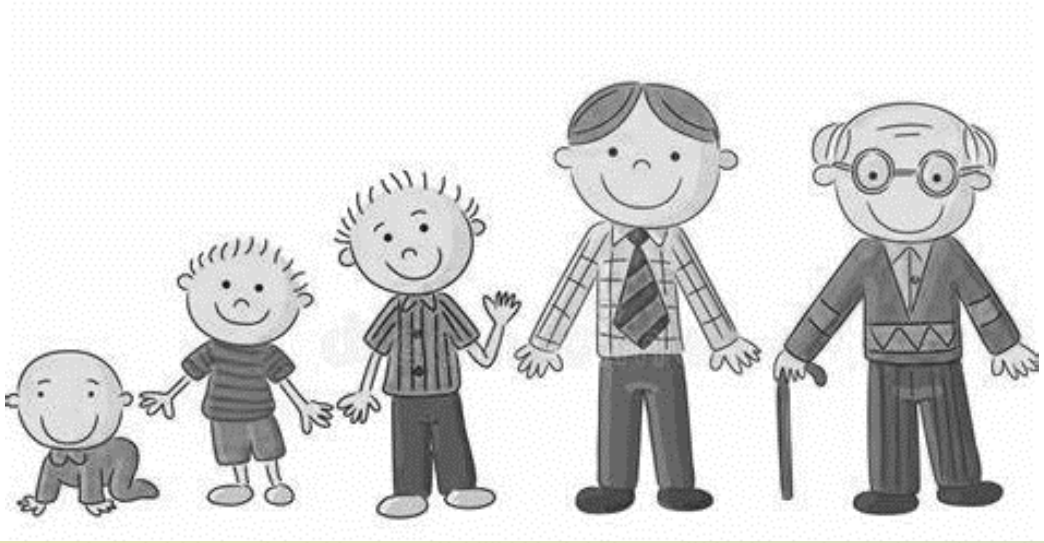
Centenara Labs

Age Better, Live Longer

- Aging is characterized by a progressive loss of physiological integrity, leading to impaired function and increased vulnerability to death.

- It is cumulative, processes that interfere with the function of the body.



One common denominator of aging is the accumulation of genetic damage throughout life

The Global Impact of Aging: A Growing Financial and Health Challenge

- **Number of people worldwide who will be age 65 and older by 2030[1]: 1 in 8**
- **Growth rate of older populations in developed countries between 2010 and 2050[2]: 71%**
- **Percentage of older Americans living with one chronic condition: 80%**

  percentage living with at least two[3]: 50%
- **Expected percentage of Americans living with cardiovascular disease in 2030[4]: 41%**
- **Frequency that an American dies from a coronary event: one every minute**

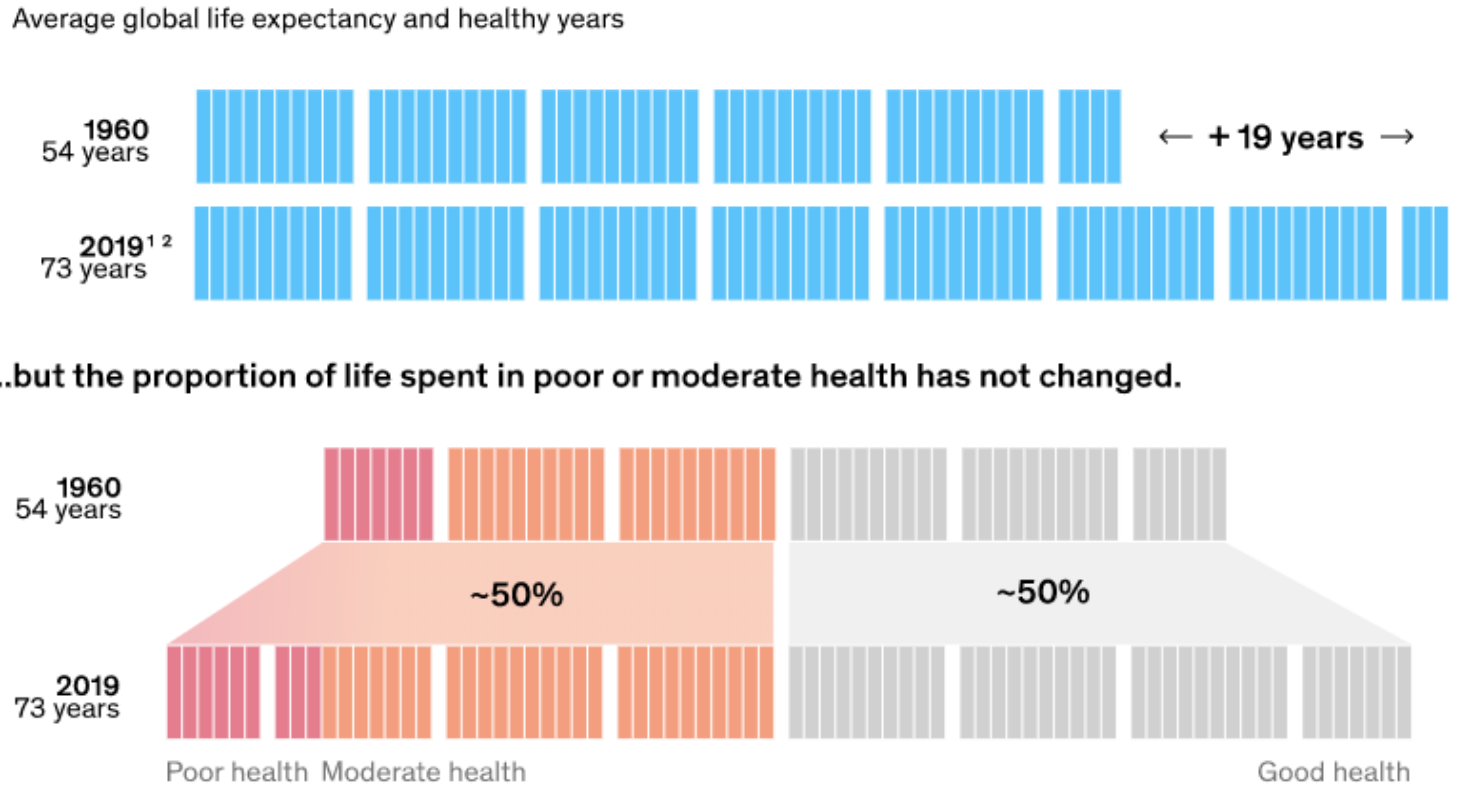
1 National Institute on Aging. "Overview: Our Aging World." *Why Population Aging Matters: A Global Perspective*.

