
# EXECUTIVE SUMMARY

**March 31, 2022**

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# 1 COMPANY OVERVIEW

Cellastra Inc., a developer of disruptive gene therapies, is a private biotech company based in the San Francisco Financial District, founded and managed by proven industry executives with a long track record of successful drug development and commercialization.

Cellastra's mission is to develop novel gene vector enabled production of anti-scarring peptides at sites of tissue injury after respiratory infections, surgery, and burns.

## 1.1 CELLASTRA'S PROPRIETARY TECHNOLOGY

Cellastra is developing a potentially revolutionizing technology (CELLEXA$^{TM}$) using a gene vector to turn on the production of a human natural lactoferrin derived anti-scarring peptide at injury sites in the lungs after respiratory infections such as COVID-19 and Respiratory Syncytial Virus (RSV) and in the skin after surgery and burn injuries. The peptide (Ensereptide (or potentially superior analogues thereof) may impact root causes of scarring by three fundamental mechanisms:

a) Broad antimicrobial effects;
b) Mitigation of upregulated immune system;
c) Pro-fibrinolytic effect by mitigation of upregulated levels of plasminogen activator inhibitors (PAI). This may counteract excessive fibrin deposition in micro-capillaries with subsequent tissue damage and scarring/fibrosis.

The three mechanisms above may be harnessed in three areas of huge unmet medical need:

**1. Pulmonary scarring** after ***Respiratory Infections:*** a) Broad antimicrobial effects potentially counteracting the initial virus infection as well as secondary bacterial or fungal infections; b) Anti-immune effects: Prevent an excessive immune response (Immune storm); c) Anti-fibrin effects: counteract excessive fibrin deposition in micro-capillaries and subsequent tissue damage and scarring/fibrosis.

**2. Scarring adhesions after *Surgery:*** The three mechanisms above may also prevent excessive dermal scarring after surgery, a great concern in aesthetic surgery not the least for women after breast augmentation, C-section, and hysterectomy**.** Internal adhesions in abdomen and pelvis are reported in majority of patients after abdominal or gynecological surgery and may cause obstruction of bowels and reproductive organs and cause death and infertility.

***3. Dermal scarring after Burn injuries:*** Cellastra has recently joined Center for Advanced Medical Products (CAMP), a Swedish government funded consortium exploring new treatment modalities in burn injuries. This is a patient group where hypertrophic and stigmatizing scarring remains an unresolved problem in 70% with often life-long suffering.

There is a strong scientific rationale to propose that scarless wound healing can be achieved using a gene vector encoding for endogenous continuous production of anti-scarring peptides at the site of injury. Three formulations of gene vectors are being developed:

- COVID-19: Virlexa ™ gene vector for inhalation, inhaled (once) into the lungs by recently exposed patients in high risk groups to prevent severe disease with acute respiratory distress syndrome (ARDS), and pulmonary /multi-organ tissue damage and fibrosis.
- Surgery: Scarlexa™ gene vector for injection, applied (once) into or under the skin before wound closure.
- Burn Injuries: Scarlexa ™ mixed with a suspension of skin cells (cultivated keratinocytes or cells obtained with a RECELL device from the patient) and sprayed back on the wound.

**Note:** An accompanying intramuscular injection (or booster dose) may be considered, particularly in patients exposed to COVID-19, to help prevent systemic spread of infection and tissue damage in multiple organs.

This proprietary technology is built and expands upon a foundation of scientific Proof of Concept Studies of the anti-scarring peptide ensereptide and the novel gene vector AAV6.2FF (see below).

## 1.2 ENSEREPTIDE FOR PREVENTION OF SCARS & ADHESIONS AFTER SURGERY AND BURN INJURIES

Swedish scientists discovered that certain polypeptides derived from human lactoferrin have potent anti-scarring properties (Nilsson et al. 2009). The most potent of these was ensereptide (PXL01), a synthetic lactoferrin sub-peptide with 25 amino acid length, which was found to disrupt excessive scar and adhesion formation in preclinical (Nilsson et al.2009) and clinical Proof of Concept Studies (Wiig et al. 2014). Time of exposure to the peptide correlated with a reduced adhesion score as seen with the improvement from three doses of peptide in water over a single dose and the further improvement when a hyaluronic acid vehicle was used in place of water in order to prolong treatment exposure to 1-2 days.

Clinical Proof of Concept of the hyaluronic acid formulation was demonstrated in a double-blind, randomized, placebo-controlled Phase 2 study in 138 patients undergoing repair surgery after ruptured hand flexor tendon. Although treatment was applied only once (as a gel on top of the tendon sheath prior to wound closure), improved hand function was demonstrated at six months follow-up using several objective measures of finger mobility. Although this was significant, the benefit no longer reached statistical significance at 12 months, as many patients had dropped out.

