UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of Earliest Event Reported): **May 8, 2018**

Esperion Therapeutics, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**001-35986**	**26-1870780**
(State or other jurisdiction of incorporation)	(Commission File Number)	(I.R.S. Employer Identification No.)

3891 Ranchero Drive, Suite 150 **Ann Arbor, MI**	**48108**
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code: **(734) 887-3903**

Not Applicable
Former name or former address, if changed since last report

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

o Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

o Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

o Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

o Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 or Rule 12b-2 of the Securities Exchange Act of 1934.

Emerging growth company o

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. o

Item 7.01 Regulation FD Disclosure.

Esperion Therapeutics, Inc. (the "Company") has prepared an investor presentation (the "Presentation") for posting on the Company's website. A copy of the Presentation is furnished herewith as Exhibit 99.1.

The information set forth under Item 7.01 and in Exhibit 99.1 attached hereto is intended to be furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934 (the "Exchange Act") or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, except as expressly set forth by specific reference in such filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	**Description**
99.1	Presentation dated May 8, 2018.

* * *

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: May 8, 2018

Esperion Therapeutics, Inc.

By: /s/ Tim M. Mayleben
Tim M. Mayleben
President and Chief Executive Officer

Esperion
The Lipid Management Company

Study 1 (1002-040)

Pivotal Phase 3 Long-Term Safety Study Supplemental Materials

MAY 8, 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 anticipated safety and efficacy profile 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 approval or necessarily be predictive of the results of future or ongoing clinical studies, 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.

Study 1 (040) Supplemental Materials

- Supplemental Materials Summary
- Comparison of Study 1 with pcsk9i Pivotal Phase 3 Long-Term Studies
  - Baseline Demographics
  - AE(s), SAE(s), Discontinuations due to AE(s), Fatal AEs
- Individual Patient Narratives for Fatal AE(s), none related to study treatment
- Adjudicated Cardiovascular Safety Events Tables
- Liver Function Test Tables
- Recent Precedents of the Efficacy of LDL-C Lowering Therapy Waning Over Time
- CVOT Powering Assumptions
- Bempedoic Acid Mechanism of Action (MOA) is inhibition of ATP-Citrate Lyase

Study 1 (040) Supplemental Materials Summary

- By design, Study 1 enrolled the oldest and highest CV risk patient population of all recently completed long-term LDL-C lowering clinical studies with high levels of smoking, obesity and elevated blood pressure
  - As a result, safety event rates were in the range expected for this high-risk population
- ALL fatal AE(s) were considered unrelated to study treatment, and pooled pcsk9i event rates (0.9%) were comparable to the 0.9% rate observed in Study 1
  - 5 were due to cardiac events, 3 of which were heart attacks (MI) within the first 61 days after randomization in patients who had had coronary events prior to entering the study
  - 5 were due to cancer; 4 lung cancer, by far the leading cause of cancer death in older people; with 80% of lung cancer deaths caused by smoking and for which symptoms typically don't appear until the cancer is advanced.
- The fully-independent DMC has consistently reviewed both the Phase 3 and CVOT safety results and recommended continuation of the program
- Measures of adjudicated cardiovascular events ALL favored bempedoic acid over placebo
- Liver Function Tests (LFTs) elevations were as expected, very low overall, and consistent with statins and ezetimibe
- As expected, LDL-C lowering efficacy with bempedoic acid was less at 52 weeks than at 12 weeks, consistent with long-term studies of ALL approved LDL-C lowering therapies
- Bempedoic acid's MOA has been conclusively demonstrated as inhibition of ATP-Citrate Lyase

Comparison of Study 1 to Recent PCSK9i Long-term Studies

- Study 1 baseline demographics indicate patients are 10 – 15 years older than patients in recent comparable long-term LDL-C lowering studies, at higher risk for cardiovascular disease due to obesity and other factors, and at higher risk for lung cancer as almost 70% are current or former smokers
- As shown on Slides 6 and 7:
  - The overall rate of AE(s) is comparable with recent long-term studies of LDL-C lowering therapies
  - The rate of serious AE(s) is comparable with recent long-term studies of LDL-C lowering therapies
  - The rate of fatal AE(s) is low overall, but to be expected for the high-risk patient population enrolled in the study who have had at least one CV event and multiple other serious risk factors including smoking, obesity, high cholesterol, diabetes, hypertension, etc.
  - An imbalance in fatal AE(s) is a function of small numbers, and has also been observed in recent long-term studies of LDL-C lowering therapies
- We include individual patient narratives for each fatal AE
  - Neoplasms benign, malignant and unspecified
  - Cardiac Disorders
  - Other

Comparison of Study 1 to Recent PCSK9i Long-term Studies

Demographics & Baseline Characteristics

Mean ± SD [a]

	Bempedoic Acid – Study 1		Alirocumab – ODYSSEY FH I		Evolocumab – DECARTES	
	Bempedoic Acid N=1,488	Placebo N=742	Alirocumab N=323	Placebo N=163	Evolocumab N=599	Placebo N=302
Demographics						
Age: years	65.8 ± 9.1	66.8 ± 8.6	52.1 ± 12.9	51.7 ± 12.3	55.9 ± 10.8	56.7 ± 10.1
Gender: % Male (M/F)	73.9% (1099/389)	71.3% (529/213)	55.7% (180/322)	57.7% (94/163)	48.4% (290/599)	46.4% (140/302)
Baseline Characteristics						
BMI: kg/m^2	29.7 ± 4.9	29.4 ± 4.9	29.0 ± 4.6	30.0 ± 5.4	29.9 ± 6.1	30.5 ± 5.9
History of ASCVD Only: % (N)	95.1% (1415)	95.3% (707)	CHD = 45.5% (147)	CHD = 47.9% (78)	CAD=15.7% (94)	CAD = 13.9% (42)
HeFH (with or without ASCVD): % (N)	4.9% (73)	4.7% (35)	99.7% (322)	100% (163)	n/a	n/a
Diabetes: % (N)	28.6% (425)	28.6% (212)	9.9% (32)	15.3% (25)	10.4% (62)	13.9% (42)
Hypertension: % (N)	78.9% (1174)	80.1% (594)	43.0% (139)	43.6% (71)	48.2% (289)	49.3% (149)
History of neoplasms benign, malignant and unspecified (including cysts and polyps)	12.4% (184)	14.3% (106)	n/a	n/a	n/a	n/a
LDL-C (mg/dL)						
LDL-C: mg/dL	103.6 ± 29.1	102.3 ± 30.0	144.7 ± 2.9	144.4 ± 3.7	104.2 ± 22.1	104.0 ± 21.6
Tobacco History: % (N)						
Current User: % (N)	16.9% (251)	13.9% (103)	12.1% (39)	18.4% (30)	14.5% (87)	15.9% (48)
Former User: % (N)	49.9% (742)	54.6% (405)	ND	ND	ND	ND
Never Used: % (N)	32.5% (484)	31.0% (230)	ND	ND	ND	ND
Missing: % (N)	0.7% (11)	0.5% (4)	ND	ND	ND	ND

