11-009

ROCHE s.r.o. IČ 49617052

Funded Non-Interventional Registry Agreement with an ACADEMIC GROUP

This Agreement, dated 18 December day of 2017

REGARDING Protocol No.: ML40461 - Study on effect of antifibrotic drugs in different subpopulations of patients with idiopathic pulmonary fibrosis - Analysis of data from the Czech EMPIRE registry with protocol number IBA0866.

BETWEEN **ROCHE s.r.o.**
with its registered office at Sokolovská 685/136f, 186 00 Praha 8, Czech Republic,
Registered in the commercial register maintained by the Municipal Court in Prague, section C, file 13202
ID No.: 49617052, VAT ID: CZ49617052
(Hereinafter known as "ROCHE")

AND **Masarykova Univerzita**
with its registered office at Žerotínovo
nám. 9, 601 77 Brno, Czech Republic,
Faculty of Medicine
Located at: Kamenice 753/5, 625 00 Brno, Czech Republic
Represented by: prof. MUDr. Jiří Mayer, CSc., dean of the Faculty
Bank account: Komerční banka, a. s., Account number 85636621/0100
Masaryk University is a public university under the Act. 111/1998 Coll., On universities, as amended
ID No.: 00216224, VAT ID: CZ00216224
(Hereinafter known as "GROUP")

Funded Non-Interventional Registry Agreement with an ACADEMIC GROUP

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THIS AGREEMENT is made by and between the following Parties:

(1) **ROCHE s.r.o.**, Sokolovská 685/136f, 186 00 Praha 8, Czech Republic , ID No.: 49617052, VAT ID: CZ49617052 (hereinafter referred to as "**ROCHE**");

(2) **Masarykova Univerzita,** with its registered office at Žerotínovo nám. 9, 601 77 Brno, Czech Republic, ID No.: 00216224, VAT ID: 00216224 (hereinafter referred to as "**GROUP**").

WHEREAS:

(A) GROUP has already set-up a non-interventional primary data collection European registry for IPF entitled EMPIRE (hereinafter the "Registry"). The up-to-date Registry protocol version 1.5 is attached hereto as ATTACHMENT 1 (hereinafter the "Protocol").

GROUP shall assume the legal responsibility attached to the Sponsor capacity, as it results from applicable laws, and from national laws and regulations, with respect to patients and the Czech Republic health authorities for non-interventional studies carried out by GROUP.

GROUP agrees to grant ROCHE certain rights to statistical analysis data entered into the Registry by Czech centres during the years 2017-2019 (hereinafter the "Data") and safety data as provided for in SDEA enclosed hereto as Attachment 4.

(B) ROCHE wishes to support the Czech part of Registry and analyses of subsets of Data, specifically Czech patients' Data. ROCHE shall therefore provide financial support to GROUP pursuant the terms and provisions of this Agreement.

The financial support given by ROCHE to GROUP pursuant to this Agreement shall not be exclusive. Accordingly, GROUP reserves the right to obtain additional financing from other third parties.

IT IS HEREBY AGREED THAT:

1 CONDUCT OF THE REGISTRY

1.1 GROUP shall undertake and maintain or has undertaken and shall maintain the Registry as the respective "Legal Sponsor" of the project as set down in the Protocol attached (ATTACHMENT 1) hereto and incorporated by reference.

1.2 GROUP is solely responsible for any legal and/or regulatory obligations associated with the conduct of the Registry.

1.3 GROUP will ensure that all Health Care Professionals ("HCP(s)") and staff who participate in the conduct of the Registry are informed of and abide by all applicable terms of this Agreement. The GROUP is entitled to share this Agreement or its parts with all HCPs, who shall take part in fulfilling the obligations hereunder, in order to comply with this requirement, with the exception of trade secrets as defined hereinafter.

1.4 The Registry shall be conducted by GROUP:

1.4.1 in accordance with the Protocol and any amendments to the Protocol. In the event the GROUP updates the Protocol, GROUP shall send this updated version to ROCHE. Upon receipt of the updated version of the Protocol by ROCHE, this updated protocol replaces the previous version of the Protocol and becomes an ATTACHMENT of this Agreement without the need to conclude any additional written addendum to this Agreement.

1.4.2 in the participating HCP practices and academic centers (hereinafter collectively the "Centers") to be selected by GROUP.

1.4.3 with Data collected / collated in accordance with the criteria specified in the Protocol.

1.4.4 in accordance with the requirements laid down by laws applicable in the countries where the Registry population and the Registry are located and notably, if relevant in the concerned country, in accordance with Good Pharmacoepidemiology Practices ("GPP"), EMA Good Pharmacovigilance Practices ("GVP") Guidelines, and all applicable local regulations.

1.5 Any changes to the Protocol that may affect processes and safety data collection related to any ROCHE product under the scope of SDEA in ATTACHMENT 4, in particular but not limited to, changes to the current version of the "IBA0866_EMPIRE_CRF_EN_AE Form" shall require prior written consent of ROCHE. Should ROCHE not agree with the change, ROCHE shall be entitled to terminate the Agreement effective upon receipt of notice of termination by GROUP.

1.6 During the time of duration of this Agreement, ROCHE reserves the right to submit, once per year, to the Steering Committee relevant scientific questions for the analysis of Data ("Data Analysis") to be performed by GROUP and following the Steering Committee's

approval. Should the Steering Committee approve Data Analysis, GROUP shall perform the Data Analysis and provide results of the Data Analysis ("Results") to ROCHE.

2 RESPONSIBILITIES

2.1 GROUP shall:

2.1.1 be solely responsible for the Registry in accordance with Article 1 of this Agreement.

2.1.2 as GROUP will use health related data (hereinafter collectively called "Health Data") for the Registry in the anonymized form, GROUP shall conduct the Registry and provide Results in accordance with the applicable laws and regulations regarding the use of such Health Data. GROUP herewith represents and warrants that the donors of Health Data (hereinafter called "Health Data Donors") have given their free and informed consent, as required in accordance with applicable local laws, for the use and/or the further use of such Health Data in projects such as the Registry hereunder, and that all requested authorizations, i.e. from the applicable Research Ethics Committee and/or Institutional Review Board, have been given. GROUP herewith represents and warrants that Results, which includes Health Data, will be provided in an anonymized manner and that GROUP will not disclose or otherwise make available to ROCHE any personal data of Health Data Donors, or give access to ROCHE to any code allowing identification of Health Data Donors. Further, ROCHE herewith represents and warrants that it will not undertake any actions to determine the personality or personal data of Health Data Donors, or to get access to any code allowing identification of the Health Data Donors.

