Small Pharma Reports Positive Top-line Data from SPL026 (DMT)-SSRI Drug Interaction Study in Patients with Major Depressive Disorder

September 27, 2023

- Cybin to acquire Small Pharma Inc. in a previously announced all-share transaction expected to close in Q4 2023, creating an international clinical-stage leader in novel psychedelic therapeutics with the largest IP portfolio in the sector -

- Results suggest that SSRIs enhance the efficacy of SPL026 (DMT) when administered to MDD patients on a stable dose of SSRIs versus patients not on SSRIs -

- At Week 4, 100% of patients in the SSRI cohort responded to SPL026 (DMT) with 92% of patients in remission from depression -

- No apparent differences in the safety and tolerability profile of SPL026 (DMT) following administration to participants in the SSRI and non-SSRI patient cohorts -

TORONTO--(BUSINESS WIRE)-- Cybin Inc. (NYSE American:CYBN) (NEO:CYBN) ("**Cybin**" or the " **Company**"), a clinical-stage biopharmaceutical company committed to revolutionizing mental healthcare by developing new and innovative psychedelic-based treatment options, commends Small Pharma Inc. ("Small Pharma"), a biotechnology company focused on short-duration psychedelic-assisted therapies for mental health conditions, on its positive safety, tolerability and efficacy data from its Phase Ib study exploring the interaction between selective serotonin reuptake inhibitors ("SSRIs") and SPL026, native N, N-dimethyltryptamine ("DMT"), in patients with Major Depressive Disorder ("MDD").

Doug Drysdale, Chief Executive Officer of Cybin, said: "With our upcoming acquisition of Small Pharma, we are excited to share its announcement of new data demonstrating that a DMT therapeutic is safe and enhances antidepressant efficacy in patients on SSRIs. This is impressive especially when combined with previously reported Phase IIa SPL026 efficacy data in MDD showing a rapid antidepressant effect and sustained remission to six months. Together, these results provide strong proof-of-concept and give us further reason to believe in the synergistic power of our combined programs, upon the closing of the transaction expected in the fourth quarter of 2023."

The purpose of the Small Pharma study was to build upon the previously reported Phase I/IIa safety and efficacy profile of SPL026 with support therapy, to assess whether SPL026 can be safely administered with or without SSRIs – the current standard of care for MDD. In the Phase I/IIa SPL026 study, patients were required to be withdrawn from SSRIs, which can be a disruptive experience. Through the SPL026-SSRI drug interaction study, Small Pharma aimed to address this requirement, which could enable broader patient recruitment on future large-scale studies, and potentially accelerate the clinical development pathway. Additionally, removing the requirement to be withdrawn from SSRIs may facilitate patient access to SPL026 earlier in the MDD treatment journey, if approved.

This open-label study investigated the safety, tolerability, pharmacokinetics, pharmacodynamics and exploratory efficacy of a single 27.5 mg intravenous infusion of SPL026, alone or in combination with SSRIs, in 17[1] patients, together with support therapy. The test cohort (N=12) (the "SSRI Cohort") consisted of patients currently on a stable treatment course of SSRIs, which have been ineffective in fully relieving their depression symptoms. The control cohort (N=5) (the "Non-SSRI Cohort") consisted of patients not currently using any pharmacological treatment to treat their depression symptoms. Patients were recruited with moderate-severe MDD as defined by a Hamilton Depression Rating Scale (HAM-D) score of ≥14. Efficacy was assessed using the Montgomery-Asberg Depression Rating scale (MADRS) to measure any change in patients' depression symptoms from baseline. Additional exploratory endpoints include the Beck Depression Inventory (BDI) to assess patients' self-reported depression.

