



MYOTONIC
DYSTROPHY
FOUNDATION

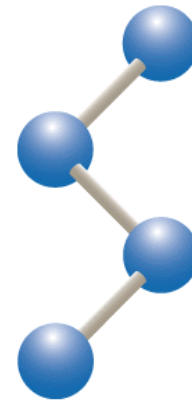
Care and a Cure



2018
MDF ANNUAL CONFERENCE
September 14-15, 2018
Nashville, TN

INDUSTRY UPDATES ON DRUG DEVELOPMENT

Matt Disney, The Scripps Research Institute and
Expansion Therapeutics



THE
SCRIPPS
RESEARCH
INSTITUTE



EXPANSION
THERAPEUTICS

Expansion is developing small molecules targeting RNA repeats

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ADVANTAGES

Oral bioavailability

Superior tissue distribution

Cross blood-brain barrier

Target disease-causing RNAs

Allows MedChem optimization

Compliments antisense

...



Routine Medicine

Expansion Board of Directors

Scott Rocklage, PhD

Chairman



Kevin Forrest, PhD

CEO



Matt Disney, PhD

Founder



Jason Hafler, PhD

Investor



Yujiro Hata, MBA

Independent



Beth Seidenberg, MD

Investor



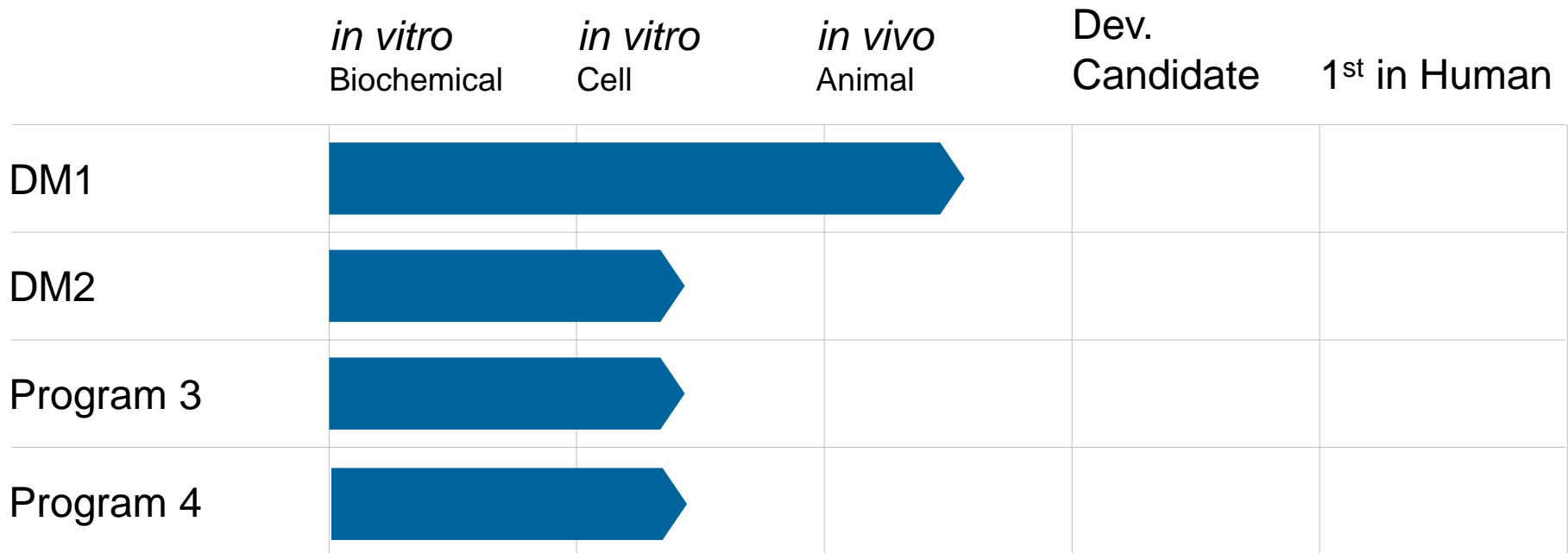
4 Campbell Murray, MD

Investor



Expansion pipeline today

5



Drug development is a long process because one needs to "do no harm."

