

June 5, 2023

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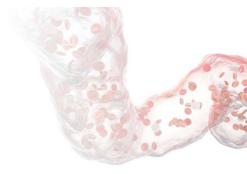
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Summary of clinical data





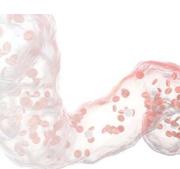


The combination of Obicetrapib and Ezetimibe observed to lower LDL-C in Patients on High Intensity Statins: Results from the ROSE2 Trial (NCT05266586).

Christie M Ballantyne, Stephen J Nicholls, Marc Ditmarsch, John J Kastelein, Douglas Kling, Danielle L Curcio, Michael H Davidson



ROSE2 trial: Obicetrapib and high intensity statin therapy



Objective To evaluate the effect of obicetrapib 10 mg in combination with ezetimibe 10 mg on top of HIS on LDL-C

Inclusion criteria

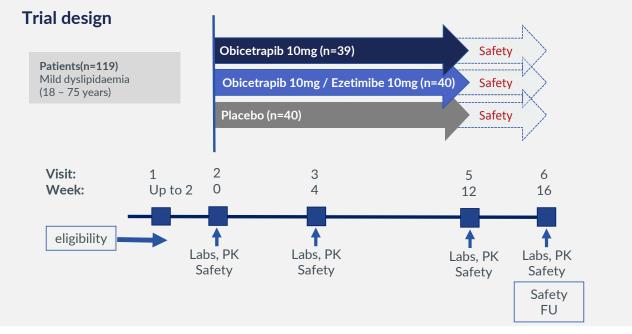
- A stable dose of High Intensity Statins (A 40 / 80; R 20 / 40) 8 weeks prior to screening
- Fasting LDL-C levels >70 mg/dL (1.8 mmol/L)

Exclusion criteria

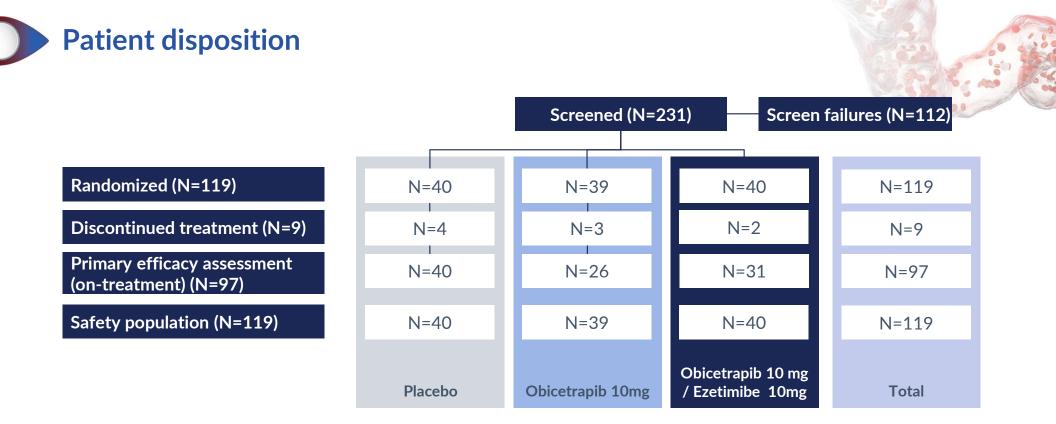
- Current significant CV disease
- HbA1c ≥10%
- Uncontrolled hypertension

Primary efficacy endpoint

• Percent change from baseline in LDL-C compared to the placebo group









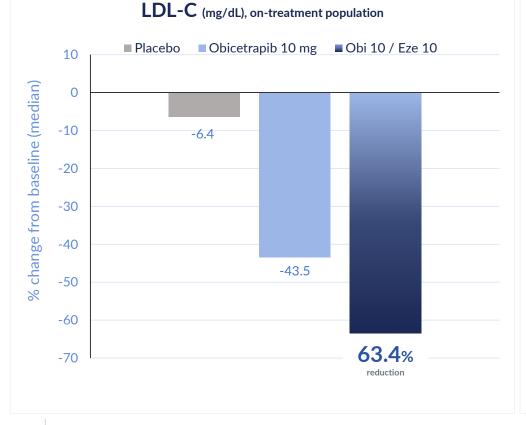


Baseline characteristics

		Placebo	Obicetrapib 10 mg	Obicetrapib 10mg /
		N=40 (%)	N=26 (%)	Ezetimibe 10 mg N=31 (%)
	Mean Age (yrs)	60.6	64.8	63.5
	Female %	35	34.6	38.7
	Mean BMI (kg/m²)	30.8	29.9	31.8
Race %	White	75	88.5	93.5
	Black / African American	22.5	11.5	6.5
Statin use (%)	Atorvastatin 40/80 mg	75	69.2	80.6
	Rosuvastatin 20/40 mg	25	30.8	19.4
Baseline level (Median)	LDL-C (mg/dL)	95.5	100	87
	HDL-C (mg/dL)	42.5	47	46



