

Investor Presentation

as of November 4, 2026

NewAmsterdam Pharma

Nasdaq: NAMS

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Obicetrapib and Obicetrapib plus Ezetimibe Could Address Significant Unmet Need in Cardiometabolic Diseases



Significant unmet need for oral LDL-C lowering therapy as adjunct to statins



Simple, once-daily, low-dose CETP inhibitor with statistically significant LDL-C lowering and effects beyond LDL, observed across three Phase 3 trials and five Phase 2 trials



Convenient oral format potentially enables broad adoption and combinations to address unmet need, if approved



Comprehensive IP protection **until mid 2043**

$8 billion+

global peak sales opportunity

>3,500 pts

of favorable safety/tolerability data comparable to placebo. Blinded data in >9,500 patients

35-40%

LDL-C lowering versus placebo as a monotherapy*

~45%

Lp(a) lowering versus placebo as a monotherapy+

~50%

LDL-C lowering versus placebo in combination** with ezetimibe

21%

observed reduction in MACE favoring obicetrapib at 1-year^

Observed beneficial effects beyond LDL, on ApoB, non-HDL-C, LDL-P, HDL-C and other markers of glycemic control, renal function, and Alzheimer's disease

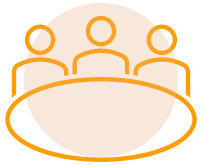
Source: Company data for obicetrapib 10mg monotherapy, *Pooled data includes BROOKLYN, TANDEM, BROADWAY Phase 3 data sets. Reduction across ITT mean, median, and LS mean. ** ROSE2 and TANDEM data, Reduction across ITT mean, median, and LS mean
+Pooled data from BROADWAY, BROOKLYN and TANDEM with Lp(a) baseline of 50-150 nmol/L. ^Data from BROADWAY trial, MACE was an exploratory endpoint measure

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Previous Years 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 end of 3Q 2026 of ~$643M*

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

2025

- Announced Alzheimer's topline
- Full AD data was presented at AAIC on July 30
- EMA submission

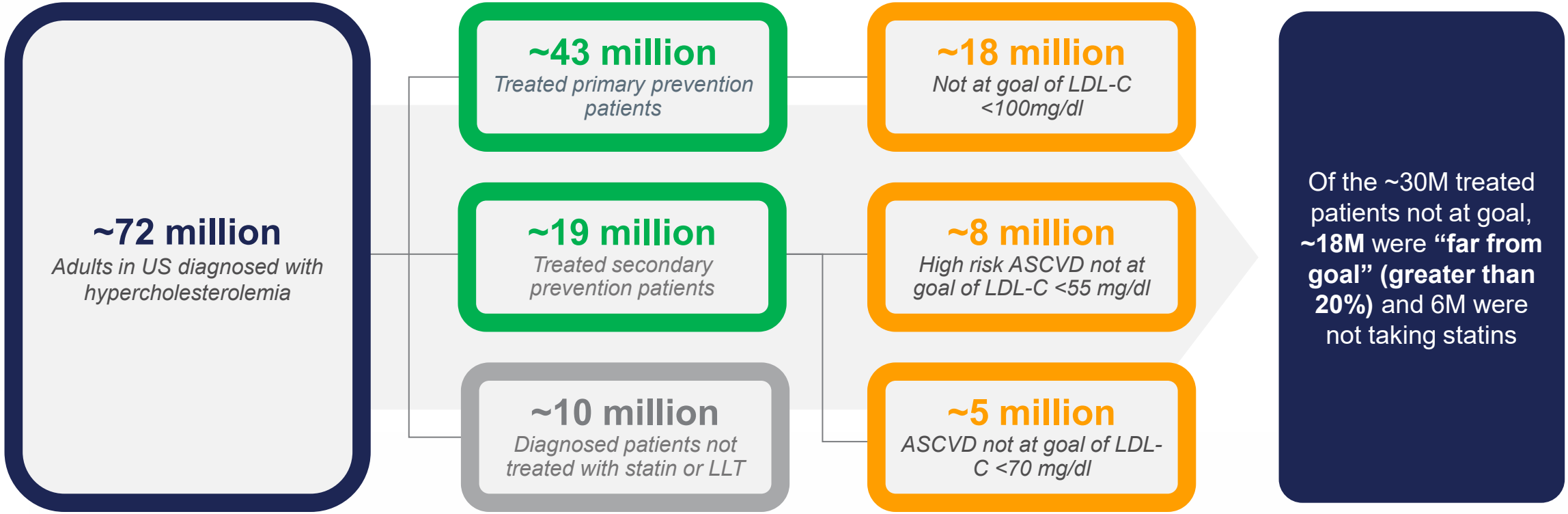
2026

- CHMP Positive Opinion
- EMA Approval
- RUBENS Phase 3 Topline

* Includes cash and cash equivalents and marketable securities

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Obicetrapib Could Address the ~30M Patients in US on Drug but not at Goal



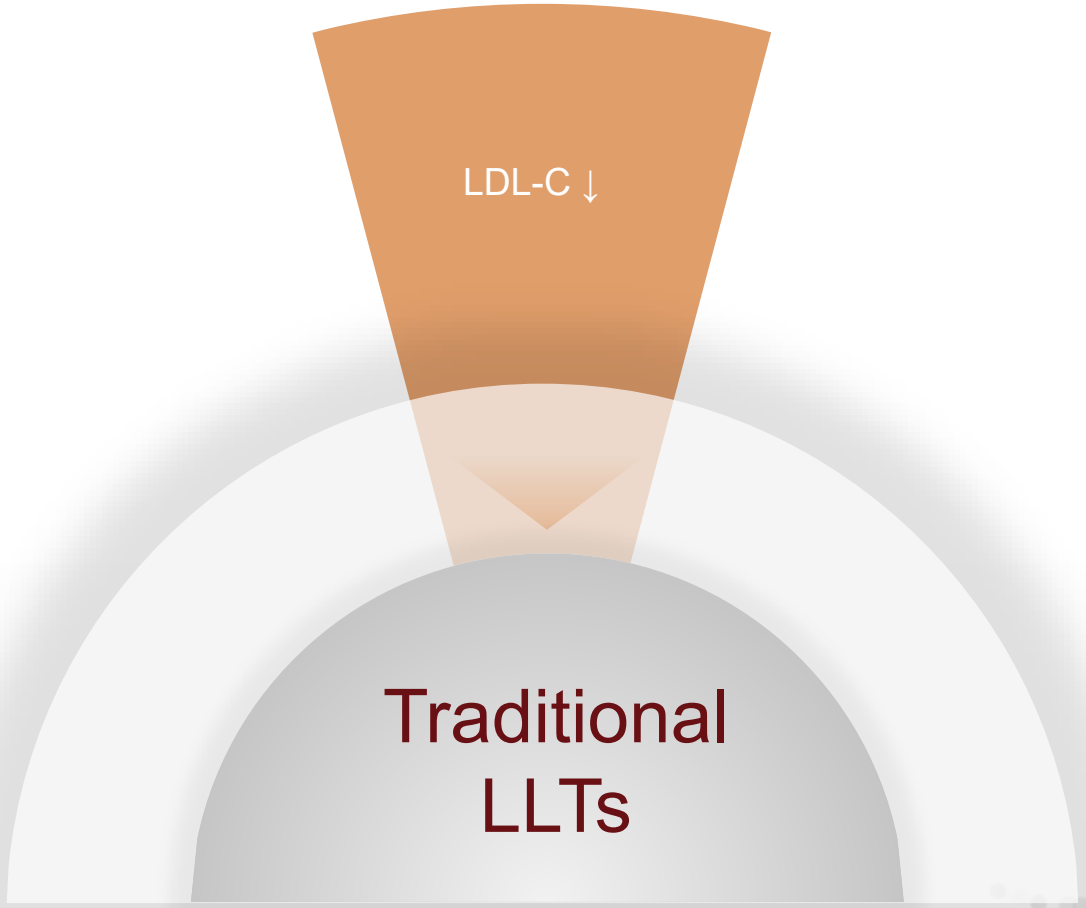
US Branded Lipid Lowering Market

Potential key factors limiting penetration include **product limitations** and **market access** hurdles:
Low prescriber enthusiasm for existing TPPs
Payors restrict access

ASCVD=atherosclerotic cardiovascular disease; HeFH=heterozygous familial hypercholesterolemia; LDL-C=low-density lipoprotein-cholesterol; LLT=lipid lowering treatment.
Source: Ortiz et al, *Journal of Medical Economics*, 2025, Vol 28, No 1, 1616-1625

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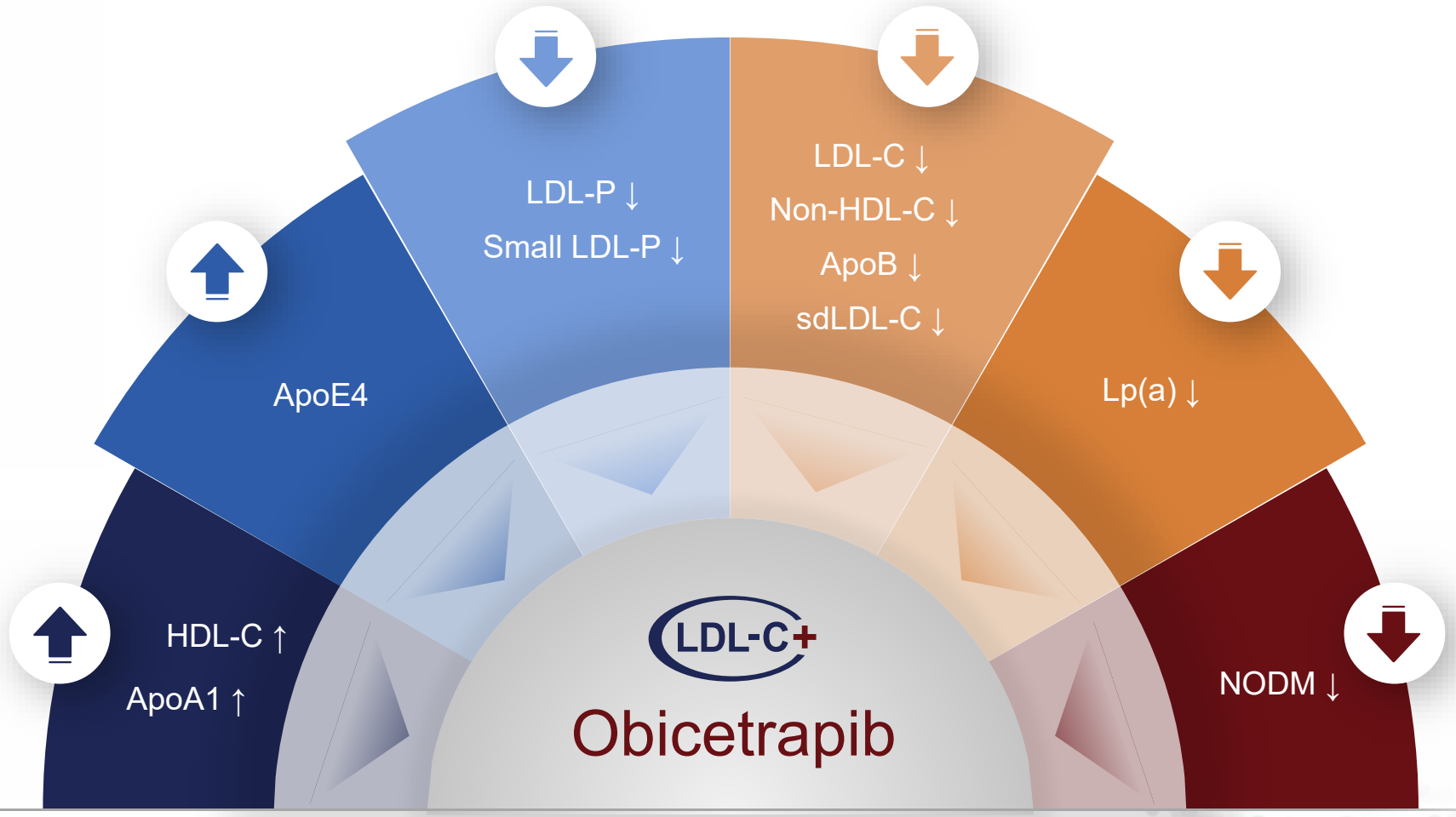
Currently, Treatment of Hyperlipidemia is One-Dimensional



LDL-C, low-density lipoprotein cholesterol; LLT, lipid lower therapy

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The Future of Hyperlipidemia Treatment Goes Beyond LDL-C



Note: NODM = New onset diabetes mellitus

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The Future of Hyperlipidemia Treatment Goes Beyond LDL-C

Obicetrapib was observed to **impact multiple risk factors,** potentially leading to more comprehensive risk management across **additional patient subpopulations**

LDL Particles

- 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^

Lp(a)

- 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

Diabetes

- **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

ApoE4

- ApoE4 is the **strongest genetic risk factor** for late-onset AD and associated with a **22-45%** increased risk of CVD[1-5]
- Approximately **20 million** patients with hyperlipidemia are at increased risk for AD
- Prevalence of ApoE4 in AD is up to **66%**[1-5]

* 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. * 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** 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 Aβ, amyloid β; AD, Alzheimer's disease; Apo, apolipoprotein; CVD, cardiovascular disese; 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

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Lipid Lowering Market Primed for Commercial Success

