Terns Pharmaceuticals Announces Positive Phase 1 Clinical Trial Results with TERN-601 Once-Daily Oral GLP-1R Agonist for the Treatment of Obesity

September 9, 2024

Statistically significant mean weight loss up to 5.5% over 28 days (4.9% placebo adjusted)

Well-tolerated with no treatment-related dose interruptions, reductions, or discontinuations even with rapid dose titration

Distinct drug properties support potential to be a leading GLP-1R agonist

Plans to initiate Phase 2 clinical trial in 2025

Company to host conference call today at 8:00 am ET

FOSTER CITY, Calif., Sept. 09, 2024 (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, today announced positive top-line data from its Phase 1 randomized, double-blind, placebo-controlled single and multiple-ascending dose (SAD and MAD) trial to assess the safety, tolerability, pharmacokinetics (PK) and pharmacodynamics (PD) of TERN-601 dosed once-daily (QD) in healthy adults with obesity or overweight.

The clinical trial results showed TERN-601 was well tolerated and demonstrated dose-dependent, statistically significant placebo-adjusted mean weight loss across all three doses evaluated in the 28-day MAD study, with maximum placebo-adjusted mean weight loss of 4.9% ($p<0.0001$) at the highest dose of 740 mg QD. Additionally, 67% of participants lost 5% or more of their baseline body weight at the top dose.

“These compelling results underscore TERN-601’s potential to be a class-leading GLP-1R agonist based on its composite profile of initial indications of efficacy, tolerability and manufacturing scalability,” said Amy Burroughs, chief executive officer of Terns. “These data validate the potential of TERN-601 for the treatment of obesity as monotherapy or in combination with agents such as TERN-501, our internally discovered, clinical stage THR-β agonist, or a GIPR modulator from our TERN-800 series. With operational preparations well underway, we look forward to swiftly advancing this promising product candidate into Phase 2 clinical development in 2025.”

“We are delighted to demonstrate potent GLP-1R agonism with TERN-601 as its distinct drug properties allowed for sustained target coverage with once-daily dosing and the evaluation of doses up to 740 mg, while being tolerable,” noted Emil Kuriakose, chief medical officer of Terns. “Importantly, we believe we have successfully identified an optimal range of clinically active, well tolerated doses to take forward in Phase 2 clinical trials, with no new dose range exploration anticipated.”

Table 1: Mean Percent Weight Change from Baseline to Day 28

	Placebo (N=9)	TERN-601 240 mg (N=9)	TERN-601 500 mg (N=9)	TERN-601 740 mg (N=9)
% weight change from baseline	-0.6%	-2.5%	-4.4%	-5.5%
% weight change placebo-adjusted (90% CI)	-	-1.9%	-3.8%	-4.9%
Exploratory p-value vs. placebo	-	<0.1	<0.01	<0.0001

TERN-601 was well tolerated with no treatment-related dose interruptions, reductions or discontinuations at any dose, despite fast titration to high doses. The majority (>95%) of treatment emergent AEs were mild. All gastrointestinal events were mild to moderate and consistent with the GLP-1R agonist class. Importantly, there were no clinically meaningful changes in liver enzymes, vital signs or electrocardiograms observed. The absence of treatment-related dose interruptions, reductions, or discontinuations with mostly mild AEs, despite aggressive titration to high doses in this 28-day study, indicates potential for further improved tolerability in subsequent studies with slower titration.

TERN-601 has distinct properties that may be advantageous for an oral GLP-1R agonist. Its low solubility and high gut permeability may result in prolonged absorption allowing for sustained target coverage and a flat PK curve, while high drug levels in the gut wall may lead to robust GLP-1R activation in the gut triggering satiety centers in the brain. Additionally, TERN-601 has a

low free fraction in circulation which, combined with the flat PK curve, may be allowing TERN-601 to be well tolerated when administered at high doses.

Table 2: Treatment Emergent Adverse Events by Maximum Severity

	Placebo (N=9)	TERN-601 240 mg (N=10)	TERN-601 500 mg (N=9)	TERN-601 740 mg (N=9)
Grade 1 (Mild)	5 (55.6%)	5 (50%)	9 (100%)	3 (33.3%)
Grade 2 (Moderate)	0	1 (10%)	0	6 (66.7%)
Grade ≥3 (Severe)	0	0	0	0
Serious Adverse Events	0	0	0	0

Terns plans to submit data from this informative clinical trial for presentation at an upcoming scientific conference.

Conference Call and Webcast
Terns will host a conference call for investors today, September 9, 2024, beginning at 8:00 a.m. ET. The live 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 TERN-601 Phase 1 Trial
The Phase 1 trial was a randomized, double-blind, placebo-controlled single and multiple-ascending dose (SAD and MAD) trial to assess the safety, tolerability, pharmacokinetics (PK) and pharmacodynamics (PD) of TERN-601 in healthy adults with obesity or overweight. The trial consisted of two parts.

Part 1 (SAD) was a single ascending dose study that evaluated five TERN-601 dose levels in healthy participants with a Body Mass Index (BMI) of ≥ 25 kg/m^2 and < 40 kg/m^2. The starting TERN-601 dose was 30 mg, with subsequent dose levels based on review of emerging safety and PK data from prior cohorts.

In Part 2 (MAD) of the trial, obese and overweight healthy adults were enrolled in cohorts that included titration of TERN-601 administered for 28 days at doses selected based on data from Part 1 (SAD). Part 2 included healthy participants with a BMI of ≥ 27 kg/m^2 to < 40 kg/m^2.

The primary endpoint of the trial was to evaluate safety and tolerability of TERN-601 administered once-daily for 28 days. Secondary endpoints included PK, efficacy as measured by body weight loss following 28 days of treatment with TERN-601, and other exploratory markers.

About TERN-601
TERN-601 is an oral, small-molecule glucagon-like peptide-1 receptor agonist, or GLP-1R agonist, internally discovered at Terns for development in obesity. TERN-601 was designed through internal structure-based drug discovery efforts employing Terns' proprietary three-dimensional QSAR model of the receptor. The ligands were further optimized based on in vitro activity, metabolic stability, and pharmacokinetic parameters. This process led to the selection of TERN-601, a potent GLP-1R agonist biased towards cAMP generation.

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 and obesity. Terns' pipeline contains three clinical stage development programs including an allosteric BCR-ABL inhibitor, a small-molecule GLP-1 receptor agonist, a THR-β agonist, and a preclinical GIPR modulator discovery effort, prioritizing a GIPR antagonist nomination candidate. 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 expectations, 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 Company's plans and expectations around the addition of key personnel; 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, 2023. Except as required by law, the Company undertakes no obligation to update publicly any forward-looking statements for any reason.

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