BOEHRINGER INGELHEIM GmbH

Information and Consent Form for Trial Subjects (template)

GENERAL GUIDELINES WHEN WRITING THE CONSENT FORM

(Keep the red text when submitting the trial version to the CT Managers. Delete these guidelines before submitting to local regulatory authorities)

1. FORMAT:

- Use a consistent font style and size throughout the document; a minimum 12 point font is preferable. Please consider the audience; some patients may require a larger font.
- The pages should contain "Page X of Y" and the version date of the document in the footer.
- **BICTMS number must be added. Localversioning can be added in addition to fulfil local needs.**
- Section headers should not float at the bottom of the page without any text.
- Before using the consent form, please print and review the document for print errors, spelling and grammar, font sizes, floating headers, etc.
- Avoid using tick boxes; this often leads to unnecessary non-compliances.

2. LANGUAGE AND READABILITY:

- Use brief, simple statements (not long, detailed, complicated explanations) using simple, layperson's language aimed at 13 – 15 year olds. Break long sentences into several shorter ones. Express only one major idea per sentence.
- Please do a "Readability Test" in MS Word as an indication check to find out whether the information you prepared is understandable to trial subjectssubjects (e.g. Grade level 8 - 10) included in this trial. Remember that the responsibility for the readability of the document remains exclusively with the author.
- Speak to your reader. Use "you/your" to refer to the potential subject. For example, write, "You must provide consent" not, "Consent must be provided".
- Avoid unfamiliar or confusing words or phrases. Avoid jargon. If a medical terminology is essential, include a layperson's definition. For example, "bruise" should be used instead of "hematoma".

3. GENERAL INSTRUCTIONS FOR USING THIS FORM:

- Instructions and suggested text are printed in 'red', with suggestions to actual text in 'black'. **Delete or replace all red text from this template when finished**.
- Sections highlighted in yellow are mandatory text and if there are any country specific changes , then the responsible CTM must consult and get approval from either local line management and/or local legal and/or local data protection/privacy contact for the requested changes.
- Please delete any parts of the consent template that are not relevant to your particular trial.
- If the consent form contains multiple procedures and/or technical terms, consider using the appendix at the end of the consent form. The use of appendices described in this

template is optional and depends on local regulations. Alternatively, the content in the appendices can be directly incorporated within the main body of the form as usual.

INFORMATION AND CONSENT FORM
FOR TRIAL SUBJECTS

TRIAL LAY TITLE: A study to test BI 655130 in patients with a flare-up of a skin disease called Generalized Pustular Psoriasis

PROTOCOL No.: 1368-0013

TRIAL SUBJECT No.: _____

EudraCT No.: 2017-004231-37

SPONSOR: Boehringer Ingelheim *(to be adapted at country level, CT Manager to insert full corporate legal name of local country)*

TRIAL DOCTOR: Name, address, telephone number

Dear Patient,

You are being asked to participate in this research trial because you have a rare and severe inflammatory skin disease called, Generalized Pustular Psoriasis (GPP) that causes inflammation in the skin and may also affect internal organs. It shows up as a recurrent flare-up (worsening GPP symptoms) with widespread pustules (small bumps on the skin that contain fluid or pus), diffuse erythema (large area of redness of the skin that looks like a sunburn), and scaling (small, hard, dry areas of the skin) accompanied by general symptoms. A flare-up can be serious and requires immediate medical care. Little is known about this rare disease so far, and current treatment options for controlling GPP flare-ups are limited.

Please read the following information carefully. It contains important information to help you decide whether to participate in this research trial. The trial staff will have a detailed interview with you to inform you about the trial and the possible benefits and risks of your participation. Ask questions about anything that is not clear at any time. You may take home an unsigned copy of this information to think about and discuss with your family, friends or family doctor before you make your decision to participate or not.

After reading and discussing the information, you should know:

- Why this research trial is being done;
- What will happen during the trial;
- Any possible benefits to you;
- The possible risks to you;
- Other options you could choose instead of being in this trial;

- How your personal information / health information will be protected during the trial and after the trial is over, and which data privacy rights you have;
- How your data and your biological samples will be collected, stored, processed, transferred and used
- Whether being in this trial could involve any cost to you; and
- What to do if you have problems or questions about this trial.

This document also includes:

- Appendix A: Visit Schedule
- Appendix B: Description of Trial Procedures and Risks
- Appendix C: Known Side Effects (Adverse Events) of the Investigational Drug(s)
- Appendix D: *move* Confidentiality / Privacy and Data Sharing *section to an Appendix if allowed by local authorities / local legal*

Your participation in this trial is voluntary. If you join this trial, you can still stop at any time. You have the right not to sign this consent form. If you do not sign, you cannot take part in this research trial. If you decide to participate, you will be asked to sign and date at the end of this form.

Your signature confirms that you agree and accept to take part in this trial and to the handling of your data as described in this form.
It is important that your personal doctor is aware that you are in a research trial because you may be taking a treatment that could affect your health. With your permission, we will notify him/her that you are taking part in this trial.

PURPOSE OF THE TRIAL

The purpose of this trial is to:

- Compare the safety, effectiveness and side effects of a single intravenous (IV) dose of the investigational drug being studied, BI 655130, with an inactive substance (placebo), in subjects with GPP, who are having a moderate to severe flare-up (GPP symptoms). A placebo is a substance that looks like the investigational drug but contains no active drug.
- Test how the investigational drug is used by the body and how fast or slow it moves through or out of the body.
- Measure the immune response of the investigational drug (when the body detects and defends itself against substances that appear unknown and harmful).
- See how genes (coded instructions for making each cell in your body) may explain and predict the response to the investigational drug.

The investigational drug, BI 655130, works by stopping the effect of a protein called IL-36 receptor involved in the development of GPP. BI 655130 is the first compound of this new class of drugs.

The investigational drug has not been approved as a treatment for any disease by <insert authority> and, thus, its use in this research trial is considered experimental.

We estimate that approximately <enter number of subjects assigned to your OPU> people will participate in this trial in <insert country of OPU> and approximately 51 subjects worldwide.

