MYOTONIC DYSTROPHY FOUNDATION

Care and a Cure

MDF 2017 Research Update

2017 MDF Annual Conference

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September 2017

Overview

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- What is the goal of MDF's research efforts?
- What we are doing to foster research & development?
- Why we are doing what we do?
- Where are we going next?

To Develop Therapies, We Need…

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- To understand DM (that gives us drug targets)
- To validate the targets (that makes sure they're disease modifying)
- To identify candidate drugs & biologics for valid targets
- To ensure that the candidates are safe & effective, starting with preclinical models & then moving through clinical trials

To do this, we need expertise, disease knowledge, tools, $$s, & time

How can MDF best make a difference?

Getting from A to B: The Need to Invest in Drug Programs & Infrastructure

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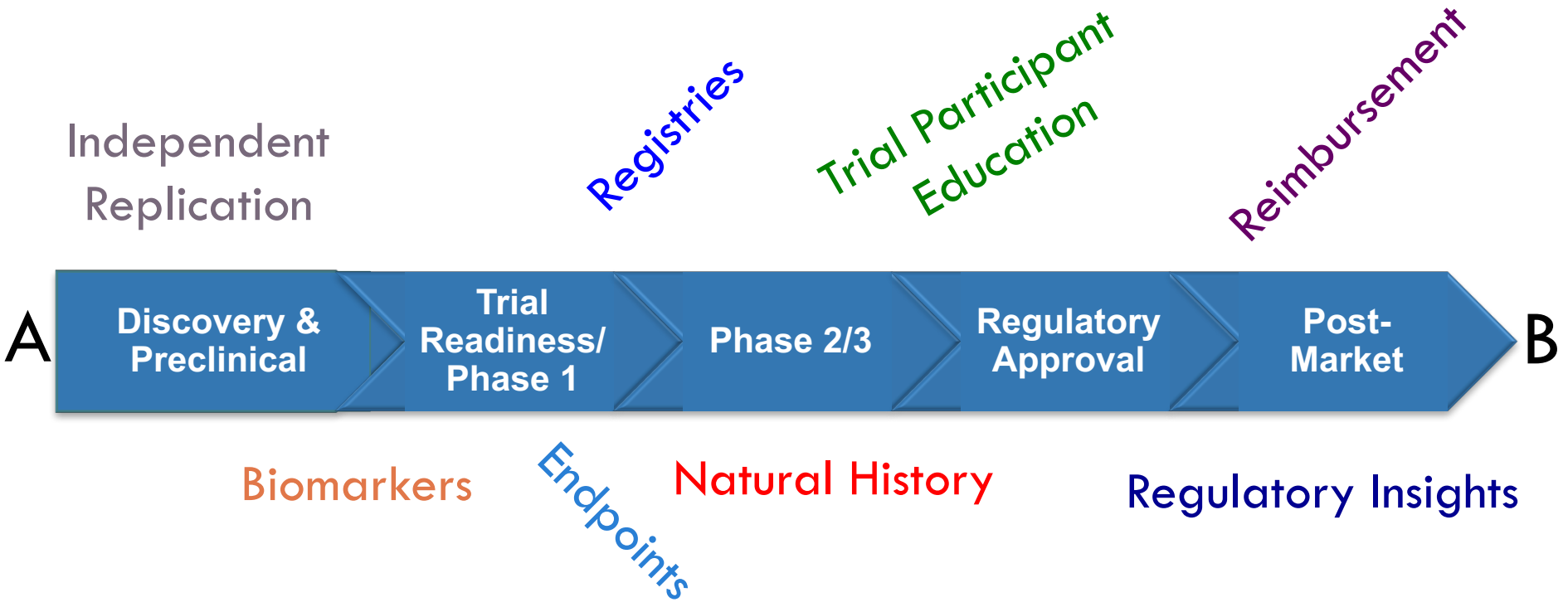

Foundations & companies invest in individual drug programs

MDF *needs* to invest in critical infrastructure that helps <u>all</u> drug programs

