

Table S1 Medication development and clinical trials of current and investigational hormonal steroids

NCT No.	Study Design	Trial Phase	Completion Year	Status	Conditions	Age (years)	Intervention	Administration route	Control	Primary Outcomes	Sponsors
NCT01616732	Primary Purpose: Treatment Allocation: Randomized Intervention Model: Parallel Assignment Masking: Triple (Participant; Care Provider; Investigator)	Phase 2	2015	Completed	Obesity in Men	18 Years to 80 Years	Testosterone	Intramuscular injection	Placebo	weight	Austin Health
NCT00104572	Primary Purpose: Treatment Allocation: Randomized Intervention Model: Parallel Assignment Masking: Quadruple (Participant; Care Provider; Investigator; Outcomes Assessor)	Phase 2	2015	Completed	Hypogonadism Diabetes Sarcopenia Osteoporosis Depression	65 Years and older	Androgel (Testosterone Gel)	Topical gel	Placebo gel	Effect of Testosterone Gel vs. Anastrozole on Bone Mineral Density	National Institute on Aging (NIA)
NCT00475501	Primary Purpose: Treatment Allocation: Randomized Intervention Model: Factorial Assignment Masking: Triple (Participant; Investigator; Outcomes Assessor)	Phase 2	2014	Completed	Male Hypogonadism Muscle Atrophy Sarcopenia Benign Prostate Hypertrophy	60 Years and older	Testosterone Enanthate	Intramuscular injection	Finasteride Placebo	1 Repetition Maximum (1-RM) Strength Testing	VA Office of Research and Development
NCT00183040	Primary Purpose: Treatment Allocation: Randomized Intervention Model: Factorial Assignment Masking: Double	Phase 2	2007	Completed	Sarcopenia Muscle Weakness Frailty	65 Years to 90 Years	Topical testosterone	Topical gel	Recombinant human growth hormone	measures of fractional synthetic rates of mixed and contractile (actin and myosin heavy chain [MHC]) skeletal muscle proteins and degradation of skeletal muscle (ubiquitin, and proteasome sub-units)	National Institute on Aging (NIA)
NCT00613782	Primary Purpose: Treatment Allocation: Randomized Intervention Model: Single Group Assignment Masking: Quadruple (Participant; Care Provider; Investigator; Outcomes Assessor)	Phase 2 Phase 3	2014	Completed	Type 2 Diabetes Hypogonadism	18 Years to 65 Years	Reandron 1000	Intramuscular injection	Placebo	Insulin Resistance	Austin Health
NCT02367105	Primary Purpose: Treatment Allocation: Randomized Intervention Model: Parallel Assignment Masking: Triple (Participant; Investigator; Outcomes Assessor)	Phase 3	2019	Completed	Obesity and Hypogonadism	65 Years to 85 Years	Testosterone	Topical gel	Placebo	Change in the Physical Performance Test	VA Office of Research and Development
NCT03054168	Primary Purpose: Basic Science Allocation: Randomized Intervention Model: Parallel Assignment Masking: Triple (Participant; Investigator; Outcomes Assessor)	Phase 3	2019	Unknown status	Sarcopenia Muscle Hypotrophy Muscle Atrophy	18 Years to 75 Years	Sustanon	Intramuscular injection	Zoladex Placebo	Muscle Protein Synthesis	University of Nottingham
NCT02938923	Primary Purpose: Treatment Allocation: Randomized Intervention Model: Parallel Assignment Masking: Quadruple (Participant; Care Provider; Investigator; Outcomes Assessor)	Phase 3	2023	Completed	Hip Fracture Frailty Sarcopenia	65 Years and older	Testosterone	Topical gel	Placebo gel	Change in six-minute walk distance at 6 months	Washington University School of Medicine
NCT02433730	Primary Purpose: Treatment Allocation: Randomized Intervention Model: Single Group Assignment Masking: Quadruple (Participant; Care Provider; Investigator; Outcomes Assessor)	Phase 4	2019	Completed	Hypogonadism	18 Years to 75 Years	Testosterone	Intramuscular injection	Placebo	lean body mass	Marianne Andersen
NCT00287586	Primary Purpose: Treatment Allocation: Randomized Intervention Model: Parallel Assignment Masking: Double (Participant; Investigator)	Phase 4	2012	Completed	Hypogonadism Atherosclerosis	60 Years and older	Testosterone Gel (Androgel)	Topical gel	Placebo	Change From Baseline in Common Carotid Artery Intima-Media Thickness (IMT)	Brigham and Women's Hospital
NCT01560546	Primary Purpose: Treatment Allocation: Randomized Intervention Model: Parallel Assignment Masking: Quadruple (Participant; Care Provider; Investigator; Outcomes Assessor)	Phase 4	2013	Completed	Type 2 Diabetes Mellitus Hypogonadism	50 Years to 70 Years	Testosterone	-	Placebo	Lean body mass	Marianne Andersen
NCT00957801	Primary Purpose: Treatment Allocation: Randomized Intervention Model: Parallel Assignment Masking: None (Open Label)	Phase 4	2015	Completed	Sarcopenia	60 Years to 85 Years	Testosterone	Intramuscular injection	Medrol	Serum Total Testosterone Measured on Treatment	The University of Texas Medical Branch, Galveston