Key Results

Safety & Tolerability

- SPL026 was well-tolerated by all patients in both the SSRI Cohort and Non-SSRI Cohort, with no apparent differences between cohorts
- No drug-related serious adverse events reported
- A small number of drug-related adverse events ("AEs") reported
    - 8 in SSRI Cohort
    - 3 in Non-SSRI Cohort
    - All deemed to be mild or moderate in severity

- Majority of drug-related AEs were resolved during the dosing visit

Exploratory Efficacy

The results reaffirmed the efficacy initially demonstrated in the Phase IIa SPL026 study. However, a marked improvement was observed between the antidepressant effect of SPL026 treatment in the SSRI Cohort compared to the Non-SSRI Cohort. While the efficacy observed in the Non-SSRI Cohort was comparable to the efficacy data previously observed in Small Pharma's SPL026 Phase IIa clinical trial, the antidepressant effects observed in the SSRI Cohort were of a greater magnitude, suggesting a potentially enhanced efficacy effect when SPL026 is administered in combination with SSRIs.

The following chart outlines the efficacy results in both cohorts at baseline and at Week 4 following the dose of SPL026 with support therapy:

	Baseline		**Week 4**	
	SSRI cohort (n=12)	**Non-SSRI cohort** (n=5)	**SSRI cohort** (n=12)	**Non-SSRI cohort** (n=5)
Mean MADRS	28.8	35.4	3.0	16.0
Response* %	-	-	100%	80%
Remission* %	-	-	92%	20%
Mean BDI	30.0	36.0	3.1	14.8

**__Response__: ≥50% reduction in MADRS from baseline; __Remission__: MADRS score ≤10*

Dr. Carol Routledge, Chief Medical and Scientific Officer of Small Pharma, said: "Our primary goal in conducting this Phase Ib study was to understand if SPL026 could be safely administered in conjunction with SSRIs to assess whether patients would need to be withdrawn from their SSRI medication in future trials. While we were very pleased that the study demonstrated that patients may not need to be withdrawn, we were not expecting to see such a marked difference in efficacy when administering SPL026 in combination with SSRIs compared to SPL026 alone. The potentially enhanced efficacy effect of a DMT-based treatment when administered with SSRIs could lead to greater therapeutic benefit for patients, and a compelling argument for positioning it earlier in the treatment pathway. This was a small study, but the findings are both interesting and encouraging and warrant further exploration."

George Tziras, Chief Executive Officer of Small Pharma, said: "These positive safety and tolerability results further support the patient access strategy for our DMT programs. There may be potential in the future to safely deliver a DMT-based treatment to patients on SSRIs that do not adequately relieve their depression symptoms. Moreover, the marked antidepressant effect seen in the SSRI patient cohort indicates the potential for a combination treatment. We look forward to exploring these findings further as part of the integrated DMT program with Cybin, subject to completion of the proposed arrangement transaction."

About Cybin

Cybin is a clinical-stage biopharmaceutical company on a mission to create safe and effective psychedelic-based therapeutics to address the large unmet need for new and innovative treatment options for people who suffer from mental health conditions.

Cybin's goal of revolutionizing mental healthcare is supported by a network of world-class partners and internationally recognized scientists aimed at progressing proprietary drug discovery platforms, innovative drug delivery systems, and novel formulation approaches and treatment regimens. The Company is currently developing CYB003, a proprietary deuterated psilocybin analog for the treatment of major depressive disorder and CYB004, a proprietary deuterated DMT molecule for generalized anxiety disorder and has a research pipeline of investigational psychedelic-based compounds.

Headquartered in Canada and founded in 2019, Cybin is operational in Canada, the United States, the United Kingdom, the Netherlands and Ireland. For company updates and to learn more about Cybin, visit www.cybin.com or follow the team on X, LinkedIn, YouTube and Instagram.

About Small Pharma

Small Pharma is a biotechnology company progressing a pipeline of short-duration psychedelic-assisted therapies for the treatment of mental health conditions. Small Pharma has a portfolio of clinical-stage DMT-based assets, SPL026 and SPL028. The Company was granted an Innovation Passport designation for SPL026 from the U.K. Medicines and Healthcare products Regulatory Agency (the "MHRA") and has a pipeline of proprietary preclinical assets.

