Esperion

The Lipid Management Company

Company Update

January 2019

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 DSE is able to successfully commercialize the bempedoic acid / ezetimibe combination pill and bempedoic acid, if approved, 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.

Poised to Change LDL-C Lowering Treatment Paradigm

"Preferred" Next-Gen Therapy

Help Patients on Maximally Tolerated Statins Achieve Their LDL-C Goal

BA and BA/EZE combo pill NDA & MAA submissions 1Q19 & 2Q19, respectively; Approvals expected 1H20

High Unmet Need

>800,000 U.S. CVD deaths annually

>18 million patients in the US not at their LDL-C goal despite broad use of statins, including >4 million patients considered "statin intolerant"

Early Managed Care Alignment

Initial payer feedback highly positive – "Tier 2" formulary status expected; generic statins as the only step through

Proven Commercial Team

"Lipid Management for Everybody"

Preparing to provide access to BA and BA/EZE combo pill to millions of patients

Funded Well-Beyond Approvals

$285 million in proforma cash at December 31st

An additional $150 million milestone payment projected 1H20

Two Non-Statin Oral Pills That Lower LDL-C and Reduce hsCRP

Complement to Standard of Care LDL-C Lowering Drugs

Bempedoic Acid / Ezetimibe Combination Pill	Bempedoic Acid

Shared Benefits:

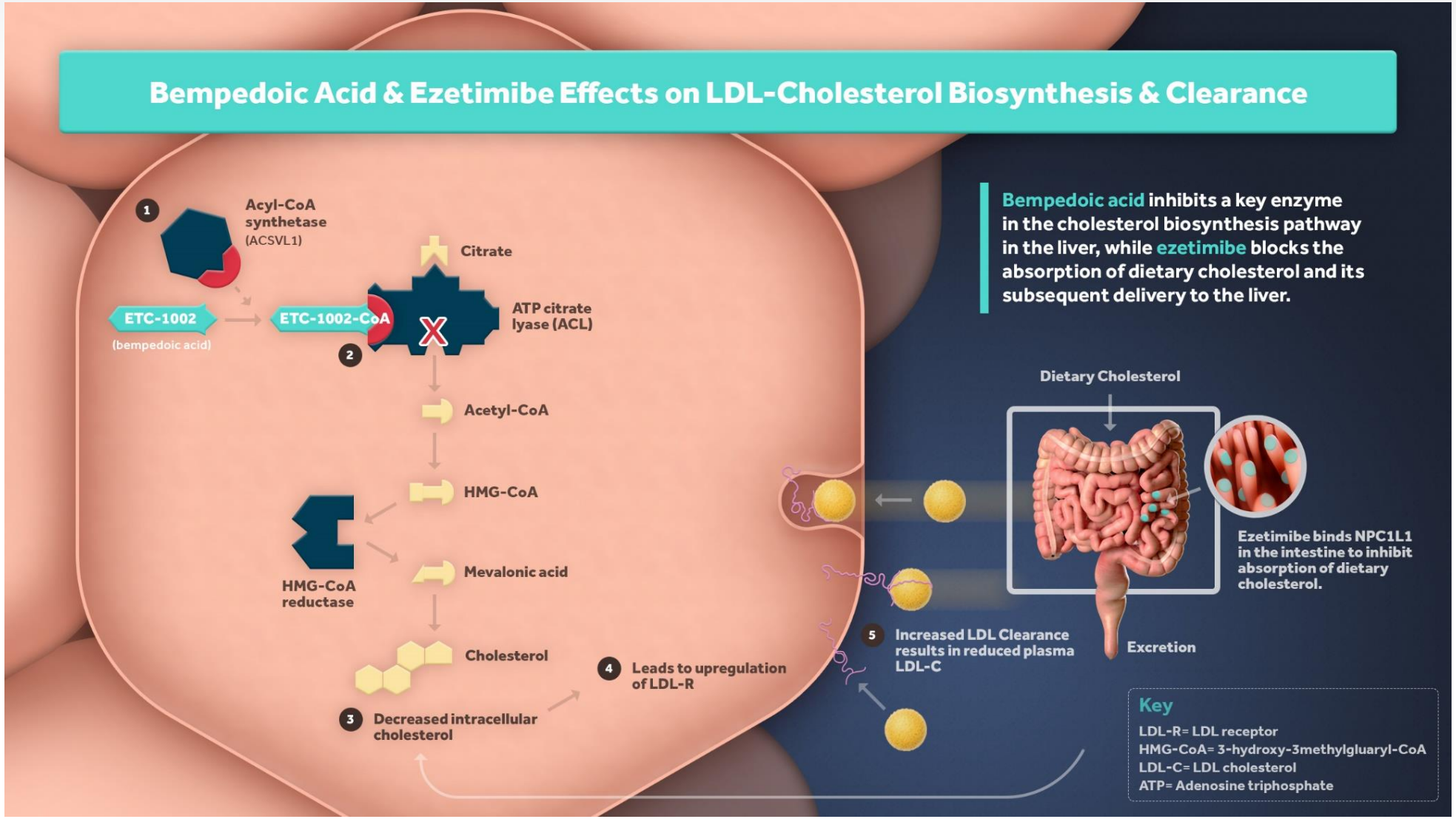
- Oral, once-daily, convenient, cost-effective therapies
- Safe and well-tolerated without increases in muscle-related adverse events
- HbA1c lowering and lower rate of new onset/worsening diabetes

- Efficacy comparable to injectable PCSK9i monotherapy (~50% LDL-C lowering) – plus differentiated hsCRP reduction
  - 35% LDL-C lowering on maximally tolerated statins
  - 43% LDL-C lowering on no background statins
  - 34% hsCRP reduction; a key marker of inflammation

- Consistent and complementary LDL-C lowering – plus differentiated hsCRP reduction
  - 18-20% LDL-C lowering on maximally tolerated statins, including high-intensity statins
  - Up to 31% LDL-C lowering on no background statin
  - 19-40% hsCRP reduction; a key marker of inflammation

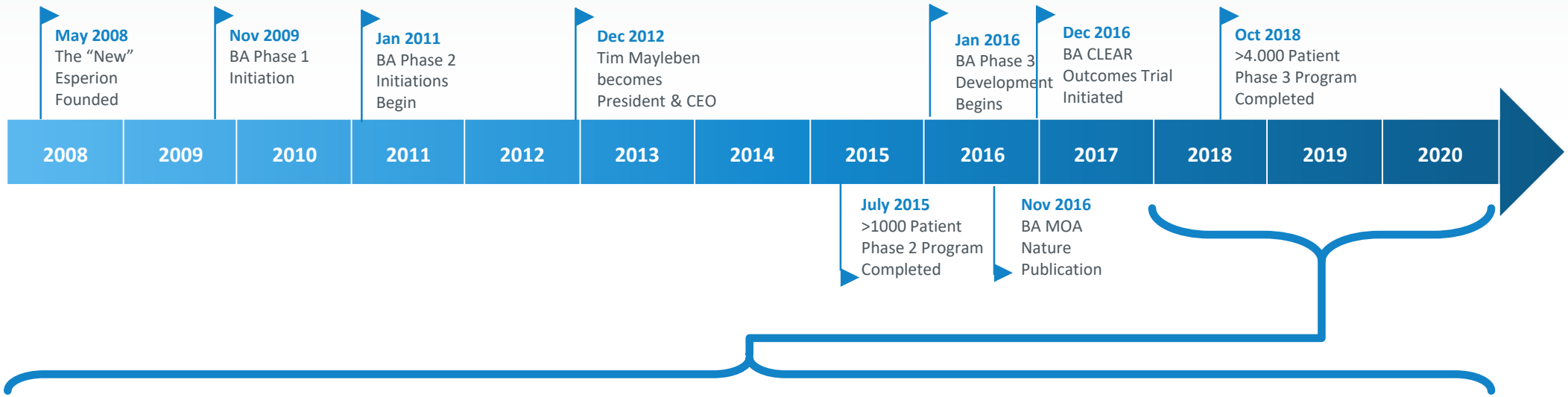
Bempedoic Acid / Ezetimibe Combination Pill and Bempedoic Acid

Complementary Non-Statin Mechanisms of Action (MOAs)