## 1.3 ENCODED GENE VECTORS SCARLEXA AND VIRLEXA

Scarlexa ™ and Virlexa ™ utilize a nonpathogenic, non-replicating, triple mutant recombinant adeno-associated viral (AAV) vector of serotype 6 (AAV6.2FF). The vector is designed to deliver the genetic code of ensereptide to cells in the wound area in the lung, or the skin, respectively, and enable continuous production of the peptide.

Transfection of epithelial cells in the lung or keratinocytes, fibroblasts or muscle cells in a dermal wound area, turns on their expression/production of ensereptide for many weeks or months, resulting in long-term treatment exposure to the bioactive peptide in the healing wound.

The beneficial effects of Virlexa and Scarlexa may be attributable to the following:

1. Broad anti-microbial effects may play a role for both. In addition, Virlexa may Potentially block COVID-19 receptors in pulmonary epithelial cells: TheAAV6.2FF vector binds to heparan sulfate (van Lieshout et al. 2018) and thus likely to heparan sulfate in angiotensin 2 converting enzyme (ACE-2) receptors throughout the respiratory and other organ systems, which may help prevent viral entry.

2. Immunomodulatory effects by mitigating increased levels of cytokine-mediated immune response ("Immune cytokine storm");

3. Fibrin modulatory effects by mitigating up-regulated levels of plasminogen activator inhibitor (PAI) and thereby preventing excessive fibrin formation:

4. Antimicrobial effects helping to prevent secondary infections during the healing process which could trigger perturbations of 2 and 3 and promote further scarring.

Thus, by prolonging the exposure to the peptide in the wound area, the gene vector may facilitate scarless wound healing in the lungs (Virlexa pulmonary delivery), or skin (Scarlexa, dermal application).

In in vivo studies in mice, the novel triple mutant vector (AAV6.2FF) induced rapid and potent transgene expression after intramuscular and intrapulmonary administration. The results obtained with this vector were superior compared with the natural AAV6 vector. Expression was significantly higher at 24 hours after transfection (101-fold higher in the muscle and 49-fold higher in the lung), favoring the recombinant vector) (van Lieshout et al. 2018).

Subsequently, the expression of ensereptide was studied using the AAV6.2FF capsid. High and durable expression of ensereptide was demonstrated for up to 11 weeks after intramuscular administration of the vector in mice. This experiment used a fusion protein which included the Fc domain of human IgG to allow for quantification of expression in vivo. This Proof-of-Concept study demonstrated a rapid increase of expression during the first week and subsequently robust and high expression levels throughout the 11-week study period. The mice were sacrificed immediately at the end of the experiment and the results demonstrated high serum levels (about 35,000 ng/mL) of tagged ensereptide and also notable expression in alveoli-bronchial lung and peritoneal tissue. Thus, an intramuscular dose could have utility in COVID-19 patients when used in combination with inhaled Virlexa, by enabling a wider distribution of ensereptide to organs outside the lungs, which could help protect against multi-organ tissue damage. This might be especially important in high-risk groups including those at risk of developing severe disease (ARDS) and so called "Long COVID syndrome."

A recent study using intramuscular administration of the AAV6.2FF vector in sheep demonstrated robust and long-term expression for more than 12 months (manuscript submitted). Ensereptide has an excellent safety profile being a sub-peptide derived from lactoferrin, which is naturally occurring in the human body and generally recognized as safe (GRAS listed by FDA) even after ingestions of gram quantities. Thus, it seems reasonable to assume that an intramuscular injection of ensereptide gene vector would be well tolerated and prove to be useful in abdominal and gynecological surgeries to help prevent intraabdominal adhesions reported in up to 90

percent of these patients. Such adhesions may cause late complications of obstructions of bowels causing ileus or of fallopian tubes between ovaries and uterus, a common cause of infertility. Such an injection also could prove to have utility in breast augmentation surgery to prevent capsule formation and contractures reported in 10-45% of women with breast implants.

### 1.4 INTELLECTUAL PROPERTY - PATENTS

Whereas the composition of matter patent of ensereptide expired in July 2019, Scarlexa ™ and Virlexa ™ are protected by a recent USPTO patent filing (July 2018) and the subsequent the continuation in part (CIP) filing on May 14, 2021. The CIP filing has composition of matter claims for the vector encoded for endogenous expression /production of a broad range of lactoferrin sub-peptides, including ensereptide and potentially superior analogues thereof. This CIP filing is based on results from an in vivo study in mice receiving intramuscular administration of the triple mutant AAV6.2FF vector encoded for ensereptide demonstrating rapid and robust expression of Fc-tagged ensereptide for up to the time the mice were sacrificed at 11 weeks. The global PCT patent filing was submitted in July 2019 but will be updated with the data from the CIP application in the US.

To further strengthen its IP position and Freedom to Operate, Cellastra has also secured patent rights to the triple mutant AAV6.2FF vector on a license from University of Guelph, ON, Canada (US Patent 10,806,802B2 {granted October 30, 2020; granted in Canada in 2021).

