Attachment no 4

Case: ZO-07-2017

TASK 1

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| No. | Study | Requirements (including standard) | Time for report preparation | Comments | Nett Price | VAT rate | Gross Price |
| 1. | **SOLUBILITY**  (kinetic, thermodynamic) | * Non-GLP * made in triplicates * The price should include any other mandatory costs required to perform the study (if not indicated otherwise in the description) |  |  |  |  |  |
| 2. | **LogD**  (shake-flask method) | * Non-GLP * made in triplicates * The price should include any other mandatory costs required to perform the study (if not indicated otherwise in the description) |  |  |  |  |  |
| 3. | **Chemical stability** | * Non-GLP * LCMS method * The price should include any other mandatory costs required to perform the study (if not indicated otherwise in the description) |  |  |  |  |  |
| 4. | **Permeability studies**:   * PAMPA (PAMPA – Parallel Artificial Membrane Permeability Assay : GI PAMPA, BBB PAMPA, Sink PAMPA, Double sink PAMPA) * Caco-2 set (CacoReady kit) | * Non-GLP * The price should include any other mandatory costs required to perform the study (if not indicated otherwise in the description) |  |  |  |  |  |
| TOTAL: | | | | | | |  |

TASK 2 -

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| No. | Study | Requirements (including standard) | Time for report preparation | Comments | Nett Price | VAT rate | Gross Price |
| 1. | **EC313 pharmacokinetic study in rats (Wistar or Spraque Deweley**:  including:   * Animal experiment, * Analytical part (Method development, Plasma analysis, Tissue sample analysis) | * Non-GLP * The PK study should include total of 18 animals devided into 2 groups (differentiated by route of administration PO, IV), 9 animals in each group, with serial sampling and terminal tissue collection at 3 selected time points (including predose sampling) * The price should include any other mandatory costs required to perform the study (if not indicated otherwise in the description) * **The price should not include the cost of animals - The ordering party will deliver the animals themselves according to the requirements of the Service Provider (providing all health and required standards)** |  |  |  |  |  |
| TOTAL | | | | | | |  |

TASK 3

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| No. | Study | Requirements (including standard) | Time for report preparation | Comments | Nett Price | VAT rate | Gross Price |
| 1. | **Metabolic stability**  (microsomes/S9 fraction) | * Non-GLP * Rat or human microsomes * The price should include any other mandatory costs required to perform the study (if not indicated otherwise in the description) * The price should not include any additional costs beyond those required to obtain the data required by the market regulator in Europe and obtain approval for Phase I clinical trials, |  |  |  |  |  |
| 2. | **Hepatocyte stability** | * Non-GLP * Rat or human hepatocytes * The price should include any other mandatory costs required to perform the study (if not indicated otherwise in the description) * The price should not include any additional costs beyond those required to obtain the data required by the market regulator in Europe and obtain approval for Phase I clinical trials, |  |  |  |  |  |
| 3. | **Metabolite identification** | * Non-GLP * The price should include any other mandatory costs required to perform the study (if not indicated otherwise in the description) * The price should not include any additional costs beyond those required to obtain the data required by the market regulator in Europe and obtain approval for Phase I clinical trials, |  |  |  |  |  |
| 4. | **Drug-drug interactions**   * inhibition of the cytochrome P450 isoform activity (screening) * inhibition of the cytochrome P450 isoform activity (IC50) | * Non-GLP * The price should include any other mandatory costs required to perform the study (if not indicated otherwise in the description) * The price should not include any additional costs beyond those required to obtain the data required by the market regulator in Europe and obtain approval for Phase I clinical trials, |  |  |  |  |  |
| 5. | **Distribution study**   * Plasma stability * Plasma protein binding (Rapid Equilibrium Dialysis) * High Sensitivity Binding Kit * Microsomal binding | * Non-GLP * The price should include any other mandatory costs required to perform the study (if not indicated otherwise in the description) * The price should not include any additional costs beyond those required to obtain the data required by the market regulator in Europe and obtain approval for Phase I clinical trials, |  |  |  |  |  |
| RAZEM | | | | | | |  |

