

# Cerenis<sup>TM</sup>

THERAPEUTICS

**The Lipid Metabolism and HDL Company**

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## Jean-Louis DASSEUX, PhD, MBA

### Founder and CEO

- More than 25 years of experience in the pharmaceutical industry (Pfizer, Esperion Therapeutics, Fournier Laboratories)
- A leading world expert in lipid metabolism, atherosclerosis and cardiovascular diseases
- Inventor of more than 70 patent families relating to HDL and the treatment of cardiovascular diseases. Two products currently in phase III clinical trials (Bempedoic acid at Esperion Therapeutics and CER-001 at Cerenis Therapeutics)
- Esperion Therapeutics sold to Pfizer for \$1.3 Billion in 2004



## Cyrille TUPIN, CPA

### CFO

- Audit Director at Sygnatures, the largest private auditing and consulting company in Toulouse, France
- More than 7 years at PWC working on high-profile business transactions

## In the short term: CER-001, a drug for treating orphan diseases

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1. A potential of value creation in the short term with an ongoing phase III study (TANGO)
2. HDL deficiency, A major unmet medical need
3. Two orphan designations for apoA-I and ABCA1 deficiency
4. Application for marketing approval before 2018
5. A manufacturing process validated on an industrial level

## CER-209: major potential in the treatment of patients with atherosclerosis and NAFLD/NASH

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1. A potential of value creation in the short term with an ongoing phase I study
2. A major unmet medical need
3. CER-209, a highly specific P2Y13 receptor agonist promoting lipid elimination

## A LISTED COMPANY WITH SUBSTANTIAL POTENTIAL IN LIPIDS METABOLISM

1. Press releases,  
OMTHERA: <http://www.astrazeneca.com/Media/Press-releases/Article/20130528-omthera>  
Esperion: <http://www.bloomberg.com/apps/news?pid=newsarchive&sid=apU2qcYcmkO4&refer=us>  
KOS: [http://www.bloomberg.com/apps/news?pid=newsarchive&sid=af\\_8tgk4fHE](http://www.bloomberg.com/apps/news?pid=newsarchive&sid=af_8tgk4fHE)

## Leading cause of death in the world

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- **1 out of 3 deaths** worldwide (source: WHO)
- **Leading cause of death in patients with liver steatosis**
- The disease category with the greatest health expenditure:
  - **\$107 bn** in the United States, in 2010
  - **\$110 bn** in Europe, in 2009

## A primary cause: atherosclerosis

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- **Atherosclerosis: accumulation of cholesterol in the vessel wall lead to formation of atherosclerotic plaques**

**Only 1/3 of the cardiovascular risk is targeted by the best current treatments**

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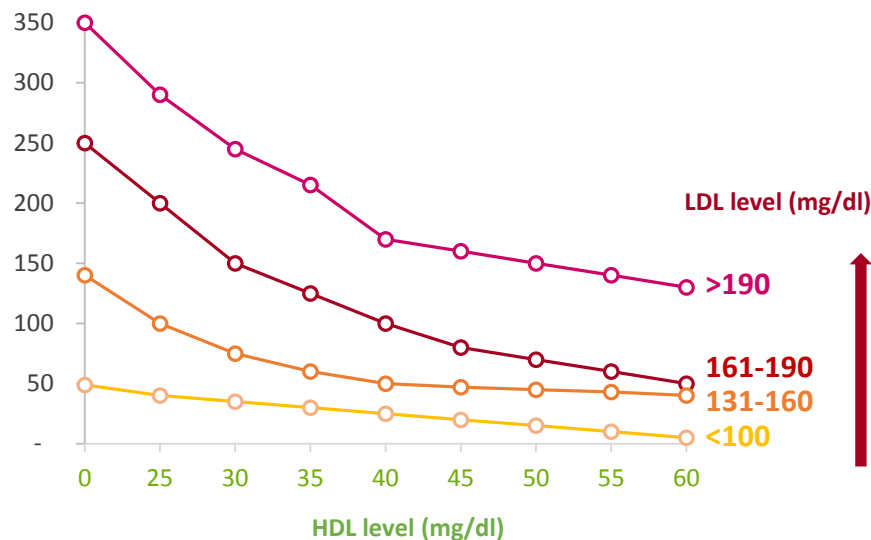
**ONLY ONE REAL SOLUTION: ELIMINATE CHOLESTEROL PLAQUE WITH CERENIS**