[a] Unless otherwise indicated [b] Median Values Full Analysis Set Population

Comparison of Study 1 to Recent PCSK9i Long-term Studies

Adverse Events (AEs)

	Bempedoic Acid – Study 1		Alirocumab – ODYSSEY FH I		Evolocumab – DESCARTES	
	Bempedoic Acid N=1,488	Placebo N=742	Alirocumab N=323	Placebo N=163	Evolocumab N=599	Placebo N=302
Any AE(s)	78.5% (1167)	78.7% (584)	81.7% (263)	79.1% (129)	74.8% (448)	74.2% (224)
Serious AE(s)	14.5% (216)	14.0% (104)	13.7% (44)	13.5% (22)	5.5% (33)	4.3% (13)
Discontinuation due to AE(s)	10.9% (162)	7.1% (53)	3.4% (11)	6.1% (10)	2.2% (13)	1.0% (3)
Fatal Adverse Events – Unrelated to Study Treatment	0.9% (13)[1]	0.3% (2)	1.9% (6)[2]	0% (0)	0.3% (2)[3]	0% (0)

[1] 13 deaths occurred in the bempedoic acid group: four due to lung cancer, one due to metastatic cancer, two myocardial infarction, one myocardial ischemia, two cardiac failure, one due to pancreatitis, one due to multiple organ failure and one due to severe ischemic apoplexy.
[2] Six deaths occurred in the alirocumab group in FH I during study treatment, two due to metastatic cancer (non-small cell lung cancer and pancreatic carcinoma with secondary Trousseau syndrome causing multiple embolic strokes), one due to acute MI, two classified as due to sudden cardiac death (congestive cardiac failure and coronary artery disease.
[3] Two deaths were from cardiac failure and myocardial infarction.

Blom et al. N Engl J Med 2014;370:1809-1819, Kastelein et al. Eur Heart J 2015;36:2996-3003

1002-040 (Study 1) Long-Term Safety Study – Safety & Tolerability

Fatal Adverse Events – *ALL JUDGED UNRELATED TO STUDY TREATMENT*

	% (Number) of Patients	
	Bempedoic acid 180 mg (N=1487)	Placebo (N=742)
Patients with Unrelated Fatal Adverse Events	**0.9% (13)**	**0.3% (2)**
Cardiac disorders (adjudicated)	0.3% (5)	0.1% (1)
Neoplasms benign, malignant and unspecified	0.3% (5)[1]	0
Infections and infestations	0.1% (1)	0.1% (1)
Gastrointestinal disorders	0.1% (1)	0
Nervous system disorders	0.1% (1)	0
Patients with Related Fatal Adverse Events	**0.0% (0)**	**0.0% (0)**

*Fatal Adverse Events are those reported starting from Day 1 when study drug is initiated through 30 days following last dose of study drug
All Fatalities Judged Unrelated to Study Medication by Investigator & Independent Adjudication Committee no issues raised by the Data Monitoring Committee
[1] One patient was listed with two co-primary causes of death of lung cancer and COPD. This one patient is listed under neoplasms.

Individual Patient Narratives

Individual Patient Narrative

Patient 1 – Unrelated Fatal AE of Malignant Lung Neoplasm

- Demographics: 71-80 years old, male (Europe)
- Relevant medical history: COPD, former smoker
- Relevant concomitant medications: n/a
- Description:
  - Day 17: AE of malignant lung neoplasm reported (CT chest scan to follow-up on a pre-existing pulmonary mass)
  - Day 29: Study drug interrupted for lung resection surgery, pathology showed NSCLC
  - Day 38: Study drug resumed
  - Day 85: Study drug discontinued due to lung neoplasm malignant
  - Day 99: Patient was hospitalized due to progression of the lung neoplasm
  - Day 114: Patient discharged from hospital
  - Day 129: Patient died (lung cancer)

Individual Patient Narrative

Patient 2 – Unrelated Fatal AE of Lung Adenocarcinoma

- Demographics: 71-80 years old, male (Europe)
- Relevant medical history: puncture of a large pleural effusion on right with no evidence of malignancy, nicotine abuse
- Relevant concomitant medications: n/a
- Description:
  - Day 3: Study drug discontinued due to muscle cramps (Note: study drug never re-started)
  - Day 27: Patient hospitalized for pleural effusion (fluid buildup in lung)
  - Day 43: Patient underwent partial pleurectomy, with drains inserted
  - Day 61: Patient diagnosed with severe lung adenocarcinoma as result of lung biopsy revealed right pleural carcinoma with pronounced tumor load
  - Day 61: Patient discharged from hospital
  - Day 61: AE reported
  - Day 87: Patient died (lung adenocarcinoma)

