Absorb GT1™
Bioresorbable Vascular Scaffold (BVS) System

℞ ONLY

Instructions for Use

Table of Contents

Abbott

1.0 DEVICE DESCRIPTION

The Absorb GT1 Bioresorbable Vascular Scaffold (BVS) System is a temporary coronary scaffold comprised of a fully bioresorbable scaffold and bioresorbable polymer coating. Absorb™ improves coronary luminal diameter in patients with ischemic heart disease and is completely resorbed by the body in approximately three years.

The Absorb GT1 BVS System includes:

- A pre-mounted polymer poly(L-lactide) (PLLA) scaffold coated with a blend of the antiproliferative drug everolimus and polymer poly(D,L-lactide) (PDLLA) in a 1:1 ratio. The available dose of everolimus on the scaffold is shown in **Table 1.0-1**.

Table 1.0-1: Drug Content in Absorb GT1 BVS

Scaffold Diameter (mm)	Scaffold Length (mm)	Drug Dose (μg)
2.5, 3.0	8	76
2.5, 3.0	12	114
2.5, 3.0	18	181
2.5, 3.0	23	228
2.5, 3.0	28	276
3.5	12	135
3.5	18	197
3.5	23	246
3.5	28	308

- Four radiopaque markers located at the end rings of the scaffold mark the scaffold length prior to deployment and after expansion in the artery. The Absorb GT1 Bioresorbable Vascular Scaffold itself is not visible under fluoroscopy.

- Two radiopaque markers, located underneath the balloon, fluoroscopically mark the working length of the balloon and the location of the undeployed scaffold of the scaffold delivery system.

- The Absorb GT1 BVS System has a rapid exchange (RX) scaffold delivery system.

- Two proximal delivery system shaft markers (95 cm and 105 cm proximal to the distal tip) indicate the position of the delivery system relative to the end of the brachial or femoral guiding catheter. The working catheter length is 145 cm.

- A shaft color change denotes the guide wire exit notch.

Note: The Absorb GT1 BVS System utilizes the identical scaffold as the Absorb BVS System used in the clinical studies. Within this document, the scaffold for both systems is referred to synonymously as the “Absorb GT1 BVS,” the “Absorb scaffold,” or “Absorb.”

Table 1.0-2: *In Vitro* Device Specifications

Scaffold Diameter (mm)	Scaffold Length (mm)	* Minimum Guiding Catheter Compatibility (ID)	** *In Vitro* Scaffold Nominal Pressure		Rated Burst Pressure – RBP		Scaffold Free Area (%)
			atm	kPa	atm	kPa	
2.5	8	6F (0.070”/1.8 mm)	6	608	16	1621	68
2.5	12	6F (0.070”/1.8 mm)	6	608	16	1621	68
2.5	18	6F (0.070”/1.8 mm)	6	608	16	1621	68
2.5	23	6F (0.070”/1.8 mm)	6	608	16	1621	68
2.5	28	6F (0.070”/1.8 mm)	6	608	16	1621	68
3.0	8	6F (0.070”/1.8 mm)	7	709	16	1621	72
3.0	12	6F (0.070”/1.8 mm)	7	709	16	1621	73
3.0	18	6F (0.070”/1.8 mm)	7	709	16	1621	73
3.0	23	6F (0.070”/1.8 mm)	7	709	16	1621	73
3.0	28	6F (0.070”/1.8 mm)	7	709	16	1621	73
3.5	12	6F (0.070”/1.8 mm)	6	608	16	1621	73
3.5	18	6F (0.070”/1.8 mm)	6	608	16	1621	73
3.5	23	6F (0.070”/1.8 mm)	6	608	16	1621	73
3.5	28	6F (0.070”/1.8 mm)	6	608	16	1621	74

* See individual manufacturer specifications for (F) equivalent.

** Ensure full deployment of the scaffold (see **Section 12.6 – Clinician Use Information, Deployment Procedure**).

Note: Deployment pressures should be based on lesion characteristics.

- A non-sterile temperature monitor for the shipping and storage of the Absorb GT1 BVS System has been included with the product. Before use of this product, check the temperature indicator located through the window in the back of the product box. Consult the product carton or carton insert for indicator legend.

2.0 INDICATIONS

The Absorb GT1 Bioresorbable Vascular Scaffold (BVS) is a temporary scaffold that will fully resorb over time and is indicated for improving coronary luminal diameter in patients with ischemic heart disease due to *de novo* native coronary artery lesions (length ≤ 24 mm) with a reference vessel diameter of ≥ 2.5 mm and ≤ 3.75 mm.

3.0 CONTRAINDICATIONS

The Absorb GT1 BVS System is contraindicated for use in:

- Patients who cannot tolerate, including allergy or hypersensitivity to, procedural anticoagulation or the post-procedural antiplatelet regimen.

- Patients with hypersensitivity or contraindication to everolimus or structurally-related compounds, or known hypersensitivity to scaffold components (poly(L-lactide), poly(D,L-lactide), platinum) or with contrast sensitivity.

4.0 WARNINGS

- **For single use only.** Do not resterilize or reuse. Note the product "Use by" date on the package.

- Careful assessment of the target lesion reference vessel diameter and selection of the appropriate scaffold diameter relative to the target lesion reference vessel diameter are required to minimize potential damage to the scaffold during post-dilatation and to ensure adequate scaffold apposition and an appropriate post-implantation minimum lumen diameter.

- **In small vessels (visually assessed reference vessel diameter ≤ 2.75 mm), on-line QCA or intravascular imaging with intravascular ultrasound or optical coherence tomography is strongly recommended to accurately measure and confirm appropriate vessel sizing (reference vessel diameter ≥ 2.5 mm). (See Section 8.1.6 – Implantation of Absorb in Small Coronary Arteries (Post Hoc Analysis))**

- If quantitative imaging determines a vessel size < 2.5 mm, do not implant the Absorb GT1 BVS. Implantation of the device in vessels < 2.5 mm may lead to an increased risk of adverse events such as myocardial infarction and scaffold thrombosis.

- Adequate lesion preparation prior to scaffold implantation is required to ensure safe delivery of the scaffold across the target lesion. It is not recommended to treat patients having a lesion that prevents complete inflation of an angioplasty balloon. It is strongly recommended to achieve a residual stenosis between 20% and 40% after pre-dilatation to enable successful delivery and full expansion of the scaffold.

- Ensure the scaffold is not post-dilated beyond the allowable expansion limits (see **Section 12.7 – Clinician Use Information, Further Expansion of the Deployed Scaffold**).

- Antiplatelet therapy should be administered post-procedure (see **Section 9.1 – Patient Selection and Treatment, Individualization of Treatment**).

- This product should not be used in patients who are not likely to comply with the recommended antiplatelet therapy.

- Judicious selection of patients is necessary, since the use of this device carries the associated risk of scaffold thrombosis, vascular complications, and / or bleeding events.

5.0 PRECAUTIONS

5.1 Scaffold Handling

- Implantation of the scaffold should be performed **only** by physicians who have received appropriate training.

- Scaffold placement should be performed at centers where emergency coronary artery bypass graft surgery (CABG) is available.

- To confirm sterility has been maintained, ensure that the inner package sterile barrier has not been opened or damaged prior to use.

- Care should be taken to control the guiding catheter tip during scaffold delivery, deployment, and balloon withdrawal. Before withdrawing the scaffold delivery system, visually confirm complete balloon deflation by fluoroscopy to avoid guiding catheter movement into the vessel and subsequent arterial damage.

- Special care must be taken not to handle or in any way disrupt the scaffold from the balloon. This is most important during catheter removal from packaging, placement over the guide wire, and advancement through the rotating hemostatic valve adapter and guiding catheter hub.

- **Do not manipulate, touch, or handle the scaffold**, as this may cause coating damage, contamination, or dislodgement of the scaffold from the delivery balloon.

- Use only the appropriate balloon inflation media. Do not use air or any gaseous medium to inflate the balloon, as this may cause uneven expansion and difficulty in deployment of the scaffold.

5.2 Scaffold Placement

- Devices (i.e., guide sheaths) that decrease the inner diameter of the guide catheter outside of the Absorb GT1 BVS minimum guide catheter compatibility (**Table 1.0-2**) must not be used with the Absorb GT1 BVS System. Do not insert a 5-in-6, or a 6-in-7 guide sheath into a 6F or 7F guiding catheter, as doing so will result in an inner diameter that is too small for use with the Absorb GT1 BVS System.

- **Do not prepare or preinflate the delivery system prior to scaffold deployment**, other than as directed. Use balloon purging technique described in **Section 12.4.4 – Clinician Use Information, Preparation, Delivery System Preparation**.

- Pre-dilatation should be performed with an angioplasty balloon. Cutting or scoring balloons can be used per physician discretion, if the lesion appears to be mildly calcified.

- When introducing the delivery system into the vessel, do not induce negative pressure on the delivery system. This may cause dislodgement of the scaffold from the balloon.

- Do not torque the catheter more than one (1) full turn.

- Use caution when advancing the Absorb GT1 BVS across the lesion. Multiple attempts to cross a lesion may lead to scaffold damage or dislodgement.

- Implanting a scaffold may lead to dissection of the vessel distal and / or proximal to the scaffold, requiring additional intervention.

  Note: In the event of edge dissections Absorb GT1 BVS or metallic everolimus-eluting stent of appropriate size should be used at the operator's discretion to completely cover dissection.

- In the event of abrupt vessel closure / total occlusion of the scaffold, a bailout implant may be inserted and deployed within the scaffold such that the Absorb GT1 BVS is

completely covered by the bailout implant. All abrupt closures must be treated as an emergency per the hospital standard of care.

Note: It is recommended that bailouts for abrupt closure / total occlusion of the scaffold be done with a metallic everolimus-eluting stent of appropriate size.

- An unexpanded scaffold may be retracted into the guiding catheter **one time only**. An unexpanded scaffold should not be reintroduced into the artery once it has been pulled back into the guiding catheter. Subsequent movement in and out through the distal end of the guiding catheter should not be performed, as the scaffold may be damaged or dislodged during retraction back into the guiding catheter.

- Should resistance be felt at any time during removal of the undeployed Absorb GT1 BVS System, please refer to the steps provided in **Section 5.4 – Precautions, Scaffold / System Removal**.

- Do not expand the scaffold if it is not properly positioned in the vessel (see **Section 5.4 – Precautions, Scaffold / System Removal**).

- The inflated balloon diameter of the system used to deploy the scaffold should approximate the diameter of the vessel. To ensure full expansion of the scaffold, the balloon should be inflated to a minimum of nominal pressure.

- **Do not exceed the Rated Burst Pressure (RBP) as indicated on the product label.** Monitor balloon pressures during inflation. Use of pressures higher than specified on the product label may result in a ruptured balloon, with possible intimal damage and dissection.

- Post-dilatation is strongly recommended for optimal scaffold apposition. When performed, post-dilatation should be at high pressure (> 16 atm) with a noncompliant balloon.

- Under-expansion of the scaffold may result in scaffold movement. Care must be taken to properly size the scaffold to ensure that the scaffold is in full contact with the arterial wall upon deflation of the balloon. All efforts should be made to ensure that the scaffold is not under dilated. Refer to **Section 12.7 – Clinician Use Information, Further Expansion of the Deployed Scaffold.**

- Balloon dilatation of any cells of a deployed Absorb GT1 BVS may cause scaffold damage. **Avoid scaffolding across any side branches ≥ 2.0 mm in diameter.** Placement of a scaffold has the potential to compromise side branch patency.

- Scaffold retrieval methods (use of additional wires, snares, and / or forceps) may result in additional trauma to the coronary vasculature and / or the vascular access site. Complications may include bleeding, hematoma, or pseudoaneurysm.

- When treating multiple lesions within the same vessel, scaffold / stent the distal lesion prior to scaffolding / stenting the proximal lesion. Scaffolding / stenting in this order obviates the need to cross the proximal scaffold during placement of the distal scaffold / stent, and reduces the chance of damaging or dislodging the proximal scaffold / stent.

- When multiple Absorb GT1 BVS or drug-eluting stents are required, only Absorb GT1 BVS or everolimus-eluting scaffolds / stents must be used. Potential interaction with

other drug-eluting or coated scaffolds / stents has not been evaluated and should be avoided.

- The extent of the patient's exposure to drug and polymer is directly related to the number of scaffolds implanted. The safety of everolimus, polymer, and polymer breakdown products was evaluated in pre-clinical studies and the biocompatibility assessment of the Absorb scaffold through its life-cycle. No everolimus, polymer, or polymer breakdown product-related safety issues were identified in dosing up to the equivalent of 94 mm of Absorb scaffolding. In the ABSORB III clinical trial, the maximum scaffolding length a patient received was 74 mm which was achieved using a total of 3 scaffolds (28, 28, 18 mm).

- It is not recommended to treat patients having a lesion with excessive tortuosity proximal to or within the lesion.

- The safety and effectiveness of the Absorb GT1 BVS in patients with prior brachytherapy of the target lesion or the use of brachytherapy for treated site restenosis in an Absorb GT1 BVS have not been established. Both vascular brachytherapy and the Absorb GT1 BVS alter arterial remodeling. The potential combined effect on arterial remodeling by these two treatments is not known.

