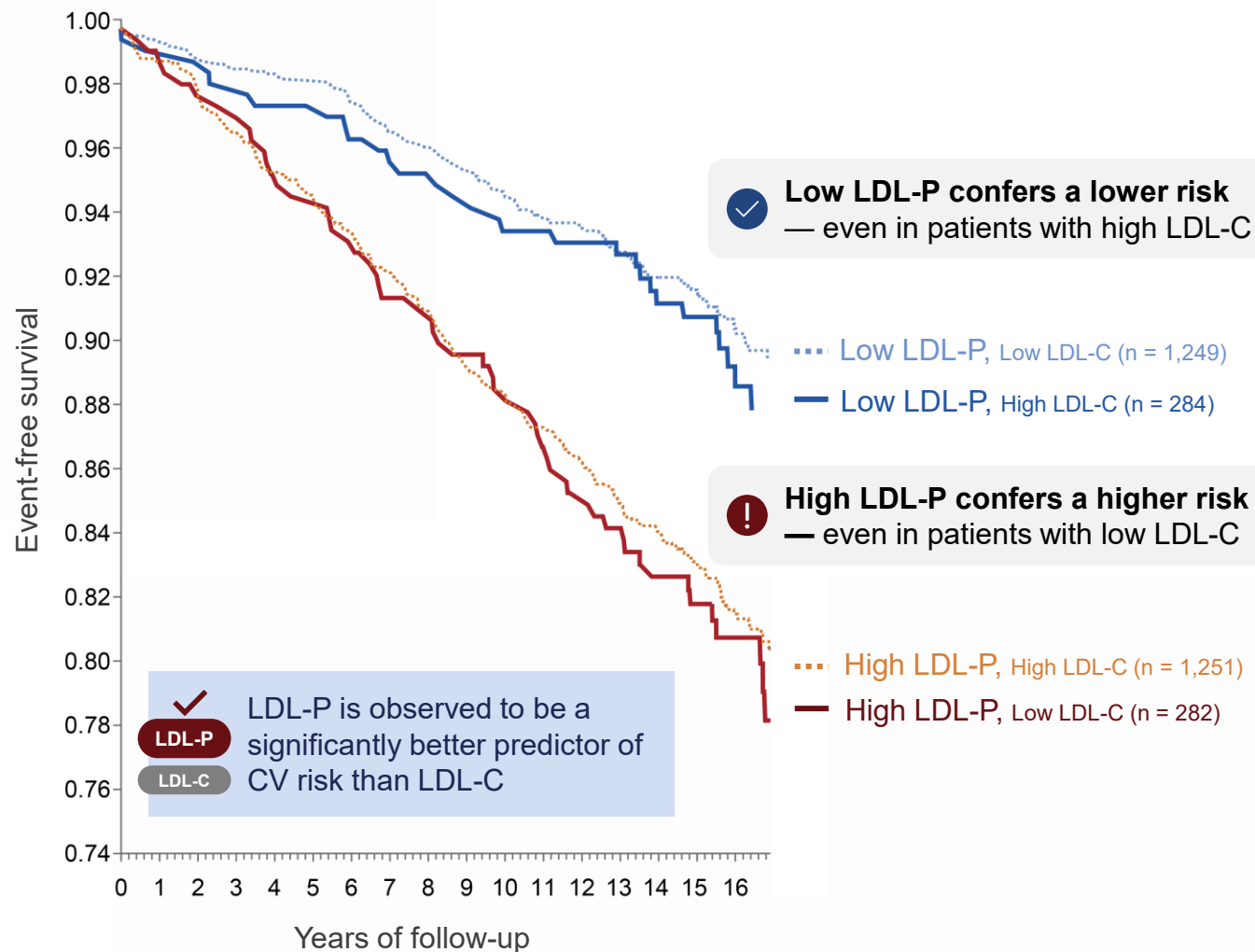
Obicetrapib's Observed MACE Reduction



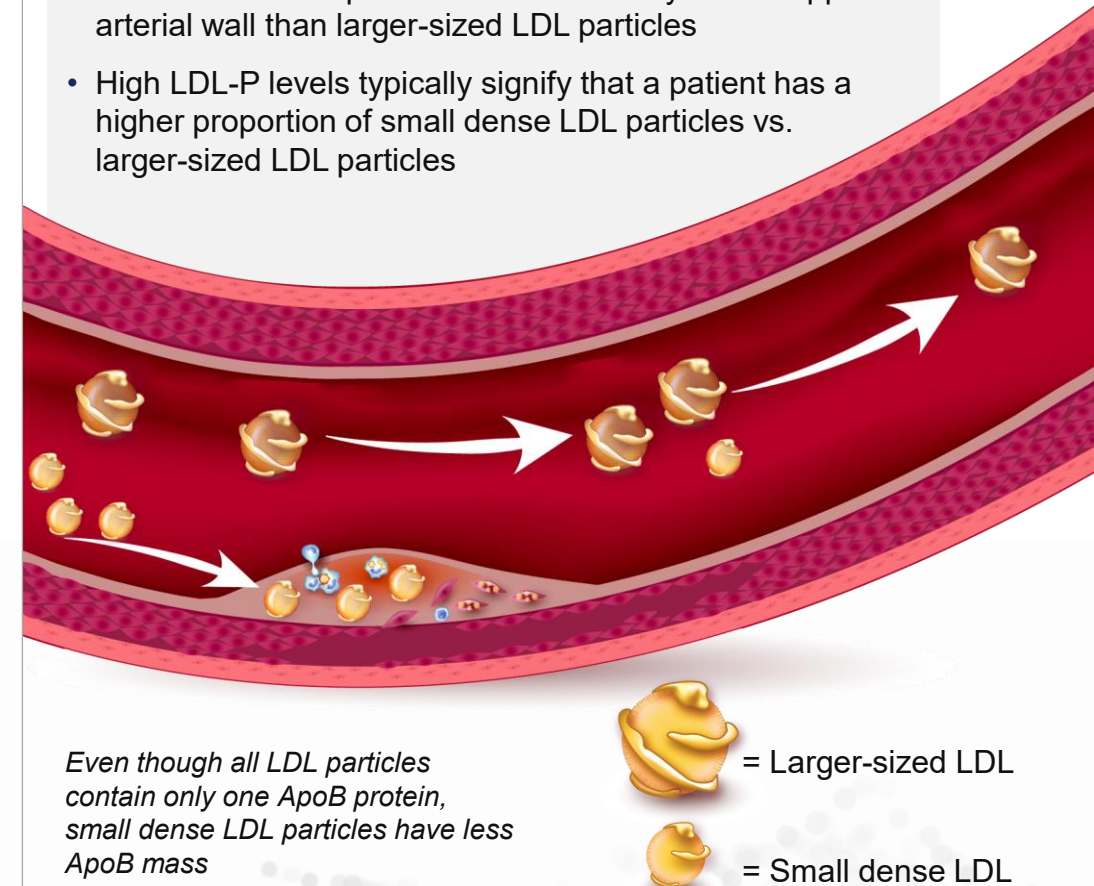


Residual LDL Particle Risk

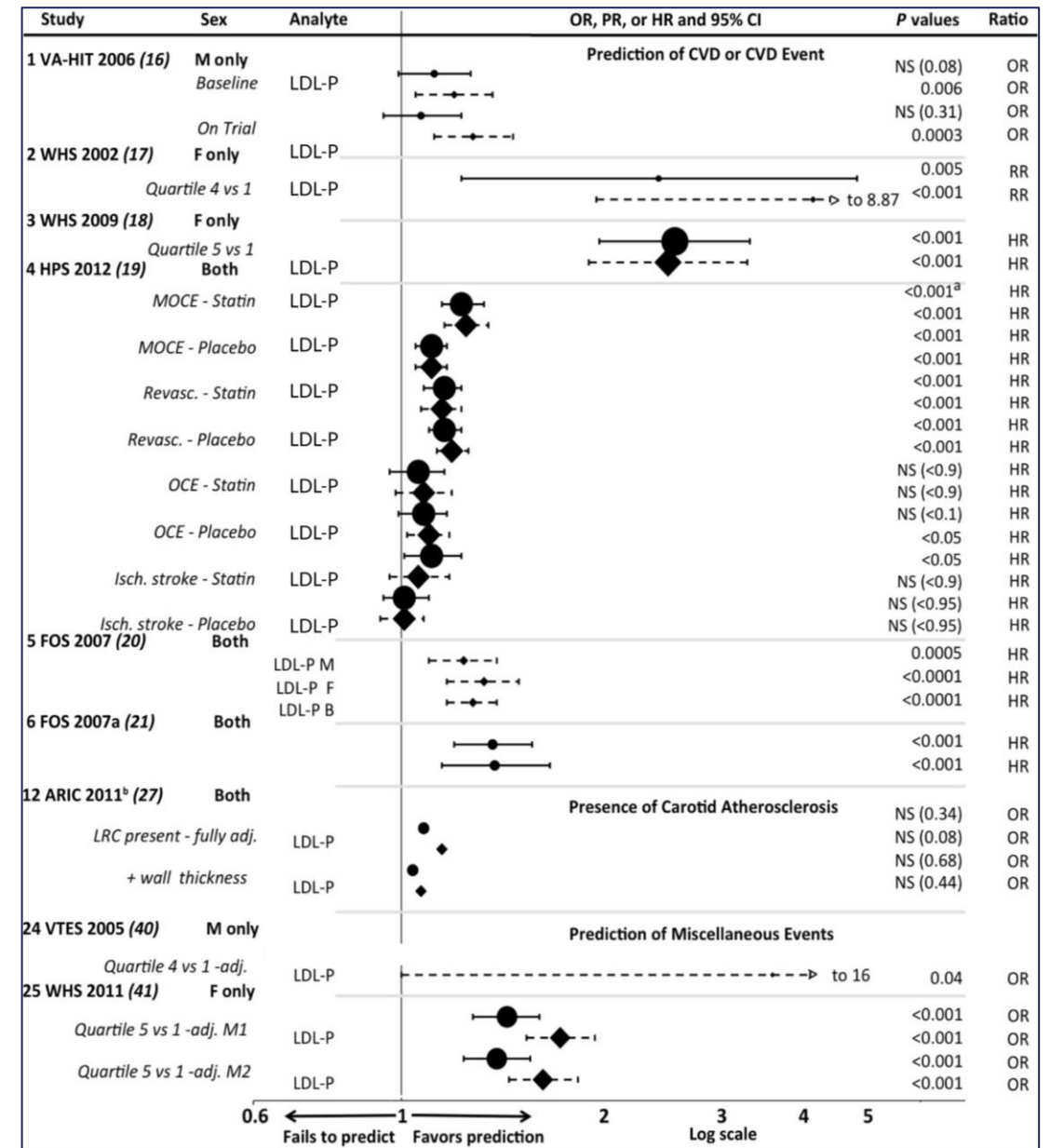
LDL-P Believed to be One of the Most Robust Predictors of Cardiovascular Risk



- Small dense LDL particles are more likely to be trapped in arterial wall than larger-sized LDL particles
- High LDL-P levels typically signify that a patient has a higher proportion of small dense LDL particles vs. larger-sized LDL particles



LDL Particles are a Strong Predictor of Risk

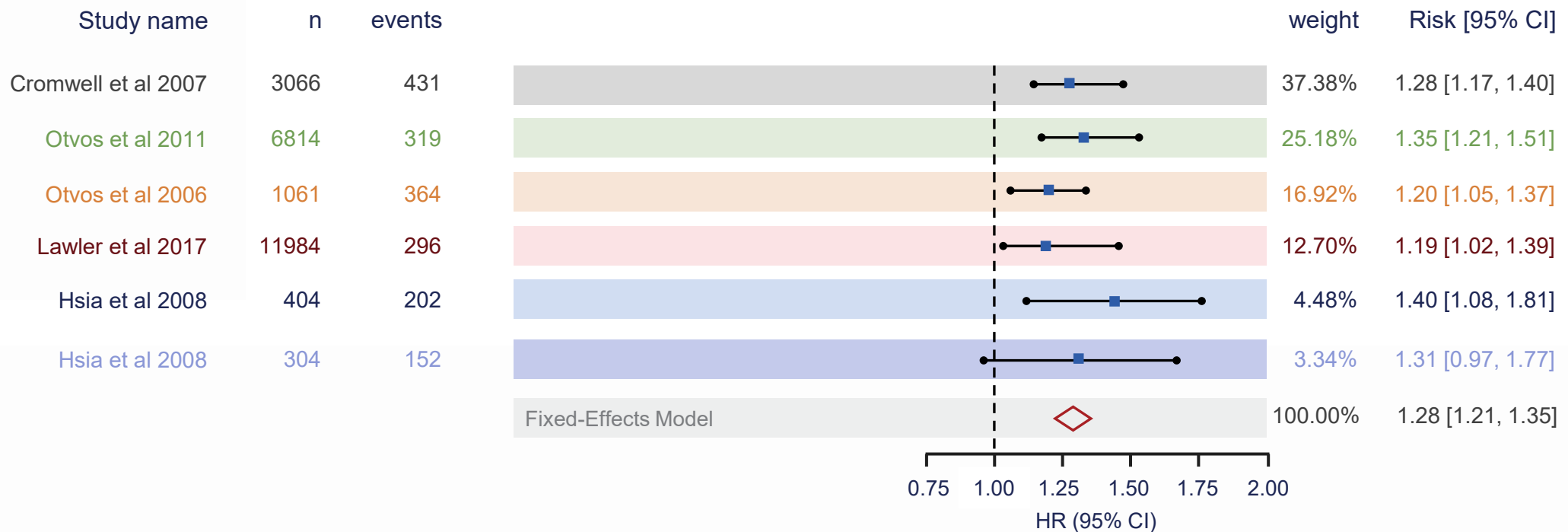


Obicetrapib Preferentially Reduces Small LDL Particles

Parameter	Pooled (n=2538)	BROADWAY (n=2041)	BROOKLYN (n=239)	TANDEM (n=182)
Baseline LDL-P (nmol/L)	988.9	923.8	1224.9	1195.4
Baseline small LDL-P	662.2	647.4	680.8	792.2
Percent reduction LDL-P	40.1%	36.3%	52.5%	60.1%
Percent reduction small LDL-P	100.6%	103.2%	102.4%	93.7%

Changes in LDL-P Associated with Increased Risk

A one standard deviation increase in LDL-P is associated with a 28% increase in cardiovascular events

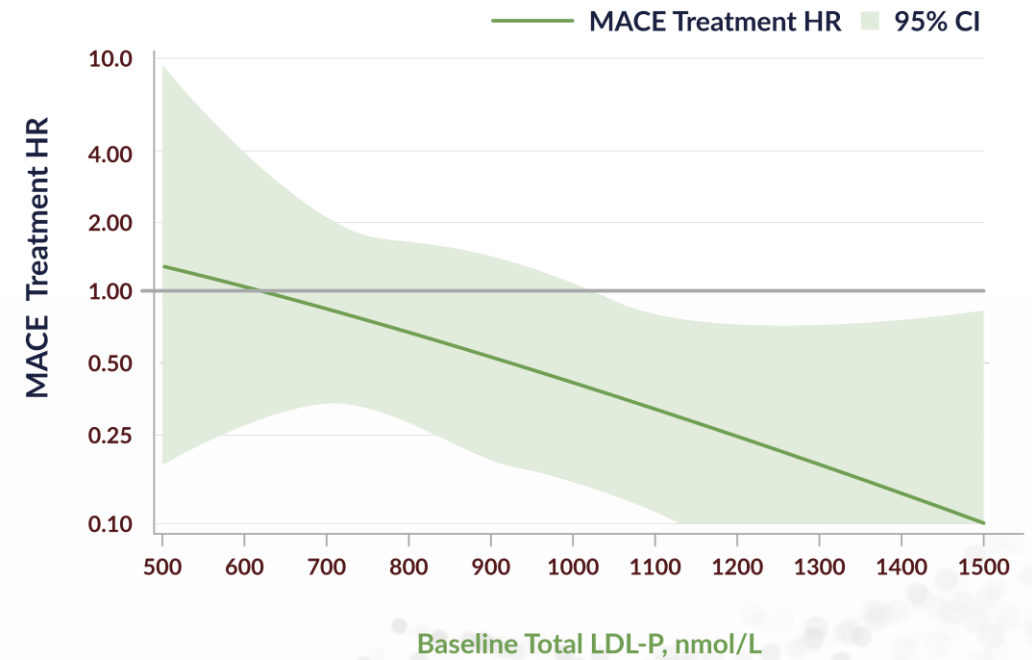
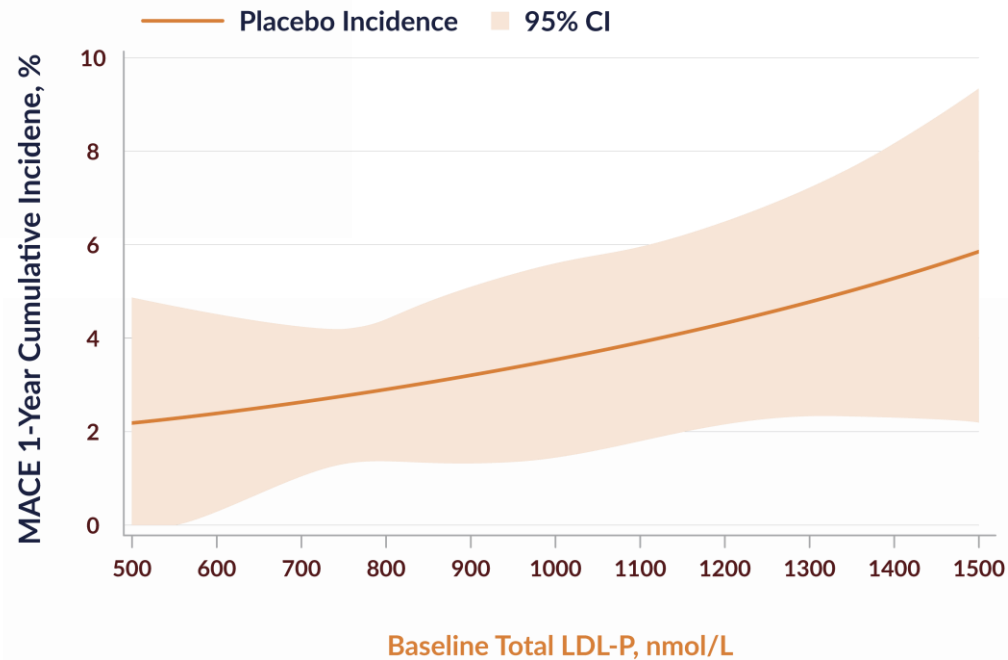


As Particle Numbers Rise, Risk Increases

Obicetrapib has greater benefit on smaller particles

Cumulative incidence of MACE* in the placebo group by baseline total LDL-P, ITT population spline P=0.14

Cumulative incidence of MACE* in the placebo group by baseline Total LDL-P, ITT population spline P=0.14



