**APPENDIX NO. 1 TO REQUEST FOR THE PROPOSAL NO. 16/2023-DUBs**

Name : \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_
Company Identification Number: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Address: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Phone no.\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Fax.\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Contact person: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ e-mail:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

To:

**Molecure S.A.**

**02-089 Warsaw, Zwirki i Wigury 101**

**VAT ID PL7282789248**

In response to request for offers 16/2023-DUBs

1. We declare that we submit this offer and we offer the following:

Part 1: In vitro safety

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **No** | **Assay** | **Assay description** | **Amount of Assay** | **Net Price** | **Net Value** | **Gross Value** |
| 1 | AMES fluctuation assay – utilizing 4 strains of Salmonella: TA98, TA100, TA1535, TA1537 with or without rat liver S9 fraction (with cytotoxicity assay) | 1 compound, 4 concentrations (48 repetitions) | 2 |  |  |  |
| 2 | hERG Human Potassium Ion Channel cell based automated patch clamp assay | IC50 determination, 1 compound, minimum 5 concentrations in duplicate | 5 |  |  |  |
| 3 | Interaction with ion channel acccording to CiPA initiative – minimum 6 different assays, automated patch clamp  | 1 compound, 3 concentrations in duplicate | 2 |  |  |  |
| 4 | Kinase inhibition panel (minimum 50 different kinases)for example: SAPK2A (p38alpha), Akt1, GSK3beta, c-Raf (Raf-1), MEK1, PKA, Fyn, PKC, CDK2/CyclinA, CDK1 /CyclinB, IKKalpha, PDGFRbeta, IGF1R, LYN, Aurora-A, CDK6 /CyclinD3, Abl, EGFR, EphB4, ALK, PI3Kgamma, Plk3, Pim1, IRAK4, TAK1, ROCK1, PI3Kalpha, PI3Kbeta, PI3Kdelta, ASK1, KDR (VEGFR2), JAK2, eEF-2K, MNK2, LOK, MLK1, mTOR, AMPKalpha1 | Screening 1 compound at 1 concentration in duplicate | 1 |  |  |  |
| 5 | Off-targets interaction panel (safety/diversity panel) for minimum 87 off-targets, for example:NK1 receptor, NK2 receptor, NK3 receptor, Rat Neuropeptide Y receptor, alpha2 Rat Adrenoceptor, Rat Opioid receptor, B1 Bradykinin receptor, H2 Histamine receptor, Glutamate Rat Ion Channel, Rat P2X Ion Channel, Rat P2Y receptor, H3 Histamine receptor, CRF1 receptor, ER NHR, MT1 receptor, CHT1, V1A Human Vasopressin / Oxytocin receptor, Cav1.2 (L-type) Rat Calcium Ion, TRH receptor, Cav1.2 (L-type) Rat Ion Channel, KWP Rat Ion Channel, KV rat Ion Channel, SKCa Rat Ion Channel, Rat Sodium Ion Channel, Rat GABAA Ion Channel, beta1 Adrenoceptor receptor, MAO-A, EP2 Prostanoid receptor, A1 Adenosine receptor, beta2 Adrenoceptor receptor, ATPase (Na+/K+), Brain, Pig, PDE5, HDAC3, Tyrosine Hydroxylase, CENPE, EG5 Human Kinesin, IP Human Prostanoid receptor, PR Human Progesterone NHR, W1 receptor, HDAC4, HDAC6, Sirtuin 1, Sirtuin 2, PTP1B, W2 receptor, HDAC11, 5-HT1, Rat GABAA Ion Channel, Adenylyl Cyclase, Guanylyl Cyclase, nAChR (alpha4/beta2) Ion Channel, B2 Bradykinin receptor, MAO-B, sigma, NET, NOP (ORL1) Opioid receptor, Acetylcholinesterase, CB2 receptor, CCK1 receptor, A2A Adenosine receptor, PDE1B, PDE2A1, PDE3A, PDE4D2, CCK2 receptor, COX1, MC4 receptor, SET, D1 receptor, CDC25A, D2S receptor, GABA transaminase, PKCalpha, GR, CB1 receptor, D3 receptor, D4.4 receptor, V2 Human Vasopressin / Oxytocin receptor, DW, ETA receptor, ETB receptor, Rat GABAA Ion Channel, A3 Adenosine receptor, GABA Rat Transporter, PPARgamma, Glutamate Rat Ion Channel, 5-LOX, alpha1 (Non-Selective) Rat Adrenoceptor, Imidazoline I2, CysLT1 receptor, H1 Histamine receptor, Rat Acetylcholine receptor, AR Androgen NHR | Screening 1 compound at 1 concentration in duplicate | 2 |  |  |  |
| 6 | Safety/off-targets panel (minimum 40 off-targets), for example:Delta DOP, mu MOP, H2 histamine receptor, alpha2A Adrenoceptor, 5-HT1A, D2S Dopamine, 5-HT2B, V1A Human Vasopressin/Oxytocin receptor, Cav1.2 (L-type) Rat Calcium Ion Channel, KV (Non-Selective) Rat Potassium Ion Channel, Rat Sodium Ion Channel, beta1 Adrenoceptor, beta2 Adrenoceptor, alpha1A adrenoceptor, Rat GABAA Ion Channel, Lck, nAChR (alpha4/beta2), NET, acetylcholinesterase, CB2, CCK1 (CCKA), A2A Adenosine receptor, PDE3A, PDE4D2, hERG, 5-HT3, COX1, COX2, 5-HT1B, SET, D1, MAO-A, kappa (KOP) receptor, GR, CB1 receptor, 5-HT2A, DW, ETA receptor, NMDA Rat Ion Channel, H1 Histamine receptor, M1 Acetylcholine receptor, M2 Acetylcholine receptor | Screening 1 compound at 1 concentration in duplicate | 2 |  |  |  |
|  |  |  |  | **TOTAL:** |  |  |