Bempedoic Acid: Beyond Statin Lipid Management

From the Developers of Lipitor to Physicians' Hands

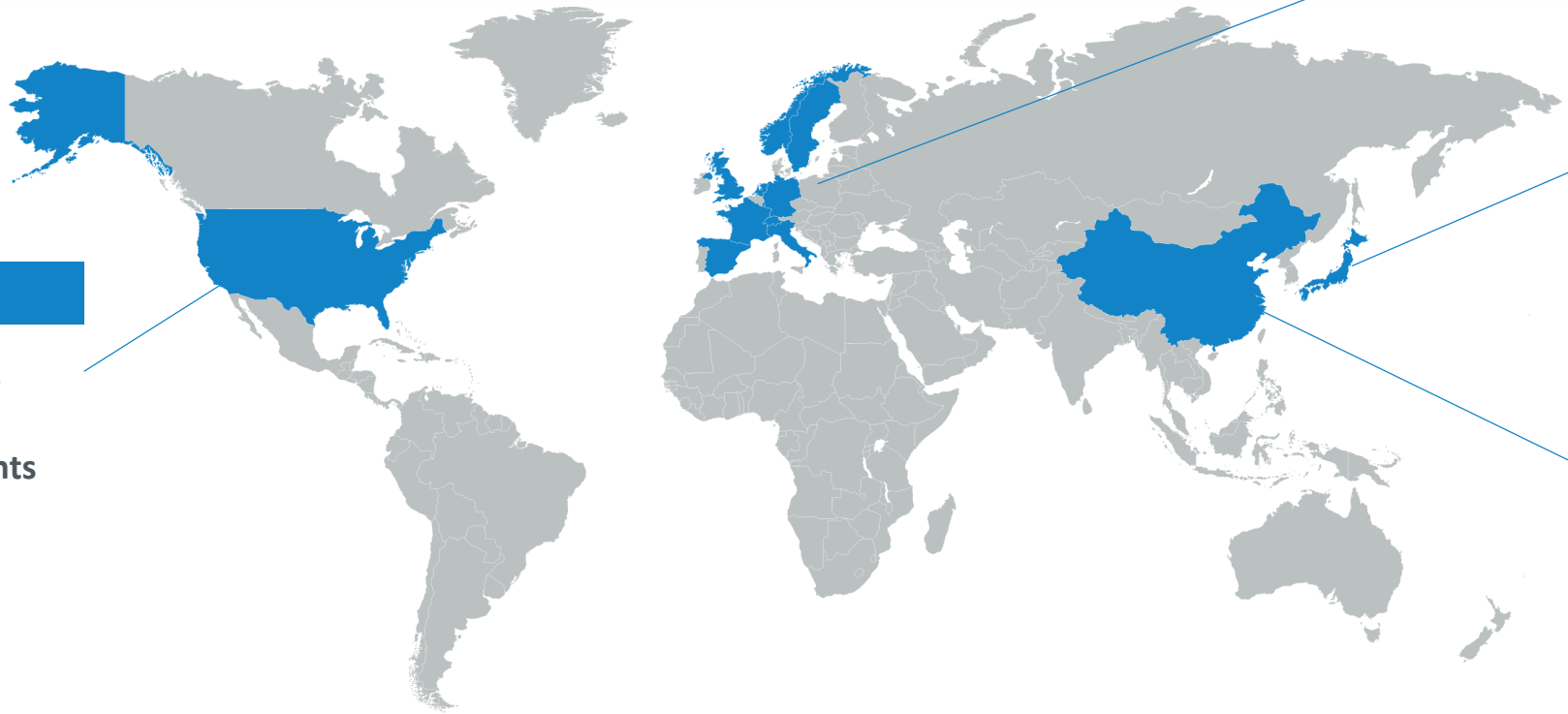


2018					2019					2020	
March	**May**	**May**	**August**	**October**	**January**	**1Q19E**	**2Q19E**	**3Q19E**	**2H19E**	**1H20E**	**1H20E**
Study 4 Topline Results	Study 1 Topline Results	Study 3 Topline Results	Study 053 Topline Results	Study 2 Topline Results	Daiichi Sankyo Europe Commercial Agreement	BA and BA/EZE NDA Submissions Ph I BA Sustained Release Results	BA and BA/EZE MAA Submissions	CLEAR Outcomes Enrollment Completed	Ph 2 BA fixed dose combination in patients with high LDL-C and T2D	Potential BA & BA/EZE NDA & MAA Approvals	Potential BA & BA/EZE First Commercial Sales

The Lipid Management Team: Addressing a Truly Global Problem

Cardiovascular Disease Remains the #1 Cause of Death Globally

- **CVD accounts for ~1 in 3 deaths in the U.S. and Europe**
- **>800,000 U.S. CVD deaths annually[1]**
- **16.3 million heart attacks, strokes, and related CV events will occur in the U.S. during 2017-2021[2]**



United States

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≈ 18.3 million addressable patients

Europe

Daiichi-Sankyo

≈ 17.5 million addressable patients

Japan

≈ 5.8 million addressable patients

China

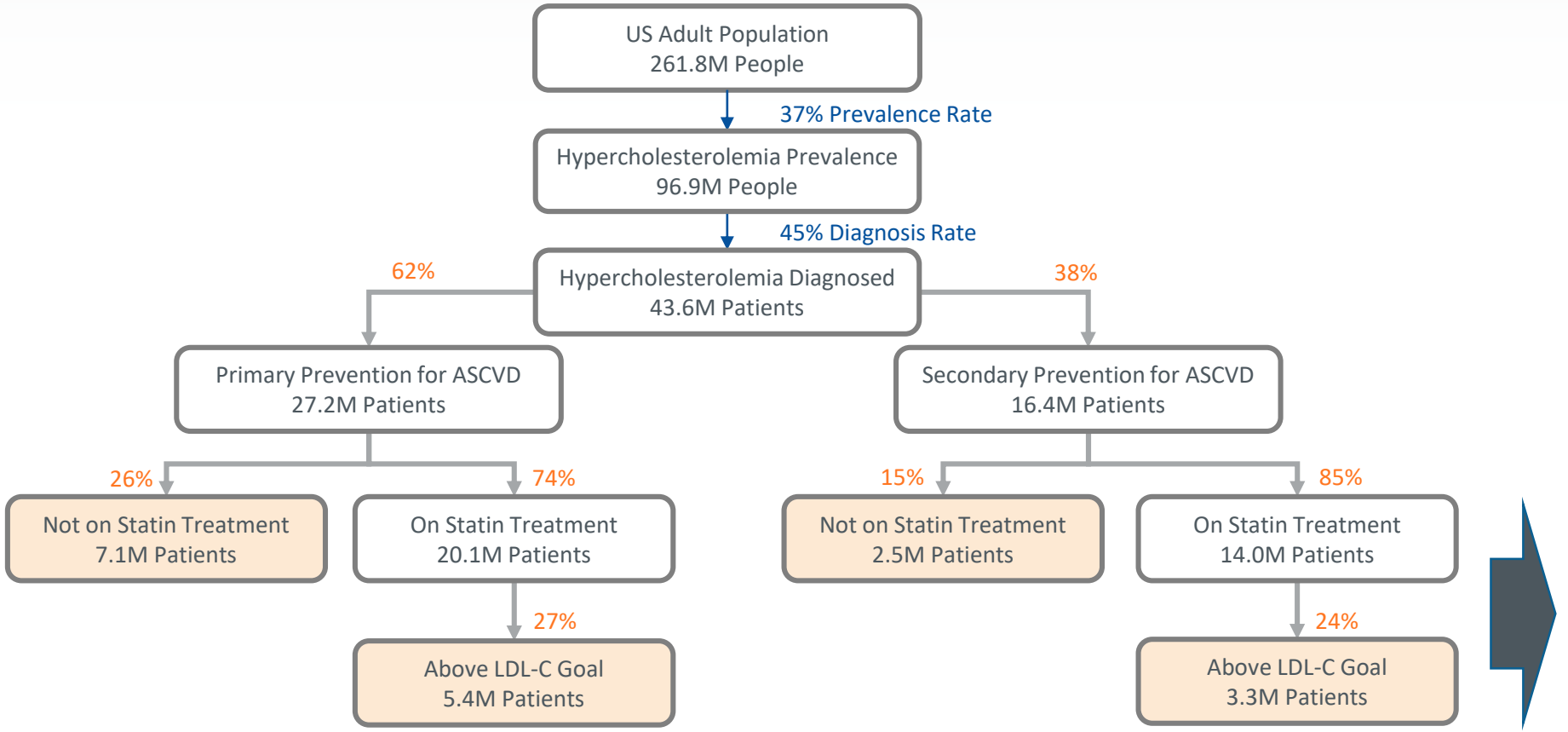
≈ 19.6 million addressable patients

Source: 1 = American Heart Association, 2 = Center for Disease Control

U.S. Target patient population for BA and BA/EZE FDC

Includes 18.3M patients

Patient Population at Peak



18.3M eligible patients

- 9.6M not on statins
- 8.7M on statins but not at goal

Secondary Research
Primary Research

Source: ZS Associates primary and secondary research, Sep-Oct 2018.
Primary research N = 350 healthcare practitioners