2 National Institute on Aging. "Humanity's Aging." *Global Health and Aging*.

3 National Center for Chronic Disease Prevention and Health Promotion, Division of Adult and Community Health. "At a Glance 2011" *Healthy Aging: Helping People to Live Long and Productive Lives and Enjoy a Good Quality of Life*.

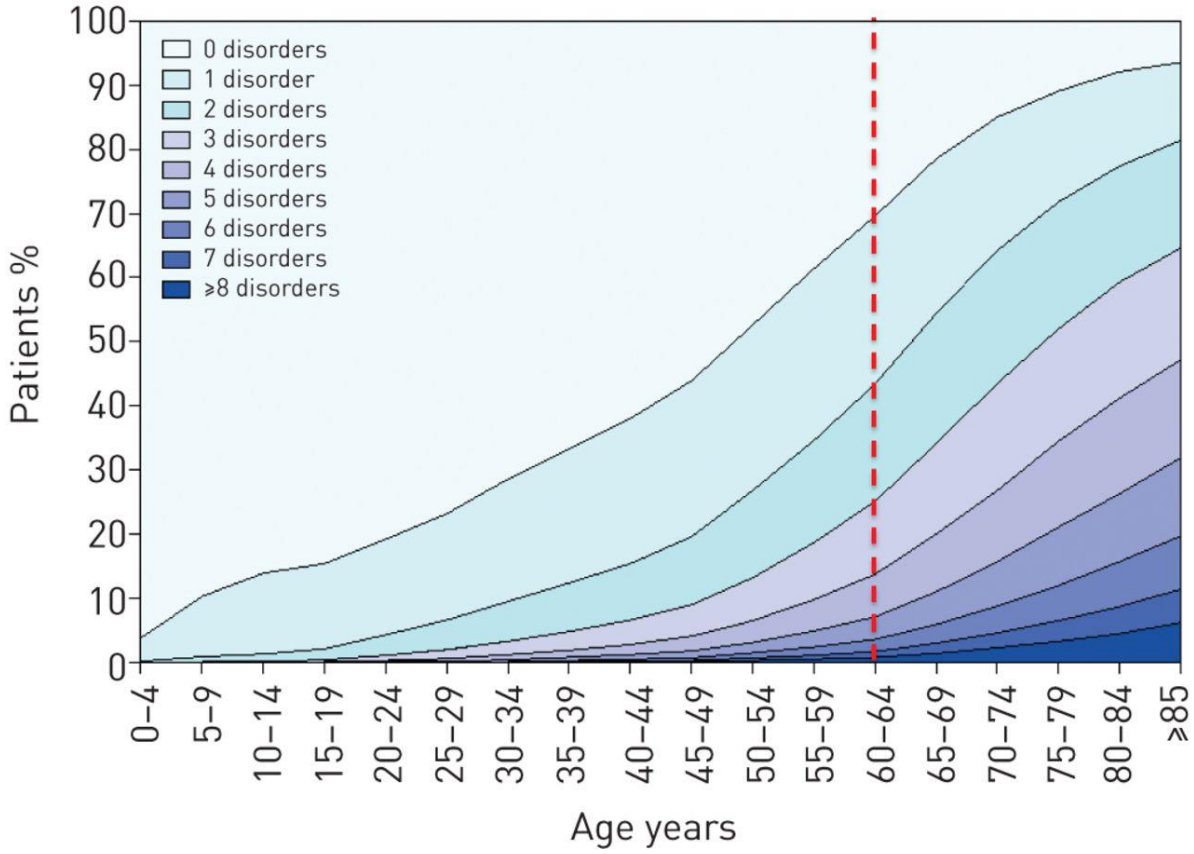
Aging Without Quality: Longer Lifespan but Decreased Well-Being

The past 60 years have seen massive improvements in global life expectancy …



Source: McKinsey Health Institute Report

The Number of Comorbidities by Age Stratum

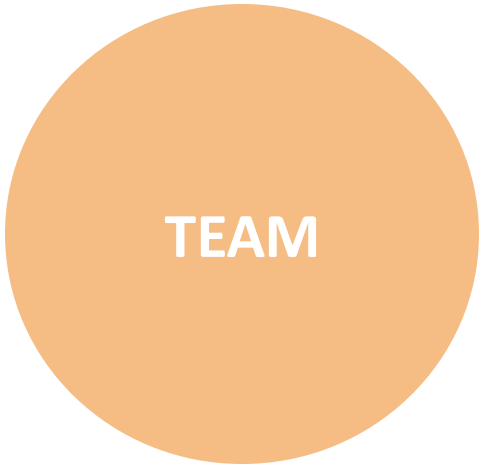


Source: Divo, M. J., Martinez, C. H., & Mannino, D. M. (2014). Ageing and the epidemiology of multimorbidity. *European Respiratory Journal*, *44*(4), 1055-1068.