### 1.5 FREEDOM TO OPERATE ANALYSIS

An independent law firm specializing in Life Science Law was contracted to make a Freedom to Operate analysis. After a thorough review of the related patent landscape, they issued a privileged and confidential report and concluded: “In our opinion, based upon the foregoing analysis, none of the issued patent claims discussed herein will be found to be infringed.”

## 2 MARKET OPPORTUNITY

Cellastra’s pipeline was selected to target areas with great unmet medical needs and address gaps representing opportunities left behind by competitors after failures with short-term treatments. Cellastra is focused on the use of a novel mechanism of viral gene therapy in the advancement of wound healing, enabling local synthesis of the agent at the site of injury for several weeks or months. Cellastra initially concentrated on prevention of scarring following surgery and burn injuries and dermal wound healing remains an area of focus. The primary compound in development is an AAV6 gene therapy vector (preliminary name Scarlexa) designed to deliver the code for an anti-scarring peptide to the area of dermal injury. With the coronavirus (SARS-CoV-2) pandemic (COVID-19) starting in 2020 and continuing into 2021, Cellastra expanded the focus to include healing in the lungs following exposure to the novel coronavirus and other pathogens.

The compound in development here is an AAV6 gene therapy vector (Virlexa) designed for pulmonary delivery. This agent could be used in the prevention or treatment of pulmonary damage following exposure to SARS-CoV-2 or other viral or bacterial infections, since the peptide has broad antimicrobial activity.

## 2.1 SCARLEXA FOR SCAR PREVENTION IN DERMAL WOUND HEALING

Scarlexa is a gene vector to be applied into or under to the skin in the wound area and is evaluated for prevention of dermal scarring after surgery and burn injuries. Based on published preclinical and clinical studies using PXL01 (ensereptide), we selected a gene vector encoded to enable endogenous synthesis of this promising anti-scaring peptide for development.

The global market for a product that improves wound healing and prevents or limits scarring is huge, easily in the billions of dollars annually. However, in order to obtain regulatory approval for a product, one needs to demonstrate efficacy using a clinical endpoint acceptable to regulatory agencies and clinically relevant. For this reason, there are a limited number of options chosen for clinical trials of scar prevention in wound healing. Of these, Cellastra chose scar prevention after breast augmentation surgery, in which external scars are troublesome in some patients who develop hypertrophic scarring and/or internal scars resulting in capsular contraction in some 15% to 45% of patients (El-Sheikh et al. 2008). These may be severe in about 10% and require reoperation. Another target indication is C-section, which has become increasingly common and is currently used globally in about 30 million women every year (including 1.4 million procedures in the US and about 6 million in China). C-section may cause hypertrophic or cosmetically challenging scarring in up to a third of Caucasian women and two thirds of Chinese women. In addition, the scars may be accompanied by internal adhesions causing bowel obstruction or infertility.

## 2.2 VIRLEXA IN SARS-COV-2 (COVID-19) AND OTHER RESPIRATORY INFECTIONS

Virlexa inhalational viral gene vector is designed to carry the code for ensereptide and enable treated cells to produce the peptide. The vector is designed based on the science demonstrating the triple efficacy of ensereptide in vitro relative to wound healing: anti-infective properties, immune modulating effects, and anti-fibrin effects. The gene vector could result in long-lasting effects for several weeks over the lifespan of the transfected cells or potentially for many months if treatment is supplemented with an intramuscular injection.

### *2.2.1 COVID-19*

The SARS-CoV-2 virus infection rate has varied in the US and in many countries and is currently decreasing in many countries and some states in the US, largely due to vaccination of millions of adults. This is not the case in many other states and countries where the vaccination rate is low and the pandemic threatens to overwhelm the medical community. Some health scientists propose that SARS-CoV-2 will become an annual infection, probably in fall to winter, just as influenza currently is. There is evolving evidence that immunity to COVID-19 from vaccination will fade after about 6 months, just as native immunity following infection may fade. In the US, the annual vaccination rate is low and new influenza cases involve millions of patients with serious infections requiring medical attention or hospitalization. There is no reason to believe this will not also be the case with COVID-19 if annual vaccinations are required. Other pulmonary viral infections already are increasing in incidence as measures in place to prevent coronavirus transmission are lifted (e.g., RSV in Southern states).

### *2.2.2 Respiratory Syncytial Virus (RSV)*

Respiratory Syncytial Virus (RSV) respiratory infection represents a great unmet medical need as no vaccines have been approved and treatment options are limited. Following inoculation of the eyes and the nose, the virus will infect the epithelial cells of the upper and lower airways, causing inflammation, cell damage, and obstruction. Worldwide, RSV is the most common cause of bronchiolitis and pneumonia in children under the age of 5 years. While it is uncommon for young adults to develop serious illness from RSV, it is now recognized as a significant cause of morbidity and mortality in certain adult populations. RSV is spread through contaminated air droplets and can cause outbreaks both in the community and in hospital settings. Each year, an estimated 5-10% of nursing home populations will experience significant morbidity and mortality caused by RSV and 30-50% of cases among immune-compromised patients are hospital acquired.

