

Study 2 (1002-047)

Pivotal Phase 3 Study Top-Line Results

October 29, 2018

#### Safe Harbor

#### **Forward-Looking Statements**

These slides and the accompanying oral presentation contain forward-looking statements and information. The use of words such as "may," "might," "will," "should," "expect," "plan," "anticipate," "believe," "estimate," "project," "intend," "future," "potential," or "continue," and other similar expressions are intended to identify forward looking statements. For example, all statements we make regarding the regulatory approval pathway for the bempedoic acid / ezetimibe combination pill and bempedoic acid and the therapeutic potential of, clinical development plan for, the bempedoic acid / ezetimibe combination pill and bempedoic acid, including Esperion's timing, designs, plans and announcement of results regarding its global pivotal Phase 3 clinical development program for bempedoic acid and the bempedoic acid / ezetimibe combination pill, Esperion's timing and plans for submission of NDAs to the FDA and MAAs to the EMA and Esperion's expectations for the market for therapies to lower LDL-C, including the market adoption of bempedoic acid and the bempedoic acid / ezetimibe combination pill, if approved, are forward looking. All forward-looking statements are based on estimates and assumptions by our management that, although we believe to be reasonable, are inherently uncertain. All forward-looking statements are subject to risks and uncertainties that may cause actual results to differ materially from those that we expected. These statements are also subject to a number of material risks and uncertainties, including but not limited to, delays or failures in Esperion's studies, that positive results from a clinical study of bempedoic acid may not be sufficient for FDA or EMA approval or necessarily be predictive of the results of future or ongoing clinical studies, that notwithstanding the completion of Esperion's Phase 3 clinical development program for LDL-C lowering, the FDA or EMA may require additional development in connection with seeking regulatory approval, that existing cash resources may be used more quickly than anticipated, and the risks detailed in Esperion's filings with the Securities and Exchange Commission. Any forward-looking statement speaks only as of the date on which it was made. Esperion disclaims any obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events or otherwise, except as required by law.



