End-to-end device compatibility and in-use stability assessment of an AAV gene therapy delivered by convection-enhanced delivery

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Disclosures

Conflict of Interest

I am an employee of Siren Biotechnology and receive salary and equity compensation, including stock options, from the company.

Forward-Looking Statements

This presentation contains forward-looking statements related to the development of investigational therapies. These statements involve risks and uncertainties that could cause actual results to differ materially from those expressed or implied. SRN-101 is an investigational product and has not been approved by the FDA for any indication. Siren Biotechnology undertakes no obligation to update these statements except as required by law.

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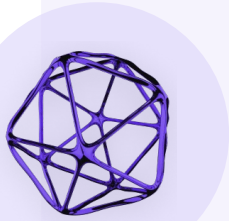
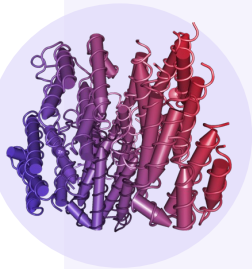
Siren has created a **new oncology modality** by combining two clinically validated platforms



AAV Gene Therapy

Can deliver therapeutic payloads to **any cell type**

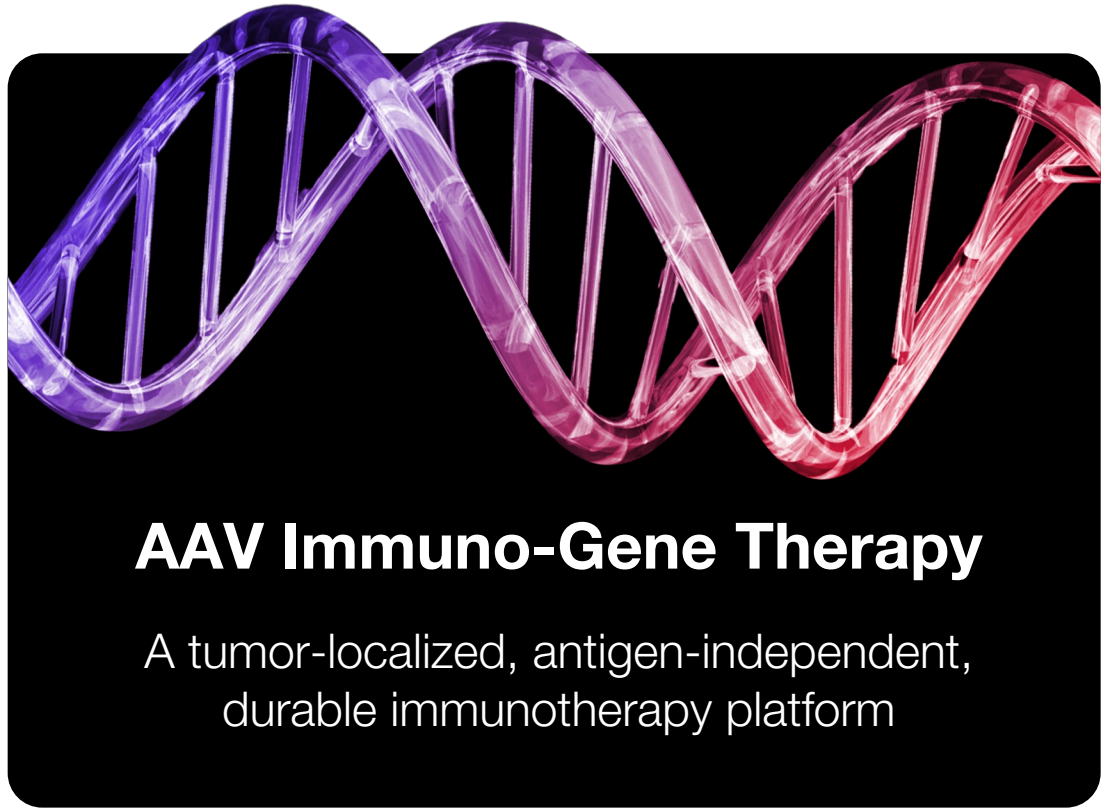
Clinically validated in both adults and children



