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Pliant's Selective Targeted Integrin-Mediated Drug Delivery Platform



November 12, 2026

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Pliant is Developing Novel Integrin-targeting Drug Delivery Products

Platform Founded on Integrin Expertise

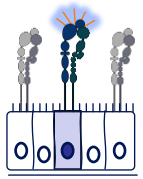
Integrin library
15,000+ proprietary small molecules (SM) and >1M annotated data points

Integrin profiling assays
Selectivity, potency, and cellular uptake to find optimized delivery binders

Delivery Optimization
Ability to “dial in” integrin selectivity and productive delivery

Pliant’s highly cell-selective drug delivery platform

Cell- & Tissue-specific payload delivery
Selective for extrahepatic tissues using integrin-targeting small molecules



Differentiated from established delivery technologies
Efficient delivery through unique mechanism of cellular internalization

Targeting previously intractable cell types
Gains access to discrete tissues by leveraging unique cell type-specific integrin expression profiles

Initial platform applications focused on RNAi delivery in diseases across multiple tissue types

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Pliant's Small Molecule RNAi Conjugates Offer Potentially Attractive Development and Commercial Profile

Target product characteristics enabled by small molecule drug delivery

- Low dose
- Subcutaneous administration
- Long-acting, infrequent dosing
- Non-immunogenic
- No PK enhancers needed
- Manufacturability

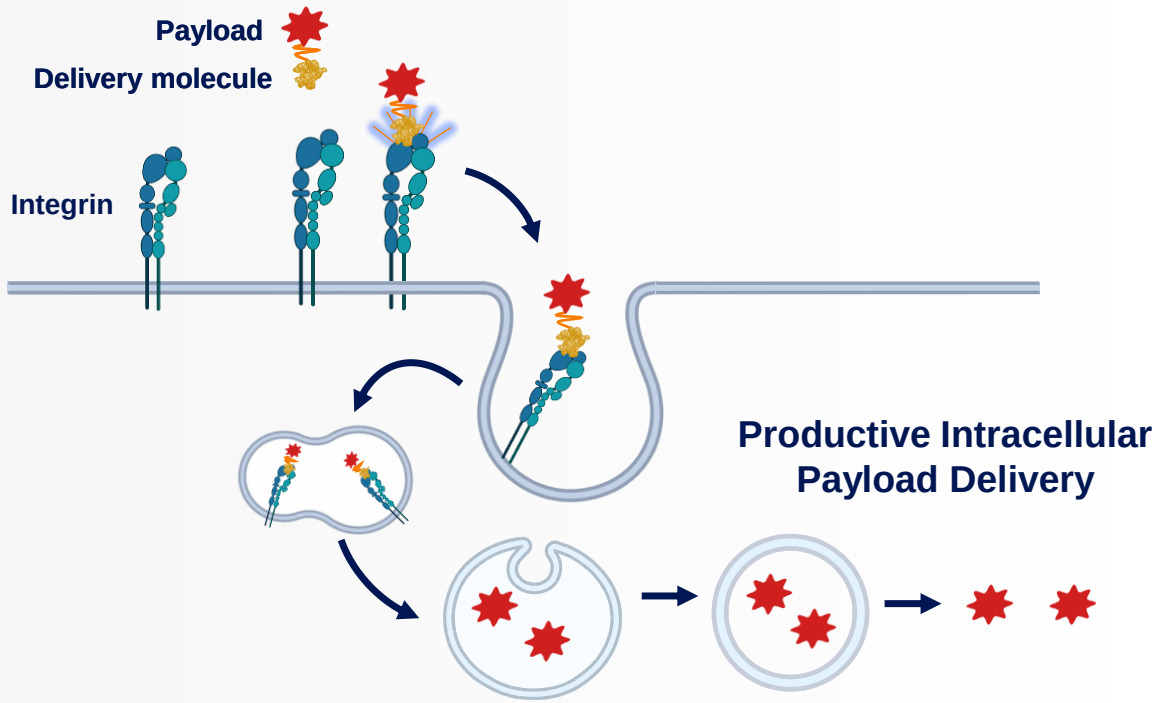
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The Integrin Receptor Target Class Holds Promise for RNAi Delivery