In this clinical trial, competitive enrolment will be used. This means that when a target number of patients (approximately 51) have entered the trial, all further enrolments will be closed. It is possible that you could be in the screening phase when the target number of patients is reached. If that happens, you may not be able to receive the treatment, even if you meet all the other requirements for entering the clinical trial and receiving the treatment.

THIS TRIAL HAS BEEN APPROVED BY <insert applicable local authorities, if required, otherwise this statement can be deleted>.

DESCRIPTION OF THE TRIAL

This trial compares the effects of the active investigational drug, BI 655130 (spesolimab), with an inactive substance (placebo) in subjects with GPP, who are having a moderate to severe flare-up.

You will be assigned by random choice to receive either the investigational drug, BI 655130, or the placebo at Visit 2 (Day 1) as follows:

- *Group 1 will receive, a single dose of BI 655130, 900 mg, by IV infusion*
- *Group 2 will receive a single dose of placebo, by IV infusion*

This process is called randomization. You will have about 66% chance of being placed in Group 1 and a 33% chance of being placed in Group 2.

The Visit 2 dose of the trial medication (investigational drug or placebo) will be double-blinded. No one (including you and the trial team) will know who is receiving the investigational drug or the placebo. This way the results of the trial will not be favored one way or another. If it becomes necessary for your care, your trial doctor will be able to find out whether you took the placebo or the investigational drug.

TRIAL PROCEDURES

Time to be spent in the trial

The time you will spend in this trial will depend on the time window between the first trial centre visit (when you agree to participate and give your informed consent) and when you have a GPP flare-up and return for the second trial centre visit. This time period can last several days, weeks or even months and cannot be predicted.

Once you have a GPP flare-up and complete Visit 2, your participation will last up to about 28 weeks (about 7 months) and require about 12 to 14 additional visits to the trial centre.

You may be asked to come to the trial centre for additional unscheduled visits. Refer to the Unscheduled Visits section below for more information.

Each trial centre visit may take between 1/2 hour and 4 hours to complete the procedures as described in Appendix A.

If applicable, please consult with your local Legal representative to clarify whether it is acceptable to have the trial tests and procedures listed in an appendix:

In Appendix A of this document you will find a detailed overview and schedule of all the visits which lists the trial tests and procedures planned at each visit. The trial doctor or the trial staff will go through this Appendix with you.

In Appendix B of this document you will find a more detailed description of the different trial tests and procedures including related risks. The trial doctor or the trial staff will go through this Appendix with you.

At trial visits, the trial doctor or trial staff will ask you about how you feel, what medications you have taken and what other health care you have received since the last trial visit.

Before the clinical research starts (screening - Visit 1)

Before any study procedures are done, you will be asked to read and sign this Information and Consent form.

The first trial visit will be a screening visit. The screening visit will include the following procedures:

- You will be asked about your medical history including history of GPP, demographics (gender, ethnicity and race), and your smoking history
- A physical exam including vital signs and your temperature will be taken
- Blood and urine tests, including a blood test for infectious disease testing
- A pregnancy blood test if you are a female able to have a child
- An electrocardiogram (ECG)
- Photographs of skin lesions (areas of your skin affected by GPP)
- You will be asked about how you feel and what medications you are taking
- The trial doctor will obtain information from your personal doctor (if different from the trial doctor) about the mutation (changes to the structure of a gene) of a certain gene (IL-36RN). If this information is not available, you will still be able to participate in this trial

The results of the tests and/or questions at the screening visit will help the trial team decide whether you can continue in this trial. If these tests show that you are eligible to participate in the trial, you will be able to continue in this trial. If you do not meet the eligibility criteria, you will not be able to continue. You should not go to another trial centre to be screened again.

If you are not having a moderate to severe GPP flare-up at the screening visit, you can still take part in this trial and then return to continue your participation when a flare-up occurs. At that time, you will be asked to confirm that you still agree to participate in this trial. If the flare-up occurs after 6 months of signing this consent form, you will be asked to sign another consent form for this trial and repeat your first visit.

INVESTIGATIONAL DRUG VISIT (VISIT 2)

You may be asked to stop taking certain medications before receiving the trial medication. The trial doctor will further discuss this with you.

If you are eligible to participate in this trial and you are having a GPP flare-up at Visit 1, Visit 1 and Visit 2 can be done on the same day.

You will receive the trial medication, BI 655130 or placebo, at Visit 2 (Day 1) by IV infusion. An IV infusion is a slow injection of the trial medication directly into your vein. It will take between 1-1/2 to 3 hours to give you the trial medication.

Your first dose of trial medication will be given to you either at the trial centre or at the hospital. The trial doctor will discuss this with you further.

FOLLOW-UP PERIOD

After receiving the trial medication at Visit 2, you will be followed-up for about 12 to 28 weeks, which includes the End of Study (EOS) Visit (see the EOS section below). The length of the follow-up period will depend on how well you respond to the trial medication.

After you receive your first dose of trial medication, you will return to the trial centre every day during the first week (Day 2 to Day 8). Depending on your response to the trial medication, the trial doctor will let you know if you need to return to the trial centre for visit Days 4 through 7 during the first week.

If your GPP worsens within the first week of receiving the trial medication, the trial doctor will treat you with Standard of Care (SoC) medication(s), which are medications usually given for treating GPP. The trial doctor will tell you the SoC medication(s) you will receive.

At Day 8 (Visit 9), if your GPP did not get better after receiving the initial dose of trial medication, and you did not receive a SoC medication(s) within the first week of receiving the initial dose of trial medication, you may receive a 900 mg dose of BI 655130 by IV infusion. The trial doctor will tell you if you are eligible to receive BI 655130 at this visit.

After Day 8 (Visit 9) and through Week 12 (Visit 14), if you have a second GPP flare-up after achieving a response to one of the following:

- the initial trial medication dose on Day 1 **OR**
- a dose of BI 655130 on Day 8 (if received) **OR**

- the SoC medication(s),

you will be able to receive a 900 mg dose of BI 655130 by IV infusion. This dose is called a rescue treatment.

If you have more than one flare-up after Visit 9, the trial doctor will treat additional flare-ups with SoC medication(s).