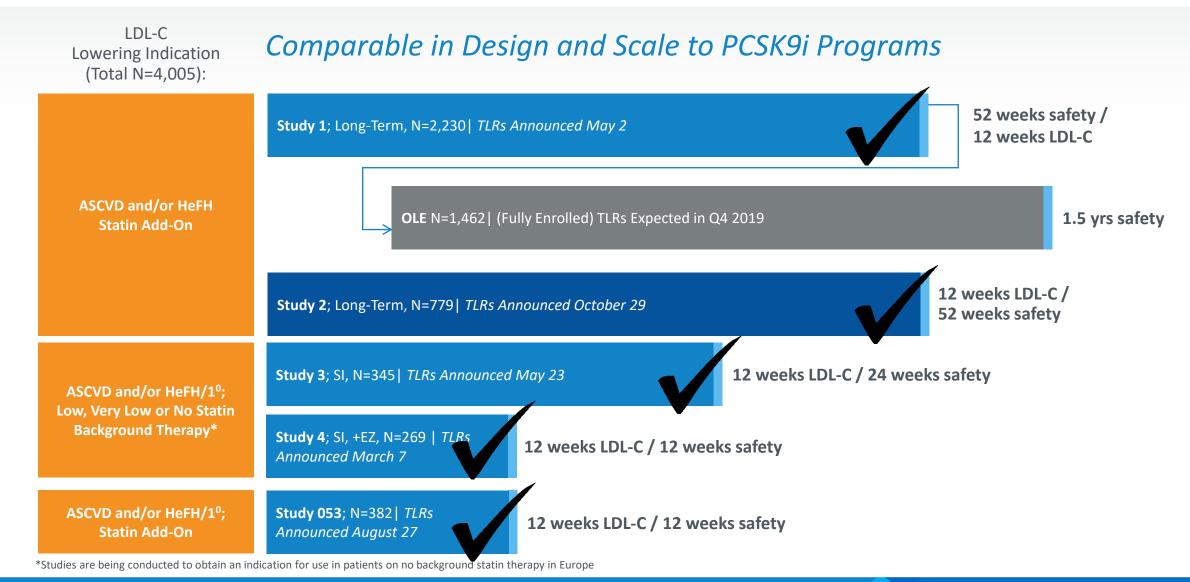


## **Bempedoic Acid Franchise**

**Development Program Updates** 

#### Bempedoic Acid / Ezetimibe Combo Pill and Bempedoic Acid Development Program

Pivotal Phase 3 Development Program Completed October 2018



Esperion
The Lipid Management Company

#### Bempedoic Acid / Ezetimibe Combo Pill and Bempedoic Acid Development Program

Clinical Development and Regulatory Strategy

#### **Global Clinical Development Programs to Support Target Label(s)**

Bempedoic Acid / Ezetimibe Combo Pill LDL-C Lowering NDA Submission (Q1 2019)

Bempedoic Acid LDL-C Lowering NDA Submission (Q1 2019)

#### LDL-C Lowering Program →

Adjunct to diet and maximally tolerated statin therapy for the treatment of adults with ASCVD and/or HeFH who require additional lowering of LDL-C

CV RR Submission (2022)

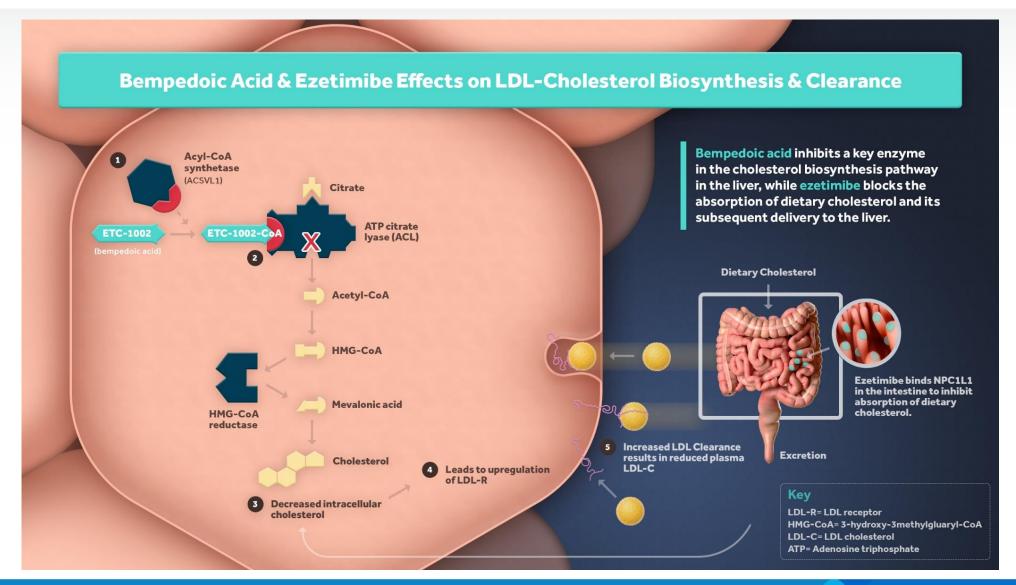
#### **CLEAR Outcomes CVOT** →

CV Risk Reduction Label in U.S. and Europe (Note: breadth of LDL-C lowering label and CV RR label will broaden similar to post-CVOT PCSK9i CV RR label 2017)



### Bempedoic Acid / Ezetimibe Combo Pill and Bempedoic Acid

Complementary Mechanisms of Action (MOAs)



### Bempedoic Acid – Study 2 Summary

Bempedoic Acid - An Important New Oral Treatment Option

In this Phase 3 study, treatment with bempedoic acid in high CV risk patients taking maximally tolerated statins provided (at 12 weeks):

- 18% LDL-C lowering
- 19% hsCRP reduction
- 0.21% HbA1c reduction in patients with diabetes

