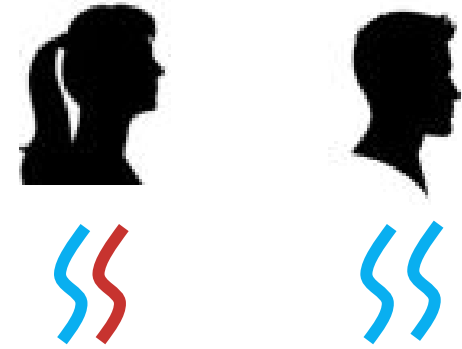


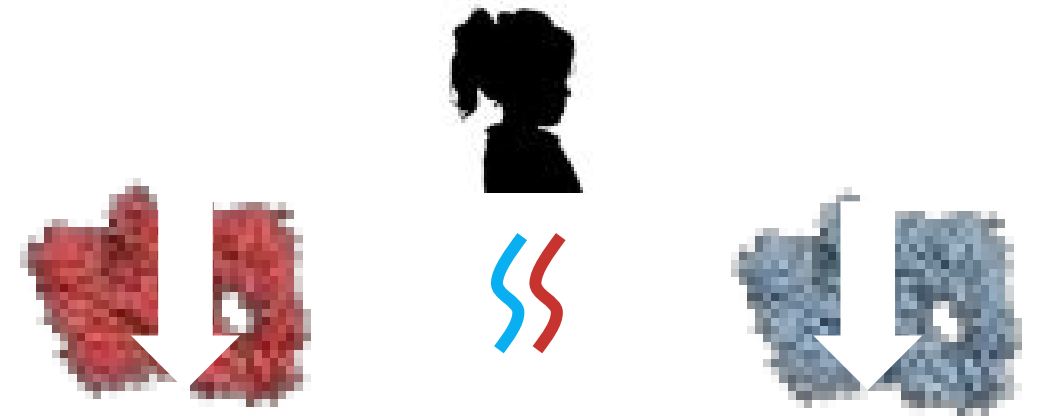
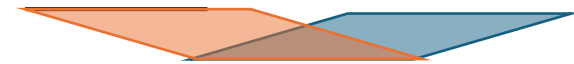
**HD BUZZ**

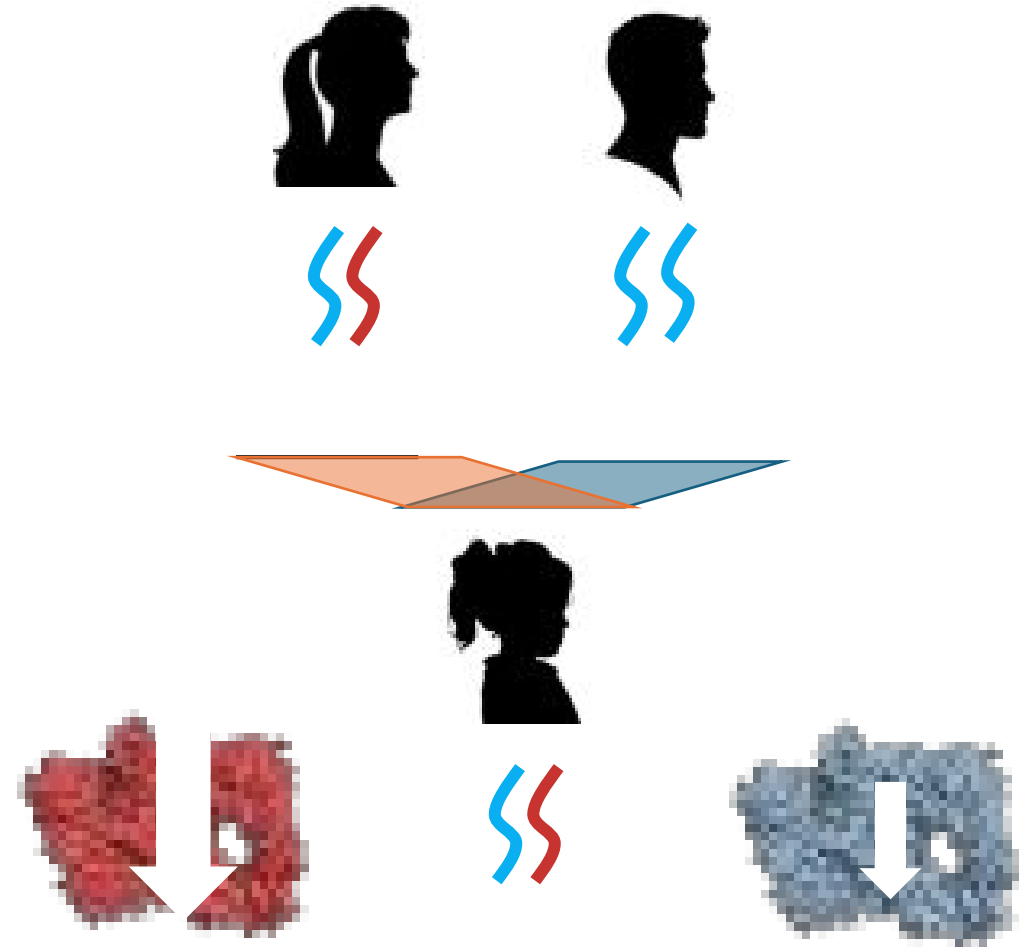
**Huntington's Disease  
Education Day**

