



**Expanding its HDL strategy into  
Immuno-oncology and  
Chemotherapeutic drug delivery**

**Acquisition of LYPRO Biosciences**

- **Over a decade of experience in HDL biology and pharmacology**
- **Scalable manufacturing expertise**
- **Broad patent estate coverage**



**HDL PARTICLES ARE IDEAL DRUG CARRIERS  
TO SELECTIVELY TARGET CANCER CELLS**

**Made up of CERENIS' apoA-I, and in the form of an HDL particle, LYPRO's Nanodisk<sup>®</sup> could be the perfect drug carrier**

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- ApoA-I, the constitutive protein of HDL, is perfectly biocompatible and tolerated by the human body
- ApoA-1 has an adaptive structure allowing for different drugs to be loaded in an HDL
- Being recognized by numerous receptors, present on the cells' membranes, HDL are able to selectively carry active drugs to a wide-range of tissues

### **LYPRO in a nutshell**

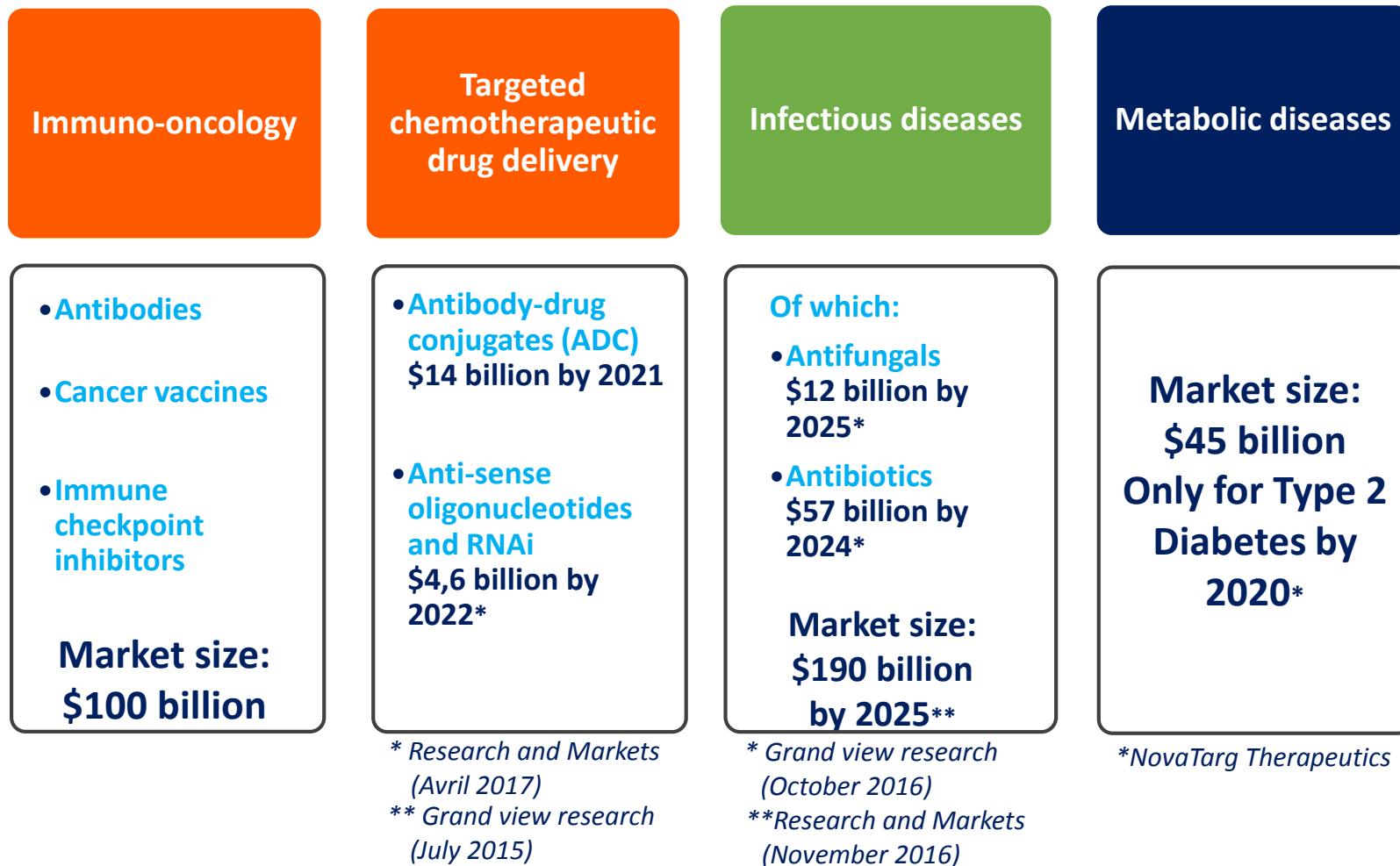
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- A California-based company with a revolutionary proprietary drug technology called Nanodisk<sup>®</sup>
- Nanodisk<sup>®</sup> are self-assembling, targetable, nanometer-scale HDL-like bioparticles able to encapsulate active drugs
- LYPRO's preclinical work has demonstrated that lipid structures, such as HDL, could be ideal delivery agent



