Official Title: An Open-Label, Multicenter, Rollover Study to Provide Continued Treatment for Participants With Advanced Malignancies Previously Enrolled in Studies of Pemigatinib

NCT Number: NCT04949191

Document Date: Original Clinical Study Protocol: 17-May-2021

Clinical Study Protocol

INCB 54828-801

An Open-Label, Multicenter, Rollover Study to Provide Continued Treatment for Participants With Advanced Malignancies Previously Enrolled in Studies of Pemigatinib

Product:	**Pemigatinib (INCB054828)**
IND Number:	**124,358**
EudraCT Number:	**2021-002207-36**
Phase of Study:	**2**
Sponsor:	**Incyte Corporation** **1801 Augustine Cut-Off** **Wilmington, Delaware, USA 19803**
Original Protocol:	**17 MAY 2021**

INVESTIGATOR'S AGREEMENT

I have read the INCB 54828-801 Protocol (dated 17 MAY 2021) and agree to conduct the study as outlined. I agree to maintain the confidentiality of all information received or developed in connection with this Protocol.

_____

(Printed Name of Investigator)

_____ _____

(Signature of Investigator) (Date)

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LIST OF ABBREVIATIONS

Abbreviations and Special Terms	Definition
AE	adverse event
CFR	Code of Federal Regulations
COVID-19	coronavirus disease 2019
CTCAE	Common Terminology Criteria for Adverse Events
ECG	electrocardiogram
eCRF	electronic case report form
EDC	electronic data capture
EOT	end of treatment
FDA	Food and Drug Administration
FGFR	fibroblast growth factor receptor
GCP	Good Clinical Practice
GDPR	General Data Protection Regulation
HIPAA	Health Insurance Portability and Accountability Act of 1996
IB	Investigator's Brochure
ICF	informed consent form
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
ID	identification
IEC	independent ethics committee
IRB	institutional review board
IRT	interactive response technology
IV	intravenous
MedDRA	Medical Dictionary for Regulatory Activities
PD-1	programmed death 1
RSI	reference safety information
SAE	serious adverse event
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
SOP	standard operating procedure
study treatment	refers to pemigatinib monotherapy or combination therapy with pemigatinib
TEAE	treatment-emergent adverse event

1. PROTOCOL SUMMARY

Protocol Title:

An Open-Label, Multicenter, Rollover Study to Provide Continued Treatment for Participants With Advanced Malignancies Previously Enrolled in Studies of Pemigatinib

Protocol Number: INCB 54828-801

Objectives and Endpoints:

Table 1 presents the primary and major/key secondary objectives and endpoints.

Table 1: Objectives and Endpoints

Objectives	Endpoints
To evaluate the long-term safety and tolerability of pemigatinib.	Frequency and nature of AEs and SAEs as assessed by CTCAE v5.0.

Overall Design:

Table 2 presents the key study design elements. Further study details are presented after the table.

Table 2: Key Study Design Elements

Study Phase	Phase 2
Clinical Indication	Treatment of patients with advanced malignancies
Population	Male and female participants at least 18 years of age who are actively receiving treatment with pemigatinib under a parent protocol and receiving clinical benefit and who do not have access to pemigatinib outside of a clinical trial.
Number of Participants	Approximately 20 participants will be enrolled from prior pemigatinib studies.
Study Design	Single-arm, open-label, rollover
Estimated Duration of Study Participation	Participants will be allowed to continue to receive pemigatinib until they meet the criteria noted in Section 7.1.
Data Safety Monitoring Board/Data Monitoring Committee	No
Coordinating Principal Investigator	Not applicable

Figure 1 presents the study design schema, and Table 3 presents the schedule of activities.

Figure 1: Study Design Schema

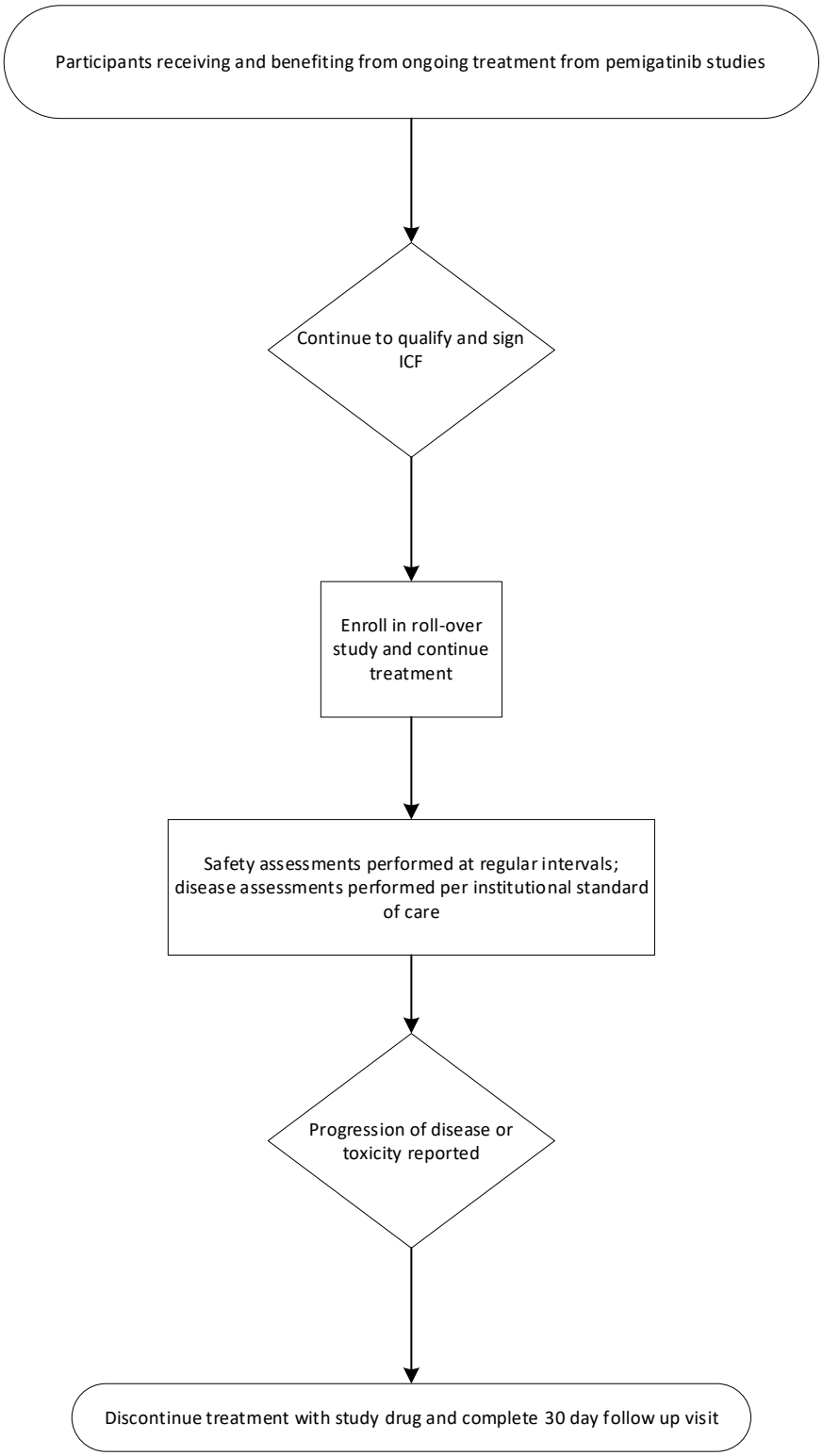

Table 3: Schedule of Activities

	Day 1 of Each Cycle	EOT	Safety Follow-Up	Comments
Informed consent	X*			*Only on Day 1 of rollover protocol.
Demography	X*			*Only on Day 1 of rollover protocol.
Contact IRT	X	X		
Dispense pemigatinib	X			
Collect remaining pemigatinib	X*	X		*Starting Cycle 2 Day 1.
Administer pembrolizumab (only for participants receiving under parent protocol)	X*			*Administer 200 mg IV once every 3 weeks on Day 1 of a 21-day cycle (3 weeks).
Administer INCMGA00012 (only for participants receiving under parent protocol)	X*			*Administer 500 mg IV once every 4 weeks on Day 1 of a 28-day cycle (4 weeks).
AE assessments	X	X	X	
12-lead ECG	X*	X		*Every 6 cycles starting from last ECG on parent study.
Ophthalmologic examinations	X*			*Every 3 cycles starting from last eye examination on parent study.
Serum chemistry	X	X		
Hematology	X*	X		*Every 3 cycles starting from last blood draw on parent study.
Disease assessment	X*			*Assess per standard of care guidelines; only report date of progression.
Urine pregnancy test	X*	X	X	*If urine test is positive, perform serum test to confirm.

