**January 15, 2019**

# SKINSTIM CLINICAL PROTOCOL

## Safety and Efficacy of Combined Bioelectric Stimulation + Biologic Therapy for the Treatment of Moderate Skin Wrinkles of Face, Hands, Neck, or Chest

**Sponsor: SkinStim**, a unit of Leonhardt's Launchpads by Cal-X Stars Business Accelerator, Inc.

**Condition To Be Treated**: Skin Wrinkles

**Background**:

The loss of skin smoothness, texture, and turgor that can occur with age or other reasons, often leads to the development of unwanted wrinkles. Current and previous treatments have been temporary or only somewhat effective in reducing wrinkles. This multi-component regimen is the most scientifically-based and cutting-edge approach for the treatment of skin wrinkles. It includes the use of both devices and biologics. The centerpiece is Bioelectric Stimulation, which involves the use of precise micro-current signals delivered to the skin that increase the local tissue expression of four pro-regenerative proteins or substances that are normally present in the skin, but become depleted with age. These signals will stimulate native skin repair by attracting stem cells, enhancing blood flow, and helping to enhance skin elasticity and cellular repair.

The bioelectric stimulation will be delivered via a mask to be worn over the face that will deliver the micro-current at a strength and comfort level that will be selected by each patient. The biologics include a hydrogel cream that provides important enhancement to the texture of the skin, and the use of two of nature's most important pro-regenerative substances, Platelet Rich Fibrin(PRF), which contains many growth factors to enhance the function of the stem cells mobilized to the skin, and a fluid derived from stem cells obtained from the human placenta post-delivery(Axolotl fluid), which contains all the substances needed at birth to form skin and every tissue of the body.

**Treatment Safety**:
Each of the components of this treatment regimen have received FDA 510K market approval based on demonstrated safety and efficacy. The combination of the components should therefore not cause any adverse interactions, and should be additive in benefit.

**Inclusion Criteria**:

1. Age: 30-75 yrs
2. Sex: Female or Male
3. Agree to be present for each of the treatments outline in the protocol

4. Agree to have de-identified photos taken of the desired treatment areas before and after treatment to assess benefit and used to demonstrate the benefit obtained.

**Exclusion Criteria:**

- Subjects who are pregnant, nursing, planning to become pregnant, and/or not using a reliable form of birth control.
- Subjects who have had prior exposure to any hyaluronic acid, or any other similar topical agent, in the 2 months preceding study enrollment through the duration of the study.
- Subjects who have had prior exposure to any botulinum toxin, or other collagen based product for facial rhytids or in the proposed treatment area in the 4 months preceding study enrollment through the duration of the study.
- Subjects who have had a prior cosmetic surgical procedure to improve facial rhytids (i.e., rhytidectomy, periorbital or eyelid/eyebrow surgery, brow lift, CO2/erbium laser resurfacing, Thermage/Thermacool radiofrequency treatment) within 3 months or who have visible scars that may affect evaluation of response and/or quality of photography.
- Ablative skin resurfacing on the glabellar area within the previous 6 months or during the study.
- Retinoid, microdermabrasion, or prescription level glycolic acid treatments within 2 months prior to study participation or during the study.
- Oral Isotretinon within the past 3 months.
- Active cut, wound, or infection on the face.
- Active HSV-1.
- History of keloids or hypertrophic scarring.
- Existing or history of skin malignancy.
- Any existing facial skin disease.
- History of collagen or vascular disease.
- Patients who have used, within 30 days, any medication that can cause dermal hypersensitivity or affect skin characteristics.
- History of autoimmune disease.
- History of any disease that inhibits pain sensation.
- Patients who have implantable pacemaker, automatic implantable defibrillator (AICD), or any other implantable electric device.

**Treatment Components (To Be Provided by the Sponsor)**:

1. **Devices**:
   A. Mettler Bioelectric Stimulator and electrodes or needles
   B. DermaPen micro-needling device
   C. LED light and microcurrent face and neck mask
   D. Centrifuge for separation of PRF from plasma in blood sample
   E. Prizm hand-held stimulator and electro massage gloves

2. **Biologics**
   F. Hydrogel based skin cream
   G. Platelet Rich Fibrin (PRF)
   H. Axolotl human placenta stem cell derived regenerative fluid

**Treatment Duration**: Each patient will be treated for a total of 3 months with decreasing frequency of clinic visits and treatments.

**Treatment Schedule**

**Bioelectric Stimulation:** Will be used at the following time points
Mettler Stimulator
Month 1: Twice weekly for 30 minutes
Months 2&3: Once/week for 30 minutes

**Prizm Stimulator**
This will be used following each delivery of BES and the Regenerative Fluid and PRF

**Microneedling**:
To follow topical delivery of the Axolotl Fluid and PRF at start of treatment, and at months 1, 2,and 3 of treatment.

**Platelet Rich Fibrin**:
Obtained from a small sample of patient's blood and prepared on-site via a low speed centrifuge and then placed topically on the targeted area of skin, and followed by microneedling to enhance penetration into the deeper layers of the skin once per month including start of treatment and then each months 1, 2 &3 of treatment.

**Axolotl Proregenerative Fluid**:
This non-manipulated fluid derived from human placental stem cells will also be delivered topically onto the surface of the skin in the targeted area of skin following or preceeding the PRF, and also followed by micro-needling to enhance penetration into the deeper layers of the skin once per month including start of treatment and then at months 1, 2, & 3 of treatment.

**Hydrogel Cream**:
This will be applied topically and massaged into the area of facial wrinkles prior to each of the bioelectric stimulation treatments.

**Pre-Treatment Assessment of Tolerability of Bioelectric Stimulation(BES):**
Each potential subject will have a test of BES applied to an arm of leg for a period of 20 minutes to simulate a facial treatment and assure tolerability of the treatment. The level of stimulation or current to be used will be selected by each patient during this test. The duration of treatments will be the same for each patient.

**Possible Side Effects of Treatment**:

There is no history of any skin burn or irritation associated with the use of this low level bioelectric stimulation, and the biologics which will be applied topically to the skin are derivatives of naturally occurring substances and also have no history of allergy, rash, or other adverse reaction. The micro-needling is a common treatment now in use in most aesthetic clinics and has not been associated with pain or adverse effects.

**End Points**:

Each patient will have a photo taken of their face with no makeup applied before and after the treatment period to document the benefit of the therapy. The photos will be graded by an experienced dermatologist not connected to the study.

**Primary End Point**: Degree of improvement judged by the professional dermatologist and the patient's own assessment as no, minimal, moderate, good, or very good improvement in skin appearance and reduction of wrinkles. These scores will be kept separate and collated and compared at the end of the study by treatment area.
**Secondary End Points**:

1. Any adverse effects thought to be possibly related to this treatment as reported to the investigator or noted by the investigator.
2. **Patient satisfaction survey (Appendix A)** which will be completed at the end of the 3 month treatment period, and again at 3 months of follow up.