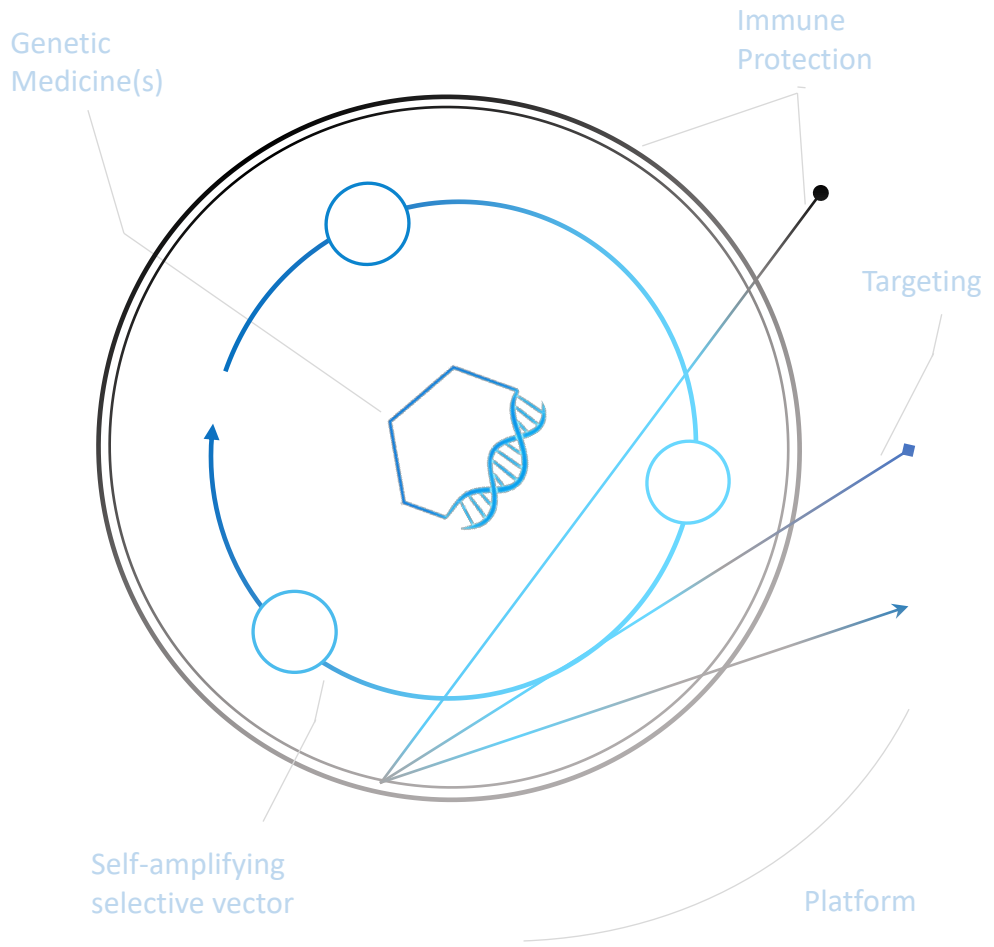
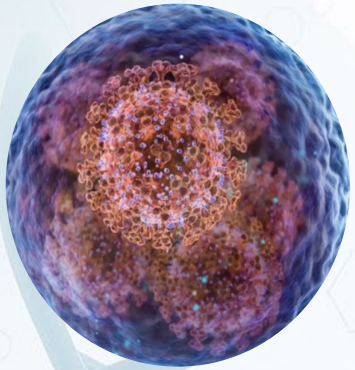
Engineering the Future of Genetic Medicine

From cancer to other complex diseases, Calidi precisely delivers genetic medicines to sites of disease



CALIDI BIOTHERAPEUTICS

Our Science: Always Evolving



NeuroNova/SuperNova: Stem cells loaded with virus

RedTail: Extracellular enveloped virus with genetic medicine payload

- Calidi pioneered the use of viruses loaded into stem cells, enhancing the efficacy of oncolytic viruses
- The stem cell membrane allows for improved tumor homing and protection from immune clearance compared to other approaches
- NeuroNova showing promising activity in advanced glioblastoma; SuperNova initiating Phase I in advanced solid tumors
- Viruses loaded into stem cells are protected against immune clearance, but the size of stem cells prohibits efficient dissemination
- RedTail platform envelops virus in *modified* human membrane to further enhance avoidance of immune clearance
- Virus is ~10,000 times volumetrically smaller than a stem cell, allowing for efficient dissemination