*”We really have not experienced much compression of morbidity to date because **we have reduced mortality more than we prevented morbidity**. Healthspan will be increased when morbidity is decreased, most effectively through raising the age of onset.”*

- From Lifespan to Healthspan expansion -

Source: Crimmins, E. M. (2015). Lifespan and healthspan: past, present, and promise. *The Gerontologist*, *55*(6), 901-911.



Centenara Labs

Swiss-based **clinical** stage biotech company with a **hub-and-spoke model** that **develops regenerative medicine therapies for age-related disorders**

Experienced team of **leading pharma drug developers and visionary scientists** working together to build a business that provides the **best translational capabilities** to the novel discoveries

Our Mission

1

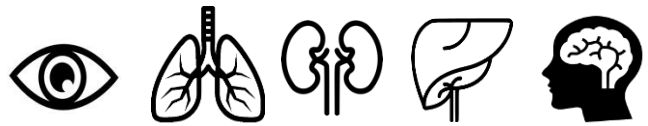
Preserving physical and mental fitness, as well as sensory capabilities, is paramount because it directly impacts the quality of life, enabling individuals to lead active, fulfilling lives well into old age

2

By addressing the root causes of decline in these areas, we offer life-changing therapies that could significantly improve the lives of many people

3

Our Focus Areas



We aim to empower individuals to sustain their independence and well-being, enabling them to enjoy a longer, healthier life

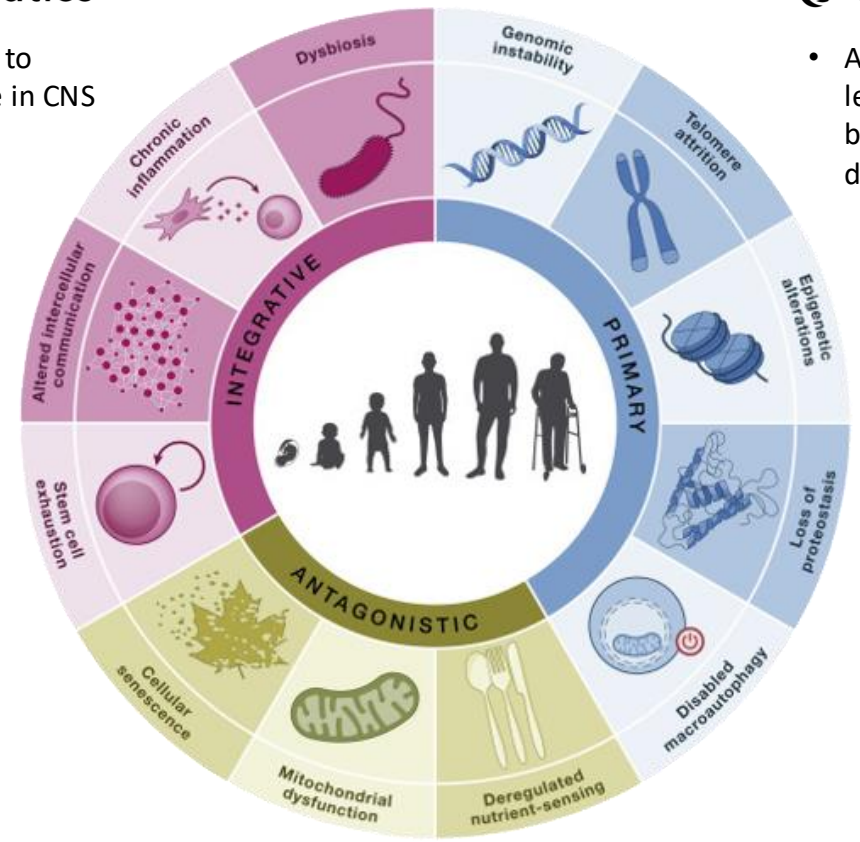
Centenara's Multi-Focused Approach: The Twelve Hallmarks of Aging

vascular therapeutics

- Targeting brain vasculature to combat age-related decline in CNS function

telomere therapeutics

- Aiming to restore telomere length, offering potential breakthroughs in aging and disease treatment.



endogena

- Retinitis Pigmentosa: Successfully completed Phase 1b/2a clinical study, demonstrating safety and early signs of efficacy. Received FDA Fast Track and Orphan Drug Designations.
- Dry-AMD: Phase 1 study planned to begin in 2025.

HEALTHY FOR LIFE RejuvenateBiomed

- Develops unique combination drugs targeting various age-related diseases with its lead clinical program already demonstrated therapeutic potential in muscle weakness induced sarcopenia.

