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Request for Proposal No. FENG/01/2025 on preclinical in vitro studies of cannabinoids and cannabinoid formulations

as part of the project entitled "Development of an innovative formulation of cannabinoids for the treatment of symptoms of irritable bowel syndrome", for which an application will be submitted for funding under the European Funds for a Modern Economy, Priority I. Support for entrepreneurs, SMART Path, call no: FENG.01.01-IP.02-002/25.

I. Name and address of the Ordering Party

CannabIBS Sp. z o.o.
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II. Type of contract

Services

III. Title of the contract

In vitro preclinical testing of cannabinoids and cannabinoid formulations
CPV code 73100000-3 Research and experimental development services

IV. Subject of the contract

The subject of the contract is in vitro preclinical testing of cannabinoids and a cannabinoid formulation (without THC in its composition).

Project start date: 1 January 2026.

IV.1 Description of the subject of the contract

The subject is the performance of in vitro genotoxicity and ADME studies on three cannabinoid preparations (CBDA, CBG and CBX).

The following in vitro studies will be performed:

- 1.1. CBDA Genotoxicity-Ames Test
- 1.1. CBG Genotoxicity-Ames Test
- 1.1. CBX Genotoxicity-Ames Test



- 1.2. CBG Genotoxicity - Chromosome Aberration Study
- 1.2. CBDA Genotoxicity Chromosome Aberration Study
- 1.2. CBX Genotoxicity Chromosome Aberration Study

1.3. CBX Plasma Protein Binding Study

1.4. CBX CYP Metabolism Study

The formulation study will consist of a combination of the cannabinoids CBD, CBDA and CBG and will be referred to as CBX.

Detailed description of the contract

1. Preclinical in vitro CBDA, CBG, CBX studies: determination of effects on cell lines

Preclinical in vitro studies will be conducted. These will be studies that confirm the safety of the oral product and will be conducted in animal cells using OECD/ISO recommended methods (or equivalent).

1.1. Genotoxicity determined by the Ames Test

according to OECD Test Guideline 471 and ICH Guideline S2(R1) (or equivalent)

Genotoxicity - Ames test for the detection of micronuclei, clastogenic and aneugenic activity. The Ames test is a reverse mutation bacterial assay using both *Salmonella typhimurium* and *Escherichia coli* (or equivalent) as test organisms. The Ames test is recommended as part of the genetic toxicology test battery and detects both point mutations and frameshift mutations as used as part of a battery of preclinical tests for new drug development.

1.1. CBDA Genotoxicity-Ames Test

1.1. CBG Genotoxicity-Ames Test

1.1. CBX Genotoxicity-Ames Test

Start date of the study: 1st month of the project.

Genotoxicity - Ames Test Timing:

- 4 weeks at life;

- 4 weeks reporting period (draft report).

Total study duration/per study: 8 weeks

Genotoxicity-Ames Test (1.1) should be performed prior to Genotoxicity Chromosome Aberration Study (1.2).

The CBDA, CBG and CBX studies may be conducted concurrently.



1.2. Genotoxicity by Chromosome Aberration Study *according to OECD Test Guideline 487 and ICH Guideline S2(R1) (or equivalent)*

This in vitro micronucleus assay is a genotoxicity test for the detection of micronuclei in the cytoplasm of interphase cells. The micronucleus assay detects micronuclei in the cytoplasm of interphase cells after the cells have been exposed to a chemical. The test detects the activity of clastogenic and aneugenic test substances in cells that have undergone cell division during or after exposure to the test substance.

1.2. CBG Genotoxicity - Chromosome Aberration Study

1.2. CBDA Genotoxicity Chromosome Aberration Study

1.2. CBX Genotoxicity Chromosome Aberration Study

Start date of the study: 3rd month of the project.

Genotoxicity - Chromosomal Aberration Study Timing:

- 8 weeks in the life phase;

- 4 weeks reporting period (draft report).

Total study duration/per study: 12 weeks

Genotoxicity Chromosome Aberration Study (1.2) should be performed after Genotoxicity-Ames Test is completed (1.1).

The CBDA, CBG and CBX studies may be conducted concurrently.

