



Distinguished Anti-Aging Expert and NYT Bestselling Author Michael F. Roizen, MD will Unveil Groundbreaking Data on promising Age Reversal Drug from Telomir Pharmaceuticals at the National Press Club

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This presentation contains forward-looking statements (as defined under the U.S. federal securities laws) of Telomir Pharmaceuticals, Inc. ("we," "us," or "our"). These statements reflect our current expectations and views of future events, including regarding our product candidate TELOMIR-1. You can identify forward-looking statements by terms such as "may," "will," "should," "expect," "plan," "anticipate," "could," "intend," "target," "project," "contemplate," "believe," "estimate," "predict," "potential", or "continue" or the negative of these terms or other similar expressions. Statements about our pre-clinical and clinical trials and expectations regarding such trials, the markets in which we operate, and statements about our other expectations, beliefs, plans, strategies, objectives, prospects, assumptions or future events (including the potential therapeutic benefits of our product candidate) are forward-looking statements. These statements are only predictions and involve significant known and unknown risks, uncertainties and other factors, which may cause our actual results, levels of activity, performance or achievements to be materially and adversely different from those expressed or implied by these forwardlooking statements. Some of these risks, uncertainties and other factors are identified in our most recent Annual Report on Form 10-K and in our other filings with the SEC, which are available at <u>www.sec.gov</u>. You should not place undue reliance on any forward-looking statement. We undertake no obligation to update or revise publicly any of the forward-looking statements after the date hereof to conform the statements to actual results or changed expectations except as required by law.

*Market size estimates in this presentation* have been determined on the basis of market research, but no assurances can be given that such estimates are accurate.





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**Questions and Answers – Kandi Amelon, Communications Consultant** 













Dr. Chris Chapman



Shoelaces

**Telomir Pharmaceuticals** is a preclinical stage pharmaceutical company focused on the development and commercialization of **Telomir-1**. Telomir-1 is

the first innovative and novel small molecule targeted at lengthening the

(Graphic: National Human Genome Research Institute)

Telomere





**Treatment Indications** – Elongating telomeres, age-related inflammatory diseases (osteoarthritis), and hemochromatosis.



### Large Market Opportunity

Osteoarthritis – \$7.4 billion worldwide in 2021, expected CAGR of 8.5% through 2030\*

**Global longevity** - according to Allied Market Research, the global longevity and anti-senescence therapy market was valued at \$25.1 billion in 2020, and is projected to reach \$44.2 billion by 2030, growing at a CAGR of 6.1% from 2021 to 2030.\*\*



Exclusive Licensing – An affiliated IP development company



### World-class Partners

IQVIA, Frontage, Eurofins, Charles River, DavosPharma, Argenta, Premier Consulting, Anthem Biosciences, and InSilicoTrials



### **Experienced Management Team**

25 years of publicly-traded pharmaceutical company experience



TELOMIR<sup>®</sup>

TELOMIR collaborated with InSilicoTrials, an innovator in leveraging AI and simulations to enhance drug development, to perform advanced AI modeling on Telomir-1. Early research has confirmed the mechanism of action of Telomir-1 and suggests that it may be a potent metal inhibitor, potentially leading to a reversal of aging through telomere regulation.



White=Hydrogen Black=Carbon Blue=Nitrogen Orange=Iron





### What do we mean by "Age Reversal" or "Anti-Aging"?

It's not the fountain of youth – it's the science of telomere elongation

While our initial proposed clinical indications for Telomir-1 are osteoarthritis and hemochromatosis, we are also more broadly studying the effect of telomere elongation on the ability of the body to repair itself, thereby potentially mitigating effects typically associated with aging.

By "age" we mean an examination in our pre-clinical animal testing of demonstrable endpoints like:

- weakness (video camera)
- Joint damage • assessment
- Dynamic weight • bearing (limb and tail) • Reduction in pain
- Clinical chemistry
- Hematology •

- Gait strength or Telomere length
  - Change in synovial • fluids
  - Fur and coat changes
  - Skin, hair and wrinkles changes

  - Behavior changes





### Effects of Telomir-1 in the Monosodium-Iodoacetate (MIA)-induced Osteoarthritis (OA) Joint Pain Model in the Aged Rat

- Adult Sprague Dawley rats at 7-9 months old will be used for the study.
- Osteoarthritis will be induced by intra-articular injection of MIA (Monoiodoacetate) in the knee joint on Day 0.
- Dosing of Telomir-1 by oral gavage will be performed from Day 3 to Day 14.
- Dynamic Weight Bearing (DWB) will be assessed at different time points (Day 4, 7, 10 and 14) for evaluation of joint nociception.





