MYOTONIC DYSTROPHY FOUNDATION

Care and a Cure

MDF 3.0: Accelerating Drug Development

September 2016

MDF 3.0: Impact

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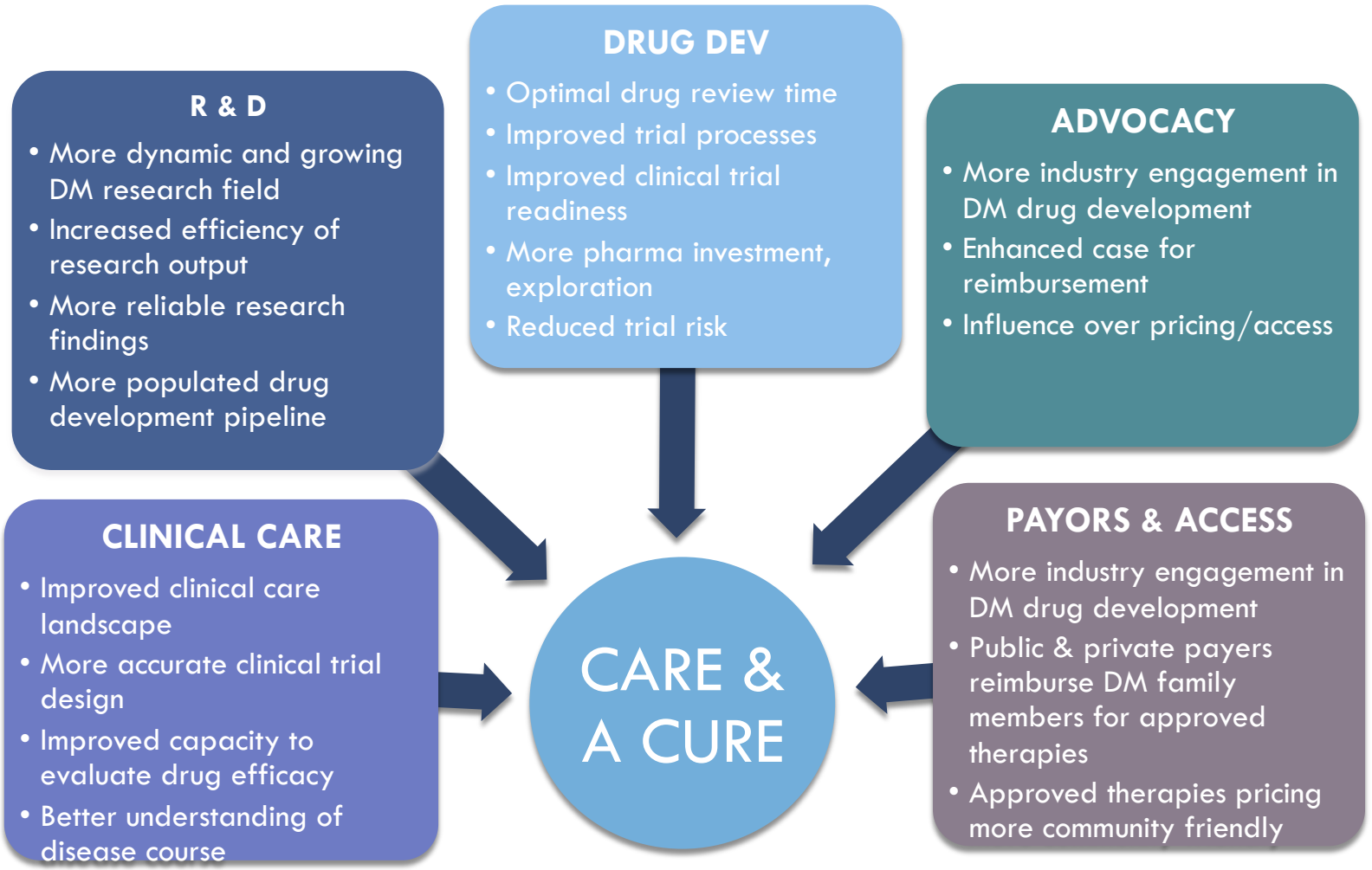