2. INTRODUCTION

2.1. Background

The rollover protocol is intended for participants currently enrolled in Incyte-sponsored studies who are continuing to receive clinical benefit from treatment with pemigatinib (monotherapy or in combination). Continued, uninterrupted treatment will be provided under this single protocol. The population for the rollover study should be consistent with the populations defined in the parent studies. The primary eligibility criterion for a participant to enter the rollover protocol is participation in an Incyte-sponsored study with pemigatinib as monotherapy or combination therapy and receiving ongoing treatment with pemigatinib. Disease assessments should be performed per standard of care, with date of progression reported and safety data collected.

Participants who have enrolled in a prior study with pemigatinib as monotherapy or combination therapy and are assessed by the investigator to continue to benefit from ongoing treatment and who are unable to access pemigatinib outside of a clinical study will be eligible.

2.2. Study Rationale

2.2.1. Scientific Rationale for Study Design

Pemigatinib is an inhibitor of the FGFR family of receptor tyrosine kinases; aberrant signaling through FGFR resulting from gene amplification or mutation, chromosomal translocation, and ligand-dependent activation of the receptors has been demonstrated in multiple types of human cancers. Fibroblast growth factor receptor signaling contributes to the development of malignancies by promoting tumor cell proliferation, survival, migration, and angiogenesis. Refer to the pemigatinib IB for additional background information on pemigatinib.

2.2.2. Justification for Dose of Pemigatinib

Participants will continue to receive uninterrupted treatment with pemigatinib as monotherapy or combination therapy during the transition to this protocol. The participants will continue to be treated with pemigatinib monotherapy or combination therapy at the dose and schedule (intermittent or continuous) that the participant is receiving under the parent protocol. For example, if the participant's dose had been reduced to 9 mg once daily continuous dosing on the parent protocol, the participant will rollover into this protocol at that dose and regimen.

2.2.3. Justification for Dose of Pembrolizumab and INCMGA00012

Participants will continue to receive uninterrupted treatment with pemigatinib in combination with either pembrolizumab or INCMGA00012 as per the parent protocol during the transition to this protocol. The participants will continue to be treated with pembrolizumab or INCMGA00012 at the dose and schedule that the participant is receiving under the parent protocol. No changes to the dose or regimen of the combination (either compound) is allowed during the transition to the rollover study.

2.3. Benefit/Risk Assessment

More detailed information about the known and expected benefits and risks and reasonably expected AEs of pemigatinib, INCMGA00012, and pembrolizumab may be found in the pemigatinib IB, INCMGA00012 IB, and KEYTRUDA® (pembrolizumab) prescribing information, respectively.

2.3.1. Benefit/Risk Assessment During the COVID-19 Pandemic

Participants to be enrolled into this study have recurrent advanced or metastatic endometrial cancer and may be at higher risk for complications if they contract COVID-19. In this Phase 2 study population, standard of care therapy options for advanced or metastatic endometrial cancer that progressed on or following platinum-based chemotherapy are limited. A European Society for Medical Oncology multidisciplinary panel highlighted the importance of clinical cancer research to find better therapeutic options for participants even during the pandemic, including potential investigational therapies similar to immunotherapy with a known survival benefit (Curigliano et al 2020). Preliminary data released based on real-world data indicate that the use of immunotherapy either alone or in combination with chemotherapy does not appear to increase the risk of hospitalization in patients with COVID-19 infection (Horn et al 2020) or cause an increased risk of mortality (Lee et al 2020). The effects of immune checkpoint inhibitors on SARS-CoV-2 infection are currently unknown. However, at early stages of SARS-CoV-2 infection, CD8+ T-cell exhaustion and PD-1 upregulation have been observed (Riva et al 2020, Zheng et al 2020). Those findings suggest that immune checkpoint inhibitors may ameliorate the early phase of COVID-19 through the reactivation of T cells expressing PD-1 (Maio et al 2020). Conversely, potential risks of cytokine release syndrome, pneumonitis, or myocarditis related to immune checkpoint inhibitor therapy may represent a clinical issue and impact a course of COVID-19 (Maio et al 2020, Sullivan et al 2020). Considering the critical medical need for alternative therapies in the setting of recurrent advanced/metastatic endometrial cancer and the importance of continuing clinical cancer research even during the pandemic and taking into account the lack of conclusive clinical data on the impact of immune checkpoint inhibitor therapy on the course of COVID-19, the sponsor is implementing additional guidance for participation in this study in the context of the COVID-19 pandemic and study treatment management in the event of SARS-CoV-2 infection (see Appendix C).

During the COVID-19 pandemic, additional risks to participants exist either related to going to a health care facility or as a result of study-related activities. The investigators need to carefully assess both the benefit/risk and the medical data (eg, performance status, past medical history, comorbidities) available at screening to determine if it is in the best interest of the potential participant to enroll and participate in the study. In addition, country-specific requirements will be followed with regard to COVID-19 testing, as specified in Appendix C. Investigators will follow up with repeated tests during the study as per medical judgment and/or local practices as well as follow up with enrolled participants who may be newly suspected of being exposed to SARS-CoV-2, have symptoms of COVID-19, or demonstrate recovery from COVID-19.

Participants will be monitored with safety procedures as described in Section 8 and with additional safety assessments as per standard of care. Additional information regarding the flexibility of assessments/visits scheduling, where possible and warranted, and a strategy for participant management during the dynamic pandemic, as applicable, are described in Appendix C.

3. OBJECTIVES AND ENDPOINTS

Table 4 presents the objectives and endpoints.

Table 4: Objectives and Endpoints

Objectives	Endpoints
To evaluate the long-term safety and tolerability of pemigatinib.	Frequency and nature of AEs and SAEs as assessed by CTCAE v5.0.

4. STUDY DESIGN

4.1. Overall Design

This rollover protocol allows study participants from multiple protocols who are receiving clinical benefit to continue to be treated during the completion of the parent study (also referred to as parent protocol). The population for the rollover study should be consistent with the population defined in each parent protocol. The primary eligibility criterion for a participant to enter the rollover protocol is participation in an Incyte-sponsored study (parent protocol) with pemigatinib as monotherapy or combination therapy and receiving ongoing treatment with pemigatinib.

Participants who have enrolled in a prior study (parent protocol) with pemigatinib as monotherapy or combination therapy and are assessed by the investigator to continue to benefit from ongoing treatment and who cannot access pemigatinib outside of a clinical trial will be eligible.

Disease assessments will be performed per standard of care, with date of progression reported and safety data collected.

Once a participant has rolled over into this protocol from a parent protocol, the database for the parent protocol will be closed and locked, and the parent protocol study will be considered completed and closed. However, the participant in the rollover protocol will still be treated as per the plan outlined in the parent protocol. The list of parent protocols is provided in Appendix B.

4.2. Overall Study Duration

The study begins when the first participant signs the study ICF. The end of the study is defined as the date of the last visit of the last participant in the study. It is estimated that an individual will participate for approximately 12 months.

The study is considered completed when the last participant's last visit has occurred.

4.3. Study Termination

The investigator retains the right to terminate study participation at any time, according to the terms specified in the study contract. The investigator is to notify the IRB/IEC of the study's completion or early termination in writing, send a copy of the notification to the sponsor or sponsor's designee, and retain 1 copy for the site study regulatory file.

5. STUDY POPULATION

Deviations from eligibility criteria are not allowed because they can potentially jeopardize the scientific integrity of the study, regulatory acceptability, and/or participant safety. Therefore, adherence to the criteria as specified in the parent protocol as well as this protocol is essential. Prospective approval of protocol deviations to recruitment and enrollment criteria, also known as protocol waivers or exemptions, are not permitted.

5.1. Inclusion Criteria

Participants are eligible to be included in the study only if all of the following criteria apply:

1. Currently enrolled and receiving treatment in an Incyte-sponsored clinical study (parent protocol) of pemigatinib as monotherapy or combination therapy.
2. Currently benefiting from and tolerating treatment with pemigatinib, as determined by the investigator.
3. Demonstrated compliance, as assessed by the investigator, with the parent protocol requirements.
4. Willingness and ability to comply with scheduled visits, treatment plans, and any other study procedures.
5. Currently have no evidence of progressive disease, as determined by the investigator, following treatment with pemigatinib as monotherapy or combination therapy.
6. Willingness to avoid pregnancy or fathering children based on the criteria below.
    a. Male participants must agree to take appropriate precautions to avoid fathering children (with at least 99% certainty) from signing of the ICF through 90 days after the last dose of pemigatinib and 6 months after the last dose of gemcitabine and/or cisplatin and must refrain from donating sperm during this period. Permitted methods that are at least 99% effective in preventing pregnancy (see Appendix A) should be communicated to the participants and their understanding confirmed. NOTE: Men being treated with gemcitabine must be advised to seek further advice regarding cryoconservation of sperm before treatment because of the possibility of infertility due to therapy with gemcitabine.
    b. Women of nonchildbearing potential (ie, surgically sterile with a hysterectomy and/or bilateral oophorectomy OR ≥ 12 months of amenorrhea) are eligible.
    c. Women of childbearing potential must have a negative serum pregnancy test at signing of the ICF and before the first dose on Day 1 and must agree to take appropriate precautions to avoid pregnancy (with at least 99% certainty) from signing of the ICF through safety follow-up (30-35 days after the last dose of pemigatinib) and through 6 months after the last dose of gemcitabine and/or cisplatin. Permitted methods that are at least 99% effective in preventing pregnancy (see Appendix A) should be communicated to the participants and their understanding confirmed.
7. Written informed consent obtained prior to enrolling in the rollover study. If consent cannot be expressed in writing, it must be formally documented and witnessed, ideally via an independent trusted witness.