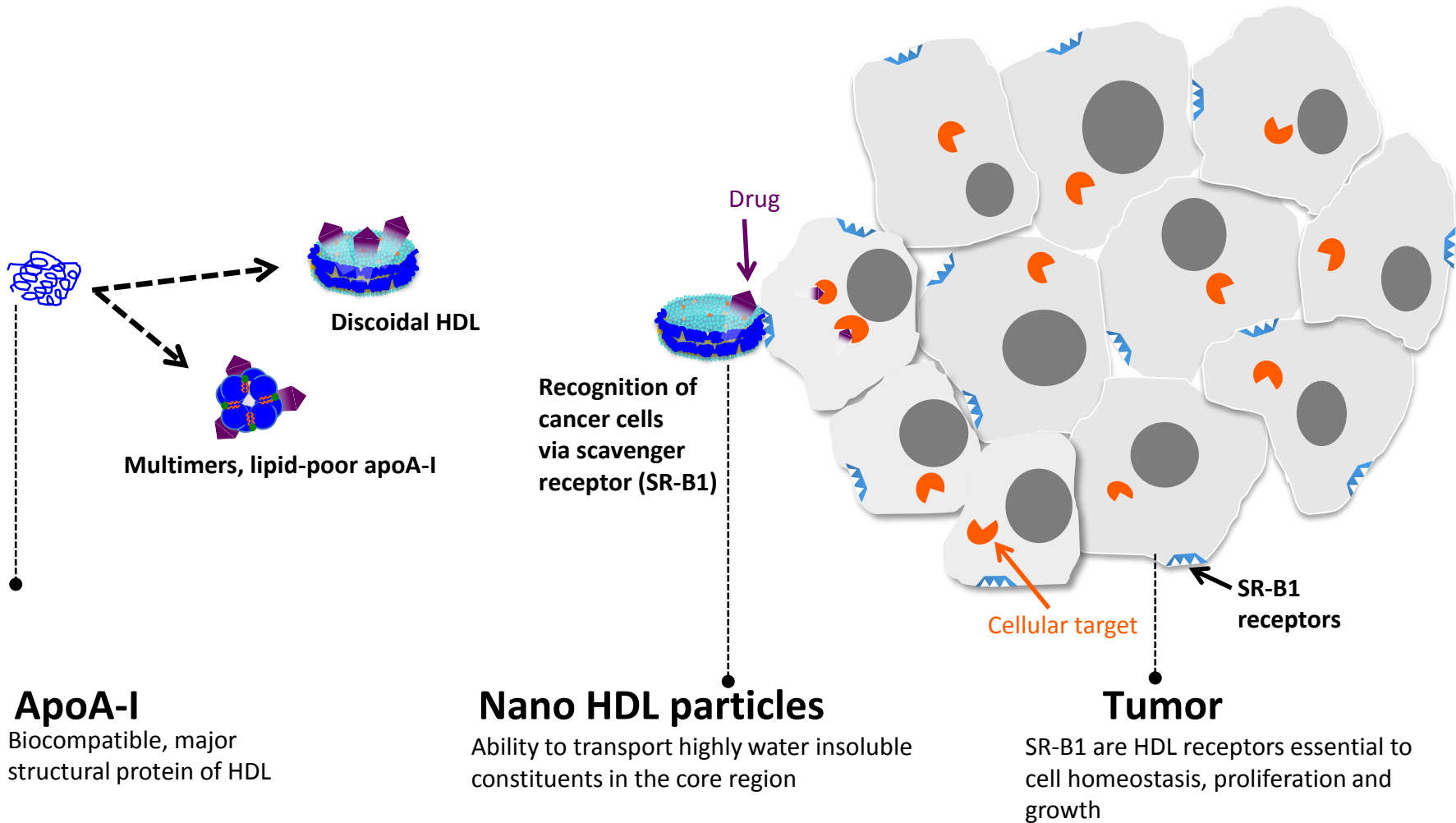
**COMBINATION OF THESE TWO TECHNOLOGIES CREATES  
A DISRUPTIVE DRUG DELIVERY TECHNOLOGY**