Part 2: ADME I

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **No** | **Assay** | **Assay description** | **Amount of Assay** | **Net Price** | **Net Value** | **Gross Value** |
| 1 | Determination of Caco-2 bidirectional permeability (pH 6.5/7.4) | 1 compound, 1 concentration | 10 |  |  |  |
| 2 | Determination of MDCKII-MDR1 bidirectional permeability | 1 compound, 1 concentration | 10 |  |  |  |
| 3 | Determination of intrinsic clearance (CLint) using liver microsomes (Human or Rat or Mouse) | 1 compound, 1 concentration | 10 |  |  |  |
| 4 | Determination of intrinsic clearance (CLint) using liver microsomes (Monkey or Dog or Minipig) | 1 compound, 1 concentration | 3 |  |  |  |
| 5 | Determination of intrinsic clearance (CLint) using intestinal microsomes (Human or Rat or Mouse) | 1 compound, 1 concentration | 3 |  |  |  |
| 6 | Determination of intrinsic clearance (CLint) using intestinal microsomes (Dog) | 1 compound, 1 concentration | 3 |  |  |  |
| 7 | Determination of intrinsic clearance (CLint) using cryopreserved hepatocytes (Rat or Mouse) | 1 compound, 1 concentration | 3 |  |  |  |
| 8 | Determination of intrinsic clearance (CLint) using cryopreserved hepatocytes (Monkey or Minipig or Human or Dog) | 1 compound, 1 concentration | 3 |  |  |  |
| 9 | Determination of plasma stability (Human or Rat or Mouse) | 1 compound, 1 concentration | 3 |  |  |  |
| 10 | Determination of plasma stability (Monkey or Dog) | 1 compound, 1 concentration | 3 |  |  |  |
| 11 | Determination of plasma protein binding (Human or Rat or Mouse) | 1 compound, 1 concentration | 10 |  |  |  |
| 12 | Determination of plasma protein binding (Monkey or Dog or Minipig) | 1 compound, 1 concentration | 3 |  |  |  |
| 13 | Microsomal protein binding (Human or Minipig or Rat or Mouse) | 1 compound, 1 concentration | 4 |  |  |  |
| 14 | Microsomal protein binding (Dog) | 1 compound, 1 concentration | 3 |  |  |  |
| 15 | Tissue homogenate protein binding (mice or rat; e.g, brain) | 1 compound, 1 concentration | 3 |  |  |  |
| 16 | Evaluation of cytochromes inhibition including: CYP1A, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, CYP3A (midazolam and testosterone as probe substrates) (HLM, 1 TA concentration), package of 8 assays | 1 compound, 1 concentration | 3 |  |  |  |
| 17 | Evaluation of cytochromes inhibition for CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6 or CYP3A (midazolam and testosterone as probe substrates) (HLM, IC50 determination), non-package | 1 compound, 8 concentrations | 6 |  |  |  |
| 18 | Blood stability (mouse or rat) | 1 compound, 1 concentration | 3 |  |  |  |
| 19 | Blood stability (human) | 1 compound, 1 concentration | 3 |  |  |  |
|  |  |  |  | **TOTAL:** |  |  |