**HDSA Centre of Excellence  
University of Washington, Tacoma**

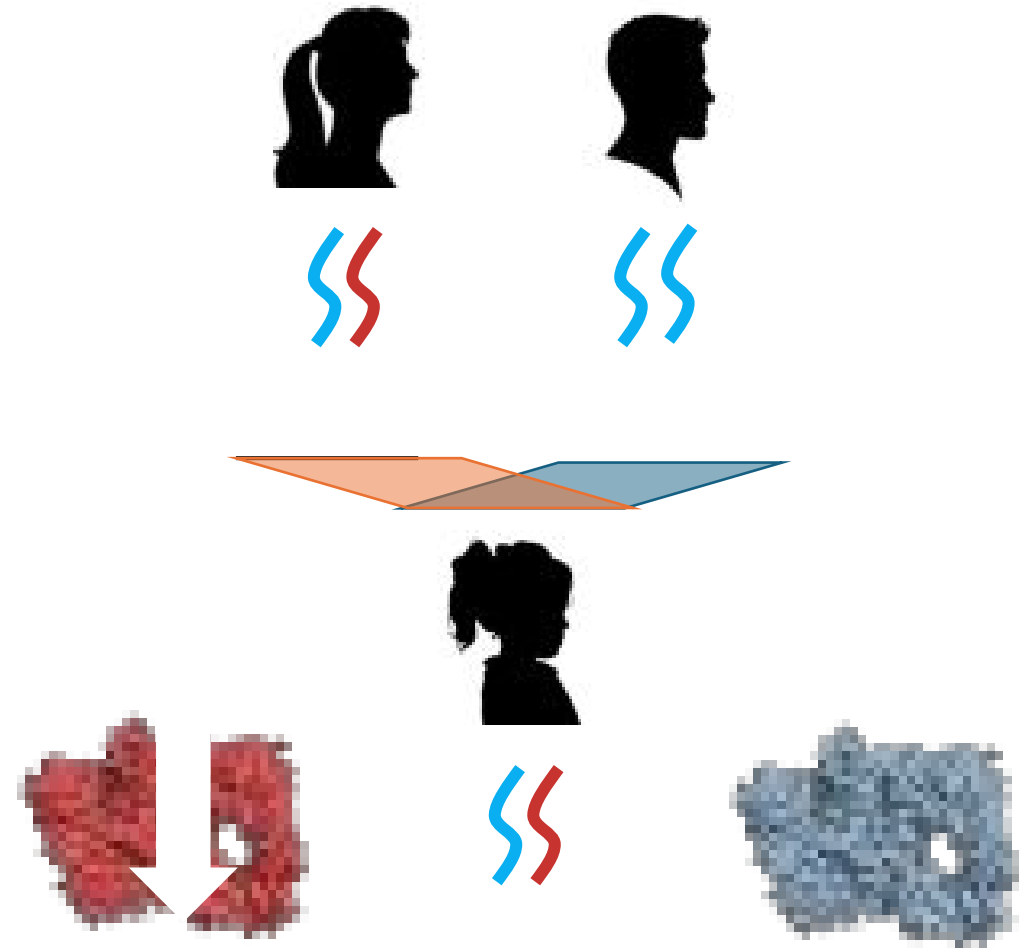


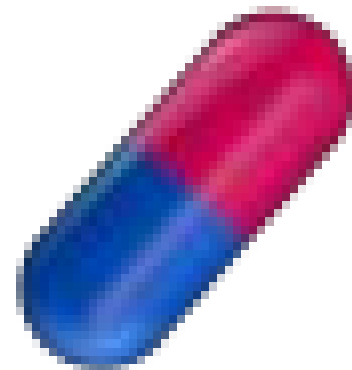
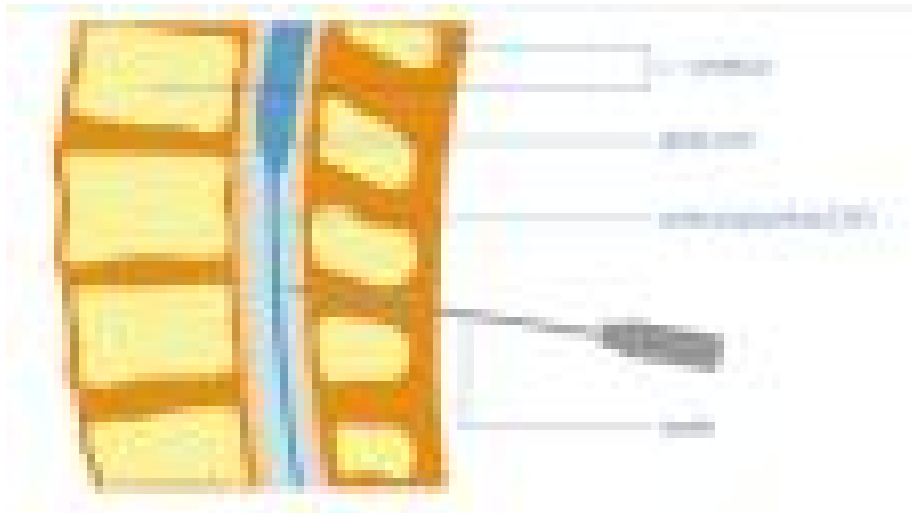
uniQure





WAVE<sup>®</sup>  
LIFE SCIENCES





HD BUZZ

PTC  
THERAPEUTICS



NOVARTIS



SKYHAWK  
THERAPEUTICS

Roche

Genentech  
*A Member of the Roche Group*

Amylam  
PHARMACEUTICALS

WAVE  
LIFE SCIENCES

VICO  
Therapeutics



uniQure

Spark  
THERAPEUTICS



### The First Domino Falls: AMT-130 Gene Therapy Slows Huntington's in Landmark Trial

In an update from uniQure, they report that their experimental gene therapy, AMT-130, has the potential to slow Huntington's disease progression in key clinical study.

By Dr Rachel Harding  
September 14, 2025  
Edited by Dr Sarah Invernizzi & Dr Emma Wilson

Promising results in a small group of people

- 12 people on high dose of AMT-130 at 3-year point
- Primary endpoint met - 75% slowing of progression (cUHDRS)