*CDC Death + NFMI + Stroke + Coronary Revasc

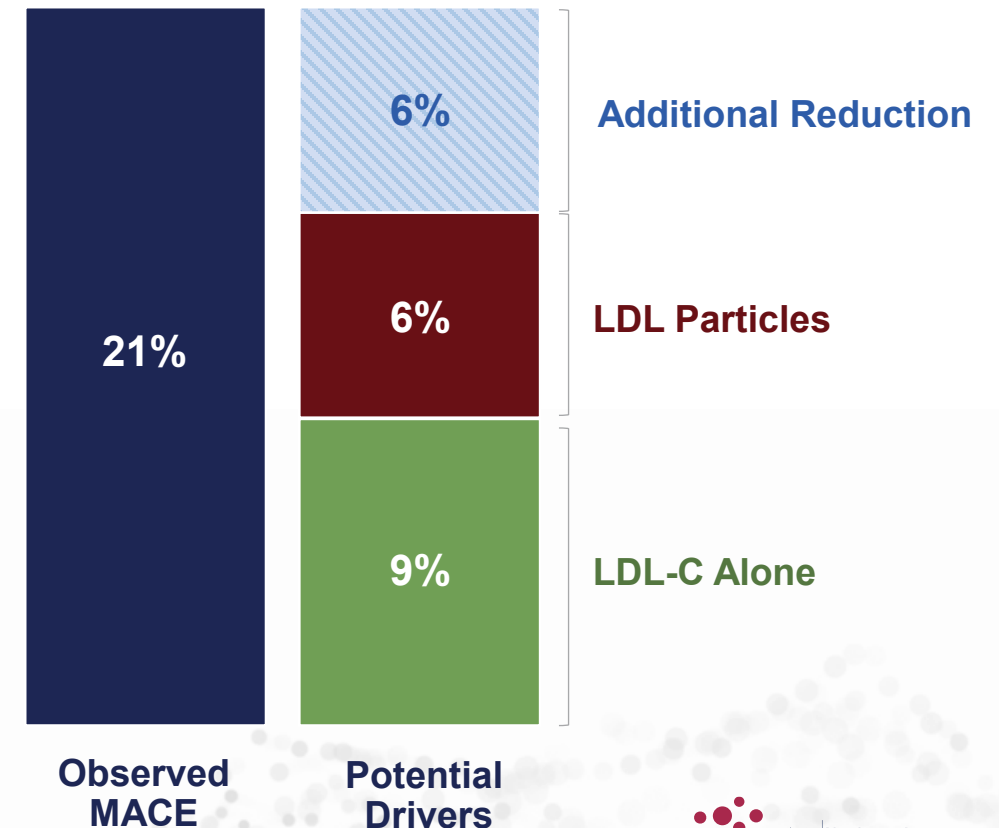
*CDC Death + NFMI + Stroke + Coronary Revasc

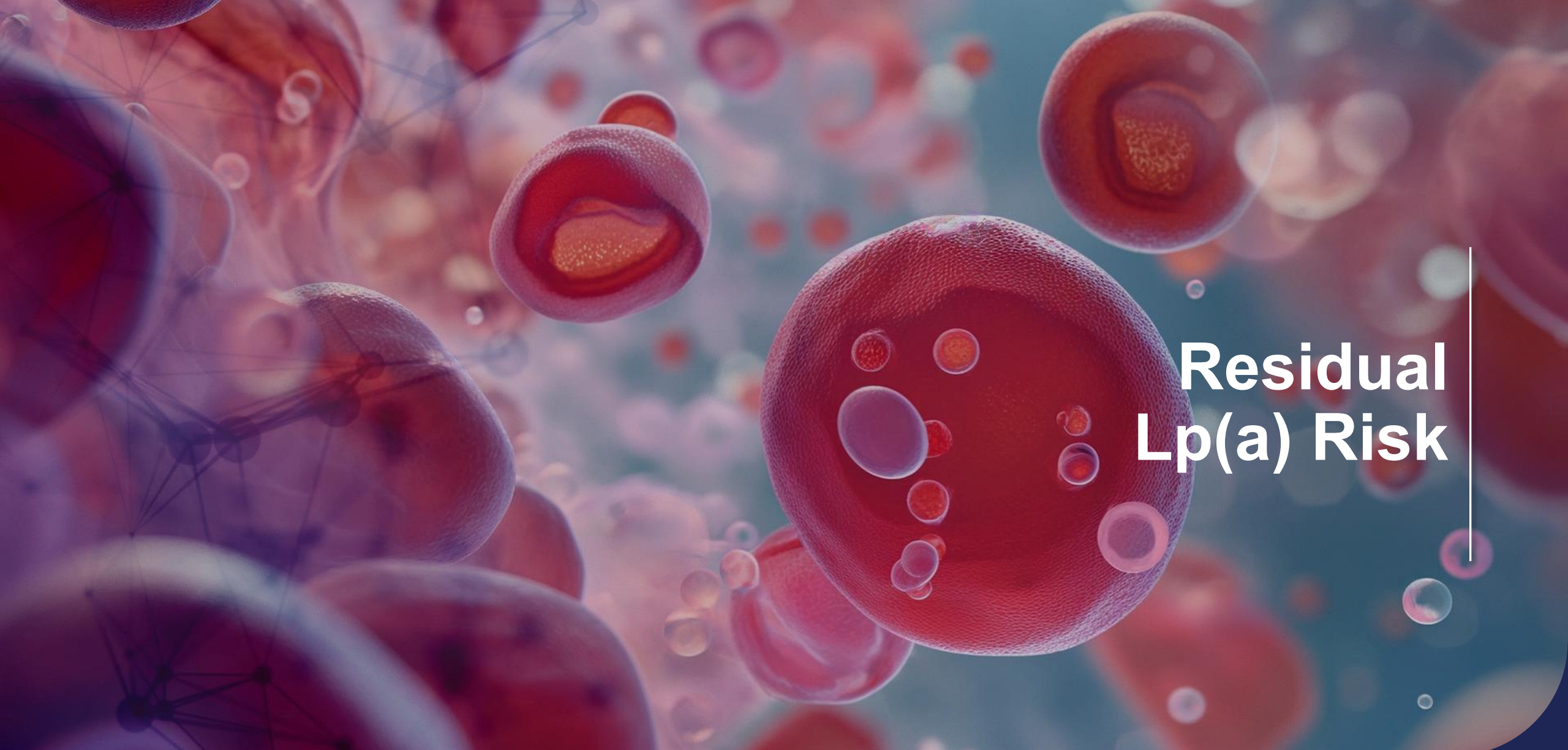
LDL-P Contributors to MACE

Methods of Estimating MACE Reduction

- 1** Treatment of particles has been associated with a 6-8% additional MACE reduction in high-risk individuals above LDL-C alone
 - 2** Based on the observed LDL-P reduction in BROADWAY, we would estimate a 15% decrease in MACE events vs 9% for LDL-C alone
 - 3** We observed a HR of 0.84 based on LDL-P, again 7% greater than the 0.91 based on LDL-C alone
- ➔ The average of these three methods is an additional 6% reduction from LDL-P

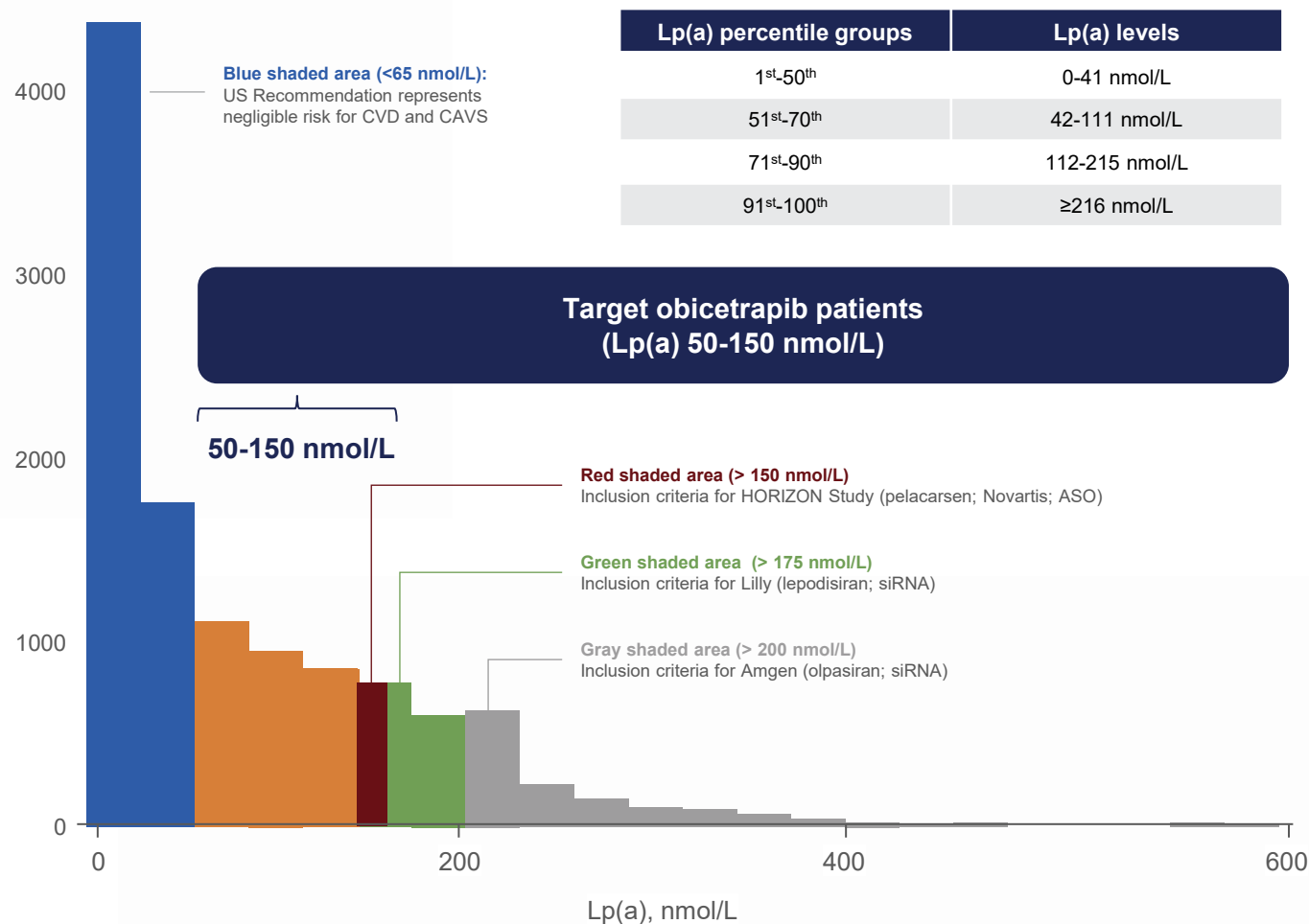
Obicetrapib's Observed MACE Reduction





Residual Lp(a) Risk

Lp(a) Concentrations Have Been Associated with Risk of ASCVD



Even with high prevalence, there are currently no pharmacologic therapies approved for reducing Lp(a)

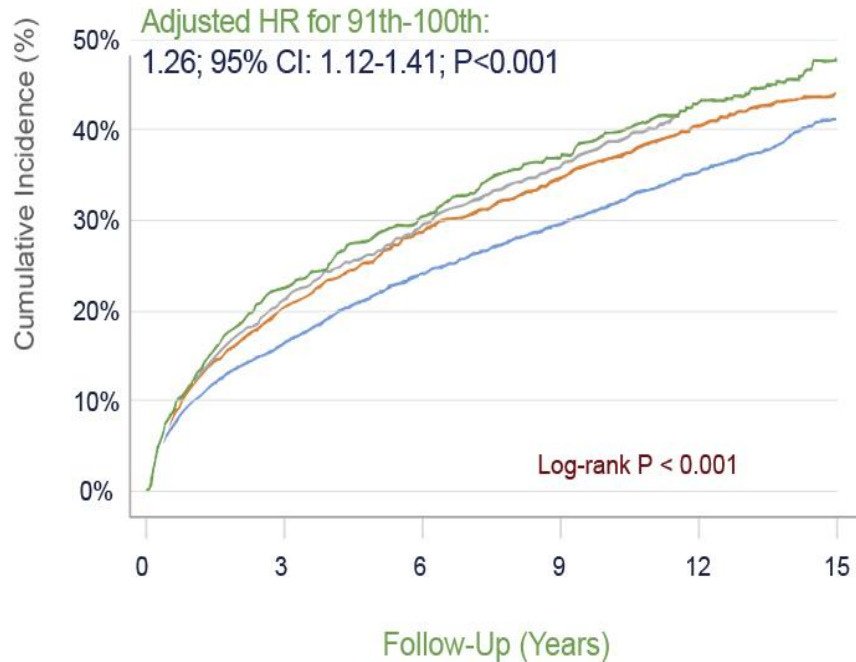
Lp(a) distribution in general population extrapolated from the graph					
Prevalence	20%	10%	5%	1%	<0.1%
Lp(a) levels	60 mg/dL	90 mg/dL	116 mg/dL	180 mg/dL	245 mg/dL
Number (US)	64,000,000	32,000,000	16,000,000	3,200,000	320,000
Number (EU)	150,000,000	75,000,000	37,500,000	7,500,000	750,000
Globally	1,400,000,000	700,000,000	350,000,000	70,000,000	7,000,000



Estimated prevalence assumes
320 million in US, 750 million in EU and 7 billion globally

Increased Risk Begins at Lp(a) Levels as Low as 40 nmol/L

Association of Lp(a) percentile group with the primary composite outcome, ASCVD patients



Composite endpoint of major adverse cardiovascular event for individuals with and without baseline ASCVD

Composite Endpoint: MACE

ASCVD (n=10,181)

No ASCVD (n=6,238)

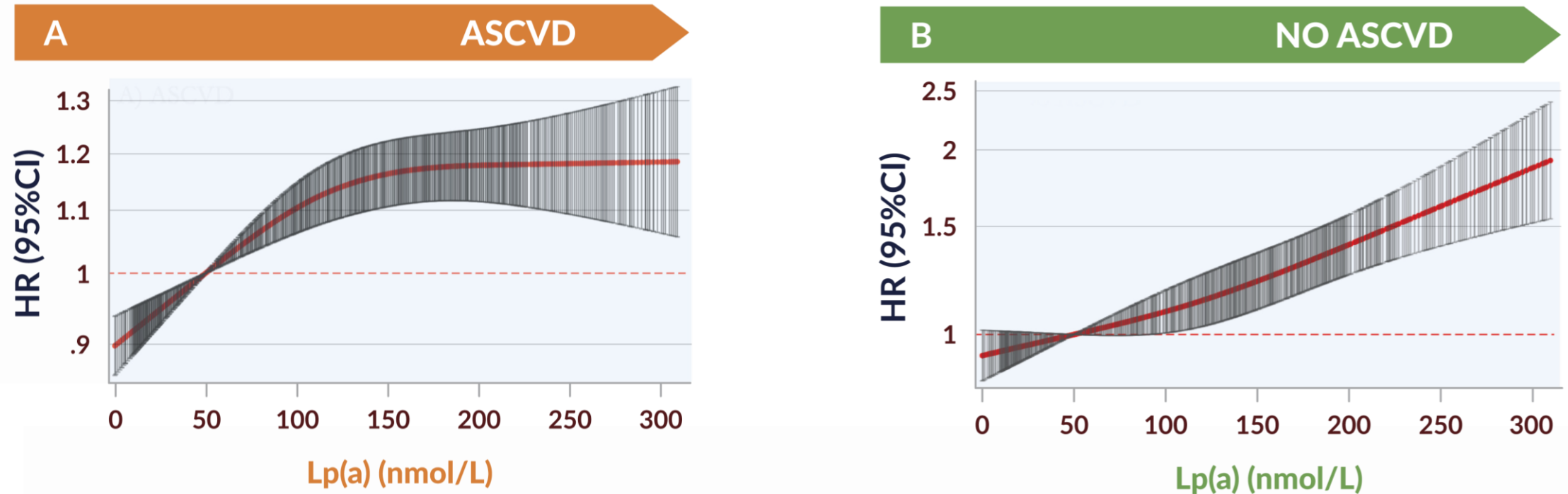
1st-50th Percentile	1,886/5,423 (34.8)	423/3,618 (11.7)
51st-70th Percentile	816/2,086 (39.1)	144/1,119 (12.9)
71st-90th Percentile	749/1,827 (41.0)	152/1,065 (14.3)
91st-100th Percentile	351/845 (41.5)	94/436 (21.6)

	Unadjusted HR (95% CI)	Adjusted HR (95% CI)	Unadjusted HR (95% CI)	Adjusted ^a HR (95% CI)
1st-50th Percentile	Reference	-	Reference	-
51st-70th Percentile	1.18 (1.09-1.28); P < 0.001	1.14 (1.05-1.24); P = 0.002	1.11 (1.92-1.35); P = 0.265	1.09 (0.90-1.32); P = 0.354
71st-90th Percentile	1.26 (1.15-1.37); P < 0.001	1.21 (1.11-1.32); P < 0.001	1.24 (1.03-1.49); P = 0.024	1.17 (0.97-1.41); P = 0.096
91st-100th Percentile	1.27 (1.14-1.43); P < 0.001	1.26 (1.12-1.41); P < 0.001	2.04 (1.63-2.55); P < 0.001	1.93 (1.54-2.42); P < 0.001

Values are n/N (%) unless otherwise indicates. ^aAdjusted for age, sex, self-reported race/ethnicity, hypertension, chronic kidney disease status, non-Lp(a) hyperlipidemia, diabetes, insulin use (in diabetic individuals), and smoking status.

MACE = major adverse cardiovascular events; other abbreviations as in Table 2.

Significant Risk for ASCVD Patients Between 50 nmol/L and 150 nmol/L



Restricted cubic spline modeling the association of continuous lipoprotein(a) levels on the primary composite outcome (myocardial infarction, ischemic stroke, coronary revascularization, cardiovascular mortality) among individuals with a history of ASCVD (A) and among those without a history of ASCVD (B). Knots were set at 41 nmol/L (50th percentile – reference), 111 nmol/L (70th percentile), and 215 nmol/L (90th percentile), and the splines are truncated at the 99th percentile (310 nmol/L). Abbreviations as in Figure 2.