5.3 Use in Conjunction with Other Procedures

- While vessel preparation in complex lesions may include the use of various mechanical atherectomy devices, the safety and effectiveness of the Absorb GT1 BVS has not been established in clinical trials with the use of either mechanical atherectomy devices (directional atherectomy catheters, rotational atherectomy catheters) or laser angioplasty catheters.

5.4 Scaffold / System Removal

- Scaffold delivery system removal prior to scaffold deployment:

  If removal of a scaffold system is required prior to deployment, ensure that the guide catheter is coaxially positioned relative to the scaffold delivery system and cautiously withdraw the scaffold delivery system into the guiding catheter. Should **unusual resistance** be felt **at any time** when withdrawing the scaffold into the guide catheter, the scaffold delivery system and the guide catheter should be **removed as a single unit**. This should be done under direct visualization with fluoroscopy.

- Withdrawal of the scaffold delivery system / post-dilatation balloon from the deployed scaffold:

  1. Deflate the balloon by pulling negative on the inflation device. Larger and longer balloons will take more time (up to 30 seconds) to deflate than smaller and shorter balloons. Confirm balloon deflation under fluoroscopy.
  2. Position the inflation device to "negative" or "neutral" pressure.
  3. Stabilize guide catheter position just outside the coronary ostium and anchor in place. Maintain guide wire placement across scaffold segment.
  4. Gently remove the scaffold delivery system / post-dilatation balloon with slow and steady pressure.

5. Tighten the rotating hemostatic valve.

Notes:

1. **If, during withdrawal of the catheter from the deployed scaffold, resistance is encountered, use the following steps to improve balloon rewrap:**
   - Re-inflate the balloon up to nominal pressure, deflate and change pressure to neutral.
   - Repeat steps 1 through 5 above.

2. After successful withdrawal of the balloon from the deployed scaffold, should **any resistance** be felt **at any time** when withdrawing the scaffold delivery system or post-dilatation balloon into the guide catheter, **remove the entire system as a single unit**.

- Failure to follow the steps and / or applying excessive force to the delivery system can potentially result in loss of or damage to the scaffold and / or delivery system components.

- If it is necessary to retain guide wire position for subsequent artery / lesion access, leave the guide wire in place and remove all other system components.

5.5 Post Implant

- **If necessary to cross a newly deployed scaffold** with a guide wire, balloon, delivery system, or imaging catheters, exercise care to avoid disrupting the scaffold geometry.

- Subsequent restenosis may require repeat dilatation of the arterial segment containing the scaffold. The long-term outcome following repeat dilatation of scaffolds is unknown.

5.6 Use in Special Populations

5.6.1 Pregnancy

Pregnancy Category C: see **Section 6.5 – Drug Information, Pregnancy**. The Absorb GT1 BVS has not been tested in pregnant women or in men intending to father children. Effects on the developing fetus have not been studied. Effects of a similar stent, XIENCE V®, on prenatal and postnatal rat development were no different than the controls. When administered at oral doses of 0.1 mg/kg or above to animals, everolimus has shown reproductive toxicity effects including embryo toxicity and fetotoxicity.[1]

Effective contraception is recommended to be initiated before implanting Absorb GT1 BVS and continued for one year after implantation. While there is no contraindication to Absorb GT1 BVS implantation during pregnancy, the risks and reproductive effects are unknown.

[1] Certican® UK label Mar 2015, Afinitor® EU authorization SPC Dec 2014, Votubia® EU SPC Sept 2014, Afinitor® US label Jan 2015, and Zortress® US label Sept 2015. Refer to www.MHRA.gov.uk, www.ema.europa.eu, and www.fda.gov for the most recent versions of these SPC/labels.

5.6.2 Lactation

See **Section 6.6 – Drug Information, Lactation**. It is unknown whether everolimus is distributed in human milk. A decision should be made whether or not to discontinue nursing prior to scaffold implantation, considering the importance of the scaffold to the mother.

5.6.3 Gender

The assessment of gender effect in the ABSORB III trial for the primary endpoint of target lesion failure (TLF) at 1 year showed no significant treatment interaction by gender (p=0.6763). Within each gender subgroup, the observed 1-year TLF rate was numerically higher in the Absorb group as compared to the XIENCE group.

5.6.4 Ethnicity

Within each ethnicity subgroup, the observed 1-year TLF rate was numerically higher in the Absorb group as compared to the XIENCE group. In the ABSORB III study, non-white subjects represented 12.5% of the population. Therefore, results in the non-white subgroup should be interpreted with caution due to the small sample size of the subgroups.

5.6.5 Pediatric Use

The safety and effectiveness of Absorb GT1 BVS in pediatric subjects have not been established.

5.6.6 Geriatric Use

The ABSORB III trial had a median subject age of 64 years, with no upper age limit. The assessment of geriatric age in the ABSORB III trial showed no relationship to the primary endpoint of TLF at 1 year.

5.7 MRI (Magnetic Resonance Imaging) Safety Information

Non-clinical testing has demonstrated the Absorb GT1 BVS is MR Conditional. A patient with this device can be safely scanned in all MR environments 3T or less.

5.8 Drug Interactions

See **Section 6.3 – Drug Information, Interactions with Drugs or Other Substances**. Several drugs are known to affect everolimus metabolism, and other drug interactions may also occur. Everolimus is known to be a substrate for both cytochrome P4503A4 (CYP3A4) and P-glycoprotein (PgP). Everolimus absorption and subsequent elimination may be influenced by drugs that affect these pathways. Everolimus has also been shown to reduce the clearance of some prescription medications when administered orally along with cyclosporine (CsA). Formal drug interaction studies have not been performed with the Absorb GT1 BVS because of limited systemic exposure to everolimus eluted from Absorb GT1 BVS (see **Section 6.2 – Drug Information, Pharmacokinetics**). Therefore, due consideration should be given to the potential for both systemic and local drug interactions in the vessel wall, when deciding to place the Absorb GT1 BVS in a patient taking a drug with known interaction with everolimus, or when deciding to initiate therapy with such a drug in a patient who has recently received Absorb GT1 BVS.

5.9 Immune Suppression Potential

Everolimus, the Absorb GT1 BVS active ingredient, is an immunosuppressive agent. Immune suppression was not observed in the ABSORB family of clinical trials. However, for patients who receive several Absorb GT1 BVS simultaneously, it may be possible for everolimus systemic concentrations to approach immunosuppressive levels temporarily, especially in patients who also have hepatic insufficiency or who are taking drugs that inhibit CYP3A4 or P-glycoprotein. Therefore, consideration should be given to patients taking other immunosuppressive agents or who are at risk for immune suppression.

5.10 Lipid Elevation Potential

Oral everolimus use in renal transplant and advanced renal cell carcinoma patients was associated with increased serum cholesterol and triglyceride levels, which in some cases required treatment. The effect was seen with both low and high dose prolonged oral therapy in a dose-related manner. When used according to the indications for use, exposure to systemic everolimus concentrations from the Absorb GT1 BVS is expected to be significantly lower than concentration exposure usually obtained in transplant patients. Increased serum cholesterol and triglyceride levels were not observed in the ABSORB family of clinical trials.

Oral administration of everolimus in combination with cyclosporine has been associated with increased serum cholesterol and triglyceride levels. Therefore, patients treated with cyclosporine should be monitored for changes in lipid profiles.

5.11 Lesion / Vessel Characteristics

The safety and effectiveness of the Absorb GT1 BVS has not been established for subject populations with the following characteristics:

- Coronary artery reference vessel diameters < 2.5 mm or > 3.75 mm
- Lesion lengths > 24 mm
- Lesions located in arterial or saphenous vein grafts
- Lesions located in an unprotected left main artery
- Ostial lesions
- Lesions located at a bifurcation
- Previously stented lesions
- Moderate to severe calcification
- Chronic total occlusion or poor flow (< TIMI 1) distal to the identified lesions
- Three-vessel disease
- Unresolved thrombus at the lesion site or anywhere in the vessel to be treated
- Excessive tortuosity proximal to or within the lesion
- Recent acute myocardial infarction (AMI)

6.0 DRUG INFORMATION

6.1 Mechanism of Action

The mechanism by which the Absorb GT1 BVS inhibits neointimal growth as seen in pre-clinical and clinical studies has not been established. At the cellular level, everolimus inhibits growth factor-stimulated cell proliferation. At the molecular level, everolimus forms a complex with the cytoplasmic protein FKBP-12 (FK 506 Binding Protein). This complex binds to and interferes with FKBP-12 Rapamycin Associated Protein (FRAP), also known as mammalian target of rapamycin (mTOR), leading to inhibition of cell metabolism, growth, and proliferation by arresting the cell cycle at the late G1 stage.

6.2 Pharmacokinetics

Everolimus elution from the Absorb scaffold post-implantation has been evaluated in a pharmacokinetic (PK) sub-study, which is part of the ABSORB III clinical trial design studying the Absorb scaffold in the United States (US). A total of 12 subjects who received only Absorb scaffolds at two investigational sites in the US were registered in the PK sub-study. All subjects had single target lesions that were treated with only Absorb. The number of scaffolds implanted per subject was one or two. The total dose of everolimus received by the subjects ranged from 181 to 443 µg. **Table 6.2-1** provides whole blood everolimus PK parameters determined from the subjects receiving Absorb.

Table 6.2-1: Pharmacokinetic Results of Everolimus after Implantation of at Least One Absorb (Individual Dose Ranged from 181 µg – 443 µg)

Pharmacokinetics of everolimus	ABSORB III PK Sub-Study
N	12
Stents/Scaffolds used	1 – 2
Dose (µg)	181 – 443
C_{max} (ng/mL)	1.085 – 4.460
AUC_{last} (ng*h/mL)	25.37 – 104.6
T_{max} (h)	0.17 – 2.37
$t_{1/2}$ (h)	45.9 – 115

Note: Ranges are provided for dose, C_{max}, AUC_{last}, T_{max}, and $t_{1/2}$

Everolimus blood concentrations were low but could be quantified up to 168 hours after implantation of the last Absorb scaffold. Although short-lived, individual C_{max} values (1.085 to 4.460 ng/mL) were slightly higher than the minimum systemic, chronically maintained therapeutic level of ≥ 3.0 ng/mL necessary to be effective for prevention of organ rejection. Blood concentrations were below 3.0 ng/mL in all subjects by 4 hours after the last scaffold deployment. The rapid disappearance of everolimus after implantation of the Absorb scaffold further limits the systemic extent of exposure. Therefore, everolimus blood concentrations seen with the Absorb scaffold are considered safe.

The pharmacokinetic profile for everolimus eluted from the Absorb scaffold has been adequately characterized and is consistent with previous clinical and nonclinical data. The PK characteristics of everolimus after deployment of the Absorb scaffold (dose range: 181 to

443 µg) were shown to be predictable due to dose-proportional behavior. The local arterial delivery and limited systemic exposure provide the opportunity for the treatment of coronary lesions with limited risk associated with systemic exposure. The pharmacokinetic profiles seen with the Absorb scaffold are considered to be safe.

6.3 Interactions with Drugs or Other Substances

Everolimus is extensively metabolized by the cytochrome P4503A4 (CYP3A4) in the gut wall and liver, and is a substrate for the countertransporter P-glycoprotein. Everolimus was shown to reduce the clearance of some prescription medications when it was administered orally along with cyclosporine (CsA). Hence, everolimus, when prescribed as an oral medication, may interact with other medications that include (but are not restricted to) inhibitors and inducers of CYP3A4 isozymes; absorption and subsequent elimination of everolimus may be influenced by drugs that affect these pathways. Formal drug interaction studies have not been performed with the Absorb GT1 BVS System. Therefore, consideration should be given to the potential for both systemic and local drug interactions in the vessel wall, when deciding to place the Absorb GT1 BVS in a subject taking a drug with known interaction with everolimus.

Everolimus, when prescribed as an oral medication, may interact with some drugs or foods including, but not limited to:

- CYP3A4 / PgP inhibitors that may increase everolimus blood concentrations:
    - Immunosuppressant cyclosporine
    - Antifungal agents (e.g., fluconazole, ketoconazole, itraconazole, ketoconazole)
    - Macrolide antibiotics (e.g., clarithromycin, erythromycin)
    - Calcium channel blockers (e.g., verapamil, nicardipine, diltiazem)
    - Protease inhibitors (e.g., nelfinavir, indinavir, amprenavir)
    - Other substances (e.g., cisapride, metoclopramide, bromocriptine, cimetidine, danazol)
- CYP3A4 inducers that may decrease everolimus drug concentrations:
    - Antibiotics (e.g., rifampin, rifabutin)
    - Anticonvulsants (e.g., carbamazepine, phenobarbital, phenytoin)
    - Non-nucleoside reverse transcriptase inhibitors (e.g., efavirenz, nevirapine**)**
    - Glucocorticoids (e.g., dexamethasone, prednisone, prednisolone)
    - HMGCoA reductase inhibitors (e.g., simvastatin, lovastatin)
    - Other (e.g., St. John's Wort)

For more detailed drug interaction information, please reference the most recent everolimus drug label. [2]

6.4 Carcinogenicity, Genotoxicity, and Reproductive Toxicity

The carcinogenicity and reproductive toxicity of the Absorb GT1 BVS have not been evaluated; however, long-term carcinogenicity and teratology studies were performed with XIENCE V, a

[2] Certican® UK label Mar 2015, Afinitor® EU authorization SPC Dec 2014, Votubia® EU SPC Sept 2014, Afinitor® US label Jan 2015, and Zortress® US label Sept 2015. Refer to www.MHRA.gov.uk, www.ema.europa.eu, and www.fda.gov for the most recent versions of these SPC/labels.

similar everolimus-eluting coronary stent system. The test results from the XIENCE V stent, as described below, are applicable to the Absorb GT1 BVS. Additionally, there is no carcinogenicity and reproductive toxicity in PLA based on historical use of PLA materials in various implant applications.

