Abbott	Clinical Investigation Plan Cover Page

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SPIRIT 48
A Clinical Investigation to Assess the Abbott Next Generation Drug Eluting Stent 48mm Everolimus Eluting Coronary Stent System in Treatment of de novo Native Coronary Artery Disease
Study Document No: ABT-CIP-10321
Version D
Date: 24-MAR-2021

Sponsor

Abbott
3200 Lakeside Drive
Santa Clara, CA 95054
USA

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Clinical Investigation Plan

[redacted]

SPIRIT 48 STUDY
A Clinical Investigation to Assess the Abbott Next Generation Drug Eluting Stent 48mm Everolimus Eluting Coronary Stent System in Treatment of de novo Native Coronary Artery Disease

Version Number	Version [redacted]
Date	[redacted]
Study Principal Investigator	[redacted]
Study Co-Principal Investigator	[redacted]
Planned Number of Sites and Region(s)	Up to 33 sites globally in the US and outside of US (OUS)
Clinical Investigation Type	Prospective, single-arm, open-label, multi-center, global (US and OUS) clinical investigation
Abbott Medical Expert	[redacted]
Sponsor	Abbott [redacted]
Clinical Investigation Monitor	Abbott
Electronic Data Capture Software	Oracle
Angiographic Core Laboratories	[redacted]
Clinical Events Committee Administration	[redacted]
Data Safety Monitoring Board	[redacted]
CIP Author of Current Version	[redacted]

[redacted]

Clinical Investigation Plan

SITE PRINCIPAL INVESTIGATOR SIGNATURE PAGE

I have read and agree to adhere to the clinical investigation plan and all regulatory requirements applicable in conducting this clinical investigation.

Site Principal Investigator

Printed name:
Signature:
Date:

Clinical Investigation Plan

COORDINATING CLINICAL INVESTIGATOR / STUDY PRINCIPAL INVESTIGATOR SIGNATURE PAGE

I have read and agree to adhere to the clinical investigation plan and all regulatory requirements applicable in conducting this clinical investigation.

[Coordinating Clinical Investigator / Study Principal Investigator]

Printed name:
Signature:
Date:

Clinical Investigation Plan

TABLE OF CONTENTS

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Clinical Investigation Plan

COMPLIANCE STATEMENT:

This clinical investigation will be conducted in accordance with this Clinical Investigation Plan, the Declaration of Helsinki, applicable Good Clinical Practices and regulations (e.g., US 21 CFR Part 50, 21 CFR Part 56, 21 CFR Part 812 and OUS ISO14155:2011) and the appropriate local legislation(s). The most stringent requirements, guidelines or regulations must always be followed. The conduct of the clinical investigation will be approved by the appropriate Institutional Review Board (IRB)/Ethics Committee (EC) of the respective investigational site and by the applicable regulatory authorities (e.g., FDA, MHRA, etc.).

[redacted]

Clinical Investigation Plan

1.0 INTRODUCTION

The SPIRIT 48mm study is a prospective, single arm, open-label, multi-center global (US and outside of US) clinical investigation to evaluate the safety and effectiveness of the ABT Next Generation Drug Eluting Stent 48 mm everolimus-eluting coronary stent system (EECSS) (called "ABT NG DES 48" hereafter) in up to 107 subjects at up to 33 sites globally. The clinical outcomes from the SPIRIT 48 study will be compared to a performance goal (PG) established using historical control data from the SPIRIT Prime Long Lesion Registry (NCT00916370)[a]. This clinical investigation will be conducted under an investigational device exemption (IDE) and is intended to support market approval of the ABT NG DES 48 in the United States.

This SPIRIT 48 study will be conducted in accordance with this CIP. All investigators involved in the conduct of the clinical investigation will be qualified by education, training, or experience to perform their tasks and this training will be documented appropriately.

1.1 Background and Rationale

Advances in coronary drug-eluting stent (DES) technology have improved the clinical outcomes associated with the treatment of complex coronary artery lesions, including long lesions. However, the currently available DES stent lengths in U.S. (maximum 40 mm)[b] are inadequate to provide complete single stent coverage of long coronary artery lesions. Globally, commercial availability of stents with 48mm length are limited in certain geographic regions, leaving physicians in these regions with the limited option of overlapping stents for long coronary lesion treatment. It was reported by Raper *et. al.* that metal stent overlap in certain situations is associated with stent fracture, malposition, restenosis and delayed vascular healing, and increases the clinical event rates[1]. In addition, Hoffmann *et. al.* reported that the use of multiple stents can also lead to increased procedure time, fluoroscopy time, contrast usage and cost, which have negative impacts on both patients and health economics[2]. Thus, Abbott identified a need for a longer stent length.

The ABT NG DES 48 is a new iteration of the XIENCE family of stents, which includes XIENCE V®, XIENCE PRIME®, XIENCE XPEDITION®, XIENCE ALPINE, XIENCE Sierra, and ABT NG DES 48. Over 13 million XIENCE family of stents have been implanted into patients with coronary artery disease (CAD) [3]. The XIENCE family of stents has been the subject of extensive clinical studies for the treatment of patients with CAD. There was a robust clinical program of Abbott-sponsored clinical investigations assesses the safety and effectiveness of the XIENCE family of stents, which encompasses over 40,000 patients across multiple geographies[3]. Overall, the safety and effectiveness of the XIENCE family of stents have been well established. As an iteration of the XIENCE family of stents, the ABT NG DES 48 is expected to be safe and effective in the treatment of coronary artery long lesions.

[a] https://clinicaltrials.gov/ct2/show/NCT00916370
[b] http://www.translumina.de/products7/TRL136_Yukon_Choice_PC_brochure_WTK_online_LR.pdf

[redacted]

Clinical Investigation Plan

2.0 CLINICAL INVESTIGATION OVERVIEW

2.1 Objective of the Clinical Investigation

The objective of the SPIRIT 48 study is to evaluate the safety and effectiveness of the ABT NG DES 48 in improving coronary artery luminal diameter in subjects with coronary artery disease (CAD) due to *de novo* native coronary artery long lesions.

2.2 Device(s) To Be Used in the Clinical Investigation

2.2.1 Name of the Device(s) Under Investigation

The study device for the SPIRIT 48 study is the ABT NG DES 48, an investigational device, with the following available sizes:

Table 2.2.1-1 ABT NG DES 48 Size Matrix

Stent Design	Product Diameter (mm)	48mm
Small	2.5	X
	2.75	X
	3.0	X
Medium	3.5	X
	4.0	X

The ABT NG DES 48 is manufactured by Abbott.

2.2.2 Intended Indication for Use

The ABT NG DES 48 is intended to be indicated for improving coronary artery luminal diameter in patients, including those with diabetes mellitus, with symptomatic heart disease due to *de novo* native coronary artery lesions (length $\leqslant$ 44 mm) with reference vessel diameters of $\geqslant$ 2.5 mm to $\leqslant$ 4.25 mm. In addition, the ABT NG DES 48 is also intended to be indicated for treating *de novo* chronic total coronary occlusions.

2.2.3 Description of the ABT NG DES 48 Stent System

ABT NG DES 48 is a balloon-expandable stent made of L-605 Cobalt Chromium (CoCr) with a poly (n-butyl methacrylate) (PBMA) and copolymer of vinylidene fluoride and hexafluoropropylene (PVDF-HFP)/everolimus coating. The stent includes two designs – small and medium. The small and medium stent design patterns of ABT NG DES 48 are identical to the respective small and medium stent designs for XIENCE Sierra Everolimus Eluting Coronary Stent System (XIENCE Sierra), and are similar to the rest of the XIENCE family of stents and MULTI-LINK VISION and MULTI-LINK 8, which are the bare-metal stents on which the XIENCE family of stents is based. ABT NG DES 48 medium stent size, (stent diameters 3.50 – 4.00 mm), will have an increased post dilatation expansion diameter up to 5.75 mm, compared to 5.50 mm for XIENCE Sierra. There is no change to the post dilatation expansion diameter for the small stent design.

[redacted]

Clinical Investigation Plan

The ABT NG DES 48 stent systems are device/drug combination products consisting of a drug-coated stent and a balloon expandable delivery system. The stent is coated with a formulation containing everolimus, the active ingredient, embedded in a non-erodible polymer, which is identical to the FDA approved XIENCE Sierra, XIENCE Alpine, XIENCE Xpedition, XIENCE PRIME and XIENCE V EECSS.

2.2.3.1 Stent Platform

Stent platform is fabricated from a single piece of medical grade L-605 Cobalt Chromium alloy. The balloon expandable stent consists of serpentine rings connected by links similar in design to the MULTI-LINK VISION Coronary Stent family and the XIENCE Sierra stent.

2.2.3.2 Anti-proliferative Drug: Everolimus

The active pharmaceutical ingredient in the ABT NG DES 48 is everolimus. Everolimus [40-O-(2-hydroxyethyl)-rapamycin], a drug provided to Abbott by Novartis Pharmaceuticals Corporation, is a novel semisynthetic macrolide immunosuppressant, obtained through chemical modification of rapamycin. Everolimus is a drug that has been evaluated in clinical investigations in the US and Europe for use in conjunction with other medications to prevent heart and renal transplant rejection. The oral form of everolimus (Certican®) had received market approval in over 65 countries. Everolimus has been approved in the United States as Afinitor and is indicated for patients with advanced renal cell carcinoma and manufactured by Novartis Pharmaceuticals Corporation. The nominal drug dose density of 100 µg/cm^2 is ABT NG DES 48, which is identical to all the other predecessors of the XIENCE family of stents.

2.2.3.3 The ABT NG DES 48 Polymer Coating

The coating of ABT NG DES 48 is identical in composition and drug to polymer ratio as the XIENCE Sierra stent coating. The primer layer is composed of poly (n-butyl methacrylate) (PBMA). The drug matrix layer is a co-polymer of vinylidene fluoride and hexafluoropropylene (PVDF-HFP), which controls the release of the drug. PVDF-HFP is blended with the anti-proliferative drug everolimus.

2.2.3.4 ABT NG DES 48 Stent Delivery System

The ABT NG DES 48 stent delivery catheter is available in a rapid-exchange (RX) design with the balloon and stent at the distal end of the catheter. The proximal lumen provides for inflation of the balloon with contrast medium and the central distal lumen permits a guidewire to facilitate advancement of the catheter. The distal and intermediate portions of the device, the tip, and tapers of the balloon are coated with HYDROCOAT™ hydrophilic coating.

Radiopaque markers are positioned on the inner member underneath the balloon to provide accurate positioning of the stent/balloon in the artery. The balloon is designed to deliver an expandable stent of known diameter and length at specified pressures. Markers located on the outside of the proximal shaft help the physician gauge the delivery catheter position relative to the guiding catheter tip. An adaption arm on the proximal end of the device provides access to the inflation lumen. It is designed with a Luer-lock fitting to facilitate connection to an inflation device. There are no novel features of this device.

[redacted]

Clinical Investigation Plan

3.0 CLINICAL INVESTIGATION DESIGN

The SPIRIT 48 study is a prospective, single-arm, open-label, multi-center clinical investigation in up to 107 subjects at up to 33 global sites to evaluate the safety and effectiveness of the ABT NG DES 48 in the treatment of *de novo* native coronary artery long lesions.

3.1 Clinical Investigation Procedures and Follow-up Schedule

A total of up to 107 subjects will be registered in the SPIRIT 48 study. Subjects registered in the study must have exactly one single *de novo* native coronary target lesion (defined in **Section 5.3**), which is eligible to be treated by a single ABT NG DES 48. Planned overlap is not allowed for the treatment of target lesion. If a bailout stent is necessary for the target lesion, a XIENCE family stent with appropriate size (including the ABT NG DES 48) must be used. A non-target lesion, if is located in a different epicardial coronary vessel than the target lesion, is allowed to be treated by stents other than the ABT NG DES 48 per site's standard of care during index procedure. All subjects must be treated with only one ABT NG DES 48.

- Lesions and stent usage: up to two treated lesions, must have exactly one long lesion that is treated by one ABT NG DES 48
    - Single lesion: one *de novo* native coronary artery long lesion (> 32 mm and ≤ 44 mm) as the target lesion, that must be treated a single ABT NG DES 48
    - Two lesions: one target lesion and one non-target lesion, each in different epicardial coronary vessels:
        - Target Lesion: one *de novo* native coronary artery long lesion (> 32 mm and ≤ 44 mm), that must be treated with a single ABT NG DES 48
        - Non-target lesion: one *de novo* native coronary artery lesion, that must be treated by stents other than the ABT NG DES 48 per site's standard of care

A maximum of 40% of subjects with two treated lesions can be registered in the study. At least 50% of the subjects will be registered at US sites.

Each subject will be followed for a two-year period. All subjects will have a hospital or office follow-up visit at 30 days, 6 months, 1 year and 2 years. An office visit is required for 1-year follow-up. All follow-ups must be conducted directly with the subject. Refer to detailed follow-up schedule in **Section 6.5.4**.

Note: If the scheduled visit occurs outside of the allowed window, it is not considered a missed visit/contact. It is a protocol deviation but still considered a completed visit.

3.2 Measures Taken to Avoid and Minimize Bias

A Clinical Event Committee (CEC) and an angiographic core laboratory will be utilized in this study to minimize bias.

3.2.1 Clinical Event Committee

A Clinical Event Committee (CEC) will review and adjudicate all clinical endpoint events. The CEC will, as appropriate, determine if the event that occurred, was clinically indicated vs. non-clinically indicated, if [redacted]

the cause of the event was cardiac or non-cardiac related or if the event was related to the investigational device, the ABT NG DES 48 or not. The CEC will also adjudicate the coronavirus disease 2019 (COVID-19) relatedness of a clinical endpoint event.

3.2.2 Angiographic Core lab

All angiographic data of this clinical investigation will be assessed by the Angiographic Core Lab. The Angiographic Core Lab will determine the type of revascularization (i.e., TLR, TVR or non-TVR), stent thrombosis, or necessary assessments. Angiography must be performed per the angiographic core laboratory guidelines. Angiographic data includes:

- Pre-procedure Morphology
- Pre-procedure quantitative coronary angiography (QCA)
- Post-procedure (Final) Morphology
- Post-procedure (Final) QCA
- Unscheduled visit Morphology and/or QCA

3.3 Suspension or Early Termination of the Clinical Investigation

While no formal statistical rule for early termination of the clinical investigation for insufficient effectiveness of the device under investigation is defined, the Sponsor reserves the right to discontinue the clinical investigation at any stage or reduce the follow-up period with suitable written notice to the investigator. Possible reason(s) may include, but are not limited to:

- Unanticipated adverse device effect (e.g., UADE) occurs and it presents an unreasonable risk to the participating subjects
- An oversight committee (e.g., Steering/Executive Committee, Data Monitoring Committee) makes a recommendation to stop or terminate the clinical investigation (such as higher frequency of anticipated adverse device effects)

Should the clinical investigation be discontinued by the Sponsor, subjects will be followed per routine hospital practice with device-related AEs reported to the Sponsor as per vigilance/commercial reporting requirements. The investigator shall return all clinical investigation materials (including devices) to the Sponsor, and provide a written statement to the IRB/EC (if applicable). All applicable clinical investigation documents shall be subject to the same retention policy as detailed in **Section 11.5** of the CIP.

A Principal Investigator, IRB/EC or regulatory authority may suspend or prematurely terminate participation in the clinical investigation at the investigational site(s) for which they are responsible. The investigators will follow the requirements specified in the Clinical Investigation Agreement.

If the Sponsor suspends or prematurely terminates the clinical investigation at an individual site in the interest of safety, the Sponsor will inform all other Principal Investigators.

If suspension or premature termination occurs, the Sponsor will remain responsible for providing resources to fulfill the obligations from the CIP and existing agreements for following the subjects

enrolled in the clinical investigation, and the Principal Investigator or authorized designee will promptly inform the enrolled subjects at his/her site, if appropriate.

4.0 ENDPOINTS

4.1 Primary Endpoint and Rationale

The Primary Endpoint of the SPIRIT 48 Study is target lesion failure (TLF) defined as a composite of cardiac death, target vessel myocardial infarction [TV-MI] (MI is per Society for Cardiovascular Angiography and Interventions (SCAI) definition[4]), and clinically indicated target lesion revascularization [CI-TLR])[c] at 1 year. The 1-year TLF will be compared to a pre-specified performance goal (PG) of 20%. More details will be found in **Section 8** for the statistical analysis plan.