- Secondary endpoint met - 60% slowing of TFC
- Compared to external control (data from Enroll-HD)

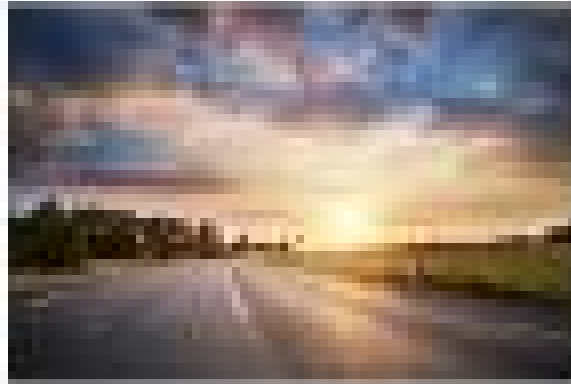
uniQure

# The path forward for AMT-130 has been bumpy



## The road ahead for uniQure: FDA says more data needed for AMT-130 gene therapy

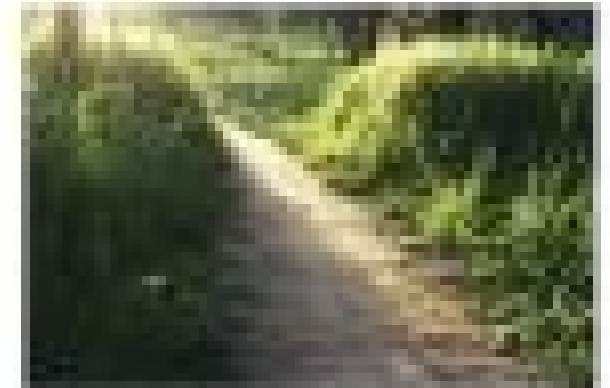
It is this road | The FDA wants more data before approving AMT-130 for Huntington's disease in the U.S. On March 2020, uniQure shared in an update that current Phase 1/2 data weren't enough for the agency. A new randomized, sham-controlled trial may be required.



By Dr Rachel Hoodley & Dr Sarah Hernandez  
March 2, 2020

## A Second Path: uniQure Plans Regulatory Filing for AMT-130 in the UK

It is this road | While the US regulatory path for AMT-130 remains complicated, uniQure announced plans to seek approval for its HD gene therapy in the UK. Here's what that means, and what might be to come.