2.1.3 define its own set of SOPs to be used for non-interventional studies.

2.1.4 be responsible for the Data management of the Registry, including the primary Data collection of Czech patients at Czech centers (listed in Tab. 1 Participating centers in the Czech Republic, EMPIRE Registry Protocol, ATTACHMENT 1) undertaken with financial support of ROCHE under this agreement.

2.1.5 conclude separate site agreements with all Centers (including Czech centers) that shall safeguard Roche's interests as provided hereunder.

2.1.6 comply with Safety Reporting obligations as detailed in Article 3.

2.1.7 set-up and maintain a Trial Master File (TMF) containing documents and written communications essential to the management of the Registry. All documents to be filed in the TMF must be clearly identifiable. The TMF must be kept in a secure location for the duration of the Registry and archived after completion of the Registry for a minimum of 15 years, and kept in an electronic form for a minimum of 15 years.

2.1.8 provide ROCHE with a copy of the Health Authorities and Ethics Committee authorizations.

2.1.9 provide ROCHE with information on the progress of the Registry, on bi-annual basis; including but not limited to project timelines.

2.1.10 provide ROCHE with Results based on variables and scientific questions approved by Steering Committee of the Registry in accordance with Art. 1.6 hereof. GROUP shall provide ROCHE with references to statistical programs and outputs on a level

of detail sufficient to allow for subsequent research reproducibility and critical assessment.

2.1.11 regularly update ROCHE in writing on the progress of Data Analyses as per art. 1.6 hereof.

2.1.12 allow ROCHE to review potential publications as set out in Article 8.

2.2 ROCHE shall:

2.2.1 have no obligations or responsibilities with respect to the conduct of the Registry.

2.2.2 review potential publications as set out in Article 8.

2.2.3 submit any safety queries related to Czech patients Data of the Registry collected at Czech centers (listed in Tab. 1 Participating centres in the Czech Republic, Registry Protocol, ATTACHMENT 1) with financial support of ROCHE under this agreement on the respective GROUP safety query form to be provided by GROUP directly to [redacted]). A submission date and a single ROCHE contact person must be indicated on the form.

3 NIS SAFETY REPORTING OBLIGATIONS

3.1 GROUP shall ensure that its staff, within one year prior to starting their work under this Agreement, have completed a GVP training. GROUP agrees to provide ROCHE with an according training certificate.

3.2 ROCHE will provide Group with training materials on the relevant GVP modules within six months of signing this Agreement. The staff of GROUP are obliged to get acquainted with these materials and this will be confirmed to ROCHE without undue delay. This procedure will be repeated each year for the duration of this Agreement.

3.3 The Parties have agreed to document their responsibilities and obligations with respect to the procedures for collecting, processing, evaluating, reporting and exchanging safety information related to primary Data collection of Czech patients at Czech centers (listed in Tab. 1 Participating centers in the Czech Republic, Registry Protocol, ATTACHMENT 1) financially supported the terms of this Agreement, in compliance with the applicable laws and regulations pertaining to safety reporting and related activities in the Safety Data Exchange Agreement (SDEA) enclosed as ATTACHMENT 4.

GROUP shall ensure that these obligations and corresponding timelines are communicated to, and are complied with, by GROUP's staff and Subcontractors.

The reporting HCP or designee is responsible for collecting and reporting initial and follow-up information for Individual Case Safety Reports (ICSRs) to GROUP. Reporting of Adverse events will be performed by HCP in the registry interface thought an e-form. This procedure will generate an e-mail in the form of an Adverse Event message sent to the ROCHE email [redacted].

4 FINANCIAL SUPPORT

4.1 GROUP has provided a budget for the primary Data collection of Czech patients of the Registry in Czech centres (listed in Registry Protocol, ATTACHMENT 1). A structured financial budget with a quantification of fixed and variable costs at an annual level is given in ATTACHMENT 3 of this Agreement. GROUP represents that the Budget is based on the

fair market value of the activities to be performed, and it provides a breakdown of all costs and expenses for variable and fixed costs including maintenance of the Czech part of the Registry including potential Data Analyses.

4.2 During the term of this Agreement (as defined in Article 11 below), ROCHE shall provide financial support for the Czech part of the Registry to GROUP in the total amount of **CZK** [redacted] including VAT, with a payment schedule set out in ATTACHMENT 2 - Schedule of Payments.

For the purpose of tax calculation, the taxable fulfillment of the performance of this Agreement is negotiated as a partial one and remuneration will be paid in several payments.

Right to remuneration for the first stage (milestone) arises on the day this Agreement enters into effect. This day is considered as a day of taxable transaction.

The date of the taxable transaction of the annual payments shall be on the anniversary of the entry into force of this Agreement. GROUP shall issue an invoice for the annual payment. The due date of the payment shall be within 60 days of the date of receipt of the invoice by ROCHE.

VAT will be applied in accordance with the regulations in force at the taxable transaction date. The tax document (invoice) shall fulfill all the requirements stipulated by the legal regulations, especially the requirements pursuant to Section 29 of Act No. 235/2004 Coll., On Value Added Tax, as amended.

The amount provided by ROCHE is final and all applicable taxes shall be the sole responsibility of the GROUP.

ROCHE recognizes that this amount does not include the additional financial support that GROUP might obtain from other ROCHE Affiliates in the event the latter would be interested in the Data.

4.3 ROCHE shall finance the Czech part of the Registry in accordance with the Schedule of Payments (ATTACHMENT 2).

4.4 GROUP undertakes to use the amount specified in Article 4.2 of this Agreement for the Czech part of the Registry only. However, ROCHE acknowledges that this amount may not represent the entirety of the financing which may be necessary to maintain the Registry.