## Targeted drug delivery nanotechnologies associated with HDL therapy have strong potential in a wide range of indications



**▶ IN THE SHORT TERM CERENIS WILL FOCUS ON ONCOLOGY**

# HDL particles are perfect delivery vehicles able to selectively bring cell killing agents to cancer cells

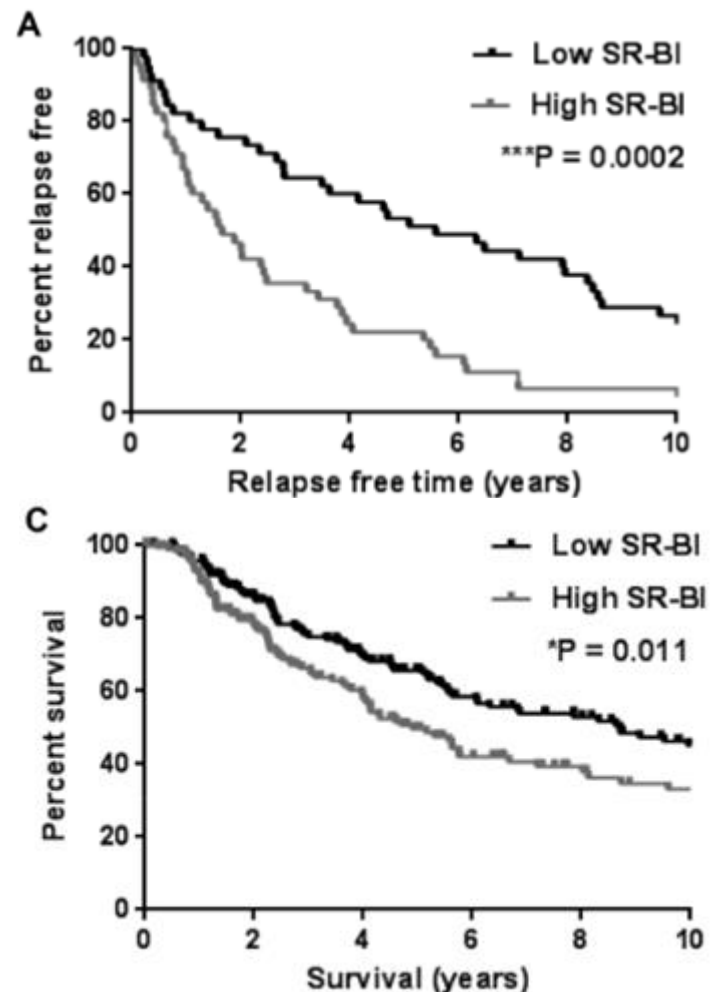


▶ **HDL'S BIOLOGICAL FEATURES SUPPORT THE SAFETY PROFILE OF THE TECHNOLOGY**

## SR-BI receptors play a key role in cancer cell proliferation

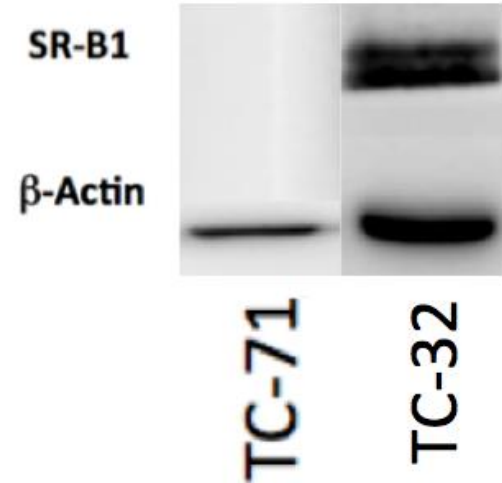
