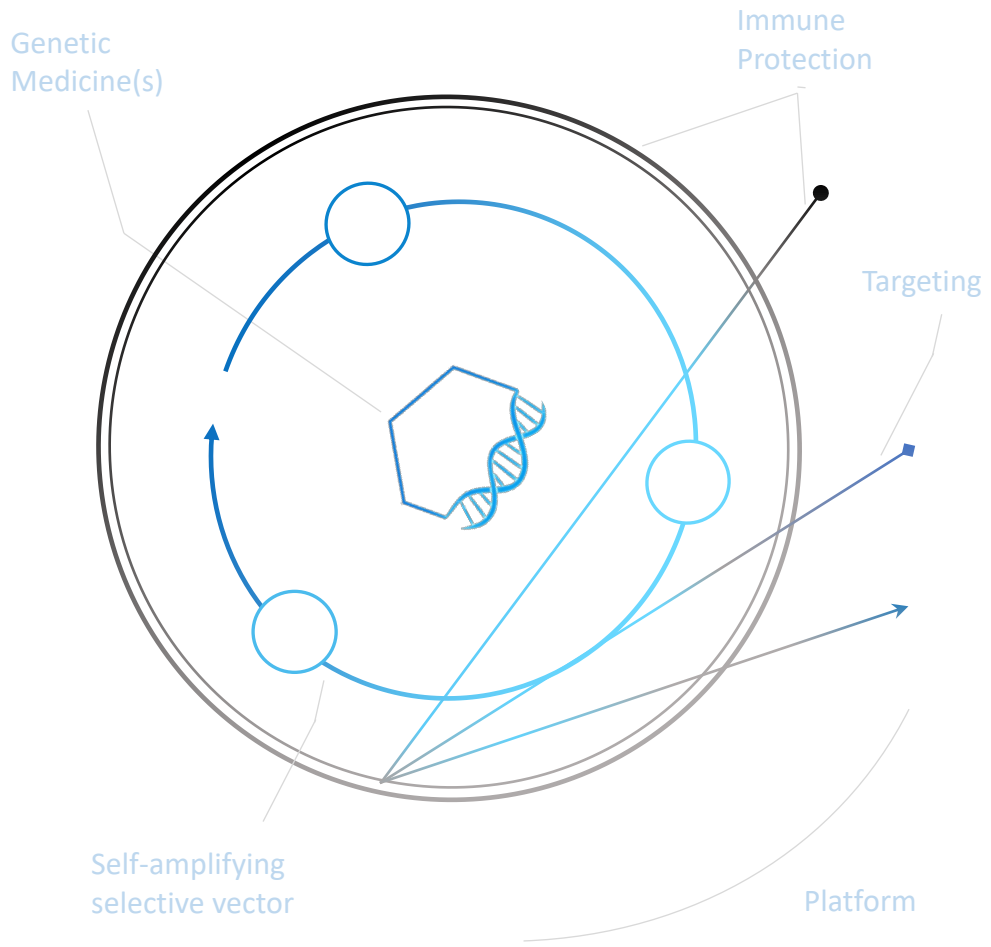
Engineering the Future of Genetic Medicine

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



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CALIDI BIOTHERAPEUTICS

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This presentation may contain forward-looking statements for purposes of the "safe harbor" provisions under the United States Private Securities Litigation Reform Act of 1995. Terms such as "anticipates," "believe," "continue," "could," "estimate," "expect," "intends," "may," "might," "plan," "possible," "potential," "predicts," "project," "should," "towards," "would" as well as similar terms, are forward-looking in nature, but the absence of these words does not mean that a statement is not forward-looking. These forward-looking statements include, but are not limited to, statements concerning upcoming key milestones, planned clinical trials, and statements relating to the safety and efficacy of Calidi's therapeutic candidates in development. Any forward-looking statements contained in this discussion are based on Calidi's current expectations and beliefs concerning future developments and their potential effects and are subject to multiple risks and uncertainties that could cause actual results to differ materially and adversely from those set forth or implied in such forward-looking statements. Forward-looking statements in this presentation may include, for example, statements about certain risks, including, but not limited to:

