Cellastra

Pioneering Targeted Scar Prevention at Wound Sites

Pulmonary Fibrosis - Burn Injuries

23 July 2025

Cellastra Mission

Cellastra is pioneering scarless wound healing by developing proprietary viral gene vectors, able to turn on production of a human anti-scarring peptide at injury sites in pulmonary fibrosis after lung infections and after severe burn injuries, both major unmet medical needs.

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Who Are We?

- Cellastra is a start-up biotech founded in San Francisco, CA
- We are **pioneering** a new form of viral gene therapy since 2018. Patent was approved 2024
- Seasoned biotech executives with extensive experience in drug and biologics development
- Distinguished Board of Directors and Scientific Advisory Board
- “Hands-on” and “pitch-in” approach to development
- Self-funded to date, seeking support

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Lead Product

- **Cellexa** is a viral adeno-associated virus gene vector based on:
  - Gene coding for **ensereptide**, a human subpeptide of lactoferrin
  - The cap gene for a proprietary triple mutant AAV6 capsid (AAV6.2FF)
  - The rep gene for AAV2
  - The helper gene elements needed for expression
  - Other selected regulatory elements required for transfection and expression
- Two drug products of the parent vector are proposed:
  - **Fibrexa** is the formulation intended for inhalational delivery
  - **Scarlexa** is the formulation intended for dermal or subdermal delivery

Discovery Approach – A Rational Design

- The human body (and all mammals) contains many proteins and peptides intended to function in host defense (innate immune system).
- Lactoferrin is a large protein with numerous functions including host defense; for example, it's present in breast milk and provides immune protection to nursing infants.
- Lactoferrin itself was tested for numerous immune properties with oral administration.
- A subpeptide of lactoferrin called ensereptide, of 25 amino acids length, has many of the same properties as the parent **molecule and is more potent for many**.

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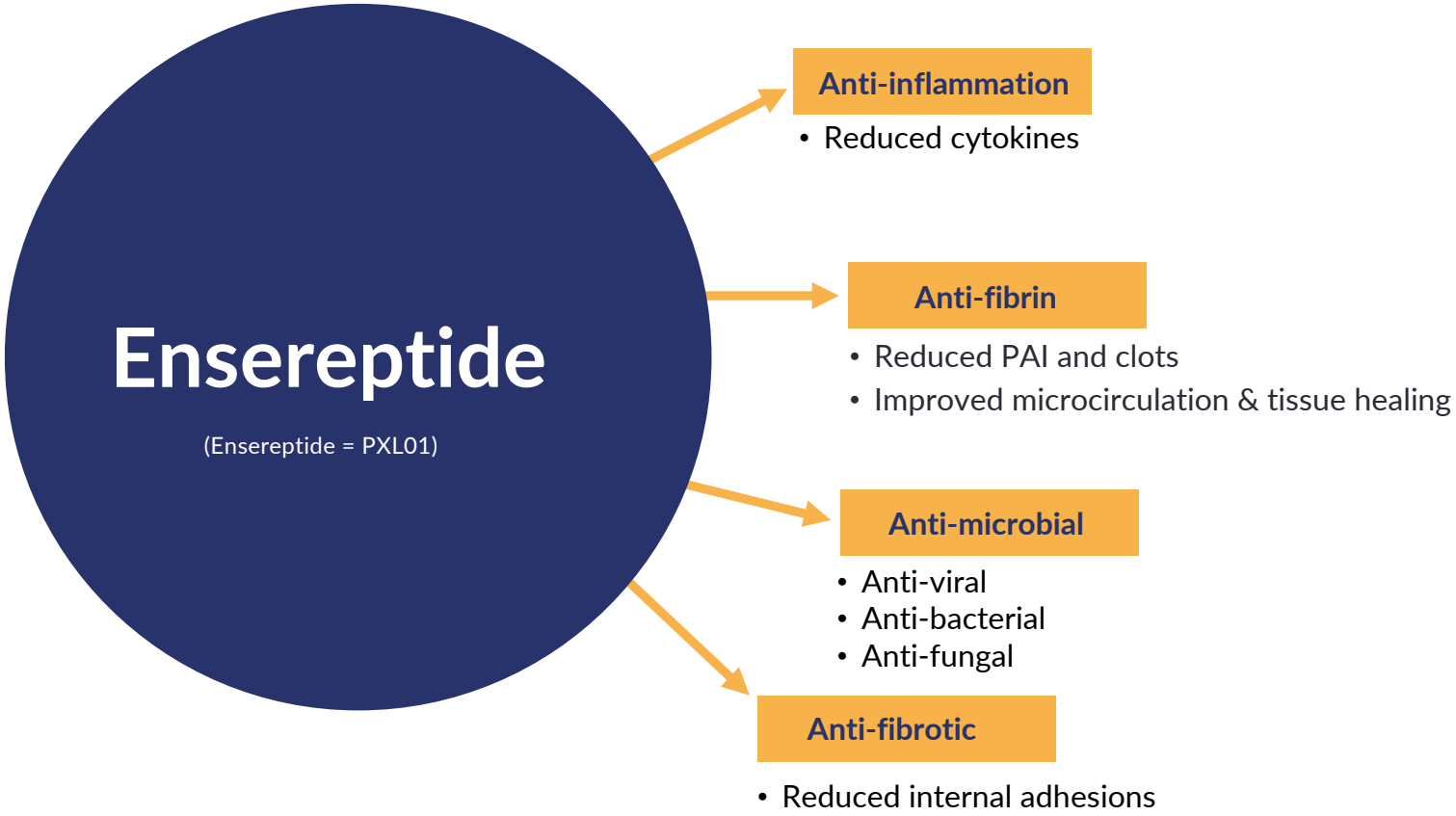
Discovery Approach – Peptide Biology