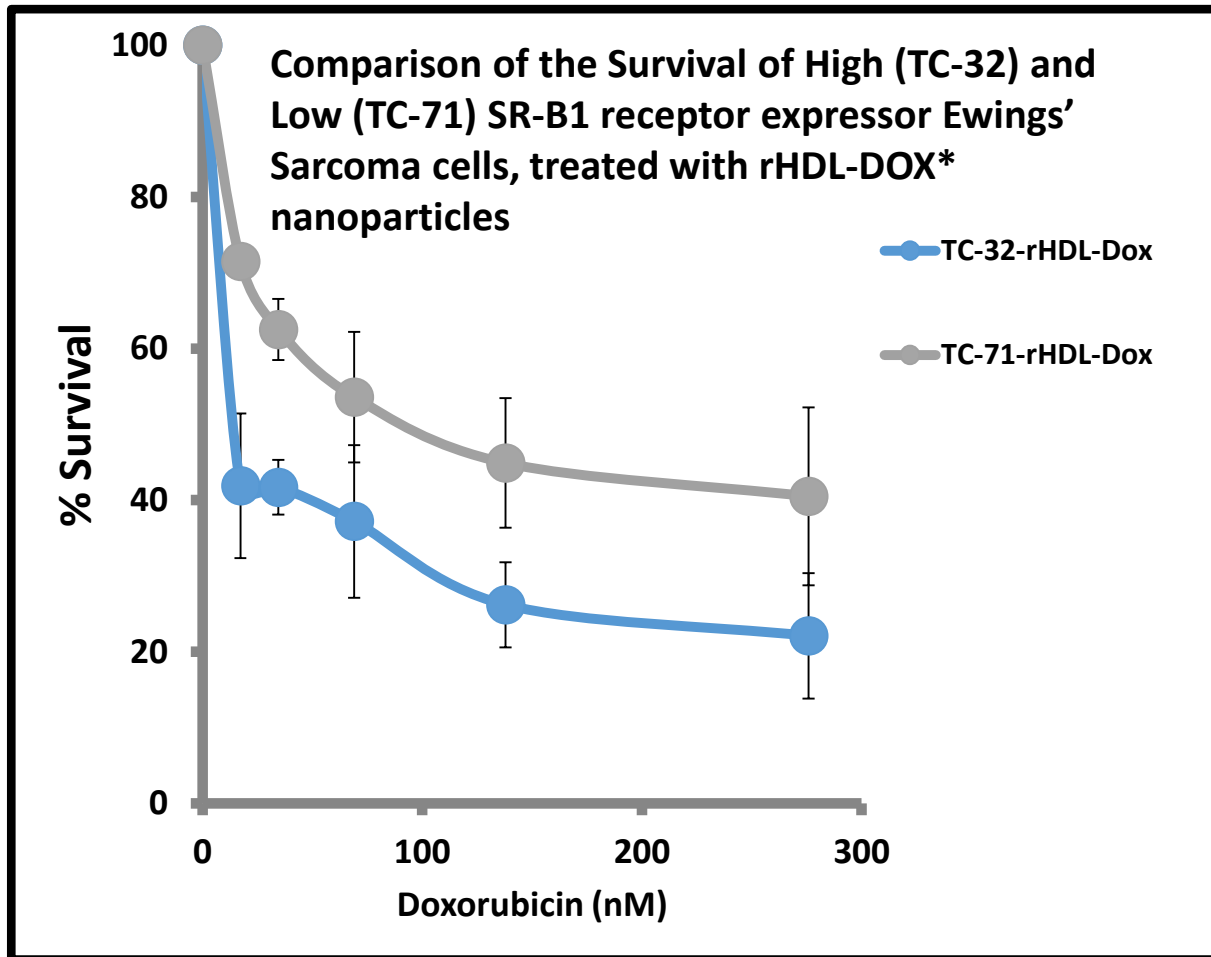
- Melanoma can be an aggressive and fatal form of skin cancer with the prevalence rising significantly over the last decade
- Once the disease is metastatic patients have a very poor prognosis
- Melanoma patients with high SR-BI expression, displayed a significantly earlier time of tumor reoccurrence compared to patients with low SR-BI expression (A). In addition patients with high SR-BI have a significant poorer outcome (C)

