



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

Item 1 Name and Address of Company

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

Item 2 Date of Material Change

September 2021

Item 3 News Releases

News releases dated September 22, September 27 and September 29, 2021.

Item 4 Summary of Material Change

TD-0148A

The Company applied for patent protection of new compositions of 2-bromo-LSD ("TD-0148A") for its use in the treatment of cluster headaches, neuropathic pain and range of mental health conditions, including depression, anxiety and PTSD, and related disorders. The Company is developing one of the new compositions of 2-bromo-LSD covered by its newly filed provisional patent application. TD-0148A is a second-generation lysergic acid diethylamide ("LSD") derivative molecule that does not cause hallucinations, and therefore not subject to controlled substance regulations. In addition, the synthesis of TD-1048A is via non-controlled substance synthetic routes and therefore not subject to controlled substance regulatory restrictions. The Company is in advanced stages of GMP manufacturing of TD-0148A and initiated the necessary preclinical IND-enabling studies for TD-0148A. TD-0148A is currently in preclinical pharmacology and other IND-enabling studies.

The Company also obtained its first set of neurological receptor binding data on TD-0148A. The data were generated by Eurofins Discovery. The receptor binding data show binding of TD-0148A to neurological receptors which are known to play key roles in neuro-psychiatric disorders. Significant TD-0148A binding was seen to receptors such as 5-hydroxytryptamine (serotonin) receptors (5-HT_{1A}, 5-HT_{2A}, 5-HT_{2B}, and 5-HT_{2C}), alpha-adrenergic receptors (alpha-1A, -2A, -2B, and -2C), beta-adrenergic receptors (beta-1, and -2), and dopamine receptors (D₁ and D_{2S}). In contrast, there is none to limited binding to receptors such as 5-HT₃, GABA-A₁, and NMDA receptors. Additional preclinical studies are underway to further determine the functional outcome of the TD-0148A binding at these receptors (where possible, outcomes include agonism, antagonism, mixed or no effect).

AP-003

In September 2021, the Company's wholly owned subsidiary, Altum Pharmaceuticals Inc. ("Altum"), and Pontificia Universidad Católica de Chile enrolled the first patient in the Phase 1 portion of the Phase 1-2 randomized placebo controlled ("IN2COVID") in

COVID-19 patients. The trial tests the Company's proprietary inhaled interferon alpha-2b product, AP-003. The IN2COVID trial (ClinicalTrials.gov Identifier: [NCT04988217](https://clinicaltrials.gov/ct2/show/study/NCT04988217)) consists of a randomized placebo Phase 1 portion in healthy subjects followed by a randomized placebo-controlled Phase 2 portion in early stage COVID-19 patients (<5 days of diagnosis of COVID-19). The IFN- α 2b treatment arms will receive BetterLife's proprietary inhaled IFN- α 2b product, AP-003, administered via nebulizer, twice daily for 10 days.

Corporate

During September 2021, the Company appointed Mr. David Melles as its Investor Relations Manager.

On September 27 and 28, 2021, the Company granted 30,000 stock options with exercise prices between \$0.27 and \$0.28 and expiry dates of December 31, 2022 and September 27, 2023 to consultants. The Company also issued, on September 27, 2021, 238,095 share purchase warrants to a company with a common director. The share purchase warrants have an exercise price of \$0.27 and expires on September 26, 2023.

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

September 29, 2021

SCHEDULE "A"



BetterLife Enrolls First Patient in Interferon alpha-2b COVID-19 Trial in Chile

VANCOUVER, British Columbia, September 22, 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 enrolled the first patient in the Phase 1 portion of the Phase 1-2 randomized placebo controlled (“IN2COVID”) in COVID-19 patients. The trial tests BetterLife’s proprietary inhaled interferon alpha-2b product, AP-003.

The IN2COVID trial (ClinicalTrials.gov Identifier: [NCT04988217](#)) consists of a randomized placebo Phase 1 portion in healthy subjects followed by a randomized placebo-controlled Phase 2 portion in early stage COVID-19 patients (<5 days of diagnosis of COVID-19). The IFN- α 2b treatment arms will receive BetterLife’s proprietary inhaled IFN- α 2b product, AP-003, administered via nebulizer, twice daily for 10 days.

