DATA ACCESS AGREEMENT

These terms and conditions govern access to the managed access datasets (details of which are set out in Appendix I) for academic, non-commercial use to which the User Institution has requested access.

The User Institution agrees to be bound by these terms and conditions.

Between _____

(called "**User Institution"** hereinafter)

And

University of Zurich Raemistrasse 71, 8006 Zurich (hereinafter called "**UZH**"),
ETH Zurich Raemistrasse 101, 8092 Zurich (hereinafter called "**ETH**"), and
University Hospital Basel Hebelstrasse 32, 4031 Basel (hereinafter called "**USB**")

(each called "**Partner**" or, together, "**Partners**" hereinafter)

Definitions

Access Rights: Rights and conditions to use the provided datasets under controlled access and under the terms and conditions laid down in this Agreement.

Registered Users*:* The individuals at the User Institution to whom Partners grant access to the Data. This includes the User, the individuals listed in Appendix II and any other individuals for whom the User Institution subsequently requests access to the Data.

Data*:* The managed access datasets to which the User Institution has requested access.

Data Producers*:* The Partners and the collaborators listed in Appendix I responsible for the development, organisation, and oversight of these Data.

Project*:* The User Institution's project for which the User Institution has requested access to these Data. A description of the Project is set out in Appendix II.

Publications*:* Includes, without limitation, articles published in print journals, electronic journals, reviews, books, posters and other written and verbal presentations of research.

Research: Research in the sense of Chapter 4 of the Swiss Human Research Act (HRA) dating September 30th, 2011.

Research Participant*:* An individual whose data form part of these Data.

***User**:* The User Institution's principal investigator for the Project and other registered users according to Appendix II.

***User Institution(s)**:* The Institution(s) that has/have requested access to the Data.

1. The User Institution agrees to **only** receive and use these Data in pseudonymized form **for the purpose of the Project** (described in Appendix II) and only for research. The User Institution further agrees that it will only use these Data for research which are within the limitations (if any) set out in Appendix I.

2. The User Institution agrees to preserve, at all times, the **confidentiality** of these Data. In particular, it undertakes not to use, or attempt to use these Data to compromise or otherwise infringe the confidentiality of information on Research Participants. Without prejudice to the generality of the foregoing, the User Institution agrees to use at least the measures set out in Appendix I to protect these Data.

3. The User Institution agrees to protect the **confidentiality of Research Participants** in any research papers or publications that they prepare by taking all reasonable care to limit the possibility of identification.

4. The User Institution agrees **not** to link or combine these Data to other information or archived data available or process the Data otherwise in a way that could **re-identify** the Research Participants, even if access to that data has been formally granted to the User Institution or is freely available without restriction.

5. The User Institution agrees to retain control of the Data and further agrees not to distribute Data obtained through this agreement to any entity or individual not covered in the submitted request. Should the User Institution wish to share these Data with an External User, the External User must complete a separate application for access to these Data and to be listed on the list of Registered Users; for the avoidance of doubt, User Institution carries at all times full responsibility and liability for any Data processing by the External User.

6. The User Institution and Registered Users acknowledge that although all reasonable efforts have been taken to ensure the accuracy and reliability of the data, the Data Producers do not and cannot warrant the results that may be obtained by using any data included therein. All contributors to these datasets disclaim all warranties as to performance or fitness of the data for any particular purpose. No indemnification for any loss, claim, damage, or liability is intended or provided by any party under this agreement. Each party shall be liable for any loss, claim, damage, or liability that said party incurs as a result of its activities under this agreement.

7. The User Institution agrees to follow the ***Fort Lauderdale Guidelines*** (https://wellcome.org/sites/default/files/wtd003207_0.pdf) and the ***Toronto Statement*** (*http://www.nature.com/nature/journal/v461/n7261/full/461168a.html*). This includes but is not limited to **recognising the contribution of the Data Producers** and including a proper **acknowledgement** in all reports or publications resulting from the use of these Data.

8. The User Institution agrees to follow the ***Publication Policy*** in Appendix III. This includes respecting the moratorium period for the Data Producers to publish the first peer-reviewed report describing and analysing these Data.

9. The User Institution agrees **not to make intellectual property claims** on these Data and not to use intellectual property protection in ways that would prevent or block access to, or use of, any element of these Data.

10. The User Institution agrees to **destroy/discard the Data** held, once it is no longer used for the Project, unless obliged to retain the data for archival purposes in conformity with audit or legal requirements. In case data and results must be archived, then data must be deleted 10 years after completion of the project, if data has not to be archived, data must be deleted no later than 2 years after start of the project; an extension can be requested via contact with Tumor Profiler Center leadership.

11. The User Institution agrees to delete data of patients with revoked consent as soon as possible, but in any case no longer than after 3 months.

12. The User Institution reports progress annually and termination of the Project latest after 3 months. The reports must be sent to info@tumorprofilercenter.ch.

13. The User Institution will notify the Partners within 30 days of any **changes or departures of Registered Users**. The notification must be sent to info@tumorprofilercenter.ch.

