Longboard Pharmaceuticals Announces Positive Topline Data from a Phase 1 Clinical Study Evaluating Central Nervous System Pharmacokinetics and Pharmacodynamics of LP352 in Healthy Volunteers

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- *LP352 exhibited a strong correlation between plasma and cerebrospinal fluid (CSF) pharmacokinetics (PK) concentration, which increased in a dose-dependent and consistent manner*
- *LP352 demonstrated early quantitative electroencephalogram (qEEG) changes, and sustained effects on qEEG activity after continuous dosing in a dose-dependent manner indicating receptor engagement*
- *Favorable safety and tolerability results were observed in this study, with adverse events (AEs) generally consistent with previous clinical studies*

LA JOLLA, Calif.--(BUSINESS WIRE)--Dec. 5, 2022-- Longboard Pharmaceuticals, Inc. (Nasdaq: LBPH), a clinical-stage biopharmaceutical company focused on developing novel, transformative medicines for neurological diseases, today announced positive topline results from a Phase 1 clinical study evaluating the central nervous system (CNS) pharmacokinetics (PK) and pharmacodynamics (PD) of LP352, an oral, centrally acting 5-HT2C superagonist, in healthy volunteers.

"We are excited to share data from our 102 study, the first known of its kind for a 5-HT2 receptor agonist, to further elucidate the potentially best-in-class profile of LP352. We believe the results of this study are encouraging as orally administered LP352 plasma and CSF PK concentration increased in a dose-dependent and consistent manner, a clear indicator that LP352 is crossing the blood brain barrier. Furthermore, the observation of demonstrated effects on qEEG activity within the first few doses and after continuous dosing suggests that LP352 engaged neurotransmitter systems and altered the EEG spectrum. We are pleased to see favorable safety and tolerability results in this study, consistent with previous work we have conducted," stated Dr. Randall Kaye, Longboard's Chief Medical Officer. "We anticipate sharing additional data to substantiate our belief that LP352 has the potential to be a safer and more efficacious treatment of seizures in a broad range of developmental and epileptic encephalopathies (DEEs), and we look forward to providing updates on the ongoing Phase 1b/2a PACIFIC study as they become available."

Study Design & Objectives:

The primary objectives of this open-label, Phase 1 study are to assess the CNS PK and PD of orally administered LP352 in healthy adult male and female participants (n=10 in each Cohort). Objectives include the characterization of plasma and CSF PK, the characterization of safety and tolerability of doses with titration and taper, and the assessment of the PK-PD relationships between plasma and CSF exposure, and PD endpoints of safety and efficacy, including quantitative electroencephalogram (qEEG) endpoints. Data being shared today relate to two doses (Cohort 1 = 6 mg and Cohort 2 = 12 mg) of LP352 three times daily (TID) that were tested over a 16-day period in addition to a screening and follow-up period. Additional cohorts of the study are ongoing.

Plasma/CSF Results:

Plasma samples were obtained on Day 1 through Day 11 (and during taper), measuring maximum concentration (Cmax), time of peak plasma concentration (Tmax), and area under the curve (AUCtau). Serial CSF samples were taken on Day 11 at multiple timepoints.

At steady state, LP352 12 mg TID mean concentrations exceeded the Ki value for 5-HT2C activity throughout the dosing interval. The vast majority of participants in Cohort 2 achieved plasma and CSF levels above the relevant Ki throughout the dosing period at steady state. LP352 exhibited a strong correlation between plasma and CSF PK concentration, which increased in a dose-dependent and consistent manner.

qEEG Results:

Serial EEGs were taken at Days -1, 1, 3 & 10, and Day 16 (at trough). LP352 demonstrated early qEEG changes within the first few doses. LP352 also demonstrated sustained, dose-dependent effects on qEEG activity after continuous dosing, thus indicating receptor engagement. LP352 engaged neurotransmitter systems and altered the EEG spectrum.

Safety / Tolerability Findings:

Favorable safety and tolerability across both cohorts were observed, with AEs generally consistent with previous clinical studies of LP352.

About LP352

LP352 is an oral, centrally acting 5-HT2C superagonist in development for the potential treatment of seizures associated with developmental and epileptic encephalopathies (DEEs) such as Dravet syndrome, Lennox-Gastaut syndrome (LGS), tuberous sclerosis complex (TSC), CDKL5 deficiency disorder (CDD), and other epileptic disorders. LP352 is designed to modulate GABA and, as a result, suppress the central hyperexcitability that is characteristic of seizures. LP352 has no detected activity at the 5-HT2B and 5-HT2A receptor subtypes. 5-HT2B and 5-HT2A receptor agonism have been associated with significant adverse side effects. LP352 has novel chemistry and attributes. It was designed to be more specific and selective for the 5-HT2C receptor subtype, giving it the potential to reduce seizures in patients with DEEs while overcoming the known or perceived safety limitations of available drugs in the 5-HT2 class. LP352 is currently being evaluated in an ongoing Ph 1b/2a clinical trial (the PACIFIC Study) in participants with DEEs, with data expected in the second half of 2023, as well as in additional supportive studies.

