Lionheart Klotho Wellnes Study
Flow Flow

Identify Candidates



Screening

Mandatory Core Arm: 30 (USA)

Screening

- Age 55-82
- Klotho level <780 pg/ml
- No cancer
- No heart/kidney failure
- No autoimmune disease or major neurrological condido-



Study Interventions

- Bioelectric-Controlled Protein Expression (NMES)



- Klotho-Promoting Diet



- Klotho-Enhancing Supplements



Advanced Arm ONLY

- AAV gene therapy injection
- Peptide stack



Measure at 0, 3, 6,1 12 Months



Muscle Health



Brain Health



Immune Health

Increase klotho levels → Improve muscle, brain, immune health

LIONHEART

IRB Submission Packet – Lionheart Klotho Wellness Study

Klotho Wellness Study

Version 1.0 — For IRB Submission
Sponsor: Lionheart Health, Inc.
Principal Investigator: Leslie Miller, MD

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1. IRB COVER SHEET (SUMMARY INFORMATION)

Study Title:
Lionheart Klotho Wellness Study: Bioelectric-Controlled Klotho+ Expression Enhanced Exercise and Klotho-Promoting Diet & Supplements, with Optional OUS Gene Therapy and Peptide Stack

Principal Investigator:
Leslie Miller, MD
Medical License: ME108787
Address: 1623 Rachel Ct, Clearwater, FL 33756

Investigators & Study Personnel

Lionheart Klotho Wellness Study
Sponsor: Lionheart Health, Inc.

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1. Principal Investigator (PI)

Leslie W. Miller, MD

Principal Investigator
Address: **1623 Rachel Ct, Clearwater, FL 33756, USA**
Medical License: **ME108787 (Florida)**

Qualifications & Experience

- Past President, **International Society for Heart, Lung, and Blood Transplantation**
- **50+ years** clinical experience in heart failure, cardiology, regenerative medicine
- **250+ peer-reviewed publications**

- Investigator in **115+ clinical studies**; Principal Investigator in **40+ trials**
- Former **Chairman of Cardiovascular Medicine**, University of Minnesota (10+ years)
- Leader in regenerative medicine, bioelectric therapy research, and advanced clinical trial design

Full CV: Attached in IRB appendix.

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2. Co-Investigators

Organized alphabetically and by functional specialty (Cardiology, Functional/Regenerative Medicine, OUS Regional Leads, etc.)

A. Cardiology, Internal Medicine & Precision Medicine

Sanjay Bhojraj, MD, FACC, FSCAI

Interventional Cardiologist • Functional Medicine Specialist
Clinic: 4740 Von Karman Ave, Suite 150, Newport Beach, CA 92660
Residence: 27762 Antonio Pkwy L1-642, Ladera Ranch, CA 92694
Medical License: **A112163 (California)**
Experience: **17 years**

Qualifications

- Fellowships: Interventional Cardiology & Cardiovascular Diseases (Henry Ford Health System)
- Former Chief Fellow, Henry Ford
- Board Certifications: Interventional Cardiology, Cardiovascular Disease
- Functional Medicine Certified (IFM)
- MIT xPro—Drug & Medical Device Development
- Specialty Credentials: TAVR, MitraClip, Watchman, CT, Echo, Nuclear, Peripheral, RPVI
- Honors: Physician of Excellence (Orange Coast Magazine), Heroes of the Heart Award

Research & Leadership

- Executive Co-Director, Mission Cardiovascular Institute
- Director, Structural Heart & STEMI Programs (Mission Hospital)
- Extensive publications in CT imaging & interventional cardiology

CV: Attached.

B. Functional, Integrative & Regenerative Medicine

Allyson Berkey, MD

Functional & Regenerative Medicine Specialist
Address: 1501 Westcliff Dr, Suite 301, Newport Beach, CA 92660
Email: allysonberkeymd@gmail.com
Medical License: **G77666 (California)**
Experience: **38 years**

Highlights

- UCLA Kinesiology (BS), University of Minnesota (MD, Residency)
- Former Medical Director, Scripps Mercy Pediatric Outpatient Clinic
- Teaching faculty, UC San Diego
- Board Certified, American Board of Regenerative Medicine (ABRM)
- Specialist in peptide therapy, cellular/exosome therapy, aesthetics, and anti-aging medicine

CV: Attached.

Bita Badakhshan, MD ("Dr. Bita")

Integrative, Family & Functional Medicine Specialist
Address: 33542 Palo Alto St, Dana Point, CA 92629
Medical License: **A116789 (California)**
Website: https://www.ocfunctionalmedicalcenter.com
Experience: **14 years**

Highlights

- Family Medicine Residency: North Shore–Long Island Jewish Health System
- Extensive experience in preventive care, integrative oncology, functional medicine
- Former staff: Center for New Medicine & Cancer Center for Healing
- Certified Personal Trainer with strong nutrition and lifestyle medicine background

CV: Attached.

Meenakshi “Meena” Verma, MD

Nephrology • Functional Medicine • Longevity Medicine
Clinic Address: 369 San Miguel Dr, Suite 370, Newport Beach, CA 92660
Phone: (949) 229-3131
Medical License/NPI: **NPI 1942463427 (California)**
Experience: **15 years**

Credentials

- Board-Certified: Internal Medicine, Nephrology, Obesity Medicine
- Fellow: Age-Management Medicine Group (AMMG)
- Stanford-Certified Genomics & Precision Health
- Certified in Peptide Therapy & Advanced Hormone Optimization

Areas of Expertise

- Metabolic health, cognitive optimization, genomics-guided longevity programs
- Biomarker-driven precision medicine
- AI-enhanced cardiac imaging

CV: Attached.

C. Precision Medicine & Family Medicine

Jared J. Szymanski, DO

Family Medicine • Precision Medicine • Preventive Genomics
NPI: **1558778274**
Address: 366 San Miguel Dr, Suite 312, Newport Beach, CA 92660
Phone: 949-770-6910
Email: szymanski.jared@gmail.com

Credentials

- DO, Lake Erie College of Osteopathic Medicine
- Fellowship in Precision Medicine
- Former **Chair, Family Medicine**—Hoag Medical Group
- Staff Physician at Hoag Hospital
- Expert in Medicine 3.0, chronic disease reversal, OMT, metabolic optimization

CV: Attached.