Treatment is primarily supportive including oxygen therapy. Ribavirin by inhalation is the only treatment currently licensed for use in children, although its use remains controversial.

## 2.3 COMPETITIVE ADVANTAGES

### *2.3.1 Dermal Scarring*

Scarlexa™ is programmed with the code for the anti-scarring peptide ensereptide. When applied directly in the wound area after surgery or burn injuries,

Scarlexa enables long-term synthesis (expression) and local exposure for several weeks or months, which is believed to be critical for robust scar prevention. Cellastra's portfolio also includes gene vectors encoded for next generation anti-scarring peptides with prolonged half-life. By contrast, previous attempts to develop scar prevention agents have failed to show long-term benefit, most likely due to treatment being limited to just the first few days or weeks after *surgery.*

### *2.3.2 COVID-19*

There are two main stages at which patients are treated for COVID-19, non-hospitalized and hospitalized. The primary aim is to prevent hospitalization and, if hospitalized, to prevent the need for mechanical ventilation. The treatment of a COVID-19 patient in the hospital is labor intensive. There is a shortage of healthcare workers able to provide all of the possible treatments that are available. However, the high cost and labor-intensive nature of some intravenous agents limited their use. With the success of vaccination and the immune protection offered by recovering from a SARS-CoV-2 infection, there is less need to try medications with little rationale for use. However, the pandemic has not disappeared and is unlikely to, so people will continue to contract the infection, especially those who are not vaccinated. At this stage, the hope is to stop the disease in the early stages and prevent the need for hospitalization, which is where Virlexa fits in. In summary:

- Virlexa can be administered and followed in an outpatient setting. By contrast, treatments such as antibody cocktails typically require hospitalizations for intravenous treatment, which is still the FDA recommended route of administration. Subcutaneous administration has recently been approved by FDA but is recommended in the label only if intravenous injection is not available. Furthermore, it may still be labor intensive as four

subcutaneous injections are given in the same session and require specialized outpatient treatment centers, as many hospitals have restrictions on bringing infected patients to hospitals to avoid spread of the virus to other patients.

- Virlexa treatment can start immediately after a COVID test is reported to be positive or even without results from such a test.
- Early treatment may be crucial to preventing ARDS (acute respiratory distress syndrome) and complications thereof, including irreversible pulmonary fibrosis.

Oral antiviral treatments are in development and Merck and Pfizer have recently obtained applied for Emergency Use Authorization (EUA) for one of these drugs.This will likely be granted by the FDA based on promising results in a large Phase 3 studies with about 1,000 patients showing about 50% and 9%, respectively, reduction in hospitalization/ and death rates. Yet, considering the limited data on long term effectiveness and potential side effects of antiviral agents, it seems likely that these may be used in combination with novel and complimentary treatment modalities such as Virlexa, if effectiveness and a good safety profile is demonstrated in early clinical studies.

# 3 DEVELOPMENT PLANS

For the two projects (Scarlexa™ and Virlexa™), Cellastra has worked out development plans from initial proof of concept and toxicology studies to IND and then to BLA. For the COVID-19 projects, Cellastra has added a step to evaluate if filing an Emergency Use Application (EUA) after completion of a Phase 2 study is feasible, provided there remains a large unmet need and strong evidence of efficacy was demonstrated. All projects are projected to go to BLA in the US and could be submitted in many other regions and countries, as the development programs follow ICH guidelines. Cellastra obtained formal bids from numerous contractors for each of the projects; while these bids are time-limited, they provide a realistic framework for the costs of development.

## 3.1 PHARMACOLOGY AND TOXICOLOGY

The pharmacology and toxicology programs are standard in many respects (e.g., acute and chronic toxicology), although they differ given the nature of the agents. Cellastra intends to seek FDA feedback on the design of planned special studies prior to undertaking these. The method of drug administration (pulmonary for Virlexa and dermal for Scarlexa) was taken into account for the preliminary study designs.

Of note, Professor Sarah Wootton's group at Guelph have already completed acute toxicology studies in mice sheep using the AAV6.2FF vector for expression of human monoclonal antibody (31C2) directed against the spike protein of SARS-CoV-2 and determined the safety profile of this AAV vector in mice and sheep as a large animal model. In both studies, plasma biochemical parameters and hematology were comparable to untreated controls. Except for mild myositis at the site of injection, none of the major organs revealed any signs of toxicity (Rghei et al., 2021).

A long-term toxicology study in sheep is ongoing using the same vector. Two week old Dorset sheep were intramuscularly administered 5e12 vg/kg of AAV6.2FF expressing a human IgG mAb

and plasma concentrations of hIgG monitored for 1 year. hIgG expression-reached a plateau and was stable over the one year monitoring period despite an increase in weight from 5 to 80 kg.

