Dear Mr., dear Mrs. ………………………………,

thank you for reading the information on PTT2.0.

Please take the time to decide, whether your child should participate in this study. Discuss your decision with your child, but also with your family and friends, if this is helpful to you. Please do not hesitate to ask us all your questions, which can help you make your decision.

1. What is PTT2.0?
   The purpose of the PTT2.0 study is the collection of research data to improve our knowledge on genetic alterations in relapsed and progressive childhood tumors. The data collected here will enable the development of new treatment strategies for patients, individualized cancer therapy and risk stratification in the future. This study has been reviewed and approved by the ethics committee of the Medical Faculty of the University of Heidelberg.

2. What are the goals of the PTT2.0 study?
   It is widely accepted that cancer is a disease resulting from genetic and epigenetic changes (i.e. changes in factors controlling genetic information) in the cells that make up the body. In this study, researchers
are trying to understand these specific genetic and epigenetic changes in tumors, and are looking for changes that can be exploited for targeted therapies (which selectively interfere with the specific changes in a tumor, as opposed to chemotherapy).

We suppose that in the near future, the tumor and the blood of all cancer patients will be analyzed in such a manner, in order to treat each patient as individually as possible.

In order to be prepared for this new era, and also to benefit today from these technical possibilities at least in part, we introduce these analyses in the PTT2.0 study. Our goal is to achieve a turnaround time of 4 weeks for the analysis of the genetic information and clinical evaluation of the changes discovered. At the same time we want to collect data on possible therapies and how to implement them.

The decision about if and which kind of therapy is given to your child based on the genetic analysis, lies solely with your treating physician. The targets identified by the genetic analysis can be used by your treating physician for his decision.

We want to document the clinical course of your child, irrespective of which treatment it receives, in order to compare the application of targeted therapies to standard chemotherapies, as well as to compare the actionability of the different targets found. By collecting this data, we hope to:
- learn more about the genetic structure of pediatric tumors
- identify common and actionable targets
- and identify the most promising therapeutic strategies

3. Why was your child selected?

Your child was selected because it was diagnosed with cancer refractory to standard of care treatment. Therefore, the genetic information of your child’s tumor obtained via PTT2.0 might be used to select novel therapeutic approaches. The consent to participate is voluntary and can be withdrawn at any time without reason, which will bear no disadvantages for your child.
4. What does the participation include?
The participation of your child in the PTT2.0 study requires the consent to participate in the following three points:

A. Use of archived tissue: Your consent to participate will allow us to analyze the tissue obtained during a planned surgical or other procedure performed during the diagnostic workup upon primary diagnosis or recurrence of your child’s tumor (i.e. bone marrow puncture, lumbar puncture etc.). This means that no tissue will be obtained specifically for the PTT2.0 study. Only residual material that is not being used for diagnostics will be used. With this consent you will also allow us to analyze previously gained samples (such as the primary tumor, first, second recurrence etc.), should they exist.

B. Analysis of a blood sample: Your consent to participate will allow us to analyze blood of your child, approx. 3-5ml (corresponding to approx. 2-3 tea spoons) for this study. The blood will be gained during routine blood sampling. The genetic information (DNA) from the blood will be extracted. The DNA will be used for targeted sequencing, which is a process that will allow us to identify many changes unique to your child and distinguishing it from the DNA of other people. We need this information in order to identify changes in the tumor, which are not detectable in normal tissue.

C. Clinical Data: Your consent to participate will allow us to collect relevant information on the health and disease of your child in this study. This information can be collected e.g. from hospital files, and can be send from your treating hospital directly to us.

5. How will the data and samples be stored and protected?
All collected tissue and blood samples of your child will be analyzed during routine diagnostics. All doctors and scientists working with these samples are bound to data protection. All samples will be sent back to the submitting institution after completion of diagnostics and validation. The data of your child as well as all results from the analyses are
stored in a protected database, and stored for at least 10 years after the end of this study.

6. Who is allowed to use the data of your child?
One of the goals of the PTT2.0 study is, to share anonymized data with other researchers (national and international academic researchers), in order to facilitate and accelerate the investigation of the causes and potential therapies of cancer. However, the PTT2.0 study group also respects the individuals providing their samples for this project, and will ensure their privacy. To achieve this, all personal identifiers, such as name of your child or address will be removed, and replaced by a unique identifier (pseudonymization). Pseudonymization means that a code consisting of numbers and/or letters will be used, possibly in combination with the year of birth (but not the complete date of birth). Only the PTT2.0 study group will be able to connect this code with information that can be used to identify your child. The coded data will be stored in to separate databases, public databases and databases with controlled access.

- **Public databases**: Information from these databases is publically available, but cannot be used to identify your child specifically. Only data on e.g. kind of tumor, age group, tumor specific mutations can be found here.

- **Databases with controlled access**: The data will only be accessible to researchers, and only be used for the study of causes of and therapeutic options for cancer.

All results from research based on data from the PTT2.0 study can be used for teaching, research, and publication including presentation at e.g. research meetings. In all cases of publication the identity of your child remains confidential.