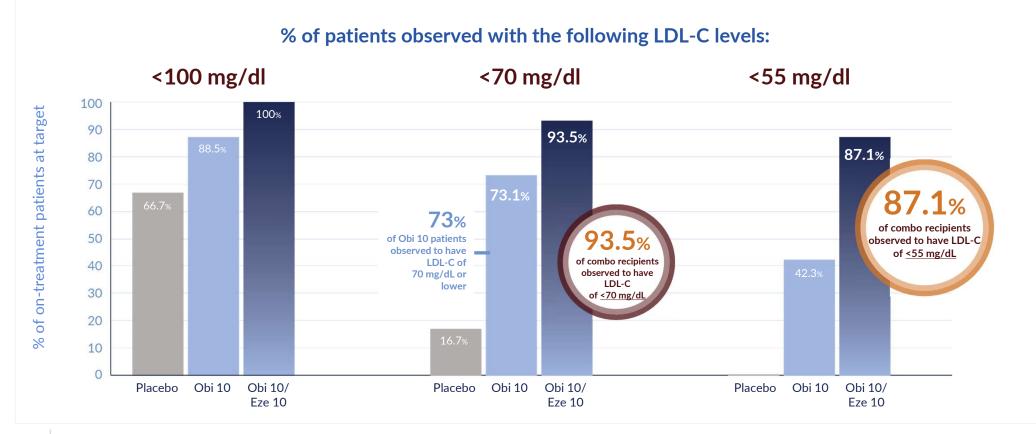
Obicetrapib/ezetimibe observed to lower LDL-C by 63.4% on top of HIS in ROSE2



Median (min, max) LDL-C levels (mg/dL) at baseline & EoT

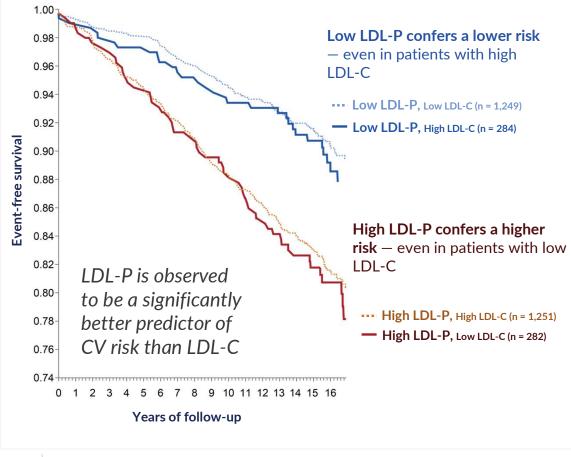
Time	Placebo	Obi 10 mg	Obi 10 / Eze 10	
	95.5	100.0	87.0	
Baseline Median	(60, 211)	(35, 189)	(62, 152)	
	(N=40)	(N=26)	(N=31)	
	88.0	55.5	39.0	
EoT Median	(55, 188)	(21, 148)	(15, 96)	
	(N=36)	(N=26)	(N=31)	
% Change	-6.4	-43.5	-63.4	
from Baseline	(-36.4, 96.7)	(-78.4, 22.6)	(-83.7, -29.7)	
(median)	(N=36)	(N=26)	(N=31)	
% Change from Baseline	-0.85	-39.20	-59.23	
LS mean (95% CI)	(-7.75, 6.05)	(-47.41, -30.99)	(-66.75, -51.71)	
P-value	-	<0.0001	<0.0001	

NewAmsterdam Source: Ballantyne CM, et al. J. of Clinical Lipidology 2023 (to be published June 3, 2023) Pharma Positive LDL goal attainment observed with ezetimibe + obicetrapib combination, including >87% of patients observed to attain <55 mg/dl LDL-C levels





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

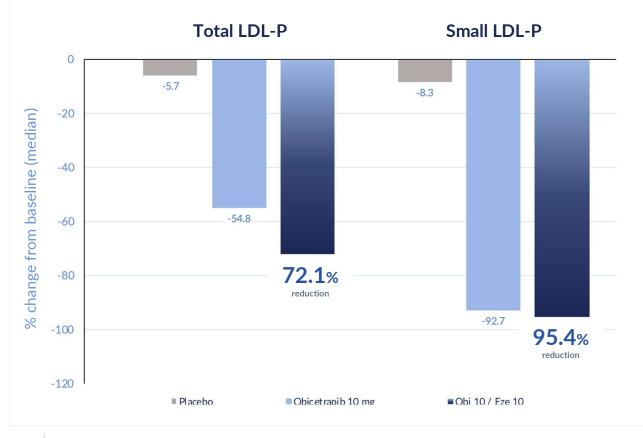


Even though all LDL particles contain only one ApoB protein, small dense LDL particles have a less massive ApoB protein = Larger-sized LDL