Lp(a) Reduction of 45% in Key Patient Population

Parameter	Pooled (n=2538)	BROADWAY (n=2041)	BROOKLYN (n=315)	TANDEM (n=182)
Baseline Lp(a)	42.7 (12.3, 171.4)	42.6 (12.2, 170.1)	45.0 (14.1, 178.5)	38.9 (11.2, 187.2)

Percent change Lp(a)

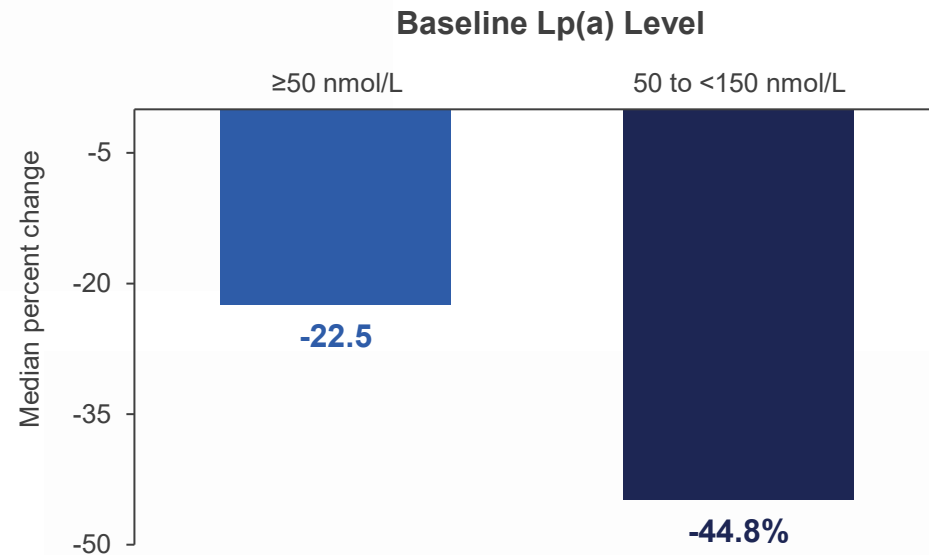
Baseline Lp(a) ≥50 nmol/L	-22.5 (-25.7, -19.3)	-21.4 (-24.9, -18.0)	-29.2 (-39.8, -18.5)	-24.8 (-38.0, -11.6)
Baseline Lp(a) 50-<150 nmol/L	-44.8 (-50.7, -38.9)	-42.8 (-49.5, -36.1)	-52.2 (-70.6, -33.7)	-52.4 (-73.5, -31.3)
Baseline Lp(a) ≥150 nmol/L	-12.8 (-15.7, -9.9)	-12.6 (-15.9, -9.3)	-13.3 (-21.2, -5.3)	-12.6 (-25.9, 0.6)

Absolute change Lp(a) (nmol/L)

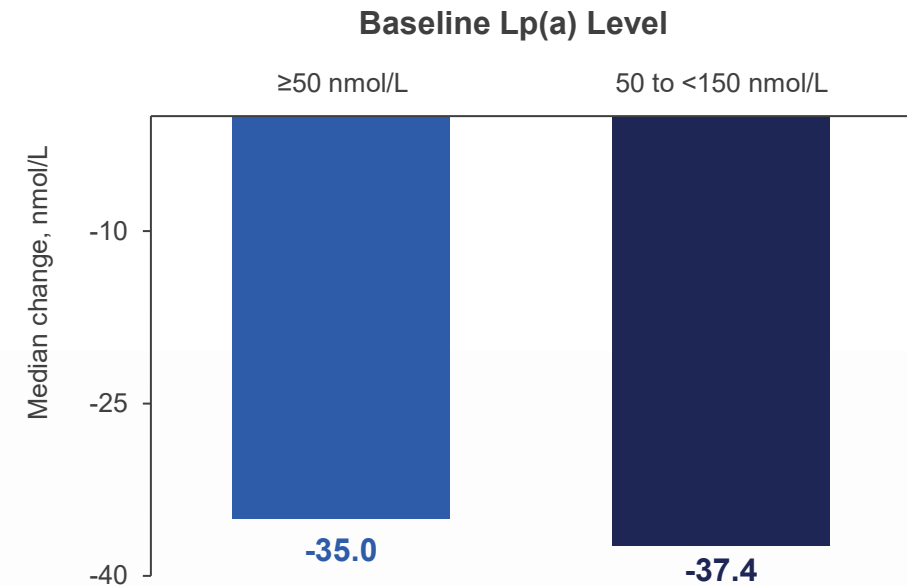
Baseline Lp(a) ≥50 nmol/L	-35.0 (-39.6, -30.3)	-33.6 (-38.7, -28.4)	-39.8 (-53.8, -25.8)	-40.0 (-61.2, -18.7)
Baseline Lp(a) 50-<150 nmol/L	-37.4 (-42.0, -32.7)	-35.8 (-40.9, -30.7)	-43.5 (-60.4, -26.6)	-43.4 (-63.4, -23.4)
Baseline Lp(a) ≥150 nmol/L	-33.1 (-41.0, -25.2)	-31.7 (-40.7, -22.7)	-37.3 (-21.2, -5.3)	-35.2 (-76.0, 5.7)

Pooled BROADWAY, BROOKLYN, and TANDEM effects on Lp(a)

Percentage Lp(a) reduction



Absolute Lp(a) Reduction

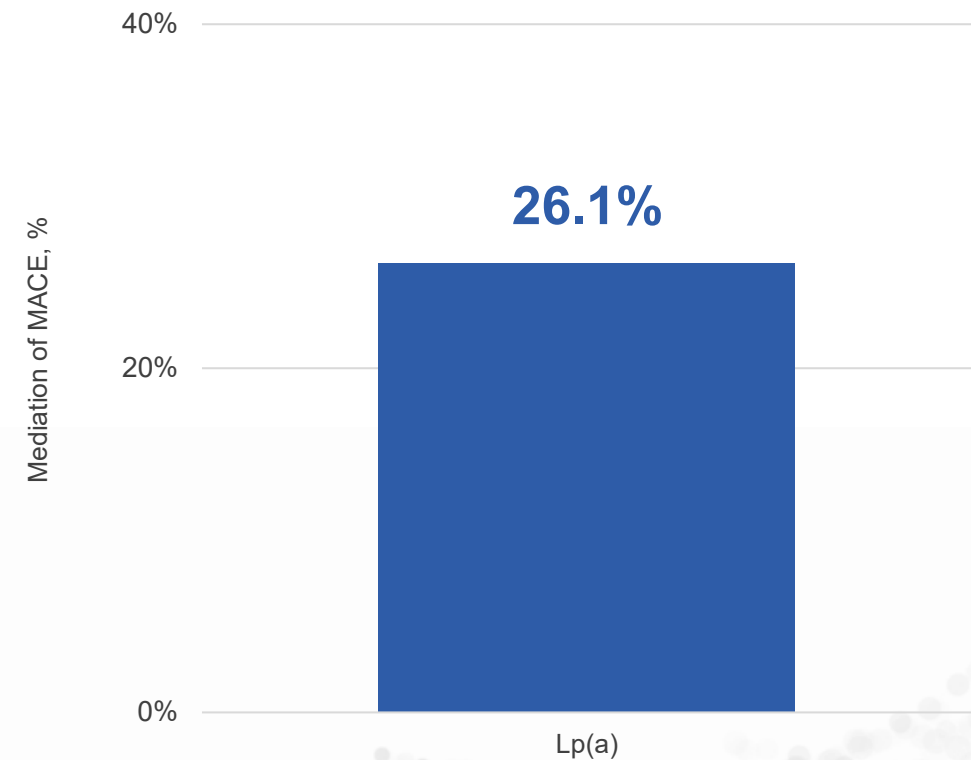


Mediation Analysis Predicts 26% of MACE Reduction from Lp(a) in BROADWAY

Multivariate Mediation of OBI MACE Reduction

A mediation analysis was performed to identify the proportion of the observed **21%** reduction in cardiovascular events potentially attributable to Lp(a)

Based on the analysis, we predict approximately **26%** of the overall change in MACE could be explained by reduction in Lp(a)



Lp(a) Contributors to MACE

Methods of Estimating MACE Reduction

1

Based on observational studies a 100 nmol/L reduction in the Lp(a) should equate to a 22% MACE reduction

- In BROADWAY we see an ~35 nmol/L reduction, predicting 8% reduction in risk of MACE at two years or a 4% reduction at one year

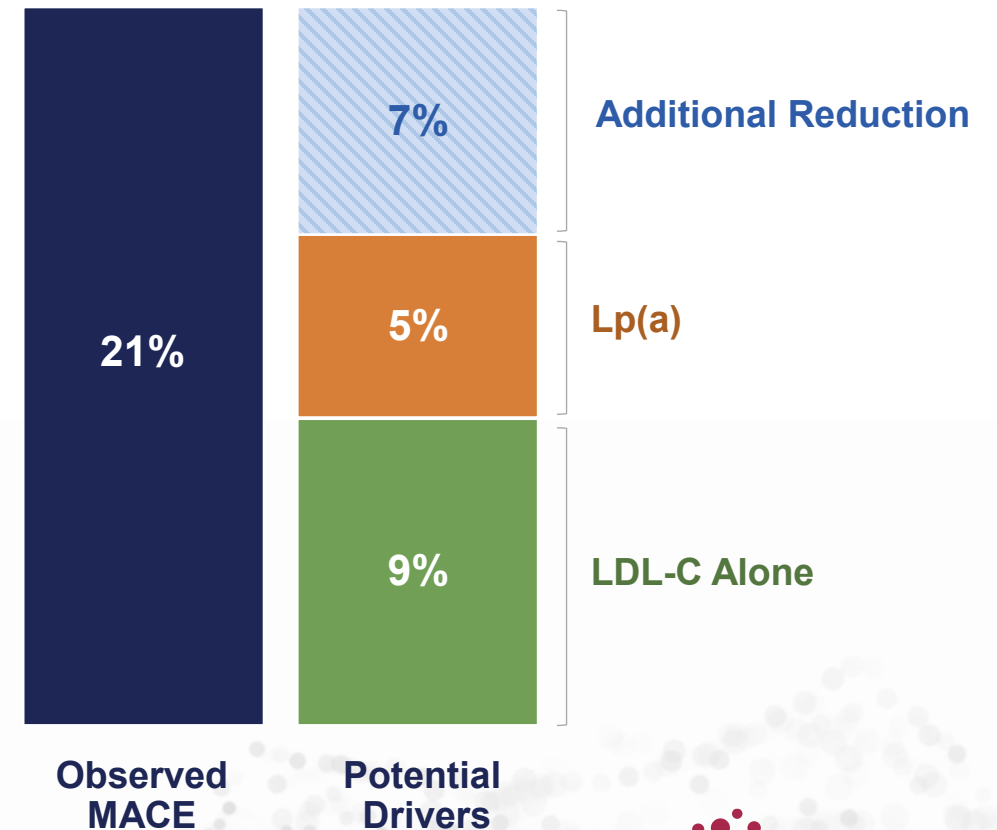
2

Mediation analysis predicts 5% contribution from Lp(a)



Based on these two methods we estimate approximately 4-5% of absolute incremental benefit is attributable to Lp(a)

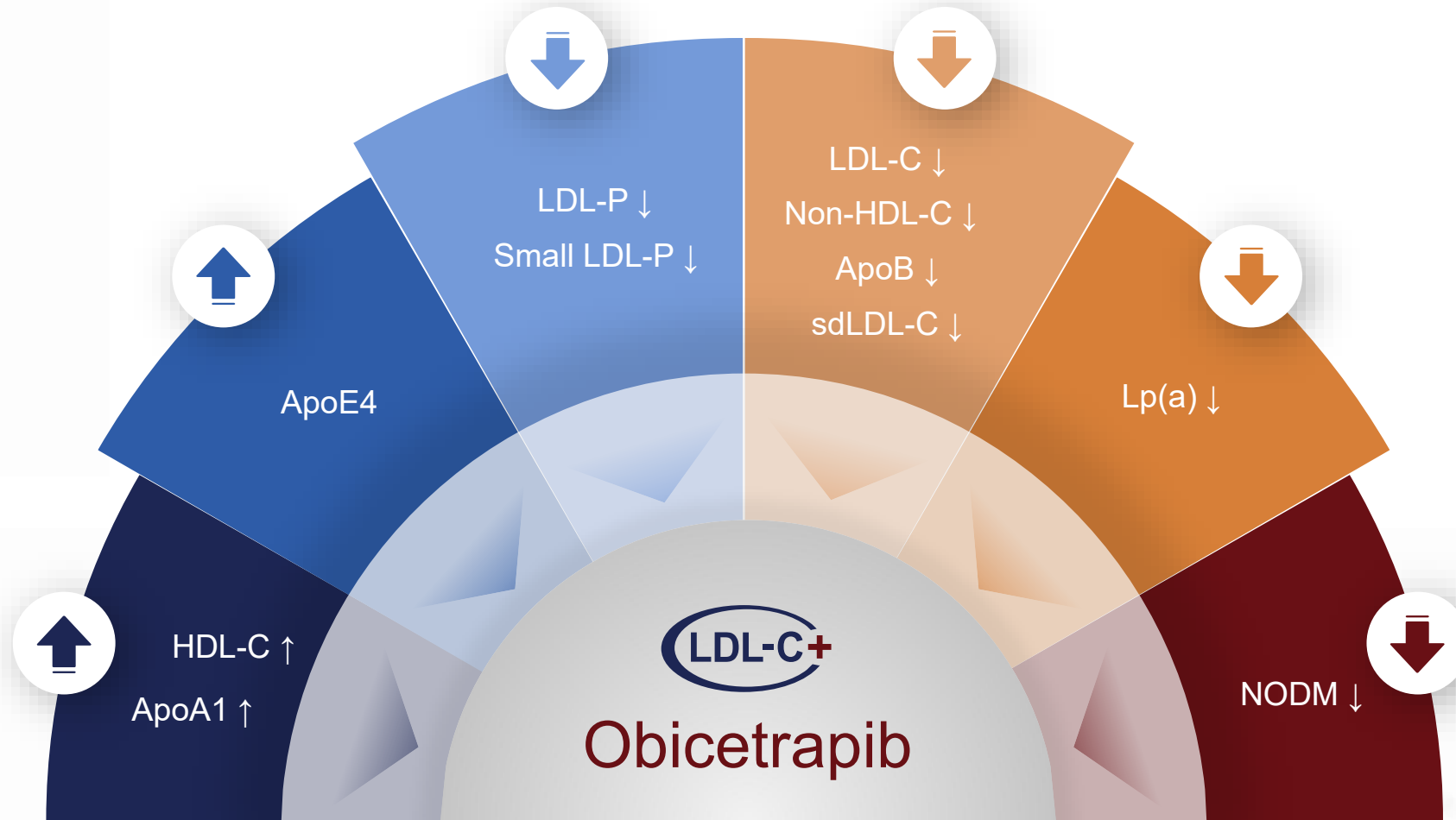
Obicetrapib's Observed MACE Reduction





Cumulative Effect

The Future of Hyperlipidemia Treatment Goes Beyond LDL-C



Explaining BROADWAY's Observed 21% MACE Reduction

Methods of Estimating MACE Reduction



Based on the CTT line, the expectation for a 33% reduction in LDL-C from placebo would be a 9% MACE reduction, after 12 months



LDL-P potentially provides 6-7% additional MACE reduction, mainly driven by small LDL-P

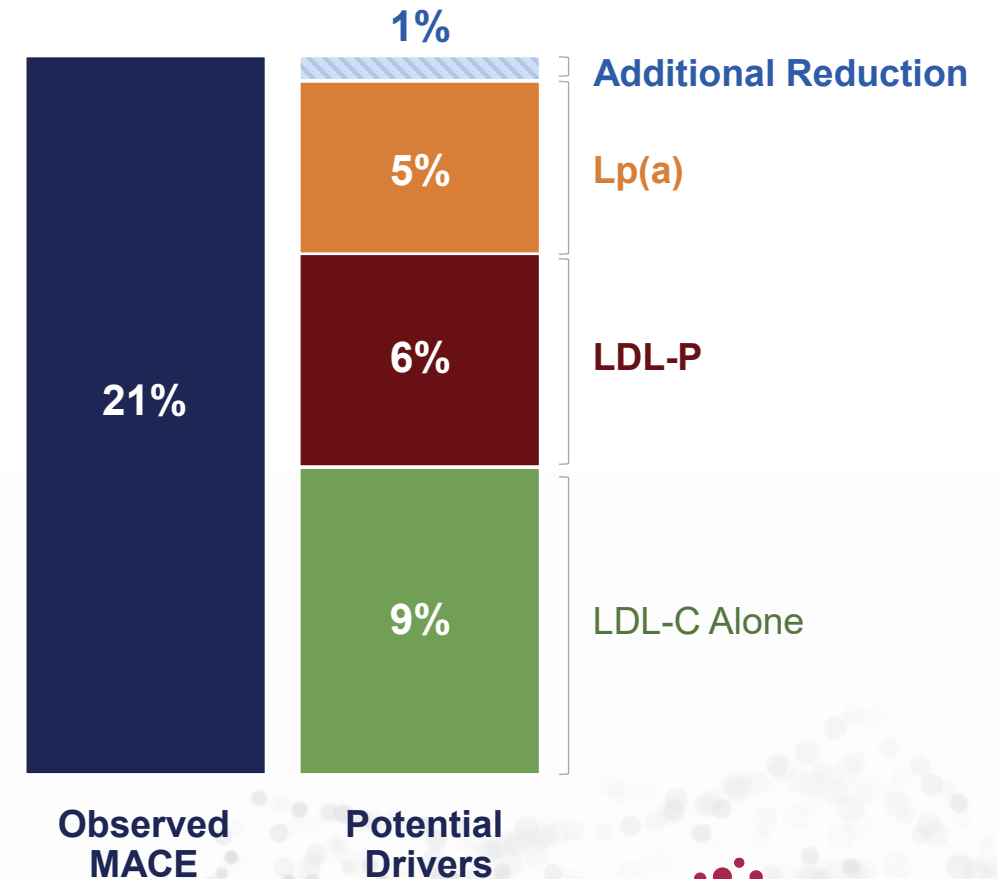


Lp(a) potentially provides an additional 5% MACE reduction



These elements may not be additive as they are correlated to some extent. In this scenario, there is room for additional reduction to be driving incremental gains

Obicetrapib's Observed MACE Reduction



Note: Actual results may differ from hypothetical calculation.

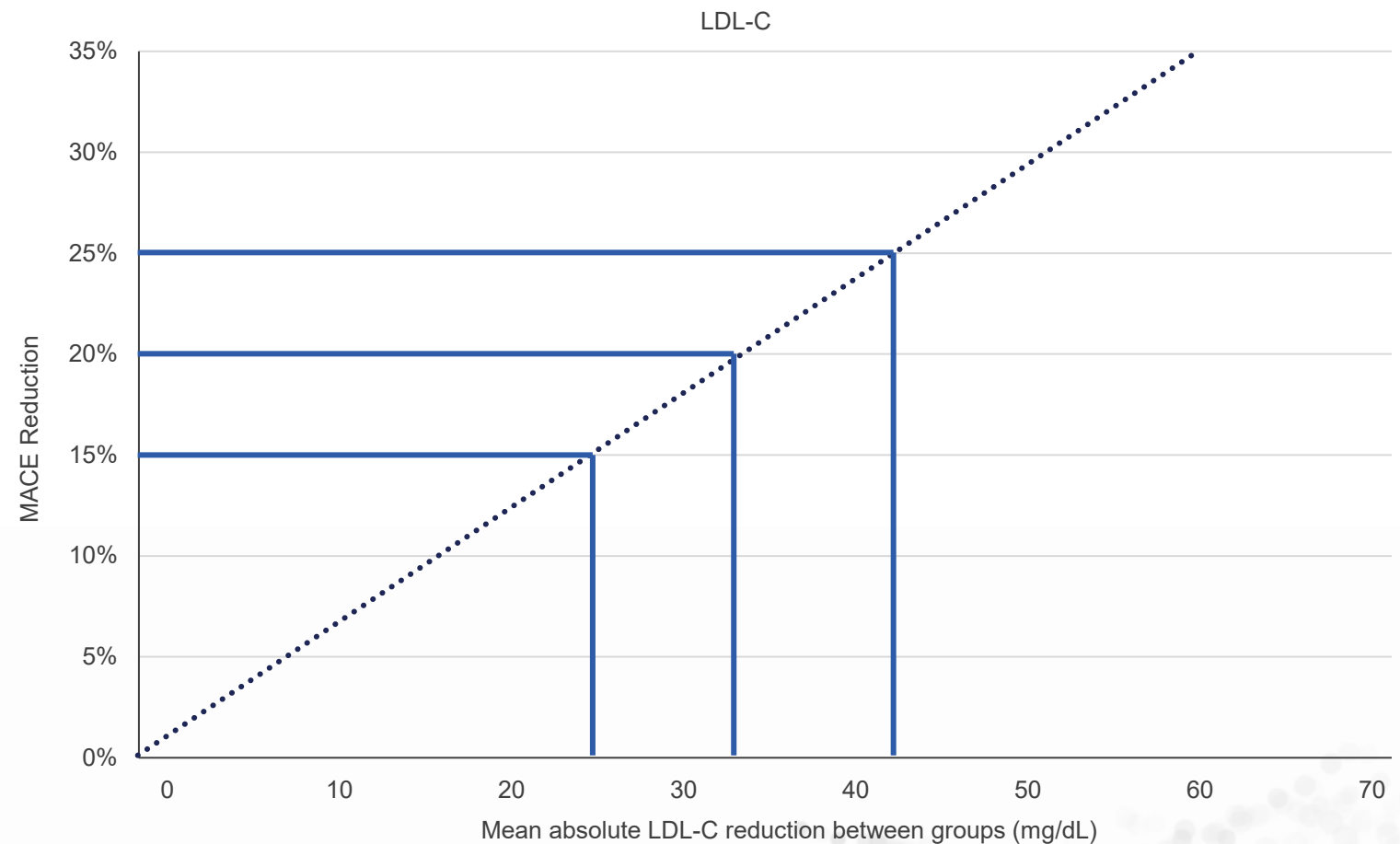
Source: Cholesterol Treatment Trialists Collaboration; Folse et al. Athero 2014, Quseda et al, Atherosclerosis 35 (2023) 165-177; Berman, A, Biery, D, Besser, S. et al. Lipoprotein(a) and Major Adverse Cardiovascular Events in Patients With or Without Baseline Atherosclerotic Cardiovascular Disease. JACC. 2024 Mar, 83 (9) 873-886; Data on file

