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PHARMACOKINETIC, SAFETY AND EFFICACY DATA OF CAPRE®, A NOVEL INVESTIGATIONAL OMEGA-3 DRUG DERIVED FROM KRILL OIL

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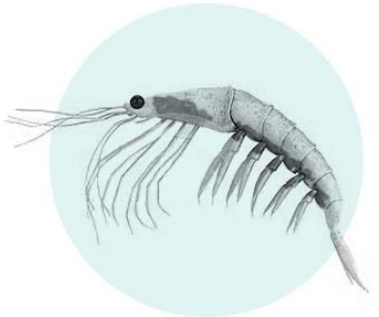
ACASTI PHARMA

CaPre®'s Novel Formulation Combines Phospholipids and Free Fatty Acid Forms of EPA and DHA

CaPre® (Acasti Pharma)



- A novel krill oil-derived mixture of PUFAs, primarily OM3, principally **EPA and DHA** present as a combination of phospholipid esters and free fatty acids
- Extracted and purified from Krill which is naturally rich in OM3 phospholipids
- CaPre® is supplied as a 1-gram hard-gel capsule containing approximately 310 mg of the sum of EPA and DHA
- First indication: for the treatment of severe hypertriglyceridemia (Phase 3)

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CaPre®'s Novel Formulation Combines Phospholipids and Free Fatty Acid Forms of EPA and DHA

	CaPre	Lovaza	Omtryg*	Vascepa	Epanova*
Sponsor	Acasti	GSK	Trygg Pharma	Amarin	AstraZeneca
Source material	Krill oil	Fish oil			
EPA/DHA (per g)	310 mg (EPA/DHA)	770 mg (EPA/DHA)	642 mg (EPA/DHA)	878 mg (EPA only)	750 mg (EPA/DHA)
Chemical form	PL esters and free fatty acids	Ethyl ester	Ethyl ester	Ethyl ester	Free Fatty Acids
Approved Dose	under investigation (4g/day)	4g/day	4.6g/d	4g/day	2 and 4g/day

**not yet marketed in USA*

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Four Clinical Studies Completed with CaPre®

Type of study	Study identifier and design	Test Product; Dose (g/day)	Number of Subjects	Duration of treatment	Population
Phase 1 PK	CAP13-101 Open-label, randomized, multiple-dose, single-center, parallel-design study	CaPre®; 1, 2 and 4	42	15 days	Healthy volunteers
Phase 1 Bridging study	PMRI 2016-4010 Single-Dose, Comparative Bioavailability Study of CaPre® 1 g Capsules compared to Lovaza® 1 g Capsules under Fasting and Fed Conditions	CaPre® and Lovaza® at 4	56	1 day (single-dose)	Healthy volunteers
Phase 2 Efficacy and Safety	PRT-API-NKPL66-CT-PIIB (COLT) Open-label, randomized, dose-ranging, multiple-center, parallel-design study	CaPre®; 0.5, 1, 2 and 4	288 total (259 on CaPre®; 29 on SoC)	8 weeks	Patients with hypertriglyceridemia (TG > 200 and < 877 mg/dL) (TG > 2.28 and < 10 mmol/L)
Phase 2 Efficacy and Safety	PRT-API-NKPL66-CT-PII (TRIFECTA) Double-blind, randomized, Placebo-controlled, dose-ranging, multiple-center, parallel-design study	CaPre®; 1 and 2	387 total (258 on CaPre®; 129 on Placebo)	12 weeks	Patients with hypertriglyceridemia (TG > 200 and < 877 mg/dL) (TG > 2.28 and < 10 mmol/L)
TOTAL SUBJECTS			**773 (no safety concerns)**		

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CAP13-101
CaPre® PK Profile Following Single and Multiple Oral Doses

Study Design

- Phase 1, open-label, randomized, multiple-dose, single-center, parallel-design study

