
SKY-0515: A Small Molecule Targeting the Cause of Huntington’s Disease
Clinical Program Update
Huntington's Australia Community Forum
October 30, 2025
SKY-0515
Learn about our RNA-targeting small molecules
falcon-hd.com / skyhawktx.com
SKYHAWK THERAPEUTICS
FALCON-HD

Disclosures

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SKY-0515 is a Type of Small-molecule Medicine Designed to Fix How the Body Processes the Huntingtin Gene

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.

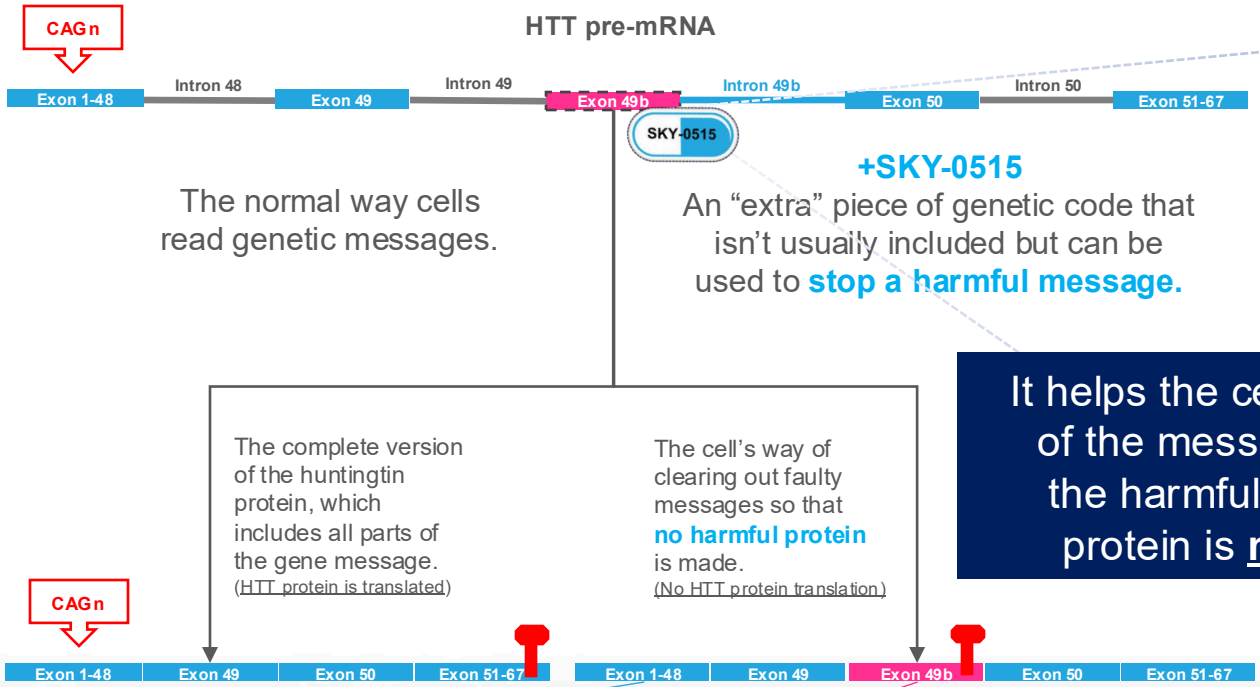


- A once-a-day pill taken by mouth
- Aims to slow the progression of Huntington's Disease
- Reduces levels of harmful proteins (mHTT and PMS1) linked to the disease
- Shown to be well-tolerated and active

*Based on early results from ongoing phase 1 data in HD patients

SKY-0515 Works by Adjusting How the HTT Gene's Message (mRNA) is Read Inside Cells

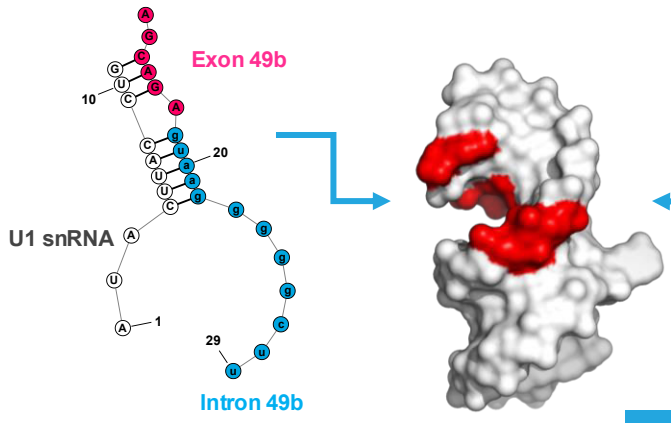
This process happens naturally in cells and **SKY-0515 helps guide it in a more beneficial way** for people with Huntington's Disease.



It helps the cell "skip" part of the message so that the harmful huntingtin protein is **not** made.

Computer models were used to predict **how SKY-0515 attaches to the HTT gene message** to help block the harmful protein from forming.

A lab method called **NMR spectroscopy** was used to confirm how SKY-0515 attaches to its RNA target.



Regular exon: A regular part of a gene message that is always included when the protein is made.

Extra exon: A hidden or extra piece of genetic code that isn't normally used but can be added to change or stop how a protein is made.

Stop code: a natural "stop signal" that prevents the cell from making a full, harmful protein.