TLF is chosen as the primary endpoint because TLF is a standard endpoint that was proposed by ARC[5] and is also recommended in FDA's draft guidance for coronary DES clinical trials[6].

4.2 Secondary Endpoint(s)[d]

- TLF in hospital, at 30 days, 180 days, and 2 years

Secondary endpoints are descriptive without a pre-specified statistical assumption.

4.3 Other Endpoint(s)[d]

Other endpoints are descriptive and include:

- Acute Success: (combined clinical and angiographic)
  - Device Success (Lesion basis)
  - Procedural Success (Subject basis)
- Clinical Endpoint in hospital and at each clinical follow-up time point (30 days, 180 days, 1 and 2 years)

  Composite:
  - All death, all MI and all revascularization (DMR)
  - Cardiac Death/MI

  Individual:
  - Any death
    - Cardiac
    - Vascular
    - Non-cardiovascular

[c] The first adjudicated COVID-19 likely related component of the primary endpoint event along with the subsequent follow-up data will be censored and will not contribute towards the primary endpoint analysis.
[d] MI is per SCAI definition.

[redacted]

- All MI
  - Q-wave MI (QMI)
  - Non-Q-wave MI (NQMI)
- TV-MI
  - Type
    - QMI
    - NQMI
- Any Revascularization
  - All TVR (including TLR)
    - ID-TVR
  - All TLR
    - ID-TLR
  - All Non-TVR
- Stent thrombosis (per ARC definition)
  - Type
    - Definite
    - Probable
    - Possible
  - Time
    - Acute (≤ 1 day)
    - Subacute (>1 day ≤ 30 days)
    - Late (>30 days ≤ 365 days)
    - Very late (>365 days)

A secondary analysis with MI per ARC 2 definition[7] and 4th universal definition[8] will be performed for all endpoints containing MI. will be performed for all endpoints containing MI.

5.0 SUBJECT SELECTION AND WITHDRAWAL

5.1 Subject Population

Subjects enrolled into this clinical investigation will be male and female subjects derived from the general interventional cardiology population. The clinical investigation will register up to 107 subjects, with a maximum of two *de novo* coronary artery lesions (among them, only one target lesion is allowed and must be treated by an ABT NG DES 48, the other lesion must be a non-target lesion and be treated by stents other than the ABT NG DES 48) in separate epicardial coronary vessels. Subjects must meet all eligibility criteria and provide written informed consent prior to conducting any investigation-specific procedures that are not considered standard of care at the site.

5.2 Subject Screening and Informed Consent

5.2.1 Subject Screening

Subjects planned to be admitted for a percutaneous coronary artery revascularization procedure should be screened for clinical investigation eligibility by a member of the research team previously trained to the CIP.

[redacted]

Subjects have signed an Informed Consent form (ICF) (Refer to **Section 5.4, Subject Enrollment and Point of Registration**) are considered enrolled in the SPIRIT 48 study. An informed consent form has to be signed prior to the index procedure of the clinical investigation.

Subject data will be collected following enrollment into the clinical investigation.

5.2.2 Informed Consent

The Investigator or his/her authorized designee (if applicable) will conduct the Informed Consent process, as required by applicable regulations and the site's IRB/EC. This process will include a verbal discussion with the subject on all aspects of the clinical investigation that are relevant to the subject's decision to participate, such as details of clinical investigation procedures, anticipated benefits, and potential risks of clinical investigation participation. Subjects must be informed about their right to withdraw from the clinical investigation at any time and for any reason without sanction, penalty or loss of benefits to which the subject is otherwise entitled. Withdrawal from the clinical investigation will not jeopardize their future medical care or relationship with the investigator.

During the discussion, the Principal Investigator or his/her authorized designee will avoid any improper influence on the subject and will respect subject's legal rights. Financial incentives will not be given to the subject. Subjects may be compensated for time and travel directly related to the participation in the clinical investigation. The subject shall be provided with the Informed Consent form written in a language that is understandable to the subject and has been approved by the center's IRB/EC. The subject shall have adequate time to review, ask questions, and consider participation. The Principal Investigator or his/her authorized designee will make efforts to ensure that the subject understands the information provided. If the subject agrees to participate, the Informed Consent form must be signed and dated by the subject and thereafter by the person obtaining the consent prior to any clinical investigation-specific procedures. The signed original will be filed in the subject's hospital or research charts, and a copy will be provided to the subject.

Failure to obtain informed consent from a subject prior to clinical investigation enrollment should be reported to Sponsor within 5 working days and to the reviewing center's IRB/EC according to the IRB's/ EC's reporting requirements.

If, during the clinical investigation, new information becomes available that can significantly affect a subject's future health and medical care, the Principal Investigator or his/her authorized designee (if applicable) will provide this information to the subject. If relevant, the subject will be asked to confirm their continuing informed consent in writing.

5.2.2.1 Special Circumstances for Informed Consent

Incapacitated individuals, defined as persons who are mentally ill, mentally handicapped, or individuals without legal authority, are excluded from the study population.

Individuals unable to read or write may be enrolled in this clinical investigation. Informed consent will be obtained through a supervised oral process. An independent witness will be present throughout the Informed Consent process. The written Informed Consent form and any other information will be read aloud and explained to the prospective subject or his/her legally acceptable representative and either will sign and personally date the Informed Consent form. The witness will also sign and personally date the

Informed Consent form attesting that the information was accurately explained, and that informed consent was freely given.

Pregnant or breastfeeding women are excluded from the study population.

All other aspects of the Informed Consent process will be in compliance with **Section 5.2.2**.

In addition, an authorization for use and disclosure of the subject's protected health information, in accordance with the Health Insurance Portability and Accountability Act (HIPAA), must be obtained from the subject or their legally acceptable representative (US subjects only).

For live cases at congresses, the subjects need to sign a specific Live Case ICF, approved by the IRB/EC and by the Sponsor, as well as by the competent authorities (e.g., FDA, or local IRB/EC), as applicable. The investigator must request Sponsor approval prior to performing a live case.

5.3 Eligibility Criteria

5.3.1 General Eligibility Criteria

Assessment for general eligibility criteria is based on medical records of the site and interview with a candidate subject. If some of the clinical or laboratory tests are not included in site standard tests or subject's medical record, they must be done after written informed consent is obtained. Subjects must meet ALL of the eligibility criteria to be considered for the clinical investigation.

5.3.2 Inclusion Criteria

5.3.2.1 General Inclusion Criteria

1. Subject must be at least 18 years of age.

2. Subject or a legally authorized representative must provide written informed consent prior to any study related procedure, per site requirements.

3. Subject must have evidence of myocardial ischemia (e.g., unstable angina, post-infarct angina, stable angina or silent ischemia) suitable for non-emergent PCI. Subject with stable angina or silent ischemia must have objective sign of ischemia as suggested by one of the following:

    - Abnormal stress or imaging stress test
    - Abnormal computed tomography-fractional flow reserve (CT-FFR)
    - Stenosis by visual estimation ≥ 70%
    - Abnormal pressure-derived indexes (FFR, instantaneous wave-free ratio [iFR], or relative flow reserve [RFR])

4. Subject must be an acceptable candidate for coronary artery bypass graft (CABG) surgery.

[redacted]

5. Subject must agree not to participate in any other clinical study for a period of one year following the index procedure.

5.3.2.2 Angiographic Inclusion Criteria

1. Only one *de novo* target lesion in native coronary artery is allowed to be treated with the investigational stent.
    - One additional non-target lesion can be treated if it is located in a different epicardial coronary vessel and NOT in left main coronary artery. The non-target lesion must be treated first and must be deemed an angiographic success.
2. The target lesion must be located in a native coronary artery with:
    - Visually estimated reference vessel diameter (RVD) of ≥ 2.5 mm and ≤ 4.25 mm.
    - Visually estimated lesion length of > 32 mm and ≤ 44 mm, and able to be covered by a single ABT NG DES 48
        - Multiple focal *de novo* lesions in an epicardial coronary vessel are allowed if the lesions can be covered by one stent. Multiple focal *de novo* lesions will be counted as a single lesion.
    - Visually estimated diameter stenosis of > 50% and < 100% with a Thrombolysis in Myocardial Infarction (TIMI) flow of ≥ 1
        - Stable angina or silent ischemia subjects must have stenosis ≥ 70%, or abnormal pressure-derived physiological indices (FFR, iFR, or RFR), unless abnormal stress or imaging stress test is evidenced

5.3.3 Exclusion Criteria

5.3.3.1 General Exclusion Criteria

1. Subject has known hypersensitivity or contraindication to device material and its degradants (everolimus, cobalt, chromium, nickel, tungsten, acrylic and fluoropolymers, etc.), or has known contrast sensitivity.
2. Subject has known hypersensitivity or contraindication to aspirin, heparin/bivalirudin, P2Y12 inhibitors (clopidogrel /prasugrel /ticagrelor), and therefore cannot be adequately pre-medicated.
3. Subject has a planned surgery or procedure necessitating discontinuation of aspirin or P2Y12 inhibitor within 12 months following index procedure.
4. Subject is receiving or will require chronic anticoagulation therapy (e.g., coumadin, dabigatran, apixaban, rivaroxaban or any other agent for any reason).

Clinical Investigation Plan

5. Pregnant or nursing subjects and those who plan pregnancy in the period up to 1 year following index procedure. Female subjects of child-bearing potential must have a negative pregnancy test done within 7 days prior to the index procedure per site standard test.

6. Subject had an acute myocardial infarction (AMI) within 48 hours of the index procedure with either of the situations below:

    - The subject is currently experiencing clinical symptoms consistent with new onset AMI, such as nitrate-unresponsive prolonged chest pain with ischemic electrocardiogram (ECG) changes

    - Elevated cardiac biomarker values have not returned to within normal limits at the time of index procedure.

7. Subject has a left ventricular ejection fraction (LVEF) < 30% within 3 months prior to the index procedure, that was documented by any method.

8. Subject is expected to require percutaneous mechanical cardiac support at the index procedure.

9. Prior PCI within the target vessel during the last 12 months prior to consent.

10. Prior PCI within the non-target vessel or any peripheral intervention during the last 30 days prior to consent.

11. At the index procedure, subject is identified to require planned stenting procedure (including staged procedures) or CABG after the index procedure.

12. Subject has received a solid organ transplant which is functioning or is active on a waiting list for any solid organ transplants with expected transplantation within 24 months.

13. Subject has a malignancy that is not in remission.

14. Subject is receiving immunosuppressant therapy or has known life-threatening immunosuppressive or severe autoimmune disease (e.g., human immunodeficiency virus, systemic lupus erythematosus, etc.). Note: corticosteroids are not included as immunosuppressant therapy, diabetes mellitus is not regarded as autoimmune disease

15. Subject has previously received or is scheduled to receive radiotherapy to a coronary artery (vascular brachytherapy), or the chest/mediastinum.

16. Subject has a platelet count < 100,000 cells/mm^3 or > 700,000 cells/mm^3.

Clinical Investigation Plan

17. Subject has renal insufficiency as defined as an estimated glomerular filtration rate (GFR) < 30 ml/min/1.73m^2 or dialysis at the time of consent[e].

18. Subject is high risk of bleeding for any reason; has a history of bleeding diathesis or coagulopathy; has had a significant gastro-intestinal or significant urinary bleed within the past six months.

19. Subject has had a cerebrovascular accident or transient ischemic neurological attack (TIA) within the past 6months, or any prior intracranial bleed, or any permanent neurologic defect, or any known intracranial pathology (e.g. aneurysm, arteriovenous malformation, etc.).

20. Subject has extensive peripheral vascular disease that precludes safe 6 French sheath insertion. Note: femoral arterial disease does not exclude the subject if radial access may be used.

21. Subject has life expectancy < 2 years.

22. Subject is, in the opinion of the Investigator or designee, unable to comply with the requirements of the study protocol or is unsuitable for the study for any reason. This includes completion of Subject Reported Outcome instruments.

23. Subject is currently participating in another clinical investigation (except for non-invasive observational studies) that has not yet completed its primary endpoint.

24. Subject intends to participate in another investigational drug or device clinical investigation (except for non-invasive observational studies) within 12 months after the index procedure.

25. Subject has other medical illness (e.g., cancer or congestive heart failure) or known history of substance abuse (alcohol, cocaine, heroin etc.) that may cause non-compliance with the protocol, confound the data interpretation or is associated with a limited life expectancy less than 2 year.

26. Presence of other anatomic or comorbid conditions, or other medical, social, or psychological conditions that, in the investigator's opinion, could limit the subject's ability to participate in the clinical investigation or to comply with follow-up requirements, or impact the scientific soundness of the clinical investigation results.

27. Subject has active symptoms and/or a positive test result of COVID-19 or other rapidly spreading novel infectious agent within the prior 2 months.

Angiographic Exclusion Criteria:

1. Target lesion/vessel meets any of the following criteria:

    - Prevents complete angioplasty balloon (plain old balloon angioplasty [POBA], scoring balloon, or cutting balloon) inflation, such as:

[e] Estimated GFR can be based on Modification of Diet in Renal Disease (MDRD) equation or Cockcroft-Gault equation (CCG).

[redacted]

- Heavy calcified lesion
- Requires additional device for lesion preparation (e.g., rotablator or laser)

- Anatomy proximal to or within the lesion that prevents proper placement of delivery system:
  - Extreme angulation (≥ 90°) proximal to or within the target lesion
  - Excessive tortuosity (≥ two 45° angles) proximal to or within the target lesion
- Involves a bifurcation of which the side branch will be jailed by the struts and requiring side branch pre-dilatation by Kissing Balloon Technique, and/or stenting.
- Is located:
  - In left main or there is a ≥30% diameter stenosis in the left main (unless the left main lesion is a protected left main (i.e. a patent bypass graft to the LAD and/or LCX arteries is present), and there is no intention to treat the protected left main lesion.
  - Within 3 mm of the origin of the LAD or LCX.
  - Within 3 mm of aorto-ostial RCA.
  - In a bypass graft or distal to anastomotic site of bypass graft.
- With total occlusion (TIMI flow 0), prior to crossing with the wire.
- Contains thrombus.
- The subject has been previously treated with a stent within 1-year prior to the index procedure such that the ABT NG DES 48 would need to cross the stent to reach the target lesion.

2. Unsuccessful target lesion pre-dilatation, defined as the presence of one or more of the following:
   - Failed for a full inflation of the pre-dilatation balloon.
   - TIMI flow grade <3 (per visual estimation).
   - Any angiographic complication (e.g. distal embolization, no-reflow).
   - Any dissection National Heart, Lung, and Blood Institute (NHLBI) grade D-F.
   - Any chest pain lasting > 5 minutes.
   - Any ST-segment depression or elevation lasting > 5 minutes.
   - Side branch requires additional dilatation/stenting caused by plaque shift, carina shift or may require additional dilatation/stenting after stent implantation, per the operator's assessment.

[redacted]

3. Non-target lesion meets any of the following criteria:
    - Is located in the target vessel
    - Is located in the left main location
    - Is restenotic from a previous stent implantation
    - Is located within a saphenous vein graft or an arterial graft
    - Is with a TIMI flow 0 (total occlusion) prior to guide wire crossing
    - Involves a complex bifurcation that needs two-stent strategy
4. Treatment of non-target lesion is not deemed successful.
    - Note: A successful treatment is defined as a treatment resulted in a mean lesion diameter stenosis < 30% in 2 near-orthogonal projections with TIMI 3 flow, as visually assessed by the physician, without the occurrence of prolonged chest pain or ECG changes consistent with MI.

5.4 Subject Enrollment and Point of Registration

A subject is considered enrolled in the clinical investigation from the moment the subject provides written informed consent.

The point of registration is when an ABT NG DES 48 is started to be delivered beyond the tip of the guide catheter, entering into a subject's vasculature.

A subject who is enrolled but not registered into this study will be considered as a screen failure. If an enrolled subject is not found meeting general eligibility criteria prior to the index procedure, or not meeting angiographic eligibility criteria during the index procedure, the subject should not be registered and should be considered as a screen failure.

5.4.1 Enrollment of Medicare Beneficiaries (US only)

This section is only applicable to sites enrolling subjects in the United States.