7. What is the benefit of your participation?
The biggest health-related benefit of the PTT2.0 study will only be accessible in a few years, and as such only the next patient generation will fully benefit from the results. However, should we detect changes in the genetic information of your child, which could inform the current
treatment of your child, this information can be used by your treating physician.

8. What are the risks for your child?

Physical risks: since we only use tissues and blood samples, that are collected during routine procedures that are conducted for diagnostic purposes independent of this study, there are practically no risks for your child. The storage of the tissue and blood samples poses only a minimal risk, since a high level of security measures are taken to protect stored specimens from unauthorized access at the German Cancer Research Center (DKFZ), the University Hospital Heidelberg, and the National Center of Tumor diseases (NCT).

Protection of privacy: There is a minimal risk, that genetic information generated in the PTT2.0 study can be connected to genetic or medical information from other databases. It is theoretically possible, however very unlikely, that security measures used to protect the data stored in the databases, are broken. Of course no employer, insurance agency, or non-authorized family members will get access to this data.

9. What happens if something is detected in the tumor or in the normal tissue of my child?

As described under (7), your treating physician has access to the results of the PTT2.0 study. Therefore your child can gain access to the data through your treating physician, if the analyses reveal a clear clinical benefit concerning the treatment of the tumor disease of your child. The molecular genetic data may only be used for therapeutic purposes. We can only evaluate the clinical benefit once at the time of analysis, not over and over. In this respect, we cannot guarantee an access to the data, if the changing scientific consensus indicates a clinical benefit. If the clinically usable information possibly concerns other family members (e.g. heritable susceptibility for (other) cancer diseases, such as breast or colon cancer), and you have consented to be informed about such a result, these results will be communicated to you in a human genetics counselling session. This only applies if you have explicitly consented to this procedure.
If potential indications for other diseases, not related to the tumor disease, are found in the DNA of your child, these will not be communicated to you.

10. Will you/your child be paid for participation?
Participation is on a strictly voluntary basis, no payments are made.

11. How can you withdraw your consent to participate in the study?
You can withdraw your consent to participate in the PTT2.0 study at any time without need for giving a reason. Please inform your treating physician.
If you withdraw your consent, the remaining samples of your child will be destroyed. Data that have already been generated as well as collected clinical data cannot be withdrawn, however no new information will be added to the PTT2.0 database. The identifiers of your child, such as name, address, complete date of birth, will be deleted. If the data have already been added to a different database, a connection of the data to your child will not be possible anymore.

12. What can you do in case of second thoughts?
If you first decide to participate in this study, and have second thoughts in the future, you can always contact us by phone (+49 6221-423387 (Dr. med. Florian Selt) or +49 6221-5637429 (PD Dr. med. Till Milde)), or by email (f.selt@dkfz.de or t.milde@dkfz.de).

Contact/Investigator
Dr. med. Florian Selt

Principal investigator:
PD Dr. med. Till Milde

Department of Pediatric Oncology and Hematology
Center for Individualized Pediatric Oncology (ZIPO) and Brain Tumors Therapy and Research Center for Pediatric Oncology and Hematology
INFORMED CONSENT FOR PARENTS

„Pediatric Targeted Therapy 2.0“—personalized pediatric oncology: targeted therapy and clinical feasibility.

Dr. __________________________ explained the PTT2.0 program to me and my child. The consent for participation in PTT2.0 program is fully voluntary. I have received written information about the program and have read it. I was allowed to ask questions about the program, which were all answered sufficiently.

With my signature I agree that tumor material and blood of my child is used for research purpose. Archived tumor material gained at a previous time point may be analyzed as well.

I have been informed and consent that the data of my child are used and analyzed for this study. The data may be passed to other researchers in pseudonymized form for research purposes. Pseudonymization means that a code consisting of numbers and/or letters will be used, possibly in combination with the year of birth (but not the complete date of birth). No third party will have access to personal records. In case of publication, the identity of my child will remain anonymous.

We want to be informed about (at the time of analysis) clinically usable changes found in the tumor tissue.

We want to be informed, if the tumor sample and the blood of our child exhibits evidence for the presence of a hereditary tumor-related syndrome.

☐ yes
☐ no

Information about hereditary alterations will be communicated within a human genetics counselling session.

I agree to participation of my child in the study. I will receive a copy of this informed consent with my signature.
Personal data of participant

Name and first name______________________________________________________________
DOB__________________________________________________________

Name and first name (mother)_____________________________________________________
Date________________________ Signature (mother)____________________________________

Name and first name (father)_______________________________________________________
Date________________________ Signature (father)_____________________________________

Confirmation of the treating physician

I have explained the PTT2.0 study including the participation requirements with the participant and his/her legal guardians. All questions have been fully answered. I have explained to the participant and his/her legal guardians that the participation is fully voluntary.

Name of the treating physician______________________________________________

Date________________________ Signature__________________________________________

Approval

The PTT2.0 Study has been submitted to the ethics committee of the University of Heidelberg and approved on XX.XX.XXXX