Telocyte

A future beyond Alzheimer's

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.

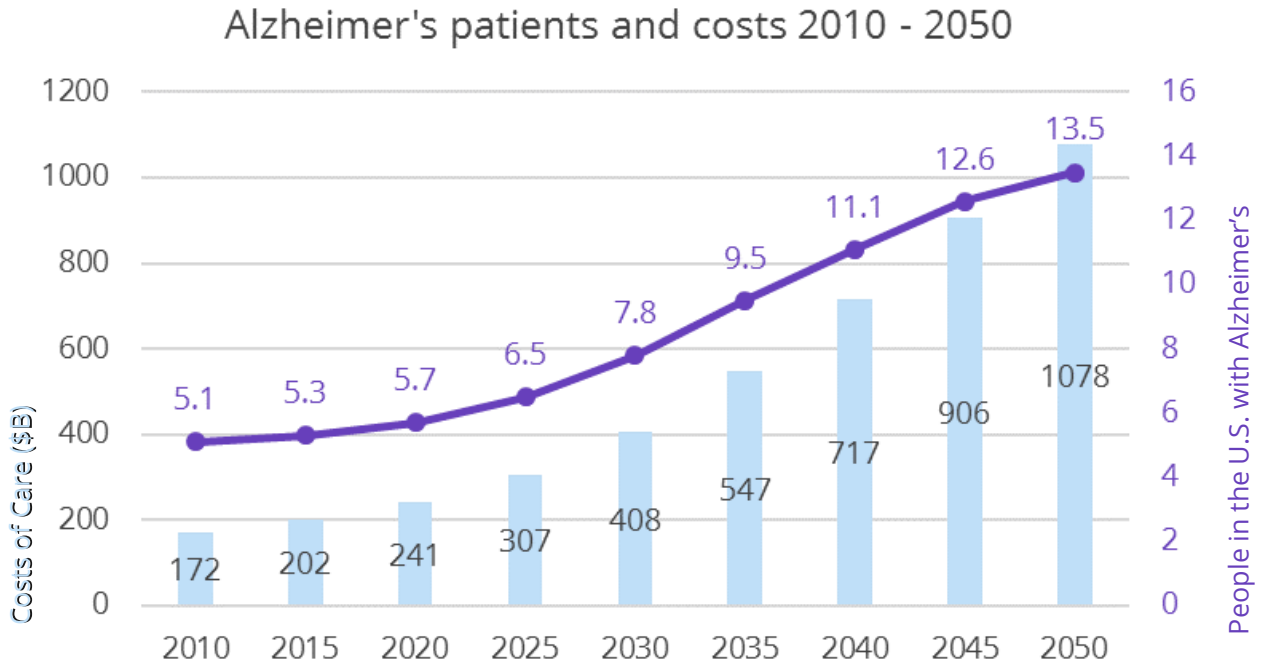
We can deliver what our investors want and our patients need:

A future beyond Alzheimer's.

TELOCYTE LLC
250 Monroe NW
Grand Rapids, MI, 49503 USA
www.telocyte.com

Market

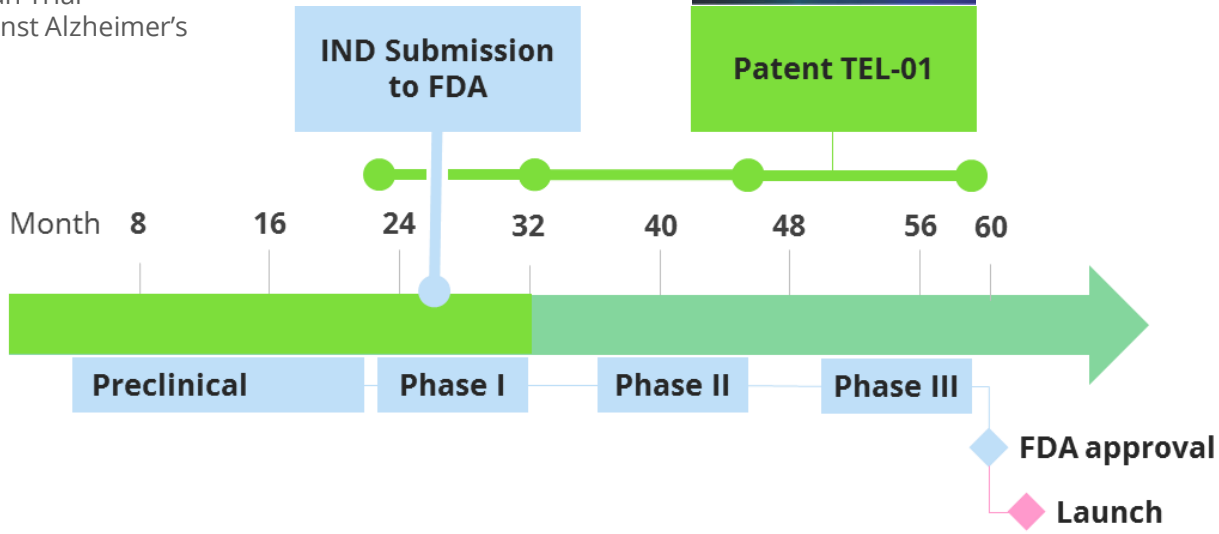
- 6.5M new AD patients per year
- $7B annual global drug sales, without clinical efficacy
- $15B annual market by 2026
- $200B US Alzheimer's costs in 2015



