Warsaw, the 28th of February 2022

REQUEST FOR PROPOSAL NO. 15/2022

We invite all entities meeting the conditions specified below to submit offers for performing Preclinical Safety Assessment Program for the drug candidate PKL-021.

The procurement carried out in accordance with the principle of competitiveness as defined in the Guidelines for the eligibility of expenditure under the European Regional Development Fund, the European Social Fund and the Cohesion Fund for 2014-2020, version of 21 December 2020.

The tender is carried out:

- in connection with the implementation by the Ordering Party of the project entitled "Use of matrix metalloproteinase inhibitor to develop an innovative therapy of preventing the development of post-traumatic and post-stroke epilepsy" /POIR.01.01.01-00-0235/20-00/ within Measure 1.1. R&D projects of enterprises, Submeasure 1.1.1 Industrial research and development work implemented by enterprises, co-financed by the European Regional Development Fund.
- in accordance with the principle of competitiveness and is not a subject of public procurement regulated by the Public Procurement Law of 11 September 2019.

I. THE ORDERING PARTY

PIKRALIDA sp. z o. o.
Uniwersytetu Poznanskiego 10
61-614 Poznan
Poland

Contact:
Joanna Lipner
j.lipner@pikralida.eu
tel. +48 608 711 071

II. DESCRIPTION OF THE SUBJECT MATTER OF THE ORDER

a) Common Procurement Vocabulary (CPV): 73111000-3 – research laboratory services

b) General Information:

The subject of the order is the performance of Preclinical Safety Assessment Program for the drug candidate PKL-021.

Pikralida sp. z o.o. is developing PKL-021, a low-molecular-weight matrix metalloproteinase 9 (MMP-9) inhibitor, as an innovative therapeutic solution protecting against the development of the post-traumatic and post-stroke epilepsy.

The Appendix no. 5 – Technical Information Package includes information regarding study design and the MSDS of PKL-021. The Appendix no. 5 will be disclosed to Bidders who express their interest in participating in the bidding procedure and will send a scan of signed confidentiality agreement (Appendix no. 4) or electronically signed confidentiality agreement (Appendix no. 4) to Joanna Lipner (j.lipner@pikralida.eu). In case the Bidder sends a scan of signed confidentiality agreement, they are obligated to send the original signed document to Joanna Lipner, Pikralida sp. z o.o., Uniwersytetu Poznańskiego 10, 61-614 Poznan, Poland.

The Appendix No. 5 (Technical Information Package) will be disclosed to interested Bidders within 48 hours after receiving of the scan of signed Appendix No. 4.

In case the Bidder and Pikralida signed the confidentiality agreement at the stage of the market research and the agreement is still valid, sending the scan of signed confidentiality agreement is not required. The Technical Information Package will be disclosed upon the Bidder express their interest in participating in the bidding procedure no. 15/2022.

c) The Scope of the Order:

i. General toxicology studies
- Acute maximum tolerated dose and 7-day repeated oral dose range finding toxicity study in the Wistar Rat, non-GLP
- Maximum tolerated dose and 7-day range finding toxicity study in a non-rodent[1], non-GLP
- 28-day repeated oral dose toxicity and toxicokinetic study in the Wistar Rat with a 14-day recovery period, GLP
- 28-day repeated oral dose toxicity and toxicokinetic study in non-rodent[1] with a 14-day recovery period, GLP

ii. Safety pharmacology studies
- hERG assay in HEK293-hERG cells in manual patch-clamp platform, GLP
- Cardiovascular telemetry study in the non-naïve non-rodent[1], GLP
- Behavioural effects in rats using the functional observational battery, GLP
- Rat respiratory safety pharmacology study, GLP

iii. Genotoxicity studies
- Bacterial reverse mutation assay (AMES), GLP
- *In vitro* micronucleus assay in CHO-WBL cells, GLP
- *In vivo* peripheral blood micronucleus assay in the rat-FMC (single sex), GLP

iv. Formulation analysis
- Development of a HPLC method for the determination of test item in dose formulation for *in vivo* studies
- Validation of a HPLC method for the determination of test item in dose formulation for *in vivo* studies

v. Bioanalysis
- Development of the bioanalytical method for the determination of the test item (PKL-021) and one metabolite concentration in the rat plasma
- Validation of the bioanalytical method for the determination of the test item (PKL-021) and its metabolite (PKL-024) concentration in the rat plasma
- Development of the bioanalytical method for the determination of the test item (PKL-021) and its metabolite (PKL-024) concentration in the non-rodent[1] plasma
- Validation of the bioanalytical method for the determination of the test item (PKL-021) and its metabolite (PKL-024) concentration in the non-rodent[1] plasma