HIGHLY CONFIDENTIAL: Based on draft unaudited data; subject to change

Phase 1A and 1B Study Overview: Testing in Healthy Volunteers

Completed	Completed
Part A: Phase 1 single dose (Healthy Volunteers)	**Part B: Phase 1 multiple doses (Healthy Volunteers)**
1 mg 6 people	1 mg QD 6 people
2 mg 6 people	3 mg QD 6 people
4 mg 5 people	9 mg QD 6 people
8 mg 6 people	Placebo 6 people
16 mg 5 people	|——14 days——|
Placebo 10 people	

QD = once daily

Main Study Goal

- Check if SKY-0515 is safe and well-tolerated
- Find the best dose to use in Phase 2

Additional Study Goals

- How SKY-0515 moves through the body
- How much it lowers HD-related markers in blood

No Increase in Side Effects, Even at Higher Doses (Up to 14 Days)

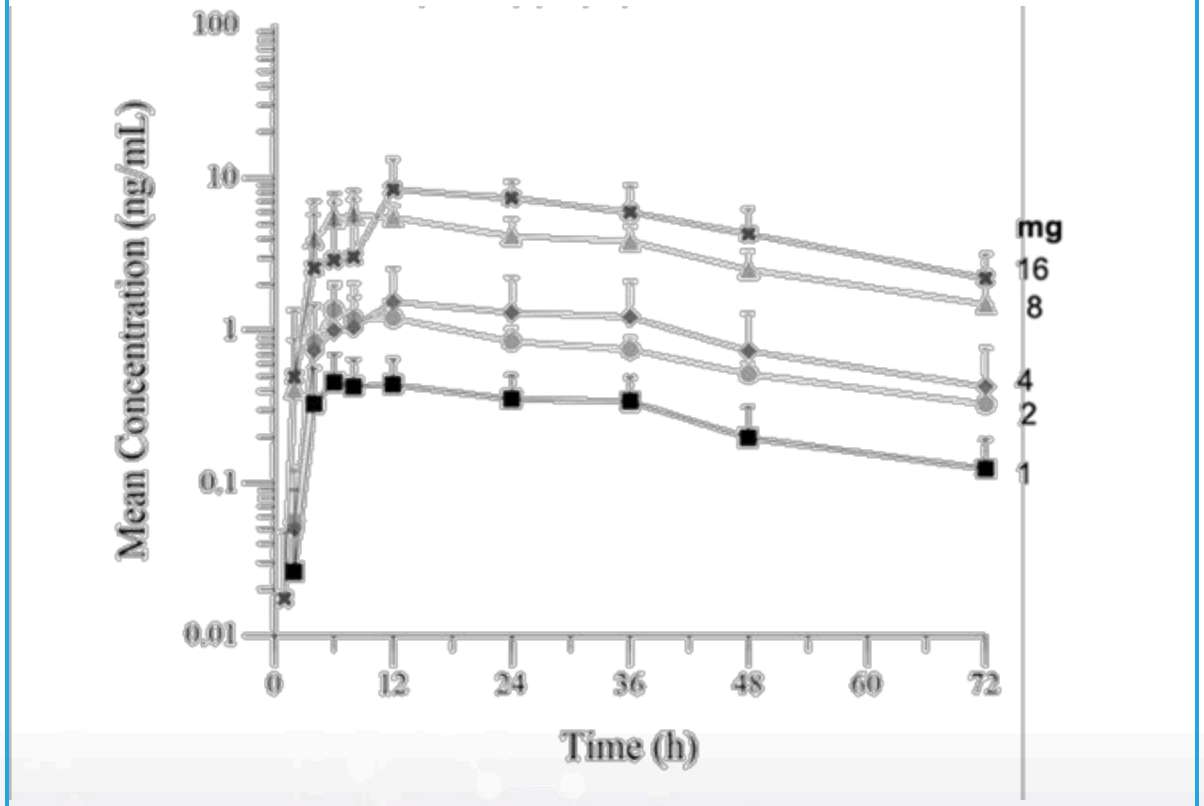
- Most side effects were **not related** to SKY-0515
- **No one** had serious side effects, stopped taking the drug, or dropped out of the study
- All side effects were **mild** and went away on their own.
- The number of people with side effects did **not increase** with higher doses.

Participants with at least one:	Placebo (n=6)	1 mg (n=6)	3 mg (n=6)	9 mg (n=6)
Any side effect	5 (83%)	6 (100%)	3 (50%)	4 (67%)
Serious side effect	0	0	0	0
Side effect causing death	0	0	0	0
Stopped treatment because of side effect	0	0	0	0
Left study because of side effect	0	0	0	0
Mild side effect	5 (83%)	6 (100%)	3 (50%)	4 (67%)
Moderate side effect	2 (33%)	0	1 (17%)	1 (17%)
Not related to study drug	5 (83%)	4 (67%)	2 (33%)	2 (33%)
Unlikely related	2 (33%)	3 (50%)	2 (33%)	2 (33%)
Possibly related (mild only)	0	1 (17%)	0	1 (17%

