OMEGA™ THERAPEUTICS

Harnessing the Power of Epigenomic Controllers

Pioneering a New Class of Programmable Epigenomic Medicines

November 2024

Disclaimer and Forward-Looking Statements

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this presentation that do not relate to matters of historical fact should be considered forward-looking statements, including without limitation statements regarding: our anticipated cash runway; our prioritization of certain preclinical programs and platform efforts; potential strategic partnership opportunities; our competitive market position and market opportunity; our expectations surrounding the applicability and potential of our product candidates and programs, development timelines; anticipated timing of regulatory submissions and filings and introduction of development candidates; and expectations regarding our programs and pipeline, including our priorities and anticipated milestones, trial design, initiation of preclinical studies and our goal of declaring additional EC development candidates. These statements are neither promises nor guarantees, but involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including, but not limited to, the following: the novel technology on which our product candidates are based makes it difficult to predict the time and cost of preclinical and clinical development and subsequently obtaining regulatory approval, if at all; the substantial development and regulatory risks associated with epigenomic controllers due to the novel and unprecedented nature of this new category of medicines; our limited operating history; the incurrence of significant losses and the fact that we expect to continue to incur significant additional losses for the foreseeable future; our need for substantial additional financing; volatility in capital markets and general economic conditions; our investments in research and development efforts that further enhance the OMEGA platform, and their impact on our results; uncertainty regarding preclinical development, especially for a new class of medicines such as epigenomic controllers; potential delays in and unforeseen costs arising from our clinical trials; the fact that our product candidates may be associated with serious adverse events, undesirable side effects or have other properties that could halt their regulatory development, prevent their regulatory approval, limit their commercial potential, or result in significant negative consequences; difficulties manufacturing the novel technology on which our EC candidates are based; our ability to adapt to rapid and significant technological change; our reliance on third parties for the manufacture of materials; our ability to successfully acquire and establish our own manufacturing facilities and infrastructure; our reliance on a limited number of suppliers for lipid excipients used in our product candidates; our ability to advance our product candidates to clinical development; and our ability to obtain, maintain, enforce and adequately protect our intellectual property rights. These and other important factors discussed under the caption “Risk Factors” in our most recent Quarterly Report on Form 10-Q and our Annual Report on Form 10-K for the year ended December 31, 2023, and our other filings with the SEC could cause actual results to differ materially from those indicated by the forward-looking statements made in this presentation. Any such forward-looking statements represent management’s estimates as of the date of this presentation. While we may elect to update such forward-looking statements at some point in the future, we disclaim any obligation to do so, even if subsequent events cause our views to change.

Omega is Pioneering the Development of a New Class of Programmable Epigenomic Medicines

Leader in Epigenomic Modulation	• Differentiated platform capable of durable gene upregulation, downregulation, and multiplexing; May enable more potent, durable, and safer therapeutics vs. existing modalities • Pre-transcriptional approach broadly applicable to nearly any human disease • Comprehensive preclinical proof-of-concept data across diverse therapeutic areas
Clinically-Validated Approach	• Clinical proof-of-mechanism established in first-in-human Phase 1 trial in HCC patients • First and only to demonstrate highly-specific targeting and intended epigenetic state change with an EC in patients • Validates epigenomic controllers as potential new class of medicines
Pipeline Positioned for Value Creation	• Strategically focused on high-value programs with clear paths to value inflection • Initial programs in obesity, liver regeneration and metabolic health • Disciplined, data-driven resource allocation to inform program advancement decisions
Strategic Partnerships	• First-in-class collaboration with Novo Nordisk to develop a novel epigenomic controller for obesity • Pursuing strategic partnerships to support development of existing programs and expand pipeline into new areas

Omega's Diverse Capabilities and Expertise Provide Foundation for Value Creation

A Clinically-Proven Platform with Broad Applicability to Nearly Any Gene

Robust R&D engine for expedited prosecution of new targets

Proprietary database of epigenomic effectors & DNA binding domains

Screened >1M unique drug targets

>100 targets validated *in silico / in vitro / in vivo* across diverse disease areas

Clinical proof-of-mechanism validates and de-risks platform

Value-focused pipeline driven by internal efforts and external strategic partnerships

Extensive delivery and formulations expertise

Precision Epigenomic Control is a Significant Technological Advance

Pre-transcriptional approach addresses limitations of other modalities

- Access to any target, independent of structure, chemistry or location; addresses undruggable/ inaccessible targets
- Uncouples PK and PD for potential safety benefit
- Exquisite specificity and bi-directional control of gene expression for therapeutic benefit
- Avoids liabilities of permanent genetic alterations
- Applicable to any human gene or disease process

Data from Completed Phase 1 First-in-Human Trial of OTX-2002 Establish Clinical Proof-of-Mechanism of Omega's Epigenomic Controller Platform

Clinical validation of epigenomic controllers as a potential new class of medicines

In Phase 1 trial of late-stage HCC patients, OTX-2002 demonstrated:

- ✓ Predictable and consistent pharmacokinetics
- ✓ Highly-specific binding at target genomic loci
- ✓ Intended epigenetic state change with on-target increase in methylation signature
- ✓ Persistent epigenetic effect throughout dosing period
- ✓ Downregulation of MYC expression observed
- ✓ 50% DCR in evaluable late-line HCC patients, with best overall response of Stable Disease
  - Within range of completed Phase 1 trials for TKIs and PD-1 monotherapies in HCC: DCR (29-65%)

Unlocks broad applicability of OMEGA platform across disease areas

Pipeline Focused on Significant Opportunities with Clear Paths to Value Inflection

Data-Driven Resource Allocation to Drive Program Advancement Decisions

Selection Framework

- **Clear biology**
- **OMEGA differentiation**
- **Delivery & technical feasibility**
- **Clinical development pathway**
- **Regulatory considerations**
- **Market opportunity**

Prioritized Pipeline and Focus Areas

Undisclosed (Novo Nordisk)	Obesity	• Multi-billion dollar opportunity • Trans-differentiation of adipose tissue offers novel strategy for management of obesity • All R&D costs reimbursed by Novo Nordisk
HNF4A	Fibrosis / Liver Regeneration	• Multi-billion dollar opportunity • Potential to durably halt or reverse liver disease • Epigenomic upregulation may offer enhanced efficacy versus exogenously administered agents
FGF21	Multiple Metabolic Indication Opportunities	• Clinically-validated target with clear development path; potential for rapid readout of therapeutic effect • May offer more potent and durable therapeutic benefit • Potential to address multiple metabolic indications where upregulation of natural expression cannot be mimicked by existing modalities
Future Pipeline Opportunities	Multiple Therapeutic Areas and Tissues	• Additional targets under evaluation for strategic partnering or internal development via disciplined, stage-gated process for program advancement

With Clinical Proof-of-Platform Established, Omega is Advancing a Focused Pipeline of High-Value Programs

TARGET GENE(S)	INDICATION	DISCOVERY	LEAD OPTIMIZATION	IND-ENABLING	PARTNER
Regenerative Medicine					
HNF4A	Fibrosis / Liver regeneration				
Metabolic					
Undisclosed	Obesity				novo nordisk®
FGF21	Multi-Indication Opportunities				

Additional gene targets under evaluation for strategic partnering or internal development via disciplined, stage-gated process for program advancement

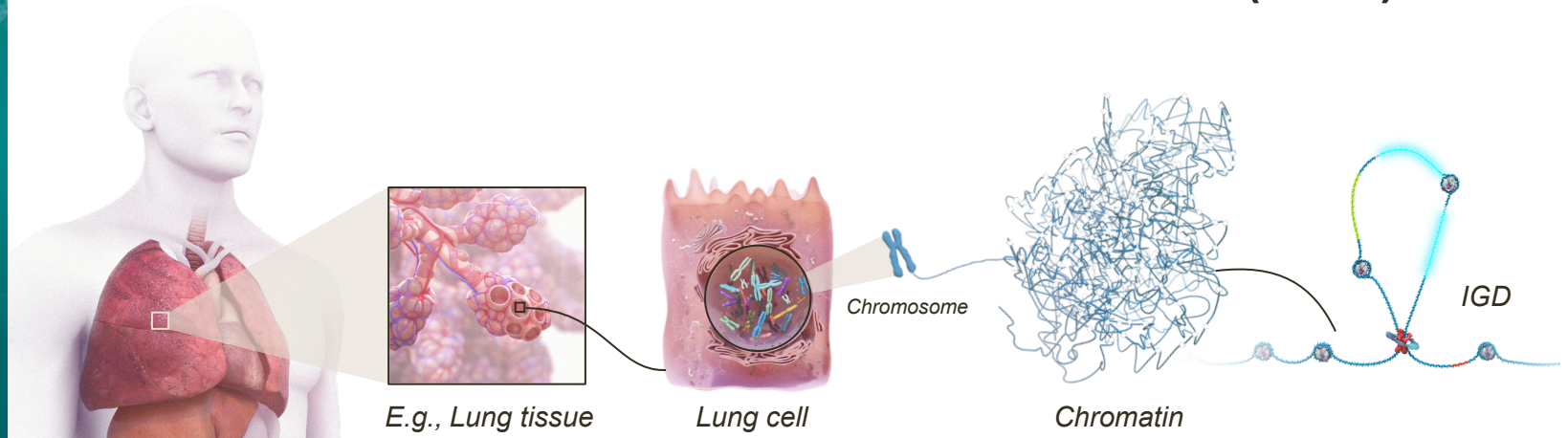
OMEGA Platform Overview

OMEGA™ THERAPEUTICS

Insulated Genomic Domains Are Nature's Control System to Regulate Gene Expression

IGDs are the fundamental structural and functional units for gene control

Nature organizes genes in evolutionarily conserved 3D loops of chromatin called Insulated Genomic Domains (IGDs)



