BROOKLYN Topline Results

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HeFH Overview

- Heterozygous familial hypercholesterolemia ("HeFH"), a genetic disorder that affects 1 in 250 persons, or approximately 30 million people worldwide, is characterized by elevated levels of low-density lipoprotein cholesterol ("LDL-C") from birth.
- Without treatment, the condition is associated with premature complications and death from accelerated development of atherosclerotic cardiovascular disease.





BROOKLYN Study Design and Baseline Characteristics

Obicetrapib on Top of Maximum Tolerated Lipid-Modifying Therapies: A Placebo-Controlled, Double-Blind, Randomized, Phase 3 Study to Evaluate the Effect of 10 mg Obicetrapib in Participants with a History of HeFH and LDL-C ≥70 mg/dL who are Not Adequately Controlled by Their Lipid-Modifying Therapies



- HeFH
- LDL-C ≥70 mg/dL
- Maximally tolerated lipid lowering therapy

Key Exclusion Criteria

- HoFH
- Uncontrolled hypertension

Endpoints

- Primary: LDL-C at day 84
- Secondary: ApoB, Lp(a), non-HDL-C, HDL-C
- Safety: AE's, vitals, laboratory

Baseline Lipids (obicetrapib 10mg mean)



Demographics

- 53% Female
- 57 years of age
- BMI: 29 kg/m²

Regions

- N. America
- S. Africa
- Europe

Baseline Lipid Modifying Therapy

- Any statin 89%
- High intensity statin: 79%
- Ezetimibe: 54%
- PCSK9i 14%
- Other 8%



Disposition of All Randomized Participants

	Placebo	Obicetrapib 10 mg	Total
Randomized	118	236	354
Completed treatment	101 (85.6)	218 (92.4)	319 (90.1)
Discontinued treatment	17 (14.4)	18 (7.6)	35 (9.9)
Discontinued due to AE's	7 (5.9)	8 (3.4)	15 (4.2)
Subject decision	4 (3.4)	4 (1.7)	8 (2.3)
Withdraw of consent	3 (2.5)	3 (1.3)	6 (1.7)
Death	2 (1.7)	2 (0.8)	4 (1.1)
Lost to follow-up	1 (0.8)	1 (0.4)	2 (0.6)
Completed the study	110 (93.2)	226 (95.8)	336 (94.9)
Discontinued study early	8 (6.8)	10 (4.2)	18 (5.1)
Adverse event	0 (0.0)	1 (0.4)	1 (0.3)



Additional Baseline Details of All Randomized Patients

	Placebo N=118	Obicetrapib 10 mg N=236	Total N=354
Mean Age (years)	56.6	57.0	56.9
Sex (F) n (%)	65 (55.1)	125 (53.0)	190 (53.7)
Region n (%)			
EMEA	83 (70.3)	182 (77.1)	265 (74.9)
North America	35 (29.7)	54 (22.9)	89 (25.1)
Race n (%)			
White	110 (93.2)	219 (92.8)	329 (92.9)
African American	3 (2.5)	3 (1.3)	6 (1.7)
Height (mean)	169.4	169.9	169.8
Weight (mean)	85.2	85.2	85.2
BMI (mean)	29.6	29.3	29.4
HeFH			
Genotyping + or DLCN >8 points or SB definite	84 (71.2)	172 (72.9)	256 (72.3)
SB possible FH diagnosis	33 (28.0)	61 (25.8)	94 (26.6)

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Additional Baseline Details of All Randomized Patients

	Placebo N=118	Obicetrapib 10 mg N=236	Total N=354
Diabetes n (%)			
Yes	26 (22.0)	47 (19.9)	73 (20.6)
No	92 (78.0)	189 (80.1)	281 (79.4)
Statin treatment			
High Dose	80 (67.8)	186 (78.8)	266 (75.1)
Low or Moderate Dose	19 (16.1)	23 (9.7)	42 (11.9)
None	19 (16.1)	27 (11.4)	46 (13.0)
Ezetimibe use			
Yes	59 (50.0)	127 (53.8)	186 (52.5)
No	59 (50.0)	109 (46.2)	168 (47.5)



Statistically Significant LDL-C Reduction Observed at Primary Endpoint of Day 84 and Maintained Through Day 365

LS Mean % change vs. placebo

LDL-C reduction over time (ITT population)







