|  |  |
| --- | --- |
| **amendment # 1 TO Clinical Trial Agreement** | **DODATEK Č. 1 KE smlouvě o klinickém hodnocení**  |
|  |  |
| **Protocol # MT-18** | **Č. protokolu MT-18** |
|  |  |
| This Amendment # 1 (“**Amendment**”), dated as of date of last signature and effective as of (“**Effective** **Date**”) between | Tento dodatek č. 1 (dále jen „**dodatek**“) se uzavírá a datuje v den posledního podpisu a je účinný dnem (dále jen „**datum** **účinnosti**“) mezi |
|  |  |
| **Syneos Health UK Limited** with principal offices located in the United Kingdom at Farnborough Business Park, 1 Pinehurst Road, Farnborough, Hampshire, GU14 7BF, United Kingdom, including its affiliates, subsidiaries, and specifically its parent company Syneos Health, LLC (hereinafter “**CRO**”) | společností **Syneos Health UK Limited** se sídlem ve Velké Británii na adrese Farnborough Business Park, 1 Pinehurst Road, Farnborough, Hampshire, GU14 7BF, Spojené království, včetně jejích poboček, dceřiných společností a konkrétně její mateřskou společností Syneos Health, LLC (dále jen „**CRO**“) |
|  |  |
| and | A |
|  |  |
| **ALK-Abelló A/S** with principal offices located in Denmark at Bøge Allé 6-8, 2970 Hørsholm, Denmark (“**Sponsor**”) | společností **ALK-Abelló A/S** se sídlem v Dánsku na adrese Bøge Allé 6-8, 2970 Hørsholm, Dánsko (dále jen „**zadavatel**“) |
| And |  |
|  | a |
| **Oblastni nemocnice Kolin a.s,- Nemocnice Stredoceského kraje** , with a place of business at Zizkova 146, 280 02 Kolin, Czech Republic Iden.number : 27256391, Tax Iden.number: CZ27256391 represented by MUDr-Petr Chudomel, MBA , director (“Institution”) | **Oblastní nemocnice Kolín a.s.- Nemocnice Středočeského kraje**, se sídlem na adrese Žižkova 146, 280 02 Kolín, Česká republika , IČ:27256391, DIČ: CZ27256391 , zastoupena: MUDr. Petr Chudomel, MBA , ředitel (dále jen „zdravotnické zařízení“) |
|  |  |
| and | a |
|  |  |
| **MUDr. Jaromir Paukert** with a place of business at Alergologická a imunologická poradna, Oblastní nemocnice Kolin, Zizkova 146, 280 02 Kolin, Czech Republic (“Principal Investigator”). | **MUDr. Jaromír Paukert,** se sídlem na adrese, Alergologická a imunologická poradna, Oblastní nemocnice Kolín, Žižkova 146, 280 02 Kolín, Česká republika (dále jen „hlavní zkoušející“). |
|  |  |
|  |  |
| WHEREAS, the Parties desire to modify the Clinical Trial Agreement with an effective date of 1.September 2020 as (“Agreement”) for the clinical trial with Sponsor DrugHDM-SLIT-tablet , encoded MT-18 entitled “A 28-day, single-armed, open-label trial to evaluate safety of the house dust mite (HDM) sublingual allergy immunotherapy (SLIT) tablet in adolescent subjects (12-17 years of age) with HDM allergic rhinitis/rhinoconjunctivitis (AR/C) with or without asthma” (“**Protocol**”) to be conducted at Institution (“**Trial**”) to involve patients participating in the Trial (“**Trial** **Subjects**”). | VZHLEDEM K TOMU, že si smluvní strany přejí upravit smlouvu o klinickém hodnocení s datem účinnosti 1.září 2020 dále jen „smlouva“) týkající se klinického hodnocení léku zadavatele –HDM-SLIT-tablet – s kódem klinického hodnocení MT-18 a názvem „28 denní, jednoramenná, otevřená klinická studie ke zhodnocení bezpečnosti sublingvální tabletové formy alergenové imunoterapie (SLIT) s obsahem alergenů z roztočů domácího prachu (HDM) u dospívajících subjektů (ve věku 12–17 let) s alergickou rinitidou/rinokonjunktivitidou způsobenou HDM s astmatem nebo bez něj“ (dále jen „**protokol**“). Tohoto klinického hodnocení (dále jen „**klinické** **hodnocení**“) prováděného ve zdravotnickém zařízení se zúčastní pacienti (dále jen „**subjekty** **hodnocení**“). |
|  |  |
| WHEREAS, in accordance with Section 26 (Entire Agreement) of the Agreement, the Parties desire to modify the specific language and hence agree to the following modifications to the Agreement: | VZHLEDEM K TOMU, že v souladu s částí 26 (Celá smlouva) smlouvy si strany přejí změnit konkrétní znění, souhlasí tedy s následujícími úpravami smlouvy: |
|  |  |
| 1. The Attachment C (Financial Arrangements Worksheet) to the Agreement is updated to correct the amount for Trial Subject Travel Reimbursement which is based on the amount specified in the ICF, said costs being effective as of 11.November 2020 Hence the Attachment C (Financial Arrangements Worksheet) to the agreement is deleted in its entirety and replaced with Attachment C (Financial Arrangements Worksheet) as attached to this Amendment.
 | 1. Příloha C (Tabulka finančního ujednání) k této smlouvě se upravuje ,tak aby se opravila částka za náhradu cestovních výdajů subjektu hodnocení , která je založena na částce uvedené v informovaném souhlasu ,přičemž částky jsou učinné od 11.listopadu 2020 . Příloha C se ruší v celém rozsahu a nahrazuje přílohou C (tabulka finančního ujednání), která je přiložena k tomuto dodatku,
 |
|  |  |
| 1. Defined terms used in this Amendment and not defined herein will have the same meanings assigned such terms in the Agreement.
 | 1. Pojmy, ať již vymezené či nevymezené v tomto dodatku budou mít stejné významy, jako je uvedeno ve smlouvě.
 |
|  |  |
| 1. All other provisions of the Agreement shall remain unaltered and given full force and effect.
 | 1. Ostatní ustanovení smlouvy zůstávají beze změny a v plné platnosti a účinnosti.
 |
|  |  |
| [SIGNATURE PAGE FOLLOWS] | [NÁSLEDUJE STRANA S PODPISY] |