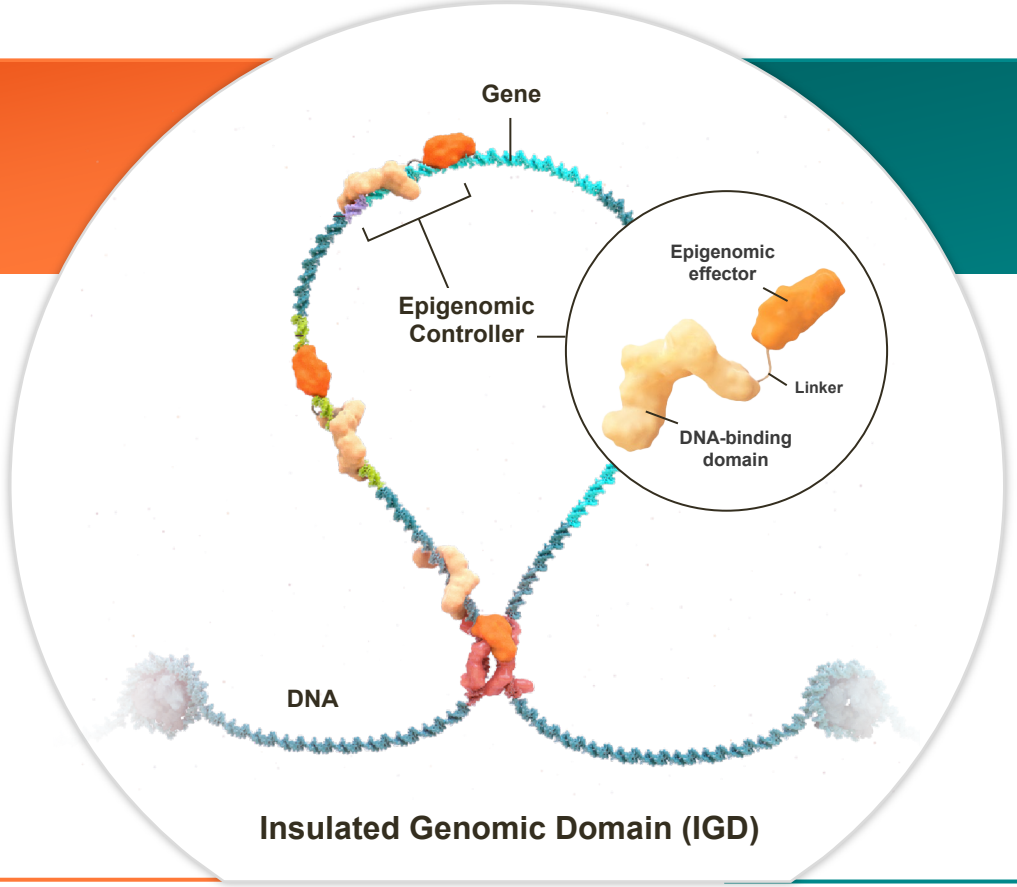
- Insulated from outside transcription by CTCF, each IGD contains 1-10 genes & their regulatory elements
- Regulators have unique DNA-sequences (**Epi**genomic **Zip**codes, "EpiZips"); can be used as drug targets
- Most diseases are caused by aberrant gene expression driven by epigenetic changes within IGDs

Source: Hnisz, D., Day, D.S., Young, R.A. *Cell.* Vol. 167, Issue 5, p1188-1200 (2016).

OMEGA Platform Engineers Programmable Epigenomic Therapeutics

BIOLOGY
New Drug Targets

- Insulated genomic domains (IGDs): Contain genes and their controlling regulators
- EpiZips: Unique regulatory sequences as precise drug targets



TECHNOLOGY
Epigenomic Controllers

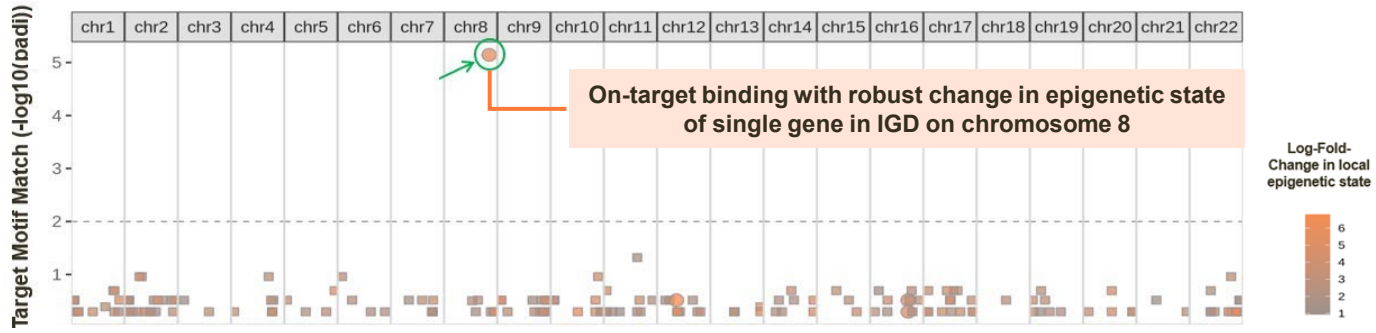
- mRNA expresses a fusion protein consisting of:
  - DNA-binding domain for site-specific targeting
  - Epigenomic effector for controlled and durable gene modulation

Pre-transcriptional control of gene expression leveraging nature's control system

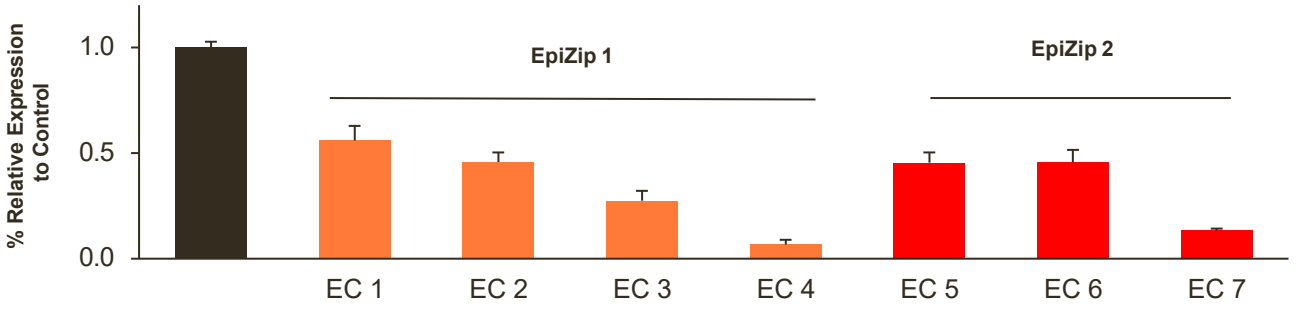
Unique Epigenomic Control at Pre-transcriptional Level

Exquisite Specificity	Precise binding to ~21 base pair sequence(s) to target a single gene or IGD genome-wide
Controlled Tunability	Bi-directional tuning and precise control on magnitude of expression
Tailored Durability	Transient PK with prospectively engineered durability tailorable to last days, weeks or months

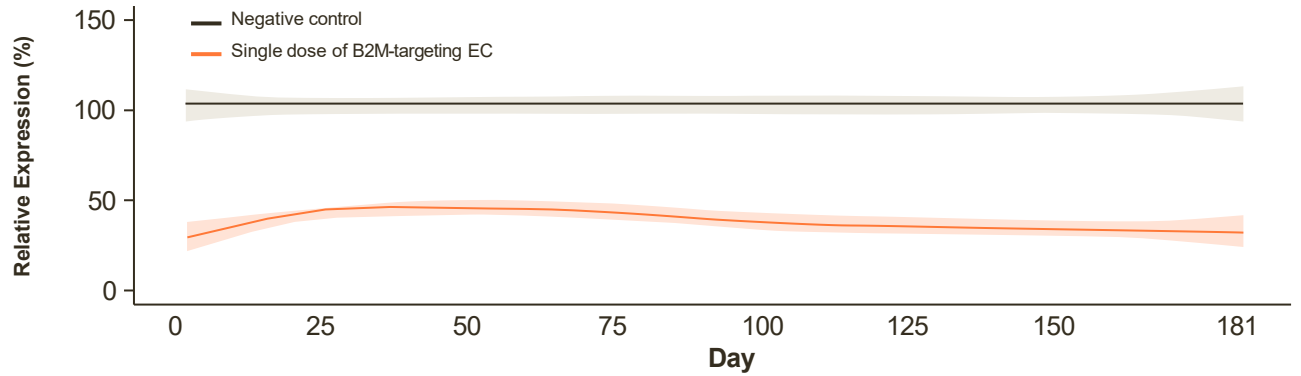
MYC



MYC



B2M

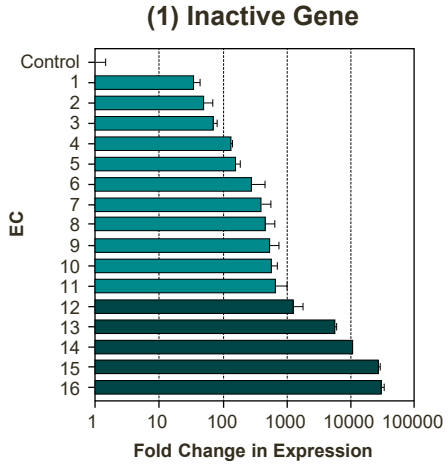


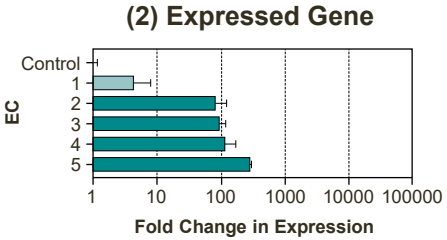
Specificity: In vitro immunoprecipitation ChiP data
Tunability and Durability: In vitro qPCR