- 42 healthy subjects enrolled into 3 groups (N= 14/group):
  CaPre® 1g daily x 15 days
  CaPre® 2g daily x 15 days
  CaPre® 4g daily x 15 days

- Drug administration 30 minutes from the start of low fat breakfast:
  - Therapeutic Lifestyle Changes (TLC) diet breakfast on Day 1 through Day 14
  - High fat (HF) breakfast on Day 15

Results

- CaPre PK profile (EPA+DHA) appears to be dose proportional both after single dose (Day 1) and multiple doses (Day 14)

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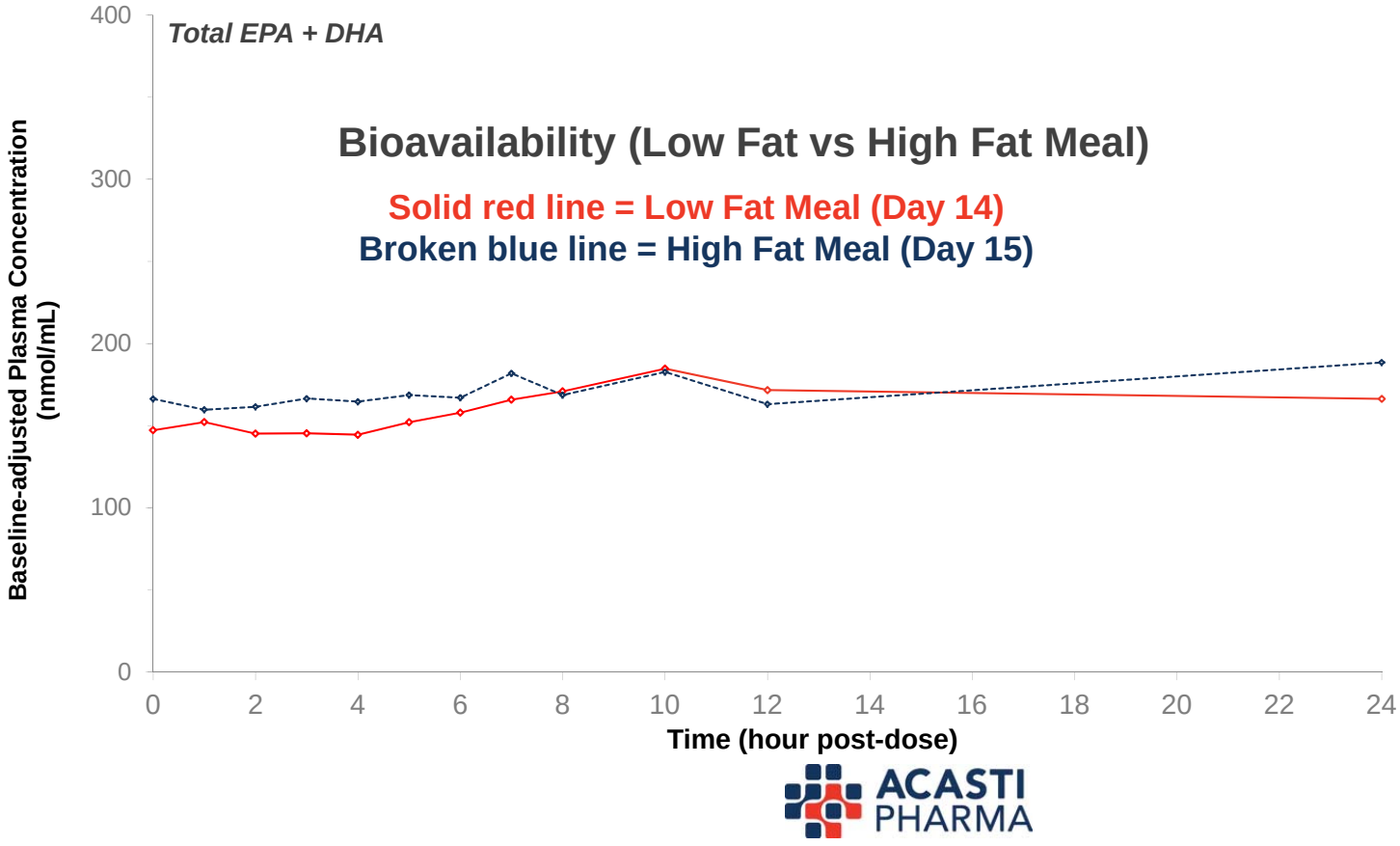
CAP13-101
CaPre® Single and Multiple Dose Pharmacokinetics – No Significant Food Effect