Individual Patient Narrative

Patient 3 – Unrelated Fatal AE of Malignant Lung Squamous Cell Carcinoma

- Demographics: 61-70 years old, female (Europe)
- Relevant medical history: former smoker
- Relevant concomitant medications: n/a
- Description:
  - Day 87: Patient diagnosed with lung squamous cell carcinoma metastatic
  - Day 87: AE reported
  - Day 141: Patient hospitalized, underwent radiation therapy
  - Day 148: Study drug discontinued due to lung carcinoma.
  - Day 156: Patient rehospitalized, underwent radiation therapy. Patient later entered home hospice care
  - Day 204: Patient died (lung adenocarcinoma)

Individual Patient Narrative

Patient 4 – Unrelated Fatal AE of Malignant Lung Neoplasm and COPD

- Demographics: 81-90 years old, male (Europe)
- Relevant medical history: end-stage COPD, abdominal aortic aneurysm, smoker
- Relevant concomitant medications: n/a
- Description:
  - Day 120: Patient underwent CT for AAA, evidence for cancer noted (approximate date)
  - Day 142: Diagnosis of lung cancer confirmed by PET scan
  - Day 142 AE reported
  - Day 252: Study drug discontinued
  - Day 268: Patient hospitalized due to increased breathlessness
  - Day 270: Patient transferred to palliative care
  - Day 303: Patient died (lung cancer and COPD)

Individual Patient Narrative

Patient 5 – Unrelated Fatal AE of Metastases to Liver

- Demographics: 71-80 years old, male (Europe)
- Relevant medical history: Bowen's disease (squamous cell carcinoma in situ), smoker
- Relevant concomitant medications: n/a
- Description:
  - Day 235: Patient presented with decreased appetite, weight loss, rash
  - Day 235: Study drug discontinued
  - Day 240: Abdominal ultrasound shows liver metastases with no primary source identified
  - Day 240: AE reported
  - Day 242: Patient hospitalized with jaundice and abdominal pain; CT scan showed diffuse malignancy within liver
  - Day 252: Patient died (metastases to liver)

Individual Patient Narrative

Patient 6 – Unrelated Fatal AE of Heart Failure

- Demographics: 71-80 years old, male (Europe)
- Relevant medical history: acute MI, stage III chronic kidney disease, heart failure, coronary revascularization, aortic aneurysm, type 2 diabetes, hypertension, CHD
- Relevant concomitant medications: aspirin, metoprolol, trapidil (anti-platelet), torsemide (diuretic), sacubitril/valsartan (Entresto), ezetimibe, atorvastatin
- Description:
  - Day 164: Patient hospitalized for edema secondary to cardiac decompensation
  - Day 169: Event reported resolved
  - Day 183: Patient hospitalized for GI discomfort
  - Day 192: Event considered resolved
  - Day 228: Patient hospitalized with severe heart failure
  - Day 228: Study drug discontinued
  - Day 228: AE reported
  - Day 228-232: Patient had tracheobronchitis, was intubated, X-ray confirmed congested upper left lobe focal abscess
  - Day 233: Patient died

Individual Patient Narrative

Patient 7 – Unrelated Fatal AE of Heart Failure

- Demographics: 61-70 years old, female (Europe)
- Relevant medical history (including co-morbidities): hypertension, ischemic heart disease, type 2 diabetes
- Relevant concomitant medications: aspirin, lercanidipine, nebivolol, aspirin, rosuvastatin
- Description:
  - Day 114: Patient felt weak at dinner, lost consciousness, could not be revived
  - Day 114: AE reported
  - Day 114: Patient died

Individual Patient Narrative

Patient 8 – Unrelated Fatal AE of Myocardial Infarction

- Demographics: 61-70 years old, female (Europe)
- Relevant medical history: acute MI, type 2 diabetes
- Relevant concomitant medications: lisinopril, amlodipine, bisoprolol, gliclazide, metformin, simvastatin
- Description:
  - Day 11: Patient hospitalized; laparoscopy revealed internal hernia. Keyhole surgery performed
  - Day 11: Study drug interrupted
  - Day 17: Event considered resolved; patient discharged from hospital
  - Day 18: Study drug resumed
  - Day 60: Last day of study drug
  - Day 61: Patient woke with shoulder pain and emergency services called. Patient went into cardiac arrest
  - Day 61: Patient died
  - Day 61: AE reported

Individual Patient Narrative

Patient 9 – Unrelated Fatal AE of Myocardial Ischemia, Hypertensive Heart Disease

- Demographics: 61-70 years old, male (Europe)
- Relevant medical history: ischemic heart disease, triple CABG, double CABG, atrial fibrillation, left ventricular heart failure, cardiomyopathy, angina, PAD requiring angioplasty
- Relevant concomitant medications: aspirin, bisoprolol, furosemide, ramipril, warfarin, eplerenone, simvastatin
- Description:
  - Day 48: Patient found dead at home
  - Day 48: AE reported

Individual Patient Narrative

Patient 10 – Unrelated Fatal AE of Myocardial Infarction

- Demographics: 61-70 years old, male (Europe)
- Relevant medical history: acute MI, heart failure, coronary revascularization, type 2 diabetes, smoking, hypertension
- Relevant concomitant medications: aspirin, insulin, metformin, liraglutide, empagliflozin, bisoprolol, nitrates, ivabradine, nicorandil, nitroglycerine, simvastatin
- Description:
  - Day 28: Patient suffered MI and died
  - Day 28: AE reported
  - Date of last known dose of study drug unknown

Individual Patient Narrative

Patient 11 – Unrelated Fatal AE of Acute Pancreatitis, Acute Cholecystitis, Pancreatic Pseudocyst, and Pancreatic Adenocarcinoma