Our Science: RedTail

Stepwise creation of the platform:
A decade of engineering to create RedTail

Step 1

Vaccinia virus engineered for **selective tumor targeting and potent lysis**

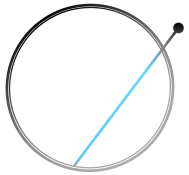
Step 2

Multiple sites for gene insertion and expression identified

Step 3

Selection of virus strain with envelope. Testing of cell lines to determine most protective envelope

Step 4

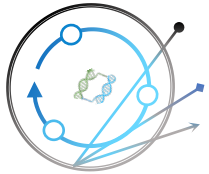


Genetic engineering to express **CD55 on envelope** to further enhance immune protection

Step 5

CLD-401:Systemic administration, potent and specific tumor lysis, and **IL-15 superagonist expression in situ**

Step 6

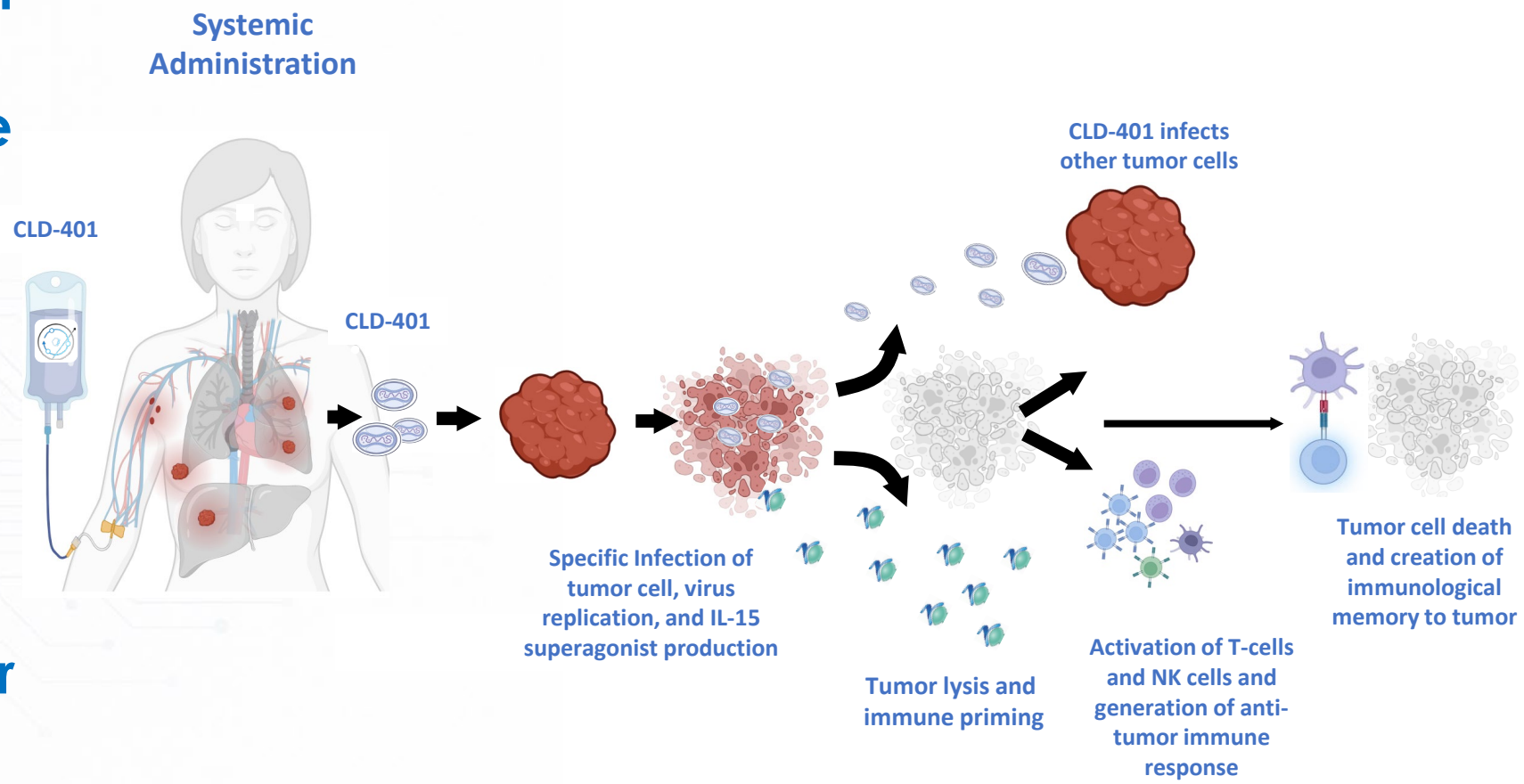


New candidates contain **multiple payloads and additional membrane-expressed proteins**

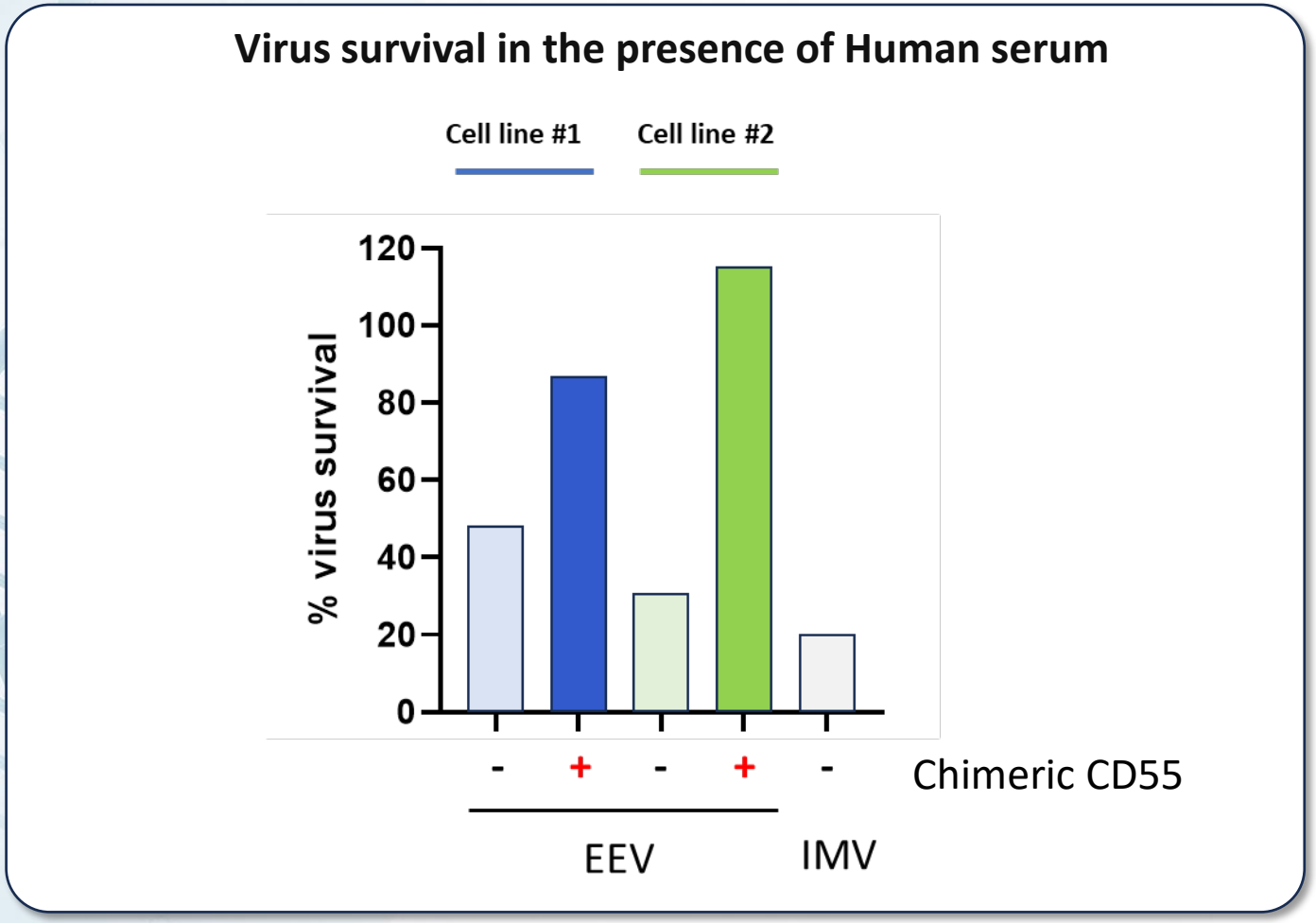
- **CLD-401 will be the first lead from the RedTail platform to enter the clinic**
- **The Phase I for CLD-401 will be in patients with advanced solid tumors**