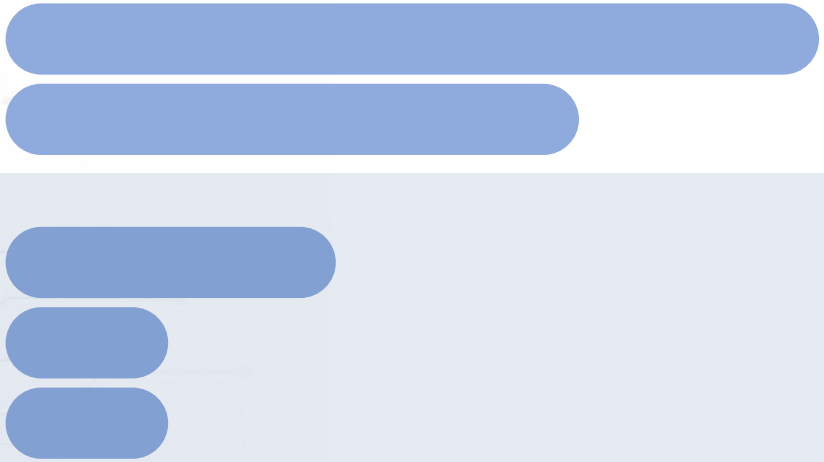
- we are a clinical stage biotechnology company developing novel genetic medicines for oncology with a limited operating history and have not generated any revenue to date from product sales;
- we have no products approved for commercial sale and have not generated revenues. We have incurred significant operating losses since our inception and we anticipate that we will incur continued losses for the foreseeable future;
- our need to raise substantial additional funding. If we are unable to raise capital when needed, or if at all, we will be forced to delay, reduce or eliminate some of our product development programs or commercialization efforts, or cease our operations altogether. In addition, the issuance of a substantial number of shares of common stock as a result of a financing could adversely affect the price of our common stock;
- our financial and business performance, including our financial projections and business metrics;
- our market opportunity;
- changes in our strategy, future operations, financial position, estimated revenues and losses, forecasts, projected costs, prospects and plans;
- our ability to retain or recruit officers, key employees and directors;
- the impact of the regulatory environment and complexities with compliance related to such environment;
- the expected costs associated with our research and development initiatives, including investments in technology and product development;
- our ability to secure sufficient funding and alternative source of funding to support when needed and on terms favorable to us to support our business objective, product development, other operations or commercialization efforts;
- our ability to enroll patients in our proposed clinical trials and development activities;
- the impact of governmental laws and regulations; and
- our ability to obtain, maintain, protect and enforce sufficient patent and other intellectual property rights for our drug candidates and technology.

Other risks and uncertainties are set forth in the section entitled "Risk Factors" and "Cautionary Note Regarding Forward-Looking Statements" in the Company's Form 10-K filed on March 31, 2025, as may be amended or supplemented by other reports we file with the SEC from time to time.

