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TITLE: Growth Hormone Replacement Therapy in Veterans with Gulf War Illness and GH Deficiency

PRINCIPAL INVESTIGATOR: Ricardo Jorge, MD

CONTRACTING ORGANIZATION: Baylor College of Medicine, Houston, TX

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14. ABSTRACT

This study is a placebo-controlled, double-blind, parallel-group randomized clinical trial (RCT) of recombinant human growth hormone (rhGH) replacement therapy (using somatropin) vs. placebo in Veterans from Operations Desert Storm/Desert Shield with a history of Gulf War Illness (GWI) and adult growth hormone deficiency (AGHD). This study will assess the efficacy and safety of rhGH in this population, as well as treatment compliance. The primary hypothesis is that participants receiving rhGH for 6-months will show improvements in body composition (i.e., truncal fat mass reduction of 5.3% or greater) compared to placebo.

15. SUBJECT TERMS
Gulf War Illness, growth hormone replacement therapy, hormonal dysregulation

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TABLE OF CONTENTS

1. INTRODUCTION:

There is a significant overlap between the symptoms of adult growth hormone deficiency (AGHD) and those of Gulf War Illness (GWI) such as fatigue, chronic pain, depression, anxiety, and cognitive dysfunction. AGHD is also associated with metabolic changes such as increased truncal fat mass, dyslipidemia, and increased cerebrovascular risk which can lead to neuroinflammation, neurodegeneration, and functional decline. Approximately 33% of veterans with a confirmed diagnosis of GWI test positive for AGHD.

Growth hormone replacement therapy (GHRT) with recombinant human growth hormone (rhGH) reverses body composition and metabolic changes. Studies on civilians with AGHD caused by other conditions such as pituitary tumors suggest GHRT improves fatigue, chronic pain, mood disturbance, cognitive function, and improves quality of life (QoL). However, the effect of growth hormone replacement therapy in veterans with AGHD associated with GWI has not been studied.

This study is a placebo-controlled, double-blind, parallel-group randomized clinical trial (RCT) of recombinant human growth hormone (rhGH) replacement therapy (using somatropin) vs. placebo in Veterans from Operations Desert Storm/Desert Shield with a history of Gulf War Illness (GWI) and adult growth hormone deficiency (AGHD). This study will assess the efficacy and safety of rhGH in this population, as well as treatment compliance. The primary hypothesis is that participants receiving rhGH for 6-months will show improvements in body composition (i.e., truncal fat mass reduction of 5.3% or greater) compared to placebo.

2. KEYWORDS:

Endocrine measures; hormonal dysregulation; HPA axis; Gulf War Illness, recombinant human growth hormone (rhGH); growth hormone replacement therapy

3. ACCOMPLISHMENTS:

What were the major goals of the project?

An overview of the major tasks is provided below and explained in greater detail in the next section.

Major Task 1: Regulatory and Administrative Start-Up Tasks	Target Month	% Complete
- Coordinate CRADA	1-3	In Progress
- Pharmacy start-up	2-7	In Progress
- Set-up billing and contracts	2-6	In Progress
- Submit IND letter requesting exemption from FDA	1-2	100%
Major Task 2: Coordinate Study Staff		
- Select members of DSMB	1-2	100%
- Develop and post job descriptions	1-2	100%
- Coordinate lab space, testing rooms, and calibrate DEXA	1-5	Pending

- Interview and hire study personnel / Train personnel	1-5	In Progress
Major Task 3: Recruitment		
- Create recruitment materials	1-3	100%
- Finalize recruitment strategy	1-3	100%
- Screen Participants	7-26	In Progress
Major Task 4: Data Collection		
- Finalize variables and create case report forms	2-7	100%
- Develop and test databases	1-6	In Progress
- Identify potential GW candidates	7-25	In Progress
- Consent patients and collect data	8-26	0%

What was accomplished under these goals?