MDF 3.0: Progress at a Glance

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3 | 2015 – 2017 $5,000,000

CLINICAL CARE

- Care Considerations
- Care Landscape Analysis and SWOT

RESEARCH

- Fund-a-Fellow Expansion
- Mouse Model Creation
- Biobank and Cell Line Library Expansion
- Mouse SOPs
- SAC Expansion and Development

DRUG DEV

- Clinical Research Network Expansion
- Biomarkers and Endpoint Development
- Industry Drug Screening Grants
- Regulatory Advocacy
- Clinical Coordinators Recognition Program
- Registry Expansion

ADVOCACY

- Muscular Dystrophy Coordinating Committee
- Federal agency advocacy for research funding
- DM Prevalence Study

PAYORS & ACCESS

- Burden of Disease Study
- Meeting with Social Security Administration & presentations at MDF conference

DRUG DEVELOPMENT: Targets

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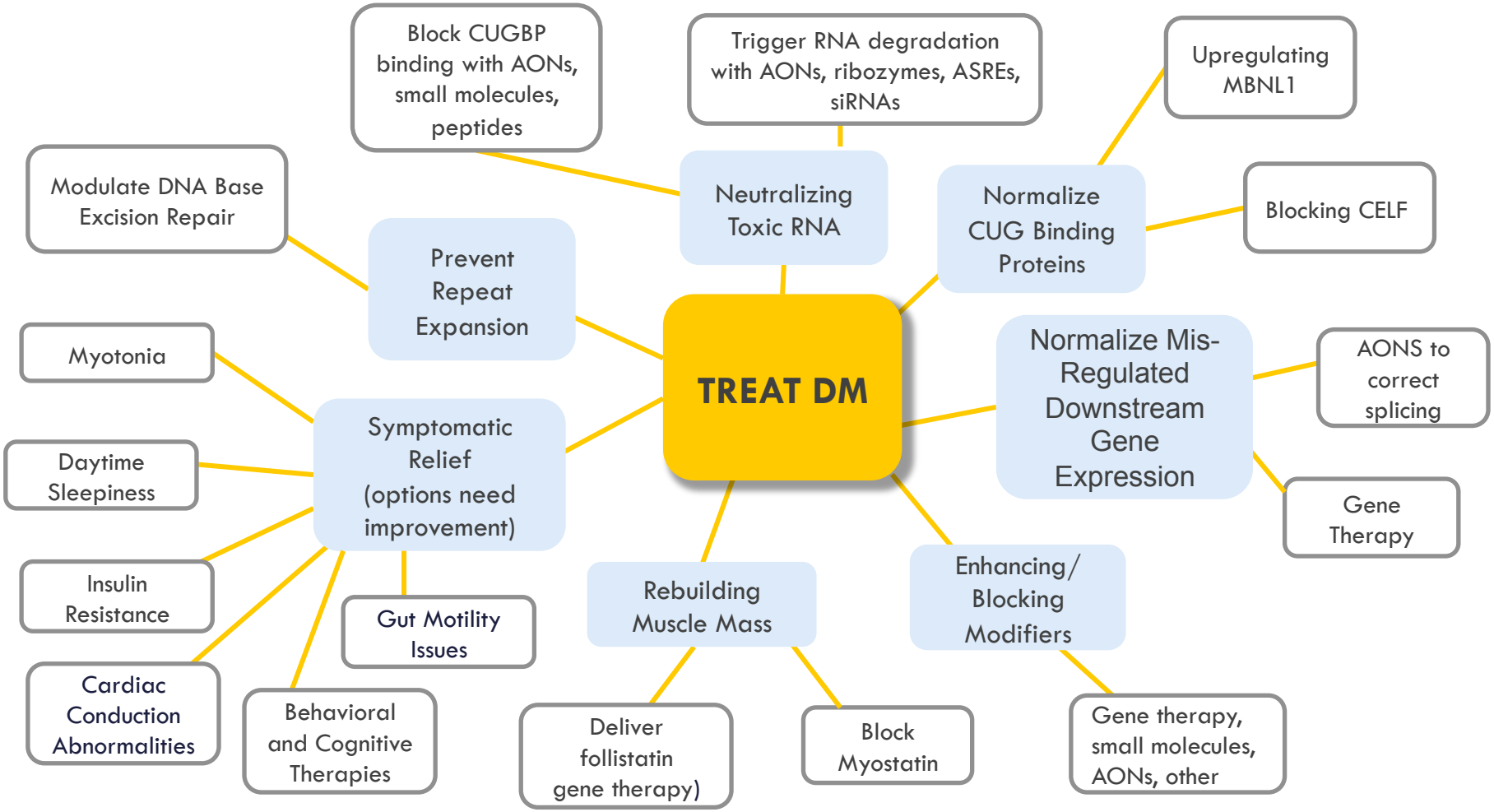

