SKYHAWK THERAPEUTICS

FALCON-HD

SKY-0515: A Daily Pill Designed To Target The Cause Of Huntington's Disease With A Potential To Help Slow Its Progression

Community Forum, Adelaide, Australia

May 12th, 2025

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Acknowledgements And Disclosures

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SKY-0515 Highlights

Skyhawk's objective is to change the way diseases are treated by creating oral medicines that target RNA, the body's instructions for making proteins.

These medicines are designed to fix or adjust how cells function, helping to treat diseases at their root cause.

- A once-a-day pill taken by mouth
- Potential to slow the progression of Huntington's Disease
- Works by reducing levels of harmful proteins linked to the disease
- Shown to be well-tolerated in healthy volunteers

*14-day study with healthy volunteers

Therapy Types Being Developed For Huntington's Disease

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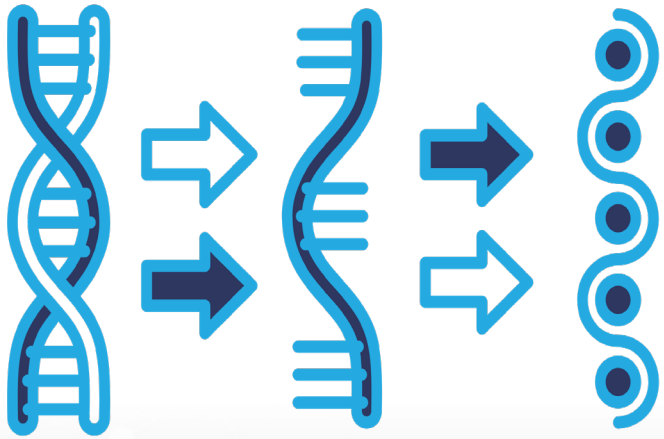
Small Molecules 		**Small**, lab-made compounds.	Usually taken as a pill.	May easily spread throughout the body, enter cells, and can be designed to reach the brain.
Nucleic Acids		**Medium**-sized, lab-made molecules.	Must be given by injection into the blood, tissue, or spinal cord.	May not spread easily throughout the body.
Biologics		**Large** molecules, made from living sources	Must be given by injection into the blood, tissue, or spinal cord.	May not spread easily in the body and some may have trouble entering cells. Certain technologies can help them reach the brain and improve how well they work.

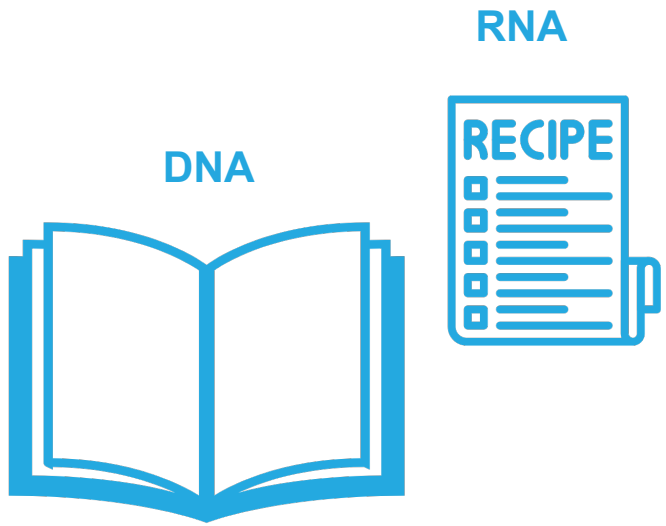
What Is RNA?

What is RNA?

A messenger in the cell.

A molecule that carries instructions from DNA to the rest of the cell for building proteins, which are essential for life.





Think of DNA as a cookbook of recipes.

RNA is like the recipe card you copy from the cookbook.

You take this card to the stove (around the cell) to make the dish (protein).

What Is An RNA-targeting Drug?

An RNA-targeting drug binds to specific parts of RNA…

Like an edit you can make to the recipe card to modify the dish.

"Add this"

"Remove that"

This can:

Change RNA function: It can stop RNA from making proteins or provide instructions to make a different protein.