The bioavailability of CaPre (total EPA+DHA) does not appear to be meaningfully affected by the fat content of a meal after multiple daily doses @4g/day (< 20% difference in AUC)

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PMRI 2016-4010

A Phase 1, Single-Dose, Comparative Bioavailability Study of CaPre®, a Novel Omega-3 Derived from Krill Oil and Lovaza® under Fasting and Fed Conditions

Study Design:

- Open-label, single-dose, randomized, *crossover*, 4 periods comparative bioavailability study

Sample Size:

- N=56 randomized

Key Pharmacokinetic Parameters:

- Total exposure to EPA and DHA in blood ($\mathbf{AUC_{0\text{-}72\ hrs}}$)
- Peak concentration of EPA and DHA in blood ($\mathbf{C_{max}}$)

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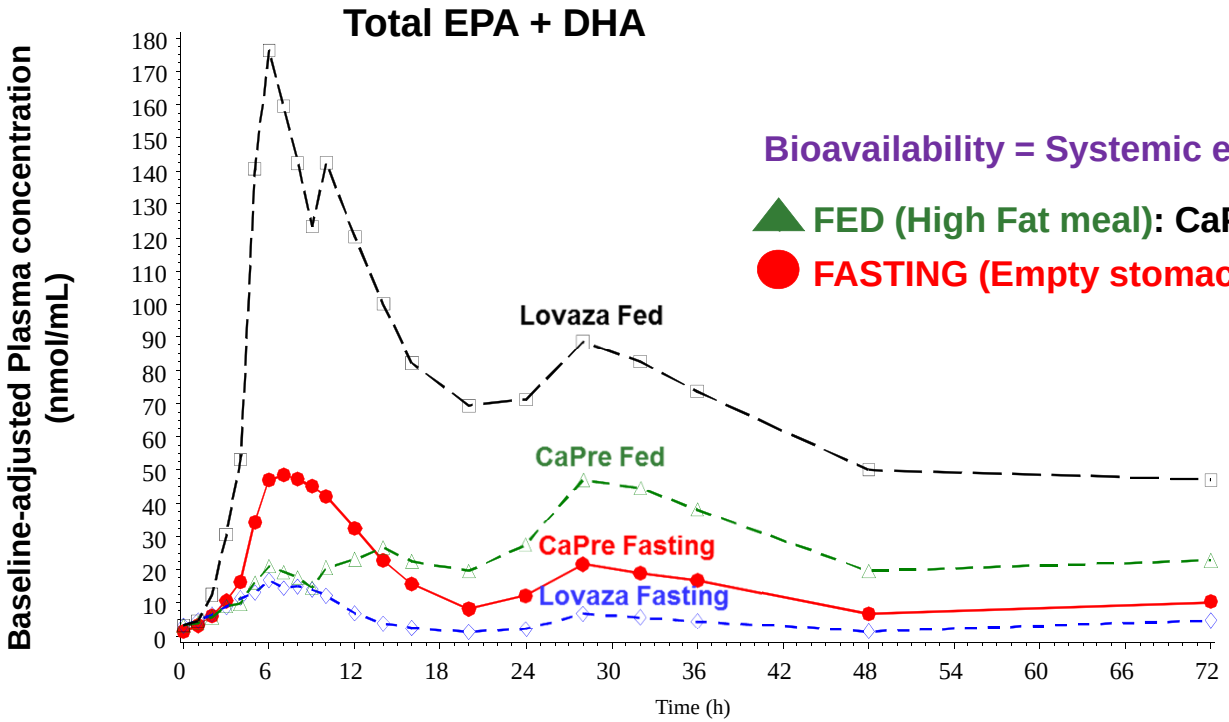
PMRI 2016-4010
Mean Plasma Baseline-Adjusted EPA + DHA Total Lipids Concentration-Time Profile Over 72h Following 4g Single-Dose of Administration Under Fasting and Fed Conditions