Administrative and Regulatory:
IRB approval was obtained from WCG IRB in August 2021. Subsequently, each site obtained local R&D and HRPO approvals in 2022. The protocol continuing review was submitted in July 2022 and approved by WCG in August 2022. Copies of the continuing review letters were forwarded to HRPO in September 2022. The study is up to date on regulatory matters.

The study was registered on clinicaltrials.gov and IND exemption letter was obtained. Pfizer agreed to provide the study medication and placebo for this study, and Dr. Jorge and Dr. Garcia are in the process of signing a CRADA with Pfizer to supply the medication. The research team is in contact with the research pharmacy, and final arrangements are dependent on the execution of the CRADA.

The subaward from Baylor to the Settle Institute for Biomedical and Clinical Research (SIBCR) for the VA Seattle site (PI: Garcia) was executed May 20, 2022. It has since expired, and Baylor is working on issuing an amendments for existing subcontracts.

Coordinate Study Staff:
The subaward for Seattle was finalized in May which delayed the personnel hiring process. Seattle hired a research nurse to join the team. She has completed the initial study credentialing process and is in the onboarding process at the VA Puget Sound. However, they are still searching for a study specific research coordinator.

In Houston, site personnel are in place. The research coordinator was hired in September 2022.

The members of the DSMB were identified in the third quarter but changed during the fourth quarter. Originally, Dr. Marco Marcelli was the endocrinologist working in Houston and Dr. Sanjay Mediwala was serving on the DSMB. However, Dr. Marcelli has since left the VA, and now Dr. Mediwala will serve as the endocrinologist in Houston and Dr. Marcelli will serve on DSMB.

The DEXA calibration was pushed back to a later date once personnel at both sites are hired and study is closer to recruiting patients.

Data Collection:
The databases are being beta-tested at this time.

What opportunities for training and professional development has the project provided?

Nothing to Report.

How were the results disseminated to communities of interest?

Nothing to Report.

What do you plan to do during the next reporting period to accomplish the goals? Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

During the next reporting period the primary focus is to finalize the CRADA with Pfizer for the study medication. Houston is diligently looking for lists of Gulf War veterans to screen and invite into the study as soon as the medication is available. Houston will continue to run system checks and troubleshoot the protocol.

VA Puget Sound (Seattle) will finalize the agreement with Quest Diagnostics for study laboratory services, as well as secure phlebotomy supplies prior to participant enrollment. Lab supplies have not been purchased because there is a national shortage, and the blood draw tube shelf life is short. Thus, supplies will be ordered as we get closer to patient enrollment. Seattle will train staff on endocrinology SOPs and cross-calibrate the DXA machines.

4. IMPACT:

What was the impact on the development of the principal discipline(s) of the project?

Nothing to Report.

What was the impact on other disciplines?

Nothing to Report.

What was the impact on technology transfer?

Nothing to Report.

What was the impact on society beyond science and technology?

Nothing to Report.

5. CHANGES/PROBLEMS:

Changes in approach and reasons for change

Nothing to Report

Actual or anticipated problems or delays and actions or plans to resolve them

Several setbacks were encountered during the first year. First, we were unaware that the reporting period began before funding was issued. Thus, we were anticipating the project's clock would start March/April 2022, yet the project date was set for October 2021. This is approximately 6 months earlier than we anticipated.

Second, the delay in regulatory approvals caused a delay in funding. Without funding we were unable to establish contracts and hire personnel. Lastly, it was not anticipated that to execute the Pfizer contract we would need to track down a former investigator from Baylor who was delinquent in her reports to Pfizer. Nonetheless, Dr. Jorge was able to reach the former investigator and is moving forward with Pfizer to establish a CRADA for the study medications.

The study is unable to launch until the study medication is in place. Nonetheless, the research team is actively working on recruitment efforts so sufficient candidates are available once the study is ready to enroll participants.

Changes that had a significant impact on expenditures

There were no significant changes affecting expenditures. Delays in hiring personnel during Year 1 resulted in lower expenditures at start-up.