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





LDL-C Responder Analysis in Obicetrapib 10mg arm





Results Consistent with Data Reported from the Company's Prior Clinical Trials





Overview of Treatment-Emergent Adverse Events – Safety Population

	Placebo N=118 n (%)	Obicetrapib 10 mg N=234 n (%)	Total N=352 n (%)
Any treatment-emergent AEs (TEAEs)	83 (70.3)	149 (63.7)	232 (65.9)
Any TEAEs by maximum severity			
Mild	47 (39.8)	84 (35.9)	131 (37.2)
Moderate	28 (23.7)	57 (24.4)	85 (24.1)
Severe	8 (6.8)	8 (3.4)	16 (4.5)
Any study drug related TEAEs	8 (6.8)	10 (4.3)	18 (5.1)
Any study drug-related TEAEs by maximum severity			
Mild	5 (4.2)	5 (2.1)	10 (2.8)
Moderate	3(2.5)	5 (2.1)	8 (2.3)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
Any TEAEs leading to discontinuation of study drug	8 (6.8)	10 (4.3)	18 (5.1)
Any treatment-emergent serious AEs (TESAEs)	8 (6.8)	13 (5.6)	21 (6.0)
Any treatment-emergent non-serious AEs	82 (69.5)	145 (62.0)	227 (64.5)
Any study drug-related TESAEs	0 (0.0)	0 (0.0)	0 (0.0)
Any TEAEs leading to death	2 (1.7)	3 (1.3)	5 (1.4)



Overview of Treatment-Emergent Adverse Events >5% in Either Population

	Placebo N=118 n (%)	Obicetrapib 10 mg N=234 n (%)	Total N=352 n (%)
Any non-serious treatment-emergent AEs	52 (44.1)	95 (40.6)	147 (41.8)
Influenza	7 (5.9)	21 (9.0)	28 (8.0)
Covid-19	8 (6.8)	15 (6.4)	23 (6.5)
Hypertension	8 (6.8)	14 (6.0)	22 (6.3)
Nasopharyngitis	5 (4.2)	15 (6.4)	20 (5.7)
Diarrhea	8 (6.8)	9 (3.8)	17 (4.8)
Upper respiratory tract infection	4 (3.4)	12 (5.1)	16 (4.5)
Back pain	6 (5.1)	7 (3.0)	13 (3.7)
Headache	6 (5.1)	7 (3.0)	13 (3.7)
Fatigue	7 (5.9)	2 (0.9)	9 (2.6)



Overview of Adverse Events of Special Interest

	Placebo N=118 n (%)	Obicetrapib N=234 n (%)
AST or ALT > 3 x ULN	O (O)	O (O)
Bilirubin > 2 x ULN	2 (1.7)	O (O)
CK > 5 x ULN	4 (3.4)	3 (1.3)
NODM or worsening of glycemic control	26 (22.0)	48 (20.5)
eGFR < 30 mL/min/1.73m2 or a 25% decrease in eGFR from baseline	10 (8.5)	10 (4.3)
Increase of Serum Creatinine \geq 0.3 mg/dL from baseline	9 (7.6)	5 (2.1)
Macular degeneration	O (O)	O (O)



Conclusions

- Primary endpoint met with LS mean reduction in LDL-C at day 84 versus placebo of 36.3% (p<0.0001). LDL-C reduction sustained at day 365 of 41.5% (p<0.0001)
- 77% of patients receiving obicetrapib achieved LDL-C below 100 mg/dl, with 51% below 70 mg/dl, and 24% below 50 mg/dl
- 34% of patients in the treatment arm achieved a greater than 50% reduction from baseline in LDL-C at day 84
- Reduction in LDL-C seen regardless of background therapy or number of therapies
- Observed to be generally well-tolerated with safety results comparable to placebo, with no increase in blood pressure or any difference from placebo in liver enzymes, hs-CRP, or renal function
- Consistent results for non-HDL-C, ApoB, and Lp(a) compared to data observed in Phase 2 studies that will be presented at an upcoming scientific conference



Study Design and Baseline Characteristics of Ongoing Phase 3 Trials

BROADWAY 1º endpoint – day 84 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 ma/dL Maximally tolerated lipid lowering therapy **Baseline Lipids (mean)** 142 150 125 98 92 100 mg/dL 50 50 0 LDL-C Non-HDL-C ApoB HDL-C ΤG **Baseline Lipid Modifying Therapy** Any statin 91% • PCSK9i 4% • High intensity statin: 65% • Other 11%

• Ezetimibe: 26%



Baseline Lipid Modifying Therapy

- Any statin >90%
- High intensity statin: 70%
- Ezetimibe: 23%



Multiple Potential Pivotal Data Readouts in Next 12 Months



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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BROOKLYN LDL-C Reduction Applied to PREVAIL Baseline Data Continues to Suggest Hypothetical 20%+ MACE Benefit



Note: Actual results may differ from hypothetical calculation. Source: Cholesterol Treatment Trialists Collaboration. Lancet. 2010 376:1670-81 Circulation. 2021;144:e564–e593 17065: Obicetrapib Lowers LDL-C in Patients Taking High Intensity Statins.

18 (1) Represents estimated average baseline LDL to be enrolled, not entry criteria. ** MACE includes cardiovascular death, myocardial infarction, stroke and non-elective coronary revascularization in adults