Pliant's proprietary integrin binders internalize and achieve effective intracellular delivery

- Integrins are cell-specific surface receptors
- Only 1 of 24 integrins is currently under clinical evaluation to deliver siRNA
- Integrin binding alone does not predict internalization and efficient drug delivery
- Pliant's small molecules induce an integrin conformation change to promote internalization and productive RNAi delivery



Pliant's expertise in small molecule–integrin binding properties unlocks this promising target class for RNAi delivery

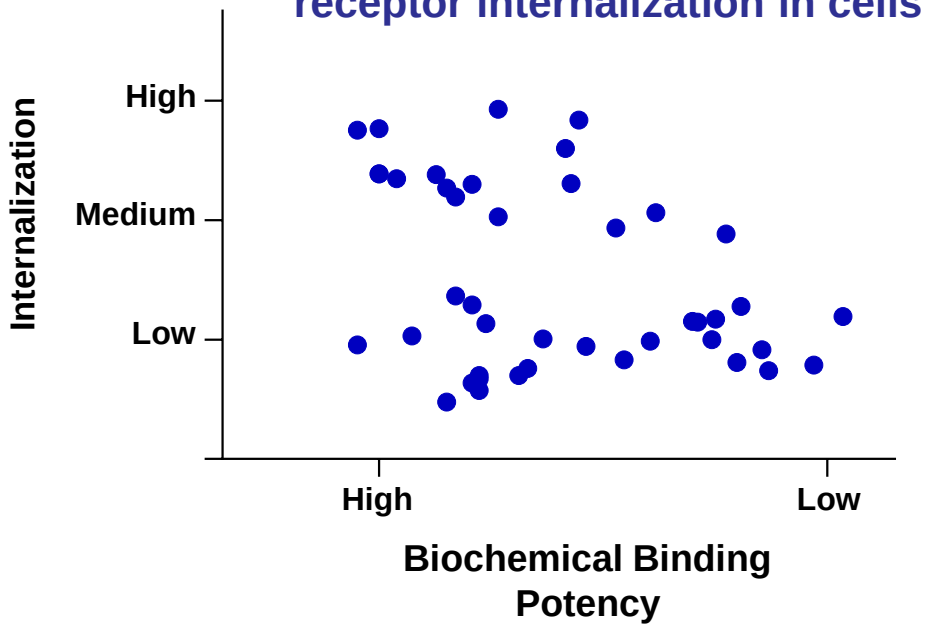
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Identifying Internalizing Small Molecules From Selective, Potent Binders

