BetterLife Pharma Prioritizes BETR-001 to Lead in Migraine and Headache Disorders, Targeting a Clinically Validated, FDA-Precedented Serotonergic Mechanism

Fully non-hallucinogenic, oral, non-scheduled 5-HT2A neuroplastogen differentiates BETR-001 from every other 5-HT2A agonist program; depression and other psychiatric disorders retained as optional future indications

Vancouver, British Columbia--(Newsfile Corp. - July 13, 2026) - BetterLife Pharma Inc. (CSE: BETR) (OTCQB: BETRF) (FSE: NPAU) ("BetterLife" or the "Company"), today announced the prioritization of its lead clinical-stage asset, BETR-001, to pursue migraine and other primary headache disorders as its lead indications. The strategic focus concentrates BETR-001's development on one of the largest, most disabling and most underserved areas of neurology, and does so through a serotonin-receptor mechanism of action that is already clinically validated and approved by the U.S. Food and Drug Administration (FDA) in multiple marketed migraine therapies.

BETR-001 is the patented, active (6R,9R) stereoisomer of 2-bromo-LSD (2-Br-LSD) - a fully non-hallucinogenic derivative of LSD that acts as a 5-HT2A partial agonist and potent "neuroplastogen." Prioritizing BETR-001 for migraine and headache aligns the asset's validated pharmacology, existing human clinical precedent, and de-risked regulatory package with a market of more than one billion patients, while preserving optionality across psychiatry and neuropathic pain.

A Migraine Mechanism That Is Already Validated - and Already Approved

Serotonin (5-HT) receptor pharmacology is the foundation of modern migraine therapy. Unlike the psychiatric indications pursued by most serotonergic programs, migraine is a field where serotonergic mechanisms of action have been repeatedly proven in the clinic and approved by regulators for more than six decades:

- **Triptans** (e.g., sumatriptan) are 5-HT1B/1D receptor agonists and remain the standard of care for acute migraine.
- **Lasmiditan** (Reyvow®), a selective 5-HT1F receptor agonist, was FDA-approved in 2019, confirming that serotonergic agonism continues to yield new, approved migraine medicines.
- **Ergot alkaloids** - dihydroergotamine and ergotamine - are lysergic-acid-derived agents acting across multiple serotonin receptors, including 5-HT2, and have been used in migraine for generations.
- **Methysergide**, FDA-approved in 1962 as a migraine preventive, is itself a lysergic-acid (LSD-related) derivative that acts through serotonin 5-HT2 and 5-HT1 receptors - the closest structural and mechanistic precedent to BETR-001.

BETR-001 sits squarely within this validated serotonergic - and specifically lysergic-pharmacology but is engineered to remove the liabilities that constrained the earlier agents: the fibrotic toxicity that limited methysergide, the vasoconstriction and cardiovascular restrictions of ergots and triptans, and the hallucinogenic activity of LSD. In short, BETR-001 pursues a mechanism the field already knows works, in a molecule designed to be safer and more patient-friendly.

Direct human precedent already exists. In a published clinical pilot study, 2-bromo-LSD (the racemic

form) reduced both the frequency and intensity of attacks in cluster headache patients, with no hallucinations or distortions and no cardiopulmonary adverse events (Karst et al., Cephalalgia, 2010). This provides rare, mechanism-confirming clinical evidence for BETR-001's activity in a severe headache disorder.

5-HT2A-Driven Neuroplasticity May Offer Benefits Beyond Symptom Relief

Beyond acute serotonergic signaling, BETR-001 is a potent neuroplastogen. Its 5-HT2A partial agonism promotes dendritic and synaptic (spine) growth - "rewiring" of neural circuits - as demonstrated in peer-reviewed preclinical work (Lewis et al., Cell Reports, 2023), which characterized 2-Br-LSD as a non-hallucinogenic LSD analog with therapeutic potential and confirmed its effects are dependent on 5-HT2A activation.

Migraine is increasingly understood as a disorder of central sensitization and maladaptive neural plasticity, in which repeated attacks drive chronification, interictal burden, and comorbid mood symptoms. A therapy that engages neuroplasticity therefore has the potential to move beyond episodic symptom control toward durable, potentially disease-modifying benefit - an attribute no existing migraine class provides. This positions BETR-001 to address not only acute and episodic migraine, but also the highest-need segments: chronic migraine, medication-overuse headache, and patients with comorbid anxiety or depression.

A Large, Disabling and Underserved Patient Population

- **Migraine affects an estimated 1.1 billion people worldwide** and is the second leading cause of years lived with disability globally - and the single leading cause of disability in people under age 50.
- **In the United States, roughly 15.5% of adults** report migraine or severe headache, with women affected roughly three times as often as men and peak prevalence during the most productive working years (ages 25-55).
- **Chronic migraine** (≥15 headache days per month) represents a particularly disabled subset; among employed U.S. adults with chronic migraine alone, lost productivity has been estimated at hundreds of millions of dollars per week.
- **Cluster headache** - often called "suicide headache" - is an orphan-designated, extraordinarily severe disorder that remains a high-unmet, de-risking beachhead for BETR-001, supported by the direct human evidence noted above.