🗧 = Small dense LDL



ROSE2 showed significant reduction in total and small LDL particles, bringing patients who had baseline elevated LDL-P to optimal parameters⁽¹⁾



Patients taking the Obi/Eze combo observed to achieve optimal LDL-P profiles

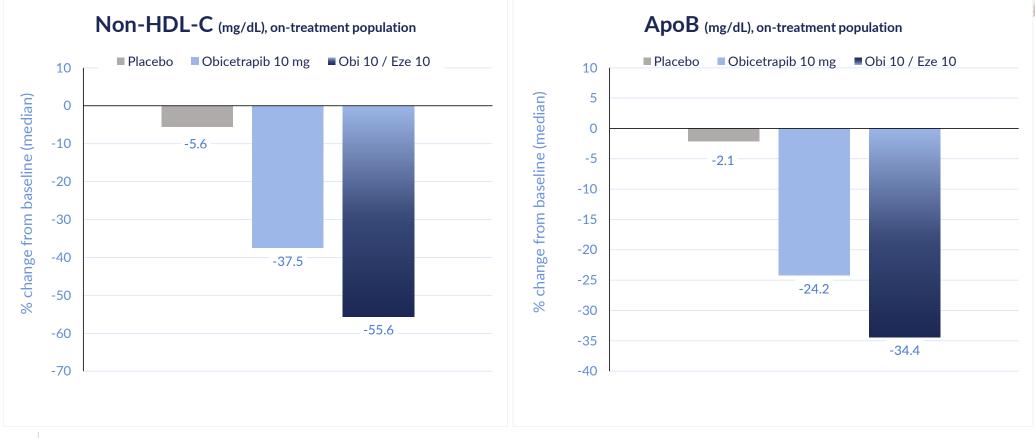
Lipoprotein fractionation 1	ROSE2 placebo	ROSE2 Obi / Obi + Eze
LDL-P (nmol/L)	1012.8	495 / 300
Small LDL-P (nmol/L)	717.5	73.4 / 47.5
LDL size (nm)	20.26	21.0 / 21.0

Key ⁽²⁾		High	Moderate	Optimal
	LDL-P (nmol/L)	>1816	935-1816	<935
	Small LDL- P (nmol/L)	>820	467-820	<467
	LDL size (nm)	≤20.5	N/A	>20.5

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Sources: 1. Ballantyne CM, et al. J. of Clinical Lipidology 2023 (to be published June 3, 2023), 2. LipoFraction NMR practitioner Guidelines

ROSE2: Non-HDL-C and ApoB percent change from baseline (Day 84)



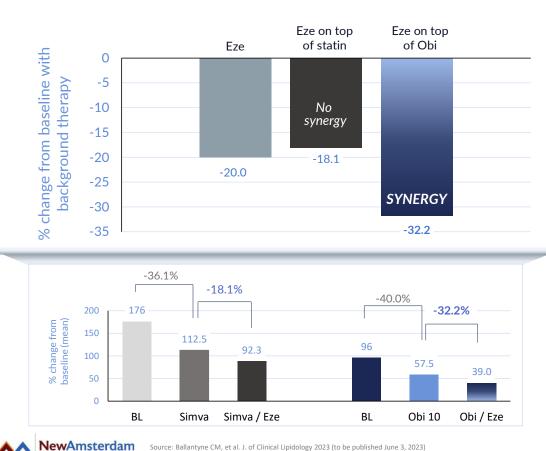
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ROSE2 Safety: TEAEs, TESAEs, and withdrawal overview (safety population)

	Placebo N= 40, N (%)	Obicetrapib 10 mg N= 39, N (%)	Obi 10 mg / Eze 10 mg N= 40, N (%)
TEAEs (%)			
TEAEs	16 (40)	8 (20.5)	11 (27.5)
Related TEAEs	2 (5.0)	4 (10.3)	5 (12.5)
Severe TEAEs	2 (5.0)	1 (2.6)(1)	O (O)
TESAEs			
TESAEs, total	1 (2.5)	1 (2.6) (1)	O (O)
Deaths	0	0	0
Withdrawal's study / medication			
TEAEs leading to discontinuation of study drug	2 (5.0)	2 (5.1) (1)	1 (2.5) (1)