/\*

|  |  |
| --- | --- |
| In the event that the parties execute this Amendment by exchange of electronically signed copies or facsimile signed copies, the parties agree that, upon being signed by all parties, this Amendment will become effective and binding and that facsimile copies and/or electronic signatures will constitute evidence of a binding agreement with the expectation that original documents may later be exchanged in good faith. | V případě, že smluvní strany tento dodatek podepíší zasláním podepsaných kopií elektronicky nebo faxem, vstoupí dodatek v platnost a stane se závazným po podpisu všemi stranami, přičemž důkazem o jeho závaznosti budou výtisky z faxu nebo elektronické podpisy. Později lze v dobré víře poskytnout originální dokumenty. |
|  |  |
| **Agreed to and accepted:** | **Souhlasí a přijímá:** |

|  |  |  |
| --- | --- | --- |
| **CRO** / **CRO** |  | **INSTITUTION** / **ZDRAVOTNICKÉ ZAŘÍZENÍ** |
|  |  |  |
|  |  |  |
| Signature / Podpis |  | Signature / Podpis |
|  |  |  |
|  |  | MUDr. Petr Chudomel, MBA |
| Printed Name / Jméno hůlkovým písmem |  | Printed Name / Jméno hůlkovým písmem |
|  |  |  |
|  |  | Předseda představenstva |
| Title / Funkce |  | Title / Funkce |
|  |  |  |
|  |  |  |
| Date / Datum |  | Date / Datum |
|  |  |  |
|  |  |  |
| Signed by CRO on behalf of SPONSOR / **Podpis CRO jménem ZADAVATELE** |  | **INSTITUTION** / **ZDRAVOTNICKÉ ZAŘÍZENÍ** |
|  |  |  |
|  |  | Signature / Podpis |
| Signature / Podpis |  |  |
|  |  | Mgr. Michael Kašpar |
|  |  | Printed Name / Jméno hůlkovým písmem |
| Printed Name / Jméno hůlkovým písmem |  |  |
|  |  | Místopředseda představenstva |
|  |  | Title / Funkce |
| Title / Funkce |  |  |
|  |  |  |
|  |  | Date / Datum |
| Date / Datum |  |  |