A 26-week carcinogenicity study was conducted to evaluate the carcinogenic potential of XIENCE V stents following subcutaneous implantation in transgenic mice. During the course of the study, there were no abnormal clinical observations that suggested a carcinogenic effect in the test group (XIENCE V stent). The test group did not demonstrate an increased incidence of neoplastic lesions when compared to the negative control group. However, the positive control and the experimental positive control groups demonstrated notable increases in the incidence of neoplastic lesions compared to either the test or the negative control group. Based on the results of this study, the XIENCE V stent does not appear to be carcinogenic when implanted in transgenic mice for 26 weeks.

In addition, a reproductive toxicity (teratology) study was conducted in female Sprague-Dawley rats. The XIENCE V stent did not affect the fertility or reproductive capability of female Sprague-Dawley rats. There was no statistical difference between the test article (XIENCE V stent) and the control system in terms of any of the evaluated parameters. The test article had no effect on litter size and caused no increase of *in utero* mortality. Additionally, the XIENCE V stent did not cause any reproductive toxicity in the offspring in this study.

Genotoxicity studies were conducted on the Absorb scaffold on bacteria *in vitro* and on mammalian cells *in vivo*. These studies included gene mutations in bacteria (Ames Test), chromosomal damage including chromosomal aberration and clastogenicity (chromosomal breakage) tests in mammalian cells, and erythrocyte micronucleus test in rodents. Based on the results of these studies, the Absorb scaffold is not genotoxic.

6.5 Pregnancy

Pregnancy Category C: There are no adequate everolimus or Absorb GT1 BVS-related studies in pregnant women. Effects of a similar stent, XIENCE V, on prenatal and postnatal rat development were no different than the controls (see **Section 6.4 – Drug Information, Carcinogenicity, Genotoxicity, and Reproductive Toxicity**). When administered at oral doses of 0.1 mg/kg or above to animals, everolimus has shown reproductive toxicity effects including embryotoxicity and fetotoxicity.[3] Effective contraception is recommended to be initiated before implanting Absorb GT1 BVS and continued for one year post-implantation. The Absorb GT1 BVS should be used in pregnant women only if potential benefits of the scaffold outweigh potential risks.

The safety of the Absorb GT1 BVS has not been evaluated in males intending to father children.

6.6 Lactation

It is unknown whether everolimus is distributed in human milk. Also, everolimus pharmacokinetic and safety profiles have not been determined in infants. Consequently, mothers should be advised of potential serious adverse reactions to everolimus in nursing

[3] Certican® UK label Mar 2015, Afinitor® EU authorization SPC Dec 2014, Votubia® EU SPC Sept 2014, Afinitor® US label Jan 2015, and Zortress® US label Sept 2015. Refer to www.MHRA.gov.uk, www.ema.europa.eu, and www.fda.gov for the most recent versions of these SPC/labels.

infants. Prior to Absorb GT1 BVS implantation, decisions should be made regarding whether to discontinue nursing or conduct an alternate percutaneous coronary intervention procedure.

7.0 ADVERSE EVENTS

7.1 Observed Adverse Events

Adverse events observed in the ABSORB family of clinical trials that are related to the key clinical outcomes of death, cardiac death, myocardial infarction (MI) (Q-wave and non-Q-wave), target lesion revascularization (TLR) (by percutaneous coronary intervention [PCI] or coronary artery bypass graft), scaffold thrombosis, ischemia-driven Major Adverse Cardiac Event (MACE) (composite of cardiac death, MI, or ischemia-driven TLR [ID-TLR]), and Target Lesion Failure (TLF) (composite of cardiac death, myocardial infarction attributable to target vessel, or ischemia-driven target lesion revascularization) are presented in **Section 8.0 – Clinical Investigations of the Absorb GT1 BVS System**. All other adverse events are included in **Section 7.2 – Adverse Events, Potential Adverse Events**.

7.2 Potential Adverse Events

Adverse events that may be associated with PCI, treatment procedures and the use of a coronary scaffold in native coronary arteries include the following, but are not limited to:

- Allergic reaction or hypersensitivity to latex, contrast agent, anesthesia, device materials (platinum, or polymer [poly(L-lactide) (PLLA), polymer poly(D,L-lactide) (PDLLA)]), and drug reactions to everolimus, anticoagulation, or antiplatelet drugs
- Vascular access complications which may require transfusion or vessel repair, including:
    - Catheter site reactions
    - Bleeding (ecchymosis, oozing, hematoma, hemorrhage, retroperitoneal hemorrhage)
    - Arteriovenous fistula, pseudoaneurysm, aneurysm, dissection, perforation / rupture
    - Embolism (air, tissue, plaque, thrombotic material or device)
    - Peripheral nerve injury
    - Peripheral ischemia
- Coronary artery complications which may require additional intervention, including:
    - Total occlusion or abrupt closure
    - Arteriovenous fistula, pseudoaneurysm, aneurysm, dissection, perforation / rupture
    - Tissue prolapse / plaque shift
    - Embolism (air, tissue, plaque, thrombotic material or device)
    - Coronary or scaffold thrombosis (acute, subacute, late, very late)
    - Stenosis or restenosis
- Pericardial complications which may require additional intervention, including:
    - Cardiac tamponade
    - Pericardial effusion
    - Pericarditis
- Cardiac arrhythmias (including conduction disorders, atrial and ventricular arrhythmias)
- Cardiac ischemic conditions (including myocardial ischemia, myocardial infarction [including acute], coronary artery spasm, and unstable or stable angina pectoris)

- Stroke / Cerebrovascular accident (CVA) and Transient Ischemic Attack (TIA)
- System organ failures:
    - Cardio-respiratory arrest
    - Cardiac failure
    - Cardiopulmonary failure (including pulmonary edema)
    - Renal insufficiency / failure
    - Shock
- Blood cell disorders (including Heparin Induced Thrombocytopenia [HIT])
- Hypotension / hypertension
- Infection
- Nausea and vomiting
- Palpitations, dizziness, and syncope
- Chest pain
- Fever
- Pain
- Death

Adverse events associated with daily oral administration of everolimus in doses varying from 1.5 mg to 10 mg daily can be found in the Summary of Product Characteristics (SPC) and labels for the drug.[4] The risks described below include the anticipated adverse events relevant for the cardiac population referenced in the contraindications, warnings and precaution sections of the everolimus labels / SPCs and / or observed at incidences ≥ 10% in clinical trials with oral everolimus for different indications. Please refer to the drug SPCs and labels for more detailed information and less frequent adverse events.

- Abdominal pain
- Anemia
- Angioedema (increased risk with concomitant ACE inhibitor use)
- Arterial thrombotic events
- Bleeding and coagulopathy (including Hemolytic Uremic Syndrome [HUS], Thrombotic Thrombocytopenic Purpura [TTP], and thrombotic microangiopathy – increased risk with concomitant cyclosporine use)
- Constipation
- Cough
- Diabetes mellitus
- Diarrhea
- Dyspnea
- Embryo-fetal toxicity
- Erythema
- Erythroderma
- Headache
- Hepatic Artery Thrombosis (HAT)
- Hepatic disorders (including hepatitis and jaundice)
- Hypersensitivity to everolimus active substance, or to other rapamycin derivates
- Hypertension

[4] Certican® UK label Mar 2015, Afinitor® EU authorization SPC Dec 2014, Votubia® EU SPC Sept 2014, Afinitor® US label Jan 2015, and Zortress® US label Sept 2015. Refer to www.MHRA.gov.uk, www.ema.europa.eu, and www.fda.gov for the most recent versions of these SPC/labels.

- Infection (bacterial, fungal, viral or protozoan infections, including infections with opportunistic pathogens). Polyoma virus-associated nephropathy (PVAN) JC virus-associated progressive multiple leukoencephalopathy (PML), fatal infections and sepsis have been reported in patients treated with oral everolimus.
- Kidney arterial and venous thrombosis
- Laboratory test abnormalities (elevations of serum creatinine, proteinuria, hypokalemia; hyperglycemia, dyslipidemia including hypercholesterolemia and hypertriglyceridemia; abnormal liver function tests; decreases in hemoglobin, lymphocytes, neutrophils, and platelets)
- Lymphoma and skin cancer
- Male infertility
- Nausea
- Nephrotoxicity (in combination with cyclosporine)
- Non-infectious pneumonitis (including interstitial lung disease)
- Oral ulcerations
- Pain
- Pancreatitis
- Pericardial effusion
- Peripheral edema
- Pleural effusion
- Pneumonia
- Pyrexia
- Rash
- Renal failure
- Upper respiratory tract infection
- Urinary tract infection
- Venous thromboembolism
- Vomiting
- Wound healing complications (including wound infections and lymphocele)

8.0 CLINICAL INVESTIGATIONS OF THE ABSORB GT1 BVS SYSTEM

Principal safety and effectiveness information for the Absorb GT1 BVS System is derived from the ABSORB III Randomized Clinical Trial (RCT) and is supported by data from the ABSORB Cohort B clinical trial, ABSORB EXTEND clinical trial, ABSORB II RCT, and ABSORB Japan RCT. In this document, these trials are collectively described as the "ABSORB family of clinical trials" or the "ABSORB trials." An overview of each of the ABSORB trials is presented in **Table 8.0-1**, and results are presented in the following subsections.

The clinical investigations outlined in this section were performed on the previous generation Absorb BVS System. The Absorb GT1 BVS has the same mode of expansion, backbone material, scaffold coating, drug density, permanent scaffold markers, and scaffold design as the Absorb BVS. The Absorb GT1 BVS differs from the Absorb BVS only in the scaffold delivery system. The Absorb GT1 scaffold delivery system utilizes the same principle of operation and materials as other Abbott Vascular RX stent / scaffold systems and coronary dilatation catheters.

Based on the identical nature of the Absorb GT1 scaffold to the Absorb scaffold, performance of the Absorb GT1 BVS can be predicted to be similar to the performance of the Absorb BVS. Within this section, the Absorb BVS and Absorb GT1 BVS System are collectively referred to as "Absorb" and the Absorb BVS and Absorb GT1 BVS are synonymously referred to as the "Absorb scaffold."

Table 8.0-1: Overview of the ABSORB Family of Clinical Trials

	ABSORB III RCT	ABSORB Cohort B	ABSORB EXTEND	ABSORB II RCT	ABSORB JAPAN RCT
Study Design	Multicenter Randomized (2:1) Single-blinded Active-Control	Multicenter Non-randomized	Multicenter Non-randomized Continued Assessment	Multicenter Randomized (2:1) Single-blinded Active-Control	Multicenter Randomized (2:1) Single-blinded Active-Control
Numbers of Patients	Total: 2008 primary analysis population Absorb: 1322 XIENCE Control: 686	Total: 101 Group 1: 45 Group 2: 56 All Absorb	Total: 812 All Absorb	Total: 501 Absorb: 335 XIENCE Control: 166	Total: 400 Absorb: 266 XIENCE Control: 134
Numbers of Enrolling Sites	193 sites for the primary analysis population	12 sites	56 sites	46 sites	38 sites
Study Geography	US and AUS	AUS, EU, NZ	AP, EU, CA, BZ	EU, NZ	JN
Vessel Sizes and Lesion Lengths	RVD: ≥ 2.5 and ≤ 3.75 mm Length: ≤ 24 mm	RVD: 3.0 mm Length: ≤ 14 mm	D_{max} ≥ 2.0 mm and D_{max} ≤ 3.3 mm Length: ≤ 28 mm	D_{max} ≥ 2.25 mm and ≤ 3.8 mm Length: ≤ 48 mm	D_{max} ≥ 2.5 mm and ≤ 3.75 mm Length: ≤ 24 mm
# of Lesion Allowed	Up to two *de novo* lesions in different epicardial vessels. No planned overlap allowed.	Up to two *de novo* lesions in different epicardial vessels. No planned overlap allowed.	Up to two *de novo* lesions in different epicardial vessels. Planned overlap allowed.	Up to two *de novo* lesions in different epicardial vessels. Planned overlap allowed.	Up to two *de novo* lesions in different epicardial vessels. No planned overlap allowed.
Scaffold / Stent Sizes	Diameter: 2.5, 3.0, 3.5 mm Length: 8, 12, 18, 28 mm	Diameter: 3.0 mm Length: 18 mm	Diameter: 2.5, 3.0, 3.5 mm Length: 12, 18, 28 mm	Diameter: 2.5, 3.0, 3.5 mm Length: 12, 18, 28 mm	Diameter: 2.5, 3.0, 3.5 mm Length: 8, 12, 18, 28 mm
Primary Endpoint(s)	One-year TLF (non-inferiority)	None	None	• Change in Mean Lumen Diameter from pre- to post-nitrate infusion at 3 years (superiority) • Change in Minimum Lumen Diameter (MLD) from pre- to post-nitrate infusion at 3 years (non-inferiority, reflex to superiority)	One-year TLF (non-inferiority)