By Dr Sarah Hernandez  
May 7, 2020

# uniQure



**Genentech**  
A Member of the Roche Group

# GENERATION-HD2 Trial for tominersen



## Roche provides an update on tominersen: What's next for this huntingtin-lowering drug?

Roche provides an update on tominersen, a huntingtin-lowering drug, following the completion of the Phase 1b trial. The drug is being evaluated in a Phase 2 trial, and the company is looking for ways to improve the drug's safety and efficacy. The company is also looking for ways to improve the drug's dosing and timing.



Roche provides an update on tominersen: What's next for this huntingtin-lowering drug?  
April 15, 2024  
Following the completion of the Phase 1b trial, Roche is looking for ways to improve the drug's safety and efficacy. The company is also looking for ways to improve the drug's dosing and timing.



An independent safety committee found no major safety concerns for the study and dosing is proceeding.

All participants will receive the 100 mg dose (or placebo) every 16 weeks - more likely to offer clinical benefit.

Data remains blinded



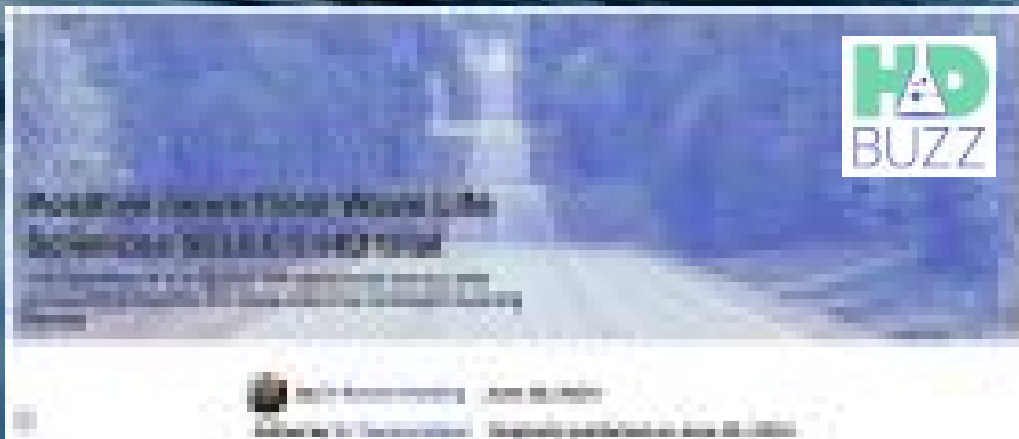
## SELECT-HD trial for WVE-003

WVE-003 is safe and well tolerated

Only lowers mHTT not wildtype HTT

Some encouraging data from brain scans and other measures

Next study in the works for trial with more people





Phase 1/2a clinical trial testing VO659



VO659 reduces mutant huntingtin levels in people with HD

It appears to be generally well-tolerated, but some participants developed radiculitis (nerve inflammation)

Vico plans to adjust dosing to reduce side effects and extend dosing intervals

A Phase 2 trial is being discussed for HD



INVEST-HD  
votoplam



POINT-HD showed that...

HD-ISS Stage 2: 10mg -> 52% slowing by cUHDRS; 5mg -> 28% slowing.

NfL remained below baseline for both doses

HD-ISS Stage 3: showed "potential signals" of benefit

Phase 3 INVEST-HD trial now launched, recruiting people with TFC=13 and early motor signs, a population where PIVOT-HD showed its strongest signal

# Splice modulators could be working to lower HTT as well as targeting somatic instability

nature communications



Article

<https://doi.org/10.1038/s41467-024-51880-0>

## Splice modulators target *PMSI* to reduce somatic expansion of the Huntington's disease-associated CAG repeat

Received: 24 July 2023

Accepted: 20 March 2024

Published online: 10 April 2024

Check for updates

Eacharish L. Molnar<sup>1,2,3</sup>, David Dao<sup>4,5,6</sup>, Kevin Daniels<sup>7</sup>, Jennie C. L. Roy<sup>8,9</sup>, Shota Shibata<sup>10,11</sup>, Iris H. Farnum<sup>12</sup>, Leo Rodriguez-Molina<sup>1</sup>, Maria Kovalenko<sup>1</sup>, Minasa Baguru<sup>1</sup>, Elizabeth Moran<sup>13</sup>, Jyoti Butani<sup>1</sup>, Tammy Ellis<sup>1</sup>, Maria Lucena<sup>1</sup>, Benjamin P. Kistner<sup>14</sup>, Jong-Min Lee<sup>15</sup>, Mary E. MacDonald<sup>16,17</sup>, Vanessa C. Wheeler<sup>18,19</sup>, Bryanne Brown Fink<sup>20,21,22</sup>, James F. Gusella<sup>1,23</sup>





## Phase 2/3 FALCON-HD SKY0515



SKY-0515 is safe and leads to dose-dependent lowering of huntingtin and PMS1

Targeting huntingtin and PMS1 could be a “two-for-one” effect on huntingtin lowering and somatic instability

Signals that cUHDRS might be improving for some participants

Phase 2/3 FALCON-HD trial is already underway but not recruiting in the US.

