I. Overview:

This annual clinical update provides a review of the ongoing experience with the Relay Thoracic Stent-Graft System with Plus Delivery System (P110038), hereafter referred to as RelayPlus, used in the treatment of thoracic aortic aneurysm or penetrating atherosclerotic ulcer covering the time period from September 1, 2023 – September 2, 2024. The original Relay Thoracic Stent-Graft with the Transport delivery system received CE Mark in April 2005 and has been commercially distributed originally in the EU and then exclusively in China and has now been retired. The RelayPlus received CE Mark in 2009 and has subsequently been commercially available globally in the EU, ASPAC including Japan and in Latin America; it has been commercially available in the United States since 2012.

In the last published clinical update (posted on terumoaortic.com, 'RelayPlus – Annual Clinical Update 2023'), five years of IDE clinical data, 5 years of the Post-Approval Study (PAS) data and over 10 years of worldwide commercial experience was presented. As presented in that previous report, the PAS was completed with 5 year follow-up on evaluable subjects. *No new clinical data is presented in this clinical update*.

The Relay Pivotal study involved two delivery system iterations: Transport and Plus. There were no modifications to the Relay Stent-Graft. Ninety-five subjects enrolled in the Pivotal study received the Relay Stent-Graft with Transport delivery system. The Plus delivery system was introduced during the clinical study on September 9, 2009, and the remaining 25 subjects in the Pivotal study, along with all 13 subjects enrolled under Continued Access, were treated with RelayPlus. There were 45 subjects enrolled in the PAS.

The Plus delivery system included the following modifications:
- Hydrophilic coating on the sheath tip
- Higher radiopacity of the sheath tip
- Longer introducer sheath
- Nitinol vs. stainless steel inner catheter to facilitate navigation and alignment

FDA approval of the RelayPlus was granted on September 21, 2012.

PMA Approval Order	https://www.accessdata.fda.gov/cdrh_docs/pdf11/P110038A.pdf
Summary of Safety and Effectiveness (SSED)	https://www.accessdata.fda.gov/cdrh_docs/pdf11/P110038B.pdf
Post Approval Study (PAS) Webpage	https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma_pas.cfm?tid=480221
Instructions for Use (IFU)	https://eifu.terumoaortic.com/TAG/US/RPlus?keycode=28-M322150222290U

II. Worldwide Device Distribution:

There have been over 25,000 devices distributed worldwide as part of the IDE, Post-Approval Study and commercially. Approximately 314 RelayPlus have been sold worldwide between September 1, 2023 and September 2, 2024. During this time, a total of 143 devices were shipped within the US, with a total of 99 devices implanted.

III. Clinical Evaluations:

US Pivotal Study:
The Relay Pivotal (Phase II) study was initiated in the US in 2007 and included 120 subjects treated with the Relay Thoracic Stent-Graft (Relay cohort) and 60 surgical control subjects (surgical control cohort). This study was designed to evaluate the safety and effectiveness of the Relay Thoracic Stent-Graft in subjects with a diagnosed thoracic aortic aneurysm or penetrating atherosclerotic ulcer. The endovascular subjects were followed to 5 years after implantation, with the final subject visit for the Pivotal study occurring in October 2015. Upon enrolling 120 subjects in the Relay cohort, the study was extended under the Continued Access provisions. This study remained open until the Relay device was commercially approved on September 21, 2012. A total of 13 subjects were enrolled in the Continued Access cohort. In the Pivotal cohort, the average length of follow-up for the endovascular subjects was 1257 days (approximately 3.4 years). At the conclusion of the study, 39 subjects of the 53 eligible (74%) completed the final 5-year visit. A 93.2% freedom from aneurysm-related mortality was achieved in the endovascular cohort. There was one conversion to open repair during follow-up. There were no aneurysm ruptures in the treated segment of the aorta. Ten subjects underwent secondary interventions. Complete details are found in the SSED (see link above).

Relay Post Approval Study:
The RelayPlus PAS was a multi-center, prospective study initiated to assess the longer term performance of the RelayPlus Thoracic Stent-Graft, along with an evaluation of device usage and training effectiveness of novice versus experienced implanters. The study involved *de novo* investigational sites that did not participate in the Relay Pivotal study. Selection criteria reflected patient anatomy consistent with the indications for use. The primary endpoint was measured as freedom from ARM at 5 years post-procedure. Aneurysm-related mortality was defined as death from rupture of the descending thoracic aortic aneurysm (DTAA) or penetrating aortic ulcer (PAU), or from any procedure intended to treat the DTAA or PAU. Secondary endpoints for the PAS were the assessment of training effectiveness and the evaluation of major device-related events and major morbidity. A total of 45 patients were enrolled in the study from March 2014 to January 2018. Follow-up of these patients was completed, as reported in the 2023 annual clinical update, with all evaluable subjects having completed 5 year follow-up. Fifteen (15) subjects completed the 5 years of follow-up, 12 subjects have expired, 8 were withdrawn by the PI, 6 subjects voluntarily withdrew and 4 are lost to follow-up.