	ABSORB III RCT	ABSORB Cohort B	ABSORB EXTEND	ABSORB II RCT	ABSORB JAPAN RCT
Major Secondary Endpoints	• Angina at 1 year • Target Vessel Revascularization at 1 year • All revascularization at 1 year • Diabetic indication at 1 year • Vasoreactivity at 3 years • Change in MLA (Mean Lumen Area) at 3 years	None	None	Change in MLA (Mean Lumen Area) at 3 years	• Late loss at 13 months • Vasoreactivity at 3 years • Change in MLA (Mean Lumen Area) at 3 years
Post Procedure Antiplatelet Therapy	Clopidogrel, prasugrel or ticagrelor 12 months minimum (or ticlopidine per site standard). Aspirin for 5 years.	Clopidogrel 6 months minimum (or ticlopidine per site standard). Aspirin for 5 years.	Clopidogrel, prasugrel or ticagrelor 6 months minimum (or ticlopidine per site standard). Aspirin for 3 years.	Clopidogrel, prasugrel or ticagrelor 6 months minimum (or ticlopidine per site standard). Aspirin for 5 years.	Clopidogrel or prasugrel 12 months minimum (or ticlopidine per site standard). Aspirin indefinitely.
Clinical Follow-ups	30, 180 days, and annually 1 to 5 years	30, 180, 270 days, and annually 1 to 5 years	30, 180 days, and annually 1 to 3 years	30, 180 days, and annually 1 to 5 years	30, 180 days, and annually 1 to 5 years
Angiographic Follow-up	3 years*	Group 1: 180 days, 2 years and 5 years (n = 45) Group 2: 1 year, 3 years, and 5 years (n = 56)	Post-procedure and 2 years*	3 years	13 months, 2 to 4 years*
Angiography, IVUS and / or OCT Follow-up	3 years*	Group 1: 180 days, 2 years and 5 years(n = 45) Group 2: 1 year, 3 years and 5 years (n = 56)	Post-procedure and 2 years*	3 years	2 to 3 years*
PK Study	Yes (12 subjects; US)	None	None	None	None
Status	Completed enrollment. Follow-up through 1 year completed. Follow-up through 5 years ongoing.	Completed enrollment and follow-up.	Completed enrollment. Follow-up through 1 year completed. Follow-up through 3 years ongoing.	Completed enrollment. Follow-up through 1 year completed. Follow-up through 5 years ongoing.	Completed enrollment. Follow-up through 1 year completed. Follow-up through 5 years ongoing.

AP, Asia Pacific; AUS, Australia; BZ, Brazil; CA, Canada; EU, Europe; JN, Japan; NZ, New Zealand; US, the United States of America
* Imaging sub-group. Three-year follow-up imaging data are not available to date..
****** On a subset of patients that were available for follow-up

8.1 ABSORB III Randomized Controlled Trial

The ABSORB III Randomized Controlled Trial (ABSORB III) is the pivotal trial supporting premarket approval of Absorb in the United States. It is a multicenter trial consisting of a lead-in group, a primary analysis group, an imaging cohort, and a pharmacokinetic group.

Enrollment in the ABSORB III primary analysis group is complete, and all subjects have completed their 1-year follow-up. Clinical follow-up through 5 years is ongoing. The ABSORB III primary analysis group was analyzed to evaluate Absorb in the primary endpoint of 1-year Target Lesion Failure (TLF) (composite of cardiac death, myocardial infarction attributable to target vessel, or ischemia-driven target lesion revascularization) compared to XIENCE. XIENCE refers to the following commercially available devices: XIENCE V, XIENCE PRIME®, XIENCE Xpedition®, XIENCE Alpine®, XIENCE Pro (outside the US only) and XIENCE Pro^{X} (outside the US only).

Results from the ABSORB III Pharmacokinetic Sub-Study, conducted in a separate and non-randomized cohort of 12 subjects, are presented in **Section 6.2 – Drug Information, Pharmacokinetics**. Enrollment in the lead-in group is complete and the imaging cohort is currently enrolling. The lead-in group and imaging cohort do not contribute to the determination of the ABSORB III primary endpoint, and therefore results from those groups are not presented.

8.1.1 Primary Objective

To evaluate the safety and effectiveness of the Absorb compared to XIENCE.

8.1.2 Design

The ABSORB III primary analysis group is a prospective, randomized (2:1 Absorb to XIENCE), single-blinded, multicenter clinical trial. This trial includes subjects with evidence of myocardial ischemia with stable angina, unstable angina, post-infarct angina or silent ischemia caused by up to two *de novo* native coronary artery lesions in separate epicardial vessels. Subjects were required to have a lesion length ≤ 24 mm in length and a RVD between 2.5 mm and 3.75 mm. Treatment of one non-target lesion with XIENCE in addition to one target lesion, per assignment, was allowed. The primary analysis group was designed to enroll 2000 subjects at 220 clinical sites in the US and Australia.

Absorb was available in diameters of 2.5, 3.0, and 3.5 mm and lengths of 8, 12, 18, and 28 mm (8 mm length was not available for 3.5 mm). All commercial sizes and diameters of XIENCE were available except for the 2.25 mm diameter and the 33 and 38 mm lengths. Overlap with the same device as assigned was allowed in the case of bailout.

The primary endpoint was TLF at 1 year, with a pre-specified hypothesis test that was designed to show that the TLF rate at 1 year in the Absorb group was non-inferior to that of the XIENCE group. The primary endpoint was evaluated in two analysis populations: (1) the intent-to-treat (ITT) population and (2) the per-treatment-evaluable (PTE) population, defined as subjects with no major protocol deviations treated with only Absorb or XIENCE at the target lesion, with the analysis based on the treatment (Absorb or XIENCE) actually received.

There were three powered secondary endpoints with pre-specified superiority hypothesis tests: Angina at 1 year, All Revascularization at 1 year and Ischemia-Driven Target Vessel Revascularization (ID-TVR) at 1 year. If the non-inferiority test of the primary endpoint TLF at

1 year was passed, superiority tests of the three secondary endpoints were to be performed.

A total of 1322 subjects were randomized to the Absorb group and 686 subjects to the XIENCE group. Clinical follow-up was planned for 30 days, 180 days, 1, 2, 3, 4, and 5 years. Following the index procedure, subjects were to be maintained on a P_2Y_{12} platelet receptor inhibitor for at least 1 year and aspirin for at least 5 years.

8.1.3 Demographics

Patients were well-matched for baseline demographics and clinical characteristics with no statistical differences identified between the study groups. Risk factors having a high prevalence in the Absorb and XIENCE arms included hypertension requiring medication (81.0% [1071/1322] and 80.6% [553/686], respectively) and dyslipidemia requiring medication (76.3% [1009/1322] and 77.7% [533/686], respectively). All diabetes mellitus comprised 31.5% (416/1320) and 32.7% (224/686), respectively, and insulin-required diabetes mellitus subjects comprised 10.5% (138/1320) and 11.2% (77/686), respectively. For cardiac status, the most common presentation in the Absorb and XIENCE arms was stable angina (57.3% [757/1321] and 60.8% [417/686], respectively). Subjects with a single diseased artery were most prevalent in the ABSORB III population (69.5% [919/1322] and 67.2% [461/686], respectively).

8.1.4 Baseline Lesion Characteristics

The mean reference vessel diameter was 2.67 ± 0.45 mm and 2.65 ± 0.46 mm in the Absorb and XIENCE groups, respectively. The mean lesion length was 12.6 ± 5.4 mm and 13.1 ± 5.8 mm in the Absorb and XIENCE groups, respectively. The mean diameter stenosis was 65.3% and 65.9% in the Absorb and XIENCE groups, respectively.

8.1.5 Results

The primary endpoint was met. For the ITT population, the TLF rate at 1 year was 7.8% (102/1313) in the Absorb arm and 6.1% (41/677) in the XIENCE arm. The difference between the two treatment arms was 1.71% with the upper bound of the 95% confidence interval being 3.93%, which was less than the pre-specified non-inferiority margin of 4.5%, p-value 0.0070 for non-inferiority (**Table 8.1.5-1**).

Table 8.1.5-1: Primary Endpoint Analysis – Per-Subject Analysis (Primary Analysis Group, ITT, Per-Protocol MI Definition)

	Absorb (N = 1322)	XIENCE (N = 686)	Difference (95% CI [1])	Non-Inferiority p-value[2]
1-Year TLF (Cardiac Death Target Vessel MI, ID-TLR[3])	7.8% (102/1313)	6.1% (41/677)	1.71% (-0.74%, 3.93%)	0.0070

[1] Two-sided 95% confidence interval by Farrington-Manning method

[2] One-sided p-value by using Farrington-Manning non-inferiority test statistic with non-inferiority margin of 4.5%, to be compared with a one-sided significance level of 0.025

[3] Ischemia-driven target lesion revascularization

Note: 1-year timeframe includes a window of ± 28 days

Note: N is the total number of subjects

Note: MI is per protocol definition: Peri-procedural MI (≤ 48 hrs post-PCI) is defined as CK-MB > 5X ULN. Spontaneous MI defined as CK-MB or Troponin > ULN plus evidence of ischemia. Q-wave MI defined as development of new, pathological Q waves in two contiguous ECG leads.

For the PTE population, the TLF rate at 1 year was 7.8% (91/1174) in the Absorb arm and 5.7%

(38/670) in the XIENCE arm. The difference between the two treatment arms was 2.08% with the upper bound of the 95% confidence interval being 4.35%, which was less than the non-inferiority margin of 4.5%. The Absorb arm was non-inferior to XIENCE regarding the primary endpoint TLF rate at 1 year in the PTE population (p = 0.0183).

The analyses of the three secondary endpoints [Angina, All Revascularization, and ID-TVR at 1 year in the ITT population] are shown in **Table 8.1.5-2**. Superiority was not met for any of the secondary endpoints with pre-specified hypothesis tests. The Angina rate at 1 year was 18.3% (238/1303) in the Absorb arm and 18.4% (125/678) in the XIENCE arm (p = 0.9256). The All Revascularization rate at 1 year was 9.1% (120/1313) in the Absorb arm and 8.1% (55/677) in the XIENCE arm. The ID-TVR rate at 1 year was 5.0% (66/1313) in the Absorb arm and 3.7% (25/677) in the XIENCE arm.

Table 8.1.5-2: Powered Secondary Endpoint Analysis – Per-Subject Analysis (Primary Analysis Group, ITT Population)

	Absorb (N = 1322)	XIENCE (N = 686)	Difference [95% CL][4]	Superiority p-value[5]
Powered Secondary Endpoint				
1-Year Angina[1]	18.3% (238/1303)	18.4% (125/678)	-0.17% [-3.77%, 3.42%]	0.9256
1-Year All Revascularization[2]	9.1% (120/1313)	8.1% (55/677)	1.02% [-1.57%, 3.60%]	N/A[6]
1-Year ID-TVR[3]	5.0% (66/1313)	3.7% (25/677)	1.33% [-0.51%, 3.18%]	N/A[6]

[1] First reported angina post-discharge (excluding angina following the index procedure through discharge, not to exceed a period of 7 days).

[2] Includes TLR, TVR non-TLR, and non TVR

[3] Ischemia-driven target vessel revascularization

[4] Without multiplicity adjustment. For Angina at 1 year, Pearson's Chi-square two-sided 95% confidence interval. For All Revascularization and ID-TVR at 1 year, exact two-sided 95% confidence interval.

[5] Compared with a two-sided significance level of 0.05. For Angina at 1 year, two-sided p-value using Pearson's Chi-square test statistic.

[6] According to the pre-specified testing sequence, further testing stopped after the superiority hypothesis test of 1-year angina was not passed. The superiority hypothesis tests of 1-year all revascularization and 1-year ID-TVR were not passed.

Note: 1-year timeframe includes a window of ± 28 days

Note: N is the total number of subjects

The safety and effectiveness results for ABSORB III primary analysis group are presented in **Table 8.1.5-3**.