DM1 disease mechanism

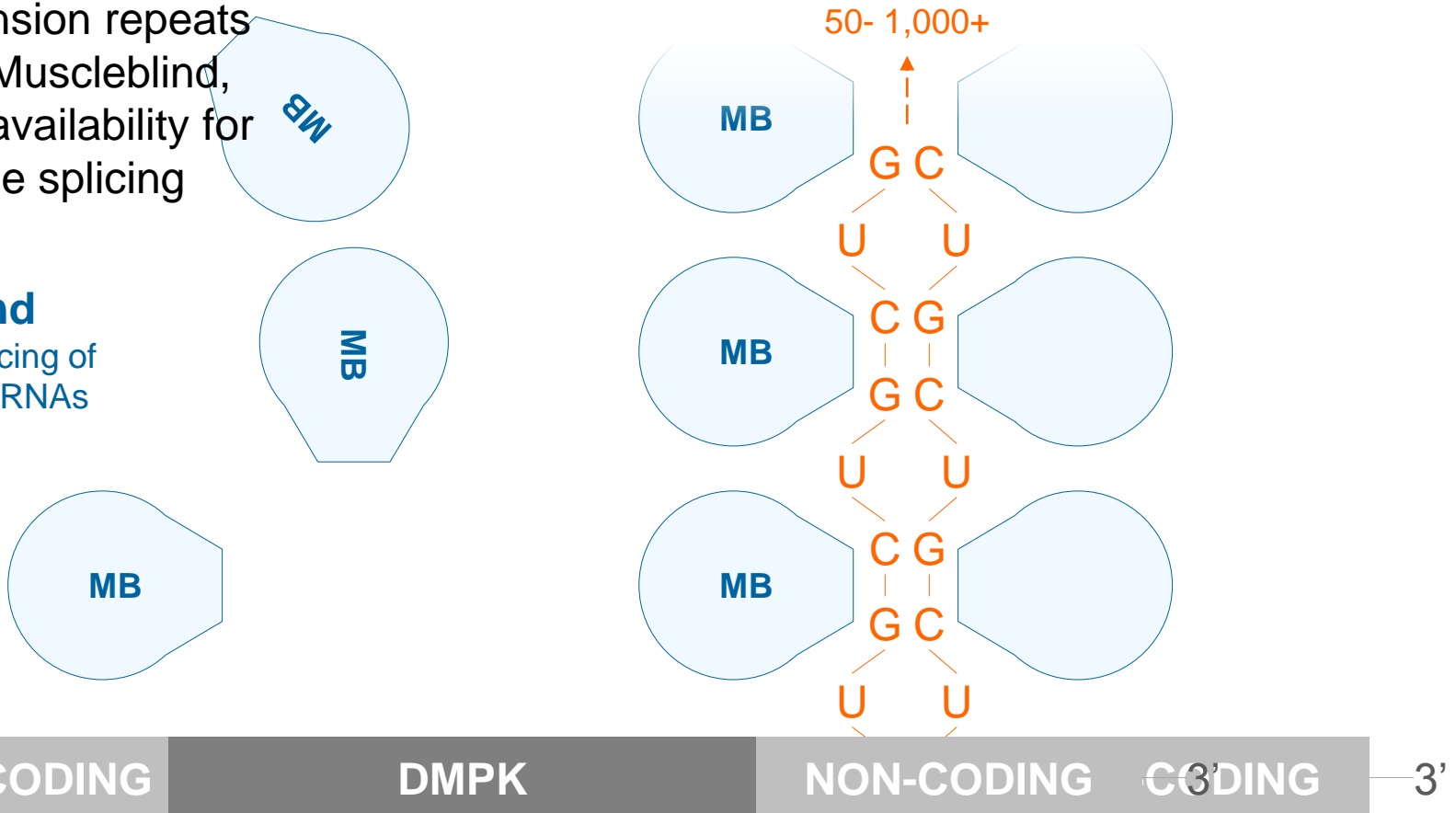
Illustrative

6

CUG expansion repeats sequester Muscleblind, limiting its availability for normal gene splicing

