

# *An ELEVIDYS Safety Update in Non-Ambulatory Patients*

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June 16, 2025



# Doug Ingram

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# Safety update regarding ELEVIDYS for non-ambulatory individuals with Duchenne

- New report of liver injury in a non-ambulatory individual with Duchenne who has passed away from acute liver failure (ALF)
- Plan to develop an enhanced immunosuppressive regimen in consultation with a panel of multi-disciplinary clinical experts, and regulators
  - Panel will evaluate data and assess Sarepta's proposed enhanced immunosuppressive regimen, which includes sirolimus
- Suspension of commercial shipments of ELEVIDYS for infusions in non-ambulatory patients until enhanced regimen is approved and in place
- Pause of ENVISION study while seeking a protocol amendment to incorporate additional immunosuppression

# Louise Rodino-Klapac, PhD

# Scientific rationale for an immunosuppression regimen with sirolimus

Sirolimus downregulates T cells that react to gene therapy

- **AAV Class Effect**
  - AAV in the liver triggers T cell response and inflammation, causing acute liver failure in severe cases
- **Enhanced Immunosuppression with Sirolimus Designed to Mitigate Acute Liver Failure Risk**
  - Data support sirolimus effective at inhibiting T cells, mitigating the inflammatory response that can lead to acute liver injury

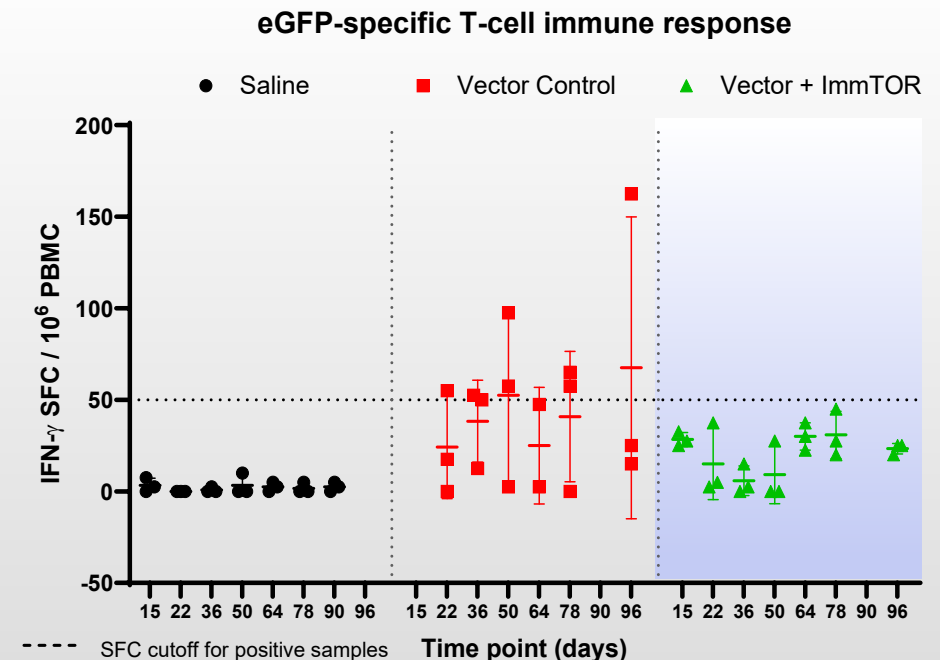
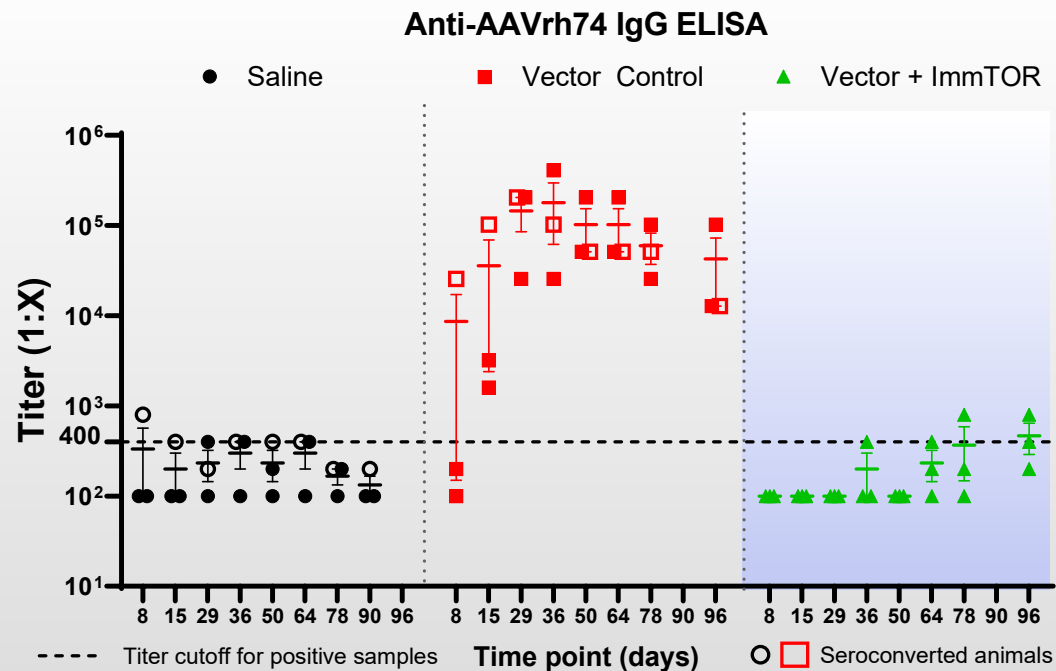
# Data support the proposed enhanced regimen