|  |  |
| --- | --- |
|  | **PRINCIPAL INVESTIGATOR / HLAVNÍ ZKOUŠEJÍCÍ** |
|  |  |
|  | Signature / Podpis |
|  |  |
|  | MUDr. Jaromír Paukert |
|  | Printed Name / Jméno hůlkovým písmem |
|  |  |
|  | Dětský lékař - alergologie |
|  | Title / Funkce |
|  |  |
|  |  |
|  | Date / Datum |

|  |  |
| --- | --- |
| **Attachment C** | **PŘÍLOHA C** |
|  |  |
| **FINANCIAL ARRANGEMENTS WORKSHEET** | **TABULKA FINANČNÍHO UJEDNÁNÍ** |
|  |  |
| FINANCE SUMMARY BOX | SHRNUTÍ FINANČNÍCH ZÁVAZKŮ |
|  |  |
| Invoice Currency:CZK | Měna platby :Kč |
| Payment Base : Visit –based: | Základ platby: na základě návštěv |
| Effective Date:11.listopad 2020 | Datum učinnosti 11.listopad 2020 |
| CRO Contracting Entity Syneos Health UK Limited  | CRO smluvní subject:Syneos Health UK Limited |

Institution / Zdravotnické zařízení :

Oblastní nemocnice Kolín, nemocnice Středočeského kraje

|  |  |  |  |
| --- | --- | --- | --- |
| **Sponsor:** | ALK-Abello A/S  |  |  |
| **Protocol Number:** | MT-18  |  |  |
| **Title:** | A 28-day, single-armed, open-label trial to evaluate safety of the house dust mite (HDM) sublingual allergy immunotherapy (SLIT) tablet in adolescent subjects (12-17 years of age) with HDM allergic rhinitis/rhinoconjunctivitis (AR/C) with or without asthma |
| **Protocol Version:** | V1.0/06-Feb-2020  |  |
| **Project:** | 7011828 |  |  |
| **Location:** | Czech Republic |  |  |
| **Overhead Percent:** | 20.00% |  |  |
| **Currency:** | CZK - Czech Koruna |  |
| **Institution:** | Oblastní nemocnice Kolín a.s. |  |
| **Principal Investigator:** | MUDr.Jaromír Paukert |  |

|  |  |
| --- | --- |
| **Trial Subject Visits 1(inclusive of applicable overhead)** | **Visit Cost** |
| Screening V1 | 10,389.30 |
| V2 Day 1 | 5,910.00 |
| TC (Phone Call) Day 8 | 1,800.00 |
| V3 Day 28 | 5,335.20 |
| TC (Phone Call) V3 + 5-7 days | 1,640.40 |
| **Total Cost Per Trial Subject** | **25,074.90** |
|  |  |
| **Additional Treatment Related Costs 2(inclusive of applicable overhead)** |
| Unscheduled Visit 3 | INVOICE |
| Screen Failure 4 | 10,389.30 |
| Urine Pregnancy Test | 171.60 |
| Trial Subject Travel Reimbursement 5 | 700.00 |
| Caregiver Travel Reimbursement 5 | 700.00 |
| SPT - Skin Prick Test if needed at Visit 2 | 997.80 |