Observations[1-4]	Key Takeaways
1  We have seen LLT market growth each year for the last 5 years	Very large opportunity – even small amounts of penetration can result in significant financial success
2  Non-statin growth continues in the high double digits	Shift towards more aggressive treatment using alternatives / adding to statins
3  Guidelines have shifted to recommend more intense and earlier intervention not only with statins, but with ezetimibe, PCSK9's and bempedoic acid	Governing bodies and KOL's are prioritizing the importance of treating to goal
4  Access to PCSK9's has been increasing, and utilization controls have been decreasing	Payers are willing to cover medications in LLT space if priced appropriately
5  PCSK9 growth continues to accelerate 10 years post launch with 45%+ growth in net sales in each of the last 2 years	Commercial success is being demonstrated and is accelerating
6  FDA labeling changes continue to support broad access and earlier treatment	Labels are less restrictive and support broad usage

1. Based on third party prescription data on file
2. Grundy SM, et al. J Am Coll Cardiol. 2019;73(24):3168-3209.
3. Lloyd-Jones DM, et al. J Am Coll Cardiol. 2022;80(14):1366-1418
4. 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

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Market Dynamics: Growth of Non-Statin (+19%) and Branded (+31%) Volume Continue to Grow Rapidly Year Over Year

Market

1 Patient Population[1]

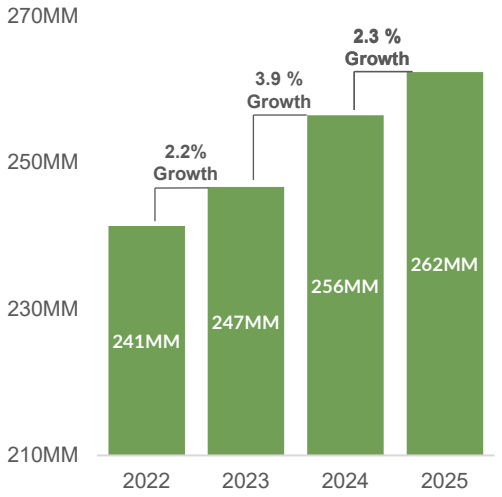
84 million
Adults in US diagnosed with hyperlipidemia

~21 million
Diagnosed patients not treated with statin or LLT

~40 million
Not at goal

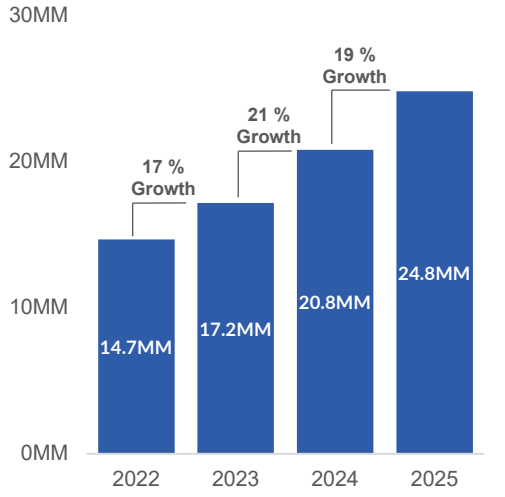
Over 60 million patients undertreated/ not treated

2 Lipid lowering Therapy TRx[2]



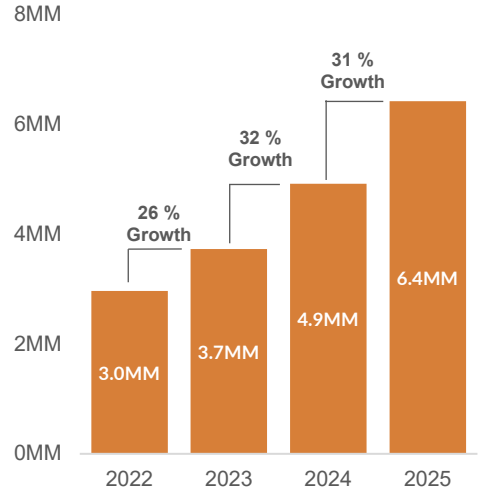
6 years of consecutive growth

3 Non-Statins[3] TRx



Non-statins growing at high double digits

4 Branded[4] TRx



Branded agents grew 31% matching last year's growth

Market Growth of 2.3% in 2025, adds 6 million additional TRx's, of which 1.5 million are branded TRx's

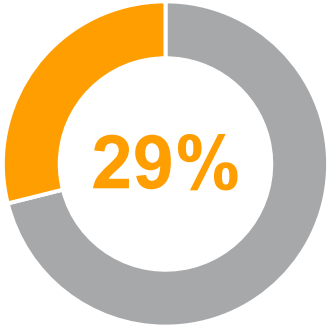
Source: Based on third party prescription data on file
1. Forian Healthcare Closed Claims and EHR Data (2022-2024)
2. All Lipid Lowering therapies: Statins, Ezetimibe and combinations; PCSK9 and BPA;
3. Non-Statins : Ezetimibe and combinations; PCSK9 and BPA;
4. Branded: PCSK9 and BPA;

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Majority of ASCVD/HeFH Patients are not Achieving LDL-C Targets

Primary prevention HeFH patients with an LDL-C target <100 mg/dL (2011-2017)[1]

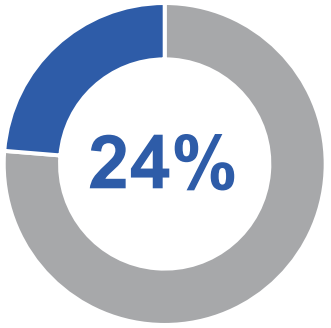
LDL-C < 100 mg/dL



<1/3 achieved LDL-C <100 mg/dL

ASCVD patients with an LDL-C target of LDL<70 or <55 mg/dL (2017-2018)[2]

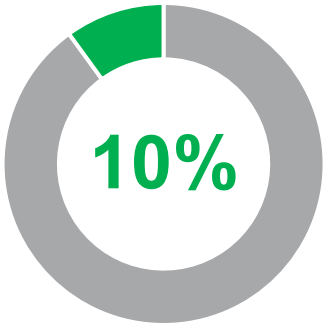
LDL-C < 70 mg/dL



~1/4 achieved LDL-C <70 mg/dL

Very high risk ASCVD patients with an LDL-C target <55 mg/dL (2020-2021)[3]

LDL-C < 55 mg/dL



10% achieved LDL-C <55 mg/dL

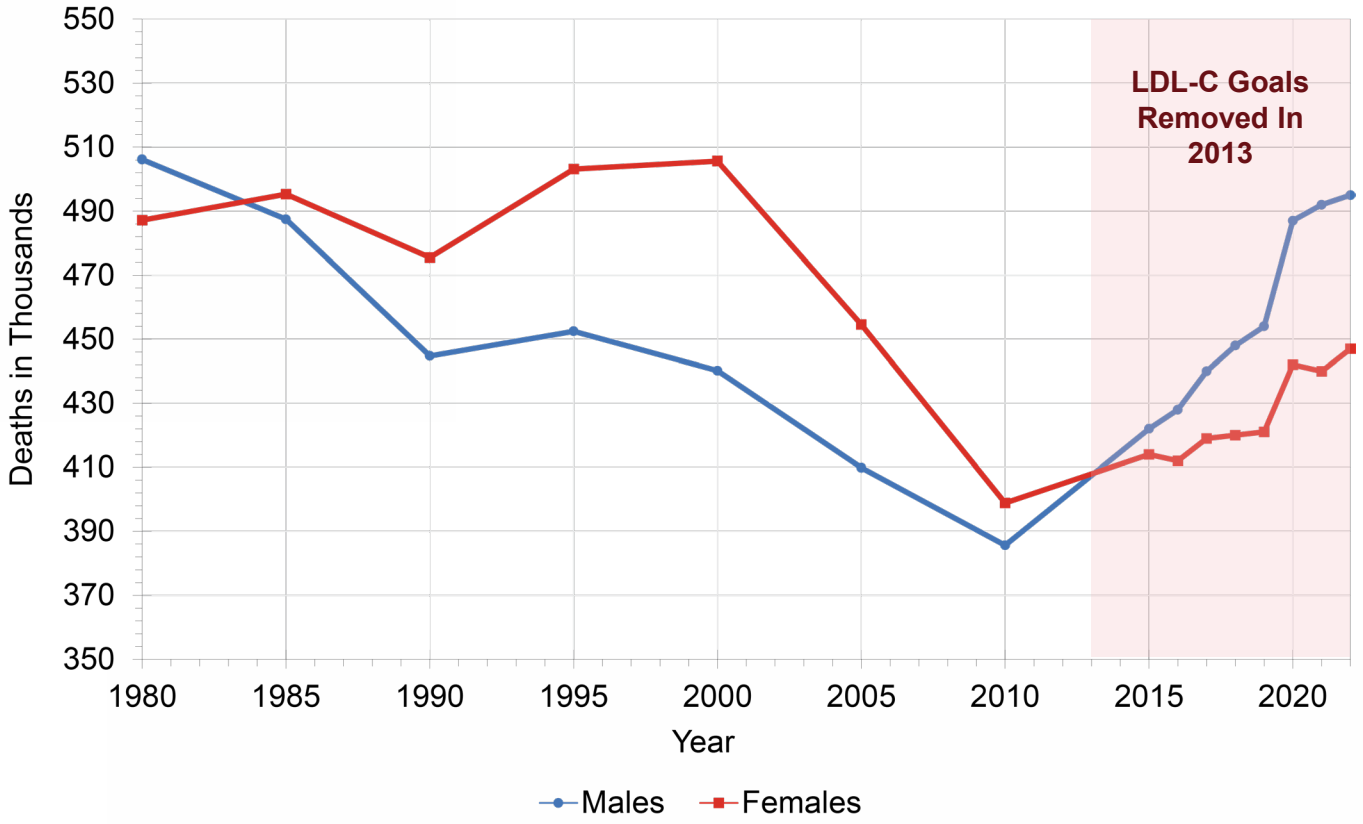
ASCVD=atherosclerotic cardiovascular disease; HeFH=heterozygous familial hypercholesterolemia; LDL-C=low-density lipoprotein-cholesterol.

1. Schreuder MM, et al. LDL cholesterol targets rarely achieved in familial hypercholesterolemia patients: A sex and gender-specific analysis. Atherosclerosis. 2023 2. Gao Y, Shah LM, Ding J, Martin SS. US trends in cholesterol screening, lipid levels, and lipid-lowering medication use in US adults, 1999 to 2018. J Am Heart Assoc. 2023;12(3):e028205; 3. Katzmann JL, et al. Simulation study on LDL cholesterol target attainment, treatment costs, and ASCVD events with bempedoic acid in patients at high and very-high cardiovascular risk. PLoS One. 2022;17(10):e0276898;

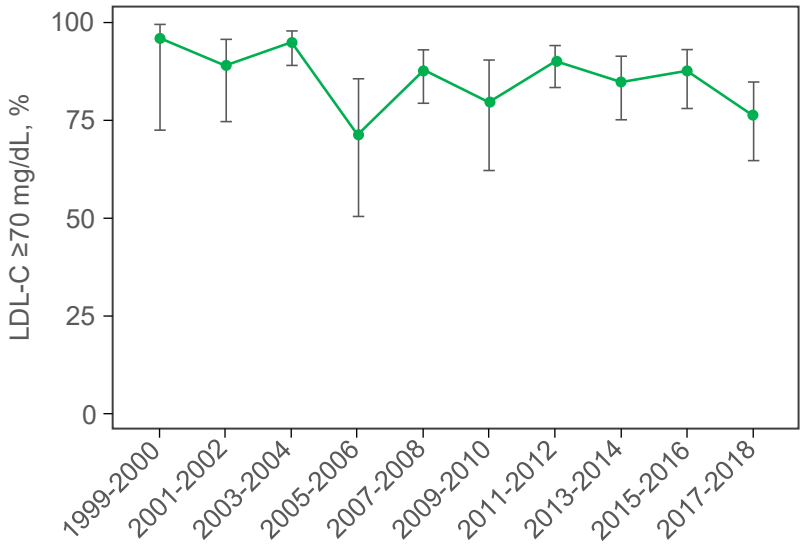
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CV Events Took an Alarming Turn Following Removal of LDL-C Guidelines in 2013

CVD Mortality Trends for US Males and Females, 1980 to 2022[1]



Trends in Prevalence of High LDL-C in US Adults, NHANES 1999-2018 with History of ASCVD[2]



~75% of ASCVD patients are NOT at their risk-based LDL-C goal

1. Martin SS, Aday AW, Allen NB, et al. 2025 Heart Disease and Stroke Statistics: A Report of US and Global Data From the American Heart Association. Circulation. doi: https://doi.org/10.1161/cir.0000000000001303 | 2. Yumin Gao, Y., et.al., US Trends in Cholesterol Screening, Lipid Levels, and Lipid-Lowering Medication Use in US Adults, 1999 to 2018, J Am Heart Assoc. 2023;12:e028205. DOI: 10.1161/JAHA.122.02820500

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Physicians Have Limited Treatment Options to Meet Patients Needs

Available and investigational treatment options have limitations

	Ezetimibe[1]	Nexletol[2]	PCSK9i[3]	Obicetrapib[5]	Obi + Eze [5]
Approval	Approved	Approved	Approved	LDL-C data 2024	LDL-C data 2024
MACE Benefit	7%	13%	15%	21%*	TBD
Observed LDL-C Reduction	25%	17%	45-50%	35-40%	49-54%
Administration	Oral (small molecule)	Oral (small molecule)	Injectable (mAb)	Oral (small molecule)	Oral (small molecule)
Dosing	10mg	180mg	140-150mg	10mg	20mg (10mg Obi + 10mg Eze)
Food Effect	No	No	No	No	No
Safety & Tolerability	Safe, well-tolerated	Tendon rupture & gout warning on label	Safe, injection site reactions	Well-tolerated compared to placebo	Well-tolerated compared to placebo
Lp(a) lowering	None	None	15-30%	34-56%	63%