Significant changes in use or care of human subjects

Nothing to Report.

Significant changes in use or care of vertebrate animals

Nothing to Report.

Significant changes in use of biohazards and/or select agents

Not applicable.

6. PRODUCTS:

Journal publications.

Nothing to Report.

Books or other non-periodical, one-time publications.

Nothing to Report.

Other publications, conference papers and presentations.

Nothing to Report.

Website(s) or other Internet site(s)

Nothing to Report.

Technologies or techniques

Nothing to Report.

Inventions, patent applications, and/or licenses

Nothing to Report.

Other Products

Nothing to Report.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name:	Ricardo Jorge, MD
Project Role:	Principal Investigator
Researcher Identifier:	0000-0001-6010-7297
Nearest person month worked:	3 CM
Contribution to Project:	Dr. Jorge oversees all aspects of the research protocol development, regulatory submissions, and CRADA negotiations.

Name:	Fuad Aloor
Project Role:	Research Coordinator
Nearest person month worked:	0.9 CM
Contribution to Project:	Mr. Aloor was recently hired and will oversee the day-to-day aspects in the trial. During his first month, he completed training and credentialing.

Name:	Uma Ramamurthy, PhD
Project Role:	Co-Investigator
Nearest person month worked:	5% effort
Contribution to Project:	Assist with the development of database.

Name:	Ruosha Li
Project Role:	Statistician
Nearest person month worked:	10% effort
Contribution to Project:	Contributed to the design of the randomization schema and statistical design.

Name:	Audri Villalon
Project Role:	Coordinator
Researcher Identifier:	0000-0001-5535-7558
Nearest person month worked:	3 CM
Contribution to Project:	Ms. Villalon assists with regulatory documents and reports as well as interviewing, hiring, and onboarding of personnel. She is also involved in case report and SOP development and database testing.
Funding Source:	No salary support

Seattle

Name:	Jose Manuel Garcia, MD
Project Role:	Co-Investigator
Researcher Identifier	0000-0002-4245-1753
Nearest person month worked:	0.6 PM
Contribution to Project:	Dr. Garcia oversees all study related activities at the Seattle site. He is responsible for development of endocrinology SOPs, calibration of DEXA (DXA) machines, hiring personnel, and ensuring regulatory documents are filed.

Name:	Megan Herodes
Project Role:	Research Coordinator
Nearest person month worked:	1.3 CM
Contribution to Project:	Ms. Herodes assists Dr. Garcia with preparation and submission of regulatory documents and SOP preparation.

Changes in the active other support of key personnel since the last reporting period

Ricardo Jorge, MD

Title:	**GH replacement therapy in Veterans with mTBI and AGHD (PIs: Garcia and Jorge)**
Effort:	1.2 calendar
Supporting Agency:	VA Cooperative Studies Program
Performance Period:	12/01/2020-11/30/2024
Funding Level:	total costs
Project Goals:	This is large multicenter study that will be examine the efficacy of rhGH to improve quality of life (QoL) among Veterans with mild TBI and GH deficiency.
Specific Aims:	When compared with placebo, GHRT will have a beneficial effect on: 1) QoL; 2) Body composition (specifically reduction of fat content and visceral fat); 3) Fatigue; 4) Chronic Pain; 4) Depression; 5) Cognitive functioning (specifically attention, memory and executive functioning
Overlap:	No overlap

Jose Manuel Garcia, MD

See PCP support document attached in the appendix. Dr. Garcia has new active clinical trial, a VA Summer Research Program, and a pending NIH grant.

What other organizations were involved as partners?

Name: Seattle Institute for Biomedical and Clinical Research (SIBCR) / VA Puget Sound Health Care System
Location: Seattle, WA
Contribution: As per the SOW, SIBCR manages external funding for researchers based at VAPSHCS. Dr. Jose Garcia serves as Co-Investigator and site PI for this project.