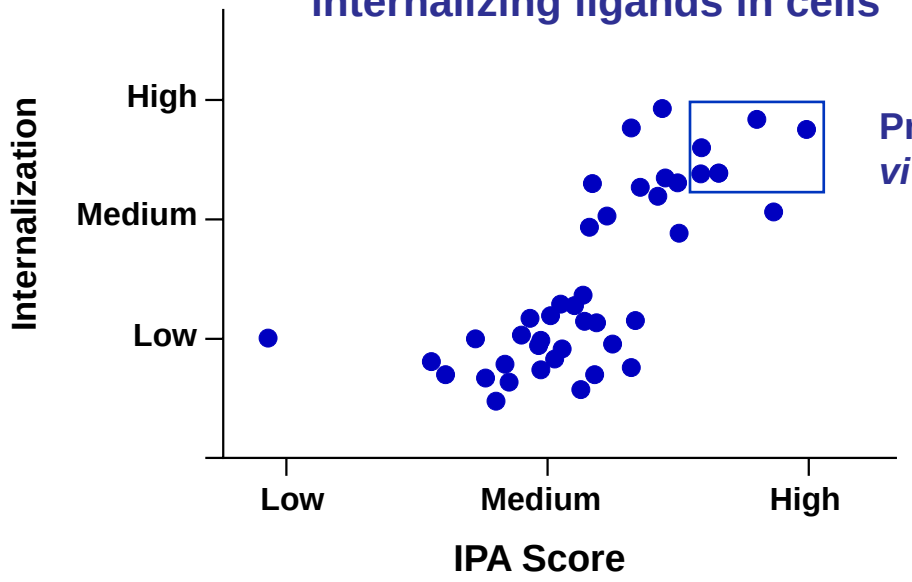
SELECTION CASCADE

- **Select integrin profile** (bioinformatics)
- **Cross-species binding**
- **Internalization predictive assay** (IPA score)
- ***in vivo* screen**

Binding potency does not predict receptor internalization in cells



IPA score identifies high internalizing ligands in cells



Prioritized for *in vivo* evaluation

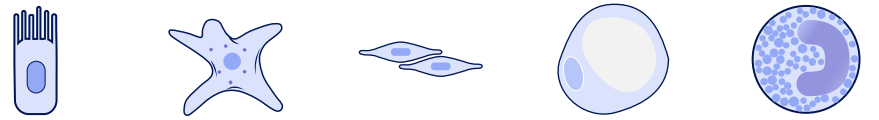
Pliant's screening cascade selects potent, selective integrin binders that actively induce internalization and payload delivery

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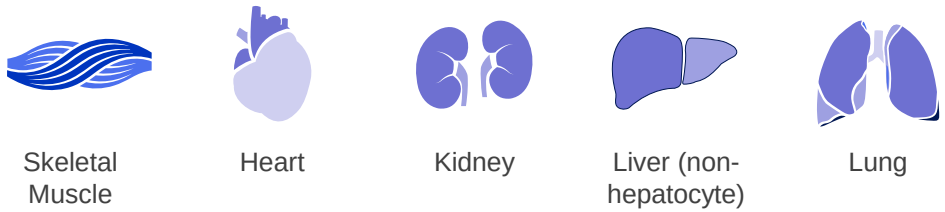
Applications of the Integrin-targeting Drug Delivery Platform

Target cells and tissues for RNAi delivery

Cell Types



Tissues



Lead RNAi Delivery Programs

1 Skeletal Muscle Selective: PLN-753-siRNA

- Deep, durable muscle-selective knockdown in mice
- Binds a skeletal muscle integrin

2 Dual Cardio-Skeletal Muscle: PLN-662-siRNA

- Combined skeletal and cardiac knockdown in mice and NHP
- Targets unique cardio-skeletal muscle integrin