Table 8.1.5-3: ABSORB III Clinical Results (Primary Analysis Group - ITT Population)

	Absorb (N = 1322)	XIENCE (N = 686)
IN-HOSPITAL OUTCOMES		
TLF (COMPOSITE OF SAFETY AND EFFECTIVENESS)	3.3% (43/1319)	3.1% (21/686)
EFFECTIVENESS		
Ischemia-Driven TLR	0.3% (4/1319)	0.6% (4/686)
TLR, CABG	0.0% (0/1319)	0.1% (1/686)
TLR, PCI	0.3% (4/1319)	0.6% (4/686)
Ischemia-Driven TVR	0.4% (5/1319)	0.6% (4/686)
SAFETY		
All Death	0.1% (1/1319)	0.0% (0/686)
Cardiac Death	0.1% (1/1319)	0.0% (0/686)
Vascular Death	0.0% (0/1319)	0.0% (0/686)
Non-cardiovascular Death	0.0% (0/1319)	0.0% (0/686)
All MI	3.0% (40/1319)	3.1% (21/686)
TV-MI	3.0% (39/1319)	2.9% (20/686)
QMI	0.1% (1/1319)	0.3% (2/686)
NQMI	2.9% (38/1319)	2.6% (18/686)
NTV-MI	0.1% (1/1319)	0.1% (1/686)
QMI	0.0% (0/1319)	0.0% (0/686)
NQMI	0.1% (1/1319)	0.1% (1/686)
Cardiac Death or MI	3.1% (41/1319)	3.1% (21/686)
30-DAY OUTCOMES		
MACE	4.9% (65/1317)	3.6% (25/686)

Note: 1-year timeframe includes a window of ± 28 days

Note: N is the total number of subjects

Note: MI is per protocol definition

Note: Major Adverse Cardiac Events (MACE) is the composite of cardiac death, all MI and ID-TLR

Table 8.1.5-3: ABSORB III Clinical Results (Primary Analysis Group - ITT Population) (continued)

	Absorb (N = 1322)	XIENCE (N = 686)
1-YEAR OUTCOMES		
TLF (COMPOSITE OF SAFETY AND EFFECTIVENESS)	7.8% (102/1313)	6.1% (41/677)
EFFECTIVENESS		
Ischemia-Driven TLR	3.0% (40/1313)	2.5% (17/677)
TLR, CABG	0.2% (3/1313)	0.4% (3/677)
TLR, PCI	2.8% (37/1313)	2.2% (15/677)
Ischemia-Driven TVR	5.0% (66/1313)	3.7% (25/677)
SAFETY		
All Death	1.1% (15/1313)	0.4% (3/677)
Cardiac Death	0.6% (8/1313)	0.1% (1/677)
Vascular Death	0.2% (2/1313)	0.0% (0/677)
Non-cardiovascular Death	0.4% (5/1313)	0.3% (2/677)
All MI	6.9% (90/1313)	5.6% (38/677)
TV-MI	6.0% (79/1313)	4.6% (31/677)
QMI	0.7% (9/1313)	0.3% (2/677)
NQMI	5.3% (70/1313)	4.3% (29/677)
NTV-MI	0.8% (11/1313)	1.2% (8/677)
QMI	0.1% (1/1313)	0.1% (1/677)
NQMI	0.8% (10/1313)	1.0% (7/677)
Cardiac Death or MI	7.5% (98/1313)	5.8% (39/677)
Cumulative ARC-defined Definite + Probable Stent / Scaffold Thrombosis (0 – 393 days)	1.54% (20/1301)	0.74% (5/675)
Acute (≤ 1 day)	0.15% (2/1320)	0.58% (4/686)
Sub-Acute (> 1 – 30 days)	0.91% (12/1315)	0.15% (1/686)
Late (31 – 365 days)	0.46% (6/1299)	0.00% (0/675)

Note: 1-year timeframe includes a window of ± 28 days

Note: N is the total number of subjects

Note: MI is per protocol definition:

8.1.6 Implantation of Absorb in Small Coronary Arteries (Post-Hoc Analysis)

In the ABSORB III trial, the target vessel size inclusion criterion was a reference vessel diameter (RVD) determined following pre-dilatation of ≥ 2.5 mm to ≤ 3.75 mm by visual estimation by the operator. In the overall ABSORB III population, 19% (375/1998) of subjects had an RVD < 2.25 mm as assessed by quantitative coronary angiography (QCA), and 81% (1623/1998) had a RVD ≥ 2.25 mm (by QCA).

Table 8.1.6-1 shows the results of a post hoc analysis of the key clinical results stratified by the QCA-assessed RVD subgroups of ≥ 2.25 mm (by QCA) and < 2.25 mm (by QCA). The 2.25 mm QCA threshold was chosen because visual estimates of coronary artery dimensions typically overestimate true vessel diameters as measured by QCA by approximately 0.25 mm.

In the RVD < 2.25 mm (by QCA) subgroup, the observed TLF rate at 1 year was 12.9% for Absorb and 8.3% for XIENCE. The difference in the TLF rate was primarily driven by a higher observed rate of target vessel MI in the Absorb group. In this small vessel subgroup, the observed definite plus probable scaffold/stent thrombosis rate at 1 year was 4.6% in Absorb vs. 1.5% in XIENCE.

In the RVD ≥ 2.25 mm (by QCA) subgroup, the observed TLF rate at 1 year was 6.7% for Absorb vs. 5.5% for XIENCE. In this subgroup, the observed definite plus probable scaffold/stent thrombosis rate at 1 year was 0.9% in Absorb vs. 0.6% in XIENCE.

Table 8.1.6-1: Clinical Results for ABSORB III Stratified by Pre-Procedure RVD Size - QCA-Assessed RVD ≥ 2.25 mm and RVD < 2.25 mm (ITT population) – 1-Year Results

	Subjects with QCA-Assessed RVD ≥ 2.25 mm		Subjects with QCA-Assessed RVD < 2.25 mm*	
	Absorb (N = 1074)	**XIENCE (N = 549)**	**Absorb (N = 242)**	**XIENCE (N = 133)**
Percentage of Subjects	81.6% (1074/1316)	80.5% (549/682)	18.4% (242/1316)	19.5% (133/682)
Pre-procedure Median RVD by QCA (mm) Range (min, max)	2.75 (2.25, 4.04)	2.72 (2.26, 4.48)	2.08 (1.39, 3.54)	2.10 (1.46, 3.49)
TLF	6.7% (71/1067)	5.5% (30/542)	12.9% (31/241)	8.3% (11/133)
Cardiac Death	0.6% (6/1067)	0.2% (1/542)	0.8% (2/241)	0.0% (0/133)
TV- MI	5.2% (55/1067)	4.6% (25/542)	10.0% (24/241)	4.5% (6/133)
ID-TLR	2.2% (24/1067)	1.5% (8/542)	6.6% (16/241)	6.8% (9/133)
Stent / Scaffold Thrombosis (Def / Prob)	0.9% (9/1058)	0.6% (3/540)	4.6% (11/238)	1.5% (2/133)

Note: N is the total number of subjects

Note: MI is per protocol definition

* ITT subjects with at least one target lesion pre-procedure RVD < 2.25 mm (core-lab measurement) are included in the analysis.

8.2 Analysis of Diabetic Subjects in ABSORB III

Patients with diabetes mellitus are at increased risk for cardiovascular morbidity and mortality and are associated with worse clinical outcomes when undergoing PCI compared with non-diabetics. In the ABSORB III trial, diabetic patients represented 31.9% (640/2006) of the overall trial population. The 1-year rates of TLF, non-hierarchically assessed cardiac death, TV-MI and ID-TLR, and stent / scaffold thrombosis for the overall population, the all diabetes mellitus (all DM) subgroup, and the all non-DM subgroup are shown in **Table 8.2-1**.

For the all DM subgroup, the observed clinical event rates in both the Absorb and XIENCE arms were higher than in the overall ABSORB III ITT population and the non-DM subgroup for most key outcome measures. For most endpoints, the event rate difference between ABSORB and XIENCE in the overall ABSORB III ITT population was similar to the event rate difference between treatment groups in the all DM subgroup and in the all non-DM subgroup.

Table 8.2-1 Subgroup Information and 1-Year Clinical Outcomes Stratified by Diabetic Status – Per-Subject Analysis (Primary Analysis Group, Intent-to-Treat Population, Per Protocol MI Definition)

	Overall ITT Population		All DM		All Non-DM	
	Absorb (N = 1322)	**XIENCE (N =686)**	**Absorb (N = 416)**	**XIENCE (N = 224)**	**Absorb (N = 904)**	**XIENCE (N = 462)**
TLF	7.8% (102/1313)	6.1% (41/677)	10.7% (44/411)	9.1% (20/220)	6.3% (57/900)	4.6% (21/457)
Cardiac Death	0.6% (8/1313)	0.1% (1/677)	0.5% (2/411)	0.0% (0/220)	0.7% (6/900)	0.2% (1/457)
TV- MI	6.0% (79/1313)	4.6% (31/677)	9.0% (37/411)	7.3% (16/220)	4.6% (41/900)	3.3% (15/457)
ID-TLR	3.0% (40/1313)	2.5% (17/677)	5.6% (23/411)	3.6% (8/220)	1.8% (16/900)	2.0% (9/457)
Stent / Scaffold Thrombosis (Def / Prob)	1.54% (20/1301)	0.74% (5/675)	3.2% (13/405)	1.4% (3/219)	0.8% (7/894)	0.4% (2/456)

Note: N is the total number of subjects
Note: MI is per protocol definition

The ABSORB III trial showed a more pronounced risk of TLF (primarily driven by an observed increased rate of target vessel MI) and definite plus probable scaffold/stent thrombosis at 1 year in diabetic patients with an RVD < 2.25 mm (by QCA) treated with Absorb compared with treatment with XIENCE. These data must be viewed with caution given the small sample size of this analysis.

8.3 Analysis of Gender in ABSORB III

A subgroup analysis by gender was conducted in the ABSORB III trial, in which female patients represented 29.5% (593/2008) of the overall trial population. The 1-year rates of TLF, non-hierarchically assessed cardiac death, TV-MI and ID-TLR, and stent / scaffold thrombosis for the overall population, female subgroup, and male subgroup are shown in **Table 8.3-1**. Compared to the overall population, females had slightly higher TLF rates for both treatment groups, which was mainly driven by numerically higher rates of TV-MI. The observed difference in scaffold thrombosis rates between the two device arms was numerically lower for females compared to males, primarily due to a disproportionally low stent thrombosis rate in male subjects treated with XIENCE.

Table 8.3-1 Subgroup Information and 1-Year Clinical Outcomes Stratified by Gender – Per-Subject Analysis (Primary Analysis Group, Intent-to-Treat Population, Per Protocol MI Definition)

	Overall ITT Population		Female		Male	
	Absorb (N=1322)	**XIENCE (N=686)**	**Absorb (N=388)**	**XIENCE (N=205)**	**Absorb (N=934)**	**XIENCE (N=481)**
TLF	7.8% (102/1313)	6.1% (41/677)	8.5% (33/386)	7.4% (15/203)	7.4% (69/927)	5.5% (26/474)
Cardiac Death	0.6% (8/1313)	0.1% (1/677)	0.3% (1/386)	0.0% (0/203)	0.8% (7/927)	0.2% (1/474)
TV-MI	6.0% (79/1313)	4.6% (31/677)	7.3% (28/386)	5.4% (11/203)	5.5% (51/927)	4.2% (20/474)
ID-TLR	3.0% (40/1313)	2.5% (17/677)	3.4% (13/386)	3.9% (8/203)	2.9% (27/927)	1.9% (9/474)
Stent / Scaffold Thrombosis (Def / Prob)	1.54% (20/1301)	0.74% (5/675)	1.56% (6/384)	1.97% (4/203)	1.53% (14/917)	0.21% (1/472)

Note: N is the total number of subjects
Note: MI is per protocol definition

8.4 ABSORB Cohort B

The ABSORB Cohort B trial was designed to assess the safety and performance of Absorb in the treatment of patients with *de novo* native coronary artery lesions.

8.4.1 Primary Objective

To assess the safety and performance of the Absorb in the treatment of subjects with a maximum of two *de novo* native coronary artery lesions located in two different major epicardial vessels.

8.4.2 Design

ABSORB Cohort B was a prospective, single-arm, open-label, multicenter study of 101 subjects enrolled at 12 clinical sites located in Europe, Australia, and New Zealand.

Subjects with up to two *de novo* native coronary artery lesions in separate epicardial vessels with visually estimated nominal vessel diameters of 3.0 mm and lesion(s) length ≤ 14 mm received a single 3.0 x 18 mm Absorb per lesion treated. There was no pre-specified primary endpoint.

Subjects were evaluated at 30 days, 180 days, 270 days, 12 months, 18 months (subset), 2 years, 3 years, 4 years and 5 years. Subjects in the first group (Group B1) had invasive imaging with qualitative coronary angiography, IVUS, IVUS-VH, and OCT at 6 months, 2 years

and 5 years while the second group (Group B2) underwent invasive imaging at 12 months, 3 years and 5 years. Vasomotor function test using nitroglycerin was done at 2-, 3- and 5-year follow-up

Following the index procedure, all subjects were to be maintained on 75 mg of clopidogrel daily for a minimum of 6 months, and aspirin (≥ 75 mg) daily throughout the length of the clinical investigation (5 years following the index procedure).

8.4.3 Demographics

The mean age of the ITT population was 62.3 years. 72.3% of subjects were men, 17.0% were current smokers, 16.8% were diabetics, 66.0% had hypertension, 85.1% had hypercholesterolemia, 25.0% had prior MI, 21.8% had a prior cardiac intervention, 14.9% had unstable angina at the time of the index procedure, and 20.8% had multi-vessel disease.

8.4.4 Clinical Results for ABSORB Cohort B

Table 8.4.4-1 shows clinical outcomes through 5 years for all subjects. The hierarchical major cardiac adverse event (MACE, a composite of cardiac death, MI, ischemia-driven TLR) rate was 6.9% (7/101) at 1 year and 11.0% (11/100) at 5 years. The overall MI rate at 5 years was 3.0% (3/100), all due to non-Q wave MIs, all occurring within 6 months of the index procedure. The overall ID-TLR rate at 5 years was 8.0% (8/100). Between 4 and 5 years there was only one additional ID-TLR event. There were no cardiac deaths or scaffold thrombosis events during the 5-year follow-up period.

