Bright Minds Biosciences Announces Positive qEEG (Quantitative Electroencephalogram) Data from its First-in-Human Phase 1 Study of Lead Compound, BMB-101

-- BMB-101 is a highly selective and potent 5-HT_{2C} agonist being developed for the treatment of refractory epilepsies and other indications, such as psychosis, addiction, and impulse control disorders

-- qEEG study was conducted in healthy individuals in Cohort 4 of the Multiple Ascending Dose arm of the study

-- Proof of Mechanism and target engagement in the brain was established using blood biomarkers and qEEG

-- In qEEG, BMB-101 demonstrated robust increase in central delta power and robust reduction in central alpha and beta power in active group, as previously reported for Anti-Epileptic Drugs (AEDs) in healthy individuals

-- Company to host webcast to discuss findings of the Phase 1 study today, August 8, 2023, at 4:30pm ET

VANCOUVER, British Columbia, Aug. 08, 2023 -- Bright Minds Biosciences Inc. (CSE:DRUG) (NASDAQ:DRUG) ("**Bright Minds**" or the "**Company**"), a biotechnology company focused on developing novel drugs for the targeted treatment of neuropsychiatric disorders and refractory epilepsy, today announced positive results of the qEEG (Quantitative Electroencephalogram) data in Cohort 4 of its first-in-human Phase 1 study of its lead compound, BMB-101. On July 20, 2023, the Company announced completion of the study, along with positive topline data that demonstrated BMB-101's excellent safety and tolerability profile in the single ascending dose, multiple ascending dose and food effects parts of the study. BMB-101 also demonstrated central target engagement and predictable plasma pharmacokinetics.

In the qEEG study, BMB-101 demonstrated:

- Central target engagement, as the treatment group was easily identified in blinded data using qEEG power signature.
- A robust increase in central delta power and robust reduction in central alpha and beta power in active group, as previously reported for Anti-Epileptic Drugs (AEDs) in healthy individuals.
- Increased gamma frontal parietal connectivity in treatment group. This constitutes an improved AED principle over benzodiazepine (GABA receptor) AED drugs.
- Power and connectivity changes were concentration dependent.

"The positive topline findings from our recently completed Phase 1 study of BMB-101, together with the observations from the qEEG portion of the study, validate our approach, as we continue to evaluate this important product candidate. BMB-101 is clearly [getting into the brain/achieving brain penetration] and activating the target receptors as we had predicted, setting us up for potential success in a number of indications that have been validated with the 5-HT_{2C} mechanism. With this study complete, BMB-101 is now a Phase 2 ready asset, and we intend to move forward with an investigative new drug submission immediately," stated Ian McDonald, CEO of Bright Minds.

"We are especially pleased that BMB-101 has demonstrated central target engagement by transient prolactin increase, and qEEG changes. The treatment group was readily identified in blinded data using the qEEG power signature. In addition, increased frontal gamma power represents an improved AED principle over [existing] benzodiazepine (GABA receptor) AED drugs. We believe that BMB-101 has the potential to be a best-in-class, novel pharmacophore 5-HT_{2C} agonist for the treatment of seizure disorders, and our team is committed to advancing this product candidate for application where serotonin 2C agonists would be useful," said Jan Torleif Pedersen, PhD, MSc, Chief Science Officer of Bright Minds.

During the EEG recording, subjects were seated with a U.S. Food and Drug Administration (FDA)- approved 19 electrode EEG headset provided by Zeto™ Inc. Channels were sampled at 250 or 500 Hz and referenced to A1/A2 channels (linked-ears reference) during recording. The EEG recording time was 10 minutes (~5 minutes resting with eyes closed and ~5 minutes resting with eyes open). There were four EEG recording timepoints: day 1 pre-dose (immediately before dosing) and post-dose (1h after dosing), and day 7 pre-dose and post-dose. Data were analyzed using the FireFly Neuroscience advanced EEG analysis platform.

BMB-101 is a highly selective and potent 5-HT_{2C} agonist being developed for the treatment of refractory epilepsies and other indications, such as psychosis, addiction, and impulse control disorders. BMB-101 demonstrated an excellent safety and tolerability profile. 5-HT_{2C} target engagement was demonstrated by transient, dose-dependent increases in prolactin. BMB-101 exhibited predictable plasma pharmacokinetics with relatively small inter-individual variability. The current formulation allows for twice-a-day oral dosing, and with further formulation development, there may be potential for once-a-day dosing. Based on these observations, the Company believes that moderate doses of BMB-101 will fully engage 5-HT_{2C} receptors, and therefore

not be dose-limited by side effects, which will help to achieve maximal efficacy in future Phase 2 studies. Dose limited side effects exhibited by first generation 5-HT_{2C} agonists have prevented exploiting the full potential of this pharmacological mechanism.

The Phase 1 study was conducted in Adelaide, Australia, by CMAX Clinical Research, a clinical trial center specializing in a range of early-phase trials and first-in-human studies. The study evaluated the safety, tolerability, pharmacokinetic (PK), and food effect of BMB-101 in healthy volunteers.