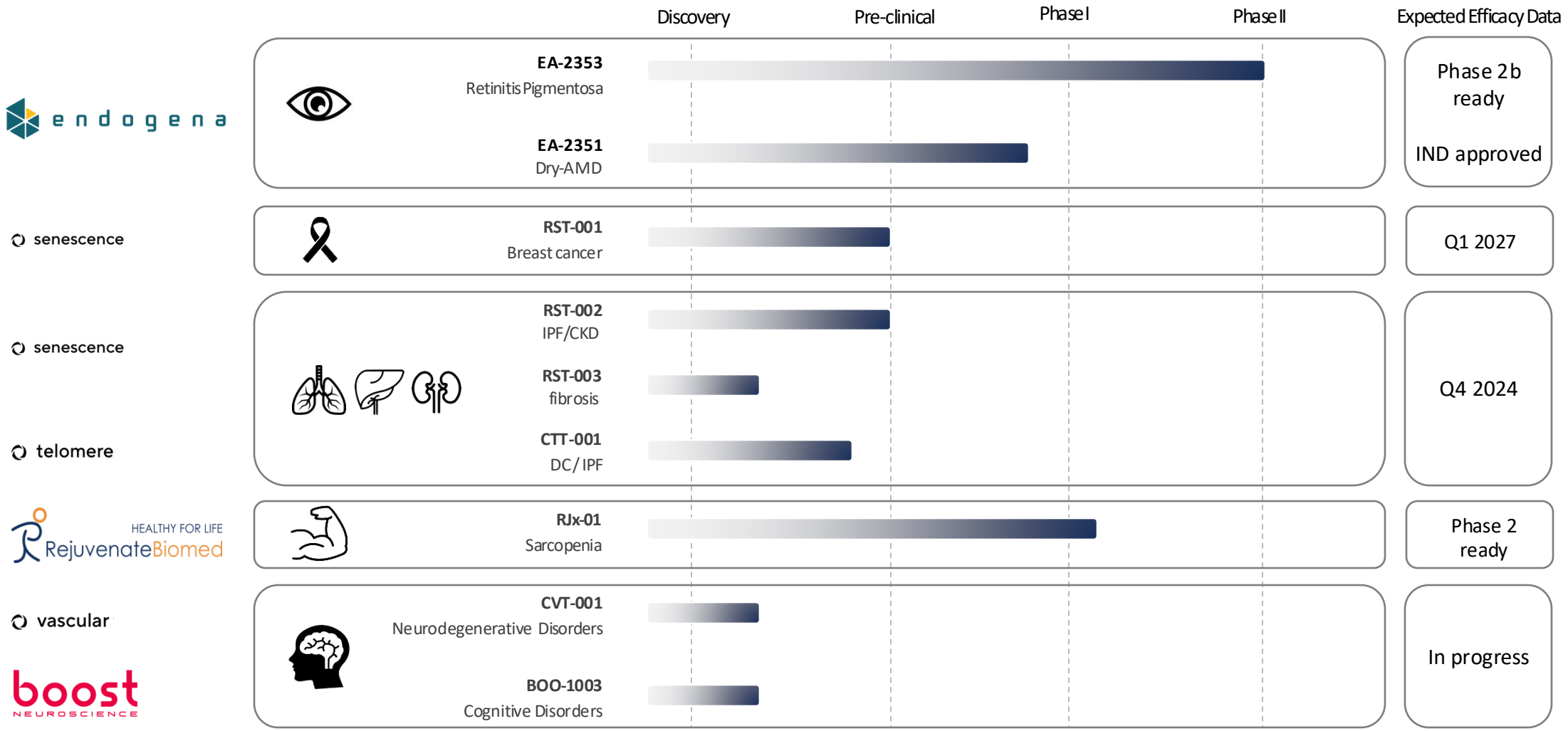
senescence therapeutics

Targeted removal of senescent cells induces a powerful anti-fibrotic effect in a variety of animal models. With several first-in-class targets identified, the platform is pioneering the next generation of fibrosis treatments

CellPress

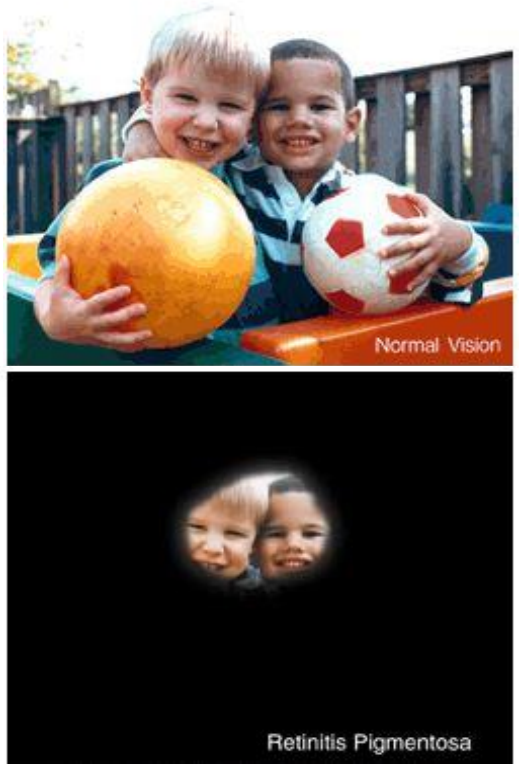
Source: From discoveries in aging research to therapeutics for healthy aging; Campisi et al. Nature 571, 183–192 (2019)
The Hallmarks of Aging; Carlos Lopez-Otin, Maria A. Blasco, Linda Partridge, **Manuel Serrano**, Guido Kremer, Cell 153, Issue 6 (2013)
Hallmarks of aging: An expanding universe; Carlos López-Otín, Maria A. Blasco, Linda Partridge, **Manuel Serrano**, Guido Kroemer, Volume 186, Issue 2 (2023)

R&D Pipeline


Discovery
Pre-clinical
Phase I
Phase II
Expected Efficacy Data
endogena
EA-2353
Retinitis Pigmentosa
EA-2351
Dry-AMD
Phase 2b ready
IND approved
senescence
RST-001
Breast cancer
Q1 2027
senescence
RST-002
IPF/CKD
RST-003
fibrosis
telomere
CTT-001
DC/ IPF
Q4 2024
HEALTHY FOR LIFE
RejuvenateBiomed
RJx-01
Sarcopenia
Phase 2 ready
vascular
boost
NEUROSCIENCE
CVT-001
Neurodegenerative Disorders
BOO-1003
Cognitive Disorders
In progress