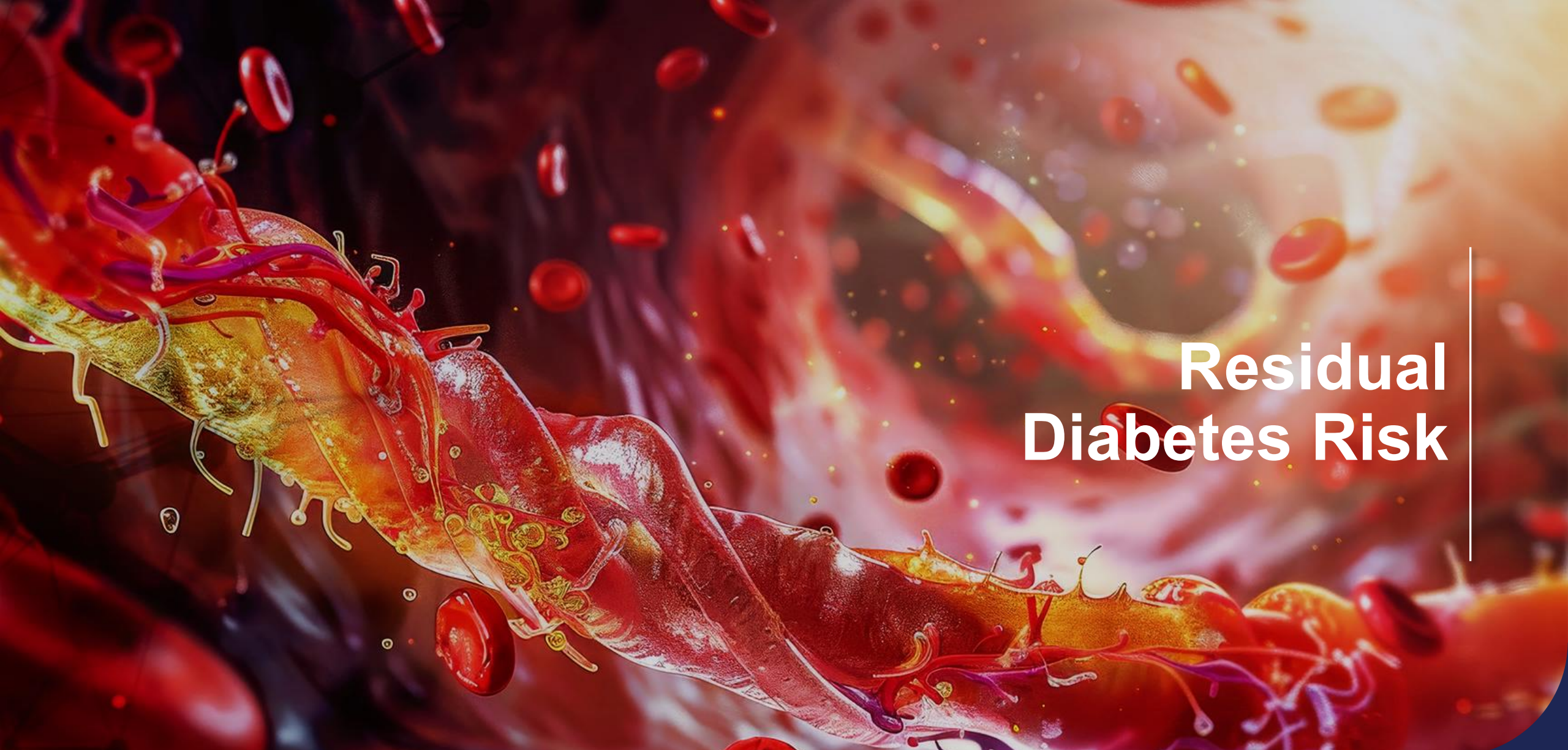
** MACE includes CHD death, myocardial infarction, ischemic stroke and coronary revascularization in adults.

LDL-C Reduction Alone Supports 20% Estimated MACE Benefit in PREVAIL

LDL-C reduction placebo adjusted	Estimated MACE Benefit
25.0%	15.3%
27.5%	16.9%
30.0%	18.4%
32.5%	19.9%
35.0%	21.5%
37.5%	23.0%
40.0%	24.5%
42.5%	26.1%
45.0%	27.6%
47.5%	29.2%
50.0%	30.7%

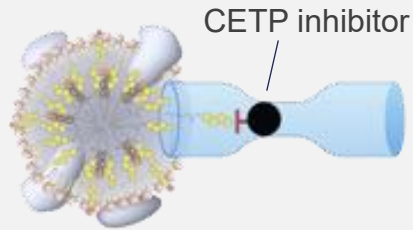
	CVOT MACE Benefit
PCSK9s ⁽¹⁾	15%
Bempedoic Acid ⁽²⁾	13%
Ezetimibe ⁽³⁾	7%





Residual Diabetes Risk

CETP Inhibition Demonstrates Potential to Improve β Cell Function



Blocking CETP increases HDL levels²

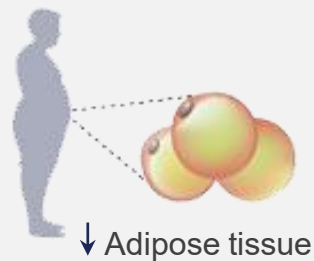
High HDL levels protect β cells by¹:

- Combating cellular lipid accumulation
- Reducing ER stress
- Preventing apoptosis

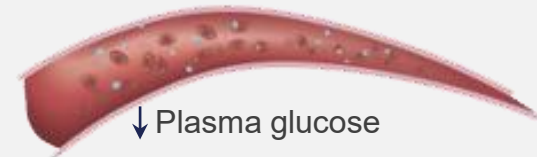
High HDL levels also promote^{1,3}:

- Insulin secretion from β cells
- Glucose uptake in peripheral tissues

High HDL/ApoA1 levels associated with less adipose tissue⁴



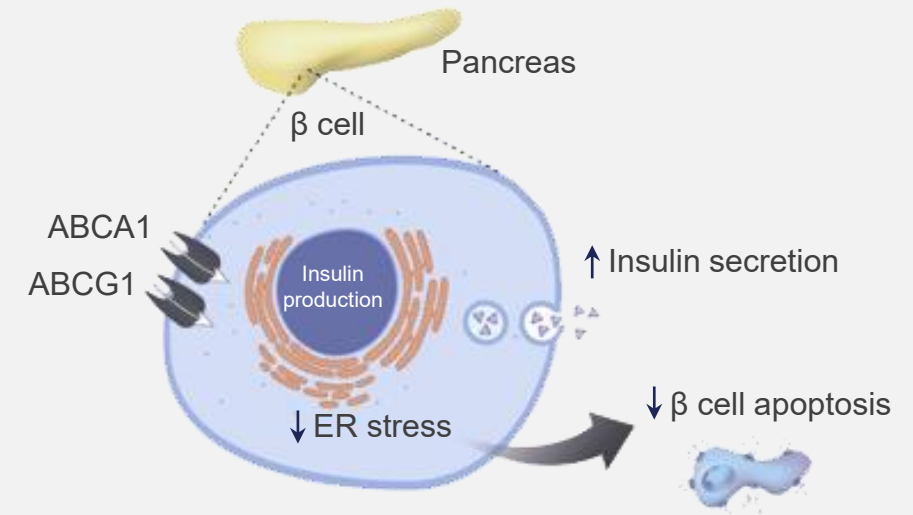
↓ Adipose tissue



↓ Plasma glucose



↑ Skeletal muscle glucose uptake by myocytes



Increases in HDL-C Reduce the Risk of Developing Type 2 Diabetes

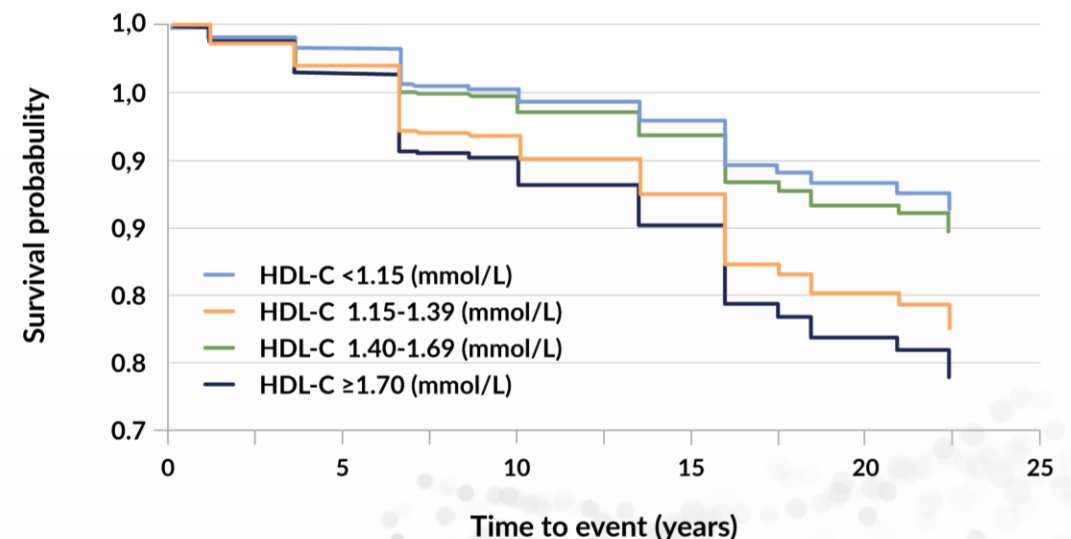
- Dose-response relationship observed between HDL-C and the risk of new-onset diabetes
- Multivariate predictive models show robust negative correlation between HDL-C and risk of future T2DM incidence
- 25-year follow-up data also show that increased HDL-C correlates with diminished T2DM risk, suggesting that HDL-C levels may influence glucose metabolism

Association between HDL-C levels and T2DM risk for baseline levels of HDL-C (mmol/L)

HDL-C, Cox model	HR (95% CI)	P=0.003
<1.15	1.00 (1.00-1.00)	
1.15-1.39	0.96 (0.60-1.52)	
1.40 - 1.69	0.48 (0.27-0.86)	
>1.69	0.45 (0.25-0.81)	

Increasing HDL-C levels across these four quartiles resulted in considerable differences in survival probabilities

Reduced risk of diabetes incidence with increased HDL-C levels



Statins Caused a Dose-dependent Increase in New Diagnosis of Type-2 Diabetes Irrespective of Age, Sex, BMI and Blood Sugar Levels

High-intensity statin regimen resulted in a 36% increased risk of new-onset diabetes

	Events (% per annum)		Observed-expected				
	Statin (n=9935)	Placebo (n=9895)	o-e	Var (o-e)	Rate ratio (CI)	Favors statin	Favors placebo
High-intensity statin							
Diabetes-related adverse events	246 (0.9)	174 (0.7)	37.0	105.0	1.42 (99% CI 1.11-1.83)		
Diabetes determined from co-medication	198 (0.8)	159 (0.6)	20.1	89.2	1.25 (99% CI 0.95-1.64)		
Subtotal: diabetes-related adverse events and co-medications	297 (1.1)	229 (0.9)	35.1	131.5	1.31 (95% CI 1.10-1.55)		
Biochemically determined diabetes	1078 (4.1)	788 (3.0)	149.3	465.7	1.38 (99% CI 1.22-1.55)		
Any new-onset diabetes	1221 (4.8)	905 (3.5)	163.9	530.8	1.36 (95% CI 1.25-1.48)		

0.60.81.01.251.502.00

Obicetrapib 10 mg Reduced HbA1c Among Patients Without Diabetes and Demonstrated a Consistent Trend Toward Lower Risk of NoD in Patients with both Normoglycemia and Prediabetes at Baseline

~70% of patients were on high intensity statins

FIGURE 2. HbA1c levels at day 365 among all patients without diabetes at baseline in BROOKLYN and BROADWAY

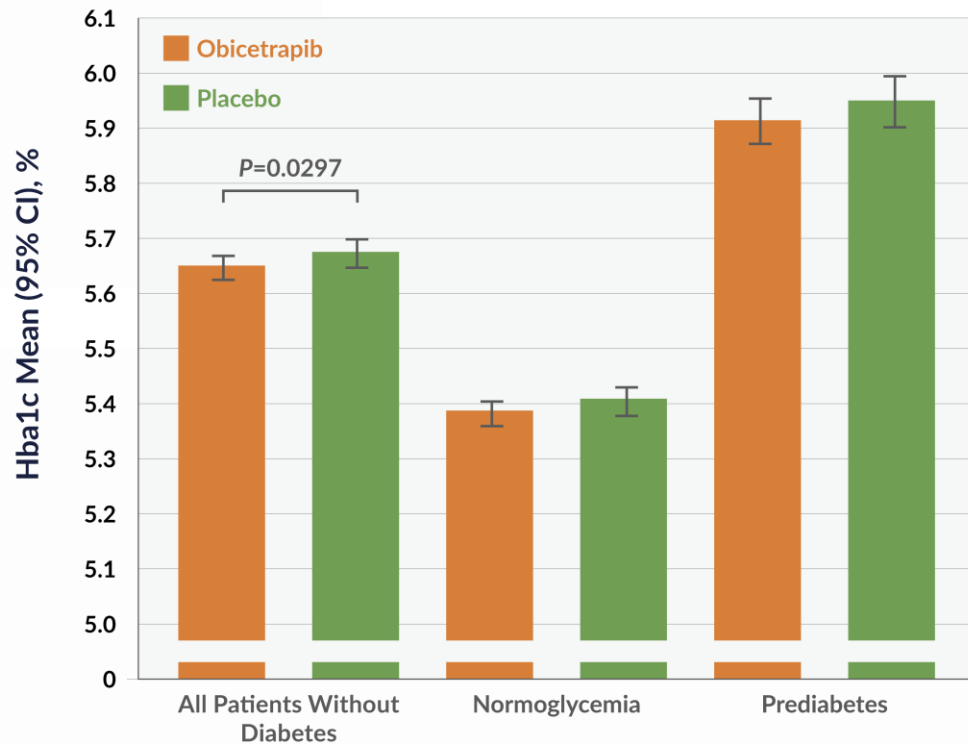
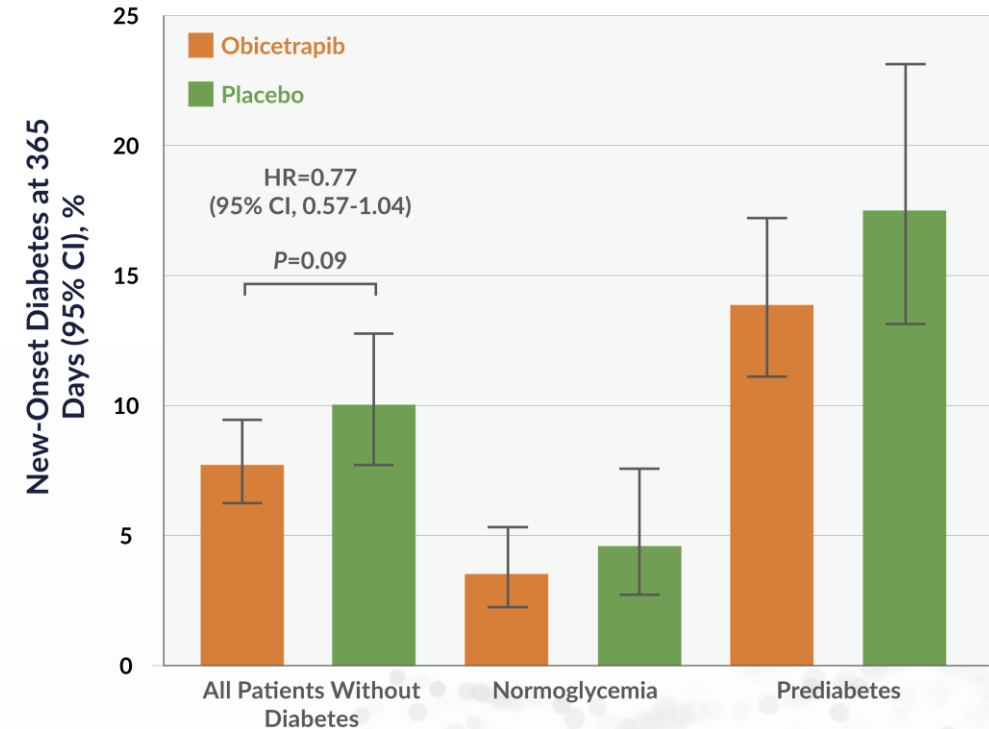
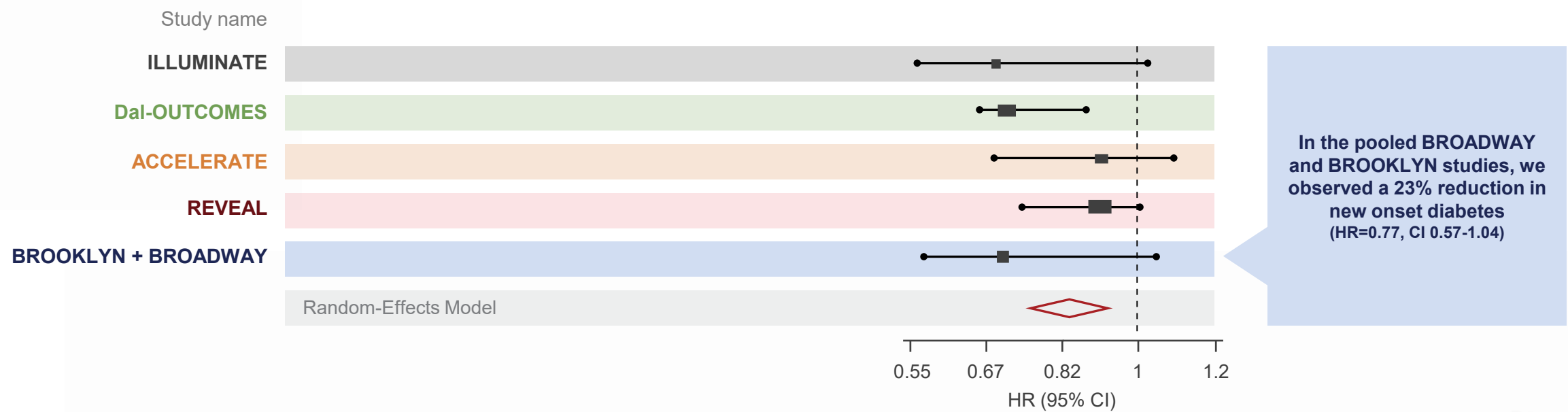


FIGURE 3. Development of NoD at day 365 among all patients without diabetes at baseline in BROOKLYN and BROADWAY



CETP Inhibition Has the Potential to Reverse Diabetes Risk, Potentially Ameliorating Key Concerns About High Dose Statins

This is consistent with the effects seen in other CETP trials that have shown 17% reduction in new onset diabetes (HR=0.83, CI 0.77-0.90)



T2D/Metabolic Syndrome Study - RUBENS

Objective: To evaluate the effect of obicetrapib and the FDC on LDL-C in patients with T2D / Met Syn