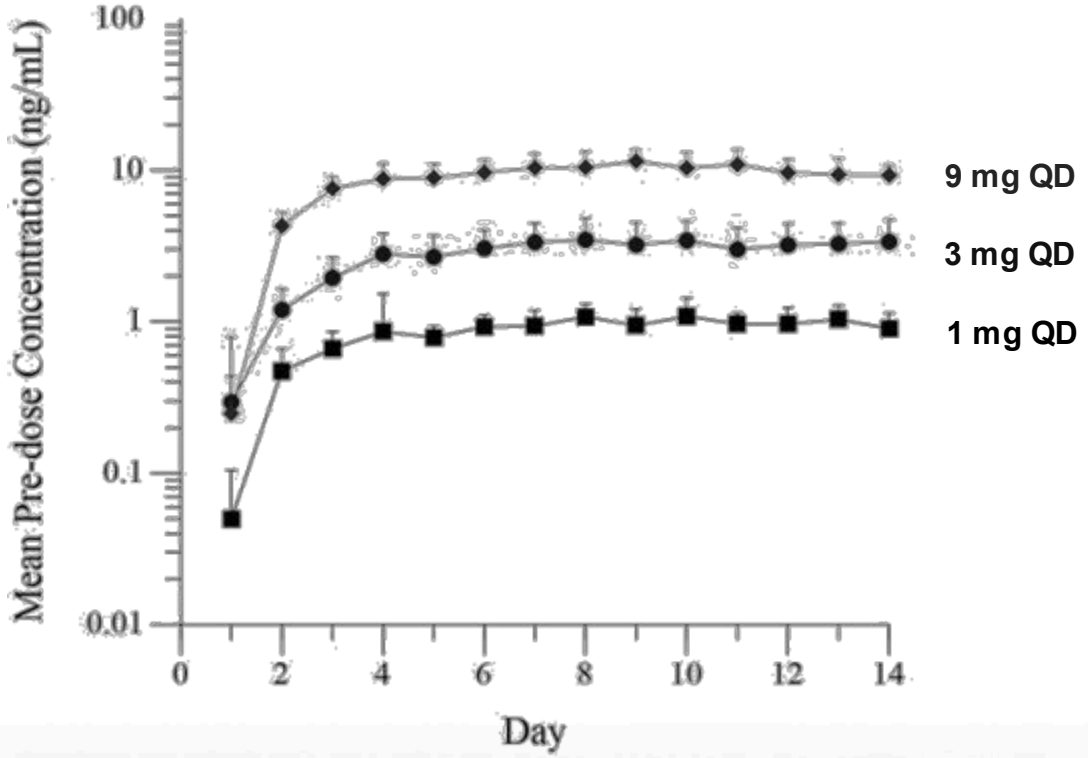
n=6 means there was a total of 6 people in the test group.

