

Supplemental Appendix 1

- I. A list of conditions and diseases for which there is evidence that senescent cells play a *causal* role in pathogenesis and therefore are alleviated by senolytic drugs.

Condition	References
Diabetes and obesity	(1-5)
Cardiac dysfunction	(6-8)
Vascular hyporeactivity/ calcification	(6)
AV fistulae	(9)
Frailty	(10-13)
Age-related muscle loss (sarcopenia)	(14)
Chemotherapy complications	(11; 13; 15-17)
Radiation complications	(18)
Cancers	(11)
Bone marrow transplant complications	(16)
Organ transplantation complications	(19; 20)
Myeloma/ MGUS	(21)
Age-related cognitive dysfunction	(22)
Alzheimer's disease	(23; 24)
Parkinson's disease	(25)
Amyotrophic lateral sclerosis	(26)
Ataxia	(10)
Obesity-related neuropsychiatric dysfunction	(27)
Renal dysfunction	(28; 29)
Urinary incontinence	(10)
Osteoporosis	(30-32)
Osteoarthritis	(33)
Age-related intervertebral disk disease	(10; 34)
Idiopathic pulmonary fibrosis	(13; 35)
Hyperoxic lung damage	(36)
Chronic obstructive pulmonary disease	(37)
Tobacco	(38)
Hepatic steatosis	(39)
Cirrhosis	(40)
Primary biliary cirrhosis	(41)
Progerias	(10; 12)
Pre-eclampsia	(42)
Macular degeneration	(43; 44)
Glaucoma	(45-47)
Cataracts	(48)
Prostatic hypertrophy	(49-51)
Psoriasis	(52)
Healthspan	(10-12)
Lifespan	(10-12)

II. Clinical trials on senotherapeutics in 2019-2020.

HSCT (human stem cell transplant) D+Q trial: Phase II open-label in bone marrow transplant survivors to reduce chemotherapy-induced frailty and senescent cell burden

HSCT (human stem cell transplant) fisetin trial: Phase II open-label in bone marrow transplant survivors to reduce chemotherapy-induced frailty and senescent cell burden

Diabetic renal disease D+Q trial: Phase IIb double-blind trial in diabetic renal disease subjects to test if the combination of Dasatinib plus quercetin reduces frailty, renal dysfunction and insulin resistance, while increasing adipose-derived stem cell function

Diabetic renal disease fisetin trial: Phase IIb double-blind trial in diabetic renal disease subjects to test if fisetin reduces frailty, renal dysfunction and insulin resistance, while increasing adipose-derived stem cell function

AFFIRM (Alleviation by Fisetin of Frailty, Inflammation, and Related Measures in Older Adult) trial: Phase II double-blind trial in elderly female subjects residing in a long-term care facility to reduce frailty, bone resorption, inflammation, and insulin resistance.

Short-term AFFIRM trial: Phase IIb double blind trial in elderly subjects with frailty to reduce senescent cell abundance

Idiopathic pulmonary fibrosis (IPF) D+Q trial: Multi-center Phase IIb trial in subjects with idiopathic pulmonary fibrosis to increase pulmonary and physical function

Osteoarthritis fisetin trial: Phase I/II trial in subjects with symptomatic knee arthritis to reduce senescence and SASP and improve MRI, physical performance and other objective clinical data.

Osteoarthritis UBOX101 trial: Randomized, double-blind, placebo-controlled study to assess the safety, tolerability, and clinical effects of single and repeat dose, intra-articular administration of a senolytic drug targeting p53/MDM2 in patients with symptomatic knee osteoarthritis.

Skeletal health fisetin trial: Phase II open-label trial to evaluate the whether fisetin improves skeletal health in the elderly as measured by percent change in amino-terminal pro-peptide of type I collagen [P1NP] and C-terminal telopeptide of type I collagen [CTX].

Skeletal health D+Q trial: Phase II open-label trial to evaluate whether D+Q improves skeletal health in the elderly as measured by percent change in amino-terminal propeptide of type I collagen (P1NP) and C-terminal telopeptide of type I collagen (CTX).

Alzheimer's disease D+Q trial: Phase I/II open-label trial to evaluate target engagement and to establish the feasibility and safety of D+Q treatment in older adults with early stage AD.

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