Terns Reports Positive Top-line Results from Phase 2a LIFT Study of FXR Agonist TERN-101 in Patients with NASH

June 14, 2021

First FXR agonist trial to demonstrate no discontinuations due to AEs, including pruritus, and both a differentiated pruritus and lipid profile in patients with NASH

First 12-week controlled trial in patients with NASH to show significant improvements in corrected T1 (cT1), an imaging marker of liver inflammation and fibrosis linked to clinical outcomes

Terns plans to initiate first NASH trial of an FXR agonist (TERN-101) in combination with a THR-β agonist (TERN-501) in 1H22

Company to host conference call and webcast at 8:30 a.m. ET today

FOSTER CITY, Calif., June 14, 2021 (GLOBE NEWSWIRE) -- Terns Pharmaceuticals, Inc. (“Terns” or the “Company”) (Nasdaq: TERN), a clinical-stage biopharmaceutical company developing a portfolio of small-molecule single-agent and combination therapy candidates for the treatment of non-alcoholic steatohepatitis (NASH) and other chronic liver diseases, today reported positive top-line results from the Phase 2a LIFT clinical trial of TERN-101, a liver-distributed farnesoid X receptor (FXR) agonist for the treatment of patients with NASH.

The LIFT study is a multicenter, randomized, double-blind, placebo-controlled, parallel-group, Phase 2a clinical trial to evaluate the safety, tolerability, efficacy, and pharmacokinetics of orally-administered TERN-101 tablets at doses of 5 mg, 10 mg and 15 mg in 100 adult patients with presumed non-cirrhotic non-alcoholic steatohepatitis (NASH). The primary objective of the clinical trial was to evaluate the safety and tolerability of TERN-101 over 12 weeks of treatment plus a four-week post-treatment follow-up period. Secondary endpoints included percent change from baseline in ALT levels and plasma pharmacokinetics of TERN-101. Exploratory efficacy endpoints included changes in liver fibro-inflammation measured by MRI corrected T1 (cT1), liver fat content by MRI proton density fat fraction (MRI-PDFF), pharmacodynamic parameters, and serum NASH biomarkers.

In the LIFT trial, TERN-101 was generally well tolerated with a similar incidence of adverse events (AEs) across treatment groups. All treatment-related adverse events were mild/moderate with no apparent dose relationship. There were no treatment-related serious adverse events, and no patient discontinued TERN-101 due to any adverse event including pruritus. The most frequent treatment-emergent adverse events included pruritus, headache, constipation, diarrhea, decreased appetite and dizziness. Pruritus was reported in four patients (16%) in the 5 mg TERN-101 arm, three patients (11.5%) in the 10 mg TERN-101 arm, four patients (17.4%) in the 15 mg TERN-101 arm and no patients in the placebo group. Three pruritus cases were Grade 2 (widespread and intermittent); the rest were Grade 1 (mild or localized). Notably, there were no Grade 3 (widespread and constant) pruritus events and no discontinuations due to pruritus. Most pruritus cases resolved during continued TERN-101 treatment.

No change in LDL cholesterol was observed in patients in the 5 mg and 10 mg TERN-101 arms as compared to placebo (Week 12 mean change: 4.8% for placebo, 6.7% for 5 mg TERN-101, 3.2% for 10 mg TERN-101, not significant). Statistically significant LDL changes were observed only in the 15 mg arm (Week 12 mean change: 15.9%, $p<0.05$). Significant decreases in HDL cholesterol were observed in all TERN-101 dose groups at Week 4 and Week 8 but returned toward baseline in the 5 mg and 10 mg dose groups without differences from placebo at Week 12. Decreases in HDL were significantly different from placebo for the 15 mg group at all observed timepoints through Week 12.

Multiple efficacy biomarkers of NASH, including corrected T1 (cT1), MRI-PDFF and ALT, were evaluated in the LIFT Study:

- Mean changes in cT1 at Week 12 were -0.8 msec for placebo, -38.0 msec ($p=0.033$) for the 5 mg arm, -57.7 msec ($p=0.002$) for the 10 mg arm, and -74.0 msec ($p<0.001$) for the 15 mg arm. Improvements of at least 80 msec in cT1 were observed in a significant proportion of patients in the 5 mg and 10 mg groups at Week 12 (as compared to placebo). Significant decreases in cT1 were also observed at Week 6 for all dose groups. cT1 is a magnetic resonance-based imaging test measuring free-water content in liver tissue, which has shown a strong correlation with inflammation and fibrosis histology and clinical outcomes in patients with liver disease.
- Mean relative changes in MRI-PDFF were -8.4% (placebo), -15.1% (5 mg), -19.7% (10 mg), and -12.9% (15 mg) at Week 12. Mean relative changes in MRI-PDFF were significant at Week 6 for the 10 mg and 15 mg dose groups compared to placebo, although these changes were not statistically significant at Week 12. MRI-PDFF is an imaging marker that measures liver fat content.
- Mean percent changes in ALT at Week 12 were -5.3% (placebo), -2.6% (5 mg), -18% (10 mg), and -13.2% (15 mg).
- No discernable trends were observed in initial analyses of the enhanced liver fibrosis (ELF) score, CK-18 and Pro-C3.

