

# BioCentury

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## Emerging Company Profile

# Omthera: Fishing expedition

By Jennifer Rhodes  
Staff Writer

**Omthera Pharmaceuticals Inc.** believes superior bioavailability and greater dosing flexibility will enable its Epanova omega-3 fatty acid to compete in the \$1 billion market for lipid-lowering drugs now occupied by Lovaza.

Epanova is a mixture of the free fatty acid forms of the omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), both of which lower triglycerides by mechanisms that are not well understood.

According to CMO Michael Davidson, a “free fatty acid is already ‘digested’ so to speak, so it’s more easily absorbed” than an ethyl ester fatty acid like Lovaza, which is the only approved prescription omega-3 product.

This means Epanova does not need to accompany a high-fat meal for better absorption and bioavailability. According to Davidson, Lovaza, an ethyl esterized combination of EPA and DHA, is more effective when taken with a high-fat meal.

In the Phase I/II ECLIPSE trial of Epanova vs. Lovaza in healthy volunteers, Lovaza’s bioavailability was about 3,954 nmol\*hour/mL with a high-fat diet vs. only about 735 nmol\*hour/mL on a low-fat diet ( $p < 0.001$ ).

By contrast, 4 g Epanova produced plasma levels of EPA and DHA that were 4.6-fold greater than levels achieved with the same dose of Lovaza in subjects on a low-fat diet (3,124 vs. 735

### Omthera Pharmaceuticals Inc.

Bedminster, N.J.

Technology: Ultra-pure mixture of the free fatty acid forms of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)

Disease focus: Metabolic

Clinical status: Phase III

Founded: 2008 by Jerry Wisler and Michael Davidson

University collaborators: None

Corporate partners: None

Number of employees: 10

Funds raised: \$40.4 million

Investors: Sofinnova Partners and New Enterprise Associates

CEO: Jerry Wisler

Patents: 2 issued covering Epanova’s coating and capsule

nmol\*hour/mL,  $p < 0.001$ ).

The need to accompany lipid-lowering medication with a high-fat meal in patients with highly elevated triglyceride levels contributes to the very problem the drug is combating. Because patients with high triglycerides should be on a low-fat diet, Davidson said, “an omega-3 product that is better absorbed with a low-fat diet would likely be a significant improvement over the ethyl ester omega-3s.”

According to its label, Lovaza lowered triglycerides by an average of 44.9% vs. a 6.7% increase for placebo in two pivotal trials in 84 adults with triglyceride levels over 500 mg/dL.

**GlaxoSmithKline plc** markets Lovaza in the U.S., **Pronova Biopharma ASA** markets the drug in Europe and parts of Asia as Omacor, while **Takeda Pharmaceutical Co. Ltd.** has exclusive rights in Japan.

According to Pronova, Lovaza had global sales of \$1.3 billion in 2010.

Epanova is being evaluated in the placebo-controlled Phase III EVOLVE trial in 330 patients with fasting triglyceride levels over 500 mg/dL, with data expected in 1H12. CEO Jerry Wisler said the company expects a more than 60% reduction in triglyceride levels with 4 g Epanova once daily.

Patients in EVOLVE are being instructed to take Epanova with a low-fat diet. The international trial has an SPA from FDA.

Omthera plans to submit an NDA in 2012 and anticipates

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PO Box 1246  
San Carlos CA 94070-1246  
Voice: 650-595-5333  
Fax: 650-595-5589  
[www.biocentury.com](http://www.biocentury.com)

**DAVID FLORES**  
President & CEO

**KAREN BERNSTEIN, Ph.D.**  
Chairman & Editor-in-Chief

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approval in 2013. The company will include safety data from three Phase III trials conducted by Tillots Pharma AG.

Tillots had been developing Epanova to treat Crohn's disease. According to Wisler, Epanova did not show efficacy in the Phase III trials for Crohn's, but showed excellent bioavailability. Tillots decided to repurpose the compound for hypertriglyceridemia before being acquired by **Zeria Pharmaceutical Co. Ltd.** in 2009. Omthera subsequently licensed Epanova in 2009.

Omthera expects Epanova will initially be taken once-daily at a starting dose of 2 g, or two pills. Davidson said this would give the product more flexible dosing and a reduced pill burden compared with Lovaza, whose daily dose is 4 g or four pills each day.

Omthera estimates there are about 5 million patients in the U.S. with triglyceride levels over 500 mg/dL.

At least one other company is hoping to take a share from Lovaza.

**Amarin Corp. plc** plans to submit an NDA this quarter for AMR101 to treat patients with triglyceride levels over 500 mg/dL. AMR101 is a 96% pure ethyl ester of EPA (ethyl-EPA) without DHA.

AMR101 met the primary endpoint of significantly reducing triglycerides from baseline to week 12 by 10.1-33% vs. placebo in two Phase III trials (see *BioCentury*, Dec. 6, 2010).

While AMR101 does not lower triglycerides as much as Lovaza, neither does it raise LDL-C, which Lovaza's label warns about.

Davidson attributes Lovaza's LDL-C increase to its DHA component which also adds to the lowering of triglycerides and raising of HDL. He told BioCentury that a "3-4% difference in LDL-C is clinically irrelevant, especially in light of the finding that DHA increases LDL-C by making the LDL particles larger, which is believed to be a beneficial effect."

Epanova is the company's only pipeline candidate. Omthera plans to start Phase III testing to evaluate the compound in combination with statin therapy in patients with triglyceride levels over 200 mg/dL this half.

Omthera plans to commercialize Epanova in the U.S. and look for partners elsewhere. Wisler said an internal sales force of less than 250 would be sufficient.

In March, Omthera raised \$33.9 million in a series B round, which Wisler said would last into 2013.

**COMPANIES AND INSTITUTIONS MENTIONED**

**Amarin Corp. plc** (NASDAQ:AMRN), Dublin, Ireland

**GlaxoSmithKline plc** (LSE:GSK; NYSE:GSK), London, U.K.

**Omthera Pharmaceuticals Inc.**, Bedminster, N.J.

**Pronova Biopharma ASA** (OSE:PRON), Lysaker, Norway

**Takeda Pharmaceutical Co. Ltd.** (Tokyo:4502), Osaka, Japan

**Zeria Pharmaceutical Co. Ltd.** (Tokyo:4559), Tokyo, Japan