CLD-401: The First RedTail Lead

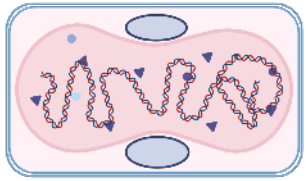
- Systemic administration
- Protected from immune clearance
- Targeted tumor cell lysis and immune priming
- IL-15 superagonist production at the tumor
- Memory response to the tumor



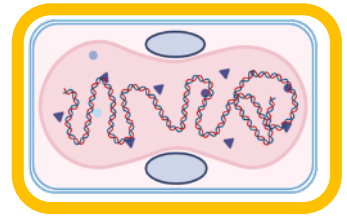
CD55 Membrane Expression Creates High Resistance to Human Complement And Inhibition of Immune Clearance



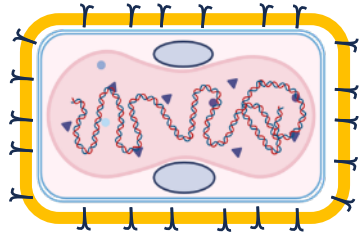
Non-enveloped form



Enveloped form



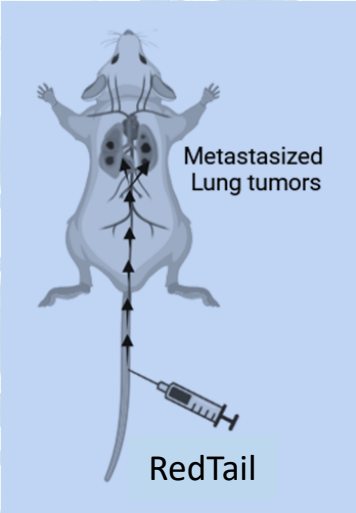
Enveloped form + CD55 receptor



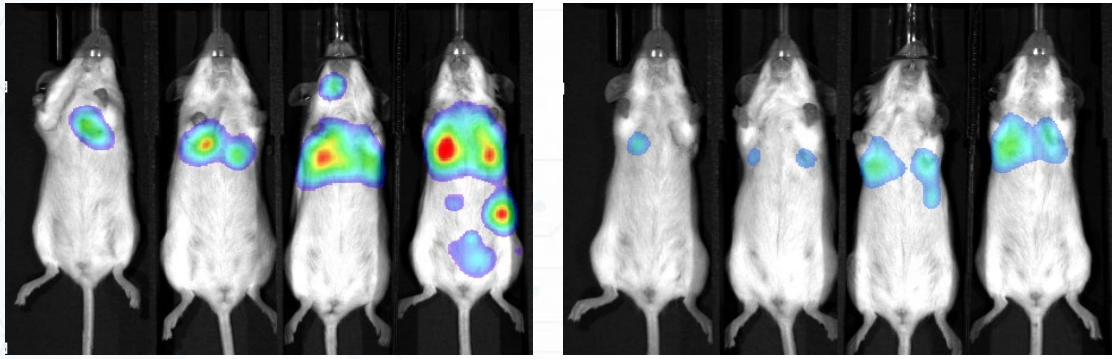
Overexpression of CD55 on cell membrane protects against complement inactivation and enhances immune evasion

Administration of RedTail Virus Eliminates Metastatic Lung Tumors

One (1) dose (5e6 PFU) was able to decrease and eliminate lung cancer and metastatic tumors into the lung.

