Cellis Ltd.
ul. Generała Zajączka 28, 01-510 Warsaw, Poland
VAT EU: PL5252640606
tel./fax (00 48 22) 59 362 77
www.cellis.eu

Warsaw, 09.04.2020 r.

REQUEST FOR QUOTATION No. 1/SS/2020

As a part of the project „Innovative cell-based glioma therapy" co-financed by European Union Founds under measures of the Operational Programme Smart Growth 2014 – 2020 under „Fast track", Cellis Ltd. request to submit price quotation for:

The service of validating research technology in established models of glioma.

1. ORDERING PARTY

Cellis Ltd.

ul. Generała Zajączka 28

01-510 Warsaw, Poland

VAT EU: 525-264-06-06

2. DESCRIPTION OF THE ORDER:

2.1 The subject of the order:

The service of validating research technology in established models of glioma.

2.2 The abovementioned order consist of:

1) Investigating research technology on the basis of protocols and compounds provided by Ordering Party (conjugates of carrier protein with specific drugs: toxins or immunomodulators; and necessary controls) in a panel of 15 human glioma cell lines comprising 2D and 3D growing cell line models.

2) Investigating research technology in orthotopic xenograft mouse models and orthotopic fully immunocompetent mouse models of glioma.

Detailed experiments to be done by the contractor are performed in the Appendix 1

„BID FORM for request for request for quotation no. 1/SS/2020"

2.3 The subject of the order specified in point 2.1 shall be received or supplied no later than 31.12.2023.

2.4 Under this invitation to tender Ordering Party does not allow partial receipt of tenders or variant offers.

2.5 CPV code:

73100000-3 Research and experimental development services

3. CONDITIONS FOR PARTICIPATION IN THE PROCEEDINGS

3.1 Contractors participating in the proceedings must fulfil following conditions:

1) Must have necessary expertise and experience - at least two documented experience in glioma models confirmed by at least two project from last two years.

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2) Must have technical potential, including:

- high-content microscopy, high-dimensional FACS, confocal microscopy, multi-photon microscopy and in vivo imaging devices (e.g. IVIS),
- fully equipped laboratory and access to animal facility,
- glioma models (e.g. LN-229, LN-308, ZH-161, ZH-305) and technologies in genomics and proteomics,
- macrophage cell lines (THP-1, BMA), blood leukocytes obtained from healthy volunteers and facility to culture them and polarize towards macrophages,
- access to glioma patients in order to obtain tumor samples directly from the patients and use for study,
- experience in performing pre-clinical studies also for commercial partners.

The statement about fulfilling conditions for participation in the proceedings is attached as Appendix 2 to this request for quotation 1/SS/2020.

3.2 The Contractor may not be personally or equity related to the Ordering Party.

A related entity is understood as:

a) related or being a subsidiary, jointly controlled or parent entity in relation to the Beneficiary within the meaning of the Accounting Act of September 29, 1994;
b) being an entity that remains with the Beneficiary or members of their bodies in such an actual or legal relationship that may raise reasonable doubts as to the impartiality in the selection of a supplier of goods or services, in particular married, consanguinity or affinity to the second degree, adoption, custody or guardianship, also through membership of the supplier's bodies;
c) being a related entity or partner entity in relation to the Beneficiary within the meaning of Regulation No. 651/2014;
d) being an entity related personally to the Beneficiary within the meaning of art. 32 section 2 of the Act of 11 March 2004 on tax on goods and services.

The Bidder is obliged to submit a relevant statement contained in Annex 3 to the Inquiry 1/SS/2020.

4. PREPARATION AND SUBMISSION OF OFFERS

4.1 Each Bidder may submit only one offer.

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4.2 Offer should be prepared in the bid form (Appendix 1 to the request for quotation 1/SS/2020). The offer must be initialled and signed by the authorised representative of the Bidder. If the offer would be signed by the person not listed in registered documents of the Contractor, the offer shall be accompanied by the appropriate power of attorney.