Note: The above data do not represent head-to-head comparisons. Actual results may differ from expectations. Obicetrapib mono and Ezetimibe combo, along with the Oral PCSK9 have not been approved by any regulatory authority. E= estimated dates. Red represents sub-optimal product charateristics.
Sources: 1. PI Zetia table 7. refers to; Gagne, C et al. Am J Cardiol 2002. LDL-C measured only using Friedewald 2. PI Nexletol; study 2. refers to; Goldberg, A et al. JAMA 2019;322(18):1780-1788. LDL-C measured using Friedewald and direct assay for LDL-C <50 mg/dL. 3. multiple studies: Blom, D et al. N Engl J Med 2014; Kereiakes, D et al. Am Heart J 2015.; Ray, K. N Engl J Med 2020. 4. Ballantyne, C et al. JACC 2023;81(16) 5. See slide 12 for LDL-C, *MACE benefit from exploratory analysis in BROADWAY at 1 year 6. MK0616 was observed to have adverse events comparable to pbo in Phase 2b trials

Limited New Therapies on the Horizon

Available and investigational treatment options have limitations

	LIPFENDRA[1] (enlicitide)	AZD0780[2]	Obicetrapib[3]	Obi + Eze [4]
Phase 3 Data Readouts	LDL-C data 2025 (CVOT data 2029E)	TBD	LDL-C data 2024	LDL-C data 2024
Current Phase	Approved	Phase 3 Ongoing	CVOT ongoing	CVOT ongoing
Observed LDL-C Reduction	50-59% (~20% with food)	35-51%	35-40%	49-54%
Administration	Oral (peptide)	Oral (small molecule)	Oral (small molecule)	Oral (small molecule)
Dosing	380mg (20mg API + 360mg SNAC)	30mg	10mg	20mg (10mg Obi + 10mg Eze)
Food Effect	Yes (8hr fast & 30min wait)	No	No	No
Safety & Tolerability	SNAC technology has previously been observed to have tolerability concerns[6]	Well-tolerated SAEs and case of AST/ALT > 5x ULN	Well-tolerated compared to placebo	Well-tolerated compared to placebo
Lp(a) Lowering	20-25%	7-20%	34-56%	63%









Note: The above data do not represent head-to-head comparisons. Actual results may differ from expectations. Obicetrapib mono and Ezetimibe combo, along with the Oral PCSK9 have not been approved by any regulatory authority. E= estimated dates. Red represents sub-optimal product charateristics.
Sources:. 1. Ballantyne, C et al. JACC 2023;81(16) 2. JACC 2025 3. See slide 12 for LDL-C 6. MK0616 was observed to have adverse events comparable to pbo in Phase 2b trials

Obicetrapib Program Designed to Overcome Limitations of Prior CETP Inhibitors

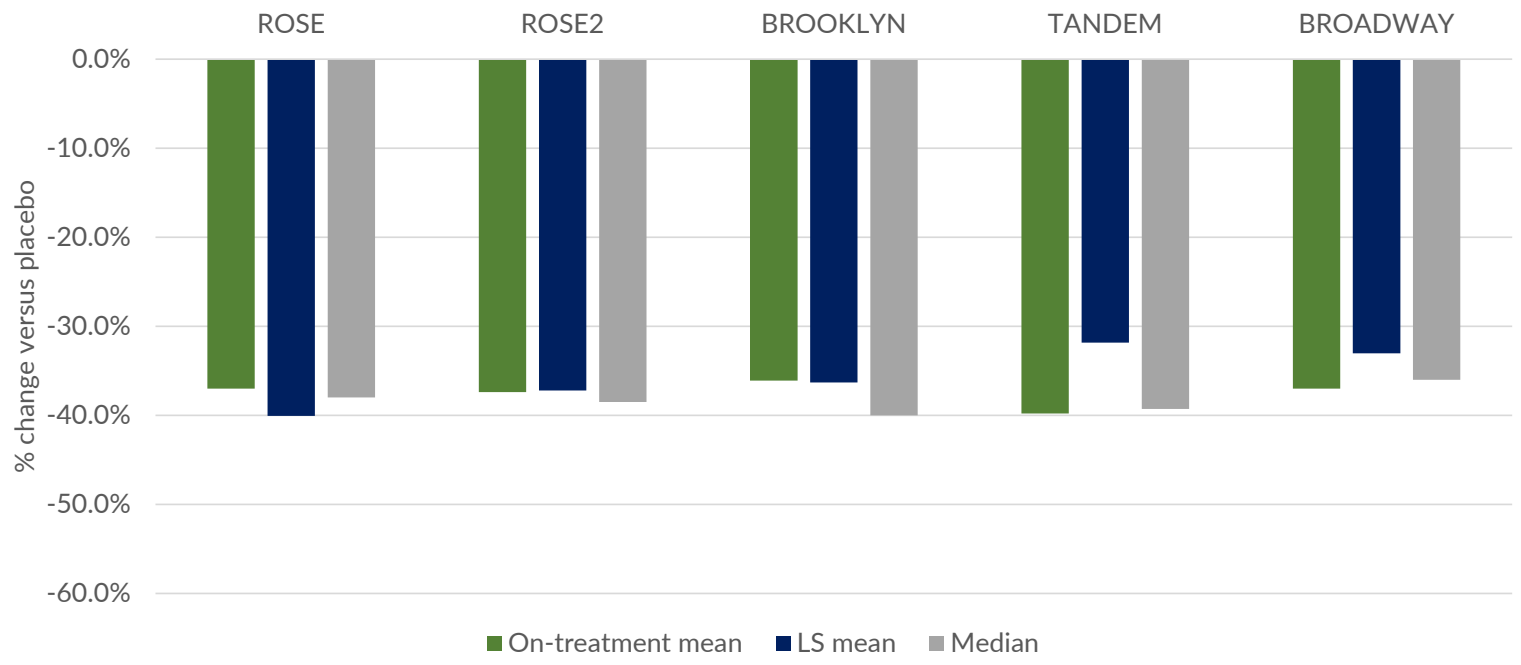
	Torcetrapib[1]	Dalcetrapib[2]	Evacetrapib[3]	Anacetrapib[4]	Obicetrapib[5]
Observed LDL-C reduction[6]	25%	7%	11-21%	17%	35-40%
CETP inhibition	35%	30%	65%	80%	97%
Dosing	60mg	600mg	100mg	100mg	10mg
Blood pressure increase	Yes	No	No	No	No
Aldosterone increase	Yes	No	No	No	No
Lp(a) lowering	unknown	unknown	20-25%	20-25%	34-56%
ApoB lowering	15%	None	15-20%	18%	22-24%
OUTCOMES STUDIES					
Name	ILLUMINATE	Dal-OUTCOMES	ACCELERATE	REVEAL	PREVAIL
Patients	15,067	15,871	12,092	30,449	9,541
Baseline LDL-C (mg/dl)	79.7	76.4	81.1	61	103
LDL-C reduction (mg/dl)	20	NS	25	11	TBD
Median follow-up	18 mo	31 mo	26 mo	49 mo	42 mo (expected)
Result (HR)	1.25	1.04	1.01	0.91	TBD
Explanation	Off target tox	No LDL-C benefit	Short follow-up but mortality benefit (HR 0.84)	Low baseline and LDL reduction	TBD

Note: The above trials and data do not represent head-to-head comparisons. Actual results may differ from expectations.
Sources: **1.** Barter et al. NEJM.2007; **2.** Schwartz et al. NEJM.2012; **3.** Lincoff et al. NEJM.2017 **4.** Bowman et al. NEJM.2017 **5.** Company Data **6.** Per PUC, if available

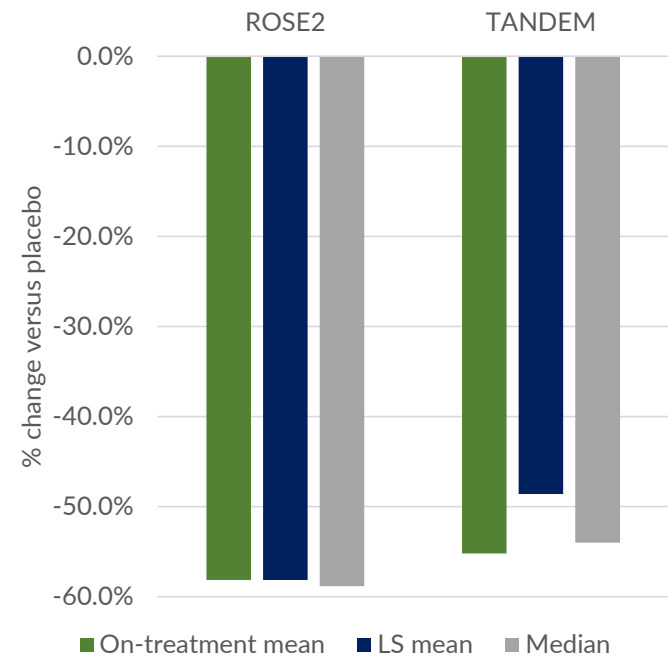
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Consistent LDL-C Reduction Observed Across Our Phase 2 and Phase 3 Trials, Independent of Background Statin and/or Multiple Lipid Lowering Therapy Usage

Obicetrapib 10 mg monotherapy



Obicetrapib plus ezetimibe



Monotherapy reductions of 35-40%

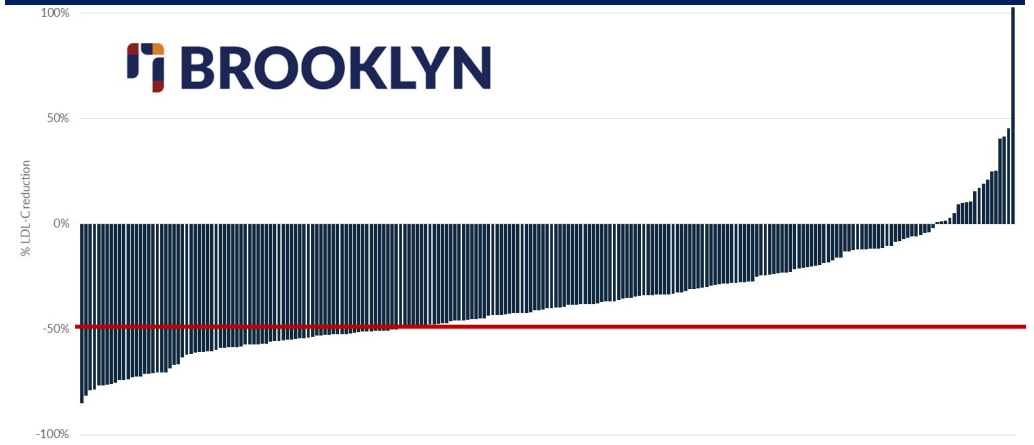
Combo reductions of 50-60%

Note: ROSE at week 8, ROSE2, BROOKLYN, BROADWAY, and TANDEM as of week 12. High intensity statin use 100% in Phase 2 trials and over 65% in Phase 3 trials.

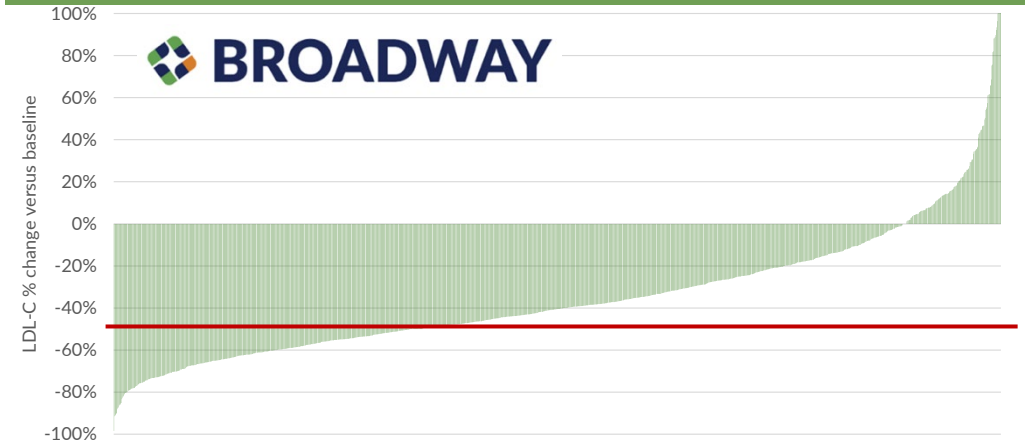
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LDL-C Responder Analysis at day 84