Modify RNA stability: It can make RNA last longer or degrade faster, changing its interactions.

Influence gene expression: It can alter how genes are expressed without altering DNA.

SKY-0515 Affects mRNA Splicing

Splicing is like editing a set of instructions for a recipe—taking out or adding ingredients can modify the final dish, helping make good proteins or stop bad ones.

SKY-0515 Adjusts How RNA Is Processed To Change Protein Production

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1 **DNA stores instructions**
Your genes contain the code for making proteins.

Transcription

2 **Pre-mRNA is created**
The body copies part of the DNA into a temporary message called pre-mRNA.

Splicing

3 **mRNA is formed**
This message gets edited (splicing) to remove extra parts, leaving only the important instructions.

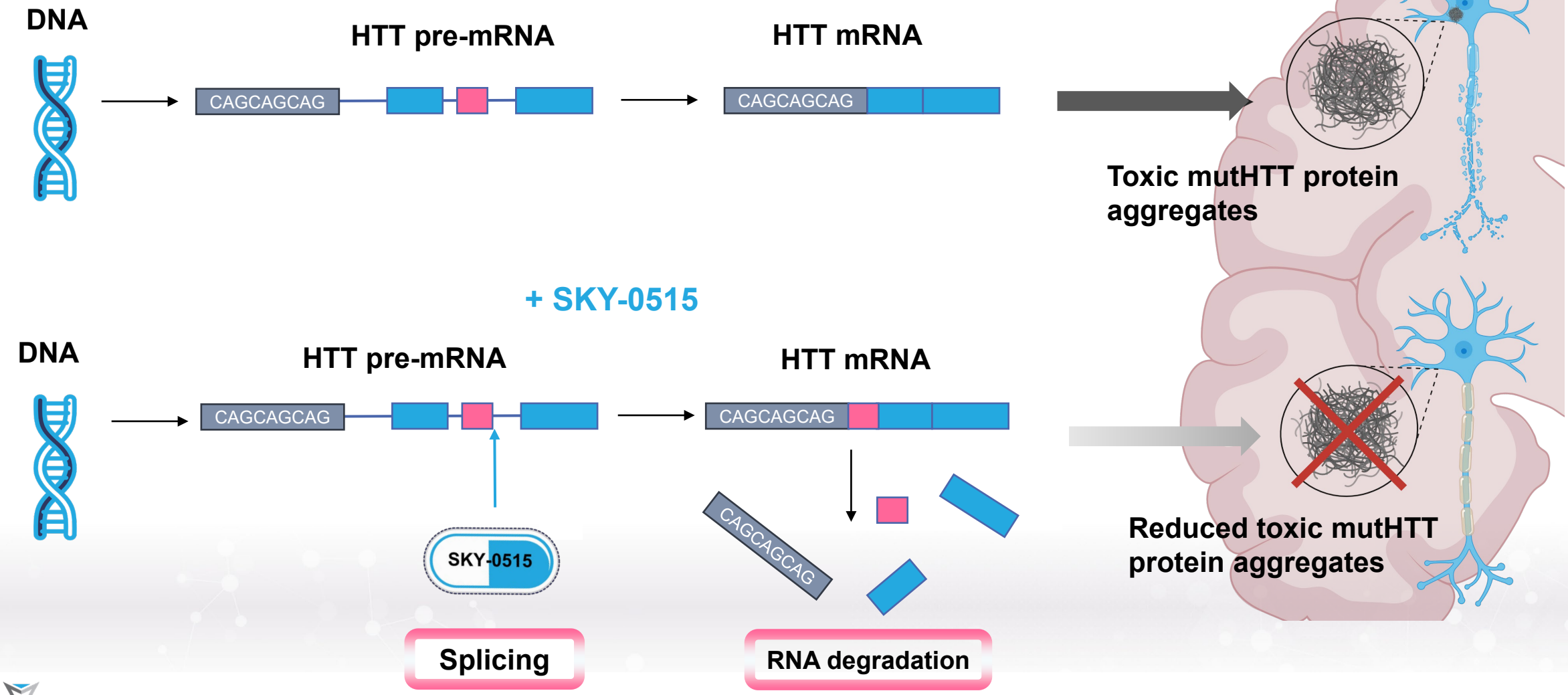
Translation

4 **Proteins are made**
The body reads the mRNA and builds proteins based on the instructions.