- Demographics: 61-70 years old, male (U.S.)
- Relevant medical history: upper abdominal pain
- Relevant concomitant medications: aspirin, ondansetron, pantoprazole, oxycodone/acetaminophen, lisinopril, pravastatin
- Description:
  - Day 30: Study drug discontinued – increase in pancreatic enzymes day 3, day 15
  - Day 47: AE of pancreatic pseudocyst reported
  - Day 228: Patient hospitalized for abdominal pain; diagnosed with hyponatremia, cholecytitis, pancreatic mass
  - Day 230: Patient diagnosed with pancreatic adenocarcinoma
  - Day 232: Patient had seizure, suffered cerebral infarct
  - Day 238: Patient discharged from hospital to hospice care
  - Day 239: Patient died

Individual Patient Narrative

Patient 12 – Unrelated Fatal AE of Ischemic Cerebral Infarction/Severe Ischemic Apoplex

- Demographics: 51-60 years old, male (Europe)
- Relevant medical history: coronary artery disease, hypertension, coronary revascularization, acute MI
- Relevant concomitant medications: aspirin, candesartan, bisoprolol, atorvastatin
- Description:
  - Day 190: Patient hospitalized with severe ischemic stroke; lysis unsuccessful; thrombectomy performed; developed cerebral bleeding
  - Day 190: AE reported
  - Day 192: Patient died

Individual Patient Narrative

Patient 13 – Unrelated Fatal AE of Multiple Organ Failure

- Demographics: 71-80 years old, male (Europe)
- Relevant medical history: COPD, angina, coronary artery disease, hypertension, ischemic stroke
- Relevant concomitant medications: atenolol, clopidogrel, candesartan, bendroflumethiazide, atorvastatin
- Description:
  - Day 219: Patient admitted to hospital for epigastric and chest pain, confirmed cholecystitis
  - Day 232: Event reported resolved, patient discharged from hospital
  - Day 328: Patient hospitalized, underwent cholecystectomy, bile duct exploration, stenting
  - Day 331: Patient developed sepsis and bile leak
  - Day 331: Study drug discontinued
  - Day 332: Patient developed multiple organ failure and died

Individual Patient Narrative (Placebo)

Patient 1– Unrelated Fatal AE of Sepsis/Multiple Organ Failure

- Demographics: 61-70 years old, male (U.S.)
- Relevant medical history: hernia repair, sleep apnea
- Relevant concomitant medications: n/a
- Description:
  - Day 170: Patient hospitalized with multiple GI complaints
  - Day 170: Study drug (placebo) discontinued due to colon neoplasm
  - Day 171: Patient underwent unsuccessful colonoscopy due to narrowing of colon
  - Day 171: Patient developed peritonitis due to a ruptured colon
  - Day 174: Patient developed septic shock with multiple organ failure and died

Individual Patient Narrative (Placebo)

Patient 2 – Unrelated Fatal AE of Myocardial Infarction (adjudicated)

- Demographics: 61-70 years old, male (Europe)
- Relevant medical history: type 2 diabetes, diabetic neuropathy, peripheral artery disease, peripheral artery bypass
- Relevant concomitant medications: Lisinopril, aspirin, insulin, liraglutide, atorvastatin
- Description:
  - Day 160: Patient died at home

Adjudicated Cardiovascular Event Tables

Study 1 Adjudicated Cardiovascular Events

- The following slide shows adjudicated cardiovascular events for Study 1
  - All adjudicated CV events
  - 5-component MACE events
  - 4-component MACE events
- These early results show a trend favoring bempedoic acid over placebo in every analysis of CV events in Study 1 which ranged from a 19% to 8% CV event reduction. This is particularly notable since event (K-M) curves in recently completed outcomes studies for the pcsk9i's didn't separate until after the first year.
  - For all CV events
  - For 5-component MACE
  - For 4-component MACE

1002-040 (Study 1) – Adverse Events of Special Interest

Rates Clinical Endpoint Adjudicated Events – Treatment Emergent AE (TEAE) Analysis

Event	% (Number) of Patients	
	Bempedoic Acid (N= 1487)	Placebo (N=742)
All Adjudicated CV Events	4.6% (68)	5.7% (42)
Five-Component MACE Adjudicated Events[1]	3.8% (57)	4.6% (34)
Four-Component MACE Adjudicated Events[2]	3.6% (54)	3.9% (29)

[1]Includes Coronary Revascularization, CV Death, Non-Fatal MI, non-Fatal Stroke, Hospitalization For Unstable Angina
[2]Includes Coronary Revascularization, CV Death, Non-Fatal MI, non-Fatal Stroke

Rates of LFT Elevations for Oral LDL-C Lowering Therapies

Rates of LFT Elevations for Oral LDL-C Lowering Therapies

- LFT elevations have been seen with EVERY previously approved and successful oral, once-daily LDL-C lowering therapy
  - Statins – 0.2% - 2.3%
  - Ezetimibe – 0.5%
- LFT elevations with approved oral LDL-C lowering therapies and bempedoic acid have never been associated with serious liver injury
  - No increases in bilirubin
  - No cases of Hy's Law
- As expected, bempedoic acid has shown a *confirmed* rate of LFT elevations that is on the low-end of reported rates of LFT elevations for approved oral LDL-C lowering therapies and almost exactly the same as ezetimibe
  - For Study 1 – 0.40%
  - Completed Integrated Data – 0.49%
  - Total Ongoing Phase 3 Program – 0.54% (all blinded data in both arms)

Bempedoic Acid Integrated Safety

LFT Elevations are Rare

Overview of Liver Function Tests (AST/ALT) - % (number) of Patients						
LFT Increases (Repeated and Confirmed)	Phase 3 – Study 1 (040)		Completed Integrated Data[1]		Total Ongoing Phase 3 Program[3]	
	Bempedoic Acid N=1,487	Placebo[2] N=742	Bempedoic Acid N=2,434	Placebo[2] N=1,227	Bempedoic Acid N=2,423	Placebo[2] N=1,119
ALT/AST > 3 x ULN	0.54% (8*)	0.13% (1)	0.58% (14*)	0.08% (1)	~0.62% (15*)	0.09% (1)

[1] Completed Phase 2/Phase 3 data includes 1002-003, -005, -006, -007, -008, -009, -014, -035, -038, -039, -048 (Study 4) and -040 (Study 1)
[2]Placebo treatment group includes patients with no background therapy; low, moderate, or high intensity statins; and/or ezetimibe; or PCSK9i
[3]Based upon blinded data review as of March 2018 for Study 3 and Study 2 subject to variability until the end of the studies and as data are "cleaned;" assumes all elevations in bempedoic acid-treated patients for Studies 2 and 3; includes final data from Study 1 and Study 4
*Two patients from -040 who rolled over in to the -050 (OLE Study) who reported an initial LFT increase were found not to meet the definition of "repeated and confirmed" LFT elevations. Incorporating these data, the rate of LFT increases for -040 would be 0.40%; Completed Integrated Data would be 0.49%; Total Ongoing Phase 3 Program would be 0.54%.