Source: Ballantyne CM, et al. J. of Clinical Lipidology 2023 (to be published June 3, 2023) (1) The severe TEAE and the TESAEs experienced in the 10 mg group was a cardiac disorder. TEAEs leading to discontinuation of the study drug included abdominal pain, tachycardia and nervous system disorders. Stronger LDL-lowering observed with ezetimibe in obicetrapib combo vs. ezetimibe with statins, potentially due to a synergistic mechanism of action for obi/eze combo⁽¹⁾



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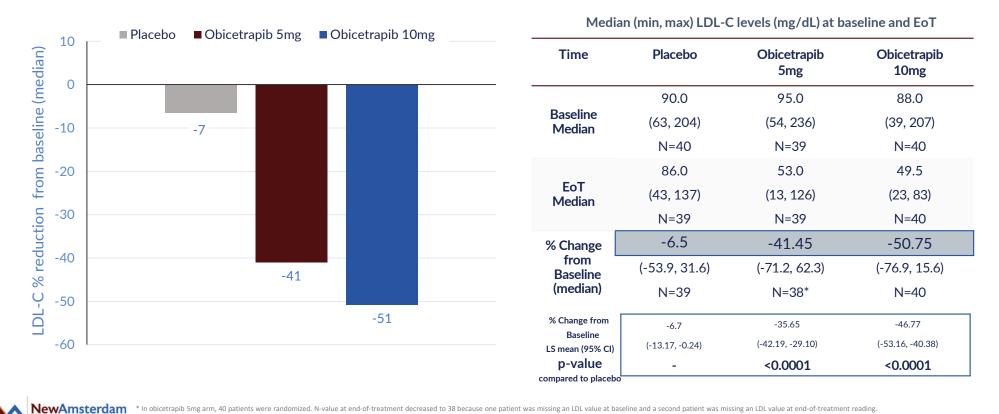
Obicetrapib is designed to promote more cholesterol excretion into the intestines (via TICE) while ezetimibe is designed to block cholesterol reabsorption into the body, synergistically enhancing fecal sterol removal of cholesterol **CETPi** Intestine LDL levels further drop CE excretion into intestines via TICE D **EZETIMIBE** NPC1L1 Stops CE reabsorption from intestines; LDL **Fecal sterol** levels further drop removal

Source: Ballantyne CM, et al. J. of Clinical Lipidology 2023 (to be published June 3, 2023) Note: The calculations included in the graphs here represent the Company's hypothetical calculation assuming one patient was treated with each drug independently.

In ROSE Phase 2b clinical trial, obicetrapib demonstrated robust LDL-C lowering as adjunct to high intensity statins¹

Preparative ultra-centrifugation (PUC) is "gold-standard" for LDL-C quantification

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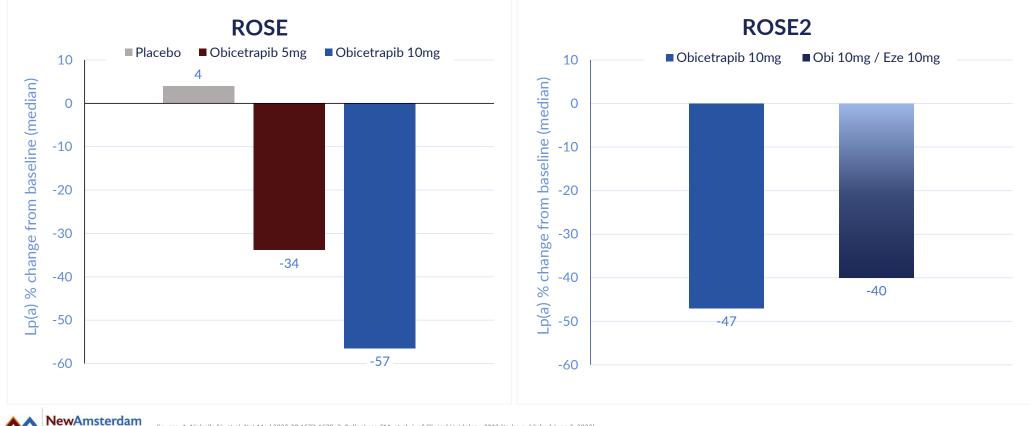


* In obicetrapib 5mg arm, 40 patients were randomized. N-value at end-of-treatment decreased to 38 because one patient was missing an LDL value at baseline and a second patient was missing an LDL value at end-of-treatment reading. Source: 1. Nicholls SJ. et al. Nat Med 2022:28:1672-1678.