Provisional approval application in the works in Australia

# A lot of progress in ~10 years

2015

First people dosed with  
huntingtin lowering  
drugs

2024

lots of clues that we  
might be on the right  
path

2025

cautious optimism that  
we might alter the  
course of HD

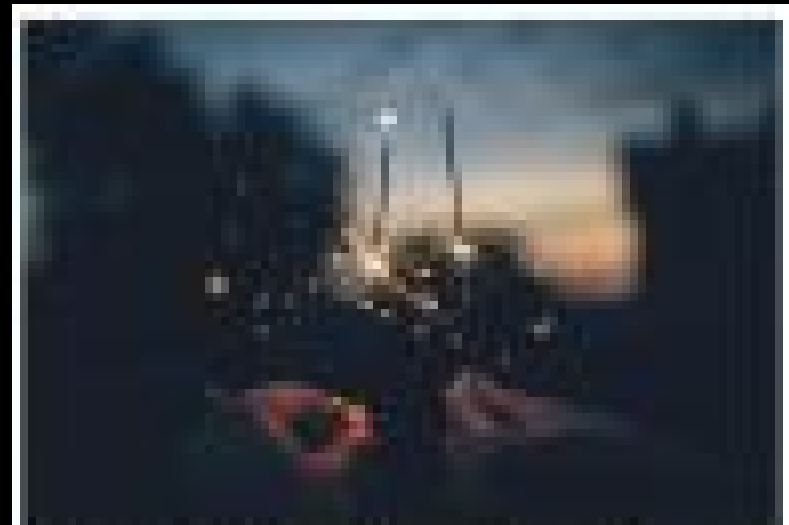


**Going boldly: First person treated in Phase 1 clinical trial by Anylam Pharmaceuticals**

A new Phase 1 clinical trial for the huntingtin-lowering drug AHN-HTT02 was initiated this week with the first dose given. Read on to learn details about the trial and how it compares to other ongoing huntingtin-lowering trials in the clinic.



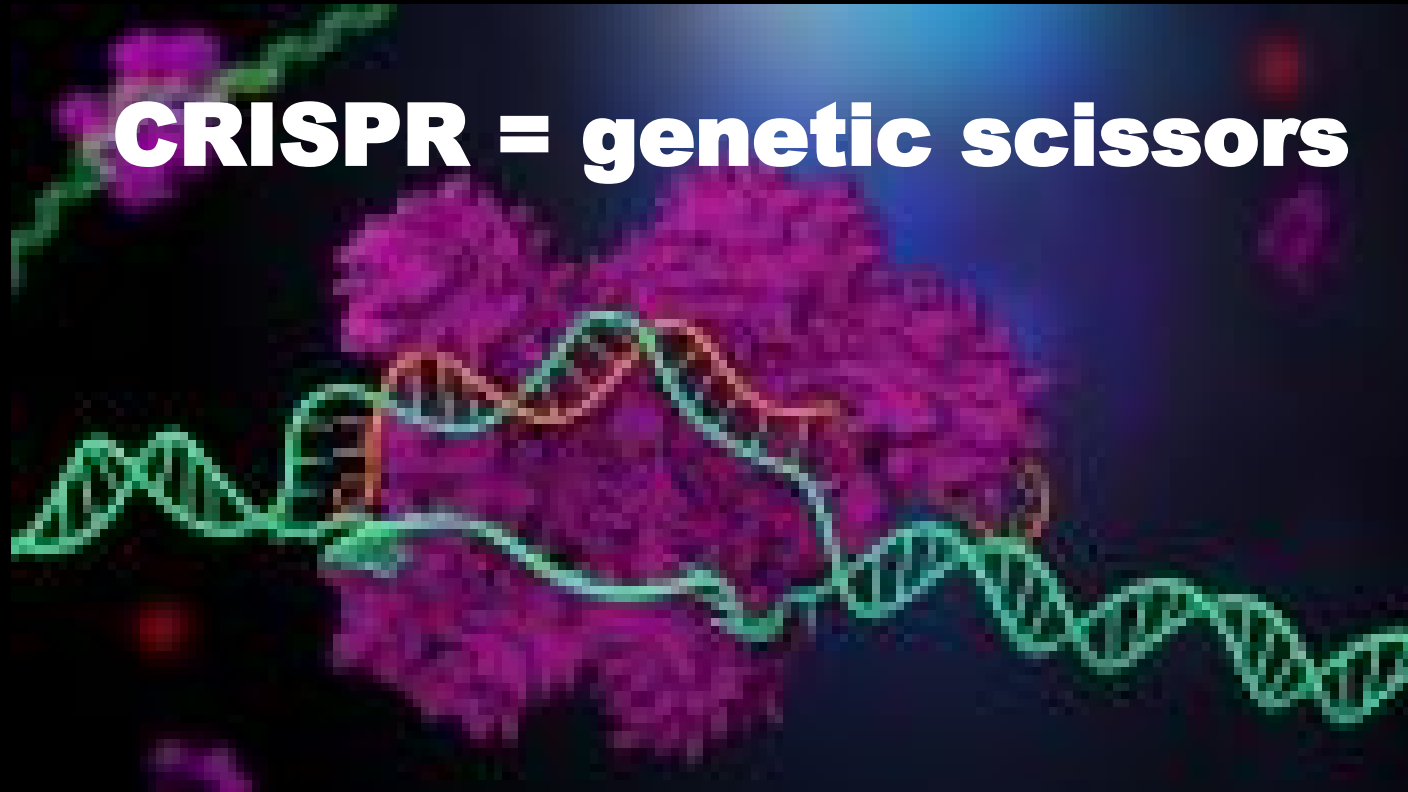
Lots of firsts in the HD clinical space!