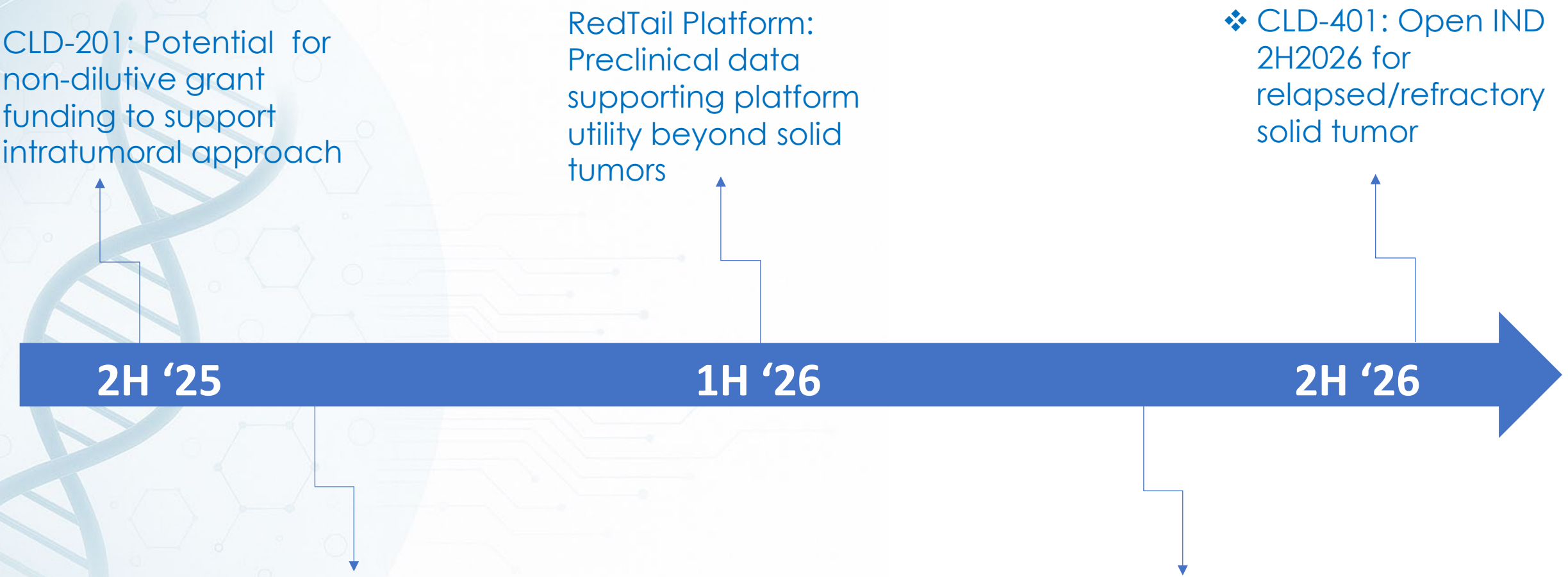
The forward-looking statements made by us in this presentation speak only as of the date hereof. Except to the extent required under the federal securities laws and rules and regulations of the Securities and Exchange Commission ("SEC"), we disclaim any obligation to update any forward-looking statement to reflect events or circumstances after the date on which the statement is made or to reflect the occurrence of unanticipated events. In light of these risks and uncertainties, there is no assurance that the events or results suggested by the forward-looking statements will in fact occur, and you should not place undue reliance on these forward-looking statements.

Calidi Pipeline: Evolving the Technology

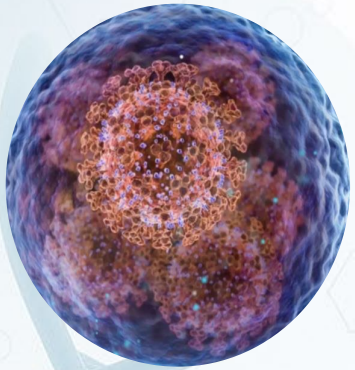
Candidate (genetic medicine)	Indications	Discovery	IND enabling	Phase I	Phase 2	Phase 3
NeuroNova	Rel/ref glioblastoma					
SuperNova	TNBC, SCCHN, sarcoma					
RedTail:						
CLD-401 (IL-15 SA)	Multiple solid tumors					
CLD-501 (undisclosed)	Myeloma, autoimmune					
CLD-601 (undisclosed)	Oncology (undisclosed)					



Upcoming Milestones



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**

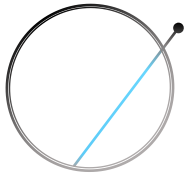
Step 2

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

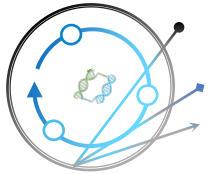


Genetic engineering to express **CD55 on envelope** to further enhance immune protection