Part 3: ADME II

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **No** | **Assay** | **Assay description** | **Amount of Assay** | **Net Price** | **Net Value** | **Gross Value** |
| 1 | Blood to plasma ratio (Human or Mouse) | 1 compound, 1 concentration | 3 |  |  |  |
| 2 | Blood to plasma ratio (Rat) | 1 compound, 1 concentration | 3 |  |  |  |
| 3 | Blood to plasma ratio (Monkey or Dog) | 1 compound, 1 concentration | 3 |  |  |  |
| 4 | Metabolite identification in vitro (liver microsomes) cold compound; Human or Monkey or Dog or Rat or Mouse) | 1 compound, 1 concentration | 2 |  |  |  |
| 5 | Metabolite identification in vitro (cryopreserved hepatocytes); cold compound; Human or Monkey or Dog or Rat or Mouse) | 1 compound, 1 concentration | 2 |  |  |  |
| 6 | Reactive metabolite assessment (glutathione trapping) (1 compound, HLM in the presence and absence of NADPH) | 1 compound, 1 concentration | 3 |  |  |  |
| 7 | CYP reaction phenotyping (CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6 or CYP3A4; recombinant enzymes) | 1 compound, 1 concentration | 3 |  |  |  |
| 8 | UGT reaction phenotyping (UGT2B7, UGT1A1, UGT1A3, UGT1A6, UGT1A9, UGT2B15, UGT1A4) (recombinant enzymes) | 1 compound, 1 concentration | 1 |  |  |  |
| 9 | Evaluation of cytochromes inhibition for CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, or CYP3A (midazolam and testosterone as probe substrates) (HLM, time-dependent inhibition (IC50 shift)) | 1 compound, 5 concentrations | 2 |  |  |  |
| 10 | Evaluation of cytochromes induction (CYP1A2, CYP2B6, CYP3A4; 3 donors; 3 concentrations; mRNA endpoint) | 1 compound, 3 concentrations | 2 |  |  |  |
| 11 | Inhibition of drug transporters including: P-gp, BCRP, MRP2, OAT1, OAT3, OATP1B1, OATP1B3, OCT1, OCT2, MATE1, MATE2-K (1 concentration) | 1 compound, 1 concentration | 1 |  |  |  |
| 12 | Inhibition of drug transporters including: BSEP (1 concentration) | 1 compound, 1 concentration | 1 |  |  |  |
| 13 | Inhibition of drug transporters for P-gp, BCRP, MRP2, OAT1, OAT3, OATP1B1, OATP1B3, OCT1, OCT2, MATE1 or MATE2-K (IC50 determination) | 1 compound, 5 concentrations | 1 |  |  |  |
| 14 | Inhibition of drug transporters for BSEP (IC50 determination) | 1 compound, 5 concentrations | 1 |  |  |  |
| 15 | Half-life  (blood; dog or monkey) | 1 compound, 1 concentration | 3 |  |  |  |
| 16 | Glutathione conjugate detection (liver S9; mouse or rat or human) | 1 compound, 1 concentration | 1 |  |  |  |
| 17 | Glutathione conjugate detection (liver S9; dog or monkey) | 1 compound, 1 concentration | 1 |  |  |  |
|  |  |  |  | **TOTAL:** |  |  |