# Preclinical Results: Sirolimus\* suppresses AAVrh74 immune response

## Study Details:

- AAVrh74.CMV.eGFP
- AAV Dose:  $1.33 \times 10^{14}$  vg/kg
- N=3 per group
- 90-105 days in life

## AAVrh74 Immune Response

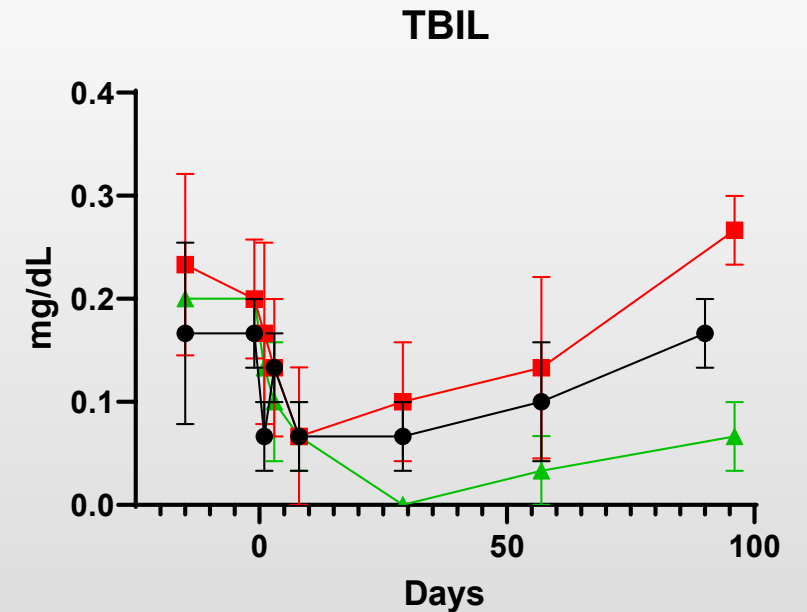
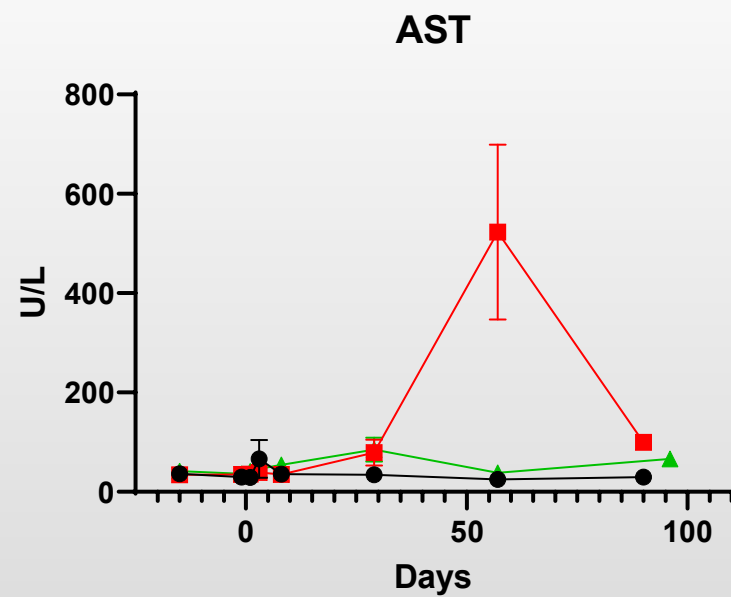
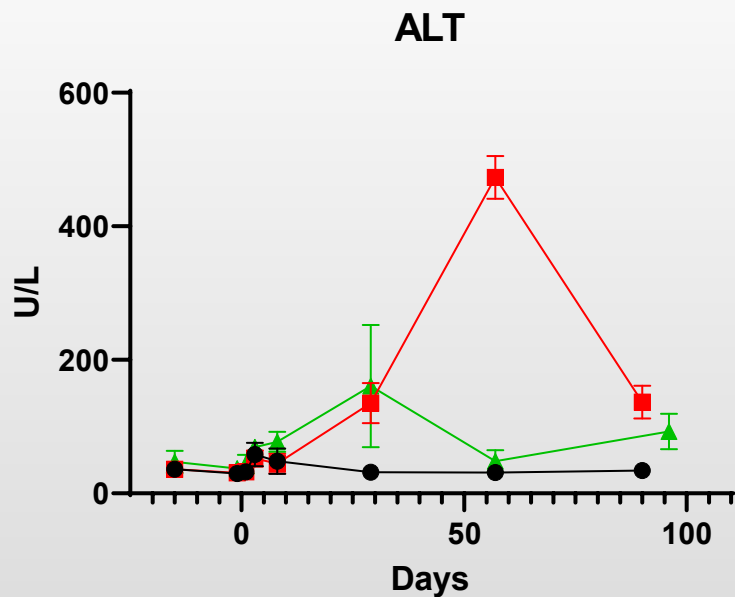


\*ImmTOR (sirolimus encapsulated LNP)

