



*Rapidly discover and develop drugs that delay or slow Huntington's disease*

# Hope, Heroes and Science

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# Where are we going?

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- u Talk about “hope”
- u What we can learn from a English country doctor
- u Who are the heroes and heroines of science?
- u What is our challenge? Suggestions on how we can address the challenges...
- u Come back to hope as a motivation to get involved... NOW



# What is HOPE?

Hope , unlike optimism, is rooted in unalloyed reality....

Hope is the elevated feeling we experience when we see – in the mind’s eye- a path to a better future. Hope acknowledges the significant obstacles and deep pitfalls along that path.

True hope has no room for delusion.



J. Groopman, *The Anatomy of Hope*



# HOPE

**Today's  
Reality**

**An  
Uncertain  
Future**

**Societal Realities**

**Health Services**

**Medical and Research Information**

**Social & Familial Relations**

**Media Representations**



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What does our path to a better  
future look like?  
A lesson from history...



# The story of the British physician Edward Jenner



DEATHS OF MALES and FEMALES from SMALL-POX.

Months Old.	Died.	Years Old.	Died.	Years Old.	Died.	Years Old.	Died.	Years Old.	Died.
0	292	0	2,235	10	226	40	43	75	4
1	181	1	1,524	15	226	45	22	80	10
2	162	2	1,197	20	240	50	13	85	1
3	456	3	669	25	148	55	10	90	0
6	646	4	628	30	93	60	19	95	1
9	588	5	1,122	35	75	70	10	Unknown	8



# Jenner's Experiment

- u Jenner was curious about the old wives tale that milkmaids could not get smallpox
- u A simple hypothesis: Infection with cowpox would give protection from smallpox.



“How do I test this hypothesis?”

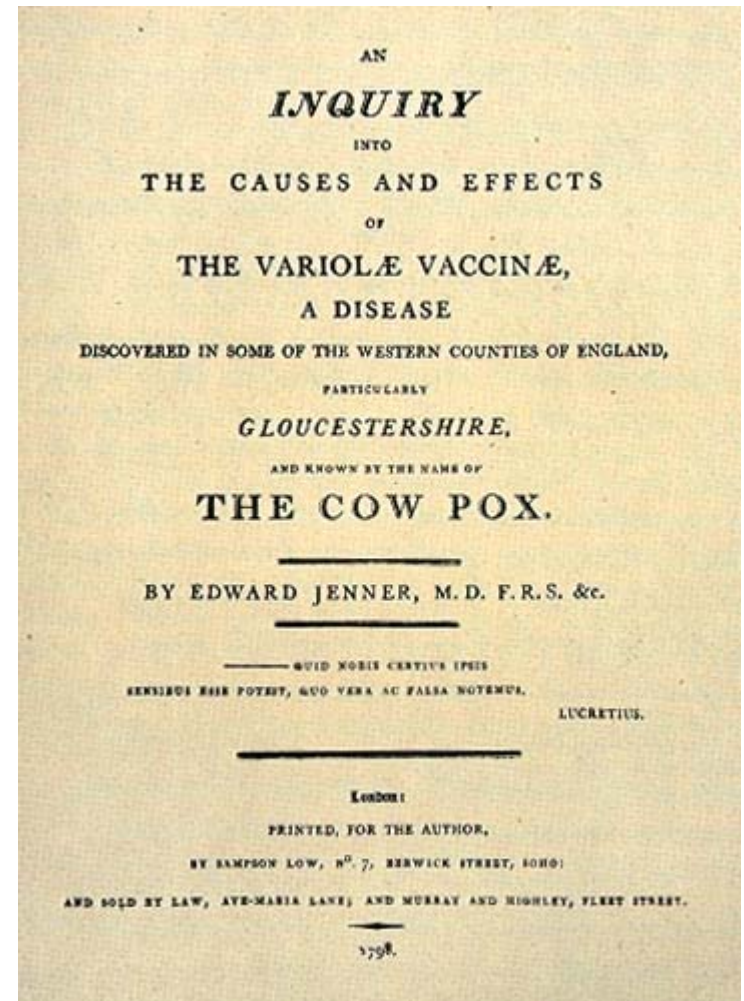
Enter our heroes: James Phipps, Sarah Nelmes, and Blossom.