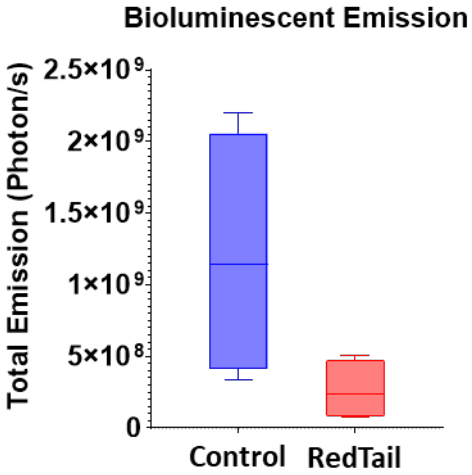


Control **RedTail**



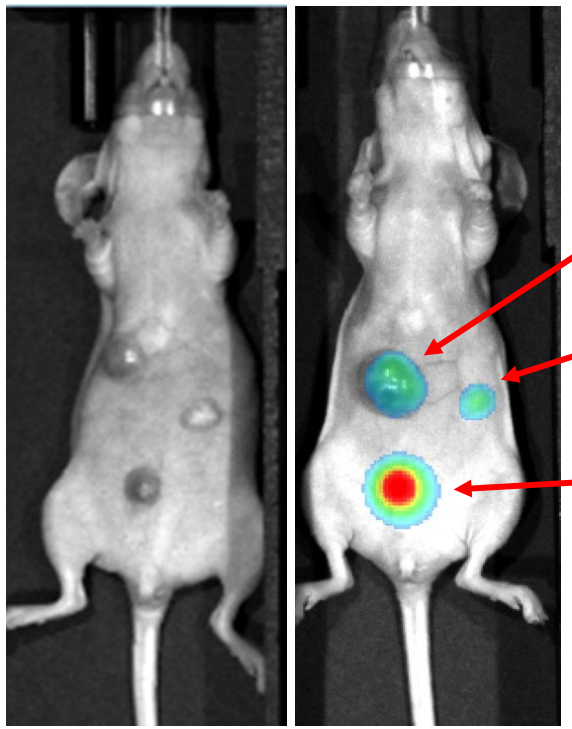
Tumor signal: Rainbow (Bioluminescence)

Bioluminescence images (tumor burden) were taken 6 days after treatment



Systemic Administration of RedTail Virus Targets and Eliminates Multiple Tumors in Preclinical Models

Mouse model bearing 3 different human solid tumor types



% Tumor Growth inhibition (Average n=5) day 10

Head and Neck SCC cancer	30%
Lung cancer	92%
Melanoma	87%

After one (1) systemic administration, RedTail virus **can target distant tumors and express selected payload** (i.e. imaging protein TurboFP635)

Remarkable Versatility: Ability to address **diverse tumor types** and adapt to the unique **tumor microenvironment** within the organism.

IL-15 Superagonist: Proven Activator of Immunity

Anktiva (IL-15 superagonist) approved for the treatment of BCG-non-responsive nonmuscle invasive bladder cancer in situ

- Drug dosed intravesically in bladder cancer at 400 mcg/kg weekly
- S.C dosing in NSCLC is 15 mcg/kg every 3 wks (80-fold lower than intravesical dose)
  - IL-15 agonists: tumor concentrations drive efficacy; systemic concentrations drive tox
    - In situ delivery of IL-15 superagonists maximizes therapeutic window

