Cardiovascular Programs

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OMNI™ Technology Platform

Superior Performance through AI-Driven Design

AnGes

About EmendoBio

- Founded in U.S. in 2016 by scientists from the Weizmann Institute, Israel
- Founding investors: OrbiMed and Takeda Ventures
- AnGes became a majority shareholder in December 2020

Management

Naoya Satoh, PhD
President & CEO

Assaf Sarid
CFO

Idit Buch, PhD
VP, Computational Biology

Roy Sirkis, PhD
VP, Biomaterials Development and Production

Board of Directors

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AnGes

Naoya Satoh, PhD
AnGes

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Columbia University

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Chief Genetic Immunotherapy, NIH

David Rawlings, MD
Director Immunity and Immunotherapies, SCRI

Andrew Kung, MD PhD
Chair Dept. Peds. Sloan Kettering

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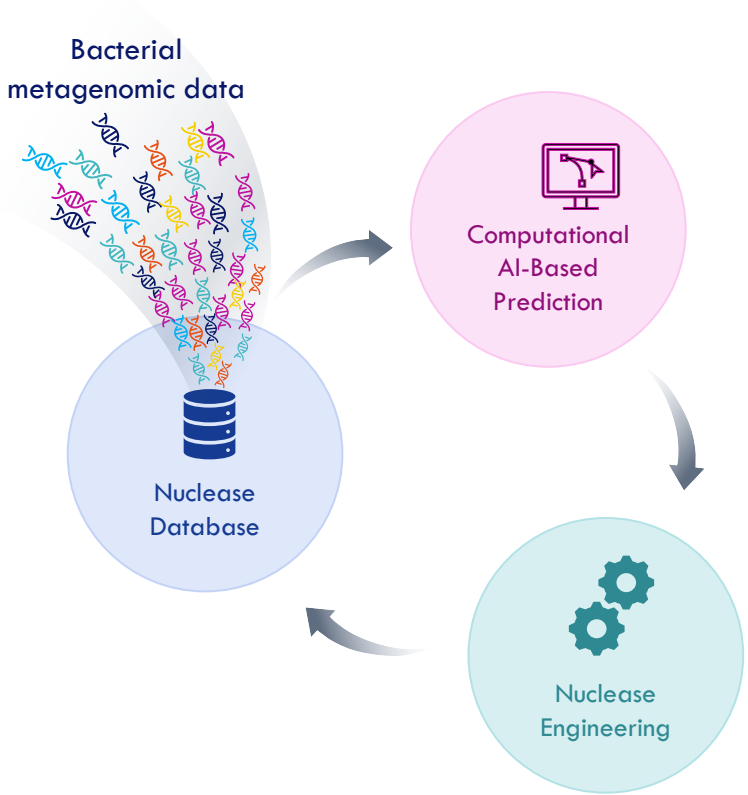
OMNI™ Platform Offers a Variety of Gene-Editing Solutions

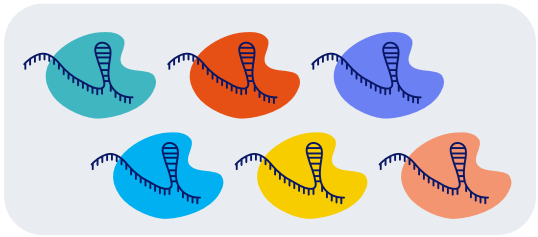
Synergistic discovery, engineering and computational technologies combine to produce a portfolio of high-performance OMNI™ nucleases

EmendoBio's Platform



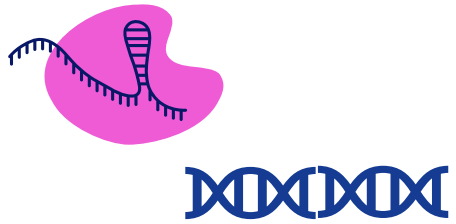
Panel of Engineered OMNI™ Nucleases

- Novel
- Highly active
- Highly specific



Optimal Therapeutic Compositions per target

- High safety profile
- Expanded range of applications
- Freedom to operate



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OMNI™ Panel Genome Accessibility