Study design: Randomized, double-blind, placebo-controlled

Main Inclusion Criteria:

- ≥ 18 years
- T2D / Metabolic Syndrome
- LDL ≥ 100 mg/dL
- TG $\geq 150 < 400$ mg/dL
- Guideline recommended LLT

Main Exclusion Criteria:

- Clinical ASCVD
- HoFH
- Uncontrolled hypertension

Primary efficacy endpoint

- % LS mean change from BL to Day 84 in LDL-C for obicetrapib & FDC using Martin-Hopkins

Key secondary efficacy endpoint

- LDL-C Goal attainment
- Lp(a), LDL-P, sdLDL

- Patients (n=300)
- T2D / Met Syn
- Guideline recommended LLT

Obi 10mg (n=100)

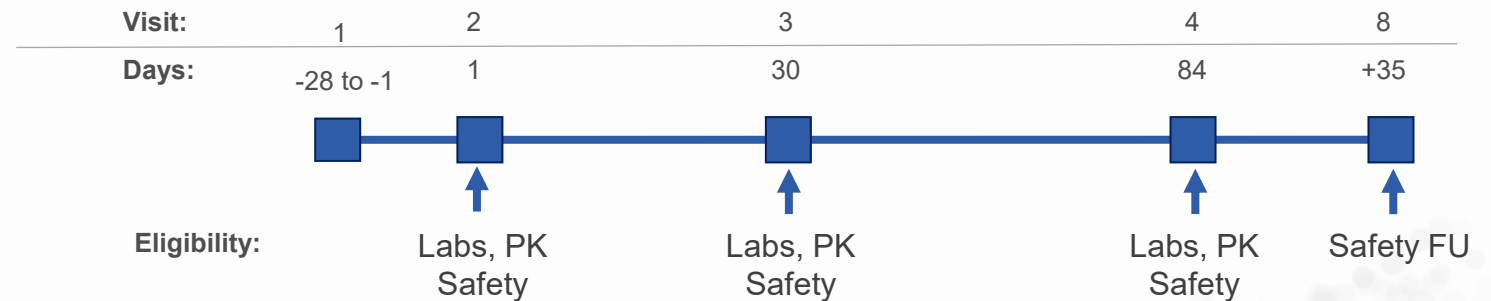
Safety FU

Obi 10 mg / EZE 10mg (n=100)

Safety FU

Placebo (n=100)

Safety FU



Commercial Update

Setting the Stage for Obicetrapib's Transformational Launch



1.
Market
Opportunity



2.
Differentiated
Product



3.
HCP
Preference



4.
Commercial
Launch

Setting the Stage for Obicetrapib's Transformational Launch



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Tailwinds are Making Lipid Lowering Space More Conducive to Commercial Success

Observations

1



We have seen LLT market growth each year for the last 5 years

2



Non-statin growth continues in the high double digits

3



Guidelines* have shifted to recommend more intense intervention not only with statins, but with ezetimibe, PCSK9's and bempedoic acid

4



Access to PCSK9's has been increasing, and utilization controls have been decreasing

5



Repatha® growth continues to accelerate 10 years post launch with +47% Rx growth in the last 12 months

Key Takeaways

Very large opportunity – even small amounts of penetration can result in significant financial success

Shift towards more aggressive treatment using alternatives / adding to statins

Governing bodies and KOL's are prioritizing the importance of treating to goal

Payers are willing to cover medications in LLT space if priced appropriately

Commercial success is being demonstrated and is accelerating

Resulting in Continued Growth and Acceleration of Brand Use

1 Lipid lowering Therapy TRx⁴

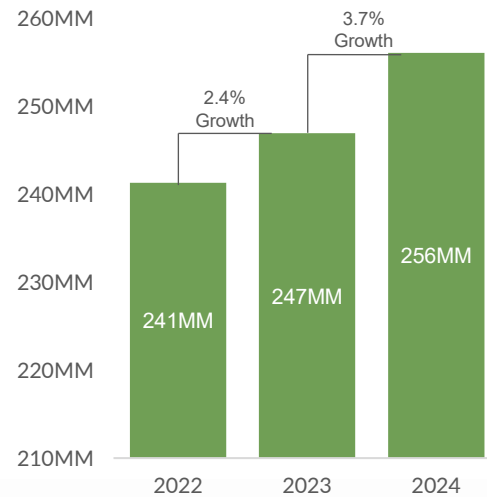
72 million¹
Adults in US diagnosed
with hypercholesterolemia

~10 million
Diagnosed patients not
treated with statin or LLT

~30 million
Not at goal

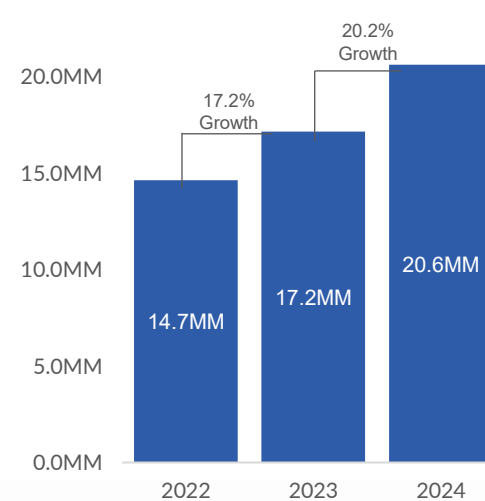
Over 40 million patients
undertreated/ not treated

2 Lipid lowering Therapy TRx¹



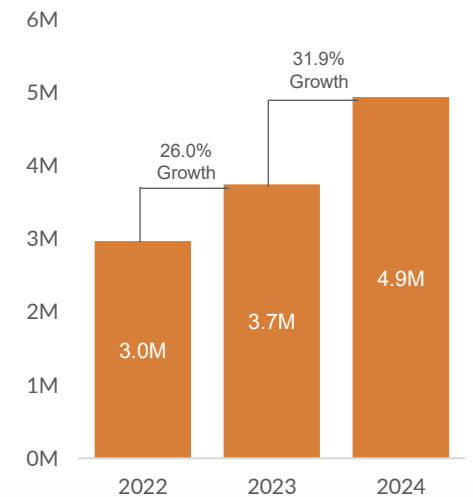
5 years of consecutive growth

3 Non-statin² TRx



Non-statins growing
at high double digits

4 Branded³ TRx



Branded agents
growing even faster

Growth of 3.7% in 2024, which is the equivalent of 9 million additional TRx's over 2023

Source: Based on third party prescription data on file

1. All Lipid Lowering therapies: Statins, Ezetimibe and combinations; PCSK9 and BPA;

2. Non-Statins : Ezetimibe and combinations; PCSK9 and BPA;

3. Branded: PCSK9 and BPA;

4. Merative Marketscan Claims Linked with Lab Data, 2019 - 2022, 12 months continuous data for each patient (6 months LB and 6 months LF from 1st observed statin treatment)

Guidelines are Being Updated for More Aggressive Intervention

Guidance for very high-risk ASCVD patients:



AHA/ACC=American Heart Association/American College of Cardiology; ASCVD= atherosclerotic cardiovascular disease; LDL-C=low density lipoprotein-cholesterol

1. Grundy SM, et al. J Am Coll Cardiol. 2019;73(24):3168-3209.
2. Lloyd-Jones DM, et al. J Am Coll Cardiol. 2022;80(14):1366-1418

3. 2025 ACC/AHA/ACEP/NAEMSP/SCAI Guideline for the Management of Patients With Acute Coronary Syndromes: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines | Circulation

U.S. Regulators are Recognizing Unmet Need in LDL-C Lowering and Acting to Address It

Language in LLT labels has evolved in recent years, reducing access restrictions and setting the stage for expanded use for treatments beyond statins

	Indication / usage updates ^{1,2,3}	
	Previous:	Updated:
	“Adjunct to diet and maximally tolerated statin therapy for the treatment of adults with HeFH or clinical ASCVD , who require additional lowering of LDL-C. ”	“ Adjunct to diet and statin therapy for the treatment of adults with primary hyperlipidemia , including HeFH, to reduce LDL-C” <i>July 2023</i>
 	“Adjunct to diet and maximally tolerated statin therapy for the treatment of adults with HeFH or established ASCVD who require additional lowering of LDL-C”	“As an adjunct to diet, in combination with other LDL-C lowering therapies, or alone when concomitant (LDL-C) lowering therapy is not possible to reduce LDL-C in adults with primary hyperlipidemia , including heterozygous familial hypercholesterolemia (HeFH)” <i>March 2024</i>

1. Integrated reviews, Nexletol and Nexlizet
2. Leqvio (inclisiran). Prescribing information. Novartis; 2024 and 2023.; Nexletol (bempedoic acid). Prescribing information. Esperion Therapeutics Inc; 2024 and 2023.
3. HeFH, ASCVD, LDL-C are fully spelled out in label

Critical Factors Improving Branded Market Dynamics



ACCESS

Changes in payer reimbursement has seen significant increases in approval rates and decreases in rejection rates^{1,2}

- 2015-2018 Repatha® approval rate: **54.1%**¹
- 2022 Repatha® approval rate: **87.5%**¹



PROMOTION

Increased product promotion and omnichannel brand marketing has enabled impactful awareness building and driven uptake

- Repatha® reinitiated DTC (branded/unbranded) in May 2024 with a run rate of **~\$60M** per annum*
- **~300** customer facing roles in 2022 increased to **600+** by 1Q 2025*



PRESCRIBERS

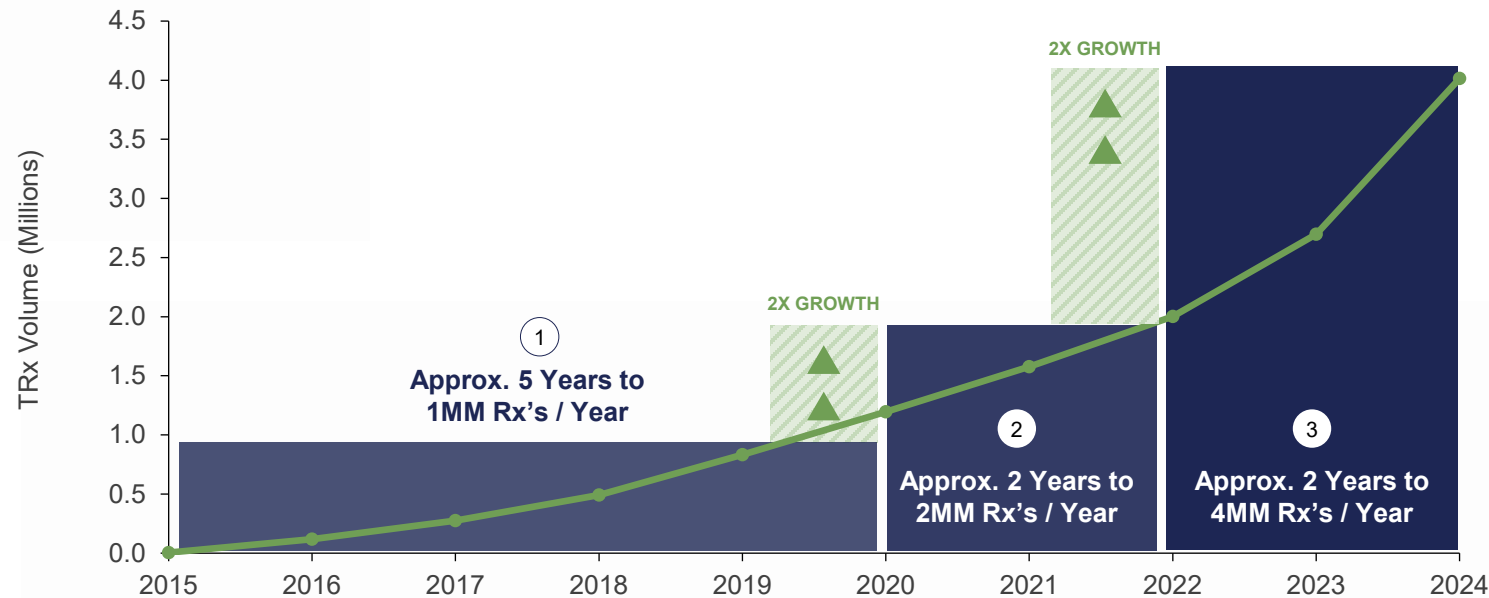
Widening prescriber target beyond specialists is expanding base to reach more HCPs treating patients in need of new LLT interventions

- Repatha® PCP writer base grew **31%** adding almost **24,000** new PCP writers in the last 12 months

... and Leading to Accelerated Growth

Accelerating growth is evidence of the demand for additional options in the LLT space

Repatha® volume continues to double every 2 years



2024 worldwide revenue of
\$2.2 Billion

US revenues of
\$1.1 Billion

WW PCSK9 class is approaching
\$4 Billion



Cardiovascular portfolio well positioned for growth into the next decade

Eight potential new

CV Pipeline Potential¹

>\$10 billion
in peak revenue
approaching
mid-2030s

Turning to **MK-0616[...]** So you provide the same efficacy, similar efficacy to the injectables in a way that is simple... So again, **significant patient population[...]**

*But both innovations, **both compounds***, we believe, have multibillion dollars.*

*Chirfi Guindo - Merck & Co., Inc. - Senior VP
& CMO for Merck Human Health*



BioPharmaceuticals – potential best in class oral PCSK9 to address high unmet need in dyslipidaemia

*“We believe that **AZD0780** has the potential to be a **\$5 billion-plus asset** and an important option for patients who urgently need novel approaches to improve their outcomes.”*

Sharon Barr, EVP
Astra Zeneca - BioPharmaceuticals R&D

Setting the Stage for Obicetrapib's Transformational Launch



1.
Market
Opportunity



2.
Differentiated
Product



3.
HCP
Preference

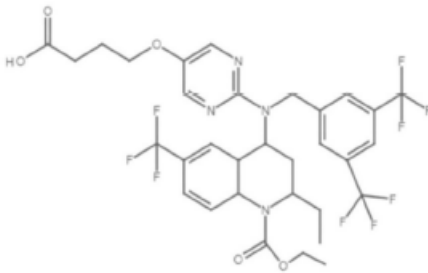


4.
Commercial
Launch

Evidence Supporting the Potential of Obicetrapib's Portfolio is Grounded in Comprehensive, Outcomes-Driven Clinical Program

1

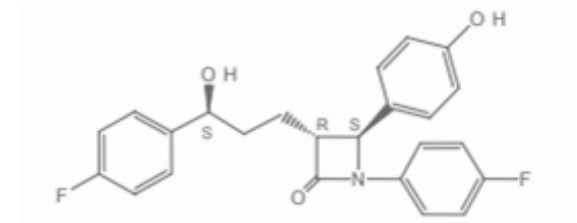
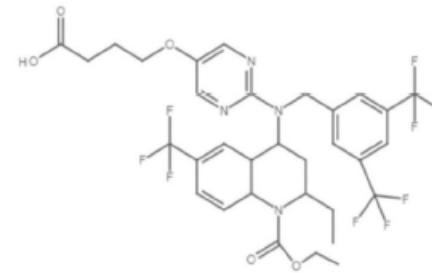
Obicetrapib