5.2. Exclusion Criteria

Participants are excluded from the study if any of the following criteria apply:

1. Able to access pemigatinib commercially or outside of a clinical trial.
2. Permanently discontinued from the parent protocol for any reason.
3. No longer meet the inclusion/exclusion criteria from the parent protocol if still receiving treatment.
4. Women who are pregnant or breastfeeding or participants expecting to conceive or father children within the projected duration of the study, starting with Day 1 of the rollover study visit through completion of safety follow-up or through 90 days from the date of last dose of study treatment.

5.3. Lifestyle Considerations

No restrictions are required.

5.4. Screen Failures

There are no screen failures for this rollover study. Only participants actively receiving treatment in another pemigatinib study (parent protocol) are eligible to enroll.

5.5. Replacement of Participants

Not applicable.

6. STUDY TREATMENT

6.1. Study Treatments Administered

Table 5 presents the study treatment information. This information is also found in the parent protocol.

Table 5: Study Treatment Information

	Study Treatment 1	Study Treatment 2	Study Treatment 3
Study treatment name:	Pemigatinib (INCB054828)	INCMGA00012 (INCB 54828-101 only)	Pembrolizumab (INCB 54828-101 only)
Dosage formulation:	Oral	IV	IV
Unit dose strength(s) /dosage level(s):	2 mg, 4.5 mg, 9 mg, 13.5 mg	500 mg/500 mg	200 mg
Administration instructions:	Taken by mouth once daily	Administered over 60 minutes once every 4 weeks (Day 1 of a 28-day cycle)	
Packaging and labeling:	Pemigatinib 4.5 mg, 9 mg, and 13.5 mg tablets will be provided in 14-count bottles; 2 mg tablets will be provided in 60-count bottles. Each bottle will be labeled as required per country requirement.	500 mg vials Each vial will be labeled as per country requirement.	Commercially labeled product
Storage:	Room temperature	Stored upright under refrigeration at 2°C to 8°C (36°F-46°F) and protected from light	Stored under refrigeration at 2°C to 8°C (36°F-46°F)
Status of treatment in participating countries:	Approved	Not approved	Approved

6.2. Preparation, Handling, and Accountability

The investigator or designee must confirm appropriate temperature conditions have been maintained during transit for all study treatments received and any discrepancies are reported and resolved before use of the study treatment.

Only participants enrolled in the study may receive study treatment, and only authorized site staff may supply or administer study treatment. All study treatment must be stored in a secure, environmentally controlled, and monitored (manual or automated) area in accordance with the labeled storage conditions with access limited to the investigator and authorized site staff.

The investigator (or designee) is responsible for study treatment accountability, reconciliation, and record maintenance (ie, receipt, reconciliation, and final disposition records). Inventory and accountability records must be maintained and readily available for inspection by the study monitor and are open to inspection at any time by any applicable regulatory authorities. The investigator or designee must maintain records that document the following:

- Delivery of study drugs (except pembrolizumab for INCB 54828-101 only) to the study site.
- Inventory of study drugs at the site.
- Participant use of the study drugs, including tablets and/or vials from each supply dispensed.
- Return of study drugs (except pembrolizumab for INCB 54828-101 only) to the investigator or designee by participants.

The investigational product must be used only in accordance with the parent protocol and this protocol. The investigator will also maintain records adequately documenting that the participants were provided the specified study drug. These records should include dates, quantities, and any available batch or serial numbers or unique code numbers assigned to the investigational product and study participants.

Completed accountability records will be archived by the site. The investigator or designee will be expected to collect and retain all used, unused, and partially used containers of study drug until verified by the study monitor (unless otherwise agreed to by the sponsor). At the conclusion of the study, the investigator or designee will oversee shipment of any remaining study drug back to the sponsor or its designee for destruction according to institutional SOPs. If local procedures mandate on-site destruction of the investigational supply, the site should (where local procedures allow) maintain the investigational supply until the study monitor inspects the accountability records in order to evaluate compliance and accuracy of accountability by the investigative site. At sites where the study drug is destroyed before monitor inspection, the monitors rely on documentation of destruction per the site SOP.

Further guidance and information for the final disposition of unused study treatments are provided in the Pharmacy Manual from the parent protocol.

6.3. Measures to Minimize Bias: Randomization and Blinding

Not applicable.

6.4. Study Treatment Compliance

Compliance with all study-related treatments should be emphasized to the participant by the site personnel, and appropriate steps should be taken to optimize compliance during the study. Compliance with study drug administration will be calculated by the sponsor based on study drug accountability and infusion records documented by the site staff and monitored by the sponsor/designee.

6.5. Dose Modifications and Interruptions

Instructions for dose modifications and interruptions for pemigatinib and/or combinations are outlined in the parent protocols.

6.6. Concomitant Medications and Procedures

Currently used medications and treatments (including over-the-counter or prescription medicines, vitamins, vaccines, and/or herbal supplements) must be recorded in the eCRF. Any medications actively being taken while the participant is on treatment under the parent protocol that will continue must be recorded in the eCRF for this study. Any addition, deletion, or change in the dose of these medications will also be recorded. Concomitant medications administered for treatment of SAEs (as defined in Section 9.2) should be recorded even if the SAE is reported beyond 30 days after the last dose of study treatment. Concomitant treatments/procedures that are required to manage a participant's medical condition during the study will also be recorded in the eCRF.

7. DISCONTINUATION OF STUDY TREATMENT AND PARTICIPANT WITHDRAWAL

7.1. Discontinuation of Study Treatment

7.1.1. Reasons for Discontinuation

Participants **must** be discontinued from study treatment for the following reasons:

- Documented disease progression.
- Pregnancy.
- Lack of treatment compliance.
- Consent is withdrawn.
- Further participation would be injurious to the participant's health or well-being, in the investigator's medical judgment.
- Unacceptable toxicity as noted in the parent protocol.
- The study is terminated by the sponsor.
- The study is terminated by the local health authority, IRB, or IEC.

7.1.2. Discontinuation Procedures

In the event that the decision is made to permanently discontinue the study treatment, the EOT visit should be conducted. Reasonable efforts should be made to have the participant return for a follow-up visit. These visits are described in Table 3. The last date of the last dose of study treatment and the reason for discontinuation of study treatment will be recorded in the eCRF.

If a participant is discontinued from study treatment:

- The study monitor or sponsor must be notified.
- The reason(s) for discontinuation must be documented in the participant's medical record and the primary reason for discontinuation must be included in the eCRF.
- The EOT visit should be performed and date recorded.
- The status of the participant should be updated to EOT in the IRT.
- Participants must be followed for safety until the time of the follow-up visit or until study treatment–related toxicities resolve, return to baseline, or are deemed irreversible, whichever is longest.

If the participant discontinues study treatment and actively withdraws consent for collection of follow-up data (safety follow-up), then no additional data collection should occur; however, participants will have the option of withdrawing consent for study treatment but continuing in the follow-up period of the study for safety assessment.

7.2. Participant Withdrawal From the Study

A participant may withdraw from the study at any time at his/her own request or may be withdrawn at any time at the discretion of the investigator for safety, behavioral, compliance, or administrative reasons.

If a participant withdraws from the study, he/she may request destruction of any samples taken for this study and/or the parent study and not tested, and the investigator must document this in the site study records. If the participant withdraws consent for disclosure of future information, the sponsor may retain and continue to use any data collected before such a withdrawal of consent.

7.3. Lost to Follow-Up

A participant will be considered lost to follow-up if he/she repeatedly fails to return for scheduled visits and is unable to be contacted by the study site.

The following actions must be taken if a participant fails to return to the clinic for a required study visit:

- The site must attempt to contact the participant and reschedule the missed visit as soon as possible and counsel the participant on the importance of maintaining the assigned visit schedule and ascertain whether or not the participant wishes to and/or should continue in the study.

- Before a participant is deemed lost to follow-up, the investigator or designee must make every effort to regain contact with the participant (where possible, 3 telephone calls and, if necessary, a certified letter to the participant's last known mailing address or local equivalent methods). These contact attempts should be documented in the participant's medical record.
- Should the participant continue to be unreachable, he/she will be considered to have withdrawn from the study.