About the Phase 1 Study

Part 1 – Single Ascending Dose

- 4 cohorts (6 drug and 2 placebo) – single dose (oral solution)
- Reached the planned top dose of 180 mg/70 kg, which approached preclinical exposure limits
- Well tolerated with predictable PK
- Most common adverse event was oral paresthesias from liquid formulation

Part 2 – Food Effect

- 12 subjects – crossover with and without breakfast, 120 mg/70kg
- Effect of food on BMB-101 levels was relatively small, and therefore BMB-101 can be administered without the need for fasting

Part 3 – Multiple Ascending Dose

- 4 cohorts (6 drug and 2 placebo) – twice a day dosing for seven days after meals
    - Reached a top dose of 150 mg/70 kg twice a day
- Biomarkers for central target engagement: Prolactin release and qEEG

Good Manufacturing Practices (GMP) production completed for BMB-101 drug substance and drug product.

Webcast Information

Bright Minds management will host a webcast to discuss the Phase 1 study as follows:

Date:	Tuesday, August 8, 2023
Time:	4:30pm ET
Webcast link:	Click here

About BMB-101

BMB-101, a highly selective 5-$HT_{2C,}$ Gq-protein biased agonist, has demonstrated compelling activity in a host of *in vitro* and *in vivo* nonclinical tests. Compared to Lorcaserin, BMB-101 exhibits strong Gq biased signaling, coupled with minimal beta-arrestin recruitment. Bright Minds believes that G-protein biased signaling translates to better tolerance profile for this second-generation 5-HT_{2C} agonist, making BMB-101 a best-in-class 5-HT_{2C} agonist. Mechanistically, Serotonin (5-Hydroxytryptamine, 5-HT) is a monoamine neurotransmitter widely expressed in the central nervous system, and drugs modulating 5-HT have made a major impact in mental health disorders. Central 5-HT systems have long been associated with the control of ingestive behaviors and the modulation of the behavioral effects of psychostimulants, opioids, alcohol, and nicotine. Results of clinical trials and animal studies indicate that 5-HT_{2C} receptor agonists may have therapeutic potential in the treatment of addiction by decreasing the intake of opioids as well as impulsive behavior that can escalate compulsive drug use. BMB-101 is a new chemical entity (NCE) and constitutes a novel scaffold 5-HT_{2C} agonist.

5-HT_{2C} agonism is a well proven anticonvulsant mechanism. In translational animal models, BMB-101 demonstrated a significant reduction in both the number and intensity of epileptic seizures and is a promising candidate for the treatment of Dravet Syndrome and other epilepsies. The Phase 1 trial (NCT 05397041) has been completed and BMB-101 is now Phase 2 ready.

About Bright Minds

Bright Minds is focused on developing novel transformative treatments for neuropsychiatric disorders, epilepsy, and pain. Bright Minds has a portfolio of next-generation serotonin agonists designed to target neurocircuit abnormalities that are responsible for difficult to treat disorders such as treatment resistant epilepsy, treatment resistant depression, PTSD, and pain. The Company leverages its world-class scientific and drug development expertise to bring forward the next generation of safe and efficacious drugs. Bright Minds' drugs have been designed to potentially retain the powerful therapeutic aspects of psychedelic and other serotonergic compounds, while minimizing the side effects, thereby creating superior drugs to first-generation compounds, such as fenfluramine, psilocybin, LSD, and ibogaine.

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This news release includes certain statements that may be deemed "forward-looking statements." All statements in this new release, other than statements of historical facts, that address events or developments that the Company expects to occur, are forward-looking statements. Forward-looking statements are statements that are not historical facts and are generally, but not always, identified by the words "expects," "plans," "anticipates," "believes," "intends," "estimates," "projects," "potential," and similar expressions, or that events or conditions "will," "would," "may," "could," or "should" occur. Forward-looking information in this news release includes statements related to potential future success in indications that have been validated with the 5-HT2C mechanism, the implementation of Phase 2 trials for BMB-101 and the submission of applications related to the same, BMB-101 becoming a best-in-class, novel pharmacophore 5-HT_{2C} agonist for the treatment of seizure disorders, and plans for future formulation development including to achievement of once-a-day dosing in respect of BMB-101. Although the Company believes the expectations expressed in such forward-looking statements are based on reasonable assumptions, such statements are not guarantees of future performance and actual results may differ materially from those in the forward-looking statements. Factors that could cause the actual results to differ materially from those in forward-looking statements include continued availability of capital and financing, results of Phase 2 clinical trials with respect to BMB-101 and other compounds that the Company may seek to test in the future, results of further development activities related to dosing and the findings specifically related to once-a-day dosing, regulatory conditions with respect to in-human drug trials, and general economic, market or business conditions. Investors are cautioned that any such statements are not guarantees of future performance and actual results or developments may differ materially from those projected in the forward-looking statements. Forward-looking statements are based on the beliefs, estimates and opinions of the Company's management on the date the statements are made. Except as required by applicable securities laws, the Company undertakes no obligation to update these forward-looking statements in the event that management's beliefs, estimates or opinions, or other factors, should change.

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