This clinical investigation will enroll Medicare beneficiaries that qualify based on the inclusion and exclusion criteria defined for this clinical investigation. This IDE clinical investigation conforms to all standards of Medicare coverage requirements. The **Risk Analysis** (**Section 15**) describes how all enrolled subjects, including Medicare beneficiaries, may be affected by the device under investigation.

A portion of the subjects enrolled in the clinical investigation display characteristics consistent with the Medicare population based on age or gender. The clinical investigation results will be analyzed by age (< 65 years and ≥ 65 years) or by gender and compared to ensure that the outcomes are similar between the Medicare and non-Medicare populations.

[redacted]

5.4.2 Historically Under-Represented Demographic Subgroups

Abbott intends to implement FDA's guidance on sex-specific data in medical device clinical investigations to ensure adequate representation of women and other traditionally under-represented demographic subgroups in this clinical investigation. As noted in the guidance, some barriers to participation of women and ethnic minorities in clinical investigations have traditionally been:

- Lack of understanding about main obstacles to participation of such subgroups in clinical research
- Inclusion/exclusion criteria potentially not needed to define the clinical investigation population may unintentionally exclude specific subgroups
- Under diagnosis of disease etiologies and pathophysiology leading to under referral of demographic subgroups
- Avoidance of specific subgroups by investigators and Sponsors due to the perception that it takes more time and resources to recruit them
- Fear of fetal consequences (for female participants)
- Family responsibilities limiting women's ability to commit time for follow-up requirements

Historically, in the SPIRIT PRIME Long Lesion Registry (LLR), which was a US study to evaluate the safety and effectiveness of XIENCE PRIME (another XIENCE family of stent) in treatment of long coronary lesions, the study population had approximately 30-40% female and an average age of 64[9]. More than 8% of the patients in the SPIRIT PRIME LLR was non-white minority ethnicity.

As the SPIRIT 48 study will also enroll subjects in US, and has almost identical inclusion/exclusion criteria on the enrollment of female and minority ethnicity as for the SPIRIT PRIME LLR, Abbott expects similar proportions of female and minority ethnicity within US for the SIPRIT 48 study compared to SPIRIT PRIME LLR. The traditional barriers for female enrollment (such as fear or fetal consequence, family plan of having new babies that may limit the ability of time commitment to trial follow-up) are not applicable to the SIPRIT 48 study due to the expected average age of the patient population. Therefore, the eligibility criteria of the SIPRIT 48 study do not introduce gender or racial bias.

Abbott will take the following steps to ensure adequate representation of women and racial or ethnic minorities in this clinical investigation:

- Provide training to investigational site personnel to ensure adequate representation of these demographic subgroups
- Regularly review enrollment data to investigate whether there is under-representation of these demographic subgroups
- Regularly review withdrawal rates for under-represented subgroups and compare these rates with that in the overall clinical investigation population
- Retrain sites on the importance of recruiting and retaining subjects in the clinical investigation as appropriate and necessary
- Approach sites without bias or consideration for specific demographic subgroups
- Have informed consent materials in alternative languages and will work with sites and IRBs/ECs on recruitment materials

[redacted]

5.5 Subject Withdrawal

A subject is considered enrolled in the clinical investigation if signed informed consent is obtained.

Subjects who are withdrawn from the study will be followed (including AE reporting) until the time of withdrawal.

Subjects who are discontinued by site or the Sponsor will not be replaced.

Each registered subject shall remain in the clinical investigation until completion of the required follow-up period; however, a subject's participation in any clinical investigation is voluntary and the subject has the right to withdraw at any time without penalty or loss of benefit. Conceivable reasons for discontinuation may include, but not be limited to, the following:

- Subject voluntary withdrawal
- Subject is withdrawn by site or sponsor
- Subject lost-to follow-up as described below
- Subject's follow-up is terminated according to **Section 3.3 Suspension or Early Termination of the Clinical Investigation**.

The Sponsor must be notified of the reason(s) for subject withdrawal. The site will provide this information to the Sponsor. Investigators must also report this to their respective IRB/EC as defined by their institution's procedure(s).

No additional follow–up will be required or data recorded from subjects once withdrawn from the clinical investigation.

However, if a subject withdraws from the investigation due to problems related to the safety or performance of the device under investigation, the investigator shall ask for the subject's permission to follow his/her status/condition outside of the clinical investigation by means of mutual agreement.

In case of subject withdrawal of consent, the site should make attempts to schedule the subject for a final clinical investigation visit. At this final follow-up visit, the subject will undergo the following assessments:

- Review and report adverse events in electronic case report form (eCRF)
- Review and report protocol and concomitant medications in eCRF
- Complete subject reported outcomes in eCRF

<u>Lost-to-Follow-up</u>

If the subject misses two consecutive CIP-required follow-up visits and the attempts at contacting the subject detailed below are unsuccessful, then the subject is considered lost-to-follow-up. Site personnel shall make all reasonable efforts to locate and communicate with the subject (and document these efforts in the source documents), including the following, for CIP-required follow-up visits:

- A minimum of two telephone calls on different days during the specified follow-up windows to contact the subject should be recorded in the source documentation, including date, time and initials of site personnel trying to make contact.

[redacted]

- If these attempts are unsuccessful, a letter (certified if applicable) should be sent to the subject.
- If a subject misses one or more non-consecutive follow-up visits, those will be considered as missed visits. The subject may then return for subsequent visits. If the subject misses two consecutive follow-up visits and the above-mentioned attempts at communicating with the subject are unsuccessful, the subject will be considered lost-to-follow-up.

Note: Telephone contact with a General Practitioner, non-clinical investigation cardiologist or relative without the presence of the subject or indirect documentation obtained via discharge letters will not be considered as subject contact.

5.6 Number of Subjects

Up to 107 subjects will be registered in the clinical investigation in order to analyze the primary endpoints. No site may register more than 20% of the total subjects.

5.7 Total Expected Duration of the Clinical Investigation

[redacted] The expected duration of each subject's participation is 2 years, including the scheduled visits and data collection for this clinical investigation that will occur at 1 month, 6 months, 1 year and 2 years. Subjects will be exited from the trial at the conclusion of their 2-year follow-up visit. Therefore, the total duration of the clinical investigation is expected to be [redacted] consisting of approximately [redacted] plus 2 years of follow-up. Subjects will be exited from the trial at the conclusion of their 2-year follow-up visits.

6.0 TREATMENT AND EVALUATION OF ENDPOINTS

6.1 Baseline Assessment

Subject preparation will occur in accordance with standard hospital policy for the care of interventional cardiovascular subjects. The baseline assessments described below must be obtained within 30 days prior to consent, unless indicated otherwise. They will be documented in the subject medical record and on the eCRF as appropriate.

The schedule of events for this trial is located in **Section 6.5.4**.

6.1.1 Subject Demographics and Medical History

Subject history will include but not be limited to the following demographics, risk factors and comorbidities: age, height, weight, body mass index (BMI), gender, hypertension, hyperlipidemia, diabetes mellitus, smoking, ischemic heart disease (history of myocardial infarction, angina pectoris, previous percutaneous or surgical coronary revascularization), congestive heart failure, renal insufficiency, liver disease, cerebrovascular disease (known carotid artery disease, history of minor or major stroke or transient ischemic attack), and chronic obstructive pulmonary disease (COPD).) All information will be obtained and recorded in eCRF.

A medication history should be documented, including:

- Anticoagulants (warfarin, unfractionated or low molecular weight heparins, etc.);

[redacted]

- Antithrombotic agents (acetylic salicylic acid, thienopyridines, glycoprotein IIb/IIIa inhibitors, direct thrombin inhibitors, etc.);
- Statins or other lipid lowering agents; beta-blockers; angiotensin converting enzyme inhibitors; angiotensin-II receptor antagonists;
- Insulin and oral hypoglycemic agents;

6.1.2 Pre-procedure Laboratory Assessments

The following laboratory assessment must be obtained at pre-procedure:

- Baseline 12-lead ECG
- Cardiac biomarker tests measuring creatine Kinase-MB (CK-MB) and troponin must be conducted. If a ST-Elevation MI (STEMI) or non-ST-Elevation MI (NSTEMI) is identified based on a cardiac biomarker level, the cardiac biomarker level has to return to normal limits prior to index procedure in order for the subject to be registered in the clinical investigation. If the subject has stable coronary artery disease or silent ischemia, the pre-procedure cardiac biomarker can be obtained during procedure from the arterial sheath but prior to any angioplasty, the lab results for cardiac biomarkers can be obtained at post-procedure.
- A pregnancy test must be administered to all female subjects of childbearing potential within 7 days prior to the procedure and return as negative.
- The latest LVEF status within the past 3 months prior to the index procedure (has to be documented by any method).

Other laboratory assessments (such as blood counts, chemistry panel and lipid panel, etc.) should be obtained per site's standard of care. Baseline laboratory results related to inclusion/exclusion criteria must be available and reviewed prior to the procedure for screening.

6.1.3 Pre-Procedure Preparation

Subjects should be prepared according to the healthcare facility's standard of care for cardiology subjects undergoing PCI. The ABT NG DES 48 mm stent or other XIENCE stents to be placed should be inspected, prepared, and implanted according to the most current instruction for use (IFU).

6.1.4 Peri-Procedure Medications

Loading dose of P2Y12 inhibitor medications (clopidogrel, prasugrel, ticagrelor, etc.):

- Follow the IFU of each drug for loading dose and timing. If not indicated in IFUs, then follow the site's standard of care.

Loading dose of aspirin:

- ≥ 300 mg must be administered 0* to 24 hours prior to PCI or up to 1-hour post-procedure.
- The aspirin loading dose may be omitted for those subjects on chronic aspirin therapy (≥ 7 days).

* Zero refers to administration immediately prior to balloon pre-dilatation of the first target lesion.

[redacted]

It is recommended that all antiplatelet medication loading doses to be given before the procedure (within 24 hours prior to procedure), at time of procedure, or post-procedure (recommended to be within 1-hour post-procedure).

6.2 Index Procedure

6.2.1 Procedures Involved in the Use of the Device Under Investigation

For appropriate use of the ABT NG DES 48, refer to the IDE IFU and the treatment strategy section **(section 6.2.4)** below.

6.2.2 Baseline Angiography

Baseline angiography of the target vessel will be completed as per the angiographic core laboratory guidelines. Angiography of the vessel not treated with the ABT NG DES 48 (if required), may be performed per site standard. Baseline (prior to pre-dilatation) angiogram must be sent to the core lab or the sponsor.

6.2.3 Procedure Information Should be Collected

The following data should be collected (including, but not limited to):

- Stent use attributes (e.g., size, diameter, overlapping, and number of stents)
- Lesion characteristics (ACC/AHA Classification Scheme of Coronary Lesions)
- All reportable adverse events (AEs) (refer to section 7.3.1 Adverse Event Reporting)

6.2.4 Treatment Strategy

The following treatment strategy must be followed during the index procedure:

- Any non-target lesion must be treated first with commercially available stents (<=38 mm) and deemed to be successful.
- Pre-dilatation of the target lesion is mandatory and deemed to be successful.
    - The pre-dilatation balloon must be shorter than the planned stent(s) length to limit pre-dilatation injury to the area to be stented (recommended 4-6 mm shorter than the planned stent).
- Select appropriate diameter of ABT NG DES 48
    - If there is considerable vessel taper it is recommended to select a stent that matches the distal RVD to avoid over expansion of the vessel.
    - Intravascular imaging is allowed per the approved ICF and per physician's discretion. If optical coherence tomography (OCT) is used for vessel size measurement, it is recommended to follow the approved IFU for guidance. Sites using OCT for vessel sizing will be asked to provide OCT images to the Sponsor. Analysis for OCT may be conducted to assess vessel sizing.

[redacted]

- Use 6 or above French guiding catheter for delivery and deployment of the ABT NG DES. A guide extension, a stronger back-up support guide catheter, as well as a buddy wire, may be considered. Deploy the ABT NG DES 48 per the IFU. Do not exceed the rated burst pressure (16 atm) as indicated in the IFU of the stent.
- Post-dilatation is strongly recommended with the following guidelines:
    - Should only be performed with balloon lengths that fit within the boundaries of the stent
    - The use of a high pressure, non-compliant balloon is strongly recommended.
    - If appropriate, the delivery balloon (stent balloon) may be used for post-dilatation.
    - If considerable vessel taper exists, post-dilate the proximal/distal stented segments with a balloon that matches the corresponding proximal/distal segment RVD, if appropriate.
- Bailout procedure for the side branch should only be done:
    - If new onset of chest pain or ECG changes that suggests ischemia occur, caused by the side branch occlusion during or after stenting, side branch dilatation can be done.
    - Side branch stenting should be avoided unless severe dissection is observed.
    - If kissing balloon is required, delivery balloon must not be used.

6.2.5 Final (Post-procedure) Angiography

In all subjects, the post-procedure target lesion angiography will be performed according to the angiographic core laboratory guidelines and must be captured in the same manner used for the pre-procedure images. The procedure is considered complete after final angiographic recording of the treatment area and the guide catheter has been removed from the subject.

Final angiography of vessels not treated with the ABT NG DES 48 (if required), may be performed per site standard.

Angiographic images of the treated lesions must be sent to the Angiographic Core Lab or the sponsor.

6.3 Post-procedure

6.3.1 Post-procedure ECG

A post-procedure ECG is required by this clinical investigation. If ECG changes were observed signaling a peri-procedure MI, at least two cardiac biomarker tests are mandatory following the required post-procedure cardiac biomarker collection time window, even when the first CK-MB test is less than 1x URL.

6.3.2 Post-procedure Cardiac Biomarker Tests

At post-procedure, at least one CK-MB test and at least one troponin test are mandatory for this clinical investigation:

- The first cardiac biomarker test must to be done between 6-10 hours post-procedure.

[redacted]

- If the first creatine kinase MB (CK-MB) test is equal or greater than 1x upper reference limits (URL) per site's standard of care (SOC), then a second cardiac biomarker test for both CK-MB and Troponin must to be done between 12-18 hours post-procedure, or prior to discharge.
- If the first CK-MB test is < 1x URL, then a second test is not required for both CK-MB and Troponin.
- Serial cardiac biomarker tests with 6-8 hours interval are strongly recommended until discharge only when CK-MB ≥ 1x URL.

6.3.3 Post–procedure medication

All subjects will be maintained on post-procedure antiplatelet medication per the latest American College of Cardiology/American Heart Association (ACC/AHA)/SCAI guidelines.

These medications can be halted for medical necessity if required. However, they must be resumed as soon as possible per physician's discretion.

Any changes in antiplatelet medications will be documented in the eCRF.

6.3.4 Other Chronic Concomitant Medications

Administration of concomitant medications other than any approved P2Y12 inhibitors and aspirin are not required in this protocol. Subjects may receive other medications as needed per physician's discretion.

6.4 Discharge Plan / Assessments

Discharge is defined as the subject leaving the treating or referral hospital. Discharge will be performed per standard of care.

Subjects that smoke or use tobacco products should be asked to attend at least one tobacco cessation class. Subjects that are diabetic should be counseled on blood sugar control in which the recommended HbA1c target is < 7%.

6.5 Follow-up Assessments

All subjects registered into the clinical investigation will have follow-up assessments, which include an office/hospital visit at the investigational center at the time points listed below.

6.5.1 Follow-up for All Subjects

Subjects registered in the clinical investigation will receive the following clinical follow-up:

- 1 month (30 ± 7 days): office visit/telephone contact (office visit is strongly recommended whenever possible)
- 6 months (180 ± 14 days): office visit/telephone contact (office visit is strongly recommended whenever possible)
- 12 months (365 ± 28 days): office visit (Note: a formal office visit is required at 12-month follow-up to ensure a thorough clinical evaluation. A telephone contact is an option *only* for subjects who would otherwise be lost to follow-up due to being unable to complete an office visit)
- 24 months (730 ± 28 days): office visit/telephone contact (office visit is strongly recommended whenever possible)

[redacted]

Clinical follow-up visits should be conducted by the investigator or trial personnel who have been trained to the protocol.

The following information will be collected at each of the time points:

- Any adverse events
- Use and compliance of protocol required antiplatelet medication
- Details of any subsequent coronary interventions (e.g., repeat PCI or CABG)

Note that information obtained through indirect contacts with a subject's healthcare provider or immediate family member will NOT be considered as a trial visit.

