

**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**

November/December 2021

**Item 3 News Releases**

News releases dated November 29, December 3 and December 9, 2021.

**Item 4 Summary of Material Change**

In November 2021, the Company’s fully-owned subsidiary, Altum Pharmaceuticals Inc. (“Altum”), and Pontificia Universidad Católica de Chile successfully completed the Phase 1 portion of the Phase 1-2 randomized placebo controlled trial (“IN2COVID”) in COVID-19 patients with the Company’s proprietary inhaled interferon alpha-2b product, AP-003. Eighteen healthy subjects were enrolled in the Phase 1 portion of the IN2COVID trial (ClinicalTrials.gov Identifier: [NCT04988217](https://clinicaltrials.gov/ct2/show/study/NCT04988217)). AP-003 demonstrated an excellent safety and tolerability profile and no serious adverse events were observed.

On December 9, 2021, the Company announced that it has obtained the first set of positive data showing anti-depressant properties of its lead compound, 2-bromo-LSD (“TD-0148A”) in animal depression models, as part of its collaboration with the laboratory of Dr. Argel Aguilar-Valles at Carleton University’s (Carleton) Department of Neuroscience. TD-0148A 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. Both single and repeat dose treatments with TD-0148A significantly reversed the depressive-like behavior in chronically-stressed female mice. The depressive-like behaviors assessed in the study included open-field test (a measure of exploratory behavior) and splash test (measure of anhedonia and self-hygiene behavior). Female mice demonstrated clear signs of depression following CVS as indicated by significant reduction in exploratory and grooming behaviors in open-field and splash tests, respectively. However, TD-0148A treatment showed anti-depressant activity by significantly reversing both depressive-like behaviors in these mice.

On December 6, 2021, the Company’s Chief Executive Officer, Dr. Ahmad Doroudian, participated in the H.C. Wainwright 2<sup>nd</sup> Annual Psychedelics Conference. The theme of the conference was “*Positioning for the Psychedelic Comeback in Mental Healthcare and Beyond*” and the conference assembled all the key thought leaders and companies in the psychedelic space.

**Item 5 Full Description of Material Change**

Refer to Item 4 and the news release in Schedule "A".

**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**

December 9, 2021

**SCHEDULE "A"**



## BetterLife Successfully Completes Phase 1 and Initiates Phase 2 Clinical Trials with Interferon Alpha-2b in Covid-19 Patients in Chile

VANCOUVER, British Columbia, November 29, 2021 – BetterLife Pharma Inc. (“BetterLife” or the “Company”) (CSE: [BETR](#) / OTCQB: [BETRF](#) / FRA: [NPAU](#)) today announced that its wholly owned subsidiary, Altum Pharmaceuticals Inc. (“Altum”), and Pontificia Universidad Católica de Chile have successfully completed the Phase 1 portion of the Phase 1-2 randomized placebo controlled trial (“IN2COVID”) in COVID-19 patients with BetterLife’s proprietary inhaled interferon alpha-2b product, AP-003.

Eighteen healthy subjects were enrolled in the Phase 1 portion of the IN2COVID trial (ClinicalTrials.gov Identifier: [NCT04988217](#)). AP-003 demonstrated an excellent safety and tolerability profile and no serious adverse events were observed.

Dr. Eleanor Fish, one of the Principal Investigators of the trial, commented, “I am confident that inhaled administration of interferon alpha-2b, AP-003 will prove to be an effective treatment against COVID-19. With increasing numbers of breakthrough infections in vaccinated individuals and the emergence of variants of concern such as Omicron, it is imperative that we have therapeutics to accelerate viral clearance in infected individuals, to avoid hospitalization, severe disease, and to limit outbreaks. With AP-003, there is the added advantage of a ‘pathogen agnostic’ broad spectrum antiviral that may have therapeutic benefits for many respiratory virus infections. And, an antiviral drug that the virus cannot become resistant to.”

Dr. Arturo Borzutzky, Study Director of the IN2COVID trial and Associate Professor and Head of Pediatric Immunology, Allergy and Rheumatology at the School of Medicine of Pontificia Universidad Católica de Chile said, “After successfully completing the Phase 1 portion of the trial, we are very excited to move on to Phase 2 and studying the effectiveness of inhaled interferon alpha-2b in COVID-19 patients, particularly given the spread of the Delta variant in Chile and the new threat of Omicron worldwide.”

“We are pleased to start the Phase 2 clinical trials using AP-003 in COVID-19 patients in collaboration with the Escuela de Medicina (School of Medicine) at the Pontificia Universidad Católica de Chile,” said BetterLife’s Chief Executive Officer, Dr. Ahmad Doroudian. “Since interferon alpha-2b is a broad acting antiviral agent, we believe BetterLife’s AP-003 will potentially be a very effective treatment against SARS-CoV-2 and variants of concern, such as the newly emerging Omicron strain. Previous results from our *in vitro* studies have also shown BetterLife’s rhIFN $\alpha$ -2b to have potent activity against the Wuhan reference strain, Alpha (B.1.1.7, UK), the Beta (B.1.351, South Africa) and the Delta SARS-CoV-2 variant (B.1.617.2, India outbreak).”