8. STUDY ASSESSMENTS AND PROCEDURES

8.1. Administrative and General Procedures

8.1.1. Informed Consent Process

A new consent will need to be obtained prior to the participant rolling over from the parent protocol to this study.

- The investigator or his/her representative will explain the nature of the study to the participant or his/her legally authorized representative and answer all questions regarding the study.
  - Informed consent must be obtained before any procedures specific to this protocol and the first dose of study treatment is administered under this protocol.
  - Informed consent must be obtained using the IRB/IEC-approved version in a language that is native and understandable to the participant. A template will be provided by the sponsor or its designee. The sponsor or its designee must review and acknowledge the site-specific changes to the ICF template. The ICF must include a statement that the sponsor or its designee and regulatory authorities have direct access to participant records.
  - The ICF must contain all required elements and describe the nature, scope, and possible consequences of the study in a form understandable to the study participant.
- Participants must be informed that their participation is voluntary. Participants or their legally authorized representative will be required to sign a statement of informed consent that meets the applicable requirements and regulations for the countries in which the study is being conducted as well as the IRB/IEC or study center.
- The participant must be informed that his/her personal study-related data will be used by the sponsor in accordance with local data protection laws. The level of disclosure must also be explained to the participant.
- The participant must be informed that his/her medical records may be examined by Clinical Quality Assurance auditors or other authorized personnel appointed by the sponsor, by appropriate IRB/IEC members, and by inspectors from regulatory authorities.

- The medical record must include a statement that written informed consent was obtained before the participant was enrolled in the study and the date the written consent was obtained. The authorized person obtaining the informed consent must also sign the ICF.
- Participants must provide consent to the most current version of the ICF during their participation in the study.
- A copy of the ICF(s) must be provided to the participant or the participant's legally authorized representative.

8.1.2. Interactive Response Technology Procedure

Each participant will obtain a new ID number when enrolling in this study. It will be different from the ID number on the parent protocol; however, the participant ID number from the parent protocol will be entered on the appropriate form of the eCRF so there is a link between the parent study and this study.

Site staff should contact the IRT to obtain the participant ID number prior to rolling the participant over into this study. Additionally, the IRT will be contacted at each regular study visit to update the study drug supply. Additional details are provided in the IRT Manual.

8.1.3. Demography and Medical History

Demographic data will be collected in the eCRF for this study and will include year of birth/age at entry to roll over study, race, and ethnicity. Medical history data will be linked from the parent protocol. NOTE: Any ongoing AEs at the time of rollover will be entered on the Adverse Event Form in the eCRF for this study.

8.1.3.1. Disease Characteristics and Treatment History

All disease history and treatment history will be linked from the parent protocol. No additional data will need to be entered for this study.

8.2. Efficacy Assessments

Participants should undergo disease assessments according to the institution's standard of care. Disease assessment details will not be captured with the exception of documenting the date of disease progression. The date of disease progression will be noted in this study's eCRF.

8.3. Safety Assessments

8.3.1. Adverse Events

NOTE: Adverse events that are ongoing at the time of rollover from the parent protocol will be entered on the Adverse Event Form in the eCRF for this study.

Adverse events will be monitored from the time the participant signs the ICF until at least 30 days after the last dose of study treatment. Adverse events for enrolled participants that begin or worsen after informed consent should be recorded on the Adverse Event Form in the eCRF regardless of the assumption of a causal relationship with the study treatment. Adverse events

(including laboratory abnormalities that constitute AEs) should be described using a diagnosis whenever possible rather than by individual underlying signs and symptoms.

Adverse events will be reported by the participant (or, when appropriate, by a caregiver, surrogate, or the participant's legally authorized representative). The investigator and any qualified designees are responsible for detecting, documenting, and recording events that meet the definition of an AE or SAE and remain responsible for following up on AEs that are serious, considered related to the study treatment or procedures, or caused the participant to withdraw from the study. Care will be taken not to introduce bias when detecting AEs and/or SAEs. Open-ended and nonleading verbal questioning of the participant, such as "How are you feeling?", is the preferred method to inquire about AE occurrences. Adverse events may also be detected when they are volunteered by the participant between visits or through physical examinations, laboratory tests, or other assessments. The definition, reporting, and recording requirements for AEs are described in Section 9.

All SAEs will be reported to the sponsor or designee within 24 hours. The investigator will submit any updated SAE data to the sponsor within 24 hours of it being available.

After the initial AE/SAE report, the investigator is required to proactively follow each participant at subsequent visits/contacts. All SAEs will be followed until resolution, stabilization, the event is otherwise explained, or the participant is lost to follow-up (as defined in Section 7.3).

8.3.2. Laboratory Assessments

See Table 6 for the list of clinical laboratory tests to be performed and Table 3 for the timing and frequency. A certified laboratory local to the investigative site will perform all clinical laboratory assessments for safety. The investigative site will enter the laboratory results and laboratory normal ranges into the eCRF. Additional tests may also be performed if clinically indicated.

Clinically significant abnormal laboratory findings are those that are not associated with the underlying disease, unless judged by the investigator to be more severe than expected for the participant's condition. All laboratory tests with values considered clinically significantly abnormal during participation in the study or within 30 days after the last dose of study treatment should be repeated until the values return to normal or baseline or are no longer considered clinically significant by the investigator or medical monitor.

NOTE: If Day 1 on the rollover study is <u>within 1 week</u> of the last laboratory sample on the parent protocol, no additional sample is required for Day 1 of the rollover study.

Table 6: Required Laboratory Analytes

Blood Chemistries	Hematology
Albumin Alkaline phosphatase ALT AST Amylase Bicarbonate or CO_2 Blood urea nitrogen Calcium (uncorrected) Chloride Creatinine Glucose Lactate dehydrogenase Lipase Magnesium Phosphate Potassium Sodium Total bilirubin Direct bilirubin (if total bilirubin is elevated above ULN) Total protein Uric acid Urea Vitamin D 1,25 Vitamin D 25-OH	Complete blood count, including: • Hemoglobin • Hematocrit • Platelet count • Red blood cell count • WBC count Differential count, including: • Basophils • Eosinophils • Lymphocytes • Monocytes • Neutrophils Absolute values must be provided for: • WBC differential laboratory results

ALT = alanine aminotransferase; AST = aspartate aminotransferase; ULN = upper limit of normal; WBC = white blood cell.
Note: Additional tests may be required, as agreed upon by the investigator and sponsor, based on emerging safety data or to rule out a diagnosis.

8.3.2.1. Pregnancy Testing

A urine pregnancy test will be required for all women of childbearing potential on Day 1 of this study and at the EOT and safety follow-up visits. Urine pregnancy tests will be performed locally as outlined in Table 3, as medically indicated (eg, in case of loss of menstrual cycle, when pregnancy is suspected), or per country-specific requirement (note that country-required urine pregnancy testing will be outlined and communicated to investigational sites under separate cover). If a urine pregnancy test is positive, the result should be confirmed with a serum pregnancy test.

If the serum pregnancy test is negative after a urine test was positive, the investigator will assess the potential benefit/risk to the participant and determine whether it is in the participant's best interest to resume study treatment and continue participation in the study.

If a pregnancy is confirmed by a serum pregnancy test, see Section 9.6 for reporting requirements.

8.4. Unscheduled Visits

Not applicable.

8.5. End of Treatment

When the participant permanently discontinues study treatment, the EOT visit should be conducted. If the EOT visit coincides with a regular study visit, the EOT evaluations will supersede those of that scheduled visit, and the data should be entered in the EOT visit in the eCRF. The participant should be encouraged to return for the follow-up visit.

8.6. Follow-Up

8.6.1. Safety Follow-Up

The safety follow-up period is the interval between the EOT visit and the scheduled follow-up visit, which should occur 30 to 35 days after the EOT visit. Adverse events and SAEs must be reported up until at least 30 days after the last dose of study treatment or until toxicities resolve, return to baseline, or are deemed irreversible, whichever is longer. Reasonable efforts should be made to have the participant return for the follow-up visit and report any AEs that may occur during this period.

8.6.2. Post-Treatment Disease Follow-Up

Participants who discontinue study treatment for a reason other than disease progression will not be required to continue disease assessments per this protocol. No additional information will be collected once treatment discontinues.

8.6.3. Survival Follow-Up

Not applicable.