Overview of Liver Function Tests for Statins and Ezetimibe[4] (AST/ALT)										
Dose	Atorvastatin		Rosuvastatin		Simvastatin		Ezetimibe		Vytorin	
	Atorva	Placebo	Rosuva	Placebo	Simva	Placebo	Eze	Placebo	Vytorin	Placebo
10mg	0.2%	-	1.1%	0.5%	-	-	0.5%	0.3%	1.7%	-
20mg	0.2%	-	1.1%	0.5%	-	-	N/A	N/A	1.7%	-
40mg	0.6%	-	1.1%	0.5%	0.9%	-	N/A	N/A	1.7%	-
80mg	2.3%	-	N/A	N/A	2.1%	-	N/A	N/A	2.6%	-

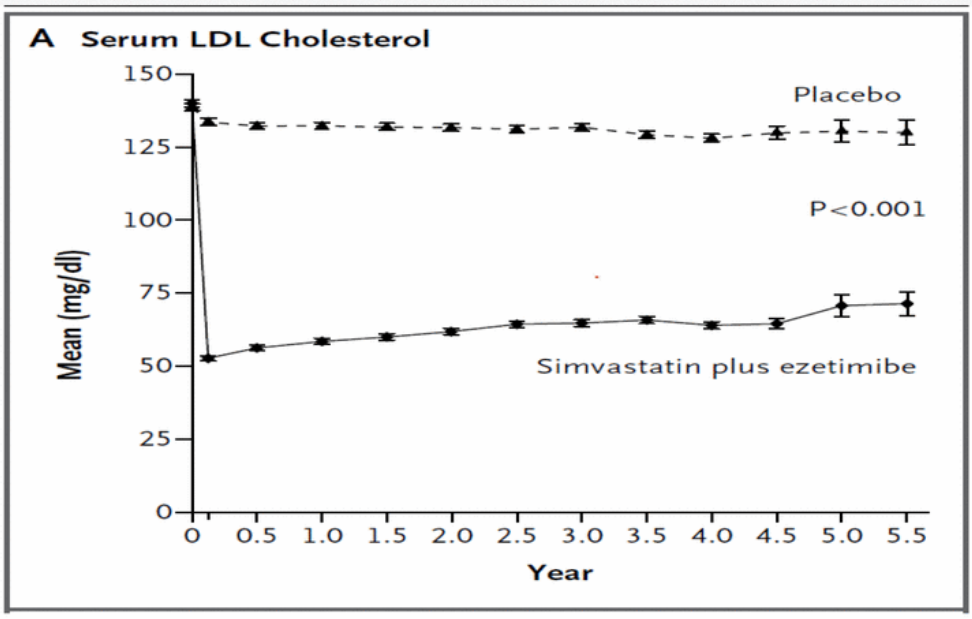
[4]Data collected from FDA approved package inserts for each drug. Note that all reported Liver Function Test increases occurred within 12 weeks of initiating therapy.

In Long-Term Studies, LDL-C Lowering Wanes Over Time

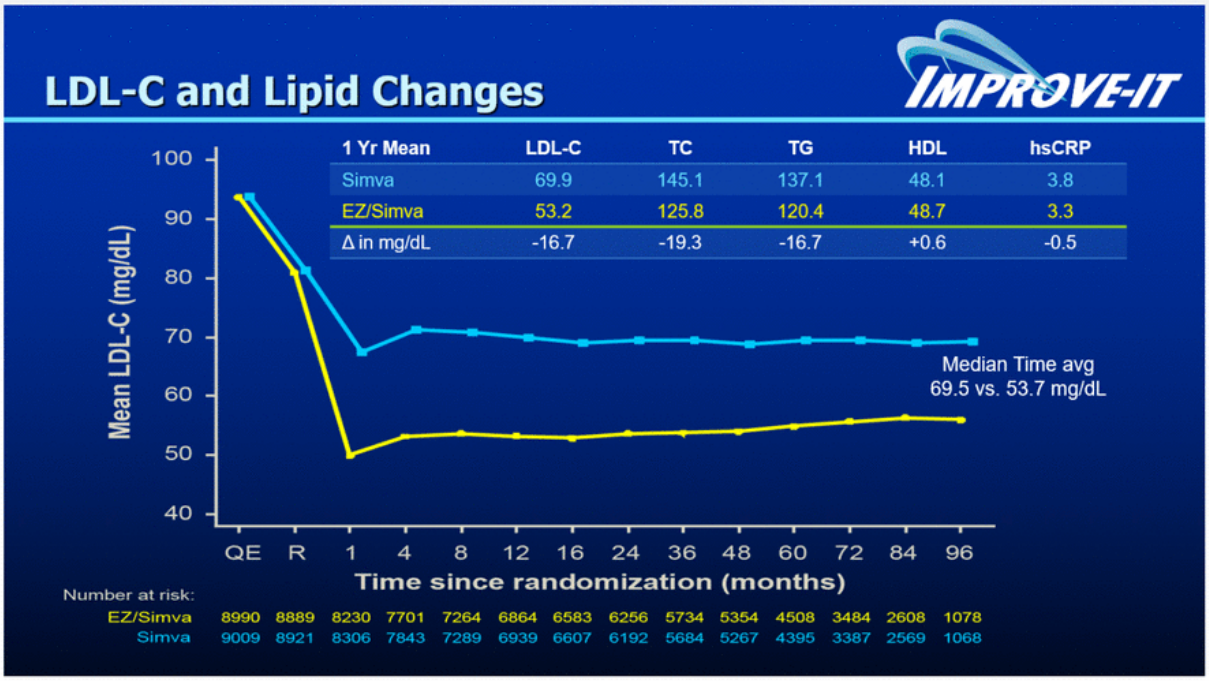
In Long-Term Studies, LDL-C Lowering Wanes Over Time