\* Mikula et al.\* (Medical University Vienna, Austria) :  
Mol Cancer Res. 2017 Oct 3. pii: molcanres.0292.2017. doi:  
10.1158/1541-7786.MCR-17-0292.



► HDL DRUG DELIVERY TARGETING HDL RECEPTORS SUCH AS SR-BI MIGHT REPRESENT A HIGHLY EFFECTIVE WAY TO TREAT CANCERS LIKE METASTATIC MELANOMA

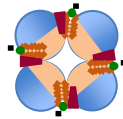
# Targeting SR-BI receptors, HDL containing Doxurobicin is a powerful anti-cancer agent



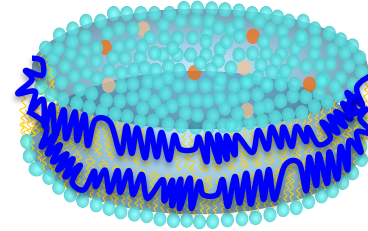
\*rHDL-DOX nanoparticles are reconstituted spherical HDL containing Doxurobicin (Personal communication by Dr. A. Lacko, University of North Texas Health Science Center, Fort Worth, TX)

▶ **SARCOMA CELLS EXPRESSING SR-B1 ARE MORE SUSCEPTIBLE TO CELL DEATH THAN THOSE WHICH DO NOT OVEREXPRESS SR-BI**

# ApoA-I with its flexible structure, is a key asset to accomodate different drug loads and target different tissues



**ApoA-1 multimeric structure**  
(2-6nm)



**Discoidal HDL**  
(7-9nm)

- The ability of monomeric apoA-I to form multimeric structures , offers the opportunity to have a carrier with adaptive capacity and a different pace of release as number of subunits increase.
- The small size of monomeric or multimeric apoA-I allows to penetrate the blood brain barrier as well as the lymph compartment.
- Cerenis delivery vehicles take advantage of the wide distribution of HDL/apoA-I receptors (SR-B1 / ABCA1/ABCG1) in tissues.