Muscleblind

Regulates splicing of hundreds of mRNAs



Lack of muscleblind causes system-wide defects

7

Myotonia

Chloride channel

Muscle strength

Bin1, Cacna1a

Insulin Resistance

Insulin receptor

Heart Defects

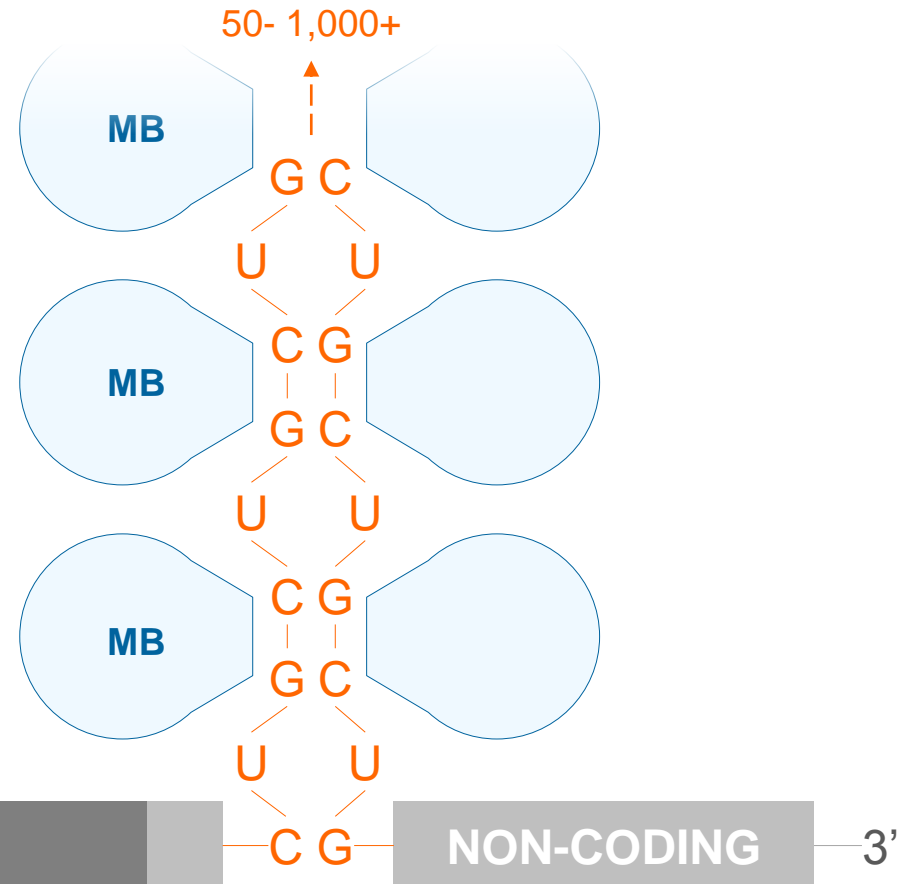
Troponin T

Sleep defects

Csnk1d

Learning/Memory

Tau

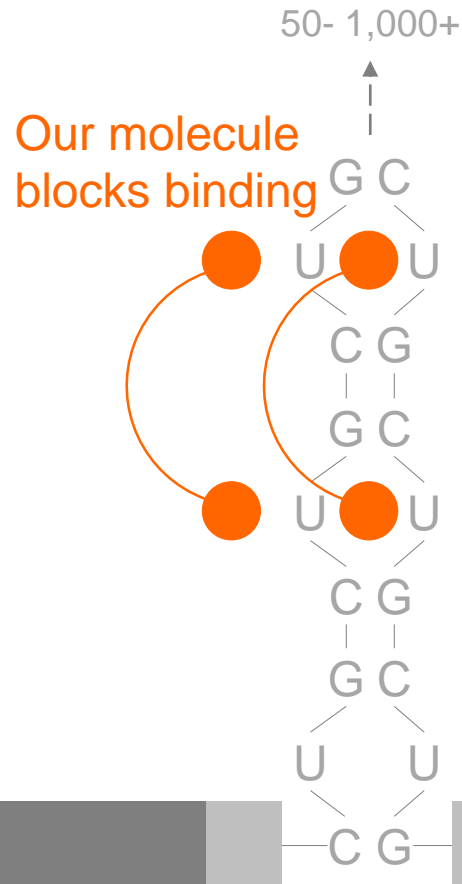
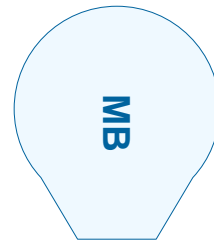