Nuclease Portfolio

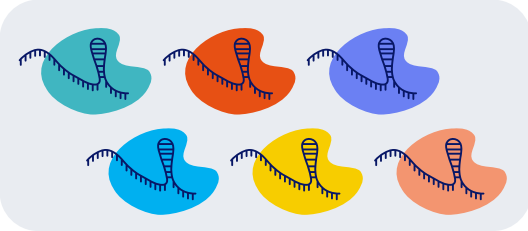
10,000 discovered nucleases

300 validated in vitro

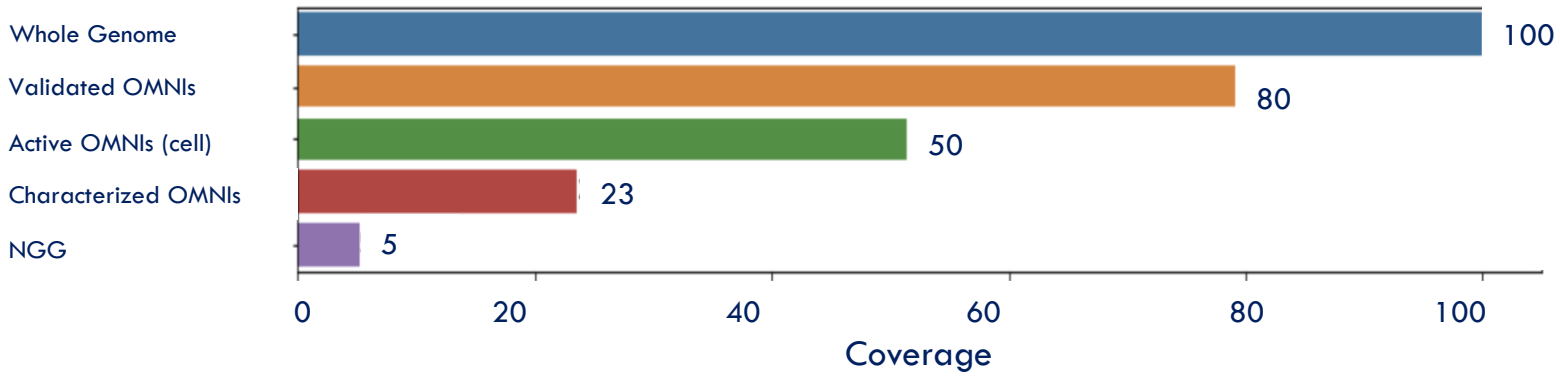
80 shown active in cells

12 characterized

2 engineered



OMNI™ Genomic PAM Coverage



The diversity of PAM sites of the OMNI™ nucleases overcomes PAM constraints and significantly widens genome accessibility, making **any gene targetable**

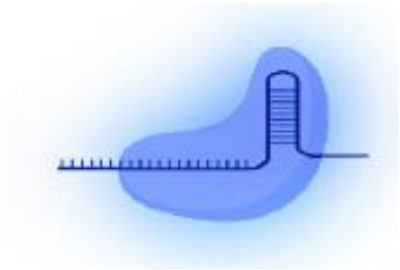
Nuclease Engineering Platform

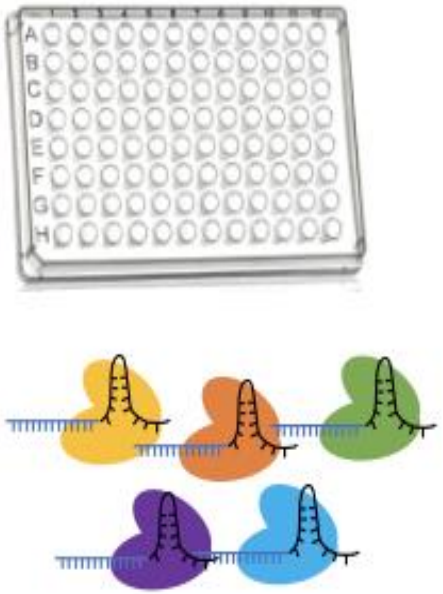
OMNI™ nuclease (from panel)

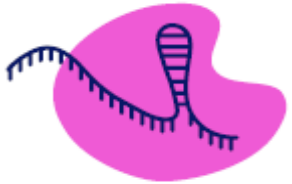
AI based engineering for variant library generation

Libraries of nuclease variants

Screening in mammalian cell line







Highly Active and Specific
Optimized OMNI™ Variants

Pipeline

Disease Area	Program	Target	Indication	Approach	Research	Lead Optimization	IND-Enabling	Phase 1
Hematology	EMD-101	ELANE	Severe Congenital Neutropenia	Allele-specific ex vivo excision				
Cardiovascular	EMD-301	LDLR	**ASCVD not at LDL-C goal** Including Heterozygous Familial Hypercholesterolemia (HeFH)	In vivo excision				
	EMD-302	ANGPTL3	**ASCVD not at LDL-C goal** Including Homozygous Familial Hypercholesterolemia (HoFH)	In vivo KO				
Ocular	EMD-201	SARM1	Glaucoma	In vivo KO				
	EMD-202	RHO	Retinitis Pigmentosa	In vivo excision				
	EMD-203	RPE65	Retinitis Pigmentosa	In vivo excision				

EMD-301 Targeting *LDLR*

Cardiovascular Program

Gaps in Dyslipidemia Management in 2023

Atherosclerotic cardiovasvolar disease (ASCVD) is the leading cause of cardiovascolar disease (CVD) morbidity and mortality -19 million CV deaths in 2020[1].