NCT01417364	Primary Purpose: Treatment Allocation: Randomized Intervention Model: Parallel Assignment Masking: Quadruple (Participant; Care Provider; Investigator; Outcomes Assessor)	Phase 4	2017	Withdrawn	Sarcopenia	60 Years to 75 Years	Testosterone enanthate	Intramuscular injection	Placebo	Muscle Strength	The University of Texas Medical Branch, Galveston
NCT00240981	Primary Purpose: Treatment Allocation: Randomized Intervention Model: Parallel Assignment Masking: Triple (Participant; Investigator; Outcomes Assessor)	Phase 4	2009	Terminated	Sarcopenia Hypogonadism Muscular Diseases	65 Years and older	Topical testosterone gel 1% (active formulation)	Topical gel	Topical gel (placebo formulation)	Changes in Physical Performance Measured by an Exercise Testing Regimen	Boston Medical Center
NCT00190060	Primary Purpose: Treatment Allocation: Randomized Intervention Model: Parallel Assignment Masking: Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor)	Phase 4	2008	Completed	Frailty Sarcopenia	65 Years and older	Transdermal testosterone gel (Testogel 1%)	Topical gel	Placebo	Lower limb muscle strength at 6 months	Manchester University NHS Foundation Trust
NCT03995251	Primary Purpose: Treatment Allocation: Randomized Intervention Model: Parallel Assignment Masking: None (Open Label)	Not Applicable	2020	Unknown	Liver Cirrhosis	18 Years to 55 Years	Testosterone	Intramuscular injection	-	Increase in Lean Appendicular Muscle Mass by more than 10% in both groups	Institute of Liver and Biliary Sciences, India
NCT00474279	Primary Purpose: Treatment Allocation: Randomized Intervention Model: Crossover Assignment Masking: Double	Phase 1 Phase 2	2004	Completed	Aging	60 Years and older	MK-677	Orally	Placebo	At 12 months: 24-hour mean growth hormone concentrations	University of Virginia
NCT04874350	Primary Purpose: Treatment Allocation: Randomized Intervention Model: Parallel Assignment Masking: Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor)	Phase 2	2023	Completed	Liver Cirrhosis Sarcopenia	18 Years and older	LPCN 1148	Orally	Placebo	Change from baseline in Skeletal Muscle Index in LPCN 1148 treated subjects compared to placebo	Lipocine Inc.
NCT01898611	Primary Purpose: Other Allocation: Randomized Intervention Model: Parallel Assignment Masking: Quadruple (Participant; Care Provider; Investigator; Outcomes Assessor)	Phase 2	2016	Completed	Frailty Syndrome	70 Years and older	Ghrelin	Subcutaneous injection	Placebo	Change in the Short Physical Performance Battery (SPPB)	University of Pennsylvania
NCT00128115	Primary Purpose: Treatment Allocation: Randomized Intervention Model: Parallel Assignment Masking: Double	Phase 2	2007	Terminated	Hip Fracture	60 Years and older	MK0677	Orally	Placebo	Proprietary Information - Exploratory (Non-Confirmatory) Trial	Merck Sharp & Dohme LLC
NCT05253287	Primary Purpose: Treatment Allocation: Randomized Intervention Model: Parallel Assignment Masking: Single (Outcomes Assessor)	Phase 2 Phase 3	2025	Recruiting	Liver Cirrhosis Fibrosis End Stage Liver Disease Digestive System Disease Physiological Effect of Drugs Growth Hormone Treatment Sarcopenia	18 Years to 80 Years	Growth Hormone	Subcutaneous injection	-	Complication free survival	Postgraduate Institute of Medical Education and Research
NCT00205686	Primary Purpose: Treatment Allocation: Randomized Intervention Model: Parallel Assignment Masking: Double	Phase 3	2005	Completed	Healthy Volunteers	65 Years to 78 Years	DHEA+exercise	Orally	Placebo	thigh muscle mass, muscle strength, intadominal fat, bone mineral density, markers of bone turnover, insulin sensitivity	Washington University School of Medicine
NCT03867357	Observational Model: Cohort Time Perspective: Prospective	-	2024	Active, not recruiting	Metastatic Prostate Cancer Androgen Deprivation Therapy	18 Years to 90 Years	Zoladex	Subcutaneous injection	-	Lean body mass (LBM) change	Seattle Institute for Biomedical and Clinical Research
NCT00254371	Primary Purpose: Treatment Allocation: Randomized Intervention Model: Parallel Assignment Masking: Double	Not Applicable	2007	Completed	Aging Low DHEA for Women Low Testosterone and DHEA for Men	60 Years and older	Androgen Replacement	Orally (DHEA); Transdermal patch (Testosterone)	-	physical performance (VO2 peak, muscle strength as measured by chest press, double knee extension, and isokinetic knee extension	Mayo Clinic

Table S2 Medication development and clinical trials of current and investigational antidiabetic agents on ClinicalTrials.gov.