Step 5

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

Step 6

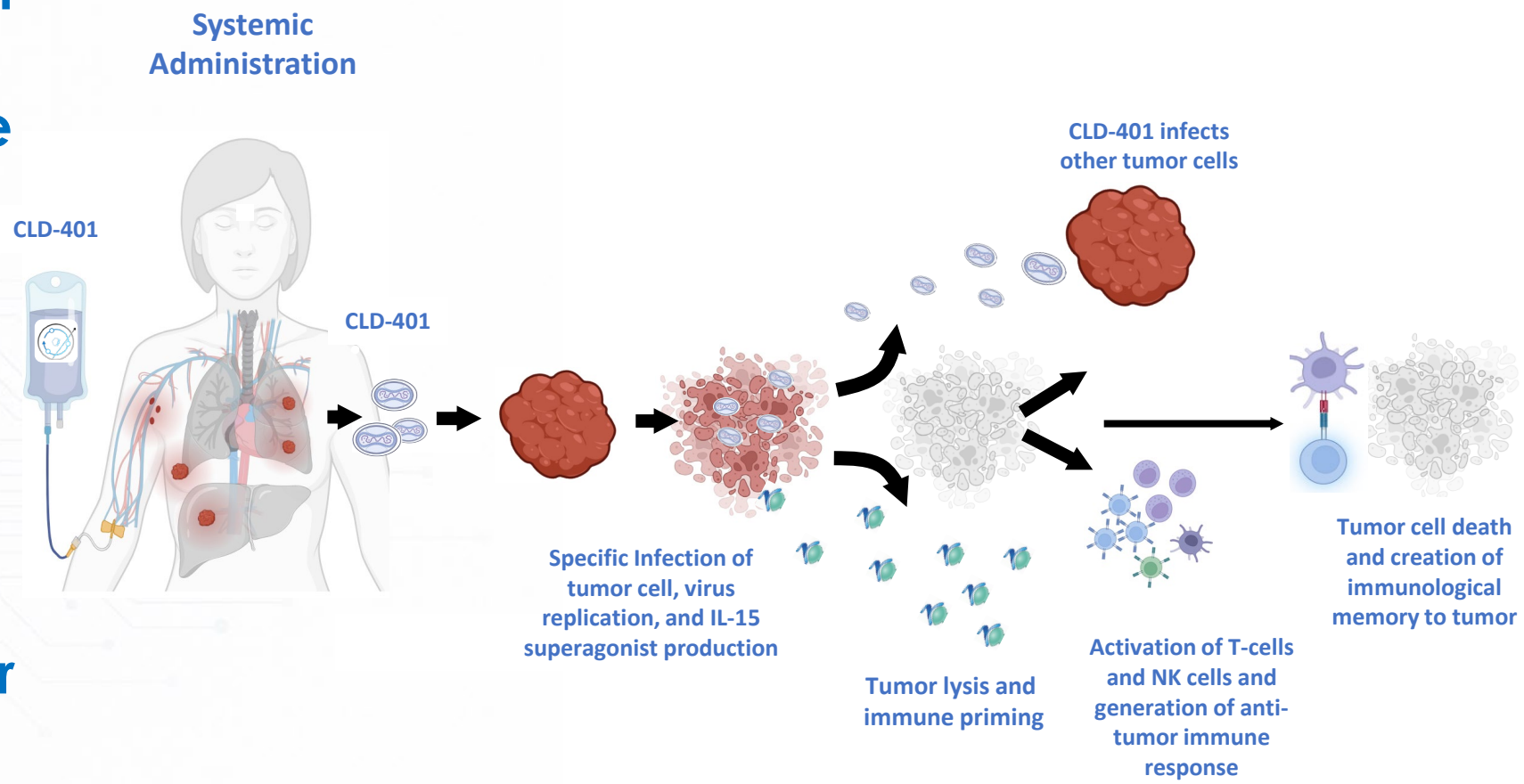


New candidates contain **multiple payloads and additional membrane-expressed proteins**