Thus, ROCHE agrees that GROUP may enter into specific agreements with other pharmaceutical companies or other legal entities so that GROUP may obtain additional financing for the Registry, provided that GROUP does not grant such pharmaceutical companies or legal entities any rights which are not compatible with those granted to ROCHE under this Agreement.

4.5 ROCHE shall not be obligated to make any payments to GROUP in excess of the amount as provided for under Article 4.2, unless such excess amount is agreed upon in writing, the fair market value is reassessed, and an amendment to this Agreement is signed by ROCHE and GROUP.

5 LIABILITY AND INDEMNITY

5.1 ROCHE is not the Sponsor and is not providing GROUP with insurance coverage.

5.2 GROUP agrees to indemnify and hold harmless ROCHE and its Affiliates employees, directors, subcontractors, and agents from and against any loss, damage, reasonable costs and expenses (including reasonable attorney's fees and expenses) incurred in connection with any claim, proceeding, or investigation arising out of this Agreement.

5.3 GROUP shall inform ROCHE of any subcontractors of GROUP, including Centres, ("Subcontractors") performing services under this Agreement. This obligation may be met by a public declaration at http://empire.registry.cz. Where GROUP contracts with Subcontractors to perform any services under this Agreement, then GROUP shall be liable for Subcontractors performance of services to the same extent as if GROUP had been acting itself.

5.4 The liability of either Party to the other under or in connection with this Agreement or arising in any other way out of the subject matter of this Agreement shall not extend to the loss of business or profit or to any incidental or consequential losses or damages.

6 INTELLECTUAL PROPERTY RIGHTS

6.1 All Data-related intellectual property rights shall be provided in the Registry protocol (ATTACHMENT 1).

For clarity, ROCHE, its Affiliates, as defined in Article 7.1 of this Agreement, and its collaboration partners shall be entitled, but not obliged, to use the Results for the following purposes, including but not limited to, publication, registration and filing, intellectual property purposes (e.g. patent application) and collaboration with other partners, any indemnification for the use of Results as per this Article 6.1 is included in the financial support provided hereunder.

6.2 Neither GROUP nor any member of GROUP shall be entitled to file patent applications for invention or discovery arising directly from the Results related to ROCHE Product. Such inventions and/or discoveries shall belong to ROCHE and ROCHE shall be solely entitled to patent ROCHE Product-related inventions and/or discoveries, provided that inventors' rights are not infringed.

7 CONFIDENTIALITY

7.1 All information obtained in connection with this Agreement, are confidential and neither Party shall, without the prior written permission of the disclosing Party or as otherwise allowed for in this Agreement, disclose the same to any third party except to the extent this may be required by applicable law. Affiliates of both Parties shall not be considered third parties for purposes of this Agreement.

"Affiliates" shall mean:

a) an organization, which directly or indirectly controls a Party to this Agreement.

b) an organization, which is directly or indirectly controlled by a Party to this Agreement.

c) an organization, which is controlled, directly or indirectly, by the ultimate parent company of a Party.

Control as per a) to c) above is defined as owning more than fifty percent of the voting stock of a company or having otherwise the power to govern the financial and the operating policies or to appoint the management of an organization.

7.2 The Parties are aware of the current participation of Boehringer Ingelheim RCV GmbH & Co KG, located at Doktor-Boehringer-Gasse 5-11, 1120 Wien, Austria (hereinafter as "BI") in the financial support of the Registry. Both Parties also acknowledge that BI reserved the right to audit the GROUP for compliance with applicable law and quality requirements agreed between GROUP and BI.

7.3 The obligations of confidentiality set out in Article 7.1 shall not apply to Confidential Information which is (i) published or generally available to the public through no fault of the receiving Party, (ii) in the possession of the receiving Party prior to the date of this Agreement and is not subject to the duty of confidentiality; (iii) obtained by the receiving Party from a third party and not subject to a duty of confidentiality.

7.4 The GROUP acknowledges and agrees that ROCHE will process in its internal IT systems and electronic databases in the context of the internal processing of data also information relating to the identification of the GROUP, including the wording of this Agreement, and that ROCHE will monitor payments and benefits granted by ROCHE or ROCHE Affiliate, including the sharing of such data with ROCHE Affiliates for cross-border collaboration with health professionals and organisations of ROCHE Affiliates, as well as handling documents that are the sources and proof of the above data.

7.5 In the event that the Act No. 340/2015 Coll., on the Special Conditions for the Effectiveness of Certain Agreements, the Publishing of such Agreements and the Register of Agreements ("**Act on the Register of Agreements**") lays down an obligation to publish this Agreement in the Register of Agreements, the Parties have agreed that the publication in the Register of Agreements according to the Act on the Register of Agreements shall be ensured by ROCHE no later than 15 days after the date on which this Agreement is fully executed and in full compliance with the requirements of the Act on the Register of Agreements.

ROCHE agrees to fill in in the form for publication of the Agreement in the register of agreements the address of the data box or e-mail of the Institution, so that the Register Administrator can send a confirmation of publication to the Institution pursuant to Article 5 Section 4 of the Act on the Register of Agreements.

The GROUP acknowledges that ROCHE is entitled to redact those parts of the Agreement which are excluded from publication under of the Act on the Register of Agreements before sending it to the Register Administrator, especially those parts that constitute a trade secret of Parties or a ROCHE Affiliate, or which are personal data unless there is a legitimate reason for their publication. For the purposes of publication of this Agreement in the Register of Agreements, a trade secret shall mean, including but not limited, Attachment 1 - the Protocol, Attachment 2 – Schedule of Payments and Attachment 3 - Budget, and the value of this Agreement.

The GROUP is allowed to publish this Agreement in the Register of Agreements only if ROCHE fails to ensure its publication within the period of time agreed to in this Article 7.4; in that case, however, the GROUP is required to obtain ROCHE's consent in writing or by e-mail with the publication of a specific form of the Agreement.

The arrangement in this Article 7.4 shall also apply *mutatis mutandis* to the publication of any amendment to this Agreement or its modification.

If the Act on the Register of Agreements does not impose the obligation to publish this Agreement in the Register of Agreements, this Article 16 shall not apply.

7.6 Without prejudice to the right of access to safety data provided in Article 2.1.6, the Parties hereto agree that if access to the Data is required at any time, for instance to provide information requested by a regulatory body or to assess/question safety, such requested access to Data shall not be unreasonably withheld.