Chronic care: The recommended LDL-cholesterol (LDL-C) thresholds now typically require multiple agents targeting LDL-C to achieve levels of <70 mg/dL

During the 1st year after an acute MI episode ~20% of patients had low adherence to statins[2]

Despite availability of multiple treatment options, most patients do not achieve the LDL-C goal[3]

1. 2023 Heart Disease and Stroke Statistics Update Fact Sheet- American Heart Association
2. Low adherence to statin treatment during the 1st year after an acute myocardial infarction is associated with increased 2nd-year mortality risk-an inverse probability of treatment weighted study on 54 872 patients. Eur Heart J Cardiovasc Pharmacother. 2021 Mar 15;7(2):141-147.
3. EU-Wide Cross-Sectional Observational Study of Lipid-Modifying Therapy Use in Secondary and Primary Care: the DA VINCI study, European Journal of Preventive Cardiology, Volume 28, Issue 11, November 2021, Pages 1279–1289.

7M Patients in the USA Not at LDL-C Goal on Current Treatments

Chronic care: Recommended therapy typically involves multiple agents and requires lifelong management[1]

Low compliance with chronic treatment[2]

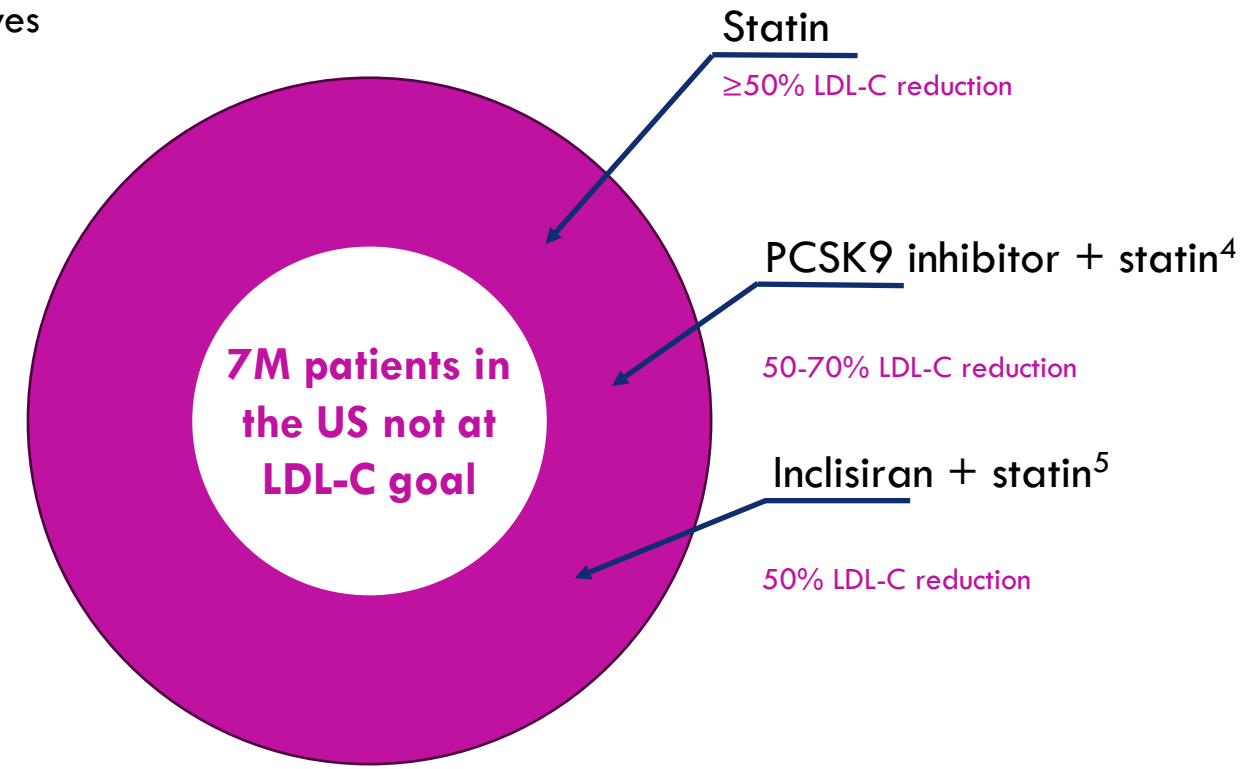
Many patients fail to achieve LDL-C goal[3]