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3. International / OUS Investigators (Advanced Arm Oversight)

Costa Rica Lead Investigator

William Rojas Flores, MD

Regenerative Medicine & Cellular Therapy Specialist
Phone: (+506) 8718-6999
Email: info@lifeboostercr.com
Address: Huacas, Santa Cruz, Guanacaste 50304, Costa Rica
Medical License: **MED 10659 (Costa Rica)**
Experience: **14+ years**

Bio Summary

- Doctor of Medicine & Surgery, Universidad de Iberoamérica
- Member, Colegio de Médicos y Cirujanos de Costa Rica
- Specialized in regenerative medicine, cellular therapies, and advanced injection-based treatments

CV: Attached.

Mexico Lead Investigator (San José del Cabo)

Patrick Sewell, MD

Interventional Radiology • Regenerative Medicine • Gene Therapy
NPI: **1043321326**
Email: drsewell@regenerativebiologyandmedicine.com
Phone: +1 (657) 610-8566
Clinic: ReHealth Cabo
Address: Plaza Koral, Edificio H, Level 5, San José del Cabo, BCS, Mexico
Residence: 23407 Unit 4, San José del Cabo, BCS, Mexico
Medical License: **MS License #14876**

Qualifications

- 30+ years clinical experience
- 130+ gene therapy patients treated
- Former NASA collaborator (robotic space surgery system design)
- Expert in interventional oncology, stem cells, PRP/PRF, minimally invasive image-guided therapies
- 34 scientific publications (ResearchGate link provided)

CV: Attached.

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4. Additional Consultants / Oversight Experts

(Optional to include—recommended for FDA and IRB transparency.)

Gregory Keller, MD

Medical License No. G22919

49 years experience

Plastic Surgeon

Graduated University of Illinois Doctorate of Medicine 1971

Address: 221 West Pueblo Street Suite A Santa Barbara, California 93105

Email: gsk@gregorykeller.com

Telephone: 805-458-9932

Plastic Surgery • Regenerative Aesthetics Bio -
Gregory Keller, MD. Internationally-known, board certified facial plastic surgeon, Dr. Keller, brings over 49 years of expertise to his state-of-the-art facility as a premier surgeon in Santa Barbara and Beverly Hills via UCLA, specializing in naturally restoring a youthful appearance and beautiful radiance to his patients.

IRB Appendix Attachments

The following documents accompany this section:

- Full CV — Dr. Leslie Miller
- Full CV — Dr. Sanjay Bhojraj
- Full CV — Dr. Allyson Berkey
- Full CV — Dr. Bita Badakhshan
- Full CV — Dr. Meena Verma
- Full CV — Dr. William Rojas
- Full CV — Dr. Patrick Sewell
- Full CV — Dr. Jared Szymanski
- Additional investigator CVs as applicable

Sponsor:
Lionheart Health, Inc.
21010 Pacific City Cir #1406
Huntington Beach, CA 92648

Study Sites:
Newport Beach, CA
New York, NY
Santa Barbara, CA
Utah (2 locations)
Mexico (4 locations, OUS arm only)
Costa Rica (OUS arm only)

Study Type: Interventional
Phase: Phase I Early Feasibility / Proof of Concept
Duration per Participant: 12 months
Total Enrollment: 45 participants
Arms:

- U.S. Mandatory Core Arm (NMES + Diet + Supplements)
- OUS Advanced Arm (adds AAV Klotho–hTERT–Follistatin Gene Therapy + Peptide Stack)

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2. STUDY PURPOSE & SCIENTIFIC RATIONALE

Purpose:
To evaluate whether increasing circulating klotho levels through bioelectric NMES stimulation, diet, supplements, and an optional OUS gene therapy arm can improve **muscle health, immune function, and cognitive performance** in adults with low klotho.

Scientific Rationale:
Klotho deficiency (<780 pg/ml) is associated with accelerated aging, inflammation, cognitive decline, and reduced muscle function.
Bioelectric protein expression, dietary optimization, supplements, and gene therapy may elevate klotho and improve biological aging markers.

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3. STUDY DESIGN (CONDENSED PROTOCOL)

Study Model:
Non-randomized, open-label, interventional feasibility trial with two arms.

A. Mandatory Core Arm (U.S.)

Participants receive for 12 months:

- **NMES bioelectric stimulation** (2–3×/week, 35–60 min)
- **Klotho-promoting diet** (delivered meals; ≥70% compliance)
- **Daily supplements** (Rejuvant, SNIP Nutrition, KlothoMaxx)

B. Advanced OUS Arm

Includes Core Arm +

- **AAV Klotho–hTERT–Follistatin gene therapy** (baseline, 6, 12 months)
- **Physician-guided peptide longevity stack** (monthly)

Primary Outcomes (Measured at 0, 3, 6, 12 months):

Muscle: grip strength, 6-minute walk, muscle mass
Brain: cognition, memory, mood
Immune: CRP, ESR, IHM immune score, gut index
Biomarkers: Full 461-marker aging panel including klotho

Secondary Outcomes:

Vision, hearing, joint pain, sexual health, skin elasticity, hair density, sleep, stress, bladder health, VO_2 max.

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4. SUBJECT POPULATION & RECRUITMENT

Inclusion Criteria

- Age 55–82
- Serum klotho <780 pg/ml
- No cancer, heart/kidney failure
- No severe immune, muscle, or brain disease
- Able to comply with diet and therapy schedule

Exclusion Criteria

- Cancer
- Pregnancy

- Stroke, TBI
- Autoimmune disease
- Severe cardiovascular or renal disease

Recruitment Methods

- Existing patients at Lionheart Longevity clinics
- Physician referrals
- Study information website
- No vulnerable populations specifically targeted

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5. RISKS & DISCOMFORTS

NMES bioelectric therapy

- Temporary muscle soreness
- Fatigue during/after sessions

Diet and supplements

- Gastrointestinal discomfort
- Rare allergy/intolerance to ingredients

Blood draws

- Bruising
- Mild pain

Advanced OUS Arm Risks (EX-US Only)

Gene therapy (AAV):

- Local inflammation
- Immune system activation
- Flu-like symptoms
- Theoretical long-term risks (low probability)

Peptide therapy:

- Injection site redness
- Hormonal/metabolic effects
- Allergic response (rare)

Risk Mitigation:

Continuous physician oversight, safety labs at each major visit, screening for contraindications.