15

Lp(a) percent reduction from baseline in ROSE¹ and ROSE²

• Lp(a) is emerging as a strong and independent marker of CVD risk and an exciting new CVD drug target



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Changes in lipid biomarkers for obicetrapib 10mg monotherapy across phase 1/2 studies



■LCL-C ■ApoB ■Non HDL-C



100

001

Obicetrapib safety profile in ROSE and across multiple studies: overview of AEs, SAEs and withdrawals

Well tolerated safety profile; Similar rates of drug discontinuation were observed for obicetrapib and placebo

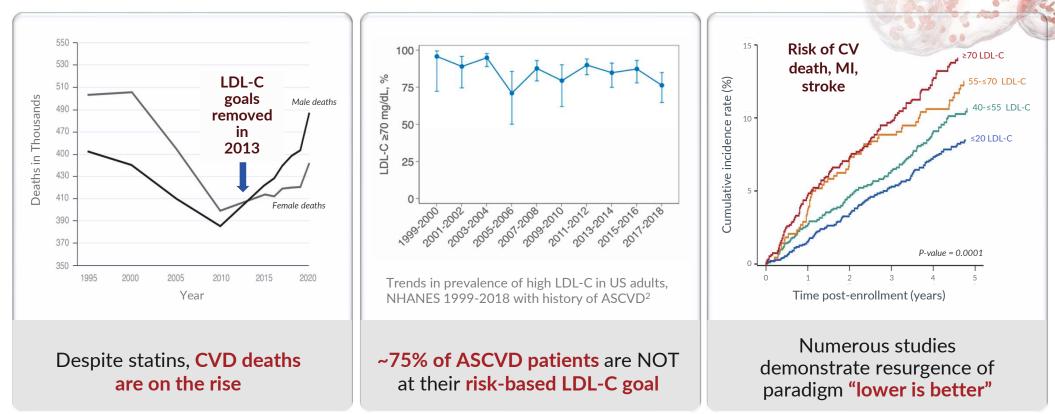
ROSE Safety	Placebo (N=40)	Obicetrapib, 5mg (N=40)	Obicetrapib, 10mg (N=40)	Pooled Safety	Comparator ⁽¹⁾ (N=231)	Obicetrapib Pooled 5mg + 10mg ⁽²⁾ (N=309)
TEAEs (%)				TEAEs (%)		
TEAEs, total	19 (47.5)	15 (37.5)	8 (20.0)	TEAEs, total	136 (58.9)	173 (55.9)
TEAEs, related	4 (10.0)	2 (5.0)	1 (2.5)	TEAEs, related	45 (19.5)	49 (15.8)
TEAEs, severe	1 (2.5)	0	0	TEAEs, severe	5 (2.2)	7 (2.3)
TESAEs				TESAEs		
TESAEs, total	2 (5.0)	0	0	*TESAEs, total	6 (2.6)	4 (1.3)
TESAEs, related	0	0	0	TESAEs, related	0	0
Deaths	0	0	0	Deaths	0	0
Withdrawals study / medicatio	on			Withdrawals study / medicat	ion	
TEAEs leading to discontinuation of study drug	1 (2.5)	0	0	TEAEs leading to discontinuation of study drug	13 (5.6)	13 (4.2)

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* There were three additional TESAEs in other obicetrapib dose arms: two in the TULIP 2.5mg arm, and one in the Lp(a) 2.5mg arm; none were considered to be related to study drug (1) The Comparator group included patients receiving placebo and non-obicetrapib monotherapy.

(2) The pooled obicetrapib group includes patients treated with obicetrapib as a monotherapy and in combination with atorvastatin, rosuvastatin and ezetimibe.

Despite availability of statins, tremendous unmet need remains – with resurgance of the "lower-is better" paradigm



Sources: Trinity NewAmsterdam Market Research Summary; Trinity quantitative market research with N = 100 PCPs and Cardiologists; Bloomberg Prescription Data; IQVIA Px Tracker. (1) Literature review suggesting hypercholesterolemia prevalence of "94mm in the US (average of He et al. 2020, Mercado et al. 2015, Muntner et al. 2013) and "137mm in EUS (average of Gomez-Huelgas et al. 2010, Guallar-Castillon et al. 2012, Tragni et al. 2012, Grau et al. 2011; (3) Rum statin-intolerant & 22mm above LDL-C target: Percentage of patients in each category estimated from Trinity quantitative market research and the – percentages were then applied to the estimated 84mm treated number above. (4) <1mm branded patients: 2020 US prescription data for Repatha, Praluent, and Nexletol/Nexlizet were pulled from the Bloomberg Prescription Data Portal that Trinity subscribes to; assuming 12 scripts/year and 70% compliance for PCSK9s (based on PCSK9 literature) and 59% compliance for Nex/Nex (based on statin literature) patient volume estimates were derived from the prescription data and extrapolated to the EUS. (5) Gaba P, et. al., Association Between Achieved Low-Density Lipoprotein Cholesterol Levels and Long-Term Cardiovascular and Safety Outcomes: An Analysis of FOURIRE-NOLE. Circulation. 2023 Feb 13. doi: 10.1161/CIRCULATIONAHA.122.063399.