[1] The selection of the non-rodent species will be confirmed after the completion of the ongoing DMPK studies.

vi. Project Management

d) The Contractor will be required to:
   i. Perform the order as a comprehensive research service.
   ii. Delegate to the project execution a team of specialists with the necessary knowledge and documented experience in the implementation of similar projects.
   iii. Organize regular project meetings to discuss project progress (frequency: at least every two weeks).
   iv. Prepare the project documentation in English.
   This includes draft study plans for review, draft reports (non-audited and audited) for review, as well as final versions of these documents. The draft reports should include all relevant study data and contributing reports. The final report should include all text, summary tables and all phase and/or contributor reports and should be a text searchable, hyperlinked, bookmarked PDF document. Tabulated summaries of each study should be delivered as well (CTD format) in word as well as PDF. Where applicable, SEND data sets should be delivered as well.
   v. Grant consent to conduct an audit of the site before signing the contract. The Ordering Party reserves the right not to sign contract in case of a negative audit result, i.e. finding any critical deficiencies.

e) The Ordering Party will deliver:
   i. Test item with corresponding CoA (PKL-021)
   ii. Internal standard with corresponding CoA (PKL-023)
   iii. Standards of the test item and the metabolite with corresponding CoA (PKL-021 & PKL-024)
   iv. The analytical procedure for the determination of the test item PKL-021 in mice plasma by LC-MS/MS
   v. The procedure for the the preparation of the dosing formulation
   vi. The analytical procedure for the determination of the test item in the dosing formulation
   vii. MSDS for the test item

f) The Timeline of the Project:

i.	Deadline for submitting the pricing proposals:	March 31, 2022
ii.	Completion of contracting process:	April 2022
iii.	Delivery of test item for DRF studies	May, 2022
iv.	Delivery of test item for GLP studies	1st week of September 2022
v.	DRF Studies initiation:	June 2022
vi.	GLP studies initiation:	September 2022
vii.	Project completion and delivery of the completed project documentation (electronic documentation):	January 31, 2023

g) Under this Request for proposal, the Ordering Party does not allow the submission of partial bids.

III. THE CONDITIONS FOR PARTICIPATION IN THE COMPETITION AND THE DESCRIPTION OF THE ASSESSMENT OF THE FULFILMENT THEREOF

a) The Request for proposal is directed to potential Contractors (Service Providers) conducting activities matching the description of the subject matter of the order i.e. they provide professional contract services in the field of preclinical safety assessment.

b) The procurement contract may be awarded to Service Providers who:
   i. offer performance of the service in accordance with the Request for Proposal no. 15/2022 and the Appendix no. 5
   ii. have a Good Laboratory Practice (GLP) certificate issued by competent national authorities
   iii. prove that no critical deficiency was found during the inspections of research sites and will present for this purpose the history of inspections (OECD GLP & FDA) in the last 5 years (2017-2021)[2]
   iv. ensure animal welfare in compliance with EU Directive 2010/63/EU and have current AAALAC accreditation (AAALAC: Association for Assessment and Accreditation of Laboratory Animal Care International)
   v. have the necessary expertise and experience, as well as technical resources and workforce capable of delivering the order
   vi. are in an economic and financial situation which allows them to duly execute the order
   vii. will do their best to execute the order in an environmentally friendly manner by ensuring that the use of materials, raw materials, energy, etc. is minimised

   Fulfilment of the conditions as above shall be evaluated based on the declaration included in the tender form filled out and signed by the Contractor (appendix No. 1).

   Copies of the Good Laboratory Practice (GLP) certificate and AAALAC accreditation, and the history of inspections (OECD GLP inspections and FDA inspections) from the last 5 years (2017-2021)[2] should be attached to the pricing proposal, so the Ordering Party could verify the Contractor's ability to perform the project.

   The Ordering Party reserves the right to ask for copies of selected documents issued by regulatory agencies after inspections which took place between January 2017[2] and December 2021. If copies of the above documents are not disclosed to the Ordering Party within ten days from the date of sending a written request for making them available, the offer will be considered invalid.

c) The following shall not be eligible:
   i. Service Providers having personal or capital relations with the Ordering Party. The term “capital or personal relations” refers to mutual relations between the Ordering Party or persons authorised to incur liabilities on behalf of the Ordering Party or persons involved in the preparation and execution of the Contractor selection procedure on behalf of the Ordering Party, and the Contractor, involving in particular the following:
      - participation in the company as a partner in a civil partnership or partnership;
      - ownership of at least 10 % of shares;
      - acting as a member of the supervisory or managing board, proxy, plenipotentiary;
      - being married, in a direct or secondary relationship of kinship or affinity or in a relationship involving adoption, custody or guardianship.

