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Protocol for Study M25-268

Idiopathic Pulmonary Fibrosis: A Phase 2a Platform Study of Investigational Products for the Treatment of Adult Subjects

VERSION:	1.3.1 (European Union Only)	DATE:	22 April 2026
SPONSOR:	AbbVie Inc.*	PLANNED NUMBER OF SITES:	125
ABBVIE INVESTIGATIONAL PRODUCT:	ABBV-142	EU CT:	2024-518013-25

FULL TITLE: A Phase 2a Multicenter Platform Study of Investigational Products for the Treatment of Adult Subjects with Idiopathic Pulmonary Fibrosis

Incorporating Versions 1.0, 1.3 (European Union Only), and 1.3.1 (European Union Only)

SPONSOR/EMERGENCY MEDICAL CONTACT:* [redacted] MD, PhD
AbbVie Inc.
1 North Waukegan Road
North Chicago, IL 60064

Office:
Mobile
Email: [redacted]

EMERGENCY 24-hour Number: +1 973-784-6402

*For European Union countries: the sponsor is AbbVie Deutschland GmbH & Co. KG. The specific contact details of the AbbVie legal/regulatory entity (person) within the relevant country are provided within the clinical trial agreement with the Investigator/Institution and in the Clinical Trial Application with the Competent Authority.

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1 PROTOCOL SUMMARY

1.1 Protocol Synopsis

Protocol Title:

A Phase 2a Multicenter Platform Study of Investigational Products for the Treatment of Adult Subjects with Idiopathic Pulmonary Fibrosis

Background and Rationale:

Idiopathic Pulmonary Fibrosis (IPF) is a rare chronic lung disease characterized by progressive, irreversible lung fibrosis, dyspnea, and loss of lung function. IPF is associated with substantial loss of quality of life and reduced life expectancy. Median survival in the absence of treatment is approximately 3 years with death most often due to respiratory failure.

Current standard of care therapies approved for treatment of IPF have been shown to reduce the rate of disease progression as measured by loss of forced vital capacity (FVC). However, disease progression and premature death still occur on these therapies. Furthermore, current standard of care therapies are associated with a high frequency of adverse effects, which frequently lead to treatment discontinuation. Thus, there is still a substantial unmet need for new therapies with greater efficacy and tolerability.

This study is a Phase 2a proof of concept platform study that will evaluate the efficacy and safety of multiple investigational products that can be assessed [redacted] in subjects with IPF.

Objective and Endpoint:

The objective is to evaluate the safety, tolerability, and efficacy of investigational products [redacted] in adult subjects with IPF.

Primary Endpoint:

- Absolute change from baseline in forced vital capacity (mL) at Week 24.

Secondary Endpoints, unless otherwise specified in the substudy specific appendixes, are:

- Absolute change from baseline in FVC (mL) at Week 52.
- Relative change from baseline in FVC (mL) at Week 24.
- Relative change from baseline in FVC (mL) at Week 52.
- Absolute and relative change from Baseline in FVC % predicted at Week 24.
- Absolute and relative change from Baseline in FVC % predicted at Week 52.
- Time to first ≥ 10% absolute decline in FVC% predicted.
- Time to first ≥ 5% absolute decline in FVC% predicted.

Please refer to the substudy specific appendixes for additional endpoints.

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Investigator(s):

Multicenter

Study Site(s):

There will be approximately 125 sites across approximately 25 countries worldwide.

Study Population:

The study will enroll subjects with IPF who are ≥ 40 years old and have a diagnosis of IPF within 7 years, with or without concomitant IPF-approved therapy.

Investigational Plan:

The study is a Phase 2a proof of concept platform study in IPF subjects. This platform study is designed as [redacted]

[redacted]

If additional [redacted] are added or [redacted]

An external Independent Data Monitoring Committee (IDMC) that is independent to AbbVie will safeguard the interests of trial subjects, assess the safety of the interventions during the trial, as well as monitor the integrity and interpretability of the trial. The IDMC will provide recommendations to the sponsor regarding ongoing trial conduct or modifications to the trial.

[redacted]

The duration of each [redacted] is from the Screening Visit to the last planned phone call or study site visit. Further details are provided in each [redacted] appendix.

[redacted]

[redacted]

Key Eligibility Criteria:

Subjects are eligible to be included in the study if they meet all of the eligibility criteria specified in the general section of the Master Protocol and at least one of the substudies. All eligibility criteria specified in the general

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section of the Master Protocol apply to all substudies. Any additional substudy-specific criteria will be described in the [redacted]

Inclusion Criteria:

- Patients aged ≥ 40 years.
- History of IPF diagnosis within 7 years of screening visit.
- Confirmed diagnosis of IPF:

  a. Diagnosis of IPF based on 2022 ATS/ERS/JRS/ALAT Guideline as confirmed by the investigator based on chest high-resolution Computed Tomography (HRCT) scan taken within 12 months of screening visit and, if available, (historical) surgical lung biopsy or transbronchical lung cryobiopsy,

  AND

  b. Usual Interstitial Pneumonia (UIP) or "probable UIP" HRCT pattern consistent with the clinical diagnosis of IPF, as confirmed by [redacted] review prior to randomization visit. Patients with an "Indeterminate" HRCT finding are eligible if a clinical diagnosis of IPF can be confirmed [redacted] based on (historical) surgical lung biopsy or cryobiopsy demonstrating a "UIP" or "Probable UIP" histopathology pattern. Subjects with an "Alternative diagnosis" HRCT finding are eligible if clinical diagnosis of IPF can be confirmed locally based on (historical) surgical lung biopsy or cryobiopsy demonstrating a "UIP" histopathology pattern.

- Either stable treatment with antifibrotics for at least [redacted] prior to screening visit or not treated with antifibrotics for at [redacted] prior to screening visit.
- FVC ≥ 45% of predicted normal at screening visit.
- Percent predicted diffusing capacity of the lungs for carbon monoxide (DLCO) corrected for hemoglobin (Hb) in a single breath ≥ 25% at screening visit.

Exclusion Criteria:

- Relevant airways obstruction defined as pre-bronchodilator forced expiratory volume 1 second (FEV_1)/FVC < 0.7 at screening visit.
- Acute IPF exacerbation diagnosis within 4 months prior to screening and/or during the screening period (investigator determined).
- Lower respiratory tract infection (e.g., infectious pneumonia, active tuberculosis) requiring antimicrobials within 4 weeks before screening visit and/or during the screening period.

Study Drug and Duration of Treatment:

[redacted] All subjects will receive the designated therapy according to each [redacted]

Additional [redacted] may be added [redacted] via a protocol amendment prior to initiation.

Date of Protocol Synopsis:

22 April 2026

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1.2 Study Schema

The general schematic of the study is shown in Figure 1, and is subject to change [redacted] are [redacted] Further details regarding the overall study design are provided in Section 4 and study procedures are located in Section 8.

See Section 5 for information regarding eligibility criteria of the [redacted] Protocol.

Details on each substudy and treatment arm are available in the [redacted]

[redacted]

1.3 Activity Schedule

Please refer to [redacted] for the required activities to be followed. The individual activities are described in detail in Section 8.

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2 INTRODUCTION

2.1 Background and Rationale

Why Is This Study Being Conducted?

IPF is a rare chronic lung disease characterized by progressive, irreversible lung fibrosis, dyspnea, and loss of lung function. IPF is associated with substantial loss of quality of life and reduced life expectancy.[1] Median survival in the absence of treatment is approximately 3 years with death most often due to respiratory failure.[2]

Current standard of care therapies approved for treatment of IPF have been shown to reduce the rate of disease progression as measured by loss of FVC. However, disease progression and premature death still occur on these therapies. Furthermore, current standard of care therapies are associated with a high frequency of adverse effects, which frequently lead to treatment discontinuation.[3] Thus, there is still a substantial unmet need for new therapies with greater efficacy and tolerability.

This is a Phase 2a proof of concept platform study that will evaluate the efficacy and safety of multiple investigational products that can be assessed as [redacted] in subjects with IPF. The platform design will maximize the operational efficiency of trial conduct in this rare disease population, and may help minimize the total number of subjects assigned to the placebo arms.

Refer to Section 1.2, Study Schema, and Section 1.3, Activity Schedule, for more information on the study design.

2.2 Benefits and Risks to Subjects

The benefit risk assessment of each substudy is discussed separately in each [redacted]

3 OBJECTIVES AND ENDPOINTS

3.1 Objectives, Hypotheses, and Estimands

Objective

The objective is to evaluate the safety, tolerability, and efficacy of investigational products as [redacted] in adult subjects with IPF.

Objectives and clinical hypotheses [redacted] are presented in each [redacted]

The estimands to the primary objective of each [redacted] are described in each [redacted]

3.2 Primary Endpoint

The primary endpoint is the absolute change from baseline in FVC (mL) at Week 24.

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3.3 Secondary Endpoints

The secondary endpoints are listed as follows:

- Absolute change from baseline in FVC (mL) at Week 52 [redacted].
- Relative change from baseline in FVC (mL) at Week 24.
- Relative change from baseline in FVC (ml) at Week 52 [redacted]
- Absolute and relative change from Baseline in FVC % predicted at Week 24.
- Absolute and relative change from Baseline in FVC % predicted at Week 52 [redacted]

Additional endpoints may be specified in individual [redacted]

3.4 Additional Endpoints

In addition, the following endpoints will be analyzed [redacted]

3.5 Safety Endpoints

Safety evaluations include AE monitoring, vital sign measurements, ECG variables, and clinical laboratory testing (hematology, chemistry, and urinalysis) as measures of safety and tolerability for the entire study duration. Clinically significant abnormal changes in physical examination findings will be reported as AEs.

3.6 Pharmacokinetic Endpoints

Plasma or serum concentrations (as applicable) for each substudy will be obtained at the visits specified in the individual [redacted]

Plasma or serum concentrations (as applicable) for each substudy will be summarized and may be used to develop population PK models for estimation of PK parameters. Furthermore, pharmacokinetic data for each substudy from this study may be combined with other studies for the development of population PK models. Exposure-response analyses may be conducted to characterize relationships between study drug exposures and clinical efficacy and safety endpoints and exploratory biomarkers, as appropriate. Additional analyses may be performed if useful and appropriate. Results from the population PK and exposure-response analyses will not be included in the clinical study report and may be reported separately.

For study drugs that are monoclonal antibodies, immunogenicity will be assessed by using a tiered approach for detecting ADAs. Neutralizing ADAs may be evaluated if useful for the interpretation of results.

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3.7 Biomarker Research

Biospecimens (e.g., blood, plasma, serum) and one optional whole blood DNA sample will be collected at specified time points as described in the [redacted] to support biomarker research.

Biospecimen sample analysis may be used to generate [redacted] Types of biomarkers derived from biospecimens may include nucleic acids, proteins, lipids, and/or metabolites, either free or in association with particular cell types. The samples may also be used to develop new therapies, research methods, diagnostic tests or technologies and may be analyzed as part of a multi-study assessment of factors influencing the subjects' response to the study treatment (or treatments of the same or similar class) or the development and progression of the subjects' disease or related conditions. Assessments may include, but are not limited to, biomarkers related to the pathway(s) targeted by the study drug or those believed to be related to the disease(s) being studied [redacted]

This research may be exploratory in nature; as such, the results should not be used for patient management, may not be included with the clinical study report, and may be performed at a non-GLP laboratory. Further details regarding the biomarker research sampling and collection are located in Section 8.6.

Provision of biospecimens for biomarker research will not be collected from sites where local regulations do not allow for the collection, use, and storage of samples as described in the protocol. The samples may be retained for up to 20 years after study completion or per local requirements.

4 INVESTIGATIONAL PLAN

4.1 Overall Study Design and Plan

This is a Phase 2a proof of concept platform study in IPF subjects. This platform study is designed as [redacted]

The general sections (Section 1 through Section 20) describe the framework for the common study elements of the platform study. The accompanying [redacted]s) (Section 21 and beyond) will present the substudy-specific information. Refer to the individual [redacted] for specific details about each substudy design and plan.

The appendix for randomization schedule (Section 16) describes the details of the randomization schedule [redacted]

Additional [redacted] can be included subsequently via a protocol amendment prior to initiation and will be included as a [redacted] If additional [redacted] are added or enrollment of existing ones are completed, the [redacted] schedule may be updated accordingly, and subjects may be randomized

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among all [redacted] according to the updated [redacted] scheme. Details on [redacted] are available in Section 16.

Data from [redacted] Therefore, additional [redacted] may enroll fewer subjects in the placebo arm [redacted]

The duration of each substudy may include a Screening Period (approximately 45 days) followed by an up to 52-week Treatment Period (Baseline - Week 52), and an optional open-label treatment period may be included as [redacted] A follow-up visit/phone call will occur after the last dose of study drug, and the duration of the follow-up period will be specified [redacted] e.g., 5 half-lives of the investigational product). The screening period may be extended to [redacted] in case of [redacted] after consultation with the sponsor's medical contact. If Day 1 visit cannot be performed in this extended timeframe, the patient will have to be screen failed.

The study site visits will occur as outlined in the Activity Schedule for each [redacted] Additional site visits for each [redacted] may be required as specified in [redacted] For further details, the schedule of activities may be found in [redacted] and the general Study Schematic may be found in Section 1.2.

[redacted]

4.2 Discussion of Study Design

Choice of Control Group

Each substudy under the Master Protocol may have its own control group, please refer to [redacted] for specific details.

Appropriateness of Measurements

Standard statistical, clinical, and laboratory procedures will be utilized in this study. All efficacy and safety-related measurements in this study are standard for assessing disease activity in subjects with IPF. All clinical and laboratory procedures in this study are standard and generally accepted.

Suitability of Subject Population

This study is designed to enroll subjects with a confirmed diagnosis of IPF, with or without concomitant [redacted] therapy.

Race and ethnicity will be collected for the purpose of the clinical trial to document the diversity and representativeness of the study population and allow evaluation of the impact, if any, of such

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demographic factors on response to treatment. As such, these data are [redacted] for the scientific objectives of the clinical trial and for the medical treatment of the subjects.

Selection of Doses in the Study

The selected study drug dosing regimens and rationales for dose selection are presented in [redacted]

4.3 Treatment After End of Study

As the subject nears study completion, the investigator will discuss the appropriate subsequent treatment with the subject.

4.4 Start and Completion of the Study

The start-of-study is defined as the date of the first site activated.

The end of each substudy is defined as the end date of the substudy participation by the last subject in the last country where the substudy was conducted (follow-up Visit/Phone call as defined in the [redacted] The specific duration of each substudy is defined in Section 4.1, which may include the Screening Period, Treatment Period, an optional open-label treatment period, and a follow-up visit or phone call.

Irrespective of the outcome of each substudy, within 1 year from the end of the substudy, the Sponsor will submit to the EU database a summary of the substudy results. The content of that summary will be done in compliance with the EU CTR.