- Peptides are difficult to turn into drugs – they have a very short half-life in the body
  - Enzymes rapidly degrade peptides (and proteins)
  - Peptides are rapidly filtered out of the blood by the kidneys
- Ensereptide demonstrated numerous properties useful in wound healing and host defense (based on published work)
- Ensereptide is a naturally occurring peptide and probably an initial product from the metabolism of lactoferrin (a similar peptide is found in cows as bovine lactoferrin metabolite)

Ensereptide targets root causes of tissue injury & scarring



Nilsson E et al, Ann Surg 2009;250(6):1021-8

Discovery Approach – Peptide Formulation

- Published work with ensereptide in prevention of adhesions following flexor tendon repair surgery used a hyaluronic acid formulation (Wiig et at., PLoS One. 2014;9(10):1–11)
- Options to increase the half-life of peptides include attaching a larger (innocuous) molecule, like the Fc component of human IgG or human albumin
- One of us (BKT) suggested using viral gene therapy to insert the genetic code for ensereptide (linked to human Fc) into cells in the area of a wound
    - An initial patent filing was submitted in 2018 and a revised application was approved in 2024

Discovery Approach – Viral Vector Design

- Numerous vectors or other systems can be used to convey genetic material into cells
  - Adeno-associated virus is the most common vector in gene therapy, mainly as it's safe and does not incorporate into the host DNA
  - AAV2 is the most common serotype in nature, which means most people have antibodies directed against it which can neutralize the vector
- Cellastra decided to use a triple-mutant AAV6 vector which had:
  - Lower immunogenicity than the parent
  - Increased transfection potential in muscle and lung tissues

Discovery Approach – Building a Viral Gene Vector

- Viral gene vector design is a decades old and evolving science
- Rational design is employed in choosing every component of the vector
- Double plasmid methods are the most used these days
  - One plasmid contains the DNA for the rep and cap genes
  - A second plasmid contains the expression cassette (gene of interest) flanked by inverted terminal repeats (ITR) and the helper genes
  - These are presented to mammalian cells (HEK293) in culture where the vector is assembled by the cell machinery
  - The vectors are purified and formulated for the chosen delivery method

Discovery Approach – Building Cellexa

- One starts with the building blocks of DNA (ATGC) and those for peptides and proteins (amino acids)
  - If you know the amino acid sequence of a peptide, you can determine the DNA sequence (3 base pairs, codon) that codes for each amino acid in the peptide
  - Note that some amino acids are coded for by more than a single DNA codon and species vary in the preferred codon for an amino acid
- DNA needs to be double stranded for replication but one can deliver a single strand and the cell will manufacture the complimentary strand (means some delay in gene expression)

