Alzheimer’s Disease (AD) is an age-related, progressive neurological disorder defined by the dysfunction and loss of neurons and synapses, with severe cognitive dysfunction. It is seen in 1-in-10 individuals over age 65 and nearly half of people over age 85. The incidence doubles about every 5 years after age 60.

Pharmaceutical companies fail to find a cure because they don’t understand the disease. Telocyte’s team understands precisely how Alzheimer’s disease works and possesses the optimal target to prevent and cure Alzheimer’s. Telocyte can move faster, with lower cost, fewer patient trials, and with effective results.

We can deliver what our investors want and our patients need:

*A future beyond Alzheimer’s.*
Market

- 6.5M new AD patients per year
- $7B annual global drug sales, without clinical efficacy
- $15B annual market by 2026
- $200B US Alzheimer's costs in 2015

Alzheimer’s patients and costs 2010 - 2050

Alzheimer’s Study Group, A National Alzheimer’s Strategic Plan: The Report of the Alzheimer’s Study Group (March 2009); Alzheimer’s Association, Changing the Trajectory of Alzheimer’s Disease: A National Imperative (May 2010); National Institute of Health Office of the Budget.
Product  

- Product: Telomerase gene therapy (TEL-01)  
  - Vector: Adeno-associated virus (AAV)  
  - Plasmid: Telomerase (hTERT and CMV)  
  - Target: Glial cells and neurons (brain)  
  - Delivery: IT (lumbar puncture, single dose)  

- Replicates the results shown in mice (mTERT) in humans (hTERT)  
  - FDA approval phase 1 Human Trial  
  - Initial results of efficacy against Alzheimer’s  
  - Proceed with phase 2 and 3
Telocyte’s therapy, TEL-01, **effective** in animal trials, can go to market quickly and efficiently

- Competing therapies, based on small molecular or antibody approaches, require extensive experimentation

TEL-01 addresses the **root cause**, rather than merely downstream symptoms or biomarkers

- Competing therapies universally fail, as they target symptoms and biomarkers alone

TEL-01 can **largely reverse the cognitive decline seen in Alzheimer’s**

- Competing therapies have never been able to slow, let alone stop or reverse cognitive decline

Telocyte is perfectly positioned to achieve FDA **expedited program status** and go to market early

- The multiple tracks for expedited approval: all apply to Telocyte’s FDA application
How Alzheimer’s works

Cell Senescence
- Shortened Telomeres
- Altered Gene Expression
- Cell Dysfunction

Upstream
- Genetic Predisposition
- Chronic Disease
- Trauma
- Hypertension
- Abnormal Microenvironment
- Radiation
- Stress/Contact
- Hormonal Factors
- Infection
- Anti-Inflammatory Therapy
- Other Variables

Downstream
- Beta Amyloid Plaques
- Tau Tangles
- Mitochondrial Dysfunction
- Slower DNA Repair
- Lower ATP/ROS Ratio
- Lower Lipid Turnover
- Poorer ROS Sequestration
- Elevated AGE Products
- Vascular Endothelial Failure
- Intermediary Changes
- Lipid Accumulation
- Other Biomarkers...

Single most effective point of intervention

Telocyte approach for curing AD

- Glial cell dysfunction as the primary cause of AD due to glia cell division causing cell aging
- Reverse cell aging by resetting gene expression
  - Glia have reduced β amyloid-binding, phagocytosis, and degradation with age

Our collaborator, Maria Blasco, CNIO’s Director, showed that we can safely restore brain function and extend healthy *mouse* lifespan by 13 - 24%

**de Jesus et al. Telomerase gene therapy in adult and old mice delays aging and increases longevity without increasing cancer.** *EMBO Mol Med* 2012; 4:691-704. [https://doi.org/10.1002/emmm.201200245](https://doi.org/10.1002/emmm.201200245)
Management Team

**Founder, President**
Michael Fossel MD, PhD
The driving force behind Telocyte, Fossel has been the leader in proposing the use of telomerase to treat age-related human disease for the past two decades, a Clinical Professor of Medicine (retired), with an MD and PhD in Neurobiology from Stanford. He authored *The Telomerase Revolution* (*Wall Street Journal* named it one of the best science books of 2015) and the Oxford University Press textbook, *Cells, Aging, and Human Disease*.

**Founder, CEO**
Peter Rayson
An experienced industry executive, Rayson provides leadership and business acumen for Telocyte. His background includes engineering management with ComputerVision, as well as working with Rolls Royce, Airbus, Ford, Jaguar Land Rover. He was the Associate Director of the Technology Innovation Center at Birmingham City University, but stepped down in 2011 when his mother was diagnosed with dementia.

**COO**
Mark Hodges
An experienced technology executive, Hodges provides effective and inspiring leadership for all Telocyte programs and services. His background includes executive experience in the aerospace and defence industries, CAD business development, including at ComputerVision with Peter Rayson. He was the General Manager of China Operations, where he managed 500 engineers across 15 offices for PTC Inc., a listed Boston engineering software firm.
Science Advisory Board

Zaven Khachaturian
PhD
SAB Member
Alzheimer’s Disease Models
NIA/NIH

Mimoun Azzouz
PhD
SAB Member
Neuroscience
Gene Therapy
Translational Research

Suzanne Hendrix
PhD
SAB Member
Alzheimer’s Disease
Statistics
Analysis
Clinical Trial Design