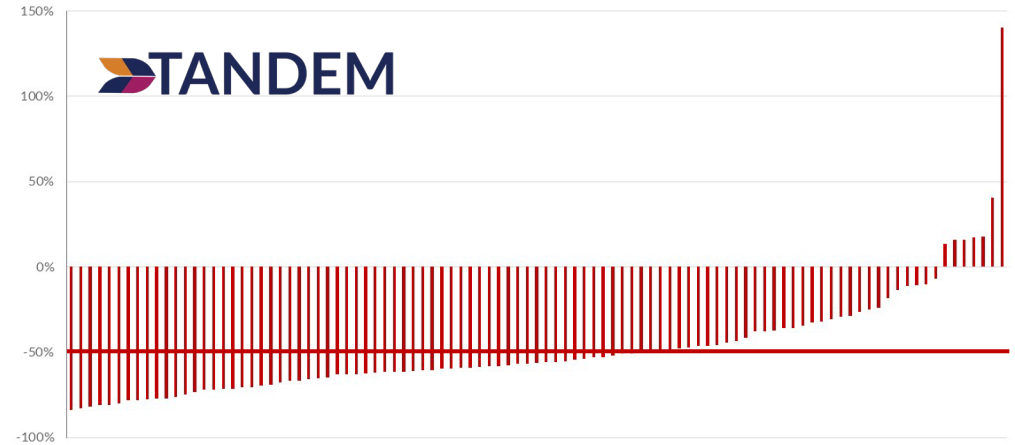
34% of patients with >50% LDL-C reduction



33% of patients with >50% LDL-C reduction



61% of patients with >50% LDL-C reduction



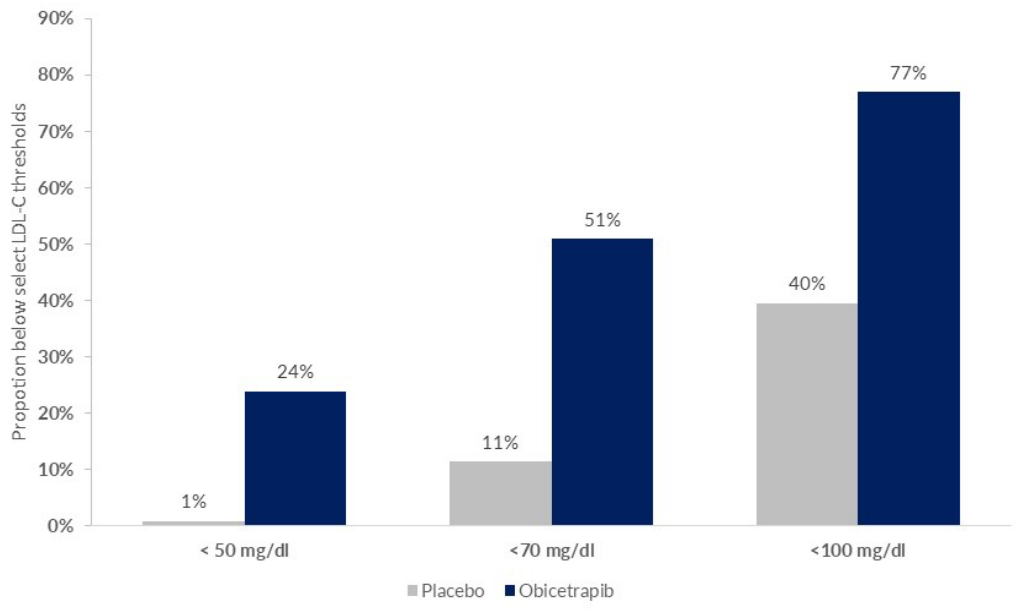
Note: each line represents a single patient in the obicetrapib 10 mg arm, five patients increase more than 100% in the BROADWAY study. TANDEM data for the FDC of obicetrapib and ezetimibe

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Greater Proportion of Patients in Obicetrapib Arm Achieved LDL-C Goal

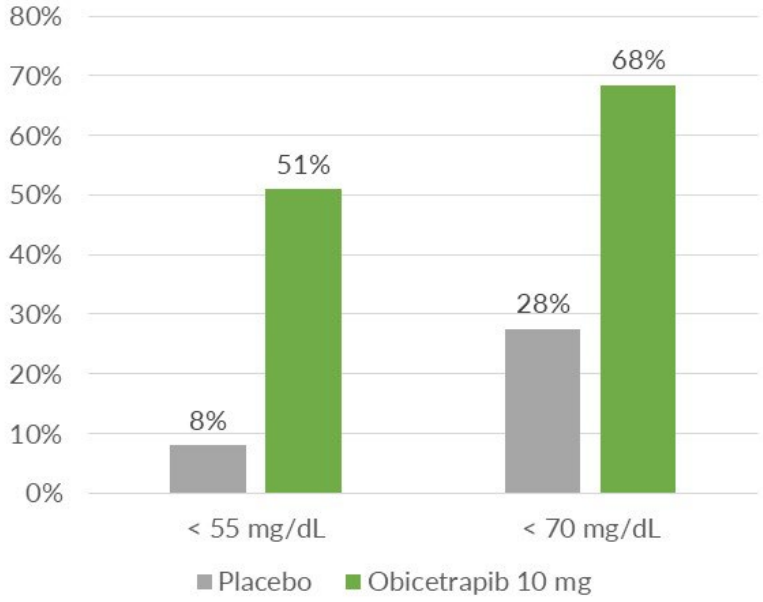
BROOKLYN

% of patients achieving LDL-C thresholds at Day 84



BROADWAY

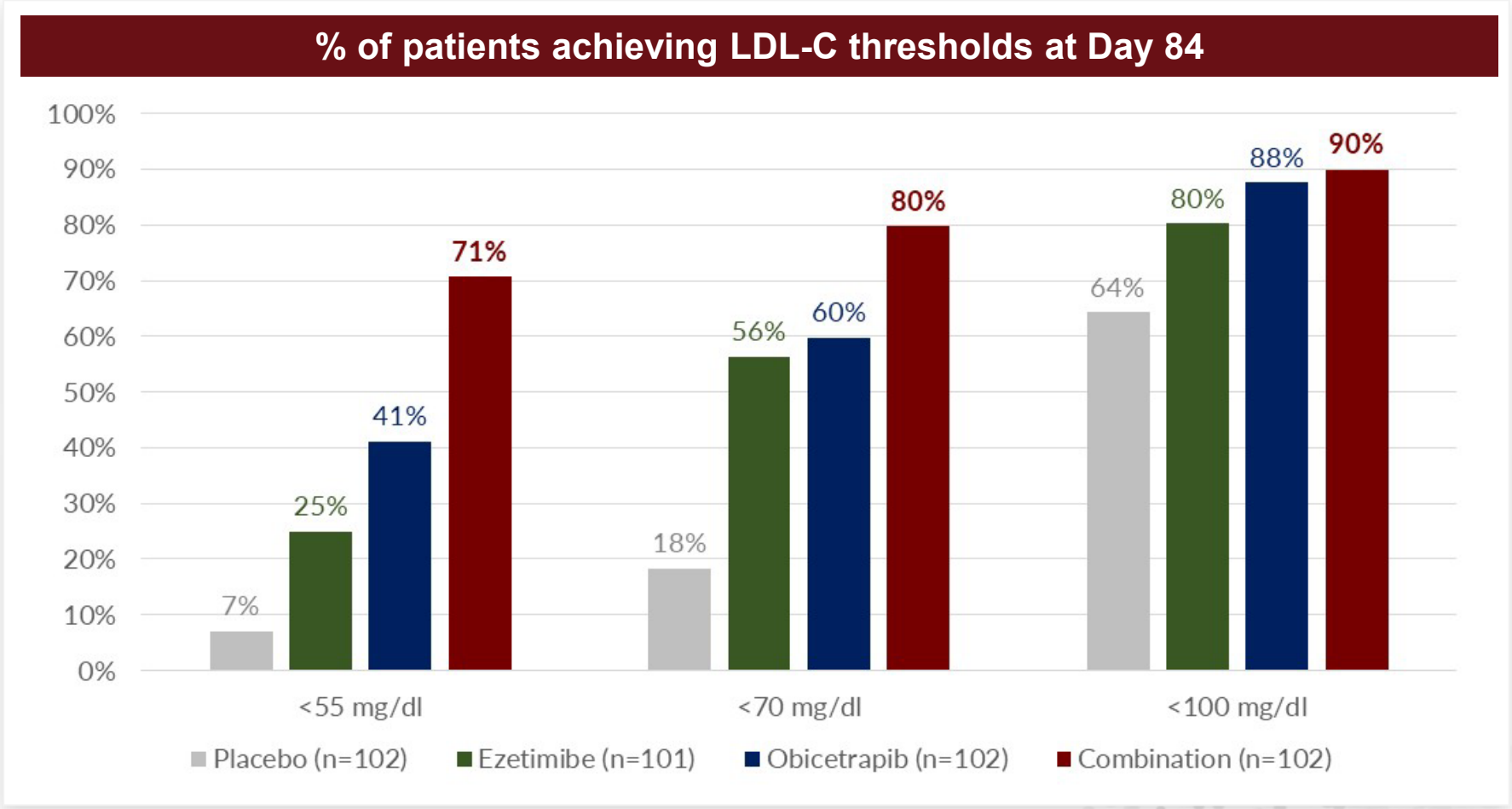
% of patients achieving LDL-C thresholds at Day 84



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Over 70% of Patients on Obicetrapib+Ezetimbe Achieved Less than <55 mg/dL

TANDEM



NewAmsterdam Pharma

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 are limitations on the interpretation of MACE data derived from both BROOKLYN and BROADWAY studies given they were not designed or powered to assess MACE. MACE data presented above may not be predictive of the MACE data we observe in PREVAIL, which has been designed to measure MACE benefit.

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MACE Benefit Observed Across Multiple Components After 1 Year of Treatment

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)
First 4-point MACE – no. (%)	44 (5.2)	70 (4.2)	0.79	(0.54-1.15)
Coronary heart death – no. (%)	5 (0.6)	8 (0.5)	0.80	(0.26-2.44)
Nonfatal MI – no. (%)	11 (1.3)	20 (1.2)	0.91	(0.44-1.90)
Stroke – no. (%)	5 (0.6)	14 (0.8)	1.39	(0.50-3.86)
Coronary revascularization – no. (%)	34 (4.0)	49 (2.9)	0.72	(0.46-1.11)

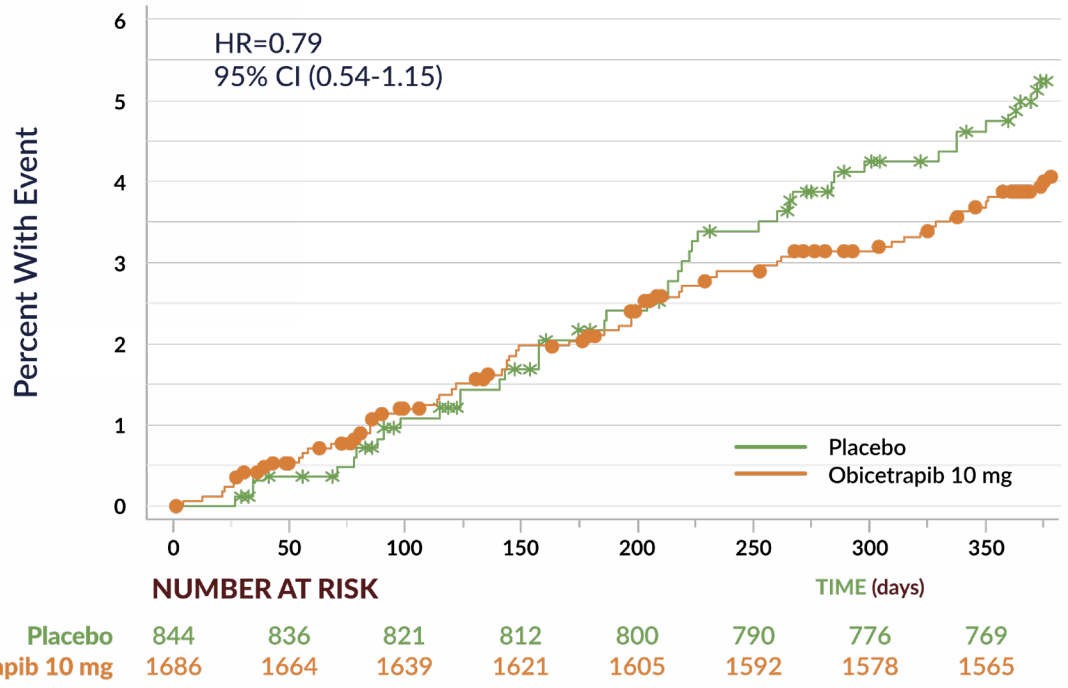
4-point MACE: CHD death, Non-fatal myocardial infarction, non-fatal stroke, coronary revascularization
(1) MACE was evaluated in BROADWAY as an exploratory endpoint. There are limitations on the interpretation of MACE data derived from both BROOKLYN and BROADWAY studies given they were not designed or powered to assess MACE. MACE data presented above may not be predictive of the MACE data we observe in PREVAIL, which has been designed to measure MACE benefit.