1.3 Plasma Protein Binding Study

according to OECD Guidance Document 249 on PBK modelling and ICH Guideline M12 (or equivalent)

Plasma protein binding (PPB) is an important parameter of drug efficacy and safety that must be investigated during any drug development program. Although regulatory guidelines exist to investigate the extent of PPB prior to the initiation of clinical trials, there are no detailed instructions on how to perform and validate such studies. CBX is being tested at 3 dose levels (3 replicates each). Blank fresh plasma samples from a variety of species including humans, rats, mice, dogs, NHPs and minipigs are spiked with the CBX drug replicates and analyzed by equilibrium dialysis. The pharmacological effect of a compound is determined by its free or unbound concentration. Unbound *in vivo* blood or plasma concentrations can be estimated by multiplying total levels by the fraction of the compound that is unbound in blood or plasma.

Start date of the study: 1st month of the project.

Plasma Protein Binding Study Timing:

- 4 weeks in life phase

- 4 weeks reporting period (draft report)

Total study duration: 8 weeks

Study required for final formulation product only, i.e. CBX.



1.4 CYP Metabolism Study

according to OECD Test Guideline project 3.32 and ICH Guideline M12 (or equivalent)

A cytochrome P450 (CYP) induction assay will be used to understand potential drug-drug interaction liabilities.

Cryopreserved hepatocytes are obtained from 3 human donors.

6 concentrations of CBX plus vehicle control in triplicate will be tested for CYP isoforms: CYP1A2, CYP2B6 and CYP3A4.

A single concentration of flumazenil is used as a negative control, while increasing doses of omeprazole (for CYP1A2), phenobarbital (for CYP2B6), and rifampicin (for CYP3A4) are used as positive controls.

The incubation period is 72 hours.

Induction of cytochrome P450 enzymes is associated with an increased prevalence of clinical drug-drug interactions.

Start date of the study: 1st month of the project.

CYP Metabolism Study Timing:

- 6 weeks in life phase

- 4 weeks reporting period (draft report)

Total study duration: 10 weeks

Required for final formulation product only, i.e. CBX.

IV.2 Division of the Order into Parts

The Order is divided into the following parts, as described in the Order above:

Part 1: Genotoxicity determined by the Ames Test

Part 2: Genotoxicity by Chromosome Aberration Study

Part 3: Plasma Protein Binding Study

Part 4: CYP Metabolism Study

Each Contractor may submit a bid for any number of parts. A separate bid must be submitted for each part of the Order.

IV.3 Other information

3.1 As a result of the performance of the contract, the Contractor will deliver to the Ordering Party:

- Signed Study Protocol(s)/Plan(s) prior to start.
- Raw data packages (electronic & paper).
- Draft study reports (within 10 working days of in-life completion).
- QA Audit Certificate (GLP)
- Final report. The report for all studies should be completed in English. The report should include a detailed description of the experiments carried out.



3.2. A detailed schedule of payments due to the Contractor from the Ordering Party will be agreed upon acceptance of the tender. Payments will be subject to the progress of the work and the Contractor's submission of the results of the work as agreed in the contract.

3.3 The Ordering Party shall provide the Contractor with the active substances CBDA, CBG and CBX. The bid should include an estimate of the active substance required for the study together with the methodology for estimating the amount of active substance.

3.4 The Contractor shall commence the Contract after obtaining the approval of the Local Ethics Committee (if approval is required). The Contractor shall be responsible for seeking consent.

3.5 The Ordering Party envisages the possibility of awarding additional contracts, in particular if the study has to be repeated.

3.6 Minimum term of validity of the tender: 30 June 2025.

V. Conditions for participation in the proceedings

1. Contractors who have a personal or capital relationship with the Ordering Party shall be excluded from the proceedings. It is necessary to attach to the bid a completed declaration of non-relationship, which constitutes Appendix No. 3 to this request for proposal.

2. A capital or personal relationship shall be understood as a mutual relationship between the Ordering Party or persons authorized to incur liabilities on behalf of the Ordering Party or persons performing activities on behalf of the Ordering Party related to the preparation and conduct of the procurement procedure and the Contractors, consisting of:

- a) participation in a company as a partner in a civil partnership or partnership, holding at least 10% of shares (unless a lower threshold is required by law), serving as a member of a supervisory or management body, proxy, attorney,
- b) being married, in a relationship of consanguinity or affinity in a direct line, consanguinity or affinity in a lateral line up to the second degree, or being related by adoption, custody or guardianship, or being in common life with the contractor, his legal deputy or members of the management or supervisory bodies of contractors competing for the contract,
- c) remaining with the contractor in such a legal or factual relationship that there is reasonable doubt as to their impartiality or independence in connection with the procurement procedure.

3. The Contractor shall have at its disposal on the date of commencement of the study the personnel and resources necessary to perform part of the contract, which shall be described in the Bid Form.