NCT No.	Study Design	Trial Phase	Completion Year	Status	Conditions	Age (years)	Intervention	Administration route	Control	Primary Outcomes	Sponsors
NCT00690534	Primary Purpose: Basic Science Allocation: Randomized Intervention Model: Parallel Assignment Masking: None (Open Label)	Phase 1	2012	Completed	Sarcopenia	18 Years to 85 Years	Insulin Regular	Intravenously	L-NMMA Sodium Nitroprusside mixed meal	Muscle protein synthesis	The University of Texas Medical Branch, Galveston
NCT03248271	Observational Model: Cohort Time Perspective: Prospective	-	2023	Withdrawn	Diabetes Sarcopenia Hypotension, Orthostatic	65 Years and older	Insulin Lispro	Intravenously	-	Body composition	Kenneth Madden
NCT01804049	Primary Purpose: Other Allocation: Randomized Intervention Model: Parallel Assignment Masking: Double (Participant; Investigator)	Phase 1 Phase 2	2018	Completed	Prediabetes	65 Years and older	Metformin	Orally	Placebo	Change in Total Lean Mass from Baseline	VA Office of Research and Development
NCT02325245	Primary Purpose: Treatment Allocation: Randomized Intervention Model: Parallel Assignment Masking: Quadruple (Participant; Care Provider; Investigator; Outcomes Assessor)	Phase 3	2017	Unknown status	Pre-frail Elderly	60 Years and older	Metformin	Orally	Placebo	Change from baseline in frailty status at 16 weeks	Indonesia University
NCT00315146	Primary Purpose: Treatment Allocation: Randomized Intervention Model: Factorial Assignment Masking: Single (Participant)	Phase 4	2007	Completed	Obesity Overweight with Indications for Weight Loss	65 Years to 79 Years	Pioglitazone	Orally	Placebo	Appendicular Non-bone Lean Mass	Wake Forest University Health Sciences
NCT00315146	Primary Purpose: Treatment Allocation: Randomized Intervention Model: Factorial Assignment Masking: Single (Participant)	Phase 4	2007	Completed	Obesity Overweight with Indications for Weight Loss	65 Years to 79 Years	Pioglitazone	Orally	Placebo	Appendicular Non-bone Lean Mass	Wake Forest University Health Sciences
NCT02305069	Primary Purpose: Basic Science Allocation: Randomized Intervention Model: Parallel Assignment Masking: Triple (Participant; Investigator; Outcomes Assessor)	Not Applicable	2012	Completed	Obesity Sarcopenia	55 Years to 75 Years	Pioglitazone	Orally	Insulin	Change in muscle protein synthesis response to simulated feeding with data reported as % fractional synthetic rate per hour	University of Nottingham
NCT02370745	Primary Purpose: Basic Science Allocation: Randomized Intervention Model: Crossover Assignment Masking: Single (Participant)	Not Applicable	2018	Completed	Sarcopenia	18 Years to 75 Years	GLP-1	Intravenously	Insulin Actrapid	Muscle protein and glucose metabolism	University of Nottingham
NCT00855166	Primary Purpose: Treatment Allocation: Randomized Intervention Model: Parallel Assignment Masking: Double (Participant; Investigator)	Phase 3	2011	Completed	Type 2 Diabetes Mellitus	30 Years to 75 Years	Dapagliflozin	Orally	Placebo	Adjusted Mean Change in Total Body Weight	AstraZeneca

Table S3 Development and clinical trials of other investigational pharmacological agents on ClinicalTrials.gov.