### Dynamic Weight Bearing System



- Bioseb's DWB allows to work with freely moving animals in a transparent cage with a matrix sensors embedded in the floor of the enclosure where the animal is free to move as it pleases.
- The animal is filmed from above for a duration of approximately 5 minutes.



- The video feed is analyzed in real-time during the test thanks to the tracking software allowing a precise analysis of the animal's posture.
- The weight bearing by the animal on each paw is measured by the sensor embedded on the mat on which the animal is walking.
- Difference between the weight the animal is putting on the MIA injected leg versus the non-injected leg will be calculated to assess the effect of Telomir-1 on joint pain.





• Whole blood will be collected for Telomer length

assessment.

### **Terminal Endpoints**

• Joint synovial fluid will be collected for inflammatory cytokines measurement







### Determining the efficacy of Telomir-1 on Mitigating the Clinical Signs of Osteoarthritis using a Femoral Induction Model in Laboratory Beagle Dogs

- Primary objective: Evaluate the efficacy of Telomir-1 for mitigating the progression of osteoarthritis based on symptomatic, radiographic, gross pathologic and histopathologic evaluations and age reversal
- **Secondary objective:** Demonstrate the safety of Telomir-1 when administered daily for 168 consecutive days
- Induction of osteoarthritis using femoral model



### Determining the efficacy of Telomir-1 on Mitigating the Clinical Signs of Osteoarthritis using a Femoral Induction Model in Laboratory Beagle Dogs

- Start of in-life phase Q2 2024 End of Live Phase (necropsy) Q4 2024
- Acclimation (SD -7 to -1); Induction Phase (SD 0 to 27); Treatment Phase (SD 56 to 196); Necropsy SD 197
- Physical examinations, gait analysis measurements (video camera), digital radiology, and hematology will occur every 4 weeks throughout the treatment phase for all 12 dogs.
- Necropsy (SD 197)
  - Femur and tibia will be separated, and the articular surfaces photographed for macroscopic cartilage damage scoring.
  - Histologic changes in the articular cartilage will be evaluated
  - Hematology, clinical chemistry, IL-17, and telomere length will be evaluated







\*One dog in each age group will not be enrolled in the treatment phase. If all the dogs within an age group are eligible for enrollment, the dog whose stage of osteoarthritis is least uniform to the broader age group based on radiographic evaluations will be excluded.











- I. Why Telomeres Matter to Longevity: Stem Cells Repair YOU
- II. Early Results Supporting Hypothesis that Telomir-1 Increases Telomere Length and that Telomir-1 May Do So By Increasing Telomerase

Kandi Amelon





### Stem Cells & Telomere Regeneration

- Stem cells are the matriarchs of the human body—the cells from which all other cells are derived. Another way stem cells are maternal: they come in and repair things
- We learned this after transplantation of a male heart into a female person...that male heart initially had an ejection fraction of 55%.
- The male heart subsequently had a heart attack. The woman got to the hospital and had blood flow to her male heart restored quickly. The heart after the restoration of blood flow had an ejection of about 30% but over 6 weeks the male heart regained an ejection fraction of 55%. On microscopic examination (Biopsy), female stem cells that repaired that male heart. (Quaini F et al: Chimerism of the Transplanted Heart NEJM 2002; 346:5-15)
- The Problem: each of us has a limited number of stem cells due to the fact they have limited telomeres and cannot reproduce more than the Hayflick limit of 70-110 times.
- That is the telomere protects your chromosomes, and is needed for replication, but gets shorter with each stem cell duplication so you as of now are limited in the duplications and repairs you can make ---really important after heart attacks and strokes but key to skin, cartilage, lung, most tissue repairs
  Dr. Michael F. Roizen



Roizen, M. Linneman, P., & Ratner, A. (2022). The Great Age Reboot: Cracking the Longevity Code for a Younger Tomorrow. National Geographic.



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- But let's say you can grow them --- they did that at Stanford for 18 patients with existing motor strokes with damage unrecovered after at least 6 years.
- They harvested their stem cells and grew them in culture by adding factors including telomerase that grew their telomeres and allowed the stem cell population to increase. They then injected the stem cells into the area of brain missing due to the stroke.
- 7 of the 18 patients had a major restoration of motor function after 6 weeks...apparently when the patients suffered the original stroke or brain damage, blood flow wasn't restored fast enough for their own stem cells to repair their brains at that time, or they didn't have enough stem cells (due to shortened telomers) to make the repairs.