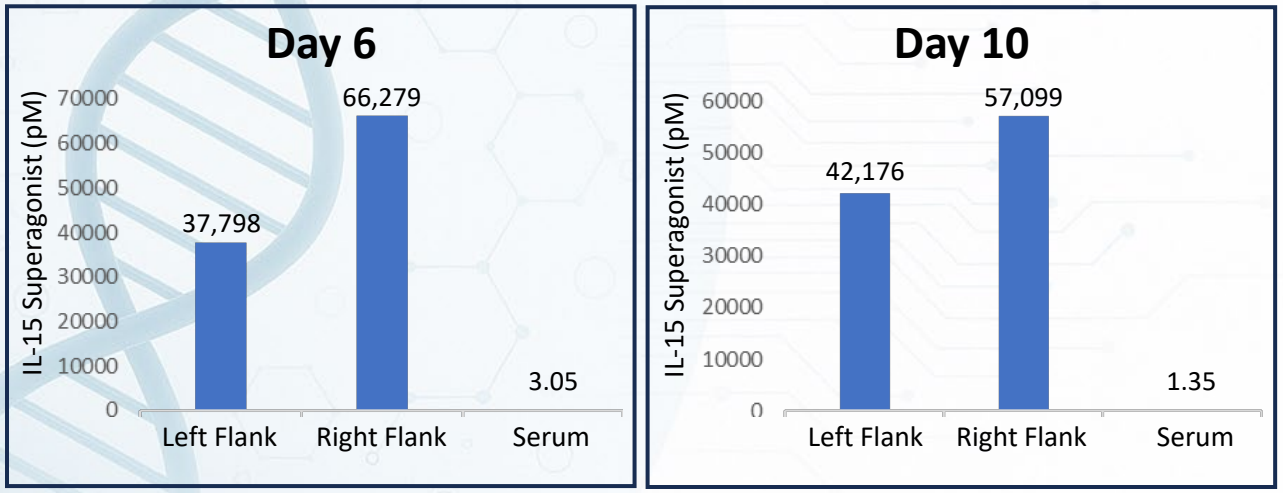
First compound out of RedTail platform delivers IL-15 superagonist directly to the tumor

- Improved activity vs. RedTail virus without IL-15 payload seen in murine models

High Levels of IL-15 Superagonist in the Tumor But Not Serum

- Serum concentration in syngeneic murine models is negligible
- Tumor concentration is much higher than achievable with systemic delivery

IL-15 Superagonist Levels in Tumor vs Serum (pM)



- EMT6 model: 1 dose at 10^6 PFU
- Average of 2 animals; each animal had implantations in the left and right flank

- **RedTail gene therapy** delivers IL-15 superagonist directly to tumors, achieving high local concentrations with minimal systemic exposure in mouse models.
- **Subcutaneous SOT101** (IL-15 superagonist) dosed at 75 µg/kg subcutaneously, reached 53.5 ng/mL in NHP plasma. By comparison, RedTail's approach maintained tumor enrichment with blood levels below 200 pg/mL in mice, potentially lowering systemic toxicity.

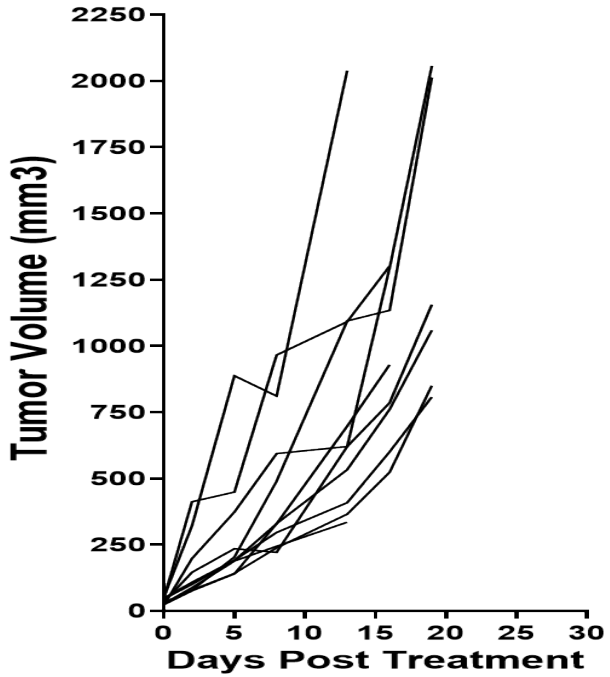
Ref: Champiat et al., *Cell Reports Medicine*, 2025