9. ADVERSE EVENTS: DEFINITIONS AND PROCEDURES FOR RECORDING, EVALUATING, FOLLOW-UP, AND REPORTING

9.1. Definition of Adverse Event

Adverse Event Definition
• An AE is any untoward medical occurrence associated with the use of a drug in humans, whether or not it is considered drug-related. • An AE can therefore be any unfavorable or unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of study treatment.
Additional Guidance for Events Meeting the Adverse Event Definition
• Any safety assessments (eg, ECG, vital signs measurements), including those that worsen from baseline, considered clinically significant in the medical and scientific judgment of the investigator (ie, not related to progression of underlying disease) are to be reported as an AE. • Abnormal laboratory test results are to be reported as an AE if they are considered clinically meaningful, induce clinical signs or symptoms, require concomitant therapy, or require changes in study treatment. Whenever possible, a diagnosis (eg, anemia, thrombocytopenia) should be recorded in the eCRF rather than the abnormal laboratory test result (eg, low hemoglobin, platelet count decreased). • Exacerbation of a chronic or intermittent pre-existing condition/disease, including either an increase in the frequency and/or intensity of the condition, is to be reported as an AE. • New conditions detected or diagnosed after the start of study treatment administration are to be reported as an AE. • Signs, symptoms, or the clinical sequelae of a suspected drug-drug interaction are to be reported as an AE. • Signs and/or symptoms from dosing errors of a study treatment (eg, overdose) or a concomitant medication are to be reported as an AE. • "Lack of efficacy," "disease progression," or "failure of expected pharmacological action" will not be reported as an AE or SAE. • A condition that leads to a medical or surgical procedure (eg, endoscopy, appendectomy) will be reported as an AE if it occurs after obtaining informed consent.

9.2. Definition of Serious Adverse Event

If an event is not an AE per the definition above, then it cannot be an SAE even if serious conditions are met (eg, hospitalization for signs/symptoms of the disease under study, death due to progression of disease).

A serious adverse event is defined as any untoward medical occurrence that, at any dose:
a. Results in death
b. Is life-threatening The term "life-threatening" in the definition of "serious" refers to an adverse drug experience that places the participant, in the opinion of the initial reporter, at immediate risk of death from the adverse experience as it occurs. This does not include an adverse drug experience that, had it occurred in a more severe form, might have caused death.

c. Requires inpatient hospitalization or prolongation of existing hospitalization

In general, hospitalization signifies that the participant has been detained (involving at least an overnight stay) at the hospital or emergency ward for observation and/or treatment that would not have been appropriate in the physician's office or outpatient setting. Complications that occur during hospitalization are AEs. If a complication prolongs hospitalization or fulfills any other serious criteria, the event is serious. When in doubt as to whether hospitalization occurred or was necessary, the AE should be considered serious.

Hospitalization for elective treatment or planned surgery (eg, stent replacement, hip surgery) is not considered an SAE.

Hospitalization for medical interventions in which no unfavorable medical occurrence occurred (ie, elective procedures or routine medical visits) is not considered an SAE.

d. Results in persistent or significant disability/incapacity

- The term "disability" means a substantial disruption of a person's ability to conduct normal life functions. This definition is not intended to include experiences of relatively minor medical significance, such as uncomplicated headache, nausea, vomiting, diarrhea, influenza, and accidental trauma (eg, sprained ankle), that may interfere with or prevent everyday life functions but do not constitute a substantial disruption.

e. Is a congenital anomaly/birth defect

f. Is an important medical event

An important medical event is an event that may not result in death, be immediately life-threatening, or require hospitalization but may be considered serious when, based on appropriate medical judgment, the event may jeopardize the participant and may require medical or surgical intervention to prevent one of the outcomes listed in the above definition. Examples of such events include new invasive or malignant cancers; intensive treatment in an emergency department or at home for allergic bronchospasm, blood dyscrasias, or convulsions that do not result in hospitalization; or development of drug dependency or drug abuse. Secondary malignancies should always be considered SAEs.

9.3. Recording and Follow-Up of Adverse Events and/or Serious Adverse Events

Adverse Event and Serious Adverse Event Recording

- Adverse events that are ongoing at the time of rollover to this study must be recorded on the Adverse Event Form in the eCRF for this study.
- An AE/SAE that begins or worsens after informed consent is signed should be recorded on the Adverse Event Form in the eCRF. AEs/SAEs should be reported for enrolled participants, but only SAEs need to be reported for screen failure participants. For detailed information, refer to the eCRF guidelines.
- When an AE/SAE occurs, it is the responsibility of the investigator to review all documentation (eg, hospital progress notes, laboratory reports, and diagnostic reports) related to the event.
- The investigator (or delegate) will then record all relevant AE/SAE information in the eCRF.
- It is **not** acceptable for the investigator to send photocopies of the participant's medical records in lieu of completing the Adverse Event Form in the eCRF.

- There may be rare instances when copies of medical records for certain cases are requested. In this case, all participant identifiers, with the exception of the participant number, will be redacted by the site staff on the copies of the medical records before submission. These records can be submitted to Incyte Pharmacovigilance by email/fax per the contact information listed as per SAE completing guidelines.
- The investigator will attempt to establish a diagnosis of the event based on signs, symptoms, and/or other clinical information. Whenever possible, the diagnosis (not the individual signs/symptoms) will be documented as the AE/SAE. When a clear diagnosis cannot be identified, each sign or symptom should be reported as a separate AE/SAE.

To the extent possible, each AE/SAE should be evaluated to determine the following:

- The severity grade (CTCAE v5.0 Grade 1 to 5). See below for further instructions on the assessment of intensity.
- Whether there is at least a reasonable possibility that the AE is related to the study treatment: suspected (yes) or not suspected (no). See below for further instructions on the assessment of causality.
- The start and end dates, unless unresolved at the final safety follow-up visit.
- The action taken with regard to study treatment as a result of the AE/SAE(s).
- The event outcome (eg, not recovered/not resolved, recovered/resolved, etc.).
- The seriousness, as per the SAE definition provided in Section 9.2.
- The action taken with regard to the event. Note: If an AE is treated with a concomitant medication or nondrug therapy, this action should be recorded on the Adverse Event Form and the treatment should be specified on the appropriate eCRF (eg, Prior/Concomitant Medications).

Assessment of Intensity

The severity of AEs will be assessed using CTCAE v5.0 Grades 1 through 5. If an event is not classified by CTCAE, the severity of the AE will be graded according to the scale below to estimate the grade of severity.

The investigator will make an assessment of intensity for each AE and SAE reported during the study and assign it to 1 of the following categories:

- **Grade 1:** Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; treatment not indicated.
- **Grade 2:** Moderate; minimal, local, or noninvasive treatment indicated; limiting age-appropriate activities of daily living.
- **Grade 3:** Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care activities of daily living.
- **Grade 4:** Life-threatening consequences; urgent treatment indicated.
- **Grade 5:** Fatal.

Assessment of Causality

- The investigator is obligated to assess the relationship between study treatment and each occurrence of each AE/SAE. If reference therapy is used in combination with an Incyte study drug or if multiple Incyte study drugs are used, then the relationship to each study drug/reference therapy must be assessed.
- A "reasonable possibility" of a relationship conveys that there are medical facts, evidence, and/or arguments to suggest a causal relationship, rather than that a relationship cannot be ruled out.

- The investigator will use clinical judgment to determine the possibility of a relationship.
- The investigator will also consult the RSI in the IB or Product Information for study drug/treatment, or marketed products, respectively, in making his/her assessment.
- Alternative causes, such as underlying or concurrent disease(s), concomitant therapy, and other risk factors, as well as the temporal relationship of the event to study treatment administration, will be considered and investigated.
- For each AE/SAE, the investigator **must** document in the medical notes that he/she has reviewed the AE/SAE and has provided an assessment of causality.
- With regard to assessing causality of SAEs:
  - There may be situations in which an SAE has occurred and the investigator has minimal information to include in the initial report. However, the causality assessment is one of the criteria used when determining regulatory reporting requirements. **Therefore, it is very important that the investigator always make an assessment of causality based on the available information for every event before the initial transmission of the SAE.**
  - The investigator may change his/her opinion of causality in light of follow-up information and submit the updated causality assessment.

Follow-Up of Adverse Events and Serious Adverse Events

- The investigator is obligated to perform or arrange for the conduct of supplemental measurements and/or evaluations as medically indicated or as requested by the sponsor to elucidate the nature and/or causality of the AE or SAE as fully as possible. This may include additional laboratory tests or investigations, histopathological examinations, or consultation with other health care professionals.
- Once an AE is detected, it should be followed in the Adverse Event Form in the eCRF until it has resolved or until it is judged to be permanent; assessment should be made at each visit (or more frequently if necessary) of any changes in severity, the suspected relationship to the study treatment, the interventions required to treat the event, and the outcome.
- When the severity of an AE changes over time for a reporting period (eg, between visits), each change in severity will be reported as a separate AE.
- Updated SAE information will be recorded in the originally completed eCRF and reported to Incyte Pharmacovigilance (either via email/fax) until resolution, stabilization, the event is otherwise explained, or the participant is lost to follow-up.
- Any updated SAE data (including SAEs being downgraded to nonserious) will be submitted to the sponsor (or designee) within 24 hours of receipt of the information.

