Terns Achieves Primary Endpoint and All Secondary Endpoints in Phase 2a DUET Trial of THR-β Agonist TERN-501 in NASH

August 8, 2023

TERN-501 demonstrated dose dependent MRI-PDFF reductions at Week 12 as a once-daily, low dose, and combinable oral therapy

TERN-501 (6mg) showed statistically significant mean relative liver fat content reduction of 45% as assessed by MRI-PDFF with 64% of patients achieving ≥30% PDFF reduction

All TERN-501 doses were well-tolerated with no gastrointestinal and no cardiovascular safety signals

Company to host conference call and webcast at 4:30 pm ET today

FOSTER CITY, Calif., Aug. 08, 2023 (GLOBE NEWSWIRE) -- Terns Pharmaceuticals, Inc. (“Terns” or the “Company”) (Nasdaq: TERN), a clinical-stage biopharmaceutical company developing a portfolio of small-molecule product candidates to address serious diseases, including oncology, non-alcoholic steatohepatitis (NASH) and obesity, today reported positive top-line results from the Phase 2a DUET clinical trial of TERN-501, an orally-administered thyroid hormone receptor-beta (THR-β) agonist, administered as a monotherapy or in combination with TERN-101, a liver-distributed farnesoid X receptor (FXR) agonist, for the treatment of NASH.

The DUET trial achieved its primary endpoint with the once-daily, orally administered TERN-501 (3 mg and 6 mg) monotherapy groups showing dose dependent and statistically significant reductions in mean relative change from baseline in liver fat content as assessed by magnetic resonance imaging, proton density fat fraction (MRI-PDFF). A liver fat content reduction of 45% was observed in the TERN-501 6 mg dose group at Week 12, compared to a 4% reduction in the placebo group (p<0.001). Additionally, all TERN-501 monotherapy doses (1 mg, 3 mg and 6 mg) achieved statistically higher proportions of patients with MRI-PDFF reduction of at least 30% compared to placebo. MRI-PDFF response rates were dose dependent with 64% of patients treated with TERN-501 (6 mg) achieving response. A reduction in liver fat content of at least 30% based on MRI-PDFF has been shown to have a high correlation with improvements in NASH when confirmed by liver biopsy.

“TERN-501 demonstrated highly encouraging efficacy results in MRI-PDFF reductions. The high degree of liver fat content reduction alongside the class-leading safety profile observed in the DUET trial create the potential for TERN-501 to be the THR-β monotherapy of choice and possibly a mainstay backbone of NASH combination therapies,” said Erin Quirk, M.D., president and head of research and development at Terns. “We sincerely thank all those who helped rapidly advance the DUET trial, including our dedicated team of investigators and clinical sites, the outstanding members of the Terns team, and, most importantly, the patients who participated in the trial.”

Primary and secondary TERN-501 monotherapy efficacy results at Week 12 are summarized below.

At Week 12	**Placebo N=21**	**TERN-501**		
		1mg N=23	3mg N=19	6mg N=22
MRI-PDFF				
Mean baseline (%)	17	16.6	19.5	17.3
Relative change (%) from BL	-4	-15	-27**	-45***
Absolute change (%) from BL	-1	-3	-5**	-8***
Patients (%) achieving ≥30% relative reduction	4%	26%*	39%**	64%***

*p<0.05, **p<0.01, ***p<0.001 versus placebo

- TERN-501 (6 mg) monotherapy demonstrated a statistically significant reduction in the secondary endpoint of a mean change in corrected T1 (cT1), a magnetic resonance-based imaging marker of liver fibro-inflammation correlated with clinical outcomes in patients with liver disease.
- TERN-501 monotherapy demonstrated improvement or trends toward improvement in plasma lipid parameters, such as LDL-C, HDL-C, triglycerides, and apolipoprotein B (ApoB).
- There were dose dependent increases in sex hormone binding globulin (SHBG), a marker of THR-β agonism in the liver; the mean SHBG increase with TERN-501 (6 mg) exceeded 120% at Week 12 and was statistically greater than placebo (p<0.001).

DUET TERN-501 safety findings:

- TERN-501 was generally well tolerated, with adverse events (AEs) being generally mild and evenly distributed across all arms, including placebo. There were no drug-related serious adverse events (SAEs).