SKY-0515 Levels in the Body Rise Steadily with Dose

SKY-0515: Single-Dose Results

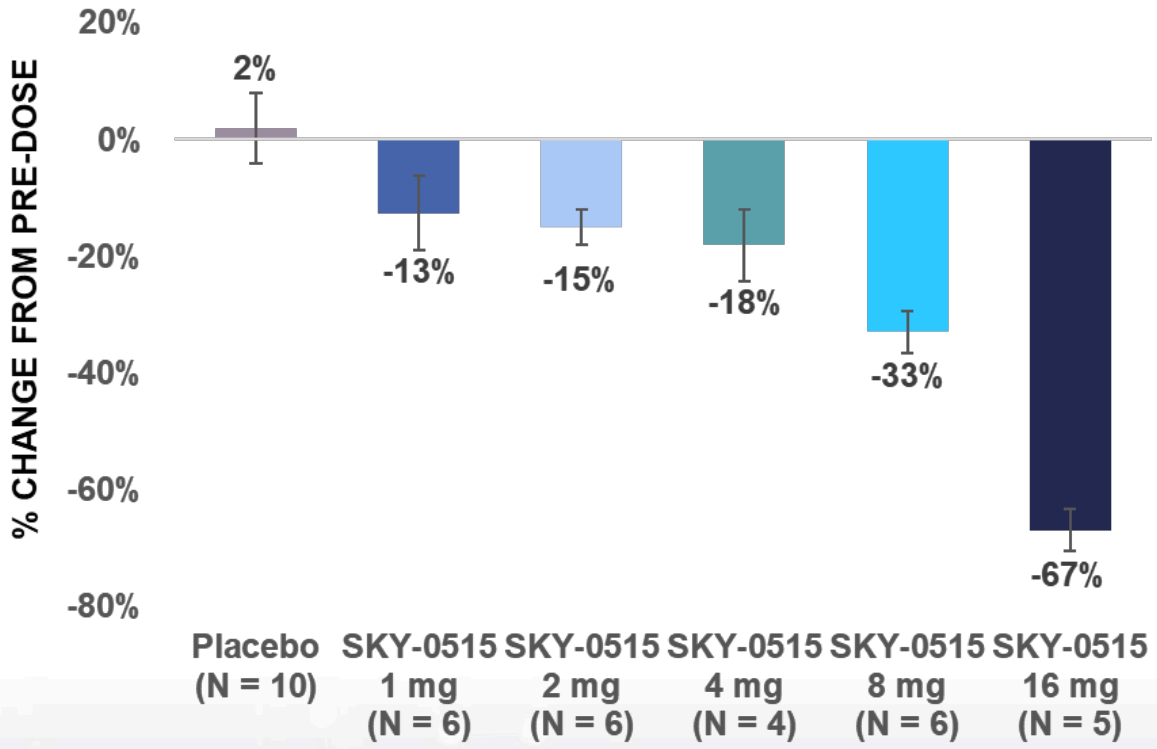


SKY-0515: Multiple-Dose Results

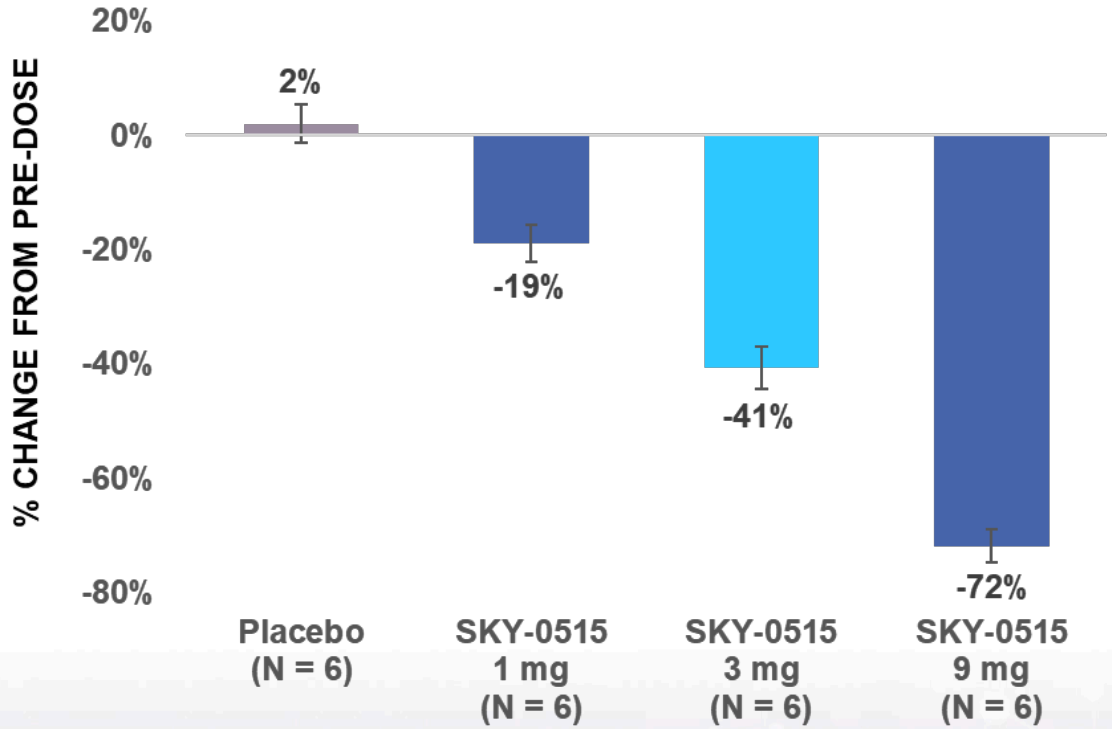


How SKY-0515 Affects the Body in Healthy People

After a single dose of SKY-0515, the amount of the harmful HTT message in the blood dropped within 24 hours*



This lower level remained consistent for at least two weeks after dosing*

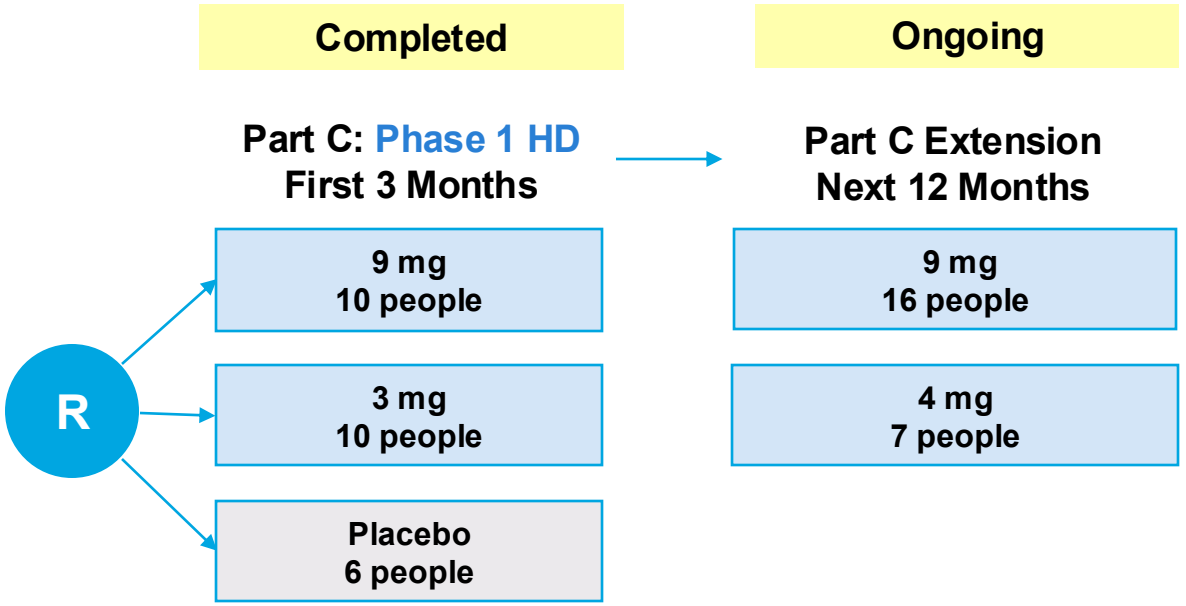


Note: Error bars represent standard error of the mean

Phase 1C Study Overview: Testing in HD Patients

SKY-0515 Phase 1 Part C

- **First 3 months:** patients receive either drug or placebo (neither doctors nor patients know which one)
- **Next 12 months**: everyone receives drug
- **Total number of patients**: 26
- **Age:** 25–70 years
- **HD stage:** Early to mid
  - TMS ≥ 6
  - IS ≥ 70
  - TFC ≥ 8



R = Randomized (assigned by chance)

Main Study Goal

- Check if SKY-0515 is safe and well-tolerated

Additional Study Goals

- How SKY-0515 moves through the body and reaches the brain
- How much it lowers HD-related markers in blood and spinal fluid
- Brain changes over time (MRI)
- Movement and thinking test results

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Who Took Part in Phase 1C of the Study

Participant Averages at Baseline ± Standard Deviation	Placebo (n= 6)	3mg (n=10)	9mg (n=10)
Sex (Male / Female)	50 M / 50 F	60 M / 40 F	40 M / 60 F
Age	58.3 ± 9.3	55.9 ± 7.2	55.9 ± 6.3
CAG repeats	41.7 ± 0.8	42.1 ± 1.9	42.9 ± 2.4
cUHDRS	11.5 ± 1.0	12.8 ± 3.0	11.3 ± 2.8
TFC	12.3 ± 8.2	12.0 ± 1.6	12.1 ± 1.9

cUHDRS = composite Unified Huntington's Disease Rating Scale (overall measure of HD symptoms and abilities)
TFC = Total Functional Capacity (how well someone can function in daily life).