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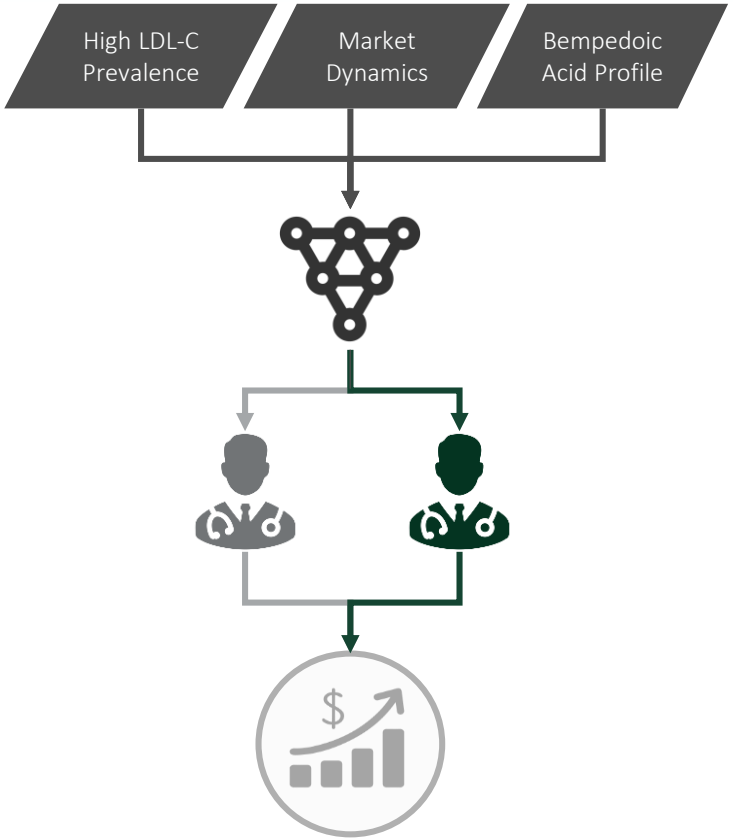
KOL and Community Physician Feedback on the Bempedoic Acid Franchise Has Been Consistently Positive

Since August 2018, Esperion has either directly or indirectly interviewed 750+ practicing US physicians and 32 US Key Opinion Leaders in Cardiology, Endocrinology, Lipidology, and Primary Care

Feedback has been consistent regarding:

- **Unmet need in the treatment of hypercholesterolemia**
  - Patients on maximally tolerated statins but not at LDL-C goal
    - Efficacy and tolerability trade-offs are real, resulting in many patients being 'on statins' yet not at LDL-C goal
  - Patients who are unable or unwilling to take a statin due to real or perceived side effects
  - HCP feedback regarding statin intolerance affecting ~15% of all hypercholesterolemia patients
- **Significant challenges associated with PCSK-9 therapy**
  - Physician effort required to obtain payor approval
  - Patient aversion to injections
  - Significant patient out-of-pocket costs
  - Overall therapy cost and burden on healthcare system
- **Positive response to Bempedoic Acid product profile – "Lipid Management for Everybody"**
  - Oral once-daily pill in monotherapy or combination with ezetimibe can lower LDL-C up to 43% on maximally tolerated statins
    - Offers a simple means to get more patients to goal, including those already taking statins
    - Offers a novel alternative for lowering LDL-C in the statin-adverse and statin-averse populations
    - Offers a convenient alternative, eliminating headaches and fears over PCSK9 approvals, cost, and administration

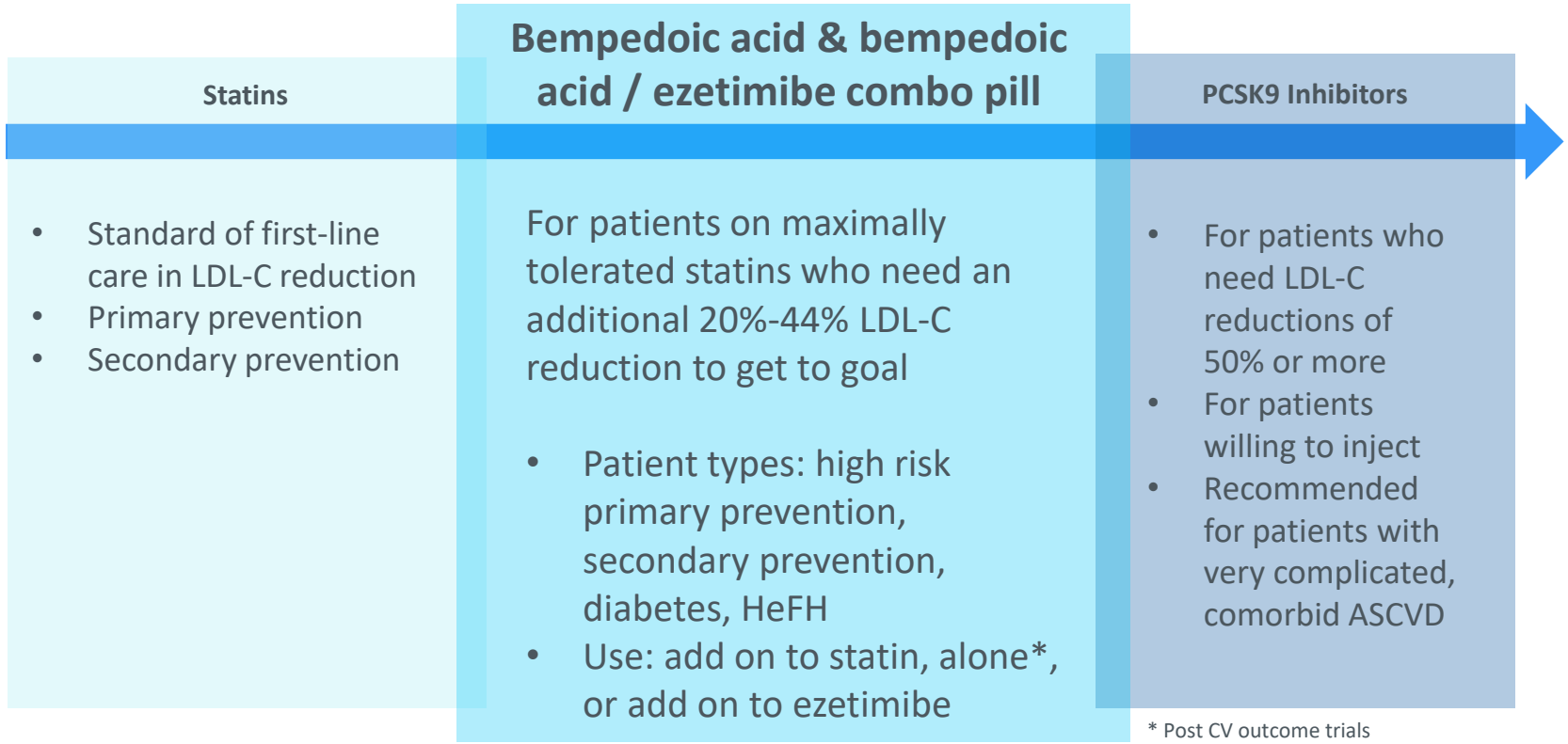


Bempedoic Acid Commercial Positioning – "Lipid Management for Everybody"

After Standard-of-Care Statins and Before Specialty PCSK9i Medicines

Where we fit

BA and BA/EZE FDC are new oral lipid lowering therapies with a unique MOA that delivers significant results alone* or in combination with other LDL-C therapies, so far more patients can finally achieve their LDL-C goals