- Drug-related AEs of interest were similar across all arms, including placebo, with similar rates of GI events, including nausea, diarrhea and vomiting. No drug-related cardiovascular AEs were observed.
- Mean change in thyroid axis hormones, including thyroid stimulating hormone (TSH), free triiodothyronine (fT3) and free thyroxine (fT4), and liver enzymes, including alanine transaminase (ALT), aspartate transaminase (AST) and gamma-glutamyltransferase (GGT), at Week 12 were similar to placebo.

DUET TERN-501 + TERN-101 combination findings:

- The combination of TERN-501 and TERN-101 (10 mg) resulted in modest improvements in MRI-PDFF mean relative change (6 mg of TERN-501 combo) and ≥30% MRI-PDFF responder rate (3 mg and 6 mg of TERN-501 combo) when compared to TERN-501 monotherapy arms in Week 12. cT1 results were comparable across mono and combo treatment arms.
    - The combination of TERN-501 and TERN 101 (10 mg) did not result in LDL increases from baseline at Week 12, suggesting TERN-501 was able to reverse FXR-mediated LDL increases.
    - Overall, these results are supportive of the ability to administer TERN-501 in combination with FXR and potentially other therapeutics.
- There were no treatment-emergent safety signals from the combination arms. TERN-101 safety and tolerability findings were generally consistent with the Phase 2a LIFT trial.

“With no FDA approved therapies, THR-β represents a key mechanism of action for the treatment of NASH, as it is the only class of treatment to have demonstrated both resolution of steatohepatitis and improvement in fibrosis in a registrational NASH study. TERN-501's impressive efficacy within a short duration and excellent safety profile is compelling especially with its once-daily, oral dosing as well as its cardiovascular and GI safety profile, the latter of which has adversely affected other NASH modalities in development,” said Mazen Noureddin, M.D., MHSc, Professor of Clinical Medicine, Academic Institute, Houston Methodist, Director of Houston Research Institute, and a principal investigator in the DUET trial. “These results add to the growing body of evidence of the safety and efficacy profile of TERN-501 and its promise as a therapy to treat the multiple facets of this disease.”

Terns plans to submit data from the DUET trial for presentation at an upcoming scientific conference.

Investor Conference Call

Terns will host an update call for investors today, August 8, 2023, beginning at 4:30 p.m. ET. The webcast of the conference call can be accessed here. A replay of the call will also be available on the Events page of the Investor Relations section of the Terns website for 30 days.

About the Phase 2a DUET Trial

The Phase 2a DUET trial (NCT05415722) is a multicenter, randomized, double-blind, placebo-controlled clinical trial in noncirrhotic NASH, designed to evaluate efficacy and safety of TERN-501 as a monotherapy and in combination with TERN-101. The trial enrolled over 160 adults with body mass index (BMI) ≥ 25 kg/m^2 and pre-cirrhotic NASH identified based on prior liver biopsy and/or imaging and clinical criteria. All participants had liver fat content measured by magnetic resonance imaging proton density fat fraction (MRI-PDFF) of ≥10%, MRI corrected T1 (cT1) relaxation time of ≥ 800 msec and met other inclusion and exclusion criteria. The trial included a 12-week treatment period and a 4-week follow-up period. The primary endpoint was the relative change from baseline in MRI-PDFF at Week 12 for TERN-501 monotherapy compared to placebo. Secondary endpoints included assessments of relative change from baseline in MRI-PDFF for TERN-501+TERN-101 combination compared to placebo and change from baseline in cT1 for TERN-501 monotherapy compared to placebo as well as for TERN-501+TERN-101 combination therapy compared to placebo.

About TERN-501

TERN-501 is a thyroid hormone receptor beta (THR-β) agonist with high metabolic stability, enhanced liver distribution and greater selectivity for THR-β compared to other THR-β agonists in development.

Preclinical studies have demonstrated that low-doses of TERN-501 achieved complete resolution of steatosis and reductions in serum lipids and hepatic inflammation and fibrosis. TERN-501 is 23-fold more selective for THR-β than for THR-α activation thereby minimizing the risk of cardiotoxicity and other off-target effects associated with non-selective THR stimulation. TERN-501 has been designed to be metabolically stable and has demonstrated low pharmacokinetic variability and potential for efficacy at a low clinical dose, making it an attractive candidate for use in fixed-dose combinations for NASH treatment.