Infrastructure Matters

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"Genzyme may have never launched its [successful] Myozyme enzyme replacement therapy for Pompe Disease if we had known what a barrier it was to not know:

- where the patients are
- the disease natural history
- the endpoints to use"

--Ed Kaye

MDF 3.0 Activities Summary

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- Research grants to increase disease understanding
- Manpower expansion - fellowships
- Animal & cell model development
- Biobank network development
- DMCRN - genetic modifier study
- Academic-industry partnerships

- Clinical trial design/ recruitment/ retention/ communication services
- Endpoint SOPs
- Standardized patient care for trial participants across clinical trial sites

- MDF Annual Conference
- Registry expansion to support post-market surveillance, etc.
- Community expansion
- Federal advocacy (FDA, NIH, DoD re: regulatory pathway & federal funding expansion

Discovery & Preclinical → **Trial Readiness/ Phase 1** → **Phase 2/3** → **Regulatory Approval** → **Post-Market**

- Registry
- Natural history
- Endpoint development
- Biomarker development/qualification
- Burden of disease & prevalence data
- Drug Development Roundtable

- Regulator relationships
- Benefit-risk data
- PFDD output

Some MDF 3.0 Products

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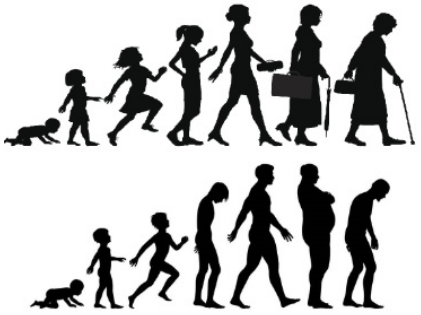
Biomarkers

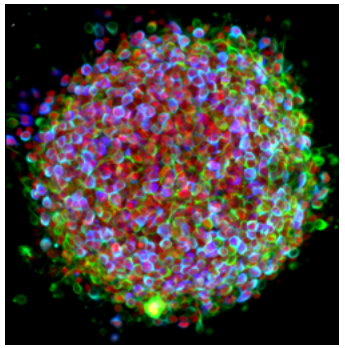


Natural History

MDF Fellows

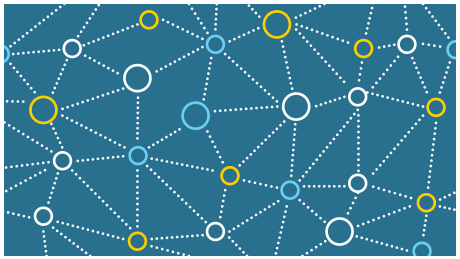
"Just work till midnight, you need to relax too"