# What do we learn from Jenner?

- u Power of observation
- u The need to test the hypothesis
- u Importance of human participation



# Let's look at the heroes and heroines of our story:

- u Jenner – courage to explore the observation that “milkmaids do not get smallpox”
- u James Phipps
- u Phipps' parents
- u Sarah Nelmes – the milkmaid (and *Blossom* the cow)
- u The 23 people who participated in Jenner's first “clinical trial” which led to publication of results in 1798.

**... and in 1980 smallpox was declared eradicated by the WHO**



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# Hope is a resource to generate action...

Eliot, Jaklin A. (2006) *The do-not-resuscitate decision: A discursive analysis of cancer patients' talk*. Adelaide. The University of Adelaide



# Our path to treatments and advancements...

Science is the effort, based on discovery, whose aim is to increase human understanding of reality.



Research



Clinical Research

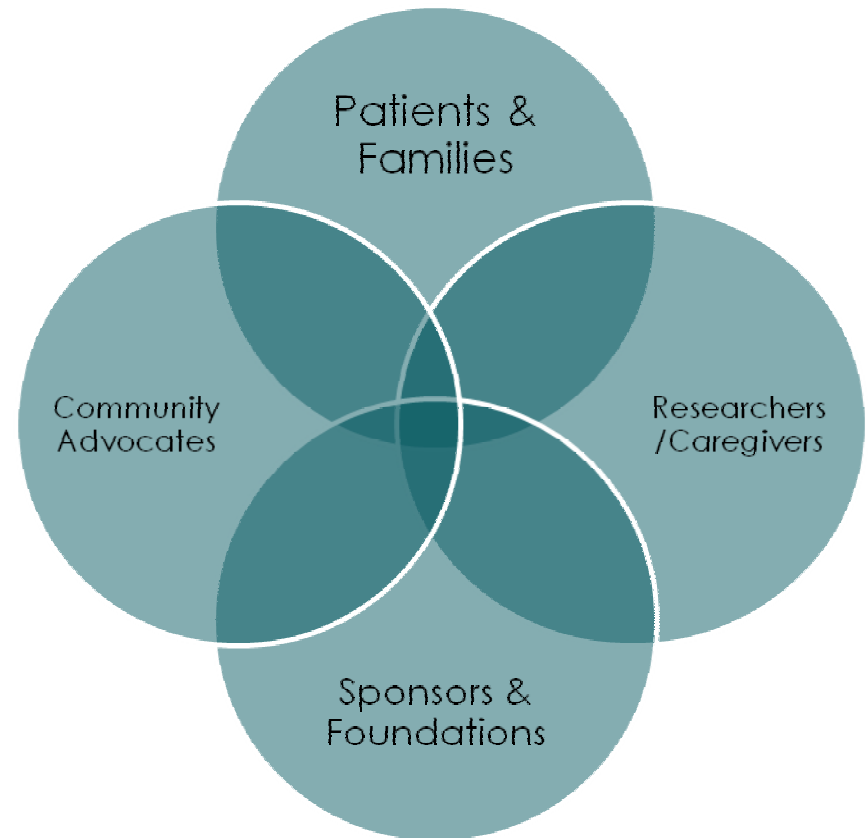


Clinical Trials



**TREATMENTS**

## The Collaboration:



# The Challenge

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- u Time is **not** on our side... and delays are common in our system
- u Less than 1% of the 1 million people with Parkinson's Disease participate in clinical trials<sup>3</sup>
- u About 5% of patients with cancer enroll in clinical trials.<sup>2</sup>
- u If just 10% of cancer patients participated in clinical trials; studies would be completed in one year instead of the current average 3-5 years.
  