Adjudicated MACE events in bempedoic acid and placebo:

- 3-component MACE: 2.7% for bempedoic acid compared to 4.7% for placebo
- 4-component MACE: 5.7% for bempedoic acid compared to 7.8% for placebo
- 5-component MACE: 6.1% for bempedoic acid compared to 8.2% for placebo

Bempedoic acid was observed to be safe and well tolerated:

- AEs, SAEs and fatal adverse events were well-balanced
- No fatal adverse events were determined to be related to study medication



Study Design

779 patients at high CV risk (ASCVD and/or HeFH) with LDL-C ≥ 100 mg/dL on stable background lipid-modifying therapy, including maximally tolerated statin therapy

Bempedoic acid 180 mg (n=522)

Placebo (n=257)

**52-Week Treatment** 

#### **Primary Objective:**

LDL-C lowering of bempedoic acid 180 mg/day versus placebo

#### **Additional Objectives:**

- hsCRP, non-HDL-C, total cholesterol, and apoB
- Safety and tolerability



Demographics & Baseline Characteristics: Full Analysis Set

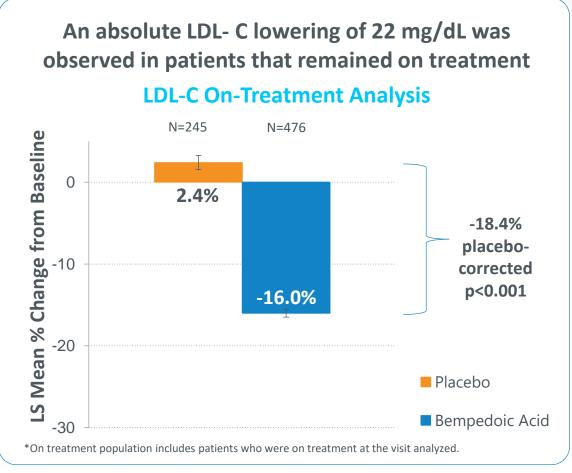
		Bempedoic Acid N=522	Placebo N=257	Total Across Study N=779
Demographics				
A	ge: years	64.1 ± 8.8	64.7 ± 8.7	64.3 ± 8.8
Gender	: % Male	62.8%	65.4%	63.7%
Race				
	White: %	94.1%	94.9%	94.4%
Baseline Characteristics				
BN	11: kg/m <sup>2</sup>	30.0 ± 5.2	30.6 ± 5.0	30.2 ± 5.2
ASCV	'D alone:	94.8%	93.8%	94.5%
HeFH (with or without	ASCVD):	5.2%	6.2%	5.5%
]	Diabetes:	29.7%	31.5%	30.3%
Нуре	rtension:	83.9%	87.2%	85.0%
Current smoker / toba	cco user:	21.1%	22.2%	21.4%
Former smoker / toba	cco user:	41.0%	42.4%	41.5%
Lipid modifying therapy use at				
High-Intensi		53.3%	52.5%	53.0%
Moderate-Intensi	, I	31.8%	31.9%	31.8%
Low-intensity Statin Including N	lo Statin:	14.9%	15.6%	15.1%

