Press Release

Skyhawk Therapeutics Announces Twelve-Month Interim Results from Phase 1/2 Clinical Trial of SKY-0515 in Huntington's Disease

Twelve-month findings showed improvement in Composite Unified Huntington's Disease Rating Scale (cUHDRS) scores from baseline of +0.38, compared to an expected decline of -0.92 points in propensity score-weighted natural history analyses of symptomatic patients

SKY-0515 patients achieved reductions of 69% mutant huntingtin protein (mHTT) at the 9 mg dose at twelve months

The Company also announces that the Australia and New Zealand (004-ANZ) portion of its Phase 2/3 FALCON-HD pivotal study completed enrollment six months ahead of schedule with 144 patients enrolled, and that the worldwide (004-WW) Phase 2/3 FALCON-HD pivotal study has expanded to eight countries

More than 175 patients are now enrolled across the SKY-0515 Phase 1/2 and FALCON-HD pivotal studies

BOSTON, Mass., June 1, 2026 - Skyhawk Therapeutics, Inc., a clinical-stage biotechnology company developing novel small molecule therapies designed to modulate RNA targets, today announced results from the twelve-month interim analysis of patients in its Phase 1/2 clinical trial evaluating SKY-0515, an investigational treatment for Huntington's disease (HD).

Treatment with SKY-0515 resulted in dose-dependent reductions in mutant huntingtin (mHTT) protein in blood of up to 69% as well as reductions in PMS1 mRNA of up to 26%. Mutant huntingtin is the primary protein responsible for HD pathology, while PMS1 is a key driver of somatic CAG repeat expansion associated with disease progression.

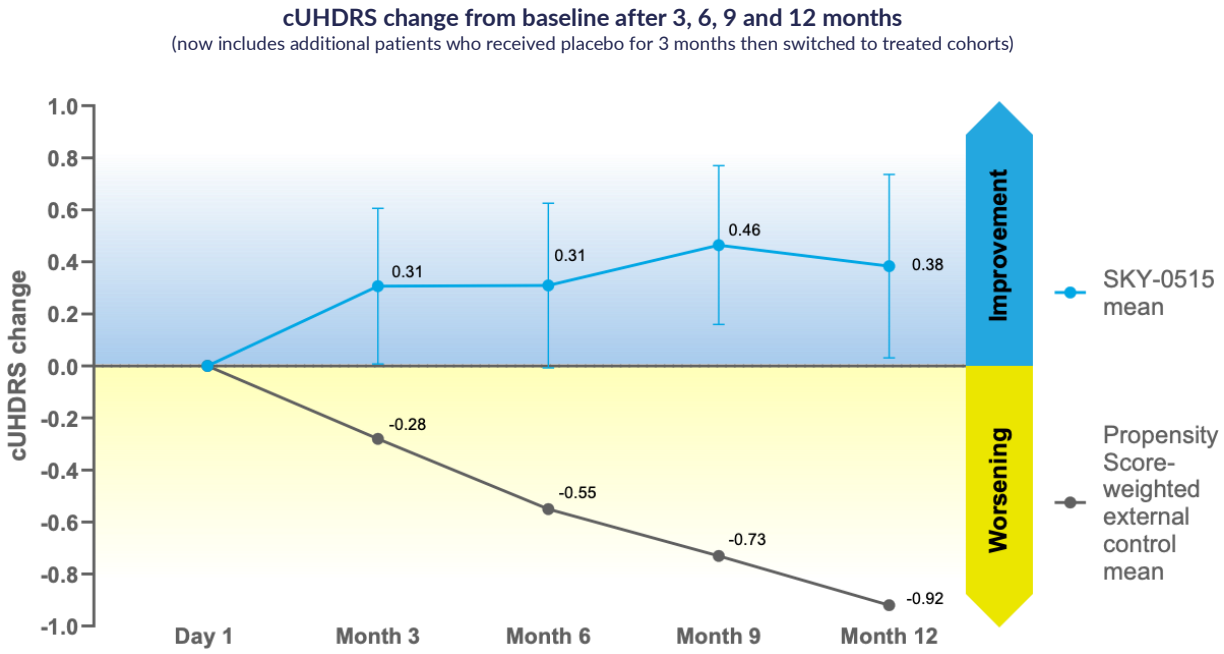
SKY-0515 has demonstrated excellent central nervous system exposure and has been generally safe and well tolerated across dose levels studied.

At three, six, nine and twelve months, patients receiving SKY-0515 demonstrated positive mean changes from baseline Composite Unified Huntington's Disease Rating Scale (cUHDRS) scores ranging from +0.31 to +0.38. These findings compared favorably with an expected worsening of -0.92 points over twelve months from propensity score-weighted analyses which use Enroll-HD and TRACK-HD natural history datasets. Favorable trends for patients on SKY-0515 were also observed across all cUHDRS subcomponents, including Total Motor Score (TMS), Total Functional Capacity (TFC), Symbol Digit Modalities Test (SDMT), and Stroop Word Reading Test (SWRT).

"Skyhawk's results show the extraordinary power of the ability to modulate RNA splicing with a small molecule, offering a therapy to patients worldwide," said Phillip Sharp, PhD, Founding Member of Skyhawk's Scientific Advisory Board and Nobel Prize Laureate for his groundbreaking work on RNA splicing. "The RNA revolution continues and I couldn't be more delighted to see what Skyhawk is doing to advance it."