8 PUBLICATION AND PUBLICITY

8.1 During the time of duration of this Agreement, GROUP shall provide ROCHE with any publication related to Data within two (2) weeks of its acceptance for publication by relevant medium.

8.2 The Steering Committee may publish the Results (as defined in art. 1.6 hereof).

8.3 In the event that any publication contains Data relating to any ROCHE product, the GROUP shall provide the manuscript to ROCHE three (3) months prior submission for publication. If any publication threatens or violates the possible patent claims or Intellectual property of ROCHE, the GROUP shall consult ROCHE regarding the contents of the publication.

8.4 If any publication threatens or violates the possible patent claims or Intellectual property of BI, the GROUP might consult BI regarding the contents of the publication.

8.5 ROCHE financial support of primary Data collection of Czech patients' and/or Results originated from financial support provided by ROCHE under this agreement will be rightfully acknowledged according to international ICMJE guidelines (http://www.icmje.org/) and for the period of duration of ROCHE financial support of the primary Data collection of Czech patients' online at EMPIRE Registry website (http://empire.registry.cz/index-en.php).

9 DATA DISCLOSURE

9.1 GROUP shall register the Registry Protocol and post the Registry results on ClinicalTrials.gov and provide the Registry results to SUKL in accordance with regulatory requirements and timelines. This posting must include all mandatory data fields. GROUP is responsible for updating posted data on any required registries as per regulatory requirements until the main Publication by GROUP per Article 8. GROUP shall provide ROCHE with link to posting.

9.2 ROCHE shall register the Registry Protocol and post the Registry results on EnCePP Register in accordance with regulatory requirements and timelines for NI-PASS/PAES. GROUP shall provide ROCHE will all necessary information required to complete all mandatory data fields. ROCHE is responsible for updating posted data on the required EnCePP Register as per regulatory requirements until the main Publication by GROUP per Article 8. ROCHE will provide GROUP with link to posting.

10 QUALITY ASSURANCE

10.1 GROUP warrants that it has a Quality Assurance Group, or access to a Quality Assurance Group, or implements quality control procedures through which GROUP will assure that its work is performed in compliance with all applicable laws, rules, regulations, applicable pharmacoepidemiology and pharmacovigilance guidelines, including but not limited to GPP, EMA Good Pharmacovigilance Practices (GVP) Guidelines, recognized industry codes of practice as well as any agreed upon Standard Operating Procedures ("SOPs"). Reports

detailing the result of audits performed by GROUP Quality Assurance GROUP may be inspected by ROCHE upon request.

10.2 GROUP warrants that it has and shall maintain all necessary licenses, authorizations, approvals, permits and registrations to perform its obligations in accordance with the terms and conditions of this Agreement and that during the term of this Agreement, all such licenses, authorizations, approvals, permits and registrations are and shall remain current and in good standing. GROUP agrees, upon ROCHE's request, to provide ROCHE with copies of all relevant records for purposes of this Agreement, including without limitation copies of all applicable licenses, authorizations, approvals, permits and registrations.

10.3 GROUP must ensure that their computer systems are complete, accurate, and reliable and have consistent intended performance. GROUP will maintain SOPs for these systems and their use. GROUP will ensure that the system data changes are documented (i.e. maintain an audit trail) and have a security system that prevents unauthorized access to data. INSTITUTION will also ensure that adequate data backup is performed. In the event of electronic data transfers between GROUP and ROCHE, the parties will define and document a secure data transfer approach.

10.4 GROUP will ensure and manage Subcontractor's satisfactory performance of services and compliance with applicable regulations and agreed SOPs which impact the Registry. GROUP will notify ROCHE in a timely manner of any critical and major findings at Subcontractor's' which have a regulatory compliance impact on the Registry.

10.5 ROCHE will have the right, but not the obligation, to audit the conduct of the work under this Agreement including that performed on behalf of GROUP by and at its Subcontractors. In the case of audit, GROUP or its Subcontractors will devise an action plan to address any findings. Access to patients' charts and dossiers cannot be granted to ROCHE.

10.6 Should any local and/or national government authority conduct, or give notice of intent to conduct, an inspection or take any other regulatory action with respect to the Registry under this Agreement, GROUP will promptly give ROCHE notice thereof and supply all information pertinent thereto. GROUP procures that it will include such obligations in any Subcontractor agreements as relevant.

10.7 As part of inspection management GROUP will promptly provide ROCHE with a copy of all communications between GROUP and any Regulatory Authority relating to the Registry.

10.8 GROUP or its Subcontractors will cooperate and assist as necessary in the implementation of action plans resulting from the inspection findings. Corrective action or actions which become necessary because of inspection findings which are due to Quality Standard deviations will not be considered to be out of the scope of this Agreement, i.e. no additional charges. In addition GROUP will, upon ROCHE's request, provide data and information that are relevant to such inspections.

10.9 Upon awareness, and in compliance with applicable international and local pharmacoepidemiology and pharmacovigilance guidelines, including but not limited to GPP, EMA GVP, GROUP must report to ROCHE any serious noncompliance or misconduct related to the Registry occurring internally, or at any Subcontractor involved in the Registry. A serious noncompliance issue is one which significantly and negatively impacts the scientific integrity of the Registry. Misconduct is defined as intentional noncompliance in connection with the conduct of a Registry including the fabrication or falsification of Registry

data. Fraud is considered to be a type of misconduct. Any such noncompliance, misconduct and fraud may be reported by ROCHE to relevant authorities.

10.10 GROUP shall produce all required documentation and data in compliance with all applicable laws, rules, regulations, recognized industry code of practice as well as the agreed procedural documentation and shall store all physical and electronic data and records at a location fit for this purpose.

11 TERM AND TERMINATION

11.1 In the event that the Registry is not approved by a competent authority or by an ethics committee, if applicable, GROUP shall promptly inform ROCHE and the Parties shall meet and discuss in good faith the extent to which this Agreement needs to be amended or terminated.

11.2 This Agreement shall become effective upon publication of this Agreement in the Agreements Register as per 7.5 by all Parties and shall continue in force for 3 years, unless otherwise terminated hereunder.