Expansion Therapeutics mechanism

Illustrative

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Now available for normal pre-mRNA splicing

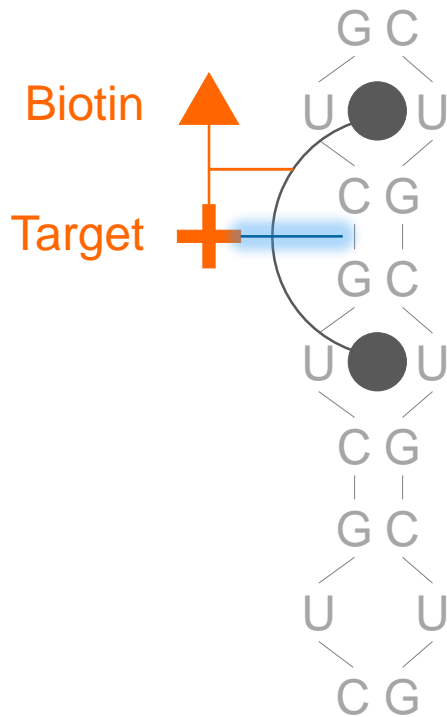


5' NON-CODING *DMPK* NON-CODING 3'

Compounds bind selectively to disease causing r(CUG) repeat

9

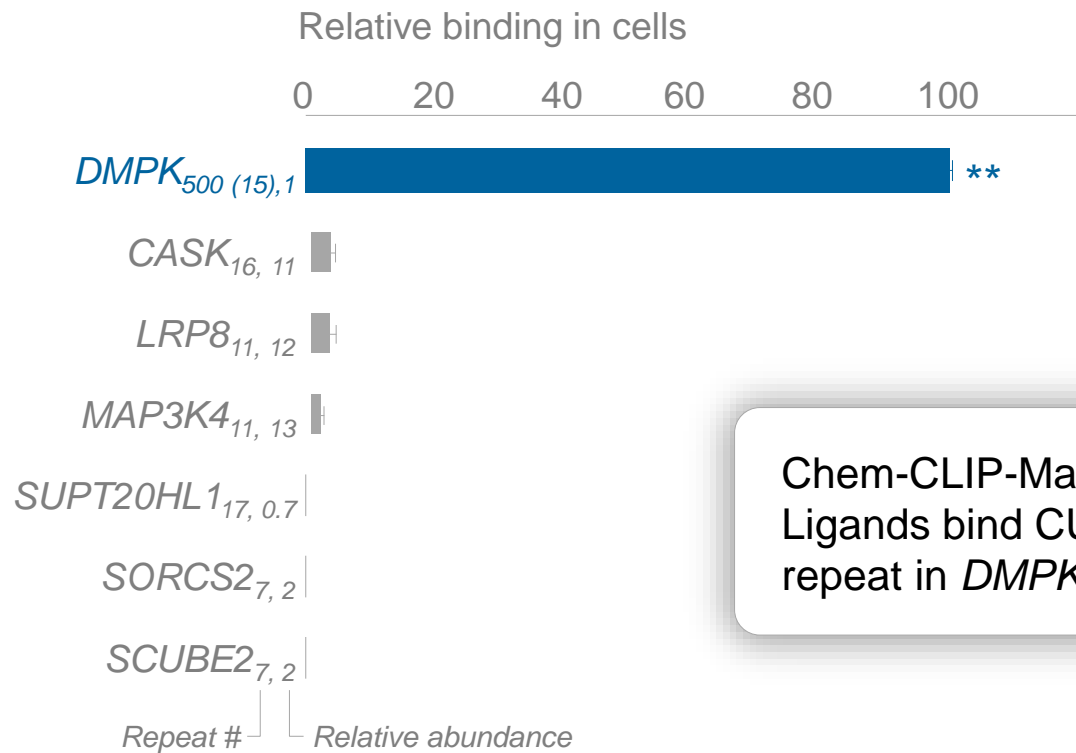
Chem-CLIP



Target Enrichment

Selectivity

Binding to DM1 Fibroblasts (CUG₅₀₀)