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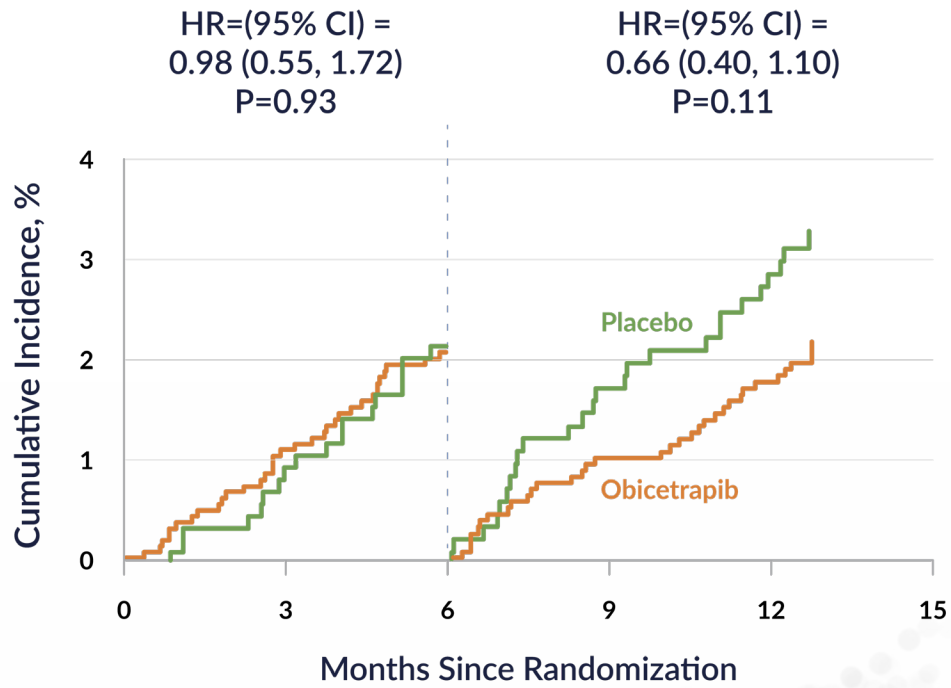
Kaplan-Meier Curve Separates at Day 200 Driven by Attenuation of MACE-4 Events in the Obicetrapib Arm

BROADWAY (1)

Kaplan Meier Curve



Landmark Analysis: Censored at 6 months



4-point MACE: CHD death, Non-fatal myocardial infarction, non-fatal stroke, coronary revascularization
(1) 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.

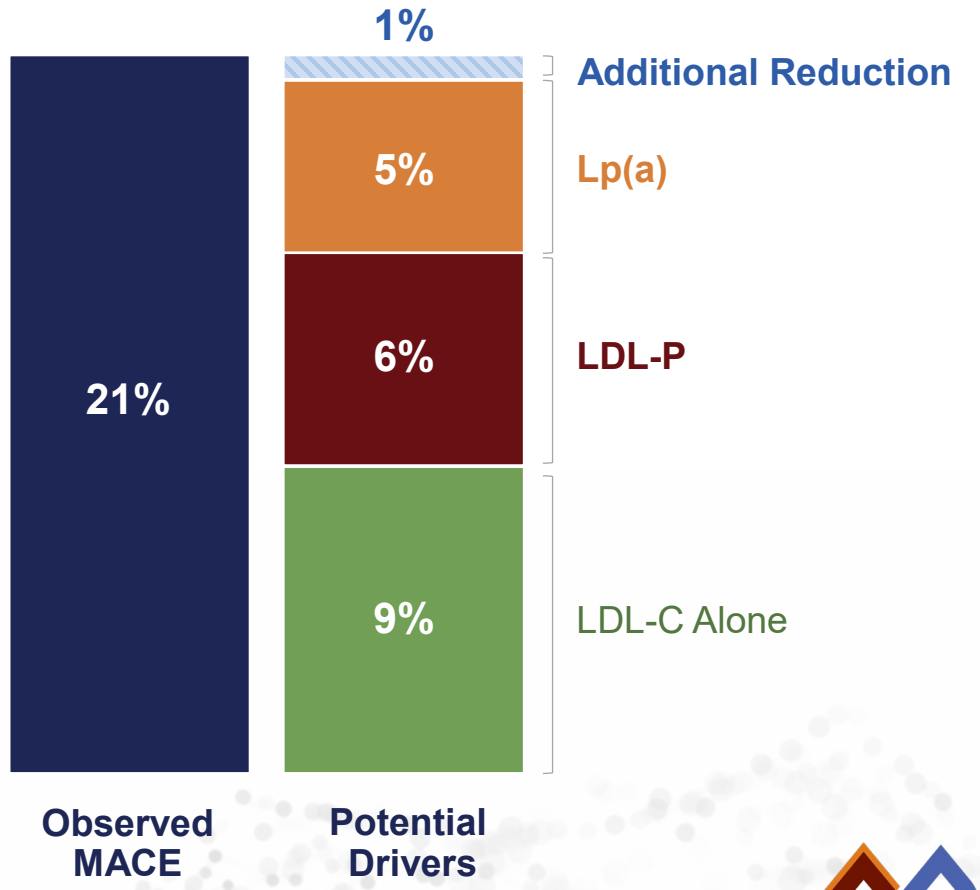
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Explaining BROADWAY's Observed 21% MACE Reduction

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 reduction potentially provides 6-7% additional MACE reduction
- Lp(a) reduction 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, Queseda 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.

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BROADWAY

Overview of Events of Special Interest

	Placebo N= 843 n (%)	Obicetrapib N= 1685 n (%)	
AST or ALT > 3 x ULN	8 (0.9)	10 (0.6)	
Bilirubin > 2 x ULN	4 (0.5)	2 (0.1)	
CK > 5 x ULN	3 (0.4)	5 (0.3)	
NODM or worsening of glycemic control	338 (40.1)	592 (35.1)	(p = 0.015)
- AE indicating new/worse type 1 or 2 diabetes	30 (3.6)	58 (3.4)	
- Initiation of diabetes medication	104 (12.3)	186 (11.0)	
- HbA1c ≥ 6.5% (where baseline HbA1c < 6.5%)	55 (6.5)	84 (5.0)	
- Two consecutive glucose values > 126 mg/dL	248 (29.4)	459 (27.2)	
- HbA1c increase from baseline > 0.5%	133 (15.8)	234 (13.9)	
- Worsening glycemic control	199 (23.6)	350 (20.8)	
Renal function worsening	77 (9.1)	127 (7.5)	
- eGFR < 30 mL/min/1.73m2	13 (1.5)	13 (0.8)	
- 25% decrease in eGFR from baseline:	70 (8.3)	115 (6.8)	
- Increase of Serum Creatinine ≥ 0.3 mg/dL from baseline	61 (7.2)	91 (5.4)	
Macular degeneration	0 (0.0)	1 (0.1)	

BROADWAY Designed to be a Predictor of PREVAIL

BROADWAY

1º endpoint – week 12

N = 2532

Obicetrapib 10 mg (2:1 randomization)

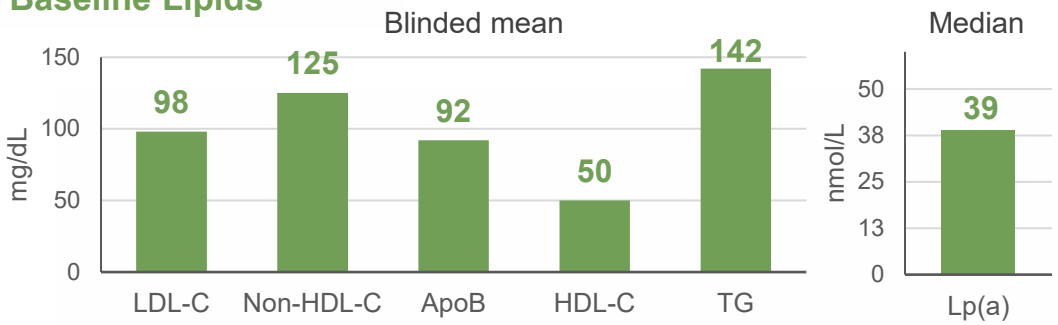
Placebo

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)

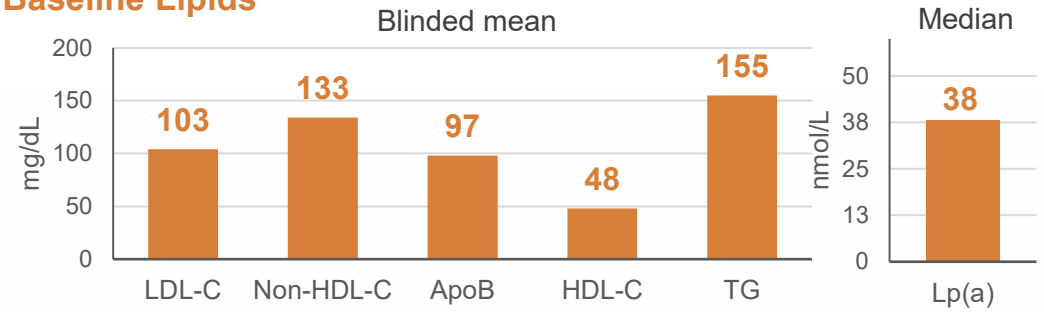
Placebo

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



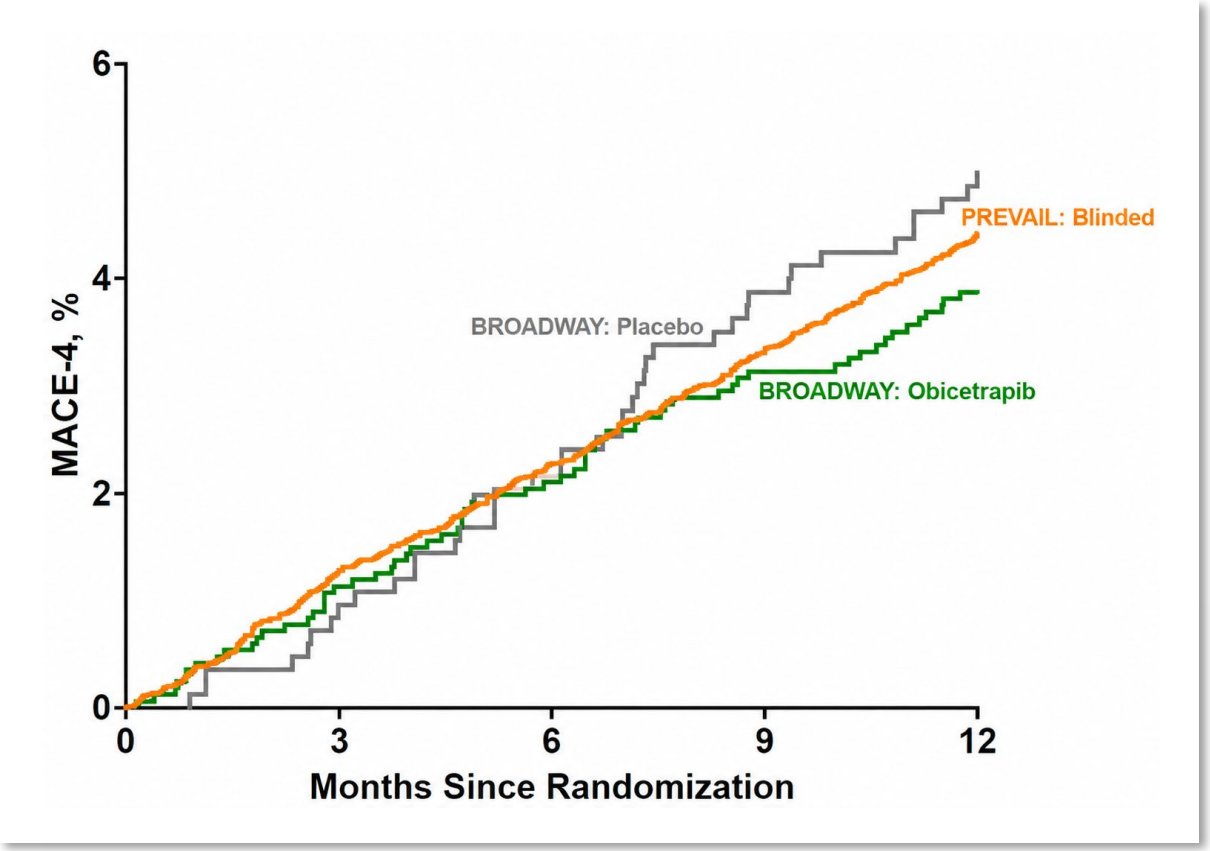
Baseline Lipid Modifying Therapy

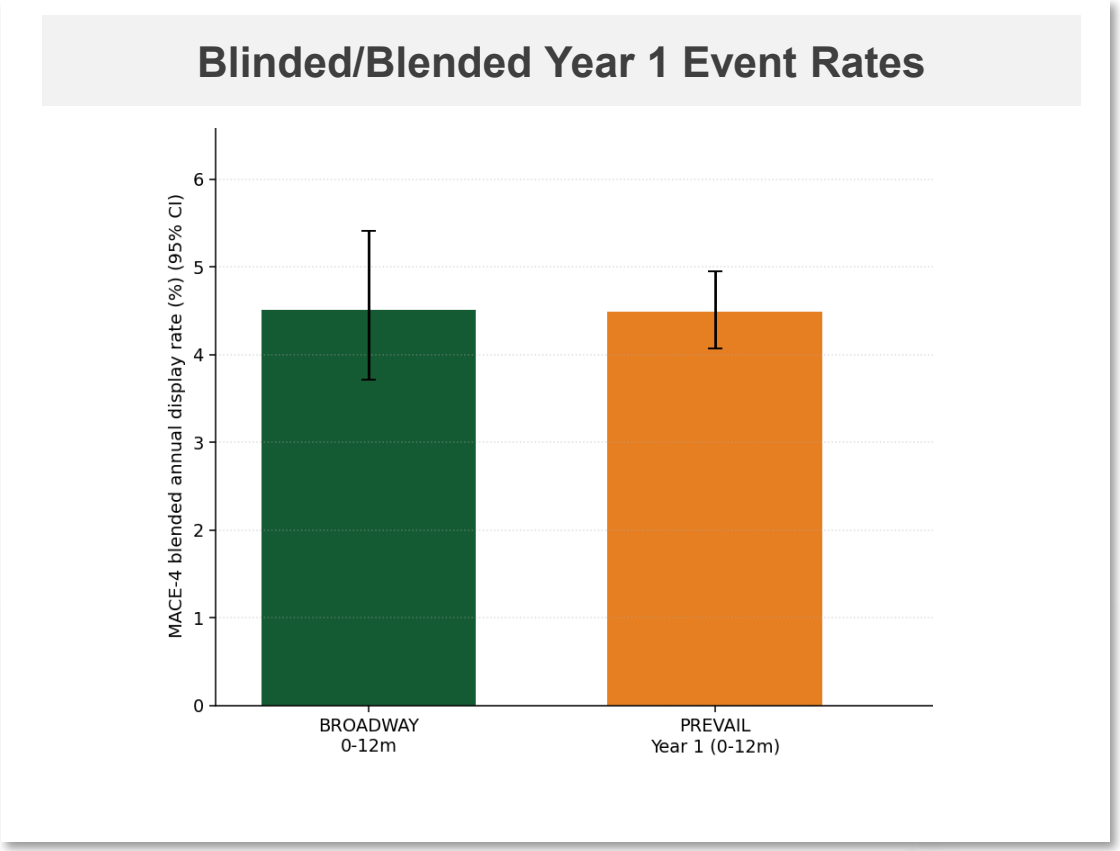
- Any statin: >90%
- High intensity statin: 70%
- Ezetimibe: 23%
- PCSK9i: 2%
- SGLT2i: 14%
- GLP-1: 6%

Source: Data on file

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Analysis of BROADWAY and PREVAIL Year 1 Event Rates(1)





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

(1) While not powered to detect a MACE benefit, we observed positive MACE-4 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. PREVAIL data is preliminary and subject to change as MACE events continue to be identified and adjudicated (including with respect to periods presented above). Additionally, Year 1 and Year 2 MACE event trends may not be indicative of future trends.