&

2

Obicetrapib + Ezetimibe



PHASE 2

TULIP

ROSE

ROSE2

JAPAN

BROOKLYN

BROADWAY

PHASE 3

TANDEM

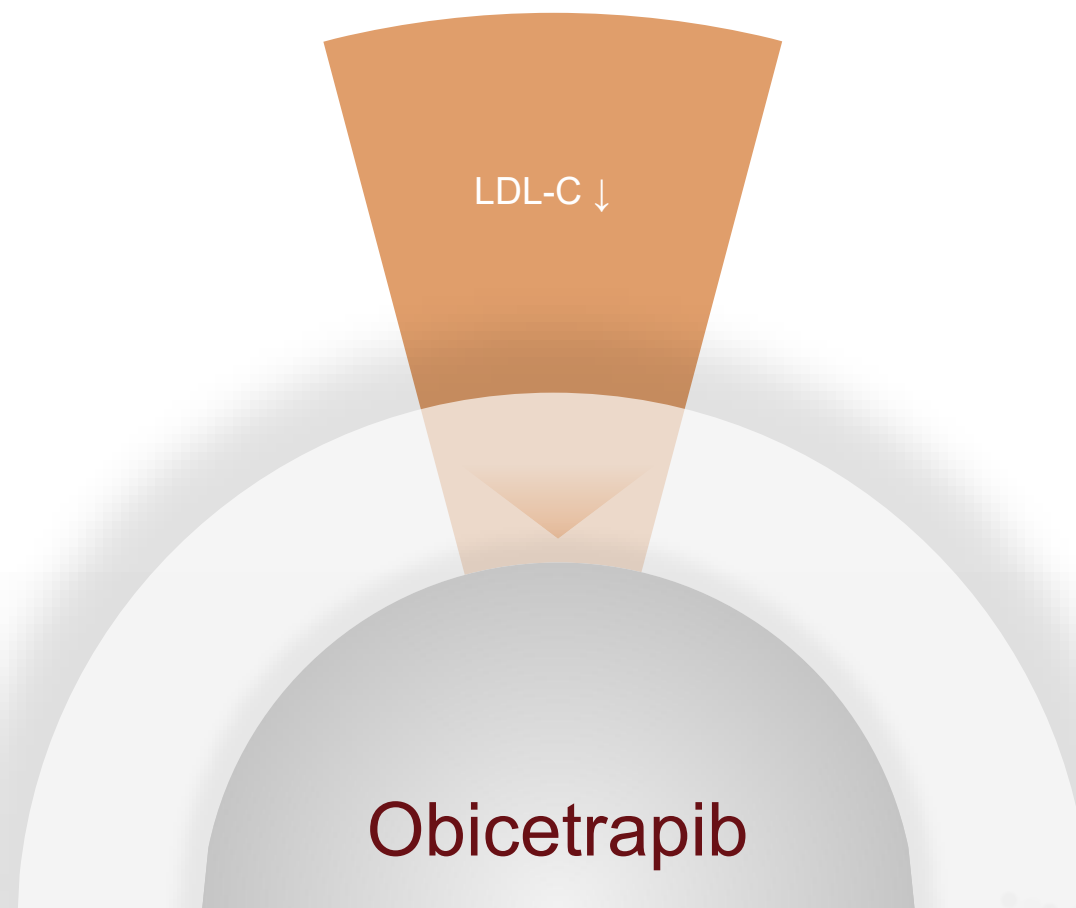
PREVAIL*

REMBRANDT*

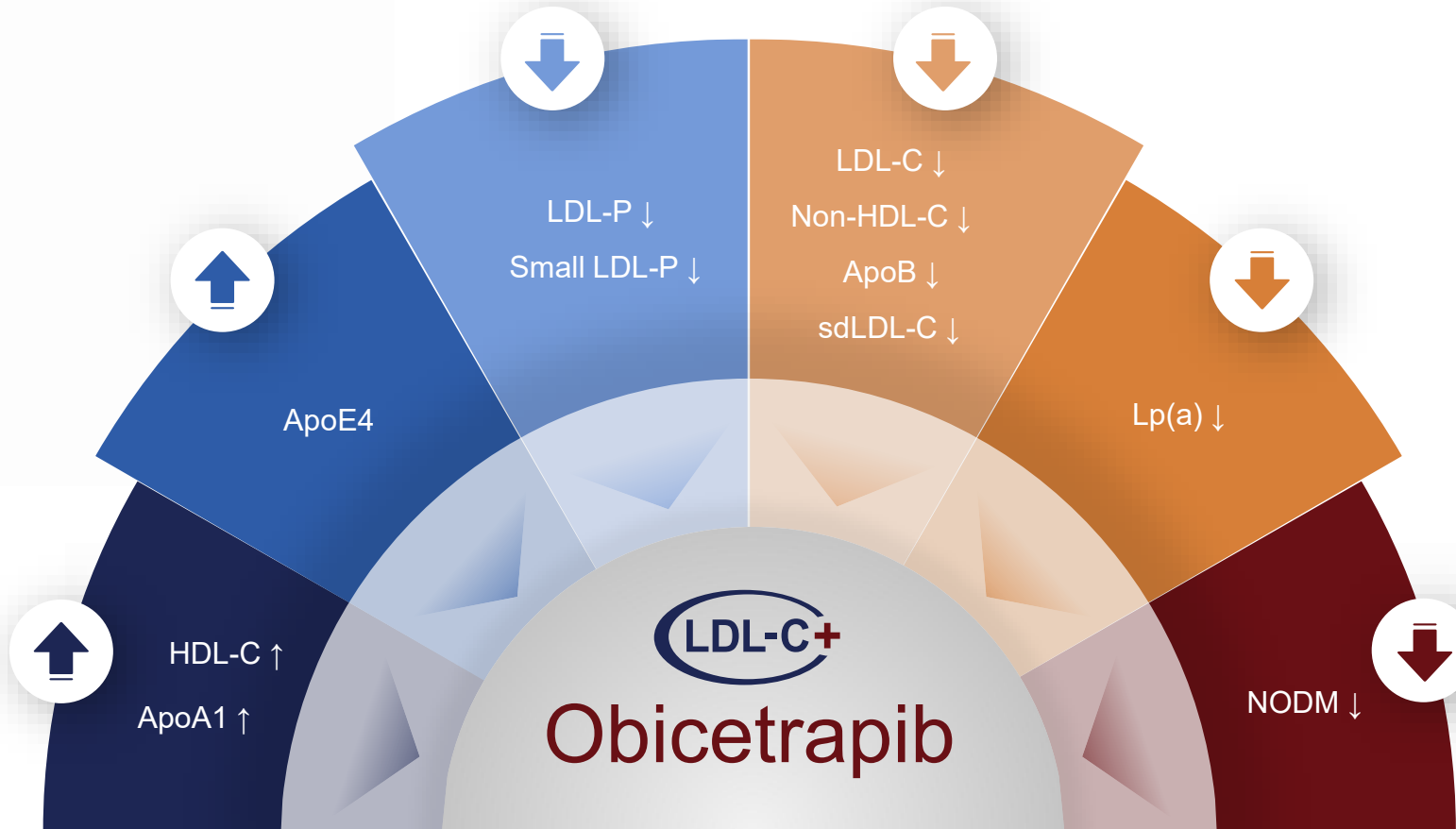
VINCENT*

RUBENS*

Currently, Treatment of Hyperlipidemia is One-Dimensional

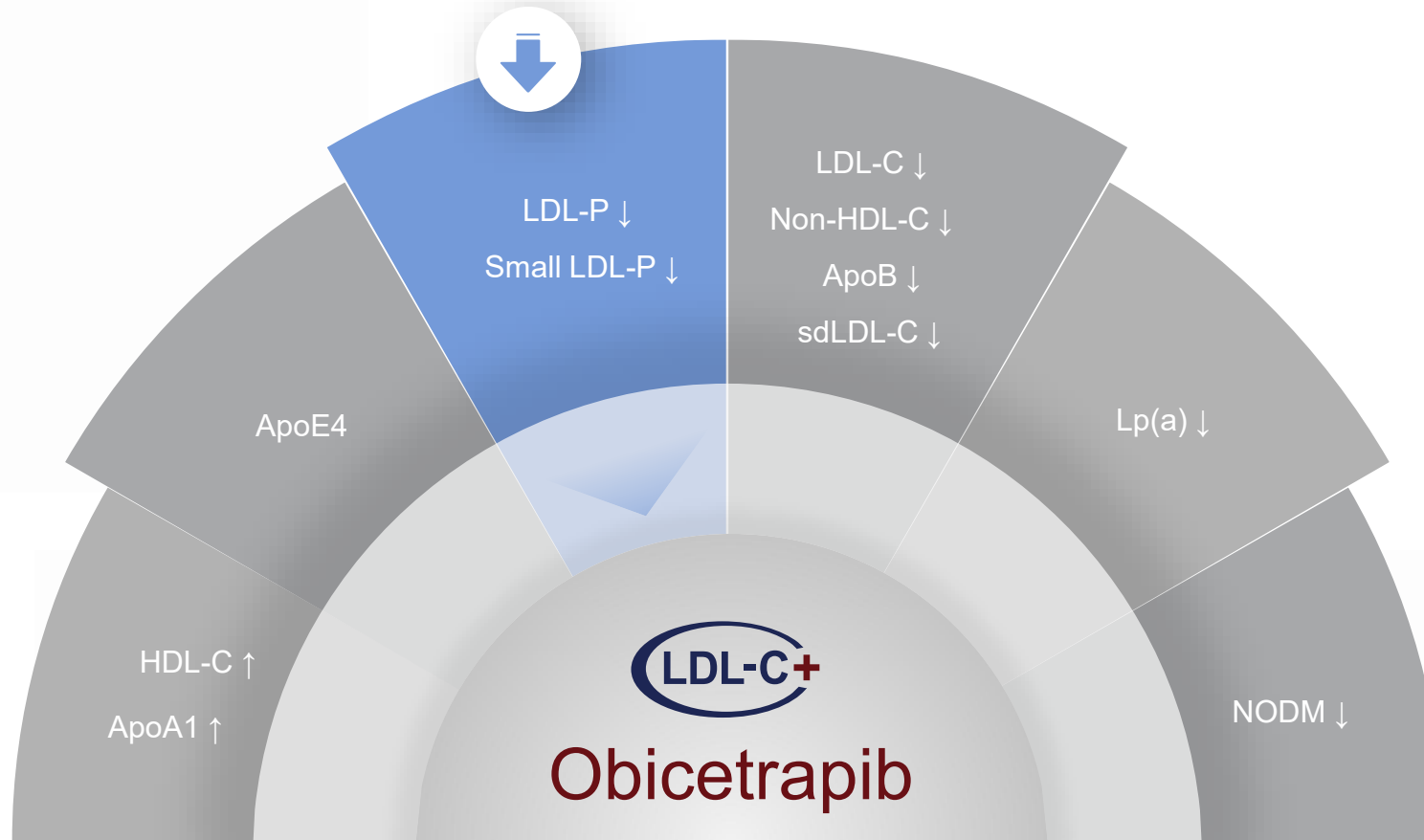


The Future of Hyperlipidemia Treatment Goes Beyond LDL-C



Obicetrapib was observed to **impact multiple factors associated with MACE**, providing more comprehensive risk management across **additional patient subpopulations**

Small LDL-P Particle Concentration

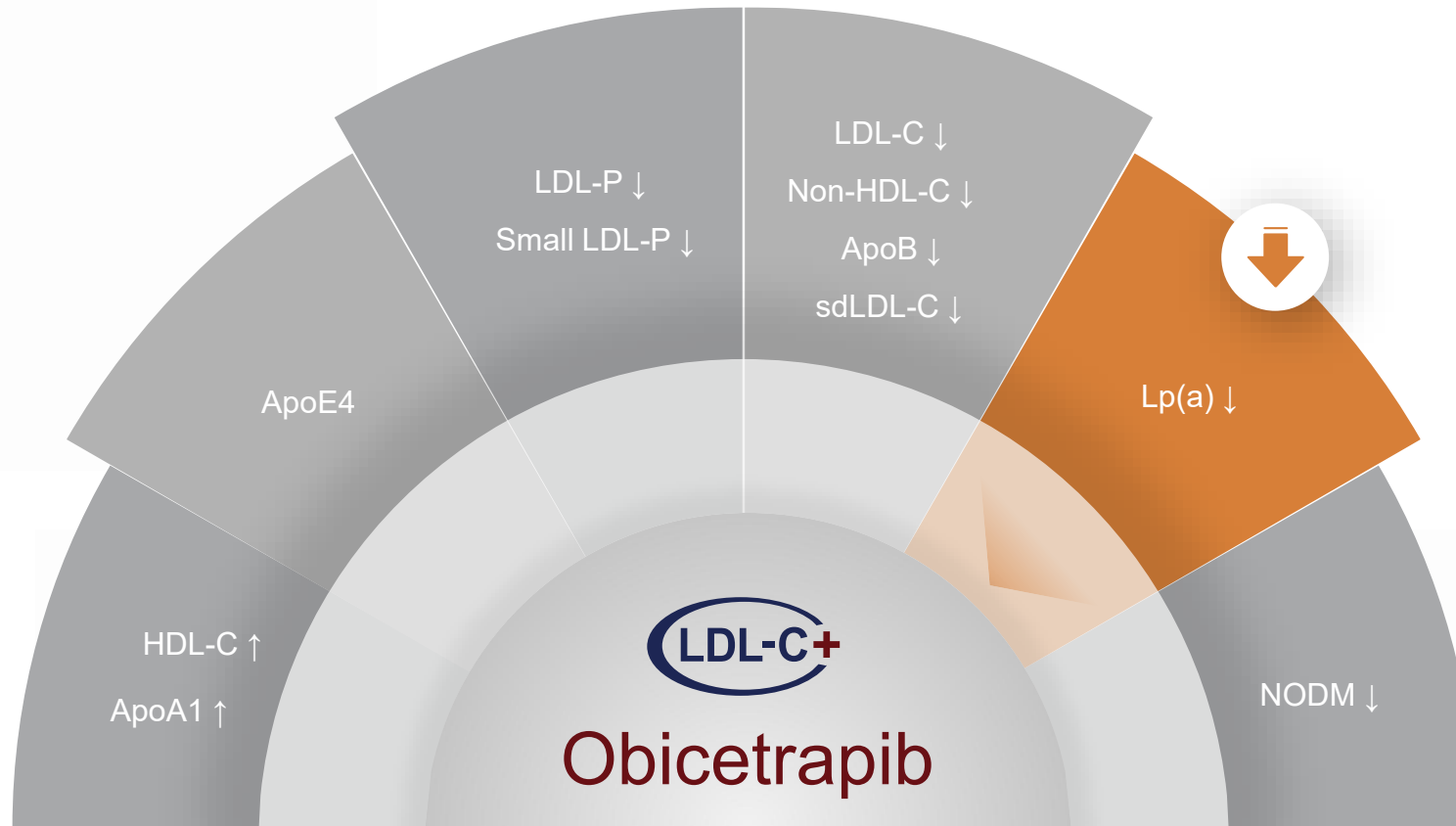


- Approximately **43 million** patients with hyperlipidemia exhibit elevated levels of **LDL-P of > 1300 nmol/L***
- Prevalence is **even higher** in individuals **with type 2 diabetes[^]**
- Presence of LDL-P is a **significant independent risk factor for coronary heart disease (CHD)**, even when traditional lipid measures like LDL-C and triglycerides are within normal ranges[^]

* Source: Toth, Peter P. et al. *Atherosclerosis*. Volume 235, Issue 2, 585 - 591.

[^]Hoogeveen RC, Gaubatz JW, Sun W, Dodge RC, Crosby JR, Jiang J, Couper D, Virani SS, Kathiresan S, Boerwinkle E, Ballantyne CM. Small dense low-density lipoprotein-cholesterol concentrations predict risk for coronary heart disease: the Atherosclerosis Risk In Communities (ARIC) study. *Arterioscler Thromb Vasc Biol*. 2014 May;34(5):1069-77. doi: 10.1161/ATVBAHA.114.303284. Epub 2014 Feb 20. PMID: 24558110; PMCID: PMC3999643.

Elevated Lp(a) Levels



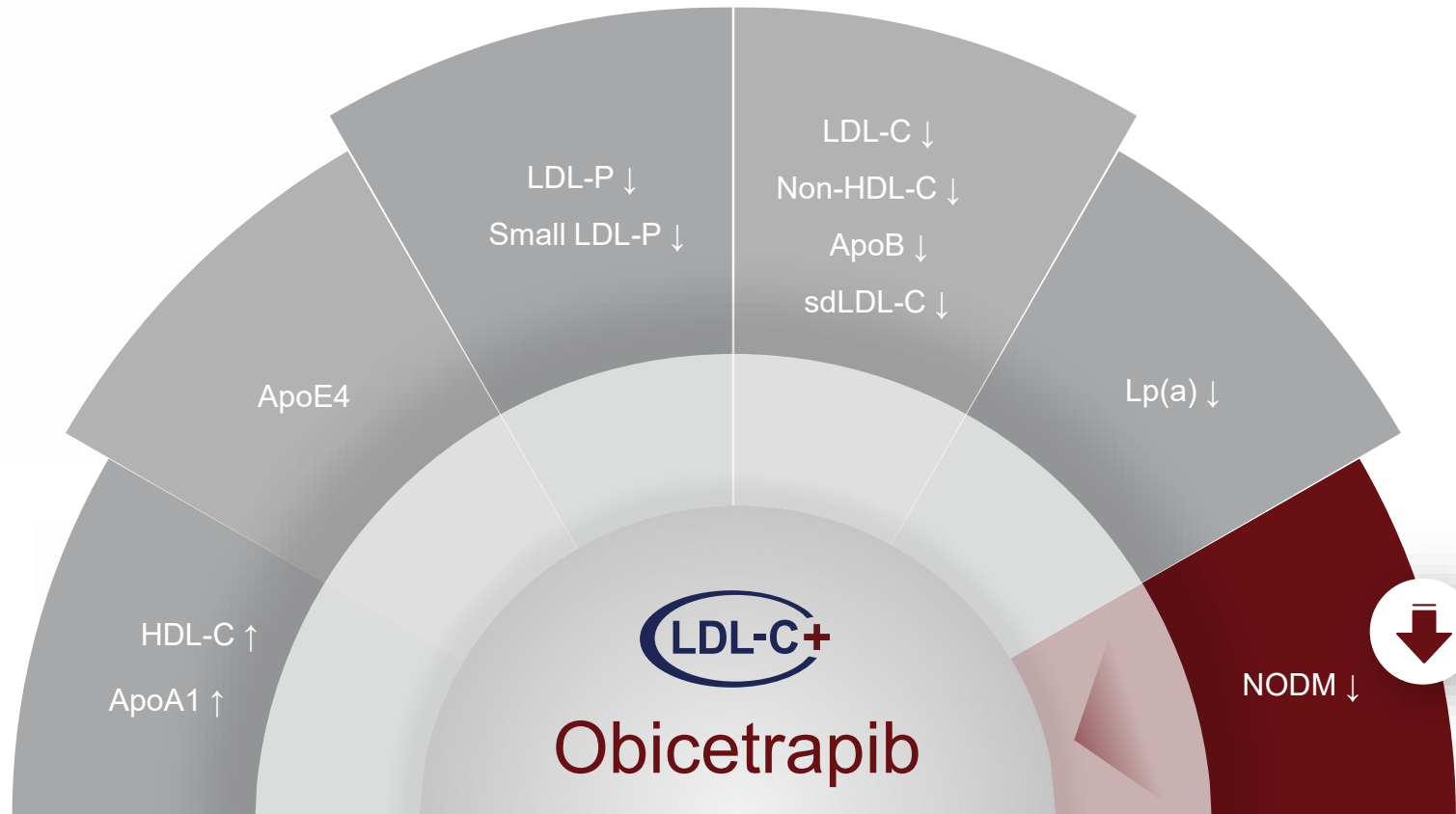
- In the US, close to **75 million** patients have an elevated Lp(a) score of **> 100-125 nmol/L** ^^**
- An estimated **14.3 million** of these patients also have hypercholesterolemia

Note: NODM = New onset diabetes mellitus

** Tsimikas et al. J Am Coll Cardiol. 2022; 80: 934-946

^^ Shapiro, M et al. Journal of Clinical Lipidology, Volume 19, Issue 1, 28 - 38

New-onset Diabetes Mellitus



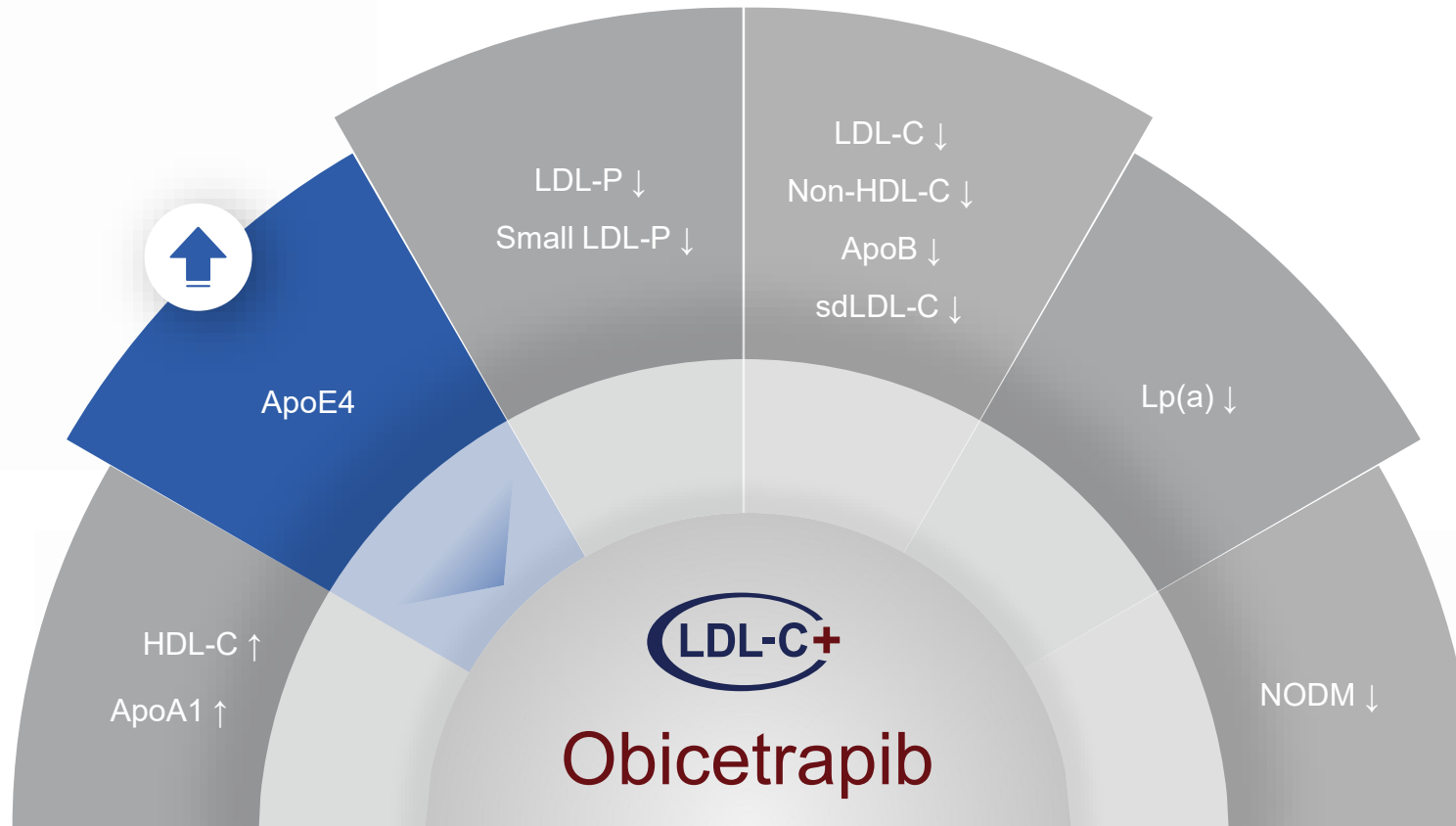
- **27.9 million** hyperlipidemia patients are estimated to have concomitant diabetes*
- In addition, there are an estimated **27.2 million**[^] individuals with hyperlipidemia that are pre-diabetic

Note: NODM = New onset diabetes mellitus

* Ray K, et al. European Journal of Preventive Cardiology (2021) 28, 1279–1289.