SKY-0515 changes splicing

This drug adjusts the editing step to stop mRNA from making harmful proteins that contribute to Huntington's disease.

SKY-0515 Aims To Reduce Toxic Mutant HTT Protein In The Brain



HD Happens Because Of A Mutation In A Gene Called HTT

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Mutation

People inherit **too many copies** of a small DNA sequence called **CAG.**

Result

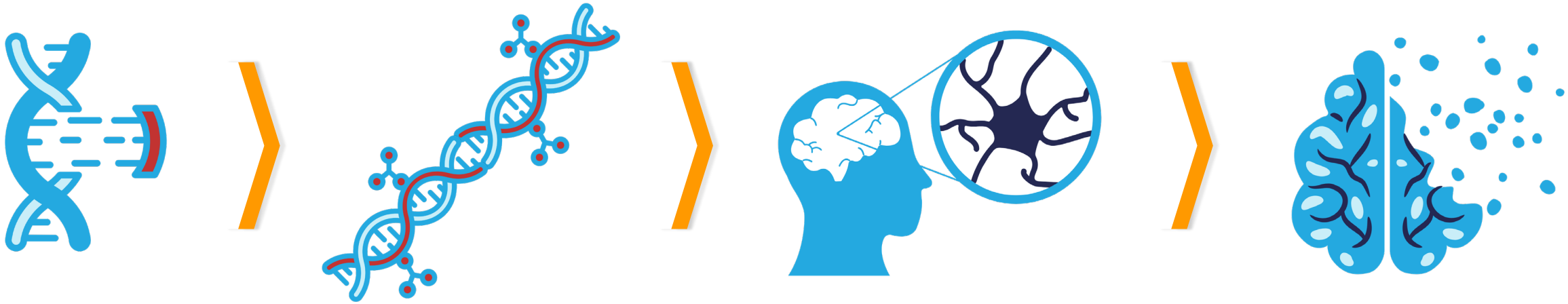
This causes the body to make a **harmful protein** that keeps growing.

Damage

The harmful protein **hurts brain cells** and makes them die.

Effect

Over time, this leads to **brain shrinkage**, affecting movement, thinking, and emotions.



CAG is a small piece of DNA that repeats too many times (36 or more) in people with HD, causing harmful effects in the brain.

PMS1 promotes CAG repeats and makes mutant HTT more harmful and worsens Huntington's Disease

PMS1 And Somatic CAG Expansion Contribute To HD Progression

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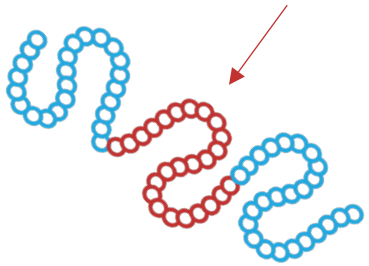
Reducing PMS1 May Slow the Disease



Born with Extra CAG Repeats

People who have HD are born with more CAG repeats in their HTT gene.

More CAG Repeats = Earlier Disease

Higher number of CAG repeats can lead to earlier onset of disease and symptoms.

CAG Repeats Increase Over Time

Over time, the number of CAG repeats expands in brain cells. This can occur at different rates in individuals and further impacts onset and progression of symptoms.

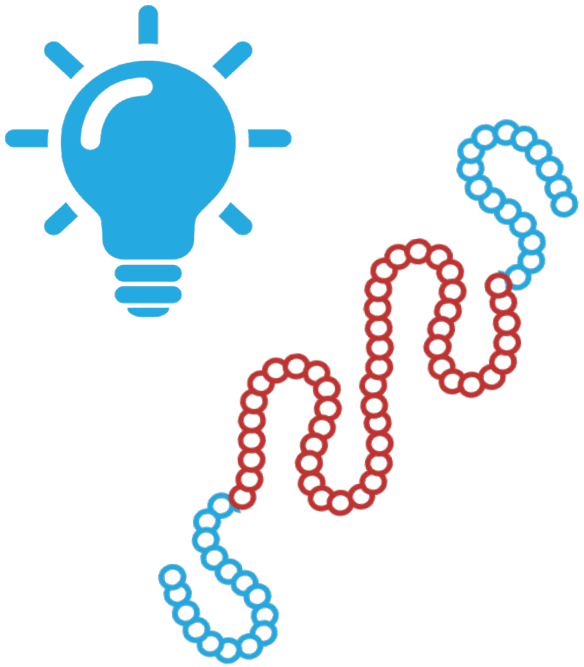
Less PMS1 =
Slower CAG growth =
Delayed disease progression