11.3 Any Party may terminate this Agreement forthwith by notice in writing to the other if the other Party commits a breach of this Agreement, which, in the case of a breach capable of remedy, shall not have been remedied within sixty (60) days of the receipt to the Party in default of a written notice identifying the breach and requiring its remedy. Such notice to terminate this Agreement shall not be issued until the matter in question has been raised in writing and discussed during the said sixty (60) day period.

11.4 The Parties shall be entitled to terminate this Agreement, by mutual agreement, in whole or in part, in the following circumstances:

11.4.1 forthwith on ethical grounds.

In case the Parties are not able to reach a mutual agreement each Party may terminate this Agreement.

11.5 In the event of premature termination of this Agreement, payments made to GROUP for achieved milestones shall remain property of GROUP.

11.6 Even in the event of premature termination of the Registry, GROUP shall provide ROCHE with Results.

11.7 Termination of this Agreement will not relieve any of the Parties of any obligation that may have accrued prior thereto. In particular, without limitation, in the event of termination of this Agreement, GROUP shall make available to ROCHE all Results, discoveries and/or inventions generated under or as a result of the Registry until the date of termination of this Agreement in accordance with Article 6. ROCHE's rights to use such Results, discoveries and/or inventions in accordance with Article 6 shall survive termination of this Agreement for an unlimited period of time.

11.8 Articles 3, 5, 6, 7, 8, 9, 11, 16 and 17 of this Agreement shall remain in force after termination of this Agreement.

12 FORCE MAJEURE

12.1 If performance of this Agreement by one of the Parties to this Agreement is prevented, hindered or delayed by reason of any cause beyond this Party's control, the other Party shall release the affected Party from its relevant contractual obligations for the duration of the event of Force Majeure and to the extent the obligations hereunder are affected by such event. The affected Party shall notify the other Party without delay, and within fifteen (15) days thereafter, provide a detailed description of the events, explaining the reason for its inability to perform or its delay in performance and specifying the period for which it is estimated that such inability or delay shall continue.

13 ENTIRE AGREEMENT

13.1 This Agreement constitutes the full understanding of the Parties related to the subject matter of this Agreement and a complete and exclusive statement of the terms of their Agreement. No terms, conditions, understanding or Agreement purporting to modify or vary the terms of this Agreement shall be binding unless hereafter made in writing and signed by both Parties.

14 AMENDMENT

14.1 This Agreement cannot be amended or modified except by the express written consent of both Parties.

15 ASSIGNMENT AND SUBCONTRACTING

15.1 Neither Party shall assign or transfer this Agreement or, subcontract any of its obligations without the prior written consent of the other Party. Provided, however all rights and obligations of ROCHE may be exercised or performed by its Affiliates, as defined in Article 7.1 of this Agreement, provided such Affiliates agree to be bound by this Agreement.

16 GENERAL PROVISION

16.1 ROCHE and GROUP have no obligation to renew this Agreement. ROCHE is not under any obligation to enter into another type of Agreement with any member of GROUP at this time or in the future.

16.2 Both ROCHE and GROUP warrant and represent to the other that both have the full right and authority to enter into this Agreement and are unaware of any impediment that would inhibit their ability to perform their obligations hereunder.

16.3 All rights vested in or created to the benefit of ROCHE under this Agreement shall be deemed to benefit to and to be assignable to any of ROCHE's Affiliates, as defined in Article 7.1 above.

16.4 Neither Party shall use the name, crest or logo of the other in any press release or product advertising or for any other commercial purpose without the prior written consent of the other.

16.5 Nothing in this Agreement shall create, imply or evidence any partnership between the Parties or the relationship between them of principal and agent.

16.6 GROUP can work with other partners in addition to ROCHE as far as these collaborations do not result in a change of the agreed Registry design, substantial changes of the

Protocol, and GROUP agrees to inform ROCHE about the other collaboration partners involved.

16.7 Legal notices under this Agreement should be addressed to:

For ROCHE:

ROCHE s.r.o.
Sokolovská 685/136f,
Karlín, 186 00 Praha 8,
Česká republika
DIČ: CZ49617052

For GROUP:

Faculty of Medicine
Masaryk University
Kamenice 753/5,
625 00 Brno
Czech Republic

16.8 All ATTACHMENTs form part of this Agreement and will have the same force and effect as if set out in the body of this Agreement.

17 APPLICABLE LAW AND JURISDICTION

17.1 This Agreement will be governed by and construed for all purposes in accordance with the substantive laws of the Czech Republic without giving effect to its choice of law principles.

17.2 The Parties shall attempt to settle all disputes arising out of or in connection with the present Agreement in an amicable way. In the event that such attempt should fail, the exclusive jurisdiction for both Parties lies in the Courts of Prague City.

IN WITNESS WHEREOF, the Parties by their duly authorized representatives have caused this Agreement to be executed as of the date first above written.

Made in two (2) original copies for and on behalf of:

Signed on behalf of:

ROCHE: ROCHE s.r.o. 18 -12- 2017

[redacted]

.....

Robin Turner
Authorized signatory

Date: 18/12/2017
dd MON yyyy

[redacted]

Patrik Krönig
2nd Authorized signatory

Signed on behalf of:
GROUP: Masarykova Univerzita

...[redacted]...