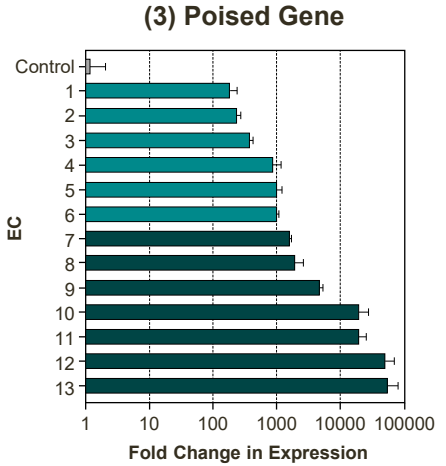
Durable Upregulation of Multiple Gene Targets

Upregulation achieved across diverse genes, including:

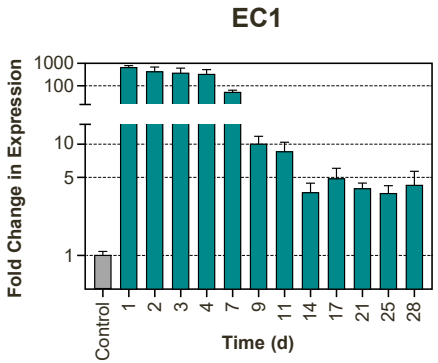
1. Genes that are inactive in a cell type of interest
2. Genes that are expressed but whose further upregulation leads to therapeutic benefit
3. Genes that are inactive or lowly-expressed but are in a poised state, ready for high activation upon pathway engagement or stimulation

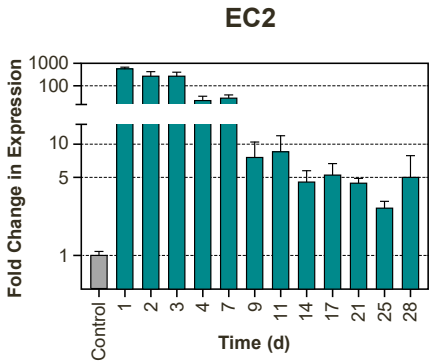


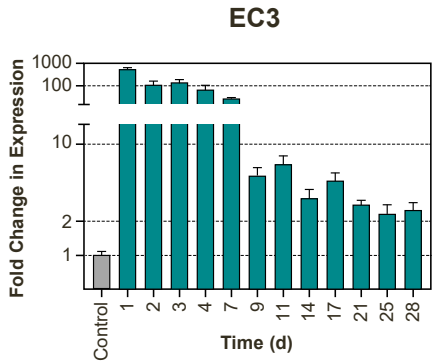


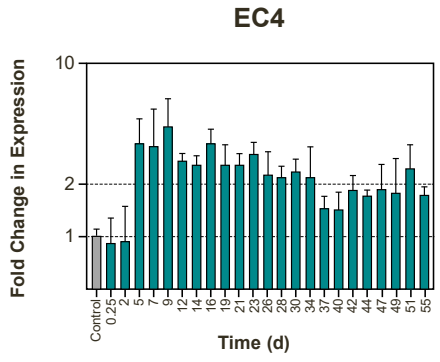


Durable upregulation following a single EC dose, weeks to months







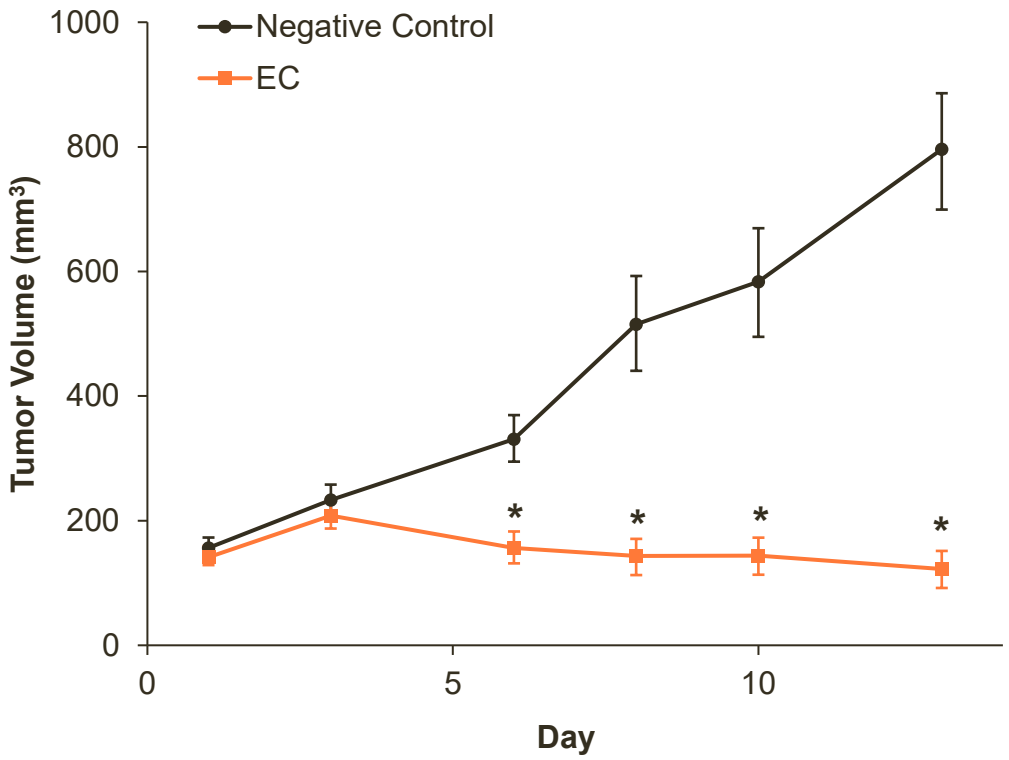


Source: Data presented at ASGCT 2024.

Proof-of-Concept Demonstrated Across Diverse Set of Disease Areas

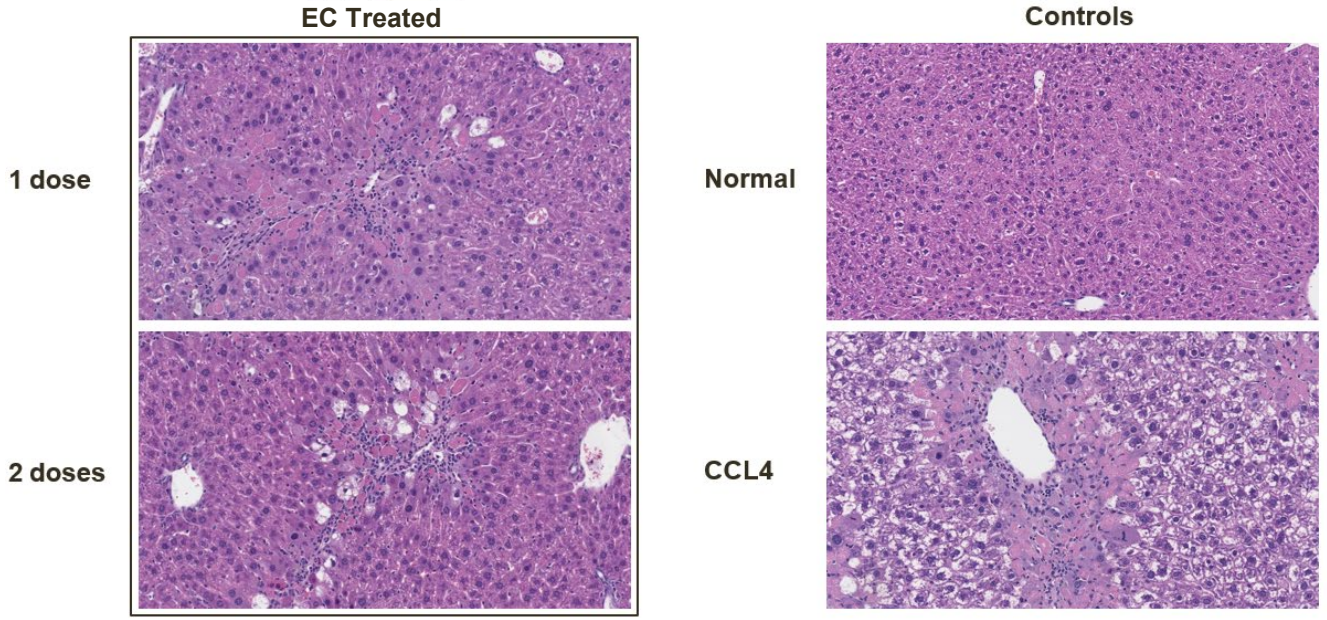
Oncology (MYC HCC)

Statistically significant inhibition of HCC tumor growth *in vivo* through direct targeting of c-MYC



Liver Regeneration (HNF4a)

Significant improvement in liver histology in murine model of fibrosis



EC ameliorates CCL4-induced hepatic fibrosis in C57BL/6J mice

*Statistically significant vs negative control, t-test p<0.05 starting on day 6

Prioritized Programs

OMEGA™ THERAPEUTICS

Thermogenesis Research Collaboration with Novo Nordisk

Opportunity For Orthogonal and Transformative Innovation In Obesity

- **Trans-differentiation of human adipose tissue:** Transitioning the epigenetic state of white to metabolically active brown fat
- **Potential first-in-class program:**
  - Epigenomic controller that regulates "browning" of human white adipose tissue
  - LNP to adipose tissue