TASK 4

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| No. | Study | Requirements (including standard) | Time for report preparation | Comments | Nett Price | VAT rate | Gross Price |
| 1. | **Cardiovascular System: telemetry by oral route in Cymonolgus monkey** | * GLP * 1 group of 4 females (15 time-points). * Concentration analysis of formulation on 2 occasions including analysis report / documentation and any other obligatory costs, * The Price should include the cost of animals (The Service Provider will provide the animals themselves) * The price should include any other mandatory costs required to perform the study (if not indicated otherwise in the description) * The price should not include any additional costs beyond those required to obtain the data required by the market regulator in Europe and obtain approval for Phase I clinical trials, |  |  |  |  |  |
| 2. | **Modified Erwin Test in rats / Functional Observational battery in rats (FOB)** (oral route) | * GLP * 4 groups – 32 females (4 time points). * Concentration analysis of formulation on 2 occasions, including analysis report / documentation. * The Price should include the cost of animals (The Service Provider will provide the animals themselves) * The price should include any other mandatory costs required to perform the study (if not indicated otherwise in the description) * The price should include any other mandatory costs The price should not include any additional costs beyond those required to obtain the data required by the market regulator in Europe and obtain approval for Phase I clinical trials, |  |  |  |  |  |
| 3. | **Respiratory study in rats** (oral route) | * GLP * 4 groups – 32 females (12 time points) * Concentration analysis of formulation on 2 occasions, including analysis report / documentation * The Price should include the cost of animals (The Service Provider will provide the animals themselves) * The price should include any other mandatory costs required to perform the study (if not indicated otherwise in the description) * The price should not include any additional costs beyond those required to obtain the data required by the market regulator in Europe and obtain approval for Phase I clinical trials, |  |  |  |  |  |
| 4. | **In vitro hERG Channel test** | * Non-GLP * Phase I (the highest concentration of Tested Item, including 1 shipment of Tested Item) * Phase II (3 additional concentrations of the Tested Item + EC50 determination) * Concentration analysis of formulation * The price should include any other mandatory costs required to perform the study (if not indicated otherwise in the description) * The price should not include any additional costs beyond those required to obtain the data required by the market regulator in Europe and obtain approval for Phase I clinical trials, |  |  |  |  |  |
| TOTAL | | | | | | |  |

TASK 5

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| No. | Study | Requirements (including standard) | Time for report preparation | Comments | Nett Price | VAT rate | Gross Price |
| 1. | **Bacterial reverse mutation test**  (AMES test done on 5 S.typhimurium strains) | * Non-GLP * OECD 471 and ICH S2(R1) Non-GLP * The price should include any other mandatory costs * The price should include any other mandatory costs required to perform the study (if not indicated otherwise in the description) * The price should not include any additional costs beyond those required to obtain the data required by the market regulator in Europe and obtain approval for Phase I clinical trials, |  |  |  |  |  |
| 2. | **In vitro chromosome aberration test on mammalian cells**  (or equivalent in vitro micronucleus test) | * Non-GLP * OECD 473 and ICH S2 (R1) or equivalent * The ordering party accepts MNA test according to OECD 487 as an equivalent   + I stage: 3h incubation   + II stage: 27h incubation * The price should include any other mandatory costs required to perform the study (if not indicated otherwise in the description) * The price should not include any additional costs beyond those required to obtain the data required by the market regulator in Europe and obtain approval for Phase I clinical trials, |  |  |  |  |  |
| TOTAL | | | | | | |  |

TASK 6

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| No. | Study | Requirements (including standard) | Time for report preparation | Comments | Nett Price | VAT rate | Gross Price |
| 1. | **Mammalian cells micronucleus test in vivo** (in rats) | * GLP * OECD 474 and ICH S2(R1) compiant, * 5 groups of animals (rats) * 10 animals per group (5F+5M), * including protocol preparation, study procedures, blood sampling, sample processing, transport to analysis, reporting, archiving * The price should not include any additional costs beyond those required to obtain the data required by the market regulator in Europe and obtain approval for Phase I clinical trials, * **The price should not include the cost of animals - The ordering party will deliver the animals themselves according to the requirements of the Service Provider (providing all health and required standards** |  |  |  |  |  |
| TOTAL | | | | | |  | |