If you decide to stop taking the trial medication early, you will be asked to continue with all of your remaining scheduled trial visits as originally planned. If you are not willing to continue with all your remaining scheduled trial visits, you will be asked to return to the trial centre for Visits 9 and 12 (if not already completed), and the End of Study Visit. If you cannot return to the trial centre, the trial staff will contact you when your scheduled visits would have occurred to ask you how you are.

UNSCHEDULED VISITS

During the Follow-up Period you may be asked to come to the trial centre for additional unscheduled visits if you have a GPP flare-up and require a rescue dose of BI 655130 or SoC medication(s), or if the trial doctor thinks the visit(s) are necessary for your safety, or if procedures were missed from a previous visit or need to be repeated.

If you receive BI 655130 at either a scheduled or unscheduled visit after Day 8 (Visit 9), you will complete the Visit 9 procedures (except for certain blood tests) as listed in Appendix A.

END OF STUDY (EOS) VISIT

You will have an "EOS" visit (Visit 14 or 15 or 16) after completing the trial or if you stop the trial early.

Your EOS visit will depend on how you respond to the trial medication and when you have your last dose of trial medication or dose of BI 655130. The trial doctor or trial staff will let you know when your EOS visit will occur.

If you complete all of your scheduled visits and have your EOS visit at either Visit 14 or Visit 15, you may be given the option to participate in an extension of this research trial using the same investigational drug, BI 655130, without the use of a placebo. If you decide to participate in the extension research trial, you will sign another Information and Consent Form.

If you do not join the extension research trial or if you decide to stop the trial early, your EOS visit will be about 16 weeks after you stop the trial medication or dose of BI 655130.

Your trial doctor will discuss your future care, any medications you require, and you will be offered standard medical care.

After your EOS Visit you will have completed this trial.

For your safety, any side effect(s) that continue after your last trial visit will be followed by the trial doctor until the side effect(s) resolve or are stable.

YOUR RESPONSIBILITIES

- You must tell your trial doctor if you previously have participated in this trial, have been in another research trial in the past 30 days or are currently in another research trial. While participating in this trial, you should not take part in another research trial, or in this trial at another site. This is to protect you from possible injury arising from such things as extra drawing of blood samples, potential medication interactions, or other hazards.
- You will receive a Trial Identification Card. It is important that you carry this card with you at all times. If you are treated by another doctor (for example, in an emergency), it is important that you tell them of your participation in this trial by showing this card.
- If you are treated by another doctor, it is important that you tell the trial staff about your treatment and what happened.
- You must follow the trial instructions provided by the trial staff, come to all scheduled trial visits, and be reasonably available for any scheduled telephone visits.
- You must call/tell the trial doctor if you experience any side effects or if you feel unwell, even if you do not know if it has anything to do with this trial.
- You must tell the trial doctor about all prescription and non-prescription drugs, herbal preparations that you are taking or planning to take.
- You will be asked to complete questionnaires (refer to Appendix A). Please complete each of them by yourself, without the help of someone else.

POTENTIAL BENEFITS

You may not personally benefit from participating in this trial, but you may contribute new information that may benefit other patients and provide the medical and scientific community with information about treatment for GPP.

However, receiving BI 655130 may help to reduce GPP symptoms and how long a GPP flare-up lasts. Therefore, you may benefit as a result of your participation in this trial. There is, however, no guarantee for that.

RISKS AND/OR DISCOMFORTS

This section is provided by the TMM for the trial drug. Any changes must be approved by the author of this section.

There are risks to taking part in any research trial. If you receive a placebo, you will not receive an active treatment for your condition. Your condition might not improve or it could get worse during the course of this trial.

If you receive active trial medication, then side effects may occur. Some of those side effects can be treated. Some side effects may go away when you stop taking the trial medication. Some side

effects can be mild, but others may continue longer or become permanent. Some may be life-threatening or fatal.

As with any drug, an allergic reaction can occur. Allergic reactions can be mild or more serious, and can even result in death. Common symptoms of an allergic reaction are rash, itching, skin problems, swelling of the face and throat, or breathing difficulties. If you think you are having an allergic reaction, call the trial doctor right away. If you are having trouble breathing, call <insert regional emergency telephone number>.

Taking BI 655130 may cause you to have one or more of the side effects (or adverse events) listed below: <List all known adverse events of each drug/product here or by using Appendix C>

If applicable, please consult with your local Legal representative to clarify whether it is acceptable to have the side effects listed in an appendix.

If using Appendix C, use the following wording:
In Appendix C of this document you will find a more detailed description of the adverse events of the trial medication including related risks. The trial doctor or the trial staff will go through this Appendix with you.

The trial doctor or the trial staff will go through the description of the known side effects with you. They are willing to discuss any questions you might have about the severity and frequency of risks and other potential discomforts. In addition to the side effects listed, there is always the risk of developing side effects which are not known at this time.

You will be monitored carefully to check for these risks. Your trial participation may be stopped if any signs of drug toxicity or other damage occurs.

You need to tell your trial doctor or a member of the trial team immediately if you experience any side effects.

The trial doctor will discuss with you the risks and benefits of the Standard of Care medication(s) which you may take during your participation in this trial.

ALTERNATIVE TREATMENTS

Instead of participating in this trial, you have other options which may include the following:

- Receive recommended treatment including <specify the standard treatment per your country/OPU>.
- Take part in another research trial.
- Receive no therapy specific to your GPP.
- Receive comfort care, also called palliative care. This type of care may help to reduce pain, tiredness, appetite problems, fever, headache, and other problems caused by your GPP. It does not treat the GPP directly, but instead tries to treat the symptoms.

Your trial doctor will discuss these options and the important potential risks and benefits with you before you decide whether you will take part in this trial.

NEW INFORMATION ABOUT THE TRIAL

During the trial, you will be notified of changes to trial procedures, newly discovered side effects or significant findings which may affect your health or willingness to participate. You may be asked to sign a new consent form that shows that you have been informed of new information relating to this trial.

INFORMATION ON BIRTH CONTROL

Based on the information provided in the Investigator's Brochure (IB) and the Clinical Trial Protocol (CTP), this section must describe the potential risks for a fetus or embryo in case pregnancy occurs during trial participation. For further guidance please refer to Contraception Guideline). This document includes a list of acceptable contraception methods meeting the requirements outlined in ICH M3 (R2).