- As shown in the next several slides, the efficacy of every approved LDL-C lowering therapy has waned over time (e.g., during long-term studies):
  - Ezetimibe
  - Vytorin (simvastatin/ezetimibe)
  - Alirocumab
  - Evolocumab
  - Pravastatin
  - Atorvastatin
- The LDL-C lowering of bempedoic acid also waned over time from 20% at 12-weeks to 16% at 52-weeks (on-treatment)

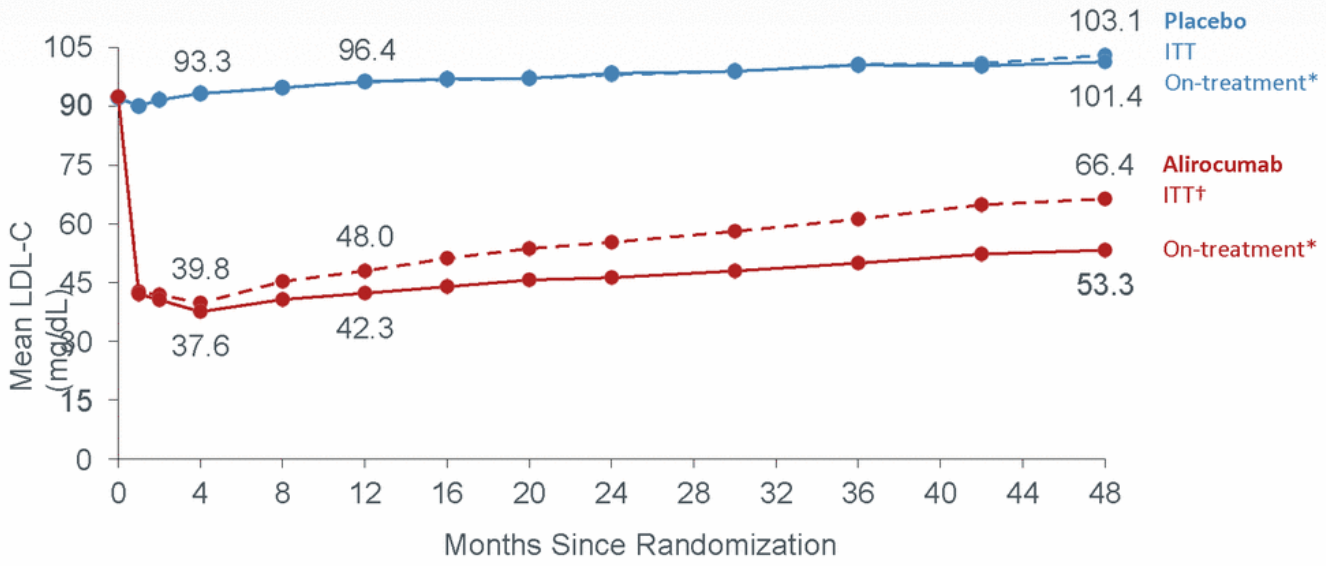
SEAS Study – Ezetimibe LDL-C Lowering Wanes Over Time



IMPROVE-IT – Ezetimibe/Simvastatin LDL-C Lowering Wanes Over Time



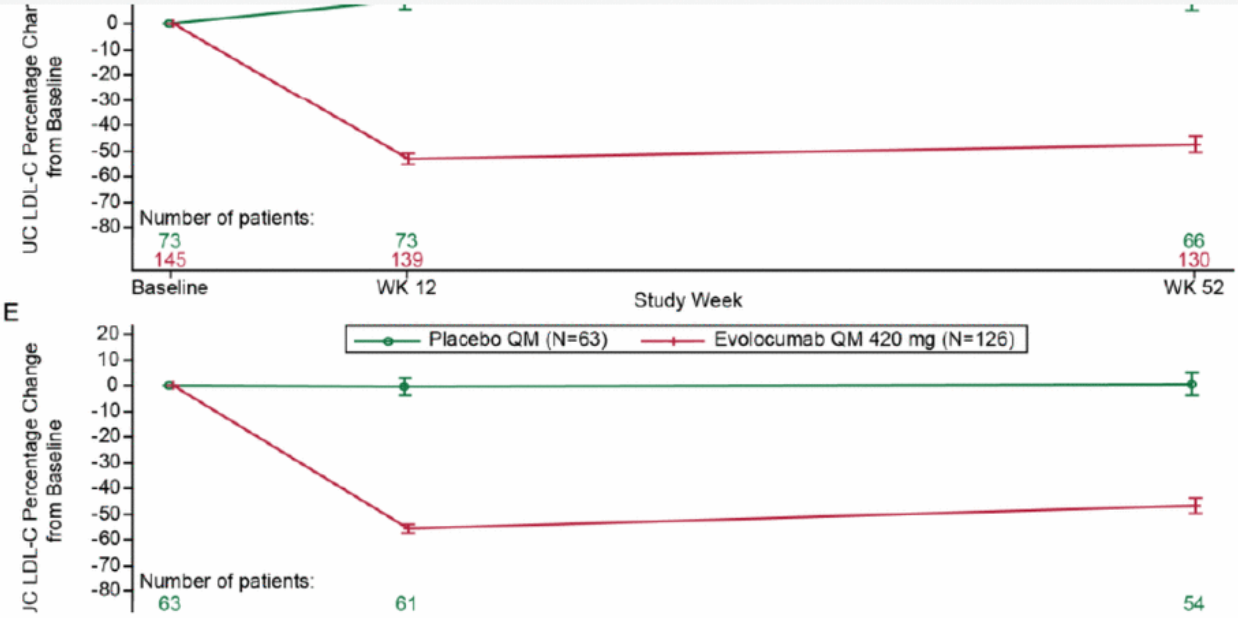
ODYSSEY Outcomes: Alirocumab LDL-C Lowering Wanes Over Time