Bioavailability = Systemic exposure (AUC) and C_{MAX}

FED (High Fat meal): CaPre < Lovaza

FASTING (Empty stomach): CaPre > Lovaza

With a high fat meal, results were expected as CaPre contains 2.5 times less EPA and DHA than Lovaza…

[1] PK Bridging Study Protocol: 2016-4010: A Single-Dose, Comparative Bioavailability Study of CaPre 1 g Capsules Compared to LOVAZA 1 g Capsules Under Fasting and Fed Conditions

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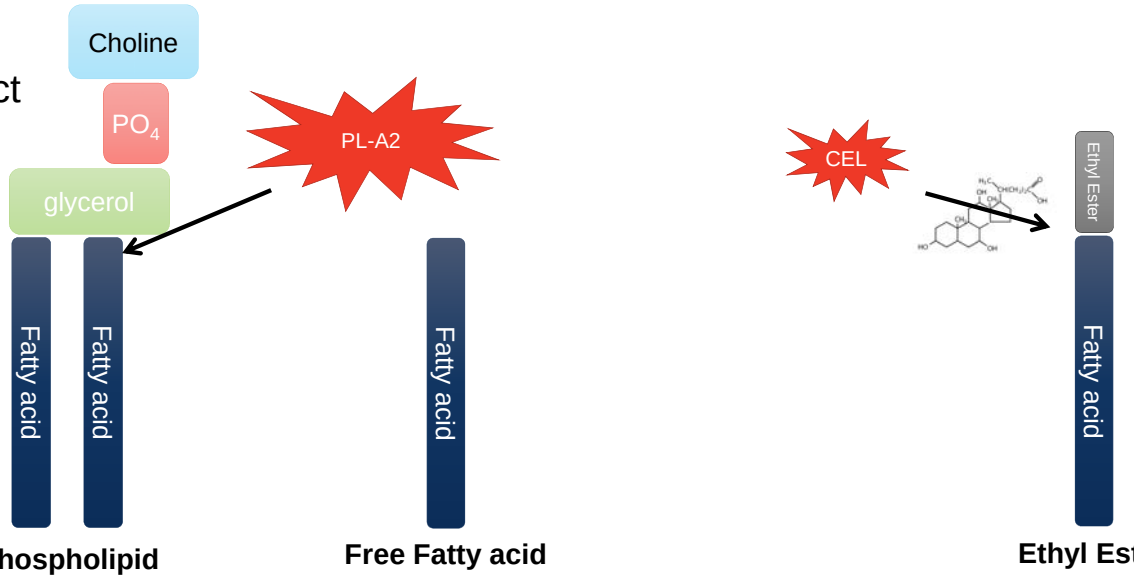
Why CaPre® Does Not Have a Significant Food Effect Compared to Ethyl Esters (EE)?

CaPre

No significant food effect

Ethyl Esters
(Lovaza, Vascepa)
Significant food effect



Phospholipid

- ❑ **Hydrolysis is primarily mediated by PL-A2, <u>not</u> a bile-salt dependent lipase such as CEL**
- ❑ **Readily accessible to lipases due to amphiphilic (interface) properties**

Free Fatty acid

- ❑ **No digestion required**

Ethyl Ester

- ❑ **Hydrolysis is mediated by carboxyl ester lipase (CEL), a bile-salt dependent lipase**
- ❑ **Dependent on the fat content of food for activity**
- ❑ **Results in lower efficiency of the hydrolysis of the EE bond**