Terns received Fast Track designation from the U.S. Food and Drug Administration for TERN-501 for the treatment of NASH in June 2021.

About Non-alcoholic Steatohepatitis (NASH)

NASH is a severe form of non-alcoholic fatty liver disease (NAFLD) that affects up to 20 million people in the United States, and up to 5% of the global population, and for which there is currently no approved therapy in the United States or Europe. In a study published in Hepatology in 2018, lifetime costs of treating and managing NASH patients in the United States in 2017 were estimated to be over $220 billion, in the absence of approved therapies. NASH is a multifaceted disease that involves three distinct pathogenic hepatic disease processes: accumulation of excess fat in the liver (steatosis), inflammation and fibrosis. In addition to these three disease processes, NASH patients often exhibit elevated levels of glucose and atherogenic lipids, are overweight or obese and accumulate excessive lipotoxic fat. Severe progression of NASH can lead to cirrhosis, decompensated liver disease and increased risk for hepatic carcinoma and liver-related mortality.

About Terns Pharmaceuticals

Terns Pharmaceuticals, Inc. is a clinical-stage biopharmaceutical company developing a portfolio of small-molecule product candidates to address serious diseases, including oncology, NASH and obesity. Terns' pipeline includes two clinical stage development programs including an allosteric BCR-ABL inhibitor and a THR-β agonist (+/- an FXR agonist), and preclinical small-molecule GLP-1 receptor agonist and GIPR modulator programs. For more information, please visit: www.ternspharma.com.

Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements about Terns Pharmaceuticals, Inc. (the "Company," "we," "us," or "our") within the meaning of the federal securities laws, including those related to the Company's expectations of timing and potential results of the clinical trials and other development activities of the Company and its partners; the potential indications to be targeted by the Company with its small-molecule product candidates; the therapeutic potential of the Company's small-molecule product candidates; the potential for the mechanisms of action of the Company's product candidates to be therapeutic targets for their targeted indications; the potential utility and progress of the Company's product candidates in their targeted indications, including the clinical utility of the data from and the endpoints used in the Company's clinical trials; the Company's clinical development plans and activities, including the results of any interactions with regulatory authorities on its programs; the Company's expectations regarding the profile of its product candidates, including efficacy, tolerability, safety, metabolic stability and pharmacokinetic profile and potential differentiation as compared to other products or product candidates; the Company's plans for and ability to continue to execute on its current development strategy, including potential combinations involving multiple product candidates; the impact of new legislation and regulatory developments on the Company's plans for its product candidates, such as the effect of the Inflation Reduction Act of 2022; and the Company's expectations with regard to its cash runway and sufficiency of its cash resources. All statements other than statements of historical facts contained in this press release, including statements regarding the Company's strategy, future financial condition, future operations, future trial results, projected costs, prospects, plans, objectives of management and expected market growth, are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "aim," "anticipate," "assume," "believe," "contemplate," "continue," "could," "design," "due," "estimate," "expect," "goal," "intend," "may," "objective," "plan," "positioned," "potential," "predict," "seek," "should," "target," "will," "would" and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology. The Company has based these forward-looking statements largely on its current expectations, estimates, forecasts and projections about future events and financial trends that it believes may affect its financial condition, results of operations, business strategy and financial needs. In light of the significant uncertainties in these forward-looking statements, you should not rely upon forward-looking statements as predictions of future events. These statements are subject to risks and uncertainties that could cause the actual results and the implementation of the Company's plans to vary materially, including the risks associated with the initiation, cost, timing, progress, results and utility of the Company's current and future research and development activities and preclinical studies and clinical trials. These risks are not exhaustive. For a detailed discussion of the risk factors that could affect the Company's actual results, please refer to the risk factors identified in the Company's SEC reports, including but not limited to its Annual Report on Form 10-K for the year ended December 31, 2022. Except as required by law, the Company undertakes no obligation to update publicly any forward-looking statements for any reason.

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