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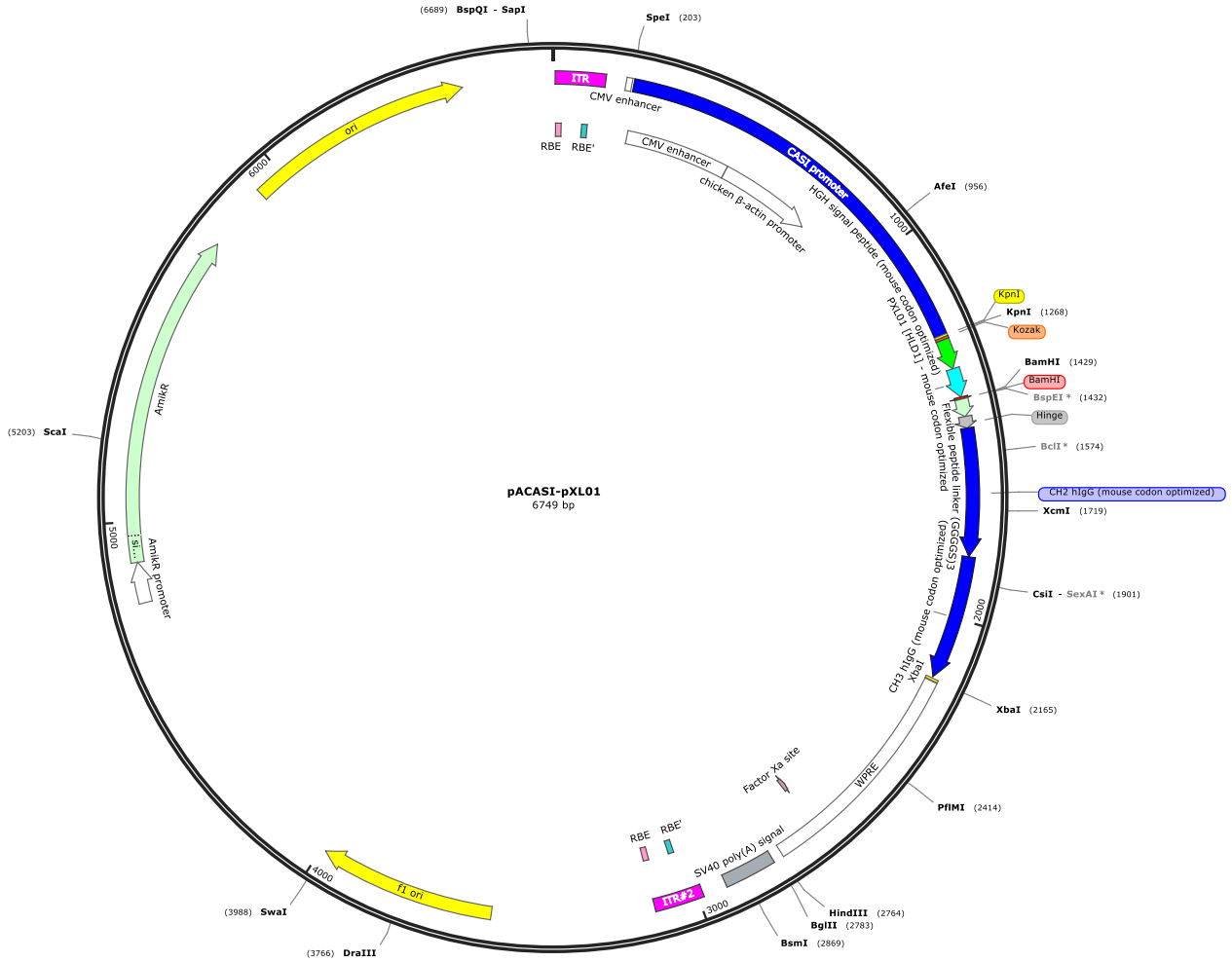
Discovery Approach - pACASI-PXL01 DNA