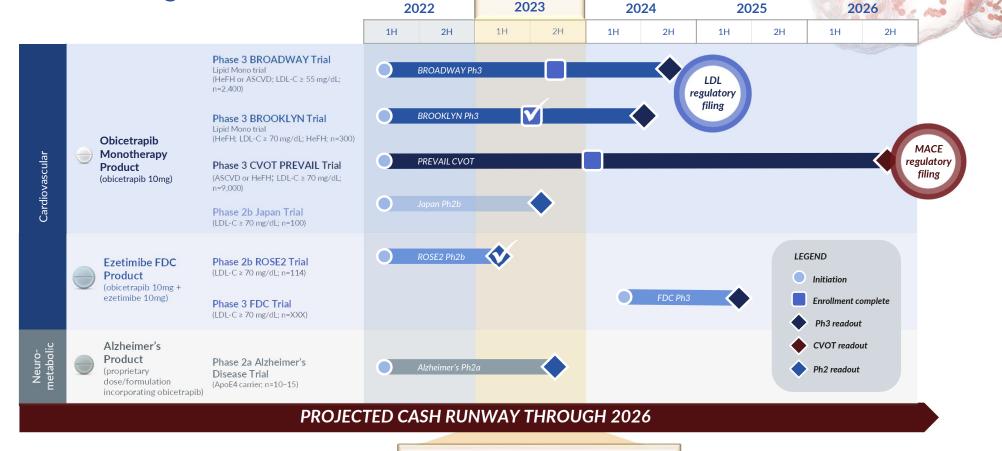


19



Clinical development

Current cash expected to fund obicetrapib development through several value-creating milestones



Numerous catalysts expected throughout 2023

Note: Other than as noted, the pipeline represents trials that are currently ongoing. Projections are subject to inherent limitations. Actual results may differ from expectations. The timing of regulatory submissions is subject to additional discussions with regulators.

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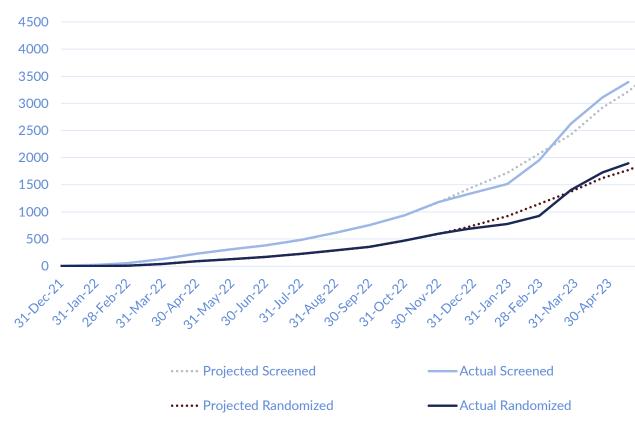


Clinical Trial Progress Update

BROADWAY enrollment on schedule to finish mid-2023

5000

- ASCVD or HeFH with • LDL \geq 55 mg/dL; n=2400
- Randomization 2:1; • obicetrapib 10 mg:placebo
- Primary endpoint: LDL-C •
- Baseline LDL-C = 102• mg/dL; Woman: 35%; Average age: 65 years



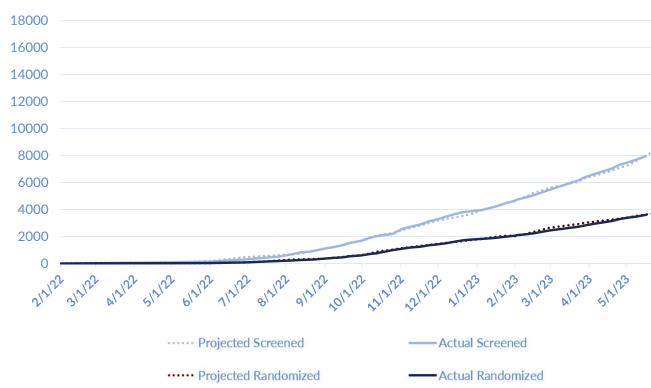


PREVAIL enrollment currently on schedule to complete 1Q 2024

ASCVD with LDL \geq 70 • 18000 mg/dL; n=9000 16000 14000 Randomization: 1:1; Obi • 10 mg vs placebo 12000

20000

- Primary endpoint: • MACE-4
- Baseline LDL: 110 mg/dL; • Women: 31%; Average age: 65 years