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6. POTENTIAL BENEFITS

Participants **may** experience improvements in:

- Strength, mobility, endurance
- Cognitive clarity, memory, mood
- Immune resilience and lower inflammation
- Biological aging markers (klotho, IMM-AGE, etc.)

Benefits **cannot be guaranteed**.

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7. DATA & SAFETY MONITORING PLAN (DSMP)

- Safety labs at baseline, 3, 6, and 12 months
- Adverse event reporting via standardized AE/SAE forms
- Immediate evaluation of any unexpected symptoms
- Study PI reviews safety outcomes quarterly
- Stopping criteria: serious unexpected adverse events related to study intervention

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8. CONFIDENTIALITY & HIPAA DATA PROTECTION

- Coded participant IDs used for all data
- Physical files stored in locked facilities
- Digital data encrypted & access-controlled
- Specimens processed only by certified laboratories
- No data shared outside study without explicit consent
- Participants may request deletion of identifiable data

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9. SHORT-FORM INFORMED CONSENT SUMMARY

Participants will be informed of:

- Study purpose and procedures
- Expected time commitment

- Potential risks and benefits
- Alternatives (standard care, declining participation)
- Voluntary nature of participation
- Right to withdraw without penalty
- Data privacy protections
- Contact information for PI and IRB

A full consent form will be provided during enrollment.

1. Participant Identification → Screening

Step 1 — Identify Candidates (Age 55–82)
⬇
Step 2 — Blood Test for Klotho

- Must be **< 780 pg/ml**
  ⬇
  Step 3 — Medical Clearance
- No cancer
- No heart/kidney failure
- No autoimmune disease
- No major neurological conditions

📌 *If eligible → Enroll into study*

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2. Enrollment → Assign to Study Arm

A. Mandatory Core Arm (30 participants, U.S.)

- Bioelectric NMES (Klotho + Follistatin signals)
- Klotho-promoting diet
- Daily supplements

B. Advanced OUS Arm (15 participants, Mexico/Costa Rica)

- All Core Protocol items **plus**
- **AAV Triple Gene Package**: Klotho + hTERT + Follistatin
- **Physician-guided peptide stack**

📌 *Participants choose OR meet criteria for the OUS Arm*

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3. Study Interventions Timeline (12 Months)

Month 0 Month 3 Month 6 Month 12
|----------|----------|----------|----------|

Mandatory Core Arm:
- NMES 2–3×/week
- Diet delivered weekly
- Supplements daily
- Labs & assessments at each milestone

Advanced OUS Arm:
- Gene Injection #1
- ----
- Gene Injection #2
- ----
- Gene Injection #3
- Peptide stack monthly (12 total)

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4. What Participants Receive Throughout Study

Bioelectric-Controlled Protein Expression (NMES)

- ↑ Klotho
- ↑ Follistatin
- Muscle stimulation + longevity signaling

Klotho-Promoting Diet

- High protein
- Low sugar
- Low carb
- Delivered meals (≥70% compliance required)

Klotho-Enhancing Supplements

- Rejuvant
- SNIP Longevity
- KlothoMaxx

Advanced Arm ONLY

- AAV gene therapy injections into thigh muscle
- Peptide stack (muscle, immune, brain) updated monthly

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5. Measurement Domains & Tools

Muscle Health

- Grip strength
- 6-minute walk
- Muscle mass (DXA/MRI)
- VO_2 max (optional)

Brain Health

- Cognitive battery (NIH Toolbox / CanTab)
- Memory assessments
- Mood/anxiety scales

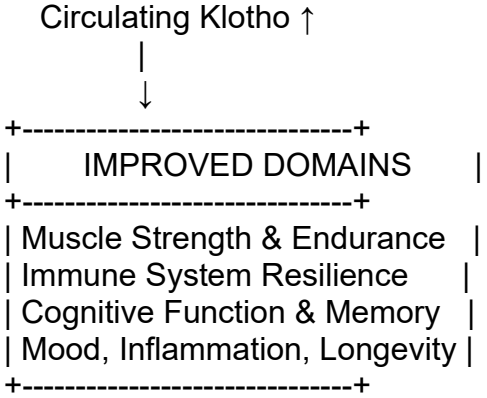
Immune Health

- CRP
- ESR / PCT
- IMM-AGE
- Gut health index
- 461-biomarker panel incl. **Klotho**

📌 Assessed at: **0, 3, 6, 12 months**

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6. Study Endpoint Schematic



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7. Study Completion → Final Evaluation

- Review of all biomarkers
- Functional tests (muscle, cognition, immune)

- Final survey + exit interview
- Recommendation for ongoing longevity care

🧾 DATA SAFETY MONITORING PLAN (DSMP)

Lionheart Klotho Wellness Study

NMES-Controlled Klotho Expression + Diet + Supplements ± OUS Gene/Peptide Arm

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1. Oversight Structure

1.1 Principal Investigator (PI)

Dr. Leslie Miller is responsible for:

- Overall safety oversight
- Review of adverse events (AEs) and serious adverse events (SAEs)
- Protocol compliance
- Ensuring risk mitigation measures

1.2 Safety Monitoring Team

Includes:

- PI (Cardiology / Regenerative Medicine)
- Study Medical Director
- Senior Clinical Research Coordinator
- Independent Medical Safety Reviewer (quarterly review)

1.3 Independent Oversight

Although not required for early-phase feasibility, an **external safety physician** will review:

- SAEs immediately
- All AEs and progress every **90 days**

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2. Safety Monitoring Procedures

2.1 Scheduled Safety Assessments

At **Baseline, 3 months, 6 months, 12 months**:

- Vital signs
- Physical examination
- Safety labs (CBC, CMP, CRP, ESR, fasting glucose, kidney/liver function)
- Klotho biomarker panel
- Adverse event review

2.2 Unscheduled Visits

Participants may be evaluated anytime concerns arise:

- New symptoms
- Device-related discomfort
- Post-gene-therapy reactions (Advanced Arm only)

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3. Adverse Event (AE) Reporting

3.1 Definition of AE

Any unfavorable change in health during study participation, regardless of causality.