TASK 7

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| No. | Study | Requirements (including standard) | Time for report preparation | Comments | Nett Price | VAT rate | Gross Price |
| 1. | **Preliminary rat study (MTD / 7 day DRF)** - oral route | * Non-GLP, * The price should include the cost of conducting MTD (Maximum Tolerated Dose) study - that is The highest dose level inducing in the tested animals (rats) the toxicity signs without significant survival impact on the test in which it is used * The price should include the cost of conducting a 7 day Dose Range Finding (DRF) study to determine the MTD of the EC313 molecule * Single dose phase – up to 3 groups, * Range finding: 4 groups (1,2,3 – treated + control group; females and males; * three doses of tested compound included (high, medium, low) * total number of rats = 25 * The price should not include any additional costs beyond those required to obtain the data required by the market regulator in Europe and obtain approval for Phase I clinical trials, * The price should include any other mandatory costs * The price should include qualification of the preclinical stage suspension formulation which is applicable and suitable for preparing the test articles used in the in vivo toxicology animal studies. This also includes ensuring the formulation is stable either when prepared daily for dosing, or the stock formulation is stable when stored in proper conditions for repeat animal dosing, * **The price should not include the cost of animals - The ordering party will deliver the animals themselves according to the requirements of the Service Provider (providing all health and required standards** |  |  |  |  |  |
| 2. | **13-weeks EC313 toxicity study with PK / TK and recovery in rats** (oral route) | * GLP, * ICH M3(R2) compliant , * toxicology study: 4 groups (1 control + 3 treated) * toxokinetics: 3 groups satellite (3 treated), * recovery study - 4 weeks * three doses of tested compound included (high, medium, low) * Total number of rats = 80 * The price should include other mandatory cost: Costs including blood collection, sample handling, bioanalytical reports, sample storage, analytical and toxicokinetic reports * The price should not include any additional costs beyond those required to obtain the data required by the market regulator in Europe and obtain approval for Phase I clinical trials, * The price should include any other mandatory costs * **The price should not include the cost of animals - The ordering party will deliver the animals themselves according to the requirements of the Service Provider (providing all health and required standards)** |  |  |  |  |  |
| TOTAL: | | | | | | |  |

TASK 8

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| No. | Study | Requirements (including standard) | Time for report preparation | Comments | Nett Price | VAT rate | Gross Price |
| 1. | **EC313 MTD study in Cynomolgus monkeys**  (oral route) | * Non-GLP * Study consisting of 2 phases:   + Phase I: Determination of MTD [Maximum Tolerated Dose (MTD)] - 1 animal (female)   + Phase II: MTD administration for 2 weeks - 1 animal (female) * The price should include other mandatory cost: Costs including blood collection, sample handling, bioanalytical reports, sample storage, analytical and toxicokinetic reports * three doses of tested compound included (high, medium, low) * The Price should include the cost of animals (The Service Provider will provide the animals themselves) * The price should include analysis report / documentation and any other obligatory costs. * The price should include any other mandatory costs * The price should not include any additional costs beyond those required to obtain the data required by the market regulator in Europe and obtain approval for Phase I clinical trials, |  |  |  |  |  |
| 2. | **13-weeks EC 313 toxicity study in Cynomolgus monkeys**  (oral route) | * GLP, * ICH M3(R2) compliant, * 13 weeks of dosing, 4 groups of 3 females * 4 weeks recovery investigation, * three doses of tested compound included (high, medium, low) * Formulation analysis on two occasions including analysis and report * The price should include other mandatory cost: toxokinetics, bioanalysis, Costs including blood collection, sample handling, bioanalytical reports, sample storage, analytical and toxicokinetic reports * the price should include TK sampling and bioanalysis, Including concentration analysis of formulation on 2 occasions and report preparation. * The Price should include the cost of animals (The Service Provider will provide the animals themselves) * The price should include any other mandatory costs * The price should not include any additional costs beyond those required to obtain the data required by the market regulator in Europe and obtain approval for Phase I clinical trials, |  |  |  |  |  |
| TOTAL PRICE: | | | | | | |  |