REGENERATIVE MEDICINE

Centenara Labs



1 AN UNMET MEDICAL NEED

- Rare, inherited retinal disease (1:4,000) caused by mutations in more than 50 genes, resulting in the degeneration of photoreceptors
- Onset at a young age and most patients are legally blind by age 40
- Reduced quality of life and autonomy
- The only treatment available Luxturna® is mutation-specific gene therapy and targets <1% of all RP patients

2 OUR COMPETITIVE EDGE

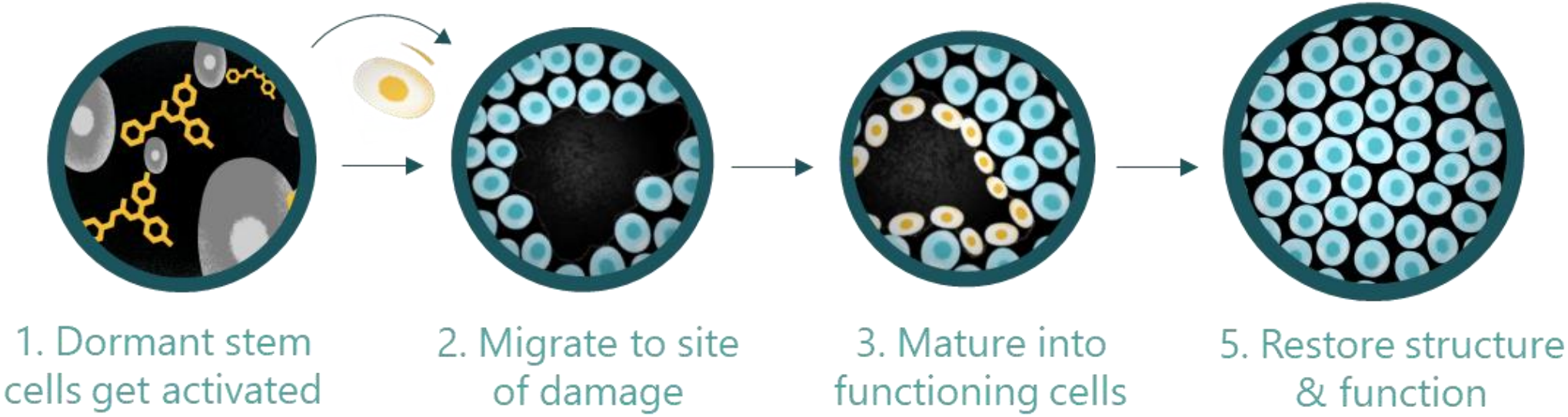
- Gene agnostic to restore anatomy and function and reverse disease progression
- **The only potential treatment for endogenous photoreceptor renewal**
- Small molecules easy to manufacture and with high stability
- Easy to administer in clinic (IVT injection)
- Strong IP position with multiple patents issued

3 OUR MARKET POTENTIAL

- 1.5m RP patients worldwide, with 300,000 RP patients in US and EU
- Projected peak worldwide **annual sales $1.5b,** reflecting the high demand and need for effective treatments

Unique concept:

Activating endogenous stem cells for regeneration



First in Human Phase 1b/2a Clinical Study

Patient Population

n=14
Age ≥18 years
RP (different mutations)

Investigator

OHSU

Retina Foundation of the Southwest

World-renowned expert **Mark Pennesi** as lead investigator

Treatment

EA-2353 suspension
One treatment cycle
(4 x weekly IVT)
(worse-seeing eye)

Primary endpoints

Safety & tolerability

Exploratory efficacy endpoints

To assess various aspects of visual function, including acuity, sensitivity, and retinal health under different conditions

Cohort 1
EA-2353 25 µg

Safety review

Cohort 2
EA-2353 50 µg

Safety review

Cohort 3
EA-2353 100 µg

Safety review

Cohort 4
EA-2353
100 µg

Key Takeaways

Primary objective to prove safety and tolerability - achieved

- **EA-2353 up to 100 µg is safe and well tolerated**
- No serious adverse events, withdrawals or discontinuations

Exploratory objective to suggest viable efficacy endpoints for future clinical trails – achieved

- EA-2353 treatment has beneficial effects on retinal structure and visual function in RP patients with advanced disease
- EA-2353 treatment yields positive results

Well-positioned for the next study

- Identified key investigators and sites with high recruitment potential and high-quality standards
- Acquired insights on optimizing the assessment schedule
- Gained valuable insights into the potential of patient stratification in the next stage of the program

- **Patient 001-001:** After treatment, the patient can distinguish between coffee and creamer no longer needing to use his finger to gauge when to stop pouring cream

- **Patient 001-002:** After treatment, the patient can see the credit card's 3-digit security number on the back without assistance, which was not possible before

- **Patient 001-004:** After treatment, the patient no longer needs a walking cane, as he can now see where he is stepping, a task he struggled with before

- **Patient 003-005:** Could previously not read the cellphone screen, following treatment he can read the cellphone screen with little difficulty

SENESCENCE

Centenara Labs

1 First-in-class therapies for diseases driven by senescence such as age-related diseases associated with fibrosis and cancer

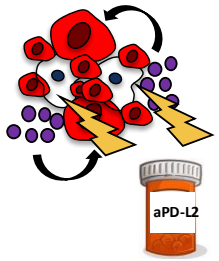
2 Senescent cell are aged cells that stop dividing and stop functioning as they used to. Their presence is associated with the secretion of SASP (inflammatory cytokines), ultimately leading to different pathalogies.