- **Collaboration validates broad applicability of the OMEGA platform**
- **Strategically complements** our internal efforts and expands our pipeline into cardiometabolic / obesity
- **Novo reimburses all R&D costs**

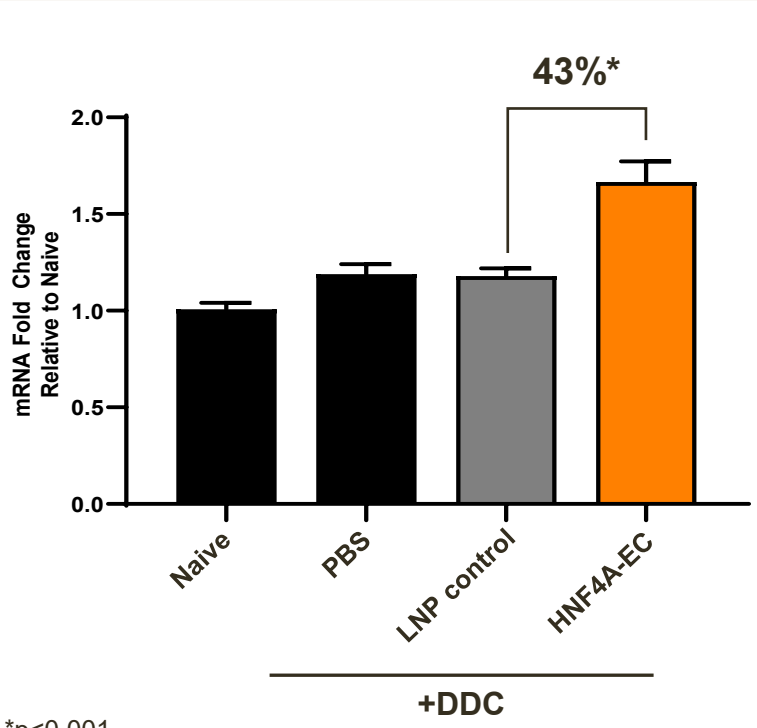
Project initiated in Q1 2024 with epigenomic controller design, discovery, and formulation

HNF4A: Potential Opportunity in Fibrotic Liver Diseases

EC Significantly Upregulated Gene Expression and Reduced Key Fibrosis Measures *In Vivo*

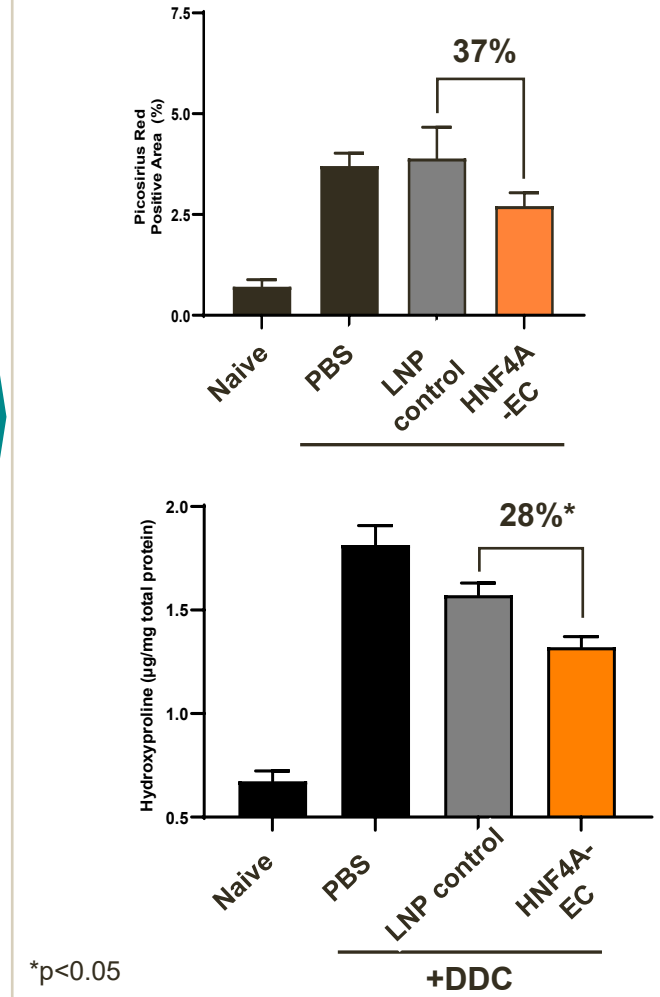
- HNF4α is a critical transcriptional regulator of hepatocyte differentiation and function; expression is dysregulated in fibrotic liver disease
- Upregulation with an EC has potential to durably mitigate liver fibrosis and restore hepatocyte and liver health; May offer enhanced efficacy vs. exogenously administered agents
- Omega's preclinical data demonstrated selective and durable upregulation of HNF4α expression, leading to decreased collagen deposition in the liver, in *in vivo* proof-of-concept studies

HNF4α Expression



*p<0.001

HNF4α Induction Conferred Protection in DDC Fibrosis Model

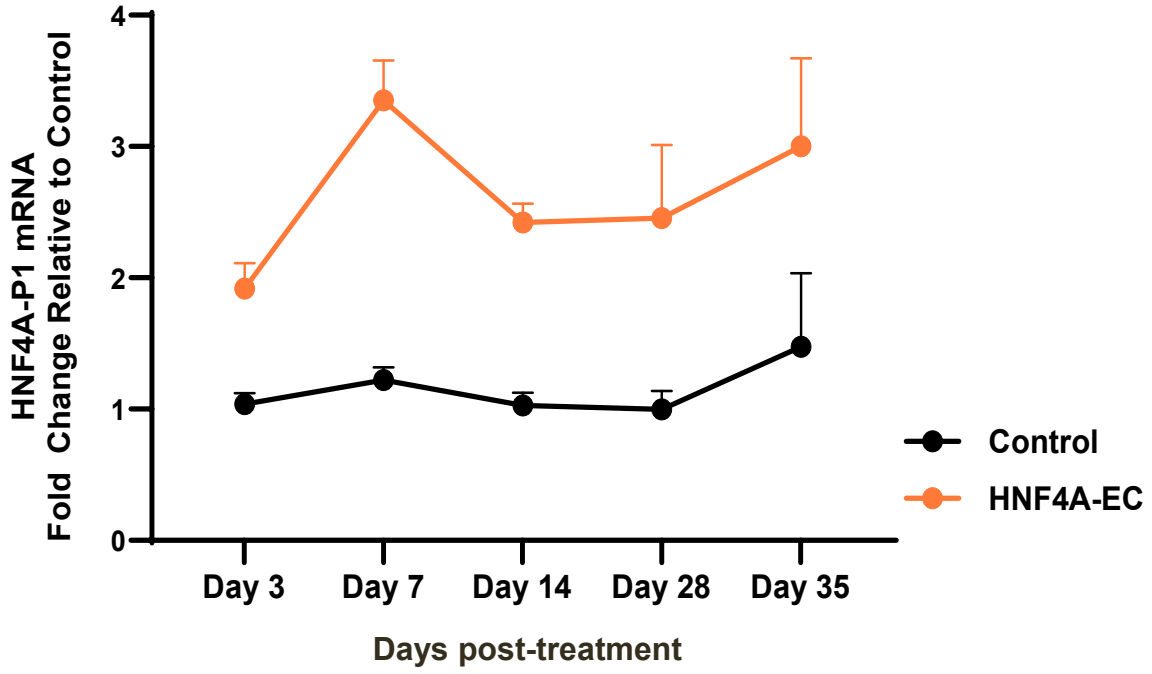


*p<0.05

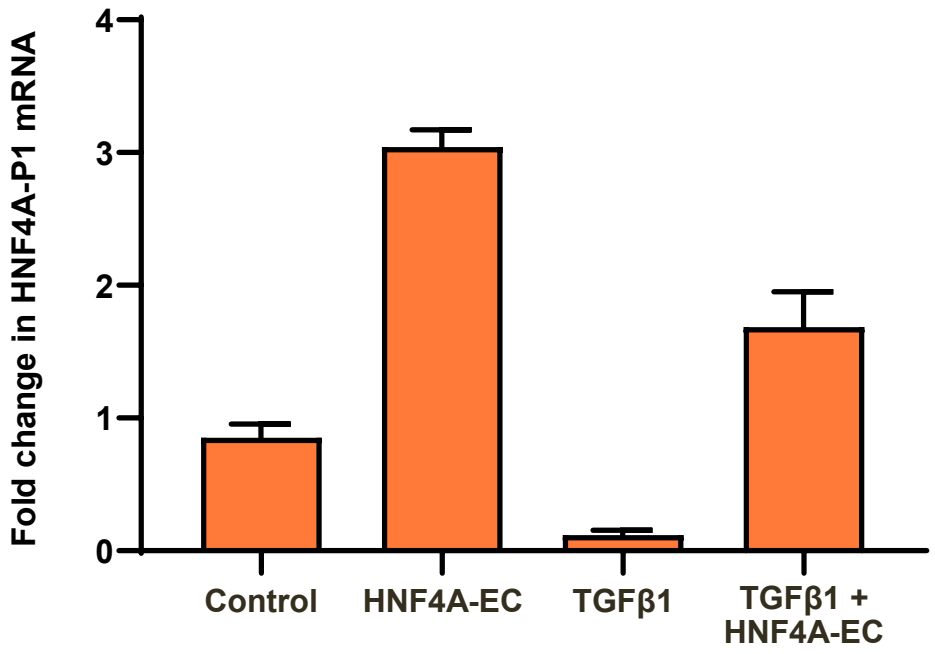
Source: Data presented at AASLD 2023. DC: development candidate

