Warszawa, 19.05.2025 r.

Request for Proposal No. FENG/03/2025 on preclinical studies in vivo studies of cannabinoids and cannabinoid formulations in non-rodents

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 vivo preclinical testing of cannabinoids and cannabinoid formulations on rodents
CPV code 73100000-3 Research and experimental development services

IV. Subject of the contract

The subject of the contract is in vivo 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 following in vivo preclinical CBDA, CBG, CBX studies in non-rodents will be performed under the contract:

3.1. CBDA MTD/DRF Studies in Non-Rodent Animals
3.1. CBG MTD/DRF Studies in Non-Rodent Animals
3.1. CBX MTD/DRF Studies in Non-Rodent Animals

3.2. CBDA Repeat Dose (28-day) Toxicity and Toxicokinetic Studies in Non-Rodent Animals
3.2. CBG Repeat Dose (28-day) Toxicity and Toxicokinetic Studies in Non-Rodent Animals

3.2. CBX Repeated Dose (28-day) Toxicity and Toxicokinetic Studies in Non-Rodent Animals

3.3. CBDA Chronic (13-week) Toxicity Studies in Non-Rodent Animals
3.3. CBG Chronic (13-week) Toxicity Studies in Non-Rodent Animals
3.3. CBX Chronic (13-week) Toxicity Studies in Non-Rodent Animals

3.4. CBDA Safety Pharmacology Cardiovascular Study in Non-Rodent Animals
3.4. CBG Safety Pharmacology Cardiovascular Study in Non-Rodent Animals
3.4. CBX Safety Pharmacology Cardiovascular Study in Non-Rodent Animals

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

The first three studies, i.e. 3.1, 3.2 and 3.3, must be conducted in that order, i.e. sequentially. Study 3.4 may be conducted after the dose levels for 3.2 have been selected.

Detailed description of the contract

3. In vivo preclinical CBDA, CBG, CBX studies in non-rodent animals

3.1. Dose Range Finding (DRF) Study in Minipigs

according to ICH Guideline M3(R2) (or equivalent)

Preliminary dose range finding and maximum tolerated dose studies in non-rodents (minipigs) of the observed effect after a post-treatment observation period. The studies will also evaluate the toxicokinetic profile of CBDA, CBG, CBX.

The objective of this preliminary study is to select the appropriate maximum dose of CBDA, CBG, CBX to be evaluated in a repeated dose (28-day) toxicity study in minipigs. Two groups of male and female minipigs will be included in this study. The study will consist of two phases: an ascending dose phase and a fixed dose phase.

Ascending dose phase

The first group will be treated with ascending daily oral doses of CBDA, CBG, CBX at ascending dose levels for 3 days per dose level, with a 4-day washout period between ascending dose levels. Toxicity will be assessed by daily observation of animals for mortality, clinical signs, and food consumption. Body weights are recorded at least twice weekly. Hematology, blood biochemistry, coagulation tests, and urinalysis will be performed before dosing and at the end of the dosing period (D31). Blood samples for analysis of plasma concentrations of CBDA, CBG, CBX will be collected on the first (D1, D8, D15, D22, and D29) and last (D3, D10, D17, D24, and D31) days of each dose level, before dosing and 30 minutes, 1, 2, 4, 8, and 24 hours after dosing. Additional samples will be collected at 48, 72, and 96 hours after the last day of each dose level. Both animals will be necropsied (D36), selected organs will be weighed, and selected tissues will be collected and preserved.

Fixed dose phase

The second group, consisting of one male and one female minipig, will be treated with daily oral administrations of CBDA, CBG, CBX at the maximum tolerated dose from the ascending dose

phase for 14 days. Toxicity will be evaluated by observing the animals daily for mortality, clinical signs, and food consumption. Body weights are recorded at least three times per week. Hematology, blood biochemistry, coagulation tests, and urinalysis will be performed before dosing and at the end of the dosing period (D14). ECG will be recorded before dosing and on D14, 1 hour after dosing. Blood samples for analysis of plasma concentrations of CBDA, CBG, CBX will be collected on D1 and D14 at pre-dose, 30 min, and 1, 2, 4, 8, and 24 h post-dose. Necropsies will be performed on both animals (D15), selected organs will be weighed, and selected tissues will be collected and preserved. Histologic analysis will be performed on limited selected tissue samples from both animals.

Start date of the study: 2nd month of the project.

