

**FORM 51-102F3  
MATERIAL CHANGE REPORT**

**Item 1 Name and Address of Company**

BetterLife Pharma Inc. (the "Company")  
1275 West 6<sup>th</sup> Avenue  
Suite 300  
Vancouver, British Columbia  
V6H 1A6

**Item 2 Date of Material Change**

March and April 2022

**Item 3 News Releases**

News releases dated March 16 and April 6, 2022

**Item 4 Summary of Material Change**

In March 2022, the Company obtained the first set of positive in vivo pharmacokinetic (PK) data confirming the bioavailability of its lead compound BETR-001 (2-bromo-LSD, formerly TD-0148A) in the brain (target tissue) and plasma of treated mice. BETR-001 is a non-hallucinogenic derivative of lysergic acid diethylamide (LSD). The Company had previously confirmed the non-hallucinogenic property of BETR-001 in the head-twitch-response (HTR) assay in mice, a model commonly used as a behavioral proxy in rodents for human hallucinogenic effects. A key objective of the current study was to confirm that lack of hallucinogenic property of BETR-001 is not due to its poor bioavailability especially in the target brain tissue.

The key PK data points from this mouse study conducted at Nucro-Technics (Scarborough, ON, Canada) include:

- A bioanalytical method was established to measure 2-bromo-LSD in mouse plasma and brain tissues.
- BETR-001 appeared quickly (10 minutes post dose) in the plasma and brain of mice following a single dose and remained detectable up to 8 hours post dose.
- Plasma and brain exposure of BETR-001 increased in a time- and dose-dependent manner.
- The mean terminal half-life of BETR-001 in plasma (~ 1.5 hours) was not significantly different among all dosing groups or between different sexes.

In April 2022, the Company obtained additional positive data confirming the anti-depressant activity of BETR-001 in preclinical models of depression. The study is part of the Company's collaboration with the laboratory of Dr. Argel Aguilar-Valles at Carleton University's (Carleton) Department of Neuroscience and evaluated the anti-depressant activity of BETR-001 on depressive-like behavior of mice in a forced swim test. The amount of time mice spend immobile (a depression-like behavior) was significantly reduced 24 hours after treatment with single dose of BETR-001 (1.0 mg/kg) compared to the untreated control group. BETR-001 had no effect on the locomotion behavior of mice in this study, suggesting the increased mobility in the forced swim test was due to its anti-depressant activity.

In March 2022, the Company issued 155,000 common shares to third parties for services rendered and pursuant to vesting of restricted stock units.

**Item 5 Full Description of Material Change**

Refer to Item 4.

**Item 6 Reliance on subsection 7.1(2) or (3) of National Instrument 51-102**

This Report is not being filed on a confidential basis in reliance on subsection 7.1(2) of National Instrument 51-102.

**Item 7 Omitted Information**

No information has been omitted on the basis that it is confidential information.

**Item 8 Executive Officer**

Further information can be obtained from Ahmad Doroudian, Chief Executive Officer of the Company, at (604) 221-0595.

**Item 9 Date of Report**

April 6, 2022

**SCHEDULE "A"**



## BetterLife Obtains In Vivo PK Data for BETR-001 Confirming its Bioavailability in Brain

VANCOUVER, British Columbia, March 16, 2022 - BetterLife Pharma Inc. (“BetterLife” or the “Company”) (CSE: [BETR](#) / OTCQB: [BETRF](#) / FRA: [NPAU](#)), an emerging biotech company focused on the development and commercialization of second generation non-hallucinogenic psychedelic analogs for the treatment of neuropsychological disorders, is pleased to announce it has obtained the first set of positive in vivo pharmacokinetic (PK) data confirming the bioavailability of its lead compound BETR-001 (2-bromo-LSD, formerly TD-0148A) in the brain (target tissue) and plasma of treated mice. BETR-001 is a non-hallucinogenic derivative of lysergic acid diethylamide (LSD). We had previously confirmed the non-hallucinogenic property of BETR-001 in the head-twitch-response (HTR) assay in mice, a model commonly used as a behavioral proxy in rodents for human hallucinogenic effects. A key objective of the current study was to confirm that lack of hallucinogenic property of BETR-001 is not due to its poor bioavailability especially in the target brain tissue.

The key PK data points from this mouse study conducted at Nucro-Technics (Scarborough, ON, Canada) include:

- A bioanalytical method was established to measure 2-bromo-LSD in mouse plasma and brain tissues.
- BETR-001 appeared quickly (10 minutes post dose) in the plasma and brain of mice following a single dose and remained detectable up to 8 hours post dose.
- Plasma and brain exposure of BETR-001 increased in a time- and dose-dependent manner.
- The mean terminal half-life of BETR-001 in plasma (~ 1.5 hours) was not significantly different among all dosing groups or between different sexes.

BetterLife's Chief Executive Officer, Dr. Ahmad Doroudian, stated that “we are very pleased with the results from our preclinical animal study demonstrating a favorable PK profile of BETR-001 in support of our IND and future clinical programs in treatment of major depressive disorder and cluster headache patients. Although 2-bromo-LSD has been tested in rodents and human studies in the past, this is the first study to characterize the brain and plasma PK profile. These results provide strong evidence that BETR-001, manufactured by our patented synthesis and formulation process can reach the target organ (brain) and achieve the desired therapeutic range. These results will be part of BETR-001’s IND enabling non-clinical package that is currently under preparation.”

## **About BetterLife Pharma**

BetterLife Pharma Inc. is an emerging biotechnology company primarily focused on developing and commercializing two compounds, BETR-001 and BETR-002, to treat neuro-psychiatric and neurological disorders.