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The Nobel Assembly at Karolinska Institute (Sweden) awarded the Nobel Prize in Physiology or Medicine 2009 jointly to Elizabeth Blackburn, Carol Greider and Jack Szostak for the discovery of how chromosomes are protected by telomeres and the enzyme telomerase.



Elizabeth Blackburn





### Stem Cells & Telomere Regeneration

- Stress **shortens** telomeres
- People who regularly eat sugar laden and processed food have **shorter** telomeres
- People who regularly do extreme physical activity have **shorter** telomeres
- Astronauts have shorter telomeres
- People who have sun burns or who smoke or vape have **shorter** telomeres
- People who regularly have short sleep times have **shorter** telomeres
- People who regularly eat healthily have **longer** telomeres
- People who regularly meditate have **longer** telomeres
- People who regularly have friends have **longer** telomeres
- People who regularly do moderate physical activity have **longer** telomeres
- People who regularly sleep 6.5 to 8.5 hours a night have **longer** telomeres
- People who regularly have sex have **longer** telomeres

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The overarching goal of the study was to evaluate evidence that TELOMIR-1 can promote telomere elongation and stability, leading to a slower progression of diseases and self-renewal.

We have limited stem cells to repair ourselves due to limits on telomeres and their shortening with each replication. Longer telomeres can give us more, meaning more ability to repair and renew ourselves.







### Stem Cells & Telomere Regeneration

- Imagine if you could repair each organ or tissue with age-related damage and make that tissue young again
- Young heart
- Young blood vessels
- Young brain
- Young joints
- Young back discs
- Young lung
- Young kidney
- Young gut

That is the promise of telomere regeneration...The ability to produce more stem cells and repair yourself.

Roizen, M. Linneman, P., & Ratner, A. (2022). The Great Age Reboot: Cracking the Longevity Code for a Younger Tomorrow. National Geographic.

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### Nasdaq: TELO

Disclaimer: While telomere elongation could have these beneficial impacts, these matters are not presently the subject of studies of Telomir-1.



# Early Data on Telomir-1 Elongating Telomeres And its Possible Mechanism of Action—Increasing Telomerase





Experimental Design for telomere length quantification. Briefly, MRC-5, HUVEC, or MSCs were grown to confluency and plated in a 12-well plate either untreated or treated with the TELOMIR-1 compound. After 48hours, DNA was extracted and then DNAs were subjected to qPCR via a kit. To evaluate our hypothesis that TELOMIR-1 influences telomere length, we conducted tests on human primary cell strains, specifically *HUVEC, MRC-5, and Bone Marrow-Derived Mesenchymal Stem Cells.* These particular strains were chosen due to their known propensity for senescence through cell passaging. Telomir-1 was evaluated for 1) cell cytotoxicity, 2) Telomere length modulation, 3) cell proliferation, and 4) TELOMIR-1-induced cell death





TELOMIR-1-mediated cytotoxicity was assessed. MRC-5, HUVEC, and MSCs were treated with TELOMIR-1 at 1, 10, 25, 50, 100, 250, 500, and 1000  $\mu$ M. TELOMIR-1 demonstrates no cytotoxicity at 1-250  $\mu$ M concentration in MRC-5 (Figure A) and HUVEC (Figure B), while at 500  $\mu$ M, a major cell loss was observed. In MSCs, cell loss was detected in culture treated with a vehicle, while TELOMIR-1 augmented the cell loss (Figure C). Therefore, MRC-5 strains and TELOMIR-1 compounds at 1-500  $\mu$ M concentrations were chosen for subsequent studies.

TELOMIR-1 cytotoxicity results and telomere length qPCR results. MRC-5, HUVEC, and MSC cells were treated with increasing concentrations TELOMIR-1 to demonstrate TELOMIR-1-induced cytotoxicity (A-C). 48-hour TELOMIR-1-treated MRC-5, HUVEC, and MSC cell DNA extracts were assayed by telomere length qPCR. Results were calculated based off of calculations using a telomere primer set that recognizes and amplifies telomere sequences, and a single copy reference primer set that recognizes and amplifies a 100 bp-long region on human chromosome 17 as an internal control (D-F). EtOH-treated cells at 1% (equivalent to 1 mM TELOMIR-1 treatment) served as a vehicle control in all experiments.

MRC-5, HUVEC, and MSCs were treated with TELOMIR-1 at 1, 50, 100, and 500  $\mu$ M concentrations (based on cytotoxicity data) and assessed for telomere length using qPCR. Telomere length was calculated as total telomere length/diploid cell. A trend where TELOMIR-1 induced telomere lengthening could be observed at concentrations greater than 1  $\mu$ M in all three cell lines, with some of the largest lengthening effects seen at 50  $\mu$ M (Figure D-F). Based on this observation, it suggests that the effect of the Telomir-1 compound is not cell-type restrictive.