* Post CV outcome trials

Who we fit

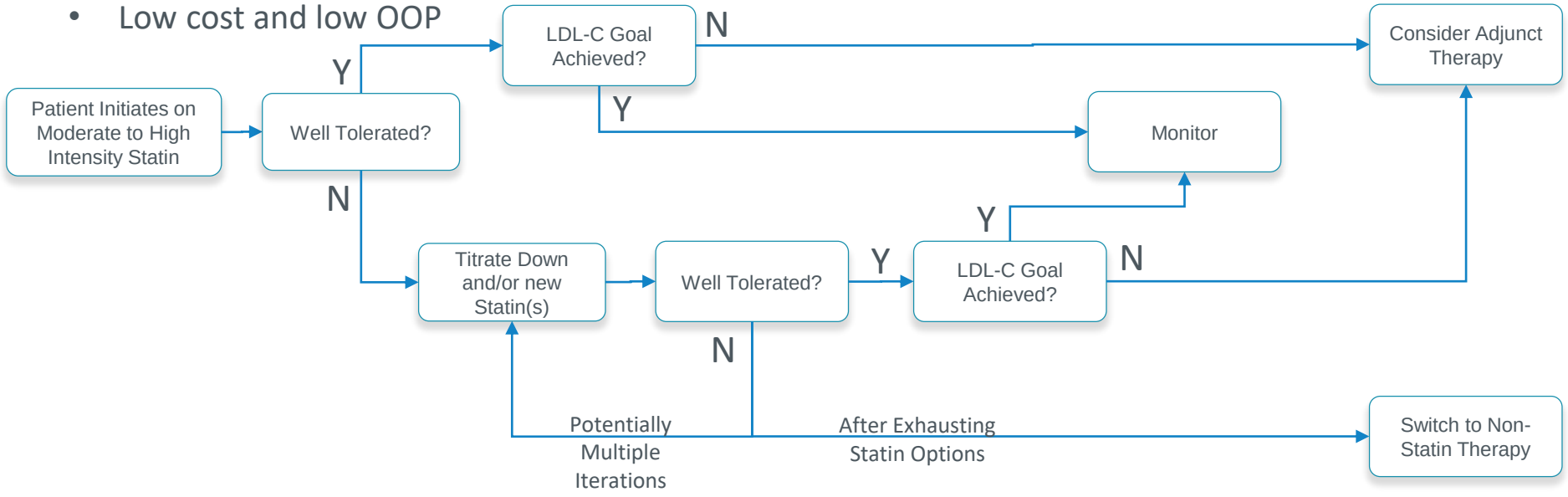
- Patients taking high-intensity statins who are not at LDL-C goal
- Patients who need additional LDL-C lowering who are taking low-dose or no statins due to muscle-related issues
- Patients with prediabetes or diabetes seeking to avoid HbA1c increases and worsening/new-onset disease
- Patients whose health insurance status compromises access to PCSK9 inhibitors
- Patients who are unwilling to take injections

Bempedoic Acid Franchise

Place in Therapy

KOL advisor consensus: In patients who are inadequately controlled or who cannot tolerate a statin, BA/EZE FDC is first add-on for low, medium and high risk 1° and stable 2° prevention patients; BA monotherapy is second add-on after ezetimibe for 1° and stable 2° prevention patients who need modest lipid lowering to get to goal and desiring

- Simplicity
- Convenience
- Low cost and low OOP



BA & BA/EZE Opportunity

- **Stable 1° or 2° prevention patients who are unable to achieve LDL-C goals with one agent**
- **Opportunity for first add on to statin in high-risk patients with LDL-C 85-97 mg/dL**
- **Should additional LDL-C lowering be required, FDC would be considered**

BA & BA/EZE Opportunity

- **1/3 of patients cannot tolerate a statin.**
- **Opportunity for 1L or add on use in low to moderate risk 1° prevention patients LDL-C 120-140 mg/dL or high risk 1° or stable 2° prevention patients LDL-C 85- 97 mg/dL**

Treatment Journey

Initial Payer Feedback for BA and BA / EZE Combo Pill

Overwhelmingly Positive

> **BA and BA/EZE combo pill will likely be 2nd Tier with generic statin as background therapy.**
>
> ***- National PBM***

> **This will be covered at branded formulary co-pay.**
>
> ***- Large Part-D Plan***

> **Covered with no steps.**
>
> ***- Large Regional Payer***

> **With contracted PCSK9/New WAC pricing, BA would be on parity at Tier 2.**
>
> ***- Large PBM***

EU Commercial Collaboration Agreement

Daiichi Sankyo Europe – EU Commercialization Agreement

- The Esperion and Daiichi Sankyo Europe (DSE) agreement is the **largest EU licensing agreement** in at least the last decade

- Significant economics to Esperion including;
  - $300 million in upfront and near-term milestones
  - $900 million in total milestones
  - Tiered royalties between 15% – 25%

- Daiichi Sankyo Europe is a strong EU commercial partner
  - **1000 person cardiovascular sales** organization to support the bempedoic acid launch in the EU
  - Fully integrated commercial organization and deep expertise in reimbursement, distribution, and medical affairs
  - European-based commercial organization driving multiple synergies with their existing CV portfolio (Lixiana, Efient, Olmesartan)
  - Responsible for one of the most successful recent cardiovascular launches in Europe (Lixiana launched in 2015)
  - Significant overlap among physicians target for bempedoic acid and those currently prescribing Lixiana

- Esperion retains control of all development with DSE responsible for all European commercial activities

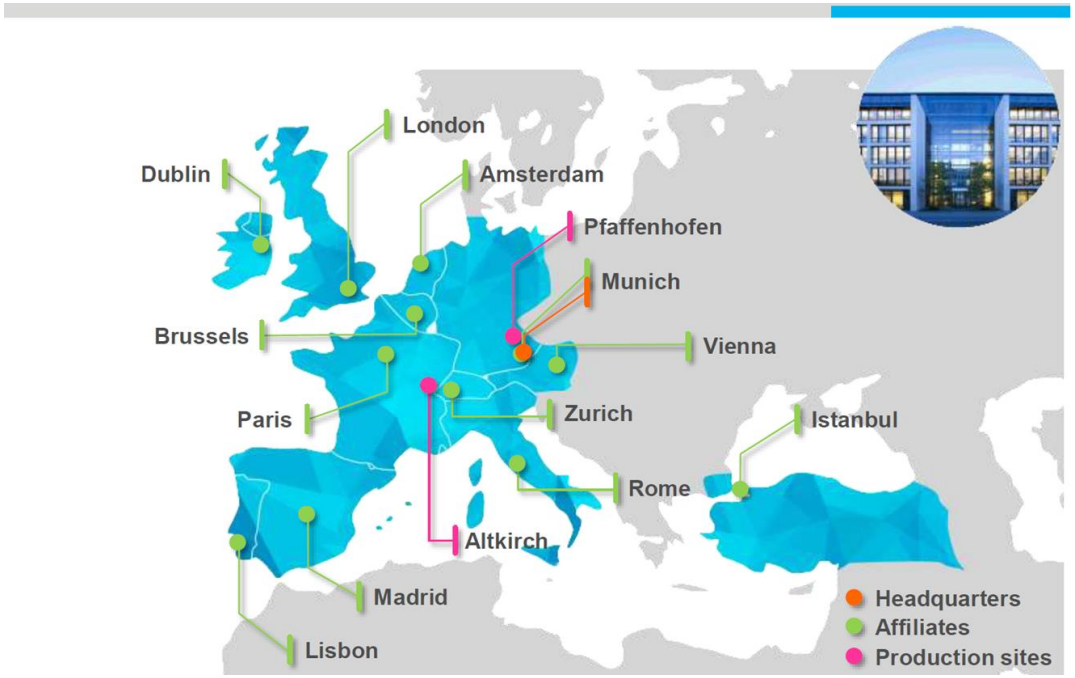
EU Commercial Collaboration Agreement – What We Wanted

- Global Pharmaceutical Company with significant resources
- Strong history in cardiovascular disease drug development and commercialization
- Recent success and experience in commercializing a cardiovascular drug in the EU
- Strong EU commercial organization with significant personnel and financial resources
- Significant economics to Esperion, reflecting the value of bempedoic acid
- Retain development and regulatory decision making for the bempedoic acid franchise
- Set a precedent for US and ROW commercial partnerships and enhancing the long-term value of Esperion and the bempedoic acid franchise

Daiichi Sankyo Europe

Global Player with a Large, European Cardiovascular Presence

- **<u>Top 25 Global Pharmaceutical Company</u>** based on revenues
- Daiichi Sankyo Europe brings together a sales organization of **<u>more than 1,000 people</u>** focusing on the cardiovascular portfolio
- Cardiovascular brands include: Lixiana (NOAC), olmesartan (Hypertension), Efient (Antiplatelet)
- History of cardiovascular innovation: discovered pravastatin



Daiichi Sankyo Europe

Success in the Cardiovascular Market – Out-Performing in this Highly Competitive Therapeutic Area

- Lixiana was launched 4th to market in 2015 in the novel oral anticoagulation (NOAC) market competing against the largest global players

- Lixiana sales in Europe: ~$400 million in 2018; ~$1 billion at peak

- Daiichi Sankyo Europe has previously achieved commercial success in the highly competitive CV therapeutic area with Olmesartan in Hypertension and Efient in antiplatelet therapies

Upcoming Milestones

Esperion 2019 Milestones & Key Events

What to Watch

Regulatory Submissions

- BA and BA/EZE combo pill NDA submissions (1Q19)
- BA and BA/EZE combo pill MAA submissions (2Q19)

Data Flow & Study Status

DATA

- **Study 201 –** Ph1 BA Sustained Release (1Q19)
- **Study 058 –** Ph2 BA/EZE combo pill in hypercholesterolemia patients with T2D (2H19)

STUDY STATUS

- **CLEAR Outcomes –** enrollment complete (3Q19)
- **Ph3 BA initiation** in Patients with High LDL-C and T2D (2H19)

Other Events

- ROW licensing / partnership(s)

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APPENDIX

Bempedoic Acid / Ezetimibe Combo Pill Phase 3 Results

Bempedoic Acid / Ezetimibe Combo Pill

An Important New Oral Treatment Option

In a pivotal Phase 3 study, treatment with the bempedoic acid / ezetimibe combination pill in high CV risk patients taking maximally tolerated statins delivered:

- 35% LDL-C lowering
- 34% hsCRP reductions
- 43% LDL-C lowering in patients taking no statin

The bempedoic acid / ezetimibe combination pill was observed to be safe and well tolerated.