6.5.2 Additional Follow-up Visits for All Subjects

Additional subject visits, such as unscheduled visits (other than the protocol required visits), may occur as clinically warranted. The following information will be collected and recorded in eCRF:

- Any adverse events
- Use and compliance of protocol required antiplatelet medication
- Details of any subsequent coronary interventions (e.g., repeat PCI or CABG)

If an unscheduled visit is conducted due to a suspected ischemic cardiac event, cardiac biomarkers and ECG may be performed per site's standard care.

All efforts must be made to obtain follow-up information on subjects who have undergone procedures or have been treated for adverse events in a non-trial-related hospital(s).

6.5.3 Unscheduled Angiography

There is no required angiographic follow-up for this clinical investigation. However, angiograms for all unscheduled revascularizations must be sent to the Angiographic Core Lab regardless of whether they are target or non-target vessel revascularizations. For all revascularizations performed on both the target lesion (TLR) and the non-target lesion of the target vessel (non-TLR), the angiographic core laboratory will determine the type of revascularization (i.e., TLR, TVR or non-TVR), stent thrombosis, or necessary assessments.

[redacted]

Clinical Investigation Plan

6.5.4 Schedule of Events

PROCEDURE/TEST	Baseline	Pre-Procedure (within 24 hours)	Procedure	Post-Procedure	1-month (30±7d) Office visit or phone contact[1]	6-month (180 ±14d) Office visit or phone contact[1]	12-month (365 ± 28d) Office visit or phone contact[2]	24-month (730 ± 28d) Office visit or phone contact[1]	Unscheduled visits
Subject Medical/Clinical History (Age, Sex, Risk Factors, Cardiac Status, Cardiac History, Medical history)	✓								
Subject Informed Consent (Must be obtained prior to any trial related testing or procedures)	✓								
General Inclusion/Exclusion Criteria	✓								
ECG	✓			✓[3]					
Pregnancy test (for all female subjects of childbearing potential only)	✓								
Latest LVEF status[4]	✓								
Angiographic Inclusion/Exclusion Criteria			✓						
Coronary Angiogram			✓						✓
Cardiac biomarker (CK-MB and Troponin) measurement(s)		✓[5]		✓[6]					
Stent and Procedure Information			✓						
Antiplatelet Medications Loading Dose		✓[7]	✓[7]	✓[7]					
Post-procedure Antiplatelet Medications				✓	✓	✓	✓	✓	✓
Adverse Events			✓	✓	✓	✓	✓	✓	✓

[1] Office visit is strongly recommended whenever possible.
[2] A formal office visit is required at 12-month follow-up to ensure a thorough clinical evaluation. A telephone contact is an option *only* for subjects who would otherwise be lost to follow-up due to being unable to complete an office visit.
[3] If post-procedure ECG changes were observed signaling a peri-procedure MI, at least two cardiac biomarker tests are mandatory following the required post-procedure cardiac biomarker collection time window, even when the first CK-MB test is less than 1x URL.

[4] LVEF within the past 3 months prior to the index procedure (has to be documented by any method)

[5] Cardiac biomarker tests measuring creatine CK-MB and troponin must be conducted. If a ST-Elevation MI (STEMI) or non-ST-Elevation MI (NSTEMI) is identified based on a cardiac biomarker level, the cardiac biomarker level has to return to normal limits prior to index procedure in order for the subject to be registered in the clinical investigation. If the subject has stable coronary artery disease or silent ischemia, the pre-procedure cardiac biomarker can be obtained during procedure from the arterial sheath but prior to any angioplasty.

[6] At post-procedure, at least one CK-MB test and at least one troponin test at post-procedure are mandatory for this clinical investigation:

- The first cardiac biomarker test must to be done between 6-10 hours post-procedure.
- If the first creatine kinase MB (CK-MB) test is equal or greater than 1x upper reference limits (URL) per site's standard of care (SOC), then a second cardiac biomarker test for both CK-MB and Troponin must to be done between 12-18 hours post-procedure, or prior to discharge.
- If the first CK-MB test is < 1x URL, then a second test is not required for both CK-MB and Troponin.
- Serial cardiac biomarker tests with 6-8 hours interval are strongly recommended until discharge only when CK-MB ≥ 1x URL.

[redacted]

[7] It is recommended that the antiplatelet medication loading dose be given before the procedure (within 24 hours prior to procedure), at time of procedure, or post-procedure (recommended to be within 1-hour post-procedure).

7.0 ADVERSE EVENTS

To comply with worldwide standards and guidelines on clinical investigation adverse event reporting, the Sponsor has adopted uniform and worldwide applicable standard definitions and reporting timelines to be used and adhered to by the investigators.

7.1 Definition

7.1.1 Adverse Event

An adverse event (AE) is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the medical device under investigation.

Note 1: This definition includes events related to the medical device under investigation or the comparator.

Note 2: This definition includes events related to the procedures involved.

Note 3: For users or other persons, this definition is restricted to events related to medical devices under investigation.

7.1.2 Serious Adverse Event

If the AE meets any of the criteria below, it is regarded as a serious adverse event (SAE).

a) Led to a death
b) Led to a serious deterioration in health of the subject, that either resulted in
    1. a life-threatening illness or injury, or
    2. a permanent impairment of a body structure or a body function, or
    3. in-patient hospitalization or prolongation of existing hospitalization, or
    4. medical or surgical intervention to prevent life threatening illness or injury or permanent impairment to a body structure or a body function.
    5. chronic disease
c) Led to fetal distress, fetal death or a congenital abnormality or birth defect

Note: A planned hospitalization for pre-existing condition, or a procedure required by the CIP, without a serious deterioration in health, is not considered to be an SAE.

[redacted]

7.1.3 Device Deficiency/Device Malfunction (if applicable)

Device deficiency is defined as an inadequacy of a medical device related to its identity, quality, durability, reliability, safety or performance, such as malfunction, misuse or use error and inadequate labeling. This includes the failure of the device to meet its performance specifications or otherwise perform as intended. Note: Performance specifications include all claims made in the labeling of the device.

A device malfunction is the failure of a device to meet its performance specifications or otherwise perform as intended, when used in accordance with the instructions for use or CIP.

7.2 Device Relationship

Determination of whether there is a reasonable possibility that an investigational product or device under investigation caused or contributed to an AE is to be **determined by the Investigator** and recorded on the appropriate CRF form. Determination should be based on assessment of temporal relationships, evidence of alternative etiology, medical/biologic plausibility, and subject condition (pre-existing condition).

7.2.1 Unanticipated (Serious) Adverse Device Effect [U(S)ADE]

Unanticipated serious adverse device effect (USADE) refers to any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

7.3 Adverse Event and Device Deficiency/Device Malfunction Reporting

7.3.1 Adverse Event Reporting

General AE Reporting

Safety surveillance and reporting starts as soon as the subject is registered in the clinical investigation. Safety surveillance and reporting will continue until the last follow-up visit has been performed, the subject is deceased, the subject concludes participation in the clinical investigation, or the subject withdraws from the clinical investigation. All adverse event data, including deaths and device deficiency data, will be collected throughout the time period defined above and will be reported to the Sponsor on a CRF. Additional information with regard to an adverse event should be updated within the appropriate CRF.

Unchanged, chronic, non-worsening or pre-existing conditions are not AEs and should not be reported. An offline form will be made available to allow the investigator to report AEs in the event the entry cannot be made in the electronic data capture (EDC) system. This does not replace the EDC reporting system. All information must still be entered in the EDC system as soon as feasible.

[redacted]

All cardiac related abnormal laboratory values should be reported as AEs.

Non-cardiac related abnormal laboratory values, in themselves, will not be considered AEs unless:

- The investigator determined that the value is clinically significant.
- The abnormal laboratory value required intervention, or
- The abnormal laboratory value required subject withdrawal from the clinical investigation.

All adverse events will be collected on each subject through the 2-year follow-up visit.

SAE Reporting

The investigator should report all SAEs to the Sponsor as soon as possible but no later than outlined below.

Clinical Site	Reporting timelines
All Sites	SAEs must be reported to the Sponsor no later than 3 calendar days from the day the site personnel became aware of the event or as per the investigative site's local requirements, if the requirement is more stringent than those outlined.

The date the site staff became aware the event met the criteria of an SAE must be recorded in the source document. The Investigator will further report the SAE to the local IRB/EC according to the institution's IRB/EC reporting requirements.

7.3.2 Unanticipated Serious Adverse Device Effect (USADE) Reporting to Sponsor and IRB

The Sponsor requires the Investigator to report any USADE to the Sponsor within 3 calendar days of the investigator's knowledge of the event, unless local requirements are more stringent, and to the IRB/EC per IRB/EC requirements.

7.3.3 Device Deficiency/Malfunction Reporting

All device deficiencies/malfunctions should be reported on the appropriate CRF form.

The investigator should report all device deficiencies/malfunctions to the Sponsor as soon as possible but no later than outlined below.

Clinical Sites	Reporting timelines
All Sites	Device deficiencies/malfunctions must be reported to the Sponsor no later than 3 calendar days from the day the site personnel became aware of the event or as per the investigative site's local requirements, if the requirement is more stringent than those outlined.

The device, if not implanted or not remaining in the subject, should be returned to the Sponsor.

Device deficiencies/malfunctions should be reported to the IRB/EC per the investigative site's local requirements.

An offline form will be made available to allow the investigator to report device deficiencies/malfunctions in the event that the entry cannot be made in the EDC system. This does not replace the EDC reporting system. All information must still be entered in the EDC system as soon as feasible.

7.3.4 Adverse Event Reporting to Country Regulatory Authorities by the Sponsor

The Sponsor will report SAEs and reportable device deficiencies/malfunctions to the country regulatory authority, per local requirements.

Note: Reportable device deficiencies/malfunctions include device deficiencies/malfunctions that might have led to an SAE if a) suitable action had not been taken or b) intervention had not been made or c) if circumstances had been less fortunate. These are handled under the SAE reporting system.

Clinical investigation SAEs and device deficiencies/malfunctions reportable per MedDEV 2.7/3 regulations will be submitted to European Competent Authorities by the Sponsor's Clinical Safety Group. Contact details are provided in [Appendix III].

8.0 STATISTICAL CONSIDERATIONS

The following section describes the statistical methods for the clinical investigation. [redacted]

8.1 Analysis Populations

The primary analysis of the primary endpoint will be based on the Full Analysis Set (FAS). All other descriptive analyses on the baseline characteristics and clinical endpoints will be performed on both the FAS population and the per-protocol (PP) population, except for that the acute success endpoint will be analyzed based on all registered population with the attempt of ABT NG DES 48 implantation.

[redacted]

8.2 Statistical Analyses

8.2.1 Primary Endpoint Analysis

The primary endpoint for this study is target lesion failure (TLF) at 1-year follow-up[c]. The hypothesis against a pre-specified performance goal (PG) of 20% is:

H_0: TLF ≥ 20%
H_A: TLF< 20%

[redacted]

8.2.2 Secondary Endpoint Analyses

Secondary endpoints will be summarized descriptively [redacted] For further details refer to the statistical analysis plan (SAP).

8.3 Sample Size Calculation and Assumptions

To test the hypothesis specified in **Section 8.2.1** for the primary endpoint of TLF at 1-year follow-up, with the following assumptions:

- One-sided alpha: 0.05
- True event rate for the primary endpoint: 10%
- Performance goal: 20%
- Attrition rate:5%

A sample size of 107 will have approximately 93% statistical power via simulation. To avoid undue influence from a single study site, each site may register at most 20% of the total subjects.

[redacted]

8.4 Timing of Analysis

The primary analysis will be performed after database lock per FAS population when all subjects in FAS population have completed their primary endpoint follow-up visit.

8.5 Subgroup Analysis

Subgroup analyses will be performed per gender, race, and age. Details are provided in the SAP.

[redacted]

8.6 Multiplicity

[redacted]

8.7 Procedures for Accounting for Missing Data

All analyses will be based on available data with missing data excluded. Any unused or spurious data will be noted as appropriate in the final report.

8.8 Success Criteria

[redacted]

8.9 Deviations from Statistical Plan

Any major changes to the statistical plan will be documented in an amendment to the statistical analysis plan. Less significant changes to the planned analyses will be documented in the final report.

9.0 DIRECT ACCESS TO SOURCE DATA/DOCUMENTS

The investigator/institution will permit direct access to source data/documents for the purpose of performing clinical investigation-related monitoring, audits, IRB/EC review and regulatory inspections.

Subjects providing informed consent are agreeing to allow clinical investigation monitors or regulatory authorities including foreign countries to review, in confidence, any records identifying the subjects in this clinical investigation. This information may be shared with regulatory agencies; however, Sponsor undertakes not to otherwise release the subject's personal and private information.

10.0 QUALITY CONTROL AND QUALITY ASSURANCE

10.1 Selection of Clinical Sites and Investigators

The Sponsor will select investigators qualified by training and experience to participate in the clinical investigation. Sites will be selected based upon review of a recent site assessment, if applicable, and the qualifications of the investigators who will participate in the clinical investigation.

10.2 Clinical Investigation Finances and Agreements

The clinical investigation will be financed by Abbott. Investigational sites will be compensated by Abbott for participation in the clinical investigation per the conditions of agreement between the Sponsor and the Investigational site.

[redacted]

10.3 CIP Amendments

Approved CIP amendments will be provided to the Investigators by the Sponsor prior to implementing the amendment. The Principal Investigator is responsible for notifying the IRB/EC or equivalent committee of the CIP amendment (administrative changes) or obtaining IRB's/EC's approval of the CIP amendment (changes in subject care or safety), according to the instructions provided by the Sponsor with the CIP amendment.

Acknowledgement/approval by the IRB/EC of the CIP amendment must be documented in writing prior to implementation of the CIP amendment. Copies of this documentation must also be provided to the Sponsor.

10.4 Training

10.4.1 Site Training

All Investigators and clinical investigation personnel are required to attend Sponsor training sessions, which may be conducted at an Investigator's meeting, a site initiation visit, or other appropriate training sessions. Over-the-phone or self-training may take place as required. Training of Investigators and clinical investigation personnel will include, but is not limited to, the CIP requirements, investigational device usage, electronic case report form completion and clinical investigation personnel responsibilities. All Investigators and clinical investigation personnel that are trained must sign a training log (or an equivalent) upon completion of the training. Prior to signing the training log, Investigators and clinical investigation personnel must not perform any CIP-related activities that are not considered standard of care at the site.

10.5 Monitoring

Sponsor and/or designee will monitor the clinical investigation over its duration according to the CIP-specific monitoring plan which will include the planned extent of source data verification.

Prior to initiating any procedure, the Sponsor monitor (or delegate) will ensure that the following criteria are met:

- The investigator understands and accepts the obligation to conduct the clinical investigation according to the CIP and applicable regulations, and has signed the Investigator Agreement or the Clinical Investigation Agreement
- The Investigator and his/her staff should have sufficient time and facilities to conduct the clinical investigation and should have access to an adequate number of appropriate subjects to conduct the clinical investigation.
- Source documentation (including original medical records) must be available to substantiate proper informed consent procedures, adherence to CIP procedures, adequate reporting and follow-up of adverse events, accuracy of data collected on case report forms, and device information.
- The Investigator/site will permit access to such records. A monitoring visit sign-in log will be maintained at the site. The Investigator will agree to dedicate an adequate amount of time to the

[redacted]

monitoring process. The Investigator and/or research coordinator will be available for monitoring visits. It is expected that the Investigator will provide the monitor with a suitable working environment for review of clinical investigation-related documents.

10.6 Deviations from CIP

The Investigator should not deviate from the CIP for any reason except in cases of medical emergencies when the deviation is necessary to protect the rights, safety and well-being of the subject or eliminate an apparent immediate hazard to the subject. In that event, the Investigator will notify Sponsor immediately by phone or in writing.

No waivers for CIP deviations will be granted by the Sponsor. All deviations must be reported to the Sponsor using the Deviation CRF. The occurrence of CIP deviations will be monitored by the Sponsor for evaluation of investigator compliance to the CIP and regulatory requirements and dealt with according to written procedures. Investigators will inform their IRB/EC or equivalent committee of all CIP deviations in accordance with their specific IRB/EC or equivalent committee reporting policies and procedures.