9.4. Reporting of Serious Adverse Events

Regardless of suspected causality (eg, relationship to study treatment), all SAEs occurring after the participant has signed the ICF through at least 30 days after the last dose of study treatment must be reported to the sponsor (or designee) immediately, without undue delay but not later than within **24 hours** of obtaining knowledge of its occurrence unless otherwise specified by the protocol. The investigator will submit any updated SAE data to the sponsor (or designee) immediately, without undue delay but not later than within 24 hours of it being available.

Investigators are not obligated to actively seek SAE information after the safety follow-up visit. If the investigator learns of any SAE, including death, at any time during this period, and he/she considers the event to be reasonably related to the study treatment or study participation, then the

investigator must notify the sponsor (or designee) within 24 hours of becoming aware of the event.

After the initial AE/SAE report, the investigator is required to proactively follow each participant at subsequent visits/contacts. All SAEs will be followed until resolution, stabilization, the event is otherwise explained, or the participant is lost to follow-up (as defined in Section 7.3).

Prompt notification by the investigator to the sponsor regarding an SAE is essential so that legal obligations and ethical responsibilities toward the safety of participants and the safety of a study treatment under clinical investigation are met.

If the SAE is not documented in the RSI of the pemigatinib IB or INCMGA00012IB for the study treatment (new occurrence) and is thought to be related to the study treatment, the sponsor or its designee may urgently require further information from the investigator for expedited reporting to health authorities. The sponsor or its designee may need to issue an Investigator Notification to inform all investigators involved in any study with the same drug that this SAE has been reported. Suspected unexpected serious adverse reactions will be collected and reported to the competent authorities and relevant ethics committees in accordance with Directive 2001/20/EC or as per national regulatory requirements in participating countries.

The sponsor has a legal responsibility to notify both the local regulatory authority and other regulatory agencies about the safety of a study treatment under clinical investigation. The sponsor will comply with country-specific regulatory requirements relating to safety reporting to the regulatory authority, IRB/IEC, and investigators.

Investigator safety reports must be prepared for suspected unexpected serious adverse reactions according to local regulatory requirements and sponsor policy and forwarded to investigators as necessary.

An investigator who receives an investigator safety report describing an SAE or other specific safety information (eg, summary or listing of SAEs) from the sponsor will review and then file it along with the IB and will notify the IRB/IEC, if appropriate, according to local requirements.

Serious Adverse Event Reporting
• Information about all SAEs is collected and recorded on the Adverse Event Form in the eCRF. • The investigator must report within 24 hours of learning of its occurrence any SAE by completing the Serious Adverse Event Report Form in English. • Follow-up information is also recorded and transmitted to Incyte Pharmacovigilance on an amended or new Serious Adverse Event Report Form, with an indication that it is follow-up to the previously reported SAE and the date of the original report. The follow-up report should include information that was not provided on the previous Serious Adverse Event Report Form, such as the outcome of the event (eg, resolved or ongoing), treatment provided, action taken with study treatment because of the SAE (eg, dose reduced, interrupted, or discontinued), or participant disposition (eg, continued or withdrew from study participation). Each recurrence, complication, or progression of the original event should be reported as a follow-up to that event, regardless of when it occurs. • Contacts for SAE reporting can be found in the Study Procedures Manual.

9.5. Emergency Unblinding of Treatment Assignment

Not applicable.

9.6. Pregnancy

Pregnancy, in and of itself, is not regarded as an AE unless there is suspicion that the study treatment may have interfered with the effectiveness of a contraceptive medication or method. When a pregnancy has been confirmed in a participant during maternal or paternal exposure to study treatment, the following procedures should be followed in order to ensure safety:

- The study treatment must be interrupted immediately (female participants only).
- If the female participant is no longer pregnant and meets the treatment continuation criteria within 14 days of the scheduled start of a cycle, study treatment may be resumed after approval has been received from the sponsor medical monitor.
- The investigator must complete and submit the Incyte Clinical Trial Pregnancy Form to the sponsor or its designee within **24 hours** of learning of the pregnancy.

Data on fetal outcome are collected for regulatory reporting and drug safety evaluation. Follow-up should be conducted for each pregnancy to determine outcome, including spontaneous or voluntary termination, details of the birth, and the presence or absence of any birth defects, congenital abnormalities, or maternal and/or newborn complications, by following until the first well-baby visit. Pregnancy should be recorded on a Clinical Trial Pregnancy Form and reported by the investigator to the sponsor or its designee. Pregnancy follow-up information should be recorded on the same form and should include an assessment of the possible causal relationship to the sponsor's study drug to any pregnancy outcome, as well as follow-up to the first well-baby visit or the duration specified in local regulations, whichever is later. Refer to the Incyte Reference Guide for Completing the Clinical Trial Pregnancy Form or Study Reference Manual.

Any SAE occurring during pregnancy of a study participant must be recorded on the Serious Adverse Event Report Form and submitted to the sponsor or its designee.

Abnormal pregnancy outcomes (eg, spontaneous abortion, fetal death, stillbirth, congenital anomalies, or ectopic pregnancy) are considered SAEs (if occurring in the study participant) and must be reported as described in Section 9.4. If an abnormal pregnancy outcome is reported in a study participant's partner, the event should be reported to the sponsor on the Clinical Trial Pregnancy Form.

9.7. Warnings and Precautions

Special warnings or precautions for the study treatment, derived from safety information collected by the sponsor or its designee, are presented in the pemigatinib IB and INCMGA00012 IB. Additional safety information collected between IB updates will be communicated in the form of Investigator Notifications. Any important new safety information should be discussed with the participant during the study as necessary. If new significant risks are identified, they will be added to the ICF.

9.8. Product Complaints

The sponsor collects product complaints on study drugs and drug delivery systems used in clinical studies in order to ensure the safety of study participants, monitor quality, and facilitate process and product improvements.

All product complaints associated with material packaged, labeled, and released by the sponsor or its designee will be reported to the sponsor. All product complaints associated with other study material will be reported directly to the respective manufacturer.

The investigator or his/her designee is responsible for reporting a complete description of the product complaint via email or other written communication to the sponsor contact or respective manufacturer as noted in the packaging information. Any AE associated with a product complaint should be recorded as described in Section 9.3.

If the investigator is asked to return the product for investigation, he/she will return a copy of the product complaint communication with the product.

9.9. Treatment of Overdose of Pemigatinib

There has been no clinical experience with overdose of pemigatinib. Treatment of overdose should consist of general supportive measures.

10. STATISTICS

This is a rollover study for participants currently receiving pemigatinib on a parent protocol. All the efficacy parameters will be analyzed in the parent protocol; no additional efficacy analysis will be performed in this protocol.

10.1. Sample Size Determination

Not applicable.

10.2. Populations for Analyses

The full analysis set/safety population includes all participants who received at least 1 dose of study treatment in this study.

10.3. Statistical Analyses

10.3.1. Disposition and Demographics

Disposition of participants and demographics will be summarized descriptively for the full analysis set.

10.3.2. Exposure

Measure of exposure for study treatment will be summarized descriptively using the safety population.

10.3.3. Safety Analyses

Adverse events/serious adverse events that are ongoing at the time of rollover will be regraded per CTCAE v5.0 if graded per CTCAE v4.03. Safety analyses will be conducted. Adverse events will be coded by the MedDRA dictionary, severity of AEs will be assessed using CTCAE v5.0 Grades 1 through 5, and TEAEs (ie, AEs reported for the first time in this protocol and within 30 days of last dose of study treatment, or any AE ongoing and defined as

treatment-emergent from the parent protocol) will be tabulated by preferred term and system organ class for all events, related events, and events of Grade 3 or higher. All AEs will be listed.

11. SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

11.1. Investigator Responsibilities

- The Protocol, Protocol amendments, ICF, IB, and other relevant documents (eg, advertisements) must be submitted to an IRB/IEC by the investigator and reviewed and approved by the IRB/IEC before the study is initiated.
- The investigator is responsible for ensuring that the safety reports provided by the sponsor are reviewed and processed in accordance with regulatory requirements, the policies and procedures established by the IRB/IEC, and institutional requirements.
- Any amendments to the Protocol will require approval from both Health Authorities and IRB/IEC before implementation of changes made to the study design, except for changes necessary to eliminate an immediate hazard to study participants.
- The investigator will be responsible for the following:
  - Providing written summaries of the status of the study to the IRB/IEC annually or more frequently in accordance with the requirements, policies, and procedures established by the IRB/IEC.
  - Notifying the IRB/IEC of SAEs or other significant safety findings as required by IRB/IEC procedures.
  - Providing oversight of the conduct of the study at the site and adherence to GCP, IRB/IEC requirements, institutional requirements, and applicable laws and country-specific regulations.
- Adhering to the Protocol as described in this document and agreeing that changes to the Protocol procedures, with the exception of medical emergencies, must be discussed and approved, first, by the sponsor or its designee and, second, by the IRB/IEC. Each investigator is responsible for enrolling participants who have met the specified eligibility criteria.
- Retaining records in accordance with all local, national, and regulatory laws but for a minimum period of at least 2 years after the last marketing application approval in an ICH region and until there are no pending or contemplated marketing applications in an ICH region, or if not approved, 2 years after the termination of the test article for investigation to ensure the availability of study documentation should it become necessary for the sponsor or a regulatory authority to review.