Baseline Lipids and hsCRP: Full Analysis Set

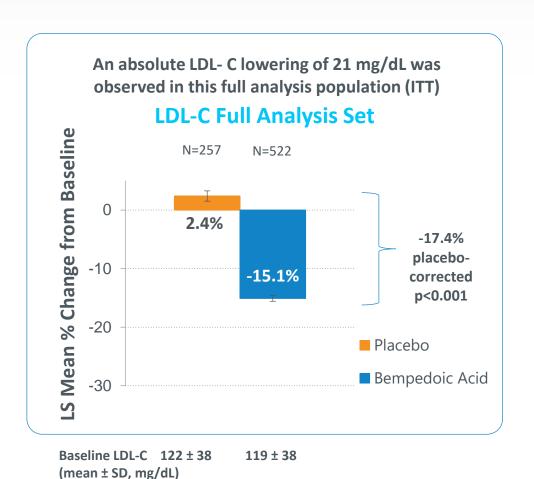
	Bempedoic Acid N=522	Placebo N=257	Total Across Study N=779
Primary Efficacy Endpoint			
LDL-C: mg/dL	119 ± 37.7	122 ± 38.3	120 ± 37.9
Secondary Efficacy Endpoints			
non-HDL-C: mg/dL	151 ± 42.7	154 ± 44.4	$152 \pm 43.3$
Total Cholesterol: mg/dL	202 ± 42.7	205 ± 46.1	203 ± 43.8
apoB: mg/dL	116 ± 29.6	119 ± 30.5	$117\pm29.9$
hsCRP: mg/L*	1.6 (0.87, 3.46)	1.9 (0.92, 3.79)	1.7 (0.87, 3.56)
Other Endpoints			
HDL-C: mg/dL	51 ± 12.9	51 ± 13.1	51 ± 13.0
Triglycerides: mg/dL*	139 (102.5, 190.0)	143 (106.0, 189.0)	140 (103.0, 189.5)

<sup>\*</sup>Median Values (Q1, Q3)

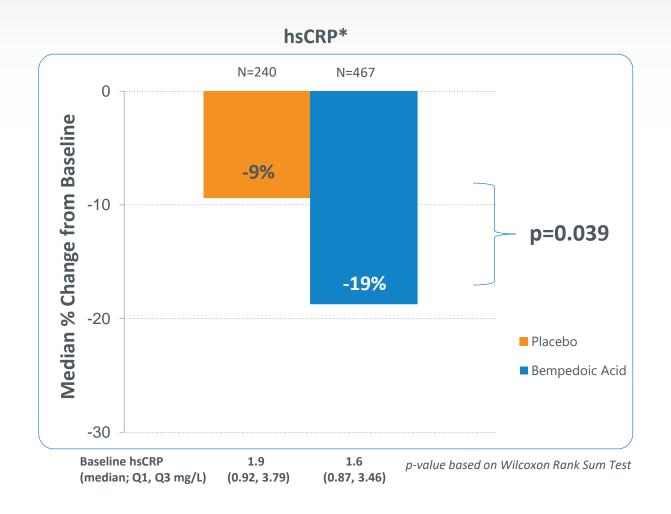
LDL-C Percent Change from Baseline at 12 weeks: On-treatment and Full Analysis (ITT)







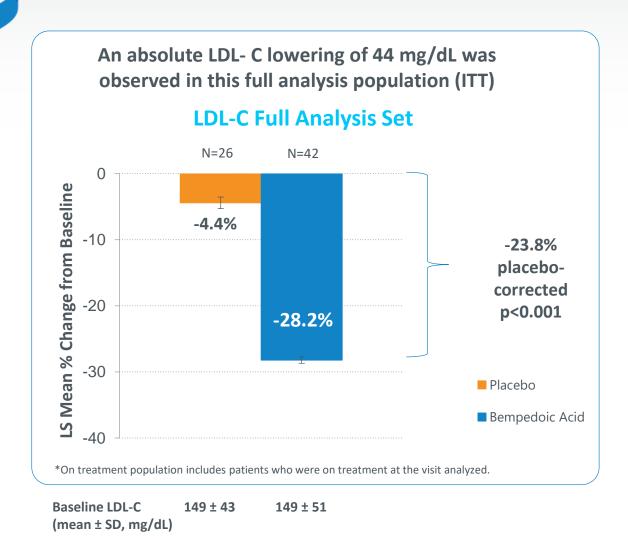
hsCRP Percent Change from Baseline at 12 weeks