[2] If the research site is operating after 2017, the history of the inspection from the beginning of its operation should be presented.

In order to document lack of grounds for exclusion, the Supplier shall attach to its bid a Declaration on lack of grounds for exclusion from the procedure due to personal or capital relations (Appendix No. 2).

ii. entities which, as a result of deliberate action or gross negligence, misled the Ordering Party when presenting the information that they are not subject to exclusion or who concealed such information or are unable to produce the documents required;

iii. entities which, as a result of carelessness or negligence misrepresented information, misleading the Ordering Party, which in consequence could have a significant impact on decisions taken by the Ordering Party in the procurement award procedure;

iv. entities which entered into an agreement with other bidders aimed at manipulating competition between bidders in the contract award procedure, which the Ordering Party is able to prove by demonstrating relevant evidence;

v. entities that have culpably committed a substantial breach of professional duties compromising its integrity, in particular where the entity failed to perform or misperformed the contract as a result of a deliberate action or gross negligence, which the Ordering Party is able to prove by demonstrating relevant evidence.

d) The bid of an excluded entity shall be deemed to be rejected.

e) The Ordering Party may exclude an entity at any stage of the procurement award procedure.

f) Submitting a bid is tantamount to accepting, without reservation, the content of this Request for proposal.

IV. BID EVALUATION CRITERIA

a) Price – Weight: 95% (95 points)

In the "Price" criterion, points shall be awarded (to two decimal places) according to the following formula:
$P_c = C_{min}/C_{cons} \times 95$
P_c – points for price criterion
C_{min} – the lowest net price
C_{cons} – net price of the bid under consideration
95 – criterion weight (95%)

b) Payment deadline – Weight: 5% (5 points)

For the criterion "Payment deadline", points shall be awarded according to the following formula:
5 points – when the payment deadline is 30 days from the date of delivery of a correctly issued invoice,
2.5 points – when the payment deadline is 14 days from the date of delivery of a correctly issued invoice,
0 points –when the payment deadline is 7 days from the date of delivery of a correctly issued invoice.

If there are two or more bids with equal score awarded, the Ordering Party shall call upon the Contractors that submitted equally scored bids to submit additional bids by the date and time specified by the Ordering Party. Contractors submitting additional bids may not offer prices higher than those offered in the previously submitted bids.

V. DEADLINE AND MODE FOR SUBMITTING BIDS

a) Bids should be delivered to the Ordering Party in line with the template provided as Appendix No. 1 to this Request for proposal. Please enclose to the pricing proposal (based on the Appendix No. 1):
   i. the detailed pricing proposal (based on company templates)
   ii. the project timeline
   iii. a copy of the GLP certificate
   iv. a copy of AAALAC accreditation
   v. the history of inspections (OECD GLP & FDA) in the last 5 years (2017-2021)
   If the site is operating after 2017, the history of the inspection from the beginning of its operation should be presented.

b) The offer should be signed physically on the document or electronically by a duly authorised representative of the Supplier.

c) Bids should be submitted electronically to the following e-mail address: pricing_offers@pikralida.eu or via the competitiveness database as a response hereto, whether personally or by post (the date of receipt shall be considered binding) to the address of the Ordering Party.

d) **The bids must be submitted by the 8th of April, 2022 until: 11:59 pm.**

e) The date of submission of a bid shall be the date of its receipt by the Ordering Party.

f) Any bids received after the deadline, to the wrong e-mail address, on the wrong form as well as incomplete bids shall not be evaluated.

g) Bids shall include a validity terms of at least 30 days from the date designated for submission of bids.

h) A Supplier may submit only one bid per Request for proposal.

i) All costs associated with the preparation of the bid shall be borne by the Service Provider / Supplier.

j) **Any inquiries regarding the subject matter of the order should be sent via the Competitiveness Database or via email to j.lipner@pikralida.eu by March 31, 2022 until: 15:00. The authorised contact person is: Joanna Lipner.**

k) Please indicate prices both as a net (without VAT) and gross value.

l) The values specified in the bid (net amount, gross amount) shall be rounded to two decimal places, following the mathematical rule for rounding numbers.

m) The bid price shall include applicable VAT, if any. The correct determination of VAT is the responsibility of the contractor. Should VAT be incorrectly determined, the bid price to be taken into consideration in the evaluation shall be net.

n) If the Bidder submits an offer in a foreign currency, it is assumed that the basis for converting the value of the offer containing the price in a currency other than PLN is the average exchange rate of PLN in relation to this currency on the date of the inquiry announced by the National Bank of Poland.

o) The Ordering Party does not allow for a bid price to be submitted in several variants.

p) The bidder may change or withdraw its bid before the bid submission deadline.