- AEs and SAEs were well balanced among the arms of the study
- No increases in muscle-related AEs; no elevations in LFTs were observed

The pivotal Phase 3, four-arm study design including a primary endpoint of LDL-C lowering, study statistics and an abbreviated 505(b)(2) regulatory pathway were discussed and agreed to with the U.S. Food and Drug Administration (FDA) in 2017.

Global Pivotal Phase 3 Study of the BA / EZ Combo Pill *(1002-053)*

Positive Top-line Results Announced August 27th, 2018; 12 Week Study

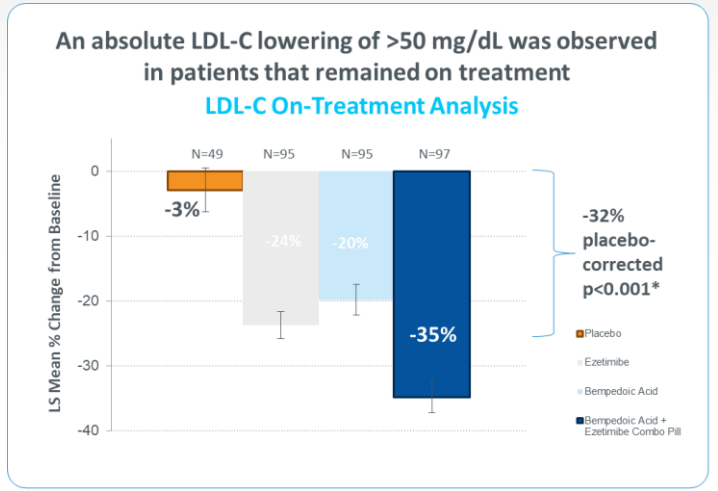
Bempedoic Acid 180mg/Ezetimibe 10mg Fixed Dose Combination Pill:

Efficacy:

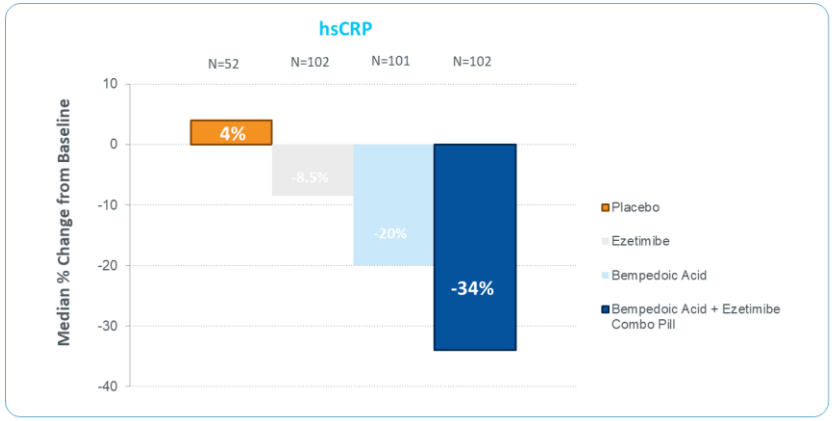
- Significantly lowered LDL-C by 35% (on treatment) (p<0.001)
- Significantly reduced hsCRP by 34% (p<0.001)
- Significantly lowered non-HDL-C, total cholesterol and apoB (p<0.001)

Safety:

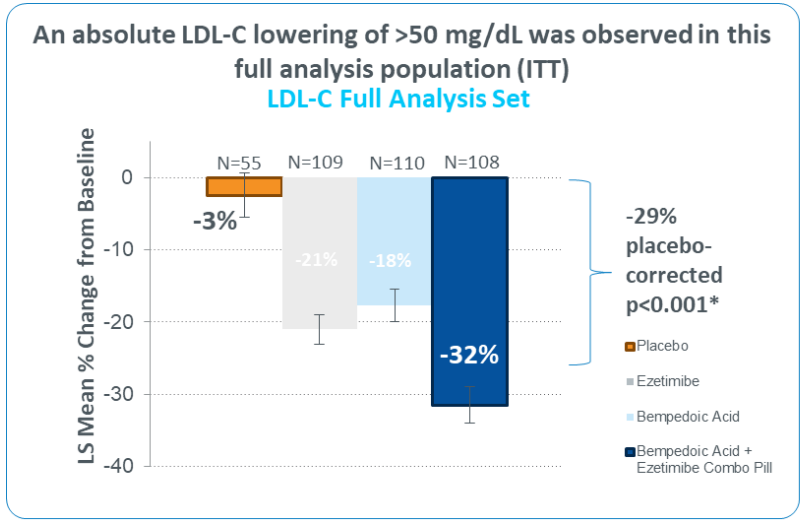
- Safe and well-tolerated in 382 ASCVD patients or high-risk primary prevention patients on maximally tolerated lipid modifying therapy over 12 weeks
- Comparable to ezetimibe with similar frequency of AEs, SAEs, muscle-related AEs and discontinuations



*p<0.001 vs PBO, EZE or BA



p-value <0.05 for both placebo and ezetimibe versus combo based on Wilcoxon Rank Sum Test



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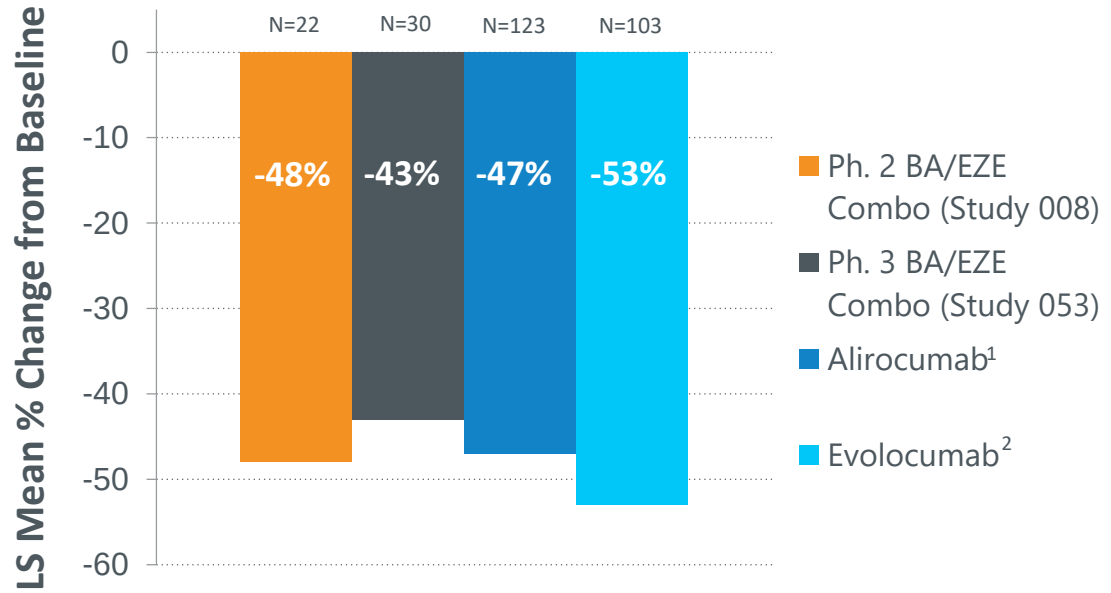
Global Pivotal Phase 3 Study of the BA / EZ Combo Pill *(1002-053)*

Efficacy Comparison in SI Patients with No Statin Background Therapy (post-hoc analysis)

% Change LDL-C at Week 12
(No Statin Background Therapy)
Post-hoc Analysis



Baseline LDL-C (mean ± SD, mg/dL)	162 ± 27	142 ± 39	142 ± 22	141 ± 27

Effects On hs-CRP:

- Bempedoic acid/ezetimibe (study 008) → -26%
- Bempedoic acid/ezetimibe (study 053) → -34%
- PCSK9-inhibitors → **no** effect on hs-CRP

Source 1: ODYSSEY Alternative; J Clin Lipidol 2015;9:758-69

Source 2: GAUSS-2; J Am Coll Cardiol 2014;63:2541–8

Global Pivotal Phase 3 Study of the BA / EZ Combo Pill *(1002-053)*

Safety and Tolerability – Overview of Adverse Events

Treatment Emergent Adverse Events (AEs)	% (Number) of Patients			
	Bempedoic Acid / Ezetimibe Combo Pill N=107	Bempedoic acid N=110	Ezetimibe N=109	Placebo N=55
Overview of AEs in All Patients (patient incidence)				
Any AE(s)	59%	62%	53%	44%
Serious AE(s)*	8%	6%	9%	2%
Discontinuation due to AE(s)	7%	8%	9%	4%
Fatal Adverse Events	0	0	0	0