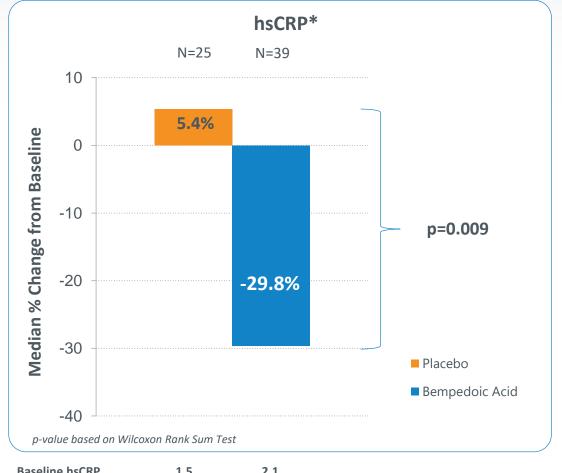


<sup>\*</sup>hsCRP is not normally distributed and so placebo adjustment is not an appropriate measure.



LDL-C Lowering and hsCRP Reduction in Patients on No Background Statin





Baseline hsCRP 1.5 2.1 (median; Q1, Q3 mg/L) (0.9, 3.3) (1.0, 5.8)

<sup>\*</sup>hsCRP is not normally distributed and so placebo adjustment is not an appropriate measure.



#### Adjudicated MACE Events in Bempedoic Acid Compared to Placebo

Major Adverse Cardiovascular Events (MACE)	% of Patients		
	Bempedoic Acid (N=522)	Placebo (N=257)	
3-component MACE	2.7%	4.7%	
4-component MACE	5.7%	7.8%	
5-component MACE	6.1%	8.2%	



<sup>3-</sup>component MACE includes CV death, nonfatal myocardial infarction (MI), and nonfatal stroke.

<sup>4-</sup>component MACE includes CV death, nonfatal myocardial infarction (MI), nonfatal stroke and coronary revascularization.

<sup>5-</sup>component MACE includes CV death, nonfatal myocardial infarction (MI), nonfatal stroke, hospitalization for unstable angina and coronary revascularization.

#### Adverse Events Are Balanced Between Treatment Groups

	% of Patients		
Treatment Emergent Adverse Events (AEs)	Bempedoic acid N=522	Placebo N=257	
Overview of AEs in All Patients			
Any AE(s)	70%	71%	
Serious AE(s)	20%	19%	
Discontinuation due to AE(s)*	11%	9%	



<sup>\*</sup>The observed difference in discontinuation frequency was not driven by any single type of adverse event or group of adverse event.

#### Fatal Adverse Events – Unrelated to Study Medication Overview



- Fatalities adjudicated as CV deaths were 0.8% in the bempedoic acid group and 0.8% in the placebo group
- The other unrelated fatalities in the bempedoic acid group included gas poisoning and sepsis as a complication of a planned abdominal surgery
- No fatal neoplasm AEs. Neoplasms as SAEs were 1.1% for bempedoic acid compared to 1.2% for placebo

	Bempedoic acid 180 mg (N=522)	Placebo (N=257)
Fatal Adverse Events — unrelated to study medication		
Cardiovascular death	0.8%	0.8%
Non-Cardiovascular death		
Septic shock <sup>1</sup>	0.2%	0.0%
Gas poisoning <sup>2</sup>	0.2%	0.0%



 $<sup>^{1}\!\</sup>text{Patient}$  died from septic shock that was a complication of planned abdominal surgery

<sup>&</sup>lt;sup>2</sup>Death was reported verbatim as CO<sub>2</sub> gas poisoning

### Example of Potential Draft Adverse Reactions Table from Package Insert

Results from 1002-047 (Study 2) Phase 3 Study

**Table 1. Adverse Reactions Occurring in ≥3%\*** 

Adverse Reaction	% of Patients		
	Bempedoic acid N=522	Placebo N=257	
Nasopharyngitis	5.2%	5.1%	
Urinary tract infection	5.0%	1.9%	
Hyperuricemia	4.2%	1.9%	
Upper respiratory tract infection	3.6%	3.5%	
Arthralgia	3.4%	3.1%	
Diarrhea	3.1%	2.7%	
Angina pectoris	3.1%	1.9%	
Osteoarthritis	3.1%	1.9%	
Myalgia	2.9%	3.1%	