The end-of-study is defined as the date of end-of-study participation by the last subject in the last country where the study was conducted (follow-up visit/phone call as defined in the [redacted]

For EU CTR submissions, irrespective of the outcome of this study, within 1 year from the end of the study, the Sponsor will submit to the EU database a summary of the study results. The content of that summary will be done in compliance with the EU CTR.

5 STUDY POPULATION

5.1 Eligibility Criteria

Subjects are eligible to be included in the study if they meet all the inclusion criteria and none of the exclusion criteria specified in this Section of the Master Protocol.

Any additional [redacted] will be described in the [redacted] Subjects will be screened for each [redacted] as per the screening activities listed in the [redacted]

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Inclusion Criteria

Consent

1. Subjects if judged by the investigator to have decision making capacity must voluntarily **sign and date an informed consent**, approved by an IEC/IRB, prior to the initiation of any screening or [redacted]

Demographic and Laboratory Assessments

2. **Individuals** at least 40 years old on the day of signing the ICF.

[redacted]

4. Are willing and able to comply with procedures required in this protocol.
5. Subjects must not be incarcerated and must be freely willing and able to provide informed consent (e.g., adults under legal protection measure [e.g., under guardianship/curatorship] or unable to express their consent and select adults under psychiatric care). Investigator's discretion should be applied.

Disease/Condition Activity

6. History of IPF diagnosis within 7 years prior to the screening visit, as per applicable ATS/ERS/JRS/ALAT guideline at the time of diagnosis.
7. Subject meets the following disease criteria:
   - Confirmed diagnosis of IPF (Appendix E)
     a) Diagnosis of IPF based on 2022 ATS/ERS/JRS/ALAT Guideline as confirmed by the investigator based on chest HRCT scan taken within [redacted] available [redacted]

        AND

     b) "UIP" or "probable UIP" HRCT pattern consistent with the clinical diagnosis of IPF, as confirmed by [redacted] review prior to randomization visit. Subjects with an "Indeterminate" HRCT finding are eligible if [redacted] demonstrating a "UIP" or "Probable UIP" histopathology pattern. Subjects with an "Alternative diagnosis" HRCT

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finding are eligible if [redacted] demonstrating a "UIP" histopathology pattern.

- FVC ≥ [redacted] of predicted normal at screening visit.
- Percent predicted diffusing capacity of the lungs for carbon monoxide (DLCO) corrected for hemoglobin [Hb] in a single breath [redacted]% at screening visit

8. Subjects are judged to be in a stable general health, as determined by the investigator based upon the results of a medical history, physical examination, laboratory profile, and a 12-lead ECG performed during the Screening Period.

Contraception

9. Pregnancy testing in female subjects of childbearing potential [refer to Section 8.13 Pregnancy Tests (Serum and Urine)]:
   - Subjects must have a **negative serum pregnancy test** at the Screening Visit and a negative urine pregnancy test at baseline prior to the first dose of study drug.
   - Subjects with a borderline serum pregnancy test at Screening must have absence of clinical suspicion of pregnancy or other pathological causes of borderline results and a serum pregnancy test ≥ 3 days later to document continued lack of a positive result (unless prohibited by local requirements).
   - Subjects with a urine pregnancy test at Baseline that is borderline or ambiguous must have a serum pregnancy test. In such cases, the subject must be excluded from participation if the serum pregnancy result is positive.
10. Female subjects of childbearing potential must practice at least 1 protocol-specified **method of birth control**, during the study and through the end of the follow-up period after the last dose of study drug as specified in substudy protocol. Female subjects of nonchildbearing potential do not need to use birth control.
11. Female subject who is not **pregnant or breastfeeding, and is not considering becoming pregnant** or donating eggs during the study through the end of the follow-up period after the last dose of study drug as specified in substudy protocol.

Concomitant Medications

12. No recent changes or planned changes to the dose or regimen for IPF therapy, defined as [redacted]

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Exclusion Criteria

Subject History

1. History of any malignancy up to 5 years prior screening, except for successfully treated nonmelanoma skin cancer or localized carcinoma in situ of the cervix.
2. History of clinically significant (per investigator's judgment) **drug or alcohol abuse** within the last 6 months.
3. History of clinically significant medical conditions or any other reason that the investigator determines would interfere with the subject's participation in this study or would make the subject an unsuitable candidate to receive study drug.
4. History of an allergic reaction or significant sensitivity to constituents of the study drug (and its excipients) and/or other products in the same class.
5. Clinically relevant or significant ECG abnormalities (per investigator's judgement), including ECG with QTcF > 450 msec (males) or > 470 msec (females).



8. In the opinion of the Investigator, other clinically significant pulmonary abnormalities.
9. Acute IPF exacerbation diagnosis within [redacted] prior to screening visit and/or during the screening period [redacted]. For acute IPF exacerbation criteria, refer to Section 9.1.
10. Lower respiratory tract infection (e.g., infectious pneumonia, active tuberculosis) requiring antimicrobials within 4 weeks before screening visit and/or during the screening period.
11. History of stroke within 6 months prior to screening.
12. History of clinically significant cardiac disease or uncontrolled atrial or ventricular cardiac arrhythmias per investigator's assessment.
13. Major surgery (major according to the investigator's assessment) performed within 3 months prior to randomization or planned during the trial period, e.g., hip replacement. Registration on lung transplantation list would not be considered as planned major surgery.
14. Inability to refrain from smoking on study visit days.

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15. High likelihood of lung transplantation (per investigator's assessment) within 6 months after Day 1.

[redacted]

17. Subjects with the following chronic or active infections:
    - Active HBV or HCV infection, defined as:
        - HBV: HBs Ag positive (+) test or detected sensitivity on the HBV DNA PCR qualitative test for subjects who are HBc Ab positive (+) (and for HB surface antibody [HBs Ab] positive [+] subjects where mandated by local requirements). For additional details see Section 8.13 (Clinical Laboratory Tests).
        - HCV: HCV RNA detectable in any subject with positive HCV Ab.
18. Are infected with HIV, defined as confirmed positive anti-HIV Ab test.
19. Subjects with a significant disease or condition other than IPF, which in the opinion of the investigator, may put the patient at risk because of participation, interfere with study procedures, or cause concern regarding the patient's ability to participate in the study or any medical condition which could lead to a life expectancy < 12 months.

Concomitant Medications

20. Subject treated with **any investigational drug** within 30 days or 5 half-lives of the drug (whichever is longer) prior to the first dose of study drug or is currently enrolled in another clinical study or was previously enrolled in this study.

5.2 Contraception

Please refer to [redacted]

5.3 Prohibited Medications and Therapy

In addition to the medications listed in the eligibility criteria, other prohibited medications and therapy applicable for each substudy will be discussed separately in the [redacted]

5.4 Prior and Concomitant Therapy

[redacted] Use of inhaled bronchodilators is permissible except within the washout time required before spirometry (refer to Section 8.15).

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Any medication or vaccine (including over-the-counter or prescription medicines, vitamins, and/or herbal supplements, supplemental oxygen) that the subject is receiving at the time of enrollment or receives during the study must be recorded from the Screening Visit through the follow-up visit (as specified in the [redacted]

Any questions regarding concomitant or prior therapy should be raised to the AbbVie emergency contact. Information regarding potential drug interactions with study drug can be located in the respective Investigator's Brochure.

Subjects must be able to safely discontinue any prohibited medications 5 half-lives or 30 days, whichever is longer, prior to initial study drug administration, unless specified differently in the eligibility criteria (Section 5.1). Subjects must be consented for the study prior to discontinuing any prohibited medications for the purpose of meeting study eligibility.

[redacted]

5.5 Screen Failures

A screen failure occurs when a subject who has consented to participate in the clinical study is not subsequently assigned to study treatment. A minimal set of screen failure information is required to ensure transparent reporting of screen failure subjects to meet the CONSORT publishing requirements and to respond to queries from regulatory authorities. Minimal information includes demography, screen failure details, eligibility criteria, and any SAE.

[redacted] Individuals who do not meet the criteria for participation in this study (screen failure) may be rescreened up to [redacted] Rescreened subjects will not be assigned a new subject number for every screening/rescreening event if the subject is rescreened for the same [redacted]

If a subject is rescreened, all screening assessments will be repeated, with the exception of the HRCT, and FSH (if applicable). Subjects who have exclusionary laboratory parameter (s) per criterion Section 5.1 are allowed to retest on the related panel(s) (e.g., exclusionary ALT requires a repeat chemistry panel) within the same screening period and must meet all inclusion and none of the exclusion criteria on the panel that is repeated. If the retest result(s) are also exclusionary, the subject is considered screen failure.

Subjects who are outside of the initial screening period as specified [redacted] with the exception of the [redacted] from the rescreening visit; and the FSH (if applicable) [redacted]

Subjects may be screened for all substudies that are recruiting subjects at the time of their screening.

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6 STUDY DRUG

Study drug information will be described in the applicable [redacted]

6.1 Treatments Administered

Study drugs refer to drugs that are used (or can be used) in this study to assess the safety and the efficacy of the Investigational Product. Investigators will assess the relationship of AEs to the use of study drugs.

AbbVie will provide study drug or matching placebo as indicated in each [redacted] AbbVie provided study drug should not be substituted or alternately sourced unless otherwise directed by AbbVie.

Upon receipt, study drug should be stored as specified on the label and kept in a secure location. Each kit will contain a unique kit number. This kit number is assigned to a subject via IRT and encodes the appropriate study drug to be dispensed at the subject's corresponding study visit. Study drug will only be used for the conduct of this study.

Upon completion of or discontinuation from study treatment, all original study drug units (containing unused study drugs) will be returned to the sponsor (or designee) or destroyed on site. All return or destruction procedures will be according to instructions from the sponsor and according to local regulations following completion of drug/device accountability procedures.

Study drug administration instructions will be provided separately in the pharmacy manual.

6.2 Packaging and Labeling

All study drugs will be supplied in quantities sufficient to accommodate the study design.

Each kit will be labeled as required per country requirements and this label must remain affixed to the kit. All blank spaces in the label should be completed by site staff prior to dispensing to the subject.

6.3 Storage and Disposition of Study Drug

Refer to the applicable [redacted] for information regarding study intervention storage and disposition.

The investigational products are for investigational use only and are to be used only within the context of this study. The study drug supplied for this study must be maintained under adequate security and stored under the conditions specified on the label until dispensed for subject use or destroyed on site as appropriate.

Sites are responsible for maintaining the investigational study drug and devices according to the storage conditions specified on the clinical label and monitoring for temperature excursions with the use of a calibrated continuous temperature monitoring device or monitoring systems. Specific guidance on appropriate temperature monitoring and temperature excursions reporting requirements will be provided separately.

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6.4 Preparation/Reconstitution of Dosage Form

Study drug preparation instructions will be provided separately in the pharmacy manual.

6.5 Selection and Timing of Dose for Each Subject

Refer to the applicable [redacted] for information regarding selection and timing of dose for each subject.

6.6 Randomization/Drug Assignment

All subjects will be assigned a unique identification number by the IRT at the screening visit. For subjects who rescreen in the same substudy (see Section 5.5), the screening number assigned by the IRT at the initial screening visit should be used.

The sponsor may review pre-enrollment screening data for eligibility prior to enrollment and/or randomization of the subjects. For subjects who meet the study selection criteria, the IRT will assign a randomization number that will encode the subject's treatment group assignment according to the randomization schedule. A subject may not be enrolled in multiple substudies except for biomarker substudies.

For subjects who do not meet the study selection criteria, the site personnel must access the IRT system and identify the subject as a screen failure.

Subjects who are enrolled will retain their subject number assigned at the screening visit throughout the study. Upon receipt of study drug, the site will acknowledge receipt in the IRT system.

Details of randomization are presented in Section 16 and [redacted]

Study drug must not be dispensed without contacting the IRT system. Study drug may only be dispensed to subjects enrolled in the study through the IRT system. The site will also contact the IRT system to provide visit date information and study drug accountability information during visits specified in [redacted]

For substudies with double blind design, the IRT will provide access to unblinded subject treatment information in the case of a medical emergency.

Contact information and user guidelines for IRT use will be provided to each site.

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7 DISCONTINUATION OF STUDY TREATMENT AND SUBJECT DISCONTINUATION/WITHDRAWAL

7.1 Withdrawal of Subjects and Discontinuation of Study

AbbVie may terminate the Master Study or any substudy prematurely, either in its entirety or at any site. The Master Study or any substudy will be discontinued or terminated in case of an unacceptable risk, any relevant toxicity, or a negative change in the risk/benefit assessment. If AbbVie terminates the study or any substudy for safety reasons, AbbVie will promptly notify the investigator. The investigator may also stop the study or any substudy at their site if they have safety concerns and promptly notify the sponsor if this occurs. Advance notice is not required by either party if the study is stopped due to safety concerns.

A subject may voluntarily withdraw or be withdrawn from the study at any time for reasons including, but not limited to following:

- The investigator believes it is in the best interest of the subject.
- The subject requests withdrawal from the study.
- In the opinion of both, the investigator and sponsor, the subject is significantly noncompliant with study procedures, which would put the subject at risk for continued participation in the trial.

Subjects must have study drug treatment discontinued immediately if any of the following occur:

- Clinically significant abnormal laboratory results or AEs, which rule out continuation of the study drug, as determined by the investigator and/or the AbbVie Therapeutic Area Medical Director.
- Eligibility criteria violation was noted after the subject started study drug and continuation of the study drug would place the subject at risk. NOTE: intentional/prospective deviations from the protocol are NOT allowed.
- Introduction of prohibited medications or dosages and continuation of the study drug would place the subject at risk.
- The subject becomes pregnant while on study drug.
- Arrhythmia or conduction abnormality, including, but not limited to prolonged QTcF, where the severity is categorized as CTCAE (Version 5.0 or most recent version) Grade 3 or higher (QTc ≥ 501 ms on at least 2 separate ECGs) [at least 2 minutes apart] obtained within 10 minutes of the initial recording.
- Subject underwent lung transplantation during the study.
- If any of the following hepatic liver test criteria are met, study drug must be discontinued immediately, the medical monitor must be notified, and a supplemental hepatic case report form must be completed (see Section 9.1 Complaints and Adverse Events and Section 9.3 Toxicity Management):

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- ALT or AST > 8 × ULN; OR
- Confirmed ALT or AST > 5 x ULN for more than 2 weeks; OR
- ALT or AST > 3 x ULN and total bilirubin > 2 × ULN (with mixed or direct predominance) or INR > 1.5; OR
- ALT or AST > 3 × ULN with presentation of related symptoms (fatigue, nausea, vomiting, right upper quadrant pain or tenderness, fever, rash, and/or eosinophilia > 5%).

Any additional substudy-specific withdrawal of subjects and discontinuation of study criteria will be described in the applicable [redacted]

All attempts must be made to determine the date of the last study drug dose and the primary reason for discontinuation of study drug or study participation. The information will be recorded on the appropriate eCRF page. However, these procedures should not interfere with the initiation of any new treatments or therapeutic modalities that the investigator feels are [redacted] to treat the subject's condition. Following discontinuation of study drug, the subject will be treated in accordance with the investigator's best clinical judgment, irrespective of whether the subject decides to continue participation in the study.