*Excludes LDL-C values after premature treatment discontinuation or blinded switch to placebo
†All LDL-C values, including those after premature treatment discontinuation, blinded down titration, or blinded switch to placebo

DESCARTES – Evolocumab LDL-C Lowering Wanes Over Time

D = Atorva 80mg, E = 80mg + Eze



WOSCOPS – Pravastatin LDL-C Lowering Wanes Over Time

Statin CVOT involving 6595 patients over 5 years

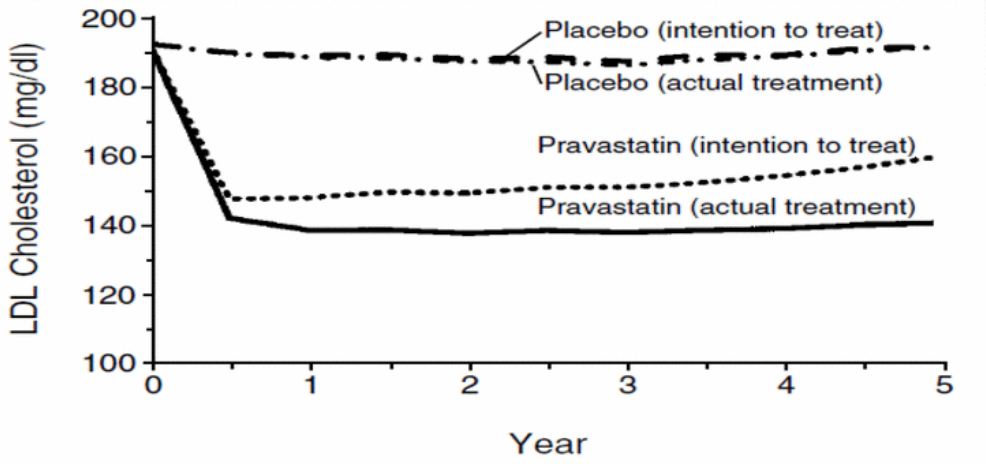
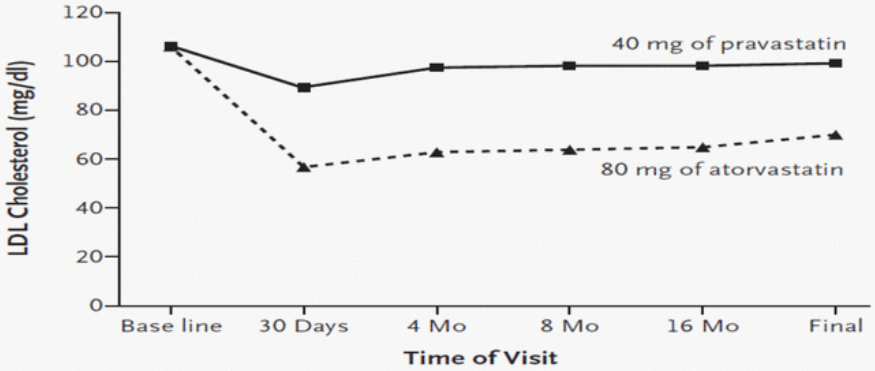


Figure 1. Effects of Pravastatin Therapy on Plasma LDL Cholesterol Levels.
To convert values for cholesterol to millimoles per liter, multiply by 0.026.

PROVE-IT – Statin LDL-C Lowering Wanes Over Time



No. of Patients						
Pravastatin	1973	1844	1761	1647	1445	1883
Atorvastatin	2003	1856	1758	1645	1461	1910

Figure 1. Median Low-Density Lipoprotein (LDL) Cholesterol Levels during the Study.
To convert values for LDL cholesterol to millimoles per liter, multiply by 0.02586.

CVOT Powering Assumptions

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Comparison of Patients Enrolled in Study 1 *vs* CLEAR Outcomes

Currently Enrolling

Mean ± SD [a]

		Bempedoic Acid – Study 1		CLEAR Outcomes
		Bempedoic Acid N=1,488	Placebo N=742	Bempedoic Acid/Placebo (1:1) Planned N=12,604
Demographics				
Age: years		65.8 ± 9.1	66.8 ± 8.6	65.5 ± 9.3
Gender: % Male (M/F)		73.9% (1099/389)	71.3% (529/213)	56.9%
Baseline Characteristics				
History of ASCVD Only: % (N)		95.1% (1415)	95.3% (707)	~70%
Diabetes: % (N)		28.6% (425)	28.6% (212)	34.9%
Hypertension: % (N)		78.9% (1174)	80.1% (594)	82.3%
LDL-C (mg/dL)				
LDL-C: mg/dL		103.6 ± 29.1	102.3 ± 30.0	135.9 ± 29.7
Baseline Statin Intensity % (N)				
No Statin or Less than Approved Daily Starting Dose		0.0% (0)	0.0% (0)	100% (12,604)
Low		6.7% (100)	6.5% (48)	0.0% (0)
Moderate		43.4% (646)	43.7% (324)	0.0% (0)
High		49.9% (742)	49.9% (370)	0.0% (0)