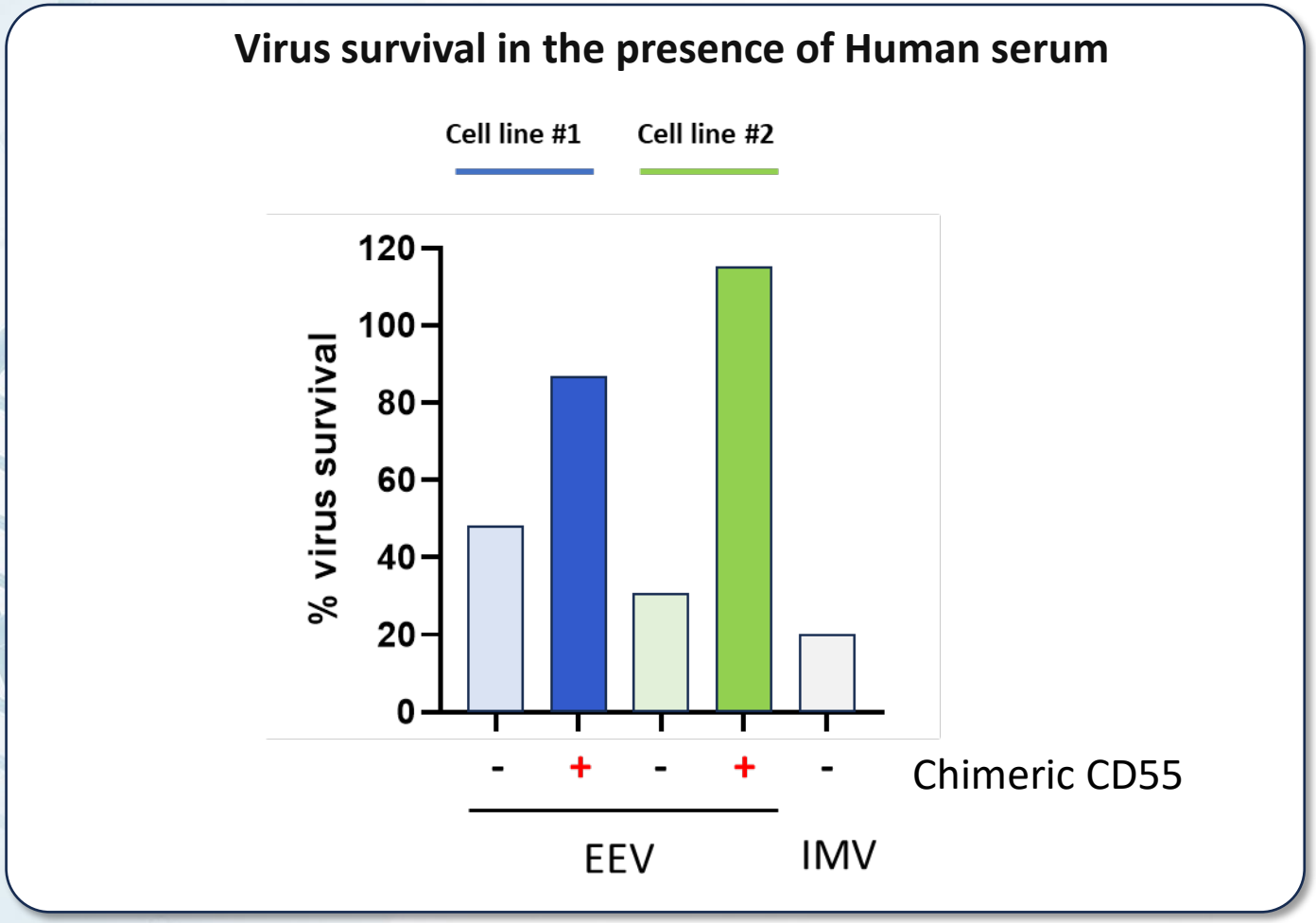
- **CLD-401 will be the first lead from the RedTail platform to enter the clinic**
- **The Phase I for CLD-401 will be in patients with advanced solid tumors**

CLD-401: The First RedTail Lead

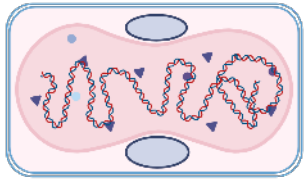
- Systemic administration
- Protected from immune clearance
- Targeted tumor cell lysis and immune priming
- IL-15 superagonist production at the tumor
- Memory response to the tumor



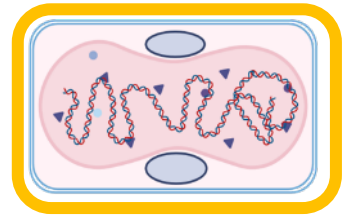
CD55 Membrane Expression Creates High Resistance to Human Complement And Inhibition of Immune Clearance