## Fundamental role of HDL in removing cholesterol

- **At each LDL level, it is the HDL level** that determines the cardiovascular risk
- **An HDL therapy that increases the number of HDL particles** is one of the best approaches for treating atherosclerosis
- **No HDL medical treatment** that can treat or eliminate atherosclerosis is yet available

## A major epidemiological study on HDL <sup>1</sup>

Incidence of cardiovascular events (per 1,000) over 10 years



**CERENIS IS THE COMPANY THAT OFFERS ONE OF THE MOST COMPREHENSIVE INNOVATIVE HDL SOLUTIONS FOR TREATING ATHEROSCLEROSIS**

1. PROCAM:  
7,152 men aged 35 to 65  
406 coronary events over 10 years

## LDL APPROACH: reduces bad cholesterol

No direct action on atherosclerotic plaque



### AVAILABLE DRUGS:

**Statins:** inhibit cholesterol synthesis

**Resins and Inhibitors:** limit intestinal absorption of cholesterol

**Fibrates:** reduce the level of triglycerides containing LDL cholesterol

**PCSK9 antibodies:** increase LDL receptors

Indirect long-term effect with no direct action on plaque: cardiac risk reduced by 1/3

## HDL APPROACH: reduces plaque

Reduces atherosclerotic plaque



### NO DRUGS YET AVAILABLE:

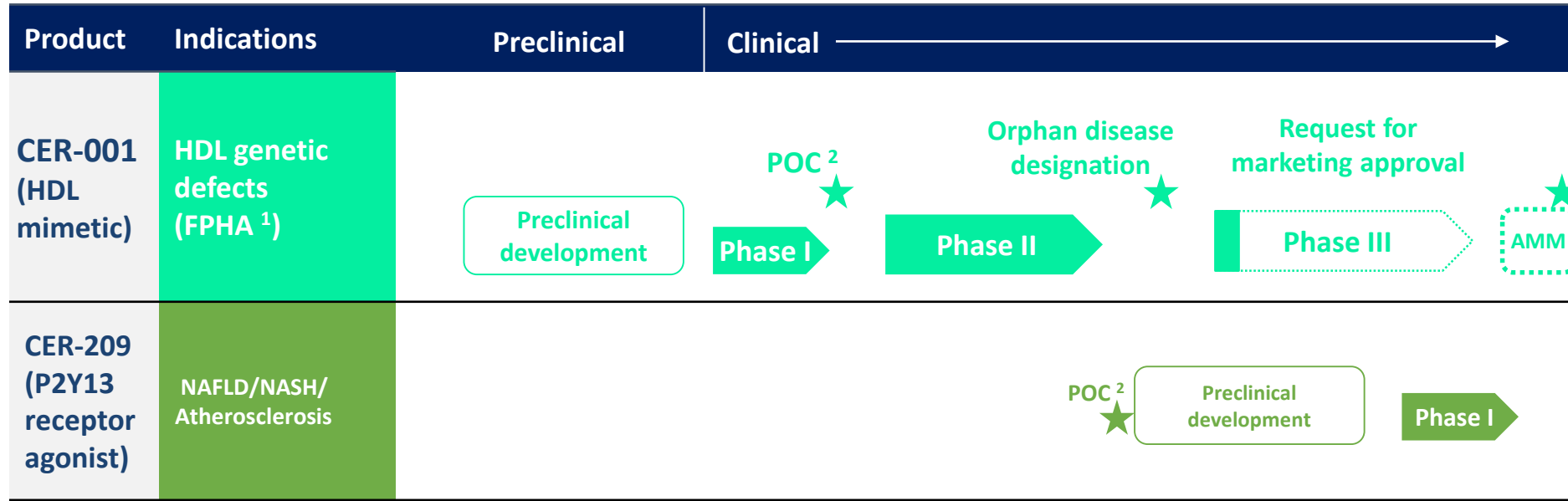
**CER-001:** CERENIS HDL mimetic candidate that reduces atherosclerotic plaque