Alzheimer's 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



Unique intervention

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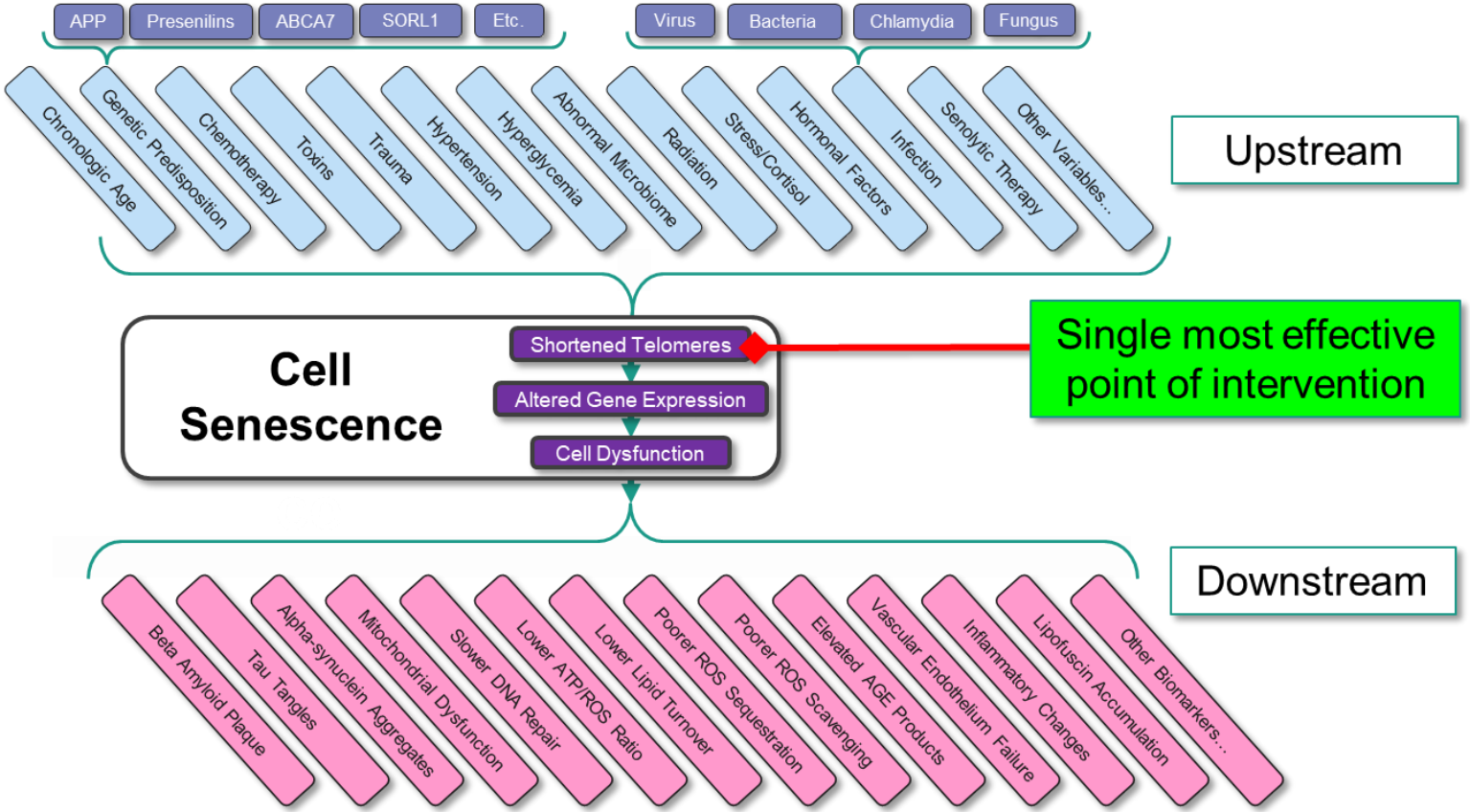
- Telocyte's therapy, TEL-01, **effective** in animal trials, can go to market quickly and efficiently
  - Competing therapies, based on small molecular or antibody approaches, require extensive experimentation
- TEL-01 addresses the **root cause**, rather than merely downstream symptoms or biomarkers
  - 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