3.2 Recording

All AEs will be:

- Documented in the secure REDCap clinical database
- Reviewed by PI within **72 hours**

3.3 Serious Adverse Events (SAE)

SAEs include:

- Hospitalization
- Life-threatening events
- Severe immune reaction
- Anaphylaxis
- Organ dysfunction

SAE Reporting Timelines:

- **Within 24 hours** to PI
- **Within 48 hours** to sponsor
- **Within 7 days** to IRB

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4. Stopping Rules

The following will trigger **immediate pause** of study interventions for an individual:

- Rapid increase in inflammatory markers (CRP > 10 mg/L unexplained)
- Unexpected severe neurological, cardiac, or immune events
- Creatinine >1.8 mg/dL or new renal impairment
- ALT/AST >3× upper limit
- Severe adverse reaction to AAV gene therapy

Study-Wide Stopping Criteria

Trial will pause if:

- ≥2 SAEs judged related to interventions
- Any suspected systemic AAV gene therapy immune cascade
- Unexpected high-risk pattern detected in safety labs

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5. Data Security & Confidentiality

- All participant data coded with unique study ID
- Encrypted digital storage
- Limited-access clinical database
- Biospecimens handled by certified laboratories
- 21 CFR Part 11–ready compliance

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6. DSM Meeting Schedule

- **Quarterly Safety Review**
- **Ad hoc meetings** if concerning trends emerge
- **Annual PI Report** summarizing all safety findings

▨ STATISTICAL ANALYSIS PLAN (SAP)

Aligned with endpoints for muscle, brain, immune, and biomarker changes

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1. Objectives & Endpoint Definitions

Primary Endpoints

Change from baseline at 12 months in:

- Muscle function (grip strength, 6MWT, muscle mass)
- Cognitive function (composite cognitive score, memory, mood)
- Immune function (CRP, ESR, IMM-AGE, gut index)
- Circulating Klotho

Secondary Endpoints (Optional)

- VO_2 max
- Sexual function score
- Joint pain score
- Vision, hearing, skin elasticity, hair density
- Sleep & stress biomarkers (cortisol)

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2. Study Groups for Analysis

Group	n	Intervention
Core Arm	30	NMES + Diet + Supplements
Advanced OUS Arm	15	Core + AAV Gene Therapy + Peptides

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3. Statistical Power

- This is a Phase I feasibility trial; power is not based on hypothesis testing.
- Target enrollment (n=45) provides sufficient precision to estimate effect sizes for a future pivotal Phase II/III trial.

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4. Analysis Populations

4.1 Intent-to-Treat (ITT)

All enrolled participants with ≥1 follow-up assessment.

4.2 Per-Protocol (PP)

Participants meeting:

- ≥70% diet compliance

- ≥75% NMES treatment attendance
- Completed ≥3 follow-up visits

4.3 Safety Population

Everyone who received at least one intervention.

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5. Statistical Methods

5.1 Continuous Variables

Examples: grip strength, klotho levels, CRP.

Analyses:

- Mean ± SD
- Paired t-test (baseline → 12 mo)
- Wilcoxon signed-rank test (non-normal)
- ANCOVA comparing groups (Core vs OUS Advanced)
    - Adjusted for age, sex, baseline klotho

5.2 Categorical Variables

Examples: improvement yes/no, AE presence.

Analyses:

- χ^2 or Fisher's exact test

5.3 Repeated Measures Modeling

For variables measured at baseline, 3, 6, 12 months:

- Mixed-effects linear regression
    - Random intercept for participant
    - Fixed effect for time and arm (Core vs OUS)

5.4 Missing Data Handling

- Missing-at-random: Multiple Imputation
- Sensitivity: Last Observation Carried Forward (LOCF)

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6. Endpoint-Specific Statistical Methods

6.1 Muscle Health

- Percent change in grip strength
- 6MWT (meters)
- Muscle mass (DXA, MRI)
  Analysis:
- Paired t-test + mixed model
- Effect size (Cohen's d)

6.2 Brain Health

- Cognitive composite score
- Memory recall score
- Mood/anxiety index
  Analysis:
- Mixed model regression
- Neurocognitive Z-score normalization

6.3 Immune Health

- CRP percent reduction
- ESR, PCT, calprotectin
- IMM-AGE score change
- Klotho trajectory modeling
  Analysis:
- Log-transformed biomarkers
- ANCOVA adjusting for baseline inflammation

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7. Gene Therapy Subgroup Analysis (Advanced Arm)

Specific analyses:

- AAV response curves (klotho increase over time)
- Early vs late peptide adjustments
- Immunological safety markers
- Local thigh reaction scoring

Models:

- Mixed-effects spline regression for biomarker kinetics
- Comparison vs Core Arm using ANCOVA

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8. Interim Analysis Plan

Interim Review at 3 and 6 Months

- Review of safety signals
- Biomarker early trend evaluation
- No stopping based on efficacy due to feasibility design

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9. Reporting & Interpretation

- Estimates will emphasize **effect sizes and confidence intervals**, not p-values.
- Results will inform the design and powering of a pivotal Phase II trial.

Risk/Benefit Analysis

Study: Lionheart Klotho Wellness Study
Interventions: NMES bioelectric klotho/follistatin expression, klotho-promoting diet & supplements, optional OUS AAV gene therapy + peptide stack

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1. Overview

This is a Phase I early-feasibility study in adults (55–82) with **low circulating klotho**. Risks arise from:

- Bioelectric neuromuscular stimulation (NMES)
- Diet and supplement program
- Repeated phlebotomy and biomarker testing
- In the Advanced OUS Arm only: AAV gene therapy and physician-guided peptide stack
- Standard research risks (privacy, time burden, psychological discomfort)

Potential benefits include **improved muscle, immune, and brain health** and better understanding of klotho-based longevity interventions.