"The increasing separation of the clinical trajectories of treated participants from natural history expectations at the twelve-month timepoint suggests exciting and sustained benefits for Huntington's patients," said Bill Haney, Co-founder and Chief Executive Officer of Skyhawk Therapeutics. "The magnitude and durability of lowering of critical biomarkers mHTT and PMS1, as well as encouraging twelve-month clinical findings across all four of the critical cUHDRS subcomponents, reinforce our confidence in SKY-0515's differentiated mechanism and potential for dramatic therapeutic impact for patients.

With enrollment in the FALCON-HD ANZ pivotal study completed ahead of schedule, we are rapidly advancing toward the next stage of development for SKY-0515 and remain committed to doing all we can to deliver a potentially transformative oral therapy to the Huntington's disease community at the earliest possible time."



Source: Skyhawk Therapeutics, Inc. 'Phase 1/2 cUHDRS scores at 3, 6, 9 and 12 months, for patients receiving SKY-0515 once-daily. Data shown reflect pooled 4 mg and 9 mg treatment groups and now includes additional patients who received placebo for three months prior to switching to active treatment (Day 1 to Month 9: n=21, Month 12: n=15),' June 2026. *Note: Error bars represent standard error of the mean. Propensity score weighting was performed using Enroll-HD and TRACK-HD datasets. Two participants with significant non-HD-related comorbidities and/or receipt of prohibited medications were excluded based on investigator assessment.*

"I am very encouraged by these continued safety and efficacy data from SKY-0515's Phase 1/2 trial in patients, including sustained improvement in patients' cUHDRS when compared with expected propensity-weighted natural history deterioration at each of three, six, nine and twelve-month prespecified analyses," said Ed Wild, Professor of Neurology at University College London. "SKY-0515 continues to reduce mHTT protein to the greatest extent demonstrated in patients, with clinical and biomarker data showing the drug is well tolerated at all doses tested.

SKY-0515's ability to reduce both mHTT and PMS1 appears to be a potent combination for treating Huntington's disease via two of its core pathogenic mechanisms," Wild added. "These Phase 1/2 trial results, due to be validated in the ongoing Phase 2/3 FALCON-HD pivotal program, give an expectation of meaningful therapeutic impact for people living with HD across the world – for whom an orally administered huntingtin-lowering treatment such as SKY-0515 will be truly transformative."

"The results we are announcing today from the ongoing Phase 1/2 trial of SKY-0515, now including data from patients who were previously on placebo, is not only exciting for Huntington's patients, their families and the generous clinical community who cares for them, but also highlights the power of Skyhawk's proprietary SKYSTAR® platform to generate potentially transformative medicines which patients can take as a daily pill, at home, for people suffering from neurological and other disabling diseases," added Sergey Pauskin, Co-founder and Head of R&D at Skyhawk. "With Skyhawk's drug candidates against a series of challenging neurological diseases advancing well through animal studies toward human trials, the possibilities offered by Skyhawk's small molecule platform are very exciting."

Huntington's disease is a rare, hereditary, and ultimately fatal neurodegenerative disorder affecting more than 40,000 symptomatic individuals in the United States, with hundreds of thousands impacted worldwide. There are currently no approved therapies shown to slow or halt disease progression.

SKY-0515 is an orally administered investigational small molecule RNA splicing modifier developed using the company's proprietary SKYSTAR® platform. SKY-0515 is designed to reduce both mHTT and PMS1 proteins.

The worldwide Phase 2/3 FALCON-HD-004-WW pivotal study is now active across eight countries.

SKY-0515's Phase 1/2 and FALCON-HD pivotal studies have now enrolled more than 175 patients.

Skyhawk expects to advance additional novel therapies targeting rare neurological diseases with no approved disease-modifying treatment into clinical development, by the end of 2027.

About SKY-0515's Phase 1/2 Clinical Study

SKY-0515's Phase 1/2 clinical trial is a first-in-human study designed to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of SKY-0515 in healthy volunteers and patients with early-stage Huntington's disease (HD).

The trial consists of three parts. Parts A and B evaluated SKY-0515 in Healthy Volunteers. Part C is a randomized, double-blind, placebo-controlled parallel-group study evaluating two dose levels of SKY-0515 in patients with early-stage HD (HD-ISS Stage 1, Stage 2, or mild Stage 3) over 84 days, followed by a twelve-month blinded extension period during which all participants receive active treatment at either a low or high dose.

Study assessments include measurements of mutant HTT protein, PMS1 mRNA, and cUHDRS. Enrollment in the Phase 1/2 study is complete.

About the Phase 2/3 FALCON-HD (004-ANZ and 004-WW) Pivotal Program

The **FALCON-HD** pivotal program (NCT06873334 and NCT07378644) is a randomized, double-blind, placebo-controlled, dose-ranging study evaluating the pharmacodynamics, efficacy and safety of SKY-0515.

FALCON-HD 004-ANZ enrolled 144 participants with Stage 2 and early Stage 3 HD across sites in Australia and New Zealand, and enrollment is complete. FALCON-HD 004-WW plans to enroll 400 participants with Stage 2 and early Stage 3 HD across more than 40 sites worldwide and is actively recruiting.

Eligible patients will receive once-daily oral SKY-0515 at one of three dose levels or placebo. The study is designed to evaluate the ability of SKY-0515 to modulate RNA splicing and reduce mHTT and PMS1 proteins implicated in Huntington's disease pathology.

Additional information regarding FALCON-HD, including participating sites and eligibility criteria, is available at ClinicalTrials.gov and www.FALCON-HD.com.

About Skyhawk Therapeutics

Skyhawk Therapeutics is a clinical-stage biotechnology company leveraging its proprietary SKYSTAR® platform to discover and develop small molecule RNA-modulating therapies for the world's most intractable diseases. For more information, visit www.skyhawktx.com.

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