[^] Footnote: Prediabetes was defined as fasting plasma glucose values of 100 to 125 mg/dL or A1C values of 5.7% to 6.4%.
Reference: National Diabetes Statistics Report | Diabetes | CDC

ApoE4 Carriers



- ApoE4 is the **strongest genetic risk factor** for late-onset AD¹⁻⁵
- Approximately **20 million** patients with hyperlipidemia are at increased risk for AD
- Prevalence of ApoE4 in AD is up to **66%**¹⁻⁵

Aβ, amyloid β; AD, Alzheimer's disease; Apo, apolipoprotein; CVD, cardiovascular disease; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; Lp(a), lipoprotein(a).
1. Abondio P et al. *Genes (Basel)*. 2019;10(3):222. 2. Feringa FM et al. *Front Aging Neurosci*. 2021;13:690372. 3. Hottman 2017. 4. Jeong W et al. *Mol Cells*. 2019;42(11):739-746. 5. Williams et al. *BMC* 2020.c

No Other Asset Provides the Comprehensive Observed Benefits of Obicetrapib and Obi-Eze to Address Cardiometabolic Risk

Clinical Profile	LDL-C+	CARD AND PCP TREATMENT PRIORITIES	EZETIMIBE	BEMPEDOIC ACID	PCSK9i (injectable)	ORAL PCSK9	OBICETRAPIB	OBI-EZE*
		MACE at Launch	•	•	•		•	•
		≥ 30% LDL-C Reduction			•	•	•	•
		ApoA1 (≥ 30% increase)					•	•
		HDL-C (≥ 30% increase)					•	•
		Lp(a)			•	•	•	•
		ApoB	•	•	•	•	•	•
		Non-HDL	•	•	•	•	•	•
		LDL-P	•	•	•	•	•	•
		Small LDL-P >80%					•	•
& Product Profile		NODM					•	•
		Easy Dosing (Including Food Effect)	•	•	•		•	•
		Oral Administration	•	•		•	•	•
		Safe and Well-Tolerated	•	•	•	•	•	•

Obicetrapib & Obi-Eze

✓ LDL-C+ Clinical Profile

✓ Safety/Tolerability Profile Comparable to Placebo

✓ Simple, oral, once daily, low-dose

Setting the Stage for Obicetrapib's Transformational Launch



1.
Market
Opportunity



2.
Differentiated
Product



3.
HCP
Preference



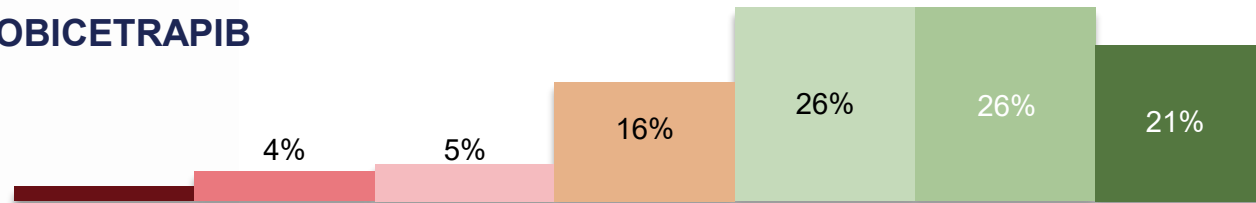
4.
Commercial
Launch

What Are Customers Saying About Obicetrapib, Obi-Eze and MK-0616?

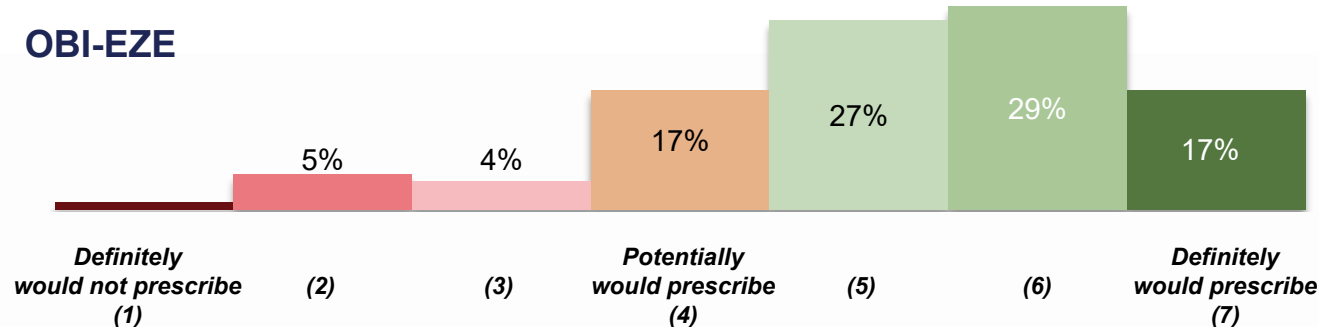


How likely are you to Rx **obicetrapib** and **obi-eze** in the first 6 months after they become available?

OBICETRAPIB



OBI-EZE

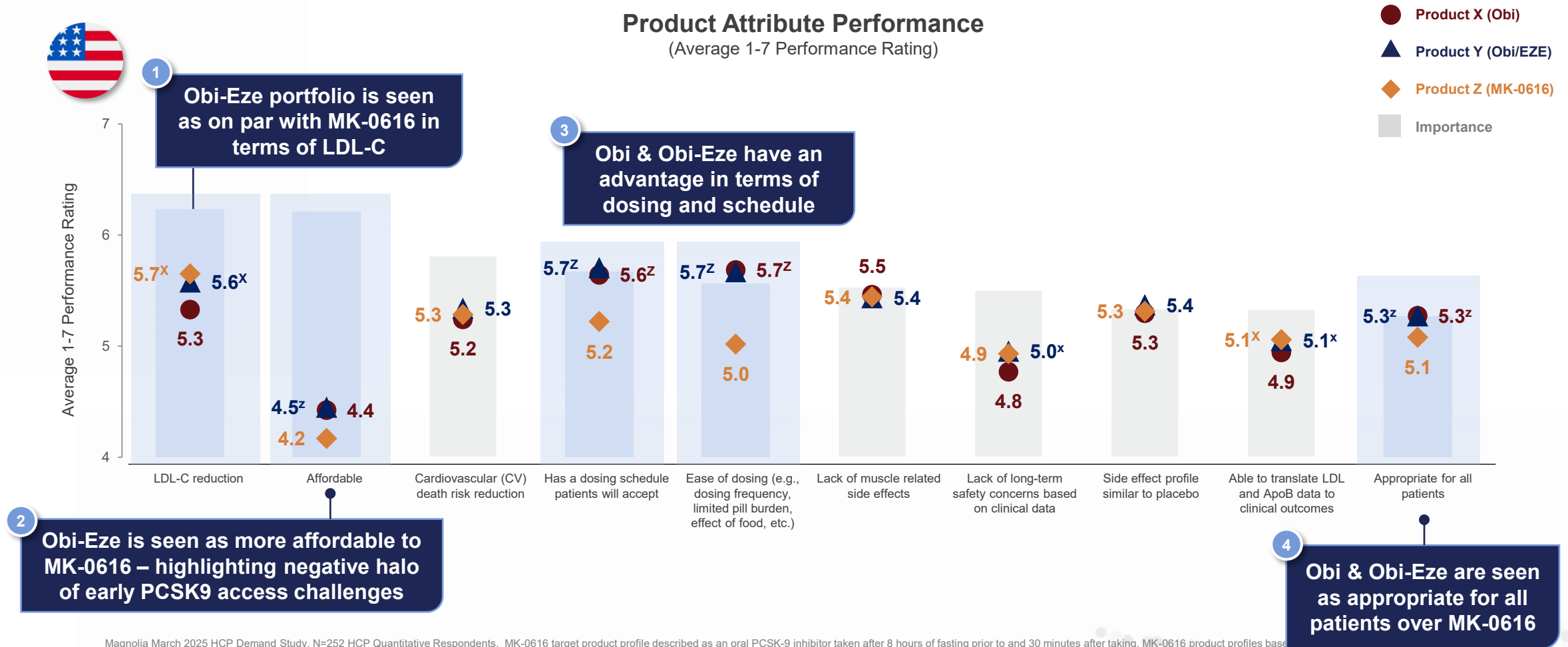


3 out of 4 HCP's
indicate a propensity to
prescribe Obi & Obi-Eze
within the first 6 months
of availability

Magnolia March 2025 HCP Demand Study, N=252 HCP Quantitative Respondents.

Obicetrapib and obi-eze target product profile described as a once daily tablet for a small molecule CETP inhibitor (or CETP + Ezetimibe for FDC) taken with or without food; with safety and efficacy profile reflecting BROADWAY, TANDEM and BROOKLYN Phase 3 results (including LDL-C, ApoB, Non-HDL-C, HDL-C, Lp(a), 4-point MACE).

Obicetrapib and Obi-Eze Perform Statistically Better than MK-0616 on Several Key Attributes



Magnolia March 2025 HCP Demand Study, N=252 HCP Quantitative Respondents. MK-0616 target product profile described as an oral PCSK-9 inhibitor taken after 8 hours of fasting prior to and 30 minutes after taking. MK-0616 product profiles based on safety and efficacy profile reflecting publicly available Phase 2 data as of January 2025 (including LDL-C, ApoB, Non-HDL-C, HDL-C, Lp(a), 4-point MACE).

Please indicate how well [Product X, Y, Z] performs on each of the following product attributes listed below. 1 indicates that the product "Performs very poorly", 4 indicates that the product "Performs moderately well" and 7 indicates that the product "Performs extremely well".

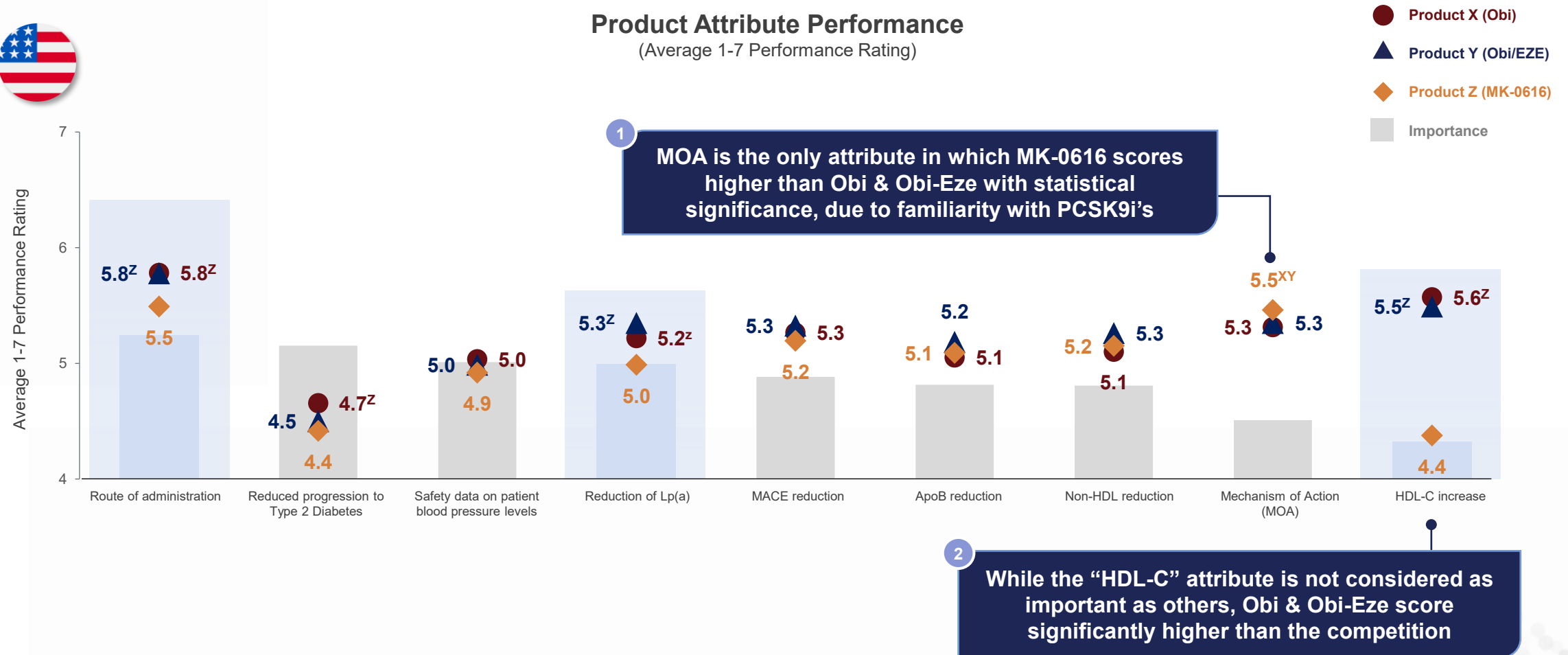
Lower case letters note significant difference between products at 90 CI; upper case letters denote significant difference at 95 CI.

*Ordered by descending product attribute importance.

Attributes that May Not Rank Highly in Today's Market Will be Considered Key Components of Differentiation in Tomorrow's Market



Product Attribute Performance (Average 1-7 Performance Rating)



Magnolia March 2025 HCP Demand Study, N=252 HCP Quantitative Respondents. Target product profiles summarized on previous slides.

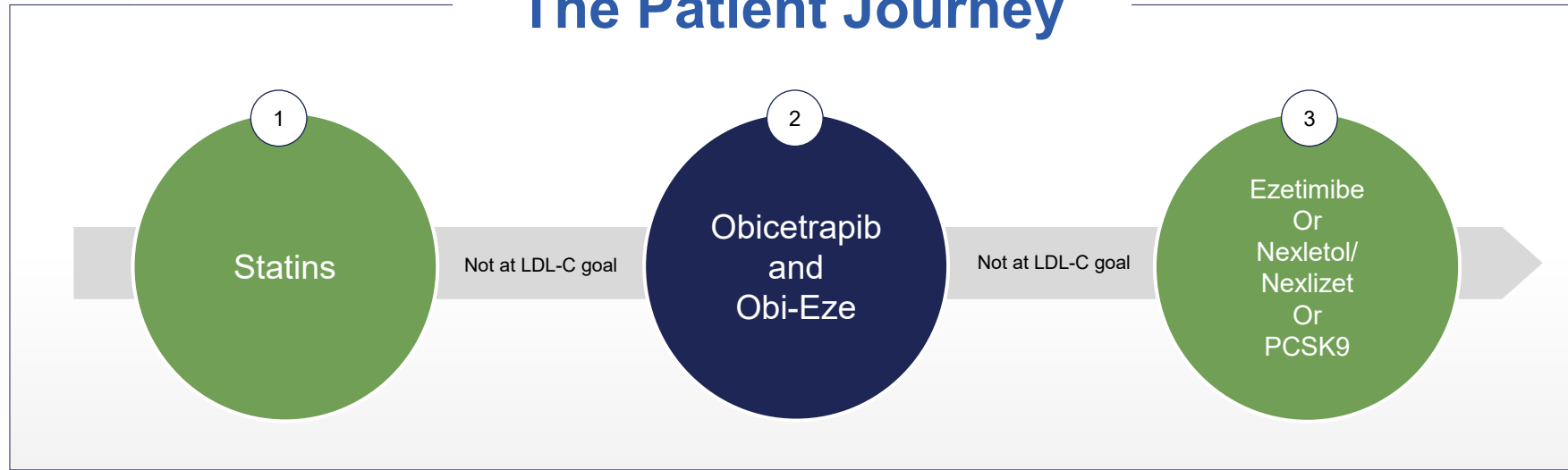
Please indicate how well [Product X, Y, Z] performs on each of the following product attributes listed below. 1 indicates that the product "Performs very poorly", 4 indicates that the product "Performs moderately well" and 7 indicates that the product "Performs extremely well"

Lower case letters note significant difference between products at 90 CI; upper case letters denote significant difference at 95 CI.

*Ordered by descending product attribute importance

With a Differentiated LDL-C+ Profile, Obicetrapib is Positioned to Become the First Choice Add-on Therapy to Statins

The Patient Journey



Why?

- Standard of care
- Oral
- Generic – payer requirement

ALL IN ONE:

- ✓ LDL-C+ efficacy
- ✓ Safe and well-tolerated in Phase 3 trials
- ✓ Oral

Balancing:

Incremental efficacy,
safety and route of
administration

Setting the Stage for Obicetrapib's Transformational Launch



1.
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2.
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Product

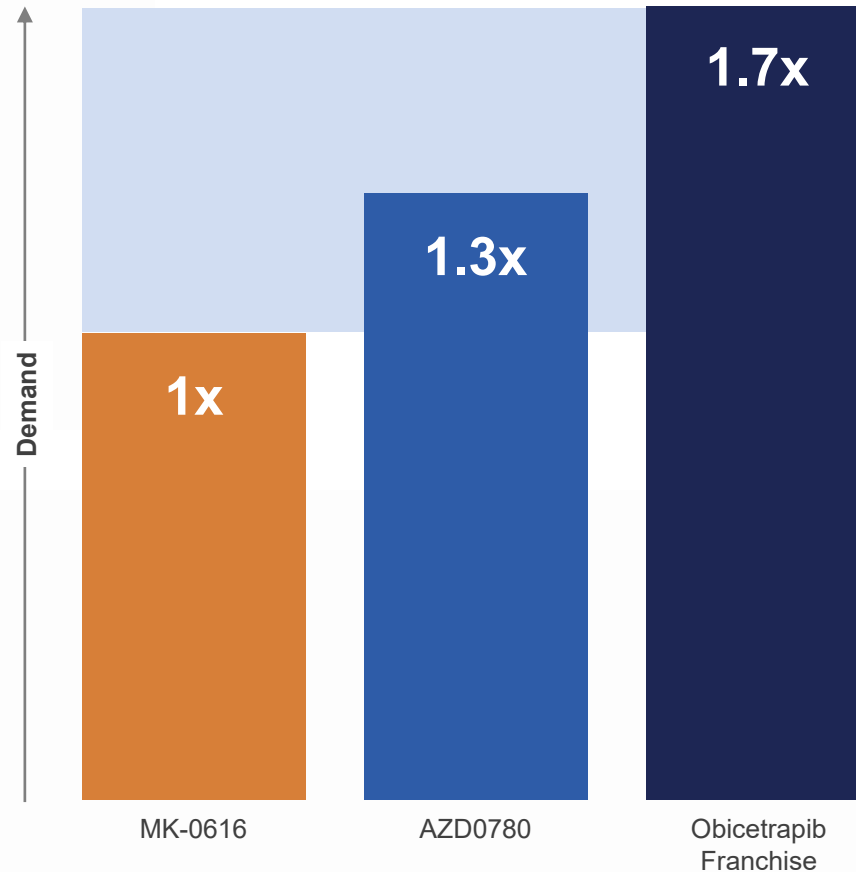


3.
HCP
Preference



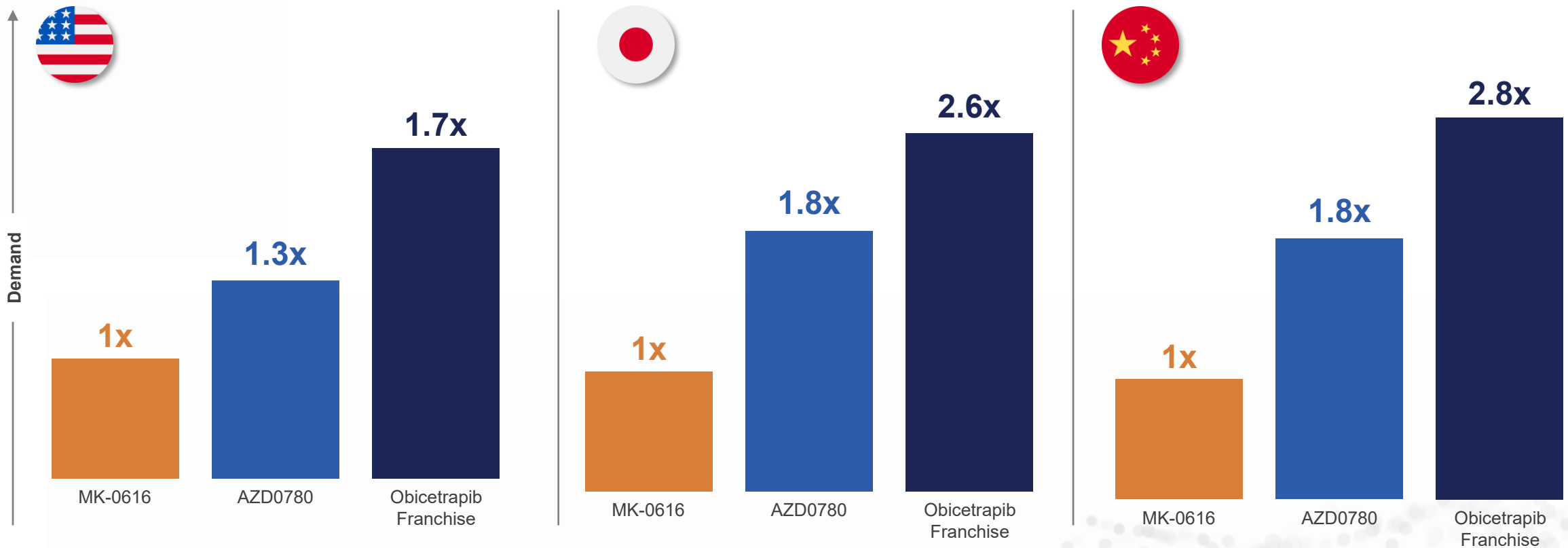
4.
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Launch