Fossel M. A Unified Model of Dementias and Age-Related Neurodegeneration. *Alzheimer's & Dementia: The Journal of the Alzheimer's Association*. January 2020. https://doi.org/10.1002/alz.12012

Competition

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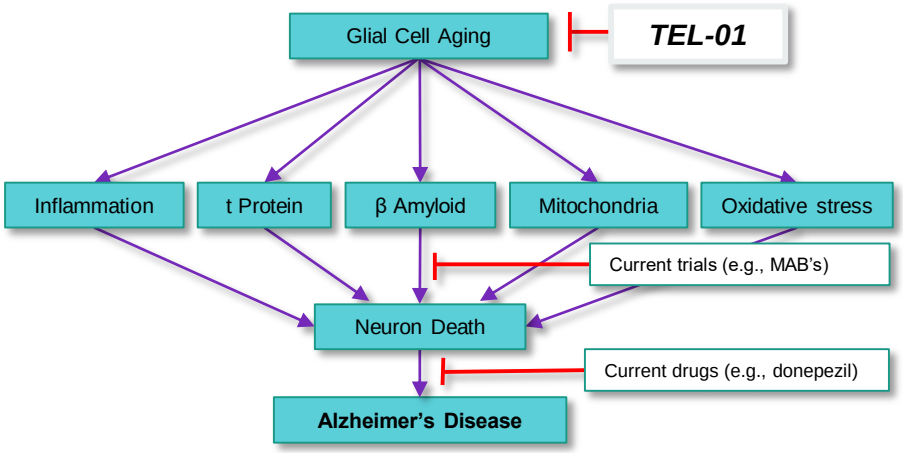
Telocyte approach for curing AD

- 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



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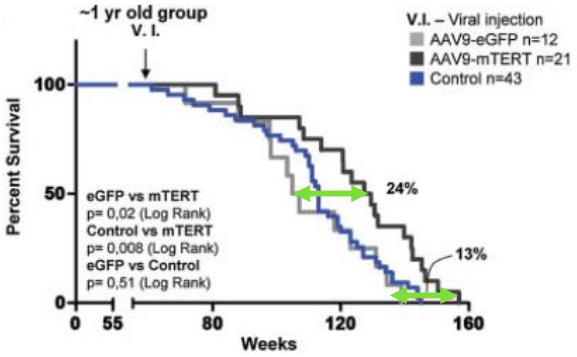
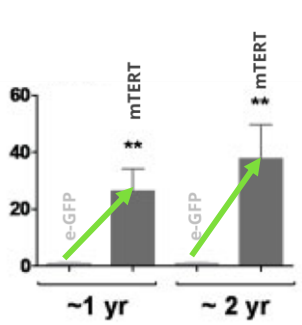
Boccardi et al. From cellular senescence to Alzheimer's disease: The role of telomere shortening. *Ageing Research Reviews. 2015;* 22:1–8. https://doi.org/10.1016/j.arr.2015.04.003
Hickman et al. Microglial Dysfunction and Defective Amyloid Clearance Pathways in Aging Alzheimer's Disease Mice. *Journal of Neurosci*. 2008; 28:8354–8360. https://doi.org/10.1523/jneurosci.0616-08.2008