4 The Contractor shall have a Certificate of Compliance with Good Laboratory Practice (or equivalent) in place on the date of commencement of testing.

To confirm the fulfillment of the above conditions, the Contractor is required to provide data and submit statements contained in Appendix No. 1 - Bid Form.

VI. Description of bid preparation

An offer prepared in accordance with the Offer Form, Appendix 1 to this enquiry should include:

- the Contractor's full name, address or registered office, telephone number;
- the date of issue of the offer;



- the expiry date of the offer - at least until 30 June 2025;
- include information on all conditions for participation in the procedure in accordance with Section V;
- refer to the number of the request for quotation - FENG/01/2025;
- at least the net price excluding VAT (in the case of prices quoted in foreign currencies, they shall be converted into PLN at the average NBP rate prevailing on the day preceding the deadline for submission of tenders) - separately for each part of the contract;
- name and surname of a person from the Contractor's side to be consulted before the commencement of works, including at the stage of preparing and evaluating the grant application.
- Table of personnel - name, role, education, years of experience, GLP responsibilities.
- Study descriptions and detailed methodology for each test - separately for each part of the contract;
 - a detailed description of the experimental design/test scheme,
 - deadline for completion of part of the contract
- List of ISO/OECD/ICH guidelines that will be followed.
- Copy of GLP certificate and relevant ISO 17025 (or equivalent) accreditation.
- Active-substance requirement calculation.
- Description of the research apparatus and infrastructure used in the studies - separately for each part of the contract;

The absence of any of the above-mentioned elements may result in the rejection of the tender on formal grounds.

The offer should be made in Polish or English.

A form of the offer other than the Offer Form (Annex 1) is acceptable, provided that the offer contains all the information contained in the Offer Form.

VII. Criteria for evaluation of tenders and their importance (weighting)

1. Admission criterion for further evaluation:

The Ordering Party will evaluate valid bids on the basis of the following criteria:

- Submission of a bid in the manner and by the deadline specified in Section. IX;
- Preparation of the bid in accordance with the requirements specified in Section VI. VI;
- Evaluation of the compliance of the bid with the description of the subject matter of the contract contained in section IV;
- only bids meeting the conditions for participation in the proceeding specified in points. IV, V, VI and IX;
- Bids that do not meet the conditions described in points. IV, V, VI and IX are rejected and are not subject to further evaluation.

2 Evaluation criteria and the way in which tenders will be evaluated

Each part of the contract is evaluated separately according to the criteria of Price and Deadline.

a. Price



Net price (excluding VAT) for the performance of each part of the contract separately, given in PLN or in a foreign currency. In the case of prices given in foreign currencies, they shall be converted into PLN at the average exchange rate of the National Bank of Poland binding on the day preceding the deadline for submission of offers. This is the total price without exclusions and including all components of the offer. Points under the Price criterion will be awarded according to the following formula:

$$A_n = (C_{\min} / C_r) \times 100 \text{ points.}$$

Where:

C_{\min} - the minimum price in the set,

C_r - price of the offer under consideration

A_n - the number of points awarded to the bid.

Maximum number of partial points: 100.

Weighting of the price criterion: 0.8

b. Deadline

The deadline for the execution of a part of the contract is the number of calendar days from the start of the study to the delivery of the report to the Contracting Authority. Points within the Term criterion will be awarded according to the following formula:

$$B_n = (T_{\min} / T_r) \times 100 \text{ points.}$$

Where:

T_{\min} - the minimum term in the set,

T_r - deadline of the offer under consideration

B_n - the number of points awarded to the bid.

Maximum number of partial points: 100.

Deadline criterion weight: 0,2

The number of points (P_n) awarded to a particular part of the contract is calculated according to the formula: $P_n = (A_n \times 0.8) + (B_n \times 0.2)$

(3) The tender which obtains the highest number of points for a given part of the contract shall be considered the most advantageous.