*No SAE reported as related to study medication

Cumulative Bempedoic Acid Phase 3 Results

Bempedoic Acid – Cumulative Phase 3 Summary

An Important New Oral Treatment Option

In the pivotal Phase 3 program, treatment with bempedoic acid in 3600 high CV risk patients taking maximally tolerated statins provided:

- 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

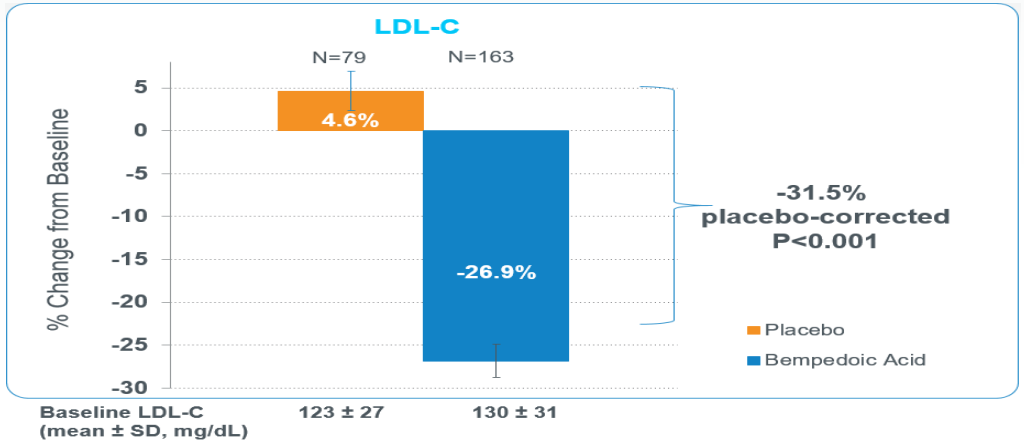
Bempedoic acid was observed to be safe and well tolerated:

- 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

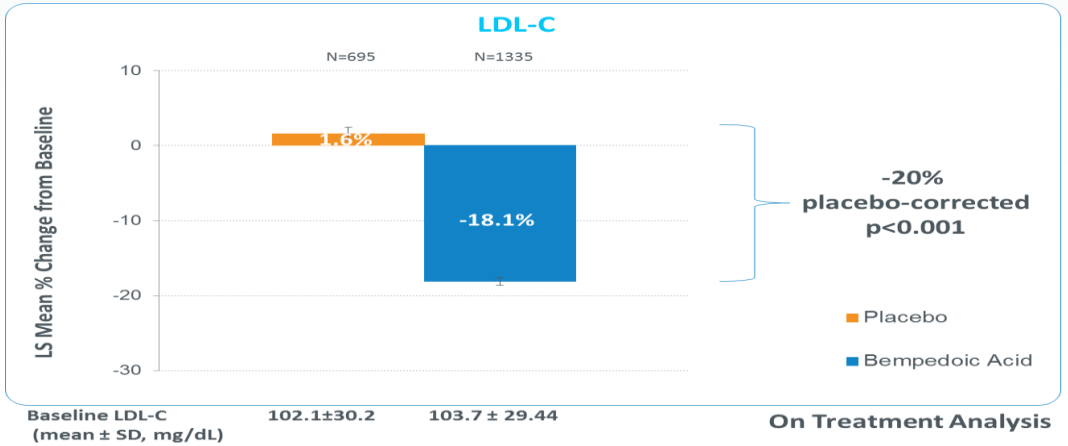
Cumulative Phase 3 Program LDL-C Lowering Efficacy

Consistent and Effective LDL-C Lowering

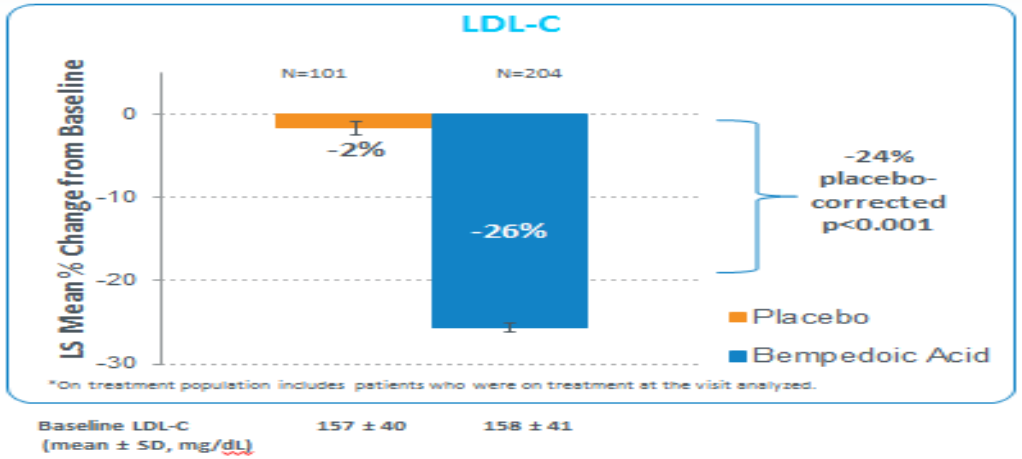
Study 4 (No Statin; 12 weeks) – 31% LDL-C Lowering



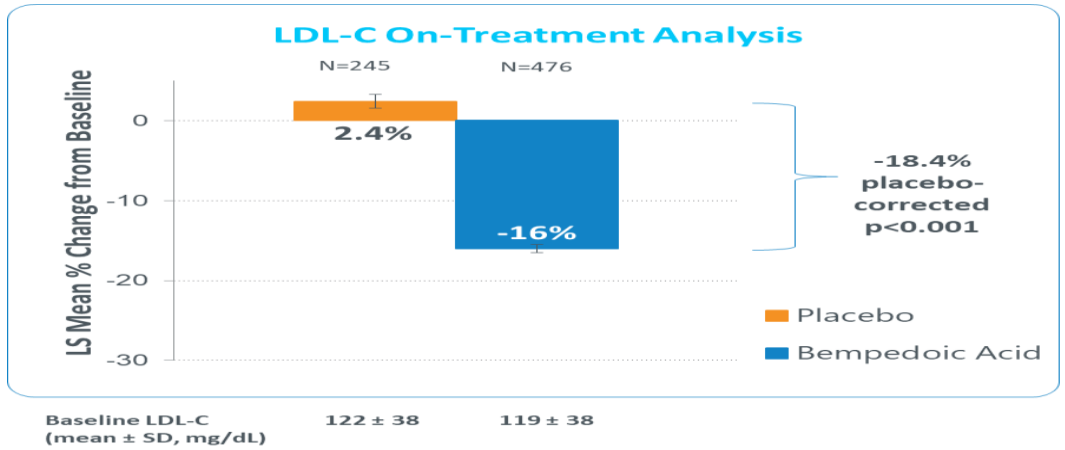
Study 1 (+Statins; 52 weeks) – 20% LDL-C Lowering



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



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



Bempedoic Acid – Cumulative Phase 3 Summary

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%

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

Bempedoic Acid – Cumulative Phase 3 Summary

Adjudicated MACE events in bempedoic acid compared to placebo

Major Adverse Cardiovascular Events (MACE)	% of Patients	
	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%

3-component MACE includes CV death, nonfatal myocardial infarction (MI), and nonfatal stroke.
4-component MACE includes CV death, nonfatal myocardial infarction (MI), nonfatal stroke and coronary revascularization.
5-component MACE includes CV death, nonfatal myocardial infarction (MI), nonfatal stroke, hospitalization for unstable angina, and coronary revascularization.