“NASH is a complex multifaceted condition, making it difficult to use just one target to treat the disease. The LIFT data are exciting because we see improvement in key non-invasive tests associated with disease severity along with an attractive safety profile with no discontinuations due to side effects,” said Rohit Loomba, MD, MHSc, director of the UC San Diego NAFLD Research Center and director of Hepatology at UC San Diego School of Medicine. “The results add to the growing body of evidence showing the promise of TERN-101 as a multi-modal therapy to treat the multiple facets of this disease.”

Summary of Week 12 Analysis

		TERN-101 tablet formulation (once-daily)		
Mean change (baseline to week 12)	Placebo N=26	5 mg N=25	10 mg N=26	15 mg N=23
LDL-c (%)	4.8%	6.7%	3.2%	15.9%*
HDL-c (%)	2.4%	-2.6%	-0.5%	-8.2%*
ALT (%)	-5.3%	-2.6%	-18.0%	-13.2%
AST (%)	0.3%	1.4%	-12.9%	-4.2%
GGT (%)	8.1%	-15.6%*	-34.2% ***	-17.6%*
ALP (%)	0.2%	2.5%	9.4%	24.4%***
cT1 (msec)[+]	-0.8	-38.0*	-57.7**	-74.0***
MRI-PDFF relative change (%)	-8.4%	-15.1%	-19.7%	-12.9%

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

[+] cT1 was conducted only at available sites (n=22, 24, 20 and 18 for placebo, 5 mg, 10 mg and 15 mg groups, respectively).

"We are encouraged by the positive effects of well tolerated doses of TERN-101 on cT1 relaxation time, a biomarker correlated with improved clinical outcomes. LIFT is the first controlled NASH trial to show significant cT1 improvement as early as Week 6. TERN-101 has the potential to be an effective component of a NASH treatment regimen. We look forward to advancing this program in our planned combination therapy trial," said Erin Quirk, MD, president, chief medical officer and head of research and development at Terns. "I would like to thank all those who have helped us rapidly advance the LIFT Study, including our outstanding team of investigators and clinical sites, the members of the Terns team, and the patients who participated in the study."

Terns plans to submit data from the LIFT Study to an upcoming scientific conference. Based on these positive results, Terns continues to plan a combination trial of TERN-101 together with TERN-501, the Company's thyroid hormone receptor beta agonist (THR-β) also in development for the treatment of NASH. The multiple ascending dose portion of the TERN-501 Phase 1 trial started in June 2021, and top-line data from the trial is expected in the second half of 2021. The combination trial of TERN-101 and TERN-501 is expected to start in the first half of 2022.

Investor Conference Call

Terns will host an update call for investors today, June 14, 2021, beginning at 8:30 a.m. ET. The webcast of the conference call will be made available at https://edge.media-server.com/mmc/p/2gsxxmta. To access the call via dial-in, please dial 1-833-665-0612 (U.S./Canada toll-free) or 1-929-517-0403 (international) using the conference code 7587739. A replay of the call will also be available on the investor page of the Terns website for 30 days.

About TERN-101

TERN-101 is a liver-distributed, non-bile acid FXR agonist that has demonstrated a differentiated tolerability profile and improved target engagement, likely due to its sustained FXR activation in the liver but only transient FXR activation in the intestine. FXR is a nuclear receptor primarily expressed in the liver, intestine and kidneys. FXR regulates hepatic expression of various genes involved in lipid metabolism, inflammation and fibrosis. Clinical studies of other FXR agonists have demonstrated significant histological NASH improvements but have also resulted in pruritus, adverse lipid changes and discontinuations.

About Terns Pharmaceuticals

Terns Pharmaceuticals, Inc. is a clinical-stage biopharmaceutical company developing a portfolio of small-molecule single-agent and combination therapy candidates for the treatment of non-alcoholic steatohepatitis, or NASH, and other chronic liver diseases. Terns' programs are based on clinically validated and complementary mechanisms of action to address the multiple hepatic disease processes of NASH in order to drive meaningful clinical benefits for patients. 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 therapeutic potential of TERN-101; the potential utility and progress of the Company's product candidates in NASH, including the clinical utility of the data from and the endpoints used in the Phase 2a LIFT Study of TERN-101; expectations of timing and potential results of the Company's clinical trials; the Company's clinical development plans and activities, including the development plans for TERN-101 in combination with TERN-501 and potentially other product candidates; the Company's expectations regarding the profile of its product candidates, including tolerability, safety, metabolic stability and pharmacokinetic profile; the Company's ability to continue to execute on its clinical strategy and plans; and the sufficiency of our cash on hand to fund our operating expenses and capital expenditures. 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 and results of the Company's current and future research and development activities and preclinical studies and clinical trials. In particular, the impact of the COVID-19 pandemic on the Company's ability to progress with its research, development, manufacturing and regulatory efforts, including the Company's clinical trials for its product candidates, will depend on future developments that are highly uncertain and cannot be predicted with confidence at this time, such as the ultimate duration of the pandemic, travel restrictions, quarantines, social distancing and business closure requirements in the United States and in other countries, and the effectiveness of actions taken globally to contain and treat the disease. 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, 2020 and Quarterly Report on form 10-Q for the three months ended March 31, 2021. Except as required by law, the Company undertakes no obligation to update publicly any forward-looking statements for any reason.

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