Progress Through Partnerships:
Consensus Building to Address Major Unmet Medical Needs
The FNIH Biomarkers Consortium Sarcopenia Initiative

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Senior Scientific Program Manager

November 4, 2013
FNIH Overview

- Sole organization authorized by the U.S. Congress to support the mission of the NIH by creating and managing public-private partnerships

- 501(c)(3) non-profit organization
  - Raised >$560 million to support >400 projects
  - 100 currently active programs

- Non-governmental
  - Independent Board of Directors
  - NIH Director/FDA Commissioner *ex-officio* FNIH Board Members

- 94 cents of every $ directly supports research programs
- Consistently rated highly on Charity Navigator
The Role and Function of FNIH

- Create innovative public-private biomedical partnerships that complement NIH priorities and advance the public health

- Partner with corporations, foundations, academia, federal agencies, and philanthropic individuals

- Serve as “honest broker”, providing a neutral forum able to engage all partners

- Enable efficient, effective collaboration

- Structure flexible donor relationships

- Manage grants, contracts, and projects efficiently
## Major FNIH Research Partnerships

### Gates Foundation Projects
**$300M**
Partner: Bill & Melinda Gates Foundation  
(6 grants in global health, AIDS, tuberculosis and malnutrition)

### Alzheimer’s Disease Neuroimaging Initiative (ADNI & ADNI 2)
**$50M**
Partners: NIA/NIBIB & 19 companies/2 non-profits

### Observational Medical Outcomes Partnership
**$28M**
Partners: FDA, PhRMA, 16 pharmaceutical partners

### Genetic Association Information Network (GAIN)
**$26M**
Partners: NHGRI, NLM & Pfizer, Affymetrix, Broad Institute, Perlegen Sciences

### Osteoarthritis Initiative (OAI & OAI 2)
**$24M**
Partners: NIAMS & Pfizer, Novartis, other pharmaceutical partners

### The Biomarkers Consortium
**$50M**
Partners: NIH, FDA, CMS, BIO, PhRMA, biopharmaceutical industry, non-profits
The Biomarkers Consortium

Fosters the exchange of knowledge and expertise among industry, academic and government leaders

- Qualifies biomarkers for specific applications in diagnosing disease, predicting therapeutic response, and improving clinical practice
- Employs rigorous, inclusive governance and project management with clearly defined goals and milestones
- Facilitate cross-sector partnerships across a broad range of disease and therapeutic areas
- Provides information to inform regulatory decision-making
- Enables pre-competitive sharing of data, resources, and expertise across stakeholders to collaboratively address unmet medical needs
Biomarkers Consortium Contributing Members

Industry Members
- Actelion Pharmaceuticals Ltd
- Amgen
- AstraZeneca
- Crescendo Biosciences
- Daiichi Sankyo, Inc.
- Eisai, Inc.
- Johnson & Johnson
- Eli Lilly and Company
- Merck, Sharpe & Dohme
- Mitsubishi Tanabe Pharma Development America
- Metabolon
- Myriad RBM
- Pfizer Inc.
- Regeneron
- Sanofi
- Takeda Pharmaceuticals USA

Non-Profit Members
- Alzheimer’s Association
- American Diabetes Association (ADA)
- American Orthopaedic Society for Sports Medicine
- Arthritis Foundation
- Autism Speaks
- Biotechnology Industry Organization (BIO)
- California Dairy Research Foundation (CDRF)
- Center for Proteomic & Genomic Research
- CHDI Foundation
- Dairy Research Institute (DRI)
- Foundation for Health Improvement & Technology
- JDRF
- Pharmaceutical Research and Manufacturers of America (PhRMA)
- PROOF Centre of Excellence
- Radiological Society of North America (RSNA)
- U.S. Pharmacopeia (USP)
Biomarkers Consortium Governance Structure

Executive Committee
NIH / FDA / CMS / industry / FNIH

- Cancer Steering Committee
- Inflammation & Immunity Steering Committee
- Metabolic Disorders Steering Committee
- Neuroscience Steering Committee

Multiple Project Teams (including the Sarcopenia I and II Projects)
Representatives from NIH, FDA, Industry, Subject Experts from Academia
The MDSC Sarcopenia Initiative

Problem Statement

- Loss of muscle mass is common in aging and wasting conditions, and is associated with weakness, poor function and lower survival.

- This important clinical condition is currently poorly recognized.

- Multiple potential interventions exist to treat or prevent muscle mass loss.

- The field needs a clinical definition to proceed with regulation formulation.
The MDSC Sarcopenia Initiative
Scope of the Problem

- Currently we are unable to identify patients that require treatment.

Clear and valid diagnostic criteria and outcome measures are needed to fulfill regulatory demands and support investments in testing interventions.

- In the US the number of older adults (≥ 65 years) is expected to double to 86.7 million near 2050 in the US.