In the event of repeated non-compliance, as determined by the Sponsor, a Sponsor's monitor or company representative will attempt to secure compliance by one or more of the following (and not limited to):

- Visiting the investigator and/or delegate
- Telephoning the investigator and/or delegate
- Corresponding with the investigator and/or delegate

Repeated non-compliance with the signed agreement, the CIP or any other conditions of the clinical investigation may result in further escalation in accordance with the Sponsor's written procedures, including securing compliance or, at its sole discretion, Sponsor may terminate the investigator's participation in the clinical investigation.

The following categories of protocol deviations will be considered as major:

- Informed Consent not obtained
- Eligibility criteria not met
  - More than one ABT NG DES 48 are implanted during index procedure
  - Non-target lesion is not successfully treated
- Serious adverse event reporting deviation
- Treatment/procedure compliance deviation

The following categories of protocol deviations will be considered as minor:

- Eligibility criteria not met except for the ones defined as major protocol deviations
- Data outside time window
- Missed visit

10.7 Quality Assurance Audit

A Sponsor representative or designee may request access to all clinical investigation records, including source documentation, for inspection during a Quality Assurance audit.

In the event that an investigator is contacted by a Regulatory Agency in relation to this clinical investigation, the Investigator will notify Sponsor immediately. The Investigator and Research Coordinator must be available to respond to reasonable requests and audit queries made during the audit process. The Investigator must provide Sponsor with copies of all correspondence that may affect the review of the current clinical investigation (e.g., Form FDA 483, Inspectional Observations, Warning Letters, Inspection Reports, etc.). Sponsor may provide any needed assistance in responding to regulatory audits.

10.8 Sponsor Auditing

1. The Sponsor shall prepare an audit plan as well as the operating procedures for the related duties, and conduct audits in accordance with the audit plan and the operating procedures.
2. Individual engaged in auditing (hereinafter referred to as "auditor") shall be different than those in charge of medical device development or monitoring.
3. The auditor shall prepare an audit report documenting the matters confirmed in the audit to certify and verify that the audit has been conducted, and submit them to the Sponsor.

10.9 Committees

10.9.1 Steering Committee

The Steering Committee is responsible for overseeing the scientific and operational aspects of the clinical investigation. This committee will meet regularly to monitor subject enrollment, general data collection and non-compliance with the CIP at individual centers, to review and act upon recommendations of the Data Safety Monitoring Board (DSMB), to review operational issues that may arise and warrant a CIP amendment or other corrective action and to determine policy regarding any publications arising from data generated from the performance of the clinical investigation.

10.9.2 Publications Committee

A Publication Committee shall be established to oversee clinical investigations publications, including publication planning and authorship determinations. Publication Committee membership may include members of the Steering Committee, Principal Investigators, a representative of the Sponsor and a statistician. The Publication Committee will determine policy and strategies regarding individual presentations and/or publications arising from clinical investigation generated data. The committee will also review all external requests for accessing clinical investigation-related data and strategies aligning with the Sponsor's presentation and publication team expectations. The committee will also follow the Sponsor's applicable policies and Standard Operating Procedures.

10.9.3 Data Safety Monitoring Board (DSMB)

The Data Safety Monitoring Board (DSMB) is an independent multidisciplinary group restricted to individuals free of apparent significant conflicts of interest. The source of these conflicts may be financial,

[redacted]

scientific, or regulatory in nature. The DSMB is typically composed of at least two physicians with experience relevant to the clinical investigation and a biostatistician.

The DSMB will serve in an advisory role to the Sponsor to ensure safety by reviewing cumulative data from the clinical investigation at prescribed intervals for the purpose of safeguarding the interests of registered subjects and those subjects yet to be registered, as well as the continuing validity and scientific merit of the clinical investigation. The composition, frequency of the meetings and the statistical monitoring guidelines are described in detail in the DSMB charter.

The DSMB may consider a recommendation for modifications or termination of the clinical investigation based on any perceived safety concerns regardless of statistical significance. The recommendations of the DSMB are not binding, and all final decisions related to clinical investigations modifications rest with the Sponsor.

10.9.4 Clinical Events Committee (CEC)

The Clinical Events Committee (CEC) is an independent adjudication body comprised of qualified physicians who are not participants in the clinical investigation. The CEC will review and adjudicate pre-specified events reported by investigators or identified by Safety personnel for the clinical investigation as defined in the CEC charter and according to definitions provided in this CIP.

11.0 DATA HANDLING AND RECORD KEEPING

Sponsor and/or its affiliates will maintain documentation of the systems and procedures used in data collection for the duration of the clinical investigation.

CRF data collection will be performed through a secure web portal and only authorized personnel will access the Electronic Data Capture (EDC) system using a unique username and password to enter, review or correct data. Passwords and electronic signatures will be strictly confidential.

The data will be subjected to consistency and validation checks within the EDC system and supplemental review by the Sponsor.

At the conclusion of the clinical investigation, completed CRF images with the date-and-time stamped electronic audit trail indicating the user, the data entered, and any reason for change (if applicable) will be provided to the investigational sites.

For the duration of the clinical investigation, the Investigator will maintain complete and accurate documentation including, but not limited to, medical records, clinical investigation progress records, laboratory reports, CRFs, signed ICFs, device accountability records (if applicable), correspondence with the IRB/EC and clinical investigation monitor/Sponsor, adverse event reports, and information regarding subject discontinuation or completion of the clinical investigation.

Clinical Investigation Plan

11.1 Protection of Personally Identifiable Information

The Sponsor respects and protects personally identifiable information collected or maintained for this clinical investigation.

The Sponsor implements technical and physical access controls to ensure that Personal Information is accessible only to and processed only on a 'need to know' basis, including periodic review of access rights, and revocation of access when an individual's employment is terminated or the individual transitions to a role that does not require access to Personal Information, and appropriate restrictions on physical access to premises, facilities, equipment, and records containing Personal Information.

The Sponsor requires the investigational sites to transfer into Sponsor's data management systems only pseudonymous Personal Information (key-coded) necessary to conduct the Clinical Investigation, such as the subject's medical condition, treatment, dates of treatment, etc. The Sponsor discloses as part of the clinical investigation informed consent process that some Sponsor representatives still may see Personal Information at the participating sites for technical support of the participating physicians on the device implant or procedures, monitoring and quality control purposes. Confidentiality of Personal Information will be observed by all parties involved at all times throughout the clinical investigation. The privacy of each subject and confidentiality of his/her information will be preserved in reports and when publishing any data.

The Sponsor data management systems and processes were designed, developed, and tested according to industry standards to appropriately safeguard Confidential Information (including any Personal Information) against unauthorized access and/or interference by third parties, intrusion, theft, destruction, loss or alteration. Clinical Investigation data are encrypted in transit and at rest.

The Sponsor maintains a Privacy Incident procedure that complies in all respects with Applicable Law and industry best practices.

11.2 Data Management Plan

A Data Management Plan (DMP) will describe procedures used for data review, data cleaning, and issuing and resolving data discrepancies. If appropriate, the DMP may be updated throughout the duration of the clinical investigation. All revisions will be tracked and document controlled.

11.3 Source Documentation

Regulations and GCP require the Investigator to maintain information in the subject's original medical records that corroborates data collected on the CRFs. In order to comply with these regulatory requirements/GCP, the following information should be included in the subject record at a minimum and if applicable to the clinical investigation:

- Medical history/physical condition of the subject before involvement in the clinical investigation sufficient to verify CIP entry criteria

[redacted]

- Dated and signed notes on the day of entry into the clinical investigation referencing the Sponsor, CIP number, subject ID number and a statement that informed consent was obtained
- Dated and signed notes from each subject visit (for specific results of procedures and exams)
- Adverse events reported and their resolution, including supporting documents, such as discharge summaries, catheterization laboratory reports, ECGs, and lab results including documentation of site awareness of SAEs and of investigator assessment of device relationship for SAEs.
- CIP-required laboratory reports and 12-lead ECGs, reviewed and annotated for clinical significance of out of range results (if applicable).

  Note: With electronic medical records some clinical sites may be able to annotate that the labs or ECG have been reviewed in the system. For those sites that do not have such capability, the labs or ECG must be printed and signed.
- Notes regarding CIP-required and prescription medications taken during the clinical investigation (including start and stop dates)
- Subject's condition upon completion of or withdrawal from the clinical investigation
- Any other data required to substantiate data entered into the CRF
- Subject reported outcome measures may be completed using CRF worksheets. These serve as the source documentation.

11.4 Case Report Form Completion

Primary data collection based on source-documented hospital and/or clinic chart reviews will be performed clearly and accurately by site personnel trained on the CIP and CRF completion. The investigator will ensure accuracy, completeness, legibility and timeliness of the data reported to the Sponsor on the CRFs and in all required reports.

Data on CRFs will be collected for all registered subjects (an ABT NG DES 48 is started to be delivered beyond the tip of the guide catheter, entering into a subject's vasculature) for the SPIRIT 48 study.

Only authorized site personnel will be permitted to enter the CRF data through the EDC system deployed by the Sponsor. An electronic audit trail will be used to track any subsequent changes of the entered data.

11.5 Record Retention

The Sponsor and Investigator/Site will archive and retain all documents pertaining to the clinical investigation as per the applicable regulatory record retention requirements. The Investigator must obtain permission from Sponsor in writing before destroying or transferring control of any clinical investigation records.

11.6 Investigational Devices Accountability

The Sponsor ships investigational products only to the Principal Investigator (the responsible leader of the investigational site) or his/her legal designee of each site, after sites receive documentation of site activation and shipping authorization is complete.

[redacted]

Clinical Investigation Plan

The Investigator or an authorized designee must maintain adequate records of the receipt and disposition of each investigational device, including part number, batch number, and serial number (if applicable), date used, subject identification, and treating physician.

Storage locations for the devices at investigational sites must be locked with access restricted only to investigators and authorized personnel.

Inventory Accountability Log supplied by the Sponsor will be used. The Inventory Accountability Log must document the disposition of all investigational devices including those that have been returned to Sponsor.

All investigational devices that are associated with a device failure or device deficiency must be returned immediately to the Sponsor.

12.0 ETHICAL CONSIDERATION

12.1 Institutional Review Board/Medical Ethics Committee Review and Approval

Institutional Review Board (IRB)/ Ethics Committee (EC) approval for the CIP and ICF/other written information provided to the subject will be obtained by the Principal Investigator at each investigational site prior to consenting and enrolling subjects in this clinical investigation. The approval letter must be received prior to the start of this clinical investigation and a copy must be provided to the Sponsor.

Any amendments to the CIP as well as associated ICF changes will be submitted to the IRB/EC and written approval obtained prior to implementation, according to each institution's IRB/EC requirements.

No changes will be made to the CIP or ICF or other written information provided to the subject without appropriate approvals, including IRB/EC, the Sponsor, and the regulatory agencies (if applicable).

Until the clinical investigation is completed, the Investigator will advise his/her IRB/EC of the progress of this clinical investigation, per IRB/EC requirements. Written approval must be obtained from the IRB/EC yearly to continue the clinical investigation, or according to each institution's IRB/EC requirements.

No investigative procedures other than those defined in this CIP will be undertaken on the enrolled subjects without the written agreement of the IRB/EC and the Sponsor.

13.0 CLINICAL INVESTIGATION CONCLUSION

The clinical investigation will be concluded when:

- All sites are closed AND
- The final report has been provided to investigators or the Sponsor has provided formal documentation of clinical investigation closure.

[redacted]

Clinical Investigation Plan

14.0 PUBLICATION POLICY

The data and results from the clinical investigation are the sole property of the Sponsor. The Sponsor shall have the right to access and use all data and results generated during the clinical investigation. The Investigators will not use this clinical investigation-related data without the written consent of the Sponsor for any purpose other than for clinical investigation completion or for generation of publication materials, as referenced in the Clinical Investigation Agreement. Single-center results are not allowed to be published or presented before the multi-center results. Any proposals for publications or presentations by the investigators must be reviewed and approved by the Sponsor in a timely manner to enable Sponsor review in compliance with the Sponsor's publication policy set forth in the Clinical Investigation Agreement.

The Sponsor will register this clinical investigation on www.clinicaltrials.gov, in accordance with the International Committee of Medical Journal Editors guidelines, or any other applicable guidelines. Sponsor shall be responsible for any such registration and results posting as required by the ClinicalTrials.gov website. Institution and/or Principal Investigator(s) shall not take any action to register the clinical investigation. A full report of the pre-specified outcomes, regardless of the results, will be made public through the ClinicalTrials.gov website no later than 12 months after clinical investigation completion, as required by section 801 of the FDA Amendments Act. If this clinical investigation is terminated early, the Sponsor will make every effort to hasten the release of the pre-specified outcomes through the ClinicalTrials.gov website.

15.0 RISK ANALYSIS

15.1 Study population

Subjects enrolled into the SPIRIT 48 study will be male and female subjects who are at least 18 years old and are derived from the general interventional cardiology population. The study will register up to 107 subjects, with a maximum of two *de novo* native coronary artery lesions in separate epicardial coronary vessels and only one long lesion (lesion length >32mm and ≤ 44mm) that is treated by a single ABT NG DES 48.

15.2 Anticipated Clinical Benefits

The currently available DES stent lengths in U.S. (maximal 40 mm) are inadequate to provide complete single stent coverage of long coronary artery lesions. Globally, commercial availability of stents with 48mm length are limited in certain geographic regions, leaving physicians in these regions with the limited option of overlapping stents for coronary long lesions treatment. However, metal stent overlap in certain situations is associated with stent fracture, malposition, restenosis and delayed vascular healing, and increases the clinical event rates[1]. Furthermore, the use of multiple stents can also lead to increased procedure time, fluoroscopy time, contrast usage and cost, which have negative impacts on both patients and health economics[2]. The introduction of ABT NG DES 48 can offer potential benefits of a single stent treatment for very long lesions by avoiding stent overlap, reducing potential procedural risks from radiation and contrast usage, and providing possible cost savings to the patients.

[redacted]

15.3 Foreseeable Adverse Events and Anticipated Adverse Device Effects

Risks associated with stenting using the ABT NG DES 48, together with their likely incidence, are described in the IFU and **Appendix IV**.

For all general risks associated with stenting/PCI procedures using DES/everolimus stents, risks conferred by the ABT NG DES 48 are anticipated to be similar to or less than overlapping stent treatment for the same total stent treatment length. Because of the long stent length, there are a few considerations specifically related to the use of the ABT NG DES 48, which are addressed below.

- Total drug dose: Although the longer length of individual ABT NG DES 48 results in a greater total amount of everolimus drug than the currently approved individual XIENCE family of stents with shorter lengths, data from the preclinical maximum dose studies and human pharmacokinetic study support that there are no systemic or vascular safety concerns associated with the total amount of drug on single, or even multiple, ABT NG DES 48 stents.

- Device deliverability: The ABT NG DES 48 delivery system utilizes the same principle of operation and materials that are currently in use by the other XIENCE family of coronary stent systems with shorter stent lengths. The deliverability was not affected by the long stent length. Bench testing using a Synthetic Arterial Model (SAM) has demonstrated that the performance of the ABT NG DES 48 satisfies the deliverability design goals, which were set to be similar to the performance of the commercially available 38 mm XIENCE family of stent systems.

- Vessel taper: Only a small amount of additional vessel taper is anticipated to be encountered with ABT NG DES 48 than is currently treated with the commercially available and widely used 38 mm XIENCE family of stents due to the incremental 10 mm length between the two stent sizes. The common practice of sizing stents to the distal vessel diameter and the maximum stent dilation limits are only slightly increased (from 5.5 mm to 5.75mm) as those provided in the current XIENCE family of stents' Instructions for Use (IFU). Abbott believes that these practices provide guidelines for safe use of the ABT NG DES 48 with regards to vessel taper.

- Side branch jailing: Side branch jailing is a general risk associated with stenting. The likelihood of side branch jailing with a 48 stent is not anticipated to be inherently different than the likelihood of side branch jailing with the same total stent length comprised of multiple overlapping stents. In fact, areas of two layers of metal created by overlapping stents may increase the risk of side branch jailing, and the use of ABT NG DES 48 can avoid stent overlap and help reduce this risk. Hence, Abbott believes that the ABT NG DES 48 will have the same overall likelihood of, and possibly lower overall risks related to, side branch jailing as compared to the same total stent length comprised of multiple overlapping stents.

