Bright Minds Biosciences Initiates the BREAKTHROUGH Study: A Phase 2 Trial of BMB-101 in Absence Epilepsy and Developmental Epileptic Encephalopathy

- *Bright Minds Biosciences announces Phase 2 Clinical trial to evaluate BMB-101 in a group of drug-resistant epilepsy disorders with high unmet needs*
- *BMB-101 is a novel highly selective 5-HT2C agonist. Its G-protein biased agonism provides an improved mechanism of action for chronic dosing*
- *Financial runway extending into 2026 enabling key data readout*
- *Conference call & KOL Event – will be held as a webcast on September 25th at 10:00 ET*

NEW YORK, September 12, 2024 – Bright Minds Biosciences Inc. (NASDAQ: DRUG), a biotechnology company focused on developing novel therapies for neurological and neuropsychiatric disorders, today announced the initiation of the BREAKTHROUGH Study, an open-label Phase 2 clinical trial evaluating the safety, tolerability, and efficacy of BMB-101, a highly selective 5-HT2C receptor agonist, in adult patients with classic Absence Epilepsy and Developmental Epileptic Encephalopathy (DEE).

Trial Design:

The BREAKTHROUGH study is designed as a basket clinical trial that will include patients diagnosed with either Absence Epilepsy (with or without Eyelid Myoclonia) or a DEE. This group of disorders consists of a range of rare epilepsy disorders, including Epilepsy with Eyelid Myoclonia (known as Jeavons Syndrome). These conditions are characterized by refractory seizures that are often resistant to current treatments. The BREAKTHROUGH study is targeting enrollment of 20 adult participants aged from 18 to 65 years old.

- Study Duration: The trial includes a 4-week baseline period where seizure activity will be monitored and recorded to establish each participant's baseline seizure frequency and EEG patterns. This will be followed by an 8-week (Absence epilepsy group) to 12-week (DEE group) treatment phase where participants will receive BMB-101. The study will conclude with a 4-week follow-up period to monitor for any lasting effects after the cessation of the drug.

Endpoints: The study's objectives are to assess the safety, tolerability and efficacy of BMB-101. The primary efficacy endpoints are to evaluate the change in frequency of generalized spike-wave discharges (GSWD) on 24-hour electroencephalogram (EEG) in participants with Absence Epilepsy and the change in seizure frequency on a daily seizure diary in participants with a DEE compared to the baseline period.

- **Open-Label Extension:** There will be a planned open-label extension trial lasting at least another 12 months that will be an option for all subjects who respond to BMB-101 as agreed upon by their physician.

“We are excited to advance BMB-101 into this next phase of clinical development as we continue to build on the promising safety and pharmacodynamic data from our Phase 1 trial,” said Ian McDonald, Chief Executive Officer of Bright Minds Biosciences. “With its unique pharmacological profile, we believe BMB-101 has the potential to be a best-in-class 5-HT2C agonist. In our Phase 1 study, we demonstrated central target engagement, which, in conjunction with the wealth of 5-HT2C data within refractory epilepsies, gives us great confidence in this study. This compound is not only poised to make a significant impact in both the DEE and Absence Epilepsy communities but also has broad applicability across the 30% of all epilepsy patients who experience drug resistance. BMB-101 offers a differentiated treatment option for patients with refractory epilepsy, where current therapies often fall short, and could provide a new standard of care for a much wider population of epilepsy sufferers. We would like to thank the AECTN and the Epilepsy Study Consortium for their contributions to our upcoming study.”

Corporate Update

Bright Minds remains committed to advancing the pipeline of novel treatments for patients with significant unmet needs in neurological disorders. Our financial position is expected to allow the completion of the BREAKTHROUGH Study and sustain operations into 2026. This financial stability allows us to maintain momentum in our clinical programs and continue exploring additional indications for BMB-101 and other assets in our pipeline.

Bright Minds is exploring the use of 5-HT2C compounds in eating disorders and the management of obesity. Bright Minds will also continue to advance its 5-HT2A and 5-HT2A/C programs within neuropsychiatric disorders with a focus on major depressive disorder, treatment-resistant depression and generalized anxiety disorder.

