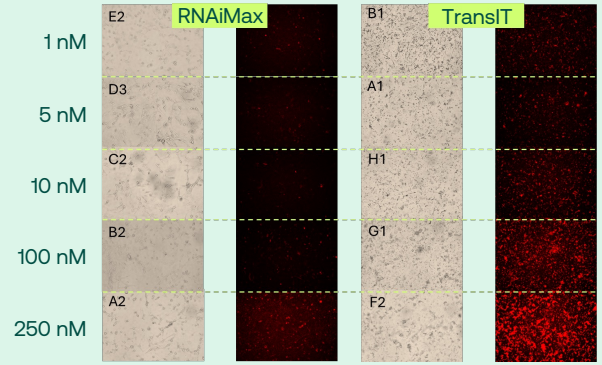
# Case Study: µMass™ identified a human-relevant signal that sharpened the mechanism of action (MoA) before IND

## Objective: supress a functional human biomarker with free-uptake siRNA delivery in 3D

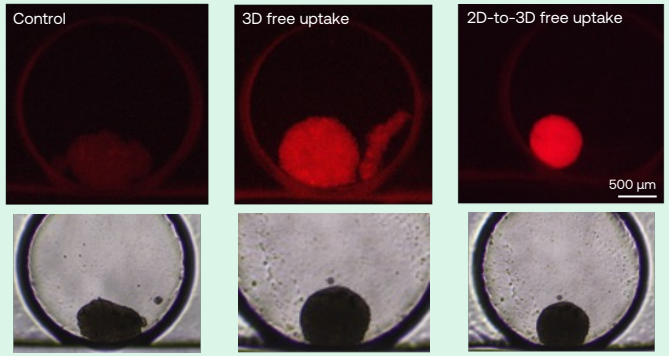
### Step 1: 2D transfection optimisation




Transfection reagents are toxic at effective concentrations in primary cells

siRNA uptake in 2D primary human cells confirmed by fluorescent labelling. Standard reagents (RNAiMax, TransIT) showed dose-dependent toxicity as per expectations

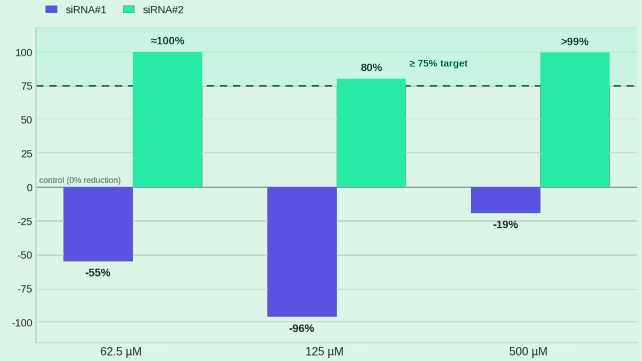
### Step 2: Free-uptake delivery in 3D




Free-floating siRNA integrated into primary, human 3D aggregates with µMass™

Free-uptake delivery confirmed by fluorescence across 2D-to-3D transition; reducing cellular toxicity vs. standard transfection. µMass™ retains siRNA in the aggregate environment throughout culture

### Step 3: Functional disease readout




A trigger-induced functional biomarker, read across candidates and doses

Disease phenotype induced by a defined trigger, generating a 4-log rise in a functional biomarker. Biomarker suppression confirmed functional disease switching