Rapid direct effect: reduction in atherosclerotic plaque

**LDL DRUGS HAVE A LIMITED EFFICACY ON PLAQUE REDUCTION**

# 10 years of R&D to achieve one of the world's most advanced HDL solutions

2005: inception of Cerenis → 2014 2015 2016 2017 2018



Financing to date



Investors



## 2 TARGETED INDICATIONS: FPHA AND NAFLD/NASH/ATHEROSCLEROSIS

1. Familial Primary Hypoalphalipoproteinemia  
2. Proof of Concept



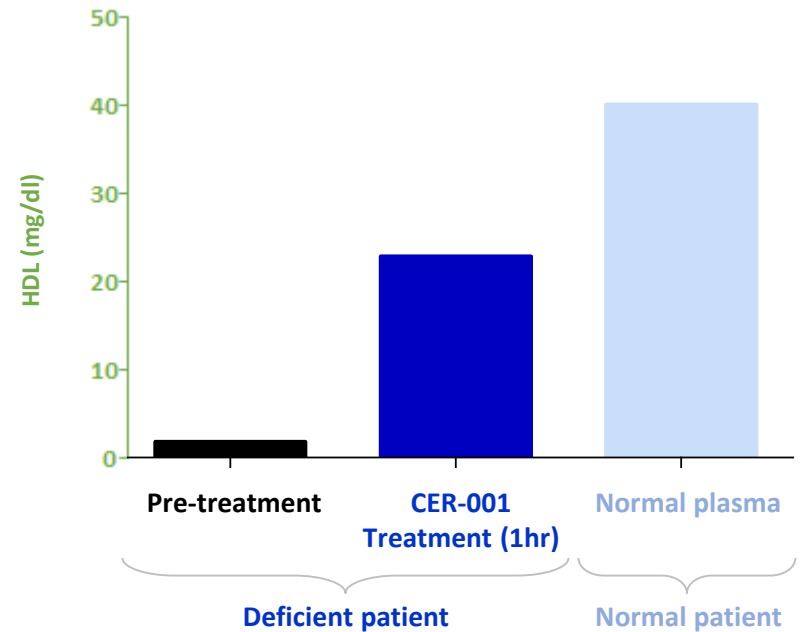
**FPHA: genetic defect affecting HDL synthesis**

- CERENIS' solution restores the blood's ability to mobilize cholesterol into HDL to facilitate its elimination

**2 orphan drug designations obtained**

- HDL deficiency (no apoA-I synthesis)
- Tangier disease (absence of ABCA1 )

**Mobilization of HDL cholesterol in the blood<sup>1</sup>**



**CERENIS: A THERAPEUTIC SOLUTION TO MEET THE UNMET FPHA MEDICAL NEED**

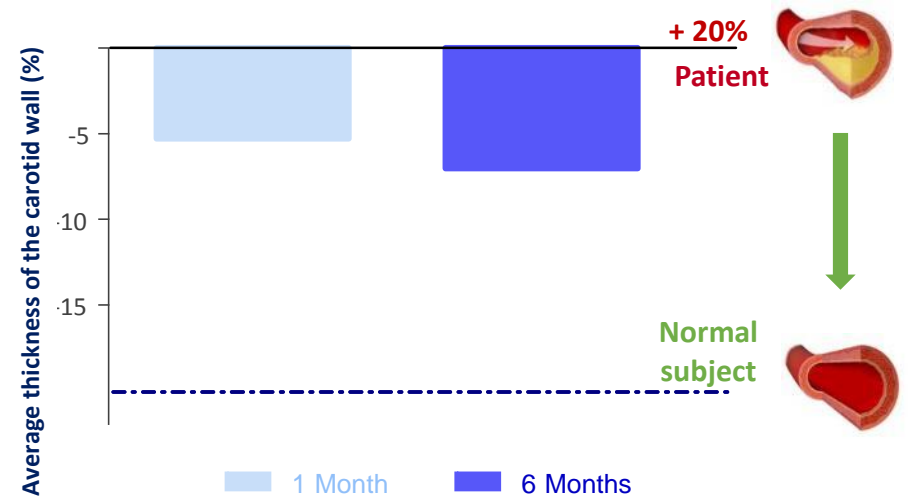
1. Company: SAMBA study

The Phase II study showed:

Reduction of the vascular wall thickness

- Behaves like a natural HDL
- Eliminates cholesterol
- Reduces plaque

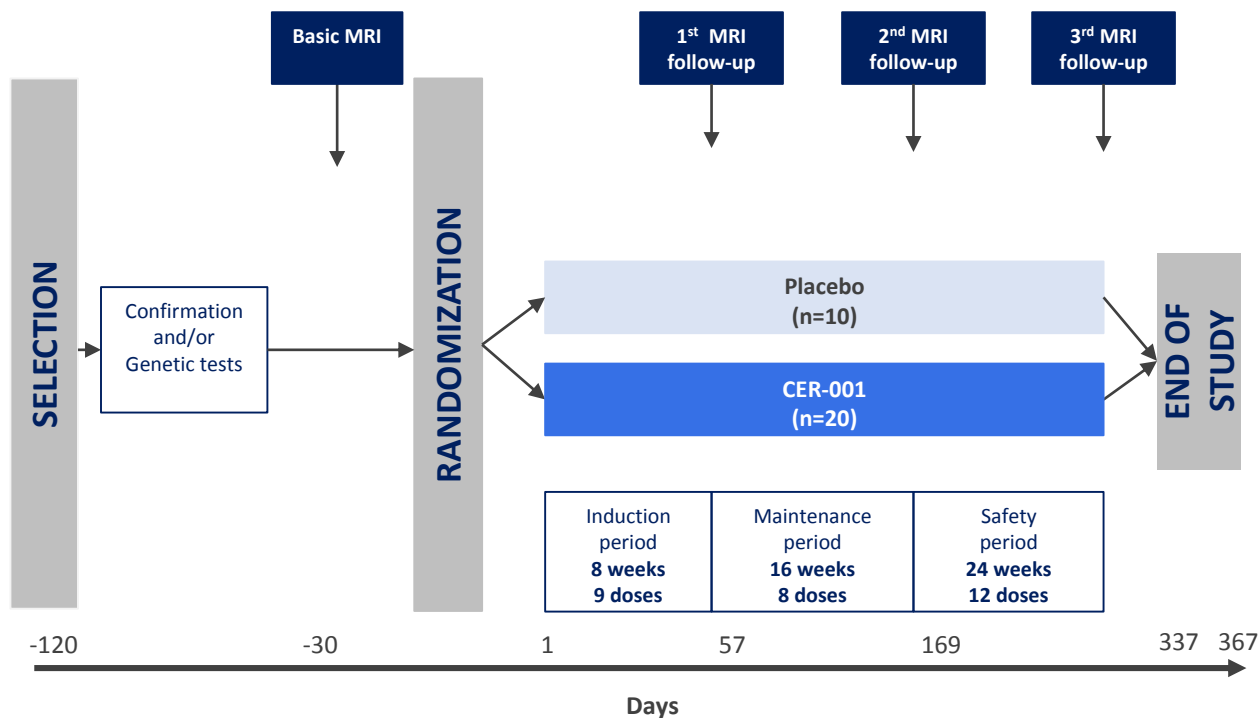
Efficacy on carotid atherosclerosis<sup>1</sup>



IN THE BODY, CER-001 BEHAVES JUST LIKE A NATURAL HDL PARTICLE

The TANGO study should show:

- A reduction in coronary plaque in the carotid



**THE TARGET OBJECTIVE IS TO OBTAIN MARKETING APPROVAL IN IDENTIFIED GENETIC DEFECTS (APOA-I AND ABCA1 DEFICIENCIES)**

## **NASH, one of the leading causes of cirrhosis in adults in the United-States<sup>1</sup>**

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- **25% of adults having NASH will develop a cirrhosis**
- **Current treatments based on lipid lowering drugs attempt to reduce LDL cholesterol but they often increase liver enzymes**

## **Cardiovascular risk : increased in patients with hepatic steatosis<sup>2</sup>**

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- **Atherosclerosis is frequently observed in patients with NASH, thus presenting high cardiovascular risk, in addition to steatohepatitis and liver inflammation**
- **Cardiovascular diseases associated : leading causes of death in patients with liver steatosis**