MTD Study in Minipigs with CBDA/CBG/CBX Timing
4 week pre-trial/acclimatization period
6-week study period (ascending and fixed-dose phases)
4-week reporting period (draft report)
14 weeks total study duration/per study

The Dose Range Finding (DRF) Study (3.1) should be conducted prior to the 28-day Repeated Dose Study (3.2).
The CBDA and CBG studies may be performed concurrently. The CBX study will be conducted after they are completed.

3.2. 28-day Repeated Dose Study of CBDA, CBG, CBX in Minipigs
according to ICH Guideline M3(R2) (or equivalent)

Repeated dose (28-day) toxicity and toxicokinetic studies in minipigs, including a recovery period, to determine the effect of repeated daily dosing and recovery of the observed effect after a post-treatment observation period, the studies will also investigate the toxicokinetic profile of CBDA, CBG, CBX.
The objective of this GLP-compliant study is to evaluate the potential toxicity of daily oral administration of CBDA, CBG, CBX to minipigs for 28 days. The minipig was selected for its background data related to the study of cannabinoids. The selected daily dosing schedule and oral route of administration are consistent with the dosing schedule and route of administration that will be used in the first planned clinical trial. After completion of treatment, designated animals will be retained for four weeks to evaluate the reversibility of any findings. Four groups of three males and three females will receive daily oral administrations of CBDA, CBG, CBX at 4 ascending dose levels for 28 days. Two additional males and two additional females will be included in the control and high dose groups for a 28-day recovery period. The high dose level will be selected based on the results of the preliminary MTD study.
Toxicity is evaluated by observing the animals for the following parameters
- Mortality and clinical signs;
- Detailed physical examinations, individual body weights, food and water consumption;
- Hematology, blood biochemistry, coagulation parameters, and urinalysis before dosing, during the last week of the dosing period (week 4), and during the last week of the recovery period (week 8);
- Ophthalmic examinations before dosing, at week 4, and at week 8;

- Toxicokinetic evaluation on D1 and D28 at pre-dose, 1, 2, 4, 8, and 24 h post-dose, and 48, 72, and 96 h post-dose for recovery animals;
- ECG on D1, week 4 (pre-dose and 2 h post-dose), and week 8;
- Complete necropsies (D29 or D57) and weighing of selected organs;
- Histologic examination of all tissues.

Start date of the study: 8th month of the project.

28-day Repeated Dose Study in Minipigs Timing:
- 4 week pre-trial/acclimatization period;
- 8-week study period including recovery period;
- 8-week reporting period (audited draft report).

Total study duration/per study: 20 weeks

28-day Repeated Dose Study (3.2) should be performed after Dose Range Finding (DRF) Study (3.1) is completed.
28-day Repeated Dose Study (3.2) should be performed prior to 13-week (Chronic) Toxicity Study (3.3).
The CBDA and CBG studies may be conducted concurrently. The CBX study will be conducted after their completion.

3.3. 13-week (Chronic) Toxicity Study of CBDA, CBG, CBX in Minipigs

according to OECD Test Guideline 409 and ICH Guideline M3(R2) (or equivalent)

The objective of this GLP-compliant study is to evaluate the potential toxicity of daily oral administration of CBDA, CBG, CBX to minipigs for 13 weeks. The minipig was selected because of its background in the study of cannabinoids. The selected daily dosing schedule and oral route of administration are consistent with the dosing schedule and route of administration that will be used in the first planned clinical trial. Upon completion of treatment, designated animals will be retained for four weeks to evaluate the reversibility of any findings. Four groups of three males and three females will receive daily oral administrations of CBDA, CBG, CBX at 4 ascending dose levels for 13 weeks. Two additional males and two additional females will be added to the control and high dose groups for a 4-week recovery period. The high dose level will be selected based on the results of the 28-day toxicity study.
Toxicity is evaluated by observing the animals for the following parameters
- Mortality and clinical signs;
- Detailed physical examinations, individual body weights, food and water consumption; hematology, blood biochemistry, coagulation parameters, and urinalysis before dosing, at weeks 4, 7, and 13 of the dosing period, and during the last week of the recovery period;
- Ophthalmic examinations before dosing, at weeks 7 and 13, and during the last week of the recovery period;
- Toxicokinetic evaluation on D1 and at weeks 7 and 13 at pre-dose, 1, 2, 4, 8, and 24 h post-dose, and 48, 72, and 96 h after the last dose for recovery animals;
- ECG pre-dose, on D1, weeks 7 and 13 (pre-dose and 2 h post-dose);
- Complete necropsies at the end of the dosing and recovery periods and weighing of selected organs;
- Histologic examination of all tissues.