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CaPre®
Phospholipids and Free Fatty Acid Forms of EPA and DHA
PK Profile

Conclusions:

- Bioavailability of the phospholipids and free fatty acids forms of EPA and DHA in CaPre® are far less affected when taken on an empty stomach as compared to the ethyl esters forms in Lovaza
- Bioavailability of Lovaza is maximal following administration with a HF meal but is dramatically reduced under fasting conditions
- Since patients with severe hypertriglyceridemia should adhere to a low fat diet, these findings suggest preserved exposure, and perhaps retained efficacy in patients taking CaPre® in either the fasted state or with a low fat diet

ACASTI PHARMA

Two Phase 2 Clinical Studies Completed with CaPre®

Type of study	Study identifier and design	Test Product; Dose (g/day)	Number of Subjects	Duration of treatment	Population
Phase 2 Efficacy and Safety	**PRT-API-NKPL66-CT-PIIB (COLT) Open-label randomized, dose-ranging, multiple-center, parallel-design study**	**CaPre®; 0.5, 1, 2 and 4 g/day**	**288 total (259 on CaPre®; 29 on SoC)**	**8 weeks**	**Patients with hypertriglyceridemia (TG > 200 and < 877 mg/dL) (TG > 2.28 and < 10 mmol/L)**
Phase 2 Efficacy and Safety	**PRT-API-NKPL66-CT-PII (TRIFECTA) Double-blind, randomized, Placebo-controlled, dose-ranging, multiple-center, parallel-design study**	**CaPre®; 1 and 2 g/day**	**387 total (258 on CaPre®; 129 on Placebo)**	**12 weeks**	**Patients with hypertriglyceridemia (TG > 200 and < 877 mg/dL) (TG > 2.28 and < 10 mmol/L)**
TOTAL PATIENTS			**675 patients randomized**		

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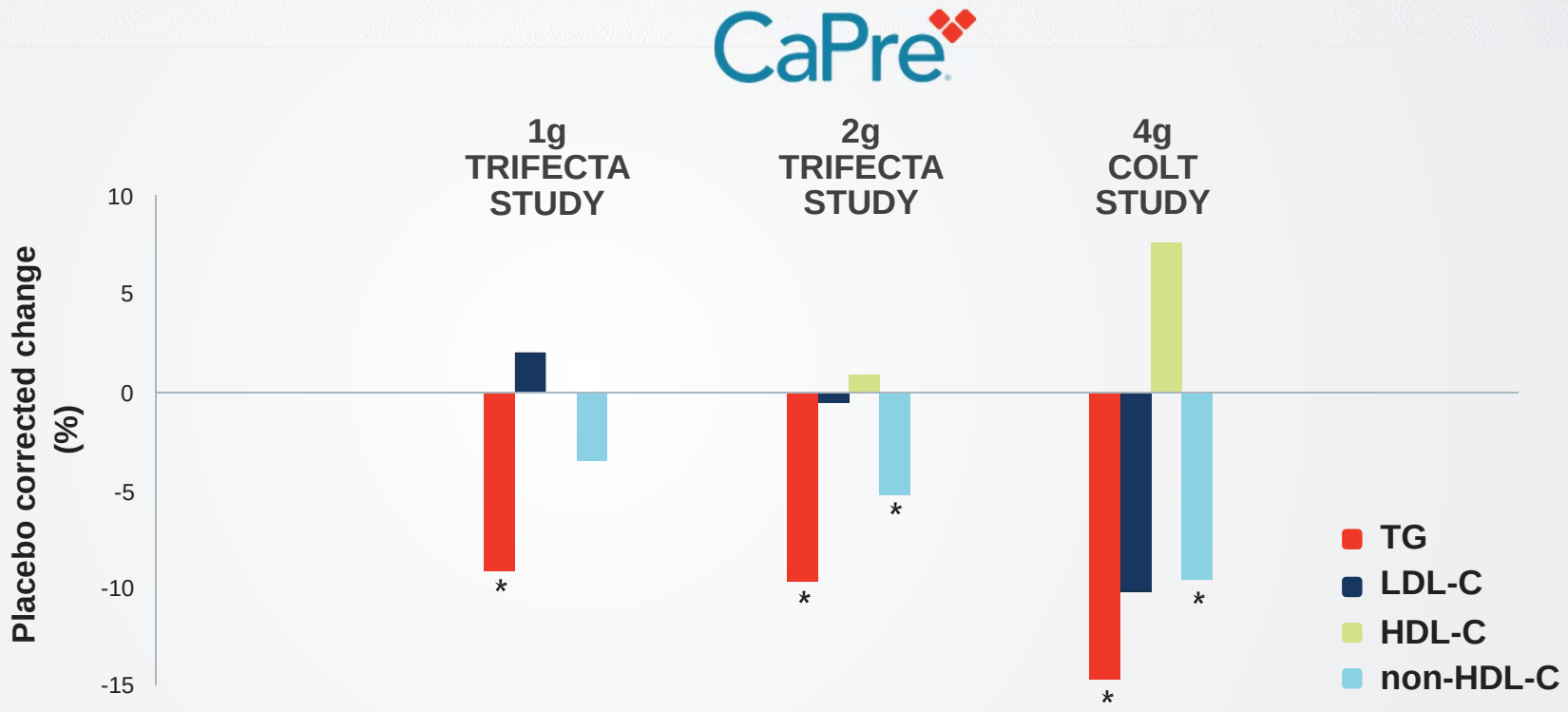
Phase 2 Study Results[1] Show CaPre® Dose Response and Potential for "Trifecta" Lipid Effect