#### High Dose Telomir-1 Induces Cell Apoptosis Instead of Necrosis in MRC-5



MRC-5 was treated with TELOMIR-1 at 500  $\mu$ M, a known concentration that led to cell loss in MRC-5. The treated cultures were then triple-stained with an anti-active Caspase-3 antibody, dead cell exclusion dye, and FITC-conjugated Annexin V, followed by flow cytometric analysis (A). TELOMIR-1 induced cell death in MRC-5, as evidenced by highlighted staining of Scarlet-conjugated dead cells and FITC-conjugated Annexin V channels. The double-positive cells were further analyzed for active Caspase-3 activity, where the population was considered apoptotic rather than necrotic (B). The heightened Caspase-3 activity indicates that the cells are going through an apoptotic cell death pathway, in contrast to necrosis.



**Apoptosis-mediated cell death in MRC-5 cells by TELOMIR-1 treatment**. (A) The population of untreated (i) and 500 µM treated (ii) MRC-5 cells on a bivariate plot of live/dead stain vs. FITC/Annexin V. Population in the lower left quadrant of (i) was further investigated with a BV650 anti-active Caspase-3 antibody (iii). Population in the upper right quadrant of (ii) was also further investigated with BV650 anti-active Caspase-3 antibody (iv). The mean fluorescence intensity (MFI) was quantified in (B).





### **Hypothesis**: TELOMIR-1 modulated telomere length via enhancing Telomerase activity.



- Previously, we've demonstrated that TELOMIR-1 did not affect telomerase activity in *passage <u>3</u>* of MRC-5 cells, which corresponded with the findings from the telomere length study.
- MRC-5 cells at **passage 4** responded to TELOMIR-1mediated telomere length modulation, whereas cells at passage 3 did not.
- Therefore, the study on telomerase activity was conducted again using passage 4 of MRC-5 cells and 3 replicates.





**Background**: MRC-5 Passage 4 (P4) cells were treated with 1, 50, 100, and 500 µM of TELOMIR-1. Cells were then lysed and processed for telomerase activity using qPCR.

Telomerase Activity, 24 hr treatment MRC5 (P4)



#### **Results**:

Telomir-1 (µM)

- TELOMIR-1 enhanced Telomerase activity in MRC-5 cells in a dose-dependent manner (~40%).
- The enhancement of telomerase activity ceased to be effective at 500  $\mu$ M, likely due to cell cytotoxicity.

Dr. Michael F. Roizen



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### Conclusions



- 1. The data confirmed our hypothesis that TELOMIR-1 affects telomere length, promoting its **extension** in primary cell strains including MRC-5, HUVEC, and MSCs (~40% increase).
- 2. TELOMIR-1 was observed to cause cell cytotoxicity at a concentration of 500  $\mu$ M in both MRC-5 and HUVEC cells.
- 3. Despite cell loss exacerbated by the ethanol vehicle, **TELOMIR-1** was effective in extending telomere length in MSC cells.
- The cytotoxic effect of 500 μM TELOMIR-1 in treated cultures was apoptotic, demonstrated by an increase in active Caspase-3 expression (less necrotic cell death, less inflammatory response, more recycled cell constituents).
- 5. Data confirmed our hypothesis that TELOMIR-1 increases telomerase activity by 40%.





Telomir Pharmaceuticals has formed a Georgetown Group --- this Group of 14 from fields of Medicine, Medical Ethics, Public Relations, Law and Economics has begun work to address obvious issues in Telomir's development:

### **1.** Formation of an Ethical Advisory Panel:

- Establish a diverse advisory panel to provide guidance on ethical issues, equitable distribution, and social implications of Telomir.
- Engage with international representatives to ensure a global perspective, especially from regions that are often underrepresented in pharmaceutical benefits.

### 2. Equitable Access Strategy:

- Develop a pricing and distribution strategy that promotes equitable access. This might be less of an issue with a small molecule that is relatively inexpensive to produce as well as might include tiered pricing models, subsidies, or partnerships with governments and NGOs.
- Collaborate with insurance companies and healthcare providers to explore coverage options, ensuring affordability for a broader population.

### **3.** Safety and Efficacy Transparency:

- Once safety is established, maintain transparency about the efficacy and limitations of Telomir-1 to prevent misinformation and unrealistic expectations.
- Publish research findings in accessible formats and languages to ensure broad understanding.





## **Questions from the Audience**

Kandi Amelon







# TELOMIR<sup>™</sup> AGE REVERSAL

## Thank You