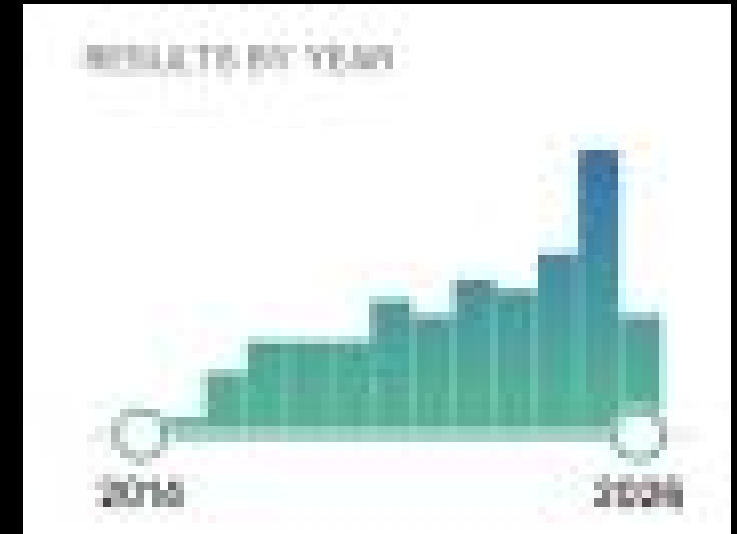
**Spark ignited: first HD patient dosed in new Roche gene therapy trial**

GenS and Roche issued a joint community letter to share that the first patient has been dosed in a new HD gene therapy trial.

# CRISPR gene therapies can make permanent genetic changes to DNA



CRISPR could be used to reduce the CAG number, lower HTT, influence a genetic modifier....



Interest in using CRISPR in HD research is growing



## CRISPR-based drugs: one giant leap for mankind

Company is the first CRISPR-based drug to reach the way through the regulatory process, with multiple Phase III studies under way. The way for similar drugs for other diseases, is it?



By Dr. Sarah Hernandez | February 14, 2018

Edited by Dr. Sarah Hernandez

**Y**ou've likely heard of CRISPR. By now, you've probably read headlines that CRISPR has been used to produce revolutionary new treatments for genetic diseases. Just 4 years after the Nobel Prize for the discovery of CRISPR was awarded, we had our approved treatment using this technology. This may have you wondering if this approach is being used to treat Huntington's disease (HD) research and what a similar drug for HD might mean for the clinic. Let's discuss.

The genetic cause is known

The mechanism of disease is already known

Genetic editing can be done outside the body

Sickle Cell	HD
✓	✓
✓	✗
✓	✗





## Cutting to the chase with CRISPR

🕒 0 min read | A new study uses “self-switching” genetic scissors to target the root cause of Huntington’s disease in mice – even after symptoms begin.

By [Sonia Márquez-Sánchez](#)

April 18, 2024

Edited by Dr Leora Fox

CRISPR “molecular scissors” cut and disrupt the CAG expanded HTT gene directly in the brain of HD mice.