### *3.1.1 Toxicity and Oncogenic Potential of AAV Gene Vectors*

AAV is considered a safe mechanism for delivery of gene therapy vectors for 3 reasons (Chandler et al. 2016).

- First, natural AAV infections in humans are common and until recently had not been associated with disease.
- Second, the recombinant AAV (rAAV) genome remains predominantly episomal, greatly reducing the risk of insertional mutagenesis and genotoxicity that was observed in clinical trials using retroviral vectors.
- Third, numerous human clinical trials and preclinical gene delivery studies in both small- and large-animal models have revealed no recognized vector toxicity other than the development of humoral and cellular immunity to the rAAV capsid. Recent studies in mice challenged the notion that rAAV was an innocuous gene therapy vector(Chandler et al. 2016).

In humans, the target organ for toxicity after systemic administration of AAV gene vectors is the liver (Sherafat 2021; George 2021). About one-third of clinical trial participants had at least one adverse event of hepatotoxicity (Sherafat 2021). Cases of hepatocellular carcinoma (HCC) are rare in such trials and cannot be ascribed to the viral gene vector.

Other common toxicities with systemic (intravenous) AAV gene therapy vectors are thrombotic microangiopathy (TMA) and neurotoxicity in dorsal root ganglion or brain (Sherafat 2021).

The oncogenic potential of AAV is very small in general and highest for systemically (intravenously) administered viral gene vectors. This potential may be independent of the gene of interest being coded for, but not the promoter/enhancer used. The target organ for toxicity after systemic administration is the liver. Administration into the skin or lungs has not been accomplished in clinical trials to date but is expected to result in extremely low oncogenic potential due to limited distribution of the viral gene vector outside the area of administration. The oncogenic potential within skin or lung can be assessed in vitro in cell cultures and in vivo in animal models. The changes to the AAV6 capsid entailed in the production of AAV6.2FF are unlikely to contribute to oncogenic potential and likely will reduce the immune response to the vector.

## 3.2 CLINICAL DEVELOPMENT

To the extent possible. Cellastra intends to follow the continuous clinical trial paradigm which is advocated for simplifying and speeding up clinical trials. In both projects, Cellastra intends to follow the Phase 1-2 paradigm (SAD-MAD study following by confirmation study) and phase this into a Phase 3 trial expanding on the results.

### 3.3 DEVELOPMENT TIMELINE AND BUDGET

The preliminary budget for Cellastra projects (Scarlexa and Virlexa) is shown in the following table, broken out by item, project, and year. This budget is based on quotes requested from various vendors for the respective projects. It assumes both projects will occur simultaneously.

**Table 1: Cellastra Preliminary Budget ($1000)**

| Project | Item | Year 1 | Year 2 | Year 3 | Year 4 | Total |
|---|---|---|---|---|---|---|
| SCARLEXA | **CMC** | $2,950 | $1,200 | $1,200 | $1,200 | $6,550 |
| | **Preclinical** | $950 | $750 | | | $1,700 |
| | **Clinical** | | | | | |
| | *Phase 1* | | $1,600 | | | $1,600 |
| | *Phase 2* | | $1,700 | $1,700 | | $3,400 |
| | *Phase 3* | | | $3,500 | $3,500 | $7,000 |
| | *Phase 3 confirm* | | | $3,500 | $3,500 | $7,000 |
| | *Phase 3 2nd Indication* | | | | $7000 | $7,000 |
| | **Regulatory** | | $250 | | $3,500 | $3,750 |
| | ***TOTAL*** | **$3,900** | **$5,500** | **$9,900** | **$18,700** | **$38,000** |
| VIRLEXA | **CMC** | $3,384 | $1,200 | $1,200 | $1,200 | $6,984 |
| | **Preclinical** | $1,600 | | | | $1,600 |
| | **Clinical** | | | | | |
| | *Phase 1* | | $1,191 | | | $1,191 |
| | *Phase 2* | | $1,696 | | | $1,696 |
| | *Phase 3* | | $6,000 | | | $6,000 |
| | **Regulatory** | | $700 | $3,500 | | $4,200 |
| | ***TOTAL*** | **$4,984** | **$10,787** | **$4,700** | **$1,200** | **$21,671** |
| **Projects Total** | | $8,884 | $16,297 | $14,600 | $19,900 | $59.671 |
| ***Operations*** | | ***$2,132*** | ***$3,911*** | ***$3604*** | ***$4776*** | ***$14323*** |
| ***Grand Total*** | | ***$11,016*** | ***$20,208*** | ***$18,104*** | ***$24,676*** | ***$73,994*** |

# 4 SUMMARY- CONCLUSION

### 4.1 VALUE PROPOSITION

- Proven management team
- Potentially Revolutionizing New Technology - encoding scarless healing of wounds and tissue injuries
- First-in-class proprietary gene vectors:
  -Scarlexa™: surgery, Burn Injuries;
  -Virlexa™: respiratory infections
- Proof of Concept:
  -Antiscarring peptide already established as safe and active in preclinical and clinical studies
  -Robust expression for weeks – months after single injection of gene vector

- Near-term exit opportunity and valuation in 1-4 years
- Dermal scar market is projected to reach 46 B USD by 2028.