Below are other risks associated with the coronary angiography, which is an integral part of the PCI procedure. These risks are not specific to the ABT NG DES 48 and may happen with any angiography procedure for heart vessels:

- Exposure to radiation
- Heart attack, stroke
- Injury to the catheterized artery
- Irregular heart rhythms (arrhythmias)

[redacted]

- Allergic reactions to the dye or medications used during the procedure
- Kidney damage
- Excessive bleeding
- Infection

There may be risks related to the device under investigation that are unknown at present. Likewise, the exact frequency of the risk may be unknown.

15.4 Residual Risks Associated with the Device Under Investigation, as Identified in the Risk Analysis Report

Residual risks are risks remaining after protective measures per Abbott's risk management process have been applied or taken. The residual risks to the subject were identified from literature review or the complaint data review of the current commercially available XIENCE family of stents.

15.5 Steps Taken to Control or Mitigate Risks

In-depth recommendations, special precautions and instructions regarding subject selection, device handling, device placement and system removal are included in the IFU.

Risks associated with the use of the ABT NG DES 48 during this clinical study are minimized through device design, investigator selection and training, pre-specified subject eligibility requirements, study monitoring to ensure adherence to the protocol and the use of a DSMB.

These risk management aspects are detailed below:

Device Design: the design of the ABT NG DES 48 includes many features aimed at minimizing potential risks. The major safety features of the device are described below:

- The stent size matrix includes longer lengths to enable better size matching between target vessel and implant.
- The initial degradation rate has been maintained relative to the predecessor to maintain vessel support until full tissue coverage has been achieved.
- The drug everolimus and drug dose density are the same as the predecessor.
- The ABT NG DES 48 is constructed from well-characterized, biocompatible materials that have undergone extensive testing.

Investigator Selection and Training: It is also stated in the IFU that the devices can only be used by physicians who have received appropriate training on how to use the device. This statement is interpreted to mean that the physician users are expected to be aware of the known and foreseeable safety risks associated with the use of the devices including the surgical and/or non-surgical treatment of these conditions.

- Only physicians who are skilled in the manipulation of catheter-based technology in the vasculature and heart and have a good understanding of the risks associated with these manipulations, will be selected as investigators for this trial.
- Emergency surgical back-up should be available as per the institution's standard procedures.

[redacted]

Clinical Investigation Plan

- The Sponsor will be available to provide technical support to answer questions regarding the function of the ABT NG DES 48.
- Pre-specified subject eligibility requirements - as stated in Section 5 of the protocol.

Ensuring strict adherence to the clinical investigation protocol

The clinical investigation will be carefully monitored by the Sponsor monitor (or designee) to ensure adherence to the Clinical Investigational Plan. Adverse events and device deficiencies will be reported to Abbott/designee and will be monitored internally for safety surveillance purposes. A DSMB will be used for the study.

15.6 Risk to Benefit Rationale

The foreseeable rates of the anticipated adverse events associated with the procedure and implantation of ABT NG DES 48 are all below 10% (see **Appendix IV**). Moreover, as detailed in **Section 15.2**, there is an unmet need for treatment of coronary long lesions, with limited options currently available. Taking these into consideration, the clinical benefit that may be expected from treatment of coronary long lesions with the ABT NG DES 48 outweigh the possible risks that subjects may experience when participating in this trial.

16.0 BIBLIOGRAPHY

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[redacted]

17.0 APPENDIX I: ABBREVIATIONS AND ACRONYMS

Acronym or Abbreviation	Complete Phrase or Definition
%DS	percent diameter stenosis
ACC/AHA	American College of Cardiology/American Heart Association
AE	adverse event
AMI	acute myocardial infarction
ARC	Academic Research Consortium
BBB	bundle branch block
BMS	bare metal stents
CABG	coronary artery bypass graft
CAD	coronary artery disease
CCG	Cockcroft-Gault equation
CEC	Clinical Events Committee
CI	clinically-indicated
CIP	clinical investigation plan
COVID-19	coronavirus disease 2019
CK-MB	creatine kinase myocardial-band isoenzyme
CT-FFR	computed tomography-fractional flow reserve
CTO	Chronic total occlusion
DD	device deficiency
DES	Drug-eluting stent
DM	device malfunction
DSMB	Data Safety Monitoring Board
DMR	death, MI, and revascularization
EC	Ethics Committee
ECG	Electrocardiogram
eCRF	electronic case report form
EDC	electronic data capture
EECS	everolimus eluting coronary stent
EECSS	everolimus eluting coronary stent system
FAS	full analysis set
FDA	Food and Drug Administration

Clinical Investigation Plan

Acronym or Abbreviation	Complete Phrase or Definition
GCP	Good Clinical Practice
GFR	Glomerular filtration rate
HIPAA	Health Insurance Portability and Accountability Act
ICF	Informed Consent Form
IDE	Investigational Device Exemption
IFU	Instructions for Use
iFR	Instantaneous wave-free ratio
IRB	Institutional Review Board
KM	Kaplan-Meier
LAD	left anterior descending coronary artery
LBBB	left bundle branch block
LCX	left circumflex coronary artery
LVEF	left ventricular ejection fraction
LVH	left ventricular hypertrophy
MDRD	Modification of Diet in Renal Disease
MedDEV	Medical Devices Directives
mg	milligram
MHRA	The Medicines and Healthcare Products Regulatory Agency
MI	myocardial infarction
mL	milliliter
mm	millimeter
N	sample size; also *N*
NHLBI	National Heart, Lung, and Blood Institute
NSTEMI	Non ST-Elevation MI
NQMI	non-Q wave myocardial infarction
OCT	optical coherence tomography
OUS	Outside of United States
PBMA	poly (n-butyl methacrylate)
PCI	percutaneous coronary intervention
PG	performance goal
PP	per protocol

[redacted]

Clinical Investigation Plan

Acronym or Abbreviation	Complete Phrase or Definition
PVDF-HFP	Polymer of vinylidene fluoride and hexafluoropropylene
QCA	quantitative coronary angiography
QMI	Q wave myocardial infarction
RCA	right coronary artery
RFR	relative flow reserve
RVD	reference vessel diameter
RX	Rapid Exchange
SAE	serious adverse event
SAP	statistical analysis plan
SCAI	Society for Cardiovascular Angiography and Interventions
SPC	Summary of Product Characteristics
ST	stent thrombosis
STEMI	ST-Elevation MI
TBD	to be determined
TIA	transient ischemic attack
TIMI	thrombolysis in myocardial infarction
TLF	target lesion failure
TLR	target lesion revascularization
TVF	target vessel failure
TVR	target vessel revascularization
UADE	unanticipated adverse device effect
URL	upper reference limit
US	United States
USADE	unanticipated serious adverse device effect

[redacted]

18.0 APPENDIX II: DEFINITIONS

ACC/AHA Classification Scheme of Coronary Lesions: Lesion-Specific Characteristics

Type A Lesions (High Success, >85%; Low Risk)	
• Discrete (< 10 mm length)	• Little or no calcification
• Concentric	• Less than totally occlusive
• Readily accessible	• Not ostial in location
• Nonangulated segment, < 45°	• No major branch involvement
• Smooth contour	• Absence of thrombus
Type B Lesions* (Moderate Success, 60-85%; Moderate risk)	
• Tubular (10-20 mm length)	• Moderate-to-heavy calcification
• Eccentric	• Total occlusions < 3 months old
• Moderate tortuosity of proximal segment	• Ostial in location
• Moderately angulated segment, > 45°, < 90°	• Bifurcation lesions requiring double guide wires
• Irregular contour	• Some thrombus present
* Type B1 lesions: One adverse characteristic * Type B2 lesions: ≥ two adverse characteristics	
Type C Lesions (Low Success, <60%; High Risk)	
• Diffuse (> 2 cm length)	• Total occlusions > 3 months old
• Excessive tortuosity of proximal segment	• Inability to protect major side branches
• Extremely angulated segments > 90°	• Degenerated vein grafts with friable lesions

ACUTE SUCCESS

Acute Success is classified according to the following definitions:

- **Device Success**

  Device success is defined as achievement of a final in-stent residual diameter stenosis of < 50% (by QCA), using only study device(s) without device malfunction. Use of a bail-out study stent is still regarded as device success unless the bail-out study stent has a device malfunction. If QCA %DS is not available, device success will be missing

- **Procedure Success**

  Procedure success is defined as achievement of a final in-stent diameter stenosis of < 50% (by QCA) using the assigned device and with any adjunctive devices, without the occurrence of cardiac death, Target Vessel MI (per ARC definition), or repeat coronary revascularization of the target lesion during the hospital stay (up to 7 days if a subject still in the hospital). If QCA %DS is not available, procedure success will be missing.

[redacted]

DEATH (Per ARC Circulation 2007; 115: 2344-2351)
All deaths are considered cardiac unless an unequivocal non-cardiac cause can be established. Specifically, any unexpected death even in subjects with coexisting potentially fatal non-cardiac disease (e.g. cancer, infection) should be classified as cardiac.

Cardiac death:
Any death due to proximate cardiac cause (e.g. MI, low-output failure, fatal arrhythmia), unwitnessed death and death of unknown cause, all procedure related deaths including those related to concomitant treatment.

Vascular death:
Death due to non-coronary vascular causes such as cerebrovascular disease, pulmonary embolism, ruptured aortic aneurysm, dissecting aneurysm, or other vascular cause.

Non-cardiovascular death:
Any death not covered by the above definitions such as death caused by infection, malignancy, sepsis, pulmonary causes, accident, suicide or trauma.

MYOCARDIAL INFARCTION [MI]

1. **Peri procedure MI**

    a. **MI per SCAI definition**[4] (J Am Coll Cardiol. 2013; 62(17):1563-70):

defined as the occurrence within 48 hours after either PCI or CABG of either:

- CK-MB above 10 x URL (*determined on a single measurement), OR
- CK-MB above 5 x URL (*determined on a single measurement), PLUS
    - new pathological Q waves in at least 2 contiguous leads or new persistent non-rate related LBBB

In the absence of CK-MB measurements and a normal baseline cardiac troponin (cTn), peri-procedural MI can also be defined as a cTn (I or T) level measured within 48 hours of the PCI rises to ≥70 x the local laboratory URL, or ≥35 x URL with new pathologic Q-waves in ≥2 contiguous leads, or new persistent LBBB.

    b. **MI per ARC 2 definition**[7](*Circulation* 2018: **137**, 2635-2650) **:**

For PCI and coronary artery bypass grafting (CABG), within 48 Hours:

[redacted]

Absolute rise in cardiac troponin (from baseline) ≥35 times upper reference limit, plus 1 (or more) of the following criteria:

- New significant Q waves or equivalent
- Flow-limiting angiographic complications
- New "substantial" loss of myocardium on imaging

Significant periprocedural myocardial injury:

Absolute rise in cardiac troponin (from baseline) ≥70 times upper reference limit.

c. MI per 4th universal definition[8] (*Circulation* 138, e618-e651, 2018).

Coronary procedure-related MI ≤ 48 hours after the index procedure is arbitrarily defined by an elevation of cTn values > 5 times of the 99th percentile URL in patients with normal baseline values. Patients with elevated pre-procedural cTn values, in whom the pre-procedural cTn level are stable (≤20% variation) or falling, must meet the criteria for a > 5-fold increase and manifest a change from the baseline value of > 20%. In addition with at least one of the following:

• New ischaemic ECG changes;

• Development of new pathological Q waves;

• Imaging evidence of loss of viable myocardium that is presumed to be new and in a pattern consistent with an ischaemic aetiology;

• Angiographic findings consistent with a procedural flow-limiting complication such as coronary dissection, occlusion of a major epicardial artery or graft, side-branch occlusion-thrombus, disruption of collateral flow or distal embolization.

2. **Spontaneous MI:** (> 48h following PCI or CABG): CK-MB > URL or Troponin > URL with baseline value < URL

MI after the periprocedural period may be secondary to late stent complications or progression of native disease. Performance of ECG and angiography supports adjudication to either a target or non-target vessel in most cases.

With the unique issues and pathophysiological mechanisms associated with these later events as well as the documented adverse impact on short and long-term prognosis, a more sensitive definition than for periprocedural MI of any elevation of troponin or CKMB above the 99 h percentile of the upper range limit (or ULN if URL is not available) is used. All late events that are not associated with a revascularization procedure will be considered simply as spontaneous.

3. **Myocardial infarctions** will also be adjudicated based on the following classification:

- **Q wave MI**

[redacted]

Development of new, pathological Q wave on the ECG (≥ 0.04 seconds in duration and ≥ 1 mm in depth) in ≥ 2 contiguous precordial leads or ≥ 2 adjacent limb leads)

- **Non-Q wave MI**

  Those MIs which are not Q-wave MI.

All Myocardial infarctions will be adjudicated by CEC by different definitions mentioned above, and also be adjudicated as to their relation to the target vessel

All infarcts that cannot be clearly attributed to a vessel other than the target vessel will be considered related to the target vessel.

STENT THROMBOSIS (Per ARC Circulation 2007; 115: 2344-2351)

- **Timing:**

Acute stent thrombosis*:	0 - 24 hours post stent implantation
Subacute stent thrombosis*:	>24 hours - 30 days post stent implantation
Late stent thrombosis†:	>30 days - 1 year post stent implantation
Very late stent thrombosis†:	>1 year post stent implantation

* Acute/subacute can also be replaced by early stent thrombosis.
† Including "primary" as well as "secondary" late stent thrombosis; "secondary" late stent thrombosis is a stent thrombosis after a target segment revascularization.

- **Categories (Definite, Probable, and Possible):**

Definite stent thrombosis

Definite stent thrombosis is considered to have occurred by either angiographic or pathologic confirmation.

Angiographic confirmation of stent thrombosis*

The presence of a thrombus† that originates in the stent or in the segment 5 mm proximal or distal to the stent and presence of at least 1 of the following criteria within a 48-hour time window:

- Acute onset of ischemic symptoms at rest
- New ischemic ECG changes that suggest acute ischemia
- Typical rise and fall in cardiac biomarkers (refer to definition of spontaneous MI)
- Non-occlusive thrombosis
  - Intracoronary thrombus is defined as a (spheric, ovoid, or irregular) non-calcified filling defect or lucency surrounded by contrast material (on 3 sides or within a coronary stenosis) seen in multiple projections, or persistence of contrast material within the lumen, or a visible embolization of intraluminal material downstream.
- Occlusive thrombus
  - TIMI 0 or TIMI 1 intrastent or proximal to a stent up to the most adjacent proximal side branch or main branch (if originates from the side branch).

[redacted]

Clinical Investigation Plan

Pathological confirmation of stent thrombosis

Evidence of recent thrombus within the stent determined at autopsy or via examination of tissue retrieved following thrombectomy.

* The incidental angiographic documentation of stent occlusion in the absence of clinical signs or symptoms is not considered a confirmed stent thrombosis (silent occlusion).
† Intracoronary thrombus.

Probable stent thrombosis

Clinical definition of probable stent thrombosis is considered to have occurred after intracoronary stenting in the following cases:

- Any unexplained death within the first 30 days‡
- Irrespective of the time after the index procedure, any MI that is related to documented acute ischemia in the territory of the implanted stent without angiographic confirmation of stent thrombosis and in the absence of any other obvious cause

‡ For studies with ST-elevation MI population, one may consider the exclusion of unexplained death within 30 days as evidence of probable stent thrombosis.

Possible stent thrombosis

Clinical definition of possible stent thrombosis is considered to have occurred with any unexplained death from 30 days after intracoronary stenting until end of trial follow-up.

STROKE

An acute symptomatic episode of neurological dysfunction attributed to a vascular cause lasting more than 24 hours or lasting 24 hours or less with a brain imaging study or autopsy showing new infarction.

- Ischemic Stroke: An acute symptomatic episode of focal cerebral, spinal, or retinal dysfunction caused by an infarction of central nervous system tissue.
- Hemorrhagic Stroke: An acute symptomatic episode of focal or global cerebral or spinal dysfunction caused by a non-traumatic intraparenchymal, intraventricular, or subarachnoid hemorrhage.
- Undetermined Stroke: A stroke with insufficient information to allow categorization as ischemic or hemorrhagic.