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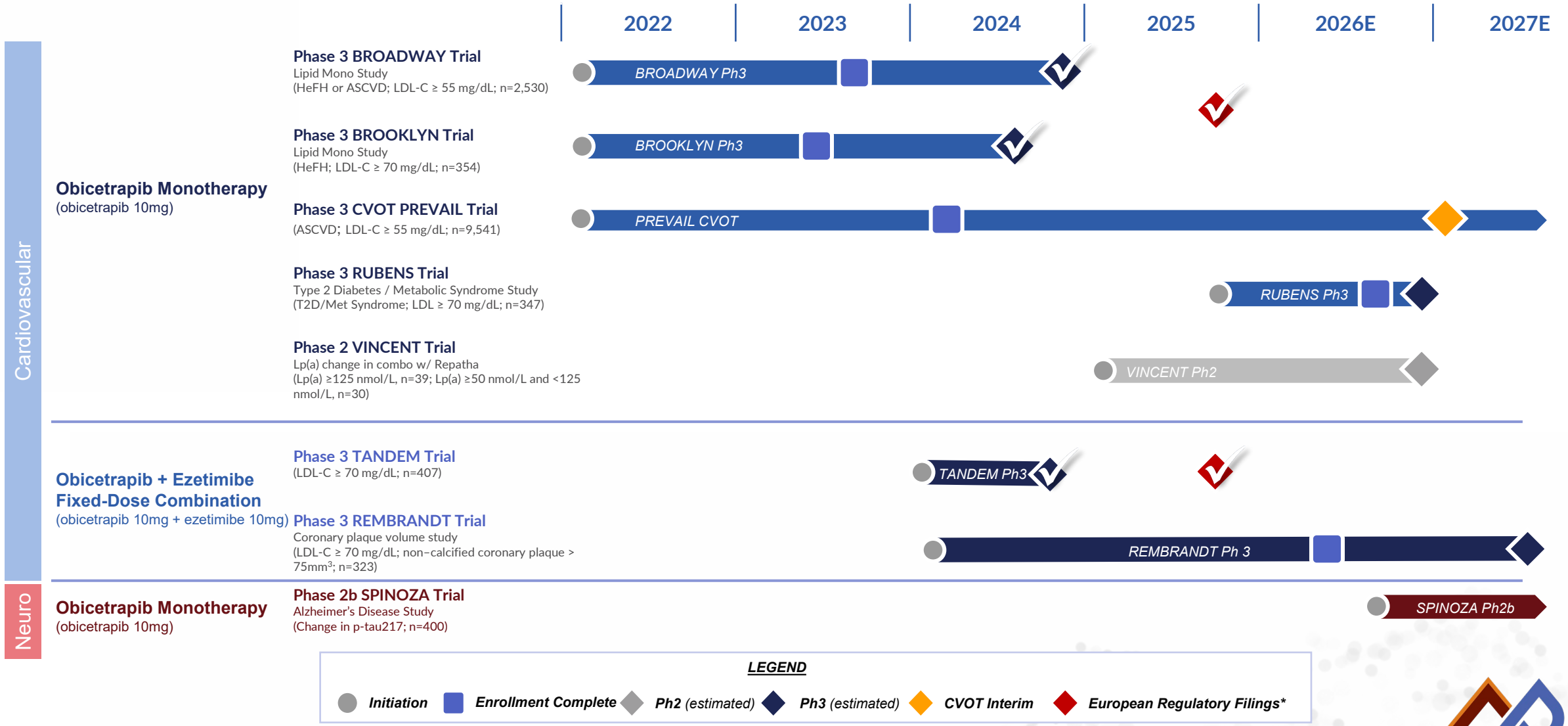
PREVAIL Designed to Apply Lessons Learned from Previous CVOTs to Reduce Risk and Demonstrate Obicetrapib's Full Benefit

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

Primary endpoint selection
Coronary heart disease (CHD) death, non-fatal MI, fatal and non-fatal ischemic stroke, coronary revascularization

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Multiple Data Readouts to Drive Future Momentum



*MAAs were filed and accepted for review by EMA, UK and Switzerland regulatory authorities

Note: Other than as noted, the pipeline represents trials that are currently ongoing. 2026 and beyond are projections and subject to inherent limitations. Actual results may differ from expectations.

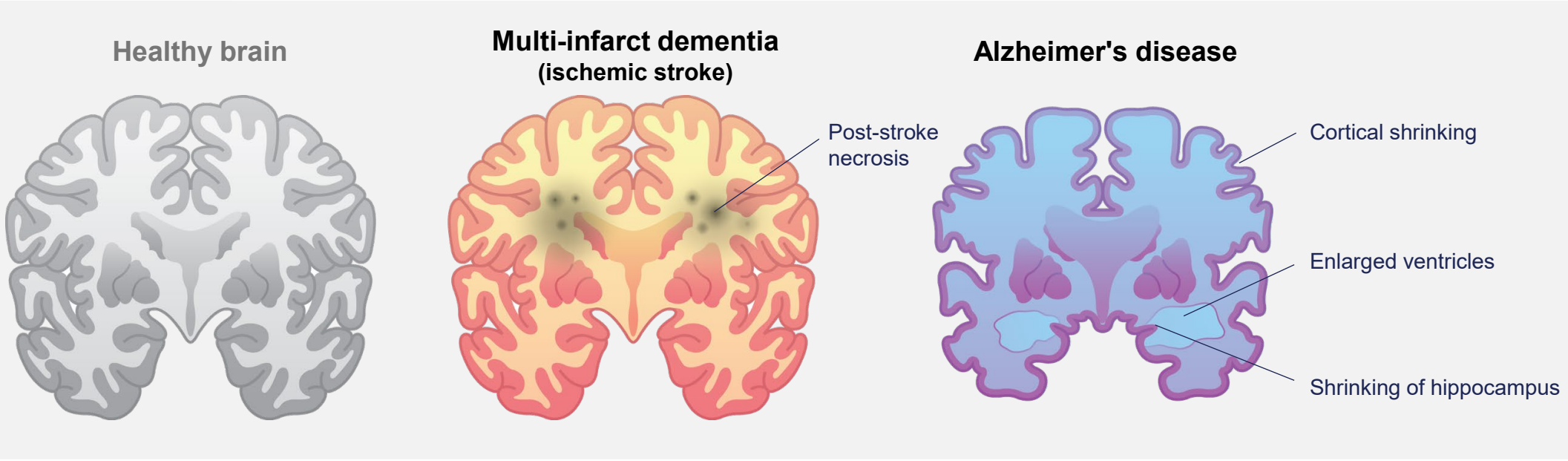
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Obicetrapib and Alzheimer's Disease

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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]

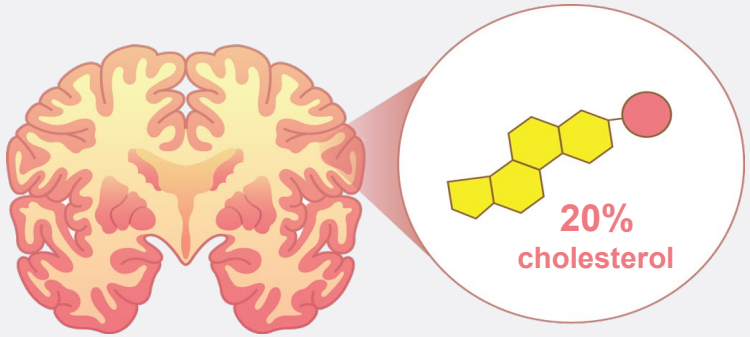
Alzheimer's disease results in the **generalized degeneration of the brain**, with over 50M people affected WW and an economic burden of >$1 trillion [2]

Source: 1. M Kivipelto et al, Stroke, 2022: 53(2) 2. Alzheimer's Disease International.

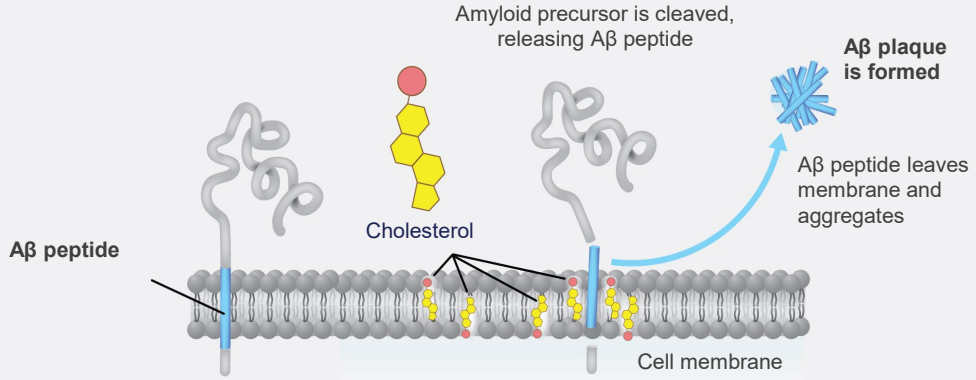
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Elevated Cholesterol Levels in the Brain Precede Formation of Amyloid-Beta (Aβ) Plaques

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



Aβ 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

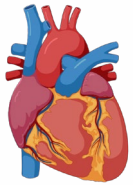
- 24S-hydroxycholesterol is a proxy for excess cholesterol that will be measured in our phase 2a clinical trial

APOE, apolipoprotein E; CNS, central nervous system.
Mahley RW. *Arterioscler Thromb Vasc Biol.* 2016;36(7):1305-1315.

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ApoE4 is a Risk Factor for Both CVD and Alzheimer's Disease[1-5]

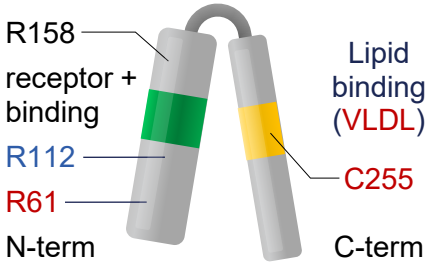
CVD



CVD Risk Factors

- ▲ Risk for CVD by 22-45%
- ▲ LDL-C
- ▼ HDL-C
- ▲ ApoC
- ▲ Lp(a)

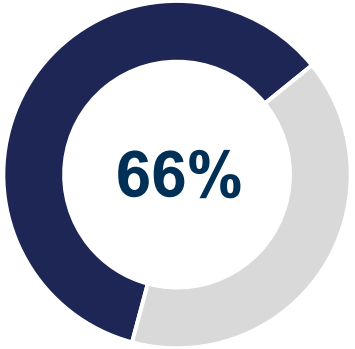
APOE4



AD Risk Factors

- ▼ Cholesterol transport and clearance
- ▲ Lipid accumulation in brain
- ▲ Aβ aggregation
- ▲ Total cholesterol
- ▼ HDL-C

Prevalence of APOE4 in AD



Elevated risk is mediated by the profound effect of APOE4 on lipid metabolism

APOE2/E2	APOE2/E3	APOE3/E3
0.5%	**11%**	**61%**

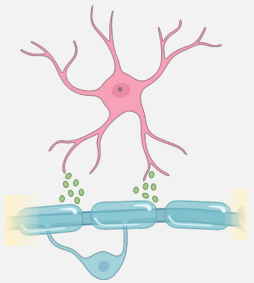
% of population with this genotype

>25% of population at increased risk

APOE4/E2 = **2%**
APOE4/E3 = **24%**
APOE4/E4 = **2%**

ApoE4-induced cholesterol dysregulation has cell-specific effects in the brain that all contribute to AD pathogenesis

- Disruption of neuronal synaptic function
- Altered astrocytic glucose metabolism
- Promotion of microglial inflammatory responses
- Impaired oligodendrocyte remyelination



Aβ, amyloid β; AD, Alzheimer's disease; Apo, apolipoprotein; CVD, cardiovascular disese; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; Lp(a), lipoprotein(a).