- The investigator must not destroy any records associated with the study without receiving approval from the sponsor. The investigator must notify the sponsor or its designee in the event of accidental loss or destruction of any study records. If the investigator leaves the institution where the study was conducted, the sponsor or its designee must be contacted to arrange alternative record storage options.
- All eCRF data entered by the site (including audit trail), as well as computer hardware and software (for accessing the data), will be maintained or made available at the site in compliance with applicable record retention regulations. The sponsor will retain the original eCRF data and audit trail.

11.2. Data Management

Data management will be performed in a validated EDC system. The investigator will be provided with access to an EDC system so that an eCRF can be completed for each participant.

The site will be provided with eCRF completion guidelines for instructions on data entry in the eCRF. The study monitor will reference the Monitoring Plan in order to ensure that each issue identified is appropriately documented, reported, and resolved in a timely manner in accordance with the plan's requirements. Other data outside the EDC system required in the study conduct of the Protocol such as documents or results transmitted to the sponsor via a central laboratory or specialized technical vendors and, as designated by the sponsor, will have their own data flow management plans, study charters, or biomarker plans, as applicable.

The sponsor (or designee) will be responsible for:

- Managing the integrity of the data and the quality of the conduct of the study, such as ensuring that study monitors perform ongoing source data verification to confirm that data entered into the eCRF by authorized site personnel are accurate, complete, and verifiable from source documents; that the safety and rights of participants are being protected; and that the study is being conducted in accordance with the currently approved Protocol and any other study agreements, ICH GCP, and all applicable regulatory requirements.
- Managing and reconciling the data generated, and/or collected including documents and results such as laboratory or imaging data analyzed centrally by a designated vendor of the sponsor.

The investigator (principal investigator or subinvestigator) will be responsible for:

- Recording, or ensuring the recording of, all relevant data relating to the study in the eCRF.
- Delivering, or ensuring the delivery of, all other results, documents, data, know-how, or formulas relating to the study to the sponsor or designee electronically and/or centrally (eg, laboratory data, imaging data, biomarker data, photographs, diary data), or as otherwise specified in the Protocol.

- Maintaining adequate and accurate source documents and trial records that include all pertinent observations on each of the site's trial participants. Source data should be attributable, legible, contemporaneous, original, accurate, and complete. Changes to source data should be traceable, should not obscure the original entry, and should be explained if necessary (e.g., via an audit trail). Source data are in general all information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents (original records or certified copies).
- Verifying that data entries are accurate and correct by physically or electronically signing the eCRF.
- Maintaining accurate documentation (source data) that supports the information entered in the eCRF, or sent to a central vendor designated by the sponsor, or as described in other study and data flow manuals.
  - Source documents provide evidence for the existence of the participant and substantiate the integrity of the data collected. Source documents are filed and available at the investigator's site. Examples of source documents are original documents, data, and records (e.g., hospital records, electronic hospital records, clinical and office charts, laboratory notes, memoranda, participants' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate copies, microfiches, photographic negatives, microfilm or magnetic media, x-rays, participants' files, and e-records/records kept at the pharmacy, at the laboratories and at medico-technical departments involved in the clinical trial).
  - Data entered in the eCRF that are transcribed from source documents must be consistent with the source documents or the discrepancies must be explained. The investigator may need to request previous medical records or transfer records, depending on the study. Current applicable medical records must be available.
- Sending participants' data, either as unique samples, or copies, or photographs, to be evaluated centrally or analyzed centrally, or both, by a qualified vendor designated by the sponsor.
- Permitting study-related monitoring, sponsor audits, IRB/IEC review, and regulatory inspections by providing direct access to source data and other relevant clinical study documents.
  - Monitoring: Qualified representatives of the sponsor or its designee, study monitors, will monitor the study according to a predetermined plan. The investigator must allow the study monitors to review any study materials and participant records at each monitoring visit.

- Auditing: Qualified representatives of the sponsor or its designee may audit the clinical study site and study data to evaluate compliance with the Protocol, applicable local clinical study regulations, and overall study conduct. The investigator must allow the auditors to review original source records and study documentation for all participants.
- Regulatory inspection: Regulatory authorities may conduct an inspection of the study and the site at any time during the development of an investigational product. The investigator and staff are expected to cooperate with the inspectors and allow access to all source documents supporting the eCRFs and other study-related documents. The investigator must immediately notify the sponsor when contacted by any regulatory authority for the purposes of conducting an inspection.

11.3. Data Privacy and Confidentiality of Study Records

The investigator and the sponsor or its designee must adhere to applicable data protection laws and regulations. The investigator and the sponsor or its designee are responsible for ensuring that sensitive personal information is handled in accordance with local data protection laws (including but not limited to HIPAA and GDPR) as applicable. Appropriate consent for collection, use and disclosure and/or transfer (if applicable) of personal information must be obtained in accordance with local data protection laws.

Participant names will not be supplied to the sponsor or its designee. Only the participant number will be recorded in the eCRF; if the participant's name appears on any other document (eg, laboratory report), it must be obliterated on the copy of the document to be supplied to the sponsor or its designee. Study findings stored on a computer will be stored in accordance with appropriate technical and organizational measures as required by local data protection laws.

Records and documents, including signed ICFs, pertaining to the conduct of this study must be retained by the investigator for 10 years after study completion unless local regulations require otherwise. No records may be destroyed during the retention period without the written approval of the sponsor. No records may be transferred to another location or party without written notification to the sponsor.

11.4. Financial Disclosure

Before study initiation, all clinical investigators participating in clinical studies subject to FDA Regulation Title 21 CFR Part 54 – Financial Disclosure by Clinical Investigators (ie, "covered studies") are required to submit a completed Clinical Investigator Financial Disclosure form that sufficiently details any financial interests and arrangements that apply. For the purpose of this regulation, "clinical investigator" is defined as any investigator or subinvestigator who is directly involved in the treatment or evaluation of research participants, including the spouse and each dependent child of the clinical investigator or subinvestigator. These requirements apply to both US and foreign clinical investigators conducting covered clinical studies.

Any new clinical investigators added to the covered clinical study during its conduct must also submit a completed Investigator Financial Disclosure Form. During a covered clinical study, any changes to the financial information previously reported by a clinical investigator must be

reported to the sponsor or its designee. At the conclusion of the covered clinical study, the clinical investigators will be reminded of their obligations. In the event that the clinical investigator is not reminded, they nevertheless will remain obligated to report to the sponsor or its designee any changes to the financial information previously reported, as well as any changes in their financial information for a period of 1 year after completion of the covered clinical study.

11.5. Publication Policy

By signing the study Protocol, the investigator and his/her institution agree that the results of the study may be used by the sponsor, Incyte Corporation, for the purposes of national and international registration, publication, and information for medical and pharmaceutical professionals. Study results will be published in accordance with applicable local and national regulations. If necessary, the authorities will be notified of the investigator's name, address, qualifications, and extent of involvement. The terms regarding the publication of study results are contained in the agreement signed with the sponsor or its designee. A signed agreement will be retained by the sponsor or its designee.

The results of this study may be published or presented at scientific meetings. If this is foreseen, the investigator agrees to submit all manuscripts or abstracts to the sponsor before submission. This allows the sponsor to protect proprietary information and to provide comments.

The sponsor will comply with the requirements for publication of study results. In accordance with standard editorial and ethical practice, the sponsor will generally support publication of multicenter studies only in their entirety and not as individual site data. In this case, a coordinating investigator will be designated by mutual agreement.

Authorship will be determined in line with International Committee of Medical Journal Editors authorship requirements.

11.6. Study and Site Closure

The sponsor or designee reserves the right to close the study site or terminate the study at any time for any reason at the sole discretion of the sponsor. Study sites will be closed upon study completion. A study site is considered closed when all required documents and study supplies have been collected and a study-site closure visit has been performed.

The investigator may initiate study-site closure at any time, provided there is reasonable cause and sufficient notice is given in advance of the intended termination.

Reasons for the early closure of a study site by the sponsor or investigator may include but are not limited to:

- Failure of the investigator to comply with the Protocol, the requirements of the IRB/IEC or local health authorities, the sponsor's procedures, or GCP guidelines.
- Inadequate recruitment of participants by the investigator.
- Discontinuation of further study treatment development.