* Indicates results reached statistical significance

[1] COLT and TRIFECTA study data (TG population in mild to moderate is 90%. About 10% were severe. Only 30% of all patients were on statins). TRIFECTA for 1g (N=130) & 2g (N=128) and COLT for 4g (N=62). HDL-C results at 4g from COLT approached statistical significance at P=0.07.

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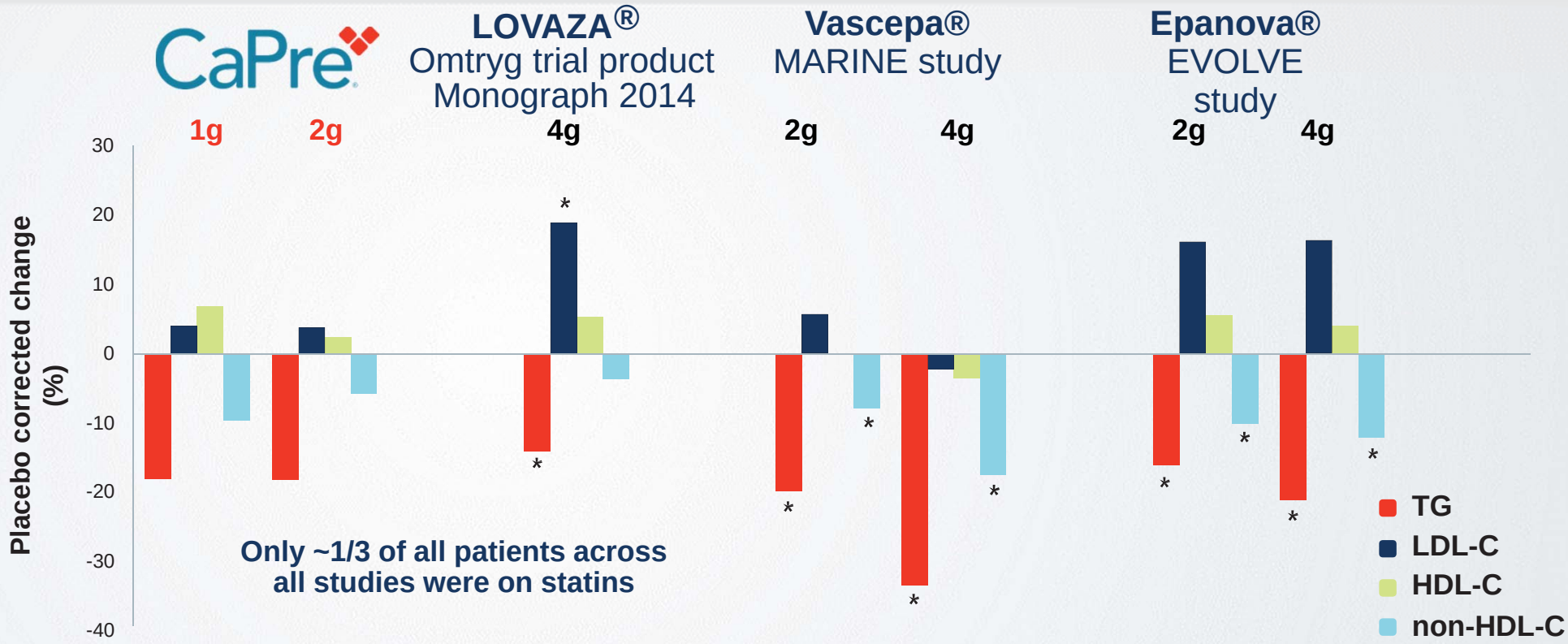
Sub-Group Analysis in Patients with Severe HTG: CaPre®[1] at 1 & 2 Grams Compares Well with Competition[2] at 2 & 4 Grams