Patient Population

- **7M patients in the U.S., 100M patients worldwide**

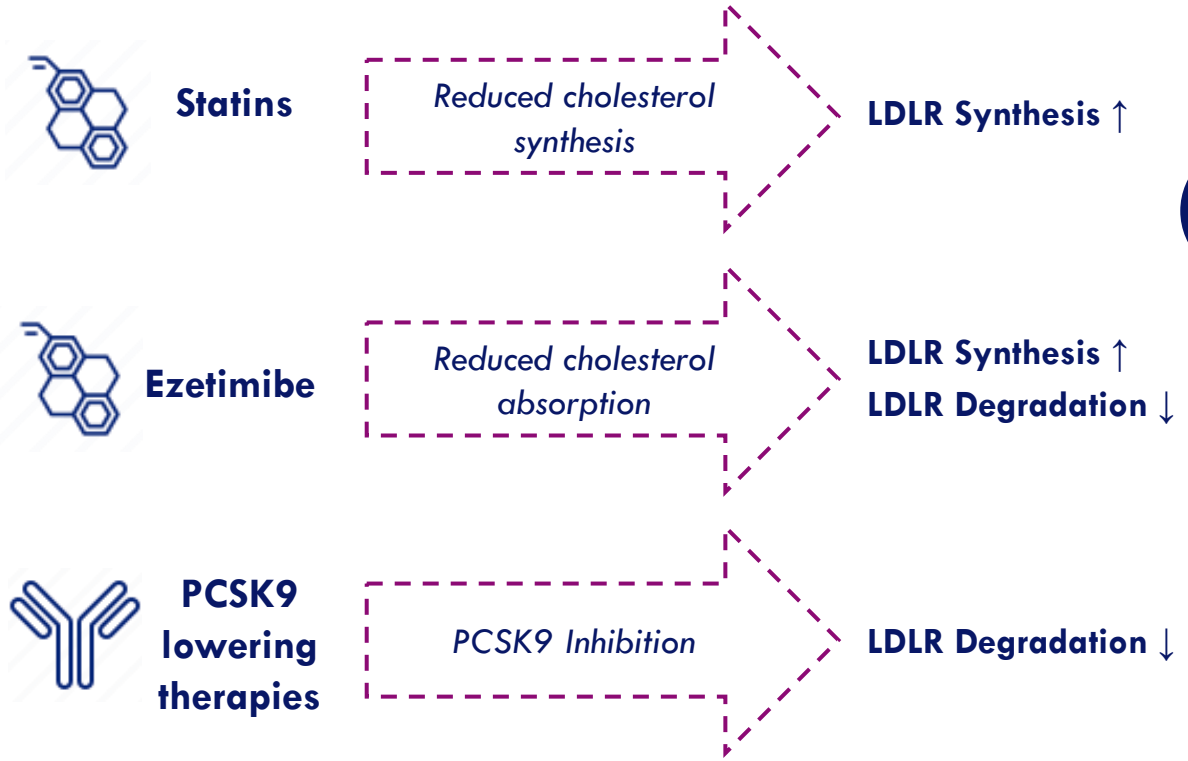
Market Size

- **$5-7B in the U.S.**



1. Intensive low-density lipoprotein cholesterol lowering in cardiovascular disease prevention: opportunities and challenges. Heart. 2021 Sep; 107(17): 1369–1375.
2. Nonadherence to lipid-lowering therapy and strategies to improve adherence in patients with atherosclerotic cardiovascular disease. Clinical Cardiology 46.1 (2023): 13-21.
3. EU-Wide Cross-Sectional Observational Study of Lipid-Modifying Therapy Use in Secondary and Primary Care: the DA VINCI study, European Journal of Preventive Cardiology, Volume 28, Issue 11, November 2021, Pages 1279–1289.
4. Efficacy and safety of alirocumab in reducing lipids and cardiovascular events, New England Journal of Medicine 372.16 (2015): 1489-1499.
5. Raal, Frederick J., et al. "Inclisiran for the treatment of heterozygous familial hypercholesterolemia." New England Journal of Medicine 382.16 (2020): 1520-1530.