## 4.2 FUNDS SOUGHT

Cellastra is seeking Series A funding of $20M USD for advancing the two projects into development. Both projects, Virlexa and Scarlexa, will reach market early/mid-Year 4 and 5, respectively. Both require manufacturing of viral gene vector which is projected to take a year. Virlexa could potentially be approved for emergency use after Phase 2, with a Phase 3 study and BLA to follow, whereas Scarlexa approval will require two Phase 3 studies per indication and a full BLA. Additional funds through Series B and C Financing will be needed to continue each project to through Phase 3 studies with potential for Exits in year 3-4.

The opportunity for an IPO should be considered on an ongoing basis and already at an early stage. An IPO for a clinical Phase biotech company with a stellar and experienced management team and a compelling portfolio may have a market cap of USD 100-200M or more indicating a potential 10 to 20-fold Return of Investment (ROI) within 24-36 months.

## 4.3 THE OFFER

- Series A – 27 M USD Ongoing Subscription period April 1 to June 1, 2022
- Series B – 27 M USD
- Series C – 27 M USD

# 5 SCIENTIFIC RISK BENEFIT ASSESSMENT – RISK MITIGATION

Scarlexa and Virlexa utilize a nonpathogenic, non-replicating, triple mutant recombinant adeno-associated viral (AAV) vector of serotype 6 (AAV6.2FF). These vectors are designed to deliver the genetic code of the anti-scarring ensereptide to cells in the wound area in the lung, or the skin, respectively, and enable continuous production of the peptide. Transfection of epithelial cells in the lung or keratinocytes, fibroblasts or muscle cells in a dermal wound area, turns on their expression/production of ensereptide for many weeks or months, resulting in long-term treatment exposure to the bioactive peptide in the healing wound.

## 5.1 RISK BENEFIT CONSIDERATIONS GENE VECTOR

### *5.1.1 Risks*

Adeno Associated Virus (AAV) gene vectors are nonpathogenic, non-replicating and do not modify DNA in the cell nucleus. Transfection leads to translation in the episomes of the genetic program delivered from the vector to enable in vivo expression / synthesis of anti-scarring peptides

- Recombinant AAV vectors are generally considered as safer than their wild type naturally occurring counterparts
- AAV6.2FF has reduced potential immunogenicity compared to AAV6
- Will be applied into or under the skin, intramuscularly, or inhaled into the lung
- Of note, Professor Sarah Wootton's group at Guelph have already completed acute toxicology studies in mice sheep using the AAV6.2FF vector for expression of human

monoclonal antibody (31C2) directed against the spike protein of SARS-CoV-2 and determined the safety profile of this AAV vector in mice and sheep as a large animal model. In both studies, plasma biochemical parameters and hematology were comparable to untreated controls. Except for mild myositis at the site of injection, none of the major organs revealed any signs of toxicity (Rghei et al., 2021.

Note risk mitigation: Cellastra does not currently plan to use intravenous administration or injections into the Central Nervous System, which in some recent studies have been associated with dose related severe adverse events (See FDA Briefing Document for Cellular, Tissue and Gene therapies Advisory Committee, September 2-3, 2021)

### *5.1.2 Gene Vector Benefit - Proof of Concept*

- The results obtained with this vector were superior compared with the natural AAV6 vector. Expression was significantly higher at 24 hours after transfection (101-fold higher in the muscle and 49-fold higher in the lung), favoring the recombinant vector) (van Lieshout et al. 2018).

Subsequently, the expression of ensereptide was studied using the AAV6.2FF capsid:

- High and durable expression of ensereptide was demonstrated for up to 11 weeks after intramuscular administration of the vector in mice. This experiment used a fusion protein which included the Fc domain of human IgG to allow for quantification of expression in vivo.
- This Proof-of-Concept study demonstrated a rapid increase of expression during the first week and subsequently robust and high expression levels throughout the 11-week study period.
- The mice were sacrificed immediately at the end of the experiment and the results demonstrated high serum levels (about 35,000 ng/mL) of tagged ensereptide and also notable expression in alveoli-bronchial lung and peritoneal tissue.
- Thus, an intramuscular dose could have utility in COVID-19 patients when used in combination with inhaled Virlexa, by enabling a wider distribution of ensereptide to organs outside the lungs, which could help protect against multi-organ tissue damages. This might be especially important in high-risk groups including those at risk of developing severe disease (ARDS) and so called “Long COVID syndrome.”

## 5.2 RISK BENEFIT CONSIDERATIONS ENSEREPTIDE

### *5.2.1 Risks*

The risks from long-term exposure to ensereptide are unknown, but are assumed to be minimal. No safety concerns were reported in:

- Preclinical in preclinical pharmacology or toxicology studies
- Phase 1 study in healthy volunteers or Phase 2 study in 138 patients, (randomized, double blind, placebo controlled)

This is not surprising as the mother molecule lactoferrin is listed on FDAs list of generally recognized as safe (GRAS listed) even after ingestion of gram quantities.