Chem-CLIP-Map:
Ligands bind CUG
repeat in *DMPK*

Results

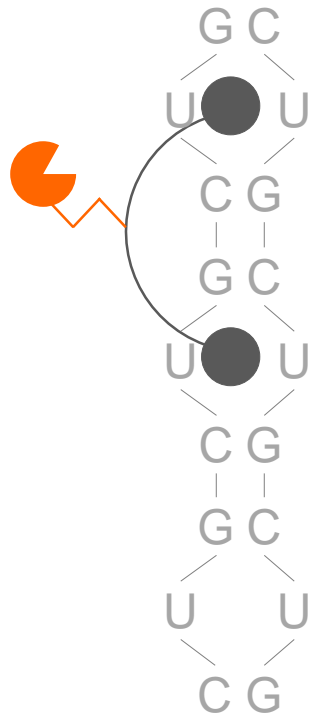
** p<0.01

Cleavage of r(CUG) with a small molecule

∞

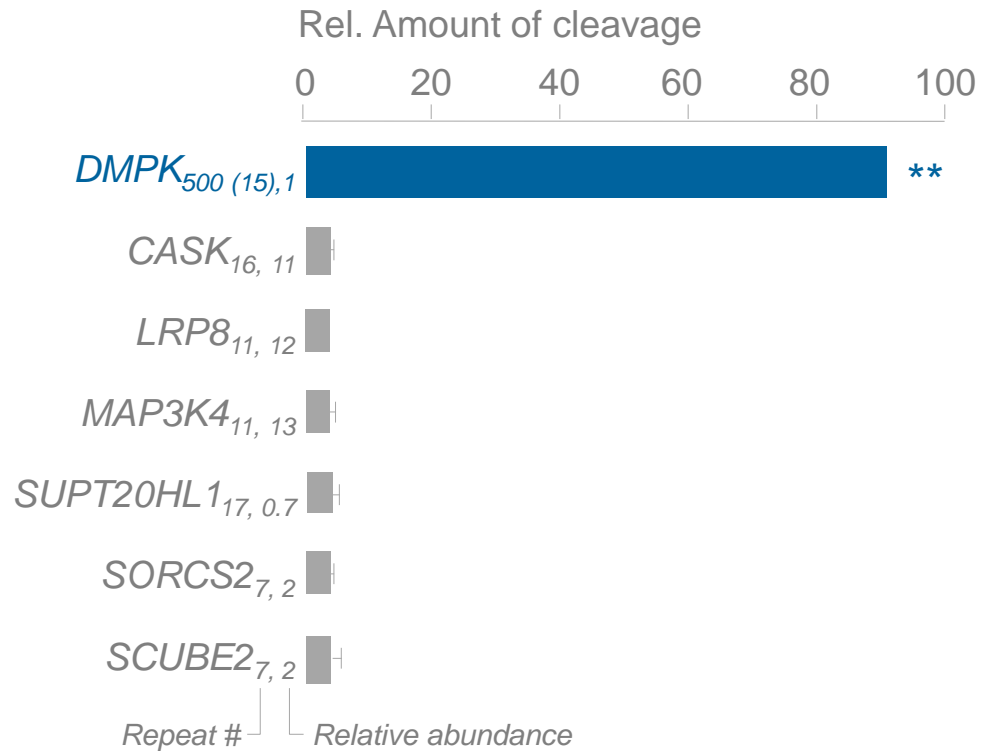
Chem-CLEAVE

Binding to DM1 Fibroblasts (CTG₅₀₀)