Initial focus on neuromuscular diseases and rare cardiomyopathy indications

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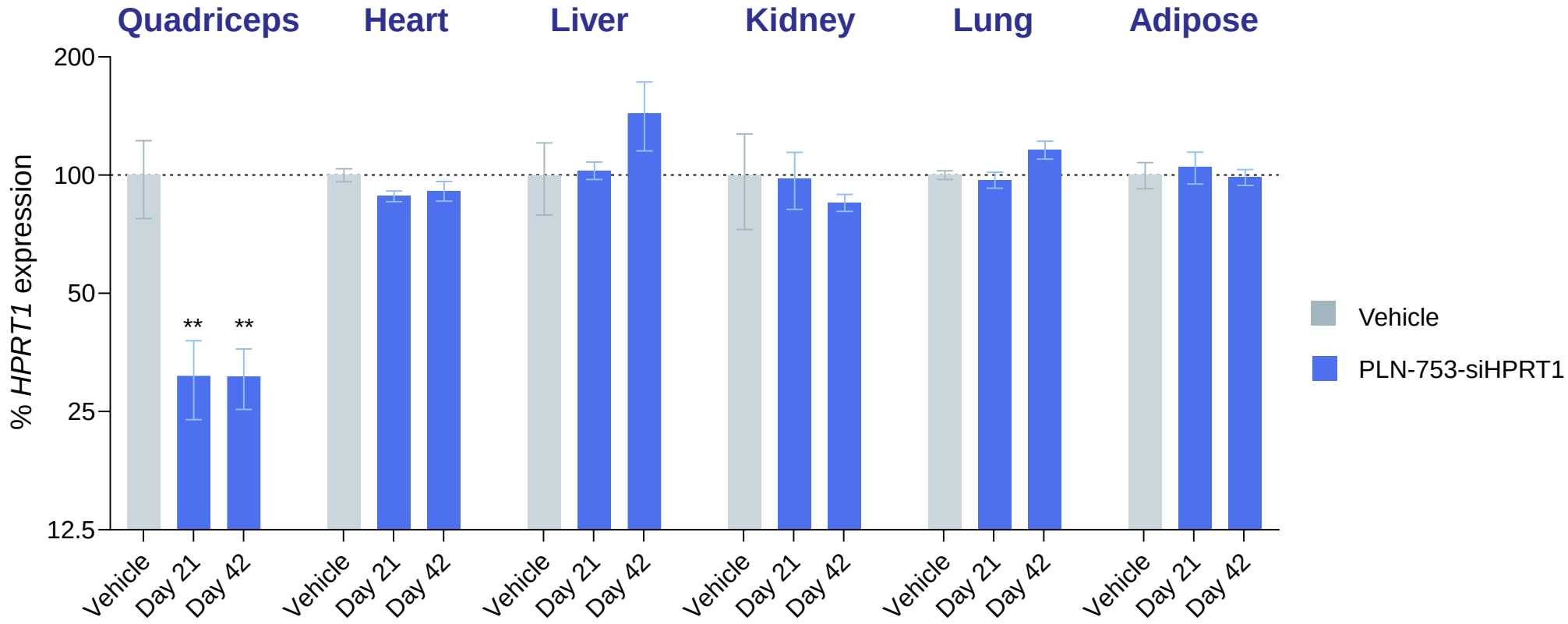
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PLN-753 for Skeletal Muscle Delivery

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PLN-753-siHPRT1 – Deep and Durable Skeletal Muscle Knockdown in Mice

*HPRT1** mRNA expression after a single low dose administered subcutaneously

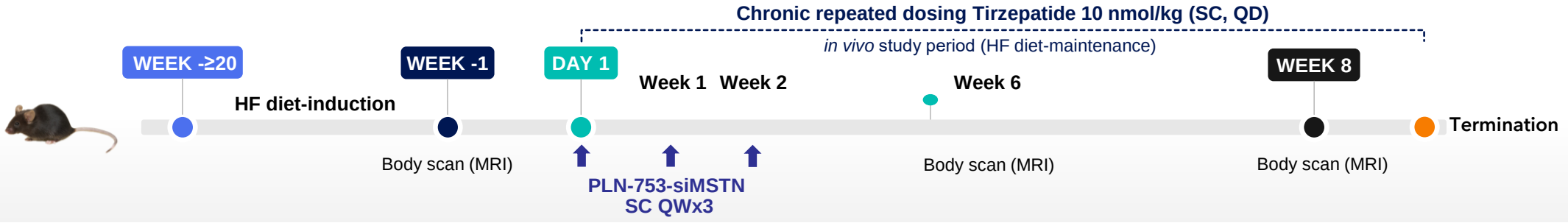


Single low-dose subcutaneous administration of PLN-753-siHPRT1 resulted in highly selective skeletal muscle delivery

n = 3 per group; mean +/- SD plotted in Log2; Vehicle is the average vehicle animals from day 21 and 42.
Ordinary one-way ANOVA with Tukey's multiple comparisons test, ** = $p < 0.01$
* *HPRT1* is a housekeeping gene