Enhanced Activity With In Situ IL15 Superagonist: Lung Cancer

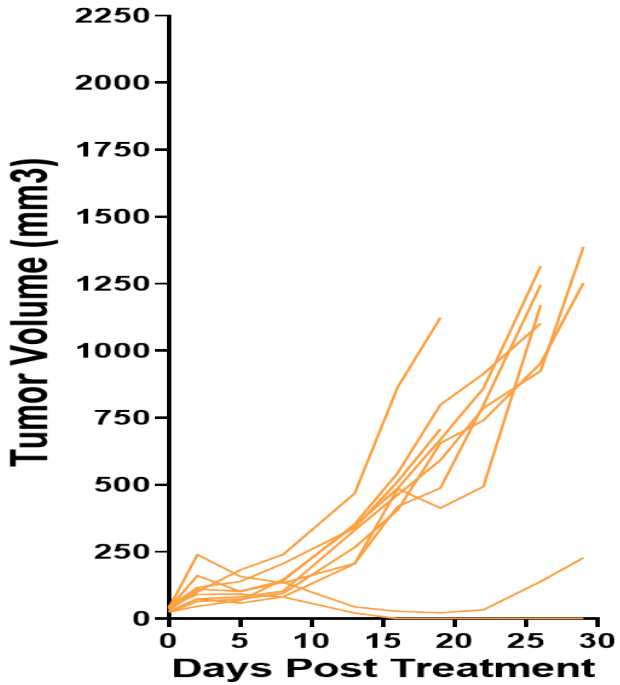
RedTail virus with the IL-15 superagonist payload drastically improves treatment efficacy

Tumor regression in a preclinical model of breast cancer (EMT6) after one (1) administration of 5e6 PFU viral particles

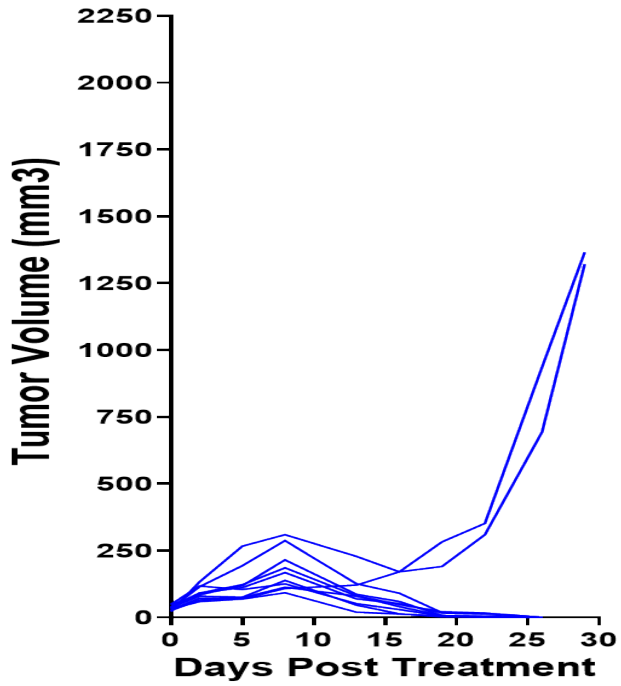
Untreated



RedTail



RedTail + IL-15-IL15α



Additional Genetic Medicine Payloads And Enhanced Targeting

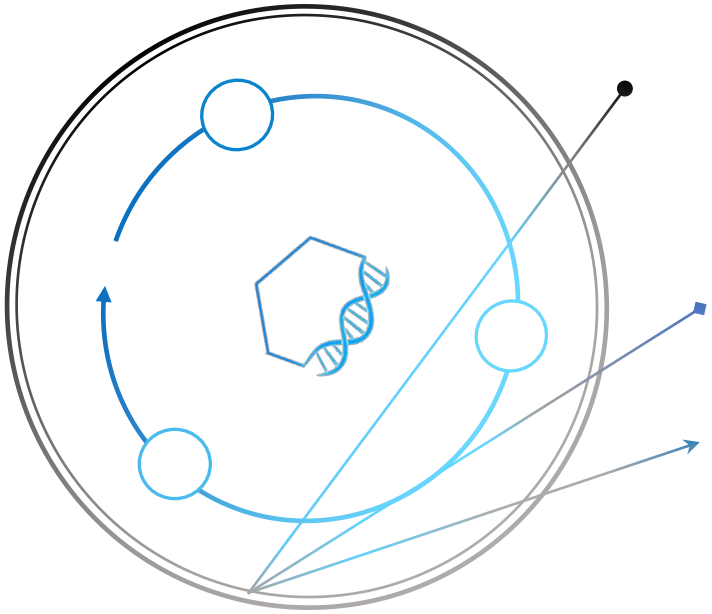
- RedTail virus is a **genetically stable, non-integrating** virus with **large insertion capacity**