Note: an event that last < 24 hours may be adjudicated as a stroke if the following treatments were used:

- Pharmacologic, i.e., thrombolytic drug administration, or

Non-pharmacologic, i.e., neurointerventional procedure (e.g., intracranial angioplasty)

REVASCULARIZATION (Per ARC Circulation 2007; 115: 2344-2351)

Target Lesion Revascularization (TLR)

[redacted]

Clinical Investigation Plan

TLR is defined as any repeat percutaneous intervention of the target lesion or bypass surgery of the target vessel performed for restenosis or other complication of the target lesion. All TLR should be classified prospectively as clinically indicated [CI] or not clinically indicated by the investigator prior to repeat angiography. The target lesion is defined as the treated segment from 5 mm proximal to the stent and to 5 mm distal to the stent.

Target Vessel Revascularization (TVR)

TVR is defined as any repeat percutaneous intervention or surgical bypass of any segment of the target vessel. The target vessel is defined as the entire major coronary vessel proximal and distal to the target lesion which includes upstream and downstream branches and the target lesion itself

Non Target Lesion Revascularization (Non-TLR)

Any revascularization in the target vessel for a lesion other than the target lesion is considered a non-TLR.

Non Target Vessel Revascularization (Non-TVR)

Revascularization of the vessel identified and treated as the non-target vessel at the time of the index procedure.

Clinically Indicated [CI] Revascularization (TLR/TVR)
A revascularization is considered clinically indicated if angiography at follow-up shows a percent diameter stenosis ≥ 50% and if one of the following occurs:

- A positive history of recurrent angina pectoris, presumably related to the target vessel;
- Objective signs of ischemia at rest (ECG changes) or during exercise test (or equivalent), presumably related to the target vessel;
- Abnormal results of any invasive functional diagnostic test (e.g., Doppler flow velocity reserve, fractional flow reserve);
- A TLR/TVR with a diameter stenosis ≥70% in the absence of the above mentioned ischemic signs or symptoms.

TARGET LESION FAILURE (TLF)
TLF is defined as a composite of all cardiac death, myocardial infarction attributed to target vessel or clinically-indicated TLR.

TARGET VESSEL FAILURE (TVF)
TVF is defined as a composite of cardiac death, MI attributed to target vessel, clinically-indicated TLR, or clinically-indicated TVR, non-TLR.

COVID-19 Relatedness Definitions
The COVID-19 relatedness to an adverse event, is adjudicated by the CEC committee into 3 categories: likely related, possibly related, or not likely related, based on the COVID-19 relatedness definitions that are described on the CEC charter. Please refer to the CEC charter for the COVID-19 relatedness definitions.

IN-STENT

Within the margins of the stent.

[redacted]

Minimal Lumen Diameter (MLD)

Minimum lumen diameter is defined as the shortest diameter through the center point of the lumen. Data are collected from two projections.

PERCENT DIAMETER STENOSIS (%DS)

The value calculated as 100 * (1 - MLD/RVD) using the mean values from two orthogonal views (when possible) by QCA.

REFERENCE VESSEL DIAMETER (RVD)

Reference vessel diameter based on QCA is derived from either the user-defined method using average diameter of proximal and distal healthy segments or the interpolated method.

RESTENOSIS

Re-narrowing of the artery following the removal or reduction of a previous narrowing.

TIMI (THROMBOSIS IN MYOCARDIAL INFARCTION) FLOW GRADES

0. No contrast flow through the stenosis.
1. A small amount of contrast flows through the stenosis but fails to fully opacify the artery beyond.
2. Contrast material flows through the stenosis to opacify the terminal artery segment. However, contrast enters the terminal segment perceptibly more slowly than more proximal segments. Alternatively, contrast material clears from a segment distal to a stenosis noticeably more slowly than from a comparable segment not preceded by a significant stenosis.
3. Anterograde flow into the terminal coronary artery segment through a stenosis is as prompt as anterograde flow into a comparable segment proximal to the stenosis. Contrast material clears as rapidly from the distal segment as from an uninvolved, more proximal segment.

19.0 APPENDIX III: SITE CONTACT INFORMATION

Contact information for each participating clinical site is available under separate cover by contacting the Sponsor.

20.0 APPENDIX IV: RISK FOR THE STUDY AND RATES OF FORSEEABLE ADVERSE EVENTS

There are risks, discomforts, and inconveniences to a subject, associated with any research (or to an embryo, unborn child or nursing infant if a subject become pregnant). These risks deserve careful thought.

While in the study, the risks and adverse effects of each are listed, but they will vary from person to person. A subject should talk with the Study Doctor if he/she has any questions. There may be some discomforts or inconveniences associated with the study tests and procedures.

Electrocardiogram

The ECG test is a recording of the electrical activity of your heart and an ECG is harmless. The ECG will be performed based on the standard of care of the hospital. The sticky pads (electrodes) that are placed on a subject's chest can sometimes cause discomfort such as redness or itching. A subject's chest may need to be shaved before attaching these pads. Irritation from shaving also may occur.

Blood Sample

The risk of inserting a needle into a vein in your arm may include temporary discomfort from the needle stick. There is also a small risk of infection, bruising, swelling, bleeding or fainting. These risks are minimized by cleansing the site carefully prior to obtaining the blood sample and applying pressure to the site after the blood sample is obtained.

Imaging Catheter, PCI, and Contrast Media

Below are the possible risks that may occur with use of ABT NG DES 48. These risks are not specific to the ABT NG DES 48 and may happen with any stent for heart vessels:

- Allergic reactions or hypersensitivity to rubber, contrast agent, anesthesia, device materials (cobalt, chromium, tungsten, nickel, methacrylic polymer, and fluoropolymer), and everolimus, anticoagulation, or antiplatelet drugs

- Vascular complications in arteries used to access the coronary artery which may require blood transfusion or surgical artery repair, including:
  - Complications at the groin or arm access site
  - Bleeding
  - Formation of an abnormal connection between an artery and the vein next to it
  - Leaking of blood from an artery to the surrounding tissue (usually as a result of a puncture to the artery)
  - Weakness in wall of artery (causing possible serious bleeding complications)
  - Partial or complete tear of the wall of the artery
  - Vessel puncture or rupture
  - Movement of air, tissue, plaque, blood clot, or device material (stent or catheter parts) downstream in the arteries resulting in blockage in blood flow
  - Nerve damage caused by compression of the nerves, injury to the nerve, or
  - interruption of blood supply to the nerves
  - Decreased blood supply to the arms and / or legs which may cause cramping or pain
- Complications at the heart arteries which may require additional treatment or surgery, including:
  - Complete blockage of the coronary artery, which may require a repeat procedure or emergency surgery to reopen the coronary artery
  - Formation of an abnormal connection between a heart artery and the vein next to it
  - Leaking of blood from a heart artery to the surrounding tissue (usually as a result of a puncture to the artery)
  - Weakness in wall of the heart artery (causing possible serious bleeding complications)
  - Partial or complete tear of the wall of the artery supplying the heart muscle
  - Puncture or rupture of the wall of the artery supplying the heart muscle
  - Movement of air, tissue, plaque, blood clot, or device material (stent or catheter parts) that partially or completely blocks the heart artery and / or implanted stent
  - Development of blood clots partially or completely blocking blood flow within the artery and / or the implanted stent
  - Narrowing or re-narrowing of the treated heart artery
- Complications in the sac around the heart which may require additional treatment, including:

  - Rapid accumulation of blood in the sac around the heart resulting in compression of the heart so it cannot pump out blood to the rest of the body which may require additional treatment or emergency surgery
  - An abnormal accumulation of blood around the heart
  - Inflammation of the tissue around the heart (causing possible chest pain)
- Irregular heartbeats (caused by abnormal electrical activity in the heart from the upper or lower heart chambers)
- Decreased blood and / or oxygen supply to part of the heart muscle which may cause:
  - Heart attack (permanent damage of an area of the heart tissue, due to interruption in the blood flow to the heart muscle)
  - Temporary spasm of the heart arteries
  - Chest pain (which may radiate to jaw or arm) or discomfort caused by inadequate supply of blood to the heart)
- Stroke or temporary stroke symptoms as a result of decreased oxygen to the brain causing blurred vision, dizziness, faintness, and numbness
- Abnormal organ function in very ill patients including:
  - Stoppage of the heart
  - Heart function failure (potentially leading to the development of fluid in the lungs and severe breathing difficulty)
  - Lung function failure (potentially leading to severe breathing difficulty)
  - Kidney failure
  - Shock (a life-threatening condition in which blood pressure is too low to maintain adequate-blood flow to your organs)
- Blood count abnormalities
- Low or high blood pressure
- Infection
- Nausea and vomiting
- Feeling of the heart beating rapidly (palpitations), dizziness, or fainting
- Chest pain
- Fever
- Pain

[redacted]

- Death

Magnetic resonance imaging (MRI): If a subject requires a magnetic resonance imaging (MRI) scan, tell the doctor or MRI technician that the subject has a stent implant. Test results indicate that the stents of the ABT NG DES 48 are MR conditional. Subjects with single or overlapped XIENCE stents can undergo MRI scans safely under the following conditions:

- Static magnetic field of 1.5 and 3 Tesla
- Maximum spatial field gradient of 3000 gauss/cm (30 T/m)
- Maximum MR system reported whole-body-averaged Specific Absorption Rate (SAR) of 2.0 W/kg for each duration of a sequence
- Normal operating mode if the MR system for both gradients and SAR
- Maximum gradient slew rate capability of 200 T/m/s

The stent(s) should not migrate in this MRI environment, and MRI may be performed immediately following the implantation of the stent of ABT NG DES 48. Prior to undergoing an MRI scan, inform the doctor that the subject has a stent of ABT NG DES 48.

There may be other risks or discomforts to a subject that are not known at this time. If important information is learned during the course of this clinical investigation, the site will be notified by the Sponsor. The Study Doctor from the site will discuss with a subject important new information that is learned during the course of this study that may affect a subject's condition or willingness to continue to take part in this clinical investigation.

If a subject is a woman who is able to become pregnant, it is expected that the subject will use an effective method of birth control to prevent exposing a fetus to a potentially dangerous agent with unknown risk. If a subject is pregnant or currently breast feeding, she should not participate in this study.

The rates of foreseeable adverse events are:

Anticipated Adverse Events	Frequency Rate Ranges

[redacted]

Clinical Investigation Plan

Category	Subcategory		Very common: ≥10%	Common: ≥ 1.0% to < 10%	Uncommon: ≥ 0.1% to < 1.0%	Rare: ≥ 0.01% to < 0.1%	Very Rare: < 0.01%
Allergic reaction or hypersensitivity to latex, contrast agent anesthesia, device materials, and drug reactions to everolimus, anticoagulation, or antiplatelet drugs.				X			
Vascular access complications which may require transfusion or vessel repair, including:	**Catheter site reactions**			X			
	Bleeding (ecchymosis, oozing, hematoma, hemorrhage, retroperitoneal hemorrhage)				X		
	Arteriovenous fistula, pseudoaneurysm, aneurysm, dissection, perforation / rupture	**Arteriovenous fistula**					X
		aneurysm			X		
		dissection		X			
		Perforation/rupture		X – for CTO patients only	X		
	Embolism (air, tissue, plaque, thrombotic material or device)	**air/ fat embolism**					X
		Arterial, aortic, peripheral embolism			X		
	Peripheral nerve injury				X		
	Peripheral ischemia						X
Coronary artery complications which may require additional intervention, including:	**Total occlusion or abrupt closure**				X		
	Arteriovenous fistula, pseudoaneurysm, aneurysm, dissection, perforation / rupture	**Arteriovenous fistula**			X		
		pseudoaneurysm			X		

[redacted]

Clinical Investigation Plan

		aneurysm			X		
		dissection		X			
		Perforation/rupture		X – for CTO patients only	X		
	Tissue prolapse/plaque shift				X		
	Embolism (air, tissue, plaque, thrombotic material, or device)				X		
	Coronary or stent thrombosis (acute, subacute, late, very late)	Thrombosis in device		X – for CTO patients only	X		
		Coronary artery thrombosis, stent thrombosis (cumulative definite/ probable, 1 year data)			X		
	Stenosis or restenosis			X			
Pericardial complications which may require additional intervention, including:	**Cardiac tamponade**						X
	Pericardial effusion				X		
	Pericarditis						X
Cardiac arrhythmias (including conduction disorders, atrial and ventricular arrhythmias)	**Aspecific**				X		
	conduction disorders				X		
	Atrial arrhythmias	**Atrial fibrillation**		X			

Clinical Investigation Plan

		Atrial flutter			X		
		Atrial tachycardia			X		
	ventricular arrhythmias	**Ventricular fibrillation**					X
		Ventricular tachycardia			X		
Cardiac ischemic conditions (including myocardial ischemia, myocardial infarction (including acute), coronary artery spasm, and unstable or stable angina pectoris)	**Myocardial Ischemia**				X		
	Myocardial Infarction			X			
	Coronary Artery Spasm						X
	unstable or stable angina pectoris			X			
Stroke/Cerebrovascular accident (CVA) and Transient Ischemic Attack (TIA)	**Stroke/CVA**	Intracaranial hemorrhage					
		Thrombotic, ischemic		X			
	TIA				X		
System organ failures	**Cardio-respiratory arrest**				X		
	Cardiac failure	**Cardiac failure Ventricular failure**			X		X

[redacted]

Clinical Investigation Plan

	Cardiopulmonary failure (including pulmonary edema)	**Acute / chronic respiratory failure**		X			
		respiratory distress			X		
		dyspnea			X		
		pulmonary edema			X		
	Renal insufficiency / failure			X			
	Shock				X		
Blood cell disorders (including Heparin Induced Thrombocytopenia (HIT)				X			
Hypotension					X		
hypertension				X			
Infection				X			
							X
					X		
					X		
Nausea and vomiting					X		
Palpitations, dizziness, and syncope	**Palpitations**				X		
	Dizziness				X		
	Syncope			X			
Chest pain				X			

Clinical Investigation Plan

Fever			X		
Pain			X		
Death		X			

Clinical Investigation Plan

21.0 APPENDIX V: DEVICE LABELING

A final draft of Device Labeling will be sent under a separate cover.

Clinical Investigation Plan

22.0 APPENDIX VI: CASE REPORT FORMS

A final draft CRF will be sent under a separate cover.

Clinical Investigation Plan

23.0 APPENDIX VII: INFORMED CONSENT FORM

A template informed consent form will be provided under a separate cover.

Clinical Investigation Plan

24.0 APPENDIX VIII: MONITORING PLAN

A copy of the Monitoring Plan can be obtained upon request from the Sponsor Clinical Project Manager for the clinical investigation.