For Female Trial Subjects

As with any investigational drug, the effect of BI 655130 on the unborn child is unknown. If you decide to take part in this trial and you are able to become pregnant, you must be willing to have a pregnancy test done at the Screening Visit, and regularly at trial visits and at the end of the trial. Further, you must avoid becoming pregnant while you take part in this trial. You cannot participate in this trial if you are pregnant, breastfeeding or plan to become pregnant during your trial participation. You must use a highly effective method of birth control and you should not breastfeed throughout this trial and for up to 16 weeks after receiving the last dose of BI 655130.

Your trial doctor will talk to you about the best method of birth control for you.

Acceptable methods of birth control for this trial are:

- Combined (estrogen and progestogen containing) hormonal birth control associated with inhibition of ovulation
- Progestogen-only hormonal birth control associated with inhibition of ovulation
- Intrauterine device (IUD) and intrauterine hormone-releasing system (IUS)
- Bilateral tubal occlusion (blocking of the fallopian tubes)
- Vasectomy of sexual partner (proven effective by absence of sperm on the ejaculation).
- Complete sexual abstinence (not to have male-female vaginal sex)

If you are pregnant or think you could be pregnant, it is important for you to tell the trial doctor or trial staff immediately. If you become pregnant during the trial, you will discontinue trial medication and be asked to continue to participate in trial visits. Your health and your baby's health will be monitored throughout your pregnancy. Even if you are no longer in the trial, your trial doctor will contact you after your baby is born to find out about the baby's health.

WITHDRAWAL FROM TRIAL PARTICIPATION

You may choose not to take trial medication or to leave this trial completely at any time. Your decision will not result in any penalty or loss of benefits to which you are otherwise entitled. Leaving the trial will not affect your future medical care.

It is important that you tell the trial doctor if you are thinking about stopping or have decided to stop so your trial doctor can evaluate the risks of stopping.

Depending on the protocol, the following section may be adapted. Please ensure the trial site understands that the discussion with the subject and the outcome regarding follow up, vital status collection, discontinuation of trial medication, and withdrawal of consent is documented in the subject's medical records.

Listed below are three possible scenarios that could stop your trial participation. Your study doctor will discuss these scenarios with you.

- **You may stop trial medication, but agree to continue participation and/or continue to be contacted**

If you decide to stop taking the trial medication, you may still continue to participate in trial visits. It is recommended that you come in to the trial centre for all of the remaining trial visits, however if you are unable to come to the trial centre, you will be asked by the trial staff if they can contact you by phone/email/mail or someone you choose (such as your family doctor, a friend, or relative), to ask about your overall health status. This will happen when your scheduled visits would have occurred up to the End of Study Visit. Alternatively, you will be asked for your permission to collect this information from your medical records <or any public records or patient search organisation – if allowed by local regulations> until the end of the trial. This information is important for the scientific value of the trial to interpret the trial results correctly. You are free to refuse this regular contact. Your decision will not affect your future medical care.

- **You may stop trial medication and participation completely and withdraw your consent**

You have the right to withdraw your consent at any time. If you decide to stop trial medication and participation, then the final assessments such as a physical examination, vital signs, laboratory tests, ECG, and questionnaires should be completed as soon as possible. This is important for your safety and well-being. After the final assessments, no further information about you will be entered into the trial database.

All data that had already been collected up to the time of withdrawal of your consent, including data gathered at any of your final assessments, will still be used to ensure the correct completion and documentation of the trial and comply with applicable law.

- **Your trial doctor may decide that you must stop**

Your trial doctor might decide to stop your trial medication or trial participation early without your consent when, in the trial doctor's judgment, it is in your best health interest to do so. Some of the reasons why this might happen are listed below:

- Your condition worsens or does not improve and an alternative treatment is medically indicated.
- The trial treatment or procedures are found to be unsafe or ineffective.
- Your inability to take the medication / participate as instructed.
- Cancellation by the sponsor or regulatory authority.
- Or for other unforeseen reasons that make it necessary to stop your participation in the trial.

If you are removed from the trial, the trial doctor will explain to you why you were removed.

CONFIDENTIALITY / PRIVACY AND DATA SHARING

The wording in this section must preferably be reproduced word-by-word in the trial specific subject information. If any changes to that wording, which would limit our ability to publish or share results and data, are mandated by an Ethics Committee or IRB or are necessary otherwise, then the responsible function (CT Leader or CT Manager) must consult local line management, local legal and/or local data protection/privacy contact. If applicable, please consult with your local legal representative to clarify whether it is acceptable to have the confidentiality, privacy, and data sharing section listed in an appendix, e.g. Appendix D.

Use of Your Personally Identifiable Information

The part of your personal information that directly identifies you, such as your name and address, will remain at the trial site and can be accessed by the trial doctor and other people at the site who are assisting with the trial or your care. This information may also be checked at the trial site by the

- sponsor, or the sponsor's representatives (including monitors hired by the sponsor through a service provider),
- ethics review board/committee that reviewed the ethical aspects of this trial, and/or
- domestic or foreign regulatory agencies such as <insert applicable regulatory bodies here, e.g. the U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA)> that approve medicines.

These persons check that the trial is carried out correctly at the trial site. They are bound by a duty of confidentiality.

Coding of Your Data

Your personally identifiable information and health information collected in this trial will be labelled with a unique code number. Coded data may also include data/information such as images (e.g. x-rays) or EEG (electroencephalograms). The code number will be used in place of your name and other information that directly and easily identifies you. Only the trial site will

have the link between your personal information and the coded data. This link will not be provided to the sponsor; only your coded data will be sent to the sponsor. The sponsor will take measures to protect the confidentiality and security of your coded data and your privacy in accordance with current law.