HNF4A-EC Selectively and Durably Upregulated P1 Isoform and Restored Dysregulated Expression Caused by TGFβ Signaling *In Vitro*

HNF4A-EC Treatment Increased HNF4α-P1 Isoform Expression for 35 Days in Primary Human Hepatocytes



HNF4A-EC Treatment Rescued TGFB1-induced HNF4α-P1 Downregulation in Primary Human Hepatocytes

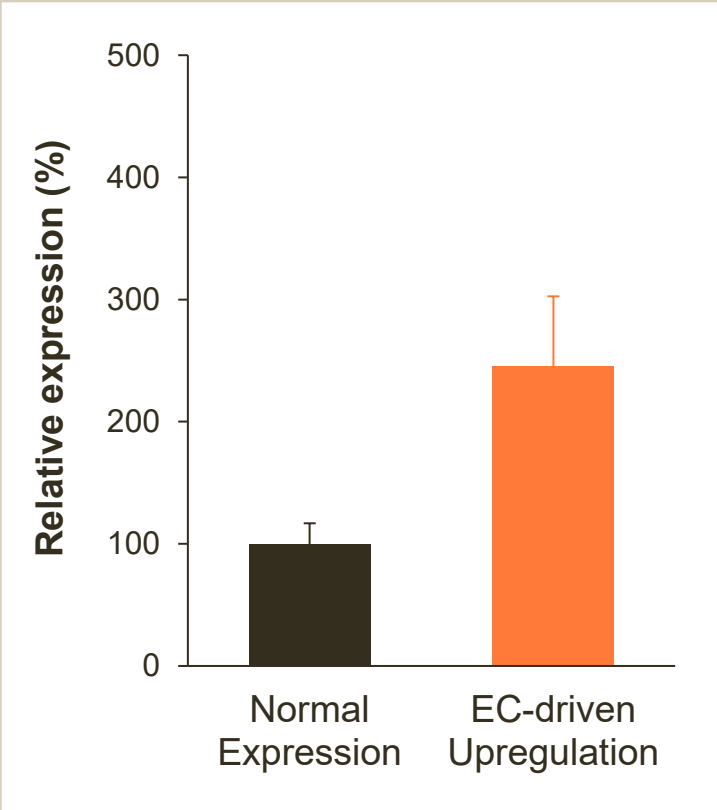


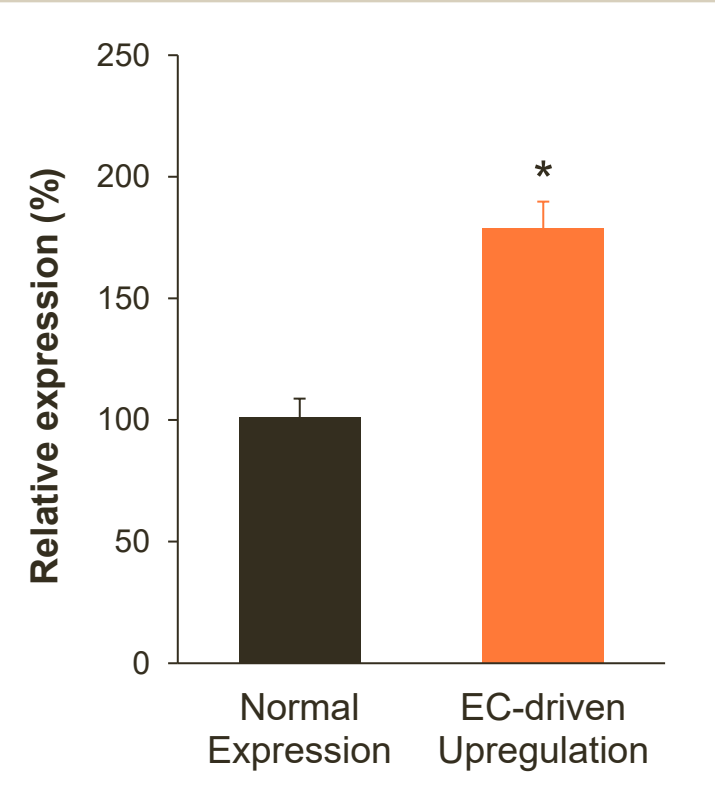
Source: Data presented at AASLD 2024.

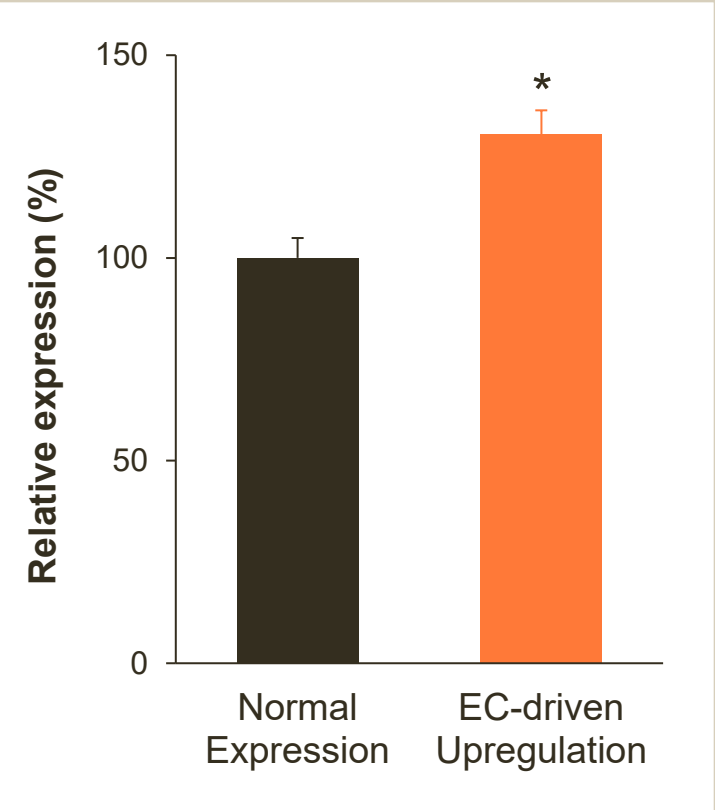
HNF4A-EC Robustly Upregulated HNF4α Expression Across Species

Increased HNF4α Expression in Healthy Liver Tissues (Over and Above Normal Expression)

Species	Mouse	Nonhuman primate	FRG Mouse
Liver Cells	Mouse (48h)	Nonhuman primate (24h)	Human (24h)





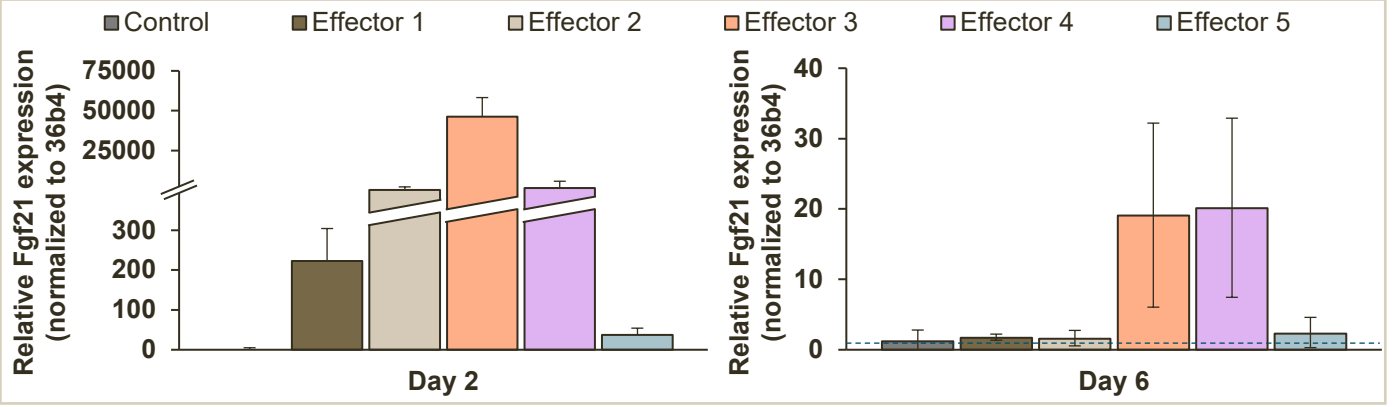


* Significant, paired t-test p<0.05

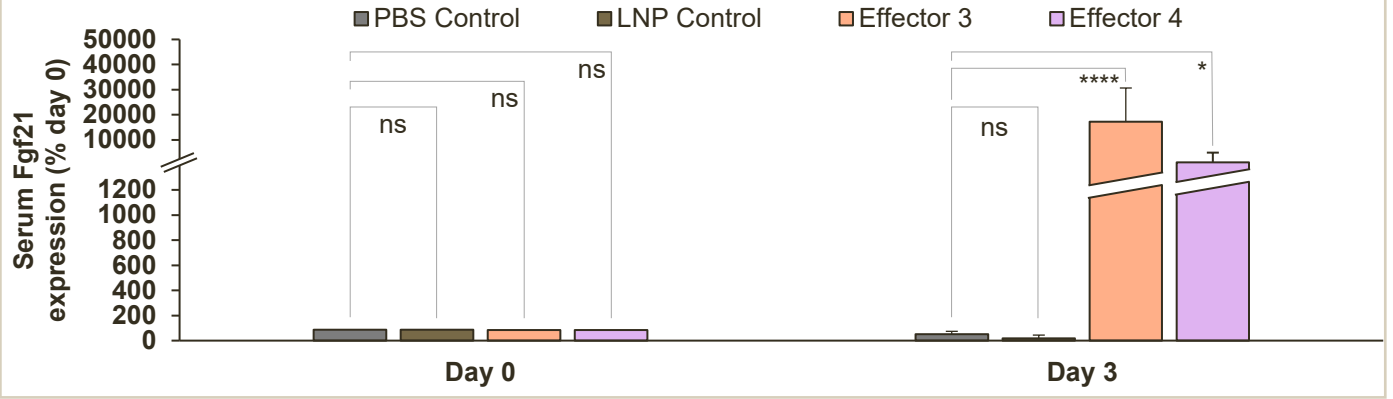
FGF21: Potential for Multi-Indication Metabolic Opportunities
Plan for Rapid Proof-of-Concept Readout of Upregulation Capabilities