- u 50% of trial delays are due to poor recruitment<sup>1</sup>
- u 86% of all clinical trials in US fail to recruit on-time<sup>1</sup>

1 CenterWatch data

2 Tufts Center for the Study of Drug Development

3 PDTrials.org



# The HD Landscape

## DIMOND

A Multi-Center, Phase 2,  
Randomized, Double-Blinded,  
Placebo-Controlled Study of  
Dimebon in Subjects with  
Huntington Disease

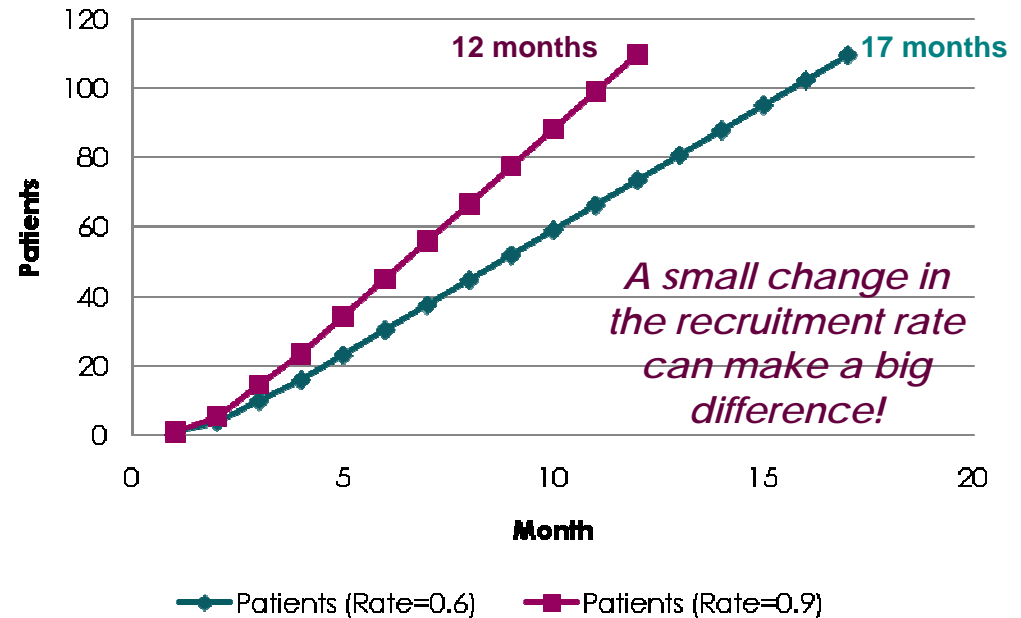
17 Centers /90 patients  
5 pts per center over 8 months  
0.6 pts/month

## DOMINO

A Multi-Center, Double-Blind, Pilot  
Study of Minocycline in Huntington  
Disease