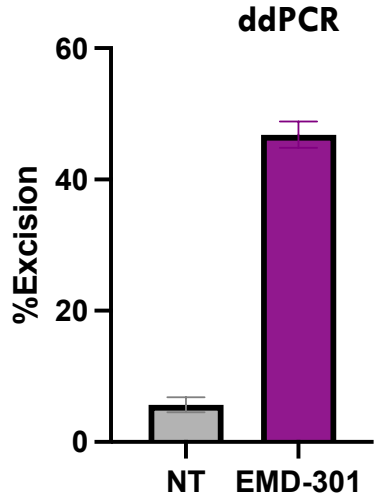
LDLR Upregulation is a Clinically Validated Approach for LDL-C Clearance and Reduced Risk for ASCVD



Direct strategy to upregulate LDLR expression

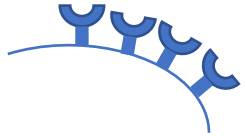
Excision in 3'UTR Leads to **Upregulation of LDLR** and **LDL-C Uptake** in Human Hepatocyte Cell Line

1.

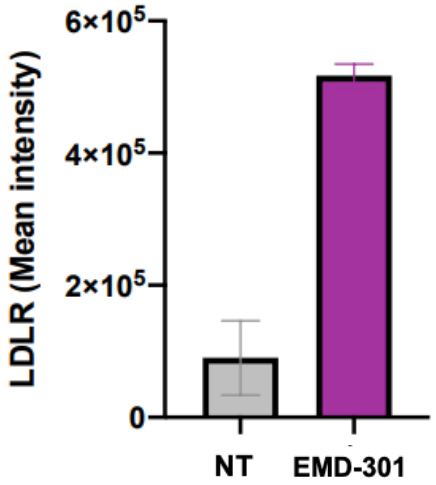


40-50% Excision

2.



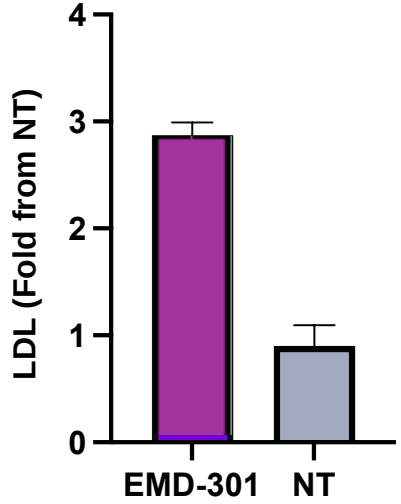
Surface LDLR ↑



~2-3 fold increase in surface LDLR

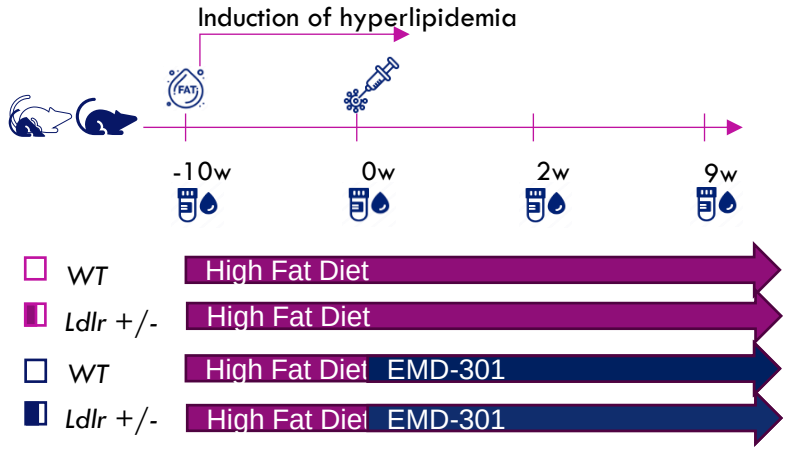
3.