Clinical Investigation Plan

25.0 APPENDIX IX: REVISION HISTORY

Amendment Number	Version	Date	Details
[redacted]			

Clinical Investigation Plan

Clinical Investigation Plan

26.0 APPENDIX X: CIP SUMMARY

Trial name and Number	CRD 999: A Clinical Investigation to Assess the Abbott Next Generation Drug Eluting Stent 48mm Everolimus Eluting Coronary Stent System in Treatment of de novo Native Coronary Artery Disease
Objective	The objective of the SPIRIT 48 study is to evaluate the safety and effectiveness of the ABT NG DES 48 EECSS in improving coronary artery luminal diameter in subjects with coronary artery disease (CAD) due to *de novo* native coronary artery long lesions.
Study Device	ABT NG DES 48: • Stent diameter: 2.5, 2.75, 3.0, 3.5 and 4.0 mm • Stent length: 48 mm
Study Design	Prospective, single-arm, open-label, multi-center, global (US and OUS) clinical investigation to evaluate the safety and effectiveness of the ABT NG DES 48 in the treatment of *de novo* native coronary artery long lesions. • Lesions and stent usage: up to two treated lesions, must have exact one long lesion that is treated by one ABT NG DES 48 o Single lesion: one *de novo* native coronary artery long lesion (> 32 mm and ≤ 44 mm) as the target lesion, that must be treated a single ABT NG DES 48 o Two lesions: one target lesion and one non-target lesion, each in different epicardial coronary vessels: ▪ Target Lesion: one *de novo* native coronary artery long lesion (> 32 mm and ≤ 44 mm), that must be treated with a single ABT NG DES 48 ▪ Non-target lesion: one *de novo* native coronary artery lesion, that must be treated by stents other than the ABT NG DES 48 per site's standard of care A maximum of 40% of subjects with two treated lesions can be registered in the study. At least 50% of the subjects will be registered at US sites.
Endpoints	Primary Endpoint: • TLF (defined as the composite rate of cardiac death (CD), target vessel myocardial infarction [TV-MI] (per SCAI MI definition), and clinically indicated target lesion revascularization [CI-TLR])[c]at 1 year Secondary Endpoints: • TLF in hospital, at 30 days, 180 days, 2 years

[redacted]

Other Endpoints:

- Acute Success: (combined clinical and angiographic)
  - Device Success (Lesion basis)
  - Procedural Success (Subject basis)
- Clinical Endpoint in hospital and at each clinical follow-up time point (30 days, 180 days, 1 year and 2 years)

  Composite:
  - All death, all MI and all revascularization (DMR)
  - Cardiac Death/MI

  Individual:
  - Any death
    - Cardiac
    - Vascular
    - Non-cardiovascular
  - All MI
    - Q-wave MI (QMI)
    - Non-Q-wave MI (NQMI)
  - TV-MI
    - Type
      - QMI
      - NQMI
  - Any Revascularization
    - All TVR (including TLR)
      - Ischemic driven (ID) -TVR
    - All TLR
      - ID-TLR
    - All Non-TVR

[redacted]

Clinical Investigation Plan

	○ Stent thrombosis (per ARC definition) ▪ Type • Definite • Probable • Possible ▪ Time • Acute (≤ 1 day) • Subacute (>1 day ≤ 30 days) • Late (>30 days ≤ 365 days) • Very late (>365 days) A secondary analysis with MI per ARC 2 definition[7] and 4 [h] universal definition[8] will be performed for all endpoints containing MI.
Sample size calculation and success criteria	[redacted]
Subject Enrollment	A total of up to 107 subjects will be registered at up to 33 sites globally. No site may register more than 20% of the total subjects. At least 50% of the subjects should be registered in US.
Subject Follow Up	All subjects will be followed for 2 years: • 1 month (30 ± 7 days): office visit/telephone contact (office visit is strongly recommended whenever possible) • 6 months (180 ± 14 days): office visit/telephone contact (office visit is strongly recommended whenever possible)

[redacted]

Clinical Investigation Plan

	• 12 months (365 ± 28 days): office visit (Note: a formal office visit is required at 12-month follow-up to ensure a thorough clinical evaluation. A telephone contact is an option *only* for subjects who would otherwise be lost to follow-up due to being unable to complete an office visit) • 24 months (730 ± 28 days): office visit/telephone contact (office visit is strongly recommended whenever possible)

Laboratory assessment	**Pre-procedure:**
	
	The following laboratory assessment must be obtained at pre-procedure:
	
	• Baseline 12-lead ECG
	• Cardiac biomarker tests measuring creatine CK-MB and troponin must be conducted. If a ST-Elevation MI (STEMI) or non-ST-Elevation MI (NSTEMI) is identified based on a cardiac biomarker level, the cardiac biomarker level has to return to normal limits prior to index procedure in order for the subject to be registered in the clinical investigation. If the subject has stable coronary artery disease or silent ischemia, the pre-procedure cardiac biomarker can be obtained during procedure from the arterial sheath but prior to any angioplasty, the lab results for cardiac biomarkers can be obtained at post-procedure.
	• A pregnancy test must be administered to all female subjects of childbearing potential within 7 days prior to the procedure
	• The latest LVEF status within the past 3 months prior to the index procedure (has to be documented by any method)
	
	Other laboratory assessments (such as blood counts, chemistry panel and lipid panel, etc.) should be obtained per site's standard of care. Baseline laboratory results related to inclusion/exclusion criteria must be available and reviewed prior to the procedure for screening.
	
	Post-procedure:
	
	• A post procedure ECG is required by this clinical investigation. If ECG changes were observed signaling a peri-procedure MI, at least two cardiac biomarker tests are mandatory following the required post-procedure cardiac biomarker collection time window, even when the first CK-MB test is less than 1x URL.
	
	• At post-procedure, at least one CK-MB test and at least one troponin test are mandatory for this clinical investigation:
	  ○ The first cardiac biomarker test must to be done between 6-10 hours post-procedure.
	  ○ If the first creatine kinase MB (CK-MB) test is equal or greater than 1x upper reference limits (URL) per site's standard of care (SOC), then a second cardiac biomarker test for both CK-MB and Troponin must to be done between 12-18 hours post-procedure, or prior to discharge.

[redacted]

Clinical Investigation Plan

	○ If the first CK-MB test is < 1x URL, then a second test is not required for both CK-MB and Troponin. ○ Serial cardiac biomarker tests with 6-8 hours interval are strongly recommended until discharge only when CKMB ≥ 1x URL.
Antiplatelet medication requirement	**Peri-procedure Medications:** <u>Loading dose of P2Y12 inhibitor medication (clopidogrel, prasugrel, ticagrelor, etc.):</u> • Follow the instruction for use (IFU) of each drug for loading dose and timing. If not indicated in the IFU, then follow the site's standard of care. <u>Loading dose of aspirin:</u> • ≥ 300 mg must be administered 0* to 24 hours prior to PCI or up to 1-hour post-procedure. • The aspirin loading dose may be omitted for those subjects on chronic aspirin therapy (≥ 7 days). * Zero refers to administration immediately prior to balloon pre-dilatation of the first target lesion. It is recommended that all antiplatelet medication loading dose be given before the procedure (within 24 hours prior to procedure), at time of procedure, or post-procedure (recommended to be within 1-hour post-procedure). **Post-procedure Medications:** All subjects will be maintained on post-procedure antiplatelet medication per the latest ACC/AHA/SCAI guidelines.
Inclusion Criteria	General Inclusion Criteria: 1. Subject must be at least 18 years of age. 2. Subject or a legally authorized representative must provide written informed consent prior to any study related procedure, per site requirements. 3. Subject must have evidence of myocardial ischemia (e.g., unstable angina, post-infarct angina, stable angina or silent ischemia) suitable for non-emergent PCI. Subject with stable angina or silent ischemia must have objective sign of ischemia as suggested by one of the following, ○ Abnormal stress or imaging stress test, ○ Abnormal computed tomography-fractional flow reserve (CT-FFR)

[redacted]

	○ Stenosis by visual estimation ≥ 70% ○ Abnormal pressure-derived physiological indices (FFR, instantaneous wave-free ratio [iFR], or relative flow reserve [RFR]). 4. Subject must be an acceptable candidate for coronary artery bypass graft (CABG) surgery. 5. Subject must agree not to participate in any other clinical study for a period of one year following the index procedure. Angiographic Inclusion Criteria: 1. Only one *de novo* target lesion in native coronary artery is allowed. ○ Additional one non-target lesion can be treated if located in the different epicardial coronary vessel other than left main coronary artery. Non-target lesion must be treated firstly and must be deemed an angiographic success. 2. The target lesion must be located in a native coronary artery with: ○ Visually estimated reference vessel diameter (RVD)) of ≥ 2.5 mm and ≤ 4.25 mm. ○ Visually estimated lesion length of > 32 mm and ≤ 44 mm, and must be covered by a single ABT NG DES 48 ▪ Multiple focal *de novo* lesions in an epicardial coronary vessel are allowed if the lesions can be covered by one stent. Multiple focal *de novo* lesions will be counted as a single lesion. ○ Visually estimated diameter stenosis of > 50% and < 100% with a TIMI flow of ≥ 1 ▪ Stable angina or silent ischemia subjects must have stenosis ≥ 70%, or abnormal pressure-derived physiological indices (FFR, iFR, or RFR), unless abnormal stress or imaging stress test is evidenced
Exclusion Criteria	General Exclusion Criteria: 1. Subject has known hypersensitivity or contraindication to device material and its degradants (everolimus, cobalt, chromium, nickel, tungsten, acrylic and fluoropolymers, etc.), or has known contrast sensitivity.

	2. Subject has known hypersensitivity or contraindication to aspirin, heparin/bivalirudin, P2Y12 inhibitors (clopidogrel /prasugrel /ticagrelor), and therefore cannot be adequately pre-medicated. 3. Subject has a planned surgery or procedure necessitating discontinuation of aspirin or P2Y12 inhibitor within 12 months following index procedure. 4. Subject is receiving or will require chronic anticoagulation therapy (e.g., coumadin, dabigatran, apixaban, rivaroxaban or any other agent for any reason). 5. Pregnant or nursing subjects and those who plan pregnancy in the period up to 1 year following index procedure. Female subjects of child-bearing potential must have a negative pregnancy test done within 7 days prior to the index procedure per site standard test. 6. Subject had an acute myocardial infarction (AMI) within 48 hours of the index procedure with either of the situations below: o The subject is currently experiencing clinical symptoms consistent with new onset AMI, such as nitrate-unresponsive prolonged chest pain with ischemic electrocardiogram (ECG) changes. o Elevated cardiac biomarker values have not returned to within normal limits at the time of index procedure. 7. Subject has a left ventricular ejection fraction (LVEF) < 30% within 3 months prior to the index procedure, that was documented by any method. 8. Subject is expected to require percutaneous mechanical cardiac support at the index procedure. 9. Prior PCI within the target vessel during the last 12 months prior to consent. 10. Prior PCI within the non-target vessel or any peripheral intervention during the last 30 days prior to consent. 11. At the index procedure, subject is identified to require planned stenting procedure (including staged procedures) or CABG after the index procedure. 12. Subject has received a solid organ transplant which is functioning or is active on a waiting list for any solid organ transplants with expected transplantation within 24 months. 13. Subject has a malignancy that is not in remission.

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Clinical Investigation Plan

	14. Subject is receiving immunosuppressant therapy or has known life-threatening immunosuppressive or severe autoimmune disease (e.g., human immunodeficiency virus, systemic lupus erythematosus, etc.). Note: corticosteroids are not included as immunosuppressant therapy, diabetes mellitus is not regarded as autoimmune disease. 15. Subject has previously received or is scheduled to receive radiotherapy to a coronary artery (vascular brachytherapy), or the chest/mediastinum. 16. Subject has a platelet count < 100,000 cells/mm^3 or > 700,000 cells/mm^3. 17. Subject has renal insufficiency as defined as an estimated glomerular filtration rate (GFR) < 30 ml/min/1.73m^2 or dialysis at the time of consent. 18. Subject is high risk of bleeding for any reason; has a history of bleeding diathesis or coagulopathy; has had a significant gastro-intestinal or significant urinary bleed within the past six months. 19. Subject has had a cerebrovascular accident or transient ischemic neurological attack (TIA) within the past 6months, or any prior intracranial bleed, or any permanent neurologic defect, or any known intracranial pathology (e.g. aneurysm, arteriovenous malformation, etc.). 20. Subject has extensive peripheral vascular disease that precludes safe 6 French sheath insertion. Note: femoral arterial disease does not exclude the subject if radial access may be used. 21. Subject has life expectancy < 2 years. 22. Subject is, in the opinion of the Investigator or designee, unable to comply with the requirements of the study protocol or is unsuitable for the study for any reason. This includes completion of Subject Reported Outcome instruments. 23. Subject is currently participating in another clinical investigation (except for non-invasive observational studies) that has not yet completed its primary endpoint. 24. Subject intends to participate in another investigational drug or device clinical investigation (except for non-invasive observational studies) within 12 months after the index procedure. 25. Subject has other medical illness (e.g., cancer or congestive heart failure) or known history of substance abuse (alcohol, cocaine, heroin etc.) that may cause non-compliance with the protocol, confound the data interpretation or is associated with a limited life expectancy less than 2 years.

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26. Presence of other anatomic or comorbid conditions, or other medical, social, or psychological conditions that, in the investigator's opinion, could limit the subject's ability to participate in the clinical investigation or to comply with follow-up requirements, or impact the scientific soundness of the clinical investigation results.

27. Subject has active symptoms and/or a positive test result of COVID-19 or other rapidly spreading novel infectious agent within the prior 2 months.

Angiographic Exclusion Criteria:

1. Target lesion/vessel meets any of the following criteria:

    - Prevents complete angioplasty balloon (plain old balloon angioplasty [POBA], scoring balloon, or cutting balloon) inflation, such as:

        - Heavy calcified lesion
        - Requires additional device for lesion preparation (e.g., rotablator or laser).

    - Anatomy proximal to or within the lesion that prevents proper placement of delivery system.

        - Extreme angulation (≥ 90°) proximal to or within the target lesion.
        - Excessive tortuosity (≥ two 45° angles) proximal to or within the target lesion.

    - Involves a bifurcation of which the side branch will be jailed by the struts and requiring side branch pre-dilatation by Kissing Balloon Technique, and/or stenting.

    - Is located:

        - In left main or there is a ≥30% diameter stenosis in the left main (unless the left main lesion is a protected left main (i.e. a patent bypass graft to the LAD and/or LCX arteries is present), and there is no intention to treat the protected left main lesion).

        - Within 3 mm of the origin of the LAD or LCX.

        - Within 3 mm of aorto-ostial RCA.

        - In a bypass graft or distal to anastomotic site of bypass graft.

    - With total occlusion (TIMI flow 0), prior to crossing with the wire.

	○ Contains thrombus. ○ The subject has been previously treated with a stent within 1-year prior to the index procedure such that the ABT NG DES 48 would need to cross the stent to reach the target lesion. 2. Unsuccessful target lesion pre-dilatation, defined as the presence of one or more of the following: ○ Failed for a full inflation of the pre-dilatation balloon. ○ TIMI flow grade <3 (per visual estimation). ○ Any angiographic complication (e.g. distal embolization, no-reflow). ○ Any dissection National Heart, Lung, and Blood Institute (NHLBI) grade D-F. ○ Any chest pain lasting > 5 minutes. ○ Any ST-segment depression or elevation lasting > 5 minutes. ○ Side branch requires additional dilatation/stenting caused by plaque shift, carina shift or may require additional dilatation/stenting after stent implantation, per the operator's assessment. 3. Non-target lesion meets any of the following criteria: ○ Is located in the target vessel ○ Is located in the left main location ○ Is restenotic from a previous stent implantation ○ Is located within a saphenous vein graft or an arterial graft ○ Is with a TIMI flow 0 (total occlusion) prior to guide wire crossing ○ Involves a complex bifurcation that needs two-stent strategy. 4. Treatment of non-target lesion is not deemed successful. Note: A successful treatment is defined as a treatment resulted in a mean lesion diameter stenosis < 30% in 2 near-orthogonal projections with TIMI 3 flow, as visually assessed by the physician, without the occurrence of prolonged chest pain or ECG changes consistent with MI.

Clinical Investigation Plan

Treatment Strategy	• Non-target lesion, if exist, must be treated first with commercially available stents (<=38 mm) and deemed to be successful.
	• Pre-dilatation of the target lesion is mandatory and deemed to be successful
	  ○ The pre-dilatation balloon must be shorter than the planned stent(s) length to limit pre-dilatation injury to the area to be stented (recommended 4-6 mm).
	• Select appropriate diameter of ABT NG DES 48.
	  ○ If there is considerable vessel taper it is recommended to select a stent that matches the distal RVD to avoid over expansion of the vessel.
	  ○ Intravascular imaging is allowed per the physician discretion. If optical coherence tomography (OCT) is used for vessel size measurement, it is recommended to follow the approved IFU for guidance. Sites using OCT for vessel sizing will be asked to provide OCT images to the Sponsor. Analysis for OCT may be conducted to assess vessel sizing.
	• Use 6 or above French guiding catheter for delivery and deployment of the ABT NG DES 48. A guide extension, a stronger support guide catheter, as well as a buddy wire, may be considered. Deploy the ABT NG DES 48 per the IFU. Do not exceed the rated burst pressure (16 atm) as indicated in the IFU of the study stent
	• Post-dilatation is strongly recommended and when performed should only be performed with balloon lengths that fit within the boundaries of the stent
	  ○ The use of a high pressure, non-compliant balloon is strongly recommended.
	  ○ If appropriate, the delivery balloon (stent balloon) may be used for post-dilatation.
	  ○ If considerable vessel taper exists, post-dilate the proximal/distal stented segment with a balloon that matches the proximal/distal segment RVD, if appropriate.
	• Bailout procedure for the side branch should only be done:
	  ○ If newly onset of chest pain or ECG changes that suggests ischemia, caused by the side branch occlusion during or after stenting, side branch dilatation can be done.

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Clinical Investigation Plan

	○ Side branch stenting should be avoided unless severe dissection is observed. ○ If kissing balloon is required, delivery balloon must not be used.
Analysis Datasets	[redacted]
Analysis	[redacted]