Use of Your Coded Data

The sponsor, its research partners and service providers (like clinical research organizations or laboratories) including companies belonging to sponsor's group, and regulatory authorities such as drug regulators, reimbursement agencies and ethics review boards may use your coded data for the following purposes:

- Analyse it to understand the trial, the trial results and the drug(s) (including side effects and efficacy) or the disease(s) studied, obtain approvals for drug(s) and reimbursements for the drug(s) in countries worldwide.
- Share it with domestic or foreign regulatory, reimbursement or other professional health care agencies worldwide such as <insert applicable regulatory bodies here, e.g. the U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA)>, that regulate medicines to fulfil reporting obligations during the trial.
- Analyse it to improve the quality of this trial and other clinical trials.

To support the review of your data, your trial doctor may code and data/information from your medical records. This will be limited to specific information relating to this trial.
The coded data may be transferred within your country or to other countries for analysis. Where the data protection rules in other countries are not as strict as the rules in your country, the sponsor will adopt appropriate measures to provide an adequate level of protection according to EU law.

Additional Use of Your Coded Data

Your coded data from this clinical trial can be combined with data from other trials. The purpose is to learn more about your disease and other diseases, different responses to treatments and new treatment options to improve quality and efficiency in the drug development process. The additional use of your coded data will not be part of another Clinical Trial.

Incidental Findings

The sponsor will only search for results that are directly related to the actual clinical trial question. To do so researchers will obtain results by combining your data with data from a large number of other individuals. Nevertheless, other results which may be of medical importance for you and your family can occur incidentally for all testing techniques applied (so-called incidental findings).
In case of incidental findings that are considered medically actionable because they have clear and immediate medical significance to your health, the Sponsor will take all justifiable efforts to inform your study doctor. Your study doctor may then discuss the impact of these incidental findings with

you.
If you are not interested in receiving this information, please let your trial doctor know.

Sharing of your anonymized data

The sponsor is convinced that access to trial data advances clinical science and medical knowledge and is in the best interest of patients and public health, provided that patient privacy is protected. Therefore, the sponsor may share with credible researchers an anonymized set of your trial data, but only for specified and approved scientific research. Anonymization means that the sponsor will delete or modify any trial data that could identify you.

Storage of your coded data

All coded data, including yours, will be kept by the sponsor. Only your trial doctor will be able to link your unique code number to you.

This link will remain at the trial site for a maximum of 30 years and will then be destroyed by the trial doctor. After that it is not possible to link your unique code number directly back to you.

Rights under data protection laws

You have the right to review which personal data the trial site and sponsor store about you. You can also request that incorrect personal data is corrected or that processing is restricted.

In order to exercise your rights please contact the trial site [if applicable: and its data protection officer (ADD EMAIL)] who will align with the sponsor. You can also ask to receive the personal information you have provided for the trial in a standardized electronic format or to have them transmitted to another person of your choice. You can also contact your local data protection authority in case of questions or concerns about the handling of your personal data. In some cases, your rights can be limited under applicable laws, especially where they conflict with the conduct of the trial and mandatory archiving requirements. In this case you will be informed accordingly.

Clinical Trial Websites and Publication
The following statement must be included and must not be modified. Additional explanations and/or websites may be added.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

The following statement must be included in European studies and is optional for other countries: A description of this trial including a summary of the trial results will also be available on the European Union web-page www.clinicaltrialsregister.eu.

The results of the trial will be published on Boehringer Ingelheim's Trial Web site (http://trials.boehringer-ingelheim.com). The website may also include a summary understandable to a layperson. The results may also appear in other clinical trial/study registries in countries in which the trial is conducted. The results will not include information that can identify you.

The results of the study may also be published in a professional journal or presented at scientific meetings. Your identity will not be disclosed in those presentations.

USE OF SAMPLES FOR THIS TRIAL

The biological samples collected from you during the trial as described under the section "Trial Procedures" and Appendix A and B will be stored, processed, and used under your code number for the purposes of this trial for analyses as follows:

Routine Safety Samples
Blood and urine will be collected for routine safety and blood for pregnancy tests (for women of child bearing potential) and will be sent to a central laboratory for analysis. Leftover samples will be destroyed once the tests are completed. The urine pregnancy testing will be done at the trial centre. The sample will be destroyed at the trial centre once the results are known.

Pharmacokinetic (PK) and Anti-Drug Antibodies/Neutralizing Antibody (ADA/Nab) Samples
Blood will be taken for PK testing to see how your body uses the investigational drug and how fast or slow it moves through or out of your body, and for ADA/Nab testing to measure your immune response to the investigational drug (when the body detects and defends itself against substances that appear unknown and harmful).

After completion of the clinical trial, the samples for PK and ADA/Nab may be used for additional testing to see how the investigational drug reacts over time. These samples will be discarded after the testing is completed but not later than 5 years after the trial is over and the sponsor completes a report that contains the trial results.

Biomarker Samples (in blood)
Blood will be taken for biomarker testing as indicated below. Biomarkers are biological molecules found in blood, other body fluids, or on cells and tissues and are a sign of a normal or abnormal process, or of a condition or disease. Biomarker testing measures how the human body is functioning.

In this study, protein biomarkers will be measured in the blood that could possibly be associated with GPP, to see changes of these biomarkers before and after receiving the trial medication. Biomarkers could be proteins or ribonucleic acid (RNA) sequences (the order of each RNA molecule). Proteins play specific roles for various body functions.

In this study, biomarker testing will be done to:

- See if the biomarkers show how the investigational drug works in your body and how

your body responds to the drug.
- Look at the changes in protein or RNA levels of certain biomarkers to see how severe the disease may be.
- Genetic testing of DNA (deoxyribonucleic acid) will be done to assess certain genes known to have mutations (changes to the structure of a gene) that cause GPP. Genes are a part of your DNA which control things like the colour of your hair or eyes. Your genes affect how you respond to drugs.

Other non-genetic biomarker testing may be done. At this time, it is not known what testing will be done.

Biomarker samples will be stored at the sponsor facilities or by an external vendor (the company hired to store the samples) for backup and will be destroyed after this trial is over and the sponsor completes a report that contains the biomarker and/or the trial results, whichever comes later.

Infectious Disease Testing
Blood will be taken to see if you have infectious diseases, such as hepatitis B or hepatitis C (a disease that affects the liver) or HIV (a blood virus that may lead to AIDS) or tuberculosis (a disease that mainly affects the lungs).

Infectious disease samples will be destroyed once the tests are completed.