VIII. Conditions for amending the contract

1. The Ordering Party envisages the possibility of amending the provisions of the contract concluded with the Contractor only if at least one of the following grounds occurs:
 - The change is necessary due to circumstances which the Ordering Party - acting with due diligence - was not able to foresee at the stage of preparing the request for quotation.
 - The change is necessary for the proper implementation of the contract due to organisational, technological, legal or formal reasons, but it does not lead to the extension of the scope of the contract beyond the assumptions specified in the request for quotation and does not change the nature of the contract in a fundamental way.
 - The change results from the modification of the co-financing conditions, in particular for reasons related to the guidelines of the financing institution, which could not have been foreseen before the conclusion of the agreement.
2. The amendments referred to in paragraph 1 shall only be admissible within the scope of:
 - the date of completion of the subject matter of the contract if, for reasons beyond the control of the Parties (e.g. changes and delays in research work, force majeure events),



- completion of the task by the date originally specified has become impossible or considerably hindered,
- dates and rules of payment, if such necessity results from the project implementation schedule or regulations of the financing institution,
 - research methods, if the change is necessary due to the results of previous research work or scientific and technological progress,
 - the scope of the research work, provided that the change does not lead to an increase in the fundamental scope or value of the contract in such a way as to justify the renewal of the competitive procedure,
 - transfer of certain scopes of work between the stages of the project, including possible transfer to a stage that was not covered by the Contractor's participation, provided that such action results from the development of the research work and does not change the fundamental character of the contract,
 - change of a person from the key research staff specified in the Request for Proposals, provided that the new person meets all the requirements specified for the function (or has equivalent / higher qualifications) and this will not result in a decrease in the quality of the contract execution.
3. In each case, in order to amend the contract to the extent indicated in paragraphs 1 and 2, it is necessary to:
- the preparation and signature by the Parties of an appropriate addendum (or other equivalent document, e.g. a memorandum of understanding),
 - to be in writing or in electronic form (qualified electronic signature or other electronic signature agreed by both Parties) under pain of nullity,
 - justification of the change and confirmation that it remains in compliance with the principle of competitiveness and does not lead to a significant extension of the subject matter of the contract or to the modification of the terms and conditions in a way that could affect the result of the procedure for selecting the Economic Operator.

IX. Place and date of submission of the offer

1 Deadline for submission of bids: until 02.06.2025.

2 The bid and its attachments should be submitted only via the Competitiveness Database portal (<https://bazakonkurencyjnoscifunduszeuropejskie.gov.pl/>).

(3) Tenders submitted after the deadline will not be considered. The date and time of receipt of the tender is decisive.

(4) The Contractor may submit only one tender.

(5) The Contractor shall bear all costs associated with the preparation and submission of the bid regardless of the outcome of the proceedings.

(6) The Contractor may, before the deadline for submission of bids, change or withdraw its bid.

(7) In the course of the examination and evaluation of tenders, the Ordering Party may request additional explanations or supplements from the Contractors concerning the contents of the submitted tenders.



(8) Communication between the Ordering Party and the Contractor in the procurement procedure, including the exchange of information, shall take place in writing via the Competitive Database.

(9) The Ordering Party shall notify the selection of the most advantageous tender through the Competitive Database (<https://bazakonkurencyjnosci.funduszeuropejskie.gov.pl/>).

(10) In the event that significant changes are made to the content of the Request for Proposals, the Contracting Authority reserves the right to extend the deadline for the submission of tenders and will inform the Competitive Database.

X. Additional information

(1) This order will be realized only if the Ordering Party signs a contract for co-financing of the project entitled 'Development of innovative cannabinoid formulation for treatment of symptoms of irritable bowel syndrome' within the scope of the call for proposals FENG.01.01-IP.02-002/25.

(2) In the event that the Ordering Party does not sign the aforementioned funding agreement, the order shall not be executed and the Parties shall have no claims against each other on this account.

(3) The Contracting Authority reserves the right to cancel this procedure in the event of failure to sign the project funding agreement. Information about the cancellation will be communicated via the Competitiveness Database.

XII. Information on the cancellation of the procedure

1. The contracting authority may cancel the procedure in the following circumstances:
 - the price of the most advantageous tender exceeds the amount which the Contracting Authority can afford to finance the Contract,
 - the Contracting Authority was not granted any funds for financing the Order,
 - the procedure suffers from a defect that cannot be removed,
 - there has been a significant change of circumstances resulting in the conduct of the proceedings or the performance of the contract not being in the interest of the Awarding Entity, which could not have been predicted earlier (e.g. change of the conditions of funding).
2. The Contracting Authority reserves the right to cancel the procedure also in other justified cases, in particular when there are unforeseen circumstances that make it impossible to sign a contract and implement the subject matter of the contract in accordance with the principle of competitiveness. In such situations, the Contracting Authority shall provide an appropriate explanation in the information on the cancellation of the procedure.
3. The Contracting Authority shall inform all Economic Operators who submitted tenders of the cancellation of the procedure, stating the reasons.

XIII. Annexes

Annex No. 1 - Offer form

Annex No 2 - Declaration of no personal or capital relations