RESEARCH: MDF Fellowship Program

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5 **ONGOING $1,500,000**

- 25 Fellows funded since 2009; fellows posters at Conference
- A 2014 evaluation:
  - >70% remained in DM research
  - 60% raised additional funding totaling over $2.5M
- Four MDF Fellows have gone to receive faculty positions and in several cases, NIH and other agency funding

Eric Wang, Ph.D.
Center for NeuroGenetics
Professor- Molecular Genetics &Microbiology
University of Florida

Yao Yao, MS, PhD
Asst. Professor
Pharmacy Practice and Pharmaceutical Sciences
University of Minnesota

Auinash Kalsotra, Ph.D.
Asst. Professor
of Biochemistry
and Medical Biochemistry
College Of Medicine
University of Illinois

Nicholas Johnson, M.D.
Neurology – Asst. Professor
University of Utah

RESEARCH: Building a Better Mouse

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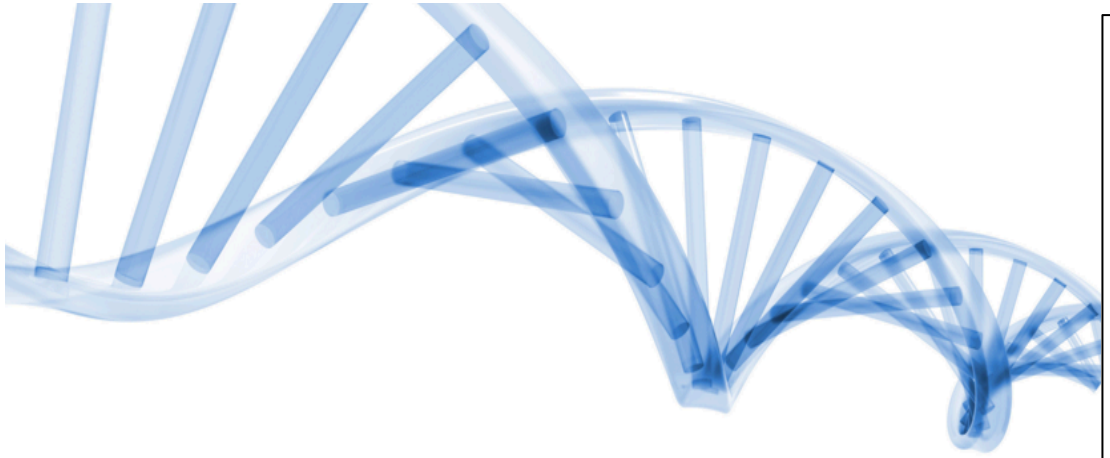
2016 – 2017 $90,000



Why do we need another mouse model?

- Genetic stability
- Better symptom profile (e.g., cognitive effects)
- Better access
- Avoiding licensing/reach-through issues
- Funding: Cat Lutz (JAX) BAC transgenic DM1 model