For subjects to be considered lost to follow-up, reasonable attempts must be made to obtain information on the subject's final status. At a minimum, 2 telephone calls must be made and 1 certified letter must be sent and documented in the subject's source documentation.

7.2 Follow-Up After Subject Discontinuation of Study Drug or from Study

To minimize missing data for efficacy and safety assessments, subjects who prematurely discontinue study drug treatment should continue to be followed at a Premature Discontinuation visit (PD visit) and a follow-up visit after the last dose of study drug to ensure that all treatment-emergent AEs/SAEs have been resolved, unless subjects have decided to discontinue the study participation entirely (withdrawal of informed consent). Subjects should be advised on the continued scientific importance of their data even if they discontinue treatment with study drug early. If a subject is willing, a follow-up phone call after the last dose of study drug may be completed to ensure all treatment-emergent AEs/SAEs have been resolved.

If a subject withdraws from study follow-up or withdraws permission for the collection of their personal data, the study staff may still use available public records to obtain information about survival status only, as appropriate per local regulations.

In the event a subject withdraws consent from the clinical study, biomarker research will continue unless the subject explicitly requests analysis to be stopped. When AbbVie is informed the subject has withdrawn and no longer wishes biomarker samples research to continue, samples will not be analyzed and no new biomarker analysis data will be collected for the withdrawn subject or added to the existing data or database(s) and samples will be destroyed. Data generated from biomarker research, before subject withdrawal of consent, will remain part of the study results.

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8 STUDY PROCEDURES

Information regarding specific procedures is provided in this section. Please refer to [redacted] for details regarding the timing and type of activities for each substudy.

8.1 Medical History

A complete medical history including demographics, medical conditions, surgical history, medication use, and history of tobacco, alcohol, and drug use will be taken at screening. A detailed IPF diagnosis history including date of diagnosis, prior IPF therapy and reasons for discontinuing, supplemental oxygen use history, prior IPF diagnostic procedures will be recorded. The subject's medical history will be updated at the Study Day 1 visit. This updated medical history will serve as the baseline for clinical assessment. Concomitant medications will be reviewed at study visits specified in [redacted]

8.2 Drug and Alcohol Screen

Subjects should have no history of clinically significant (per investigator's judgment) drug or alcohol abuse within the last 6 months.

Urine specimens will be tested at the screening visit for the presence of drugs of abuse. The panel for drugs of abuse will minimally include the drugs listed below. Any positive result must be assessed for clinical significance. These analyses will be performed by the certified central laboratory chosen for the study.

- Opiates
- Barbiturates
- Amphetamines
- Cocaine
- Benzodiazepines
- Alcohol
- Phencyclidine
- Methadone
- Oxycodone

8.3 Adverse Event Assessment

Please refer to Section 9.2.

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8.4 Clinical Outcome Assessments

COAs may be administered to capture the experience of the subject directly via patient-reported outcomes (PROs) and functioning through performance outcomes (PerfOs).

Refer to each [redacted] for specific COAs and PerfOs that will be administered for each substudy.

[redacted]

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[redacted]

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[redacted]

8.5 Pharmacokinetic Sampling

Blood samples for PK analysis will be collected at time points specified in the [redacted]

For study drugs that are monoclonal antibodies, blood samples for ADA/nAb analysis will be collected at time points specified in the applicable [redacted]s).

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Blood samples for PK and ADA/nAb (if applicable) [redacted] may also be stored and used for biomarker research. Additional information on the collection, handling/processing, and disposition of samples can be found in the [redacted] and the study-specific laboratory manual(s).

8.6 [redacted]

[redacted]

8.7 12-Lead Electrocardiogram

12-Lead Electrocardiogram (Single Only)

Resting 12-lead ECGs will be obtained singly as specified in the [redacted]

The ECG acquired prior to dosing will serve as the baseline measurements for clinical assessment.

When an ECG is scheduled at the same time as a blood collection, the ECG will be obtained prior to the blood collection. ECGs occurring near meals will take place prior to meals.

ECGs will be acquired after the subject has been in the supine position for at least 5 minutes. Subjects will be instructed to remain completely stationary (no talking, laughing, deep breathing, sleeping, or swallowing) for approximately 10 seconds during the ECG recording. While ECGs are being acquired, subjects and staff are prohibited from having devices (e.g., cellular telephones, fans, heaters, etc.) that emit electrical interference in the room.

ECG Safety Review

Each ECG will be evaluated by an appropriately trained medical practitioner at the study site (the "local reader"). The local reading of the ECG will be used by the investigator for subject safety assessments, including AE determination and management, and decision on whether a subject will be discontinued from the study.

The local reader will sign and date all the ECGs collected in this study and provide a global interpretation for each ECG using the following categories:

- Normal ECG
- Abnormal ECG – NCS
- Abnormal ECG – CS
- Unable to evaluate

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All local reader evaluations of ECGs will be entered into the source documents. If the global interpretation is Abnormal (NCS or CS), the local reader will provide further information (e.g., sinus bradycardia, arrhythmia). The QTcF will be calculated and documented for all ECGs.

All ECG source documentation will be retained at the study site. The automatic cardiograph reading (i.e., cardiograph-generated measurements and interpretations) will not be collected for analysis.

8.8 Height and Weight

Height will be measured at screening only. Body weight will be measured at scheduled visits as specified in Section 1.3. The subject will wear lightweight clothing and no shoes during weighing.

8.9 Vital Signs

Vital sign determinations of systolic and diastolic blood pressure, pulse rate, respiratory rate, and body temperature will be obtained at visits as specified in [redacted] Specific Activity Schedule. Blood pressure and pulse rate should be measured after the subject has been sitting for at least 3 minutes.

Measurements should be assessed consistently throughout the study. Vital signs measurements determined prior to dosing on Day 1 will serve as baseline.

[redacted]

8.11 Physical Examination

A complete physical examination, including height (at Screening only) and weight, will be performed at the designated study visits as specified in Section 1.3. Subsequent physical examinations will be limited to evaluations of throat, chest, and heart. The physical examination performed on Study Day 1 will serve as the baseline physical examination for the entire study. Physical examination abnormalities noted at the Baseline Visit prior to the first dose of study drug should be recorded in the subject's medical history. Any significant physical examination findings after the first dose will be recorded as AEs. All findings, whether related to an AE or part of each subject's medical history, will be captured on the appropriate eCRF page.

At any time, a symptom-directed physical examination can be performed as deemed [redacted] by the investigator.

8.12 Dispense Study Drug

Study drug will be dispensed to subjects beginning at Baseline (Day 1) and as specified in [redacted] The first dose of study drug will be administered after all other predose procedures are completed. At the visits

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specified in [redacted] the site personnel will review returned study drug kits, and empty study drug packaging to verify compliance (if applicable).

8.13 Clinical Laboratory Tests

The blood samples for serum chemistry tests will be collected following a minimum 8-hour fast prior to study drug administration (except for the screening visit, which may be nonfasting). For orally administered study drugs, subjects whose visits occur prior to the morning dose of study drug should be instructed to fast after midnight until the blood sample is collected in the morning and thereafter take their study drug with food. Subjects whose visits occur after the morning dose of study drug should be instructed to fast after breakfast until the study visit occurs. At the Study Day 1 visit, a fasting blood sample should be collected prior to the first dose of study drug. Blood samples should still be drawn if the subject did not fast for at least 8 hours. Fasting or nonfasting status will be recorded in the source documents and on the laboratory requisition. The baseline laboratory test results for clinical assessment for a particular test will be defined as the last measurement prior to the initial dose of study drug.

A certified laboratory will be used to process and provide results for the clinical laboratory tests. Laboratory reference ranges will be obtained prior to the initiation of the study.

Instructions regarding the collection, processing, and shipping of these samples will be provided by the central laboratory.

If a laboratory test value is outside the reference range and the investigator considers the laboratory result to be clinically significant, the investigator will:

- repeat the test to verify the out-of-range value;
- follow the out-of-range value to a satisfactory clinical resolution; or
- discontinue the subject from the study or require the subject to receive treatment; in this case, the laboratory result will be recorded as an AE.

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Clinical Laboratory Tests		
Hematology	**Clinical Chemistry**[e]	**Other Tests**
Hematocrit Hemoglobin Red blood cell (RBC) count White blood cell (WBC) count WBC differential (% and absolute values): Neutrophils Bands Lymphocytes Monocytes Basophils Eosinophils Platelet count (estimate not acceptable)	hsCRP Blood urea nitrogen (BUN) Urea Creatinine Total bilirubin Direct and indirect bilirubin Gamma-glutamyl transferase (GGT) Lactate dehydrogenase (LDH) Albumin Alanine aminotransferase (SGPT/ALT) Aspartate aminotransferase (SGOT/AST) Alkaline phosphatase Sodium Potassium Calcium Inorganic phosphorus Uric acid Cholesterol Total protein Glucose Triglycerides Bicarbonate Carbon Dioxide Chloride Creatine kinase Magnesium Estimated Glomerular Filtration (eGFR)	**Screening Blood Tests** HBs Ag HBs Ab HBc Ab HBV DNA PCR reflex only HCV Ab HCV RNA reflex only HIV-1 and HIV-2 **Other Laboratory Tests** Serum pregnancy (bHCG) test Urine pregnancy test (Local) OPTIONAL: Follicle-stimulating hormone (if needed to confirm postmenopausal status) Urine Drug Screen Tests
Coagulation		
International normalized ratio (INR) Partial Thromboplastin Time (PTT), activated PTT Prothrombin Time (PT)		
Urinalysis		
Specific gravity Ketones pH Protein Blood Glucose Leukocyte esterase Nitrite Bilirubin Microscopic examination (if needed)		

[redacted]

e. Minimum 8-hour fast prior to study drug administration (except for the screening visit, which may be nonfasting).

Pregnancy Tests (Serum and Urine)

Pregnancy testing should not be performed for postmenopausal women.

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A qualitative serum pregnancy test will be performed at Screening and a urine pregnancy test or serum (per local guidelines) will be performed at baseline (or upon confinement in each period) for all female subjects of childbearing potential.

The serum pregnancy test will be sent to and performed by the central laboratory. If the serum pregnancy test is positive the subject is considered a screen failure. If the serum pregnancy test is borderline, the serum pregnancy test should be repeated ≥ 3 days later to determine eligibility.

If the repeat serum pregnancy test is:

- Positive, the subject is considered a screen failure;
- Negative, the subject can be enrolled into the trial;
- Still borderline, ≥ 3 days later, this will be considered documentation of continued lack of a positive result and the subject can be enrolled into the study (unless prohibited per local requirements) in the absence of clinical suspicion of pregnancy and other pathological causes of borderline results.

Additional urine pregnancy tests will be performed at visits indicated in the Activities Schedule for individual [redacted] More frequent pregnancy tests can be performed throughout the study at the investigator's discretion or if required per local/country requirements. Use of highly sensitive urine pregnancy tests (detection of at least 25 IU/L hCG) at baseline and postbaseline are preferable.

- If the baseline urine pregnancy test is negative, then dosing with study drug may begin.
- If any urine pregnancy test at baseline or postbaseline is borderline or ambiguous, a serum pregnancy test is required. In such cases, the subject must be excluded from study if the serum pregnancy result is positive.
- Monthly pregnancy testing should be performed during treatment, including at the last dose and until the end of the follow up period for the AbbVie product as specified in [redacted] If the monthly tests are done at home, then the results need to be communicated to the site.
- Unless a woman is suspected to have become pregnant, additional pregnancy testing during the clinical trial is not [redacted]

Clinical Chemistry

A minimum 8-hour fast will be [redacted] for blood samples to be drawn for chemistry (except for the screening visit, which may be nonfasting). If a subject is not able to fast when [redacted] due to unforeseen circumstances, the nonfasting status will be recorded in study source documentation.

Urinalysis

Urinalysis will be completed by the central laboratory at all required visits. Specified abnormal macroscopic urinalyses defined as leukocytes, nitrite, protein, ketones, or blood greater than negative, or glucose greater than normal will be followed up with a microscopic analysis at the central laboratory.

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Hepatitis Screening

All subjects will be tested for the presence of HBV and HCV at Screening.

Hepatitis B Virus (HBV)

Subjects will be tested for the presence of HBV at Screening using the following tests:

- HBs Ag (Hepatitis B surface antigen)
- HBc Ab/anti-HBc (Hepatitis B core antibody)
- HBs Ab/anti-HBs (Hepatitis B surface antibody)

A positive result for HBs Ag will be exclusionary.

A negative result for HBs Ag will trigger automatic reflex testing for core antibodies (HBc Ab) and surface antibodies (HBs Ab).

1. A negative test result for HBc Ab does **not** require HBV DNA PCR qualitative testing and the subject may be enrolled (Figure 2, Scenarios A and B).
2. For a subject who has had a HBV vaccination (should document in the medical history), a positive test result for HBs Ab is expected, the HBV DNA PCR qualitative testing is **not** required and the subject may be enrolled (Figure 2, Scenario B).*
3. For subjects without a history of HBV vaccination, and where mandated by local requirements, a positive result for HBs Ab requires HBV DNA PCR testing (automatic reflex testing; Figure 2, Scenario B).
4. A positive test result for HBc Ab requires HBV DNA PCR testing (automatic reflex testing) (Figure 2, Scenarios C and D). A result for HBV DNA that exceeds detection sensitivity will be considered positive and will be exclusionary. A subject with a negative result for HBV DNA may be enrolled.

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Hepatitis C Virus (HCV) Screening

Blood samples for HCV serology will be obtained at the Screening Visit. A positive HCV Ab will trigger a HCV RNA test. A subject will not be eligible for study participation if test results indicate active Hepatitis C (HCV RNA detectable in any subject with anti HCV Ab).

HIV Testing

HIV testing will be performed at Screening. The investigator must discuss any local reporting requirements to local health agencies with the subject. The site will report confirmed positive results to their health agency per local regulations, if [redacted] If a subject has a confirmed positive result, the investigator must discuss with the subject the potential implications to the subject's health and the subject should receive or be referred for clinical care promptly. A subject will not be eligible for study participation if test results are positive. AbbVie will not receive results from the testing.

8.14 Unscheduled Visits

An Unscheduled Visit should be performed when the subject comes in for a medical visit for evaluation and assessment. During Unscheduled Visits, blood and urine samples may be obtained for the laboratory tests listed in Section 8.13, or for other tests, at the investigator's discretion.

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Visits for dispensing new study drug in case of temperature excursion, loss or damage are not considered an Unscheduled Visit. In addition, visits to only retest a lab will not be considered an Unscheduled Visit.

