Warsaw, 23.04.2020 r.

To participants in the proceeding

Applicable: Request for quotation no. 1/SS/2020 from 09.04.2020 r.

Ordering Party – Cellis Sp. z o.o. - informs about a change in the content of the Request for quotation no. 1/SS/2020 from 09.04.2020 r. and in the "BID FORM for request for quotation no. 1/SS/2020" constituting the Appendix 1 and in the "STATEMENT CONCERNING PERSONAL / CAPITAL CONNECTIONS BETWEEN THE BIDDER AND THE ORDERING PARTY for request for quotation no. 1/SS/2020" constituting the Appendix 3 to the above Request for quotation.

In the request for quotation point 3.2

– before change:

„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."

after change:

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

Equity 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:

a) Being a partner to civil law partnership or commercial law partnership,

b) Holding at least 10% of shares, if lower threshold does not result from law or is not specified by Managing Authority for the Operational Programme,

c) **Being a member of a supervisory or management corporate body, a holder of general commercial power of attorney, an authorised representative,**

d) **Being married to, being in direct consanguinity or affinity, second degree consanguinity or affinity of the second degree collaterally or by adoption or guardianship**.“

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

– before change:

„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;**

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.”

after change:

“Equity 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:

a) **Being a partner to civil law partnership or commercial law partnership,**

b) **Holding at least 10% of shares, if lower threshold does not result from law or is not specified by Managing Authority for the Operational Programme,**

c) **Being a member of a supervisory or management corporate body, a holder of general commercial power of attorney, an authorised representative,**

d) **Being married to, being in direct consanguinity or affinity, second degree consanguinity or affinity of the second degree collaterally or by adoption or guardianship.”**

In addition, in Appendix 1 „BID FORM for request for quotation no. 1/SS/2020" point 1 „Detailed calculation of the cost" the Ordering Party added information on the net amount offered.

The changes introduced in this letter are binding on bidders and should be treated as a modification of the content of the request for quotation no. 1/SS/2020 of 09.04.2020r and "BID FORM for request for quotation no. 1/SS/2020" constituting the Appendix 1 and in the "STATEMENT CONCERNING PERSONAL/ CAPITAL CONNECTIONS BETWEEN THE BIDDER AND THE ORDERING PARTY for request for quotation no. 1/SS/2020" constituting the Appendix 3 to the above Request for quotation.

The deadline and method of submitting offers is extended until **May 16, 2020 at 23:59**.

Sincerely,

Magdalena Król
Member of the Board

CELLIS Sp. z o.o.
ul. Gen. Zajączka 28
01-510 Warszawa
NIP: 525-264-06-06

Appendices:

Changed Appendix 1 Bid form

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

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

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 net price _____ PLN / USD / EUR / OTHER ……

and gross price _____PLN / USD / EUR / OTHER……..[1]

1. Detailed calculation of the cost:

No	Product/ Activities	Net price	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**.		

[1] Confirm by ticking or adding relevant information

No	Product/ Activities	Net price	Gross price
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		

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

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

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.

_____ _____

Date and place

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

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

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

Equity 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:

a) Being a partner to civil law partnership or commercial law partnership,
b) Holding at least 10% of shares, if lower threshold does not result from law or is not specified by Managing Authority for the Operational Programme,
c) Being a member of a supervisory or management corporate body, a holder of general commercial power of attorney, an authorised representative,
d) Being married to, being in direct consanguinity or affinity, second degree consanguinity or affinity of the second degree collaterally or by adoption or guardianship.

_____ _____

Place and date

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