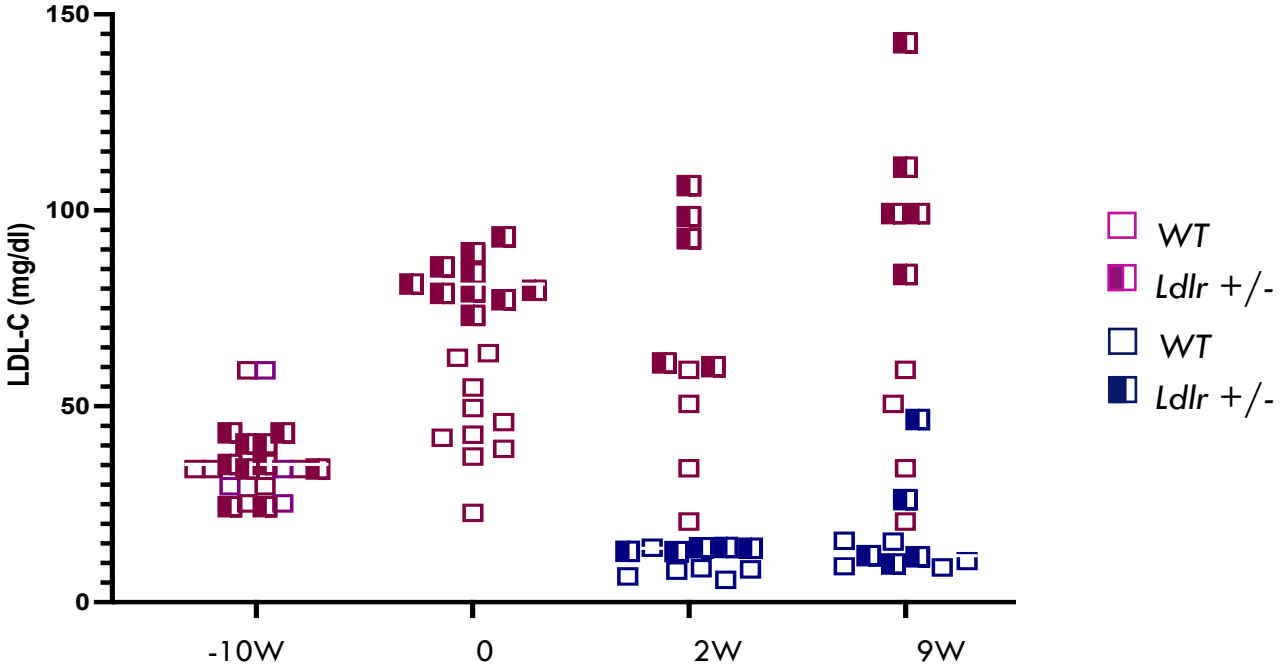
LDL-C Uptake ↑

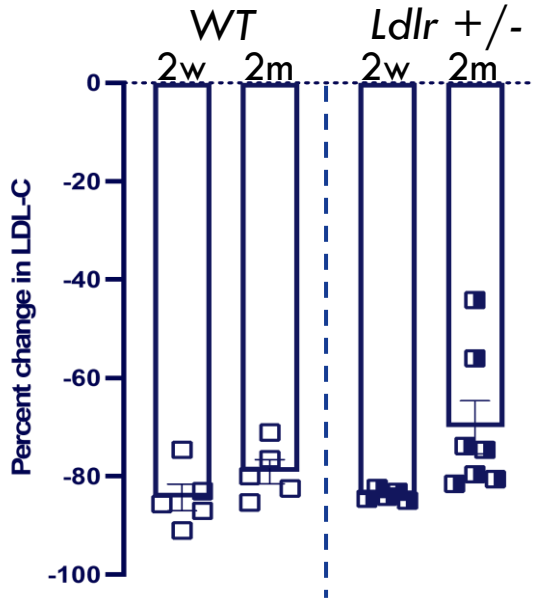


HepG2 liver cells treated by electroporation with nuclease and guide RNA

Treatment in vivo with mEMD-301 Leads to >80% LDL-C Clearance







Genomic Safety

Off-target ID and validation

In-silico prediction

→ ±350 targets predicted

In-vitro assay

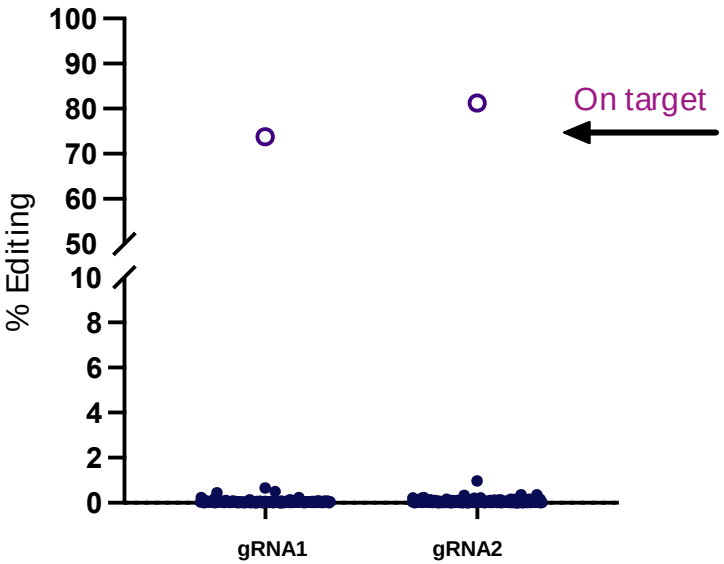
→ 5 off-targets detected

Cell based assay

→ No off-target detected in U2OS cells

rhAmpSeq

→ No validated off-targets



Competitive Advantage

EMD-301 targeting LDLR

Product name	Company	Target	Technology	Route of administration	Dosing frequency	Clinical stage	LDL reduction rates
Alirocumab/ Evolumab + statin	Regeneron/ Amgen	PCSK9	Antibody	IP	Every 2-4 weeks	FDA/EU approved	50-70%
Inclisiran + statin	IONIS	PCSK9	siRNA	IP	Every 6 months	FDA/EU approved	50%
VERVE-101	Verve	PCSK9	Base editing	IV	Single dose	Phase I-II	50%
EMD-301	EmendoBio	LDLR	3'UTR excision	IV	Single dose	Preclinical	80%*