8.15 Spirometry

Spirometry will be performed to assess pulmonary function beginning at Screening and as specified in the [redacted] Spirometry measurements will be performed according to ATS/ERS 2019 guidelines[10] at specific timepoints as described in [redacted] FVC will be assessed using standardized spirometry equipment which will be provided centrally. Only these spirometers are to be used for this trial. Spirometry results will be centrally reviewed.

The spirometry test must meet the criteria for acceptability and repeatability as defined in the 2019 ATS/ERS guidelines on standardization of lung function testing.[10]

Spirometry will be conducted with the patient in a seated position. Efforts should be made to schedule the spirometric measurements at approximately the same time of the day, at least within the same half-day (morning vs. afternoon), with reference to baseline measurement (Day 1). On days of study visits, patients should be encouraged to refrain from vigorous activity and avoid smoke, dust, or areas with strong odors (e.g., perfumes) at least 1 hour of pulmonary function testing.

If treated with bronchodilators, washout according to [redacted] should be advised before spirometry and documented in the source documents.[10]

[redacted]

The following parameters will be measured as part of the spirometry assessment:

[redacted]

The [redacted] Global Lung Function Initiative Equations" will be used to calculate the predicted values.[11]

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8.16 DLCO

[redacted] to assess carbon monoxide diffusion capacity during the single breath diffusion test and [redacted] Single breath diffusion test will be carried out according to the ATS/ERS guidelines.[12,13]

Two acceptable DLCO measurements along with the corresponding alveolar volume will be taken at the time points specified in the [redacted] schedule of activities and recorded. Up to five DLCO measurement attempts may be made on the same day to obtain two acceptable DLCO measurements. The measured DLCO (mL/min/mmHg) [redacted] will be entered into the eCRF when DLCO measurements are conducted per the substudy specific activity schedule.

To obtain the predicted DLCO normal values (mL/min/mmHg), different sites may use different prediction formulas, based on the equipment they use. In any case, the calculation method used must be in compliance with the ATS/ERS guideline on DLCO measurements and the prediction formula appropriate for that method.

[redacted]

8.17 Chest high-resolution Computed Tomography (HRCT)

A [redacted] chest HRCT can be used to determine eligibility [redacted]

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Confirmation of diagnosis must be available prior to randomization visit. To perform an HRCT within the trial, all local regulatory requirements to perform an HRCT have to be met.

[redacted] the HRCT scan should be performed as close to screening date as possible as part of the study during the screening period, preferably once eligibility is confirmed based on other parameters, to avoid [redacted] scans for patients who are found ineligible based on other criteria.

9 SAFETY CONSIDERATIONS

9.1 Complaints and Adverse Events

Complaints

A complaint is any written, electronic, or oral communication that alleges deficiencies related to the physical characteristics, identity, quality, purity, potency, durability, reliability, safety, effectiveness, or performance of a product/device. Complaints associated with any component of this investigational product must be reported to AbbVie.

Product Complaint

A product complaint is any complaint related to the biologic or drug component of the product or to the medical device component(s).

For a product this may include, but is not limited to, damaged/broken product or packaging, product appearance whose color/markings do not match the labeling, labeling discrepancies/inadequacies in the labeling/instructions (e.g., printing illegible), missing components/product, device damage or not working properly, or packaging issues.

Product complaints concerning the investigational product and/or device must be reported to AbbVie within 24 hours of the study site's knowledge of the event.

Reporting will be done via EDC. The date the product complaint details are entered into EDC and the form is saved represents the date reported to AbbVie. A back-up paper form will be provided for reporting complaints related to unassigned product or in the event of an EDC system issue. If a back-up paper form is used, the date the form is emailed to RD_PQC_QA@abbvie.com represents the date reported to AbbVie.

All follow-up information is to be reported to the sponsor (or an authorized representative) and documented in source as required by the sponsor. Product complaints associated with AEs will be reported in the study summary. All other complaints will be monitored on an ongoing basis. Product complaints occurring during the study will be followed up to a satisfactory conclusion.

Medical Complaints/Adverse Events and Serious Adverse Events:

An AE is defined as any untoward medical occurrence in a subject or clinical investigation subject administered a pharmaceutical product and which does not [redacted] have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal

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(investigational) product, whether or not the event is considered causally related to the use of the product.

Such an event can result from use of the drug as stipulated in the protocol or labeling, as well as from "special situations" such as accidental or intentional overdose, medication error, occupational or accidental exposure, off-label use, drug abuse, drug misuse, or drug withdrawal, all which must be reported whether associated with an AE or not. Any worsening of a pre-existing condition or illness is considered an AE. Worsening in severity of a reported AE should be reported as a new AE. Laboratory abnormalities and changes in vital signs are considered to be AEs only if they result in discontinuation from the study, necessitate therapeutic medical intervention, meets protocol-specific criteria (see Section 9.3 and each [redacted] regarding toxicity management), and/or if the investigator considers them to be clinically significant.

The investigators will monitor each subject for clinical and laboratory evidence of AEs on a routine basis throughout the study. All AEs will be followed to a satisfactory conclusion.

An elective surgery/procedure scheduled to occur during a study will not be considered an AE if the surgery/procedure is being performed for a pre-existing condition and/or the surgery/procedure has been pre-planned prior to study entry. However, if the pre-existing condition deteriorates unexpectedly during the study (e.g., surgery performed earlier than planned), then the deterioration of the condition for which the elective surgery/procedure is being done will be considered an AE.

If any of the following events are reported, then the following supplemental report must be completed. For substudy specific events requiring the supplemental report form refer to Complaints and Adverse Events section in each [redacted]

Event	Supplemental Report
Discontinuation of study drug due to a hepatic-related AE **Any hepatic-related SAE** **ALT or AST > 8 × ULN;** **Confirmed ALT or AST > 5 x ULN for more than 2 weeks;** **ALT or AST > 3 x ULN and total bilirubin > 2 × ULN (with mixed or direct predominance) or INR > 1.5;** **ALT or AST > 3 × ULN with presentation of related symptoms (fatigue, nausea, vomiting, right upper quadrant pain or tenderness, fever, rash, and/or eosinophilia > 5%).**	Hepatic AE eCRF

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If an AE, whether associated with study drug or not, meets any of the following criteria, it is to be reported to AbbVie clinical pharmacovigilance as a SAE within 24 hours of the site being made aware of the SAE (refer to Section 9.2 for reporting details and contact information):

Death of Subject	An event that results in the death of a subject.
Life-Threatening	An event that, in the opinion of the investigator, would have resulted in immediate fatality if medical intervention had not been taken. This does not include an event that would have been fatal if it had occurred in a more severe form.
Hospitalization or Prolongation of Hospitalization	An event that results in an admission to the hospital for any length of time or prolongs the subject's hospital stay. This does not include an emergency room visit or admission to an outpatient facility.
Congenital Anomaly	An anomaly detected at or after birth, or any anomaly that results in fetal loss.
Persistent or Significant Disability/Incapacity	An event that results in a condition that substantially interferes with the activities of daily living of a study subject. Disability is not intended to include experiences of relatively minor medical significance such as headache, nausea, vomiting, diarrhea, influenza, and accidental trauma (e.g., sprained ankle).
Important Medical Event Requiring Medical or Surgical Intervention to Prevent Serious Outcome	An important medical event that may not be immediately life-threatening or result in death or hospitalization, but based on medical judgment may jeopardize the subject and may require medical or surgical intervention to prevent any of the outcomes listed above (i.e., death of subject, life threatening, hospitalization, prolongation of hospitalization, congenital anomaly, or persistent or significant disability/incapacity). Additionally, any elective or spontaneous abortion or stillbirth is considered an important medical event if no other serious criterion is applicable. Examples of such events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse.

The following definitions will be used for SAR and SUSAR:

SAR	Defined as all noxious and unintended responses to an IMP related to any dose administered that result in an SAE as defined above.
SUSAR	Refers to individual SAE case reports from clinical trials where a causal relationship between the SAE and the IMP was suspected by either the sponsor or the investigator, is unexpected (not listed in the applicable Reference Safety Information) and meets one of the above serious criteria.

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AbbVie will be responsible for SUSAR reporting for the IMP in accordance with global and local requirements, including reporting to Eudravigilance database in accordance with EU Clinical Trial Regulation.

AEs will be monitored throughout the study to identify any of special interest that may indicate a trend or risk to subjects.

Acute IPF Exacerbations

Acute exacerbation will be defined as an acute, clinically significant, respiratory deterioration characterized by evidence of new widespread alveolar abnormality, including all of the following:[14]

- Acute worsening or development of dyspnea typically less than one month duration.
- Imaging with new bilateral ground-glass opacity and/or consolidation superimposed on a background pattern consistent with IPF.
- Respiratory deterioration not fully explained by cardiac failure or fluid overload.

Acute IPF exacerbation event will be investigator-determined, and additional information will be collected in AE supplemental eCRF. *The AEs will not be adjudicated.*

Adverse Events of Special Interest

Refer to each [redacted] for substudy-specific AESIs.

Adverse Event Severity and Relationship to Study Drug

The investigator will rate the severity of each AE according to the NCI CTCAE Version 5.0.[15]

If no specific criteria per CTCAE v. 5.0 guidelines are available for the reported event, the event should be graded per the investigator's judgment:

- Grade 1 (Mild); asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated
- Grade 2 (Moderate); minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental activities of daily living
- Grade 3 (Severe); medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care activities of daily living
- Grade 4 (Severe); Life-threatening consequences; urgent intervention indicated
- Grade 5 (Severe); Death related to AE

  Note: a semicolon indicates "or" within the description of the grade.

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The investigator will use the following definitions to assess the relationship of the AE to the use of study drug:

Reasonable Possibility	After consideration of factors including timing of the event, biologic plausibility, clinical judgment, and potential alternative causes, there is sufficient evidence (information) to suggest a causal relationship.
No Reasonable Possibility	After consideration of factors including timing of the event, biologic plausibility, clinical judgment, and potential alternative causes, there is insufficient evidence (information) to suggest a causal relationship.

Pregnancy

While not an AE, pregnancy in a study subject must be reported to AbbVie within 24 hours after the site becomes aware of the pregnancy. Subjects who become pregnant during the study must be discontinued (Section 7.1). If a pregnancy occurs in a study subject or in the partner of a study subject, information regarding the pregnancy and the outcome will be collected.

In the event of pregnancy occurring in a subject's partner during the study, written informed consent from the partner must be obtained prior to collection of any such information. AbbVie will provide a separate consent form for this purpose. Pregnancy in a subject's partners will be collected from the date of the first dose through the last study visit (refer to the [redacted]

The pregnancy outcome of an elective or spontaneous abortion, stillbirth or congenital anomaly is considered a SAE and must be reported to AbbVie within 24 hours after the site becomes aware of the event.

9.2 Safety Manual

Methods and Timing of Safety Assessment

Study procedure-related serious and nonserious AEs (e.g., contusion secondary to blood draw during screening) will be collected from the time the subject signs the study-specific ICF.

During study treatment, all AEs will be collected through the follow-up period specified in [redacted] whether solicited or spontaneously reported by the subject.

After the [redacted] specified follow up period, only spontaneously reported SAEs will be collected. Those SAEs which have a causal relationship to study treatment must be reported to AbbVie without undue delay. Nonserious AEs will not be collected.

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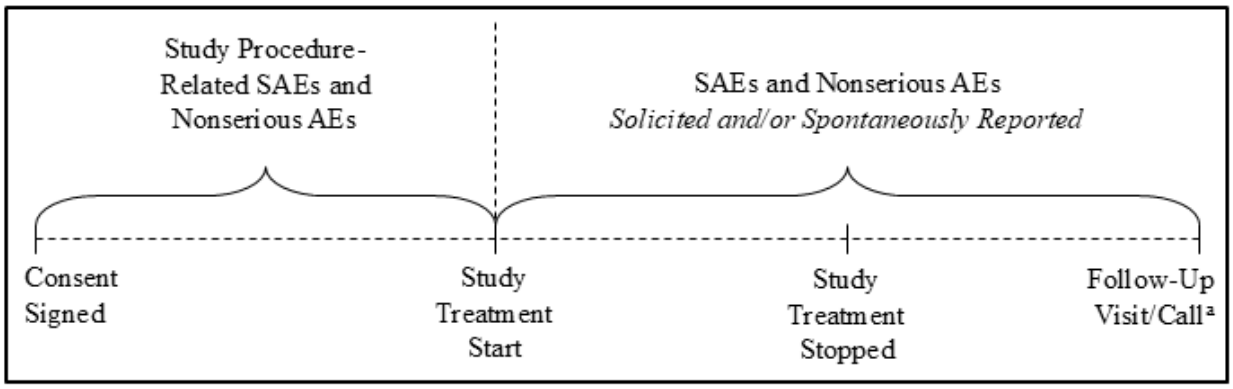

a. As specified in the Follow up period in each [redacted]

Reporting Adverse Events and Intercurrent Illnesses

In the event of an SAE, whether associated with study drug or not, the investigator will notify Clinical Pharmacovigilance within 24 hours of the site being made aware of the SAE by entering the SAE data into the EDC system. SAEs that occur prior to the site having access to the EDC, or if the EDC system is not operable, should be documented on the SAE nonCRF forms and emailed (preferred route) or faxed to Clinical Pharmacovigilance within 24 hours of the site being made aware of the SAE.

Email: PPDINDPharmacovigilance@abbvie.com
FAX to: +1-847-806-2062 Backup: +1-847-935-2844

For safety questions, contact the Internal Medicine Safety Team at:

TA Safety Team
Email: SafetyManagement_InternalMedicine@abbvie.com

For any subject safety concerns, please contact the physician listed below:

Primary Therapeutic Area Medical Director
EMERGENCY MEDICAL CONTACT:
[redacted] **MD, PhD**
AbbVie Inc.
1 North Waukegan Road
North Chicago, IL 60064

Contact Information:

Office: [redacted]
Mobile:
Email:

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In emergency situations involving study subjects when the primary Therapeutic Area Medical Director is not available by phone, please contact the 24-hour AbbVie Medical Escalation Hotline where your call will be re-directed to a designated backup AbbVie Therapeutic Area Medical Director:

HOTLINE: +1 (973) 784-6402

SUSAR Reporting

AbbVie will be responsible for SUSAR reporting for the IMP in accordance with global and local requirements, including EU Clinical Trial Regulation, and Appendix A of the Investigator Brochure will serve as the RSI. The RSI in effect at the start of a DSUR reporting period will be used to determine expectedness until the RSI that was submitted at the time of the DSUR becomes approved by all applicable regulatory authorities. For follow-up reports, the RSI in place at the time of occurrence of the 'suspected' Serious Adverse Reaction will be used to assess expectedness.

9.3 Toxicity Management

The below study toxicity management consists of safety monitoring (review of AEs/SAEs on an ongoing basis), and, if applicable, interruption of study drug dosing with appropriate clinical management and/or discontinuation of the subjects from study drug.

Refer to the toxicity management sub section of each [redacted] measures.