Bempedoic Acid – Cumulative Phase 3 Summary

Fatal Adverse Events – Unrelated to Study Medication Overview

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

- 16 Phase 3 and CVOT DMC reviews, covering several thousand patient years. To date, the DMC has recommended the trials continue, 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 was 1.9% in the bempedoic acid arm and 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%

*Other fatal AEs include:

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

Bempedoic Acid – Cumulative Phase 3 Summary

LFT Elevations

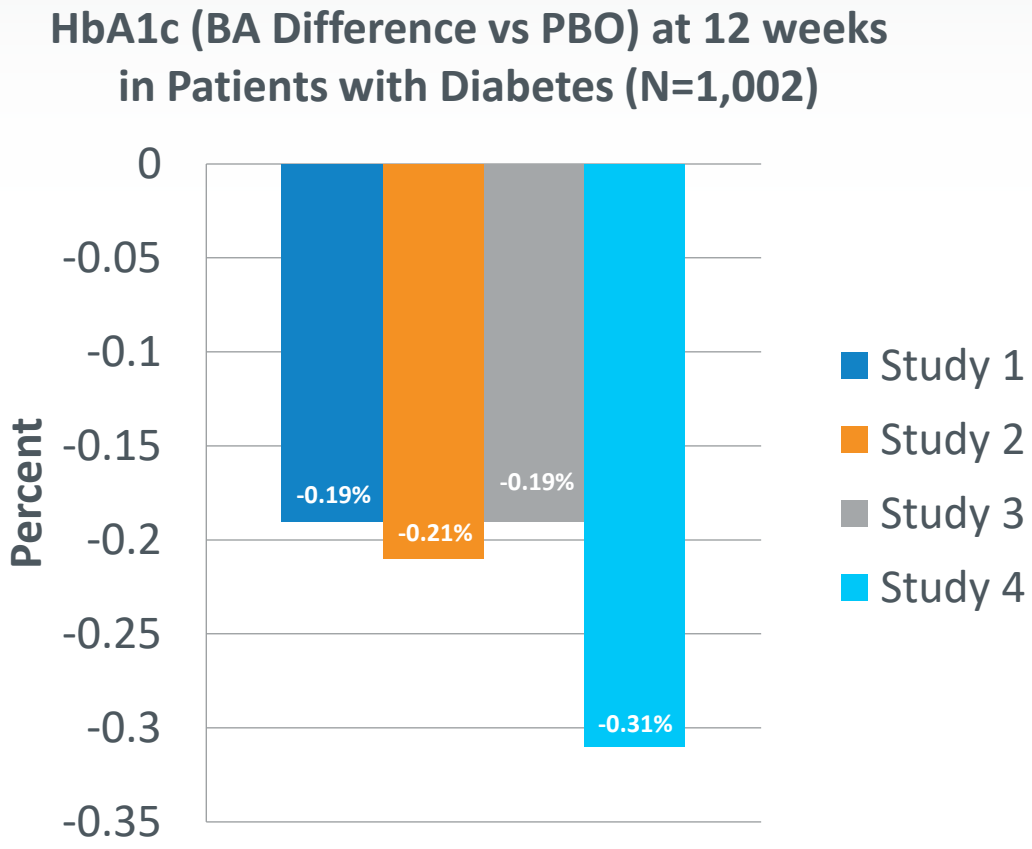
Overview of LFT Elevations > 3x ULN (ALT/AST)		
Drug Name	**Drug Arm**	**Placebo**
FDA Approved Drugs[1]		
Simvastatin 40mg – 80mg	0.9% - 2.1%	-
Atorvastatin 10mg - 80mg	0.2% - 2.3%	-
Vytorin 10mg/10mg – 80mg	1.7% - 2.6%	0.6%
Rosuvastatin 5-40 mg	1.1%	0.5%
Ezetimibe 10 mg	0.5%	0.3%
Phase 3 Development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

1 = Data collected from FDA approved package inserts for each drug.
2 = Cumulative Phase 3 Program: Bempedoic acid n=2424, placebo=1197

Bempedoic Acid – Cumulative Phase 3 Summary

Consistent Reductions in HbA1c and New Onset Diabetes

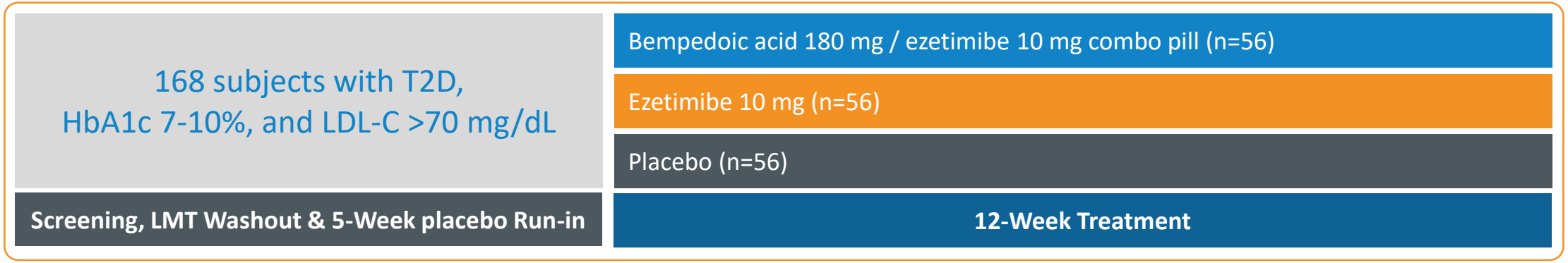
- 4 out of 5 patients with diabetes over age 65 die from ASCVD
- **Cumulative Phase 3 data demonstrate that new onset or worsening of diabetes occurred less frequently in patients taking statins plus bempedoic acid (4.0%) than in patients taking statins plus placebo (5.6%)**
- Statins, especially high-intensity 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.



Ongoing Clinical Studies

Bempedoic Acid / Ezetimibe Combination Pill Phase 2 Study

Patients with T2D and Elevated LDL-C: Top-Line Results in 2H19

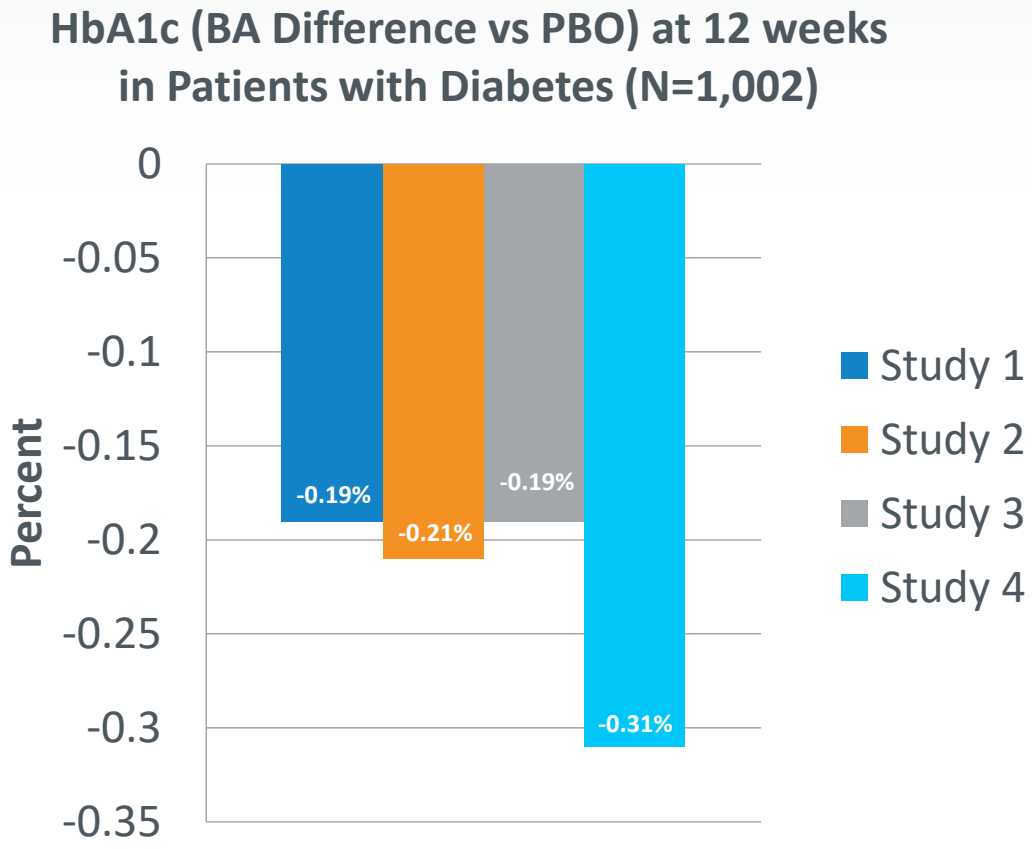


- **Co-Primary Objectives**
  - LDL-C lowering efficacy of the bempedoic acid / ezetimibe combination pill vs placebo
  - LDL-C lowering efficacy of the bempedoic acid / ezetimibe combination pill vs ezetimibe
- **Secondary Objectives**
  - hsCRP, non-HDL-C, ApoB, total cholesterol and TGs
  - Safety and tolerability
- **Exploratory Objectives**
  - HbA1c, fasting glucose, fasting insulin, insulin resistance, beta cell function, and additional glycemic measurements