The CRISPR tool is self-inactivating, switching itself off after editing, improving safety.

Toxic protein levels reduced  
~90%

Mice showed improved movement, behavior, and lifespan



# Non-interventional studies

## Registries



The global registry for Juvenile onset Huntington's Disease

## Observational studies



Map the progression of the earliest HD related changes be found in young gene-positive adults

# Surveys



The image is a screenshot of a social media post from HDYO. At the top, the HDYO logo is displayed in colorful letters. Below the logo is a large image of a hand holding a black pen, writing on a document with blue horizontal lines. The text "HDYO Survey Series" is overlaid in white on the bottom part of the image. Below the image are two blue buttons: "View" on the left and "Download" on the right. At the bottom of the post, there is a pink text box with the text "Share Your Voice to Help ALL People Impacted by HDI".

HDYO

HDYO Survey Series

View Download

Share Your Voice to Help ALL People Impacted by HDI



Global study with thousands of people

Yearly visits

Vast amounts of data  
How HD unfolds  
Tracking symptoms

Clinical trial design

New targets

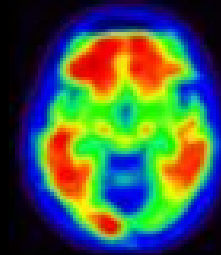
# Observational research and local trials



CSF Donation



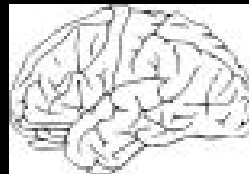
JHD & At-risk youth



Imaging studies



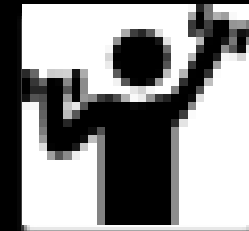
Cognitive testing



Brain Donation



Medication Combinations



Exercise and PT/OT



# Living an active and healthy lifestyle can help some HD symptoms



## HD changes for a healthier brain

In 2018, there were ~17 million people living with dementia. By 2050 that number is expected to climb to 70 million. Changes in the 10 factors highlighted here can protect brain health and be applied for Huntington's disease.

Dr Sarah Hernandez | September 25, 2024



## 2024 HD Buzz Prize: Social Skills – The Hidden Gem in Improving Quality of Life for People with Huntington's Disease?

We're proud to announce Molly Chavry as a 2024 HD Buzz Prize winner! Social skills for her have impacted to a better quality of life in people with HD. Huntington's Disease Chavry suggest that 'hidden gems' impact QoL in HD.

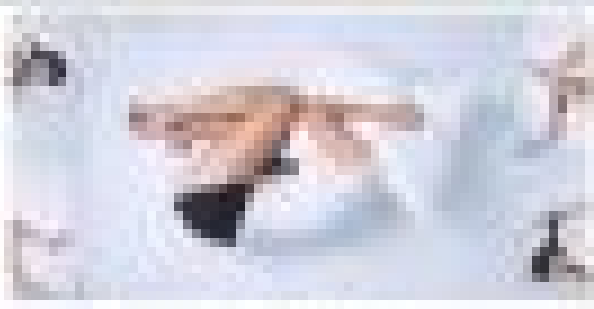
Molly (Molly) Chavry | November 08, 2024



## Brain Gym: Staying Mentally Active May Slow Huntington's Disease

New research suggests that cognitive engagement - keeping your brain busy with activities like reading, puzzles, or learning new skills - could help protect the brain, possibly slowing progression of symptoms of Huntington's disease.

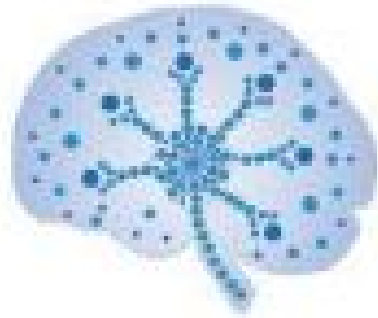
Molly (Molly) Chavry | February 24, 2025



## Waking up early: Sleep is important before Huntington's disease symptoms appear

Our sleep-wake cycle (circadian rhythm) is critical to staying healthy. Research in Huntington's disease (HD) patients suggests sleep changes may occur before other symptoms appear. Just because sleep patterns aren't changed, doesn't mean...