For Asian/Pacific region:
Infectious disease samples will be destroyed once the tests are completed with the exception of the HIV confirmation sample (if analysed i.e. in case HIV screen test result is positive). The sample will be stored at least 7 years and then be automatically destroyed.

The samples or parts of them may be transferred to the sponsor, its research partners and service providers (like clinical research organizations or laboratories) including companies belonging to the Boehringer Ingelheim Group of Companies.

SAMPLES FOR OPTIONAL RESEARCH

As an optional part of this trial, you are being asked to allow the collection and storage of blood samples for potential future scientific research.

As another optional part of this trial, you will be asked to have skin biopsies taken at selected trial visits.

You will be provided with separate consent forms with information so that you can decide whether or not you want to participate in these optional parts.

COMPENSATION / COSTS

Sample text provided below. Amend in accordance with local legal requirements or insurance.

This trial is funded by the sponsor. The sponsor will pay the trial doctor and/or institution for his/her expenses, time, and effort to conduct this trial. The trial doctor and the institution/Hospital have no other financial ties to Boehringer Ingelheim.

Sample text if using a CRO; amend as needed.
The sponsor has signed a contract with <insert applicable CRO> to conduct this trial. The sponsor will, on behalf of <CRO> pay the trial doctor and/or institution for his/her expenses, time, and effort to conduct this trial. The trial doctor and the institution/Hospital have no other financial ties to Boehringer Ingelheim.

There will be no additional costs to you for your participation in this trial. All trial procedures including lab work, tests, doctor visits, <include if applicable per your OPU budget: hospital stays to receive the trial medication,> and trial medication are provided to you free of charge by the sponsor, Boehringer Ingelheim, and will not be billed to you or your insurance carrier as long as you are participating in the trial. You will receive <enter amount and/or a description of a payment schedule> to cover out-of-pocket expenses such as meals and parking for visits that are required as part of the trial.

The sponsor will be the owner of the trial results. If commercial products or other valuable discoveries result from research using your samples and/or data, these products and discoveries may be owned, patented, licensed, or otherwise developed for commercial sale by the sponsor, other researchers, or companies. If this should occur, you will not receive any financial benefits or compensation or other proprietary interest from any commercial products or discoveries that may result from such research.

INJURY / INSURANCE

Please work with local legal to ensure that the below follows local regulations.
You will receive necessary medical treatment in the event that an injury or illness results because of your participation in this trial. If your insurance or other third-party coverage does not cover the cost of the necessary medical treatment or care, the sponsor will cover the cost if the injury or illness is due to the trial medication or procedures, and you have followed the trial doctor's instructions. Financial compensation for lost wages, disability or discomfort due to an injury is not generally available. You do not give up any legal rights by signing this form. You do not release the sponsor, institution, trial doctor or their agents from any liability for negligence by signing this form.

EMERGENCY CONTACT / ETHICS CONTACT

Suggested sample text provided below. You can adapt this section and add in any local regulations as needed.
If you have questions concerning side effects, the conduct of the trial, or for any other reason you may contact <*leave the following text intact for each site to customize in their site-specific ICF*> Dr. _____at _____ or the Trial Coordinator, _____, at _____ at ANY TIME. You have the right at any time, upon request, to be informed by the above trial doctor of your condition and the effects of the investigational drug on you.

In case of an emergency, please contact <*leave the following text intact for each site to customize in their site-specific IC*> Dr. _____ at tel. _____ OR go to the nearest hospital emergency department.

If you have any questions about your rights as a trial subject, please contact your family doctor, lawyer, or write to the committee that reviewed the ethical aspects of this trial at: <insert ethics committee name and contact here>

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Information and Consent Form for Trial Subjects (template)

APPENDIX A: VISIT SCHEDULE

Boxes marked with an X show what will happen at each visit. Descriptions of these procedures are listed in Appendix B.

Trial Procedures	**Screening**	**Treatment Visit**	**Follow-up Period**													
Visit Number	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14 or EOS[1]**	**15 or EOS[2]**	**16 EOS[3]**
Visit Week		**1**							**2**		**3**	**4**	**8**	**12**	**13-18**	**16-28**
Visit Day	-1	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**15**	**22**	**29**	**57**	**85**	**92-127**	**113-197**
Discuss this trial, demographics and medical history, including gene mutation	X															
Physical exam, vital signs, and temperature	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
ECG	X	X							X	X	X	X	X	X	X	X
Blood and urine tests for safety,	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Blood or urine for pregnancy testing for women of child bearing potential	X	X							X	X	X	X	X	X	X	X
Blood for infectious disease testing	X													X	X	X
Blood tests for PK and ADA/Nab		X			X				X	X	X	X	X	X	X	X
Blood tests for: genetic biomarker testing (DNA[4]); RNA and protein biomarkers		X	X	X					X	X		X		X	X	X
Blood tests for biomarker testing		X							X			X				
Receive trial medication (BI 655130 or placebo)		X														
Receive BI 655130 (if needed and if eligible)									X	X						
Photographs of skin lesions	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Complete questionnaires		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

[1] Visit 14 will be done as your EOS visit only if you did not require a rescue dose with BI 655130 or if you required a rescue dose with BI 655130 before Week 7 and you are eligible to participate in the extension research trial.

[2] Visit 15 will be done as your EOS visit only if you required a rescue dose with BI 655130 after Week 7 and you are eligible to participate in the extension research trial.

[3] Visit 16 EOS will be done 16 weeks after your last dose of trial medication or BI 655130 if you are not eligible to participate in the extension research trial.

[4] DNA testing will only be done at Visit 2.

APPENDIX B: DESCRIPTION OF TRIAL PROCEDURES AND RISKS
<CUSTOMISE THIS LIST AS NEEDED>

Ensure the flowchart in the protocol matches the procedures as described in the CTP text and that all research related procedures are included in the Appendix. The definitions below are suggested descriptions and risks and can be edited as needed. Additional procedural and associated risk definitions may need to be added. It may not be feasible to describe every possible risk; however, subjects must be informed of all risks to consider which may influence their decision to participate.

The trial doctor or the trial staff will go through the description of the trial procedures and related risks with you. Please ask any questions you might have. In addition to the risks listed, there is always the chance of developing risks which are not known at this time.