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2. Potential Risks

2.1 NMES Bioelectric Stimulation (Core & OUS Arms)

Risk Types

- Local muscle soreness, fatigue, or cramping
- Mild skin irritation or redness at electrode sites
- Temporary discomfort during higher-intensity sessions
- Very rare risk of arrhythmia in predisposed patients

Mitigation

- Pre-screening for cardiac disease and implanted devices
- Gradual titration of stimulation intensity
- Real-time monitoring by trained staff
- Immediate stoppage of session if discomfort occurs
- Documentation and review of any device-related AEs

2.2 Klotho-Promoting Diet

Risk Types

- Gastrointestinal discomfort (bloating, constipation, diarrhea)
- Intolerance to specific components (e.g., high protein)
- Possible interaction with existing metabolic conditions (e.g., diabetes, kidney disease)

Mitigation

- Exclusion of significant kidney failure or uncontrolled metabolic disease
- Diet customization by qualified nutrition professionals
- Ongoing monitoring of weight, renal function, and metabolic labs
- Ability to modify meal plans if adverse symptoms occur

2.3 Supplements (Rejuvant, SNIP Nutrition, KlothoMaxx)

Risk Types

- GI upset (nausea, reflux, diarrhea, constipation)
- Headache or mild systemic symptoms
- Rare allergic reactions to ingredients
- Potential interactions with existing medications

Mitigation

- Review of full medication and allergy history before enrollment
- Use of established dosing ranges
- Clear instructions for participants to report new symptoms
- Option to discontinue or adjust supplements if side effects arise
- Physician review of all suspected supplement-related events

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2.4 Blood Draws and Biomarker Panels

Risk Types

- Mild pain or bruising at venipuncture site
- Rare infection, hematoma, or lightheadedness
- Time burden and inconvenience

Mitigation

- Performed by trained phlebotomists
- Use of sterile technique
- Observation after blood draws when indicated
- Limiting total blood volume to safe levels for age and size

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2.5 AAV Gene Therapy (Advanced OUS Arm Only)

Risk Types

- Local injection-site pain, redness, or swelling
- Acute inflammatory or immune reaction (flu-like symptoms, fever, malaise)
- Possible transient elevation of liver enzymes or inflammatory markers
- Theoretical long-term risks of gene transfer (e.g., insertional mutagenesis, persistent immune activation) though risk is considered low with modern AAV vectors
- Unknown risks due to investigational nature of klotho–hTERT–follistatin gene combination

Mitigation

- Gene therapy restricted to **OUS sites** with appropriate regulatory/ethical approvals
- Rigorous pre-screening including labs and clinical exam
- Administration by experienced physicians in controlled settings

- Post-injection observation and scheduled safety labs (liver, kidney, inflammation markers)
- Clear stopping rules and study pause criteria in case of serious immune or systemic reactions
- Detailed gene therapy consent specific to this arm

2.6 Physician-Guided Peptide Stack (Advanced OUS Arm Only)

Risk Types

- Injection site redness, discomfort, or infection
- Potential hormonal or metabolic changes (blood pressure, glucose, lipids) depending on peptides used
- Headache, fatigue, or sleep disturbance
- Rare allergic or idiosyncratic reactions

Mitigation

- Physician-determined selection and dosing based on medical history and labs
- Monthly review and adjustment of peptide regimen
- Routine safety labs and vital signs monitoring
- Immediate discontinuation of specific peptides if concerning changes occur

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2.7 Psychosocial and Time-Burden Risks

Risk Types

- Time commitment for visits, NMES sessions, travel (especially OUS arm)
- Possible frustration if expected improvements are not achieved
- Anxiety related to extensive biomarker testing or gene therapy considerations

Mitigation

- Clear explanation of visit schedule before consent
- Option to withdraw at any time without penalty
- Access to study staff to address concerns and provide support

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2.8 Privacy and Confidentiality Risks

Risk Types

- Potential breach of confidentiality of health and biomarker data

Mitigation

- Use of coded study IDs instead of names on data files
- Encrypted databases and restricted access to identifiable information
- Secure transfer of lab data from external laboratories
- Compliance with applicable privacy regulations and IRB/HIPAA standards

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3. Potential Benefits

3.1 Direct Benefits to Participants

Participants **may** experience:

- Improved **muscle strength and endurance** (e.g., better grip strength, walking distance)
- Enhanced **cognitive function, memory, and mood**
- Reduced **inflammatory markers** and improved **immune resilience**
- Favorable changes in **biological aging biomarkers**, including klotho
- Personalized feedback on health status via extensive biomarker testing

However, **benefit is not guaranteed**, and participants are informed that the interventions are investigational.

3.2 Indirect and Societal Benefits

- Generation of feasibility data on a **multi-modal klotho-targeted longevity protocol**
- Insight into integration of **bioelectric stimulation, diet, supplements, and gene therapy**
- Effect size estimates to design a larger, adequately powered pivotal trial
- Contribution to scientific understanding of klotho, hTERT, follistatin, and immune/muscle/brain aging relationships
- Potential future development of safer, more effective **healthspan-extension therapies** for broader populations

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4. Risk Minimization & Favorable Risk/Benefit Assessment

Several design features are intended to **minimize risk**:

- Restriction to **older adults with low klotho and acceptable baseline health**
- Exclusion of participants at elevated risk for serious complications
- Non-invasive or minimally invasive procedures in the **Core Arm** (NMES, diet, supplements)
- Advanced OUS interventions (gene therapy/peptides) only under enhanced monitoring and regulatory oversight
- Frequent safety assessments and predefined **stopping rules** for individuals and the study overall
- Robust data security and confidentiality safeguards

Given:

- The **potential for meaningful improvement** in muscle, immune, and brain function,
- The high unmet need for safe, non-toxic strategies to **extend healthspan**, and
- The layered safety measures and strict eligibility criteria,

the **overall risk/benefit ratio is considered acceptable** for a Phase I early-feasibility study, particularly as a preparatory step toward future, more definitive trials.