# Preclinical Results: Sirolimus\* effectively mitigates liver enzyme elevations

- Saline
- Vector Control
- ▲ ImmTOR + Vector

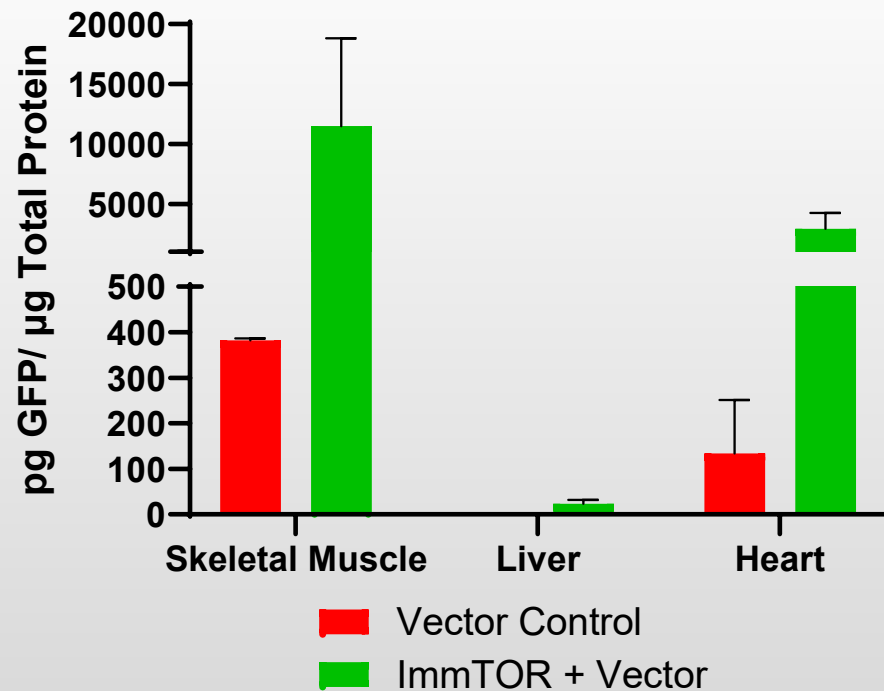
## Key Liver Function Tests



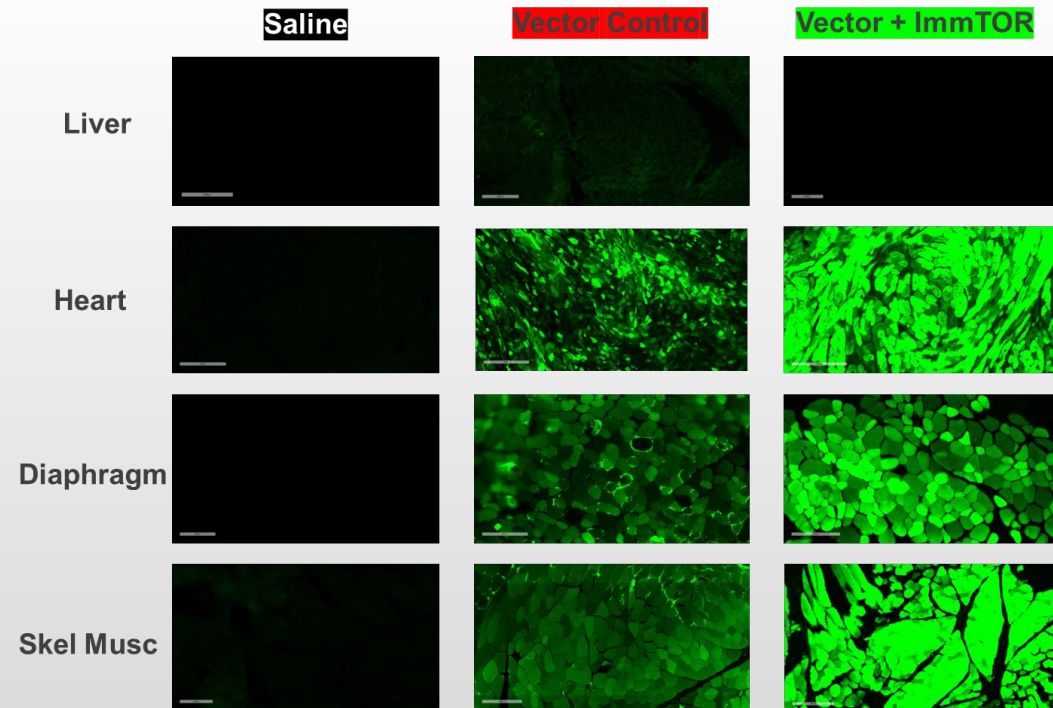
\*ImmTOR (sirolimus encapsulated LNP)

# Preclinical Results: Confirming gene expression in target tissue

## GFP Expression (ELISA)



## GFP Expression (IF)



# Enhanced risk mitigation plan

# Summary of enhanced risk mitigation plan

## Commercial setting

- **Non-ambulatory patients**
  - Suspend shipment of ELEVIDYS until alignment with expert panel and regulators on risk mitigation such as enhanced immunosuppression regimen
  - Commitment to ongoing vigilance and learning
- **Ambulatory patients**
  - No changes to treatment protocol or patient experience (steroid regimen remains the same)
  - Ongoing practice of administering corticosteroids before and after ELEVIDYS infusion
  - Post-treatment monitoring for elevated liver enzymes to continue

## Clinical setting

- Paused dosing in ENVISION study to allow for the evaluation of a protocol amendment
- Amendment to introduce sirolimus as part of the immunosuppressive approach

# Doug Ingram

# Q&A