Celgene International Sàrl
Route de Perreux
2017 Boudry
Svizzera
Tel: 0041 32 72

Amendment #1
to Clinical Trial Agreement
Protocol No. CC-5013-MDS-005

BETWEEN

The Company **Celgene International Sarl** (hereinafter the **Company**), tax code no. 34304, VAT number 582145, located in 2017 Boudry, Switzerland, Route de Perreux 1, represented by **Anna Fitzmaurice** (Associate Director Site Contracts), on behalf of the parent company **Celgene Corporation**, with headquarters in 86 Morris Avenue, Summit, NJ 07901, USA **("Celgene")**;

AND

The **Azienda U.S.L.** no. 8 in Cagliari (hereinafter called the "**Azienda**") TAX Code and VAT ID number no. 02261430926, with registered office in Selargius (Su Planu), Via Piero della Francesca, 1 represented by the General Director Dr. Emilio Simeone

WITNESSETH

- Celgene International Sarl has entered into a financial Agreement with the Hospital relating to a Clinical Trial CC-5013-MDS-005 entitled "***A Phase 3, Multicentre, Randomized, Placebo-Controlled, Parallel Group Study to Compare the Efficacy and Safety of Lenalidomide (Revlimid) vs. Placebo in Subjects With Transfusion Dependent Anemia Due to IPSS Low or Intermediate-1 Risk myelodysplastic syndrome without deletion 5q [31] and Unresponsive to of refractory to erythropoiesis stimulating agents***" (hereinafter the "Trial") at the Struttura Complessa di Ematologia e CTMO dell'Ospedale Oncologico-Businco di Cagliari, under the responsibility of **Dr. Emanuele Angelucci**;
- pursuant to Amendment no. 3 to the Protocol, approved by the Ethics Committee on 17/10/2012 (hereinafter the "Amendment"), the follow-up period of the study will be extended up to a maximum of 5 years.

The Recitals form an integral part of this Amendment.

THE PARTIES STIPULATE AND AGREE AS FOLLOWS:

1. Celgene previously released Protocol Amendment # 3 (the "Protocol Amendment") for the above Study. The Protocol Amendment extended the Follow-up period up to 5 years. By this Amendment, Celgene amends the budget set out in the Agreement that covers the conduct of the Study by including the following further activities.

   Due to the extension of the Follow-up period, the maximum number of Follow-up visits per patients is increased from 6 to 20. Each individual Follow-up visit will be compensated according to the cost already set out in the Budget Section of the Agreement.

   Although the estimate used for preparation of the budget included in the Agreement is based on a maximum of 12 cycles, the Protocol permits a patient to be treated for more than 12

cycles. Any additional cycles will be paid for by Celgene based on the cost of the 12 cycles provided for in the Agreement.

Following these changes, the parties agree to amend Article 6 to the Agreement with the new Article 6 herein attached to this Amendment, which shall replace and supersede the said Article.

Art. 6

As remuneration for the services included in this agreement, regarding 10 patients, the Company agrees to pay the Azienda, through bank transfer in favour of Azienda USL N.8 di Cagliari at:

Banco Di Sardegna Servizio Tesoreria – Viale Bonaria - Cagliari
IBAN Code:IT29G0101504800000070188775
BIC SARDIT3S

The following amounts :

1) BUDGET OVERVIEW : *For each evaluable patient who completes the Study in accordance with the Protocol, Sponsor, through CRO, will compensate the Institution remuneration as specified below :*

VISITS	**Clinical fees, in Euros, ex tax**
Screening	1,569.00€
Cycle 1	906.00€
Cycle 2	800.00€
Cycle 3	500.00€
Cycle 4	1,350.00€
Cycle 5	350.00€
Cycle 6	350.00€
Cycle 7	1,169.00€
Cycle 8	350.00€
Cycle 9	350.00€
Cycle 10	350.00€
Cycle 11	350.00€
Cycle 12	350.00€
Discontinuation	375.00€
28 Day post treatment	363.00€
Follow-up (x 20 visits)	44.00€/visit
TOTAL per patient in Euros, ex tax. *	**10,962.00 €**

**** per evaluable and complete case= Screening+ 12 Cycles + discontinuation + 28 day follow up+ 20 follow up + 1 additional BM***

Fees include overhead

Assume average treatment duration for patients is 1.5 years {70% (263) of subjects will discontinue treatment at 6 months and 30% (112) of subjects will remain on study for 48 months for a total average treatment duration of 18.5 months.}

Additional Costs:

Screen Failure = 350€ max of 6	2,100.00€
Additional BM Aspirate Q 24 weeks after Day 169	600.00€
Additional Cycle from Cycle 13 will be paid by Celgene 350.00 € per Cycle	350.00€

The sums shown comprise all payments due in connection with the conduct of the study including staff payments, unless otherwise indicated. For the avoidance of doubt the sums shown comprise all payments due for any and all examinations, including but not limited to those examinations which may incur an extra cost on the Institution.