3 Our scientific co-founder Prof. Manuel Serrano discovered a novel mechanism that senescent tumour cells use to evade the immune system that is undertaken to develop therapies specifically targeting this mechanism

4 Overall, targeting senescence is a highly attractive therapeutic strategy given its pleiotropic effects on underlying causes of diseases

aPD-L2 has *in vivo* anti-tumor Activity that Synergizes with Standard of Care Chemotherapy for TNBC

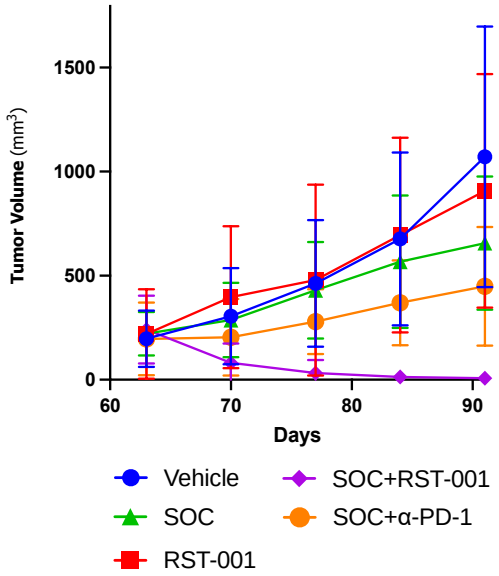
TNBC post-SoC



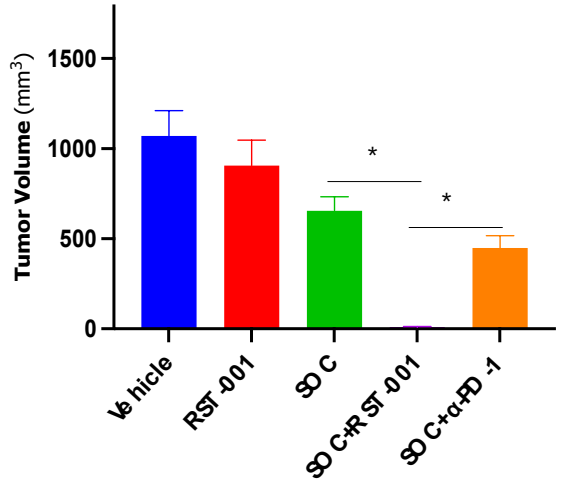
aPD-L2 treatment removes senescent cancer cells

Tumor fully regresses

Tumor Growth Kinetics



Final Tumor Volume



Error bars represent SD. *p<0.0001

- Combining aPD-L2 with senescence-inducing chemotherapy (doxorubicin) completely ablated tumors in a breast cancer mouse model, whereas aPD-1 plus doxorubicin only induced a moderate reduction in tumor volume
- The maintenance of tumor regression with the aPD-L2 + chemotherapy combination relies on cytotoxic T cell activity, as depleting CD8+ T cell results in tumor regrowth.

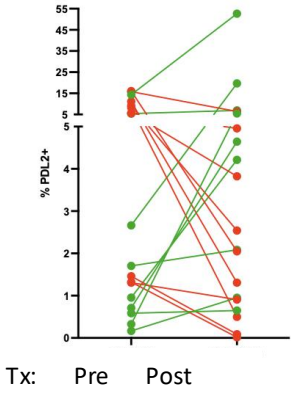
Translational Work in Oncology

- Analysis of target expression in primary tumor samples reveals that aPD-L2 treatment might be effective in 90% of Triple-Negative Breast Cancer cases and 38% of Hormone Receptor-Positive/HER2-Negative (HR+/HER2-) cases
- Mode of action now include activation of innate immunity and Antibody-Dependent Cellular Cytotoxicity (ADCC)
- PD-L2 blockade demonstrates greater efficacy than anti-PD-1/L1 therapies in killing human breast cancer cells in vitro

PDL-2 expression in primary human TNBC samples

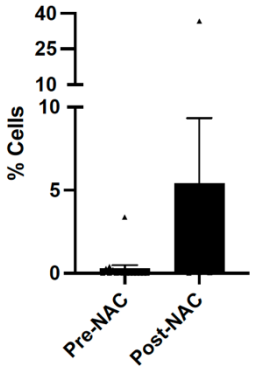
PDL-2 vs. PD(L)-1

PD-L2 pre/post-Tx



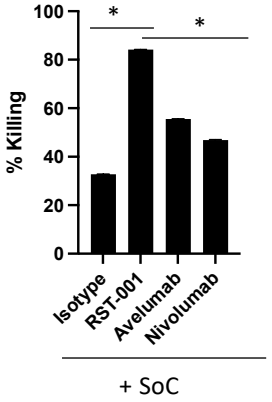
- *90% pts CPS>1%*
- *47.4% pts ↑ post-tx*

PD-L2 in senescence



- *% PD-L2⁺/SA-bGal⁺ cells ↑ post-tx*

TNBC killing by immune cells

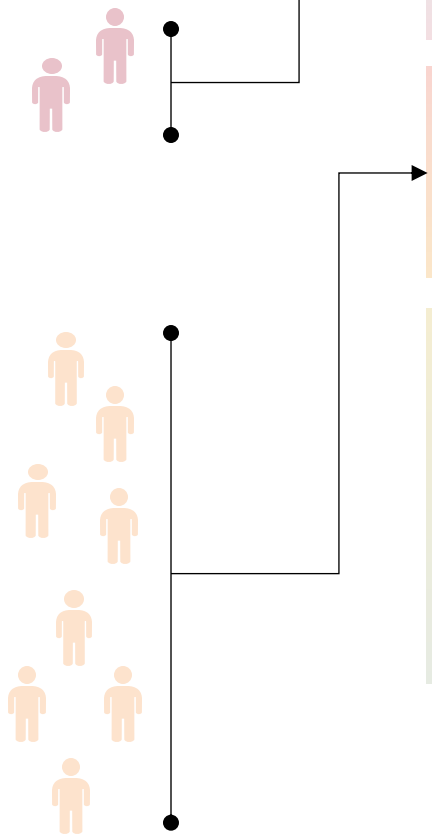


- *aPD-L2 kills TNBC cells more potently than anti-PD-1/-L1*

Pre-clinical

- Cyno half-life translateable to human dosing every 5 weeks
- No overt tox (no cytokine storm or immune cell depletion
- Oncology trial design for multiple indications including BC

aPD-L2 Treatment has Potential to Target a Distinct, Molecularly-defined TNBC Patient Subgroup