Demand Studies Support Obicetrapib and Obi-Eze as a Preferred Add-on LLT Over MK-0616 and AZD0780

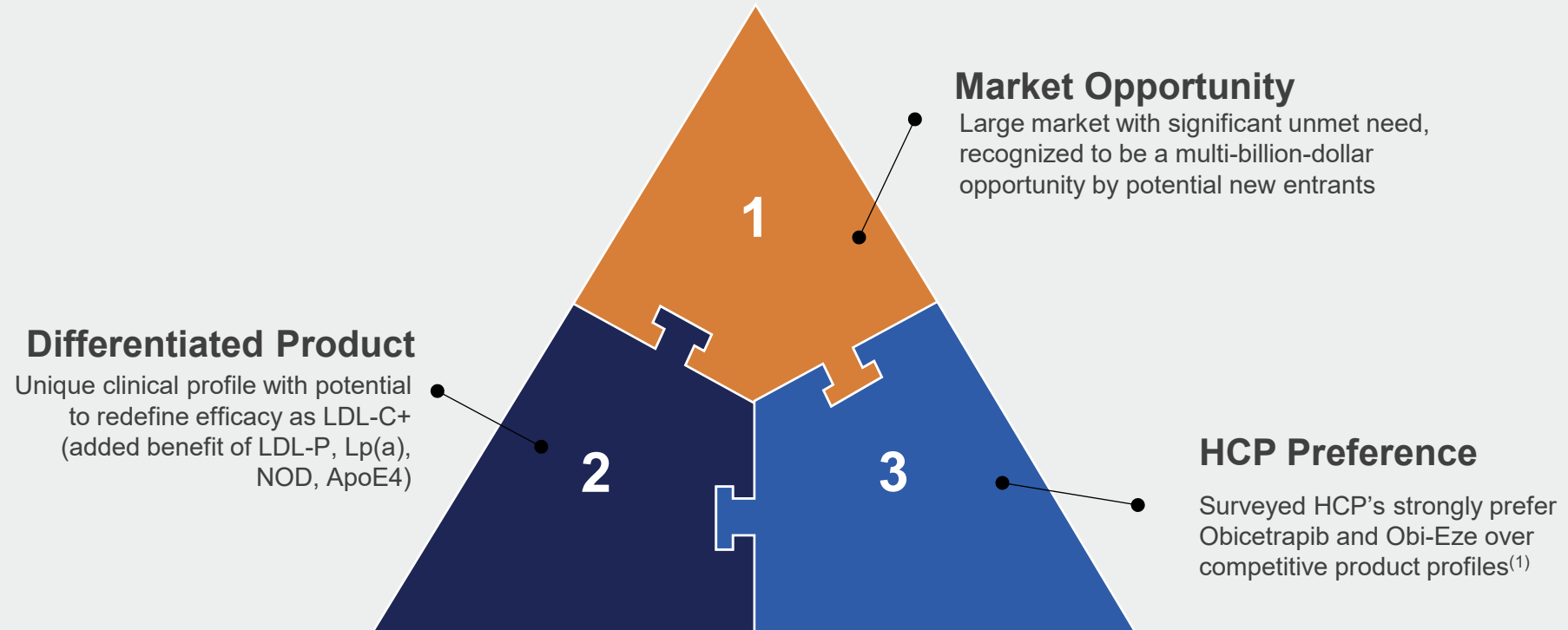


Preferential Demand for Obicetrapib Franchise Across Global Markets

Preference transcends diverse cultures, treatment preferences and healthcare systems



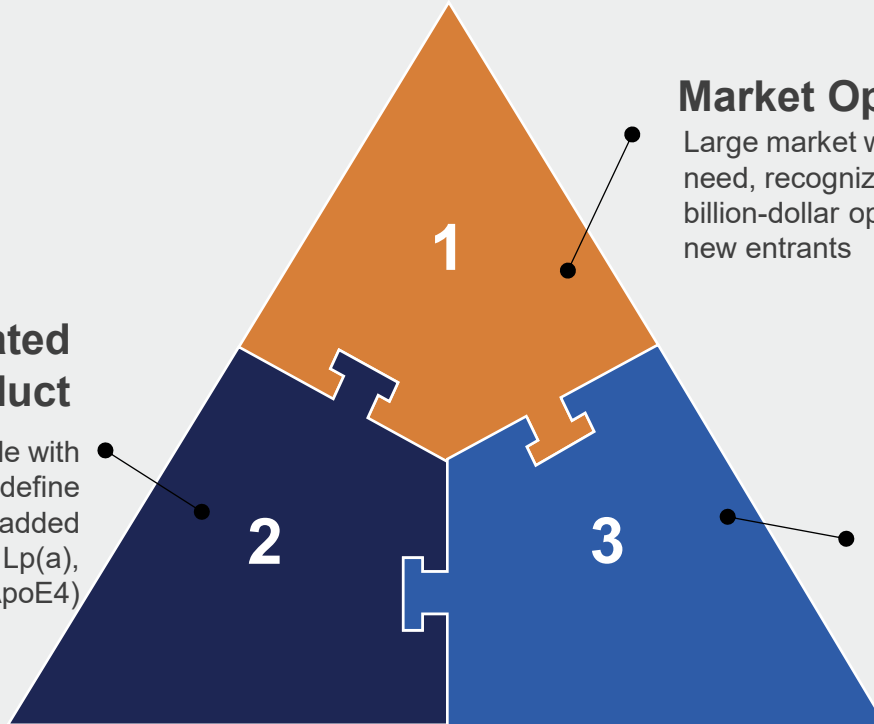
Obicetrapib's Blockbuster Potential



Obicetrapib's Blockbuster Potential

Differentiated Product

Unique clinical profile with potential to redefine efficacy as LDL+ (added benefit of LDL-P, Lp(a), NOD, ApoE4)



Market Opportunity

Large market with significant unmet need, recognized to be a multi-billion-dollar opportunity by potential new entrants

HCP Preference

Surveyed HCP's strongly prefer Obicetrapib and Obi-Eze over competitive product profiles ⁽¹⁾

\$8 Billion+
potential worldwide
market opportunity

Access Not Expected to be a Barrier to Success

Primary & Secondary Payer Research

- 3 US Payer Advisory Boards
- >40 Direct Payer Engagement Discussions
- 2023 Payer & Office Manager Research
- Secondary Analytics including payer coverage policies

- 1 “Control” of branded LLT space has led to broad coverage of PCSK9s and BA (Commercial/ PartD)
- 2 Evidence suggests plans have also reduced PA restrictions on branded LLTs
- 3 Obicetrapib is anticipated to establish a new class of LLT medications (CETPi)
- 4 Incremental value lies in differentiated data beyond LDL-C (LDL-P, Lp(a), new onset diabetes, ApoE4)
- 5 Payor feedback consistently reinforces broad access (Commercial and Medicare Part D) based on Product TPP

* 3 US Payor Advisory Boards held April 14, 2023, September 22, 2023, April 12, 2024
Solstice Health Communications - Primary Research - 20 Plan MD and Pharm D; Initiated October 25, 2023
Solstice Health Communications - Primary Research - 16 Office (PCP & Cardiology) managers; Initiated December 13, 2023

The Stage is Set for Obicetrapib's Transformational Launch

The Obicetrapib and Obi/Eze launch aims to surpass current branded LLT growth trends with enhanced demand in a receptive and dynamic market



Market opportunity continues to expand in a receptive environment



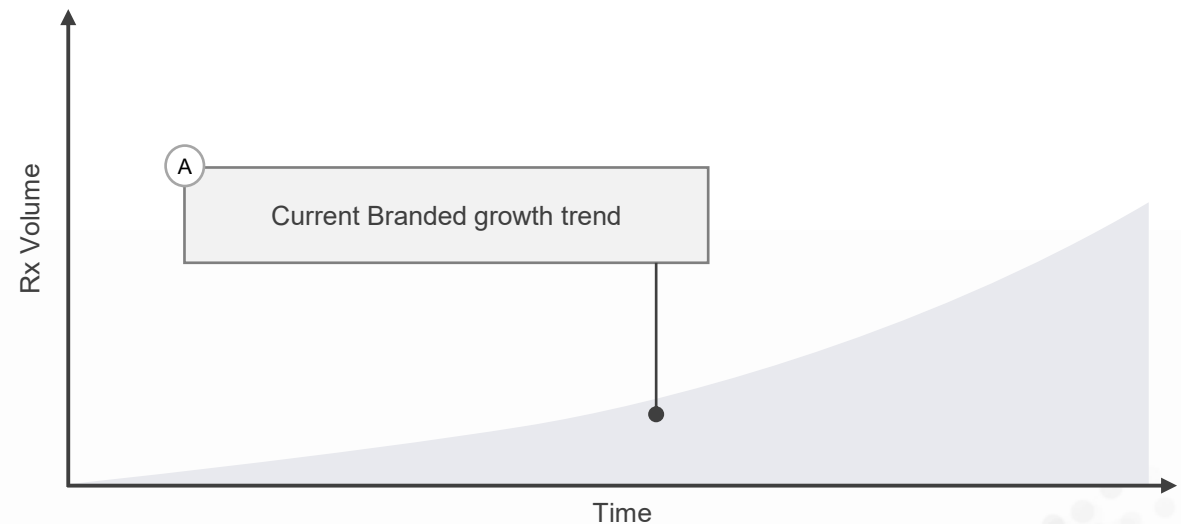
Differentiated product provides meaningful benefit beyond LDL-C



HCP preference strongly favors obicetrapib franchise in surveyed HCPs ⁽¹⁾



Commercial launch aims to revolutionize LLT with LDL-C+ profile



Graphic and launch curves are for illustrative purposes only

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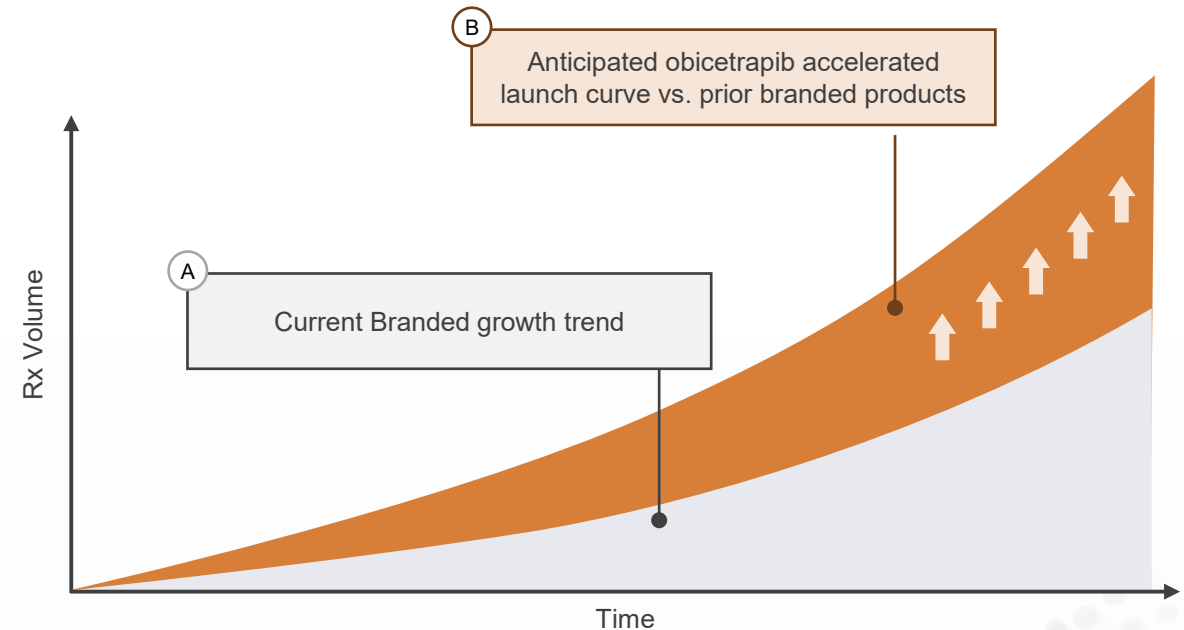
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OUR END GAME

Lives Changed by Obicetrapib

PATIENT

AGE:	59
SEX:	Female
MEDICAL HISTORY:	High LDL-C, High Lp(a), Elevated CAC score, Adopted, unknown family history
MEDICATIONS:	statin
LIFESTYLE:	Working professional, moderately active
OCCUPATION:	CFO



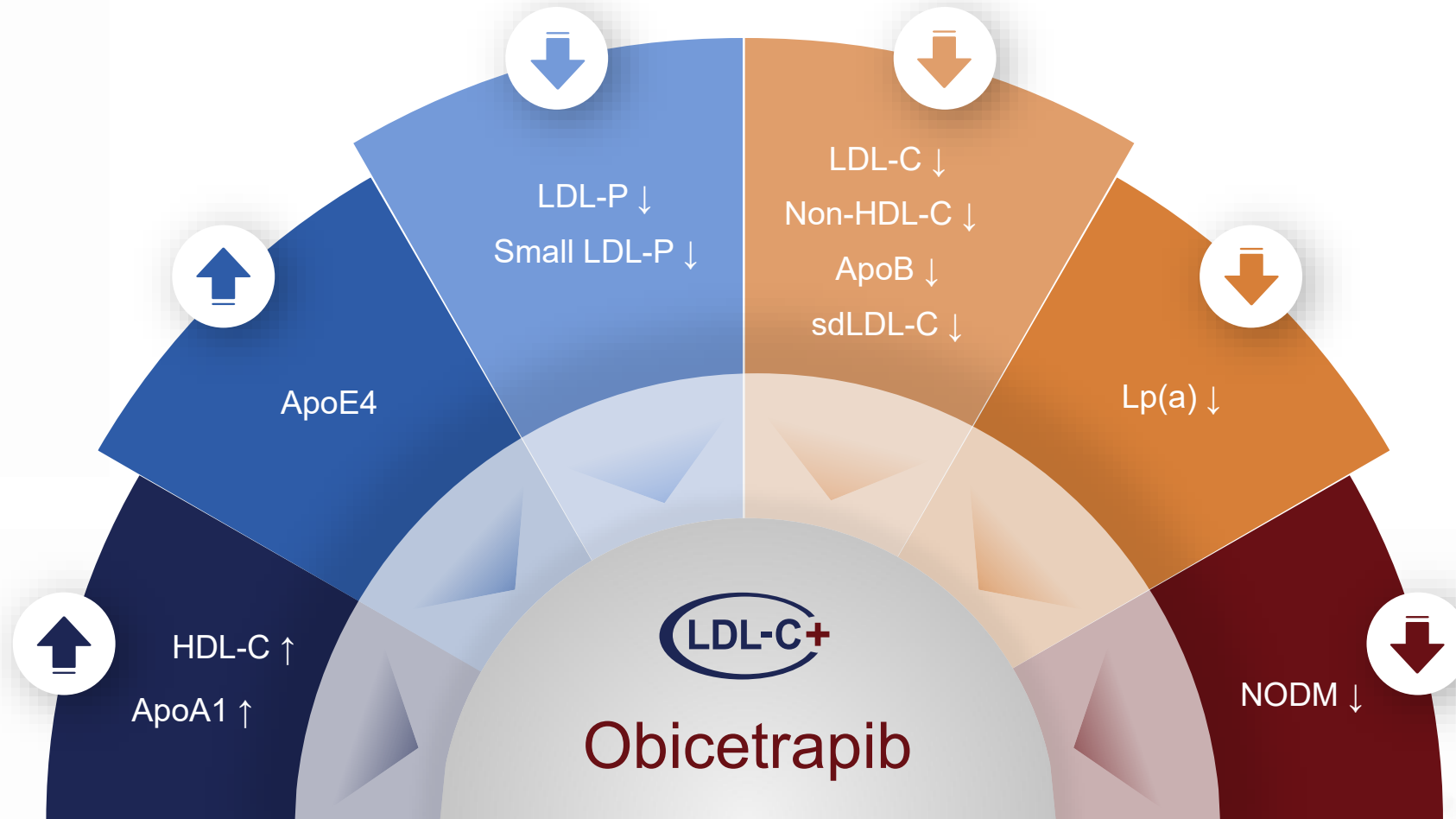
“Having heart disease weighs on me every day. I feel like I am a walking time bomb, waiting for it to be my turn to have a heart attack or stroke. I’ve worked so hard to take care of myself, but I still have markers that put me at high risk. I’m so grateful to have a cardiologist helping me take control, but I’m always thinking – **is it enough?**”

Kari B.

Doing Everything Right, Still Living in Fear

Closing

The Future of Hyperlipidemia Treatment Goes Beyond LDL-C



The NewAmsterdam Value Proposition



Clinical Expertise:

Data driven clinical development increases probability of success



Differentiated Target Product Profile:

Phase 2 data demonstrates obicetrapib's potential impact on multiple CVD risk factors



Unmet Need:

Significant need for a potent, convenient, well-tolerated low-dose oral therapy



Experienced Leadership and Team:

Expanding team comprised of cardiometabolic and biotechnology industry executives



KOL Support:

Physician community aware of unmet need and eager to leverage obicetrapib's differentiated profile to achieve desired clinical benefit, if approved



CMC Expertise and Manufacturing Capacity:

Preparing to meet anticipated demand for obicetrapib and FDC, creating redundancy, expanding capacity and building inventory



Commercial Excellence:

Track record of blockbuster launch success and innovative go-to-market model



Strong Balance Sheet:

Cash sufficient to fund ongoing trials and support US commercial launch

Our Mission is Clear and Simple



At NewAmsterdam Pharma, we are **advancing a new era of life-saving treatment** for cardiovascular disease and other lipid-related conditions.

By prioritizing patients with high unmet needs and those who are underserved by current therapies, we are working toward a reality where cardiovascular disease is **no longer the #1 killer of people worldwide.**

Q&A

Thank You



NewAmsterdam
Pharma