**► CERENIS HDL PLATFORM: A « ONE STOP » DRUG DELIVERY PARTNER**



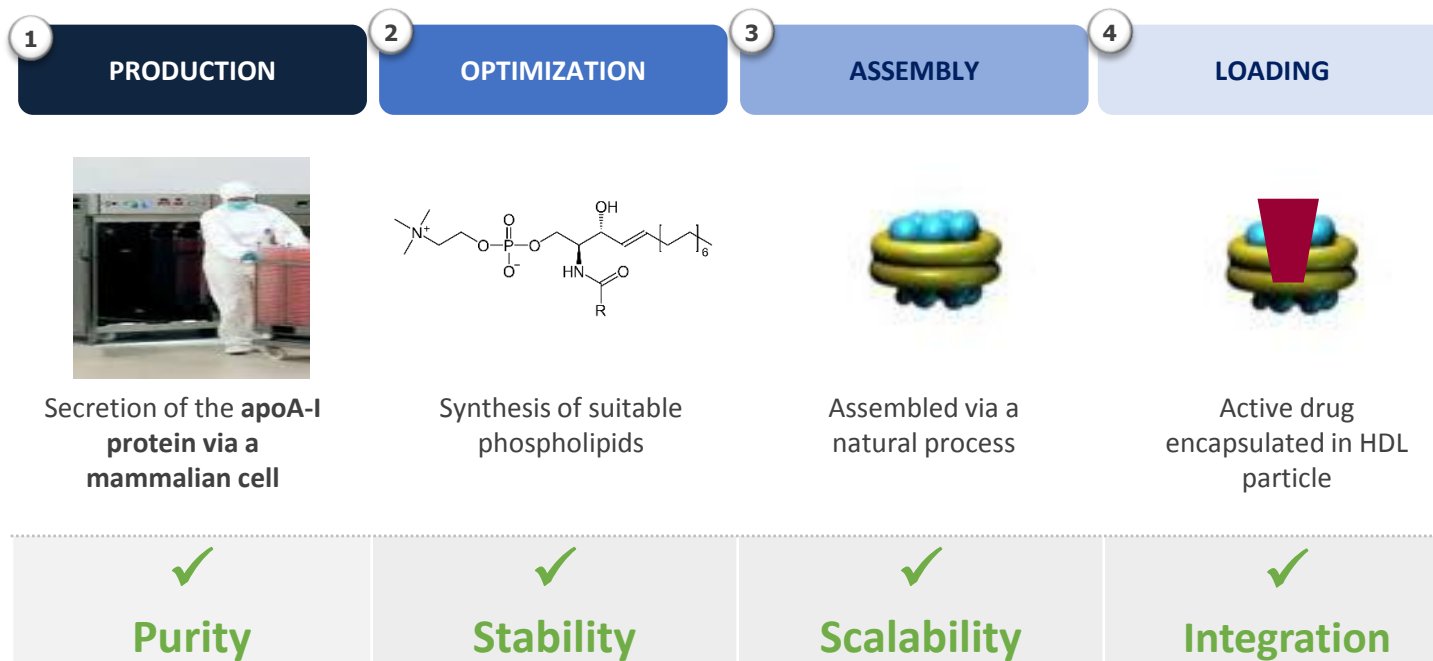
# HDL particles have strong advantages over existing drug delivery technologies

	HDL particles
<b>Safety and efficacy</b> ✓	Natural structure stabilized by apolipoproteins, particularly apolipoprotein A-I (apo A-I) and uniquely capable of delivery of biologically active molecules to tissues and circulating cell in humans.
<b>Biocompatibility</b> ✓	Once the load is delivered, the remaining apoA-I is rapidly and safely integrated in the natural lipoprotein metabolism pathways leading to no accumulation of empty carrier.
<b>Strong ability to target specific cells</b> ✓	HDL particles are recognized by the SR-B1 receptor expressed on cancer cells' surface. The receptor-mediated uptake of the payload, enable delivery of the drug carried in the core of the HDL particle.
<b>Adaptive structure</b> ✓	ApoA-I is flexibly and adaptive, from lipid-poor apoA-I, to discoidal and large spherical particles, allowing different types and quantities of drug payloads for different applications in cancer chemotherapy and antigen carrying immuno-oncologic applications.
<b>Proprietary manufacturing process</b> ✓	Cerenis owns the right to an exclusive, validated, and scalable manufacturing process to produce apoA-I, apoA-I peptides and HDL on an industrial scale.
<b>Indications</b> ✓	Cerenis unique and broad IP covers composition of matter and methods of use (indications).