Reduced PMS1 Slows CAG Expansion

A protein called PMS1 affects the rate of increase in CAG repeats.

Somatic CAG Expansion is the increase in CAG repeats in specific cells over time.

HD Is Caused By Mutant HTT And Worsened By PMS1



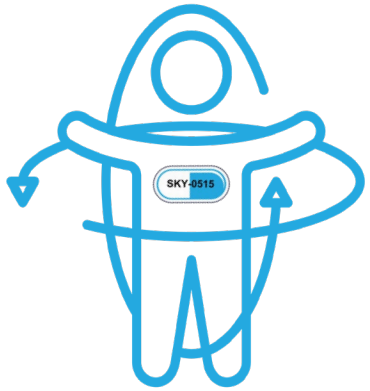
Mutant HTT is a damaged protein caused by extra CAG repeats in the DNA. The CAG can continue to expand over time affecting the severity of the Huntington's disease.

PMS1 is one of the proteins that help control CAG expansion, linked to the development of HD.

SKY-0515 Is A Daily Pill Designed To Potentially Slow Down Or Reduce The Damage Caused By HD

The pill is taken by mouth, once-a-day.

The pill spreads throughout the body, including the brain.

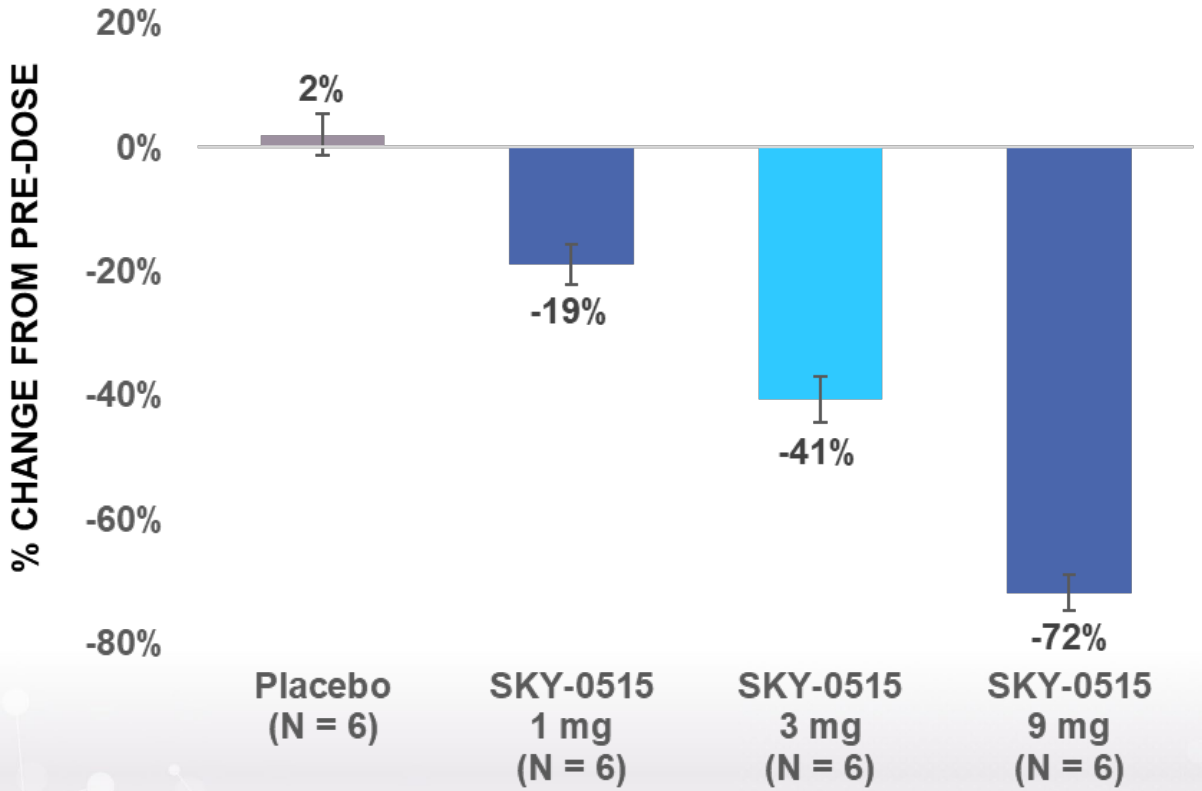


It lowers the amount of harmful HD protein (HTT), which might prevent brain cell damage.

It also reduces another protein (PMS1), which might slow the CAG repeats expansion.

Clinical Effects Of SKY-0515 On HTT mRNA In Blood After 14 Days Of Dosing In Healthy Volunteers

Multiple Dose Study (daily dosing for 14 days)
Average Reduction in HTT mRNA Level in Blood over 24 Hours



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Standard Clinical Development Program

May 2025

Small cohort
Healthy volunteers and/or patients

Medium cohort of patients

Large cohort of patients

Preclinical	Phase 1	Phase 2	Phase 3
Lab and animal studies	**Safety studies** May be able to detect early markers of efficacy (Biomarkers)	**Safety and dose-finding efficacy studies** Establish early signs that the drug may be working (Biomarkers, clinical assessments)	**Confirmation of safety and efficacy** Establish significant clinical benefit (Clinical assessments, biomarkers)

SKY-0515-004-ANZ (FALCON-HD) is a Phase 2 study enrolling HD patients in Australia and New Zealand

Eligibility Criteria For SKY-0515-004-ANZ

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Inclusion Criteria

Participants must:

- Be ≥ 25 years old at the time of informed consent.
- Have genetically confirmed Huntington's disease (CAG ≥ 40 in the HTT gene).
- Meet the following screening criteria:
- Total Functional Capacity (TFC) ≥ 10
- Total Motor Score (TMS) ≥ 6