VI. NOTICE OF AWARD

The bidder shall be notified that his bid was awarded via e-mail. The results of the procedure, in accordance with the principle of competitiveness, shall be made public using the same notification mode as for the Request for proposal.

VII. MATERIAL PROVISIONS OF THE AGREEMENT AND THE CONDITIONS FOR AMENDING THE SAME

a) The Supplier shall be obligated to conclude an agreement in line with the conditions included herein and in the tender.
b) The Ordering Party reserves the right to award a supplementary contract to the selected Contractor (the Contractor selected in the procedure np. 15/2022). The additional order cannot exceed 50% of the value of the basic order.
c) The subject of the supplementary order will be consistent with the subject of the basic order.
d) No substantial amendments shall be made to the provisions of the agreement concluded considering the contents of the bid constituting the basis for selecting contractor, unless:
    i. such amendments relate to implementation of additional services or supplies from the existing Contractor, not included in the basic contract, if they have become necessary, and the following conditions are jointly met:
        - the Contractor may not be changed due to economic or technical reasons, in particular regarding interchangeability or interoperability of equipment, services or installations, ordered under the basic contract,
        - changing the Contractor would cause considerable inconvenience or increase the costs for the Ordering Party,
        - the value of each subsequent amendment does not exceed 50% of the contract value initially specified in the agreement,
    ii. the amendment does not change the nature of the agreement, and the following conditions are jointly met:
        - the need to amend the agreement is caused by a force majeure understood as an event or combination of events or circumstances beyond the control of the Parties, which substantially hinder or prevent the performance of particular Party's obligations under the agreement, which could not have been foreseen, prevented or overcome had that Party acted with due diligence,
        - restrictions are introduced due to an epidemic emergency state being declared on the territory of the Republic of Poland,
        - the value of the amendment does not exceed 50% of the contract value initially specified in the agreement,
    iii. the amendment does not change the character of the agreement, and the total value of the amendment is lower than the amounts specified in provisions issued pursuant to Article 11 section 8 of the Public Procurement Law that are behind the obligation to notify the Publications Office of the European Union, while being lower than 10% of the order value originally indicated in the contract.

    Any amendments to the agreement to be concluded as a result of the procedure must be made in writing in order to be valid.
e) Information regarding contractual penalties:
    i. Should any Party terminate the Agreement or withdraw therefrom for reasons attributable to the Contractor, the Ordering Party shall charge a contractual penalty equal to 5% of the contract value.
    ii. The evidence basis for the calculation of contractual penalties shall be a debit note of the Ordering Party delivered to the Contractor in the form of an e-mail message to the address indicated in the bid/agreement.
    iii. The Ordering Party shall have the right to deduct the contractual penalties from the supplier's remuneration.
    iv. The Ordering Party shall have the right to claim damages in excess of the amount of contractual penalties specified in the Agreement on general terms.
    v. The contractual penalties shall be payable within 7 days from the date of delivery of the debit note to the Contractor by the Ordering Party.
    vi. The contractual penalties shall be cumulative.

VIII. OTHER

a) The Ordering Party reserves the right to cancel the procedure at any stage, without giving reasons therefor.
b) The issuance of this Request for proposal does not oblige the Ordering Party to accept a particular bid, in whole or in part, and does not oblige it to provide explanations or reasons for accepting or rejecting a particular bid.
c) The Ordering Party reserves the right to request additional information, documents, or clarifications.
d) In justified cases, at any time before the deadline for submission of bids, Pikralida sp. z o.o. may modify or supplement the content of the Request for proposal. The Ordering Party shall inform about the changes made using the same mode as for notifying the public about the Request for proposal.
e) This Request for proposal does not oblige Pikralida sp. z o.o. to enter into an agreement.
f) The Ordering Party shall not be responsible for any costs or expenses incurred by bidders in connection with preparation and submission of the bid.
g) The Ordering Party reserves the right to reject an abnormally low bid.[3]

IX. APPENDICES TO THE REQUEST FOR PROPOSAL

a) Appendix no. 1: Tender form template.
b) Appendix no. 2: Declaration of personal and capital relations with the Ordering Party.
c) Appendix no. 3: Statement regarding the fulfilment of the information obligation provided for in Article 13 or Article 14 of the GDPR.
d) Appendix no. 4: Confidentiality agreement template.
e) Appendix no. 5: Technical Information Package (disclosed after signing the confidentiality agreement).

[3] An abnormally low bid shall mean a bid with a total price (including the applicable VAT) lower than 70% of the price of all bids submitted under the procedure.