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: N/A

QUAD CHARTS: N/A

9. APPENDICES: Dr. Jose Manuel Garcia updated support document.

PREVIOUS/CURRENT/PENDING SUPPORT
GARCIA, JOSE, MD, PhD,

PREVIOUS (past 5 years)

Title:	**Metabolic and QOL effects of GH in mTBI (PI: Garcia)**
Effort:	0.1 calendar months
Supporting Agency:	Pfizer
Grant Officer:	Daliza Crane; daliza.crane@pfizer.com
Performance Period:	11/30/2016-07/01/2022
Funding Level:	Total Costs
Project Goals:	The goal of this project is to explore the role of GH replacement in veterans with mild TBI and AGHD.
Specific Aims:	Determine the effects of GH replacement in patients with AGHD due to TBI

Title:	**Genetic Approaches to Aging Training Grant (PI: Rabinovitch)**
Effort:	0.1 calendar months
Role:	Co-Investigator/Mentor
Supporting Agency:	NIH/NIBIB, T32AG000057
Grant Officer:	Max Guo, PhD; max.guo@nih.gov
Performance Period:	5/1/2013-4/30/2021
Funding Level:	Annual Direct Costs
Project Goals:	This training program provides support for 8 postdoctoral and 8 predoctoral trainees in studies of the biology of aging.
Specific Aims:	The goal of our program is to train new independent investigators who will utilize molecular and genetic techniques to investigate the biology of aging.

Title:	**Examining SSRI- Induced Disruption of Pubertal Growth Spurt (PI: Calarge)**
Effort:	0.6 calendar months
Role:	Co-Investigator
Supporting Agency:	NIH/NICHD, R21HD097776
Grant Officer:	Zhaoxia Ren, MD, PhD; zren@mail.nih.gov
Performance Period:	1/1/2019-12/31/2020
Funding Level:	Total Costs
Project Goals:	This project will study the effect of SSRI exposure on growth in children.
Specific Aims:	1) Compare the effect of fluoxetine and sertraline on markers of GH function in peripubertal youth. 2) Establish the persistence of fluoxetine-induced disruption of GH function in peripubertal youth. 3) Examine the causal relation between fluoxetine-induced disruption in GH function and longitudinal growth in peripubertal youth.

Title:	**Intramuscular Mechanisms of Cancer Cachexia (PI: Li)**
Effort:	1.2 calendar months
Role:	Co-Investigator
Supporting Agency:	NIH/NIMS, R01AR067319
Grant Officer:	Rebecca Liddell Huppi, PhD; liddellr@exchange.nih.gov
Performance Period:	10/1/2015-7/31/2020
Funding Level:	Annual Direct Costs

Project Goals:	The goal for this study is to determine novel intramuscular mechanisms contributing to muscle wasting in cancer cachexia.
Specific Aims:	1) To determine whether UBR2 is a key E3 ubiquitin ligase responsible for cancer-induced muscle wasting. 2) To determine whether site-specific acetylation of C/EBPβ mediates cancer-induced UBR2 upregulation. 3) To determine the signaling mechanism that mediates cancer-induced acetylation of C/EBPβ.

Title:	**Novel Pharmacologic Risk factors for Common Non-AIDS defining Cancers in Individuals with Well-controlled HIV Infection (PI: Chiao)**
Effort:	0.6 calendar months
Role:	Co-Investigator
Supporting Agency:	NIH/NIBIB, R01CA206476
Grant Officer:	Rebecca Liddell Huppi, PhD; liddellr@exchange.nih.gov
Performance Period:	6/10/2016-5/31/2020
Funding Level:	Total Costs
Project Goals:	The goal for this study is to find drugs that can modify the risk of cancer in HIV-infected patients.
Specific Aims:	1) a) To measure the effect of the duration of specific classes of cART medications on the risk of each of the 8 NADCs of interest in a cohort of veterans with well-controlled HIV, adjusting for known risk factors for each type of cancer, and b) to assess the extent of cancer risk that is mediated by metabolic disorders. 2) a) To measure the effect of duration of specific classes of common medications used to treat metabolic disorders known to impact cancer risk, utilized by HIV-infected individuals (e.g., statins, metformin, beta-blockers and ACE-Inhibitors) on the risk of developing the 8 NADCs of interest in a cohort of veterans with well-controlled HIV-infection; and b) to assess the extent that the observed cancer risk association from these common metabolic disorder- related medication is primarily mediated through their impacts on metabolic disorder control.