Hepatic AEs and Abnormal Laboratory Values: Post-Baseline occurrence of one or more of the following hepatic test abnormalities (confirmed on a second separate sample at least 48 hours apart):

- ALT or AST > 8 × ULN;
- ALT or AST > 5 × ULN for more than 2 weeks;
- ALT or AST > 3 × ULN and Total Bilirubin > 2 × ULN or international normalized ratio [INR]> 1.5;
- ALT or AST > 3 × ULN with the appearance of fatigue, nausea, vomiting, right upper quadrant pain or tenderness, fever, rash, and/or eosinophilia (> 5%).

Subjects who meet any of the above criteria will interrupt study drug and should be evaluated or an alternative etiology of the ALT or AST elevation and managed as medically appropriate. If applicable, the alternative etiology should be documented in the eCRF.

A thorough investigation of potential etiologies for elevated transaminases should be conducted (e.g., trauma, acetaminophen use, viral hepatitis, alcohol ingestion), and the subject should be followed closely for clinical progression.

Subjects for whom treatment is discontinued for elevated hepatic liver tests should have transaminases and bilirubin levels repeated by the central laboratory within 48 to 72 hours after the initial finding if possible, and then monitored closely until levels normalize or return to baseline. If a subject cannot

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return to the site for liver function testing, a local laboratory may be used. Elevations in hepatic liver tests at the local laboratory must be reported immediately to the medical monitor, and the subject must have the tests repeated and sent to the central laboratory as soon as possible (ideally within 48 to 72 hours).

If an alternative, reversible cause of transaminase elevation and/or increased bilirubin or clinical jaundice has been identified, study drug administration may be resumed once transaminases or bilirubin return to baseline or are ≤ 2 x ULN, whichever is higher. Approval of the medical monitor is required before resumption of study drug. Upon resumption of study drug, transaminases and bilirubin should be assessed weekly for 4 weeks.

If a protocol-defined transaminase or bilirubin elevation interruption threshold recurs during the treatment period (with confirmation of the initial elevation by repeat testing within 48 to 72 hours), then the study drug must be permanently discontinued, regardless of the presumed etiology.

10 STATISTICAL METHODS & DETERMINATION OF SAMPLE SIZE

10.1 [redacted]

[redacted]

10.2 Definition for Analysis Populations

The FAS includes all randomized subjects who received at least 1 dose of study drug. The FAS will be used for all efficacy and baseline analyses.

The Safety Analysis Set consists of all subjects who received at least 1 dose of study drug.

The FAS and Safety Analysis Set for each substudy are defined [redacted]

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10.3 Handling Potential Intercurrent Events

The estimand corresponding to the primary efficacy objective is the difference between active treatment and placebo in the mean absolute change from baseline through Week 24 in FVC for subjects with IPF and who received at least one dose of study treatment.

Primary and Secondary Endpoint(s)

The primary and secondary endpoints are defined in Section 3.2 and Section 3.3, respectively.

For subjects who have an intercurrent event of premature treatment discontinuation or initiation of another IPF treatment that requires a withdrawal from the study, according to the study design, these subjects will have a premature discontinuation (PD) visit for their last efficacy evaluation. No further evaluations will occur after the PD visit. Data collected after the intercurrent event (i.e., after the PD visit) will be excluded from the primary analysis.

Supplementary analysis will be performed using treatment policy strategy for handling these intercurrent events.

10.4 [redacted]

[redacted]

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10.5 Statistical Analyses for Safety

Safety analyses will be performed on the safety analysis set for [redacted]based on the treatment subjects actually receive. Safety will be assessed by AEs, AESIs, weight, vital signs, clinical laboratory data, and 12-lead ECGs. Details on the safety analyses will be provided in the SAP.

AEs will be coded using MedDRA. A TEAE is defined as an AE that began or worsened in severity after the first dose of study drug and within the follow up period after the last dose of study drug specified in each [redacted] The number and percentage of subjects experiencing TEAEs will be tabulated using MedDRA SOC and preferred term as well as by severity and by relationship to the study drug as assessed by the investigator. Summaries (i.e., number and percentages) of TEAEs, SAEs, deaths, AEs leading to discontinuation, and AESIs will be provided.

For laboratory test and vital signs variables, mean change from Baseline before the first dose of study drugs and percentage of subjects with evaluations meeting criteria for predefined PCS values will be summarized.

Additional analysis details will be provided in the SAP of each substudy.

10.6 [redacted]

[redacted]

10.7 Population PK and Exposure-Response Analyses

Interim (pre-database lock) population PK and exposure-response analyses may be initiated prior to full enrollment of study participants in any substudy. These analyses will be conducted by a pre-specified internal unblinded group that is not involved or in charge of study conduct.

Study drug concentration information that may unblind the study will not be reported to study sites or blinded personnel.

For study drugs that are monoclonal antibodies, immunogenicity data (e.g., incidence of treatment-emergent ADA) will also be analyzed by the internal unblinded group.

10.8 Overall Type I Error Control

Overall type I error control is not planned for this phase 2 proof of concept study.

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10.9 Sample Size Determination

In general, the sample size for each substudy is determined based on the statistical considerations for estimating the difference between the intervention group and the control group for the primary endpoint of FVC change from baseline. Please refer to the [redacted] for the determination of the sample size of the corresponding substudy.

10.10 Protocol Deviations

AbbVie does not allow intentional/prospective deviations from the protocol except when [redacted] to eliminate an immediate hazard to study subjects. The investigator is responsible for complying with all protocol requirements, written instructions, and applicable laws regarding protocol deviations. If a protocol deviation occurs (or is identified), the investigator is responsible for notifying IEC/IRB, regulatory authorities (as applicable), and AbbVie.

11 GENERAL CONSIDERATIONS: REGULATORY, ETHICS, AND STUDY OVERSIGHT

11.1 Independent Ethics Committee/Institutional Review Board

The protocol, informed consent form(s), recruitment materials, and all subject materials will be submitted to the IEC/IRB for review and approval. Approval of both the protocol and the informed consent form(s) must be obtained before any subject is enrolled. Any amendment to the protocol will require review and approval by the IEC/IRB before the changes are implemented to the study. In addition, all changes to the consent form(s) will be IEC/IRB approved.

11.2 Ethical Conduct of the Study

The study will be conducted in accordance with the protocol, ICH guidelines, EU Clinical Trial Regulation, applicable regulations, and guidelines governing clinical study conduct and the ethical principles that have their origin in the Declaration of Helsinki. Responsibilities of the investigator are specified in Section 13.

11.3 Subject Confidentiality

Before subject data are shared with AbbVie, the study investigator and staff will replace the subject's name, address, and contact information with a generic code which AbbVie cannot link to that subject's identity to protect the confidentiality of the data.

For the personal data that AbbVie Deutschland GmbH & Co KG acting as sponsor of the submitted study ("AbbVie Deutschland") controls and maintains, AbbVie Deutschland has developed a robust security program focused on due diligence in design, managed change, and information security governance. Information Security policies govern the Information Security functions including identity and access

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management, operations, infrastructure, application, and third-party security requirements. The risk-based AbbVie Data Classification Tool dictates the level of scrutiny and control required for the relevant activities per AbbVie's Information Security policies taking into account the sensitivity of the data.

AbbVie Deutschland has a data protection impact assessment program to ensure and document the appropriate controls and safeguards stated above are in place for clinical trial data that it controls and maintains, and these processing activities respect privacy of clinical trial subjects. AbbVie Deutschland also maintains robust security incident response policies and procedures, including requirements for the containment of any data-related incidents, the mitigation measures where needed, and notification to authorities or affected individuals where required.

AbbVie Deutschland as the sponsor shall document any personal data breaches for which it is a controller and notify the competent national supervisory authority where required without undue delay and at the latest within 72 hours after becoming aware of such an incident. AbbVie Deutschland shall create and maintain appropriate records of such an incident.

11.4 Study Subject Information and Informed Consent

The investigator or their representative will explain the nature of the study to the subject, the benefits and risks anticipated from participation in the study, and answer all questions regarding this study. Prior to any study-related screening procedures being performed on the subject or any medications being discontinued by the subject in order to participate in this study, the informed consent statement will be reviewed, signed, and dated by the subject or their legally authorized representative, the person who administered the informed consent, and any other signatories according to local requirements. A copy of the signed informed consent will be given to the subject and the original will be placed in the subject's medical record. An entry must also be made in the subject's dated source documents to confirm that informed consent was obtained prior to any study-related procedures and that the subject received a signed copy.

Information regarding benefits for subjects and information regarding provisions for treating and/or compensating subjects who are harmed because of participation in the study can be found in the informed consent form.

Samples for optional pharmacogenetic and pharmacokinetic analyses or other exploratory analyses will only be collected if the subject has voluntarily signed and dated a separate written consent form for this testing that has been approved by an IRB/IEC, after the nature of the testing has been explained and the subject has had an opportunity to ask questions. Additionally, participation in the Open Label Extension (if applicable) is optional and subjects will only roll over after completing the Treatment Period if they voluntarily sign and date a separate written consent for this. The separate written consent may be part of the main consent form. If the subject does not consent to the testing or participation in Open Label Extension, it will not impact the subject's participation in the study.

11.5 Independent Data Monitoring Committee

An external IDMC composed of clinicians and statisticians independent of AbbVie and with relevant expertise in their field will periodically review unblinded safety data from the ongoing study. The IDMC

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is responsible for safeguarding the interests of trial subjects, assessing the safety of the interventions during the trial, as well as for monitoring the integrity and interpretability of the trial. The IDMC will provide recommendations to the sponsor regarding ongoing trial conduct or modifications to the trial as described in a separate IDMC charter.

In order to maintain sponsor blinding, an external statistical data analysis center is responsible for performing the analyses described in the DMC charter as well as additional analyses requested by the IDMC and facilitating interpretation and answering questions that arise before, during or after IDMC review.

A separate IDMC charter will be prepared outside of the protocol to further describe the roles and responsibilities of the IDMC members, frequency and scope of the data reviews, and expectations for blinded communications.

11.6 For EU CTR submissions - Publication Policy

AbbVie as the sponsor has proprietary interest in this study. Authorship and manuscript composition will reflect joint cooperation between multiple investigators and sites and sponsor personnel. Authorship will be established prior to the writing of the manuscript. As this study involves multiple centers, no individual publications will be allowed prior to completion of the final clinical study report of the multicenter study except as agreed with the sponsor.

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.

Investigators are NOT employed by the organization sponsoring the study. There is an agreement between investigators and the sponsor (or its agents) that restricts the investigator's rights to discuss or publish study results after the study is completed.

AbbVie requests that any investigator or institution that plans on presenting/publishing results, provide written notification of their request 60 days prior to their presentation/publication. AbbVie requests that no presentation/publication will be instituted until 12 months after a study is completed or after the first presentation/publication, whichever occurs first. A delay may be proposed for a presentation/publication if AbbVie needs to secure patent or proprietary protection.

12 GENERAL CONSIDERATIONS: RISK MANAGEMENT AND QUALITY ASSURANCE

12.1 Source Documents and Case Report Form Completion

The investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported. All source documents should be attributable, legible, contemporaneous, original, accurate, and complete to ensure accurate interpretation of data. Clinical site monitoring is conducted to ensure that the rights and well-being of human subjects are protected, that the reported trial data

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are accurate, complete, and verifiable, and that the conduct of the trial is in compliance with the currently approved protocol, ICH GCP, and applicable local regulatory requirement(s), including EU Clinical Trial Regulation.

12.2 Data Quality Assurance

AbbVie will ensure that the clinical trial is conducted in accordance with the protocol and with a quality management system that will define quality tolerance limits in order to ensure human subject protection and reliability of study results. Data will be generated, documented, and reported in compliance with the protocol, ICH GCP, and applicable regulatory requirements, including EU Clinical Trial Regulation.

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13 APPENDIX A. RESPONSIBILITIES OF THE INVESTIGATOR

Protocol M25-268: A Phase 2a Multicenter Platform Study of Investigational Products for the Treatment of Adult Subjects with Idiopathic Pulmonary Fibrosis

Protocol Date: 22 April 2026

Clinical research studies sponsored by AbbVie are subject to the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practices (GCP), as well as applicable laws, regulations, and guidelines. Certain laws, regulations, or guidelines may apply to conduct of the study at investigator's site even if such laws, regulations, or guidelines originate in a foreign jurisdiction. The investigator agrees and acknowledges that applicable laws or regulations may require AbbVie to submit inspection reports, instances of significant noncompliance with the study protocol, or other documents regarding conduct of the study at the investigator's site to regulatory authorities, and such documents may be publicly disclosed by such authorities. In signing the Investigator Agreement, the investigator is agreeing to the following:

1. Conducting the study in accordance with ICH GCP, the applicable regulatory requirements, current protocol, and making changes to a protocol only after notifying AbbVie and the appropriate Institutional Review Board (IRB)/Independent Ethics Committee (IEC), except when [redacted] to protect the subject from immediate harm.
2. Personally conducting or supervising the described investigation(s).
3. Informing all subjects, or persons used as controls, that the drugs are being used for investigational purposes and complying with the requirements relating to informed consent and ethics committees (e.g., IEC or IRB) review and approval of the protocol and its amendments.
4. Reporting complaints that occur in the course of the investigation(s) to AbbVie.
5. Reading the information in the Investigator's Brochure/safety material provided, including the instructions for use and the potential risks and side effects of the investigational product(s).
6. Informing all associates, colleagues, and employees assisting in the conduct of the study about their obligations in meeting the above commitments.
7. Maintaining adequate and accurate records of the conduct of the study, making those records available for inspection by representatives of AbbVie and/or the appropriate regulatory agency, and retaining all study-related documents until notification from AbbVie.
8. Maintaining records demonstrating that an ethics committee reviewed and approved the initial clinical protocol and all of its amendments.
9. Reporting the following to AbbVie within 1 calendar day of becoming aware:
   - Any unanticipated problems involving risks to human subjects
   - Any departure from relevant clinical trial regulation, GCP, or the trial protocol that has affected or is likely to affect to a **significant** degree the following:
     - Rights, safety, physical or mental integrity of the subjects in the clinical trial
     - Scientific value of the clinical trial, reliability or robustness of data generated

   Where required by local regulation, inform relevant Ethics Committees / Institutional Review Boards and other appropriate individuals (e.g., Co-ordinating Investigator, Institution Director).
10. Providing direct access to source data documents for study-related monitoring, audits, IEC/IRB review, and regulatory inspection(s).

Signature of Principal Investigator | Date

Name of Principal Investigator (printed or typed)

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14 APPENDIX B. LIST OF PROTOCOL SIGNATORIES

Name	Title	Functional Area
[redacted]		TA MD
		Statistics

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15 APPENDIX C. COUNTRY-SPECIFIC REQUIREMENTS

Any coded data (as defined under General Data Protection Requirements) that is transferred to AbbVie's parent company, AbbVie Inc., in the United States, or other AbbVie affiliates is done under internal agreements, which include an EU approved model contract pertaining to data transfers to controllers. A copy can be obtained by sending an email to privacyoffice@abbvie.com. Any transfers of Coded Data to AbbVie's research partners outside the EU will be done in compliance with the international data transfer restrictions that apply under EU data protection laws.