Modifiers/
Endpoints



iPSC Lines

BAC Mouse



DMCRN

FDA

Regulatory

DRUG Development: Targets

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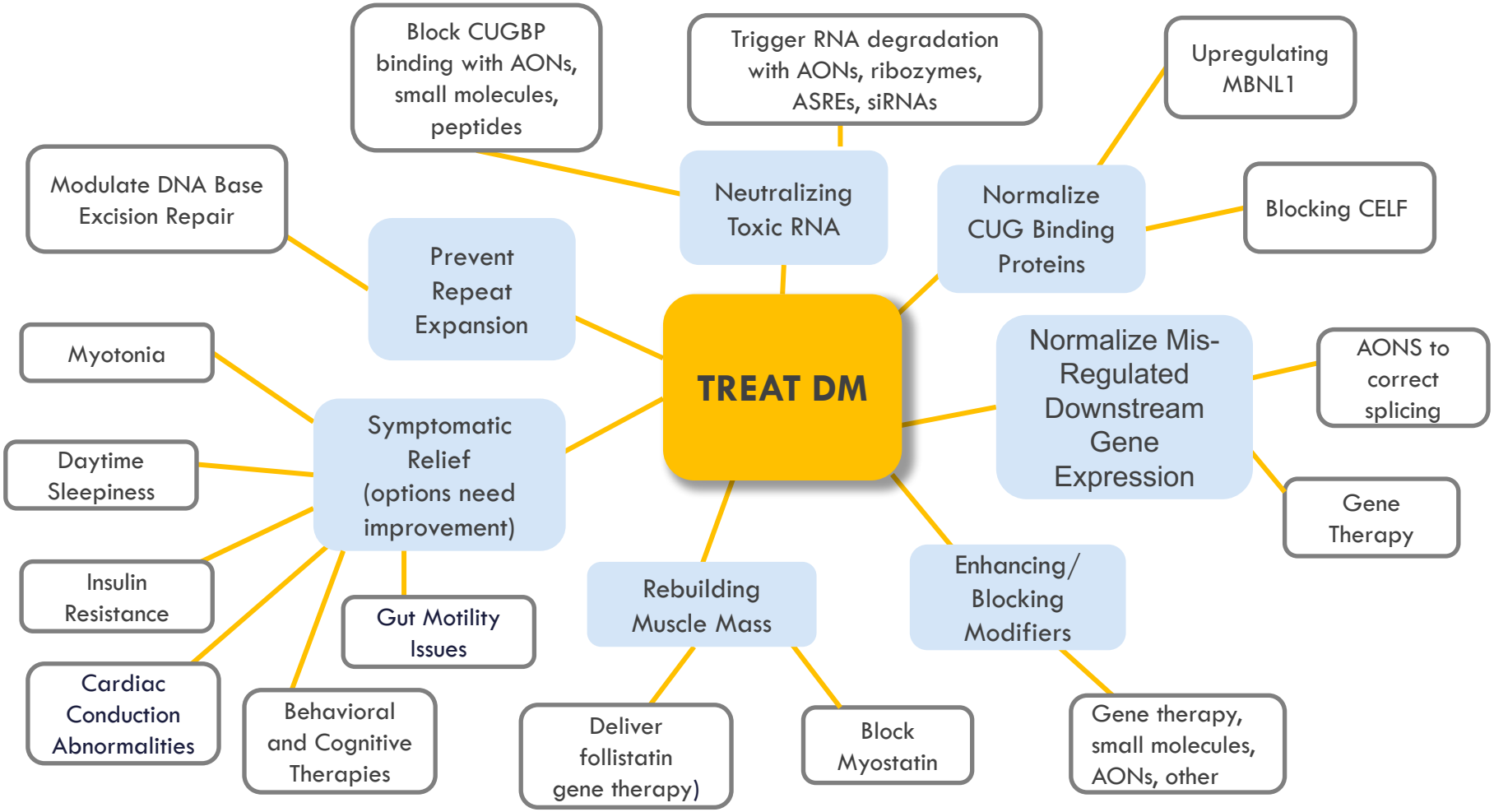

Seeking a Drug that Actually Works

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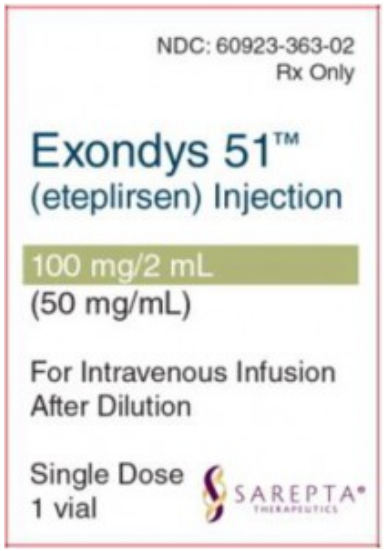
- A DM drug will be expensive, very expensive
- Strong efficacy & safety data will be needed to get it approved
- Strong efficacy data will be needed to get the payers to, well, pay for it

vs.