SKY-0515 Continues to Show a Good Safety Record

Results After 3 Months

- Side effects were similar between people taking placebo, 3 mg, and 9 mg of SKY-0515.
- No important changes were seen in lab tests, heart readings, or vital signs.

Severe side effects:

- **Headache** (possibly related): went away within 10 days
- **Psychosis** (unlikely related): went away in 3 days

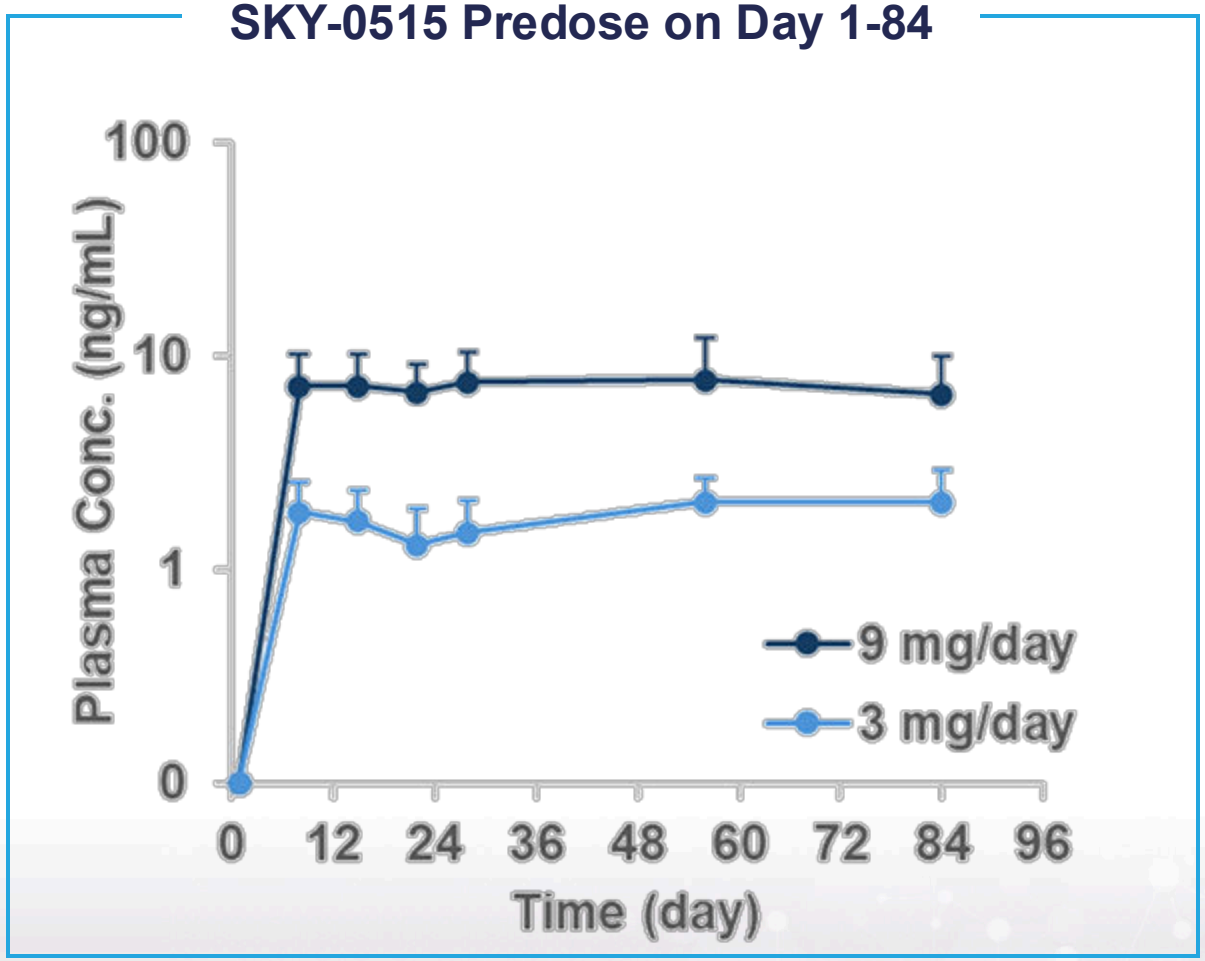
Moderate side effects:

- **Headache** (possibly related): went away in 3 days
- **Fall** (not related to the drug)

All participants have now been on SKY-0515 for at least 6 months.