“We are excited to be able to initiate this trial of 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. “The team, as well as the trial center, are the leaders in Chile in conducting COVID-19 trials.”

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, “We are pleased to be partnering with Altum to bring AP-003 to COVID-19 patients.” He added, “There are several reasons why there is a need for an effective, easy to administer, non-invasive treatment, such as AP-003, for COVID-19. These reasons include: emergence of SARS-CoV-2 variants, not knowing the duration of protection afforded by the current vaccines and the reality of breakthrough infections in vaccinated individuals.”

Dr. Eleanor Fish, one of the Principal Investigators of the trial, commented, “AP-003, being a Type I interferon, is a broad acting antiviral agent and, therefore, may be effective in all the scenarios described by my colleague Dr. Borzutzky.” Dr. Fish is a Professor in the Department of Immunology, University of Toronto, and Emerita Scientist at the Toronto General Hospital Research Institute, University Health Network. Dr. Fish is the principal author of the exploratory trial published in 2020 in Frontiers of Immunology titled “Interferon- α 2b Treatment for COVID-19”, which examined the outcome of treating a cohort of 77 individuals with confirmed COVID-19 admitted to Union Hospital, Wuhan, China, with inhaled interferon- α 2b. The study revealed the therapeutic benefits of Interferon- α 2b treatment in patients with early COVID-19. The authors concluded that a randomized clinical trial was warranted in moderate cases of COVID-19 and “treatment with IFN- α 2b may benefit public health measures aimed at slowing the tide of this pandemic, in that this exploratory study demonstrated that duration of viral shedding was shortened, and lung abnormalities and systemic inflammation were significantly reduced.” The current IN2COVID trial in Chile was designed to test these.

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.

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>.

About University Health Network

University Health Network consists of Toronto General and Toronto Western Hospitals, the Princess Margaret Cancer Centre, Toronto Rehabilitation Institute, and The Michener Institute of Education at UHN. The scope of research and complexity of cases at University Health Network has made it a national and international source for discovery, education and patient care. It has the largest hospital-based research program in Canada, with major research in arthritis, cardiology, transplantation, neurosciences, oncology, surgical innovation, infectious diseases, genomic medicine and rehabilitation medicine. University Health Network is a research hospital affiliated with the University of Toronto.

For more information, visit: www.uhn.ca



Contact Information

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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.



BetterLife Files Patent for TD-0148A for Treatment of Cluster Headaches and Related Disorders

VANCOUVER, British Columbia, September 27, 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 applied for patent protection of new compositions of 2-bromo-LSD for its use in the treatment of cluster headaches, neuropathic pain and range of mental health conditions, including depression, anxiety and PTSD, and related disorders.

BetterLife is developing one of the new compositions of 2-bromo-LSD (“TD-0148A”) covered by its newly filed provisional patent application. TD-0148A is a second-generation lysergic acid diethylamide (“LSD”) derivative molecule that does not cause hallucinations, and therefore not subject to controlled substance regulations. In addition, the synthesis of TD-1048A is via non-controlled substance synthetic routes and therefore not subject to controlled substance regulatory restrictions.

BetterLife is already in advanced stages of GMP manufacturing TD-0148A and initiated the necessary preclinical IND-enabling studies for TD-0148A. TD-0148A is currently in preclinical pharmacology and other IND-enabling studies and in 2022, BetterLife will file its IND and start Phases 1 and 2 in healthy subjects for major depressive disorder.

Ahmad Doroudian, CEO of BetterLife, commented, “The inventions covered by this provisional patent filing hold great promise, and helps us advance on our path to becoming a leader in the psychedelic drug space which is estimated to become a US\$6.85-billion industry by 2027. We are excited to be developing and bringing to market treatments addressing cluster headaches, neuropathic pain and range of mental health conditions, including depression, anxiety and PTSD, and related disorders.”