12 Centers/114 subjects  
9 pts per center over 16 months  
0.6 pts/month

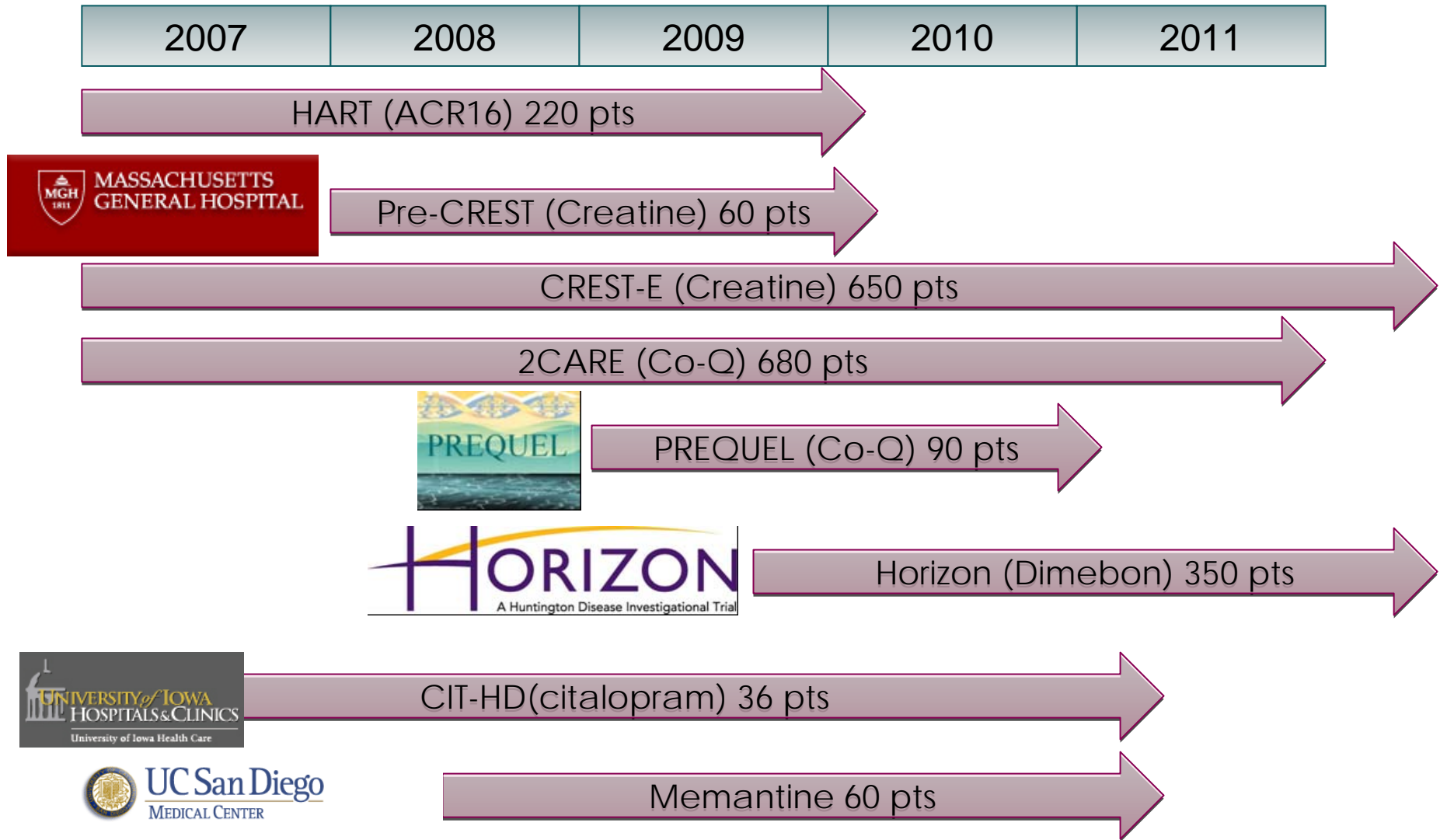
## Patient Recruitment



Assumptions:  
12 centers / 110 pt. study  
Comparing recruitment rates of  
0.6 and 0.9 pts/month



# Studies in Progress or Planning

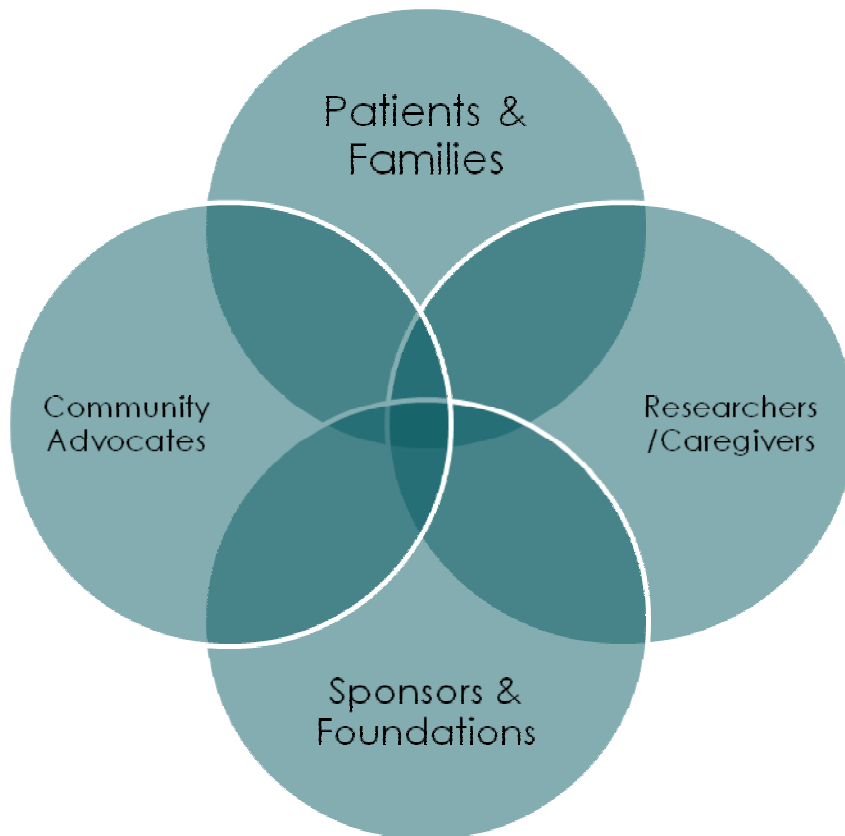


**2,100+ participants**



# What can we do?

## The Collaboration:



## The Best Solution is a Shared Solution:

Decrease clinical trial delays (e.g. recruitment, contracts, etc.)