## **About BetterLife Pharma**

BetterLife Pharma Inc. is an emerging biotechnology company engaged in the development and commercialization of next generation psychedelic products for the treatment of mental disorders. Utilizing drug delivery platform technologies, BetterLife is also refining and developing drug candidates from a broad set of complementary interferon-based technologies which have the potential to engage the immune system to fight virus infections, such as the coronavirus disease (COVID-19) and human papillomavirus.

For further information, please visit [www.abetterlifepharma.com](http://www.abetterlifepharma.com).

## **About Pontificia Universidad Católica de Chile**

Founded in 1888, Pontificia Universidad Católica de Chile is currently one of the leading higher education institutions in Latin America, ranked first in the continent for three years in a row by the Times Higher Education Ranking. Universidad Católica aspires to achieve excellence in the creation and transfer of knowledge and in providing a Catholic-based educational experience that motivates both personal growth and the development of an inquisitive and critical mind. One of its objectives is to educate persons who are committed to the construction of a more just and prosperous society. The University is an important national center for research in social sciences, natural sciences, health, economics, agriculture, philosophy, theology, arts and literature. Located in a young and geographically distant country, the University believes that maintaining an active exchange program with foreign universities is crucial for academic development.

For further information, please visit <https://www.uc.cl/en>

## **Contact Information**

### **BetterLife Pharma:**

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### **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.



## H.C. Wainwright 2<sup>nd</sup> Annual Psychedelics Conference, BACK TO THE FUTURE!

VANCOUVER, British Columbia, December 3, 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 that Dr. Ahmad Doroudian will be participating in the H.C. Wainwright 2<sup>nd</sup> Annual Psychedelics Conference. The event will be held virtually on Monday, December 6, 2021.

The theme of the conference is “*Positioning for the Psychedelic Comeback in Mental Healthcare and Beyond*”. This event will assemble all the key thought leaders and companies in the space to discuss this paradigm shift.

Dr. Doroudian’s presentation will be available starting Monday, December 6 at 7:00 am EST. BetterLife invites you to register and attend this [event](#).

Conference registration and further information can be found at <https://hcwevents.com/psychedelics/>. For inquiries, please contact H.C. Wainwright at [lk@hcwco.com](mailto:lk@hcwco.com).

### **About BetterLife Pharma**

BetterLife Pharma Inc. is an emerging biotechnology company primarily focused on developing and commercializing two compounds, TD-0148A and TD-010, to treat neuro-psychiatric and neurological disorders.

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 TD-0148A 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 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.

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 and insomnia. 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 [BetterLife Pharma](#).

## **Contact Information**

### **BetterLife Pharma:**

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BetterLife Pharma

## BetterLife Obtains Positive TD-0148A Data in Preclinical Models of Depression

VANCOUVER, British Columbia, December 9, 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 the first set of positive data showing anti-depressant properties of its lead compound, 2-bromo-LSD ("TD-0148A") in animal depression models, as part of its collaboration with the laboratory of Dr. Argel Aguilar-Valles at Carleton University's (Carleton) Department of Neuroscience.

TD-0148A 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. Both single and repeat dose treatments with TD-0148A significantly reversed the depressive-like behavior in chronically-stressed female mice. The depressive-like behaviors assessed in the study included open-field test (a measure of exploratory behavior) and splash test (measure of anhedonia and self-hygiene behavior). Female mice demonstrated clear signs of depression following CVS as indicated by significant reduction in exploratory and grooming behaviors in open-field and splash tests, respectively. However, TD-0148A treatment showed anti-depressant activity by significantly reversing both depressive-like behaviors in these mice.

"We are very excited to confirm the projected anti-depressant properties of TD-0148A in rodent depression models conducted by Dr. Aguilar-Valles and his team. There is a high unmet need for novel anti-depressants for the treatment of major depressive disorder ("MDD") and treatment-resistant depression ("TRD") and these early data provide evidence for the therapeutic potential of TD-0148A as an anti-depressant. BetterLife is fully focused on bringing TD-0148A to the US IND stage and into the clinic as soon as possible, and our collaborations with global experts such as Dr. Aguilar-Valles, a leading scientist in depression research, will help us realize our vision," said 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 properties of TD-0148A in our models. The high rate of resistance to SSRI and other first-line treatments in MDD indicates an urgent unmet need for alternative anti-depressant treatments. LSD and other psychedelic drugs have been shown to have anti-depressant effects, and non-hallucinogenic derivatives of these drugs such as TD-0148A represent a promising alternative."

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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).

## **Contact Information**

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