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May 13, 2016

BY E-MAIL

Bone Medical Ltd.,
Ground Floor, 16 Ord Street,
WEST PERTH WA, 6005

Attention: Phil Wingate
Company Secretary and Director

Re: FDCA and CSA Assurances

Ladies and Gentlemen:

This letter is furnished to Bone Medical Ltd. ACN 009 109 755 (to be renamed Botanix Pharmaceuticals Limited) (the "Company") pursuant to your request that we present an opinion as to whether activities concerning the development and marketing of a drug product containing synthetic cannabidiol for the treatment of skin disease in the United States can be legally conducted under the relevant laws and regulations of the United States.

This firm has acted in the role of regulatory counsel to the Company in the U.S. Food and Drug Administration ("FDA"), and U.S. Drug Enforcement Administration ("DEA") areas. In such capacity, we have reviewed the Company's Prospectus dated May 13, 2016 (the "Prospectus") in connection with the offering and listing of its securities on the financial market conducted by ASX Limited ACN 008 624 691 ("ASX").

Opinion

Subject to the qualifications set forth in this opinion letter, we are of the opinion that, if the Company obtains all registrations, permits, licenses and other approvals and otherwise complies with all Applicable Laws, the Company can legally conduct its business of developing synthetic cannabidiol for the treatment of skin diseases in the United States under the Applicable Laws. In connection with our opinion we have reviewed the Applicable Laws.[1]

[1] Most states also regulate controlled substances and it is worth noting that the federal CSA does not generally pre-empt state law. 21 U.S.C.§ 903.

Applicable Laws

In addition to the opinion expressed above, you requested a summary of some of the requirements and limitations imposed by the laws applicable to the development, testing and potential approval for human use of synthetic cannabidiol ("Applicable Laws"). The requested summary is as follows:

> Controlled substances are drugs or other substances with a potential for abuse.[2] The federal Controlled Substances Act ("CSA"), and regulations promulgated by the Drug Enforcement Administration ("DEA") among other things, imposes requirements and limitations on the research, manufacture, distribution, prescribing, importation, and exportation of controlled substances in the United States.[3] The CSA is primarily administered and enforced by the DEA.[4]
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> The CSA classifies controlled substances into five schedules.[5] Each schedule is associated with a different level of risk of diversion and abuse and, thus, with a different level of regulation.[6] Schedule I, the most restrictive schedule and that which imposes the greatest restrictions and regulatory requirements, includes substances with no currently accepted medical use in treatment in the United States.[7] A substance's schedule dictates the requirements regarding record keeping and reporting, physical security, quotas, and prescription limitations.[8]
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> The plant Cannabis sativa L. is currently controlled in Schedule I of the CSA.[9] Congress placed "marihuana" in Schedule I of the CSA and defined "marihuana" as all parts of the plant Cannabis sativa L., with certain exceptions for the parts of the plant that are not the source of cannabinoids. Cannabidiol or CBD derived from the cannabis plant is controlled under Schedule I of the CSA because it is a naturally occurring constituent of marijuana, that is, it is a derivative or compound of the cannabis plant and thus meets the statutory definition of marijuana.[10]
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> The CSA, and its implementing regulations, require every person who, unless otherwise exempt, engages in or proposes to engage in the manufacture, distribution, dispensing,

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2 *See* 21 U.S.C. § 812.

3 21 U.S.C. § 801, et seq; 21 C.F.R. Part 1300, et seq.

4 21 U.S.C. § 871(a) and 28 C.F.R. § 0.100(b).

5 21 U.S.C. § 812.

6 *See id.*

7 *Id.*

8 *See e.g.*, 21 C.F.R. §§ 1301.72, 1304.22, 1303.12, 1303.21, 1306.11.

9 21 U.S.C. § 812 Schedule I (d) and 21 C.F.R. § 1308.11(d)(23).

10 The term "marihuana" means all parts of the plant Cannabis sativa L., whether growing or not; the seeds thereof; the resin extracted from any part of such plant; and every compound, manufacture, salt, derivative, mixture, or preparation of such plant, its seeds or resin. 21 U.S.C. § 802(16); 21 U.S.C. § 812(c), Schedule I (d) and 21 C.F.R. § 1308.11(d)(23).

research, importation, or exportation of any controlled substance to obtain a DEA registration.[11] Registrants must also comply with certain security, recordkeeping and reporting requirements regarding the controlled substances they handle in conducting these activities.[12] In addition, manufacturers of Schedule I and II controlled substances must apply for and obtain quotas for the manufacture and procurement of those controlled substances.[13] To export Schedule I or II controlled substances, such as CBD, the exporter must be registered with DEA must apply for and obtain an export permit from DEA for each proposed export.[14]

Federal law permits research on Schedule I substances, if certain conditions are met. To conduct research on a Schedule I substance, the researcher must first obtain a registration under the CSA from DEA.[15] To receive such a registration, the Department of Health and Human Services (HHS) must determine that the researcher is qualified and competent and the proposed research must be determined to have merit.[16] Applying for such a registration requires submission of a detailed protocol to the DEA describing, among other things, the location where the research will take place and the security provisions for storing and dispensing the controlled substance to prevent diversion.[17] Certain research may also require an Investigational New Drug Application under the Federal Food, Drug, and Cosmetic Act (FDCA), as described below.[18] Researchers using Schedule I substances are required to comply with DEA regulations regarding registration, security, record-keeping, reporting, and disposal.[19]

The FDCA prohibits the introduction or delivery for introduction of a new drug into interstate commerce absent an approved New Drug Application (NDA) or effective Investigational New Drug Application (IND).[20] The term "drug" is defined broadly to include articles "intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man" and "intended to affect the structure or any function of the body of man or other animals."[21] The term "new drug" is defined as any drug that "is not

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11 21 U.S.C. §§ 822(a)-(b), 823, 957; 21 C.F.R. §§ 1308.11(a), 1301.13.