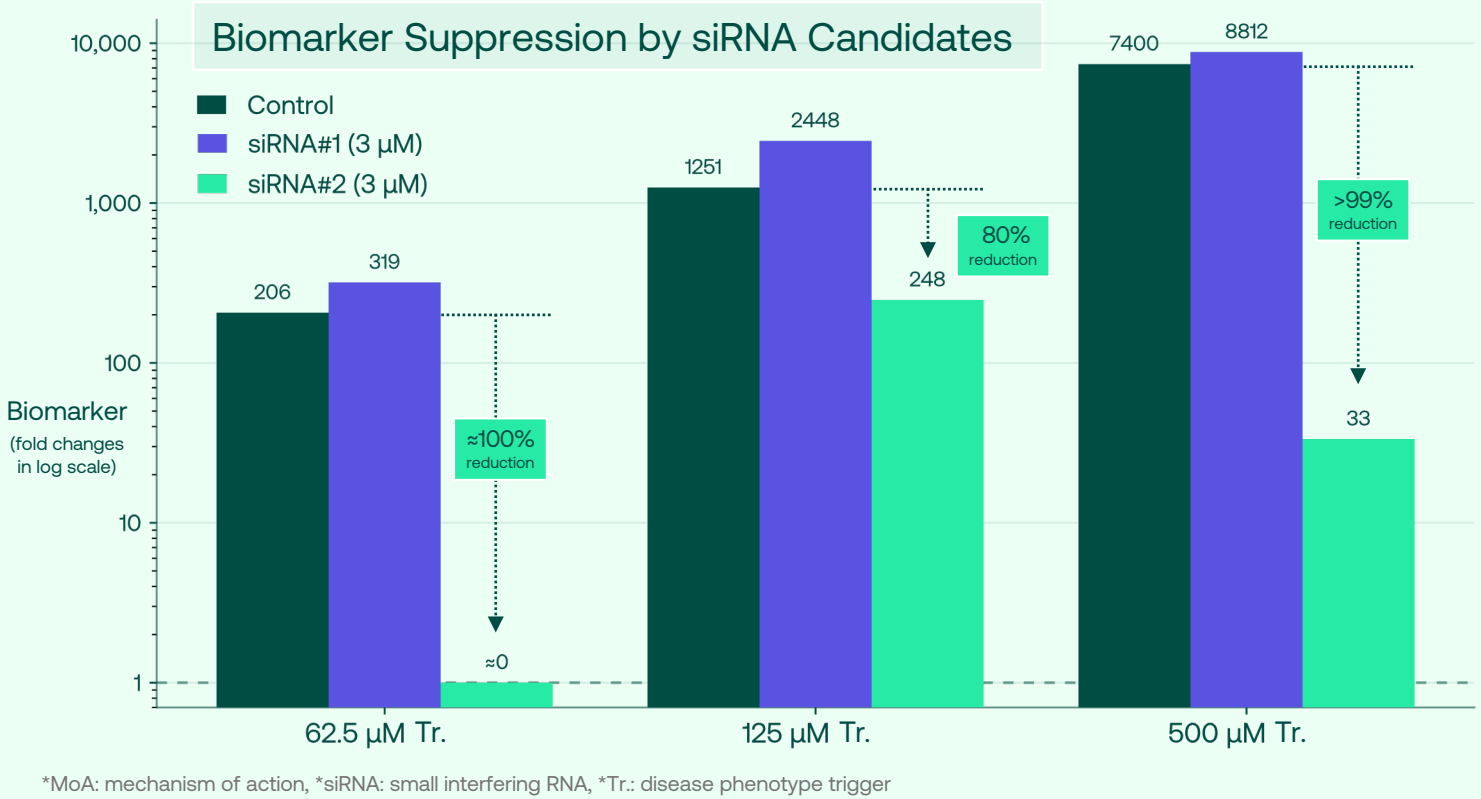
Set up: 1 week → Uptake optimization: 2 weeks → Results assays: 1 week

*siRNA: small interfering RNA

*Free uptake: siRNA delivered without transfection reagent

*qPCR: quantitative polymerase chain reaction

# Outcome: assumption challenged. Human 3D aggregates and µMass™ flagged the candidate the mouse data didn't




*MoA: mechanism of action, *siRNA: small interfering RNA, *Tr.: disease phenotype trigger

## How it was tested

siRNA delivered by free uptake into human, primary 3D aggregates in µMass™
Disease phenotype was triggered across three concentrations, and functional human biomarker measured at Day 5

## What the data showed

>80% phenotypic reduction of functional biomarker across all tested concentrations

siRNA#1 had no effect, unambiguous lead selection on a functional human endpoint.
The MoA observed in µMass™ differed from what the mouse model predicted

## Next steps for the program

Characterize the MoA divergence — Verify potency in multiple donors — Test durability — Add mechanical load (Re-plate™)

Assay results within four weeks — GLP-like, SOP-based workflows — ISO-certified facilities