~20% of TNBC patients are PD-L1 high and are eligible to receive anti-PD-L1 / PD-1 therapy

Unmet Need:

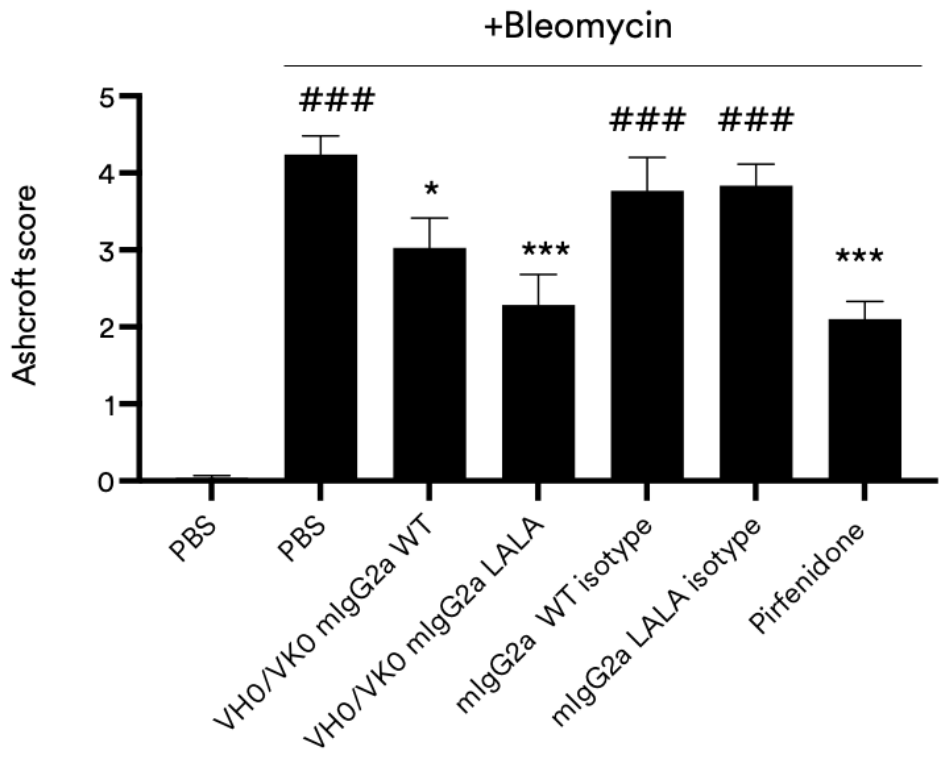
~80% of TNBC patients are PD-L1 low, hence chemotherapy remains frontline with only PFS of 5 – 6 months

Value proposition:

- ~20% of all TNBC patients are PD-L2 high
- High PD-L2 levels, but not PD-L1 levels, are associated with a significantly reduced 3-year PFS and OS among TNBC patients in response to SoC
- PD-L2 may also serve as a negative prognostic biomarker for response to SoC therapy