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16 APPENDIX D. RANDOMIZATION SCHEDULE

This study will be initiated [redacted] The Part 1 is the double blind treatment period (52 weeks) and will consist of [redacted] all subjects will be invited to participate in an optional Part 2 which will include a [redacted] The randomization will be stratified by baseline [redacted] The study schematic is presented in Figure 3.

[redacted]

If additional substudy(ies) are added or enrollment of existing ones are completed, the randomization schedule may be updated accordingly, and subjects may be randomized among all enrolling treatment arms according to the updated randomization scheme.

Each update to the randomization schedule will be documented in this appendix.

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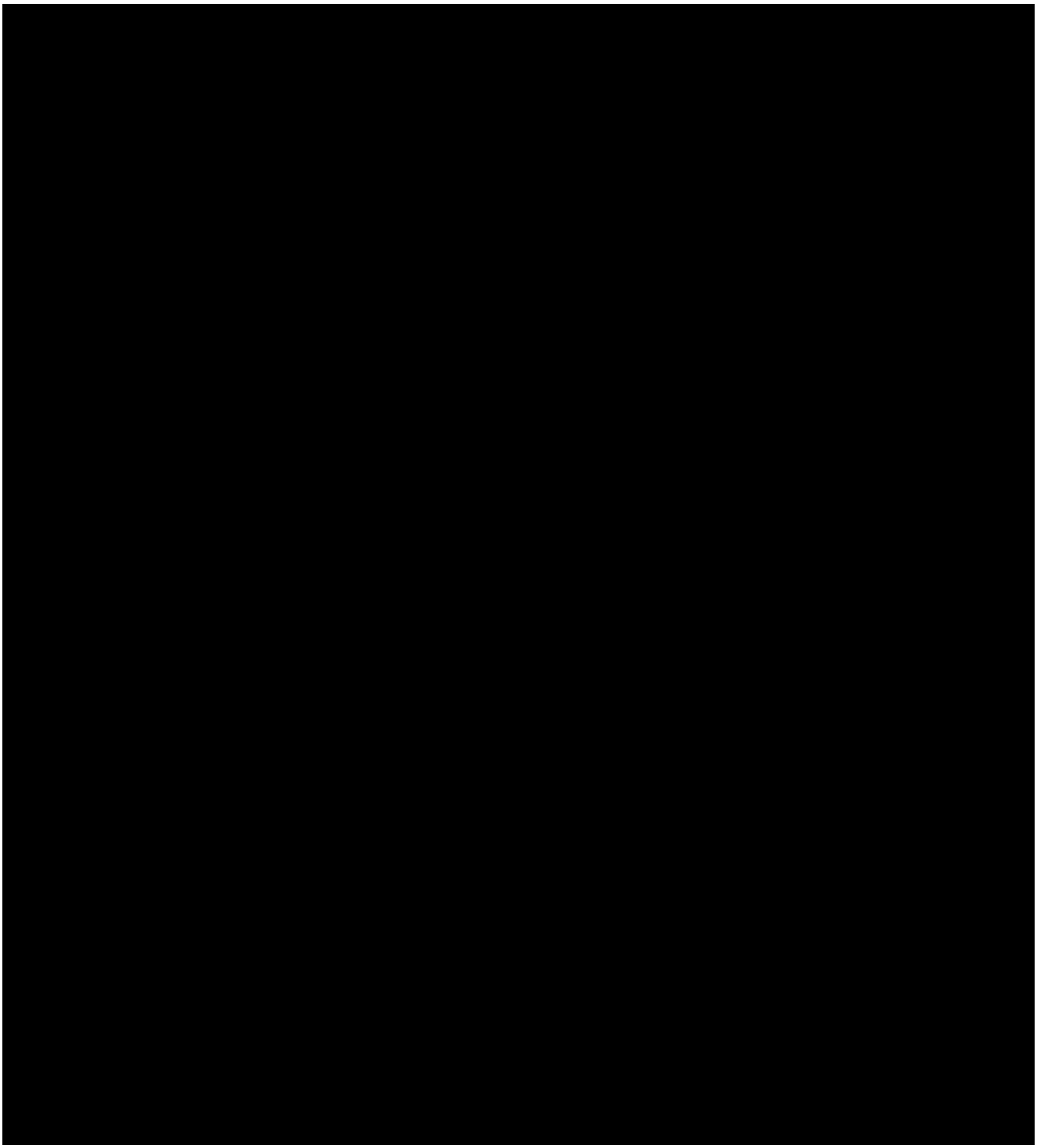

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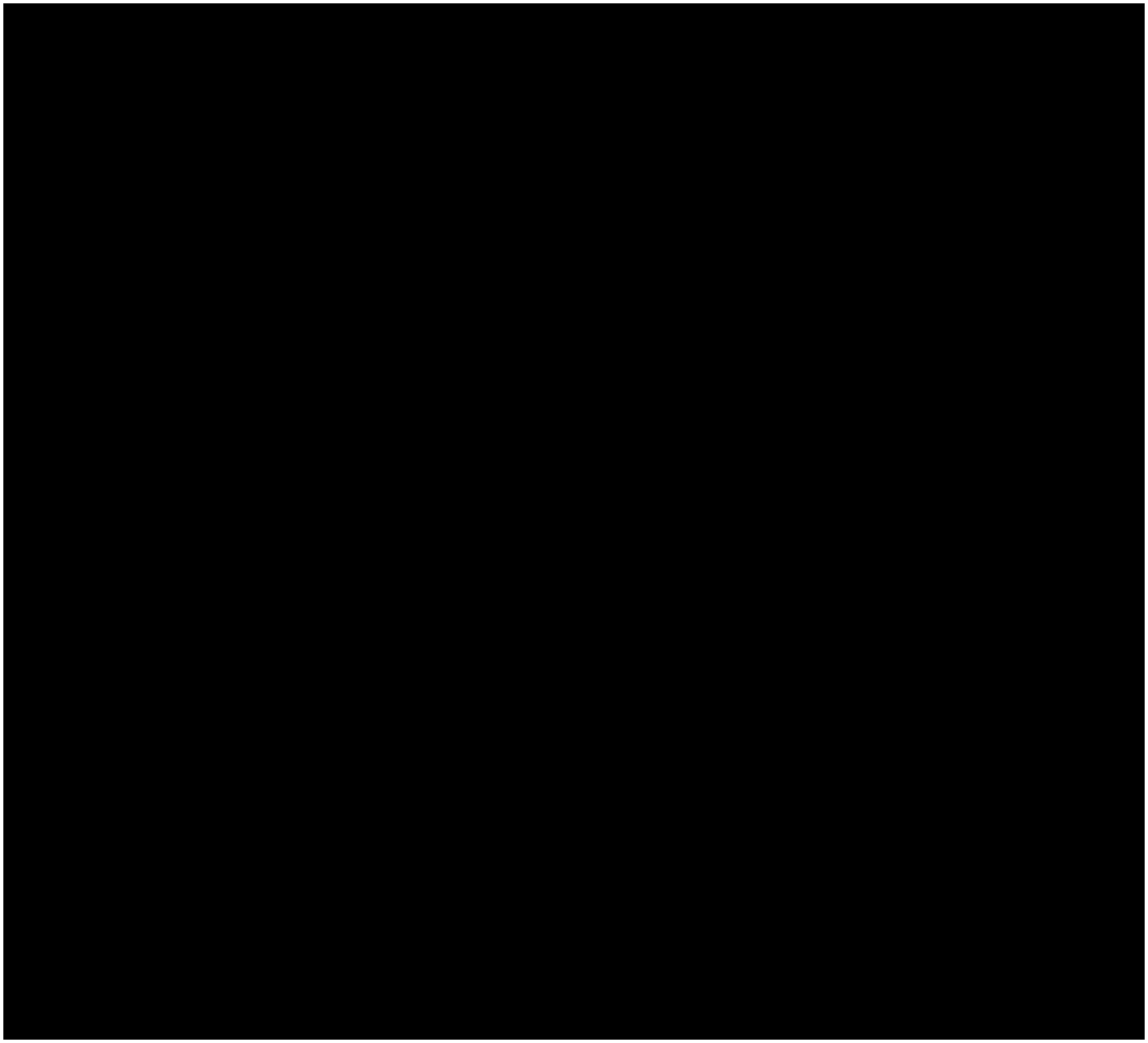

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18 APPENDIX F. STUDY-SPECIFIC ABBREVIATIONS AND TERMS

Abbreviation	Definition
[redacted]	
AAC	Anaphylaxis Adjudication Committee
ABBIOS	AbbVie BIOsignal System
ADR	Adverse drug reaction
AE	adverse event
AESI	adverse event of special interest
ALAT	Latin American Thoracic Association
ALT	alanine aminotransferase
AST	aspartate aminotransferase
ATS/ERS	American Thoracic Society/European Respiratory Society
BID	twice daily
CD	Crohn's disease
CFR	Code of Federal Regulations
CL/F	apparent clearance
COA	clinical outcome assessment
COVID-19	coronavirus disease - 2019
CS	clinically significant
CYP	cytochrome P450
DILI	drug-induced liver injury
DLCO	diffusing capacity of the lungs for carbon monoxide
DMC	data monitoring committee
ECG	electrocardiogram
eCRF	electronic case report form
EDC	electronic data capture
[redacted]	
EU	European Union
EudraCT	European Clinical Trials Database
FAS	full analysis set
FDA	Food and Drug Administration
FEV_1	forced expiratory volume in the first one second

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Abbreviation	Definition
FEV_1/FVC	ratio of the FEV_1 to the FVC
FEF25-75	forced expiratory flow between 25% and 75% of exhaled volume
FSH	follicle-stimulating hormone
FVC	forced vital capacity
GCP	Good Clinical Practice
Hb	hemoglobin
hCG	human chorionic gonadotropin
HIV	human immunodeficiency virus
HR	heart rate
HRCT	high-resolution Computed Tomography
ICF	informed consent form
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
IDMC	Independent Data Monitoring Committee
IEC	Independent Ethics Committee
IMP	Investigational Medicinal Product
IPF	Idiopathic Pulmonary Fibrosis
IRB	Institutional Review Board
IRT	interactive response technology
ISO	International Organization for Standardization
ITT	Intent-to-Treat
IV	Intravenous(ly)
[redacted]	[redacted]
LABA	long-acting beta2-agonist
LAMA	long acting muscarinic antagonist
L-PF	Living with Pulmonary Fibrosis
L-PF-Symptoms	Living with Pulmonary Fibrosis Symptoms module
L-PF-Impacts	Living with Pulmonary Fibrosis Impacts module
mAb	Monoclonal antibody
MAD	Multiple-ascending dose
MedDRA	Medical Dictionary for Regulatory Activities
N/A	not applicable
NCI CTCAE	National Cancer Institute Common Terminology Criteria for Adverse Events

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Abbreviation	Definition
NCS	not clinically significant
NOAEL	No-observed-adverse-effect level
NRS	numeric rating scale
PCS	potentially clinically significant
[redacted]	
PK	pharmacokinetic(s)
POC	Proof-of-concept
PPD	Purified protein derivative
PRO	patient-reported outcome
PT	prothrombin time
PTT	partial thromboplastin time
[redacted]	
QTcF	QT interval corrected for heart rate using Fridericia's formula
RSI	Reference Safety Information
SABA	short-acting beta2 agonist
SAD	single ascending dose
SAE	serious adverse event
SAMA	short-acting muscarinic antagonist
SAP	Statistical Analysis Plan
SAR	Serious Adverse Reaction
[redacted]	
SOC	system organ class
SpO_2	peripheral oxygen saturation
[redacted]	
SUSAR	Suspected Unexpected Serious Adverse Reaction

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Abbreviation	Definition
[redacted]	
TEAE	treatment-emergent adverse event
UADE	unanticipated adverse device effect
[redacted]	
ULN	upper limit of normal
US	United States
USADE	unanticipated serious adverse device effect
[redacted]	
V/F	apparent volume of distribution

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19 APPENDIX G. REFERENCES

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[redacted]

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[redacted]

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20 APPENDIX H. PROTOCOL SUMMARY OF CHANGES

Previous Protocol Versions

Protocol	Date
Version 1.0	18 August 2025
Version 1.1 (United States Only)	05 January 2026
Version 1.2 (United Kingdom Only)	02 March 2026
Version 1.3 (European Union Only)	11 February 2026

Master Protocol:

The purpose of this version is to update the protocol with regard to a Health Authority request for information:

[redacted]

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21 APPENDIX I. [redacted] APPENDIX: ABBV-142 MONOTHERAPY

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Substudy 1 Appendix for Clinical Study Protocol M25-268, ABBV-142 vs Placebo
ABBV-142 Monotherapy

SPONSOR:	AbbVie Inc.	ABBVIE INVESTIGATIONAL PRODUCT:	ABBV-142

SUBSTUDY 1 FULL TITLE: Randomized, Double-blind, Placebo-controlled Phase 2a Proof-of-Concept Study of ABBV-142 for the Treatment of Adults Subjects with Idiopathic Pulmonary Fibrosis

For any protocol section not contained below, refer to the master protocol.

