

c 035/mvB/2019

AMENDMENT No. 2 TO CLINICAL TRIAL AGREEMENT

DODATOK ZMLUVY Č.2 O KLINICKOM SKÚŠANÍ

This Amendment to Clinical Trial Agreement ("Amendment") is between

Tento dodatok zmluvy o klinickom skúšaní (ďalej „dodatok“) sa uzatvára medzi

F.Hoffmann-La Roche Ltd Grenzacherstrasse 124
CH-4070 Basel, Switzerland (Hereinafter referred to as the 'Sponsor')

F.Hoffmann-La Roche Ltd Grenzacherstrasse 124
CH-4070 Bazilej, Švajčiarsko (ďalej iba "zadávateľ")

represented by

zastúpený

IQVIA RDS Slovakia, s.r.o. ("CRO/IQVIA"), having a place of business at Vajnorska 100/B, 83104 Bratislava, Slovak Republic, Organisation No.: 45942269, Filed in the Companies register of the District Court Bratislava I., section: Sro, File no: 69023/B represented by: Aurelia Mojzesova, holder of procurator

IQVIA RDS Slovakia, s.r.o. (ďalej „CRO/IQVIA“), so sídlom na adrese Vajnorská 100/B, 83104 Bratislava, Slovenská republika, IČO: 45942269, Zapísaná v Obchodnom registri Okresného súdu Bratislava I., oddiel: Sro, vl.č: 69023/B, v zastúpení: MUDr. Aurélie Mojšesová, prokurista

and

a

Univerzitná nemocnica Bratislava, having a place of business at Pazitkova 4, 821 01, Bratislava, Slovak Republic, Organisation Identification No.: 318 138 61, Tax Identification No.: 202 1700 549, represented by MD Renata Vandriakova, MPH, director of the UNB (Hereinafter referred to as the 'Medical Facility')
Working place for the study: Nemocnica Ruzinov
Investigator: MUDr. Viera Hancinova

Univerzitná nemocnica Bratislava, so sídlom na Pazitkova 4, 821 01, Bratislava, Slovenská republika, Identifikačné číslo organizácie: 318 138 61, Daňové identifikačné číslo: 202 1700 549, zastúpená: MUDr. Renatou Vandriakovou, MPH, riaditeľkou UNB (ďalej iba "zdravotnícke zariadenie")
Pracovisko skúšania: Nemocnica Ružinov
Skúšajúca: MUDr. Viera Hancinová

and is effective as of the date last signed below

a nadobúda účinnosť dňom podpísania poslednou zmluvnou stranou nižšie

WITNESSETH:

ÚVODNÉ VYHLÁSENIA:

WHEREAS, IQVIA, Sponsor and the Institution are parties to an agreement entitled Clinical Trial Agreement for Protocol **A Randomized, Double-Blind, Double-Dummy, Parallel-Group Study To Evaluate The Efficacy And Safety Of Ocrelizumab In Comparison To Interferon Beta-1a (Rebif®) In Patients With Relapsing Multiple Sclerosis**, hereinafter referred to as the 'Study' effective as of 24.10.2011 and as amended (the "Agreement"), and the parties desire to amend such Agreement;

Spoločnosť IQVIA, zadávateľ a Zdravotnícke zariadenie sú zmluvnými stranami zmluvy s názvom Zmluva o klinickom skúšaní pre protokol **Randomizované, dvojito zaslepené, dvojito maskované skúšanie v súbežných skupinách pre hodnotenie účinnosti a bezpečnosti ocrelizumabu v porovnaní s interferónom beta-1a (Rebif®) u pacientov s relabujúcimi formami sklerózy multiplex**, ďalej iba "klinické skúšanie", ktorá nadobudla účinnosť dňa 24.10.2011 v znení neskorších dodatkov (ďalej „zmluva“), a zmluvné strany si želajú zmeniť a doplniť túto zmluvu.

WHEREAS, the Budget shall be amended due to Protocol Amendment version H dated 03/08/2018.

Rozpočet sa má zmeniť podľa dodatku k protokolu verzia H zo dňa 03/08/2018.

CTA Amendment – Slovakia – 05/4/2019- [PI name: Hancinova MD F.Hoffmann La Roche ,
WA21092
from English to Slovak by MultiTrans on 08/04/2019.]
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NOW THEREFORE, in consideration of the mutual promises and covenants set forth herein, and other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, the parties hereby agree to amend the Agreement as follows:

1. Budget

The Budget shall be amended due to Protocol Amendment version H dated 03/08/2018. Therefore, the budget is hereby amended, with a summary of changes as follows:

OLE budget:

1. OLE: Visits amended to reflect the OLE extension timelines.

2. Optional RBR : ICF, Collection of blood sample as well as CSF (per lumbar puncture) added to Conditionals.

The Budget is hereby deleted in its entirety and replaced by the attached Budget.

All terms and conditions of the Agreement not expressly amended by this Amendment remain in full force and effect.

