# Reviva Pharmaceuticals Announces Intent to File an IND for Brilaroxazine in Psoriasis After Promising Preclinical Data

Brilaroxazine topical liposomal-gel formulation (brilaroxazine lipogel) demonstrated proof-ofconcept efficacy in the imiquimod-induced psoriatic mouse model

IND submission for brilaroxazine lipogel in psoriasis expected in 2024

Reviva has filed composition of matter patent for brilaroxazine-lipogel and a separate patent for use in the treatment of psoriasis

Preclinical efficacy data presented at the ISID 2023 meeting

CUPERTINO, Calif., May 11, 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 promising preclinical data on the potential of novel serotonin-dopamine stabilizer brilaroxazine for the treatment of psoriasis at the First International Societies for Investigative Dermatology (ISID) Meeting in Tokyo, Japan, May 10-13, 2023. The ISID poster is available at revivapharma.com/publications.

"The multifaceted activity of brilaroxazine offers the promise to improve the quality of life and provide a novel treatment option for patients with psoriasis, an inflammatory condition stemming from serotonin and dopamine dysfunction," said Laxminarayan Bhat, Ph.D., Founder, President, and CEO of Reviva. "We were excited to present encouraging preclinical data at ISID 2023 highlighting the therapeutic potential of brilaroxazine lipogel, a novel, proprietary lipogel formulation for the topical treatment of psoriasis. We have filed a composition of matter patent for brilaroxazine-lipogel and a separate patent for its use in psoriasis. Mental illness, including schizophrenia and depression, is a major comorbidity in patients with psoriasis. Brilaroxazine has established a well-tolerated safety profile with robust efficacy in about 300 patients with schizophrenia from Phase 1B and Phase 2 studies. To further explore this therapeutic potential, we intend to submit an investigational new drug application (IND) for brilaroxazine lipogel in psoriasis in 2024."

Psoriasis is a chronic dermal inflammatory disease with a global prevalence of ~125 million. Dopamine (D) and serotonin (5-HT) signaling pathways play an important role in the pathobiology of psoriasis, and lead to increased inflammatory mediators (TNF- $\alpha$ , IFN- $\gamma$ , IL-1 $\beta$ , IL-6, IL-8), keratinocyte activation and deterioration, and worsening symptoms. Current treatments include multiple modalities but are limited by long-term side effects (topicals), toxicities (orals) or risk of immunogenicity, serious infection, and malignancy (biologics). Brilaroxazine (RP5063) is a modulator of D and 5-HT receptors with multifaceted activity that may affect underlying psoriasis pathology. Preclinical studies in the imiquimod-induced

psoriatic mouse model (BALB/c) were used to evaluate the potential of topical liposomal-gel formulation of brilaroxazine for the treatment of psoriasis.

# Key poster highlights support the therapeutic potential of brilaroxazine lipogel in psoriasis:

- Brilaroxazine lipogel treatment group compared to imiquimod-induced psoriatic group:
  - Consistently and significantly lowered Psoriasis Area and Severity Index (PASI) scores on Days 3-12 (P=0.03), with maximum difference on Days 11-12
  - Significantly lowered Baker's score (P=0.003)
  - Significantly lowered serum biomarkers Ki-67 (P=0.001) and TGF-β (P=0.008)
- Provides initial proof-of-concept (PoC) for the brilaroxazine topical liposomal-gel formulation
- Supports D and 5-HT receptors as viable psoriasis targets and offers an initial glimpse at changes indicating anti-inflammatory, anti-fibrotic, and anti-proliferative effects
- Brilaroxazine formulation with the lipogel delivery system offers a potential option for psoriasis, which has links to mental illness (as high as 36%)

#### About Reviva's Lead Drug Candidate Brilaroxazine

Brilaroxazine 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 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 Psoriasis**

Psoriasis is a systemic immune-mediated dermal inflammatory disease with genetic components that presents as recurrent episodes of hyperkeratotic, erythematous plaques and silvery-coated scales on the skin, symmetrically distributed to the extensor (knees, elbows), scalp, and lumbosacral (trunk) regions. This common, incurable, chronic disease cycles with flares for weeks or months, then subsides periodically or remissions. With a global prevalence of approximately 125 million, this condition manifests as phenotypically distinct subtypes, with plaque psoriasis accounting for over 80% of cases. Mental illness (e.g. anxiety, depression, schizophrenia) is a major comorbidity in patients with psoriasis. Dopamine (D) and serotonin (5-HT) signaling pathways play an important role in the pathobiology of psoriasis, and lead to increased inflammatory mediators (TNF-α, IFN-γ, IL-1β, IL-6, IL-8), keratinocyte activation and deterioration, and worsening symptoms. Current treatments include multiple modalities but are limited by long-term side effects (topicals), toxicities (orals) or risk of immunogenicity, serious infection, and malignancy (biologics).

#### **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.

## **Corporate Contact:**

Reviva Pharmaceuticals Holdings, Inc. Laxminarayan Bhat, PhD www.revivapharma.com

#### **Investor Relations Contact:**

LifeSci Advisors, LLC Bruce Mackle bmackle@lifesciadvisors.com

RedChip Companies, Inc. Todd McKnight (917) 349.2175 RVPH@redchip.com