Title:	**Long-acting ghrelin for cancer cachexia (PI: Soliman)**
Effort:	1.2 calendar months
Role:	Co-Investigator
Supporting Agency:	NIH/NCI, R44CA174094
Grant Officer:	Patricia A. Weber, PhD; weberpa@mail.nih.gov
Performance Period:	7/1/2017-3/31/2020
Funding Level:	Annual Direct Costs
Project Goals:	This project will study the effects of a novel long acting ghrelin on different murine models of cancer- related anorexia and cachexia.
Specific Aims:	Methods for cGMP production of the long-acting ghrelin will be put in place. We will perform IND-enabling GLP toxicity and immunogenicity studies using the cGMP material. These studies are needed prior to beginning human trials. Once fully developed, this long- acting ghrelin derivative would provide a patient-friendly cachexia therapy that would significantly improve the prognosis and quality of life in patients with cancer and also in patients with other chronic disorders such as congestive heart failure (CHF) and chronic obstructive pulmonary disease (COPD).

Title:	**Validation of Macimorelin as a Test for Adult Growth Hormone Deficiency (PI: Garcia)**
Effort:	0.6 calendar months
Supporting Agency:	Aeterna Zentaris, Inc.
Grant Officer:	Jill Steeley; jill.steeley@ergomedplc.com
Performance Period:	2/8/2016-9/30/2019
Funding Level:	Annual Direct Costs
Project Goals:	The goal for this study is to determine the role of macimorelin as a diagnostic test for adult growth hormone deficiency.
Specific Aims:	Validate the use of macimorelin as a test for AGHD diagnosis.

Title:	**A 6-Week, Randomized, Doubleblind, Sponsor-Open Study to Assess the Effect of Repeated Subcutaneous Administration of PF-06946860 on Appetite in Participants with Advanced Cancer and Anorexia, Followed by an 18-Week Open-Label Treatment Period (Site PI: Garcia)**
Effort:	0.1 calendar months
Supporting Agency:	Pfizer, Inc.,C3651010
Performance Period:	10/2021-09/2022
Funding Level:	Dependent on enrollment
Project Goals:	To Assess the Effect of Repeated Subcutaneous Administration of PF-06946860 on Appetite in Participants with Advanced Cancer and Anorexia,
Specific Aims:	To Assess the Effect of the GDF-15 antibody PF-06946860 on Appetite in Participants with Advanced Cancer and Anorexia, Followed by an 18-Week Open-Label Treatment Period

Title:	**A Phase 1b, 12-Week, Open-Label Study to Assess the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics Following Repeated Subcutaneous Administrations of PfF06946860 in Patients with Non-Small Cell Lung Cancer and Cachexia (Site PI: Garcia)**
Effort:	0.1 calendar months
Supporting Agency:	Pfizer, Inc.,C3651009
Grant Officer:	Kirsten Duncan, PharmD; kirsten.duncan@pfizer.com
Performance Period:	11/2020-06/2022
Funding Level:	Dependent on enrollment
Project Goals:	This project will study the safety and tolerability of the novel agent PF06946860 in NSCLC suffering from cachexia.
Specific Aims:	The specific aims for the study include to assess the safety, tolerability, pharmacokinetic and pharmacodynamics of repeated doses of this novel agent in patients with cachexia due to NSCLC. This multicenter, regulatory study will set the basis for future studies in cachexia.