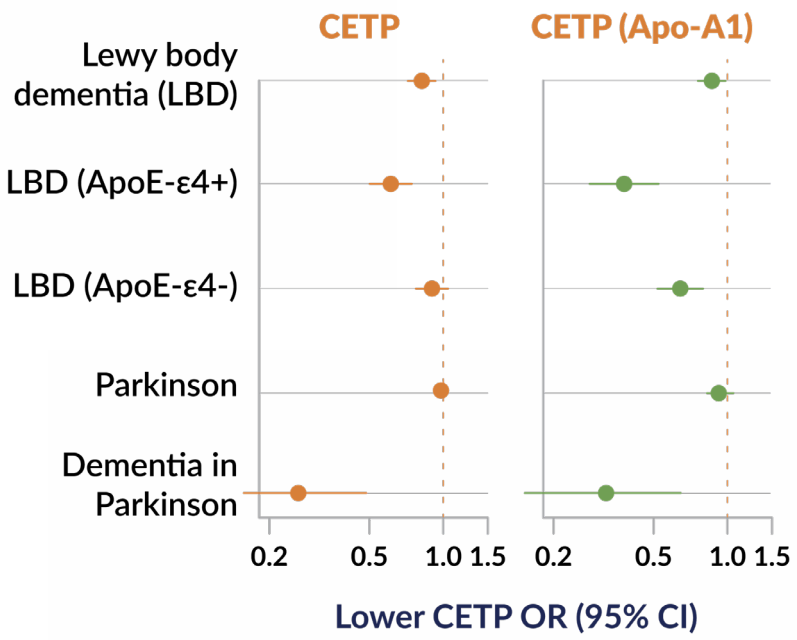
1. Abondio P et al. *Genes (Basel)*. 2019;10(3):222. 2. Feringa FM et al. *Front Aging Neurosci.* 2021;13:690372. 3. Hottman 2017. 4. Jeong W et al. *Mol Cells.* 2019;42(11):739-746. 5. Williams et al. BMC 2020.c

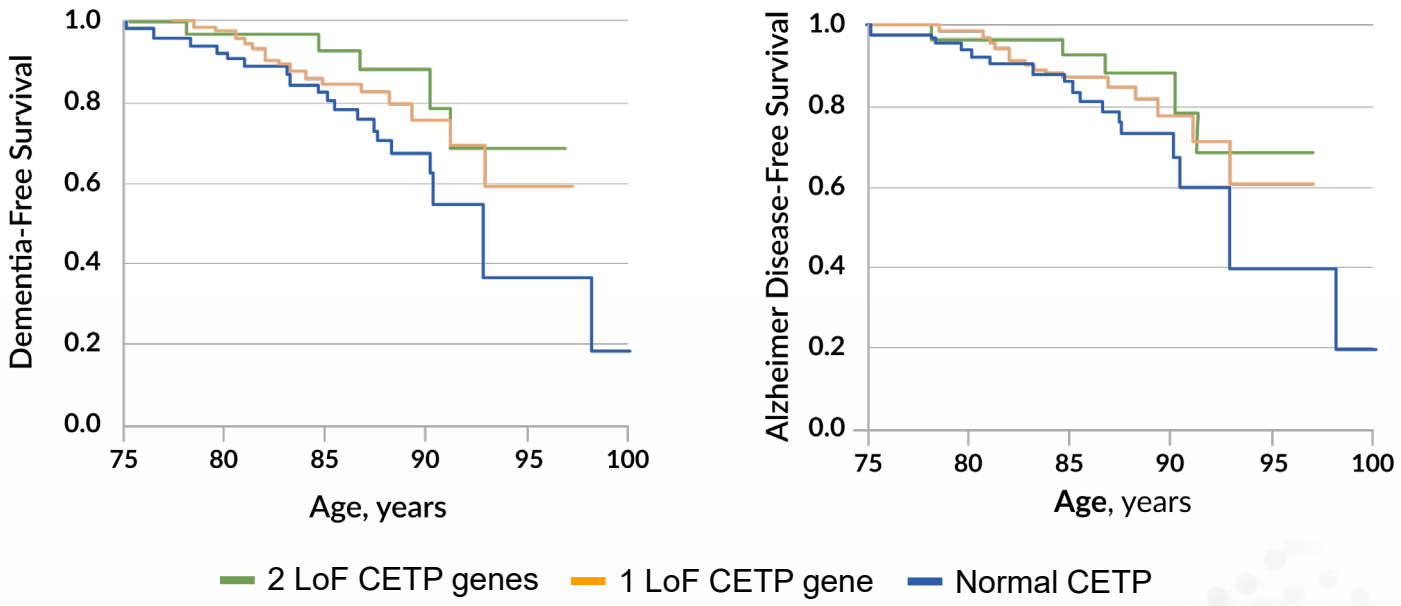
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CETP Loss-of-Function (LoF) Genotype May be Associated with Slower Memory Decline and Lower AD Risk

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



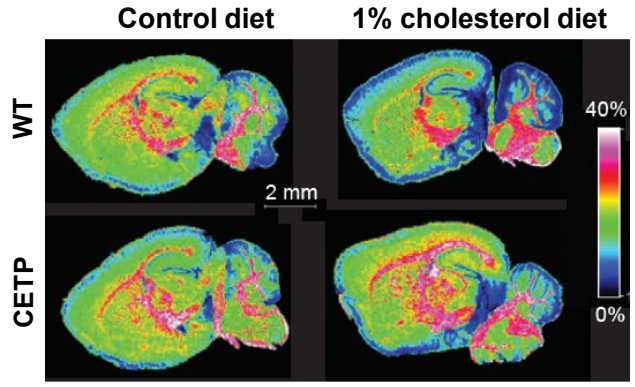


Source :JAMA, January 13, 2010—Vol 303, No. 2

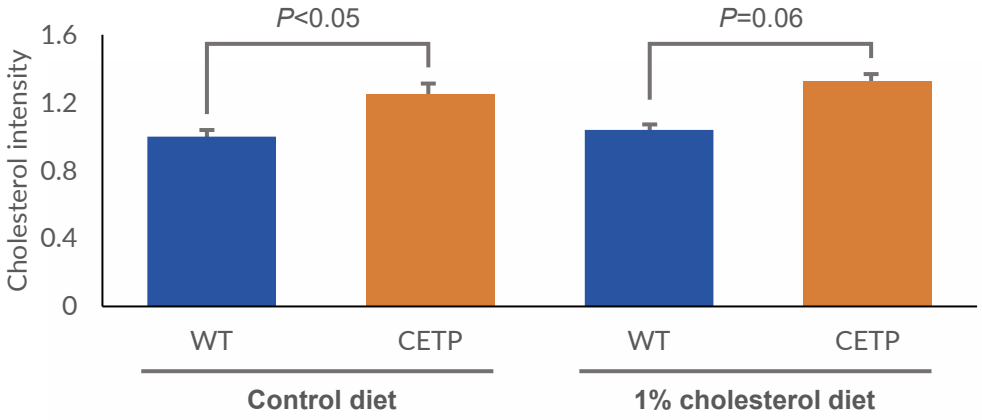
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CETP Knock-in Mice Have Increased Brain Cholesterol Levels and CETPi Observed to Rescue Cognition in Preclinical Models of CETP-induced AD

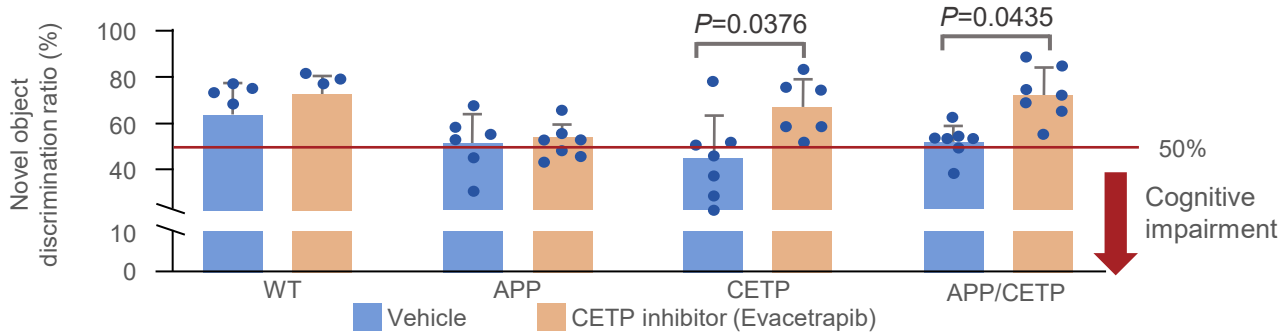
CETP transgenic mice have lower plasma HDL-C levels and increased brain cholesterol levels[1]



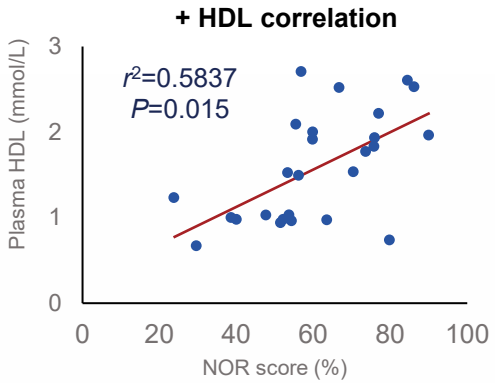
Increased CETP demonstrates 22% increased brain cholesterol levels on high cholesterol diet



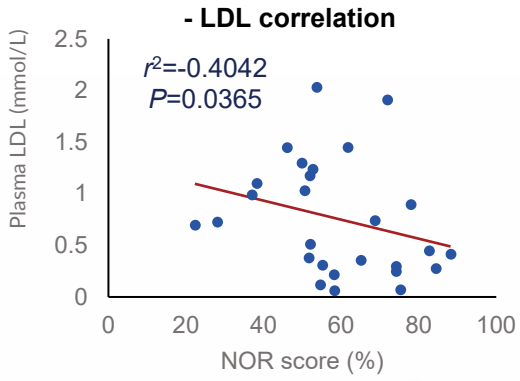
CETP inhibition with evacetrapib led to cognitive improvement [2,3]



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 brain[4]

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.

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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).

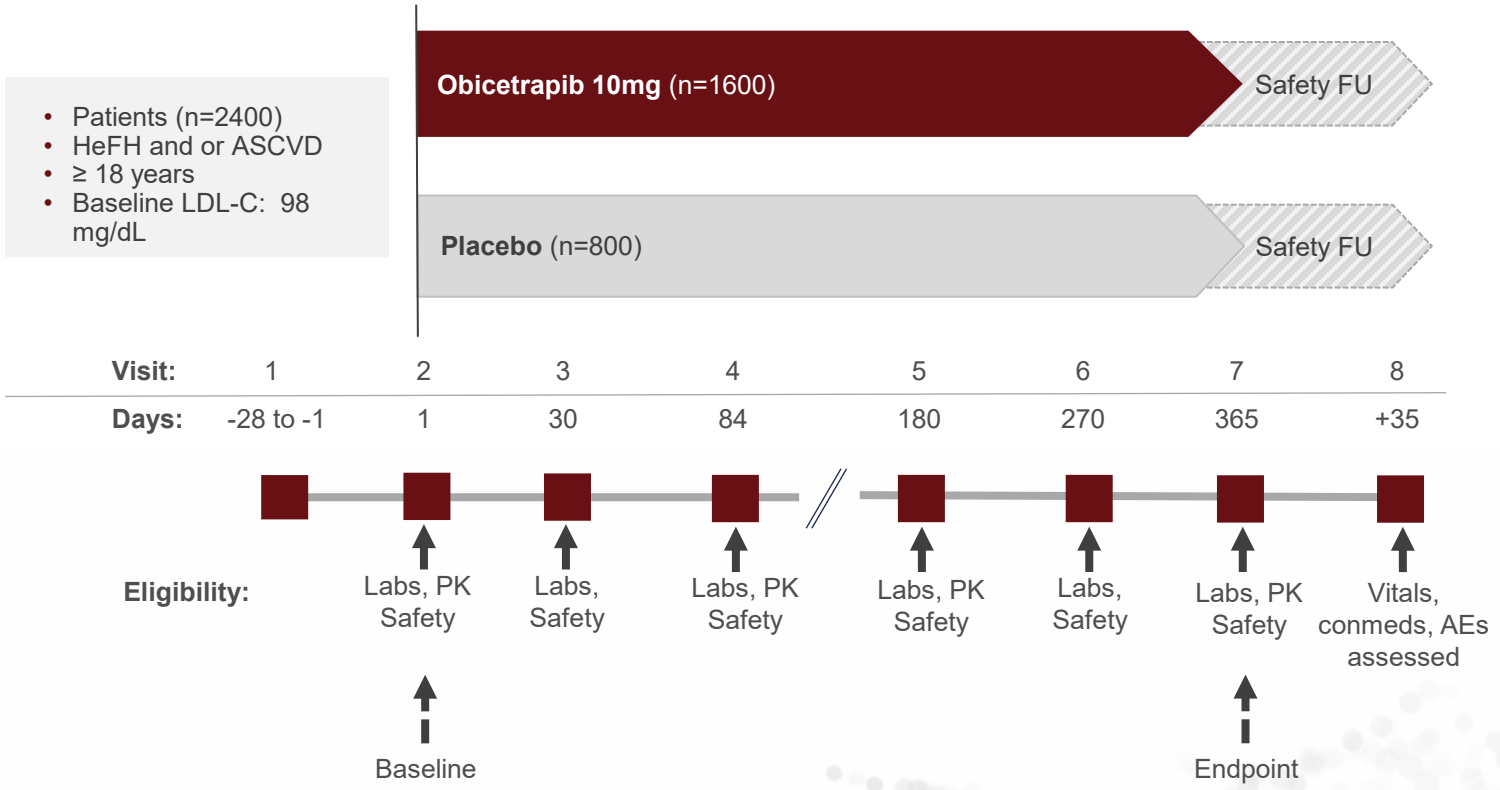
Main Exclusion Criteria:

- CV disease < 3 months
- HoFH
- Uncontrolled hypertension

Biomarker Endpoints:

- p-tau217
- Ratio of Aβ42 to Aβ40 (Aβ42/Aβ40)
- GFAP
- NFL
- p-tau181

.