This DNA map shows the composition of the ensereptide and helper gene plasmid

A second plasmid (not shown) codes for the AAV6.2FF cap and AAV2 rep genes



Discovery Approach – Transfection

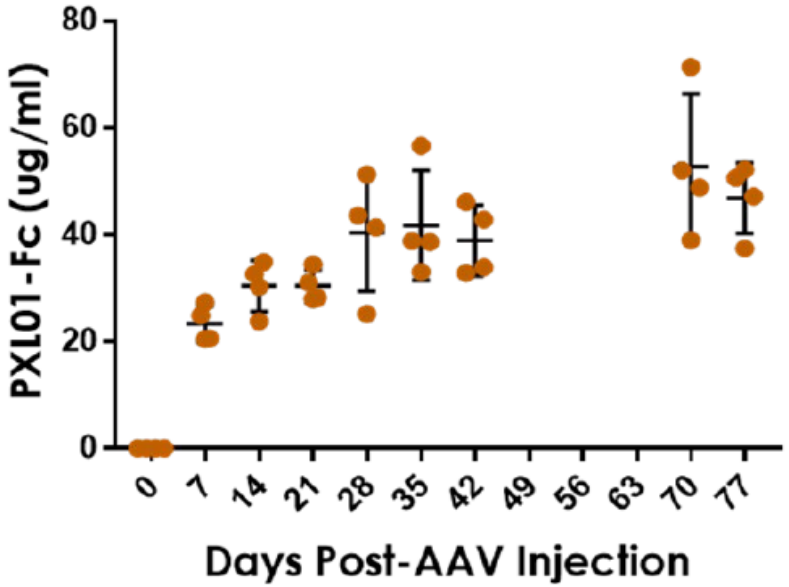
- Transfection is the process (similar to infection) in which the vector gets into target cells and is processed
  - The usual components of the virus needed for its replication in cells are not included in the vector
  - The vector is not replicated by the cells and is metabolized within a few days or less
  - The vector is transported into the cell nucleus where its genetic contents inside the expression cassette are processed by the cell machinery
  - This process depends on the usual DNA to RNA processing to result in production of a peptide or protein in the cell's cytoplasm
- Transfection of cells in the wound area turns the cells into little factories which produce the **ensereptide-linker-Fc fusion protein**, key to scarless wound healing
  - The short linker peptide is important to allow ensereptide to bind without Fc being in the way

Preclinical Studies – A First Step

- Manufacturing (to GMP standards) of a viral gene therapy is expensive
  - Most of the cost is for purification of the vector from mammalian cells
  - Plasmids, made in bacterial cells, also are expensive
- Cellastra initially had the vector made at a university site according to laboratory standards
- An initial proof-of-concept (POC) study was performed at the university laboratory and demonstrated positive results
- Additional POC studies can be done with engineering grade vector or with laboratory grade vector

Robust expression of Ensereptide (in mouse)

- Robust expression in mouse plasma until sacrifice on Day 77
- Intramuscular administration of encoded vector for ensereptide (PXL01)
- Fc (human IgG constant domain) tag added to the gene construct
  - Enables quantification expression
  - Prolongs half-life in plasma



Balb/c mice were intramuscularly administered $1x10^{10}$ vector genomes of AAV6.2FF expressing PXL01 fused to the Fc domain of human IgG1 (PXL01-Fc). Plasma levels of PXL01-Fc were measured over time until ***the experiment was terminated at 77 days post AAV-administration***

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Preclinical Studies – General Comments

- Cellastra has obtained quotes for preclinical studies from 2 established laboratories
- All safety pharmacology and toxicology studies will be performed according to Good Laboratory Practice (GLP) standards
  - Standard safety pharmacology studies will be performed as required by FDA and ICH prior to submission of an IND (investigational new drug exemption)
  - Acute toxicology studies will be performed prior to IND submission
  - Special toxicology studies will be discussed with FDA at a pre-IND conference
- All POC studies will be performed at GLP or near-GLP standards and will include an extensive safety component
- Safety studies of the AAV6.2FF capsid were conducted as were published studies of the vector with various expression cassettes
  - No safety concerns were noted in these
  - Slide of acute toxicity studies is below

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Preclinical Studies – Next Steps in POC

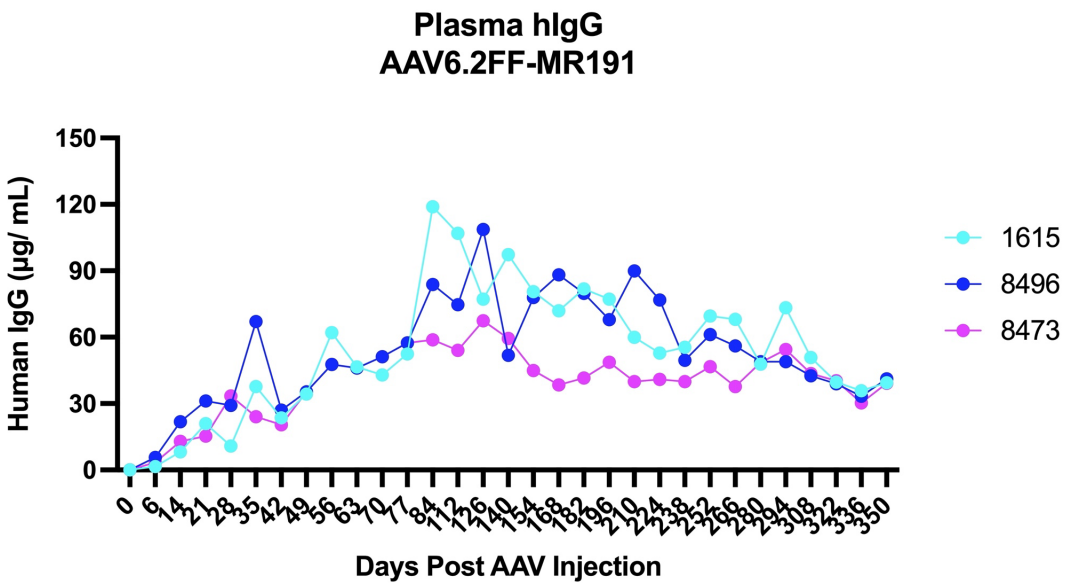
- Standard animal models will be employed in POC studies of the ensereptide viral gene vector
  - Proof of Concept 1: Efficacy against respiratory inflammation (LPS model)
  - POC 2: Lung scarring prevention - pivotal efficacy model (BLM model)
  - Pre-clinical efficacy study of Fibrexa in a hamster or transgenic mice SARS-CoV-2 Model
  - Efficacy of viral uptake with inhaled vector
  - Biodistribution study (GLP)
  - Repeat-dose biodistribution study (GLP) if required