Bempedoic Acid – Cumulative Phase 3 Summary

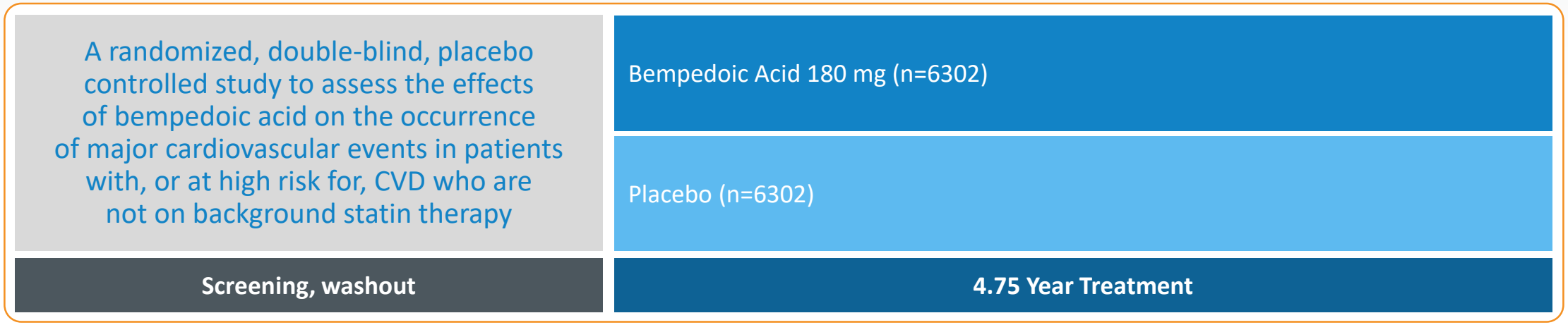
Consistent Reductions in HbA1c and New Onset Diabetes

- 4 out of 5 patients with diabetes over age 65 die from ASCVD
- **Cumulative Phase 3 data demonstrate 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.



CLEAR Outcomes CVOT to Support CVD Risk Reduction

ASCVD/High-Risk 1° Prevention CVOT: Top-Line Results Expected by 2022



- **Study Initiated Q4 2016;** all countries approved; full enrollment expected by 3Q19
- **Primary Endpoint:** Effect of bempedoic acid vs placebo on four-component MACE
  - CV death, non-fatal MI, non-fatal stroke, or coronary revascularization (minimum of 1437 events)
- **Target Enrollment:** ~12,600 patients randomized 1:1; ~900 sites, 30 countries
- **Baseline LDL-C levels:** 100-190 mg/dL in 2° prevention and ≥ 100 mg/dL in 1° prevention; expected mean baseline > 135 mg/dL
- **Study Chairman:** Steven Nissen M.D.
- **Co-Principal Investigators**: A. Michael Lincoff M.D. and Stephen Nicholls M.D.

CLEAR Outcomes: Designed for Success

- CLEAR Outcomes is designed for success for the following reasons:
  - Enrolling patients who are on no statin or less than the lowest approved daily starting dose of a statin – and at high baseline CV disease risk (secondary prevention or high-risk primary prevention)
  - Enrolling patients with significantly higher mean baseline LDL-C levels (~135 mg/dL) compared to ODYSSEY and FOURIER (~90 mg/dL) and IMPROVE-IT (~69 mg/dL)
    - Absolute mg/dL LDL-C lowering – not % LDL-C lowering – drives CV risk reduction benefit (CTT)
  - Patients mean duration of treatment in CLEAR will be ~4 years compared to 2.2-2.8 years in ODYSSEY/FOURIER
    - Longer treatment duration produces greater relative risk reduction (CTT analysis)
- Powered to show at least a 14% CV RR benefit with high potential to deliver better CV risk reduction than recent CVOTs
- Potential for “upside” CV RR benefit due to the hsCRP reductions and high baseline hsCRP levels
- Post-CVOT we expect a much broader label similar to the recent precedent established with evolocumab

NASH Program and Sustained Release formulation

Program Development

- NASH is a chronic liver disease marked by increased hepatic fat, inflammation, and liver cell damage that eventually leads to increased liver-related mortality
- Aberrant fatty acid biosynthesis is believed to be a key contributing factor to the pathogenesis of NASH
- Inhibition of ACL by ETC-1002-CoA reduces both cholesterol and fatty acid biosynthesis
- Similar to fatty acid synthesis inhibition by Acetyl-Coenzyme A Carboxylase (ACC) inhibitor therapies, bempedoic acid treatment reduces liver fat and inflammation, and improves insulin sensitivity in several well-accepted preclinical models of metabolic disease/NASH
- In an insulin-independent model of NASH, bempedoic acid treatment improved multiple metabolic abnormalities and promoted anti-inflammatory and anti-fibrotic effects, which results in a reduced NAFLD activity score and inhibition of fibrosis progression.

Next Steps

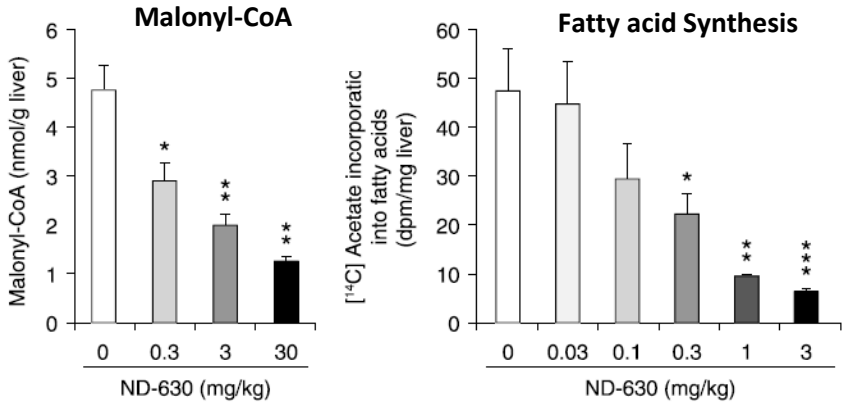
- Finalize mechanistic investigations in STAM™ mice and assess potential translation to humans
  - Data available around YE18
- Complete Phase 1 Study of the sustained release formulation of bempedoic acid
  - Differentiates the LDL-C lowering program from the NASH program
  - Dose optimization for NASH-related outcomes
- Announce Phase 2 NASH development plans and timelines in 1H19

Acute Effects of Bempedoic Acid and Gilead's GS-0976 (ND-630) on Fatty Acid Metabolism in Rats and Human

Mechanism Marker: Liver Malonyl-CoA Levels and Fatty Acid Synthesis

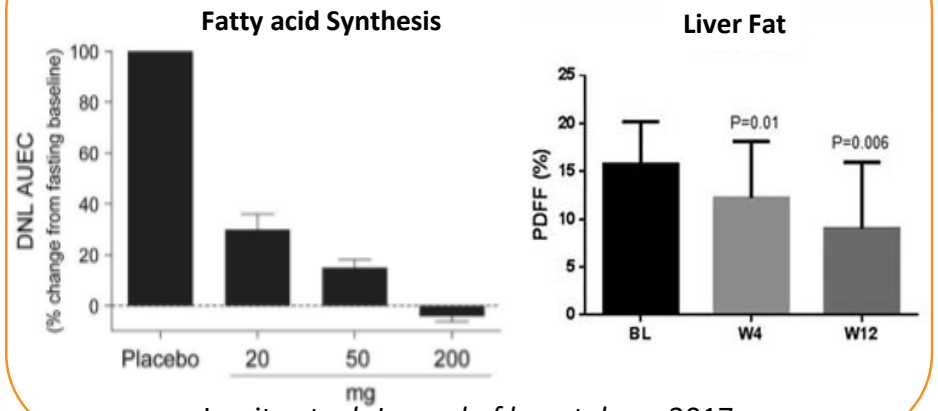
Rat → **Human**

ND-630 (GS-0976)



Harriman *et. al.* PNAS; 2016

ND-630 (GS-0976)



Lawitz *et. al. Journal of hepatology*; 2017

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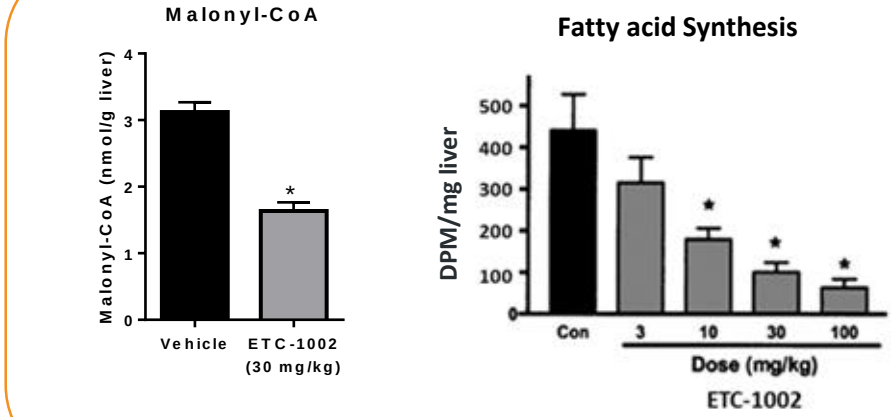

Pinkosky *et al. JLR;* 2013, Cramer *et al. JLR*;2004

→ **Human ?**