All sums are in Euros (€).

Remuneration for Screen Failure:

- *A Screen Failure is a potential study patient who has signed a declaration of informed consent after receiving an explanation of the study, but has failed to satisfy the inclusion and/or exclusion criteria or was not randomized for other reasons.*

  Maximum six (6) Screen Failures will be paid during the study.

  Remuneration per Screen Failure: 350 €

Patients who have been withdrawn from/dropped out of the study:

- *If an evaluable, randomized patient must be withdrawn from the study for the reasons indicated in the study protocol, a pro rata payment will be made according to the number of completed investigation appointments, as set out in the Budget Overview.*

Additional appointments / Unscheduled Visit:

- *If, in accordance with the study protocol, additional appointments are required, prior authorization must be obtained from CRO or Sponsor. Payment will be made on a case-by-case basis and after submission of an invoice for the costs previously authorized.*

2) PATHOLOGY SERVICES

Fees per sending of original samples, paraffin block or slides: ***600 €.***
Please refer to Lab Manual for details.

The total amount payable for the Study under this Agreement may not exceed ***111,720 Euros*** *without the prior written consent of Celgene/CRO even under a quantum merit theory. This assumes 10 patients and 6 screen failures: 16 Screening Visits, 120 Cycles and 200 Follow Up visits, 10 discontinuation visits and 10 x 28 day post treatment visits, 10 additional biopsies.*

All sums are in Euro (€).
All costs mentioned here are net costs, excluding VAT.

The total number of patients foreseen for the study is 10. So the total sum foreseen is ***111,720 €*** *= including 6 screen failures.*

BENEFICIARY

Payment will be executed by CRO on behalf of the sponsor on a quarterly basis. Invoices for this work will be addressed to Celgene International Sàrl, but sent for Payment to the following address:

PRA International
ATT. Orsolya Tatrai
500 South Oak Way
Green park
Reading
United Kingdom
Ref: (CC-5013-MDS-005)

GENERAL PAYMENT TERMS:

i) *Payments will be made every 3 months, within 45 days upon receipt of a note for payment to be followed by a valid VAT invoice.*

ii) *Payments for each visit will be made after the pages of the case report form corresponding to the visit are filled out, monitored and collected.*

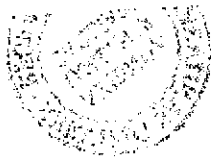
iii) *Payments for major protocol violators will be made up to and including the visit where the violation occurred, but will not cover visits made after the violation. Payments for subjects that are protocol violators due to missed or delayed Study visits may be paid at Sponsor's discretion.*

iv) *All costs mentioned here are net costs, excluding VAT.*

The remuneration is to be declared for tax assessment by the payee. The relevant income tax regulations should be taken into account.

Clarification of concepts related to payments:

Evaluable patient:
An evaluable patient means a patient recruited and randomized in accordance with the protocol, fulfilling all the eligibility criteria and with acceptable data quality.



Evaluable and Complete Case:

An "Evaluable and Complete Case" shall be one in which a participant is an Eligible Participant, has completed the specified Study period, and has been evaluated in accordance with the Protocol.

Discontinuations:

Should the Study be prematurely discontinued, the remuneration will be calculated on a pro rata temporis basis.

Laboratory Costs:

A fee for collecting and processing samples is included in the patient budget. The samples will be analyzed in a central laboratory and no costs will therefore be incurred by the Institution.

The amounts as per Art. 6 will be paid to the Azienda, after the issue of a note followed by a regular invoice according to this schedule:

- *30% of the above mentioned amount will be given to the ASL no. 8 to cover management costs,*
- *The remaining 70% net of instrument and laboratory tests (enclosed to this deed) will be apportioned to the participants in the trial according to the decision of the Principal Investigator.*

2. All unchanged terms and conditions of the Agreement remain in full force and effect as the current conditions of the Agreement.

3. This Amendment shall become effective from the last date signature.

Read, approved and signed.

The **Azienda U.S.L. N. 8 di Cagliari**

The General Manager

Dr. Emilio Simeone

Date _____

The **Principal Investigator** (to consent)

Dr. Emanuele Angelucci

Date 05/02/2014

Celgene International Sarl

Legal Representative

Date 18 December 2013

Anna Fitzmaurice
Associate Director Site Contracts
Celgene International
Switzerland

ALLEGATO ALLA DELIBERAZIONE

N. 144 DEL 10 FEB. 2014

IL DIRETTORE AMMINISTRATIVO (Dott. Sergio Salis) IL DIRETTORE SANITARIO (Dott. Ugo Storelli)

IL DIRETTORE GENERALE (Dott. Emilio Simeone)

Il presente allegato è composto da n° 06 fogli di n° 06 pagine.