4.3 Offer must include all attachments required by the Ordering Party confirmed to be true.

4.4 Contractor must submit with the offer copy (scan) of relevant Register of Business Activity, applicable to country of residence of Contractor, issued not earlier than three (3) months before the deadline for submission the offer to demonstrate the absence of grounds for exclusion.

4.5 The offer must be submitted by May 9, 2020 r. (23:59)

4.6 Offer must be send to the e-mail address: office@cellis.eu

4.7 Offers received after deadline or incomplete will not be considered.

4.8 The offer should include the validity date (at least 90 days from the submission deadline).

4.9 Submitting the tender means acceptance of the conditions stated therein.

4.10 The Bidder may request the Ordering Party to clarify the content of the request for quotation. Inquiries can be submitted in writing or electronically, to the e-mail address given in the request for quotation. The awarding entity shall answer questions that have been received no later than by the end of half of the deadline for submission of tenders, except that the answer should be given at least 2 (two) days before the submission deadline. Answers to questions will be published on the page on which the request for quotation was published and sent to the Bidder who submitted the questions.

5. OFFER EVALUATION CRITERIA

5.1 The Ordering Party will evaluate offer based on the following criteria:

Methods of assessment – according to the formula below:

$$Pi=Pi(C) + Pi(Q)$$

where:

Pi – the amount of points received

Pi(C) – points for the „Price" criterium

Pi(Q) – points for the "Professional qualifications and experience of proposed staff/ personnel" criterium

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- Criterium „Price" – weight 80%

„Price" criterium will be calculated as follows:

Pi(C)=(Cmin : Ci) x 80

where:
Pi(C) – the amount of points given for the „Price" criterium
Cmin – the lowest price among all valid and non-rejected offers
Ci – the price of the currently evaluated offer

In the "Price" criterium Bidder may obtain 80 points.

- Criterium „ Professional qualifications and experience of proposed staff/ personnel" – weight 20%
  - (a) at least one person with two years' experience in glioma studies proofed by the list of min. 5 scientific papers published in this field and / or participation to min. 2 scientific projects in this field, (b) at least one person with two years' experience in clinical trials conducted in patients with glioma/glioblastoma and (c) at least one person with activity in cancer / neuro scientific associations - 40 points;
  - (a) at least one person with two years' experience in glioma studies proofed by the list of min. 5 scientific papers published in this field and / or participation to min. 2 scientific projects in this field and (b) at least one person with two years' experience in clinical trials conducted in patients with glioma/glioblastoma – 30 points;
  - at least one person with two years' experience in glioma studies proofed by the list of min. 5 scientific papers published in this field and / or participation to min. 2 scientific projects in this field – 20 points.

5.2 All calculations will be made to two decimal places.

5.3 The most advantageous offer will be considered the one which obtains the highest number of points.

5.4 The Awarding Entity reserves the right to ask the Bidder about the content of submitted bids, including to supplement missing powers of attorney, statements or documents indicated in the request for quotation (except for the extent to which they are subject to evaluation in the bid evaluation criteria).

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6. **ORDER COMPLETION DATE :** 36 months

7. **NOTICE OF SELECTION OF THE BEST TENDER**

The Bidder will be notified by e-mail (to e-mail address indicated in the bid form). In addition, information of the results of the proceedings will be published on the website of Ordering Party (www.cellis.eu).

8. **CHANGES IN THE AGREEMENT**

8.1 All modification to the agreement, which will be concluded as a result of the proceeding, must be in writing under pain of nullity.

9. **ADDITIONAL INFORMATION**

9.1 The Ordering Party reserves the right to cancel this procedure at any stage, without providing reasons.

9.2 This request for quotation does not oblige Cellis Sp. z o o. [Ltd.] to conclude an agreement.

10. **CONTACT**

Cellis Sp. z o.o. [Ltd.]

ul. Generała Zajączka 28

01-510 Warsaw, Poland

Contact person: Małgorzata Sęktas, e-mail m.sektas@cellis.eu

Any question about request for quotation may be submitted via e-mail

Appendices:

Appendix 1 Bid form

Appendix 2 Statement on the compliance with conditions for participation in the proceedings

Appendix 3 Statement concerning personal / capital connections between the Bidder and the Ordering Party.