- Expecting increased comorbidities and need for institutionalization.
The MDSC Sarcopenia Initiative

The Ultimate Goal

- Create an evidence-based definition by generating:
  - Clear and valid diagnostic criteria and outcome measures acceptable to clinicians, FDA, and health insurers, including CMS
  - Opportunities to develop and test potential interventions on low muscle mass and strength, to improve the health of the older adult
  - Clinical recognition and practice guidelines for screening, diagnosis and management
The MDSC Sarcopenia Initiative

Sarcopenia I Project Goals

- Use cross-sectional and prospective data from several aging studies to evaluate criteria for sarcopenia diagnosis, based on shared operational definitions of performance, strength, body composition (pooled analyses completed)

- Present findings to a broad professional audience for feedback and recommendations (Consensus Meeting, co-sponsored by FDA, FNIH and NIA took place on May 8-11, 2012 in Baltimore, MD)

- Publish findings and define a consensus/multi-stakeholder definition of clinically important sarcopenia (manuscripts ready for submission)
Sarcopenia Project Accomplishments

1. The FNIH Sarcopenia Project: Rationale, Study Description and Recommendations (Studenski S, et al.)

2. Cut-points in grip strength for the clinical definition of slowness with weakness (Alley D, et al.)

3. Cut points for low appendicular lean mass identifying older adults with weakness (Cawthon P, et al.)

4. Criteria for clinically important weakness and reduced muscle mass and their longitudinal association with incident mobility disability and mortality (McLean R, et al.)

5. Comparison of Handgrip to Leg Extension Strength for Predicting Slow Gait Speed in Older Adults (Fragala M, et al.)

6. Consensus Definition Comparisons (Dam T, et al.)

Data Pooling
(~ 10 observational and clinical data sets)

Joint Team Recommendations

Project Team

Consensus Conference
May 2012 – Baltimore, Maryland
The MDSC Sarcopenia I Project

Conclusions

- Through the Biomarkers Consortium Sarcopenia Project, evidence-based candidate criteria were established:

  Weakness + Low Lean Mass
  Low lean mass + Weakness + Slow walking speed

- Based on this consensus, further biomarker analyses have become possible in future clinical trials

- A series of manuscripts was submitted to the Journal of Gerontology Medical Sciences in June 2013 - currently in review before publication
Sarcopenia I Results Dissemination Strategy

- Publications of results as a series of papers in a major peer-review journal (expected in late 2013 or early 2014)
- Public announcements, webinar, conference to disseminate the findings of the research after the paper publications to be organized by NIA, NIH
- FNIH press-release planned at the same time
- Invited ASBMR “Cutting Edge Discoveries in Muscle Biology, Disease and Therapeutics” Presentation at the upcoming ASBMR Annual Meeting in Baltimore, MD – scheduled for Oct. 3, 2013
- Innovator Presentation at the Partnering for Cures Meeting of FasterCures in New York, NY
The MDSC Sarcopenia II Project

Project Overview

- **Main Goal**
  - Validate and confirm the predictive validity of the candidate criteria established in phase I.

- **Core Hypothesis**
  - Analysis of populations with higher levels of mobility limitation and with muscle wasting disorders will exhibit stronger associations of the candidate criteria with outcomes.

- **Duration and Estimated Budget**
  - 30 months; $1.5M
The MDSC Sarcopenia II Project Team

**Project Team Chair:**
- Rosaly Correa-de-Araujo M.D., M.Sc., Ph.D. - NIA, NIH

**Principal Investigators**
- Shalender Bhasin, M.D. – Brigham’s and Women’s Hospital, Harvard Medical School
- Roger Fielding, Ph.D. – Tufts University
- Christine Liu, M.D. – Tufts University
- Susan Greenspan, M.D. – University of Pittsburgh
- Tamara Harris, M.D., M.S. – NIA, NIH
- Denise Orwig, Ph.D., University of Maryland
- Jay Magaziner, Ph.D., M.S. – University of Maryland

**Biostatisticians**
- Subashan Perera, Ph.D., University of Pittsburgh
- Michelle Shardell, Ph.D., University of Maryland
- Thomas Travison, Ph.D., Brigham’s and Women’s Hospital, Harvard Medical School
- William Hawkes, Ph.D., University of Maryland

**Foundation for NIH**
- Maria Vassileva, Ph.D.

**Academic Advisors:**
- Steven kritchely, PhD, Wake Forest University
- Thuy-Tien Dam, M.D. – Columbia University
- Maren Fragala, Ph.D. - University of Central Florida
- Douglas Kiel, M.D., M.P.H. – Harvard Medical School
- Stephanie Studenski, M.D., M.P.H. – University of Pittsburgh
- Anne Kenny, M.D., University of Connecticut

**Professional Organization Representative (ASBMR):**
- Keith Hruska, M.D.

**Federal Government Representatives:**
- Dragos Roman, M.D. – FDA
- Luigi Ferrucci, M.D. - NIA, NIH
- Lyndon Joseph, Ph.D. – NIA, NIH
- Judy Hannah, Ph.D. – NIA, NIH

**Industry Representatives:**
- Olivier Benichou, Eli Lilly
- Julie Chandler, M.D., Merck
- Suzette Perera, Ph.D., Abbott Nutrition
## The MDSC Sarcopenia II Project