prof. MUDr. Jiří Mayer, CSc.
Authorized signatory

19 -12- 2017

Date: .....
dd MON yyyy

MASARYKOVA UNIVERZITA
Lékařská fakulta
625 00 Brno, Kamenice 5
5

ATTACHMENT 1

SEE FINAL REGISTRY PROTOCOL

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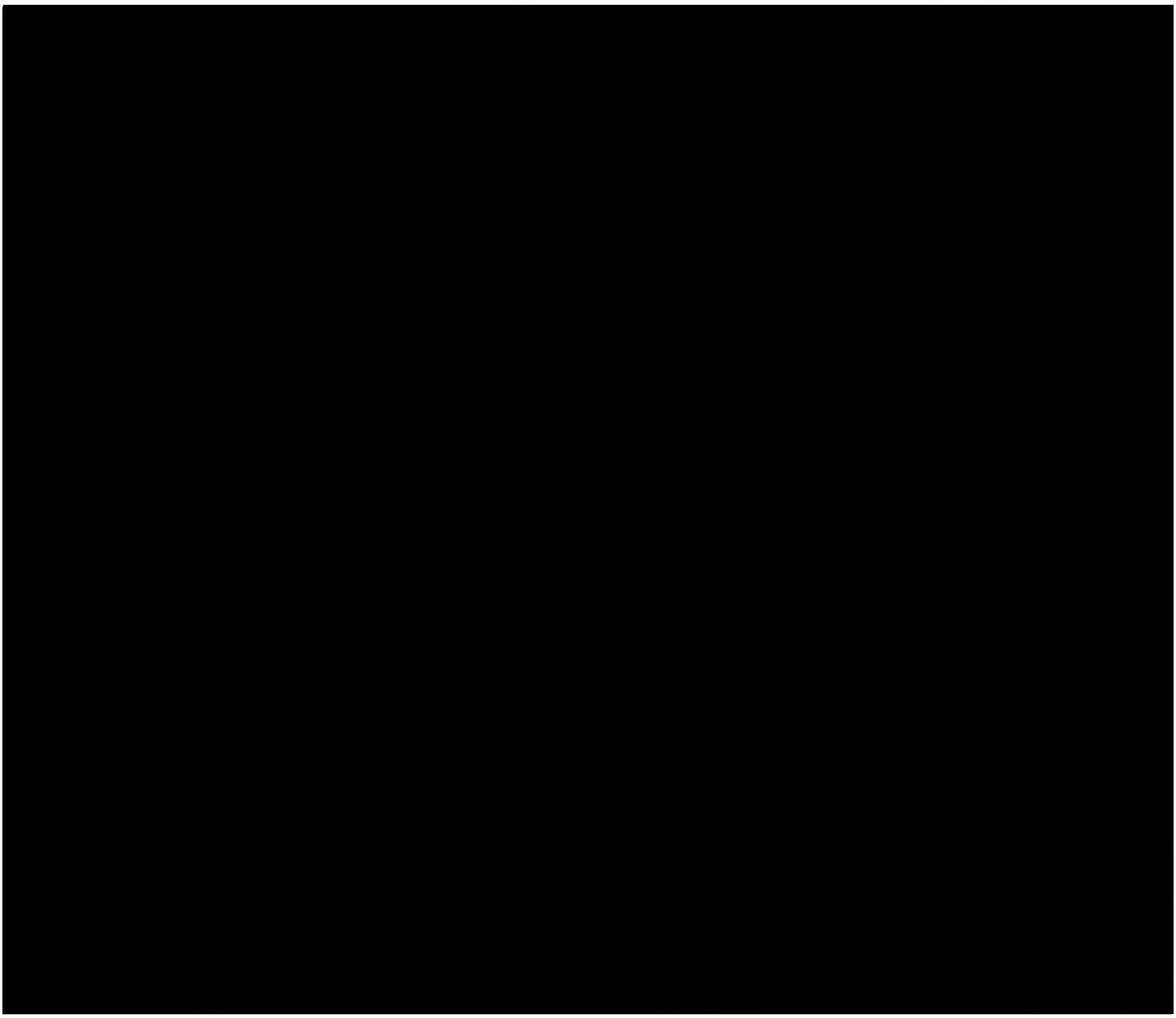
ATTACHMENT 2

SCHEDULE OF PAYMENTS



ATTACHMENT 3

BUDGET

ATTACHMENT 4

SAFETY DATA EXCHANGE AGREEMENT

BACKGROUND

A. ML-40461 - Study on effect of antifibrotic drugs in different subpopulations of patients with idiopathic pulmonary fibrosis. Analysis of data from the Czech EMPIRE registry, with protocol number IBA0866 ("the STUDY").

ROCHE shall provide financial support for the Czech part of the Registry according to timelines and milestones as per Study Agreement ("NISA").

B. This Safety Data Exchange Agreement (hereinafter referred to as "SDEA") describes the procedures and time frames and defines the responsibilities that both Parties will employ for ensuring compliance with the applicable laws and regulations pertaining to safety reporting and its related activities, as well as related activities for the Study.

C. The terms and conditions of the NISA are incorporated and made part of this SDEA. To the extent the terms and conditions of this SDEA conflict or are inconsistent with any terms or conditions of the NISA, the terms and conditions of the NISA shall take precedence unless otherwise agreed by both Parties in writing.

D. The relevant International Council for Harmonisation (ICH) guidelines, the latest European Union Pharmacovigilance guidelines and applicable European Union legislation, the United States (US) Code of Federal Regulations, Title 21, and relevant local regulations form the basis of the information to be exchanged between the Parties and to be reported to the regulatory authorities, as applicable.

NOW, THEREFORE, the Parties agree the following terms:

1. Definitions

All acronyms and capitalized terms not otherwise defined in the body of this SDEA are set forth in Appendix 1.

2. Single Case Management

2.1 Collection of Single Case Reports

Masaryk University will be responsible for collecting all Adverse Events (AEs). It is understood and agreed that Masaryk University will perform adequate due diligence with regard to obtaining follow-up information on incomplete AE reports. Masaryk University is not responsible for not receiving follow-up reports, provided that adequate efforts have been made to obtain them.

All AEs must be collected for patients receiving a Roche product.

Masaryk University shall amend the EMPIRE protocol Pharmacovigilance section according to the changes stipulated in section 2 hereof within 6 months of the effective date of this Agreement. Masaryk University shall notify investigators and Czech centers about their PV obligations by email within 2 weeks of the effective date of this Agreement.

2.2 Tracking of Safety Information

Masaryk University will track all safety reports collected as per Section 2.1 (Collection of Single Case Reports), originating from the Study for the Product.

2.3 Exchange of Single Case Reports

AE Reports, where the patient has been exposed to the studied Roche Product(s), will be sent to the Roche contact specified in Appendix 2 of this SDEA in the format described below. Transmission of these reports (initial and follow-up) will be electronically via email and within the timelines specified below:

- Adverse events
    - All AE reports will be performed by HCP in the registry interface through an e-form. This procedure will generate an e-mail in the form of an Adverse Event message sent immediately after filling the pre-defined fields in the e-form by HCP to the email contacts listed in APPENDIX 2.