Target Depletion

Tests Target Binding



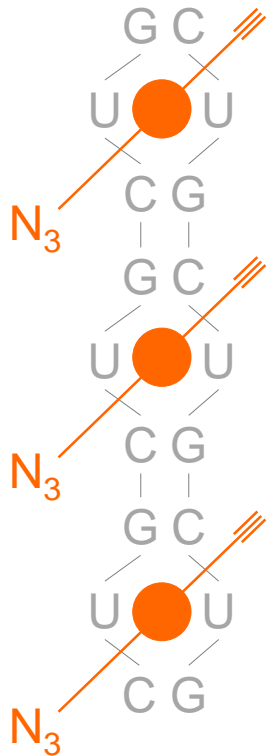
Results

** p<0.01

Getting r(CUG) to make its own drug

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Chem-CLICK



Binding-
triggered
reaction



On-site drug
synthesis
in cells



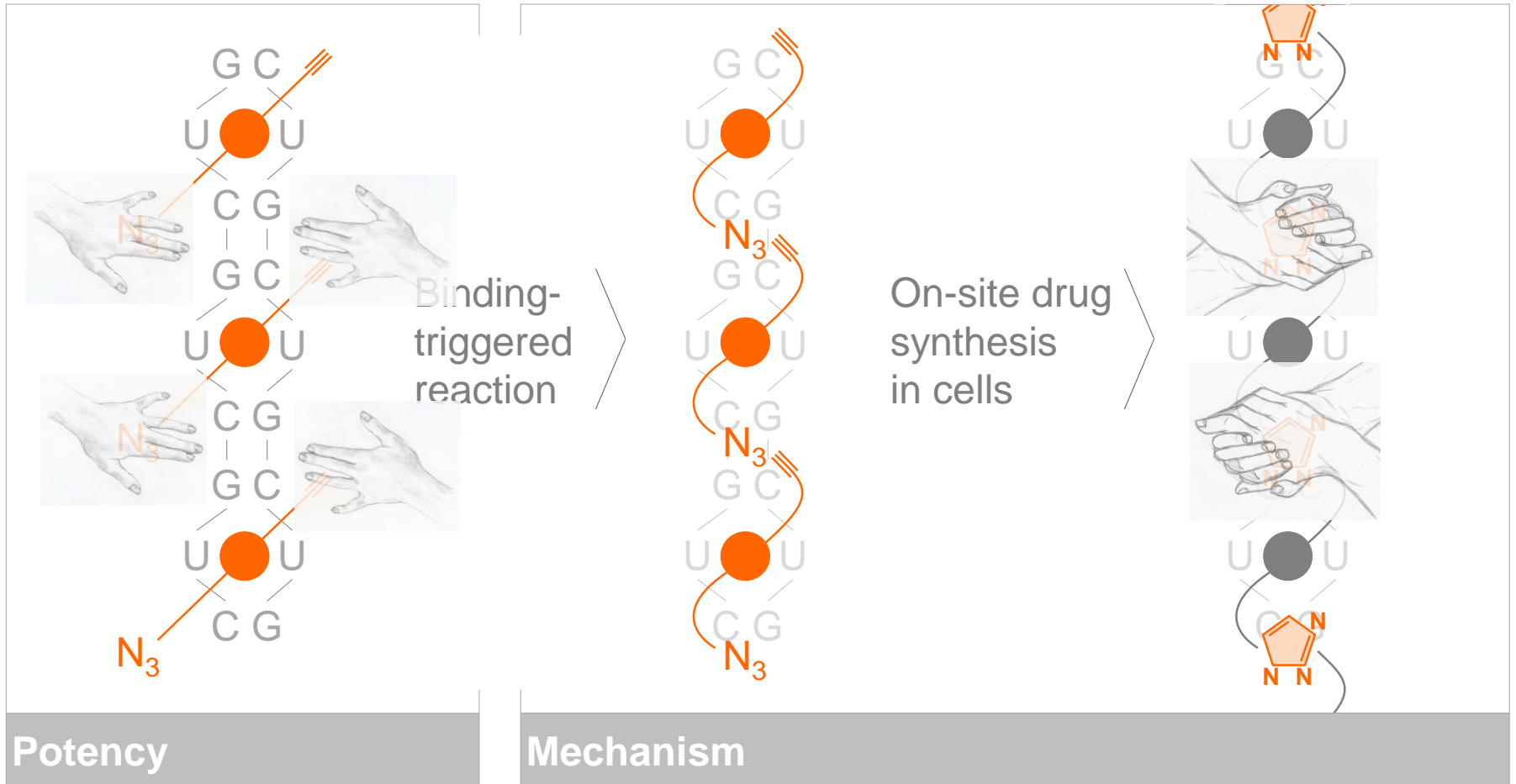
