**Written Testimony on Geroscience from Dr. Laura Niedernhofer, MD, PhD      September 15, 2022**

Geroscience refers to the fact that advanced chronologic age is the greatest risk factor for most diseases. Therefore, developing therapeutics that disrupt the biologic changes that universally occur with advanced chronologic age is logical but also potentially highly impactful to human health.
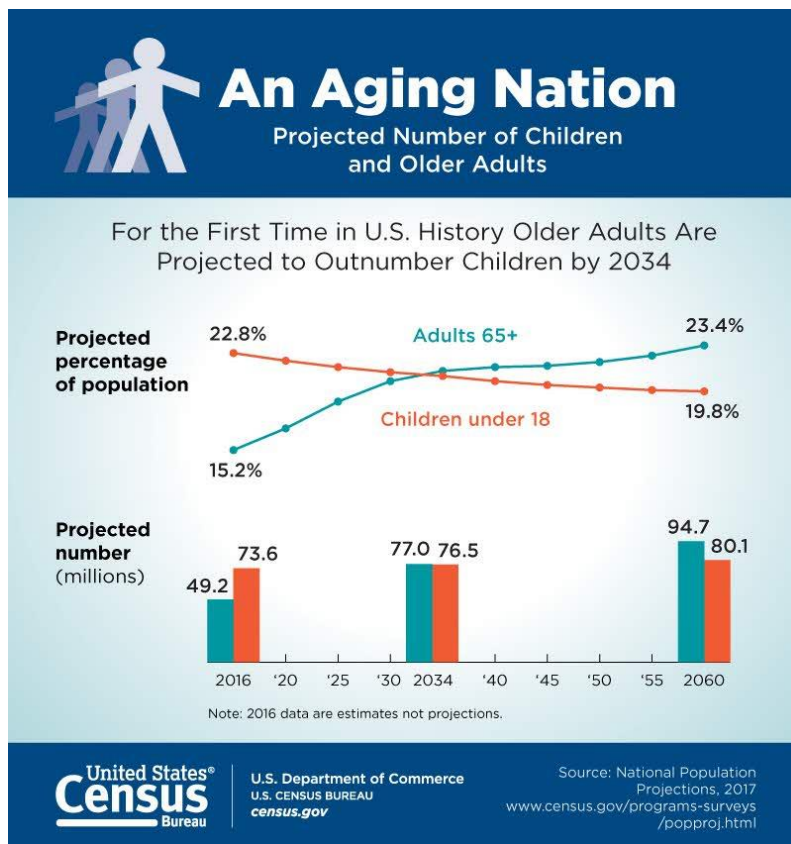
A Geroscience approach is anticipated to affect the health of the elderly to a greater extent than curing any single disease of old age, including curing Alzheimer's disease or cancer.

Importantly, Geroscience aims to extend how long individuals are healthy, not how long they live, what we refer to as extending _healthspan_.
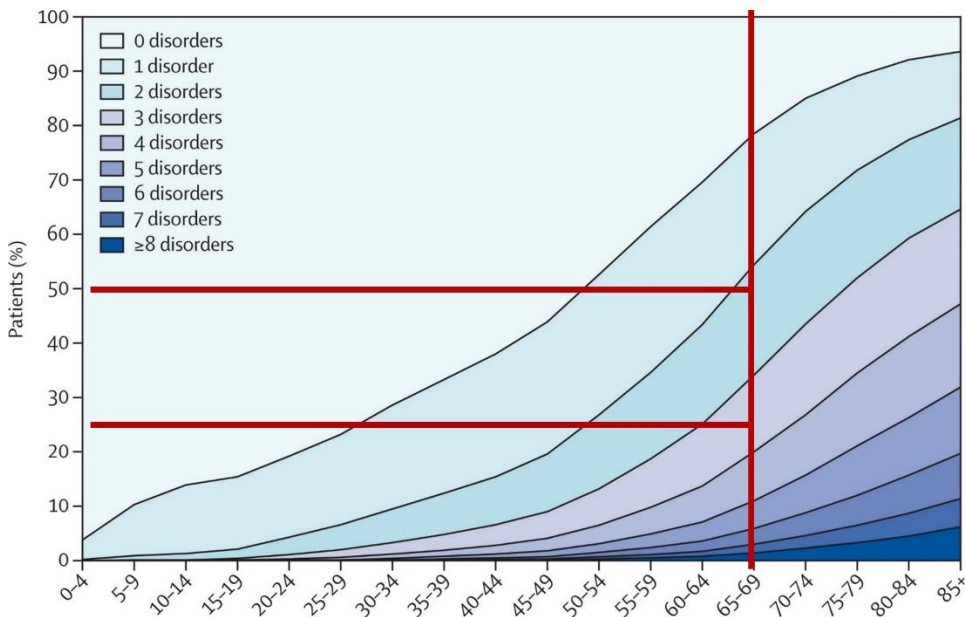
Geroscience is based on three facts:

1) First, we are in an unprecedented period in human history in which the number of elderly is doubling and surpassing the number of young people. This establishes the need for a new approach to prevent our healthcare system from becoming overwhelmed and healthcare costs skyrocketing.

**Our aging population:**



2) Second, the _majority_ of people over the age of 65 have two or more chronic diseases. Hence, curing a single disease of old age will not dramatically improve the health of the elderly.

**Frequency of diseases by chronological age:**



**Diseases where chronologic age is the greatest risk factor:**

- ➢ Osteoporosis
- ➢ Cardiovascular disease
- ➢ Neurodegenerative diseases
- ➢ Osteoarthritis
- ➢ Type II diabetes
- ➢ Cancer
- ➢ Macular degeneration
- ➢ Intervertebral disc degeneration

3) Third, chronologic age contributes to the risk of most diseases to a much greater extent than other risk factors that we are currently treating. Thus, therapeutics targeting aging biology have the potential to be not only useful for many diverse diseases but also highly effective at doing so compared to current first-line drugs.
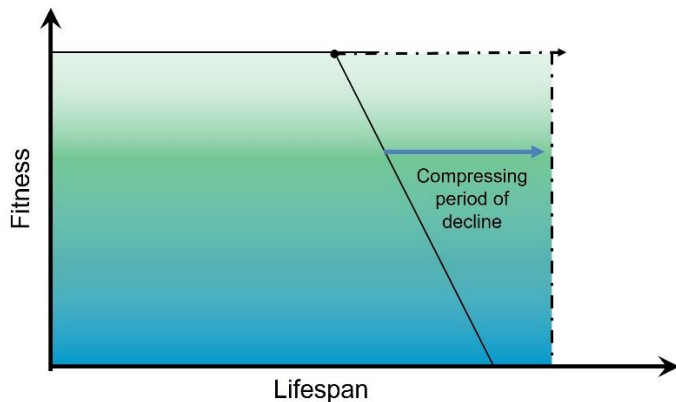
**Impact of chronic age on disease risk relative to other risk factors that we currently treat:**

Geroscience-guided therapeutics are predicted to:

- Target multiple common chronic diseases
- Be more impactful on human health than treating other disease risk factors
- Be efficacious in most people because aging biology is largely universal
- Extend human healthspan not lifespan
- Reduce health care costs by ~$38T annually
- Not require de novo drug development and testing, reducing the time and cost before therapies are available

**Goal of Geroscience:**



Currently, where Geroscience stands today:

- There is ample evidence that certain molecular and cellular events occur in most if not all people with advanced chronologic age.
- There is also ample evidence that some of these events can be therapeutically targeted in humans and in disease models.
- We have in-hand FDA-approved drugs that target and stop or reverse these molecular and cellular events of aging biology.
- We also have extensive data from animal models (pre-clinical data) demonstrating that Geroscience-guided therapies prevent, attenuate, or reverse age-related diseases affecting most organ systems. This includes heart disease, Alzheimer's disease, and diabetes.
- There exists at least one drug that appears to simultaneously stave-off diabetes, heart disease, cancer, and cognitive impairment. There are also numerous other candidate Geroscience drugs already approved by the FDA and in clinical use.
- There is a lot of activity in terms of the development of therapeutic interventions that target aging biology, primarily in academic centers and gaining traction in the pharmaceutical industry.

