Reviva Pharmaceuticals Announces Positive Safety Data from Drug-Drug Interaction Clinical Study of Brilaroxazine

– Topline data for pivotal Phase 3 RECOVER trial evaluating brilaroxazine for schizophrenia expected in mid-2023

– Brilaroxazine is a serotonin/dopamine modulator with a differentiated pharmacological and safety profile

CUPERTINO, Calif., Dec. 15, 2022 — Reviva Pharmaceuticals Holdings, Inc. (NASDAQ: RVPH) ("Reviva" or the "Company"), a clinical-stage pharmaceutical company developing therapies that seek to address unmet medical needs in the areas of central nervous system (CNS), cardiovascular, metabolic, and inflammatory diseases, today announced positive data from its recently completed clinical drug-drug interaction (DDI) study investigating the potential effect of CYP3A4 enzyme on brilaroxazine in healthy subjects. The CYP3A4 enzyme plays a pivotal role in helping the body metabolize and remove small foreign molecules and is primarily found in the liver and intestine. DDI evaluation is a critical clinical pharmacology study required by the U.S. Food and Drug Administration (FDA) and other regulatory agencies globally for approving a new drug to market. Brilaroxazine is a serotonin/dopamine modulator in late-stage clinical development for the treatment of schizophrenia.

"We are pleased to have achieved positive results from our DDI study with brilaroxazine, which further demonstrated its differentiated pharmacological and safety profile. Our latest data reinforce that brilaroxazine may have the potential to provide an advantage over other treatments for patients taking multiple drugs who are at higher risk of experiencing adverse drug interactions or even discontinuation of their medications due to those interactions," said Laxminarayan Bhat, Ph.D., Founder, President, and CEO. "We look forward to submitting these data to the FDA along with the results from our pivotal Phase 3 trials as part of our New Drug Application (NDA) for brilaroxizine in schizophrenia."

Following FDA guidelines, the DDI clinical study was designed to evaluate the drug interaction effect of a strong CYP3A4 inhibitor or inducer when co-administered with brilaroxazine in healthy volunteers. A strong CYP3A4 inhibitor, itraconazole, slightly increased brilaroxazine C_{max}, AUC_{last} and AUC_{inf} by 6, 16 and 13%, respectively, in healthy volunteers (N=11). Similarly, a strong CYP3A4 inducer, phenytoin, in healthy volunteers (N=16) decreased brilaroxazine C_{max}, AUC_{last} and AUC_{inf} by 33, 56 and 53%, respectively. Reviva believes that brilaroxazine's clinical safety is further reinforced with the positive results of this DDI study, which found no clinically significant interaction when combined with a CYP3A4 inhibitor.

Brilaroxazine is currently being evaluated in RECOVER, a pivotal global Phase 3, randomized, double-blind, placebo-controlled, multicenter study designed to assess the safety and

efficacy of brilaroxazine in approximately 400 patients with acute schizophrenia compared to placebo. Brilaroxazine will be administered at fixed doses of 15 mg or 50 mg once daily for 28 days. A 52-week open-label extension study with flexible doses of 15 mg, 30 mg, or 50 mg will further evaluate the long-term safety and tolerability of brilaroxazine in patients with stable schizophrenia. Topline data is expected in mid-2023.

About DDI Clinical Studies

Drug-drug interaction (DDI) clinical studies are an imperative step in the new drug approval process. DDI studies help identify potential adverse reactions that may be caused by interactions between multiple drugs, leading to unintended reactions, toxic side effects, or in some cases, a lack of therapeutic efficacy. With the rise in polypharmacy to treat comorbidities, alongside prevalent substance abuse, drug-drug interactions have become a critical factor to consider when treating schizophrenia. Approximately 50% of prescribed drugs and over 25% of antipsychotics currently on the market are known to cause drug interactions with CYP3A4 inhibitors and can lead to side effects. Findings from DDI studies help to inform drug labeling that is then used by healthcare providers to aid in therapeutic decision-making.

About Brilaroxazine

Brilaroxazine (RP5063) is a new chemical entity with potent affinity and selectivity against key serotonin and dopamine receptors implicated in schizophrenia and its comorbid symptoms. In a multinational, multicenter, double-blind Phase 2 study in 234 patients with acute schizophrenia or schizoaffective disorder, brilaroxazine met its primary endpoint, reducing Positive and Negative Syndrome Scale (PANSS) total score and demonstrating statistically significant improvements for secondary endpoints evaluating social functioning, and positive and negative symptoms, and directional improvements for depression and cognition. In this completed Phase 2 study, brilaroxazine met all safety endpoints with no weight gain, no increase in blood sugar and lipids, and no cardiac or endocrine adverse effects compared to placebo. A full battery of regulatory compliant toxicology and safety pharmacology studies has been completed for brilaroxazine. The U.S. Food and Drug Administration (FDA) has agreed to consider a potential ‘Superior Safety’ label claim if there is a positive outcome on a relevant endpoint in a pivotal Phase 3 study in patients with schizophrenia. Reviva intends to develop brilaroxazine for other neuropsychiatric indications including bipolar disorder, major depressive disorder (MDD) and attention-deficit/hyperactivity disorder (ADHD). Additionally, brilaroxazine has shown promising efficacy for pulmonary arterial hypertension (PAH) and idiopathic pulmonary fibrosis (IPF) with mitigation of lung fibrosis and inflammation in translational animal models. Reviva believes brilaroxazine has the potential to delay disease progression in PAH and IPF. Brilaroxazine has received Orphan Drug Designation by the U.S. FDA for the treatment of these conditions. To learn more about the clinical and preclinical data available for brilaroxazine, please visit revivapharma.com/publications.

About Reviva

Reviva is a clinical-stage biopharmaceutical company that discovers, develops, and seeks to commercialize next-generation therapeutics for diseases representing unmet medical needs and burdens to society, patients, and their families. Reviva's current pipeline focuses on the central nervous system, respiratory and metabolic diseases. Reviva's pipeline currently includes two drug candidates, RP5063 (brilaroxazine) and RP1208. Both are new chemical entities discovered in-house. Reviva has been granted composition of matter patents for both RP5063 and RP1208 in the United States (U.S.), Europe, and several other countries.

Forward-Looking Statements

This press release contains certain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934 and the Private Securities Litigation Reform Act, as amended, including those relating to the Company's Phase 3 RECOVER study and timing of topline data, product development, clinical and regulatory timelines and expenses, market opportunity, ability to raise sufficient funding, competitive position, possible or assumed future results of operations, business strategies, potential growth opportunities and other statements that are predictive in nature. These forward-looking statements are based on current expectations, estimates, forecasts and projections about the industry and markets in which we operate and management's current beliefs and assumptions. These statements may be identified by the use of forward-looking expressions, including, but not limited to, "expect," "anticipate," "intend," "plan," "believe," "estimate," "potential, "predict," "project," "should," "would" and similar expressions and the negatives of those terms. These statements relate to future events or our financial performance and involve known and unknown risks, uncertainties, and other factors which may cause actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Such factors include those set forth in the Company's filings with the Securities and Exchange Commission. Prospective investors are cautioned not to place undue reliance on such forward-looking statements, which speak only as of the date of this press release. The Company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise.

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