### *5.2.2 Ensereptide Benefit - Proof of Concept*

Anti-scarring effects have already been demonstrated in:

- Gold standard scar prevention rat model
- Double blind, placebo controlled randomized Phase 2 clinical study in 138 patients (repair surgery of ruptured hand flexor tendon).
- It is believed that a major advantage of using gene vector technology in our program is to enable endogenous production of the anti-scarring peptide and long-term treatment exposure at the site of injury for several weeks or months, likely needed to show long term benefit at 6 and 12 months follow up in pivotal registration studies. Most previous clinical studies with promising anti-scaring agents have only used treatment injections during the first few days or weeks, which may result in too short treatment exposure for long term benefit (See section 1.2.3.1).

**Note:** It is possible that an intramuscular injection (in combination with an intradermal/ subdermal application of Scarlexa or inhaled Virlexa) may provide long term benefit for >6-12 months based on data from long term follow of studies in sheep using the same gene vector. Considering the unique safety of natural human lactoferrin and derivates thereof, this may have broad utility by securing long term benefit in a number of conditions:

- Reduced risk of hypertrophic scarring at > 6-12 months follow-up after surgery or burns
- Reduced risk of fibrosis in lungs and other organs in patients with Long-COVID
- Reduced risk of internal intra-abdominal adhesions after C-section, gynecological and abdominal surgeries
- Potential utility as a new treatment paradigm in chronic autoimmune diseases (by down regulating elevated cytokines), and atherothrombotic diseases (by down regulating elevated f fibrinolysis inhibitor PAI (plasminogen activator inhibitor).

Preliminary Long term follow data of such potential benefits could be collected during the 5 year follow-up period stipulated in current FDA Guidelines for gene therapy clinical studies.

# 6 SCIENTIFIC REFERENCES


Boerma, Ties, Carine Ronsmans, Dessalegn Y Melesse, Aluisio J D Barros, Fernando C Barros, Liang Juan, Ann-Beth Moller, et al. 2018. "Global Epidemiology of Use of and Disparities in Caesarean Sections." Lancet (London, England) 392 (10155): 1341–48. https://doi.org/10.1016/S0140-6736(18)31928-7.

Childs, Arielle, Andrew R. Zullo, Nina R. Joyce, Kevin W. McConeghy, Robertus Van Aalst, Patience Moyo, Elliott Bosco, Vincent Mor, and Stefan Gravenstein. 2019. "The Burden of Respiratory Infections among Older Adults in Long-Term Care: A Systematic Review." BMC Geriatrics 19 (1): 1–10. https://doi.org/10.1186/s12877-019-1236-6.

El-Sheikh, Yasser, Roberto Tutino, Casey Knight, Farough Farrokhyar, and Nicolas Hynes. 2008. "Incidence of Capsular Contracture in Silicone versus Saline Cosmetic Augmentation Mammoplasty: A Meta-Analysis." The Canadian Journal of Plastic Surgery = Journal Canadien de Chirurgie Plastique 16 (4): 211–15. https://doi.org/10.1177/229255030801600403.

Falsey, Ann R, and Edward E Walsh. 2005. "Respiratory Syncytial Virus Infection in Elderly Adults." Drugs Aging 22 (7): 577–87. https://doi.org/10.1016/j.medmal.2018.01.008.

Ghai, Ria R., Ann Carpenter, Amanda Y. Liew, Krystalyn B. Martin, Meghan K. Herring, Susan I. Gerber, Aron J. Hall, Jonathan M. Sleeman, Sophie VonDobschuetz, and Casey Barton Behravesh. 2021. "Animal Reservoirs and Hosts for Emerging Alphacoronaviruses and Betacoronaviruses." Emerging Infectious Diseases 27 (4): 1015–22. https://doi.org/10.3201/eid2704.203945.

Han, Linda L, James P Alexander, and Larry J Anderson. 1999. "Respiratory Syncytial Virus Pneumonia among the Elderly: An Assessment of Disease Burden." The Journal of Infectious Diseases 179 (1): 25–30. https://doi.org/10.1086/314567.

Holmdahl, Lena, Elsa Eriksson, Mohammed Al-Jabreen, and Bo Risberg. 1996. "Fibrinolysis in Human Peritoneum during Operation." Surgery 119 (6): 701–5. https://doi.org/10.1016/S0039-6060(96)80196-6.

Ivarsson, M I, M Bergström, E Eriksson, B Risberg, and I Holmdahl. 1998. "Tissue Markers as Predictors of Postoperative Adhesions." BJS 85 (11): 1549–54. https://doi.org/10.1046/j.1365-2168.1998.00859.x.

Kelland, Kate. 2020. "Don't Use Gilead's Remdesivir in Hospitalized COVID-19 Patients, WHO Says." Medscape 23 Novembe.