Potency

Mechanism

Getting r(CUG) to make its own drug

12

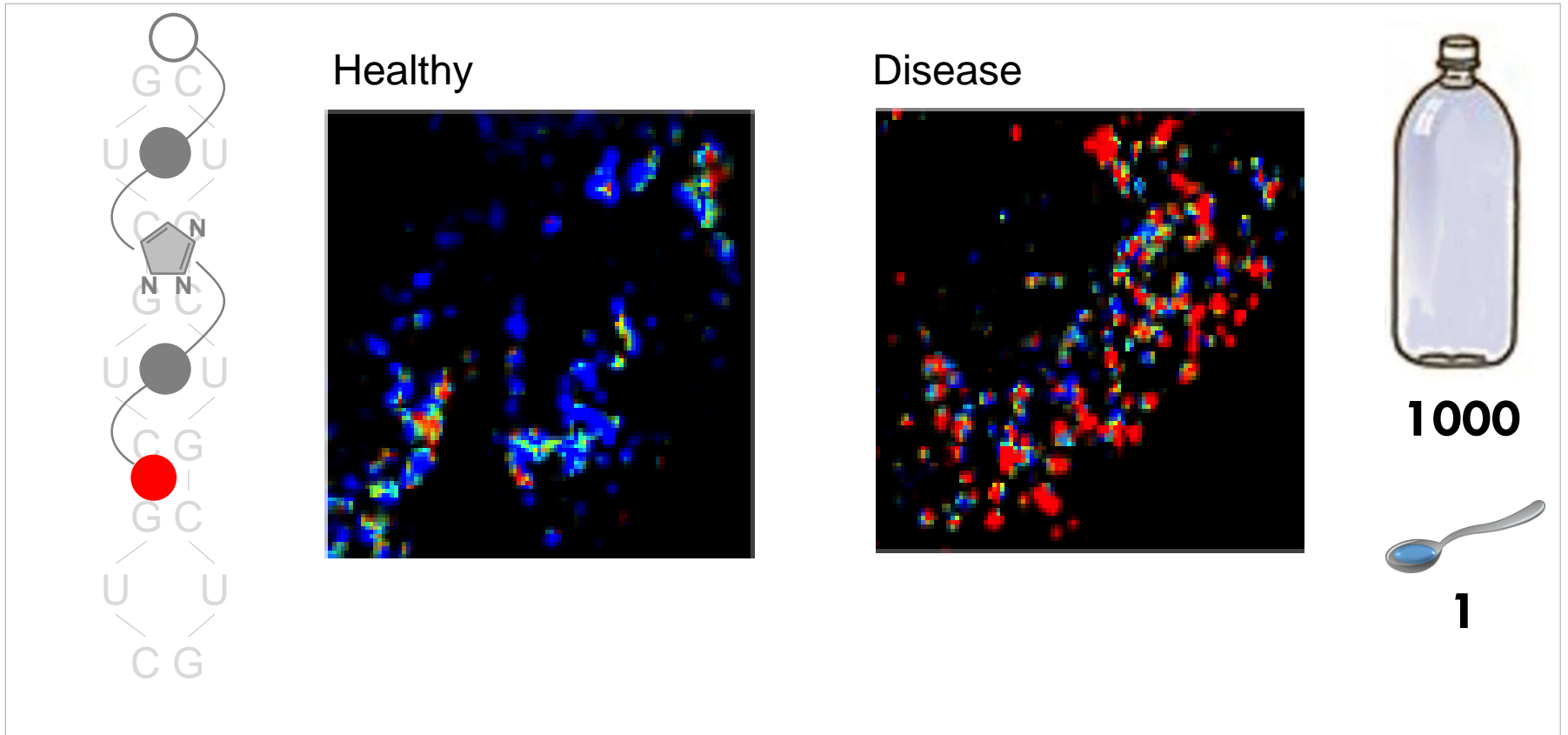
Chem-CLICK



Chem-CLICK imaging

13

Chem-CLICK



Pre-clinical,
250
compounds

3 - 6 years

Clinical Trials,
5 Compounds
& 3 Phases

Phase 1
20

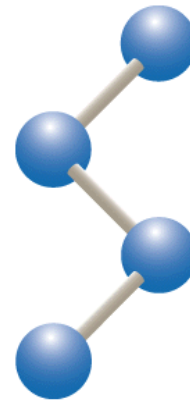
Phase 2
100

Phase 3
1000