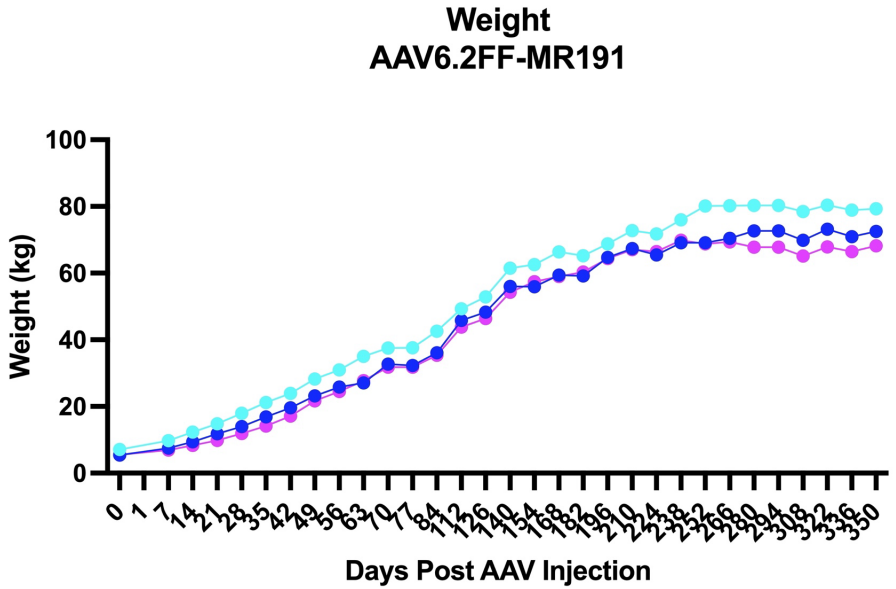
Preclinical Studies – Proposed Pharm-Tox Studies

- Genetic toxicity assessment studies
- Cardiovascular and respiratory safety study
- Acute Toxicity (MTD) study (non-GLP) of Fibrexa (mouse, hamster, other)
- Single-Dose Toxicology Study of Fibrexa in C57BL/6 Mice
- Repeat-Dose Toxicology Study of Fibrexa in C57BL/6 Mice
- Single-Dose Biodistribution Study of Fibrexa in Mice

Preclinical toxicology studies with AAV6.2FF

- Acute toxicology study in mice — DOI:10.3390/biomedicines9091186
- Acute toxicology study in sheep — DOI:10.3390/biomedicines9091186
- Chronic pharmacology study in sheep — Ongoing





Clinical Studies – General Comments

- FDA and other regulatory agencies have been conservative with their approach to gene therapy
- Long-term safety of gene therapy is not known
  - A chance of unexpected immune reactions late after treatment exists, as seen with cancer immunotherapy
  - Acute immune reactions generally target the liver (systemic administration)
  - Autoantibodies can inactivate the vector or attack transfected cells
- Best approach is to target serious diseases with well-defined diagnosis and measurable endpoint(s)
  - Serious or orphan diseases allow for faster approval in a smaller population
  - Must demonstrate medical and statistical efficacy in a primary endpoint
- Cellastra's AAV technology (Scarlexa and Fibrexa) is **delivered at the injury site**. This **eliminates systemic distribution** of gene vector which has been associated with potential safety concerns in clinical use.