*Indicates results reached statistical significance

[1] Subgroup analysis on CaPre® Phase 2 TRIFECTA study data in patients with severe HTG; (N=10 for 1g & N=14 for 2g). Results are not statistically significant for TG which may be explained by small number of patients. Results for LDL-C, HDL-C, non HDL-C are based on descriptive statistics only (no statistical testing conducted).

[2] Lovaza 4g (N=103), Vascepa 2g/4g (N=73/76), Epanova 2g/4g (N=100/99)

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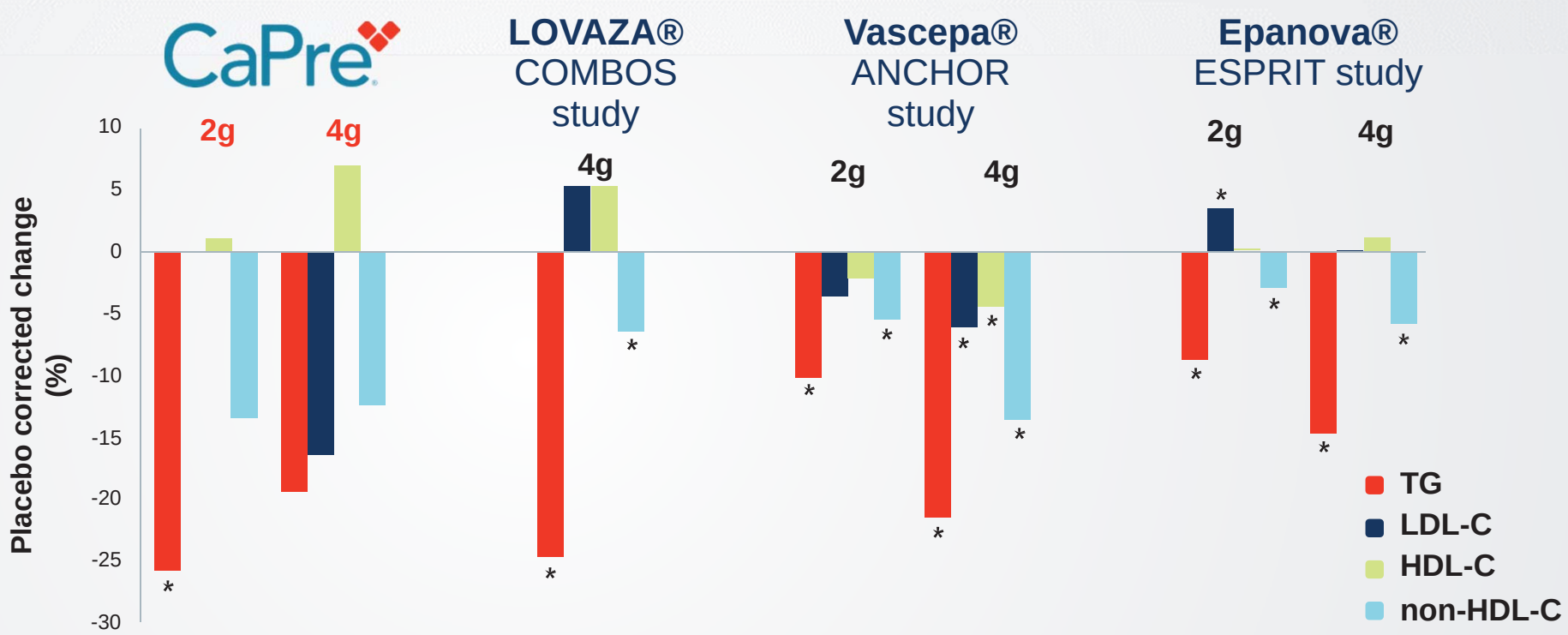
Sub-Group Analysis in Patients Treated with Statins[1] vs Independent Competitor Data[2]: Potential for CaPre® "Trifecta" Effect