Title:	**Metabolomics approach to characterize the effects of androgen deprivation therapy on skeletal muscle in prostate cancer patients (PIs: Anderson and Dash)**
Effort:	0 calendar months
Role:	Co-Investigator
Supporting Agency:	NIH/ UW Center for Translational Muscle Research Pilot Grant, P30AR074990
Grant Officer:	Emily Carifi, emily.carifi@nih.gov
Performance Period:	06/2021-02/2022

Funding Level:	total costs
Project Goals/Aims:	To establish the role of androgen-dependent molecular pathways leading to androgen deprivation therapy (ADT)-induced sarcopenia in men with prostate cancer assessed by targeted metabolomics perturbations in skeletal muscle and plasma which will be associated with sarcopenia.

CURRENT

Title:	**Mechanisms of action of ghrelin in muscle and adipose tissue in cancer-related cachexia (PI: Garcia)**
Effort:	2.4 calendar months
Supporting Agency:	Department of Veterans Affairs
Grant Officer:	Kimberlee Potter, PhD; Kimberlee.Potter@va.gov
Performance Period:	10/1/2015-9/30/2025
Funding Level:	Total Costs
Project Goals:	The goal of this project is to characterize the mechanisms leading to muscle and fat preservation by ghrelin in the setting of cancer-related cachexia
Specific Aims:	1) Characterize the mechanisms mediating the effects of ghrelin in skeletal muscle in the setting of sarcopenic obesity. 2) Determine the mechanisms mediating the effects of ghrelin on adiposity and adipocyte function in sarcopenic obesity. 3) Establish the extent to which GHSR-1a mediate the effects of ghrelin in sarcopenic obesity.

Title:	**Neurobehavior, Neuropathology, and Risk Factors in Alzheimer's Disease (MPI: Peskind, Kraemer)**
Effort:	0.1 calendar months
Role:	Co-Investigator/Mentor
Supporting Agency:	NIH/NIA, T32AG052354
Grant Officer:	Dallas Anderson, PhD; andersda@nia.nih.gov
Performance Period:	5/1/2022-4/30/2027
Funding Level:	Total Costs
Project Goals:	The objective of our research training program is to provide interdisciplinary training for basic science, clinical, and translational researchers so that they will be able to advance clinical hypotheses about the etiology, pathophysiology, and treatment of AD and related disorders.
Specific Aims:	Our training program is the only formal program at the University of Washington focused on training investigators to carry out basic, clinical, and translational research in AD and related neurodegenerative dementing disorders.

Title:	**The role of mitochondria in ADT-induced sarcopenia in prostate cancer patients (PI: Garcia)**
Effort:	1.2 calendar months
Supporting Agency:	Department of Defense/CDMRP, W81XWH1810461
Grant Officer:	Melanie Neagley, PhD; Melanie.a.Neagley.ctr@mail.mil
Performance Period:	9/1/2018-8/31/2023
Funding Level:	Total Costs
Project Goals:	This project will study the role of mitochondria in prostate cancer patients undergoing ADT.
Specific Aims:	The specific aims of this proposal are to determine the extent to which ADT induces changes in: 1) Lean body mass (LBM) measured by X-ray densitometry

(DEXA), and muscle performance measured by handgrip strength, actigraphy, stair climbing power, 6-minute walk test, and VO2 peak. 2) Mitochondrial function assessed in-vivo by magnetic resonance spectroscopy and optical spectroscopy (31P MRS/OS) and ex-vivo in muscle biopsy specimens by measuring different aspects of mitochondrial metabolism and function including biomarkers of mitochondrial content and oxidative phosphorylation, mitochondrial respiration, mitochondrial biogenesis, mitophagy and production of reactive oxygen species (ROS). 3) Fatigue and HR-QOL scores as measured by well-validated questionnaires: Functional Assessment of Cancer Therapy–Prostate (FACT-P), European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-30) and Expanded Prostate Cancer Index Composite (EPIC) Assessment.