About Longboard Pharmaceuticals

Longboard Pharmaceuticals, Inc. is a clinical-stage biopharmaceutical company focused on developing novel, transformative medicines for neurological diseases. Longboard is working to advance a portfolio of centrally acting product candidates designed to be highly selective for specific G protein-coupled receptors (GPCRs). Longboard's small molecule product candidates are based on more than 20 years of GPCR research. Longboard is evaluating LP352, an oral, centrally acting 5-hydroxytryptamine 2C (5-HT2C) receptor superagonist, with no detected activity at the 5-HT2B and 5-HT2A receptor subtypes. LP352 is currently being evaluated in a Phase 1b/2a clinical trial, the PACIFIC Study, and being developed for the potential treatment of seizures associated with a broad range of developmental and epileptic encephalopathies (DEEs). Longboard is also evaluating LP659, a centrally acting, sphingosine-1-phosphate (S1P) receptor subtypes 1 and 5 modulator, in development for the potential treatment of multiple neurological diseases. Longboard holds rights to other product candidates, including LP143 and nelotanserin, through a License Agreement with Arena Pharmaceuticals, Inc.

Forward-Looking Statements

Certain statements in this press release are forward-looking statements that involve a number of risks and uncertainties. In some cases, you can identify forward-looking statements by words such as "potential", "focused on", "anticipate", "expects" and "advance", and include, without limitation, statements about the following: the potential of LP352, including to be a safer and more efficacious treatment of seizures associated with DEEs and in a broad range of DEEs, to be best-in-class, and reduce seizures in patients with DEEs while overcoming the known or perceived safety limitations of available drugs in the 5-HT2 class; the timing and results of clinical data for LP352; updates on the Company's Pacific Study; the potential for LP659, including to treat multiple neurological diseases, and the Company's other product candidates; and the Company's focus and ability to advance a portfolio of product candidates. For such statements, Longboard claims the protection of the Private Securities Litigation Reform Act of 1995. Actual events or results may differ materially from Longboard's expectations. Factors that could cause actual results to differ materially from the forward-looking statements include, but are not limited to, the following: topline data may not reflect the complete or final results of a particular study or trial, and are subject to change; risks related to Arena's acquisition by Pfizer; Longboard's limited operating history, financial position and need for additional capital; Longboard will need additional managerial and financial resources to advance all of its programs, and you and others may not agree with the manner Longboard allocates its resources; risks related to the development and commercialization of Longboard's product candidates; Longboard's product candidates are in the early phase of a lengthy research and development process, the timing, manner and outcome of research, development and regulatory review is uncertain, and Longboard's product candidates may not advance in research or development or be approved for continuing development or marketing; the regulatory process of the U.S. Food and Drug Administration and comparable foreign authorities is lengthy, time consuming and inherently unpredictable; enrolling participants in Longboard's ongoing and intended clinical trials is competitive and challenging; the impact of geopolitical and macroeconomic events, including the COVID-19 pandemic, on Longboard's clinical trials and operations, the operations of Longboard's suppliers, partners, collaborators, and licensees, and capital markets, which in each case remains uncertain; risks related to unexpected or unfavorable new data; nonclinical and clinical data is voluminous and detailed, and regulatory agencies may interpret or weigh the importance of data differently and reach different conclusions than Longboard or others, request additional information, have additional recommendations or change their guidance or requirements before or after approval; results of clinical trials and other studies are subject to different interpretations and may not be predictive of future results; risks related to relying on licenses or collaborative arrangements; other risks related to Longboard's dependence on third parties; competition; product liability or other litigation or disagreements with others; government and third-party payor actions, including relating to reimbursement and pricing; risks related to regulatory compliance; and risks related to Longboard's and third parties' intellectual property rights. Additional factors that could cause actual results to differ materially from those stated or implied by Longboard's forward-looking statements are disclosed in Longboard's filings with the Securities and Exchange Commission (SEC). These forward-looking statements represent Longboard's judgment as of the time of this release. Longboard disclaims any intent or obligation to update these forward-looking statements, other than as may be required under applicable law.

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