<sup>\*</sup>Please note this is a DRAFT for example purposes based only on Study 047 and based on a 3% cut-off – this is not considered final



## **Cumulative Phase 3 Program Results**

(Studies 1002-040, -046, -047 and -048)

### Bempedoic Acid – Cumulative Phase 3 Summary

Bempedoic Acid - An Important New Oral Treatment Option

In the cumulative Phase 3 program, treatment with bempedoic acid in high CV risk patients taking maximally tolerated statins provided (at 12 weeks):

- 18% to 31% LDL-C lowering
- 19% to 33% hsCRP reduction
- 0.19% to 0.31% HbA1c reduction in patients with diabetes

Adjudicated MACE events in bempedoic acid and placebo:

- 3-component MACE: 1.9% for bempedoic acid compared to 2.3% for placebo
- 4-component MACE: 3.8% for bempedoic acid compared to 4.2% for placebo
- 5-component MACE: 4.0% for bempedoic acid compared to 4.6% for placebo

Bempedoic acid was observed to be safe and well tolerated:

- AEs, SAEs, LFTs and fatal adverse events were well-balanced
- No fatal adverse events were determined to be related to study medication
- 83% of the patients in the cumulative dataset were studied over 52-weeks



Adjudicated MACE events in bempedoic acid compared to placebo

	% of Patients		
Major Adverse Cardiovascular Events (MACE)	Bempedoic Acid (N=2424)	Placebo (N=1197)	
3-component MACE	1.9%	2.3%	
4-component MACE	3.8%	4.2%	
5-component MACE	4.0%	4.6%	



<sup>3-</sup>component MACE includes CV death, nonfatal myocardial infarction (MI), and nonfatal stroke.

<sup>4-</sup>component MACE includes CV death, nonfatal myocardial infarction (MI), nonfatal stroke and coronary revascularization.

<sup>5-</sup>component MACE includes CV death, nonfatal myocardial infarction (MI), nonfatal stroke, hospitalization for unstable angina, and coronary revascularization.

Adverse Events Are Balanced Between Treatment Groups

Treatment Emergent Adverse Events (AEs)	% of Patients		
	Bempedoic acid N=2424	Placebo N=1197	
Overview of AEs in All Patients (patient incidence)			
Any AE(s)	73%	73%	
Serious AE(s)	14%	13%	
Discontinuation due to AE(s)*	11%	8%	



<sup>\*</sup>The observed difference in discontinuation frequency was not driven by any single type of adverse event or group of adverse event.

Fatal Adverse Events – Unrelated to Study Medication Overview



All fatal AEs were determined to be unrelated to study medication by the investigator

- We have had 16 Phase 3 as well as CVOT DMC reviews, covering several thousand patient years. To date, the DMC has recommended the trial continue as designed and conducted, without modification.
- Neoplasms as SAEs were 1.1% for bempedoic acid compared to 0.9% for placebo
- 3-Component MACE, which includes CV death, nonfatal MI, and nonfatal stroke, is 1.9% in the bempedoic acid arm to 2.3% in the placebo arm

	Bempedoic acid 180 mg (N=2424)	Placebo (N=1197)
Fatal Adverse Events – unrelated to study medication		
Cardiovascular death	0.4%	0.3%
Non-Cardiovascular death		
Neoplasms	0.2%	0.0%
Sepsis/septic shock	0.1%	0.1%
Other*	0.1%	0.0%

<sup>\*</sup>Other fatal AEs include:

- Gas poisoning (bempedoic acid)
- Pancreatic pseudocyst (bempedoic acid)

LFT Elevations

Overview of LFT Elevations > 3x ULN (ALT/AST )			
Drug Name	Drug Arm	Placebo	
FDA Approved Drugs <sup>1</sup>			
Simvastatin 40mg – 80mg	0.9% - 2.1%	-	
Atorvastatin 10mg - 80mg	0.2% - 2.3%	-	
Vytorin 10mg/10mg – 80mg	1.7% - 2.6%	0.6%	
Rosuvastatin 5-40 mg	1.1%	0.5%	
Ezetimibe 10 mg	0.5%	0.3%	
Phase 3 Development Program <sup>2</sup>			
Bempedoic Acid 180 mg	0.7%	0.3%	

<sup>1 =</sup> Data collected from FDA approved package inserts for each drug.