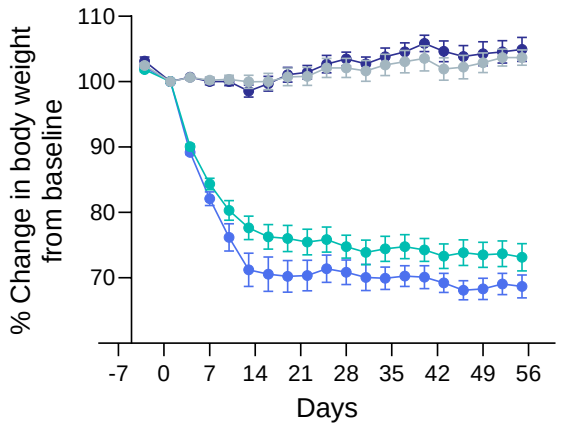
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PLN-753-siMSTN Preserved Lean Mass in Combination with Tirzepatide

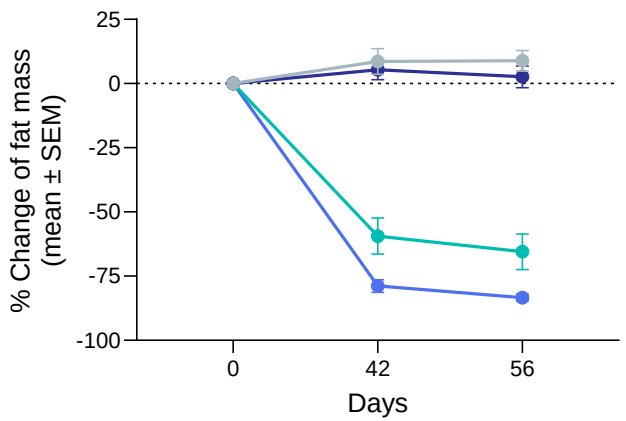


Longitudinal MRI Body Scan Results

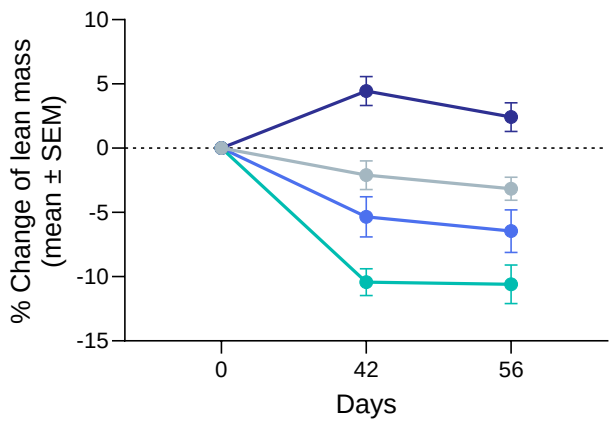
% Body weight change



Fat tissue mass change



Lean mass change



Vehicle | PLN-753-siMSTN (QWx3) | Tirzepatide | Tirzepatide + PLN-753-siMSTN (QWx3)

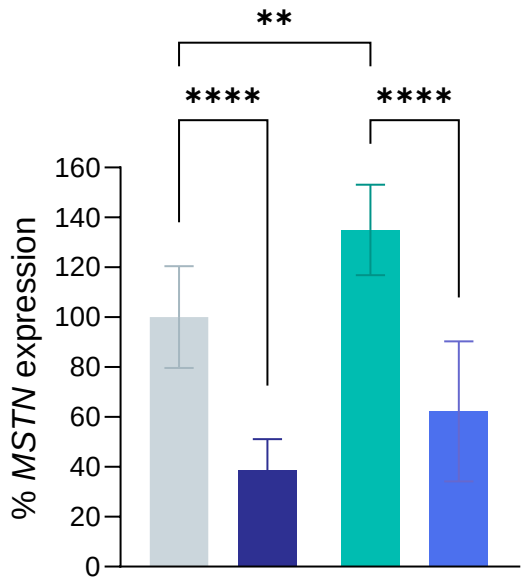
In combination with tirzepatide, PLN-753-siMSTN preserved lean mass and enhances fat mass loss