BETR-001 (formerly TD-0148A), which is in preclinical and IND-enabling studies, is a non-hallucinogenic and non-controlled LSD derivative in development and it is unique in that it is unregulated and therefore can be self-administered. BetterLife's synthesis patent for BETR-001 eliminates regulatory hurdles and its pending patent for composition and method of use covers treatment of depression, cluster headaches, post-traumatic stress disorder and other neuro-psychiatric and neurological disorders. The global depression drugs market reached US\$12.41 billion in 2019 and is projected to reach near US\$25 billion by 2030. According to the WHO, depression is one of the leading causes of disability, impacting approximately 265 million people in the world.

BETR-002 (formerly TD-010), which is in preclinical and IND-enabling studies, is based on honokiol, the active anxiolytic ingredient of magnolia bark. BetterLife's pending method of use and formulations patent covers treatment of anxiety related disorders including benzodiazepine dependency. The global benzodiazepines market is expected to grow to US\$4.15 billion in 2017 (from US\$3.48 billion in 2019) at a CAGR of 2.25%.

BetterLife also owns a drug candidate for the treatment of viral infections, such as COVID-19, and is in the process of seeking strategic alternatives for further development.

For further information, please visit [BetterLifePharma](https://www.betterlifepharma.com).

## **Contact Information**

David Melles, Investor Relations Manager

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Phone: 1-778-887-1928

## **Cautionary Note Regarding Forward-Looking Statements**

No securities exchange has reviewed nor accepts responsibility for the adequacy or accuracy of the content of this news release. This news release contains forward-looking statements relating to product development, licensing, commercialization and regulatory compliance issues and other statements that are not historical facts. Forward-looking statements are often identified by terms such as "will", "may", "should", "anticipate", "expects" and similar expressions. All statements other than statements of historical fact, included in this release are forward-looking statements that involve risks and uncertainties. There can be no assurance that such statements will prove to be accurate and actual results and future events could differ materially from those anticipated in such statements. Important factors that could cause actual results to differ materially from the Company's expectations include the failure to satisfy the conditions of the relevant securities exchange(s) and other risks detailed from time to time in the filings made by the Company with securities regulations. The reader is cautioned that assumptions used in the preparation of any forward-looking information may prove to be incorrect. Events or circumstances may cause actual

results to differ materially from those predicted, as a result of numerous known and unknown risks, uncertainties, and other factors, many of which are beyond the control of the Company. The reader is cautioned not to place undue reliance on any forward-looking information. Such information, although considered reasonable by management at the time of preparation, may prove to be incorrect and actual results may differ materially from those anticipated. Forward-looking statements contained in this news release are expressly qualified by this cautionary statement. The forward-looking statements contained in this news release are made as of the date of this news release and the Company will update or revise publicly any of the included forward-looking statements as expressly required by applicable law.



## BetterLife's BETR-001 Demonstrates BETR-001 Anti-depressant Activity in Preclinical Models of Depression

VANCOUVER, British Columbia, April 6, 2021 - BetterLife Pharma Inc. ("BetterLife" or the "Company") (CSE: [BETR](#) / OTCQB: [BETRF](#) / FRA: [NPAU](#)), an emerging biotech company focused on the development and commercialization of cutting-edge treatments for mental disorders, is pleased to announce it has obtained additional positive data confirming the anti-depressant activity of its lead compound 2-bromo-LSD ("BETR-001") in preclinical models of depression. The study is part of BetterLife's collaboration with the laboratory of Dr. Argel Aguilar-Valles at Carleton University's (Carleton) Department of Neuroscience.

BETR-001 is a second-generation Lysergic Acid Diethylamide ("LSD") derivative molecule that BetterLife believes will mimic the therapeutic potential of LSD without causing psychedelic effects, such as hallucinations. The current study evaluated the anti-depressant activity of BETR-001 on depressive-like behavior of mice in a forced swim test. The amount of time mice spend immobile (a depression-like behavior) was significantly reduced 24 hours after treatment with single dose of BETR-001 (1.0 mg/kg) compared to the untreated control group. BETR-001 had no effect on the locomotion behavior of mice in this study, suggesting the increased mobility in the forced swim test was due to its anti-depressant activity.

"We are very pleased with these preclinical results as they show that BETR-001 efficacy in the forced swim test is consistent with 2-bromo-LSD's 5-HT<sub>2A</sub> agonist activity, promotion of neural plasticity, and its anti-depressant effect in stress-induced preclinical depression model, as demonstrated in previous studies by BetterLife. The mounting evidence on BETR-001 efficacy in preclinical models of depression leaves little doubt on its therapeutic potential in depression and related disorders," stated BetterLife's Chief Executive Officer, Dr. Ahmad Doroudian.

Dr. Argel Aguilar-Valles commented, "We are pleased to collaborate with the BetterLife team in demonstrating the anti-depressant activity of 2-bromo-LSD (BETR-001) in various preclinical models that are established in our laboratory. LSD and other psychedelic drugs have been shown to have anti-depressant effects, and non-hallucinogenic derivatives of these drugs such as BETR-001 represent a promising alternative."

BetterLife is also pleased to present an interview by Dr. Doroudian with Proactive Investors discussing the anti-depressant activity of BETR-001. The interview can be viewed at [https://youtu.be/ZSukpIRsZ\\_I](https://youtu.be/ZSukpIRsZ_I).

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BetterLife also owns a drug candidate for the treatment of viral infections such as COVID-19 and is in the process of seeking strategic alternatives for further development.

For further information, please visit [BetterLife Pharma](#).

## **About the Department of Neuroscience at Carleton University**

Carleton Neuroscience has an international reputation for research on stress and its effects on brain functioning and mental health. The department has an interdisciplinary approach to understanding the emergence, prevention and treatment of mental and physical disorders.

For more information, please visit [www.carleton.ca/neuroscience](http://www.carleton.ca/neuroscience).

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