|  |  |  |  |
| --- | --- | --- | --- |
| Footnotes:  |  |  |  |
| (1) Cost inclusive of, but is not limited to, the following: staff time with the Trial Subject during procedures, study drug dispensing and accountability, AE/SAE reporting, CRF/eCRF completion, meeting attendance, audits, monitoring visits, assignment of subject and randomization numbers.  |
| (2) If applicable, will be reimbursed after CRF data is entered by Institution.  |
| (3) To be paid based on actual procedures performed, plus applicable additional services and overhead.  |
| (4) Pursuant to the Agreement, 1 (one) Screen Failure for 4 (four) randomized Trial Subjects will be reimbursed at the cost in the table above. Failure to adhere to the above limits will not create Sponsor or CRO liability for any compensation attributed to the non-adherence to these terms and conditions of payment.  |
| (5) Trial Subject and Caregiver Travel Reimbursement for site visits will be reimbursed as per IRB/EC approved Informed Consent Form after CRO receipt of invoice and receipts reflecting actual costs.  |
| "INVOICE" = invoiced items will be reimbursed by Sponsor under terms in the Agreement.  |
| Payments will be prorated based on the number of visits completed; visit payments will be based upon CRFs completed.  |
| All costs above include applicable overhead (operating costs).  |

**Principal Investigator / Hlavní zkoušejicí**

**MUDr.Jaromír Paukert**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Sponsor:** | ALK-Abello A/S  |  |  |  |  |  |  |  |
| **Protocol Number:** | MT-18  |  |  |  |  |  |  |  |
| **Title:** | A 28-day, single-armed, open-label trial to evaluate safety of the house dust mite (HDM) sublingual allergy immunotherapy (SLIT) tablet in adolescent subjects (12-17 years of age) with HDM allergic rhinitis/rhinoconjunctivitis (AR/C) with or without asthma |
| **Protocol Version:** | V1.0/06-Feb-2020  |  |  |  |  |  |  |
| **Project:** | 7011828 |  |  |  |  |  |  |  |
| **Location:** | Czech Republic |  |  |  |  |  |  |  |
| **Overhead Percent:** | 20.00% |  |  |  |  |  |  |  |
| **Currency:** | CZK - Czech Koruna |  |  |  |  |  |  |
| **Institution:** | Oblastní nemocnice Kolín a.s. |  |  |  |  |  |  |
| **Principal Investigator:** | MUDr.Jaromír Paukert |  |  |  |  |  |  |

|  |  |
| --- | --- |
| **Trial Subject Visits 1(inclusive of applicable overhead)** | **Visit Cost** |
| Screening V1 | 10,389.30 |
| V2 Day 1 | 5,910.00 |
| TC (Phone Call) Day 8 | 1,800.00 |
| V3 Day 28 | 5,335.20 |
| TC (Phone Call) V3 + 5-7 days | 1,640.40 |
| **Total Cost Per Trial Subject** | **25,074.90** |
|  |  |
| **Additional Treatment Related Costs 2(inclusive of applicable overhead)** |
| Unscheduled Visit 3 | INVOICE |
| Screen Failure 4 | 10,389.30 |
| Urine Pregnancy Test | 171.60 |
| SPT - Skin Prick Test if needed at Visit 2 | 997.80 |
|  |  |

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Footnotes:  |  |  |  |  |  |  |  |  |  |  |  |
|  | (1) Cost inclusive of, but is not limited to, the following: staff time with the Trial Subject during procedures, study drug dispensing and accountability, AE/SAE reporting, CRF/eCRF completion, meeting attendance, audits, monitoring visits, assignment of subject and randomization numbers.  |  |  |  |
|  | (2) If applicable, will be reimbursed after CRF data is entered by Institution.  |  |  |  |
|  | (3) To be paid based on actual procedures performed, plus applicable additional services and overhead.  |  |  |  |
|  | (4) Pursuant to the Agreement, 1 (one) Screen Failure for 4 (four) randomized Trial Subjects will be reimbursed at the cost in the table above. Failure to adhere to the above limits will not create Sponsor or CRO liability for any compensation attributed to the non-adherence to these terms and conditions of payment.  |  |  |  |
|  | "INVOICE" = invoiced items will be reimbursed by Sponsor under terms in the Agreement.  |  |  |  |
|  | Payments will be prorated based on the number of visits completed; visit payments will be based upon CRFs completed.  |  |  |  |
|  | All costs above include applicable overhead (operating costs).  |  |  |  |