*In a mouse model

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Summary

EMD-301 cardiovascular program

- Uses a proprietary approach to increase LDLR level by excision in 3'UTR
- Demonstrated an 80% reduction in LDL-C in a mouse model
- Expected high safety profile with no off-targets detected
- Potential new treatment option for 7M (U.S.) underserved patients
- FDA INTERACT meeting completed

EMD-302 Targeting *ANGPTL3*

Cardiovascular Program

ASCVD Including Homozygous Familial Hypercholesterolemia (HoFH)

Inhibition of ANGPTL3 induces clearance of triglyceride-rich lipoproteins upstream of low-density lipoprotein production

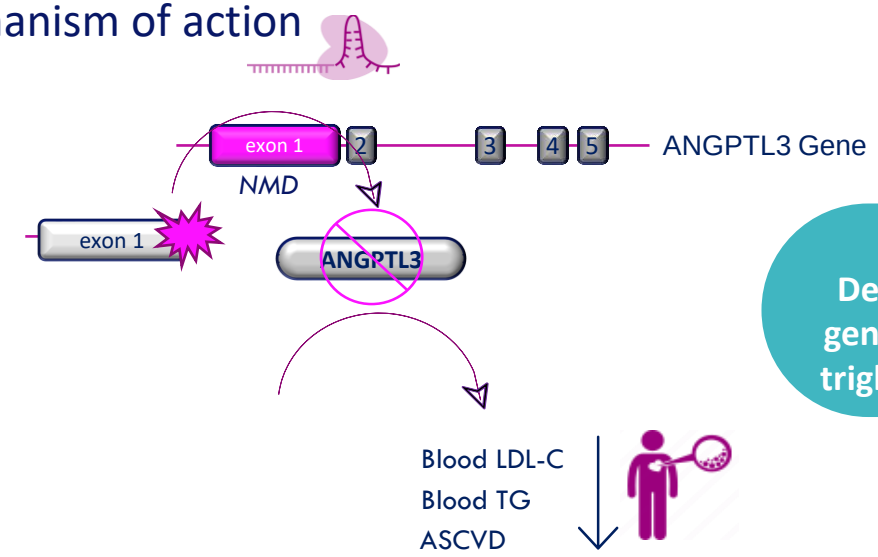
ANGPTL3 as a therapeutic target:

- Clinical validation of efficacy[2]
- Safety and MoA validated by human genetics[3]

High unmet need

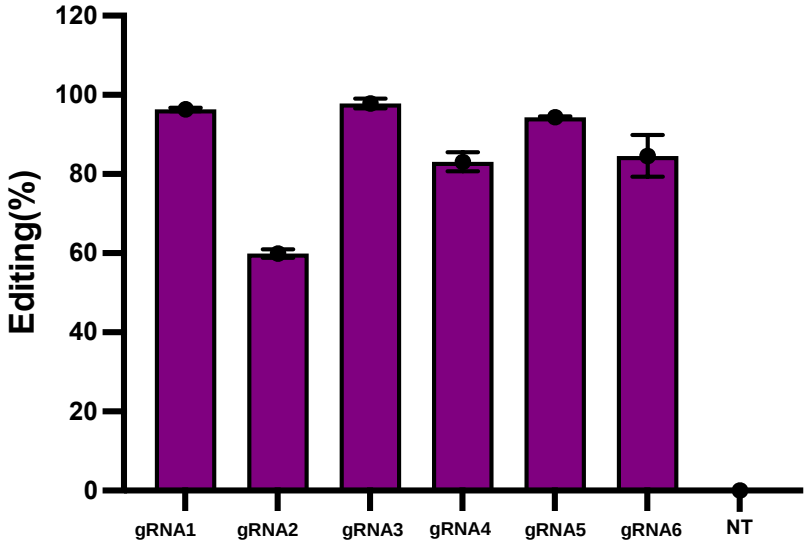
- 7M patients in US1 / EU not at LDL-C goal on oral statins+PCSK9[1]
- 47% of HoFH patients not at LDL-C goal