- Proof-of-concept established with **IL-15 superagonist**
  - High levels of **in situ delivery** of payload
  - **Enhanced activity** in tumor models with payload

- Potential to deliver additional cytokines, chemokines, Mabs, etc
  - Potential for **multiple payloads** delivered in one virus

- **Human cell "programmable"** membrane to allow for enhanced targeting

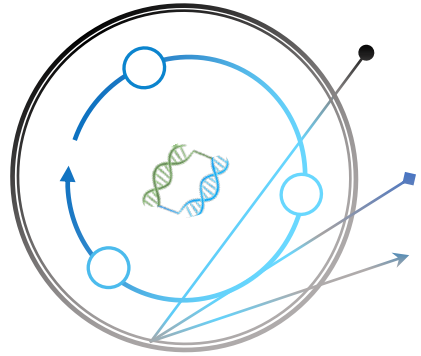
- Commercial scale **COGs** for RedTail estimated to be **similar to antibody or other protein-based therapies**



RedTail: Potential to Expand Outside of Oncology

Lead: CLD-401

Next-Generations



Oncology

- Envelope and CD55 expression facilitate survival in the complement-rich bloodstream, enabling systemic dissemination
- Viral replication depends on cell proliferation, active mitogenic signaling and enhanced nucleotide biosynthesis
  - E.g: Tumor cells.
- Payload(s) expressed as virus replicates
  - Immune-stimulating payloads used in oncology

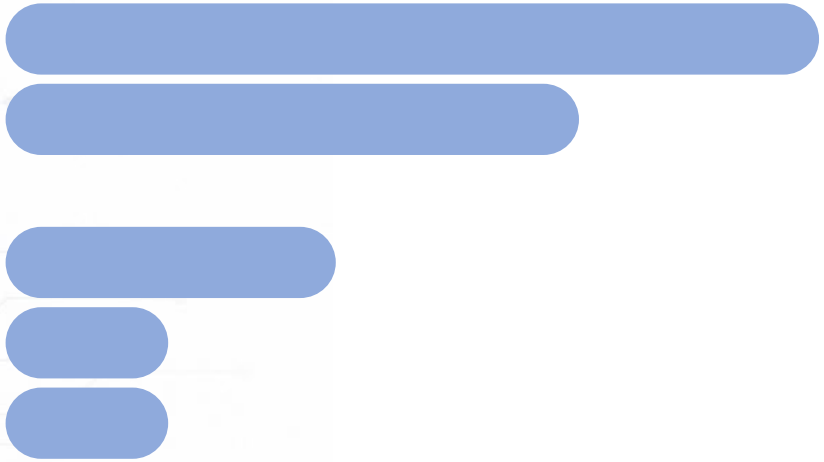
Precision Oncology and Other Diseases

Additional Add-ons:

- Envelope can be used to target other cell types
  - Envelope engineering for “programmable” targeting
  - Viral replication in proliferative cells like activated B- cells
- Oher Payload(s)
  - Immune-suppressive payloads to be used **in autoimmunity**
  - Alternative cancer therapeutic payloads

Calidi Pipeline: Evolving the Technology

Candidate (genetic medicine)	Indications	Discovery	IND enabling	Phase I	Phase 2	Phase 3
NeuroNova	Rel/ref glioblastoma					
SuperNova	TNBC, SCCHN, sarcoma					
RedTail:						
CLD-401 (IL-15 SA)	Multiple solid tumors					
CLD-501 (undisclosed)	Myeloma, autoimmune					
CLD-601 (undisclosed)	Oncology (undisclosed)					



Calidi: A Commitment to Using Capital Efficiently

Calidi continues to improve its financial position

- ❖ New management team brought in
  - ✓ New CEO, CMO, and Board Chairman appointed to drive value
- ❖ Improving the balance sheet
  - ✓ Debt reduced from >$8M to $1.7M (1Q25); projected to be $0.6M by end of 2025
- ❖ Reducing operating costs
  - ✓ G&A expenses reduced by 34% 1Q24-1Q25; plans to reduce costs further
- ❖ Rapidly advancing the pipeline
  - ✓ CLD-401 will be advanced rapidly as proof-of-concept for RedTail
- ❖ Potential for non-dilutive capital
  - ✓ Pharma partnerships in discussion around the RedTail platform