IN WITNESS WHEREOF, this Amendment has been executed by the parties hereto through their duly authorized officers on the date(s) set forth below.

S ohľadom na vzájomné dohody a záväzky uvedené v tomto dokumente a riadne a primerané protiplnenie, ktorého prevzatie a dostatočnosť sa týmto potvrdzuje, sa zmluvné strany týmto dohodli na zmene a doplnení zmluvy takto:

1. Rozpočet

Rozpočet sa zmení kvôli dodatku k protokolu verzii H zo dňa 03/08/2018. Týmto sa mení rozpočet a súhrn zmien bude nasledovný:

Rozpočet nezaslepeného predĺženia skúšania (OLE):

1. OLE: Návštevy sa zmenili tak, aby odrážali časový harmonogram predĺženia OLE.

2. Voliteľné hodnotenie prínosov a rizík (RBR): do podmienok bol pridaný formulár ICF, odber vzorky krvi aj CSF (pri lumbálnej punkcii).

Rozpočet sa týmto v celom rozsahu vypúšťa a nahrádza sa priloženým rozpočtom.

Všetky podmienky zmluvy, ktoré sa výslovne nezmenili ani nedoplnili týmto dodatkom, zostávajú plne platné a účinné.

NA ZNAK SÚHLASU S VYŠŠIE UVEDENÝM zmluvné strany uzatvárajú tento dodatok prostredníctvom podpisov svojich riadne oprávnených zástupcov ku dňu(-om) uvedenému(-ým) nižšie.

ACKNOWLEDGED AND AGREED BY IQVIA RDS Slovakia s.r.o./
POTVRDENÉ A ODSÚHLASENÉ IQVIA RDS Slovakia s.r.o.:

By/
Za: _____

Name/
Meno: _____

Title/
Funkcia: _____

Date/
Dátum: _____

ACKNOWLEDGED AND AGREED BY SPONSOR (IQVIA executing on Sponsor's behalf)/
POTVRDENÉ A ODSÚHLASENÉ ZADÁVATEĽOM (podpísané spoločnosťou IQVIA v mene
zadávateľa)

By/
Za: _____

Name/
Meno: _____

Title/
Funkcia: _____

Date/
Dátum: _____

ACKNOWLEDGED AND AGREED BY Univerzitná nemocnica Bratislava/ Univerzitná
nemocnica Bratislava

By/
Za: _____

Bratislava
S. MPH

Name/
Meno: _____

Title/
Funkcia: _____

Date/
Dátum: _____

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ACKNOWLEDGED AND AGREED BY MUDr. Viera Hancinova.
POTVRDENÉ A ODSÚHLASENÉ MUDr. Viera Hančinová :

By/
Za: _____

Date/
Dátum: _

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JLA47285_SVK_en_Roche_WA21092_ex-US_AP_Prot Amend v.H_Budget_2018.12.18 (002)_HB_Translated on 08-Apr-2019-1



BUDGET

Description	Short Name	Amount in EUROS
OLE Screening visit	OLE SV	52.65
Visit 12	V12	166.95
Visit 13	V13	145.80
Visit 14	V14	69.90
Visit 15	V15	89.85
Visit 16	V16	148.95
Visit 17	V17	219.00
Visit 18	V18	244.35
Visit 19	V19	32.25
Visit 20	V20	229.95
Visit N-2	VN-2	32.25
Visit N	VN	229.95
Screen-Fail Week 12	SF W12	59.55
Screen-Fail Week 24	SF W24	87.75
Screen-Fail Week 12	SF W36	59.55
Screen-Fail Week 12	SF W48	87.75
Total		1,956.45

Additional payments

Description	Short Name	Amount in EUROS
Bcell Follow-Up	Bcell FU	68.25
Delayed Dosing Visit	Delayed	127.35
Unscheduled Visit	UNV	61.95
Withdrawal visit	WD	76.80
		334.35
		€

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**Conditional procedures -
Invoicable items**

Description	Amount in EUROS
Magnetic resonance imaging, brain including brain stem (MRI); without contrast material, followed by contrast material(s) and further sequences (eg, proton)	
Interpretation and Report; Magnetic resonance imaging, brain including brain stem (MRI); without contrast material, followed by contrast material(s) and further sequences (eg, proton)	
Patient Reimbursement, Expenses, Patient Travel - Per Visit	
TTC Code: Genomics consent; DNA consent; Genetics (RBR)	2.10
Collection of samples, any method including blood, serum, (RBR and Biomarker samples)	1.80
TTC Code: Collection of specimen; urine, urine collection (Formerly TTC code 99010) (JVC testing)	0.90
Lab handling and/or shipping of specimen(s)	2.10
Electrocardiogram, routine ECG (EKG) with at least 12 leads, 12 lead ECG, 12-lead ECG: Includes tracing, interpretation and report	6.45
European Quality of Life Questionnaire (EuroQol) (EQ-5D); self-administered	2.25
Treatment Satisfaction Survey, General	1.35
SF-36	1.65
Collection of CSF per lumbar puncture	31.95