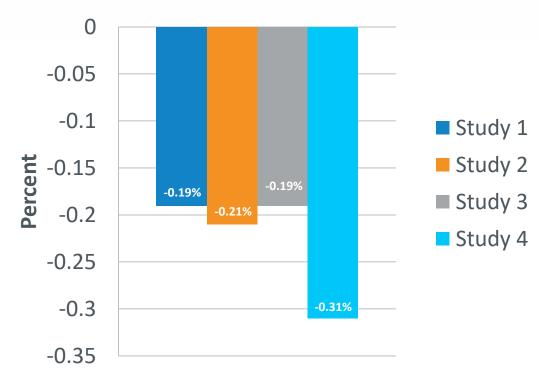
<sup>2 =</sup> Cumulative Phase 3 Program: Bempedoic acid n=2424, placebo=1197

#### **Cumulative Phase 3 Data**

#### Consistent Reductions in HbA1c and New Onset Diabetes

- 4 out of 5 patients with diabetes over age 65 die from ASCVD
- Cumulative Phase 3 datasets showed that new onset or worsening of diabetes occurred less frequently in patients taking statins plus bempedoic acid (4.0%) than in patients taking statins plus placebo (5.6%)
- Statins, especially high-intensity statins, lower LDL-C but increase HbA1c and new onset or worsening of diabetes
  - Statin class label: increases in HbA1c and fasting serum glucose have been reported with statins
  - Rosuvastatin's label contains additional language including: significantly higher frequency of diabetes in patients taking rosuvastatin (2.8%) vs placebo (2.3%). HbA1c was significantly increased by 0.1% in rosuvastatin-treated patients compared with placebo-treated patients.

## HbA1c (BA Difference vs PBO) at 12 weeks in Patients with Diabetes (N=1,002)



### Two Targeted Non-Statin Oral LDL-C Lowering Therapies

Therapies to Complement All LDL-C Lowering Therapies, Providing Even Greater LDL-C Lowering

#### **Bempedoic Acid / Ezetimibe Combination Pill**

- Efficacy comparable to injectable PCSK9i monotherapy (~50% LDL-C lowering) plus differentiated hsCRP reduction
- Profile:
  - Once-daily, convenient, cost-effective, oral combination pill
  - 35% LDL-C lowering on maximally tolerated statin therapy
  - 43% LDL-C lowering on no background statin therapy
  - 64% total LDL-C lowering when combined with atorva 20 mg
  - 34% hsCRP reduction; a key marker of inflammation
  - Safe and well-tolerated without increases in muscle-related adverse events
- NDA submission for LDL-C lowering indication in Q1 2019