Russell Swerdlow
MD
SAB Member
Neurology
Alzheimer’s Disease
FDA Clinical Trials

Joseph Araujo
PhD
SAB Member
Neuroscience
Veterinary Medicine
Translational Research
Detailed clinical program

| Eapsed Months from Investment Date | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 | 32 | 33 | 34 | 35 | 36 | 37 | 38 | 39 | 40 | 41 | 42 | 43 | 44 | 45 | 46 | 47 | 48 | 49 | 50 | 51 | 52 | 53 | 54 |
|-----------------------------------|---|---|---|---|---|---|---|---|---|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|

$10.3M investment round 1 → $15.1M investment round 2

**FDA ENGAGEMENT**
- Pre-IND Meeting
- FDA IND Submission
- Approval to proceed from FDA
- Phase I Human trial results available to FDA
- FDA approval for Phase II or 'Fasttrack' Phase III trials
- Phase II Human trial results available to FDA

**PRE-CLINICAL TRIALS**
- Update CRO Gap Analysis
- Meeting request to FDA
- Pre-clinical IP submission
- Test specification & lab process
- Animal Toxicity Tests commence
- Animal Toxicity Tests completed

**TEL-01 MANUFACTURE & SUPPLY**
- TEL-01 Manufacturing process begins
- TEL-01 for Animal Toxicity available
- TEL-01 GMP for Phase I trials available
- TEL-01 GMP for Phase II trials available

**CLINICAL (HUMAN) TRIALS**
- Phase I
  - Phase I IP submission
  - Phase I candidates selected and success criteria confirmed
  - Phase I trials commence
  - Phase I trials completed
- Phase II
  - Phase II IP submission
  - Phase II candidates selected and success criteria confirmed
  - Phase II trials commence
  - Phase II trials completed

**FDA ENGAGEMENT** continues with further milestones and processes.
## Expedited program status speeds approval

- The FDA facilitates breakthrough therapies in a quicker go-to-market, if they meet a set of criteria. These criteria apply to TEL-01.
- If expedited program status is approved, our planning can be sped up by approximately one year.

### Reasons for denial EP status, N=109

<table>
<thead>
<tr>
<th>Reason for Denial</th>
<th>Count (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Trial or analysis issues</td>
<td>78 (72%)</td>
</tr>
<tr>
<td>2 Lack of substantial improvement</td>
<td>58 (53%)</td>
</tr>
<tr>
<td>3 Lack of data</td>
<td>18 (17%)</td>
</tr>
<tr>
<td>4 Safety concern</td>
<td>12 (11%)</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>14 (13%)</td>
</tr>
</tbody>
</table>

#### 1 Trial or analysis issues
- Alzheimer's is uniformly fatal, TEL-01 addresses an unmet medical need
- TEL-01 provides substantial improvement over existing therapies

#### 2 Lack of substantial improvement
- Animal trials show a substantial improvement in brain function

#### 3 Lack of data
- Clinical data is well documented, published and peer-reviewed

#### 4 Safety concern
- Safety concerns are unlikely due to the track record of AAV9, hTERT is a gene known to the human body

- 50% of ep-status resubmissions were granted
<table>
<thead>
<tr>
<th>Risk</th>
<th>Chance, Impact</th>
<th>Mitigation strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FDA</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Refuses IND permit</td>
<td>low</td>
<td>Resubmit&lt;br&gt;Respond to FDA concerns and resubmit the permit request</td>
</tr>
<tr>
<td>Refuses 'expedited programs' status</td>
<td>low</td>
<td>Continue FDA process&lt;br&gt;Instead of receiving a 12-month acceleration, we would continue our current timeline for FDA trials and commercialization</td>
</tr>
<tr>
<td>Requires an additional species</td>
<td>low</td>
<td>Add animal study in parallel&lt;br&gt;No delay to the program, but increased cost of 2nd animal</td>
</tr>
<tr>
<td><strong>Immune response</strong></td>
<td>low</td>
<td>Adjust steroid preload&lt;br&gt;Intrathecal route offers a low probability for an immune response</td>
</tr>
<tr>
<td>Empty virions</td>
<td>low</td>
<td>Adjust CMC with supplier&lt;br&gt;Probabilities are falling with advancing technology</td>
</tr>
<tr>
<td><strong>Cytokine storm</strong></td>
<td>low</td>
<td>Admit if needed&lt;br&gt;CRS is extremely unlikely as we are not changing genes or using CAR-T therapy, and is not seen with AAV alone</td>
</tr>
<tr>
<td>Other side-effects</td>
<td>low</td>
<td>Monitor and treat as indicated&lt;br&gt;Side effects related to therapy have been beneficial rather than adverse and incidental side effects of AAV alone have not slowed clinical trials</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Risk</th>
<th>Chance, Impact</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Efficacy</td>
<td>low</td>
<td></td>
</tr>
<tr>
<td>Cells don't respond</td>
<td>low</td>
<td>Share CMC risk contractually&lt;br&gt;Aldevron, our plasmid vendor was specifically chosen for their quality and FDA CMC compliance.</td>
</tr>
<tr>
<td>Other therapies work better</td>
<td>negligible</td>
<td>Negligible likelihood&lt;br&gt;Other therapeutic approaches have uniformly failed to have any effect whatsoever on disease course</td>
</tr>
<tr>
<td><strong>Competition</strong></td>
<td>medium</td>
<td>Fast route to market&lt;br&gt;Rapidly finish up development and go to market with a successful competitor with broad market access</td>
</tr>
</tbody>
</table>

**Post-mitigation**<br>low risks with FDA and TEL-01 safety and efficacy<br>low risk of competing therapies putting pressure on margins, as these cures are expected to be less effective, facing strong competition from TEL-01 worldwide

**LOW RISK**