N = 10 per group

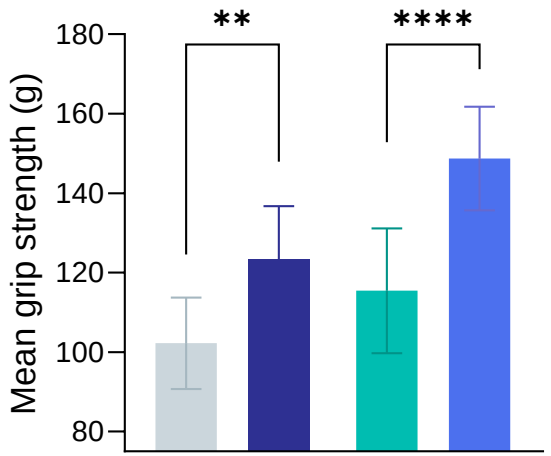
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Reduced Target Gene Expression Increases Muscle Volume and Function

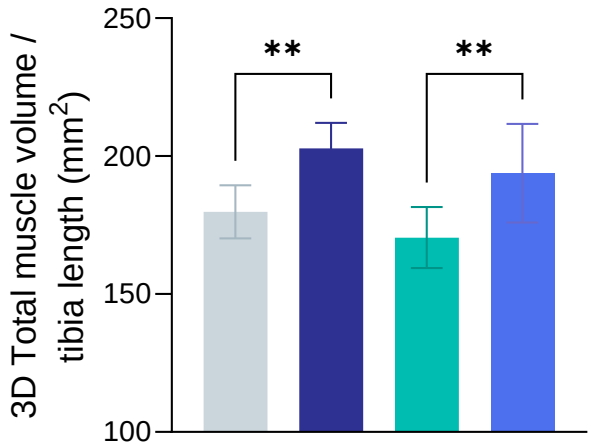
Quadriceps *MSTN* mRNA Levels
Day 56 (EOS)



Muscle Volume
Day 56 (EOS)



Grip Strength
Day 56 (EOS)



Vehicle | PLN-753-siMSTN (QWx3) | Tirzepatide | Tirzepatide + PLN-753-siMSTN (QWx3)

PLN-753-siMSTN establishes functional proof-of-concept for skeletal muscle selective RNAi delivery

Mean +/- SD plotted; Ordinary one-way ANOVA with Tukey's multiple comparisons test, ** = p < 0.01, **** = p< 0.0001

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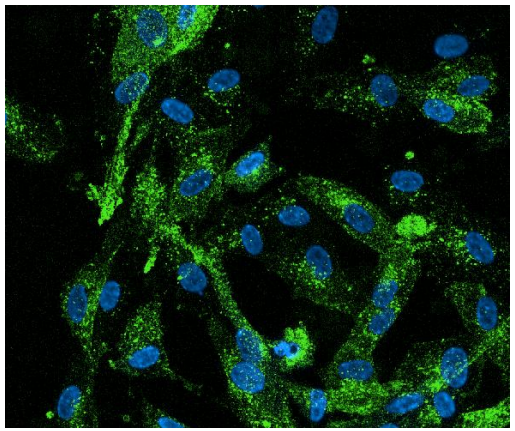
PLN-662 for Cardio-Skeletal Muscle Delivery

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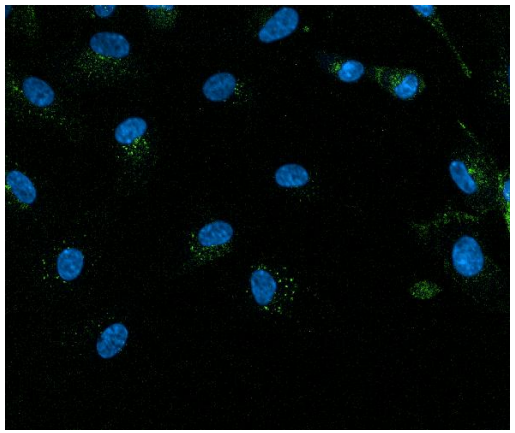
PLN-662 Leverages a Unique Integrin for Cardio-skeletal Muscle Delivery