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APPENDIX A. INFORMATION REGARDING EFFECTIVENESS OF CONTRACEPTIVE METHODS AND DEFINITIONS

Definitions

WOCBP: A woman who is considered fertile following menarche and until becoming postmenopausal unless permanently sterile (see below).

Women in the following categories are not considered WOCBP:

- Premenarchal
- Premenopausal with 1 of the following:[a]
  - Documented hysterectomy
  - Documented bilateral salpingectomy
  - Documented bilateral oophorectomy
- Postmenopausal
  - A postmenopausal state is defined as no menses for 12 months without an alternative medical cause.
    - A high FSH level in the postmenopausal range may be used to confirm a postmenopausal state in women not using hormonal contraception or HRT. However, in the absence of 12 months of amenorrhea, confirmation with 2 FSH measurements in the postmenopausal range is required.
  - Females on HRT and whose menopausal status is in doubt will be required to use 1 of the nonhormonal, highly effective contraception methods if they wish to continue their HRT during the study. Otherwise, they must discontinue HRT to allow confirmation of postmenopausal status before study enrollment.

For male participants of reproductive potential[b]

The following methods during the Protocol-defined timeframe in Section 5.1 are highly effective:

- Use of a male condom plus partner use of an additional contraceptive method when having penile-vaginal intercourse with a woman of childbearing potential who is not currently pregnant.
- Vasectomy with medical assessment of the surgical success (verified by site personnel's review of the participant's medical records)
- Sexual abstinence[c]
  - Abstinence from penile-vaginal intercourse

The following are **not** acceptable methods of contraception:

- Periodic abstinence (calendar, symptothermal, post ovulation methods), withdrawal (coitus interruptus), spermicides only, and lactational amenorrhea method.
- Male condom with cap, diaphragm, or sponge with spermicide.
- Male and female condom used together.

Note: Men with a pregnant or breastfeeding partner must agree to remain abstinent from penile-vaginal intercourse or use a male condom during each episode of penile penetration.

For female participants who are WOCBP

The following methods during the Protocol-defined timeframe in Section 5.1 that can achieve a failure rate of less than 1% per year when used consistently and correctly are considered as highly effective birth control methods:

- Combined (estrogen and progestogen containing) hormonal contraception associated with inhibition of ovulation[d]
  - oral
  - intravaginal
  - transdermal
- Progestogen-only hormonal contraception associated with inhibition of ovulation[d]
  - oral
  - injectable
  - implantable[e]
- Intrauterine device[e]
- Intrauterine hormone-releasing system[e]
- Bilateral tubal occlusion[e]
- Vasectomized partner[e,f]
- Sexual abstinence[c]

FSH = follicle-stimulating hormone; HRT = hormone replacement therapy.

[a] Documentation can come from the site personnel's review of the participant's medical records, medical examination, or medical history interview.

[b] If the male participant has a partner with childbearing potential, the partner should also use contraceptives.

[c] In the context of this guidance, sexual abstinence is considered a highly effective method only if defined as refraining from heterosexual intercourse during the entire period of risk associated with the study treatments. The reliability of sexual abstinence needs to be evaluated in relation to the duration of the clinical study and the preferred and usual lifestyle of the participant.

[d] Hormonal contraception may be susceptible to interaction with the investigational medicinal product, which may reduce the efficacy of the contraception method. In this case, 2 methods of contraception should be used.

[e] Contraception methods that in the context of this guidance are considered to have low user dependency.

[f] Vasectomized partner is a highly effective method of avoiding pregnancy provided that partner is the sole sexual partner of the WOCBP study participant and that the vasectomized partner has received medical assessment of the surgical success.

Source: Clinical Trials Facilitation and Coordination Group 2020.

APPENDIX B. LIST OF PARENT PROTOCOLS

INCB 54828-101 (FIGHT-101)

INCB 54828-201 (FIGHT-201)

INCB 54828-202 (FIGHT-202)

APPENDIX C. COVID-19 PANDEMIC MITIGATION STRATEGIES AND INSTRUCTIONS

The COVID-19 global pandemic presents challenges to the ongoing conduct of clinical trials. In line with regulatory guidance regarding clinical trial execution during the pandemic, the sponsor has issued the following Protocol considerations to ensure participant safety is maintained and adequate benefit/risk analyses are applied relative to participation in the study and the completion of study procedures and objectives while maintaining the investigational product supply chain.

Recognizing the dynamic nature and flexibility required to manage the impact of the pandemic on this clinical trial, additional details will be incorporated into respective study manuals and site-specific monitoring plans as applicable, with institutional requirements as warranted, and communicated and discussed with investigative sites as needed. Relevant test results will be documented in the eCRF, and applicable changes to the ICF will be made and monitored.

Given the critical medical need for alternative treatments for patients in the setting of recurrent advanced/metastatic endometrial cancer and the importance of continuing cancer research, a positive COVID-19 screening test should not result in definitive exclusion. Participants with a positive COVID-19 test during screening may be reassessed for eligibility in the study only after normalization of their COVID-19 screening test and clinical recovery as per the investigator's evaluation.

SARS-CoV-2 Infection and Participation in the Study

Benefit/risk assessment in the context of the COVID-19 pandemic is provided in Section 2.3.1. During the COVID-19 pandemic, additional risks to participants exist either related to going to a health care facility or as a result of study-related activities. It is at the principal investigator's discretion to balance the risk/benefit while considering the participant's safety, existing comorbidities, and current malignancy. In addition, country-specific requirements are to be followed with regard to COVID-19 testing.

Study Site Visits

If local travel restrictions, isolation requirements, or the investigator's benefit/risk assessment determines it to be unsafe for participants to attend study visits at the investigational site, the site staff may elect to pursue the following:

- In order to minimize participant risk, study visits may be conducted via telemedicine modalities (phone or video) or as per site institutional guidelines. At a minimum, a review of AEs and concomitant medications must be completed. On-site visits should be conducted whenever feasible and are required for administration of study treatment. The participant may also be asked to undergo additional safety laboratory assessments.

- In order to support investigator oversight of participant safety and disease management, the participant may be asked to undergo some laboratory tests or study procedures (eg, imaging) at a local laboratory or facility closer to the participant's residence rather than at the investigational site. In this case, the study physician will provide the participant with the list of parameters to be checked. These tests should be performed in certified laboratories and ensure data may be transferred to the investigational site.
- Some tests, such as ECG or computed tomographic scan assessments, may require longer windows due to the COVID-19 pandemic and may be performed outside the regularly scheduled visit window or may be conducted at the next scheduled visit. It is the investigator's responsibility to check with the facility (if performed at a different facility) that the data will be obtained and available for evaluation. General procedures performed outside of protocol time windows will be captured as protocol deviations due to COVID-19 in the eCRF.

Study Treatment Management in the Event of SARS-CoV-2 Infection

If a participant develops a SARS-CoV-2 infection, the event should be reported as an SAE (if it meets the SAE definition requirements) and appropriate medical intervention provided.

Postbaseline COVID-19 testing should follow country-specific requirements depending on the extent of the COVID-19 pandemic, local institutional guidance, or the investigator's clinical judgment. For participants who are diagnosed with COVID-19 during the study (positive COVID-19 test) or presumed (test pending/clinical suspicion) to be affected by SARS-CoV-2 infection, study treatment should be delayed until COVID-19 test normalization and clinical recovery. Prior to restarting treatment, the study medical monitor should be notified regarding the participant's condition; that is, the participant should be afebrile for 72 hours and SARS-CoV-2–related symptoms (if any) should have recovered for a minimum of 72 hours.

Safety monitoring following COVID-19 infection should be implemented as per institutional guidance or clinical judgment (eg, coagulation factors). Concomitant medication administered for treatment of SARS-CoV-2 infection should be carefully considered for potential drug-drug interactions and recorded in the clinical database (EDC).

COVID-19 Vaccination

Participants may receive the COVID-19 vaccine as long as it is not a live vaccine. A live COVID-19 vaccine requires prior consultation with the medical monitor. COVID-19 vaccination will be captured in the eCRF as a concomitant medication. Administration of study treatment may be delayed to ensure vaccination is completed and acute AEs (if any) are managed. The medical monitor may be consulted if needed.

Clinical Trial Monitoring

Study monitoring visits could be postponed; however, the site monitor and sponsor will continue to employ off-site monitoring practices such as routine communication methods (eg, phone calls, emails, video visits) with the sites to get information on trial progress, participant status, and information on issue resolution. The study monitor may remotely review data entered into the

EDC for accuracy and completeness if allowed by the national regulatory body, investigational site, and/or in compliance with local authorities.

Reimbursement of Additional Expenses

The sponsor will reimburse for any extraordinary expenses, keeping appropriate documentation as evidence (eg, travel expenses for the local laboratory visit[s], the costs of local [proximate] laboratory tests).

APPENDIX D. PROTOCOL AMENDMENT SUMMARY OF CHANGES

Not applicable.

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