**Evidence for feasibility of targeting aging biology:**

1) Centenarians illustrate that the human body is capable of being healthy late in life
   a. They experience 20+ years of disease-free life than the average person
   b. They spend <2.5-fold less on healthcare in the last 2 years of life than the average person
2) Diseases for which there is evidence that targeting aging biology is efficacious

- ➢ Alzheimer's disease and neuromuscular dysfunction
- ➢ Pulmonary fibrosis
- ➢ Non-alcoholic fatty liver disease, steatosis, and fibrosis
- ➢ Osteoporosis and osteoarthritis
- ➢ Kidney disease
- ➢ Coronary artery and cardiovascular disease
- ➢ Frailty
- ➢ COVID-19

**Other conditions of accelerated aging in which patients stand to benefit from Geroscience therapies, in addition to the chronologically aged:**

- ➢ Cancer survivors
- ➢ Chronic HIV patients
- ➢ Socioeconomic stress
- ➢ Astronauts
- ➢ Genetic diseases including Down's syndrome and Hutchinson Gilford Progeria

**Existing FDA approved drugs that target multiple aspects of aging biology that are candidate Geroscience therapeutics:**

- ➢ Metformin
- ➢ Rapamycin
- ➢ Acarbose
- ➢ Canagliflozin
- ➢ Aspirin
- ➢ Dasatinib
- ➢ Navitoclax
- ➢ Inhibitors of HSP90, SGLT2i, LSD1, angiotensin-converting enzyme or angiotensin receptor, BCL-2, tyrosine kinase, cardiac glycoside

**Natural products available over-the-counter that are candidate Geroscience therapeutics:**

- ➢ Quercetin
- ➢ Fisetin
- ➢ N-Acetyl Cysteine
- ➢ Piperlongumine
- ➢ Luteolin
- ➢ Curcumin

**Other potential benefits of expansive Geroscience research:**

- ➢ What is learned could be applied in organ transplantation to expand the number and age of organ donors and recipients.

➢ It is now clear that events across the entire human lifespan impact how we age. Understanding how will potentially benefit every person in this country.

➢ What is learned could be applied to extend the health of farm animals to improve productivity (eggs, milk, wool)

**Key barriers to progress:**

- Adequate funding to pursue Geroscience research in a timely fashion
- Lack of the physician scientists and infrastructure needed to support clinical trials in geriatrics
- Lack of public knowledge about Geroscience
- Lack of biomarkers that report how well an individual is aging better than their chronological age does

**The federal government could facilitate Geroscience by providing:**

- Federal funding dedicated to supporting Geroscience research across multiple disciplines
- Support for training of physician scientists knowledgeable about clinical trials in geriatric patients
- Funding and support to create the infrastructure needed to advance Geroscience research, including sharing of biospecimen and data.
- Facilitating both the collection and dissemination of information across diverse race, ethnic, and socioeconomic groups

**Ethical and societal implications:**

Although this is not my area of expertise, I can offer my opinion. Aging biology affects virtually every aspect of how an individual interacts with the world: communication, transportation, housing needs, healthcare needs. The elderly exit the workforce while requiring significantly more help. As the number of chronologically aged continues to increase, we as a society will have to accommodate all of this. Geroscience offers an alternative where we aim to keep those of advanced chronologic age healthy, independent, active, able to work if they choose, and able to contribute to the economy. Given the wealth of scientific evidence supporting Geroscience, it would be irresponsible not to try this alternative. I cared for four parents or grandparents over the last two decades each of whom had multiple co-morbidities and I can attest that it is time-consuming, costly, and heartbreaking.

**BIOGRAPHY          Laura J. Niedernhofer, MD, PhD**

Laura Niedernhofer joined the University of Minnesota in July 2018 to direct the new Institute on the Biology of Aging & Metabolism and Medical Discovery Team on the Biology of Aging. She is a Professor in the Department of Biochemistry, Molecular Biology and Biophysics at UMN. Dr. Niedernhofer's expertise is in DNA damage and repair, genome instability disorders, cellular senescence, and aging biology. Her research program is centered on studying fundamental mechanisms of aging and developing therapeutics to target them. She contributed to the discovery of a new class of drugs called senolytics. Laura has served on study section for NCI, NIEHS, and NIA. She has been awarded for research in aging, cancer and environmental health science and was the 2018 recipient of the Vincent Cristafolo Rising Star in Aging Research awarded by the American Federation for Aging Research (AFAR). She is currently serving on the Advisory Council to the Division of Aging Biology at NIA and on the Board of Directors for American Federation of Aging Research. Laura was recently nominated to The Academy for Health and Lifespan Research.