Investor Call

Bright Minds Biosciences will host an investor call on September 25, 2024 at 10:00 ET to discuss the BREAKTHROUGH Study. The call will feature key opinion leaders (KOLs) in the

field of epilepsy who will provide insights into the significance of the BREAKTHROUGH Study and the potential impact of BMB-101 on the treatment landscape.

Registration and Participant Details:

Investors and interested parties can register for the call HERE or by visiting the Bright Minds Biosciences website at www.brightmindsbio.com. A replay of the call will be available following the event.

About BMB-101

BMB-101 is a novel scaffold 5-HT2C Gq-protein biased agonist developed using structure-based drug design. It was explicitly designed for chronic treatment of neurological disorders where tolerance and drug resistance are common issues. Biased agonism at the 5-HT2C receptor is one of its key features and adds another layer of functional selectivity within a well-validated target. BMB-101 works exclusively via the Gq-protein signaling pathway and avoids beta-arrestin activation, which is crucial to minimize the risk of receptor desensitization and tolerance development. This provides a novel mechanism, anti-epileptic drug designed to provide sustained seizure relief in hard-to-treat patient populations. In preclinical studies, BMB-101 has demonstrated efficacy in animal models of Dravet Syndrome and numerous models of generalized seizures.

In Phase 1 clinical studies, BMB-101 was given to 64 healthy volunteers in a Single Ascending Dose (SAD), Multiple Ascending Dose (MAD) and food-effects study. BMB-101 was demonstrated to be safe and well tolerated at all doses. No Serious Adverse Events (SAEs) were observed, and Adverse Events (AEs) were mild in nature and in line with on-target effects for serotonergic drugs.

An extensive target-engagement study was conducted using both fluid biomarkers (transient prolactin release) and physical biomarkers (Quantitative Electroencephalogram, qEEG). Both methods confirmed robust central target engagement. A qEEG signature typical for anti-epileptic drugs was observed, with a selective depression of EEG power at frequencies observed during epileptic seizures. Furthermore, a potentiation of frontal gamma-power was observed in this study which could indicate the potential for improved cognition.

About Bright Minds Biosciences

Bright Minds Biosciences is a biotechnology company developing innovative treatments for patients with neurological and psychiatric disorders. Our pipeline includes novel compounds targeting key receptors in the brain to address conditions with high unmet medical need, including epilepsy, depression, and other CNS disorders. Bright Minds is focused on delivering breakthrough therapies that can transform patients' lives.

Bright Minds Biosciences has developed a unique platform of highly selective serotonergic agonists exhibiting selectivity at different serotonergic receptors. This has provided a rich portfolio of NCE programs within neurology and psychiatry.

Forward-Looking Statements

This news release contains "forward-looking information". Often, but not always, forward-looking statements can be identified by the use of words such as "plans", "expects", "is expected", "budget", "scheduled", "estimates", "forecasts", "intends", "anticipates", or "believes" or variations (including negative variations) of such words and phrases, or state that certain actions, events or results "may", "could", "would", "might" or "will" be taken, occur or be achieved. Forward-looking statements in this news release include design, progress, and completion of the BREAKTHROUGH *Study, future clinical development of BMB-101, and future intended use or therapeutic benefit of BMB-101 to treat refractory epilepsy disorders. A variety of factors, including known and unknown risks, many of which are beyond our control, could cause actual results to differ materially from the forward-looking information in this news release. These factors include the company's financial position and operational runway, regulatory risk to operating in the pharmaceutical industry, and inaccuracies related to the assumption made by management relating to general availability of resources required to operate the studies noted in this news release. Additional risk factors can also be found in the Company's public filings under the Company's SEDAR+ profile at www.sedarplus.ca. Forward-looking statements contained herein are made as of the date of this news release and the Company disclaims any obligation to update any forward-looking statements, whether as a result of new information, future events or results or otherwise. There can be no assurance that forward-looking statements will prove to be accurate, as actual results and future events could differ materially from those anticipated in such statements. The Company undertakes no obligation to update forward-looking statements if circumstances, management's estimates or opinions should change, except as required by securities legislation.*

Accordingly, the reader is cautioned not to place undue reliance on forward-looking statements.

The Canadian Securities Exchange has neither approved nor disapproved the information contained herein and does not accept responsibility for the adequacy or accuracy of this news release.

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