**CURRENTLY NO APPROVED THERAPIES ADDRESSING BOTH ATHEROSCLEROSIS  
NASH/NAFLD, MAJOR GLOBAL HEALTH CHALLENGES**

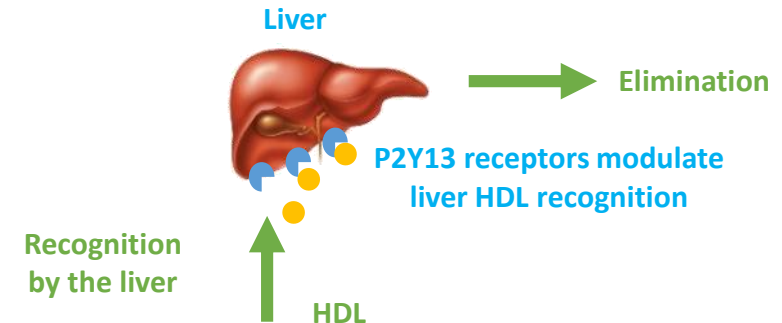
*1: American Liver Foundation: Franque S. M. et al. Journal of Hepatology, 2016, vol. 65, 425-443*

*2: World J Gastroenterol 2015 June 14; 21(22): 6820-6834*

### CER-209

- First drug candidate in the category of oral P2Y13 receptor agonists
- Newly-patented molecule coming from Cerenis' research
- Major asset in NASH and NAFLD treatment

### CER-209 stimulates the activity of HDL receptors

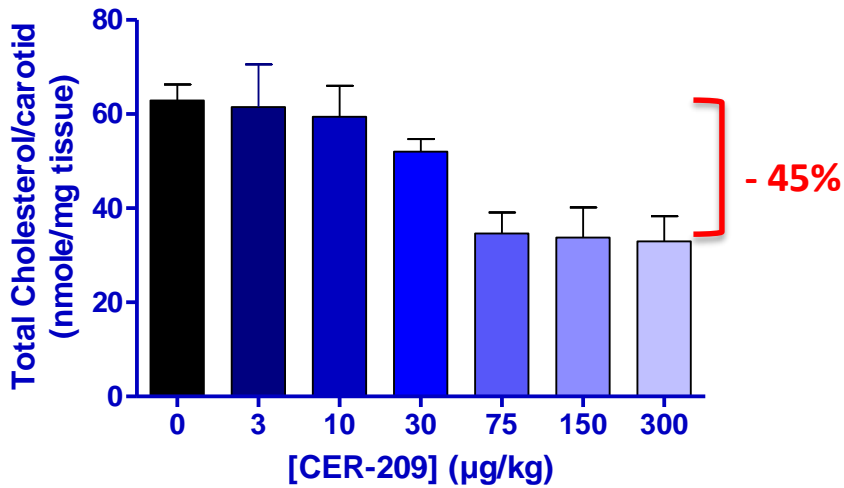


- Promoting HDL recognition and lipid elimination by the liver, through the activation of natural metabolic pathways mediated by the P2Y13 receptor
- A new mechanism of action which involves the last steps of the RLT pathway

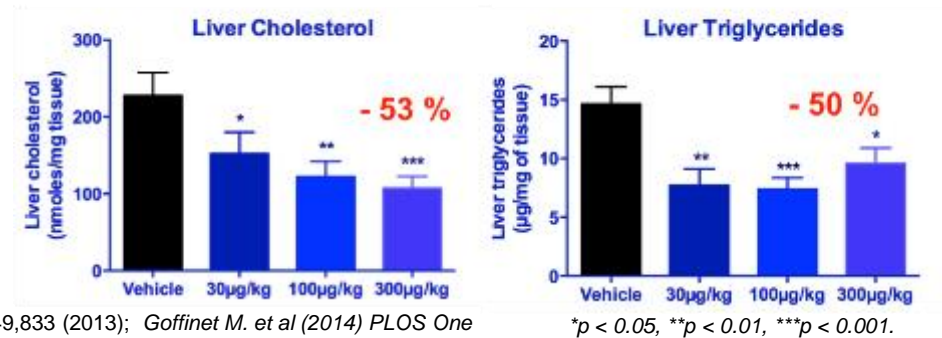
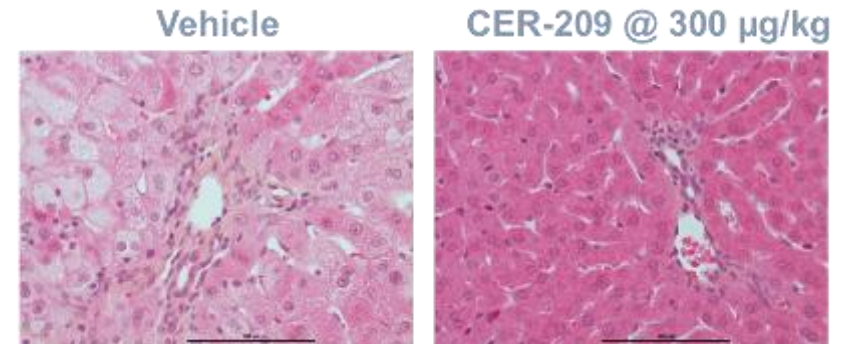
## A POTENTIAL BREAKTHROUGH TREATMENT FOR BOTH HEPATIC STEATOSIS (NASH AND NAFLD) AND ATHEROSCLEROSIS