Engineered Cytokines

Potent immunomodulatory and **anti-tumor effects**

Activity **independent of tumor antigens**



AAV Immuno-Gene Therapy

A tumor-localized, antigen-independent, durable immunotherapy platform

SRN-101, the lead asset in Siren's platform, is designed for broad oncology applications

Kuwahara et al., Molecular Therapy Oncology 2026. DOI: 10.1016/j.omton.2026.201183

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High-grade glioma: the first of many indications for SRN-101

Regulatory & Development Advantage

Orphan indication

Clear, near-term clinical endpoints

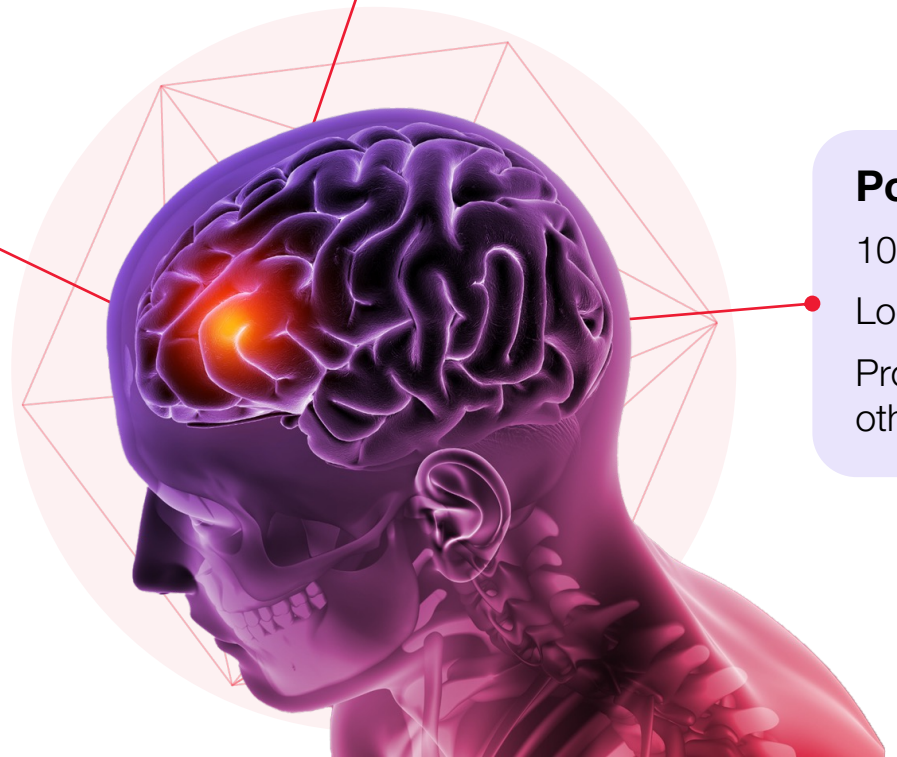
Familiar MRI-guided CED delivery paradigm

Unmet Need

Median survival of 6-12 months

5-year survival is <5%

No effective therapies



Potential for Platform Leverage

100+ different primary brain cancers

Local delivery is well-validated

Proof-of-mechanism here is scalable to other solid tumor cancers

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MRI-guided intratumoral CED enables precise tumor-restricted expression with minimal systemic exposure

- ☑ Reduces both systemic cytokine toxicity risks + AAV localization risks
- ☑ Enables lower total doses
- ☑ Results in high intratumoral concentrations of SRN-101