COMMISSION MOUSE FROM JACKSON LABS

MOUSE DISTRIBUTION: JACKSON LABS

MDF SAC SUBCOMMITTEE TO OVERSEE PROJECT

RESEARCH: Cell lines for Screening

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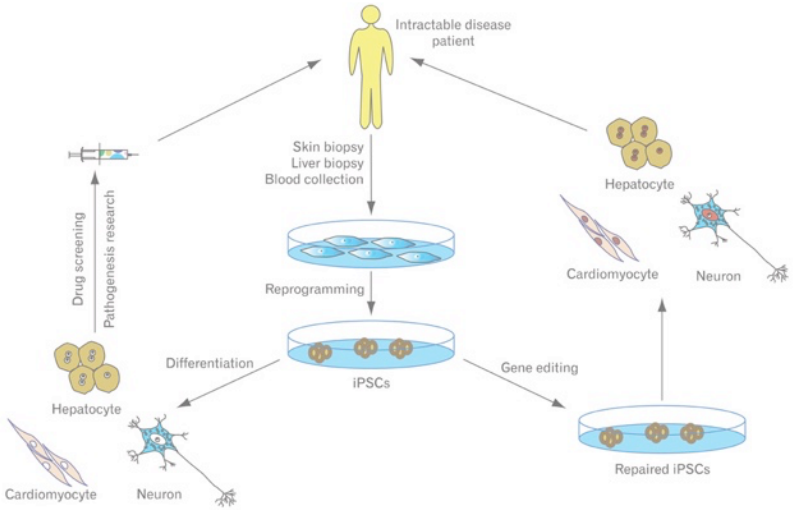
7 | 2016 – 2017 $106,000

Why do we need new cell lines?

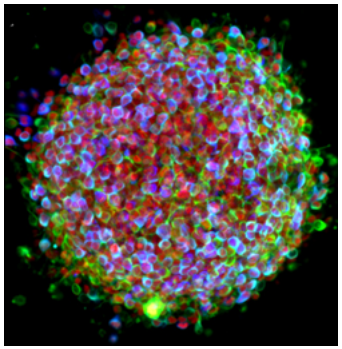
- Deriving specific cell types for screen
- Improving flexibility and availability through iPSCs housed at an NIH source
- Avoid licensing and reach-through issues
- Funding: NHCDR/NINDS, 4 DM1 & 4 DM2 lines



COMMISSION MOUSE FROM NHCDR-NINDS

CELL LINE DISTRIBUTION: NHCDR

MDF SAC SUBCOMMITTEE TO OVERSEE PROJECT



NINDS iPSC cluster

DRUG DEVELOPMENT: Endpoints RFA

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2016 – 2017 $150,000

ENDPOINTS RFA:

- **Develop new or refine existing endpoints for DM**
- **$150,000, 1 yr award**
- **Funding: Donovon Lott (UFL) for skeletal muscle MRI**
- **Upper & lower extremity; correlate with variety of functional measures**
- **25 subjects**
- **Strong MRI track record at UFL, inc. initiating qualification process for DMD**
- **Project requires FDA consultation**

DRUG DEVELOPMENT: Biomarkers

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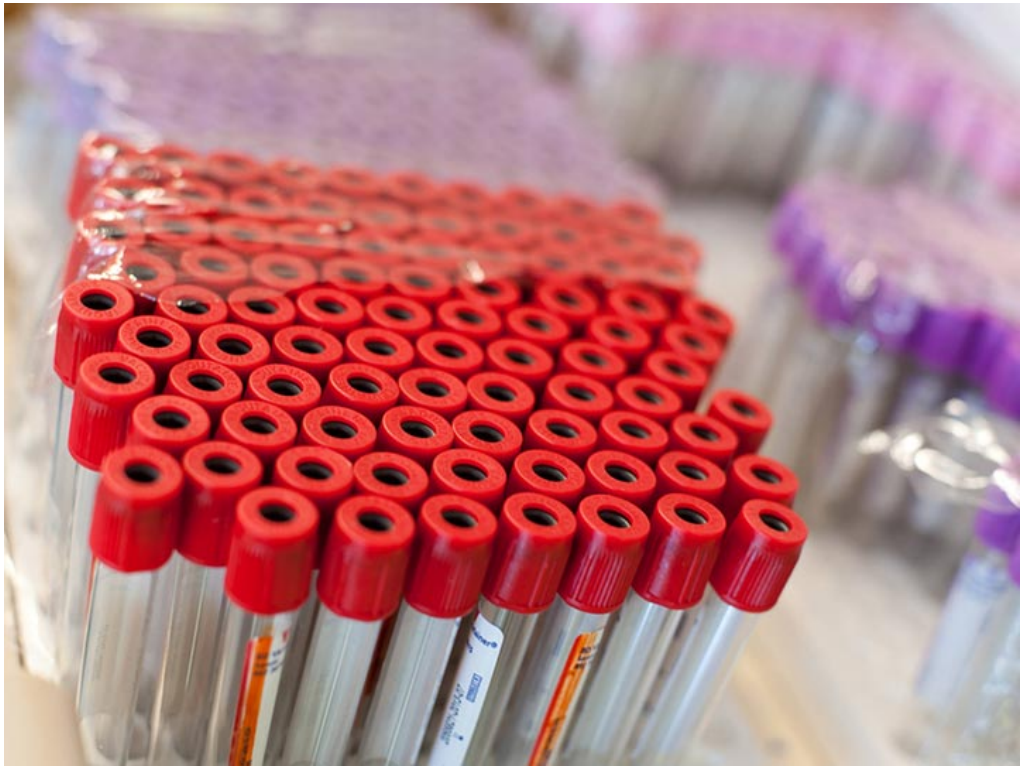
2016 – 2017 $150,000