14. The User Institution will notify the Partners prior to any significant **changes to the protocol** for the Project.

15. The User Institution will notify the Partners as soon as (in any case no longer than after 1 month) it becomes aware of **a breach of the terms or conditions** of this agreement.

16. This Agreement terminates without further ado after completion of the Project. After termination, Clauses 2-5, 7-10 and 20 shall prevail.

17. The **Partners may terminate this agreement** only due to either significant changes to the protocol or of the framework conditions or in case of Clause 19 (altered terms). Termination shall be made by written notice to the User Institution within a time limit of 3 three months. In this case, the User Institution will be required to destroy any Data held, including copies and backup copies. This clause does not prevent the User Institution from retaining these data for archival purpose in conformity with audit or legal requirements.

18. The User Institution accepts that it may be necessary for the Data Producers to alter the **terms of this agreement** from time to time. As an example, this may include specific provisions relating to the Data required by Data Producers other than the Partners. In the event that changes are required, the Data Producers or their appointed agent will contact the User Institution to inform it of the changes and the User Institution may elect to accept the changes or terminate the agreement.

19. If requested, the User Institution will allow **data security and management documentation** to be inspected to verify that it is complying with the terms of this agreement.

20. The User Institution agrees to distribute a **copy of these terms to the Registered Users**. The User Institution will procure that the Registered Users comply with the terms of this agreement.

21. For the avoidance of doubt, the existence of this contract is dependent on the validity of the Consortium agreement.

22. This agreement (and any dispute, controversy, proceedings or claim of whatever nature arising out of this agreement or its formation) shall be construed, interpreted and governed by the **laws of Switzerland** (without its conflict of law principles) and shall be subject to the exclusive jurisdiction at the competent **court(s) in Basel**.

Agreed for User Institution

Signature:	
Name:	
Title:	
Date:	
Corresponding address & Email	

Principal Investigator at User Institution

I confirm that I have read and understood this Agreement.

Signature:	
Name:	
Title:	
Date:	
Corresponding address & Email	

Agreed for the Partners (individually UZH, ETH, USB)

For UZH

Signature:	
Name:	
Title:	
Date:	
Corresponding address & Email	

For ETH

Signature:	
Name:	
Title:	
Date:	
Corresponding address & Email	

For USB

Signature:	
Name:	
Title:	
Date:	
Corresponding address & Email	

APPENDIX I – DATASET DETAILS
APPENDIX II —PROJECT DETAILS
APPENDIX III — PUBLICATION POLICY

APPENDIX I – DATASET DETAILS (to be completed by the data producer before passing to applicant)

Dataset reference (EGA Study ID and Dataset Details)

Technology/Platform	Description	
Digital Pathology	Quantitative measurement of biomarker expression, immune cell counts and spatial immune cell distribution on digitized immunohistochemistry slides	☐
Single-cell CyTOF	In-depth characterization of tumor and immune compartments at single-cell resolution based on metal tagged antibodies targeting surface markers and intracellular signaling pathways	☐
IMC	High-dimensional, spatially resolved analysis of the tumor microenvironment at single-cell resolution based on metal tagged antibodies. Regions of interest are defined in conjunction with digital pathology	☐
FMI	Massively parallel sequencing of cancer-related genes in tumor specimens using the FoundationOne®CDx test. A qualitative next generation sequencing based in vitro diagnostic test using targeted high throughput hybridization-based capture technology for detection of substitutions, insertion and deletion alterations (indels), and copy number alterations (CNAs) in 324 genes and select gene rearrangements, as well as genomic signatures including microsatellite instability (MSI) and tumor mutational burden (TMB) using DNA isolated from formalin0fixed paraffin embedded (FFPE) tumor tissue specimens.	☐
scDNA and scRNA	Massively parallel sequencing at single -cell resolution of both DNA (scDNA) and RNA (scRNA) for the study of tumor microenvironment, tumor cellular composition, cell type-specific expression patterns, somatic copy number alteration, and the immune cell component	☐
cfDNA	Massively parallel sequencing of cancer-related genes in cell-free DNA. Relevant drugs are suggested from a list of approved therapies based on this state-of-the-art molecular diagnostic test	☐
bkRNA	Massively parallel sequencing of mRNA to characterize the transcriptomic status at tissue-level. Gene expression, signaling pathways, splicing landscape, and novel putative epitopes for targeted treatment, among other characteristics, can be investigated with bulk transcriptomics	☐
Proteotyping	Unbiased quantification of the proteotype at tissue-level. Cellular phenotypes are revealed by the study of the abundances and interactions of over 3000 proteins. Additionally, the absolute quantification of selected targets is performed by the “antibody-free ELISA” approach	☐
Pharmacoscopy	Quantitative measurement at single-cell resolution of ex vivo response to relevant drugs and drug combinations using automated microscopy, single-cell image analysis, and machine learning	☐
4i DRP	Image-based analysis of multi-scale molecular response to drug treatments, including multicellular phenotypes (cell-cell interactions and spatial patterns), single-cell phenotypes (cell cycle state, morphology and intracellular organelles, and signaling pathways activity	☐