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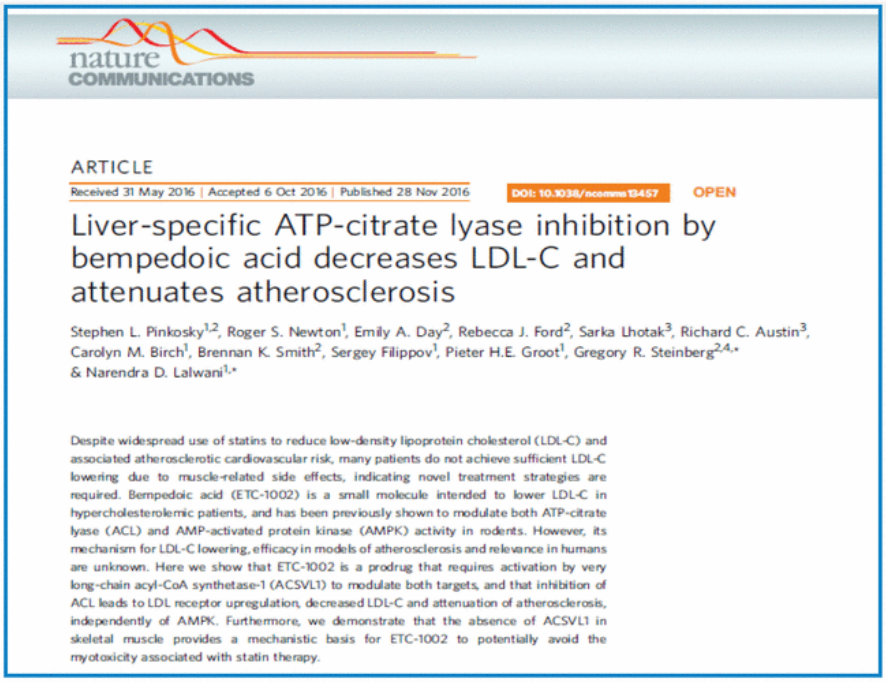
CLEAR Outcomes Powering Assumptions

- Designed to provide greater than 85% power to detect an ~14% relative risk reduction in the primary endpoint of the bempedoic acid treated group as compared with placebo
- Study expected to complete with a minimum of 1437 patients experiencing the primary endpoint and with all patients required to be on study drug for a minimum of two years
- Patient population comprised of high risk patients with or without ASCVD unable to benefit from therapeutic doses of statins
  - **Background therapy: No statin or "less than approved daily starting doses of statins"**
- Expected and current baseline LDL-C: ~135 mg/dL
  - With an expected 27% LDL-C lowering by bempedoic acid (similar to Study 4), the calculated unit (mg/dL) reduction is ~36 mg/dL, a reduction in LDL-C that predicts a relative risk reduction of ~20%, according to the Cholesterol Treatment Trialists formula
- Powering calculations assume that 10% of patients will discontinue treatment at study start.
  - Targeted patients have less available/effective options to control lipids and are more motivated to continue in the study – Study 048 had a lower drop out rate due to AEs
  - Statin related "side effects" unlikely to occur since statin usage will be minimal

Mechanism of Action

Bempedoic Acid Mechanism – ATP-citrate lyase inhibition



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ARTICLE

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Liver-specific ATP-citrate lyase inhibition by bempedoic acid decreases LDL-C and attenuates atherosclerosis

Stephen L. Pinkosky[1,2], Roger S. Newton[1], Emily A. Day[2], Rebecca J. Ford[2], Sarka Lhotak[3], Richard C. Austin[3], Carolyn M. Birch[1], Brennan K. Smith[2], Sergey Filippov[1], Pieter H.E. Groot[1], Gregory R. Steinberg[2,4,*] & Narendra D. Lalwani[1,*]

Despite widespread use of statins to reduce low-density lipoprotein cholesterol (LDL-C) and associated atherosclerotic cardiovascular risk, many patients do not achieve sufficient LDL-C lowering due to muscle-related side effects, indicating novel treatment strategies are required. Bempedoic acid (ETC-1002) is a small molecule intended to lower LDL-C in hypercholesterolemic patients, and has been previously shown to modulate both ATP-citrate lyase (ACL) and AMP-activated protein kinase (AMPK) activity in rodents. However, its mechanism for LDL-C lowering, efficacy in models of atherosclerosis and relevance in humans are unknown. Here we show that ETC-1002 is a prodrug that requires activation by very long-chain acyl-CoA synthetase-1 (ACSVL1) to modulate both targets, and that inhibition of ACL leads to LDL receptor upregulation, decreased LDL-C and attenuation of atherosclerosis, independently of AMPK. Furthermore, we demonstrate that the absence of ACSVL1 in skeletal muscle provides a mechanistic basis for ETC-1002 to potentially avoid the myotoxicity associated with statin therapy.

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ETC-1002/Bempedoic Acid Mechanism Summary

LDL-C Lowering via Tissue Specific ACL Inhibition

- **ETC-1002 is a prodrug and inhibits cholesterol synthesis by inhibition of ACL – an enzyme upstream of HMG-CoA reductase**
- ACL inhibition by ETC-1002-CoA
  - ETC-1002-CoA directly inhibits recombinant human ACL while parent ETC-1002 does not
  - ETC-1002-CoA inhibits cholesterol synthesis in primary human liver cells
  - ETC-1002-CoA increases LDL receptor activity in human liver cells
- ETC-1002 (prodrug) conversion to ETC-1002-CoA (active form)
  - Catalyzed by ACSVL1, an enzyme highly expressed in liver and not expressed skeletal muscle
  - ETC-1002-CoA is not detected in rodent skeletal muscle in vitro or in vivo
  - ETC-1002-CoA is not detected in primary human skeletal muscle cells in vitro or human skeletal muscle microsomes
  - Unlike statins, treatment with ETC-1002/bempedoic acid does not result in cholesterol synthesis inhibition nor promote skeletal muscle toxicity in vitro

Adapted from Pinkosky et al. Nature Communications. 2016 Nov 28; DOI: 10.1038/ncomms13457

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