- Independence Scale (IS) ≥ 70
- Adhere to local contraceptive regulations if applicable.
- Provide signed informed consent and comply with study requirements.
- If previously in a tominersen study, the last dose must have been at least 12 months before dosing with SKY-0515-004-ANZ.

Participants cannot join if they:

- Have other significant neurological or medical conditions.
- Have conditions that would interfere with assessments (e.g., implanted shunts).
- Have had active malignancy in the last five years (excluding specific skin cancers).
- Have a history of severe allergic reactions to the study drug.
- Are currently using drugs that affect HTT mRNA or protein levels.
- Have elevated liver function test results.
- Test positive for HBsAg, HepC, or HIV antibodies.
- Are pregnant, planning pregnancy, or currently breastfeeding.
- Have a history of substance abuse or other conditions that may interfere with participation.

Clinical Trial FAQ's

Why are clinical trials needed?

Clinical trials aim to answer key questions, such as:

- Does the new medicine work?
- Is it more effective than existing treatment options?
- Does it have any side effects?

These studies are crucial in helping healthcare professionals determine which medicines are best suited for individuals. However, it is important to know that participation in a clinical trial does not guarantee access to a better treatment.

If you have more questions, please speak to a healthcare professional.

Who conducts and regulates clinical trials

Clinical trials may be conducted by governments, pharmaceutical companies, hospitals, and universities. They are strictly regulated by laws, ethical standards, and codes of conduct.
Before a trial can begin, it must be approved by the Ethics Committee of each clinical site involved

Are there benefits of participating in a trial?

Taking part in a clinical trial may offer several benefits, including:

- Contributing to the development of new medications that may change the course of Huntington's disease for current and future generations.
- Access to medical experts and facilities.
- Ongoing medical monitoring by experts throughout the trial.

What happens before a clinical trial?