LIONHEART HEALTH, INC.

Informed Patient Consent Form

Lionheart Klotho Wellness Study / Klotho Wellness Program Clinical Trial

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SECTION 1 — STUDY SUMMARY (READ FIRST)

Mandatory Participant Requirements

All participants must agree to:

1. **Klotho-favoring diet:** Eat healthy, low-carb, low-sugar, high-protein meals **≥70%** of the time.
   Optional home delivery: Metabolic Meals, Tempo.
2. **Bioelectric EMS Exercise (BodStim™ / Wiemspro Suit):**
   - Minimum: **20 minutes 2×/week**
   - Wear suit for **1 hour 2×/week**
   - Maximum use: **3×/week**

3. **Daily Supplements:**
   Supplements for **muscle, brain, and immune health** (all klotho-favoring).

Required Assessments at Baseline, 6 Months, and 12 Months

- Full aging biomarker blood panel (up to 500 biomarkers, including klotho)
- Muscle strength and mass tests
- Brain function tests (cognition, mood, memory)
- Immune and gut health tests

Optional Add-On Therapies (Patient Choice)

a. Hyperbaric oxygen
b. LED red light
c. Cold plunge
d. Nature therapy
e. Sleep/breathing coaching
f. Yoga & meditation
g. Peptide therapy
h. Hormone optimization
i. AI-enhanced MRI
j. PEMF therapy
k. Bioelectric enhanced PRF
l. Sexual, joint, skin, or weight-loss therapies

SECTION 2 — ADVANCED ARM (OUS ONLY)

For participants treated in **Mexico or Costa Rica**:

1. **Gene therapy injections** (thigh muscle): klotho, follistatin, hTERT
2. **Klotho-expressing stem cell infusions** (optional)
3. **Wharton's Jelly and exosome treatments**
4. **Physician-directed AI-assisted peptide stack** (monthly adjustments)

SECTION 3 — BACKGROUND & SPONSOR HISTORY

Lionheart Health, Inc. is a 2022 spinout of Leonhardt Ventures (founded 1982).
Key history:

- **600,000+ patients** treated globally using Leonhardt medical devices & biologics
- First organ regeneration performed in **1988 (animal)** and **2001 (human)**
- First bioelectric regeneration paper published in *Circulation* (1999)

- Mettler Electronics, ElectroMed, and Wiemspro — all FDA 510(k) cleared — have performed **>1,000,000+ treatments each** with **no serious adverse events reported**

Primary suppliers include:
• Mettler (1957) — bioelectric stimulator
• ElectroMed Technologies — WellnessPro
• Wiemspro (2015) — EMS suit
• Metabolic Meals (2009) — nutrition program
• Rejuvant, SNIP Nutrigenomics, Hop Box — supplement suppliers

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PART 1 — WHAT DOES MY PARTICIPATION INVOLVE?

1. Introduction

You are being invited because your physician believes this program may benefit your muscle, immune, and brain health without interfering with your existing treatments. Participation is **voluntary**.

Signing consent means you:
✓ Understand the study
✓ Agree to the procedures
✓ Allow use of your health information for the study

---

2. Purpose of This Research

This trial supports the **XPRIZE Healthspan Competition**. Lionheart Health is a **Top-40 global semifinalist** (from 600 entries).

This study evaluates whether:

✓ **Klotho-favoring diet**
✓ **Klotho-increasing supplements**
✓ **BodStim/Wiemspro EMS bioelectric exercise**

can improve:

- Muscle health
- Brain health
- Immune resilience
- Biological age & longevity

Participants also gain optional access to hyperbaric oxygen, red light therapy, peptides, hormone balancing, meditation/yoga, PRF, PEMF, sleep optimization, and more.

The Advanced OUS Arm receives **gene therapy (klotho + hTERT + follistatin)**.

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3. What Will Happen Before You Begin? (Screening)

Before starting, you will undergo:

- Medical history review
- Medication review
- Vital signs
- Physical exam
- Blood tests (organ function, inflammatory markers, klotho, aging biomarkers)
- Brain function assessment
- Sleep/breathing evaluation
- Muscle function assessment
- Immune & gut health assessment
- Cancer screening (if indicated)
- Pregnancy test (if applicable)

Results determine if you are eligible to continue.

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4. What Will I Do During the Study?

Mandatory Components

1. **Eat healthy klotho-favoring meals ≥70% of the time**
2. **Use the BodStim™ Wiemspro EMS suit 2–3× per week**
3. **Take daily klotho-supporting supplements**

Optional Add-Ons

You may choose any of these (included unless otherwise specified):

- Hyperbaric oxygen
- LED therapy
- PEMF
- Bioelectric PRF
- Peptides
- Wharton’s Jelly / Exosomes
- Nature therapy

- Yoga & meditation
- Sleep optimization

Advanced OUS Arm Only

- Gene therapy injections (baseline, 6, 12 months)
- Physician-supervised peptide stacks
- Stem cells (optional)

SECTION 5 — REQUIRED STUDY MEASUREMENTS

You must complete **minimum** tests at:

Baseline / 6 Months / 12 Months

- Muscle strength & mass
- Cognitive tests (memory, executive function, mood)
- Immune & gut testing
- Aging biomarkers (up to 500 markers)

Optional Tests

- AI-enhanced MRI
- Peak VO_2
- Full sleep/breathing diagnostic evaluation

SECTION 6 — COSTS & GUARANTEES

Program Options

Program	Cost	Guaranteed Biological Age Reversal
Basic	$39,000	5 years or money-back
Intermediate	$79,000	7 years or money-back
Advanced	$205,000	10 years or money-back (goal 20 yrs)

Costs Included

1. All healthy meals delivered
2. BodStim™ Wiemspro EMS suit
3. All daily supplements
4. All physician consultations

5. All lab tests (blood, saliva, urine)
6. All required muscle, brain, immune tests
7. Immune, brain, joint, sexual health therapies
8. Weight loss & toning program
9. Optional VO_2 max testing

Not Included

- Gene therapy (~$124,000)
- AI-Enhanced MRI ($2,600 per scan)
- Travel costs

SECTION 7 — DO I HAVE TO PARTICIPATE?