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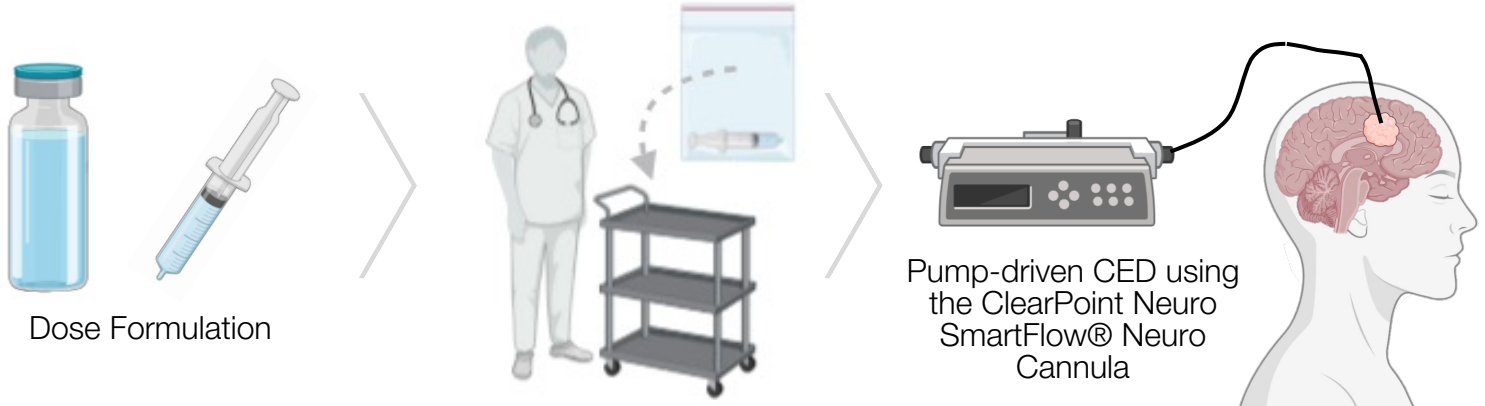
Clinical workflows present risks to drug integrity

SRN-101 Clinical Workflow

Preparation → **Transport** → **Administration**



Dose Formulation

Pump-driven CED using the ClearPoint Neuro SmartFlow® Neuro Cannula

Pharmacy Manual

Administration Manual

Potential Risks

Material loss, inactivation, or structural instability due to:

- Physical stresses
- Material contact
- Temperature changes
- Holding time(s)

Device compatibility and in-use stability studies that mimic real world clinical workflows are critical to confirm product strength, integrity, and function are maintained

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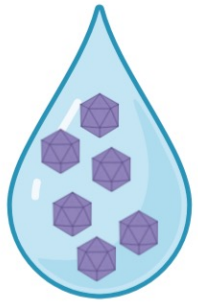
Our device compatibility study design was informed by our clinical protocol for our Phase I/II trial

Clinical dose preparation

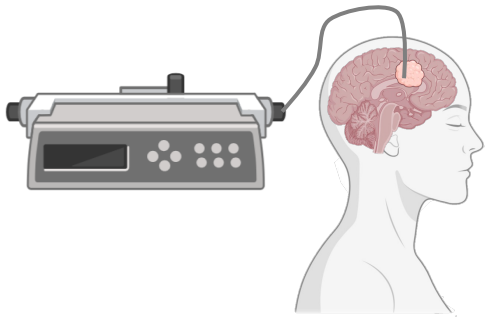


Investigational product dilution

Intermediate dilution
Infusate volume

Convection-enhanced delivery (CED)

SmartFlow® Neuro Cannula



Pump-mediated infusion

Infusion flow rate
Infusion duration

Clinical imaging

Real-Time MRI

Contrast agent

Compatibility study parameters

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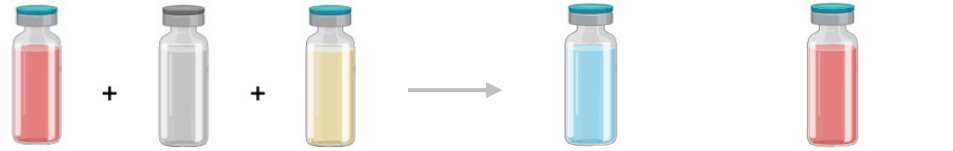
Device Compatibility and In-use Stability Study Design