Mechanism of action



EMD-302
Designed to KO the *ANGPTL3* gene in hepatocytes, to reduce triglycerides levels in the blood

In-vitro results demonstrate high editing efficiency

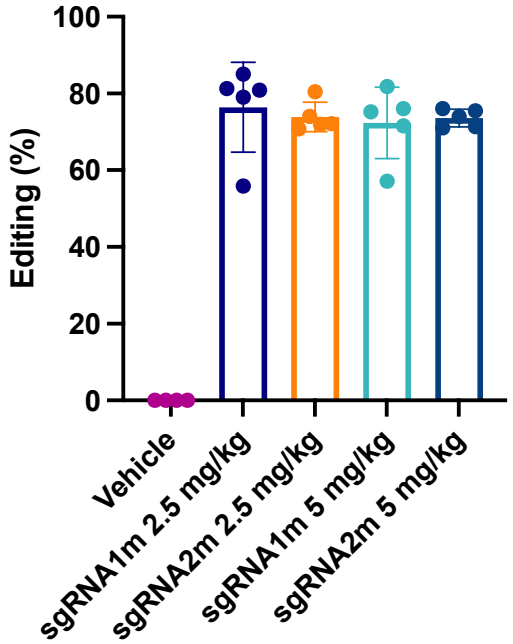


1. O'Donoghue et al., Circulation. 2022;146:1109–1119
2. Evinacumab, an ANGPTL3 Inhibitor, in the Treatment of Dyslipidemia Sosnowska B, et al. J Clin Med. 2022
3. Lifelong Reduction in LDL Cholesterol Due to a Gain-of-Function Mutation in *LDLR* *Bjornson, E., et al.* Circulation: Genomic and Precision Medicine. 2021;14:e003029

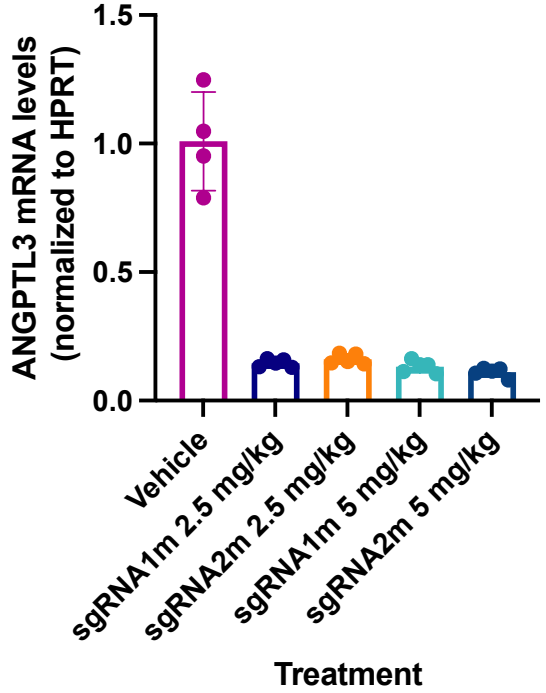
In-vivo preclinical Data to Proof of Concept

Highly efficient knock-out of the *ANGPTL3* gene leads to over 95% reduction in protein levels in a mouse model

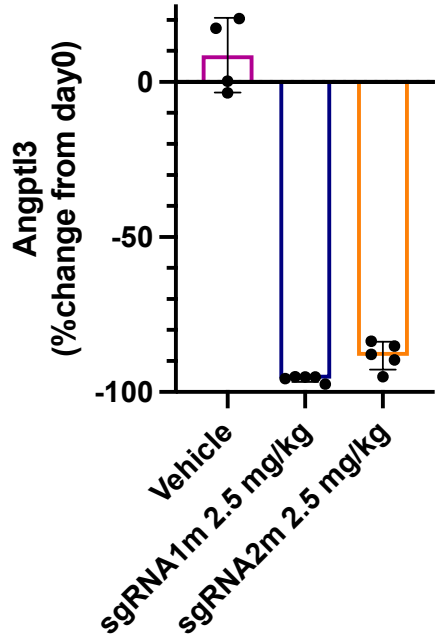
Editing (NGS)



ANGPTL3-mRNA (qPCR)



ANGPTL3 protein (ELISA)



Summary

EMD-302 cardiovascular program

- Uses a proprietary approach to knock out *ANGPTL3* using a novel non-NGG nuclease
- Demonstrated over 95% reduction in ANGPTL3 protein in a mouse model
- Potential new treatment option for 7M underserved patients
- Initial PoC studies completed