No. Participation is **voluntary**.
You may withdraw **at any time** without penalty or loss of care.

SECTION 8 — POSSIBLE BENEFITS

Benefits are not guaranteed, but may include:

- Improved muscle strength & endurance
- Enhanced cognitive performance & mood
- Improved immune system resilience
- Decreased inflammation
- Biological age reversal
- Longer healthspan

SECTION 9 — POSSIBLE RISKS

Bioelectric Procedures

- Skin irritation
- Muscle soreness
- Irregular heartbeat (rare)
- Allergic reaction
- Blood clots or stroke (very rare)
- Skin burns (rare)

Supplements

- Headache
- Nausea
- Insomnia
- Allergic reaction

Gene Therapy (Advanced OUS Only)

Significant Risks:

- Immune reaction
- Organ damage (heart, liver, kidney)
- Severe inflammation
- Brain fog
- Death (extremely rare, theoretical)

General Risks

- Blood draw discomfort
- Emotional distress
- Unknown risks

Pregnancy, breastfeeding, or trying to conceive **are prohibited**.
Participants must avoid pregnancy for **12 months** after treatment.

SECTION 10 — WHAT HAPPENS TO MY SAMPLES?

Blood samples will be used for:

- Aging biomarkers
- Immune tests
- Klotho levels
- Safety labs

Remaining samples may be stored for future research (with optional separate consent).

SECTION 11 — NEW INFORMATION

If new risks emerge, you will be informed and may withdraw.

SECTION 12 — OTHER TREATMENTS

You must report all medications, supplements, and therapies during the program.

SECTION 13 — WITHDRAWAL

You may withdraw at any time.
Previously collected data will still be used unless you request otherwise before enrollment.

SECTION 14 — EARLY TERMINATION

The study may stop early due to:

- Safety concerns
- Ineffectiveness
- Regulatory decisions
- Sponsor decision

SECTION 15 — AFTER THE STUDY

Data will be analyzed, published, and submitted to XPRIZE judging committees.
You will not be personally identified.

SECTION 16 — CONFIDENTIALITY

Your data will be:

- Coded
- Encrypted
- Stored securely
- Viewed only by authorized personnel

Regulators, monitors, and XPRIZE evaluators may access your records.

SECTION 17 — COMPLAINTS & COMPENSATION

If injured, you will receive medical attention.
You may pursue arbitration or legal remedies if applicable.

SECTION 18 — FUNDING & ORGANIZATION

This study is sponsored by Lionheart Health, Inc.
Investigators and clinics are compensated but participants are not.
You will not receive royalties or financial benefit from any discoveries.

CONTACT INFORMATION

Medical Questions / Adverse Events

Dr. Leslie Miller
Chief Medical Officer
📞 813-476-3933
✉ lmiller1429@gmail.com

Research & Complaints Contact

Suhani Khandelwal
Research Coordinator
📞 929-557-9363
✉ suhanikhandelwal05@gmail.com

SIGNATURE PAGE

DocuSign Template Structure (Recommended)

Recipients

- **Participant** (Required signer)
- **Study Doctor / Investigator** (Optional co-signer)
- (Optional) **Witness**

Tabs / Fields to Add

For the *participant*:

- Text fields:

    - Participant Full Name
    - Date of Birth
    - Email
    - Phone
- Checkboxes / Radio buttons:
    - “I have read and understand this form”
    - “I agree to participate in the Lionheart Klotho Wellness Study”
    - Program choice (Basic / Intermediate / Advanced)
    - Arm choice (USA Core vs Advanced OUS – if applicable)
- Initial fields:
    - Initial next to **Risks Section**
    - Initial next to **Pregnancy & contraception clause**
    - Initial next to **Costs/financial section**
    - Initial next to **Optional therapies**
- Signature fields:
    - Participant Signature
    - Date Signed
- Optional: signer attachment field if you want them to upload labs/ID.

For the *study doctor*:

- Name (auto from DocuSign routing)
- Signature
- Date Signed

For the *witness* (optional):

- Name
- Signature
- Date Signed

2️⃣ DocuSign-Ready eConsent Text

(You can paste this into DocuSign as one or multiple “documents” and overlay fields where indicated.)

LIONHEART HEALTH, INC.

LIONHEART KLOTHO WELLNESS STUDY
DIGITAL INFORMED CONSENT FORM (eCONSENT)

Participant Full Name: _____
Date of Birth: ____ / ____ / _____
Email: _____
Phone: _____

---

1. STUDY SUMMARY

Please read this section carefully. You will be asked to confirm that you understand and agree.

Purpose:
The Lionheart Klotho Wellness Study is a clinical research program designed to investigate whether:

- A **klotho-favoring diet**
- **Bioelectric EMS exercise** (BodStim™ / Wiemspro suit)
- **Daily klotho-supporting supplements**
- *(and for some participants, optional advanced therapies such as gene therapy, stem cells, peptides, and other longevity therapies)*

can improve **muscle, brain, and immune health** and may help **extend healthspan**.

Mandatory Participant Requirements

By joining the study, I understand I must:

1. Eat healthy, klotho-favoring food **at least 70% of the time**.
2. Exercise with the **BodStim™ Wiemspro EMS suit**:
    - At least **20 minutes, 2× per week**, and
    - Wear the suit **1 hour, 2× per week** (max 3×/week).
3. Take **daily supplements** for muscle, brain, and immune health as directed.

Key Study Assessments (Required)
At **baseline, 6 months, and 12 months**, I will complete:

- Blood tests for aging biomarkers (including klotho)
- Muscle strength and mass testing
- Brain function testing (cognition, mood, memory)
- Immune and gut health testing

[ ] **I have read and understand the Summary above.**
[INITIAL SUMMARY HERE]

---

2. OPTIONAL THERAPIES

I may choose to receive additional therapies including some or all of the following:

- Hyperbaric oxygen
- LED red light therapy
- PEMF
- Cold plunge
- Yoga, meditation, nature experiences
- Sleep and breathing optimization
- Bioelectric enhanced PRF injections
- Peptide therapies
- Hormone balancing
- AI-enhanced MRI
- Joint, sexual, brain, skin and weight-management therapies

I understand these are **optional**, may carry additional risks, and will be **logged for research** if I receive them.