Eligibility criteria must be met in order to participate in a clinical trial. Having the disease does not automatically make someone eligible for a study. Similarly, if someone is not eligible for this study, they may be eligible for other studies.

What happens during a clinical trial?

The treatment process depends on the trial. Some medications are taken at home, while others require clinic visits. Participants may need regular assessments to monitor effects.

What happens after a clinical trial?

Depending on the results, there will be a decision about what to do next:

- To proceed to another trial phase.
- To stop the research.
- Or to seek regulatory approval for the medication to be available for use.

SKY-0515-004-ANZ (FALCON-HD) Site Locations

Australia

Flinders Medical Centre

Bedford Park, South Australia 5042

Principal Investigator: Karyn Boundy

The Perron Institute

Nedlands, Western Australia 6009

Principal Investigator: Daniel Clarke

Westmead Hospital

Westmead, NSW 2145

Principal Investigator: Florence Chang

John Hunter Hospital

New Lambton Heights, NSW 2305

Principal Investigator: Natalia Murray

The University of Queensland

Royal Brisbane Women's Hospital, Herston, QLD 4006

Principal Investigator: Robert Adam

Calvary Health Care Bethlehem

Caulfield South, VIC 3162

Principal Investigator: Yenni Lie

The Royal Melbourne Hospital

Parkville, VIC 3050

Principal Investigator: Dennis Velakoulis

New Zealand

Auckland City Hospital

Auckland, 1023

Principal Investigator: Richard Roxburgh

Wellington Hospital

Wellington, 6021

Principal Investigator: David Bourke

New Zealand Brain Research Institute

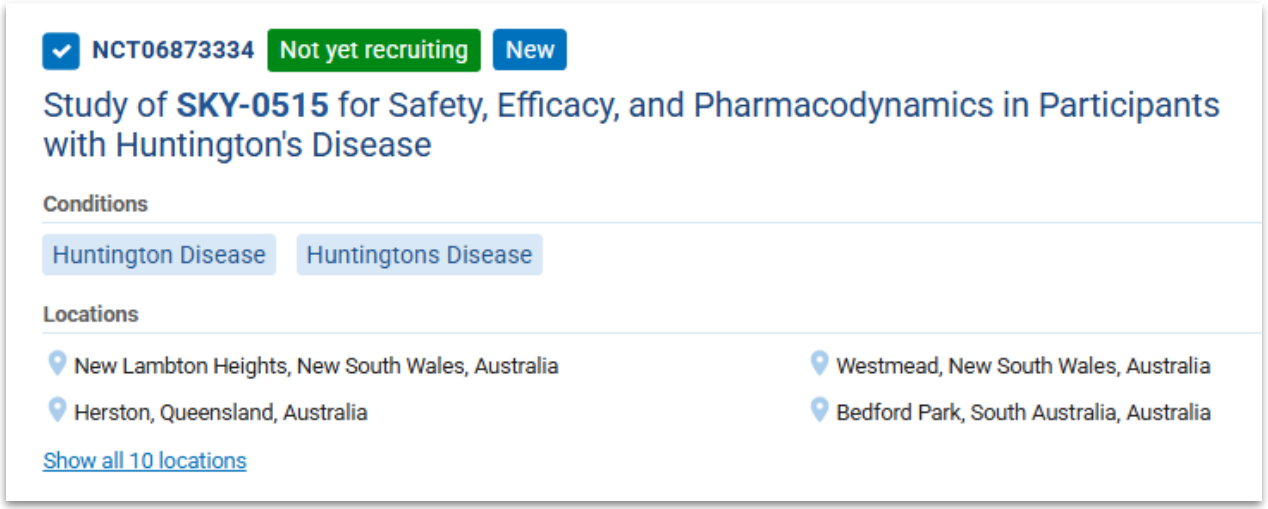
Christchurch, 8011

Principal Investigator: Tim Anderson

For More Information

Study Information:

- Visit: **ClinicalTrials.gov**
- Key Term Search: **SKY-0515**
- Identifier: **NCT06873334**



General Questions / Inquiries:

- Email: **SKY0515trials@skyhawktx.com**