Table 8.4.4-1: Key Clinical Outcomes of ABSORB Cohort B (ITT Population) through 5 Years

	30 days (N = 101)	6 months (N = 101)	1 year (N = 101)	2 year (N = 100*)	3 year (N = 100*)	4 year (N = 100*)	5 year (N = 100*)
COMPOSITE EFFECTIVENESS AND SAFETY							
MACE	2.0% (2/101)	5.0% (5/101)	6.9% (7/101)	9.0% (9/100)	10.0% (10/100)	10.0 (10/100)	11.0 (11/100)
EFFECTIVENESS							
Ischemia-Driven TLR	0.0% (0/101)	2.0% (2/101)	4.0% (4/101)	6.0% (6/100)	7.0% (7/100)	7.0% (7/100)	8.0% (8/100)
TLR, CABG	0.0% (0/101)	0.0% (0/101)	0.0% (0/101)	0.0% (0/100)	0.0% (0/100)	0.0% (0/100)	0.0% (0/100)
TLR, PCI	0.0% (0/101)	2.0% (2/101)	4.0% (4/101)	6.0% (6/100)	7.0% (7/100)	7.0% (7/100)	8.0% (8/100)
Ischemia-Driven TVR	0.0% (0/101)	2.0% (2/101)	4.0% (4/101)	8.0% (8/100)	10.0% (10/100)	10.0% (10/100)	11.0% (11/100)
SAFETY							
Cardiac Death	0.0% (0/101)	0.0% (0/101)	0.0% (0/101)	0.0% (0/100)	0.0% (0/100)	0.0% (0/100)	0.0% (0/100)
All MI	2.0% (2/101)	3.0% (3/101)	3.0% (3/101)	3.0% (3/100)	3.0% (3/100)	3.0% (3/100)	3.0% (3/100)
QMI	0.0% (0/101)	0.0% (0/101)	0.0% (0/101)	0.0% (0/100)	0.0% (0/100)	0.0% (0/100)	0.0% (0/100)
NQMI	2.0% (2/101)	3.0% (3/101)	3.0% (3/101)	3.0% (3/100)	3.0% (3/100)	3.0% (3/100)	3.0% (3/100)
Scaffold Thrombosis	0.0% (0/101)	0.0% (0/101)	0.0% (0/101)	0.0% (0/95)	0.0% (0/95)	0.0% (0/95)	0.0% (0/95)

*One subject lost to follow-up at 2-year follow-up.

Note: MACE: Cardiac death, MI, ischemia-driven TLR

Note: MI per protocol definition: : Q-wave MI defined as new pathological Q wave on the ECG; Non-Q wave MI defined as elevation of CK level to ≥ 2 times ULN with elevated CK-MB in the absence of pathological Q-waves.

8.4.5 Intravascular Ultrasound (IVUS) Outcomes

Paired IVUS data at post-procedure, 6-month, 2-year, and 5-year follow-up for 21 lesions from Group 1 subjects are shown in **Table 8.4.5-1**, and at post-procedure, 1, 3, and 5 years for 30 lesions from Group 2 subjects are shown in **Table 8.4.5-2**. Over the course of 5 years follow-up there were variable changes in vessel area, scaffold area, lumen area, and plaque area over time between Groups 1 and 2.

Table 8.4.5-1: Paired IVUS Results at Post-Procedure, 6 Month, 2 Year, and 5 Year (Group 1, ITT Population)

	Post-procedure (L = 21)	6-Month (L = 21)	2-Year (L = 21)	5-Year (L = 21)
Average Vessel Area (mm^2)	14.56 ± 3.82	14.92 ± 3.78	15.88 ± 4.02	15.28 ± 4.53
Average Scaffold Area (mm^2)	6.75 ± 1.19	6.63 ± 1.16	7.52 ± 1.79	N/A
Average Lumen Area (mm^2)	6.75 ± 1.19	6.59 ± 1.20	7.24 ± 1.91	7.46 ± 2.45
Average Plaque Area (mm^2)	7.81 ± 2.98	8.33 ± 2.88	8.64 ± 2.85	7.75 ± 2.62

Note: Data are presented as Mean ± SD. L is the number of lesions with a paired measurement for the specific variable.
Note: Follow-up windows were: 6 months ± 14 days; 2 year ± 2 months; 5 year ± 28 days

Table 8.4.5-2: Paired IVUS Results at Post-Procedure, 1, 3, and 5 Year (Group 2, ITT Population)

	Post-procedure (L = 30)	1-Year (L = 30)	3-Year (L = 30)	5-Year (L = 28)
Average Vessel Area (mm^2)	13.61 ± 2.40	14.15 ± 2.61	14.25 ± 2.57	13.23 ± 2.70
Average Scaffold Area (mm^2)	6.31 ± 0.86	6.37 ± 0.97	7.05 ± 1.39	N/A
Average Lumen Area (mm^2)	6.31 ± 0.86	6.31 ± 1.01	6.70 ± 1.48	6.48 ± 1.50
Average Plaque Area (mm^2)	7.30 ± 1.85	7.84 ± 1.92	7.55 ± 1.58	6.79 ± 1.90

Note: Data are presented as Mean ± SD. L is the number of lesions with a paired measurement for the specific variable.
Note: Follow-up windows were: 1 year ± 28 days; 3 year ± 28 days; 5 year ± 28 days

8.4.6 Optical Coherence Tomography (OCT) Analysis

Serial OCT analysis at baseline, 6 months, 2 and 5 years in 13 lesions from Group 1 are shown in **Table 8.4.6-1**, and at baseline, 1, 3, and 5 years for 17 lesions in Group 2 are shown in **Table 8.4.6-2**. In both groups, there was an increase in neointimal area accompanied by an increase in scaffold area, resulting in a stable lumen diameter. Strut coverage by neointima was nearly complete at 6 months and 1 year for Groups 1 and 2, respectively.

Table 8.4.6-1: Paired OCT Results at Post-Procedure, 6 Months, 2 and 5 Years (Group 1, ITT Population)

Group 1 OCT (paired)	Post-procedure (L = 13)	6-Month (L = 13)	2-Year (L = 13)	5-Year (L = 13)
Lumen Area (mm^2)	7.28 ± 1.24	6.04 ± 1.20	6.17 ± 1.44	6.38 ± 1.47
Scaffold Area (mm^2)	7.55 ± 1.17	7.79 ± 1.20	8.54 ± 1.71	N/A
Mean Neointimal Area (mm^2)	N/A	1.53 ± 0.36	2.22 ± 0.47	N/A
% of Uncovered Struts	96.97 ± 6.83	1.80 ± 1.63	1.40 ± 2.37	N/A

Note: Data are presented as Mean ± SD or %. L is the number of lesions with a paired measurement for the specific variable.

Note: Follow-up windows were: 6 months ± 14 days; 2 year ± 2 months; 5 year ± 28 days

Table 8.4.6-2: Paired OCT Results at Post-Procedure, 1, 3 and 5 Years (Group 2, ITT Population)

Group 2 OCT (paired)	Post-procedure (L = 17)	1-Year (L = 17)	3-Year (L = 17)	5-Year (L = 17)
Lumen Area (mm^2)	7.54 ± 0.88	5.94 ± 1.29	6.01 ± 1.49	5.93 ± 1.53
Scaffold Area (mm^2)	7.61 ± 0.83	7.45 ± 0.84	8.61 ± 1.98	N/A
Mean Neointimal Area (mm^2)	N/A	1.42 ± 0.71	2.39 ± 0.68	N/A
% of Uncovered Struts	97.65 ± 5.56	3.03 ± 2.81	1.70 ± 1.59	N/A

Note: Data are presented as Mean ± SD. L is the number of lesions with a paired measurement for the specific variable.

Note: Follow-up windows were: 1 year ± 28 days; 3 year ± 28 days; 5 year ± 28 days.

Although serial IVUS and OCT studies demonstrated late lumen enlargement and an increase in BVS area at 2 years (Group 1) and at 3 years (Group 2), there were some inconsistencies in measurement trends between the imaging modalities (IVUS vs. OCT) and between Groups 1 and 2 at 5 years.

8.4.7 Vasomotor Function Outcomes

At the 3-year follow-up, 27 patients from Group 2 underwent vasomotor function testing with nitrate administration (**Table 8.4.7-1**). The in-scaffold mean lumen diameter increased from 2.45 ± 0.37 mm (pre-nitrate) to 2.50 ± 0.39 mm (post-nitrate administration). At the 5-year follow-up, a total of 57 patients from the full Cohort B (23 from Group 1 and 34 from Group 2) completed vasomotor function tests with nitrate administration (**Table 8.4.7-1**). The in-scaffold mean lumen diameter increased from 2.48 ± 0.38 mm (pre-nitrate) to 2.56 ± 0.37 mm (post-nitrate administration). These data indicate that the Absorb-treated segment can vasodilate in response to physiologic stimuli.

Table 8.4.7-1: Vasomotor Function by Nitroglycerine Injection at 2, 3 and 5 Years (PTE Population[1])

	Mean Luminal Diameter (mm)					
	Group B1 2 Y (L = 33)		Group B2 3 Y (L = 47)		Full Cohort 5 Y (L = 57)	
	Pre-NTG	Post-NTG	Pre-NTG	Post-NTG	Pre-NTG	Post-NTG
Proximal	2.48 ± 0.46	2.65 ± 0.42	2.51 ± 0.39	2.63 ± 0.48	2.53 ± 0.44	2.64 ± 0.43
Distal	2.26 ± 0.41	2.40 ± 0.40	2.28 ± 0.33	2.41 ± 0.35	2.26 ± 0.41	2.39 ± 0.39
Scaffold	2.44 ± 0.37	2.47 ± 0.35	2.45 ± 0.37	2.50 ± 0.39	2.48 ± 0.38	2.56 ± 0.37

[1] Per treatment Eligible Population

Note: Data are presented as Mean ± SD. L is the number of lesions with a paired measurement for the specific variable.

8.5 ABSORB EXTEND

The ABSORB EXTEND study is a global continued access registry designed to expand treatment with Absorb in a broader patient population including subjects with more complex lesions.

8.5.1 Primary Objective

To continue the assessment of the safety and performance of Absorb in a population of up to 1000 subjects with a maximum of two *de novo* native coronary artery lesions each located in different epicardial vessels.

8.5.2 Design

ABSORB EXTEND is a prospective, single-arm, open-label clinical study that enrolled 812 subjects at up to 58 global sites. Subjects with a maximum of two *de novo* native coronary artery lesions, each located in different epicardial vessels, a target lesion length ≤ 28 mm and reference vessel sizes that were suitable for treatment with Absorb were registered.

Clinical follow-up is scheduled at 30 days, 180 days, and at 1, 2, and 3 years.

Following the index procedure, all subjects were to be maintained on an IFU-specified dose of ADP antagonist for a minimum of 6 months, and aspirin (≥ 75 mg) daily throughout the length of the clinical investigation (3 years following the index procedure).

8.5.3 Demographics

The mean age was 61.1 ± 10.8 years, 74.3% (603/812) of the subjects were male, 23.2% (188/812) were tobacco users, 69.3% (563/812) had hypertension requiring medication, 67.7% (550/812) had dyslipidemia requiring medication, 28.5% (230/807) had a prior MI, and 26.5% (215/812) were diabetic.

8.5.4 Clinical Results for ABSORB EXTEND

Data out to 3 years for ABSORB EXTEND are presented in **Table 8.5.4-1**. The composite endpoint of TLF is presented using the protocol World Health Organization (WHO) definition for MI and is based on hierarchical counts. The TLF rate for ABSORB EXTEND was 5.1% (41/811) at 1 year, 6.9% (56/807) at 2 years and 9.0% (55/613) at 3 years. Note that not all subjects have reached 3-year follow-up

Table 8.5.4-1: Key Clinical Outcomes of ABSORB EXTEND (ITT Population) through 3 Years

	ABSORB EXTEND (N = 812)		
	1-Year	**2-Year**	**3-Year**
TLF	5.1% (41/811)	6.9% (56/807)	9.0% (55/613)
Cardiac Death	0.7% (6/811)	1.1% (9/807)	1.5% (9/613)
TV-MI	3.3% (27/811)	4.2% (34/807)	5.2% (32/613)
ID-TLR	2.3% (19/811)	4.1% (33/807)	4.9% (30/613)
Definite/Probable Stent/Scaffold Thrombosis	1.0% (8/808)	1.5% (12/799)	2.0% (12/603)

Note: 1-year timeframe includes a window of ± 28 days

Note: N is the total number of subjects

Note: MI per WHO definition: Q wave MI defined as new pathological Q wave on the ECG; Non-Q wave MI defined as elevation of CK level to ≥ 2 times ULN with elevated CK-MB in the absence of new pathological Q-waves.

8.6 ABSORB II Randomized Clinical Trial

The ABSORB II Randomized Clinical Trial RCT (ABSORB II) is the first randomized controlled trial comparing Absorb to XIENCE.