\* Fabre ACC et al., *Hepatology* 2010;52:1477–1483 / Serhan N. et al., *Biochim. Biophys Acta* 2013;1831:719–725 / Goffinet M. et al., *PLoS ONE* 2014;9:e95807

**Plaque regression in mice treated with CER-209\***



**Regression of liver steatosis in high-cholesterol diet rabbits treated with CER-209\***



Cerenis US Patent 8,349,833 (2013); Goffinet M. et al (2014) PLOS One

\*p < 0.05, \*\*p < 0.01, \*\*\*p < 0.001.

**CER-209 HAS A STRONG POTENTIAL FOR THE TREATMENT OF NASH AND NAFLD**

\* P2Y13 receptor agonist CER-209 decreases both atherosclerosis and liver steatosis in vivo: Rudi Baron, Marine Goffinet, Nadia Boubekeur, Claudine Tardy, Guy Cholez, Daniela C. Oniciu, Narendra D. Lalwani, Jean-Louis H. Dasseux and Ronald Barbaras



## The success of the Single Dose Tolerance study (SDT) with CER-209 showed, as expected:

- No drug related safety nor tolerance issues identified
- The pharmacokinetics observations support CER-209 once daily oral dosing

## Design: randomized, double-blind and placebo controlled phase I study

- Primary endpoint: determine safety and tolerance as well as pharmacokinetics/pharmacodynamics after administration of escalating doses of CER-209 to healthy volunteers
- Patients: 24 subjects treated in 4 cohorts of 6
- 4 patients have received CER-209 drug-candidate and 2 the placebo
- Oral administration of escalating doses of 1, 3, 10 and 30 mg

**NEXT STEP: LAUNCH OF THE MULTIPLE DOSES TOLERANCE STUDY**

- 9 patent families protecting the products, indications and manufacturing / diagnostic methods

PRODUCT	INDICATION	MANUFACTURING/DIAGNOSTIC
<p><b>Family 1:</b> Formulation of CER-001 and its uses</p>	<p><b>Family 4:</b> Treatment of Dyslipidemias</p>	<p><b>Family 2:</b> Manufacturing methods for reconstituted HDL particles and highly-homogenous resulting populations of HDL particles</p>
<p><b>Family 6:</b> HDL mimetic peptide including CER-522</p>		<p><b>Family 3:</b> Companion diagnostics and dosage of CER-001</p>
<p><b>Family 7:</b> P2Y13 receptor agonists (CER-209)</p>		<p><b>Family 5:</b> Synthetic sphingomyelin synthesis / production methods</p>
<p><b>Family 8:</b> PPAR agonists (CER-002)</p>		<p><b>Family 9:</b> Carrier particles for administering drugs</p>

**NO COMPETITOR CAN REPRODUCE THE CHARGED NANOPARTICLE, EVEN PARTIALLY**



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Esperion: <http://www.bloomberg.com/apps/news?pid=newsarchive&sid=apU2qcYcmkO4&refer=us>  
KOS: [http://www.bloomberg.com/apps/news?pid=newsarchive&sid=af\\_8tgk4fHE](http://www.bloomberg.com/apps/news?pid=newsarchive&sid=af_8tgk4fHE)

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