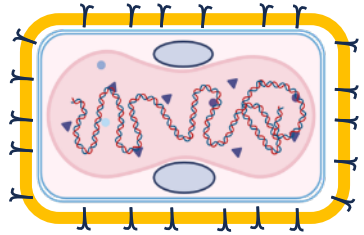
Non-enveloped form



Enveloped form



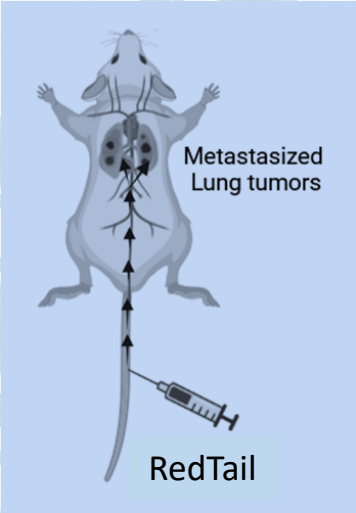
Enveloped form + CD55 receptor



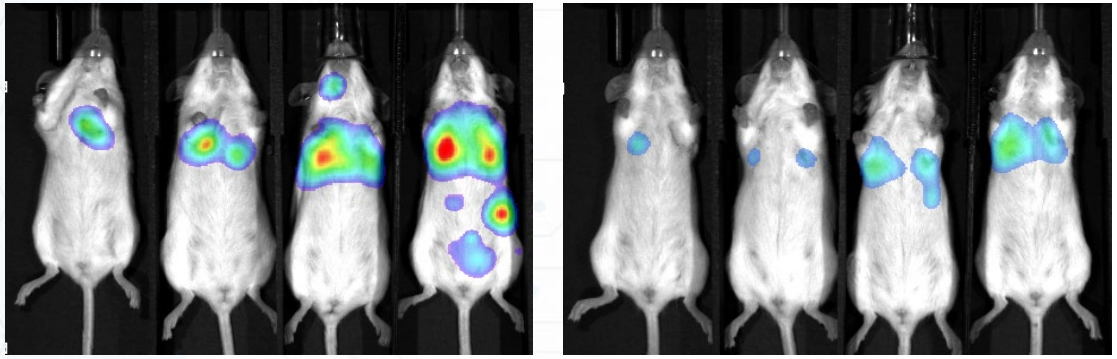
Overexpression of CD55 on cell membrane protects against complement inactivation and enhances immune evasion

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.

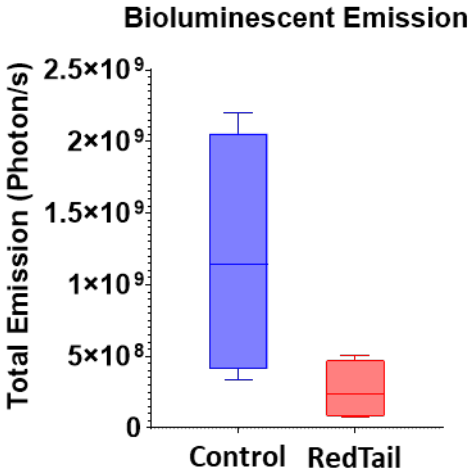


Control **RedTail**



Tumor signal: Rainbow (Bioluminescence)

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



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

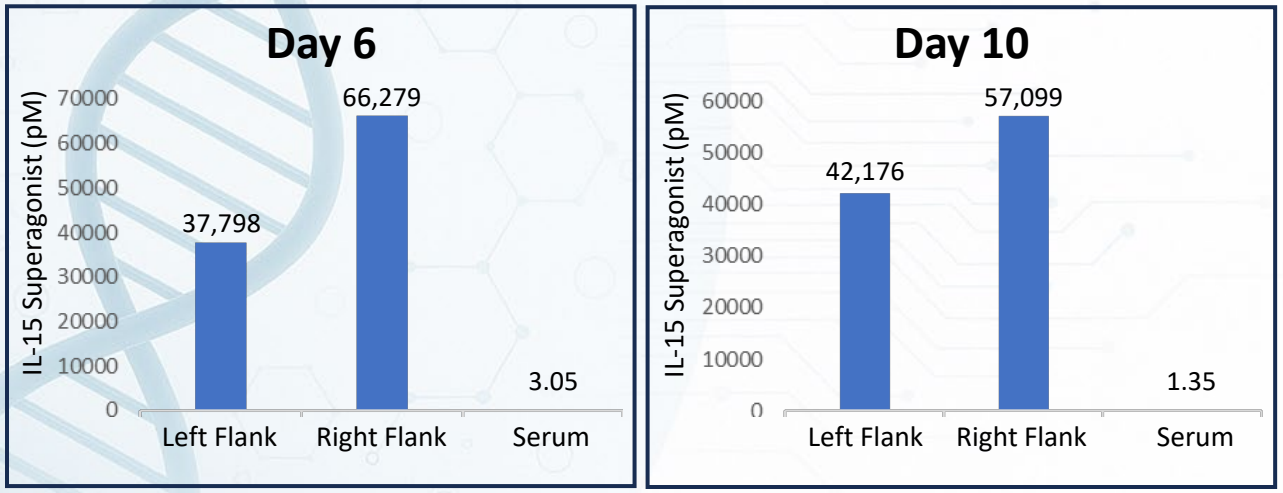
First compound out of RedTail platform delivers IL-15 superagonist directly to the tumor