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21 SUBSTUDY 1 APPENDIX FOR CLINICAL STUDY PROTOCOL M25-268, ABBV-142 VS PLACEBO

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21.1 [redacted] 1 Specific Activity Schedule

Part 1:

ABBV-142 Substudy-Specific Activity Schedule	Screening	Baseline	[redacted]
	Up to approximately Day -45	Day 1 (± 3 days)	
INTERVIEWS & QUESTIONNAIRES			
Informed consent	X		
Eligibility criteria	X	X	
Medical/surgical history	X		
Alcohol and nicotine use	X		
Adverse event assessment	X	X	X X X X X X X X X X X X X X X X
Prior/concomitant therapy	X	X	X X X X X X X X X X X X X X X X
Name, date, and time of last dose of bronchodilator (if applicable)	X	X	X X X X X X X X X X X X X X X

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ABBV-142 Substudy-Specific Activity Schedule	Screening	Baseline	[redacted]													
	Up to approximately Day -45	Day 1 (± 3 days)														
Contraceptive counseling (review and document continued compliance with pregnancy avoidance recommendations in the source records with females of childbearing potential)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
[redacted]																
Qualitative patient interviews (optional, to be conducted within 14 days after Week 52 visit, not applicable if PD visit)															X	
LOCAL LABS & EXAMS																
12-lead ECG	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Height (screening only) and weight	X				X			X			X				X	
Vital signs & [redacted] vital signs	X														X	

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ABBV-142 [redacted] Specific Activity Schedule	Screening	Baseline	[redacted]													
	Up to approximately Day -45	Day 1 (± 3 days)														
[redacted]		X	X	X	X	X	X	X	X	X	X	X	X	X		
[redacted]																
Full physical examination	X	X														
Physical examination (limited to throat, chest, heart)			X	X	X	X	X	X	X	X	X	X	X	X	X	
Urine pregnancy test (only for females of childbearing potential, and monthly test may be performed at home during Follow Up period)		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Spirometry	X	X	X	X	X	X	X	X		X		X		X	X	
Chest HRCT (refer to Master Protocol Section 8.17 for details)	X															
[redacted]																

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ABBV-142 [redacted] pecific Activity Schedule	Screening	Baseline	[redacted]
	Up to approximately Day -45	Day 1 (± 3 days)	
[redacted]			
DHT provisioned at screening visit	X		
[redacted]			
DHT returned to site			X
CENTRAL LABS			
[redacted]			

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ABBV-142 [redacted] Specific Activity Schedule	**Screening**	**Baseline**
	Up to approximately Day -45	**Day 1 (± 3 days)**

[redacted]

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ABBV-142 [redacted] Specific Activity Schedule	**Screening**	**Baseline**	[redacted]
	Up to approximately Day -45	**Day 1 (± 3 days)**	
[redacted]			
℞ TREATMENT			
[redacted]			

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Part 1a (OPTIONAL PK COHORT): Collections in addition to those specified in Part 1

Study Day	Baseline: Day 1 (± 3 days)		[redacted]
Timepoints	1h After EOI	4h After EOI	[redacted]
INTERVIEWS & QUESTIONNAIRES			
Adverse Event Assessment for on-site PK visits only			X X X X
LOCAL LABS & EXAMS			
[redacted]			
CENTRAL LABS			
[redacted]			

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Part 2 (OPTIONAL OPEN-LABEL EXTENSION)

ABBV-142 [redacted] pecific Activity Schedule	Day 1 (activities in addition to all those listed in Part 1 Week 52)	[redacted]												
INTERVIEWS & QUESTIONNAIRES														
Adverse event assessment		X	X	X	X	X	X	X	X	X	X	X	X	X
Prior/concomitant therapy		X	X	X	X	X	X	X	X	X	X	X	X	X
Name, date, and time of last dose of bronchodilator (if applicable)		X		X			X			X			X	X		
[redacted]														
Contraceptive counseling (review and document continued compliance with pregnancy avoidance recommendations in the source records with females of childbearing potential)		X	X	X	X	X	X	X	X	X	X	X	X	X		
LOCAL LABS & EXAMS														
12-lead ECG							X							X		
Height (screening only) and weight							X							X		
Vital signs & orthostatic vital signs														X		
[redacted]																

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ABBV-142 [redacted] Specific Activity Schedule	Day 1 (activities in addition to all those listed in Part 1 Week 52)	[redacted]
[redacted]		
Physical examination (limited to throat, chest, heart)		X X X X X X X X X X X X X X
Urine pregnancy test (required only for females of childbearing potential, and monthly test may be performed at home during Follow Up period)		X X X X X X X X X X X X X X X
Spirometry		X X X X X X X X X X X X
[redacted]		

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ABBV-142 [redacted] Specific Activity Schedule	Day 1 (activities in addition to all those listed in Part 1 Week 52)	[redacted]
CENTRAL LABS		
[redacted]		
TREATMENT		
[redacted]		

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21.2 Substudy 1 Introduction

Refer to Master Protocol Section 2.1 for Background and Rationale.

Benefit and Risk to Subjects

Benefits

[redacted]

ABBV-142 is currently being characterized in a Phase 1 study (M25-265) in healthy volunteers. [redacted] dose was selected for ABBV-142 in Study M25-268. [redacted]

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[redacted]

21.3 Substudy 1 Objectives, Hypothesis, Estimand, and Endpoints

Objective

The objective is to evaluate the safety, tolerability, and efficacy of ABBV-142 compared with placebo in adult subjects with IPF.

Hypothesis

It is hypothesized that ABBV-142 will be safe and well tolerated in adults with IPF, and ABBV-142 therapy will reduce FVC decline in IPF subjects.

Estimand

The estimand corresponding to the primary efficacy objective for the ABBV-142 substudy is the difference between ABBV-142 and placebo in mean absolute change from baseline through Week 24 in FVC for subjects with IPF and who received at least one dose of study treatment. [redacted] Data after this event will be imputed with an unfavorable value.

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Endpoints

Please see Master Protocol Section 3. In addition, the following substudy-specific secondary, additional, exploratory and safety endpoints will be evaluated.

Secondary Endpoints

- Change from baseline in L-PF overall score at Week 24 and 52.
- Time to first absolute decline from baseline in FVC % predicted of ≥ 10%
- Time to first relative decline from baseline in FVC % predicted of ≥ 10%
- Time to first absolute decline from baseline in FVC % predicted ≥ 5%
- Time to first relative decline from baseline in FVC % predicted ≥ 5%



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[redacted]

Exploratory Endpoints

[redacted]

Safety Endpoints

[redacted]vital signs will be collected as measures of safety and tolerability for the entire study duration, in addition to safety endpoints described in Master Protocol Section 3.

21.4 Substudy 1 Investigational Plan

Overall Study Design and Plan

Substudy 1 is a Phase 2a proof of concept, multicenter, randomized, double-blind substudy to evaluate the safety, tolerability, and efficacy of ABBV-142 in IPF subjects.

[redacted] will include 2 treatment arms, 1 ABBV-142 treatment arm and 1 matching placebo arm.

[redacted]

The duration of Substudy 1 will include a Screening Period (up to approximately 45 days) followed by a 52 week Treatment Period (Baseline - Week 52), and an optional [redacted] open-label treatment period. A follow-up visit/phone call will occur approximately 120 days after the last dose of study drug.

Part 1: Treatment Period

This substudy will include a 52 week double blind treatment period. The absolute change in FVC, as primary endpoint, will be assessed at Week 24 since small molecule inhibitors of LPA_1 demonstrated meaningful reduction in FVC decline over 26 weeks in Phase 2 clinical trial.[7] Additional analysis related to the change in FVC is also planned at Week 52 (Master Protocol Section 3.3).

[redacted]

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[redacted]

Optional Part 1a: PK Cohort

[redacted]

Optional Part 2: Open Label Extension

Following the completion of the 52-week double blind treatment period, study subjects that elect to participate in the OLE will start receiving active treatment during the Week 52 visit at the end of the treatment period (Part 1).

Follow-up Period

The follow-up period for ABBV-142 will be completed with a follow-up visit or phone call after the last dose of study drug. The duration of the follow-up period is approximately 120 days for the planned dose of [redacted] Based on preliminary PK data from the ABBV-142 FIH study (Section 8 of the current ABBV-142 Investigator's Brochure) [redacted]

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Discussion of Study Design

Choice of Control Group

The control group will consist of subjects randomly assigned to receive placebo. Comparative analyses utilizing a double-blind, placebo-controlled design will provide unbiased assessments of efficacy and safety.

All subjects, including those assigned to the placebo arm, are allowed to continue their concomitant use [redacted]IPF therapy, as specified in Section 21.5 and Section 21.7. Subjects assigned to either treatment arm may also initiate treatment with approved and commercially available IPF therapy after withdrawing from the study as specified in Master Protocol Section 7.1.

The rationale for including a placebo control in Sub-Study 1 is to ensure robust, unbiased evaluation of ABBV-142 efficacy and safety. [redacted] Therefore, allowing participants to enroll with or without their existing IPF treatment is consistent with current standard of care practices.

All trial participants will be allowed to continue receiving the supportive standard of care for IPF they were receiving at baseline, in line with IPF guidelines and local best practices. Approved standard of care options for patients with IPF include anti-fibrotics [redacted] as well as supportive therapies such as short-course systemic steroids or oxygen therapy if applicable, for the management of symptoms.[10]

Selection of Doses in the Study

For the ABBV-142 treatment arm in Part 1 (double-blind treatment period) and optional Part 2 (open label extension), ABBV-142 will be evaluated at a fixed dose of [redacted] mg administered as an [redacted] IV infusion.

The dose and dosing regimen for ABBV-142 is selected based on extrapolation of preclinical pharmacology data and analysis of preliminary PK and safety data from the ABBV-141 Phase 1 [redacted] and the [redacted] The [redacted] Finally, [redacted] toxicology study is predicted to provide preliminary exposure-safety margins of approximately [redacted] (based on $C_{max,ss}$ and AUC_{ss}), further supporting this dose regimen in the present clinical study.

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Please refer to the current ABBV-142 Investigator's Brochure for further information on the GLP [redacted] (Section 7.4) and preliminary data from the ABBV-142 FIH Study M25-265 (Section 8).

21.5 Substudy 1 Specific Eligibility Criteria

Subjects are eligible to be included in the [redacted] if they meet all of the eligibility criteria listed in Master Protocol Section 5 and [redacted] specific eligibility criteria below.

Inclusion Criteria

Concomitant Medications

1. No recent changes or planned changes to the dose or regimen for IPF therapy, defined either:
   a) Receiving a stable dose* of IPF-[redacted] therapy [redacted] for at least [redacted] weeks prior to screening visit with no plans to change the concomitant therapy during trial participation, OR

      **stable therapy is defined as the individually and general tolerated regimen of [redacted] [redacted] (no dose changes) for at least [redacted] weeks prior to screening visit.*[11]
   b) Not currently receiving concomitant IPF-approved therapy at Screening (either naïve to IPF-approved therapy or previously discontinued an IPF [redacted] therapy at least [redacted] weeks prior to screening visit or drug-specific, 5 half-lives elimination period if longer than [redacted] weeks), and with no plans to change the concomitant therapy status during trial participation.

Exclusion Criteria

1. Participants with a supine SBP of < 100 mmHg (confirmed by retest within 15 minutes) at screening or prior to Day 1 study drug treatment will be excluded from participation in this study.
2. [redacted]
3. Subjects with a history of hypotension, orthostatic hypotension, or syncope [redacted] will be excluded.

21.6 Substudy 1 Prohibited Medications and Therapy

There are no additional prohibited medications for this substudy other than what is listed in Master Protocol Section 5.4.

21.7 Substudy 1 Prior and Concomitant Therapy

[redacted] but they are not allowed in combination with one another. Concomitant [redacted] medications and other long-term medications for other

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conditions that are not expressly prohibited are allowed. All subjects receiving a stable dose of IPF standard of care treatment at Baseline should maintain their concomitant treatments without dose changes through the end of the study. Doses of these medications may be decreased only in the event of safety or tolerability issues. Initiating and/or changing doses of these medications are prohibited during the study, except when the subjects meet the criteria for rescue therapy.

Also refer to Master Protocol Section 5.4.

21.8 Substudy 1 Specific Contraception Recommendations

Contraception Requirements for Females

Subjects must follow the following contraceptive guidelines as specified:

- Females, Nonchildbearing Potential

  Females do not need to use birth control during or following study drug treatment if considered of nonchildbearing potential due to meeting any of the following criteria:

  1. Premenopausal female with permanent sterility or permanent infertility due to one of the following:
     - Permanent sterility due to a hysterectomy, bilateral salpingectomy, bilateral oophorectomy
     - Non-surgical permanent infertility due to Mullerian agenesis, androgen insensitivity, or gonadal dysgenesis; investigator discretion should be applied to determining study entry for these individuals.
  2. Postmenopausal female
     - Age > 55 years with no menses for 12 or more months without an alternative medical cause.
     - Age ≤ 55 years with no menses for 12 or more months without an alternative medical cause AND a follicle-stimulating hormone level ≥ 30 IU/L.

- Females, of Childbearing Potential

  If a female does not meet the definition of a female of nonchildbearing potential above, she would be considered to be a female of childbearing potential.
  - Review and document pregnancy avoidance recommendations with females of childbearing potential.
  - At each visit, the study staff should review the pregnancy avoidance recommendations with each female of childbearing potential and document this discussion in the subject's source records (see Substudy Activities Table in Section 21.1).
    - Females of childbearing potential must avoid pregnancy while taking study drug(s) and for at least 120 days after the last dose of study drug

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- Females of childbearing potential must use a contraceptive method listed below that is highly effective (with a failure rate of < 1% per year, when used consistently and correctly):
  - Combined (estrogen and progestogen containing) hormonal birth control (oral, intravaginal*, transdermal*, injectable*) associated with inhibition of ovulation-initiated at least 30 days prior to study Baseline Day 1.
  - Progestogen-only hormonal birth control (oral, injectable*, implantable*) associated with inhibition of ovulation initiated at least 30 days prior to study Baseline Day 1.
  - Bilateral tubal occlusion*/ligation (can be via hysteroscopy, provided a hysterosalpingogram confirms success of the procedure).
  - Intrauterine device.
  - Intrauterine hormone-releasing system.
  - Vasectomized partner (provided the partner has received medical confirmation of the surgical success of the vasectomy and is the sole sexual partner of the trial subject).
  - Practice true abstinence, defined as: Refraining from heterosexual intercourse when this is in line with the preferred and usual lifestyle of the subject (periodic abstinence [e.g., calendar, ovulation, symptothermal, post-ovulation methods] and withdrawal are not acceptable).

If required per local regulations, either 2 highly effective methods or an additional effective method of contraception should be used along with one of the highly effective methods above (excluding true abstinence). These include a barrier method (preferably a male condom with or without spermicide*; other barrier methods include female condom*, cap*, diaphragm* or sponge* with spermicide*) or a progestogen-only oral hormonal contraception*, where inhibition of ovulation is not the primary mode of action.

Contraception recommendations related to use of concomitant therapies prescribed should be based on the local label. (Methods of contraception not approved or certified in Japan are marked with an asterisk [*])

Contraception Requirements for Males

Male contraception is not required for this substudy.

21.9 Substudy 1 Study Drug

Treatments Administered

AbbVie will provide ABBV-142 study drug and matching placebo.

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[redacted]

Each dose of ABBV-142 or matching placebo will be administered [redacted] The times of each drug administration (start and end times of infusion) will be recorded to the minute.

Storage and Disposition of Study Drug

[redacted]

Randomization

Subjects will be randomized in a 2:1 ratio to receive ABBV-142 or placebo. Randomization will be stratified by concomitant use of nintedanib or pirfenidone at baseline (yes or no).

All AbbVie personnel with direct oversight of the conduct and management of the trial (with the exception of AbbVie Drug Supply Management Team) will remain blinded through the database lock for the primary analysis (at Week 24). The investigator, study site personnel, and the subject will remain blinded to each subject's treatment throughout the 52-week treatment period (i.e., Part 1). To maintain the blind, the generic name or ABBV-142 infusion bags and syringes as well as placebo infusion bags and syringes provided for the study will be identical in appearance. The IRT will provide access to unblinded subject treatment information in case of a medical emergency.

[redacted]

21.10 Substudy 1 Discontinuation of Study Treatment and Subject Discontinuation/Withdrawal

Withdrawal of Subjects and Discontinuation of Study

Refer to Master Protocol Section 7.1 for any applicable study treatment and subject discontinuation/withdrawal criteria.