2.4 Case Transmission Verification of Single Case Reports

The Parties will ensure that all single case reports have been adequately received by Roche, via Masaryk University emailing Roche a monthly line-listing documenting single case reports sent by Masaryk University to Roche in the preceding time period. The periodic line-listing will be exchanged within seven (7) calendar days of the end of the agreed time period.

Confirmation of receipt should be received within seven (7) calendar days of receipt.

Following Case Transmission Verification, single case reports which have not been received by Roche shall be forwarded by Masaryk University to Roche within five (5) calendar days from request by Roche.

3. Reporting to Regulatory Authorities

Roche as the Marketing Authorization Holder will be responsible for the reporting of individual case safety reports from the study to the regulatory authority in compliance with applicable regulations. However, this does not impact the individual HCP's responsibility to report Adverse Drug Reactions in line with the applicable local legislation.

4. Queries

Queries related to the Study will be answered by Masaryk University. However, responses to all safety queries from regulatory authorities related to Roche Product or for publications will be discussed and coordinated between the Parties. The Parties agree that Roche shall have the final say and control over safety queries relating to the Roche Product. Masaryk University agrees that it shall not answer such queries from regulatory authorities and other sources relating to the Roche Product independently but shall redirect such queries to Roche.

Both Parties will use all reasonable effort to ensure that deadlines for responses to urgent requests for information or review of data are met. The Parties will clearly indicate on the request the reason for urgency and the date by which a response is required.

5. Safety Crisis Management

In case of a safety crisis, e.g.,

- where safety issues have a potential impact on the indication(s), on the conduct of the Study,
- may lead to labeling changes or regulatory actions that limit or restrict the way in which the Product is used, or
- where there is media involvement,

the Party where the crisis originates will contact the other Party as soon as possible.

The Parties agree that Roche shall have the final say and control over safety crisis management issues relating to the Roche Product. Masaryk University agrees that it shall not answer such queries from media and other sources relating to the Product but shall redirect such queries to Roche. For contact details see APPENDIX 2.

6. Language

English will be used as the common language for all safety information exchanged between the Parties.

7. Contacts

All transfer of safety information between the Parties will be made through the designated or alternate contact person(s) listed in APPENDIX 2, will be reviewed annually and updated accordingly as agreed by the Parties by e-mail correspondence. The Parties shall inform each other of changes in the contact details affecting critical processes such as single case management and safety crisis.

8. Records

All Parties will maintain reports and all related documentation (or true copies of these documents) for a time period required by the applicable laws and regulations in the territories for which they are responsible, taking into account the minimum archiving period worldwide.

9. Compliance with pharmacovigilance agreement/audit

The Parties shall follow their own procedures for adherence to AE reporting timelines.

Each Party shall monitor and, as applicable, request feedback from the other Party regarding AE report timeliness in accordance with its own procedures. The Parties agree to provide written responses in a timely manner to inquiries from the other Party regarding AE reports received outside the agreed upon Agreement timelines. If there is any detection of trends of increasing or persistent non-compliance to transmission timelines stipulated in this Agreement, both Parties agree to conduct ad hoc or institute a regular joint meetings to address the issue.

In case of concerns related to non-compliance of processes, other than exchange timelines, with this Agreement, the Parties will jointly discuss and collaborate on clarifying and resolving the issues causing non-compliance. Every effort will be made by the non-compliant Party to solve the non-compliance issues and inform the other Party of the corrective and preventative actions taken.

Upon justified request, given sufficient notice of no less than sixty (60) calendar days, an audit under the provisions of this Agreement can be requested by either Party. The Parties will then discuss and agree in good faith upon the audit scope, agenda and execution of the audit. The requesting Party will bear the cost of the audit.

10. Amendments

The Parties agree to revise this SDEA to comply with new or amended legal or regulatory requirements as necessary, or as and when required; provided, however, that no subsequent alteration, amendment, change or addition to this SDEA shall be binding upon the Parties hereto unless in writing, with reference to this SDEA and signed by the respective authorized personnel of the Parties.

11. Term and Termination of SDEA

This SDEA becomes effective on the date upon which the last Party executes the NISA and remains in full force and effect as long as the reporting obligations under applicable laws and regulations for the Parties exist.

IN WITNESS WHEREOF, the Parties by their duly authorized representatives have caused this Safety Data Exchange Agreement to be executed as of the date first above written.

Made in *two (2)* original copies for and on behalf of:

Signed on behalf of:

ROCHE: F. Hoffmann-La Roche Ltd

[redacted]

..... Date: 18/12/2017

Robin Turner DD/MMM/YYYY

Authorized signatory

[redacted]

Patrik Kronig

2nd Authorized signatory

Signed on behalf of:

GROUP: Masaryk University, Faculty of Medicine, prof. MUDr. Jiří Mayer, CSc., Dean of the Faculty

[redacted]

..... Date: 19 -12- 2017 .....

prof. MUDr. Jiří Mayer, CSc. DD/MMM/YYYY

Authorized signatory

MASARYKOVA UNIVERZITA
Lékařská fakulta
625 00 Brno, Kamenice 5
5

APPENDIX 1: Definitions

The definitions below are based on the International Council for Harmonisation (ICH) guidelines and Food and Drug Administration (FDA) regulations. The use of italic font in this section refers to definitions taken from the ICH guidelines and/or FDA and EMA regulations. Other definitions relate to the company specific Global Processes and Procedures Glossary.

- **Adverse Event (AE)**

  "Any untoward medical occurrence in a patient or clinical trial subject administered a medicinal product and which does not necessarily have a causal relationship with this treatment. An Adverse Event (AE) can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product."

  (Source: Clinical Safety Data Management: Definitions and Standards for expedited Reporting, ICH E2A, 1994)

- **Awareness Date**

  The date any Party (including employees of affiliates or agents acting on behalf of either Party), first has knowledge of the minimum data elements as defined by ICH E2A guideline. At the very least, the following data must be provided for a case to be considered as valid:

  - *an identifiable reporter*,*
  - *an identifiable patient**(i.e., either CRF number, patient/subject number, initials, gender, date of birth, age or age group),*
  - *a drug/counterfeit drug,*
  - *an adverse event (or a special situation report).*

  *For AE reports from social media sources, verified contact details (e.g., email address) are considered an identifiable reporter.