Preparation

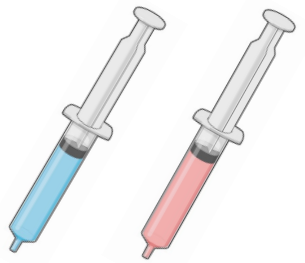


SRN-101 Diluent Contrast

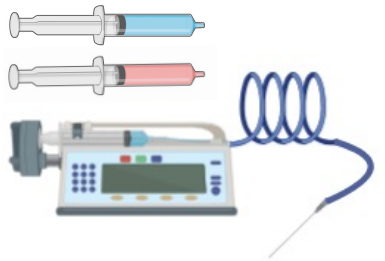
Low IP concentration

High IP concentration

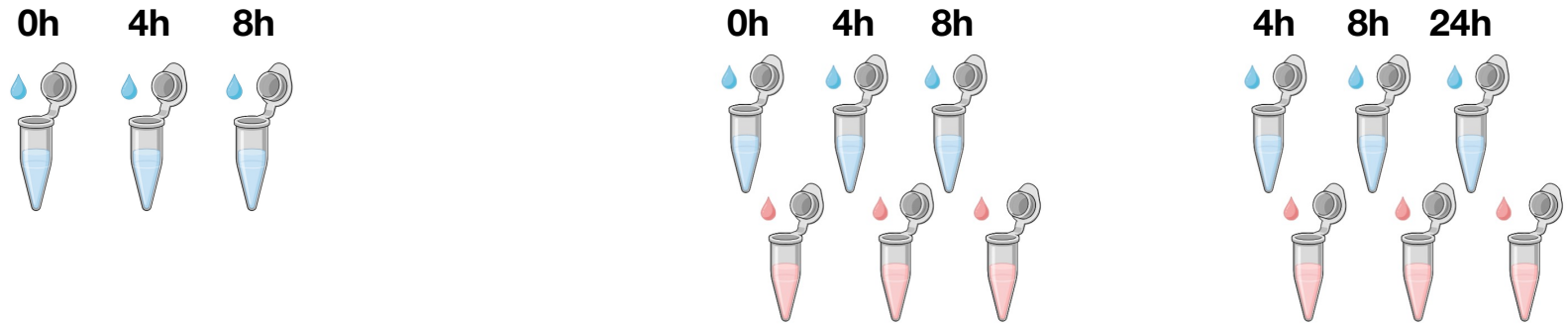
Transport



Administration



Sampling



Assessment of Critical Quality Attributes

Genome titer | Potency | Capsid titer | Subvisible particulate matter

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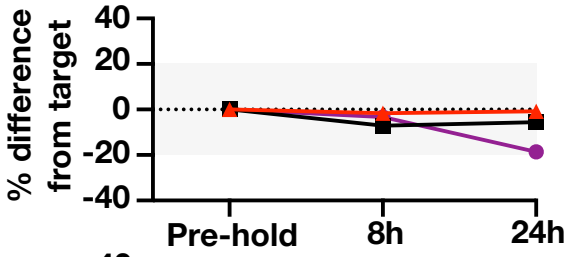
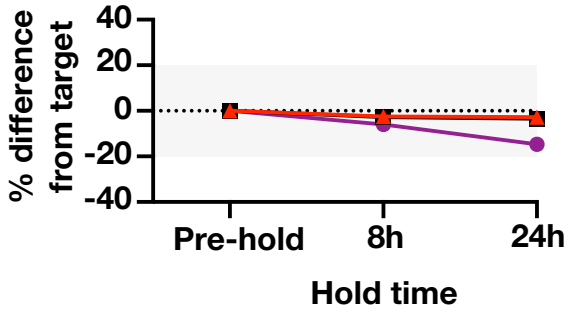
SRN-101 demonstrates strong compatibility with clinical workflows

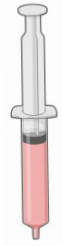
Compatibility with intermediate containers