### Data Sets Selected for the Analyses

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Investigators / Affiliations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hip Fracture 3 Study Cohort</td>
<td>205 w</td>
<td>Denise Orwig, PhD</td>
</tr>
<tr>
<td>Hip Fracture 4 Study Cohort</td>
<td>180 w</td>
<td>Jay Magaziner, PhD, MS</td>
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<td>University of Maryland</td>
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<tr>
<td>LIFE-P Study</td>
<td>424 w &amp; m</td>
<td>Roger Fielding, PhD</td>
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<tr>
<td></td>
<td></td>
<td>Christine Liu, MD</td>
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<tr>
<td></td>
<td></td>
<td>Tufts University</td>
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<td>VIVE-2 Study</td>
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<td>Frailty in LTC Study</td>
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<td>Susan Greenspan, MD</td>
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<td>Health ABC Study</td>
<td>459 m</td>
<td>Tamara Harris, MD</td>
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<td>TOM Trial</td>
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<td>TEEM Trial</td>
<td>309 m</td>
<td>Brigham and Women’s Hospital, Harvard Medical School</td>
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## The MDSC Sarcopenia II Project

### Timeline Summary

<table>
<thead>
<tr>
<th>Year 1</th>
<th>Year 2</th>
<th>Year 3</th>
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<tbody>
<tr>
<td>Preliminary data analysis of each participant study</td>
<td>Conduction of data analyses including pooling data</td>
<td>Writing papers, submitting for publication. Go-No-Go Decision</td>
</tr>
<tr>
<td>Identification of potential gaps, better defining characteristics of each participant study’s population, variables of special attention. Go-No-Go Decision</td>
<td>Interpreting data</td>
<td>Holding consensus conference</td>
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<tr>
<td>Reassessing methodological approach</td>
<td>Holding regular group calls for discussion</td>
<td>Summarizing and publishing consensus definition for sarcopenia</td>
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<tr>
<td>Holding regular group calls for discussion</td>
<td>Start development of dissemination strategy</td>
<td>Dissemination strategy implementation</td>
</tr>
<tr>
<td>Preliminary data analysis of each participant study</td>
<td>Conduction of data analyses including pooling data</td>
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</tbody>
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The MDSC Sarcopenia II Project
Addressing a Significant Unmet Medical Need Through

- Evidence-Based Approach
  - Clear and valid diagnostic criteria and outcome measures
  - Development and testing potential interventions on low muscle mass and strength
  - Clinical recognition and practice guidelines for screening, diagnosis and management

- Precompetitive Collaboration of All Relevant Stakeholders

- Impact on
  - Public health
  - Drug development
  - Regulatory decision making
  - Researchers/clinicians
  - Patients
## The MDSC Sarcopenia II Project
### Budget Estimate

<table>
<thead>
<tr>
<th></th>
<th>Year 1</th>
<th>Year 2</th>
<th>Year 3 (6 months)</th>
<th>Total</th>
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<tbody>
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<td>Consensus Conference</td>
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<td><strong>Total Request</strong></td>
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<td>$540,000</td>
<td>$400,000</td>
<td>$1.5M</td>
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*FNIH Costs include direct legal and project management expenses and 25% fee on direct expenses*
The MDSC Sarcopenia II Project

Anticipated Funding Request

- For large companies:
  $150K-$200/year for 2 years for a total funding commitment of $300-$400K
- For medium-sized companies:
  $120-150K/year for 2 years, for a total funding commitment of $240-$300K
- For non-profits or small organizations:
  $10-$30K total

*All commitments can be stretched over 3 years if requested by the funder.
The MDSC Sarcopenia II Project

Potential Stakeholders

- Pharmaceutical Companies
- DEXA Equipment Manufacturers
- Strength Assessment and Training
- Sports Companies
- Food Companies
- Health Organizations
Acknowledgements

- **The Project Team Leaders:**
  For the Sarcopenia I Project: Stephanie Studenski, MD, University of Pittsburgh
  The Sarcopenia II Project: Rosaly Correa-de-Araujo, M.D., NIA, NIH

- **Metabolic Disorders Steering Committee (MDSC) Co-Chairs:**
  Myrlene Staten, MD - NIDDK/NIH and David Kelley, MD - Merck Research Labs

- **Sarcopenia I Project Funders:**
  Abbott Nutrition, Amgen, Eli Lilly, Merck, Novartis, DRI, NIA, FDA

- **The Biomarkers Consortium Sarcopenia I and II Project Team Members:**
  Dawn Alley, Peggy Cawthon, Thuy-Tien Dam, Chhanda Dutta, Luigi Ferrucci, Maren Fragala, Jack Guralnik, Judy Hannah, Tamara Harris, Anne Kenny, Steven Kritchevsky, Bob McLean, Dragos Roman, Ali Mohamadi, Carmen Sceppa, Michelle Shardell, Qian-Li Xue, Olivier Benichou, Julie Chandler, Doug Kiel, Suzette Pereira, Dan Rooks, Roger Fielding, Shalender Bhasin, Denise Orwig, Jay Magaziner, Susan Greenspan, Subashan Pereira

- **FNIH Colleagues:**
  Maria Freire, Jessica Ratay, David Wholley
Thank you
For more information and questions:
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