Fluorescently tagged PLN-662 demonstrates integrin-specific cell internalization

PLN-662-AF647

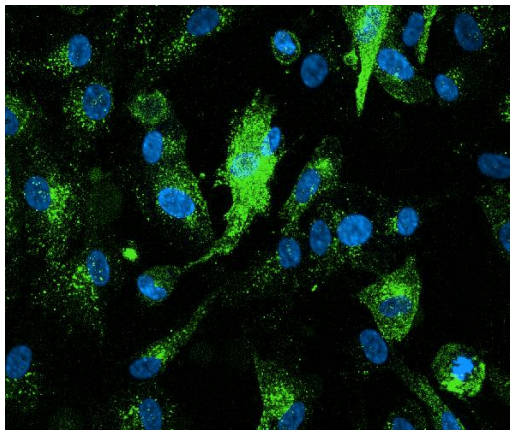


PLN-662-AF647
+ antibody blocking cardio-skeletal muscle integrin



Blockade of binding & internalization

PLN-662-AF647
+ antibody blocking skeletal muscle integrin (PLN-753)



No blockade of binding & internalization

Pliant's integrin platform unlocks RNAi delivery for cardio-skeletal muscle

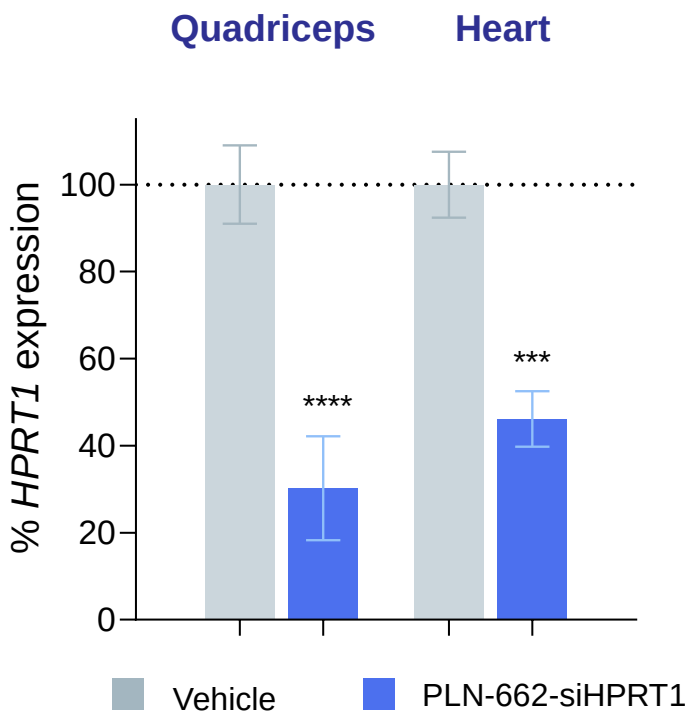
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PLN-662-siHPRT1 – Robust Cardio-skeletal Muscle Knockdown in Mouse & NHP