Name of project that created the dataset
TuPro 1.0

Names of other data producers/collaborators

TuPro Data	Responsible TuPro PI(s)
Digital Pathology	Holger Moch, Viktor Koelzer, Markus Tolnay
CyTOF	Bernd Bodenmiller
IMC	Bernd Bodenmiller
FMI	Holger Moch
scDNA-seq	Niko Beerenwinkel
cfDNA	Ilaria Alborelli, Markus Tolnay
scRNA-seq	Niko Beerenwinkel
bkRNA-seq	Gunnar Raetsch
Proteotyping	Bernd Wollscheid
Pharmacoscopy	Berend Snijder
4iDRP	Lucas Pelkmans

Specific limitations on areas of research
None

Minimum protection measures required

File access*: The User Institution and Registered Users, including the institutional Information Technology Director or his/her designee, acknowledge the partners' expectation that they have reviewed and agree to handle the requested dataset(s) according to the current dbGaP Security Best Practices, including its detailed description of requirements for security and encryption. These include, but are not limited to:*

- *All Approved Users have completed all required computer security training required by their institution.*
- *The data will always be physically secured (e.g., through camera surveillance, locks on doors/computers, security guard).*
- *Servers must not be accessible directly from the internet, (e.g., they must be behind a firewall or not connected to a larger network) and unnecessary services should be disabled.*
- *Use of portable media (e.g., CD, flash drive or laptop) is discouraged, but if necessary then they should be encrypted consistent with applicable law.*
- *Updated anti-virus/anti-spyware software is used.*
- *Security auditing/intrusion detection software that regularly scans and detects potential data intrusions should be in place.*
- *Strong password policies for file access are used.*

- *All copies of the dataset are destroyed, as permitted by law and local institutional policies, whenever any of the following occurs:*
    - *the Data Access Agreement expires and renewal is not sought;*
    - *access renewal is not granted;*
    - *destruction of the dataset is requested; and*
    - *continued use of the data would no longer be consistent with the Data Access Agreement.*

In addition, User Institution and Registered Users agree to keep the pseudonymized data secure and confidential at all times and to adhere to information technology practices in all aspects of data management to assure that only authorized individuals can gain access to the datasets. This agreement includes the maintenance of appropriate controls over any copies or derivatives of the data obtained through this Data Access Agreement.
User Institution and Registered Users agree to notify the partners of any unauthorized data sharing, breaches of data security, violations in the presentation and publication embargo period, or inadvertent data releases that may compromise data confidentiality within 24 hours of when the incident is identified. As permitted by law, notifications should include any known information regarding the incident and a general description of the activities or process in place to define and remediate the situation fully. Within 3 business days of the partners notification, the User Institution, through the Registered User and the Institutional Signing Official, agree to submit to the partners Data Access Committee a more detailed written report including the date and nature of the event, actions taken or to be taken to remediate the issue(s), and plans or processes developed to prevent further problems, including specific information on timelines anticipated for action.
All notifications and written reports of data security incidents should be sent to: info@tumorprofilercenter.ch.
The partners or another entity designated by the partners may, as permitted by law, also investigate any data security incident. Registered Users agree to support such investigations and provide information within the limits of applicable laws and regulations. In addition, User Institution and Registered Users agree to work with the partners to assure that plans and procedures that are developed to address identified problems are mutually acceptable and consistent with applicable law.

APPENDIX II – *USER INSTITUTION's* PROJECT DETAILS (to be completed by the Requestor)

User Institution and Registered Users agree that information about themselves and their approved research use can be used for internal purposes and posted publicly on the Tumor Profiler Center website. The information includes the name of the User Institution and Registered Users, abstract, summary statements and used dataset. In addition, citations of publications resulting from the use of the dataset may be posted on Tumor Profiler Center data repository websites.

Details of dataset requested i.e., EGA Study and Dataset Accession Number

Brief abstract of the Project in which the Data will be used (500 words max)

All Individuals at the User Institution to be named as registered users

Name of Registered User	*Institutional Email*	*Job Title*	*Supervisor**

All Individuals that should have an account created at the EGA

Name of Registered User	Institutional Email	Job Title

APPENDIX III – PUBLICATION POLICY

Partners intend to publish the results of their analysis of this dataset and do not consider its deposition into public databases to be the equivalent of such publications. Partners anticipate that the dataset could be useful to other qualified researchers for a variety of purposes. However, some areas of work are subject to a publication moratorium.

The publication moratorium covers any publications (including oral communications) that describe the use of the dataset. For research papers, publication should not occur until 12 months after these data were first made available on the relevant hosting database, unless the Partners has provided written consent to earlier submission.

In any publications based on these data, please describe how the data can be accessed, including the name of the hosting database (e.g., The European Genome-phenome Archive at the European Bioinformatics Institute) and its accession numbers (e.g., EGAS00000000029), and acknowledge its use in the following form: “The results published here are in whole or part based upon data generated by members of The Tumor Profiler Study. Information about the study and the succession initiative Tumor Profiler Center can be found at http://tumorprofilercenter.ch”