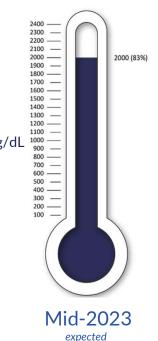
Update on phase 3 trial enrollment

BROOKLYN



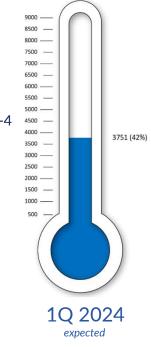
BROADWAY ASCVD or HeFH with LDL \geq 55 mg/dL N=2400

2100 2000 1900 1800 1700 Randomization: 2:1 1600 1500 Obi 10 mg vs placebo 1400 1300 Primary Endpoint: LDL-C 1200 -1100 Baseline mean LDL: 102 mg/dL 1000 900 Women: 35% 800 -700 Average Age: 65 years 600 -500 400 -300 200 -100



PREVAIL ASCVD with LDL ≥ 70 mg/dL N=9000

Randomization: 1:1 Obi 10 mg vs placebo Primary Endpoint: MACE-4 Baseline mean LDL: 110 mg/dL Women: 31% Average Age: 65 years



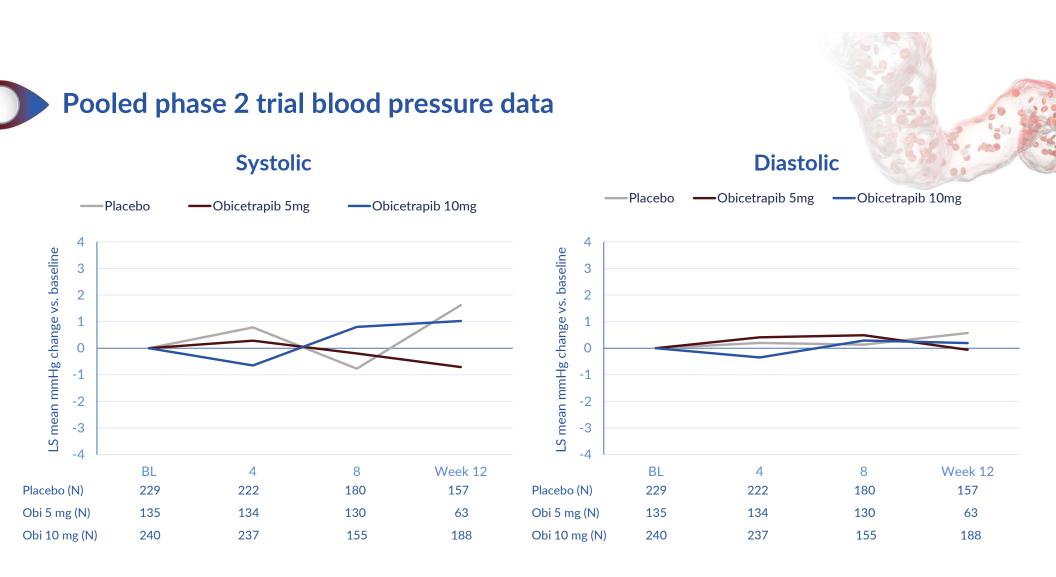
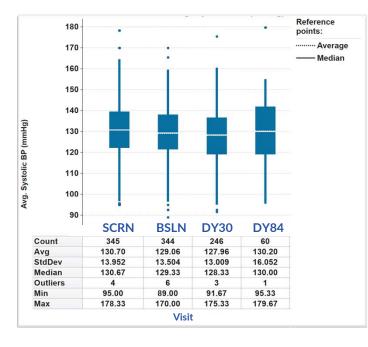




Table 2.3 Pooled Analysis TULIP, OCEAN & ROSE

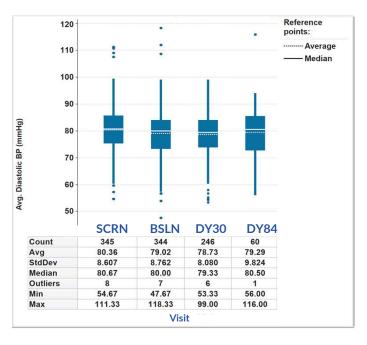
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BROOKLYN: Aggregate blinded average blood pressure is stable over time



Average Systolic BP (mmHg) by Visit

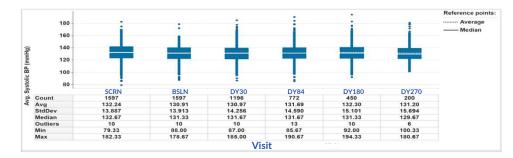
Average Diastolic BP (mmHg) by Visit





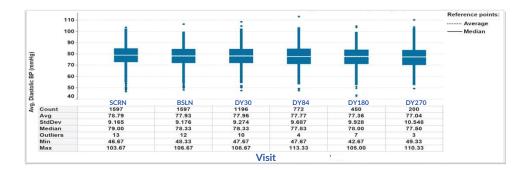
BROOKLYN Medical Monitoring Meeting 10 May 2023; Data cut-off 25 April 2023