Title:	**Improving Patient-Important Outcomes with Testosterone Replacement in Hypogonadal Men with a Prior History of Cancer (MPI: Garcia, Basaria)**
Effort:	1.8 calendar months
Supporting Agency:	NIH/NCI, R01CA239208
Grant Officer:	Ashley Smith, PhD; smithas@mail.nih.gov
Performance Period:	5/8/2019-4/30/2025
Funding Level:	Total Costs
Project Goals:	This project will study the efficacy of testosterone replacement on cancer-related fatigue in male cancer survivors who report fatigue and have testosterone deficiency.
Specific Aims:	1) To compare the efficacy of weekly testosterone injections versus placebo on our primary outcome, fatigue, in cancer survivors with testosterone deficiency. 2) To compare the effects of weekly testosterone injections on sexual function (sexual activity score, sexual desire, erectile function), well-being, mood and QOL. 3) To determine whether testosterone administration improves body composition, muscle strength and physical activity more than placebo.

Title:	**Improving cancer-related fatigue, sexual dysfunction and quality of life in older men with cancer and androgen deficiency (MPI: Garcia, Basaria, DelFabbro)**
Effort:	1.8 calendar months
Supporting Agency:	NIH/NIA, R01AG061558
Grant Officer:	Sergei Romashkan, MD, PhD; (301) 435-3047; romashks@nia.nih.gov
Performance Period:	8/1/2019-4/30/2025
Funding Level:	Total Costs
Project Goals:	This project will study the effects of testosterone in elderly men with androgen deficiency and cancer.
Specific Aims:	1) To compare the efficacy of weekly testosterone injections versus placebo on our primary outcome, fatigue, in men with cancer and testosterone deficiency. 2) To compare the effects of weekly testosterone injections on sexual function (sexual activity score, sexual desire, erectile function), QOL (including mood, well-being and loss of productivity) and burden on the caregivers. 3) To compare the efficacy of testosterone administration versus placebo on body composition, muscle strength and physical function.

Title:	**foresiGHt: A multicenter, randomized, parallel-arm, placebo-controlled (double-blind) and active-controlled (open-label) trial to compare the efficacy and safety of once-weekly lonapegsomatropin with placebo and a daily somatropin product in adults with growth hormone deficiency (Site PI: Garcia)**
Effort:	0.1 calendar months
Supporting Agency:	Ascendis Pharma Endocrinology Division A/S, TCH-306
Grant Officer:	Olu Lawson, Clinical Trial Manager; o.lawson@accelsiors.com
Performance Period:	5/13/2021-Present
Funding Level:	Dependent on enrollment
Project Goals:	To compare the efficacy and safety of once-weekly lonapegsomatropin with placebo and a daily somatropin product in adults with growth hormone deficiency
Specific Aims:	1) To compare safety; and 2) to compare efficacy of a new long acting GH formulation to placebo and to daily GH in patients with AGHD.

Title:	**GH replacement therapy in Veterans with mTBI and AGHD (PIs: Garcia and Jorge)**
Effort:	1.2 calendar
Supporting Agency:	VA Cooperative Studies Program
Performance Period:	12/01/2020-11/30/2024
Funding Level:	total costs
Project Goals:	This is large multicenter study that will be examine the efficacy of rhGH to improve quality of life (QoL) among Veterans with mild TBI and GH deficiency.
Specific Aims:	When compared with placebo, GHRT will have a beneficial effect on: 1) QoL; 2) Body composition (specifically reduction of fat content and visceral fat); 3) Fatigue; 4) Chronic Pain; 4) Depression; 5) Cognitive functioning (specifically attention, memory and executive functioning

Title:	**Growth Hormone Replacement Therapy in Veterans with Gulf War Illness and GH Deficiency (PI: Jorge)**
Effort:	2.4 calendar months
Supporting Agency:	Department of Defense/CDMRP, W81XWH2110450 (Subaward #7000001651)
Performance Period:	10/01/2021-09/29/2024
Funding Level:	Total Costs (subaward)
Project Goals:	This project is a multicenter, VA, randomized clinical trial of GH vs placebo in Veterans with Gulf War Illness and AGHD
Specific Aims:	To establish the safety and efficacy of GH replacement in individuals with AGHD and GWI.