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Appendix 1 BID FORM for request for request for quotation no. 1/SS/2020

Stamp of the Bidder

Name _____
Address _____
Phone no._____

Contact person: _____
e-mail: _____

Ordering Party:
Cellis Sp. z o.o.
Generała Zajączka 28
01-510 Warsaw, Poland
VAT EU: PL5252640606

According to the Request for quotation no 1/SS/2020 as a part of the project „Innovative cell-based glioma therapy" co-financed by European Union Founds under measures of the Operational Programme Smart Growth 2014 – 2020 under „Fast track", I submit tender:

I offer a gross price _____PLN / USD / EUR / OTHER……..*

1. Detailed calculation of the cost:

No	Product/ Activities	Gross price
1.	Real-time observation of the co-culture of macrophages and cancer cells using time-lapse microscopy in vitro. This study should be done in order to track fluorescently labeled carrier protein transfer from one cell to another. This should be done on the human LN-229, LN-308, ZH-161 and ZH-305 and human monocyte-derived macrophages. **At least three independent valid experiments should be done**.	

*** Confirm by ticking or adding relevant information

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2.	Observation of the fluorescently labeled carrier protein transfer from one cell to another in vivo in mice using in vivo imaging by fluorescence molecular tomography and ex vivo high-dimensional FACS, confocal microscopy and alternatively multi-photon microscopy. This should be done on at least two of the following human glioma cells: LN-229, LN-308, ZH-161 and ZH-305 and human monocyte-derived macrophages. **At least three independent valid experiments should be done, n=5 mice per group**. The same experiment will be done in orthotopic syngeneic glioma models using GL-261 cells syngeneic to C57BL/6 mice and SMA-560 cell syngeneic to VMD/k mice.	
3.	Efficacy in vitro - screening of the compounds provided by Ordering Party and **selection of at least three candidates** for further studies. The in vitro screening will be done on the following human glioma cells: LN-229, LN-308, ZH-161 and ZH-305 co-cultured with human monocyte-derived macrophages and a human macrophage cell line at different time-points (e.g. 24, 48 and 72 hrs). The readout should be number of cells in co-culture measured by FACS and live/dead staining. **At least three independent valid experiments should be done for each cell line for each compound**. This can be complemented in glioma samples directly obtained from surgery by a novel method based on high-content imaging and computer vision and machine learning algorithms.	
4	Pharmacokinetic study of the three compounds administered in macrophages, as selected in previous study. Two cell lines will be selected based on the previous study. Macrophages containing compound of interest will be administered to healthy and brain tumor bearing mice (two models) and mice will be sacrificed at time-points: 1, 4, 8, 16, 24, 48 and 72 hrs. The controls will be plain drug and protein-carrier drug conjugate. **At least two independent experiments will be done with n=5 mice per group**. The contractor will provide Cellis with mouse tissues from this experiment for further studies (liver, lungs, spleen, kidneys, heart, brain, blood.	
5	Investigation of changes within the tumor micro-environment (in glioma in vivo) after administration of macrophages loaded with two compounds provided by Ordering Party. This should be done by single cell RNAseq and high-dimensional flow cytometry. This study should be complementary with the previous one and should be done on at least two of the following human glioma cells: LN-229, LN-308, ZH-161 and ZH-305 and human monocyte-derived macrophages. At least three controls should be used: PBS, macrophages with plain carrier protein and plain drug. **At least three independent valid experiments should be done, n=3 mice per group**. To understand the microenviromental changes in syngeneic fully immunocompetent mice this study will be done also in orthotopic syngeneic glioma models using GL-261 cells syngeneic to C57BL/6 mice and SMA-560 cell syngeneic to VMD/k mice.	
6.	Investigation of efficacy of macrophages loaded with compounds provided by Ordering Party. Tumor size assessed by MRI and mice survival will be the outcomes of this experiment. This study should be complementary with the previous one and should be done on at least two of the following human glioma cells: LN-229, LN-308, ZH-161 and ZH-305 and human monocyte-derived macrophages. At least four controls should be used: PBS, standard therapy, macrophages with plain carrier protein and protein carrier with the drug. **At least two independent valid experiments should be done, n=15 mice per group.**	
7	Investigation of efficacy of macrophages loaded with compounds provided by Ordering Party on PDX models. Tumor size and mice survival will be the outcomes of this experiment. This study should be complementary with the previous one and should be done on PDX mice models and human monocyte-derived macrophages. At least four controls should be used: PBS, standard therapy, macrophages with plain carrier protein and protein carrier with the drug. **At least two independent valid experiments should be done, n=15 mice per group**. As in point 3 This can be complemented in glioma samples directly obtained from surgery by a novel method based on high-content imaging and computer vision and machine learning algorithms.	
	Total	