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 the only 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, migraines, 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 www.abetterlifepharma.com.

Contact Information

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BetterLife Obtains TD-0148A Receptor Binding Data for IND-Enabling Pharmacology Studies

VANCOUVER, British Columbia, September 29, 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 it has obtained its first set of neurological receptor binding data on its lead compound, 2-bromo-LSD (“TD-0148A”). The data were generated by Eurofins Discovery.

TD-0148A is a second-generation Lysergic Acid Diethylamide (“LSD”) derivative molecule that BetterLife believes will mimic the projected therapeutic potential of LSD without causing undesirable psychoactive dissociative side effects, such as hallucinations. The receptor binding data show binding of TD-0148A to neurological receptors which are known to play key roles in neuro-psychiatric disorders. Significant TD-0148A binding was seen to receptors such as 5-hydroxytryptamine (serotonin) receptors (5-HT1A, 5-HT2A, 5-HT2B, and 5-HT2C), alpha-adrenergic receptors (alpha-1A, -2A, -2B, and -2C), beta-adrenergic receptors (beta-1, and -2), and dopamine receptors (D1 and D2S). In contrast, there is none to limited binding to receptors such as 5-HT3, GABA-A1, and NMDA receptors. Additional preclinical studies are underway to further determine the functional outcome of the TD-0148A binding at these receptors (where possible, outcomes include agonism, antagonism, mixed or no effect).

These TD-0148A receptor binding studies are being conducted by Eurofins Discovery at its state-of-the-art facilities at Eurofins Cerep, DiscoverX and Panlabs. “We are pleased to be partnering with Eurofins Discovery and the global Eurofins Discovery team for these TD-0148A primary and safety pharmacology studies as part of TD-0148A’s IND-enabling preclinical data package. TD-0148A is a potential novel new therapy to treat debilitating psychiatric and neurological disorders with high unmet need, such as depression, post-traumatic stress disorder and cluster headaches. As the lead compound in BetterLife’s neuro-psychiatric pipeline, and protected by several BetterLife owned patents (granted and provisional), BetterLife is fully focused to bring TD-0148A to US IND and the clinic as soon as possible,” said BetterLife’s Chief Executive Officer, Dr. Ahmad Doroudian.

BetterLife also announces the appointment of Mr. David Melles as Investor Relations Manager. “We are very pleased to welcome David Melles to our team. His experience in the investor relations field will be extremely valuable to BetterLife’s progress,” said Dr. Doroudian.

As an experienced investor relations professional, Mr. Melles comes to BetterLife with an extensive track record of financial market understanding, global business know-how, and thorough research capabilities. Over the last number of years, he has developed customized sales funnel activities, produced timely industry research/reporting, and delivered optimized marketing strategies in both the North American and Japanese marketplace. Lastly, his financial market experience, from sell-side to buy-side, will be a great complement to the existing team.

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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 www.abetterlifepharma.com.

About Eurofins Discovery

Eurofins Discovery, a business operating under the Eurofins BioPharma Services division, has supported drug discovery research for over 40 years. Eurofins is recognized as the industry leader for providing drug discovery researchers the largest and most diverse portfolio of standard and custom in-vitro safety and pharmacology assays and panels for drug screening and profiling. In addition to in-vitro safety pharmacology strengths, Eurofins Discovery also offer a broad portfolio of over 3500 drug discovery services and 1800 products. These include in-vitro assays, cell-based phenotypic assays, safety pharmacology and efficacy, ADME toxicology, medicinal chemistry design, synthetic chemistry, and custom proteins and assay development capabilities. Eurofins Discovery supports a variety of drug discovery targets such as GPCRs, Kinases, Ion Channels, Nuclear Hormone Receptors and other proteins and enzymes. The Eurofins Discovery capabilities, expertise, knowledge and skill sets enable it to provide clients the benefit of being able to work with a single outsourcing provider for all their drug discovery programs.

For more information, please visit: <https://www.eurofinsdiscoveryservices.com/>

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