In the best interests of subjects, study drug must be permanently discontinued for participants experiencing the events listed below:

[redacted]

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[redacted]

See specific toxicity management details in Section 21.12.

21.11 Substudy 1 Study Specific Procedures

Substudy-specific procedures are provided in this section. Please see Master Protocol Section 8 for all other procedures.

Digital Health Technology

At sites where the DHT is available and accepted for use as a data collection tool in clinical trials, [redacted] DHT will collect [redacted] data to quantify [redacted] for the purpose of assessing treatment effect [redacted]

[redacted]

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[redacted]

Vital Signs

Frequent monitoring of vital signs [redacted] as specified in Section 21.1 [redacted] Specific Activity Schedule, or per local institutional guidelines is required.

Also refer to Master Protocol Section 8.9.

[redacted]

At all study visits, including the screening visit, participants will be carefully monitored for symptoms associated with low BP, [redacted]

[redacted]

[redacted]

When measurements of [redacted] vital signs (blood pressure and pulse rate) are scheduled at the same time as a [redacted], the measurement of [redacted] vital signs will be obtained prior to the blood collection. Whenever possible, measurements of vital signs [redacted]

During [redacted] assessments, participants will be queried for any of the following symptoms that may potentially indicate hypotension [redacted]

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Should any subject's pre- or post-dose measurements meet the Hypotension/Orthostatic Hypotension [redacted] (see Section 21.12 Toxicity management for additional guidelines).

[redacted]

Part 1 All Study Subjects

[redacted]

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Subjects Participating in Part 1a PK Cohort

For subjects participating in the Part 1a optional PK cohort, additional [redacted] vital signs monitoring will be collected along with pharmacokinetic sample collections during PK visits (e.g., Weeks 1, 2, 24, 25, and 26, see Section 21.1 Table Part 1a PK COHORT), except for subjects that choose [redacted] collection [redacted]

Subjects Participating in Part 2 Open label extension

For subjects participating in the Part 2 Open label extension, [redacted] vital signs measurements will be taken on study Day 1, Week 24 and Week 52 /premature discontinuation (see Section 21.1 Table Part 2 Open-label extension).

Pharmacokinetic And Anti-drug Antibody/Neutralizing Anti-drug Antibody Sample Handling, Processing and Shipment

Collection, Handling/Processing and Disposition of Samples for Analysis

[redacted]

Part 1 and Part 2:

On dosing days, ABBV-142 PK samples should be collected by venipuncture at predose (preferably within 30 minutes prior to start of [redacted] **and** post-dose (preferably within 30 minutes after the end of [redacted] at the visits specified in the Substudy 1 Specific Activity Schedule for Part 1 and Part 2.

On Day 1 of Part 1 (i.e., dosing Day 1), the ABBV-142 PK sample should only be collected at the postdose timepoint (i.e., preferably within 30 minutes after [redacted]

On dosing days [redacted] samples should be collected by venipuncture at predose (i.e., preferably within 30 minutes prior to [redacted] at the visits specified in the Substudy 1 Specific Activity Schedule for Part 1 and Part 2.

Optional Part 1a (PK cohort):

On dosing days, ABBV-142 PK samples should be collected by venipuncture at the visits and timepoints specified in the Substudy 1 Specific Activity Schedule for Part 1a, in addition to the collections specified in the Activity Schedule for Part 1.

[redacted]

- Collection by venipuncture at the study site
- At-home collection by venipuncture by a home health nurse (when applicable)

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[redacted]

Additional information on the collection, handling/processing and disposition can be found in the study-specific central laboratory manual according to instructions from AbbVie.

[redacted]

Additional information on the collection, handling/processing and disposition of blood samples can be found in the study-specific central laboratory manual according to instructions from AbbVie.

Measurement Methods

[redacted]

Also refer to Master Protocol Section 8.4.

21.12 Substudy 1 Safety Considerations

Complaints and Adverse Event

Refer to Master Protocol Section 9.1.

If any of the following events are reported, then the following supplemental report must be completed.

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[redacted]

Toxicity Management

Refer to Master Protocol Section 9.3 for study toxicity management measures.

[redacted]

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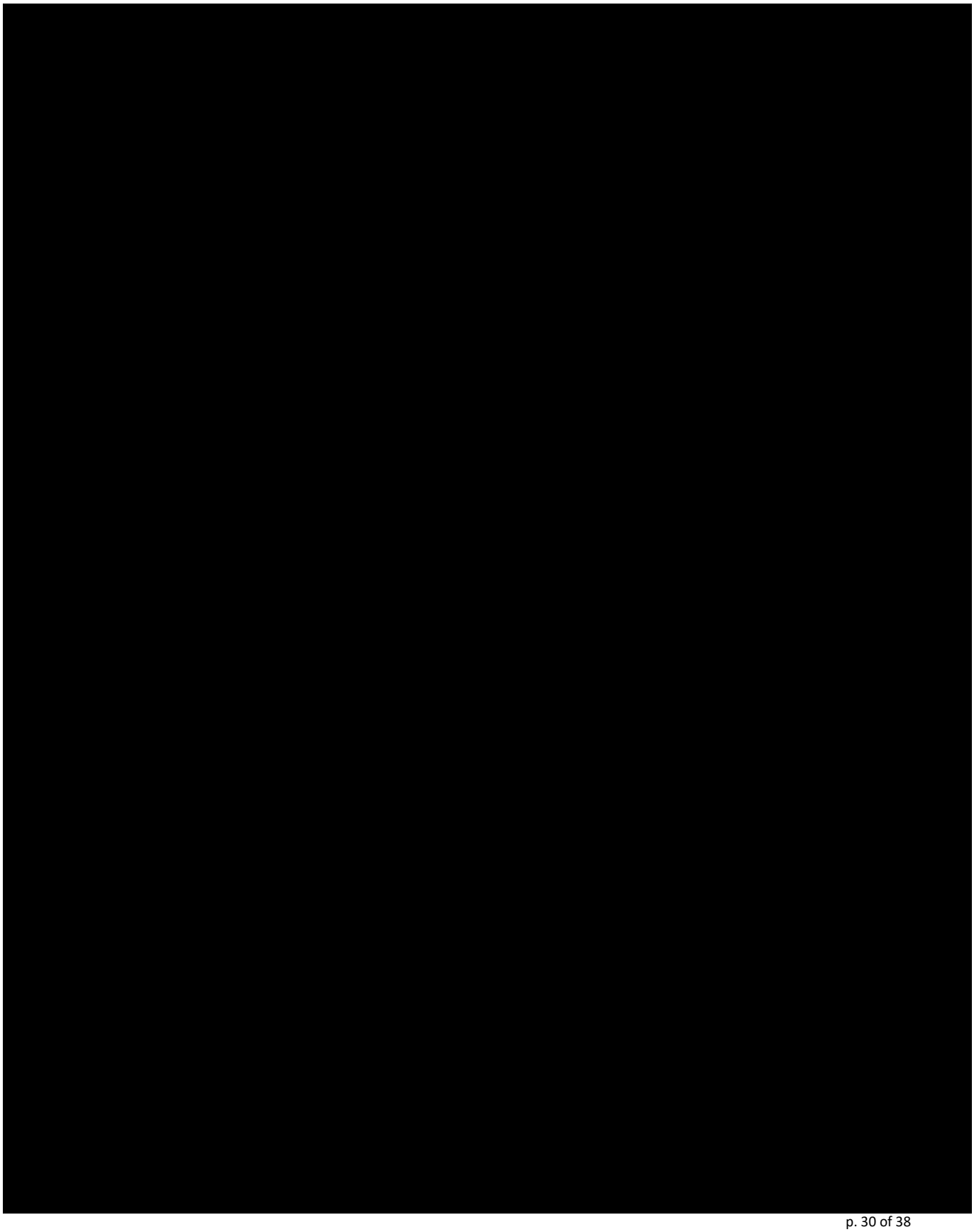
[redacted]



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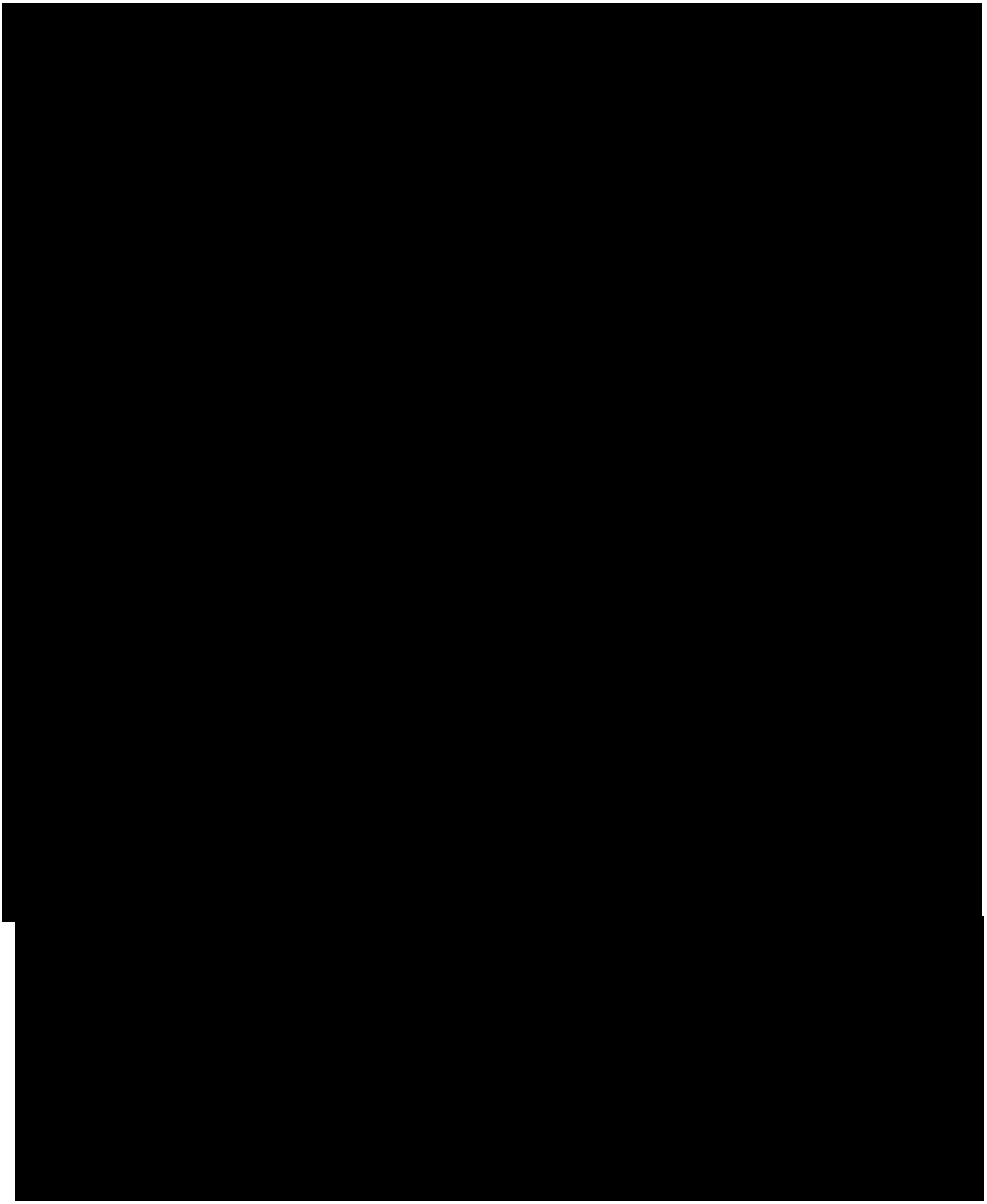

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21.13 Substudy 1 Statistical Methods and Determination of Sample Size

Refer to Master Protocol Section 10 and substudy specific details below.

Hypotheses for Primary/Secondary Efficacy Objective

The clinical hypothesis corresponding to the primary efficacy objective is:

The mean absolute change from baseline in FVC at Week 24 for subjects treated with ABBV-142 is less than that of the placebo group.

Definition of Analysis Populations

The following population will be used for efficacy analyses:

- FAS_IS1 Population: The FAS_IS1 population includes all subjects enrolled and randomized in Substudy 1 (ABBV-142 or placebo) who received at least 1 dose of study drug. The FAS_IS1 Population will be used for the primary efficacy analyses for Substudy 1.

The following population will be used for safety analyses:

- SA_IS1 Population: The SA_IS1 Population includes all subjects who received at least 1 dose of study drug from Substudy 1 (ABBV-142 or placebo). The SA_IS1 Population will be used for safety analyses for Substudy 1.

Additional analysis population(s) will be defined in the SAP for the supplementary analyses using concurrent or non-concurrent control groups across multiple substudies.

IDMC

Refer to Master Protocol Section 11.5 for study IDMC information.

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[redacted]

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21.14 [redacted] Abbreviations and Terms

Abbreviation	Definition
[redacted]	
ADA	antidrug antibodies
AESI	adverse event of special interest
BP	blood pressure
DHT	Digital Health Technology
DBP	diastolic blood pressure
[redacted]	
FIH	first in human
FVC	forced vital capacity
GPS	global positioning system
IA	interim analysis
IDMC	Independent Data Monitoring Committee
IPF	Idiopathic Pulmonary Fibrosis
IRR	infusion-related reaction
LPA_1	lysophosphatidic acid receptor 1
L-PF	Living with Pulmonary Fibrosis
mAb	monoclonal antibody
MVPA	Moderate to Vigorous Physical Activity
NAb	neutralizing antibodies
NRS	numeric rating scale
OH	orthostatic hypotension
PD	pharmacodynamic
PEF	peak expiratory flow
PGIC	Patient Global Impression of Change
PGIS	Patient Global Impression of Severity
PK	pharmacokinetic
Q4W	every 4 weeks
RUO	Research Use Only
SA_IS1	safety population in Substudy 1

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Abbreviation	Definition
SAD	single ascending dose
SAP	statistical analysis plan
SBP	systolic blood pressure
SpO_2	peripheral oxygen saturation
VAS	visual analog scale

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21.15 [redacted] References



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21.16 Substudy 1 Summary of Changes



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Version: 1.0 **Date:** 22-Apr-2026 **Company ID:** 22Apr2026-bba52184-0d5b-4a15-bf02-82f2933f5615-1.0-en

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[redacted]	22-Apr-2026 20:26:30 UTC	Approver - Statistics
	22-Apr-2026 15:33:29 UTC	Approver

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Study M25268 - A Phase 2a Multicenter Platform Study of Investigational Products for the Treatment of Adult Subjects with Idiopathic Pulmonary Fibrosis - Protocol Version 1-3-1 (EU Only) - EU CT 2024-518013-25 - 22Apr2026

Version: 1.0 **Date:** 22-Apr-2026 **Company ID:** 22Apr2026-8083298c-e7e1-4b5e-b35f-1da8accc4a7d-1.0-en

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	22-Apr-2026 15:36:04 UTC	Approver