AMENDMENT #2 TO EPIDEMOLOGY AND OUTCOMES RESEARCH AGREEMENT

BETWEEN Azienda Ospedaliera di Cosenza AND inVentiv Health Clinical UK Ltd. acting for and on behalf of Bristol-Meyers Squibb EMEA SARL, with registered office at 3 rue Joseph Moier, 92506 Rueil-Malmaison, France CONCERNING THE CONDITIONS AND PROCEDURES FOR CONDUCTING THE OBSERVATIONAL STUDY "Long-term experience with abatacept SC in routine clinical practice"

STUDY: "Long-term experience with abatacept SC in routine clinical practice."

PROTOCOL NUMBER: IM 101348ST

THIS AMENDMENT, when signed by all parties, will set forth certain agreements by and between inVentiv Health Clinical UK Limited, with its principal office at Thames House, 17-19 Marlow Road, Maidenhead, Berkshire SL6 7AA, England together with its Affiliates (hereinafter "CRO") who is acting for and on behalf of Bristol-Meyers Squibb EMEA SARL, with registered office at 3 rue Joseph Monier, 92506 Rueil-Malmaison, France (hereinafter "BMS") and the Azienda Ospedaliera Ospedaliera di Cosenza with registered office at via S. Martino, s.n.c., tax and VAT no. 01987250782 (hereinafter "Institution"). Institution and the CRO shall be referred to individually as "Party" and collectively as the "Parties".

WHEREAS, the Parties have an Epidemiology and Outcomes Research Agreement in place effective as of April 10st 2015 ("Agreement");

that with the amendment 1 to the Agreement, last signature of 30.11.2016, the PI Dr Pierluigi Frugiuele has been replaced by Dr. Antonio Greco.

WHEREAS, the Parties wish to nominate a new principal investigator since the former investigator, Dr. Antonio Greco, is no longer working at the Institution, the change was approved by the Ethical Committee of Institution on 21.12.2017 (Effective Date).

IT IS AGREED AS FOLLOWS:

i) Dr. Francesco Marcianò (hereinafter the "New Investigator") has agreed to and hereby assumes the obligations of Dr Antonio Greco (the "Investigator") in relation to the Study under the provisions of the Agreement, in the role as the investigator. The Investigator ceases to be part of the Agreement and the New Investigator assumes the obligations and responsibilities borne by the Investigator under the Agreement.

And

EMENDAMENTO 2 ALLA CONVENZIONE DELLO STUDIO OSSERVAZIONALE

TRA L'Azienda Ospedaliera di Cosenza AND inVentiv Health Clinical UK Ltd che agisce in nome e per conto di Bristol-Meyers Squibb EMEA SARL con sede legale in 3 rue Joseph Moier, 92506 Rueil-Malmaison, Francia (di seguito "BMS") CONCERNENTE CONDIZIONI E MODALITA' PER L'ESECUZIONE DELLO STUDIO OSSERVAZIONALE "Esperienza a lungo termine con abatacept sottocute nella pratica clinica: Studio ASCORE"

STUDIO: "Esperienza a lungo termine con abatacept sottocute nella pratica clinica." PROTOCOLLO NUMERO: IM 101348ST

QUESTO EMENDAMENTO, quando sarà firmato da tutte le parti, stabilirà alcuni accordi da e tra inVentivHealthClinical UK Limited, con la sua sede principale in Thames House, 17-19 Marlow Road, Maidenhead, Berkshire SL6 7AA, Inghilterra insieme ad i suoi affiliati (di seguito "CRO") che agisce in nome e per conto di Bristol-Meyers Squibb EMEA SARL con sede legale in 3 rue Joseph Moier, 92506 Rueil-Malmaison, Francia (di seguito "BMS") (allegato 1) e Azienda Ospedaliera di Cosenza con sede legale in Via S. Martino, s.n.c., codice fiscale e partita iva n. 01987250782 (di seguito "Azienda"). L'Azienda e la CRO sono singolarmente come "Parte" collettivamente come "Parti".

PREMESSO che le Parti hanno in atto un Contratto per lo studio osservazionale ("Contratto") che è stato firmato il 10 Aprile 2015;

che con emendamento 1 al Contratto, ultima sottoscrizione del 30.11.2016, è stato sostitutito il P.I. dr. Pierluigi Frugiuele con il dr. Antonio Greco.

CONSIDERANDO che, le Parti intendono nominare un nuovo sperimentatore principale poiché il precedente sperimentatore, il dr. Antonio Greco, non opera più presso l'Azienda, cambio approvato dal Comitato Etico dell' Azienda in data 21.12.2017 (Data di Efficacia).

SI CONVIENE QUANTO SEGUE:

i)II Dr. Francesco Marcianò (da qui in poi "il nuovo Sperimentatore") accetta di assumere gli obblighi del Dr. Antonio Greco (lo Sperimentatore) in merito allo studio oggetto del Contratto, nel ruolo di Sperimentatore. Lo Sperimentatore non sara' del Contratto e piu' parte il nuovo Sperimentatore assume gli obblighi responsabilità dello Sperimentatore Principale secondo il Contratto.

In tutto l'accordo, in cui il Dr Antonio Greco è



Throughout the Agreement, where Dr. Antonio Greco is mentioned as the Investigator, the name shall be replaced by the name of the new Investigator Dr Francesco Marcianò	indicato come lo Sperimentatore, il nome sarà sostituito dal nome del nuovo Sperimentatore Dr. Francesco Marcianò	
All other provisions of the Agreement will remain unchanged and will be fully applicable to this Assignment. This Amendment shall become effective as of the Effective Date of approval of the Ethical Committee of the Institution.	Tutte le altre disposizioni del Contratto rimarranno invariate e saranno pienamente applicabili a questa Assegnazione. Tale modifica entra in vigore a partire dalla data di Efficacia.	