- FGF21 is a hepatocyte-derived hormone involved in energy homeostasis, and implicated in multiple metabolic indications
- Preclinical models are well-established and their translatability to clinical trial outcomes understood
- Pre-transcriptional upregulation of FGF21 in liver, where it is naturally produced, may offer greater potency and durability compared to existing modalities
- Upregulation proof-of-concept demonstrated *in vitro* and *in vivo*

In *Vitro* Upregulation Observed Across Multiple Epigenomic Effectors



FGF21 Upregulation *In Vivo*



* p<0.05, **** p< 0.0001

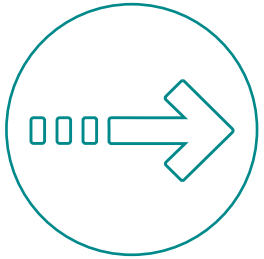
Strategic Partnerships Core to Omega's Corporate Strategy

Partnering Strategy

Support development of prioritized programs

Extend pipeline into additional high-value targets and tissues

Advance further development of OTX-2002 or other assets



Actively engaged in dialogue with potential partners to bring in non-dilutive capital and advance pipeline priorities

Pioneering a New Class of Programmable Epigenomic Medicines

OMEGA™ THERAPEUTICS

- Pre-transcriptional gene modulation enables durable gene upregulation, downregulation, and multiplexing
- Clinical proof-of-mechanism validates epigenomic controllers and de-risks OMEGA platform
- Advancing pipeline of select high-value programs with clear value creation opportunities
- Platform enables rapid prosecution of new targets and IGD biology driven by data science and advanced computational genomics
- Cash runway into Q2 2025; balance sheet of $30.4 million as of September 30, 2024


OMEGA™
THERAPEUTICS

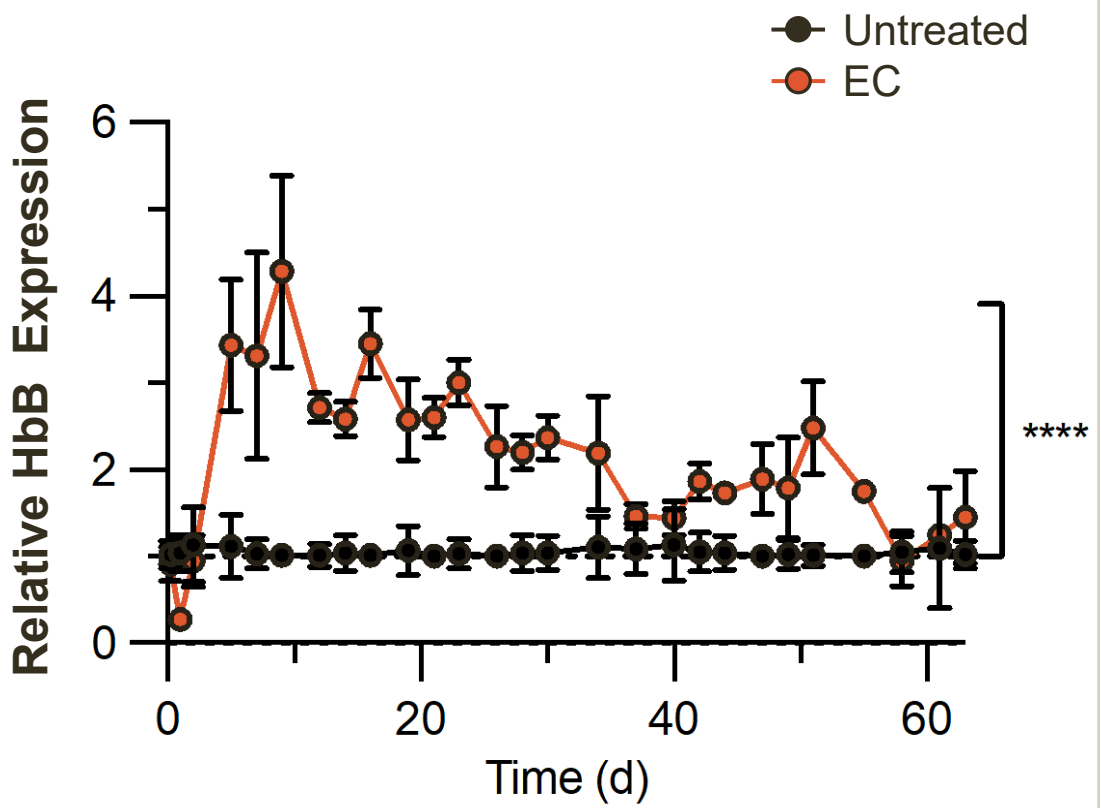
Building Value Through Differentiated Capabilities

Additional Sample Data

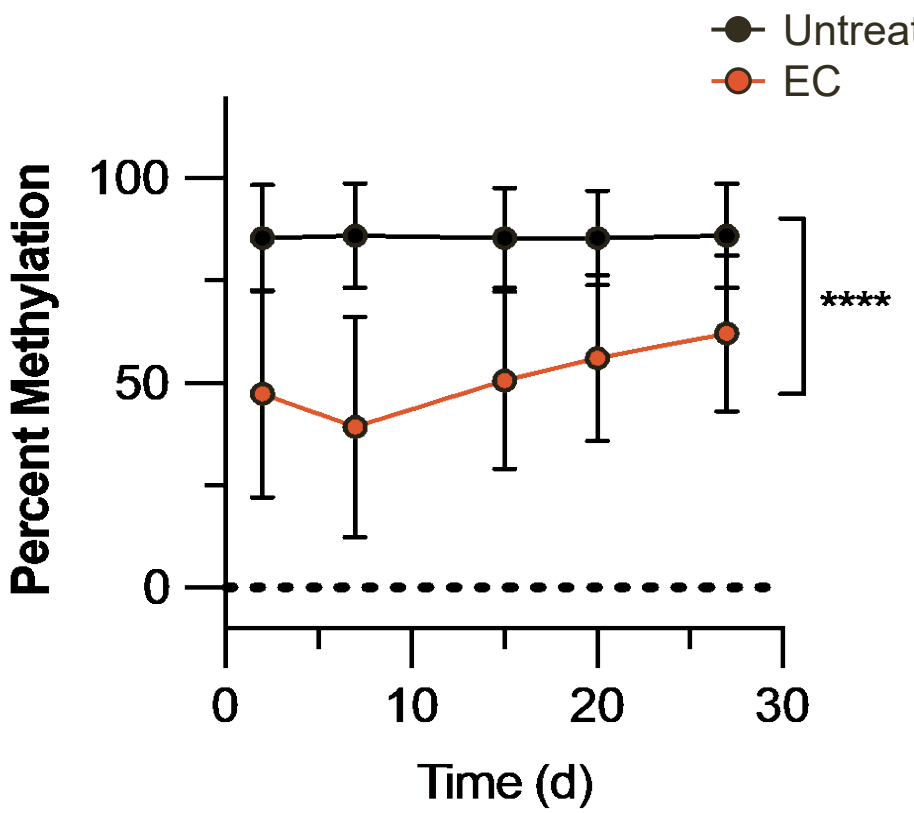
OMEGA™ THERAPEUTICS

HBB: Durable Upregulation Observed for ~2 Months With Single Administration; No DNA Sequence Changes as Associated with Transgenic Approaches