Procedure	Description	Risks
Blood Tests and Blood Drawing	Approximately 600 mLs (40 tablespoons) of blood samples for the whole trial will be drawn to test your blood for: • Safety and pregnancy • Infectious diseases • PK and ADA/Nab • Biomarkers • Genetic biomarkers At each visit approximately 15-75 mLs (1-5 tablespoons) of your blood will be taken from a vein in your arm. If at any time during this trial your blood tests show there may be a problem with your liver, you will be asked to return for additional tests to see why. Additional blood tests to check your liver function and hepatitis will be done.	As with all blood sampling, there is a risk of mild pain, local irritation, bleeding or bruising (a black and blue mark) at the puncture site. Furthermore, there is a small risk of light-headedness and/or fainting. In rare cases, the puncture site can also become infected or nerves may be damaged, inducing long-lasting abnormal sensations (paresthesia), impaired sensation of touch and persistent pain. Frequent blood collection may cause anemia (low red blood cell count), which may create a need for blood transfusions.
Blood pressure test	A blood pressure test measures the pressure in your arteries as your heart pumps.	The squeezing of an inflated blood pressure cuff on your arm may be uncomfortable. It usually takes only a few seconds.
ECG (electrocardiogram)	A painless test which measures the electrical activity of your heart.	There may be some skin irritation from the ECG electrode pads or pain when removing these pads from your chest.

Procedure	Description	Risks
Intravenous (IV) Infusion	The investigational drug, BI 655130, or placebo will be given to you by an IV infusion, which is a slow injection of the trial medication directly into your vein using an IV catheter. It will take between 1-1/2 to 3 hours to receive the IV infusion. You will be monitored during the IV infusion and for about 2 hours after receiving BI 655130 or placebo. If you have a reaction to the IV infusion, you may be given medications to help reduce a reaction before you receive another IV infusion.	You may feel mild pain, local irritation, bleeding or bruising (a black and blue mark) at the puncture site (where the needle is inserted). There is also a small risk of light-headedness and/or fainting. In rare cases, the site where the needle is inserted can become infected or nerves may be damaged, and cause long-lasting abnormal sensations, damaged sensation of touch and lasting pain. During an IV infusion, tissue damage can occur if the infusion is not given directly into the vein. Your skin near the vein could become warm, swell, hurt, or get red. A blood clot or an air bubble could form, which could block a blood vessel in another part of your body. There could be an increase or decrease in electrolyte levels (the amount of certain salts and other chemicals in your blood), causing health problems. Some of these side effects could be very serious. Over time, getting a lot of injections or infusions can cause a vein to become hard or scar, which can make it difficult to put a needle into the vein to give you a shot or to take blood.
Photographs	Photographs will be taken of the affected areas of your skin (such as, the front and back trunk, legs and arms). You will not be personally recognized in the photos taken.	Please refer to the "Confidentiality" section of this consent form for information on how your personal information is managed.

Procedure	Description	Risks
	Photographs may be used in a presentation or publication about this trial. The use of the photograph may include news releases, professional conferences, websites and exhibits related to this research trial.	
Physical examination	A routine manual examination your trial doctor performs to check your overall health. The trial doctor will assess your symptoms of GPP.	This examination generally produces little pain or discomfort.
Pregnancy test	A pregnancy test measures a hormone in the body called human chorionic gonadotropin (HCG). This hormone is present in your body when you are pregnant. A pregnancy test is done using your blood and/or your urine. You cannot participate in a clinical trial if you are pregnant or planning to become pregnant.	**Pregnancy tests using blood:** As with all blood sampling, there is a risk of mild pain, local irritation, bleeding or bruising (a black and blue mark) at the puncture site. Furthermore, there is a small risk of light-headedness and/or fainting. In rare cases, the puncture site can also become infected or nerves may be damaged, inducing long-lasting abnormal sensations (paresthesia), impaired sensation of touch and persistent pain. **Pregnancy tests using urine**: Because this procedure involves normal urination, there should not be any discomfort and no known risks.

Procedure	Description	Risks
Questionnaires	You will complete the following questionnaires to assess your GPP symptoms: **FACIT-fatigue (Functional Assessment of Chronic Illness Therapy - Fatigue scale):** to see how tired you are. **PSS (Psoriasis Symptom Scale):** to see how bad your GPP symptoms have been. **Pain VAS (Visual Analog Scale):** a measure of how much pain you have. **DLQI (Dermatology Life Quality Index):** to see how your skin problem has affected your life. DLQI will not be completed on Days 2-7. **EQ-5D-5L (EuroQol-5 Dimensions-5 Levels):** a measure of your current health status. It will take about 30 minutes to complete all of the questionnaires. It is important that you complete the questionnaires yourself and not ask others to do it for you. If needed, the trial staff can read the instructions, questions, and response options to you. You can then tell the trial staff member your answer.	You might find the questionnaires are long, or upsetting, or tiring. You might not like some of the questions or feel uncomfortable answering them. You do not have to answer any questions that make your feel uncomfortable.

Procedure	Description	Risks
Urine test (urinalysis)	Urine tests are used to look for the presence of red blood cells (high levels of protein) which may indicate a kidney problem and excreted minerals that can cause kidney stones. A sample of your urine is also likely to be checked for bacteria that cause infection.	Because this procedure involves normal urination, there should not be any discomfort and no known risks.
Vital signs: Temperature, heart rate, breathing rate, and blood pressure	The act of taking vital signs is the recording of body temperature, pulse rate (or heart rate), blood pressure, and respiratory rate, but may also include other measurements. Before receiving the trial medication your temperature will be taken. If you have a fever, the trial doctor may decide to give you medication to treat the fever.	These are routine procedures with little risk. Please also see definition for "blood pressure test" above.

APPENDIX C: KNOWN SIDE EFFECTS (ADVERSE EVENTS) OF THE INVESTIGATIONAL DRUG(S)

Taking BI 655130 may cause you to have one or more of the side effects (or adverse events) listed in the table below. The trial doctor or the trial staff will go through the description of the side effects with you. Please ask any questions you might have. In addition to the side effects listed, there is always the risk of developing side effects which are not known at this time.