8.6.1 Primary Objective

ABSORB II is a randomized clinical trial designed to compare the safety, effectiveness and performance of Absorb compared to the XIENCE in the treatment of *de novo* native coronary artery lesions.

8.6.2 Design

ABSORB II is a prospective, randomized (2:1 Absorb to XIENCE), active-controlled, single-blinded, multicenter (Europe and New Zealand) clinical trial registering 501 subjects. Target lesions were up to two *de novo* native coronary artery lesions, each located in different major epicardial vessels, all with an angiographic luminal diameter between 2.25 mm and 3.8 mm as estimated by on-line quantitative coronary angiography (QCA), and a lesion length of ≤ 48 mm. Planned overlapping of study devices was allowed for treatment of long lesions.

The co-primary endpoints are vasomotor function assessed by the change in mean lumen diameter between pre- and post-nitrate infusion at 3 years (superiority) and the minimum lumen diameter change from post-procedure to 3 years (non-inferiority, reflex to superiority).

Clinical follow-up is scheduled at 30 days, 180 days, 1 year, and annually through 5 years.

Following the index procedure, all subjects were to be maintained on an IFU-specified dose of ADP antagonist for a minimum of 6 months, and aspirin (≥ 75 mg) daily throughout the length of the clinical investigation (5 years following the index procedure).

8.6.3 Demographics

The mean age was 61.5 ± 10.0 and 60.9 ± 10.0 years in the Absorb and XIENCE arms, respectively. The patient population was predominantly male (75.5% in the Absorb arm and 79.5% in the XIENCE arm). There was a high prevalence of hypertension (69.0% vs. 71.7%) and dyslipidemia (75.2% vs. 80.1%) for Absorb and XIENCE arms, respectively. Over 20% of the study population was diabetic (23.9% vs. 24.1% for Absorb and XIENCE arms, respectively).

8.6.4 Results

Safety and effectiveness results in the ITT population out to 2 years are presented in **Table 8.6.4-1**. The TLF rate at 1 year was 4.8% (16/331) in the Absorb arm and 3.0% (5/165) in the XIENCE arm; and the definite / probable stent / scaffold thrombosis rate at 1 year was 0.9% (3/329) in the Absorb arm and 0.0% (0/164) in the XIENCE arm. At 2 years, the TLF rate was 7.0% (23/328) in the Absorb arm and 3.0% (5/164) in the XIENCE arm, and the stent/scaffold thrombosis rates were 1.5% (5/325) and 0.0% (0/163) in the Absorb and XIENCE groups, respectively.

Table 8.6.4-1: ABSORB II Clinical Results (ITT population) through 2 Years

	ABSORB II (N=501)			
	1-Year		2-Year	
	Absorb N = 335	XIENCE N = 166	Absorb N = 335	XIENCE N = 166
TLF	4.8% (16/331)	3.0% (5/165)	7.0% (23/328)	3.0% (5/164)
Cardiac Death	0.0% (0/331)	0.0% (0/165)	0.6% (2/328)	0.0% (0/164)
TV-MI	4.2% (14/331)	1.2% (2/165)	5.2% (17/328)	1.2% (2/164)
ID-TLR	1.2% (4/331)	1.8% (3/165)	2.7% (9/328)	1.8% (3/164)
Definite/Probable Stent/Scaffold Thrombosis	0.9% (3/329)	0.0% (0/164)	1.5% (5/325)	0.0% (0/163)

Note: 1-year timeframe includes a window of ± 28 days

Note: N is the total number of subjects

Note: MI is per protocol definition: Q wave MI defined as new pathological Q wave on the ECG; Non-Q wave MI defined as elevation of CK level to ≥ 2 times ULN with elevated CK-MB in the absence of new pathological Q-waves.

8.7 ABSORB Japan Randomized Controlled Trial

The ABSORB Japan Randomized Controlled Trial (ABSORB Japan) is the pivotal trial to support the approval of Absorb in Japan.

8.7.1 Primary Objective

The objective of ABSORB Japan is to compare the safety and effectiveness of Absorb in Japanese subjects with ischemic heart disease caused by *de novo* native coronary artery lesions compared to the XIENCE stent.

8.7.2 Design

ABSORB Japan is a prospective, randomized (2:1 Absorb to XIENCE), active-controlled, single-blinded, multicenter clinical trial in Japan registering 400 subjects. Treatment of up to two *de novo* native coronary artery lesions, each lesion located in a different major epicardial vessel, was allowed. The maximum target vessel diameter (D_{max}), by quantitative methods, was required to be ≥ 2.5 mm and ≤ 3.75 mm, and the lesion length was to be ≤ 24 mm (by visual estimation). Treatment of one non-target lesion with XIENCE was allowed.

Absorb was available in diameters of 2.5, 3.0, and 3.5 mm and lengths of 8, 12, 18 and 28 mm (the 8 mm length was not available for 3.5 mm diameter). All commercial sizes and diameters of XIENCE were available except for the 2.25 mm diameter and the 33 and 38 mm lengths. Overlap with same device as assigned was allowed in the case of bailout.

The primary endpoint of the study is TLF (composite of cardiac death, myocardial infarction attributable to target vessel, or ischemia-driven target lesion revascularization) at 1 year. The hypothesis test was designed to show non-inferiority of Absorb to XIENCE with a pre-specified non-inferiority margin of 8.6% at one-sided alpha level of 0.05..

Powered secondary endpoints include: in-segment late loss at 13 months by angiography (non-inferiority with a non-inferiority margin of 0.195 mm); in-device mean lumen area change from

post-procedure to 3 years by IVUS (superiority); and in-device mean lumen diameter change, between pre- and post-nitrate infusion at 3 years by angiography (superiority).

Clinical follow-up is planned at 30 days, 180 days, and at 1, 2, 3, 4 and 5 years. All subjects undergo coronary angiography pre- and post-procedure, at 13 months and at 3 years. In addition, a subgroup of 120 subjects will undergo evaluation of vasoreactivity responses to acetylcholine (ACh) at 4 years.

Following the index procedure, all subjects were to be maintained on an IFU-specified dose of ADP antagonist for a minimum of 12 months, and aspirin (80 mg) for an indefinite period.

8.7.3 Demographics

The population was predominantly male (78.9% in the Absorb arm, 73.9% in the XIENCE arm). The mean age was 67.1 ± 9.4 years in the Absorb arm and 67.3 ± 9.6 years in the XIENCE arm. There was a high prevalence of hypertension (78.2% vs. 79.9% for Absorb and XIENCE arms, respectively) and dyslipidemia (82.0% vs. 82.1% for Absorb and XIENCE arms, respectively). Over 30% of the population was diabetic (36.1% vs. 35.8% for Absorb and XIENCE arms, respectively). The proportion of patients with two (or more) lesions treated were 10.9% (29/266) in the Absorb arm and 9.7% (13/134) in the XIENCE arm.

8.7.4 Results

The safety and effectiveness results for the ABSORB Japan trial are presented in **Table 8.7.4-1**. The TLF rate at 1 year was 3.8% (5/133) in the XIENCE arm and 4.2% (11/265) in the Absorb arm (difference 0.39%, 95% CI -4.68% to 4.18%), which met statistical non-inferiority ($p < 0.0001$). The observed definite/probable stent/scaffold thrombosis rate at 1 year was 1.5% for both Absorb and XIENCE arms.

Table 8.7.4-1: ABSORB Japan Clinical Results through 1 Year (ITT Population)

	Absorb (N = 266)	XIENCE (N = 134)
COMPOSITE EFFECTIVENESS AND SAFETY		
TLF	4.2% (11/265)	3.8% (5/133)
EFFECTIVENESS		
Ischemia-Driven TLR	2.6% (7/265)	2.3% (3/133)
TLR, CABG	0.0% (0/265)	0.0% (0/133)
TLR, PCI	2.6% (7/265)	2.3% (3/133)
Ischemia-Driven TVR	4.9% (13/265)	3.8% (5/133)
SAFETY		
All Death	0.8% (2/265)	0.0% (0/133)
Cardiac Death	0.0% (0/265)	0.0% (0/133)
Vascular Death	0.4% (1/265)	0.0% (0/133)
Non-cardiovascular Death	0.4% (1/265)	0.0% (0/133)
TV-MI	3.4% (9/265)	2.3% (3/133)
QMI	1.1% (3/265)	0.0% (0/133)
NQMI	2.3% (6/265)	2.3% (3/133)
All MI	3.4% (9/265)	2.3% (3/133)
QMI	1.1% (3/265)	0.0% (0/133)
NQMI	2.3% (6/265)	2.3% (3/133)
Cardiac Death or MI	3.4% (9/265)	2.3% (3/133)
Cumulative ARC-defined Definite + Probable Stent / Scaffold Thrombosis (0-365 days)	1.5% (4/262)	1.5% (2/133)
Acute (≤ 1 day)	0.0% (0/266)	0.0% (0/133)
Sub-Acute (> 1-30 days)	1.1% (3/265)	0.8% (1/133)
Late (31-365 days)	0.4% (1/262)	0.8% (1/133)

Note: 1-year timeframe includes a window of ± 28 days

Note: N is the total number of subjects

Note: MI is per protocol definition: Peri-procedural MI (≤ 48 hrs post-PCI) is defined as CK-MB > 5X ULN. Spontaneous MI defined as CK-MB or Troponin > ULN plus evidence of ischemia. .Q-wave MI is defined as development of new, pathological Q wave on the ECG in ≥ 2 contiguous leads.

9.0 PATIENT SELECTION AND TREATMENT

9.1 Individualization of Treatment

Risks and benefits should be considered for each patient before using the Absorb GT1 BVS System. Patient selection factors to be assessed should include identifying appropriately sized vessels for Absorb GT1 BVS implantation and judgment regarding the potential for non-compliance with antiplatelet therapy.

In small vessels (visually assessed reference vessel diameter ≤ 2.75 mm), on-line QCA or intravascular imaging with intravascular ultrasound or optimal coherence tomography is strongly recommended to accurately measure and confirm appropriate vessel sizing (≥ 2.5 mm). Implantation of the device in vessels < 2.5 mm may lead to an increased risk of adverse events such as myocardial infarction and scaffold thrombosis.

Antiplatelet drugs should be used in combination with the Absorb GT1 BVS per ACC / AHA and ESC guidelines. Physicians should use the information from the ABSORB family of clinical trials, coupled with the current literature on drug-eluting stents / scaffolds and the specific needs of individual patients, to determine the specific antiplatelet dose and duration to be used for their patients in general practice. In ABSORB III, all patients were to be maintained on 75 mg of clopidogrel daily or 5 or 10 mg of prasugrel daily (10 mg preferred in most patients) or 90 mg twice daily of ticagrelor for a minimum of 12 months, and ≥ 75 mg of aspirin daily for the length of the clinical investigation.

Special consideration should be given to those patients with recently active gastritis or peptic ulcer disease.

It is very important that the patient comply with the post-procedural antiplatelet recommendations. Premature discontinuation of prescribed antiplatelet medication could result in a higher risk of thrombosis, MI, or death. Prior to PCI, if a surgical or dental procedure is anticipated that requires early discontinuation or temporary interruption of antiplatelet therapy, the interventionalist and patient should carefully consider whether an everolimus-eluting scaffold and its associated recommended antiplatelet therapy are the appropriate PCI choice. Following PCI, should a surgical or dental procedure be recommended, the risks and benefits of the procedure should be weighed against the possible risk associated with premature or temporary discontinuation of antiplatelet therapy.

Patients who require premature discontinuation of antiplatelet therapy secondary to significant active bleeding should be monitored carefully for cardiac events, and once stabilized, have their antiplatelet therapy restarted as soon as possible per the discretion of their treating physicians.

10.0 PATIENT COUNSELING AND PATIENT INFORMATION

Similar to metallic stents, physicians should consider the following in counseling patients about this product:

- Discuss the risks associated with scaffold placement
- Discuss the risks associated with an everolimus eluting bioresorbable vascular scaffold
- Discuss the risks of early discontinuation of the antiplatelet therapy

- Discuss the risks of late thrombosis with scaffold use in higher risk patient subgroups
- Discuss the risk / benefit issues for this particular patient
- Discuss alternation to current life style immediately following the procedure and over the long term

The following patient materials are provided for this product:

- A Patient Information Guide, including information on coronary artery disease, the implant procedure and the Absorb GT1 BVS System (provided to physician, on-line at http://www.abbottvascular.com, or by calling customer service 1-800-227-9902).
- A Scaffold Implant Card, including both patient information and scaffold implant information (provided in package).

11.0 HOW SUPPLIED

Sterile – This device is E-beam radiation-sterilized. Non-pyrogenic. Do not use if the package is open or damaged.

This single-use device cannot be reused on another patient, as it is not designed to perform as intended after the first usage. Changes in mechanical, physical, and / or chemical characteristics introduced under conditions of repeated use, cleaning, and / or resterilization may compromise the integrity of the design and / or materials, leading to contamination due to narrow gaps and / or spaces and diminished safety and / or performance of the device. Absence of original labeling may lead to misuse and eliminate traceability. Absence of original packaging may lead to device damage, loss of sterility, and risk of injury to the patient and / or user.