**HDL PARTICLES ARE NATURAL MOLECULE CARRIERS READILY DELIVERED TO  
TISSUES AND CIRCULATING CELLS**

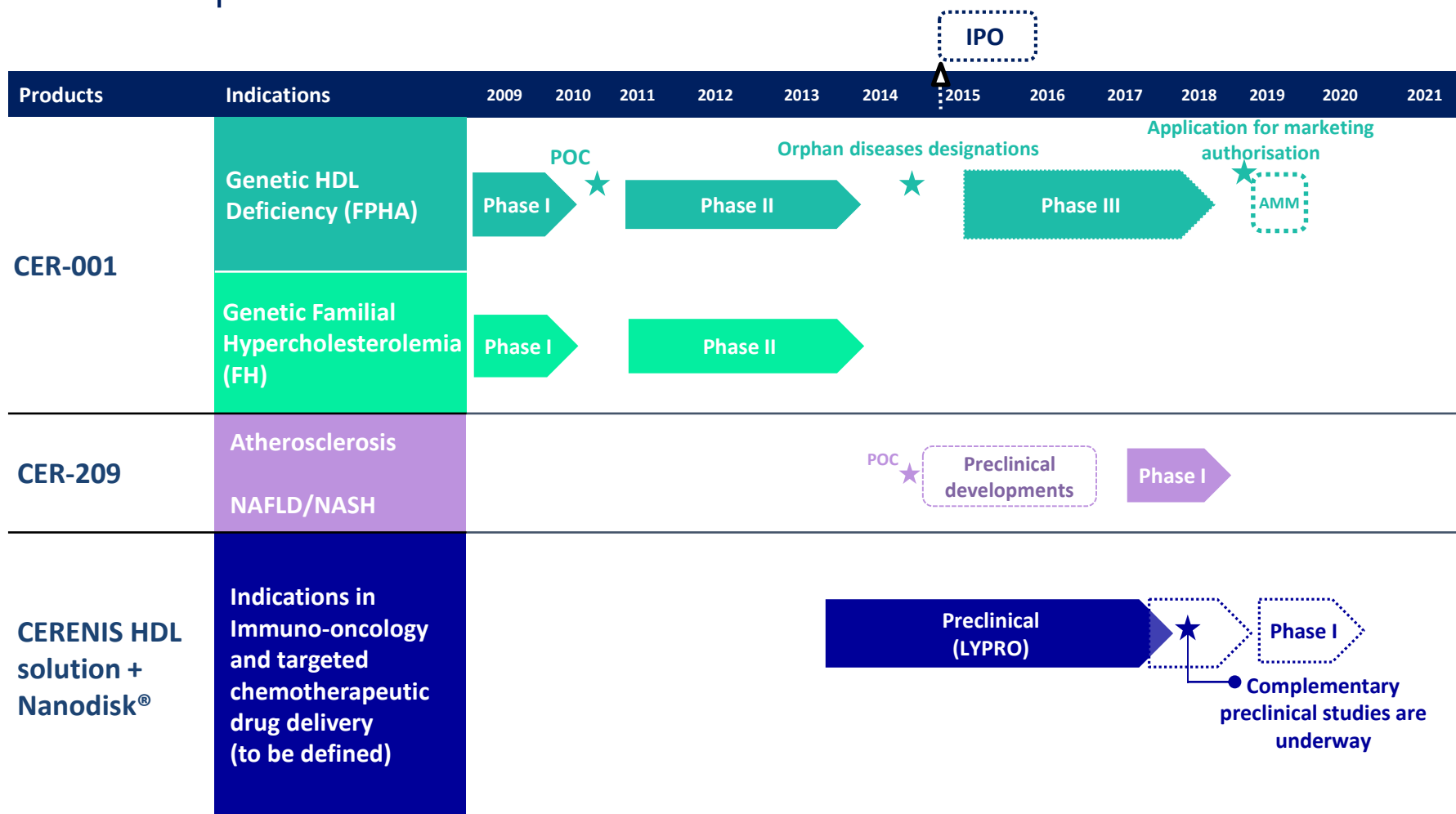
# Cerenis holds the proprietary manufacturing process for natural recombinant human apoA-I and HDL particles



- Manufacturing costs that will lead to substantial savings at scale-up
- An economically-viable HDL manufacturing process



**NO COMPETITOR CAN REPRODUCE THE CHARGED APOA-I CONTAINING NANOPARTICLE**



**IMMUNO-ONCOLOGY AND CHEMOTHERAPEUTIC FIELDS REPRESENT NEW MARKET OPPORTUNITIES FOR CERENIS' HDL SOLUTION**