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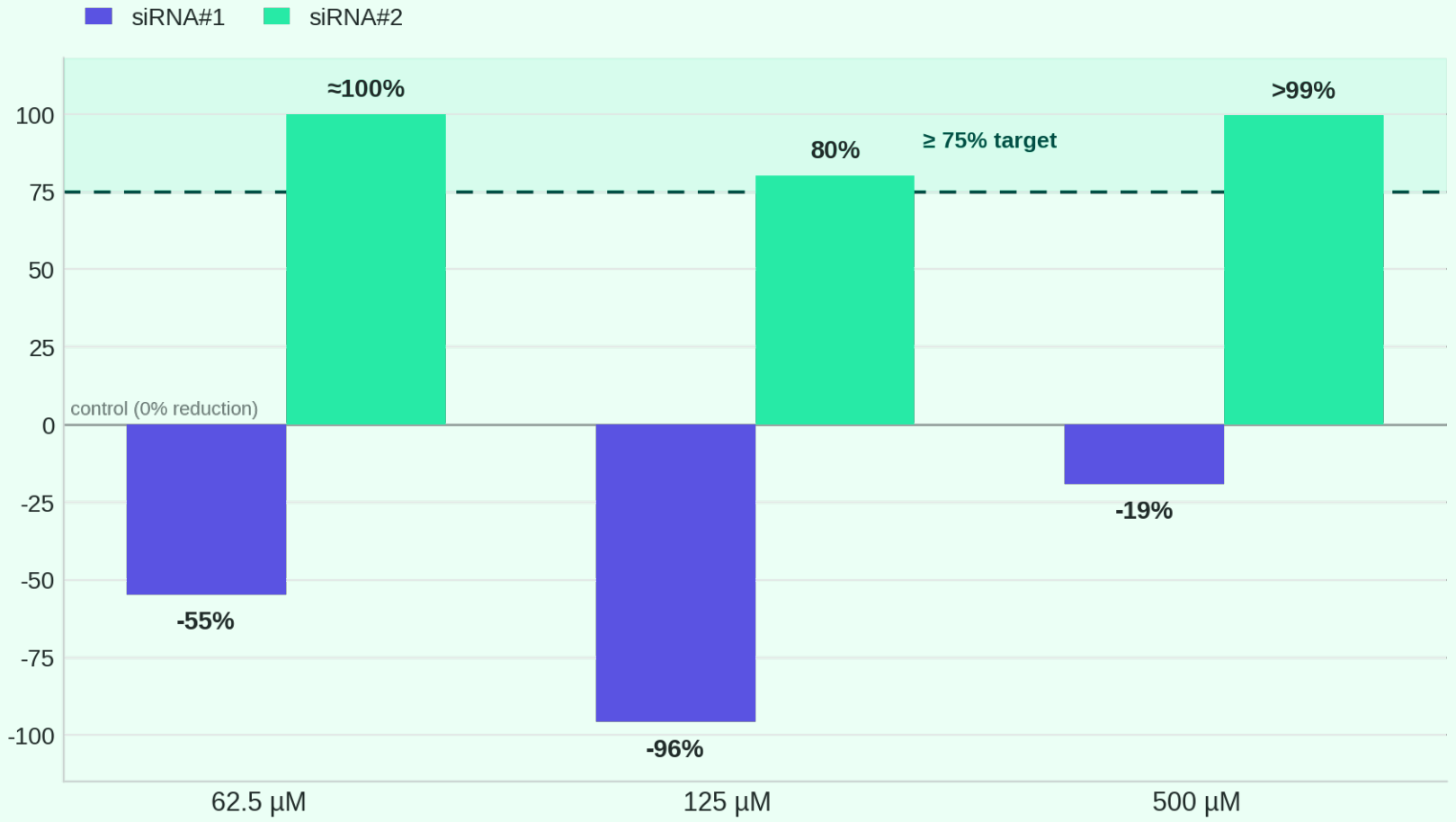
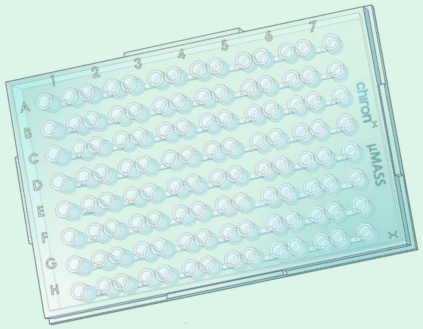
Reduction of biomarker in %

(higher = more disease phenoptype suppression)



# Gain access to µMass™ for your program

## Whether you need study execution, in-house platform access, or a tailor-made solution—chiron offers multiple ways to engage

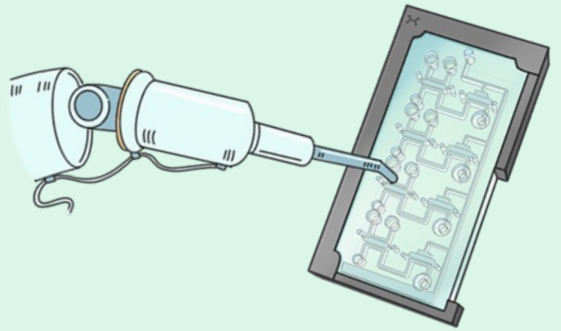



### Device Sales

Device sales via technology transfer: bring µMass™ into your own laboratory as a consumable platform; compatible with standard workflows and equipment

### Contract Research Services

Outsource studies to chiron for rapid, expert execution, generating human-relevant, decision-ready data with no internal burden



### Model Co-development

Co-develop a bespoke model with chiron that fits your specific therapeutic, disease, or translational application

# Why work with chiron?

Human-relevant insights, for more informed decision making, resulting in lower a financial burden for drug development

## Difficult-to-access insights, made measurable

- Direct comparison of multiple treatments and donors on one platform
- Cell-therapy and advanced-modality testing where animal models are poorly predictive
- 3D solid tumour models that better capture tumour structure

## More learning, at a lower cost per data point

- Generate large, comparable datasets that can be fed to predictive platforms
- Enable leaner clinical trials, reducing the development timeline
- Rapid application development and assay processing

# Thank You