- 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.

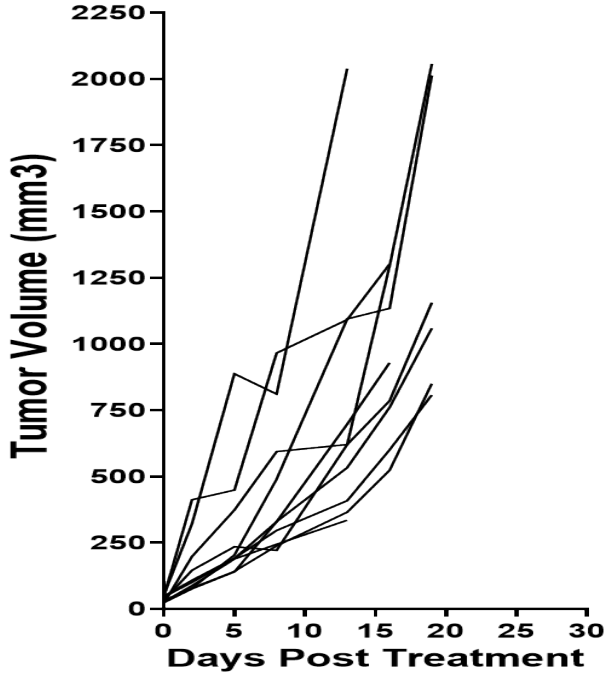
Ref: Champiat et al., *Cell Reports Medicine*, 2025

Enhanced Activity With In Situ IL15 Superagonist: Lung Cancer

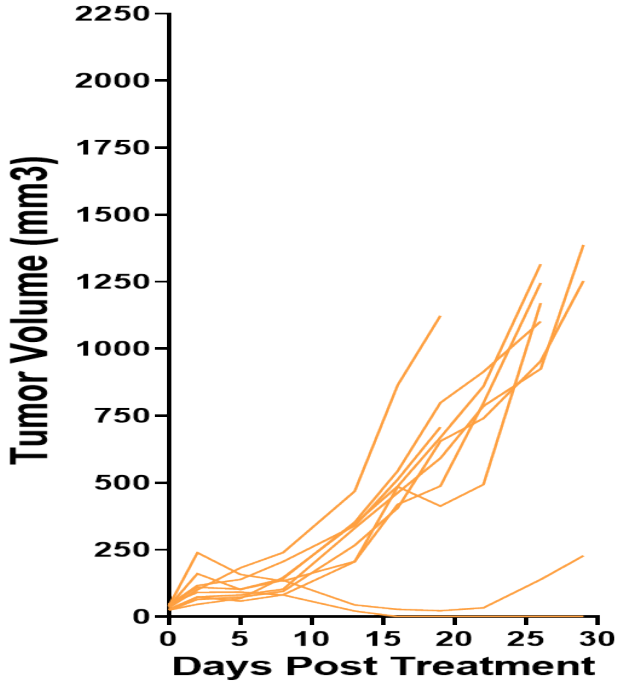
RedTail virus with the IL-15 superagonist payload drastically improves treatment efficacy

