Reviva Pharmaceuticals Announced Preclinical Efficacy Data on Brilaroxazine in IPF at the 2023 American Thoracic Society International Conference and Publication in Medical Research Archives

Brilaroxazine, a novel serotonin-dopamine modulator with multifaceted activities has the potential to treat idiopathic pulmonary fibrosis (IPF)

Brilaroxazine improved survival and lung function, and reduced lung fibrosis and inflammation in a bleomycin-induced rodent model of IPF

U.S. FDA has granted Orphan Drug Designation to brilaroxazine for IPF indication

CUPERTINO, Calif., May 25, 2023 — 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), respiratory and metabolic diseases, has presented preclinical data on the novel serotonin-dopamine modulator brilaroxazine in idiopathic pulmonary fibrosis (IPF) at the 2023 American Thoracic Society (ATS) International Conference which took place in Washington, DC, USA, May 19-24, 2023. The Company also announced acceptance of this data for publication in *Medical Research Archives*. The ATS poster and online publication will be available at revivapharma.com/publications.

"The improvement in survival and lung function, coupled with significant reduction in fibrosis and proinflammatory cytokines in the bleomycin-induced rodent model of IPF reinforces the multifaceted action of brilaroxazine," said Laxminarayan Bhat, Ph.D., Founder, President, and CEO of Reviva. "This preclinical evaluation in IPF provides proof-of-concept support for the potential of brilaroxazine to treat pulmonary fibrosis and inflammation stemming from underlying dysfunction in serotonin signaling in the lung. Brilaroxazine has already received Orphan Drug Designation by the U.S. FDA for IPF."

Idiopathic pulmonary fibrosis (IPF) is a debilitating lung disease involving chronic inflammation and progressive alveolar fibrosis that leads to destroyed architecture, reduced capacity, impaired oxygenation, and declined function. While two treatments Nintedanib (Ofev®) and Pirfenidone (Esbriet®) – have been approved by the Food and Drug Administration (FDA), the ability to address unmet needs is still limited by inadequate improvements in lung function decline, disease progression and survival rates. Most IPF patients suffer from chronic mental illness (e.g. depression, psychosis).

Serotonin (5-HT) signaling plays a key role, via $5\text{-HT}_{2A/2B/7}$ receptors, in the vasoactive effect on pulmonary arteries and lung myofibroblast actions. Brilaroxazine displays a high affinity and functional activity for the $5\text{-HT}_{2A/2B/7}$ receptors and moderate affinity for the serotonin

transporter. Brilaroxazine's effects on vascular fibrosis (5-HT_{2B} receptor), proliferation (5-$H_{2A/2B}$ receptor), relaxation (5-HT_{2A} receptor), inflammation (5-HT_{7} receptor), and pro-inflammatory cytokines have created interest in the potential to treat IPF. Brilaroxazine was evaluated in a bleomycin (BLM)-induced rat model of IPF receiving either brilaroxazine 15 mg twice daily for 21 days starting at day 1 (BT) or at day 10 (BI).

Key highlights from the poster presentation and publication support the potential of brilaroxazine to improve fibrosis and inflammation in rat model of IPF

- Brilaroxazine demonstrated efficacy with significant improvements in key endpoints in the bleomycin (BLM)-induced rat model of IPF.
- Statistically significant improvements with brilaroxazine vs BLM group include:
    - Prolonged survival
        - 90% (BT) and 89.5% (BI) vs 62% survival rate (P<.05, Day 21)
    - Improved lung function
        - Improved arterial pulse pressure (BT: P<0.05, BLM)
        - Restored cardiac output (BT: P<0.01, BLM)
        - Normalized blood oxygen levels (BT: P<0.05, BLM)
        - Reduced blood lactate levels (BT: P<0.01, BLM; BI: P<0.05, BLM)
        - Reduced respiratory resistance (BT: P<0.05, BLM)
    - Anti-fibrotic effects
        - Decreased hydroxyproline content (BT: P<0.05, BLM; BI: P<0.01, BLM)
        - Lower lung weight (BT: P<0.05)
        - Reversed BLM induced total cell counts (BT and BI: P<0.05, BLM) and protein levels (BT: P<0.05, BLM)
        - Reduced BLM-induced fibrotic changes based on Ashcroft Score and Masson's trichrome staining (BT: P<0.001)
    - Anti-inflammatory effects
        - Decreased MCP-1 (BT: P<0.05, BLM)
        - Decreased IP10 and RANTES (BT and BI: P<0.01, BLM)

About Idiopathic Pulmonary Fibrosis (IPF)

IPF is a progressive, debilitating, and fatal lung disease that affects approximately 3 million people worldwide. IPF is characterized by inflammation and fibrosis of the lungs, hindering the ability to process oxygen and causing shortness of breath. Mortality from IPF is increasing steadily worldwide with a median survival time from diagnosis of 2-5 years. It is estimated that there will be between 28,000 and 65,000 deaths in Europe and between 13,000 and 17,000 deaths in the United States from IPF per year. Treatment involves either early referral for lung transplantation, palliative care, and clinical trials. Various interventions, including commonly used agents (e.g., corticosteroids and immunosuppressants), are limited and not supported in current guidelines. While two treatments Nintedanib (Ofev®), and Pirfenidone

(Esbriet®) – have been approved by the Food and Drug Administration (FDA), the ability to address unmet needs is still limited by inadequate improvements in lung function decline, disease progression and survival rates. Most patients with IPF suffer from chronic mental illness (e.g. depression, psychosis).

About Brilaroxazine

Brilaroxazine is an in-house discovered 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 improvement of overall drug treatment outcomes using Clinical Global Impression (CGI) scale and 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. Positive data from a clinical drug-drug interaction (DDI) study investigating the potential effect of CYP3A4 enzyme on brilaroxazine in healthy subjects supports no clinically significant interaction when combined with a CYP3A4 inhibitor. 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 and intends to develop brilaroxazine for these pulmonary indications. Brilaroxazine has already 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, brilaroxazine and RP1208. Both are new chemical entities discovered in-house. Reviva has been granted composition of matter patents for both brilaroxazine 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 RECOVER Phase 3 trial, including expectations therefor and the timing of topline data, the Company's expectations regarding the anticipated clinical profile of its product candidates, including statements regarding anticipated efficacy profile, product development, clinical and regulatory approval pathways, timelines 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 most recent Annual Report on Form 10-K for the fiscal year ended December 31, 2022, and the Company's other filings from time to time 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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