Safety Pharmacology studies are conducted in accordance with applicable regulatory guidelines, including ICH S7A and S7B guidelines.

Start date of the study: 18th month of the project.

13 Week (chronic) minipig toxicity study timing:
- 4 week pre-trial/acclimatization period;
- 17-week study period including recovery period;
- 8-week reporting period (audited draft report).

Total study duration/per study: 29 weeks

13-week (chronic) Toxicity Studies (3.3) may be conducted after completion of 28-day Repeated Dose Studies (3.2).
The CBDA and CBG studies may be conducted concurrently, but the CBX study may not be conducted until the first two studies (CBDA and CBG) have been completed.
Depending on the results of the 28-day studies, it is possible to conduct a combined 13-week CBDA and CBG study in minipigs by including 2 dose levels (low and high) of CBDA and CBG and conducting a 5-dose group study. This will reduce the overall cost and number of animals.

3.4. Cardiovascular assessment by radiotelemetry after a single oral dose of CBDA, CBG, CBX in minipigs

according to OECD Test Guideline 409 and ICH Guideline S7A (or equivalent)

This safety pharmacology cardiovascular study in minipigs is designed to determine the appropriate dose levels for subsequent repeat dose studies.
This GLP-compliant study will evaluate the potential adverse effects of CBDA, CBG, and CBX treatment on the cardiovascular system of minipigs following a single oral administration. Minipigs are recognized as an appropriate model for cardiovascular safety pharmacology studies and significant historical control data are available for this species. They will also be used in the main non-rodent toxicology study. The selected route of administration for this study is oral, consistent with that planned for the first clinical trial.
Two male and two female minipigs will be orally dosed with vehicle (peanut oil) and CBDA, CBG, and CBX at three dose levels (5 ml/kg) with a seven-day washout period between doses based on an ascending dose schedule. These dose levels will be selected based on the results of the preliminary minipig maximum tolerated dose (MTD) study.
Cardiovascular recordings will be made in conscious animals surgically implanted with radiotelemetry transmitters. Cardiovascular parameters, including heart rate, arterial blood pressure (systolic, diastolic, and mean), body temperature, and ECG waveforms (from which the ECG intervals PR, QRS, QT, and QTc are derived) will be collected continuously for at least 20 hours prior to dosing to establish baseline measurements, and then continuously for at least 90 minutes before and after each dose (on days 1, 8, 15, and 22).
Mortality is recorded twice daily. Body weight is measured at least weekly, both before and after dosing on each dosing day. Blood samples will be collected before and four hours after dosing on each dosing day (D1, D8, D15, and D22) to determine plasma exposure to CBDA, CBG, and CBX.

Start date of the study: 8th month of the project.

Cardiovascular assessment by radiotelemetry after a single oral administration in minipigs timing:
- 4 weeks pretrial/acclimatisation period;
- 4 weeks study duration;
- 4 weeks reporting period (draft report).

Total study duration/ per study: 12 weeks

Cardiovascular assessment (3.4) may be conducted after completion of 28-day Repeated Dose Studies (3.2).
The CBDA and CBG studies may be conducted concurrently, but the CBX study may not be conducted until the first two studies (CBDA and CBG) have been completed.

IV.2 Division of the Order into Parts

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

Part 1: Dose Range Finding (DRF)
Part 2: 28-day Repeated Dose Study
Part 3: 13-week (Chronic) Toxicity Study
Part 4: Cardiovascular assessment by radiotelemetry after a single oral dose

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.

5. On the date of commencement of the research, the Contractor should have a system of ensuring the welfare of animals used for research aimed at the protection of animals, which should be confirmed with the appropriate certificate.

To confirm the fulfilment 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/03/2025;
- 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
- 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:

An = (C min / Cr) x 100 points.

Where:

C min - the minimum price in the set,

Cr - price of the offer under consideration

An - 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:
Bn = (T min / Tr) x 100 points.
Where:
T min - the minimum term in the set,
Tr - deadline of the offer under consideration
Bn - the number of points awarded to the bid.
Maximum number of partial points: 100.
Deadline criterion weight: 0,2

The number of points (Pn) awarded to a particular part of the contract is calculated according to the formula: Pn = (An x 0.8) + (Bn x 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://bazakonkurencyjnosci.funduszeeuropejskie.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.funduszeeuropejskie.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 proposalsFENG.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 Honor