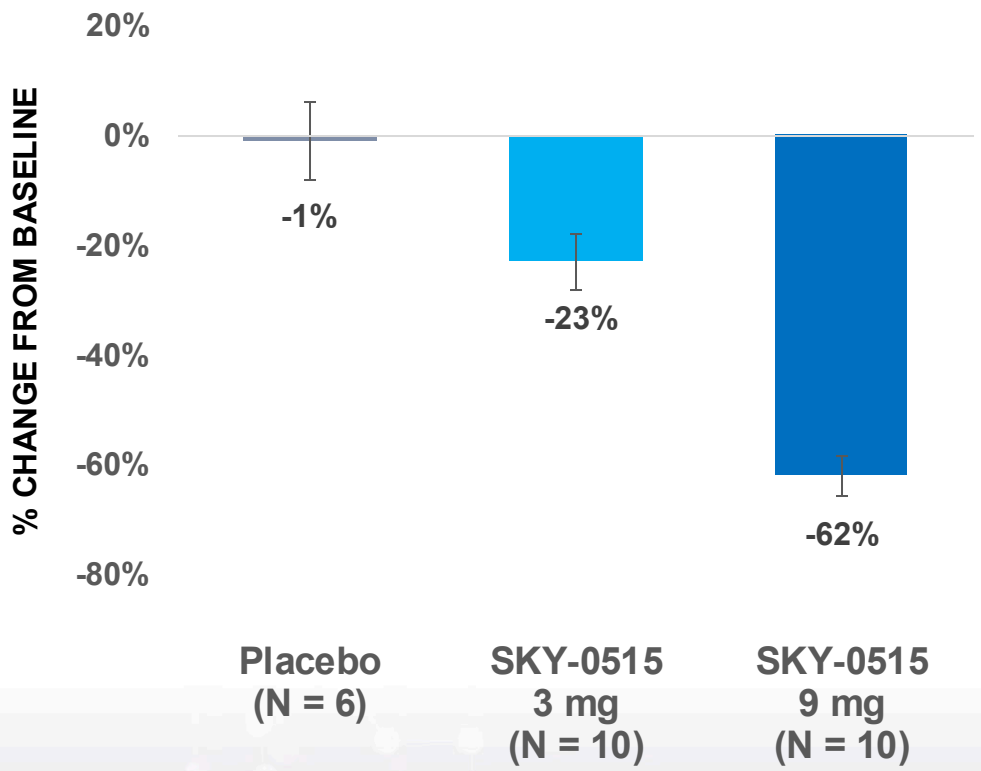
In HD Patients, SKY-0515 Works the Same Way as in Healthy Volunteers

- SKY-0515 levels **rise steadily** with the dose
- We also know that SKY-0515 reaches the brain effectively with **73% to 84%** exposure

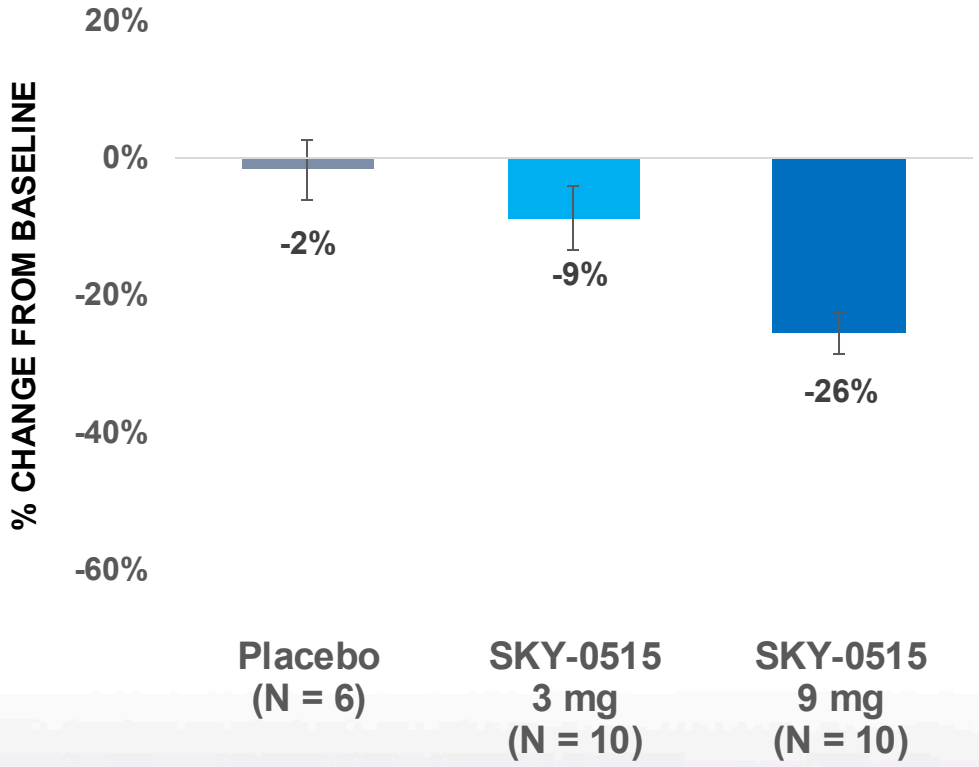


SKY-0515 Reduces HTT and PMS1 mRNA in Blood – the Higher the Dose, the Greater the Drop