Title:	**A Multicenter, Open-Label, Extension Trial to Investigate Long Term Efficacy and Safety of Lonapegsomatropin in Adults with Growth Hormone Deficiency (Site PI: Garcia)**
Effort:	0.1 calendar months
Supporting Agency:	Ascendis Pharma Endocrinology Division A/S, TCH-306-EXT
Grant Officer:	Olu Lawson, Clinical Trial Manager; o.lawson@accelsiors.com
Performance Period:	5/20/2022-Present
Funding Level:	Dependent on enrollment
Project Goals:	To assess the long-term safety of once-weekly lonapegsomatropin in adults with growth hormone deficiency (GHD/AGHD) who participated in trial TCH-306.

Title:	**Summer Research Program**
Effort:	0.6 calendar months
Supporting Agency:	Department of Veterans Affairs
Performance Period:	05/01/2022-04/30/2025
Funding Level:	Total Costs
Project Goals/Aims:	This project enhances the diversity of the biomedical, behavioral, clinical, health services and rehabilitative research workforce by providing research experiences and related opportunities that can enrich the pool of individuals from diverse backgrounds, including nationally underrepresented groups, veterans, and disabled individuals who will be available to compete for future research opportunities in the mission areas of importance to the VA.

PENDING

Title:	**SArcopenia in men with Prostate Cancer undergoing ADT (SAP-ADT) (MPI: Garcia, Gharib)**
Effort:	2.4 calendar months
Supporting Agency:	NIH/NCI, R01CA279220
Performance Period:	04/01/2023-03/31/2028
Funding Level:	Total Costs
Project Goals:	We propose to follow men with prostate cancer starting ADT for one year to establish how best to measure sarcopenia, identify clinical and biochemical predictors of this complication, and apply state-of-the-art multi-omics methods to characterize the molecular mechanisms in skeletal muscle that lead to sarcopenia. The data generated will provide essential information on tools to measure sarcopenia that are clinically meaningful to patients, shed light on new pathways and targets for this condition, and establish markers of sarcopenia that could allow for early diagnosis and improved selection of patients and outcomes for future clinical trials.
Specific Aims:	1) ADT will decrease muscle strength, physical performance, appendicular lean body mass (aLBM), and QOL and that these changes will be clinically meaningful. 2) ADT will alter molecular profiles (at transcript, protein, and metabolite levels) in muscle and plasma as measured by an unbiased multi-omics approach, and this will be associated with the development of sarcopenia. 3) Specific pathways probed in plasma and muscle, and impairments in clinical parameters including muscle strength and physical performance, aLBM, and PROs at baseline will predict the development of sarcopenia upon starting ADT.

OVERLAP

There is no scientific or budgetary overlap amongst current or pending projects. If all pending applications are funded, the percent effort on funded projects will be adjusted to maintain sponsored support at or below 12 calendar months.

The following statements assure:

I certify that the current and pending support provided here is current, accurate, and complete;

I agree to update such disclosure at the request of the agency prior to the award of support and at any subsequent time the agency determines appropriate during the term of the award;

I have been made aware of these disclosure requirements as required under Section 223(a)(1) of the William M. (Mac) Thornberry National Defense Authorization Act for Fiscal Year 2021 (https://www.govinfo.gov/content/pkg/PLAW-116publ283/pdf/PLAW-116publ283.pdf).

I am aware that false, fictitious, or fraudulent statements or claims may result in criminal, civil, or administrative penalties (218 USC 1001).

Signature: 

Date: 09/13/2022