Support the patient registries (e.g. COHORT, REGISTRY)

Improve access to clinical trials for patients and families

Ensure quality data from well designed studies

Education and outreach to the community

HDTrials.org





# Some suggestions...

## u Clinical Trial Center Award for Performance and Care

- Awarded to centers for their efforts to improve patient care of people with HD through participation in clinical trials
- Recognize centers that use best practices in making studies more efficient, improve quality and provide a positive participant experience



## u HDSA Clinical Trial Ambassadors

- An ambassador in every chapter who is a resource and advocate for clinical trial participation
- Trained and re-trained to bring reliable and accurate information and news to the community
- Know the centers in their area; a “voice” for participants and carers



## u HDTrials.org

- Will serve as an important tool to match subjects with studies!



# CHDI Discovery Pipeline

## Active Programs:

Energy Homeostasis  
Histone Deacetylases  
Htt Processing  
Modulation of Htt Levels  
Inflammation  
Neurotransmission  
Phosphodiesterases  
Protein Folding  
Transcriptional  
Dysregulation  
Trophic Factors

42  
Projects



# CHDI Discovery Pipeline - Highlights

## u HDAC4 – a clear priority

- Data for HDAC4 (+/-)-R6/2 genetic cross from Gill Bates are encouraging

## u Antisense Oligonucleotides (ASOs)

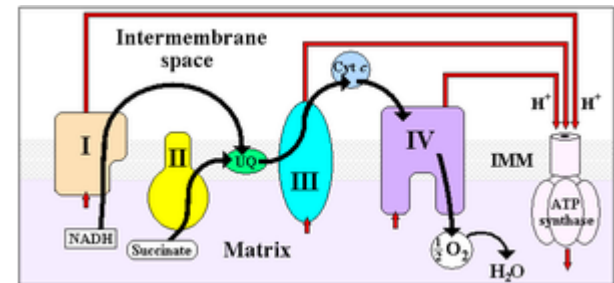
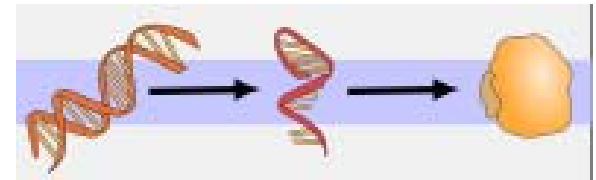
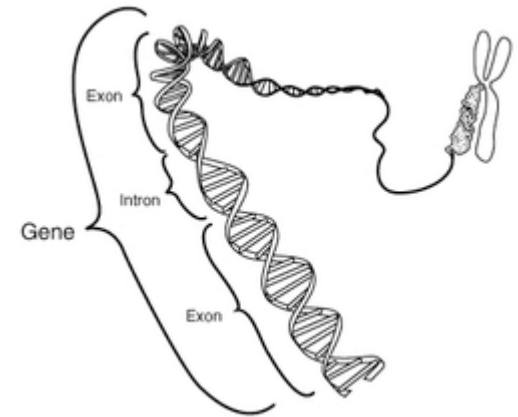
- Goal to nominate a set of lead ASOs for further pre-clinical testing by the end of the year.