NCT No.	Study Design	Trial Phase	Completion Year	Status	Conditions	Age (years)	Intervention	Administration route	Control	Primary Outcomes	Sponsors
NCT01550107	Primary Purpose: Treatment Allocation: Randomized Intervention Model: Parallel Assignment Masking: Triple (Participant; Investigator; Outcomes Assessor)	Phase 4	2017	Completed	Sarcopenia	65 Years and older	Allopurinol	Orally	Lactose tablets	Improvement in Muscle energetics as measured by MR-spectroscopy	University of Dundee
NCT03452488	Primary Purpose: Treatment Allocation: Randomized Intervention Model: Parallel Assignment Masking: Double (Participant, Investigator)	Phase 2	2021	Completed	Sarcopenia Gait Disorders in Old Age Muscle Weakness	65 Years and older	BIO101	Orally	Placebo	Gait speed measured during the 400MW test	Biophytis
NCT02575235	Primary Purpose: Prevention Allocation: Randomized Intervention Model: Parallel Assignment Masking: Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor)	Early Phase 1	2016	Completed	Sarcopenia	60 Years and older	Cetylpyridinium Chloride	Orally	Placebo	Change from baseline in procollagen type III N-terminal peptide	Seoul National University Hospital
NCT02297997	Primary Purpose: Prevention Allocation: Randomized Intervention Model: Parallel Assignment Masking: Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor)	Early Phase 1	2015	Completed	Sarcopenia	60 Years and older	Cetylpyridinium Chloride	Orally	Placebo	Change from baseline in procollagen type III N-terminal peptide	Seoul National University Hospital
NCT05666310	Primary Purpose: Treatment Allocation: Randomized Intervention Model: Parallel Assignment Masking: Double (Participant; Investigator)	Phase 4	2026	Active, not recruiting	Sarcopenia Osteoporosis	65 Years and older	Denosumab	Subcutaneous injection	Placebo	Percentage change from baseline in muscle mass (kg) measured by D3-Creatine	Nami Safai Haeri
NCT01660126	Primary Purpose: Treatment Allocation: Randomized Intervention Model: Parallel Assignment Masking: Double (Participant; Investigator)	Phase 4	2016	Completed	Subclinical Hypothyroidism	65 Years and older	Levothyroxine	Orally	Placebo	Thyroid-specific quality of life - Hypothyroid symptoms and Fatigue symptoms (co-primary outcomes)	NHS Greater Glasgow and Clyde
NCT04354896	Primary Purpose: Treatment Allocation: Randomized Intervention Model: Parallel Assignment Masking: Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor)	Phase 4	2018	Completed	Subclinical Hypothyroidism Sarcopenia	65 Years and older	Levothyroxin	Orally	Placebo	Physical performance	Insel Gruppe AG, University Hospital Bern
NCT03784495	Primary Purpose: Treatment Allocation: Randomized Intervention Model: Parallel Assignment Masking: Quadruple (Participant; Care Provider; Investigator; Outcomes Assessor)	Not Applicable	2015	Completed	Sarcopenia	65 Years and older	Melatonin	Orally	Placebo	Change in Total Fat Mass and Total Free Fat Mass (DXA)	Azienda di Servizi alla Persona di Pavia
NCT05284604	Primary Purpose: Treatment Allocation: Randomized Intervention Model: Parallel Assignment Masking: Quadruple (Participant; Care Provider; Investigator; Outcomes Assessor)	Phase 1 Phase 2	2023	Withdrawn	Frailty	65 Years to 85 Years	Mesenchymal Stem Cells (MSCs)	Intravenous infusion	-	Adherence	VA Office of Research and Development
NCT03119610	Primary Purpose: Basic Science Allocation: Randomized Intervention Model: Parallel Assignment Masking: Quadruple (Participant; Care Provider; Investigator; Outcomes Assessor)	Phase 1 Phase 2	2019	Completed	Obesity Sarcopenic Obesity Sarcopenia Aging Sedentary Lifestyle	60 Years to 99 Years	Oxytocin nasal spray	Intranasally	Placebo nasal spray	Change in Body Weight	Sara Espinoza
NCT00509405	Primary Purpose: Treatment Allocation: Randomized Intervention Model: Parallel Assignment Masking: Quadruple (Participant; Care Provider; Investigator; Outcomes Assessor)	Phase 3	2010	Completed	Healthy	65 Years to 80 Years	Potassium citrate	Orally		BMD at L2-L4 by DEXA and microarchitectural composition of bone in both tibia and radius	Kantonsspital Baselland Bruderholz
NCT03788252	Primary Purpose: Prevention Allocation: Randomized Intervention Model: Parallel Assignment Masking: None (Open Label)	Phase 4	2020	Completed	Chronic Kidney Diseases	20 Years and older	Renamezin	Orally	Non-Renamezin	Change of 6-meter walking speed at 24 weeks	Gumi Cha Medical Center