Clinical Studies - Fibrexa for interstitial lung diseases (Rationale)

- Delivery to lungs by inhalation or intranasal administration
- Transfection enables expression of peptide for the 30-day life cycle of lung epithelial cells (or fibroblasts)
- Multiple mechanisms of action include:
  - Direct antibacterial or antiviral actions
  - Immunomodulation to shut down overactive immune system
  - Anti-fibrin effects to prevent blood clot formation in lung vasculature
  - Potentially stop the cascade of events leading to pulmonary fibrosis
  - Prevent acute exacerbations in pulmonary fibrosis that are often fatal

Clinical Studies - Fibrexa for interstitial lung diseases (Potential Clinical Endpoints)

- Changes in respiratory parameters from baseline to study endpoint in vector-treated group vs. placebo-treated group
  - Forced expiratory volume in 1 second (FEV1)
  - Forced viral capacity (FVC)
  - Oxygen saturation of blood
  - Requirement for supplemental oxygen
- Survival in the two groups
- Quality of Life measures over time
- Clinical assessments of disease progression

Endpoint of the study are expected to be 6 months (primary) and 3 and 12 months (secondary) with safety followed for at least 5 years

Clinical Studies – Severe Burn Injuries

- In severe burns, skin grafts are required to restore barrier function to avoid dehydration and pathogen entry
- Skin grafting is critical but difficult to achieve
  - Intact skin for large grafts can be difficult to find in many burn patients
  - Grafts do not always take
  - Healing after burns often results in scars which are esthetically displeasing and can limit function or movement
- Unburned skin often is collected and cells separated and cultured prior to spraying them back on the wound
- Procedures to enhance the survival and spread of the cells are needed

Clinical Studies – Gene Therapy in Severe Burn Injuries

- Cellastra's approach would be a combination of viral gene therapy and cell therapy
  - Human skin cells in culture would be treated with the viral ensereptide gene vector
  - After a few days, treated and nontreated cells would be applied to separate burn injuries following a standard protocol for harvesting and using such grafts
- The initial approach would be to use normal human skin cells of various types (keratinocytes, fibroblasts, melanocytes) to demonstrate that the treatment has no harmful effects
- A second approach would be assessment of such treated and grafted cells in animal models of burns or dermal injury

Why Now?

- Cellastra received a patent for our gene vector product in 2024, which gives protection for the novel approach to wound healing
- The viral vector we chose is also patented giving dual protection to our approach
- We have demonstrated the feasibility of our approach in an experiment in mice
- The efficacy and safety of ensereptide and of the viral vector have been demonstrated
- The indications we have targeted are life-threatening conditions with inadequate treatment options
- A relatively small initial investment could open up a novel, exciting approach to treating serious wounds

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Why Cellastra?

- Cellastra is composed of experienced professionals who have brought numerous drugs to clinical studies (IND) and to market (NDA, NDS, MAA, etc.) or contributed to the multi-billion dollar acquisition of companies in early stages of development
- We are experienced in drug, device, and biologic development for the US and international markets and computer literate
- While we are mostly senior scientists, we have a hands-on approach and are adept at doing the job, at least partly as we have no funds to pay for help (and most people want a salary)
- We know what we're doing, have experience doing it, and are excited about this project (and sharing the experience with new, younger people we could bring onboard with funding)

What's Next?

- Our initial interest is in developing the ensereptide gene vector, but the technology could be applied to a host of other innate peptides with anti-inflammatory or immunomodulating properties
- The initial indication is for pulmonary fibrosis caused by an infection (SARS-CoV-2, RSV, influenza are examples), but other causes including idiopathic and environmental (e.g., black lung, respiratory burn injuries)
- Further expansion in burn injuries could include patients not requiring grafts, many of whom experience abnormal healing
- Dermal would healing is another area to explore, especially in patients who show abnormal healing patterns in the past (e.g., hypertrophic scarring)
- Post-surgical adhesions, which can be painful, limit bodily functions, or be life-threatening, are another potential area to explore.

Funding Requested

- Cellastra has been self-funded to date and we work without pay
- We seek about $1 million to conduct all of our proof-of-concept studies
- Another $6 million would be required to get to IND, most of it for manufacturing a batch according to GMP
- We have projected the budget requirements and clinical studies for taking the viral gene vector through clinical trials to an early (Phase 2 data) or full (Phase 3 data) biologics license application (BLA) in the US
- The people at Cellastra and the fund-raising team thank you for your time and efforts in reviewing this pitch