Note: Davidson MH et al. 2025. Manuscript in preparation.

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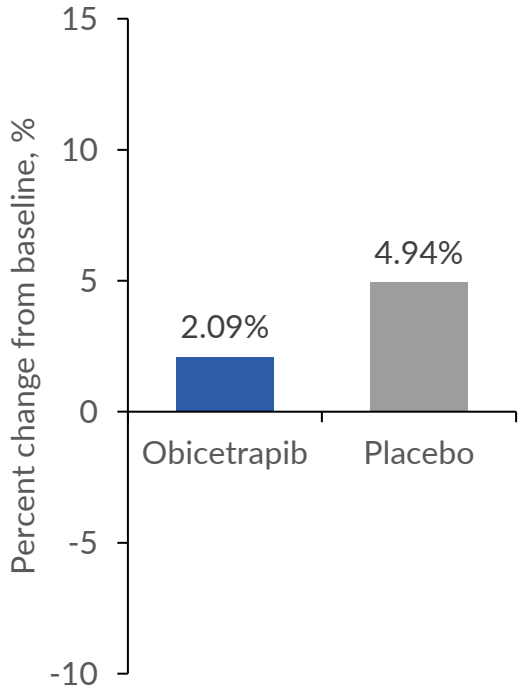
Significant Reduction in p-tau217 Progression Over 12 Months Observed with Greater Reductions as ApoE4 Risk Factors Increase

2.84% benefit between obicetrapib and placebo (*P*=0.025)

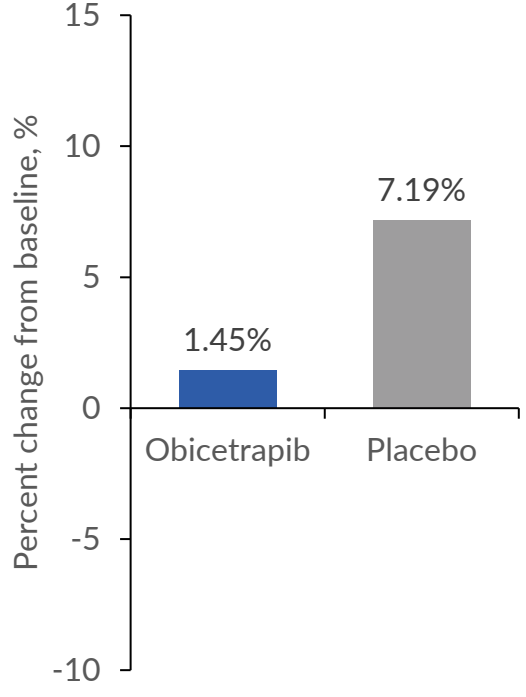
5.74% treatment benefit in *ApoE4* carriers (*P*=0.022)

20.5% treatment benefit in *ApoE4* homozygotes (*P*=0.010)

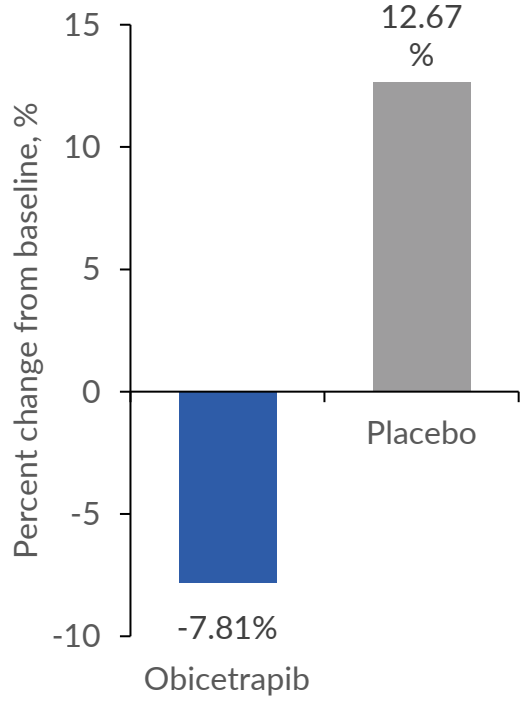
Full Analysis Set*
(n=1535)



ApoE4 Carriers*
(n=367)



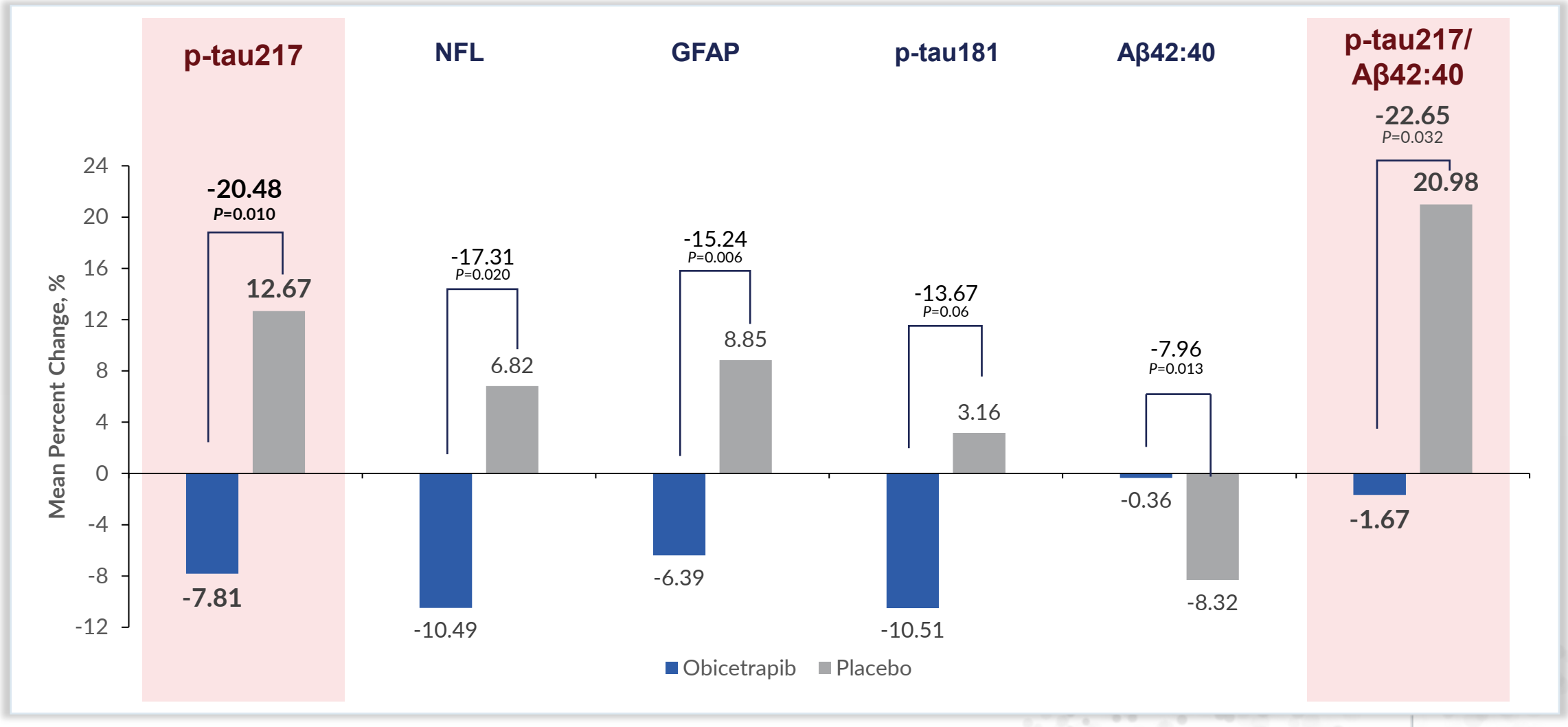
ApoE4 Homozygotes*
(n=29)



*Results reflect adjustment for mean-centered baseline p-tau217 and mean-centered age. Participants with known ApoE status (based on phenotypic analysis), baseline p-tau217 above the lower limit of quantification (LLQ), and available end-of-study p-tau217 were included in the current analyses.
ApoE, apolipoprotein E; p-tau, phosphorylated tau. ApoE4 carriers defined as ApoE3/E4 or ApoE4/E4, based on phenotypic analysis
Davidson MH et al. 2025. Journal of Prevention of Alzheimer's Disease

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Obicetrapib's Impact on Additional AD Biomarkers in E4/E4 Carriers



Aβ, amyloid beta; AD, Alzheimer's disease; GFAP, glial fibrillary acidic protein; NFL, neurofilament light chain; p-tau, phosphorylated tau.
Davidson MH et al. 2025. Journal of Prevention of Alzheimer's Disease

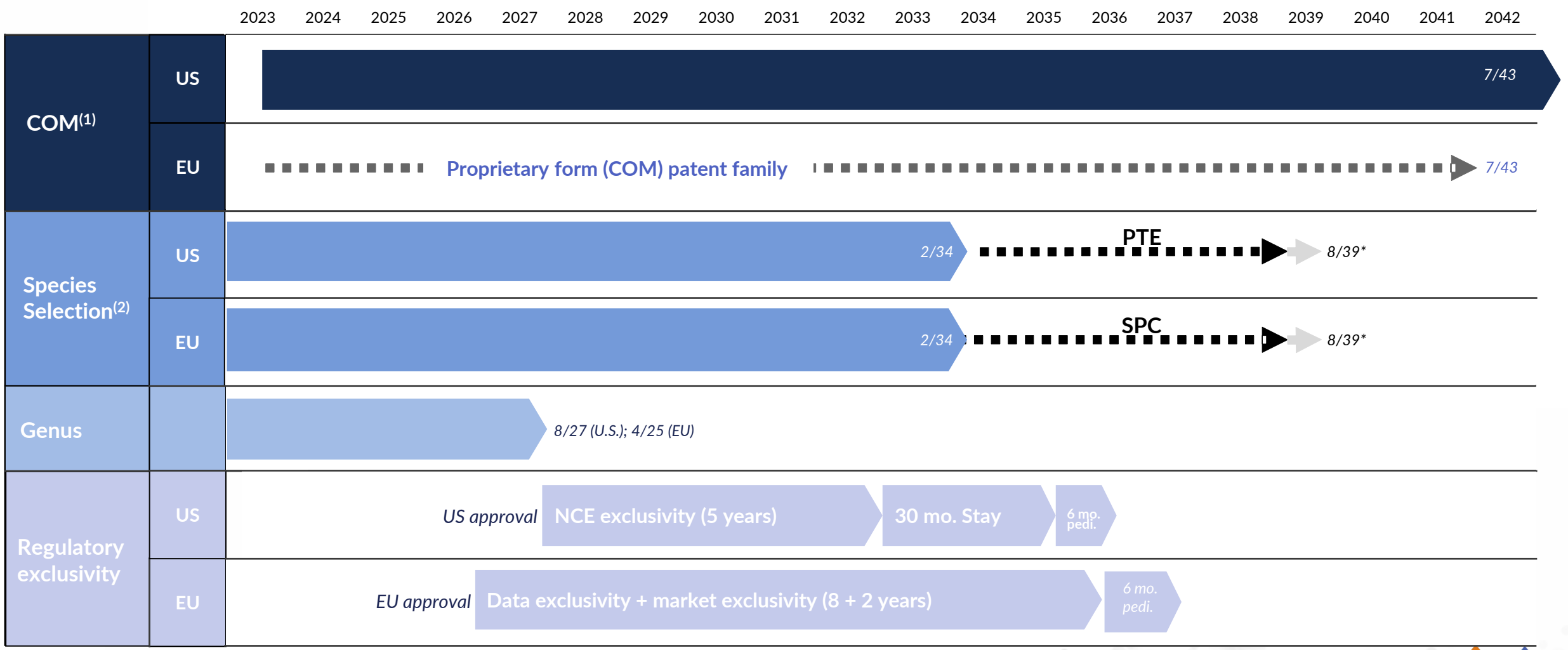
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Intellectual Property

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Comprehensive Patent Portfolio with Composition of Matter IP into 2043



Note: Regulatory approval and exclusivity dates are illustrative and shown for information purposes only; actual results may differ.
Filled colors = granted patents & dotted lines = pending patents; one patent only to be selected for SPC/PTE; an earlier US approval leads to earlier regulatory expiry & shorter PTE;
*including pediatric extension 6m; actual results may differ from expectations. (1) US 12,006,305. (2). Low dose/ species selection patents US 10,653,692, US 11,013,742, US 11,642,344; US 12,186,315 statin combo patent US 10,300,059

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Thank You

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