BIOMARKER RFA:

- Development of a biomarker for a specific drug program or a biomarker of general utility; should be a path to regulatory qualification
- $150,000, 1 yr award
- Taking recommendation for funding to Board

DRUG DEVELOPMENT: PHENO-DM1

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10 | 2017 – 2018 $120,000

PHENO-DM1 Study:

- **Leverage existing NIHR (UK) grant to Newcastle**
- **$120,000, 18 month award**
- **Funding: Hanns Lochmuller, to extend 1 yr natural history study in 200-400 subjects to 2 yrs**
- **Upper & lower extremity; correlate with variety of functional measures**
- **25 subjects**
- **20 measures (inc. MRC strength, 10MWT, nine-hole peg, DM1Activ, FVC/FEV, MDHI, Mini Mental)**

DRUG DEVELOPMENT: Benefit-Risk Study

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11 2015-2016 $75,000

CRITICAL REGULATORY QUESTION:

- Does drug's clinical benefit outweigh risk?
- **Improving, halting or slowing muscle weakness = greatest benefit to study participants**
- **Reducing fatigue = least benefit**
- Loss of appetite was the best tolerated risk
- 1:1000 chance of liver damage was the least tolerated

REGULATORY ADVOCACY

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2015--2016 $100,000

- All-day FDA workshop at MDF conference 2015
  - Moderator: former FDA Deputy Commissioner Dr. Stephen Spielberg
  - Topics:
    - Patient-Focused Drug Development
    - Endpoint Validation Group
    - Neurology Review Division
    - Biomarkers Validation Group
    - >70 attendees from industry, academia, NIH
    - Publication submitted August 2016
- Patient Focused Drug Development Meeting at MDF conference 2016
  - Significant participation confirmed from FDA leadership
  - First formally approved Externally-Led PFDD for FDA
  - Will include testimony from MDF conference attendees on burden of disease and input on desired impacts of treatments
  - Proceeds to inform FDA Neurology Review Division via regulatory framework
- Outreach to European Medicines Agency ongoing