#### **Bempedoic Acid**

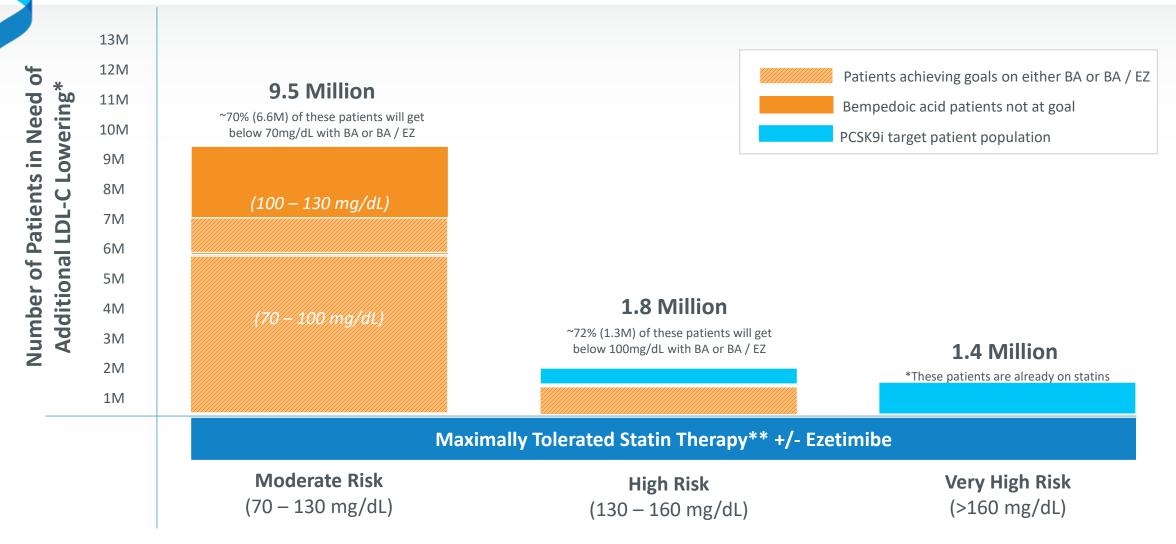
- Consistent and complementary LDL-C lowering plus differentiated hsCRP reduction
- Profile:
  - Once-daily, convenient, cost-effective, oral pill
  - 18-20% LDL-C lowering on statins, including high-intensity statins
  - Up to 30% LDL-C lowering on no background statin therapy
  - 19-40% hsCRP reduction; a key marker of inflammation
  - Safe and well-tolerated without increases in muscle-related adverse events
- NDA submission for LDL-C lowering indication in Q1 2019

Bempedoic Acid / Ezetimibe Combination Pill and Bempedoic Acid are *Not* a Replacement for Statins or Ezetimibe



#### 12-13M ASCVD and/or HeFH Patients with Elevated LDL-C

Bempedoic Acid Franchise Addresses Most Patients Not at LDL-C Treatment Goal



<sup>\*</sup>Excludes Low CVD Risk patients because, by definition, they do not need additional LDL-C lowering



<sup>\*\*</sup>Includes patients only able to tolerate less than the approved daily starting dose of a statin (considered statin intolerant)



Q&A

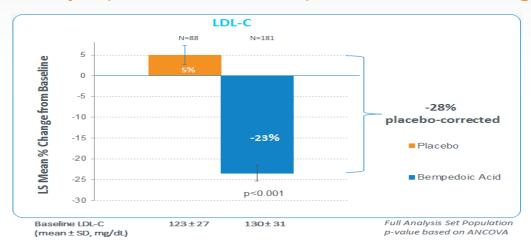


# **APPENDIX**

### Phase 3 Efficacy Snapshot (LDL-C)

Consistent and Efficacious LDL-C Lowering

#### Study 4 (No Statin; 12 weeks) – 28% LDL-C Lowering



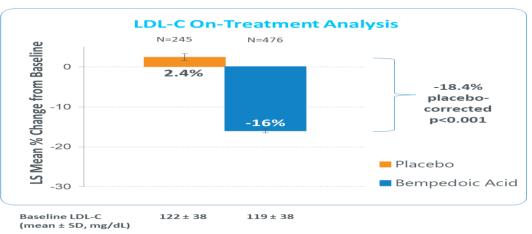
#### Study 3 (No Statin; 24 weeks) – 24% LDL-C Lowering



#### Study 1 (+Statins; 52 weeks) - 20% LDL-C Lowering



#### Study 2 (+Statins; 52 weeks) – 18% LDL-C Lowering



### 1002FDC-053 (BA/EZE Combo Pill) Phase 3 Efficacy Study

LDL-C Percent Change from Baseline at 12 weeks