6 - 7 years

FDA Review,
Large Scale
Manufacturing

0.5 - 2 years



THE
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EXPANSION
THERAPEUTICS

We are at the beginning of a long process

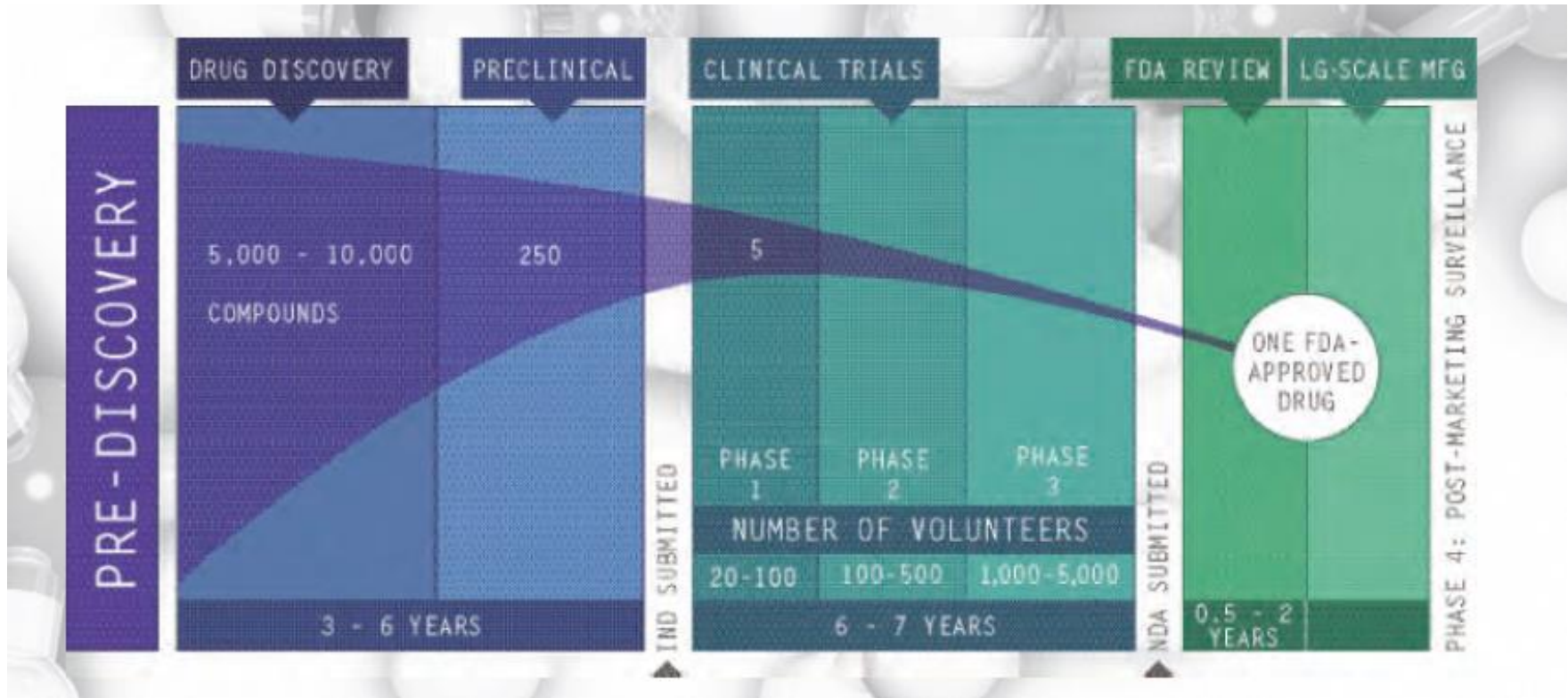


Figure from:

http://www.innovation.org/drug_discovery/objects/pdf/RD_Brochure.pdf