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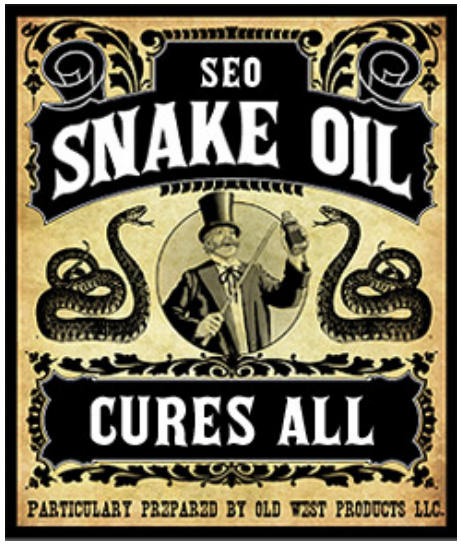

MDF is Pushing Companies Toward the Opportunities in DM

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- Promote corporate investments in therapies by de-risking with DM infrastructure investments
- Reduce the risks *regardless* of the company, therapeutic target or therapeutic modality
- We don't know what drug(s) or drug combinations will work (or not work)
- So—attract as many companies as possible & facilitate them all
- Test all drug candidates rigorously & draw lessons from those that work (& and those that don't—see Ionis)
- MDF has met with > 11 companies this year alone, to discuss opportunities & needs (& to twist arms!)

Making the Case that DM is "Tractable"

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- Prevalence: at least 30K in the US, likely significantly understated (more data soon)
- Clear diagnostics; compelling & well-understood disease mechanism (viable targets)
- Preclinical POC established for different targets in the pathogenic cascade
- New preclinical tools (mouse, iPSCs soon)
- Ability to get rapid molecular readout (splicing) of target engagement/modulation in early stage clinical trials; potential biomarker qualification
- Ability to use quantitative molecular readout in dose ranging studies
- Ability to get physiological readout of disease modification in early stage clinical trials
- Building natural history; concerted effort on registration endpoints, including international coordination on endpoint SOPs
- Existing, validated PROM for DM1: MDHI; existing PFDD data—patient/caregiver values
- MDF strengths: registry, recruitment/retention, aid trial design/conduct, communication
- DM1 patient care considerations being disseminated internationally (DM2, CDM soon)
- Centers of excellence program in the US (DMCRN—8 sites; potential central IRB) & effort to coordinate with EU

MDF 4.0 Needs Summary

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- Mouse model repository
- Drug testing facility
- Mouse SOPs
- Emerging Opps Fund
- Biobank network
- Fellows/early stage investigator support

- Enhanced DMCRN staffing/efficiency
- DMCRN evolution to trial *and* research network
- Centralized site review board; master trial agreement
- Community education

- Post-market registry (regulatory & payer)
- Evidence to support care considerations
- Clinical trial guidance document development
- Payer outreach/activities

- Registry expansion (clinical & longitudinal data)
- Non-invasive biomarkers; qualification
- Patient/caregiver education

- Build on EMA relationships (European regulatory body)
- Expanded benefit-risk studies
- Accumulate/distribute clinical trial lessons learned

Filling the Gaps in Infrastructure

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Want to Make it Easy for Drug Developers to Say Yes to DM
Ask: Where Do You See Remaining Needs?

MDF is committed to filling gaps at all stages in pre-competitive space to de-risk drug discovery & development

MDF's Bottom Line

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To eliminate every barrier that causes Biotech & Pharma to hesitate in making a commitment to working on DM

Actually, You are the Bottom Line

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- FDA & EMA will not approve a drug unless it makes a clinically meaningful difference for you—patients & caregivers
- DM drugs will be expensive; payers will not reimburse the costs of a drug unless it makes a clinically meaningful difference for you
- To do a trial, companies need to know what a drug has to do to make a clinically meaningful difference for you
- MDF looks at each stage of therapy development, asking how we can reduce or eliminate barriers & make DM attractive for drug developers
- Activities like the MDFR, the PFDD meeting, & the session on CNS endpoints help facilitate the discovery, development, approval, & reimbursement of drugs that make a meaningful difference for you
- Anything less but a truly effective/reimbursable drug is not success