In Vitro Hemoglobin Activation



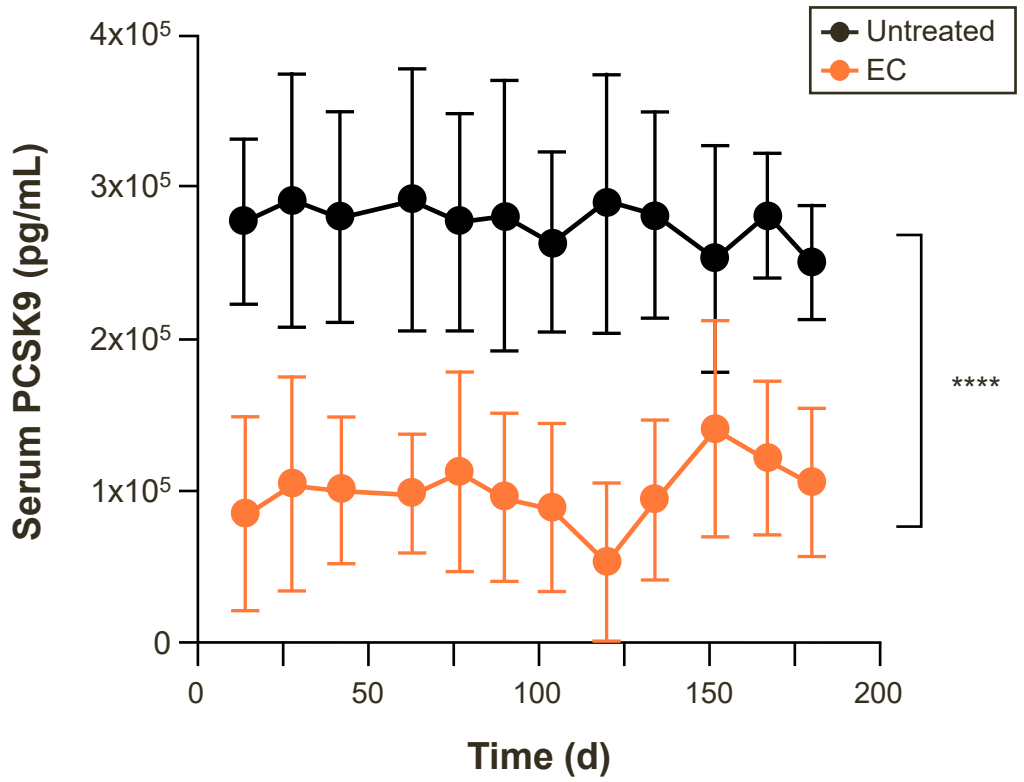
Change in Epigenetic State



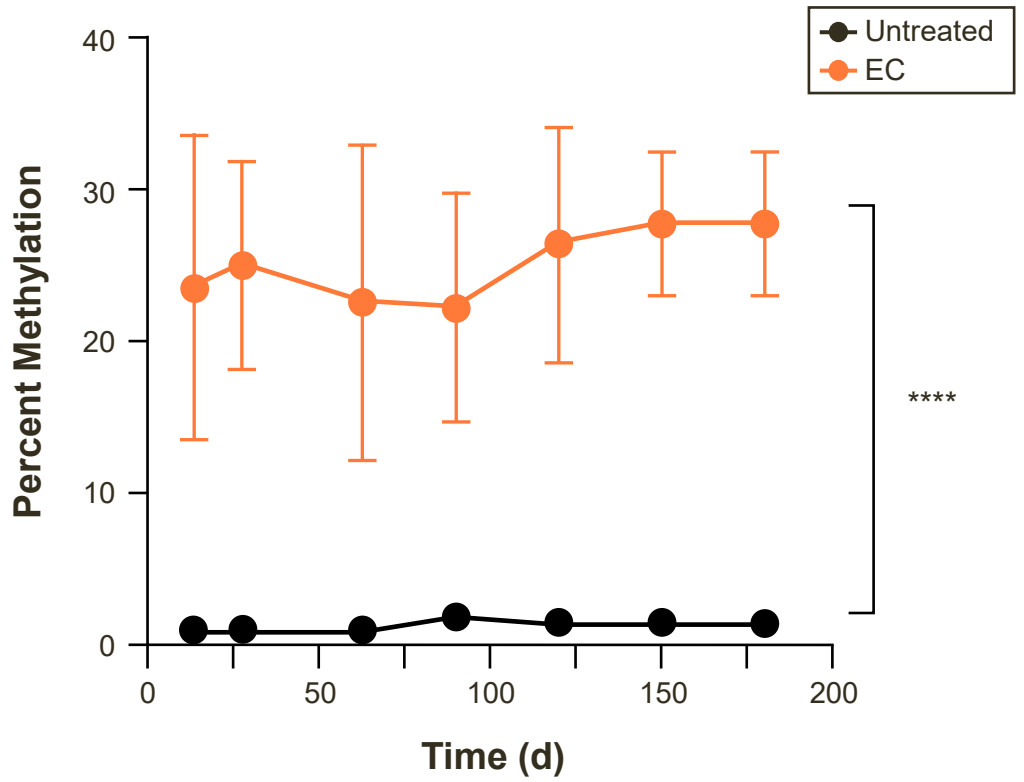
****p<0.0001

PCSK9: Durable Downregulation Maintained Through 6 Months Following Single Administration; Enables Less Frequent Dosing

In Vivo PCSK9 Downregulation



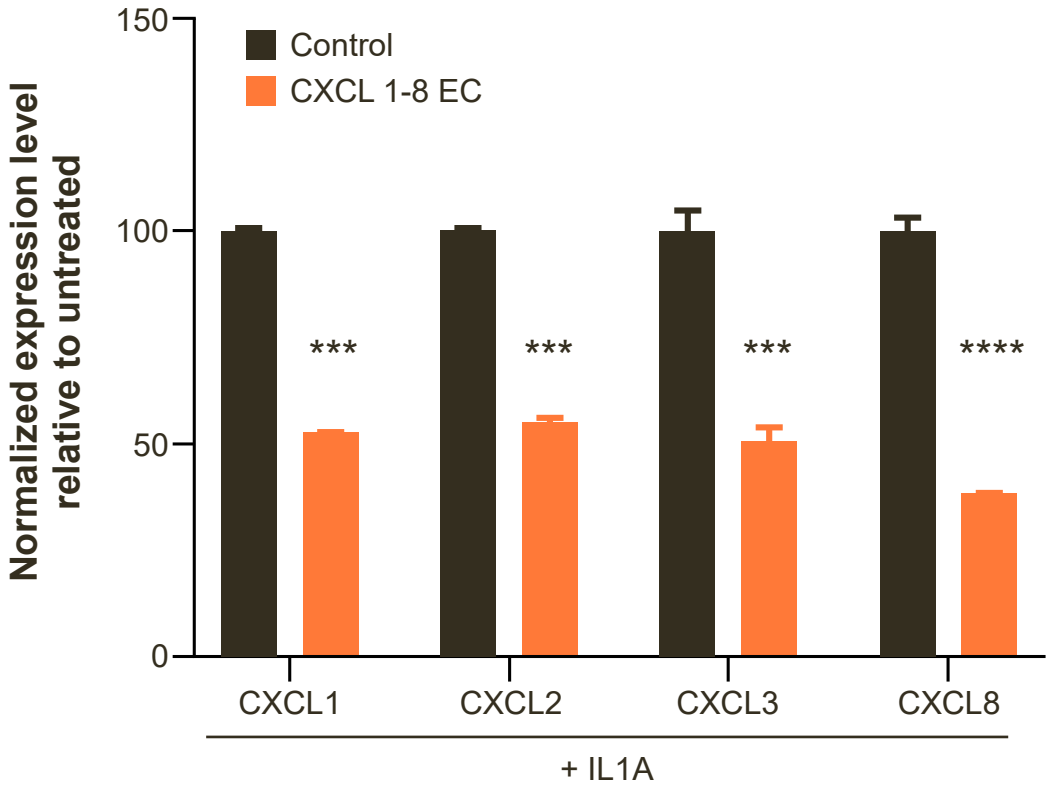
Change in Epigenetic State



**** p<0.0001

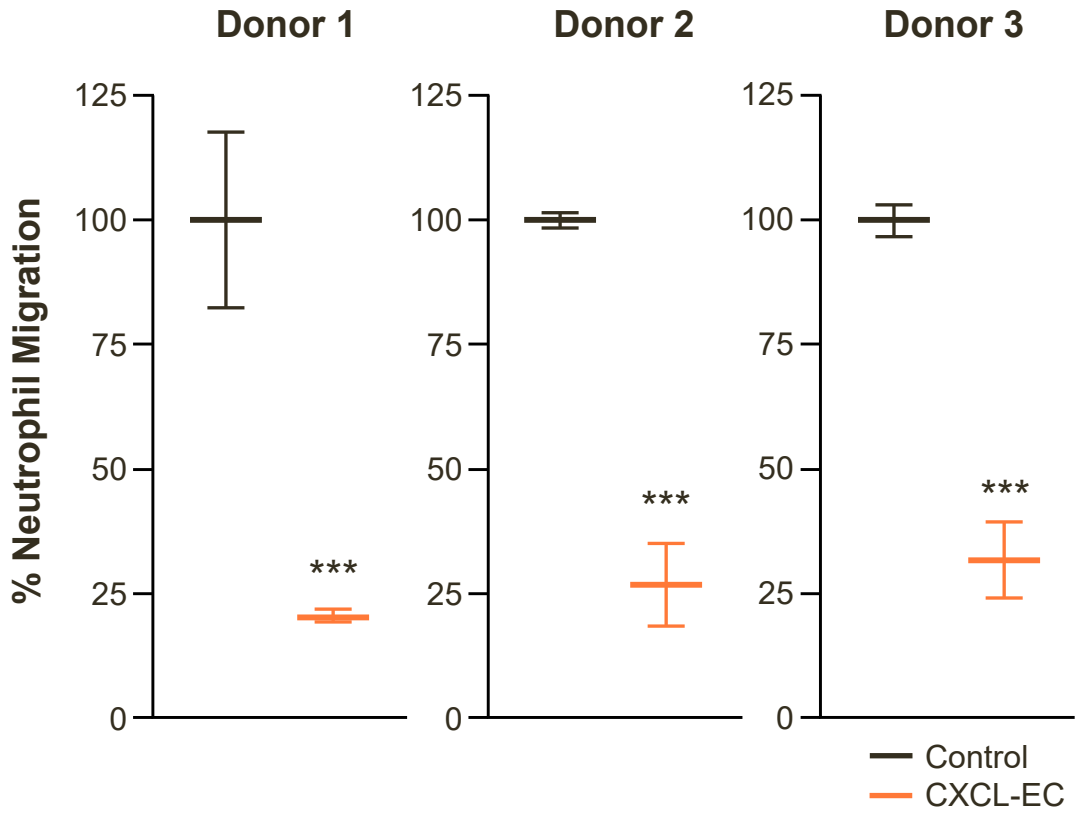
Multigenic Targeting of CXCL1-8 Downregulated Chemokine mRNA Expression and Reduced Neutrophil Migration in Donor Lung Fibroblasts *In Vitro*