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

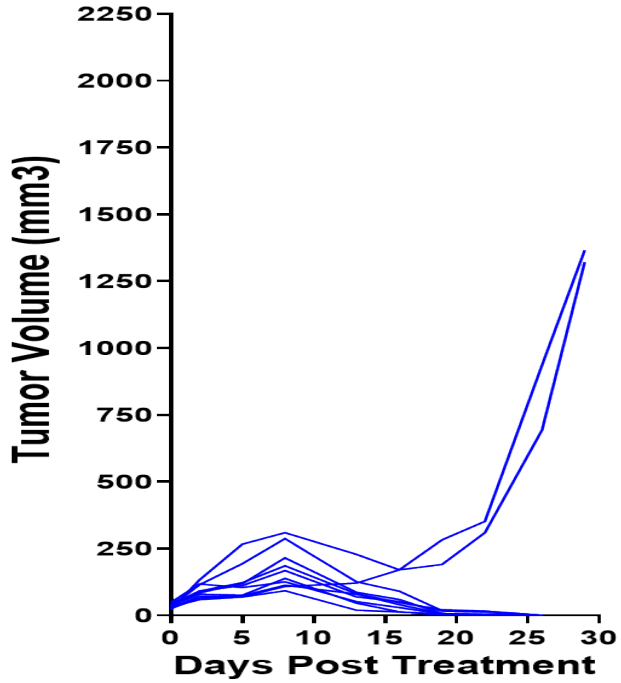
Untreated



RedTail



RedTail + IL-15-IL15α



Additional Genetic Medicine Payloads And Enhanced Targeting

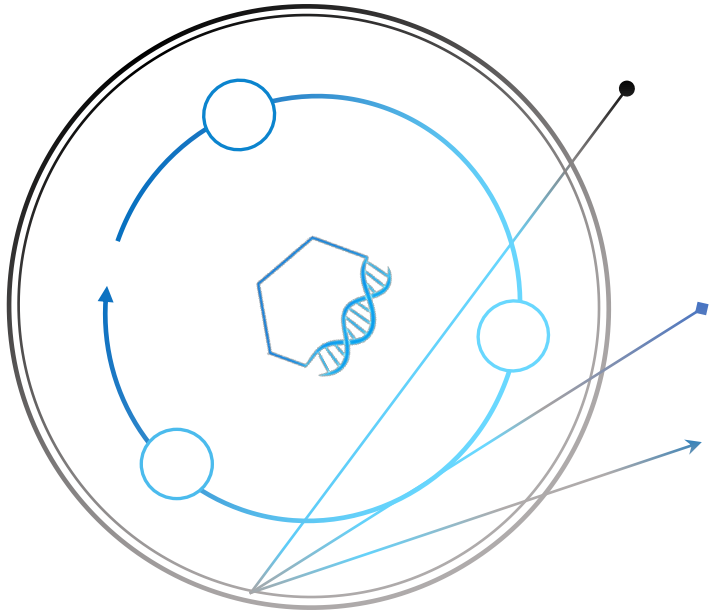
- RedTail virus is a **genetically stable, non-integrating** virus with **large insertion capacity**

- 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

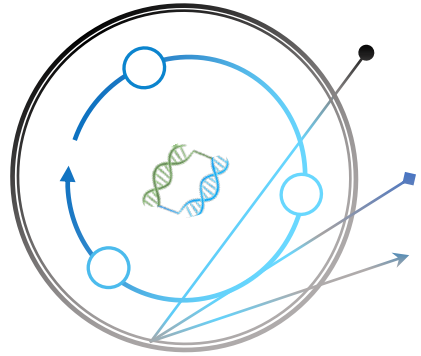
- Commercial scale **COGs** for RedTail estimated to be **similar to antibody or other protein-based therapies**



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

Capitalization Table

Securities Outstanding (as of August 8, 2025)	Common Stock Equivalents *
Common stock outstanding	3,576,446
Warrants (WAEP $11.00)	1,291,539
Warrants ($1,380.00)	111,772
Options (WAEP $88.36)	176,794
Forward Purchase Agreements	5,501
Fully Diluted	5,162,052

* Common stock adjusted for reverse split that was effective 8/4/2025.

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 $1.4M (2Q25); projected to be $0.6M by end of 2025
- ❖ **Reducing operating costs**
  - ✓ G&A expenses reduced by 25% 1H24-1H25; 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