1. We offer the total price for the order execution (PART 1): .................................. (PLN/EUR/USD/GBP)\* Net ……………………………… (PLN/EUR/USD/GBP)\* Gross\*\*
2. We offer the total price for the order execution (PART 2): .................................. (PLN/EUR/USD/GBP)\* Net ……………………………… (PLN/EUR/USD/GBP)\* Gross\*\*
3. We offer the total price for the order execution (PART 3): .................................. (PLN/EUR/USD/GBP)\* Net ……………………………… (PLN/EUR/USD/GBP)\* Gross\*\*
4. Invoice due date – \_\_\_\_\_\_ days from the date of delivery of a correctly issued invoice.
5. We declare that we are acquainted with the contents of the Request for the Offer. We consider ourselves bound with specified requirements and rules of the conduct. We declare to fully accept the presented rules and conditions. We also declare that we were provided with all the necessary information to prepare the offer.
6. **We declare that price includes all costs related to execution of the order.**
7. We declare that we consider ourselves bound by this offer for the time specified in the offer, ie. \_\_\_\_\_ days after the date set for the submission of tenders (minimum 30 days).
8. We declare to conclude an agreement in the place and time specified by the Ordering Party, if we are awarded the contract.
9. We declare that the offer does not contain confidential information within the meaning on counteraction to unfair competition acts\*.
10. We declare that the offer contains information constituting a business secret within the meaning of the counteraction to unfair competition acts. Such information is contained in the following documents\*:

…………………………………………………………………………………………………………………………………………………………….

*\** *Delete (scratch off) as appropriate*

*\*\*Please note that a supplier providing services to a VAT registered customer in another Member State without being established there will not charge any VAT on their invoice. The customer will reverse-charge the transaction. Therefore, please provide only Net values.*

*.............................* ........................................................

 *Date* / *legible signature or the signature and stamp
of the Contractor / person / persons authorized
to act on behalf of the Contractor\*\*/*

*\*\*Signature(-s) or the person(-s) authorized to act on behalf of the Contractor. Name stamp is required in the case of an illegible signature.*

**APPENDIX NO. 2 TO REQUEST FOR THE PROPOSAL NO. 16/2023-DUBs**

STATEMENT CONCERNING FULFILLMENT OF THE REQUIREMENTS SET OUT IN PART IV OF THE REQUEST FOR OFFERS

We declare that ………………………………………………………………………………………………………………………. (company name)

fulfils the following conditions:

1. We declare that we have the necessary qualifications to carry out the described activity.
2. We declare that we have the appropriate technical potential and personnel capable of performing the contract.
3. We declare that we are in a good economic and financial standing, which assures proper execution of the order.
4. We declare that we will pursue the contract in a way that is beneficial to the environment by minimizing the consumption of materials, raw materials, energy, etc.

*.............................* ........................................................

 *Date* / *legible signature or the signature and stamp
of the Contractor / person / persons authorized
to act on behalf of the Contractor\*/*

*\*Signature(-s) or the person(-s) authorized to act on behalf of the Contractor. Name stamp is required in the case of an illegible signature.*

**APPENDIX NO.3 TO REQUEST FOR THE PROPOSAL NO. 16/2023-DUBs**

**Statement regarding personal and capital connections
with the Ordering Party**

I, undersigned …………………………… acting in the name of the Contractor under the name …………………………………………

**declare that:**

1. The Contractor **has not** any personal or capital connections with the Ordering Party as mentioned in paragraph 3 below**\***.
2. The Contractor **has** a personal or capital link with the Ordering Party\*/ persons authorized to take on commitments on behalf of the Ordering Party\*/ persons responsible for the preparation and the execution of the process of selecting the contractor\* by (please indicate the type of connection referred to in paragraph 3, point 1 to 4)\*\*:

…………………………………………………………………………………………………………………………………………………………..

1. Capital or personal relationship is understood as relations between the Ordering Party or individuals authorized to take commitments on behalf of the Ordering Party or those acting on behalf of the Ordering Party in order to prepare and implement the contractor selection procedure, and the Contractor, including in particular:
2. participation in the company, in a civil or limited partnership.
3. holding at least 10 % shares or interests.
4. serving a function of a member of the supervisory organ, a member of the management organ or proxy.
5. having family ties, such as by marriage, by lineage at first or second degree, by adoption, guardianship or custody.