Kulmala, Henrik K, Laura P Van Lieshout, Bradley Thompson, and Sarah K Wootton. 2020. "Manufacture of an AAV6 Triple Mutant Ensereptide-Fc Vector and in Vivo Expression of the Peptide in Mice Following Intramuscular Administration."

Langford, Bradley J., Miranda So, Sumit Raybardhan, Valerie Leung, Duncan Westwood, Derek R. MacFadden, Jean-Paul R. Soucy, and Nick Daneman. 2020. "Bacterial Co-Infection and Secondary Infection in Patients with COVID-19: A Living Rapid Review and Meta-Analysis." Clinical Microbiology and Infection, no. xxxx. https://doi.org/10.1016/j.cmi.2020.07.016.

Lieshout, Laura P. Van, Geoff Soule, Debra Sorensen, Kathy L. Frost, Shihua He, Kevin Tierney, David Safronetz, et al. 2018. "Intramuscular Adeno-Associated Virus-Mediated Expression of Monoclonal Antibodies Provides 100% Protection Against Ebola Virus Infection in Mice." Journal of Infectious Diseases 217 (6): 916–25. https://doi.org/10.1093/infdis/jix644.

M Scott-Coombes, D, Simon Whawell, and J N Thompson. 1995. The Operative Peritoneal Fibrinolytic Response to Abdominal Operation. The European Journal of Surgery = Acta Chirurgica. Vol. 161.

Marshall, Clement D, Michael S Hu, Tripp Leavitt, Leandra A Barnes, H Peter Lorenz, and Michael T Longaker. 2018. "Cutaneous Scarring: Basic Science, Current Treatments, and Future Directions." Advances in Wound Care 7 (2): 29–45. https://doi.org/10.1089/ars.2006.8.243.

Nilsson, Elin, Camilla Björn, Veronika Sjöstrand, Kerstin Lindgren, Mattias Münnich, Inger Mattsby-Baltzer, Marie Louise Ivarsson, Kjell Olmarker, and Margit Mahlapuu. 2009. "A Novel Polypeptide Derived from Human Lactoferrin in Sodium Hyaluronate Prevents Postsurgical Adhesion Formation in the Rat." Annals of Surgery 250 (6): 1021–28. https://doi.org/10.1097/SLA.0b013e3181b246a7.

Pan, Hongchao, Richard Peto, Quarraisha Abdool Karim, Marissa Alejandria, Ana Maria Henao-Restrepo, César Hernández García, Marie-Paule Kieny, et al. 2020. "Repurposed Antiviral Drugs for COVID-19 –Interim WHO SOLIDARITY Trial Results." MedRxiv, January, 2020.10.15.20209817. https://doi.org/10.1101/2020.10.15.20209817.

Prescott, Hallie C, and Todd W Rice. 2020. "Corticosteroids in COVID-19 ARDS: Evidence and Hope During the Pandemic." JAMA, September. https://doi.org/10.1001/jama.2020.16747.

Rghei, Amira D, van Lieshout, Laura P, McLeod BM, et al. 2021. "Safety and Tolerability of the Adeno-Associated Virus Vector, AAV6.2FF, Expressing a Monoclonal Antibody in Murine and Ovine Animal Models " Biomedicines 9:1186, 14 pages. https://doi.org/10.3390/biomedicines9091186

Steiner, Claudia A. ., Zeynal Karaca, Brian J. Moore, Melina C. Imshaug, and Gary Pickens. 2017. "Surgeries in Hospital-Based Ambulatory Surgery and Hospital Inpatient Settings, 2014." Agency for Healthcare Research and Quality May: 2005–13. https://www.ncbi.nlm.nih.gov/books/NBK442035/pdf/Bookshelf_NBK442035.pdf.

Stewart, Kyana D, Veronica Nguyen, and Sean Nguyen. 2013. "RSV Infection in the Immunocompromised Host." US Pharm 38 (11): 8–10.

Szpaderska, Anna M, and Luisa A DiPietro. 2005. "Inflammation in Surgical Wound Healing: Friend or Foe?" Surgery 137 (5): 571–73. https://doi.org/10.1016/j.surg.2005.01.006.

Weiser, Thomas G, Alex B Haynes, George Molina, Stuart R Lipsitz, Micaela M Esquivel, Tarsicio Uribe-Leitz, Rui Fu, et al. 2016. "Size and Distribution of the Global Volume of Surgery in 2012." Bulletin of the World Health Organization 94 (3): 201-209F. https://doi.org/10.2471/blt.15.159293.

Wiig, Monica E, Lars B Dahlin, Jan Friden, Lars Hagberg, Soren E Larsen, Kerstin Wiklund, and Margit Mahlapuu. 2014. "PXL01 in Sodium Hyaluronate for Improvement of Hand Recovery after Flexor Tendon Repair Surgery : Randomized Controlled Trial." PLOS One 9 (10): 1–11.