Average Systolic BP (mmHg) by Visit

Average Diastolic BP (mmHg) by Visit



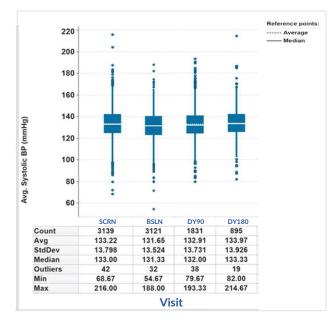


BROADWAY Medical Monitoring Meeting 10 May 2023; Data cut-off 25 April 2023

28

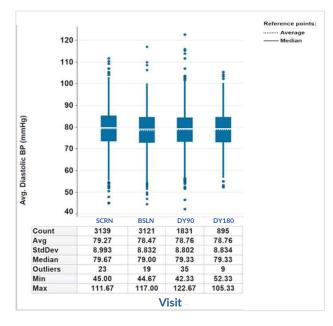
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Average Systolic BP (mmHg) by Visit

Average Diastolic BP (mmHg) by Visit





PREVAIL Medical Monitoring Meeting 10 May 2023; Data cut-off 25 April 2023

We have selected a Fixed Dose Combination (FDC) of Obicetrapib + Ezetimibe

- We recently completed a bioavailability study comparing two FDC formulations of obicetrapib + ezetimibe to the component products
- An FDC formulation was selected based on comparable bioavailability and is planned to be advanced into a Phase 3 safety & efficacy trial
- An End-of-Phase 2 meeting has been granted by FDA and scheduled for June 2023 to review the design of our Phase 3 study
- The Phase 3 trial is expected to begin in 1Q 2024
- We currently expect to submit an NDA for the FDC on or around the same time as the obicetrapib monotherapy

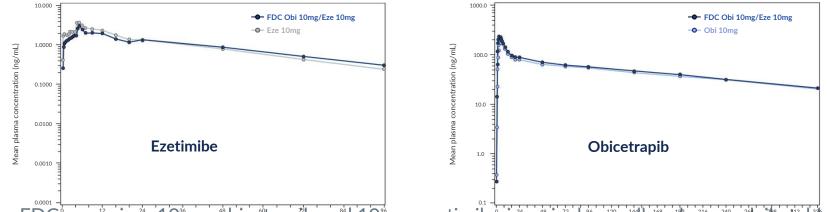
Fixed-Dose Combo Tablet



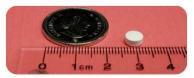


Fixed dose combination Obi + Eze: Development update

• FDC formulation observed to have comparable pharmacokinetic (PK) profiles to individual products



- The FDC comprises 10 mg object rapib and 10 mg ezetimibe in a single, small or at, once daily tablet, with CoGs comparable to object rapib 10 mg tablet
- FDC Phase 3 trial is planned to start in Q1 2024
- The planned manufacturing site for FDC was selected and technology transfer is ongoing for anticipated NDA readiness and commercial supply





Proposed fixed dose combination phase 3 trial design



Inclusion criteria Trial design • LDL-C \geq 70 mg/dL • ASCVD, ASCVD risk equiv, or HeFH Obi 10mg (n=100) Randomized (1:1:1:1), • • 18-75 years double-blind, placebo-Obi/Ezi 10mg (n=100) controlled **Primary endpoint** • Patients(n=400) Placebo (n=100) Percent change from baseline in LDL-C compared to placebo 3 2 Visit: 1 4 5 4 Up to 2 0 12 Week: 16 Eligibility ╋ Labs. PK Labs. Labs. Labs, **Primary efficacy endpoint** РΚ PΚ Safety PΚ Safety Safety • Percent change from baseline in LDL-C for Safety the combination therapy group compared to Safety the placebo group FU



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Summary of key messages

- ROSE2: 63% median LDL-C reduction observed in patients on high intensity statins with obicetrapib 10mg in combination with ezetimibe
- Japan Phase 2: 46% median LDL-C reduction observed with obicetrapib 10mg; largely consistent with observed results from obicetrapib 10mg across six clinical trials (Range 43-51%) and potentially enabling PMDA regulatory path for approval aligned with the rest of the world
- Well tolerated in Phase 2 trials and Phase 3 blinded safety, including frequent blood pressure assessments, is encouraging
- Robust reductions in Lp(a) and small LDL particles as well as documented diabetes benefits in the CETP inhibitor class are encouraging
- FDC formulation selected with Phase 3 initiation anticipated in Q1 24
- Enrollment in Phase 3 trials is progressing on-track with completion of the two pivotal LDL trials expected in H2 24 and CVOT expected in H2 26