12 *See gen.* 21 C.F.R. §§ 1301.71-93, 1304.01-55, 1306.01-27, 1311.01-305, 1312.01-32, 1317.01-95.

13 21 U.S.C. § 826; 21 C.F.R. § 1303.11-27.

14 21 U.S.C. §§ 957, 953; 21 C.F.R. §1312.21(a).

15 21 U.S.C. § 823(f).

16 *Id.*; 21 C.F.R. § 1301.32.

17 21 C.F.R. § 1301.18.

18 21 U.S.C. § 355(i).

19 21 C.F.R. §§ 1301.71, 1301.75-76, 1304.01-55, 1317.01-95.

20 21 U.S.C. § 331(d); 21 U.S.C. § 355(a). Interstate commerce is presumed. 21 U.S.C. § 379A. Moreover, even if a finished product does not move in interstate commerce (*e.g.*, if it is shipped only intrastate), the interstate commerce requirement is satisfied if any of the components of the finished product (*e.g.*, active or inactive ingredients, packaging components) moved in interstate commerce. *U.S. v. Regenerative Sciences, LLC*, 741 F.3d 1314, 1321-1322 (2014); *see also* FDA Compliance Policy Guide 100.200.

21 21 U.S.C. § 321(g).

generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling ..."[22] Cannabidiol containing products intended for use in the diagnosis, cure, mitigation, treatment or prevention of disease meet the definition of a drug and the definition of a new drug under the FDCA and therefore require an approved NDA before they can be marketed.

In order to study an unapproved new drug in the U.S., the FDCA requires a valid IND.[23] An IND is required when a drug is studied in humans even if such study is intended solely for research purposes.[24] An IND must contain sufficient information to demonstrate that the drug product is safe for testing in humans and that the clinical protocol is properly designed for its intended objectives.[25] As indicated above, both FDA and DEA must approve that protocol when it governs research with a Schedule I controlled substance.

After a sponsor has gathered sufficient evidence to show that a drug is safe and effective for use in humans, the sponsor submits a NDA to FDA for review. An NDA must contain data regarding the abuse potential of the drug.[26] Upon FDA approval of an NDA containing a Schedule I substance, after conducting a scientific and medical evaluation, HHS will recommend a change in schedule to a lower schedule or removal from the schedules.[27] DEA must issue an interim final rule within 90 days rescheduling the drug.[28] Interested persons may comment on the rescheduling and request a hearing. After this process, DEA will issue a final scheduling determination.[29] A Schedule I drug may not be legally marketed in the United States until it is rescheduled into Schedule II – V or otherwise decontrolled.

FDA has previously approved synthetic cannabinoid drug products, namely, nabilone (Cesamet), for the treatment of nausea and vomiting associated with chemotherapy[30] and dronabinol (Marinol), for the treatment of anorexia associated with weight loss in patients with AIDS and nausea and vomiting associated with chemotherapy.[31] Cesamet is

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22 21 U.S.C. § 321(p).

23 21 U.S.C. § 355(i).

24 21 U.S.C. § 355(i), 21 C.F.R. Part 312.

25 21 C.F.R. § 312.22.

26 21 C.F.R. § 314.50(d)(5)(vii).

27 21 U.S.C. § 811(b).

28 *Id.*

29 *Id.*

30 *See* Cesamet (nabilone), Prescribing Information, available at https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=bb582d64-0f51-11df-8a39-0800200c9a66.

31 *See* Marinol (dronabinol), Prescribing Information, available at https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=5bbac0b1-ddc2-400b-8e0d-1e1d484720ca.

currently controlled in Schedule II. DEA initially placed Marinol, the FDA approved drug product in Schedule II, however, in 1999, DEA transferred Marinol into Schedule III.[32]

Consent

We consent to being named in the Prospectus as being responsible for the preparation of this letter. Except for this letter, we (a) have not authorized or caused the issuance of the Prospectus, (b) are not responsible for any matter included in or omitted from this Prospectus, (c) make no representation or warranty, either express or implied, with respect to the accuracy or completeness of the information contained in the Prospectus, and (d) disclaim liability to any persons in respect of any statement included in or omitted from the Prospectus.

This letter is given solely for the benefit of the Company and it directors in connection with the issue of the Prospectus and is not to be relied on or disclosed to any other person or used for any other purpose or quoted or referred to in any public documents or filed with any government body or other person without our prior consent.

Please do not hesitate to contact us if you require any further information.

Sincerely,

Michelle L. Butler

MLB/vam

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32 *See* 51 Fed. Reg. 17476 (May 13, 1986); 52 Fed. Reg. 11042 (Apr. 7, 1987); 64 Fed. Reg. 35928 (July 2, 1999).