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2. Professional qualifications and experience of proposed staff/ personnel

a) Name and surname: …….

No.	Publication title	Journal	Date

No.	Project title	Unit or financial agency	Time

No.	Description of clinical trial	Unit or financial agency	Time

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No.	Name of the cancer/neuro scientific association

b) Name and surname: ……..

No.	Publication title	Journal	Date

No.	Project title	Unit or financial agency	Time

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No.	Description of clinical trial	Unit or financial agency	Time

No.	Name of the cancer/neuro scientific association

3. The Bidder declares that time of completing the order is _____ days / months.

4. The Bidder declares that all costs of the completion the order have been included in the price. The Price includes all reagents, laboratory plastics and using of equipment (except conjugates of carrier protein with specific drugs: toxins or immunomodulators, and necessary controls, that will be provide by the Ordering Party).

5.The Bidder declares that the offer will be valid for 60 days.

6. The Bidder declares that is familiar with Request for quotation, accept the conditions stated therein and does not raise any objection to completion the order in accordance with these conditions.

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_____ _____

Date and place

Signature of the Bidder /
Person authorized to act on behalf of the Bidder

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Appendix 2 STATEMENT ON THE COMPLIANCE WITH CONDITIONS FOR PARTICIPATION IN THE PROCEEDINGS for Request for quotation no. 1/SS/2020

Bidder

_____

(name and address of the Bidder)

1) The Bidder declares that have necessary expertise and experience - at least two documented experience in glioma models confirmed by at least two project from last two years.

No.	Project title	Unit or financial agency	Time

2) The Bidder declares that have technical potential, including:

- high-content microscopy, high-dimensional FACS, confocal microscopy, multi-photon microscopy and in vivo imaging devices (e.g. IVIS),
- fully equipped laboratory and access to animal facility,
- glioma models (e.g. LN-229, LN-308, ZH-161, ZH-305)and technologies in genomics and proteomics,
- macrophage cell lines (THP-1, BMA) and blood leukocytes obtained from healthy volunteers.

3) The Bidder declares that the data contained in the offer are true and adequate.

_____ _____

Date and place

Signature of the Bidder /
Person authorized to act on behalf of the Bidder

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Appendix 3 STATEMENT CONCERNING PERSONAL / CAPITAL CONNECTIONS BETWEEN THE BIDDER AND THE ORDERING PARTY for request for quotation no. 1/SS/2020

(Place)_____, date_____

Stamp of the Bidder

Statement concerning personal / capital connections between the Bidder and the Ordering Party

I, undersigned_____ declare, that:

Have not any personal or capital connections with the Ordering Party

A related entity is understood as:

a) related or being a subsidiary, jointly controlled or parent entity in relation to the Beneficiary within the meaning of the Accounting Act of September 29, 1994;
b) being an entity that remains with the Beneficiary or members of their bodies in such an actual or legal relationship that may raise reasonable doubts as to the impartiality in the selection of a supplier of goods or services, in particular married, consanguinity or affinity to the second degree, adoption, custody or guardianship, also through membership of the supplier's bodies;
c) being a related entity or partner entity in relation to the Beneficiary within the meaning of Regulation No. 651/2014;
d) being an entity related personally to the Beneficiary within the meaning of art. 32 section 2 of the Act of 11 March 2004 on tax on goods and services.

_____ Place and date

_____ Signature of the Bidder / Person authorized to act on behalf of the Bidder