* Indicates results reached statistical significance

[1] CaPre subgroup analyses on patients treated with statins: TRIFECTA for 2g (N=39) and COLT for 4g (N=22). For CaPre 2g, results for LDL-C, HDL-C, and non HDL-C are based on descriptive statistics only (no statistical testing was conducted). For CaPre 4g, no results are statistically significant which may be explained by small number of patients.

[2] All patients on a statin background: Lovaza (N=122 for 4g), Vascepa (N= 234 for 2g, N=227 for 4g), Epanova (N=209 for 2g, N=207 for 4g). Statins have been shown to enhance the efficacy of OM3 products – Vascepa NDA 202057. Statistical review, section 4.2 ''Other special/Subgroup populations', p107; and Maki K et al. Clin. Ther. 2013.

ACASTI PHARMA

CaPre® is Safe and Well Tolerated

- Altogether, the 4 clinical Phase 1 & 2 studies included 773 subjects:
  - 611 subjects received CaPre® between 0.5g to 4g daily for up to 12 weeks
- Among all treatment-emergent adverse events (all causalities) with an occurrence greater than 2% of subjects (CaPre® all doses pooled) and greater than placebo :
  - Only diarrhea emerged at an incidence of 2.2%
- No treatment–related SAE reported
- Acasti has conducted a comprehensive nonclinical toxicology program which did not identify any significant safety concern

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CaPre® May Deliver a More Complete Lipid Management Solution for Patients with Severe HTG[1]

Drug Composition	Products	Therapeutic Effect				
		TG	LDL-C	HDL-C	Non-HDL-C	Food Effect
EPA + DHA Omega-3 Phospholipids/Free Fatty Acids	CaPre®	↓	— / ↓	— / ↑	↓	None
EPA + DHA Omega-3 Ethyl Esters	LOVAZA & Generics	↓	↑	—	↓	Significant
EPA only Omega-3 Ethyl Esters	VASCEPA	↓	—	—	↓	Significant
EPA + DHA Omega-3 Free Fatty Acids	EPANOVA	↓	↑	—	↓	None

Positive effect Neutral effect Negative effect

[1] In Phase 2 clinical studies, CaPre showed positive effects on TGs, HDL-C and non-HDL-C, and no deleterious effects (and potentially positive effects) were noted on LDL-C. Competitor information from prescription information and SEC company filings.

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Thank You!

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