Animal trial shows restored brain function

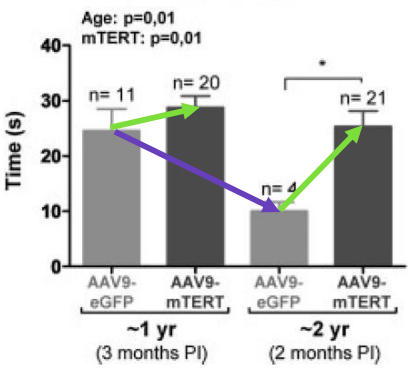
- Our collaborator, Maria Blasco, CNIO's Director, showed that we can safely restore brain function and extend healthy *mouse* lifespan by 13 - 24%

AAV9-eGFP = ineffective gene
AAV9-mTERT = cure restoring brain function

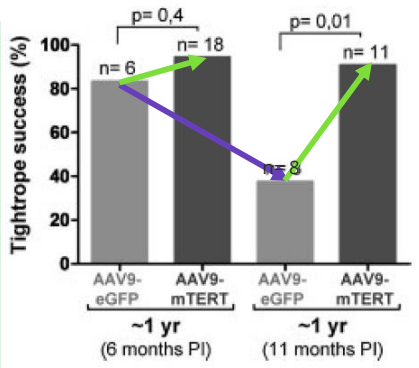




fold change in mRNA



coordination and balance



neuromuscular coordination

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

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 back ground 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

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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

alzheimer's association | Alzheimer's & Dementia
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION
jad2020
The Campaign to Prevent Alzheimer's Disease by 2020

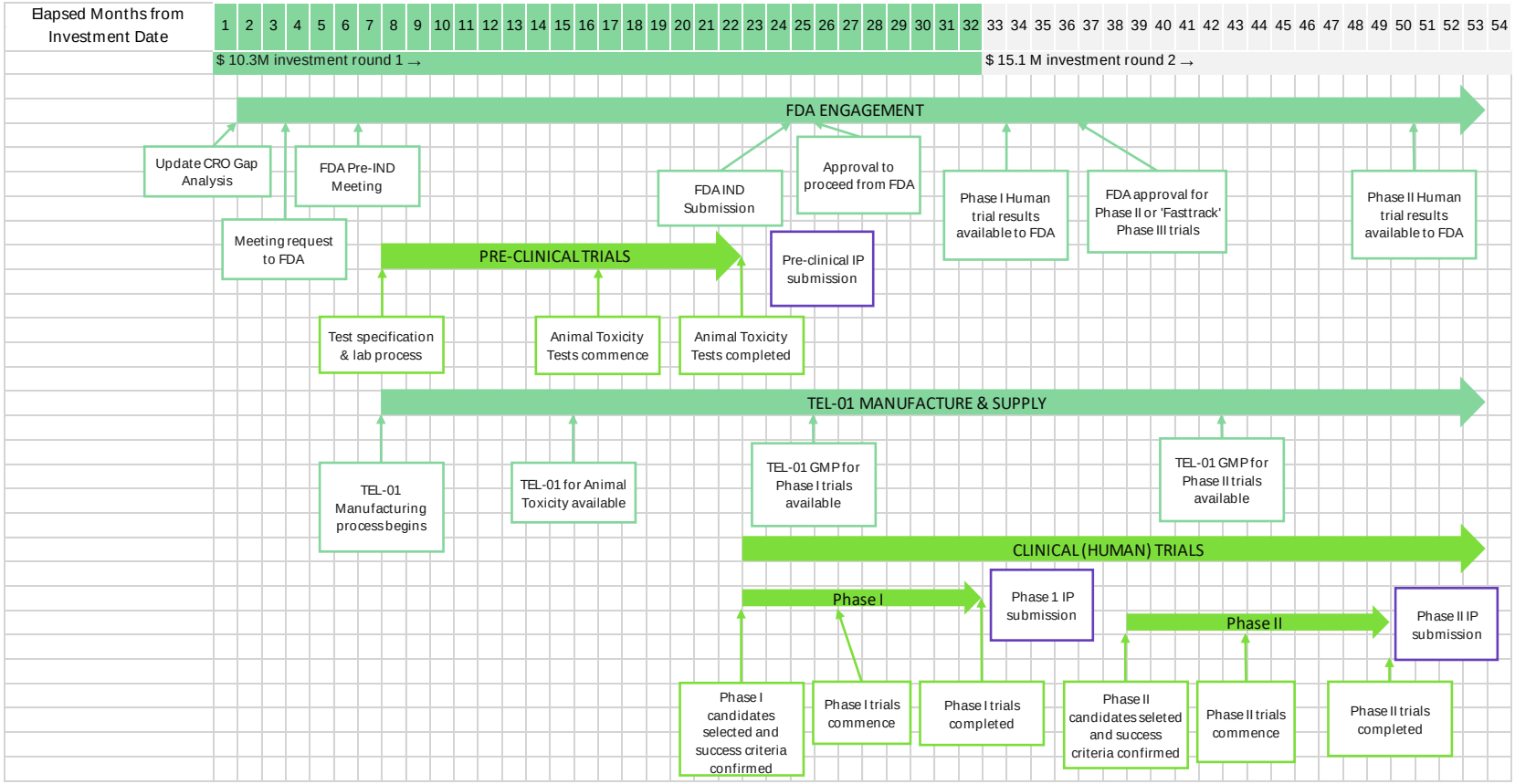
The University Of Sheffield.