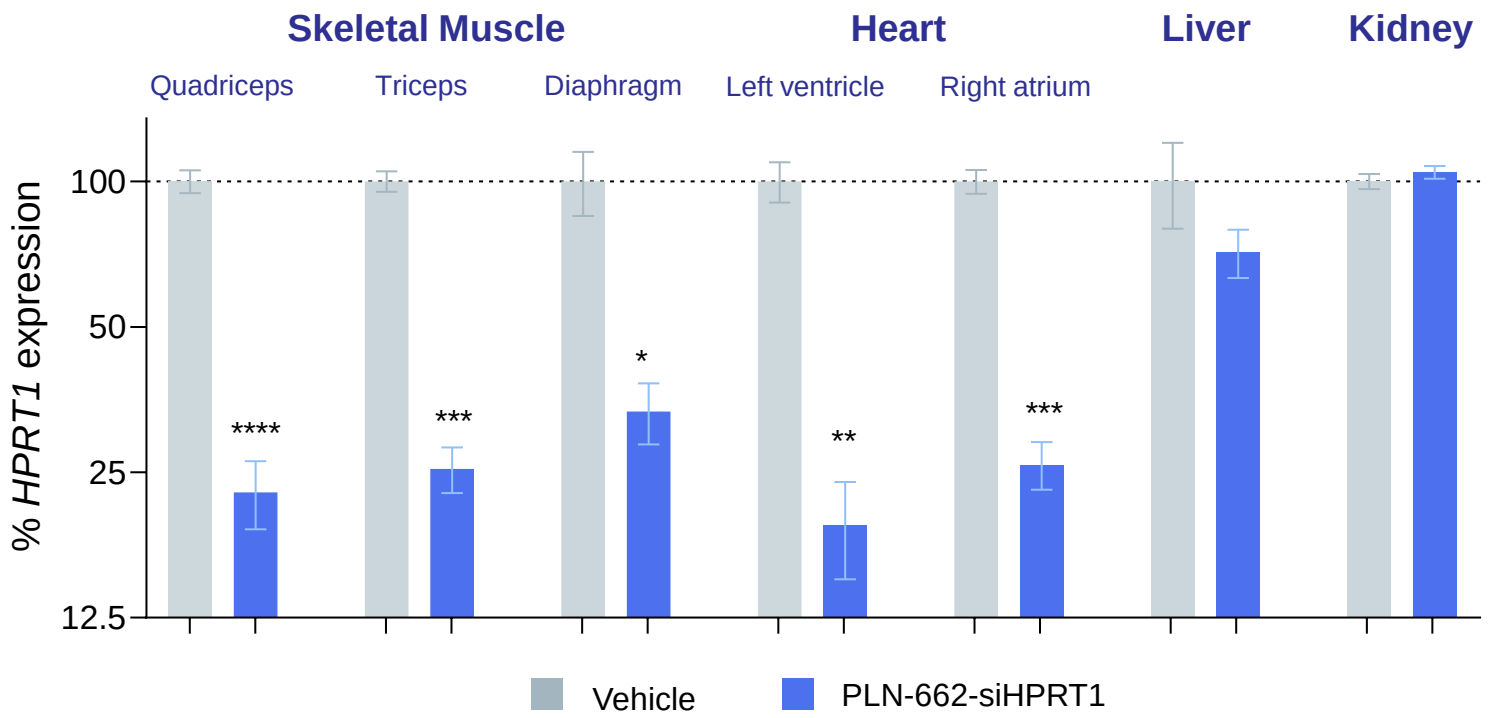
Mouse *HPRT1* mRNA knockdown at day 21

QWx3, SC



NHP *HPRT1* mRNA knockdown at day 57

QWx4, SC



Deep skeletal muscle and cardiac target gene knockdown in NHPs opens cardiovascular and neuromuscular disease opportunities

Mouse, n = 4 per group, mean +/- SD. NHP, n = 3 per group, mean +/- SD plotted in Log2. SC = subcutaneous
Unpaired T test with Welch's correction, * = p < 0.05, ** = p < 0.01, *** = p < 0.001, **** = p < 0.0001

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Summary & Next Steps



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Integrin Drug Delivery Platform – Summary and Next Steps

Integrin RNAi Delivery Platform

- Selective delivery to extrahepatic cells and tissues
- Validated *in vivo* with mouse to NHP translatability
- Expanding across additional payloads and tissues
- Multiple potential products from each delivery molecule

Neuromuscular & Cardiomyopathy Focus

- Multiple lead programs advancing in parallel
- Deep, durable knockdown after a single dose
- Delivers to both skeletal muscle and the heart
- Severe diseases with high unmet need

Attractive development and commercial profile

- **Low doses**
- **Subcutaneous administration**
- **Long-acting, infrequent dosing**
- **Non-immunogenic**
- **No PK enhancers needed**
- **Manufacturability**

Advancing toward INDs for select neuromuscular & rare cardiomyopathy indications

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