Despite recent innovation, current preventives (topiramate, beta-blockers, and the CGRP antibodies and gepants) leave a large share of patients inadequately controlled, intolerant of side effects, or facing significant cost and access barriers - sustaining a multibillion-dollar unmet need that a well-tolerated, oral, at-home, non-scheduled therapy is well positioned to serve.

Differentiated From Every Other 5-HT2A Agonist Program

The current wave of 5-HT2A agonist development - including programs built around LSD, psilocybin, and their analogs - is almost entirely directed at psychiatric indications and, critically, retains the hallucinogenic activity of the parent psychedelics. Those programs remain controlled substances requiring specialized clinics, prolonged in-clinic dosing, and monitoring by mental-health professionals. BETR-001 is fundamentally different on every axis:

- **Fully non-hallucinogenic** - no "trip," no head-twitch response in preclinical models, enabling routine outpatient use.
- **Not a controlled substance** - removing scheduling, distribution, insurability and access barriers.
- **Oral, at-home self-administration** - no specialized clinics, no monitored dosing sessions, no accompanying cost and resource burden.
- **Aimed at neurology and pain, not crowded psychiatry** - BETR-001 pursues migraine and headache, where the serotonergic mechanism is already approved, rather than competing in the

saturated psychedelic-psychiatry field.
- **De-risked and protected** - prior human efficacy signal in headache, an improved cardiac-safety profile versus LSD, no tolerance on repeat dosing, and a granted U.S. composition-of-matter patent providing coverage to 2042.

Together, these attributes make BETR-001 the only 5-HT2A neuroplastogen positioned to deliver the therapeutic benefits associated with this receptor while being suitable for broad, everyday prescribing in a mainstream neurology indication.

Depression and Additional Indications Retained as Future Optionality

BETR-001's neuroplastogenic mechanism and demonstrated activity in preclinical depression and anxiety models mean that major depressive disorder, anxiety, PTSD, neuropathic pain, and traumatic brain injury / concussion remain attractive future indications. Under the new strategy these are retained as optional, value-expanding opportunities to be advanced opportunistically or through partnerships, while the Company concentrates its lead development resources on the migraine and headache franchise.

Development Status and Next Steps

BetterLife has completed its FDA pre-IND meeting for BETR-001, has initiated the final the IND-enabling toxicity study, and substantially completed GMP scale-up manufacturing (achieved without using LSD as a starting material). The Company anticipates filing its Investigational New Drug (IND) application in 1Q 2027.

Management Commentary

"Migraine is one of the world's largest and most disabling conditions, and it is one of the few areas where serotonergic pharmacology is not experimental - it is already approved and prescribed every day. BETR-001 lets us pursue that validated mechanism with a molecule that is non-hallucinogenic, non-scheduled, and taken as a simple oral pill at home. That combination is unique among 5-HT2A programs, and we believe it gives BETR-001 a clear, differentiated path to patients who need better options."

- Dr. Ahmad Doroudian, Chief Executive Officer, BetterLife Pharma Inc.

About BETR-001

BETR-001 is the active (6R,9R) stereoisomer of 2-bromo-LSD, a fully non-hallucinogenic derivative of LSD and a potent 5-HT2A neuroplastogen. It is designed as an oral, at-home therapy that is not restricted as a controlled substance. BETR-001 is protected by a granted U.S. composition-of-matter patent with coverage to 2042, with additional filings underway in other major markets.

About BetterLife Pharma Inc.

BetterLife Pharma Inc. is a biotechnology company engaged in the development of cutting-edge treatments for neuro-psychiatric and neurological disorders. Its lead asset, BETR-001, is a non-hallucinogenic, non-controlled 5-HT2A neuroplastogen.

For more information, visit the Company's website and its continuous-disclosure filings on SEDAR+ at www.sedarplus.ca.

Contact

Ahmad Doroudian, Chief Executive Officer
Email: Ahmad.Doroudian@blifepharma.com
Phone: 1-604-221-0595

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This press release contains forward-looking statements and predictions. These forward-looking statements, by their nature, necessarily involve risks and uncertainties that could cause actual results to differ materially from those contemplated by the forward-looking statements. BetterLife considers the assumptions on which these forward-looking statements are based to be reasonable at the time they were prepared, but cautions that these assumptions regarding future events, many of which are beyond the control of the Company, may ultimately prove to be incorrect. Factors and risks which could cause actual results to differ materially from current expectations include, among other factors, those related to the timing or successful completion of the Company's development plans including, but not limited to, synthesis of its compounds, obtaining regulatory approval, and the success of pre-clinical and clinical studies. Forward-looking information is based upon a number of assumptions and estimates of management at the date the statements are made. Risk factors include, among other things, BetterLife's ability to raise capital to complete its plans and fund its studies, and assumptions are inherently subject to significant economic, social, political, competitive, regulatory and other uncertainties. The Company disclaims any intention or obligation to update or revise any forward-looking statements, whether as a result of new information, future events, or except as required by law. For additional information on risks and uncertainties relating to these forward-looking statements, investors should consult the Company's ongoing continuous disclosure and other filings found on SEDAR+ at www.sedarplus.ca.

Selected References

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