  **For reports from healthcare professionals, "a patient" is considered an identifiable patient criterion.

  The minimum data elements should be obtained initially prior to transmitting the information to the other Party. In the event that an AE report is lacking minimum data elements, this report should not be forwarded to the other Party until all the minimum data elements are gathered. The originating Party will ensure prompt follow-up as necessary.

- **European Medicines Agency (EMA)**

  The centralized European regulatory authority for the European Union (EU) member states.

- **European economic area (EEA)**

  European Union (EU) plus Iceland, Liechtenstein and Norway.

- **Food and Drug Administration (FDA)**

  The agency within the U.S. Department of Health and Human Services protecting the public health by assuring the safety, effectiveness, quality, and security of human and veterinary drugs, vaccines and other biological products, and medical devices.

- **International Council for Harmonisation (ICH)**

  International Council for Harmonization of Technical Requirements for Registration on Pharmaceuticals for Human Use.

- **Non-interventional study (NIS)**

  NIS are carefully designed and conducted epidemiological studies, specifically observational (non-interventional, non-experimental). In observational studies, the physician "observes and evaluates results of ongoing medical care without 'controlling' the therapy beyond normal medical practice."

  Note: The prescription of the medicine is clearly separated from the decision to include the patient in the study.

  For EEA Affiliates, please refer to the definition below from EMA GVP Module VIII: *"A non-interventional study is a study fulfilling, cumulatively, the following requirements:*

  1. *The medicinal product is prescribed in the usual manner in accordance with the terms of the marketing authorization;*
  2. *The assignment of the patient to a particular medical treatment is not decided in advance by a trial protocol but falls within current practice;*
  3. *No additional diagnostic or monitoring procedures are applied to the patients above those applied in course of routine clinical practice; and 4. epidemiological methods are used for the analysis of collected data.*

  (Sources: CIOMS, Current Challenges in Pharmacovigilance: Pragmatic Approaches. Report of CIOMS Working Group V. Geneva; World Health Organization [WHO], 2001 and FDA Guidance for Industry E2E Pharmacovigilance Planning, 2005).

- **Product**

  The Roche product that is the subject of the study as defined in the corresponding protocol.

- **Single case reports**

  A document providing the most complete information related to an individual case at a certain point of time. An individual case is the information provided by a primary source to describe adverse events/special situation reports following the administration of one or more medicinal products to an individual patient at a particular point of time.

APPENDIX 2: Contact Details

Roche Contacts:

[redacted]

ENTER NAME OF External NIS Initiator Contacts:

[redacted]

APPENDIX 3: EMPIRE REGISTRY – CRF

13th JULY 2016

ADVERSE EVENT

- **Basic information**
  - Type of report (selection)
    - Initial
    - Follow-up
  - Race of patient
    - Asian
    - Black
    - White
    - Other
  - Weight
  - Height
  - Pregnancy (yes/no)
  - Weeks
- **Type of adverse event**
  - Type of adverse event (selection)
    - Nausea
    - Dyspepsia
    - Emesis
    - Diarrhoea
    - Anorexia nervosa
    - Photosensitive reaction
    - Rash
    - Dizziness
    - Fatigue
    - Fever
    - Weight loss
    - Weight gained
    - Obstipation
    - Abdominal pain
    - Dyspnoea
    - Cough

- Elevated liver enzymes
- Liver failure
- Bleeding
- Loss of appetite
- Other

➢ Please specify
➢ Grade

- 1- Mild
- 2- Moderate
- 3 - Severe
- 4 - Life threatening
- 5 - Death

❖ **Adverse event**

➢ Onset date of the adverse event (dd.mm.yyyy) (date)
➢ Stop date of the adverse event (dd.mm.yyyy) (date)
➢ Was the adverse event serious (SAE)? (yes/no)
➢ Specify serious adverse event (checkbox)

- Death
- Life-threatening event
- Patient required hospitalisation or existing hospitalisation was prolonged
- Persistent or significant disability/incapacity
- Congenital birth defect
- Required intervention to prevent permanent impairment or damage

➢ Is there a reasonable causal relationship with the drug administered? (selection)

- Yes
- No
- Cannot be excluded

➢ What is the indication of this drug? (selection)

- IPF
- Non-IPF

➢ Type of non-IPF medication (text)
➢ IPF medication (selection)

- N-acetylcysteine
- Protein pump inhibitors
- Corticosteroids
- Azathioprine
- Pirfenidone
- Nintedanib

- Investigational drug (specify)
- Other

➢ Please specify
➢ Who is the marketing authorization holder? (selection)
- Boehringer Ingelheim
- Roche
- Trommsdorff
- Zentiva
- Mundipharma
- Bristol-Meyers
- Aspen Pharma
- Other

➢ Please specify
➢ Is the patient treated with this drug within the clinical trial (CT)? (yes/no)
➢ Is the patient treated with this drug within the compassionate use program (CUP)? (yes/no)
➢ Was the Adverse event already reported within the CUP or CT? (yes/no)
➢ Please insert CUP/CT number and sponsor (text)
➢ Please insert site number in this CT/CUP (text)
➢ Please insert patient ID in this CT/CUP (text)

❖ **Assessment of the adverse event**

➢ AE treatment (yes/no)
➢ Type of treatment (text)
➢ Formulation (text)
➢ Total daily dose at onset (dose, unit) (text)
➢ Route of administration (text)
➢ Start date of treatment of AE (dd.mm.yyyy) (date)
➢ End date of treatment of AE (dd.mm.yyyy) (date)
➢ Indication for use (text)
➢ Concomitant therapy (relevant) (text)
➢ Is there a reasonable causal relationship between the event and the concomitant therapy? (yes/no)
➢ Concomitant diagnoses (relevant) (text)
➢ Outcome of AE (selection)
- The AE completely subsided
- The condition improved
- The condition worsened
- Unknown

➢ Action taken with suspect drug due to event (selection)
- Continued
- Reduced
- Discontinued
- Increased
- Completed according to protocol
- Discontinued and reintroduced
- Not applicable

➢ Comments (text)

Please insert telephone number and email in case any further details are needed (text)