IN TESTIMONY WHEREOF, CRO and Institution have A testimonianza di quanto sopra, la CRO e l'Azienda hanno prodotto questo Emendamento caused this Amendment #2 to be executed in 2 n. 2 eseguito in 2 originali originals. For inVentiv Health Clinical UK Ltd/ Per inVentiv Health Clinical UK Ltd: (Signature)/(Firma) Name/Nome: Karen Turner Date/Data: 21 FEB 2018 Finance Director Title/Titolo: For Institution/ Per l'Azienda: Divettore Generale (Signature)/(Firma) Oll 115 MAR 2010 Name/Nome: dr. Achille Gentile Title/Titolo:General Director/II Direttore GeneraleDate/Data: Read and acknowledge/ Letto e accettato For New Investigator/Per il Nuovo Sperimentatore:

Title/Titolo: The Investigator/ Lo Sperimentatore Date/Data: 1310312018

(Signature)/(Firma)

Name/Nome: Dr. Francesco Marcianò



POWER OF ATTORNEY

We, inVentiv Health Clinical UK Limited (registered no: 01772610), whose registered office is at Thames House, 17-19 Marlow Road, Maidenhead, Berkshire England SL6 7AA (the "Company") irrevocably appoint **Karen Turner** (the "Attorney") as our attorney to enter into discussions, negotiate, agree, execute and terminate contracts, including any annex or amendment thereto, on behalf of the Company, with investigative sites, hospitals and research institutions in connection with the Company's operations in the UK and any other jurisdiction in which the Company has an established branch, up to the value of EUR 100'000 ("Site Contracts").

We undertake to ratify and confirm whatever the Attorney shall, in our name or on our behalf, do or purport to do by virtue or in pursuance of this power of attorney and to indemnify and to keep our attorney indemnified against all costs, claims, expenses, proceedings, obligations and liabilities incurred or suffered by our attorney by reason, directly or indirectly, of the exercise or purported exercise of any power conferred on our attorney by this power of attorney.

This power of attorney shall last for an indefinite period unless either (1) revoked by the Company by giving ten day's notice in writing to the Attorney or (2) the Attorney's employment with the Company or with any related, affiliated, parent or subsidiary company of the Company terminates, or notice to terminate the Attorney's employment is given (either by the Attorney or the Company or any related, affiliated, parent or subsidiary company of the Company) for any reason; or (3) the death of the Attorney, or the Attorney becoming bankrupt or an order is made by a court having jurisdiction in matters concerning mental disorder for the Attorney's detention or for the appointment of a receiver, guardian or other person to exercise powers with respect to his property or affairs.

This power of attorney shall be governed by the laws of England and Wales.

Executed as a deed by us on December 03, 2013

EXECUTED as a Deed by inVentiv Health Clinical UK Limited acting by a director

Trevor Paul Hanbury

Director

In the presence of:

Witness name Shaz Majeed

Witness address: Inventiv Health, Thames House, Maidenhead

Witness occupation: Administrative Assistant

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02/12/2013





LETTER OF DELEGATION PROTOCOL NUMBER IM 101-348ST LONG TERM EXPERIENCE WITH ABATACEPT SC IN ROUTHNE CLINICAL PRACTICE

To whom it my concern,

I, for and on behalf of BRISTOL-MYERS SQUIBB EMEA, with its registered office at 3 Rue Joseph Monier, Rueil-Malmaison, France, BP 325, 92505 ("SPONSOR") delegate to PHARMANET GmbH with its registered office at Obere Wiltisgasse 52, CH-8700, Kusnacht/ZH, Switzerland and to inVentiv Health Clinical UK, with its registered office at Thames House, 17-19 Marlow Road, Maidenhead, SL6 7AA, United Kingdom, and its affiliated companies in Austria, The Netherlands, Germany, UK, Italy, Greece, France and Spain, and such other countries as may be added to the study from time to time by written agreement between the SPONSOR and PHARMANET GmbH or/and inVentiv Health Clinical UK, the following responsibilities in as far as permitted according to the laws of the applicable countries in respect of the above study:

- 1. Preparing and signing documents required by the local ethics committees, central ethics committees and regulatory authorities.
- 2. Corresponding with ethics committees for study-related purposes
- Corresponding with regulatory authorities for study-related purposes, including the submission of regulatory documents
- 4. Monitoring and managing the study
- 5. Managing standard form clinical trial agreements with investigators and/or institutions
- 6. Negotiating, signing, and executing Agrements with Hospitals, Investigators and Vendors, on behalf of BMS.

The delegation of the above described responsibilities means that PHARMANET GmbH and/or inVentiv Health Clinical UK and such other affiliated companies as described above shall be authorized to assume some or all of the above mentioned responsibilities, but solely if and insofar as permitted under applicable law and to take all measures necessary in order to apply with this delegation under applicable law.

PHARMANET GmbH and/or inVentiv Health Clinical UK and its affiliated companies, as addressed above, shall be authorized to grant power of substitution to sub-delegate some or all responsibilities listed above within the scope of this letter of delegation.

The delegation and authorization shall be valid until the end of the above study unless earlier revoked by the SPONSOR in writing.

Study to be conducted in the following countries:

Netherlands	X
United Kingdom	X
Austria	X
France	Х
Germany	Х
Italy	Х
Spain	X

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Delegation Letter



Switzerland	X
Greece	X

BRISTOL-MYERS SQUIBB EMEA

Name: Manuela Le BARS

We hereby accept delegation of the above responsibilities,

PHARMANET GmbH

inVentiv Health Clinical UK

Name:

Name:

Title: Signature: Title: Director Signature:

Date:

Date:

Soundh

Delegation Letter