Footnotes:

[1] Total study sample of 18. However, 17 participants were evaluable.

Cautionary Notes and Forward-Looking Statements

Certain statements in this news release relating to the Company and Small Pharma are forward-looking statements and are prospective in nature. Forward-looking statements are not based on historical facts, but rather on current expectations and projections about future events and are therefore subject to risks and uncertainties which could cause actual results to differ

materially from the future results expressed or implied by the forward-looking statements. These statements generally can be identified by the use of forward-looking words such as “may”, “should”, “could”, “intend”, “estimate”, “plan”, “anticipate”, “expect”, “believe” or “continue”, or the negative thereof or similar variations. Forward-looking statements in this news release include statements regarding impacts on Small Pharma’s strategy as a result of the results of the Phase Ib study; the potential enhanced efficacy effect of a DMT-based treatment when administered with SSRIs, and the impact of same, including enabling broader patient recruitment on future large-scale studies, potentially accelerating the clinical development pathway, a greater therapeutic benefit for patients and facilitating patient access to SPL026 earlier in the MDD treatment journey; the potential approval to allow patients; the potential for a combination treatment with SSRIs and SPL026; completion and timing of the proposed arrangement transaction between Small Pharma and Cybin; and Cybin’s proprietary drug discovery platforms, innovative drug delivery systems, novel formulation approaches and treatment regimens for mental health disorders.

These forward-looking statements are based on reasonable assumptions and estimates of management of the Company at the time such statements were made. Actual future results may differ materially as forward-looking statements involve known and unknown risks, uncertainties, and other factors which may cause the actual results, performance, or achievements of the Company to materially differ from any future results, performance, or achievements expressed or implied by such forward-looking statements. Such factors, among other things, include: implications of the spread of COVID-19 on the Company's operations; fluctuations in general macroeconomic conditions; fluctuations in securities markets; expectations regarding the size of the psychedelics market; the ability of the Company to successfully achieve its business objectives; plans for growth; political, social and environmental uncertainties; employee relations; the presence of laws and regulations that may impose restrictions in the markets where the Company operates; and the risk factors set out in each of the Company's management's discussion and analysis for the three months ended June 30, 2023, and the Company’s annual information form for the year ended March 31, 2023, which are available under the Company's profile on SEDAR+ at www.sedarplus.ca and with the U.S. Securities and Exchange Commission on EDGAR at www.sec.gov. Although the forward-looking statements contained in this news release are based upon what management of the Company believes, or believed at the time, to be reasonable assumptions, the Company cannot assure shareholders that actual results will be consistent with such forward-looking statements, as there may be other factors that cause results not to be as anticipated, estimated or intended. Readers should not place undue reliance on the forward-looking statements and information contained in this news release. The Company assumes no obligation to update the forward-looking statements of beliefs, opinions, projections, or other factors, should they change, except as required by law.

Cybin makes no medical, treatment or health benefit claims about Cybin’s proposed products. The U.S. Food and Drug Administration, Health Canada or other similar regulatory authorities have not evaluated claims regarding psilocybin, psychedelic tryptamine, tryptamine derivatives or other psychedelic compounds. The efficacy of such products has not been confirmed by approved research. There is no assurance that the use of psilocybin, psychedelic tryptamine, tryptamine derivatives or other psychedelic compounds can diagnose, treat, cure or prevent any disease or condition. Rigorous scientific research and clinical trials are needed. Cybin has not conducted clinical trials for the use of its proposed products. Any references to quality, consistency, efficacy and safety of potential products do not imply that Cybin verified such in clinical trials or that Cybin will complete such trials. If Cybin cannot obtain the approvals or research necessary to commercialize its business, it may have a material adverse effect on Cybin’s performance and operations.

Neither the Neo Exchange Inc. nor the NYSE American LLC stock exchange have approved or disapproved the contents of this news release and are not responsible for the adequacy and accuracy of the contents herein.

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