REIMBURSEMENT & ACCESS: Burden of Disease Study

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2015 – 2016 $50,000

GOAL: DOCUMENT ANNUAL MEDICAL COSTS OF DM DIAGNOSIS

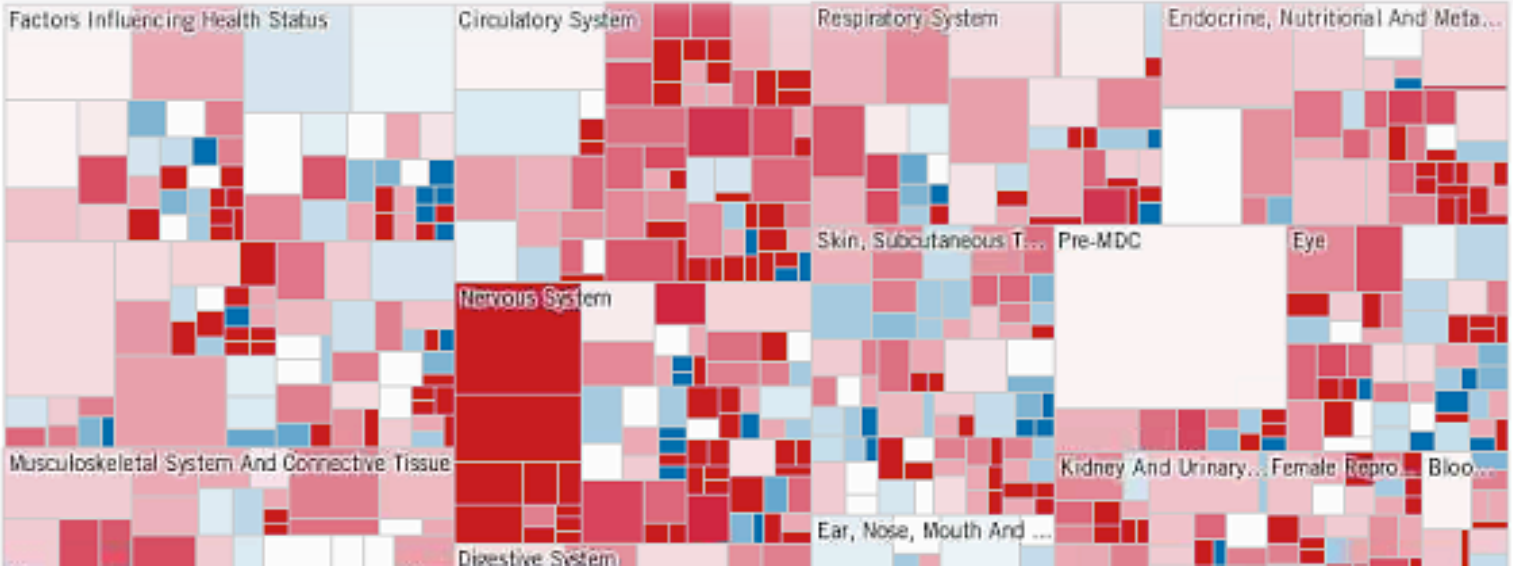
TARGET AUDIENCE: PAYERS & POLICY MAKERS

PARTNERS: MAYO CLINIC & OPTUM LABS

- REACH: >100M CLAIMS & 300K MATCHED MEDICAL RECORDS

STATUS: PRELIMINARY FINDINGS DUE FALL 2016

NEXT STEPS: CMS DATA FOR EMPLOYMENT, EDUCATION & QOL



FEDERAL ADVOCACY: Prevalence Study

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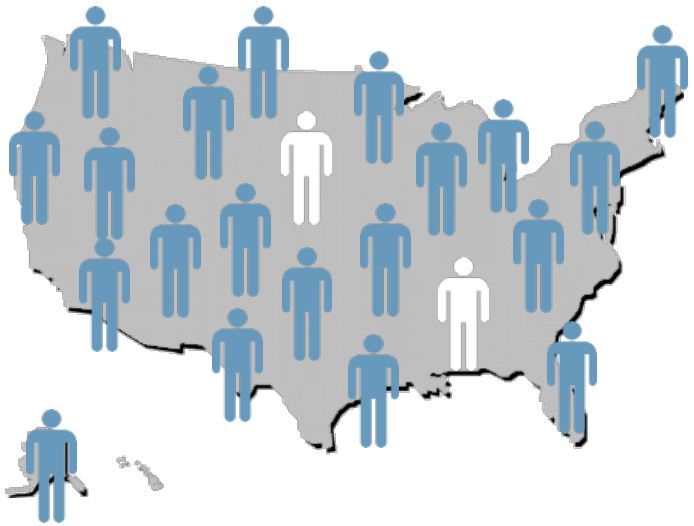
14 | 2015 – 2017 $ 575,000

GOAL: Define mutation and pre-mutation load in US population

TACTIC: Two-phased project

- Phase I: develop and validate a scalable, inexpensive methodology
  - Award to Nick Johnson, UUT 2015
  - Assay complete
- Phase II: measure the frequency of DM1 and DM2 expansions in the general population via +/- 70,000 newborn blood spots
  - One application received
  - Phase II RFA review November 2016

THE UNIVERSITY OF UTAH



DRUG DEVELOPMENT: Network & Natural History Data Expansion Project

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15 **ONGOING $700,000**

GOAL:

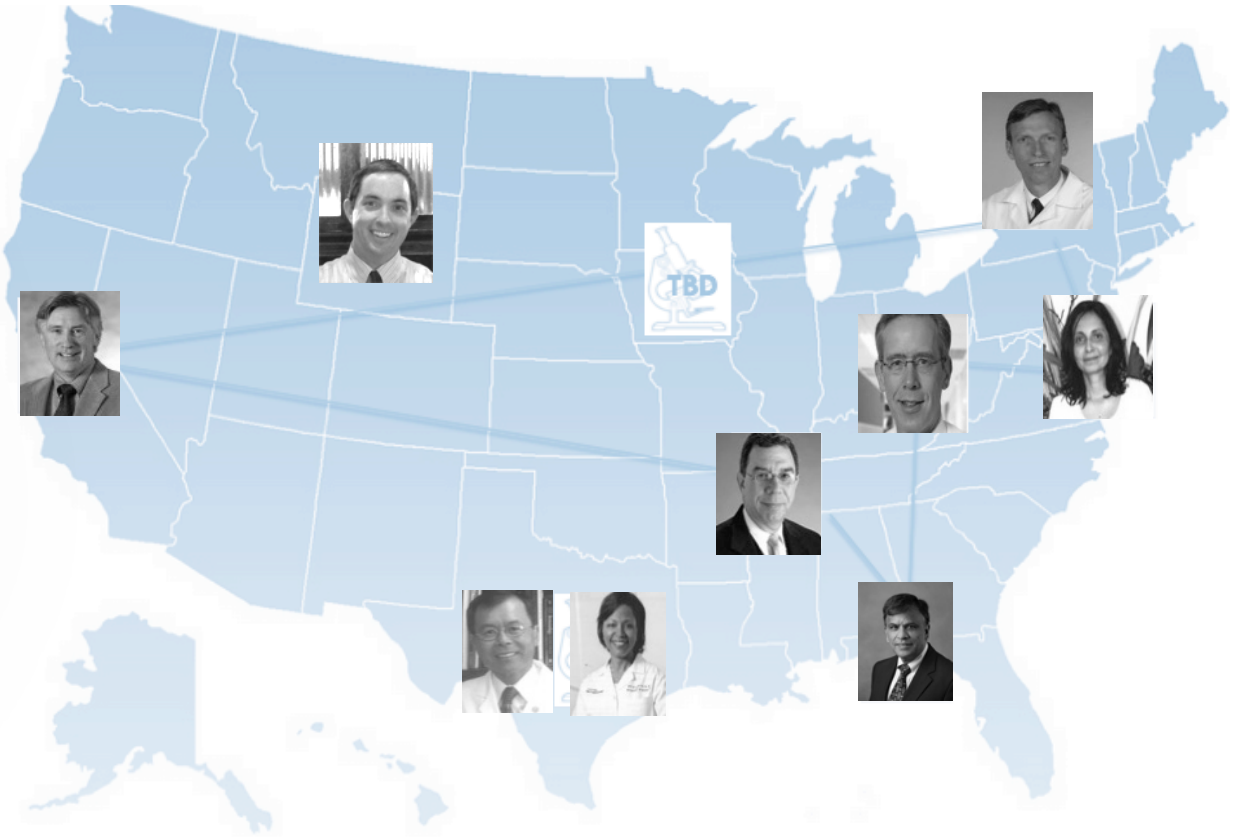
- National network of study & trial sites
- Increase natural history data collection

IMPACT:

- Improved trial infrastructure
- Drive study & trial efficiencies
- Capture more natural history data
- Create centralized, accessible database

TACTICS:

- Annual multi-site grants based on milestones



Drug Development: DM Advantages

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DM is Tractable

- Prevalence: about 30K in the US, likely significantly understated
- Compelling and well-understood disease mechanism
- Preclinical POC established for different targets in the pathogenic cascade
- Ability to get rapid molecular readout (splicing) of target engagement/modulation in early stage clinical trials
- Ability to use molecular readout in dose ranging studies
- Ability to get physiological readout of disease modification in early stage clinical trials
- Concerted effort on endpoints, including efforts to coordinate endpoint SOPs internationally
- Existing registries provide data, patient location and trial facilitation
- Patient care considerations being disseminated internationally
- Centers of excellence program in the US (DMCRN) & effort to establish & coordinate with EU

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