Pentara

KU MEDICAL CENTER
The University of Kansas

InterVivo SOLUTIONS

Detailed clinical program



Expedited program status speeds approval

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- 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

FDA *Therapy addresses "serious conditions and fills an unmet medical need"*
FDA *"Demonstrates substantial improvement over available therapy"*

- Alzheimer's is uniformly fatal, TEL-01 addresses an unmet medical need
- TEL-01 provides substantial improvement over existing therapies

Telocyte's:

1 Science Advisory Board has ample experience with **FDA trials and analysis**

- Experience with FDA trials improves odds of success 20% → 61% (FDA, 2015)

2 Animal trials show a **substantial improvement** in brain function

3 **Clinical data** is well documented, published and peer-reviewed

4 **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

Reasons for denial EP status, N=109	
1 Trial or analysis issues	**78 (72%)**
• Trial design issues	45 (41%)
• Sample issues	39 (36%)
• Endpoint issues	29 (27%)
• Results too preliminary	19 (17%)
• Flawed post-hoc analysis	17 (16%)
2 Lack of substantial improvement	**58 (53%)**
3 Lack of data	**18 (17%)**
• No clinical data	4 (4%)
• Incomplete data	14 (13%)
4 Safety concern	**12 (11%)**
Miscellaneous	**14 (13%)**
• Not a serious condition	2 (2%)
• Other	12 (11%)

Risks

Risk		Chance, Impact	Mitigation strategy
FDA	Refuses IND permit	o low 3-month delay	**Resubmit** Respond to FDA concerns and resubmit the permit request
	Refuses 'expedited programs' status	o low No change from current program	**Continue FDA process** Instead of receiving a 12-month acceleration, we would continue our current timeline for FDA trials and commercialization
	Requires an additional species	o low Additional costs and delays	**Add animal study in parallel** No delay to the program, but increased cost of 2nd animal
Safety	Immune response	o low 2-month delay	**Adjust steroid preload** Intrathecal route offers a low probability for an immune response
	Empty virions	o low 2-month delay	**Adjust CMC with supplier** Probabilities are falling with advancing technology
	Cytokine storm	o low 1-month delay	**Admit if needed** CRS is extremely unlikely as we are not changing genes or using CAR-T therapy, and is not seen with AAV alone
	Other side-effects	o low No delay	**Monitor and treat as indicated** Side effects related to therapy have been beneficial rather than adverse and incidental side effects of AAV alone have not slowed clinical trials

Risk		Chance, Impact	Mitigation strategy
Efficacy	AAV9 vector fails	o low 6-month delay	**Share CMC risk contractually** Lonza, our AAV vendor was specifically chosen for their vector quality and FDA CMC compliance
	Cells don't respond	o low 6-month delay	**Share CMC risk contractually** Aldevron, our plasmid vendor was specifically chosen for their quality and FDA CMC compliance.
	Other therapies work better	o negligible ! Therapy denied	**Negligable likelihood** Other therapeutic approaches have uniformly failed to have any effect whatsoever on disease course
Competition	Competing therapy	o medium 2-30% lower margins	**Fast route to market** Rapidly finish up development and go to market with a successful competitor with broad market access

Post-mitigation

o low risks with FDA and TEL-01 safety and efficacy

o 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

investment profile

LOW RISK