As of September 2018, BI 655130 has been given to 212 subjects in ongoing and clinically completed trials. BI 655130 was well tolerated. Most reported adverse events were of mild or moderate intensity, but there have also been a small number of patients experiencing severe or serious adverse events in clinical trials. It is unknown whether these adverse events were caused by BI 655130. Overall adverse events observed in subjects who received BI 655130 were comparable to adverse events observed in those who received placebo and no dose-limiting adverse effects were observed.

If you receive the investigational drug, then adverse events may occur which may or may not be caused by BI 655130. Some of those adverse events can be treated. Some side effects may go away when you stop taking the trial medication. Some adverse events can be mild; but others may by more severe, continue for longer or become permanent. Some may be life-threatening or fatal.

All drugs can potentially cause an allergic reaction. Allergic reactions may vary from mild (rash, hives, itching) to severe (which may include difficulty breathing, swelling of the face or throat, low blood pressure, or passing out). A severe allergic reaction requires immediate medical treatment and could result in permanent disability or death. It is important to tell your trial doctor about any past allergic reactions that you may have had to other drugs including antibody drugs (which are usually given into a vein or injection under the skin).

Giving trial medication into your vein may result in an infusion reaction with symptoms such as fever, flushing of the skin, itching, rash or a decrease in blood pressure. If you are receiving trial medication into your vein, your trial doctor will monitor for signs of an adverse reaction while you are getting the drug into your vein.

Infusion reactions typically resolve after stopping or slowing down the infusion, sometimes additional medication is required. If you think you are having an allergic reaction, call the trial doctor right away. If you are having trouble breathing, call <insert regional emergency telephone number>.

Name of Drug	Known Adverse Events or Side Effects
BI 655130	Currently there are no identified side effects of BI 655130. So far, BI 655130 has been tested in healthy volunteers for up to four weeks of dosing and in one trial in patients with generalized pustular psoriasis (GPP) and palmoplantar pustulosis (PPP). BI 655130 was well tolerated and adverse events were mostly mild or rarely moderate. In the four-week-trial in healthy volunteers, headache appeared to be reported more frequently in subjects treated with 20 mg/kg BI 655130 than in the other treatment groups. Two subjects experienced dyspnoea (shortness of breath) only in the 20 mg/kg group. Additionally, diarrhea, nausea, and nasopharyngitis (inflammation of the nose and throat) appeared to occur more often in subjects who received BI 655130 than in subjects who received placebo. There were no severe or serious adverse events. In the trial investigating the effects of BI 655130 in 7 patients with generalized pustular psoriasis, adverse events reported most frequently were arthralgia (joint pain) (3 patients, 42.9%) and eosinophilia (high levels of a certain type of white blood cell), chills, peripheral oedema (swelling caused by too much fluid in the body tissues), pyrexia (fever), upper respiratory tract infection, and eczema (a condition that causes the skin to become inflamed, itchy, red, cracked, and rough) each reported in 2 patients (28.6%). It is not known whether any of these adverse events were caused by BI 655130. There were no severe or serious adverse events. In the trial investigating the effects of BI 655130 in 59 patients with palmoplantar pustulosis, adverse events reported most frequently were nasopharyngitis (inflammation of the nose and throat) and headache. These adverse events occurred with a comparable frequency in patients treated with BI 655130 and placebo. It is unknown, whether BI 655130 caused any of these adverse events. Based on the preceding trials in healthy volunteers and patients with GPP and PPP, no specific drug-related risks are anticipated. The infusion of any protein can result in local or general allergic reactions. These reactions may also occur by administration of BI 655130. Moreover, there is the risk of local infusion site reactions (swelling, warmth, redness and pain at the infusion site). This usually resolves without any treatment, but can be uncomfortable for a few hours or days.

Name of Drug	Known Adverse Events or Side Effects
BI 655130 – cont'd	Infusion reactions have been reported occasionally in the clinical trials using BI 655130; the event was reported in patients treated with placebo and patients treated with BI 655130. As an inhibitor of the immune mediator IL36R (gene), BI 655130 affects a target of the immune (body defense) system which could decrease the body's defense ability against certain types of infection or tumor diseases. However, repeated dose studies in animals at very high doses and also first data from studies in humans do not suggest that inhibition or absence of IL36R would increase the risk for infectious or tumor diseases.

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DECLARATION OF INFORMED CONSENT

This page may be revised as appropriate.

Remember: If the consent and the subject information are two separate documents, the consent form must refer to the version and date of the Subject Information form.

TRIAL SUBJECT No.: _____

My signature on this consent form means that:

- I understand that I am being asked to participate in a research trial to test an investigational drug, BI 655130, in patients with a flare-up of Generalized Pustular Psoriasis.
- I have had this trial explained to me by _____.
- I have read, or have had it read to me, each page of this document including its appendices (Appendix A: Visit Schedule, Appendix B: Description of Trial Procedures and Risks, and Appendix C: Known Side Effects (Adverse Events) of the Investigational Drug) Appendix D; Confidentiality / Privacy and Data Sharing (according to local regulations) and the Declaration of Informed Consent and understood all these documents.
- I have had all of my questions answered fully and to my satisfaction.
- I was given sufficient time to think in peace and quiet and decide whether to participate.
- I have been told that my participation is voluntary and I can withdraw at any time without giving any reasons.
- I voluntarily consent to participate in this trial.
- I will be given a signed copy of this consent document for my records.

Name of Trial Subject (*please print*)	**Consent Signature of Trial Subject**	**Date**

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Information and Consent Form for Trial Subjects (template)

STATEMENT OF INVESTIGATOR / TRIAL DOCTOR / STUDY COORDINATOR:

I certify that I have explained to the above individual(s) the nature and purpose of the trial and the possible benefit and risks associated with participation. I have answered any questions that have been raised and the potential trial subject has received a copy of this signed consent document.

I acknowledge my responsibility for the care and well-being of the above trial subject, to respect the rights and wishes of the subject, and to conduct the trial according to applicable Good Clinical Practice guidelines and regulations.

Name of Health Care Professional (*please print*)	**Signature of Health Care Professional**	**Date**