*\** *Delete (scratch off) as appropriate*

*\*\* Fill in only if personal or capital connections ore present*

*............................................. ..............................................................*

 *Date* / *legible signature or the signature and stamp
of the Contractor / person / persons authorized*

 *to act on behalf of the Contractor\*\*\*/*

*\*\*\* Signature(-s) or the person(-s) authorized to act on behalf of the Contractor. Name stamp is required in the case of an illegible signature.*

**APPENDIX NO. 4 TO REQUEST FOR THE PROPOSAL NO. 16/2023-DUBs**

DECLARATION OF COMPLIANCE WITH THE INFORMATION OBLIGATIONS PROVIDED FOR IN ARTICLE 13 OR ARTICLE 14 OF THE GDPR

**I hereby declare that I have complied with the information obligations provided for in Article 13 or Article 14 of the GDPR1) towards natural persons from whom I have obtained, directly or indirectly, personal data in order to compete for the award of a public contract in this procedure.2**

 .....................................................

*signature(-s) or the person(-s) authorised to*

*act on behalf of the Contractor*

*and a name stamp/name stamps\**

*\*name stamp in the case of an illegible signature*

1) Regulation (EU) 2016/679 of the European Parliament and of The Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation) (O.J. EU L 119 of 04.05.2016, p. 1).

2) If the contractor does not provide personal data other than data directly related to the contractor or if the application of the information obligation is excluded pursuant to Article 13(4) or Article 14(5) of the GDPR, the contractor shall not make the declaration (delete the declaration wording by, for instance, crossing it out).

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

INFORMATION CLAUSE

Pursuant to [Article 13(1) and (2)](https://sip.legalis.pl/document-view.seam?documentId=mfrxilrtgm2tsnrrguytsltqmfyc4mzuhaztimztgq) of Regulation (EU) [2016/679](https://sip.legalis.pl/document-view.seam?documentId=mfrxilrtgm2tsnrrguyts) of the European Parliament and of The Council [of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive](https://sip.legalis.pl/document-view.seam?documentId=mfrxilrvgaytgnbsge4a) 95/46/EC (“**GDPR**”), we hereby inform that:

* Your personal data is controlled by Molecure spółka akcyjna (joint-stock company) with its registered office in Warsaw, address: Żwirki i Wigury 101, 02-089 Warsaw, entered in the register of entrepreneurs of the National Court Register, kept by the District Court for the capital city of Warsaw, 12th Commercial Division of the National Court Register, under KRS Number 0000657123, e-mail address: contact@molecure.com, tel. 22 552 67 24 (“**Controller**” or „**Company**”). In matters relating to personal data protection, please contact Marta Borkowska, e-mail: m.borkowska@molecure.com, tel. 22 552 67 24.
* Your personal data will be processed on the basis of Article 6(1)(c) of the GDPR for the purpose of the tendering procedure conducted on a competitive basis, under which you have responded to the request for quotation.
* Your personal data will be stored for a period of 5 years from the end of the year when the performance of the agreement with you is complete. If your bid is not selected, your personal data will be stored for a period of 5 years from the end of the year when the tender procedure you submit your bid for has ended.
* Your provision of personal data is voluntary, yet necessary to participate in the tender procedure conducted by the Company on a competitive basis.
* Your personal data will not be subject to automated decision-making pursuant to Article 22 of the GDPR;
* you have the right:
* of access your personal data;
* to rectification of your personal data;
* to request from the controller restriction of processing of personal data, subject to the cases referred to in Article 18(2) of the GDPR;
* to file a complaint with the President of the Personal Data Protection Office, if you believe that the processing of your personal data violates the GDPR provisions;
* to erasure of personal data, except the cases referred to in Article 17(3) (b), (d) or (e) of the GDPR;
* to data portability referred to in Article 20 of the GDPR, except and subject to the cases indicated there
* you do not have the right to object to the processing of personal data on the basis of Article 21 of the GDPR, since the legal grounds for the processing of your personal data is Article 6(1)(c) of the GDPR.
* Your personal data may be transferred outside the European Economic Area. However, if in the course of business it becomes necessary that your personal data be transferred outside the European Economic Area on account of your obligations, we will make every effort and ensure that the receiving entities observe the principles set forth in the GDPR, int. al. that they meet the requirements of the Privacy Shield framework.
* Your provision of data is voluntary.