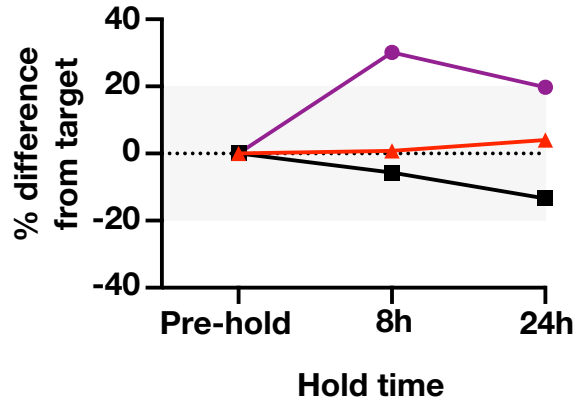
Low IP concentration



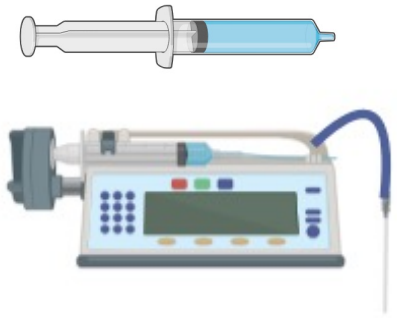


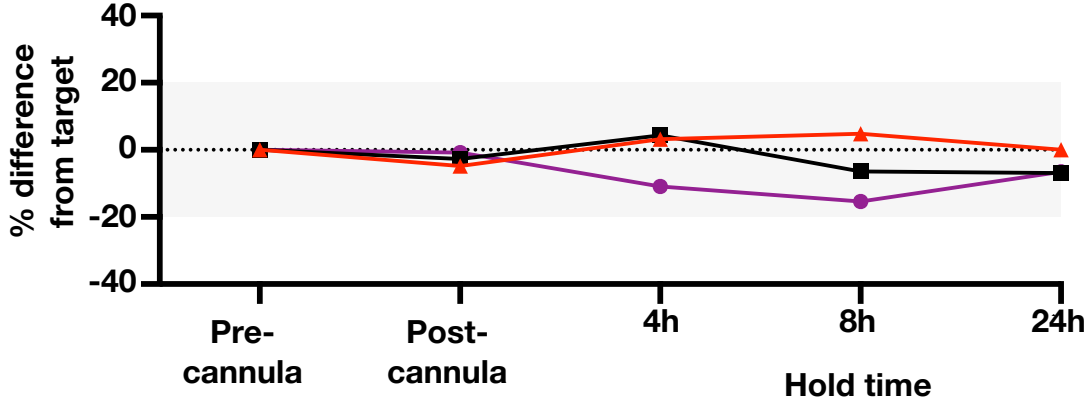
High IP concentration

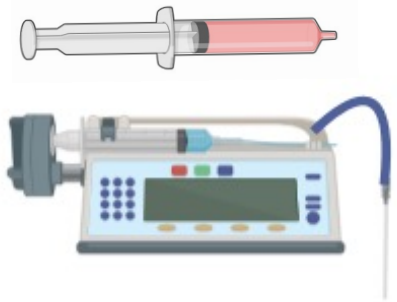


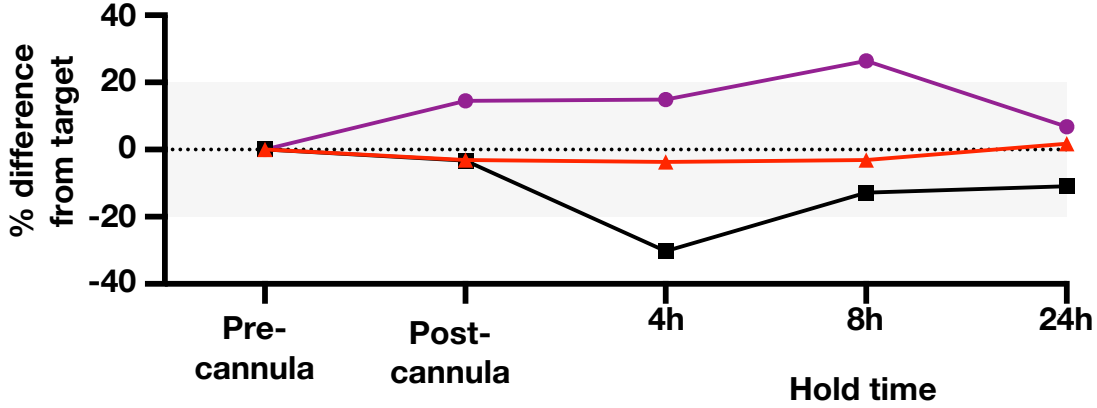


Compatibility with CED device + infusion parameters









Genome titer Capsid titer Potency

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CONCLUSIONS

SRN-101 was demonstrated to be compatible with:

- Pharmaceutical dose preparation workflows
- CED device and infusion parameters
- All materials utilized in dose preparation and delivery
- Environmental conditions
- Hold times representative of real-world clinical workflows

This data contributed to the clearance of two fully U.S.-based INDs (a Phase 1 IIT and a Phase 1/2) in adult recurrent high-grade glioma

This study provides a robust framework for later phase development and future BLA submission

Poster #2241 covers our large animal pig safety data

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