Average drop in HTT mRNA (blood) After steady dosing



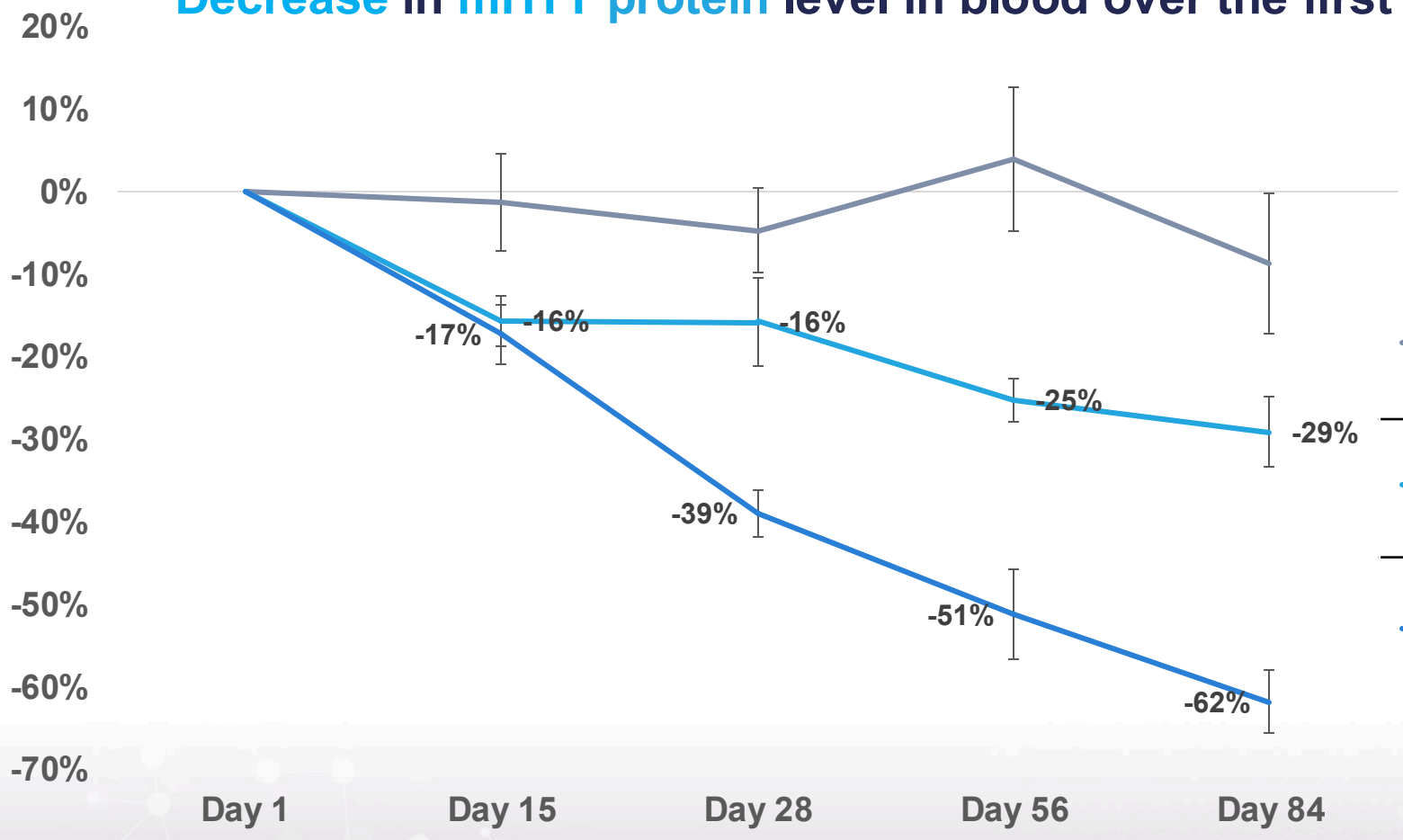
Average drop in PMS1 mRNA (blood) After steady dosing



Note: Error bars represent the standard error of the mean.

The More SKY-0515 Is Taken, the More It Lowers the Harmful HD Protein Over Time

Decrease in mHTT protein level in blood over the first 84 days of treatment



	Mean % Change from Baseline mRNA
Placebo	
3mg	-23%
9mg	-62%

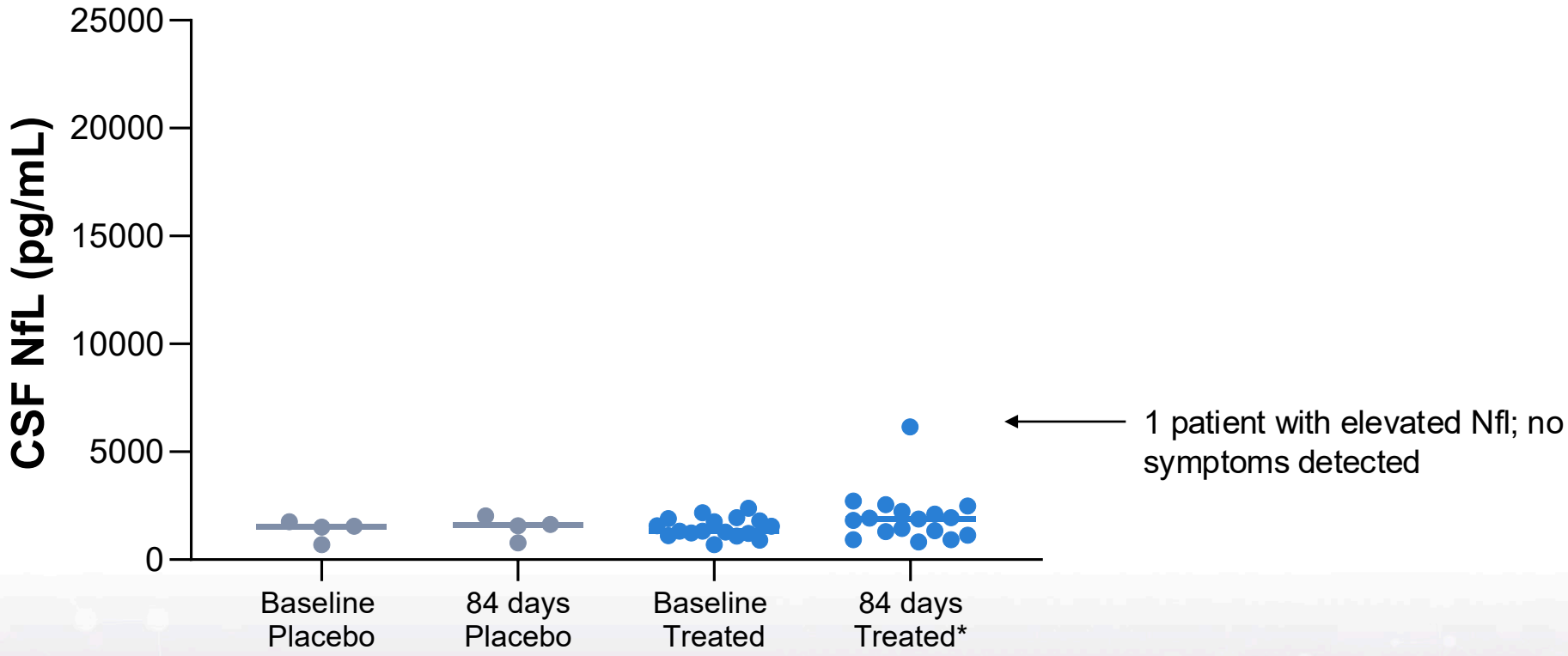
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mRNA and Protein Lowering