Contents – One (1) Absorb GT1 Bioresorbable Vascular Scaffold (BVS) System; one (1) temperature monitor

Storage – Store at or below 25°C (77°F); excursions permitted to 30°C (86°F)

12.0 CLINICIAN USE INFORMATION

12.1 Inspection Prior to Use

Prior to using the Absorb GT1 BVS System, carefully remove the system from the package and inspect for bends, kinks and other damage. Verify that the scaffold does not extend beyond the radiopaque balloon markers and that it is still well-crimped onto the balloon catheter. Do not use if any defects are noted.

12.2 Materials Required

- Appropriate arterial sheath
- 2–3 syringes (10–20 cc)
- 1,000 u/500 cc heparinized normal saline (HepNS)
- 6F / 0.070" / 1.8 mm minimum inner diameter guiding catheter(s) of appropriate shape for the target vessel
- Rotating hemostatic valve with 0.096 inch (2.44 mm) minimum inner diameter
- 0.014 inch (0.36 mm) x 175 cm (minimum length) guide wire
- Torque device
- Guide wire introducer
- Contrast diluted 1:1 with heparinized normal saline
- Appropriate sized pre-dilatation angioplasty balloon
- Appropriate sized post-dilatation noncompliant angioplasty balloon
- Inflation device
- Three-way stopcock
- Appropriate anticoagulation and antiplatelet drugs

12.3 Vessel and Lesion Selection

- **Quantitative imaging is recommended** for the assessment of target vessel diameter at baseline for appropriate Absorb GT1 BVS size selection.

- In small vessels (visually assessed reference vessel diameter ≤ 2.75 mm), on-line QCA or intravascular imaging with intravascular ultrasound or optical coherence tomography is strongly recommended to accurately measure and confirm appropriate vessel sizing (≥ 2.5 mm). (See **Section 4.0** – **Warnings**)

- The target vessel diameter ranges to be treated in the procedure are indicated in **Table 12.3-1**, along with the Absorb GT1 BVS diameter to be used.

Table 12.3-1: Target Vessel Diameter Ranges and Absorb GT1 BVS Diameter to be Used (Quantitative Imaging)

Target Vessel Diameter Distal and Proximal	Absorb GT1 BVS Diameter to be Used
≥ 2.5 mm and < 2.75 mm	2.5 mm
≥ 2.75 mm and < 3.25 mm	3.0 mm
≥ 3.25 mm and ≤ 3.75 mm	3.5 mm

- **If visual estimation is used:**
    - **Use the pre-dilatation balloon, when inflated, to assist in sizing the vessel.**
- For cases where the combination of target vessel diameter and target lesion length is appropriate to be treated by more than one scaffold size, the selection of scaffold size can be made per the judgment of the physician.

12.4 Preparation

12.4.1 Packaging Removal

Note: The foil pouch is the sterile barrier. Sterile product is contained within this one pouch — there is no secondary pouch.

- Peel the pouch open from the top corner.
- Carefully remove the delivery system from its protective tubing for preparation of the delivery system.
- Do not bend or kink the hypotube during removal.

12.4.2 Dual Layer Sheath Removal

1. While holding the distal catheter shaft with one hand, grasp only the yellow outer sheath with the other hand and gently slide the sheath distally.
2. A longitudinal split on the inner sheath will open up and be visible.
3. The stylet and dual layer sheath are removed simultaneously from the delivery system by continuing to slide the yellow sheath distally until the inner and outer layers of the dual layer sheath as well as the stylet are free from the catheter system. See **Section 5.1 – Precautions, Scaffold Handling.** Do not use the device if the sheath cannot be removed as indicated.
4. Verify that the scaffold does not extend beyond the radiopaque balloon markers and no scaffold struts are lifted. **Do not use if any defects are noted.**

12.4.3 Guide Wire Lumen Flush

1. Flush the guide wire lumen with HepNS until fluid exits the guide wire exit notch.
   Note: Avoid manipulation of the scaffold while flushing the guide wire lumen as this may disrupt the placement of the scaffold on the balloon.

12.4.4 Delivery System Preparation

1. Prepare an inflation device / syringe with diluted contrast medium.
2. Attach an inflation device / syringe to stopcock; attach it to the inflation port of the product.
   Do not bend the product hypotube when connecting to the inflation device / syringe.
3. With the tip down, orient the delivery system vertically.
4. Open the stopcock to delivery system; pull negative for 30 seconds; release to neutral for contrast fill.
5. Close the stopcock to the delivery system; purge the inflation device / syringe of all air.
6. Repeat steps 3 through 5 until all air is expelled. If bubbles persist, do not use the product.
7. If a syringe was used, attach a prepared inflation device to the stopcock.
8. Open the stopcock to the delivery system.
9. Leave on neutral.

Note: The labeled scaffold diameter refers to expanded scaffold inner diameter.

12.5 Delivery Procedure

1. Prepare the vascular access site according to standard practice.
2. **Pre-dilate the lesion to match the reference vessel diameter with a percutaneous transluminal coronary angioplasty catheter.** Pre-dilatation should be performed with an angioplasty balloon which can also be utilized to properly size the vessel.

   Note: Limit the length of the pre-dilatation by the PTCA balloon to avoid creating a region of vessel injury that is outside the boundaries of the Absorb GT1 scaffold.
3. Administer a standard dose of intracoronary nitroglycerine prior to finalizing the RVD within the target zone.
4. Maintain neutral pressure on the inflation device. Open the rotating hemostatic valve as wide as possible.
5. Backload the delivery system onto the proximal portion of the guide wire, while maintaining guide wire position across the target lesion.
6. Advance the delivery system over the guide wire to the target lesion. Utilize radiopaque balloon markers to position the scaffold across the lesion; perform angiography to confirm scaffold position.

   Note: If removal of a scaffold system is required prior to deployment, ensure that the guide catheter is coaxially positioned relative to the scaffold delivery system and cautiously withdraw the scaffold delivery system into the guiding catheter. Should **unusual resistance** be felt **at any time** when withdrawing the scaffold into the guide catheter, the scaffold delivery system and the guide catheter should be **removed as a single unit**. This should be done under direct visualization with fluoroscopy.
7. Tighten the rotating hemostatic valve. The scaffold is now ready to be deployed.

12.6 Deployment Procedure

1. **CAUTION: Refer to product label for *in vitro* scaffold inner diameter, nominal pressure and RBP.**
2. Prior to deployment, reconfirm the correct position of the scaffold relative to the target lesion using the radiopaque balloon markers.
3. Deploy the scaffold slowly, by pressurizing delivery system **in 2-atm increments over 5 seconds**, until scaffold is completely expanded. Maintain pressure for 30 seconds. Fully expand the scaffold by inflating to nominal pressure at a minimum; accepted practice generally targets an initial deployment pressure that would achieve a scaffold inner ratio of about 1.1 times the reference vessel diameter.

   CAUTION: Do not exceed the labeled rated burst pressure RBP of 16 atm (1621 kPa) or maximum deployment diameter of the scaffold.
4. Fluoroscopic visualization during scaffold expansion should be used in order to properly judge the optimum scaffold diameter as compared to the proximal and distal native coronary artery diameters (reference vessel diameter). Optimal scaffold expansion and proper apposition require that the scaffold be in full contact with the arterial wall.
5. If necessary, the delivery system can be repressurized or further pressurized to ensure complete apposition of the scaffold to the artery wall.

   Fully cover the entire lesion and balloon-treated area (including dissections) with the Absorb GT1 scaffold, allowing for adequate scaffold coverage into healthy tissue proximal and distal to the lesion.
6. Deflate the balloon by pulling negative on the inflation device for 30 seconds. Confirm complete balloon deflation before attempting to move the delivery system. If unusual resistance is felt during scaffold delivery system withdrawal, pay particular attention to the guiding catheter position.

   Note: See **Section 12.8 – Clinician Use Information, Removal Procedure** for instruction on withdrawal of scaffold delivery system.
7. Confirm scaffold position and deployment using standard angiographic techniques. For optimal results, the entire stenosed arterial segment should be covered by the scaffold. Fluoroscopic visualization during scaffold expansion should be used in order to properly judge the optimum expanded scaffold diameter as compared to the proximal and distal coronary artery diameter(s). Optimal expansion requires that the scaffold be in full contact with the artery wall, which can be facilitated with the use of routine angiography and post-dilatation. Intravascular ultrasound (IVUS) or optical coherence tomography (OCT) can be used to confirm scaffold apposition to the artery wall.
8. **Post-dilatation is strongly recommended for optimal scaffold apposition.** When performed, follow the instructions in **Section 12.7 – Clinician Use Information, Further Expansion of the Deployed Scaffold**, as long as the post-dilated segment is within the allowable expansion limits of the scaffold.

12.7 Further Expansion of the Deployed Scaffold

1. **DEPLOYED SCAFFOLDS SHOULD NOT BE LEFT UNDER DILATED.**

   Deployed scaffolds should be well-apposed to the vessel wall. To achieve optimal scaffold apposition, post-dilatation is strongly recommended, especially for small vessels. When performed, post-dilatation should be at high pressure (> 16 atm) with a noncompliant balloon*.

   ***Note:** Limit choice of noncompliant balloon nominal diameter to be no more than 0.5 mm above the scaffold nominal diameter to stay within the scaffold's maximum expansion limit. **The compliance chart of the noncompliant balloon selected must be carefully reviewed prior to dilatation and an appropriate maximum pressure used to ensure that the scaffold is not over dilated.**

   The scaffolded segment should be carefully recrossed with a prolapsed guide wire to avoid disrupting the scaffold geometry. Post-dilatation must only be done with balloons sized to fit within the boundaries of the scaffold.

   CAUTION: Do not dilate the scaffold beyond the dilatation limit which is 0.5 mm above the nominal diameter. Over-dilatation may result in scaffold damage.

Nominal Scaffold Diameter	Dilatation Limit
2.5 mm	**3.00 mm** **Maximum post-dilatation diameter**
3.0 mm	**3.50 mm** **Maximum post-dilatation diameter**
3.5 mm	**4.00 mm** **Maximum post-dilatation diameter**

2. If more than one Absorb GT1 BVS is needed to cover the lesion and balloon-treated area, it is suggested that, to avoid the potential for gap restenosis, the scaffolds be overlapped by a minimum of 1 mm and a maximum of 4 mm. The least amount of overlap is recommended. To ensure that there are no gaps between scaffolds, the balloon marker bands of the second Absorb GT1 BVS should be positioned inside the deployed scaffold, just above the marker beads, prior to expansion. It is recommended not to use more than two Absorb GT1 BVS to treat one lesion.
3. Ensure the final scaffold diameter matches the reference vessel diameter to **ENSURE GOOD SCAFFOLD APPOSITION**. Reconfirm scaffold position and angiographic results. Repeat inflations until achieved.

12.8 Removal Procedure

Withdrawal of the scaffold delivery catheter / post-dilatation balloon from the deployed scaffold:

1. Deflate the balloon by pulling negative on the inflation device. Larger and longer balloons will take more time (up to 30 seconds) to deflate than smaller and shorter balloons. Confirm balloon deflation under fluoroscopy.
2. Position the inflation device to “negative” or “neutral” pressure.
3. Fully open the rotating hemostatic valve.
4. Stabilize guide catheter position just outside coronary ostium and anchor in place. Maintain guide wire placement across scaffolded segment.
5. Gently remove the scaffold delivery system with slow and steady pressure.
6. Tighten the rotating hemostatic valve.

If, during withdrawal of the catheter from the deployed scaffold, resistance is encountered, use the following steps to improve balloon rewrap:

- Re-inflate the balloon up to nominal pressure, deflate and change pressure to neutral.
- Repeat steps 1–5 above.
- Re-evaluate the scaffolded region once the balloon is removed to ensure optimal apposition.

Note: See **Section 5.4 – Precautions, Scaffold / System Removal** for specific delivery system removal instructions.

13.0 TRADEMARKS

Absorb GT1 and Absorb are trademarks of the Abbott Group of Companies.

XIENCE V, XIENCE PRIME, XIENCE Xpedition, and XIENCE Alpine are registered trademarks of the Abbott Group of Companies.

Certican, Afinitor, Votubia, and Zortress are registered trademarks of Novartis Pharmaceuticals, Inc.

Abbott Vascular
3200 Lakeside Drive
Santa Clara, CA 95054 USA

CUSTOMER SERVICE
TEL: (800) 227-9902
FAX: (800) 601-8874
Outside USA TEL: (951) 914-4669
Outside USA FAX: (951) 914-2531

Graphical Symbols for Medical Device Labeling

Manufacturer	REF Catalogue number	F French size	RX Rapid Exchange	30°C (86°F) EXCURSIONS Excursions permitted to temperature	Separate collection for waste electrical / electronic equipment
MANUFACTURED BY Manufactured by	Do not reuse	Do not resterilize	25°C (77°F) Upper limit of temperature	MR MR Conditional MR Conditional	
Use by	Date of manufacture	LOT Batch code			Rx ONLY CAUTION: Federal (USA) law restricts this device to sale by or on the order of a physician
Inner diameter	Outer diameter	STERILE R Sterilized using irradiation	Guiding catheter		
Consult instructions for use	Contents (numeral represents quantity of units inside)	CAUTION: Consult instructions for use for warnings and precautions	Non-pyrogenic	Do not use if package is damaged	