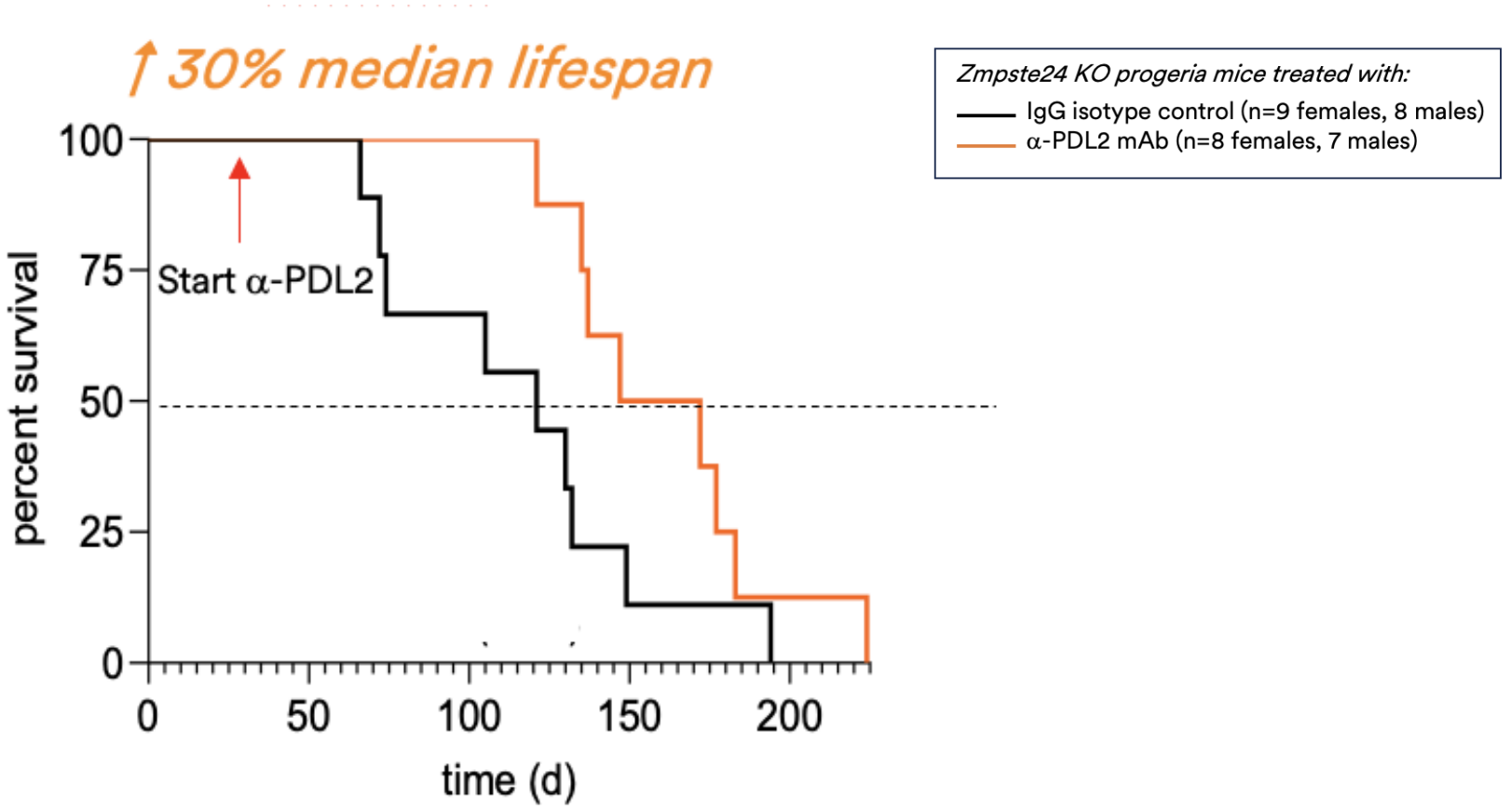
Given that SoC induces senescence and upregulation of PD-L2 in TNBC, combination with aPD-L2 is a rational approach to elicit complete responses and improve clinical outcome

Idiopathic Pulmonary Fibrosis mouse model



Anti-PDL2 therapy significantly reduces lung weight and hydroxyproline levels in mice, mirroring the effects of Pirfenidone and establishing aPD-L2 as a potent new treatment option in the battle against IPF

aPD-L2 Treatment in Healthy Aging



aPD-L2 significantly prolongs lifespan (+30%) and dramatically reduces kidney and cardiac fibrosis in a progeria* mouse model, showcasing its potent anti-aging effects.

*The Zmpste24 Progeria model is a genetically engineered mouse that lacks the Zmpste24 enzyme, leading to premature aging symptoms similar to human Progeria due to the accumulation of defective prelamin A.

Key Takeaways

1

Addressing vision loss with two innovative programs

- **Retinitis Pigmentosa**: Safe, well-tolerated with early signs of clinical efficacy, received FDA Fast Track and Orphan Drug Designations
- **Dry-AMD**: IND clearance in October 2023, Phase 1 study to commence in 2025

2

Targeted therapy for TNBC to approaching clinical development

- Lead program targeting TNBC, addressing cancer escape mechanisms post-SoC
- Proprietary antibody in IND-enabling studies

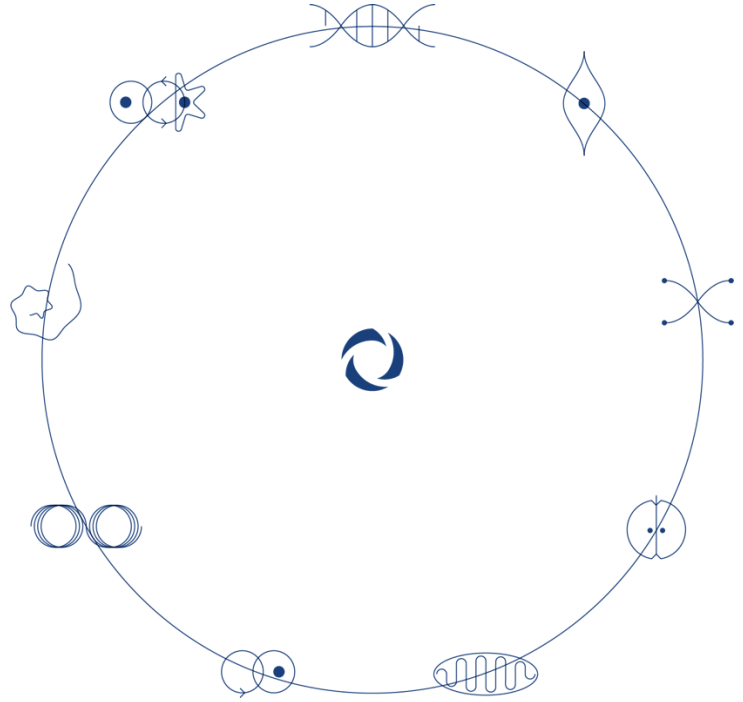
3

Breakthrough in fibrosis treatment:

- Robust pre-clinical data in fibrosis models, such as IPF and CKD, supported by a novel and differentiated MoA.
- Our early-stage target discovery platform identified 5 First-in-class targets.

4

Our hub-and-spoke model and diversified portfolio, strong regulatory support, innovative approach, and pipeline progress position us for future growth and success in addressing unmet age-related medical needs.



Centenara Labs

Age Better, Live Longer

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Curing age-related diseases to help
people live longer & healthier lives

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