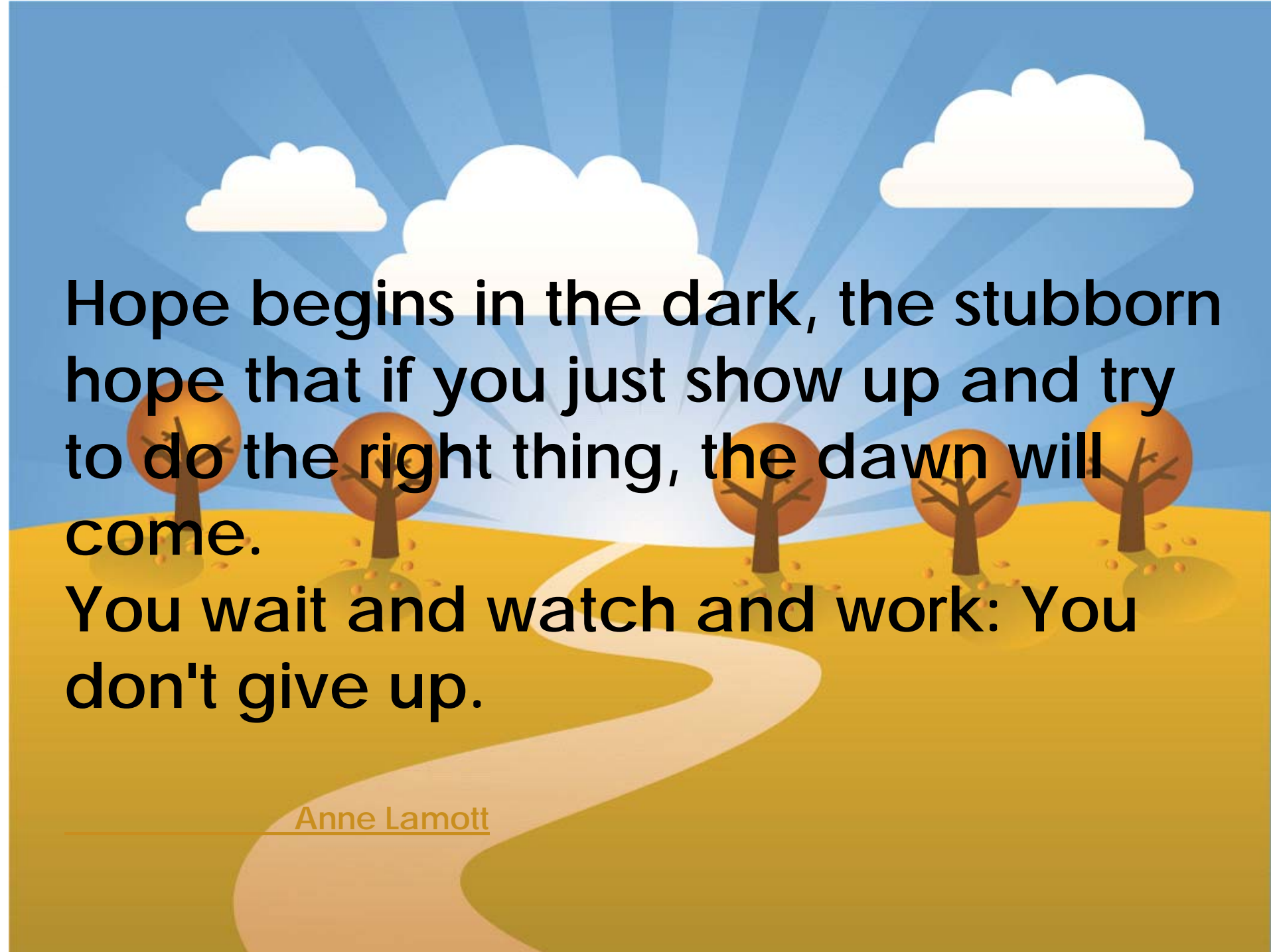
## u PDE4 Modulators for Cognition(...and beyond?)

- Evaluation of the published literature on the potential pro-cognitive, neuroprotective, motor, and anti-inflammatory effects of these inhibitors has led to CHDI's interest in evaluating inhibitors for PDE4, PDE2, PDE1/5 and PDE10.
- Currently evaluating a compound in our in vitro and in vivo assay platforms to assess the potential as an HD therapeutic.

## u MITO-HD

- Finding biomarkers for energy defects in HD





Hope begins in the dark, the stubborn hope that if you just show up and try to do the right thing, the dawn will come.

You wait and watch and work: You don't give up.

Anne Lamott

# Thank you

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HD Patients and Families

HD Families who have participated in FuRST Focus Groups

CHDI Colleagues:

Robi Blumenstein

Dan van Kammen

Robert Pacifici

Beth Borowsky

LaVonne Goodman

Louise Vetter

Collaborators:

Ken Evans, OCBN

Anthony Vaccarino, OCBN

Marta Newby, UTSW