Dr Sarah Hernandez | March 15, 2024



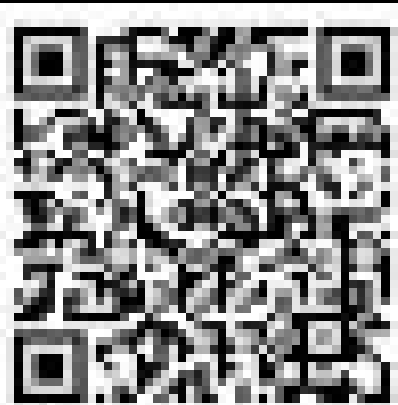
**HARVARD  
BRAIN TISSUE  
RESOURCE CENTER**

allan institute

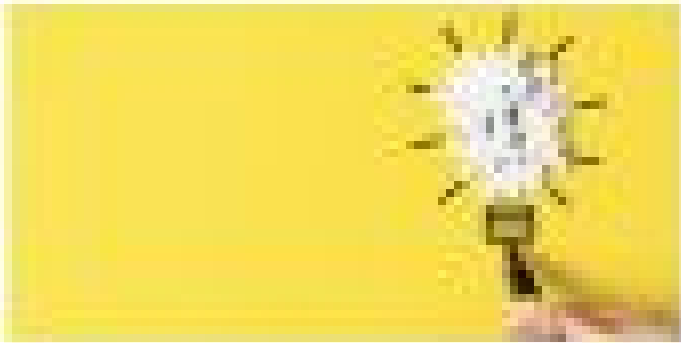


**UW Medicine**

LABORATORY MEDICINE  
& PATHOLOGY



**brain  
donations  
support  
science**



## New insights into Why Huntington's Disease Has Delayed Onset

A highly-anticipated scientific paper has landed! This new work challenges current theories in Huntington's disease research, uncovering how runaway CAG repeats erode cell identity in certain types of brain cells, leading to their death.

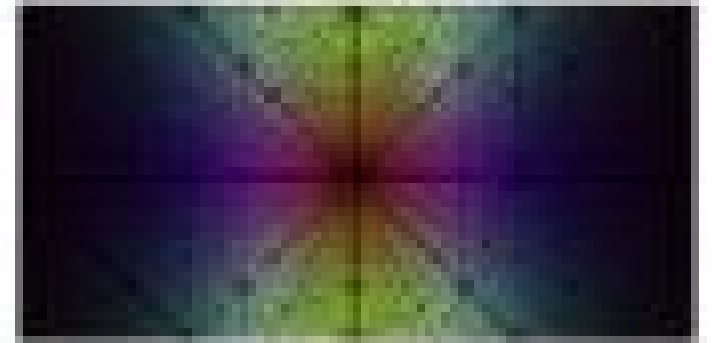
Dr Sarah Hernandez | January 26, 2024



## Hats off to brain donors on Brain Donation Awareness Day

May 7 is Brain Donation Awareness Day. Today we highlight the selfless donation that many HD families have made, sending our gratitude, sharing research updates made with those precious brains, and detailing resources for brain donation.

Dr Sarah Hernandez | May 07, 2024



## Understanding expansions at the single cell level

Scientists have looked at CAG expansions in brains from people with HD to see which cells are affected

Dr Rachel Harding | March 02, 2024

### Article

## Long somatic DNA-repeat expansion drives neurodegeneration in Huntington's disease

Robert B. Handmaker,<sup>1,2,3\*</sup> Sava Kashef,<sup>1,2,3\*</sup> Hans M. Reed,<sup>1,2,3</sup> Steven Tan,<sup>1,2</sup> Woo-Seok Lee,<sup>1,2</sup> Tara M. McDonald,<sup>1,2</sup> Kay Morris,<sup>1</sup> Nolan Komatsu,<sup>1,2</sup> Christopher D. Mullaly,<sup>1,2</sup> Nadya R. Morakabati,<sup>1</sup> Melissa Goodman,<sup>1,2</sup> Gabriel Lind,<sup>1,2</sup> Rhys Kohli,<sup>1,2</sup> Elizabeth Lawton,<sup>1</sup> Marisa Hagan,<sup>1,2</sup> Kiko Ishihara,<sup>1,2</sup> Sabine Bonetto,<sup>1,2,3,4,5,6,7</sup> and Steven A. McCarroll<sup>1,2,3,4,5,6,7,8,9,10,11</sup>

First Published: [https://doi.org/10.1016/j.neuron.2024.01.010](#)

## Cell-type-specific CAG-repeat expansions and toxicity of mutant huntingtin in human striatum and cerebellum

Abstract: [https://doi.org/10.1016/j.neuron.2024.01.010](#)

Keywords: [https://doi.org/10.1016/j.neuron.2024.01.010](#)



Huntington's Disease  
Society of America

# HD Trialfinder



Huntington's  
Disease  
Foundation

Dedicated to Research



Huntington Society of Canada

# HUNTINGTON

Société Huntington du Canada

HD BUZZ