Coordinated Downregulation of mRNA Expression



***p<0.001, ****p<0.0001

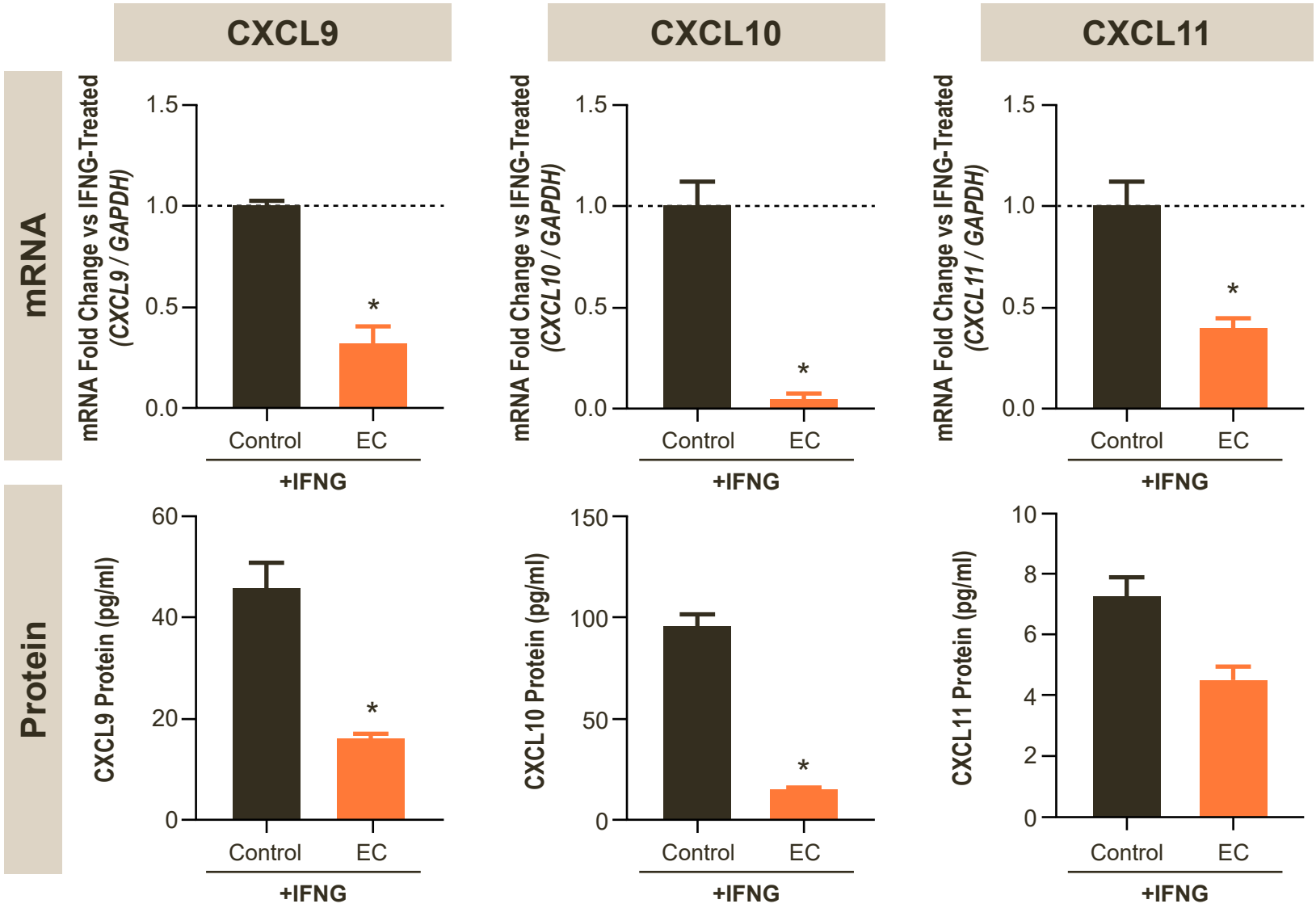
Significant Decrease in Neutrophil Migration

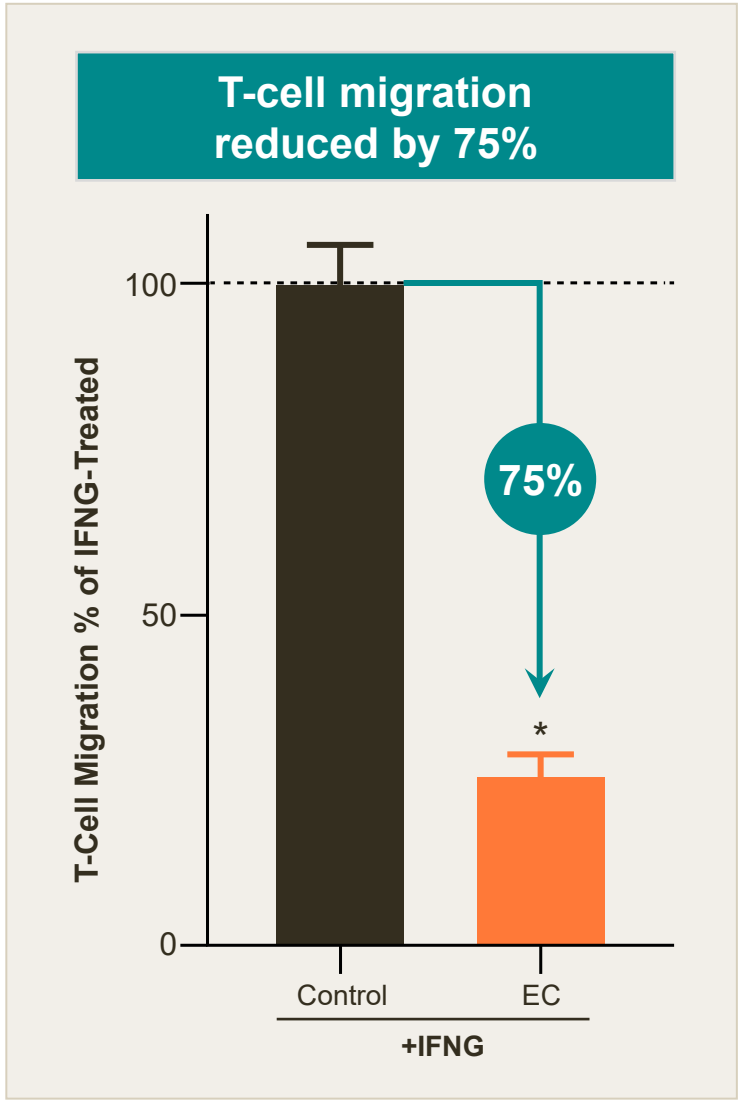


Supernatants from IMR90 cells stimulated with IL1A; ***p<0.001

Source: Data presented at International mRNA Health Conference 2023.

CXCL 9-11-Targeting EC Reduced mRNA Expression and Protein Levels in IFNG-Stimulated Primary Human Hepatocytes





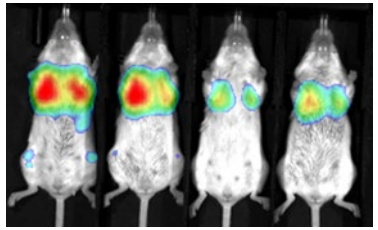
Source: Data presented at AASLD 2023. *p<0.05

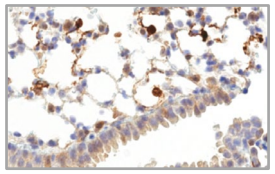
Omega Has Extensive Internal Delivery Capabilities

Additional Proprietary LNPs Targeting CNS, Joints, Skin and Adipose in Development

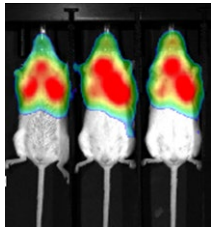
Lung (Systemic & Inhaled)

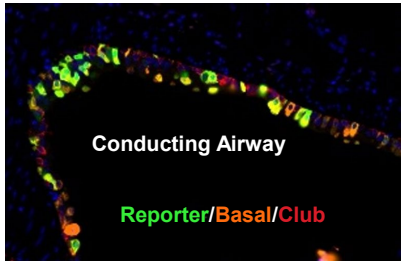
Systemic





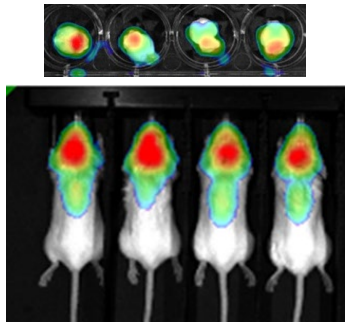
Intratracheal





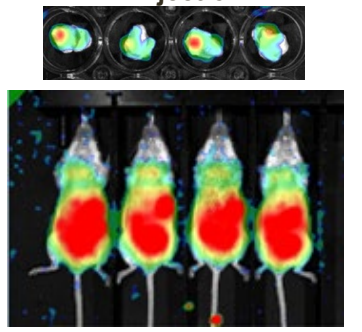
CNS

Intrathecal

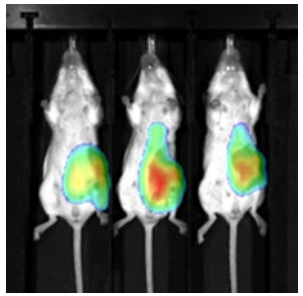


Pancreas

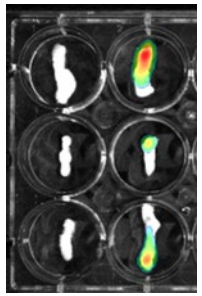
IP injection



Adipose tissue



Subcutaneous injection

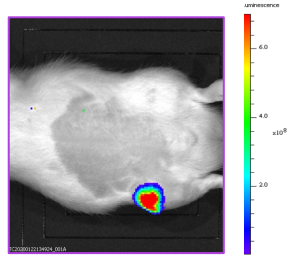


Inguinal fat pads

OMEGA™ THERAPEUTICS

Delivery Capabilities

Joint



Intraarticular administration

Dermis