Note: Error bars represent the standard error of the mean. Excludes Day 84 data for patient that discontinued 9 mg treatment at day 73.

No Significant Signs of Nerve Damage Seen After Three Months of Treatment

CSF NfL levels: A nerve health marker measured in spinal fluid before treatment and after 84 days.



* One subject removed who had covid just prior to 84 day sample

Summary: SKY-0515 3-Month Study Results

Safety

- So far, SKY-0515 looks **well-tolerated.**
- **No significant signs** of harmful side effects, even at higher doses.
- **No significant signs** of nerve damage (based on a marker called NfL).

How the Drug Moves in the Body

- The amount of SKY-0515 in the body **increases steadily** as the dose increases.
- It **reaches stable levels** in about a week.
- It gets **into the brain effectively.**

How the Drug Works

- At the 9 mg dose, SKY-0515 **lowered mHTT by 62%.**
- It also **lowered** another related marker, **PMS1, by 26%.**

*These results are early (up to 3 months). More results will come as the study continues

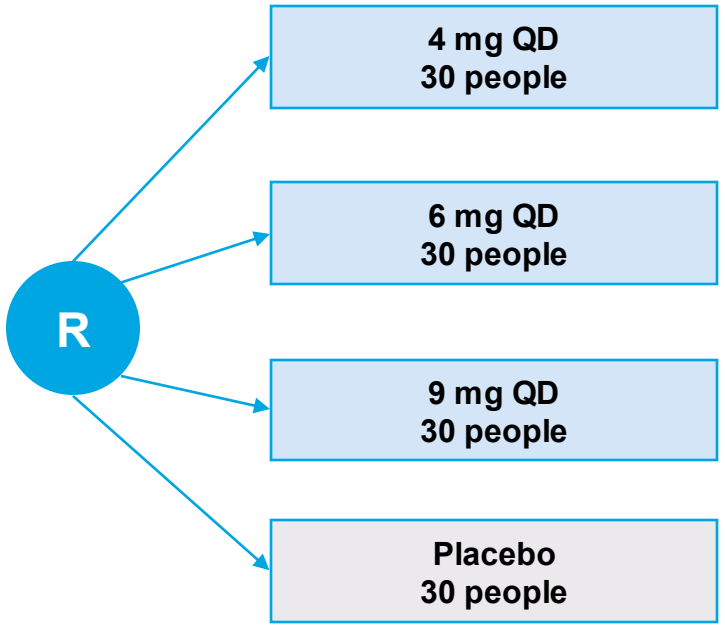
SKY-0515 (FALCON HD): Phase 2/3 study in HD patients in Australia and New Zealand

SKY-0515 Phase 2/3 Study

- **12 months total**
- **Participants randomly receive either SKY-0515 or placebo** (neither doctors nor patients know which one)
- **Total number of patients**: 120
- **Age:** 25 and up
- **HD gene expansion**:
  - CAG ≥ 40
- **HD stage:** Early to mid
  - TMS ≥ 6
  - IS ≥ 70
  - TFC ≥ 10

Currently Enrolling Patients

Phase 2/3
(Stage 2 – 3 HD Patients)



Main Study Goal

- Measure changes in mHTT in the blood

Additional Goals:

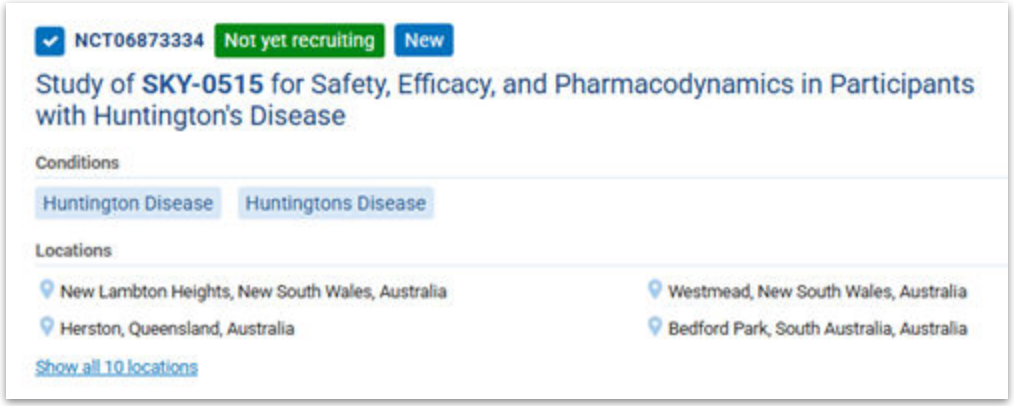
- Check safety (any side effects or serious side effects)
- Measure brain changes (size of a brain area called the caudate)
- Track movement, thinking, and daily function (using clinical tests)
- See if treatment helps slow down or delay HD progression

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Study Information

Study Information:

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



General Questions / Inquiries:

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