[ ] **I understand that these optional therapies are not required and may have additional risks.**
[INITIAL OPTIONAL HERE]

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3. ADVANCED OUS ARM (IF APPLICABLE)

Some participants treated at **international (OUS) locations** may also receive:

- Gene therapy injections into thigh muscle (klotho, follistatin, hTERT)
- Klotho-expressing stem cell infusions
- Wharton's Jelly and exosome treatments
- Physician-directed, AI-assisted peptide stack

These are investigational procedures with additional risks, including serious immune or organ-related events.

[ ] I am being enrolled **only in the USA Core Program (no gene therapy).
[ ] I am being enrolled **in the Advanced OUS Arm and understand I will receive gene therapy and/or related advanced biologics.

[INITIAL OUS CHOICE HERE]

---

4. PROGRAM LEVEL & COSTS

I understand there are fee-based program options with **biological age reversal guarantees**:

- [ ] **Basic Program – $39,000**
  Guarantee: reverse biological age by **5 years** or money-back.
- [ ] **Intermediate Program – $79,000**
  Guarantee: reverse biological age by **7 years** or money-back.
- [ ] **Advanced Program – $205,000**
  Guarantee: reverse biological age by **10 years** or money-back
  (20-year goal in alignment with XPRIZE Healthspan goals).

Included in Program Fees

- All healthy meals delivered
- BodStim™ Wiemspro EMS suit
- Daily supplements
- Physician consultations
- Required tests (muscle, brain, immune, aging biomarkers)
- Immune, brain, joint, sexual health, body toning/weight-loss therapies
- All blood, urine, and saliva tests
- VO_2 max testing (if selected)

Not Included

- Gene therapy (may cost up to ~$124,000)
- AI-enhanced MRI (~$2,600 per scan)
- Travel costs to and from clinics

[ ] **I understand the program cost structure, what is included, and what is not included.**
[INITIAL COSTS HERE]

---

5. RISKS & DISCOMFORTS

I understand that all medical and research procedures involve risks.
Risks may include, but are not limited to:

Bioelectric Procedures

- Rash, skin irritation, blistering or burns
- Muscle soreness or fatigue
- Irregular heartbeat or blood clot (rare)
- Headache, chest pain, or other cardiovascular symptoms

Supplements

- Headache
- Nausea or GI upset
- Insomnia
- Allergic reaction

Gene Therapy (Advanced OUS Arm Only)

- Strong immune reactions
- Organ damage (heart, liver, kidneys)
- Brain fog, fatigue
- Serious complications including **death (rare, but possible)**

General Study Risks

- Discomfort from blood draws
- Emotional distress from test results or procedures
- Unknown or unanticipated risks

I agree to immediately report any new or unusual symptoms to the study doctor.

[ ] **I have read and understand the risks described above.**
[INITIAL RISKS HERE]

---

6. PREGNANCY & CONTRACEPTION

I understand that:

- The effects of these interventions on an unborn child or nursing infant are **unknown**.
- I **must not** participate if I am pregnant, breastfeeding, or actively trying to conceive.
- I must use **effective birth control** during the study and for **12 months** after my last treatment.
- If I become pregnant or father a child, I will notify the study doctor immediately and may be withdrawn for safety reasons.

[ ] **I understand and agree to the pregnancy/contraception requirements.**
[INITIAL PREGNANCY HERE]

---

7. POTENTIAL BENEFITS

I understand that benefits **cannot be guaranteed**, but may include:

- Improved muscle strength, endurance, and body composition
- Improved cognitive function, memory, and mood
- Stronger immune function and reduced inflammation
- Reversal of biological age and potentially longer healthspan

[ ] **I understand that benefits are not guaranteed.**
[INITIAL BENEFITS HERE]

---

8. CONFIDENTIALITY

- My data will be coded and stored securely.
- Only authorized staff, regulators, monitors, and XPRIZE evaluators may access my records for research purposes.
- Results may be published or presented, but I will **not** be personally identified.

[ ] **I understand how my data and samples will be used and protected.**
[INITIAL CONFIDENTIALITY HERE]

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9. VOLUNTARY PARTICIPATION & WITHDRAWAL

- My participation is **voluntary**.
- I may withdraw at **any time** without penalty or loss of medical care.
- Data collected up to the time of withdrawal may still be used in the study unless I revoke permission before joining.

[ ] **I understand that participation is voluntary and I may withdraw at any time.**
[INITIAL VOLUNTARY HERE]

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10. QUESTIONS, NEW INFORMATION, AND CONTACTS

If I have questions or experience side effects, I will contact:

Clinical Contact
Dr. Leslie Miller – Chief Medical Officer
Phone: 813-476-3933
Email: lmiller1429@gmail.com

Research / Complaints Contact
Suhani Khandelwal – Research Coordinator
Phone: 929-557-9363
Email: suhanikhandelwal05@gmail.com

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11. CONSENT TO PARTICIPATE

Please confirm the following by checking the box and signing.

[ ] **I confirm that I have read (or had read to me) this Informed Consent Form for the Lionheart Klotho Wellness Study. I have had the opportunity to ask questions, and my questions have been answered to my satisfaction. I voluntarily agree to participate in this study.**

Participant Signature: [SIGN HERE – PARTICIPANT]
Date: [DATE SIGNED – PARTICIPANT]

---

12. WITNESS (IF REQUIRED)

I attest that the participant signed this consent form willingly in my presence.

Witness Name (print): _____
Signature: [SIGN HERE – WITNESS]
Date: [DATE SIGNED – WITNESS]

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13. STUDY DOCTOR / INVESTIGATOR DECLARATION

I have explained the study purpose, procedures, risks, and alternatives to this participant and believe they understand what participation involves.

Study Doctor / Senior Researcher Name: _____
Signature: [SIGN HERE – STUDY DOCTOR]
Date: [DATE SIGNED – STUDY DOCTOR]