Core-lab reported data from the RelayPlus Post-Approval Study subjects through 2023 (refer to FDA's Post-Approval Studies (PAS) Database):

RelayPlus Post-Approval Study - Core-lab reported data							
	30-days	**1 Year**	**2 Years**	**3 Years**	**4 Years**	**5 Years**	**Total subjects**
Eligible for Follow-up	45	42	36	29	26	19	
Subjects with visit data	42	36	29	25	21	13	
Subjects with CT Scan	42	34	28	23	19	13	
Subjects with X-Ray	41	33	24	19	16	10	
Events							
Aneurysm-related Mortality	4.4% (2/45)	0	0	0	0	0	2
All-cause Mortality	4.4%	4.8%	5.6%	6.9%	7.7%	10.5%	12

RelayPlus Post-Approval Study - Core-lab reported data							
	30-days	**1 Year**	**2 Years**	**3 Years**	**4 Years**	**5 Years**	**Total subjects**
	(2/45)	(2/42)	(2/36)	(2/29)	(2/26)	(2/19)	
Major Adverse Events	6.7% (3/45)	2.3% (1/42)	0	0	0	0	4
Aneurysm Rupture	0	0	0	0	0	0	0
Conversion to Open Surgery	0	0	0	0	0	0	0
All Endoleaks*							
Type Ia	0	0	0	3.4% (1/29)[a]	0	0	1
Type Ib	0	0	0	3.4% (1/29)[b]	0	0	1
Type II	4.4% (2/45)	2.3% (1/42)	2.8% (1/36)	0	3.8% (1/26)	0	5
Type III	0	0	0	1	3.8% (1/26)[d]	5.3% (1/19)[d]	1
Type IV	0	0	0	0	0	0	0
Unknown	0	0	0	0	0	0	0
Aneurysm Sac Enlargement (> 5 mm)*	0	4.8% (2/42)[c,d]	2.8% (1/36)[d]	6.9% (2/29)[d,e]	7.7% (2/26)[d,e]	5.3% (1/19)[e]	3
Loss of Device Integrity	0	0	0	0	0	0	0
Migration > 10 mm		0	2.8% (1/36)[f]	3.4% (1/29)[a]	0	0	2
Loss of Patency	0	0	0	0	0	0	0
Any Secondary Intervention	0	2.3% (1/42)	0	0	0	0	1

*x is the number of subjects who reported that event, and y is the number of subjects with follow-up/adequate imaging to assess the parameter.

[a] Subject 512-106: Type Ia endoleak detected at 3-year follow-up, with associated caudal migration of the proximal neck and expansion of the proximal aorta. Subject expired 1538 days (~4 years) post implant due to atherosclerotic cardiovascular disease.

[b] Subject 503-101: Type Ib endoleak detected at 3-year follow-up. No migration or aneurysm sac increase.

[c] Subject 502-105: sac increase of 6.3 mm at 1 year, decreased to -5.4 mm from baseline at 2 years, further decreased to -11.8 mm from baseline at 3 years. No migration or endoleak.

[d] Subject 513-103: sac increase of 7.6 mm at 1 year, ongoing at 2, 3 and 4 years. No migration. Type II endoleak detected at 4 years which was reclassified by the Core Lab as a Type III endoleak when seen at the 5-year follow-up. No secondary intervention performed to date

[e] Subject 512-101: sac increase of 6.1 mm at 3 years, persisted at 4 and 5 years, possibly due to secondary aneurysm present below treated area. No migration or endoleak.

[f] Subject 502-104: experienced cranial migration of the distal neck at 2 years, likely attributed to lengthening of the aorta. Subject expired 1889 days (~5 years) post implant due to intracerebral hemorrhage.

Commercial access to RelayPlus is granted if the physician possesses the required experience needed to perform an endovascular procedure and has completed the required in-service device training for new users. Delivery and deployment rates for experienced versus novice implanters have been evaluated and while the number of subjects treated by experienced implanters remains small, there appears to be no notable differences in outcomes compared to those of novice implanters.

Procedural parameters were also compared, and experienced implanters had slightly longer procedural and fluoroscopy time, with slightly less blood loss and contrast used. Procedural related MAEs were slightly higher in the experienced group, however, the experienced centers consistently perform implants on challenging anatomy, which present a higher risk for MAEs. Overall, the review does not support any clinically meaningful differences between subjects treated by experienced vs

novice users in terms of patient demographics or outcomes providing evidence of training effectiveness.

IV. Worldwide Recalls, Safety Communications and Field Safety Notices:

There have been no US recalls, safety communications and/or Field Safety Notices issued for RelayPlus during this reporting period.

In 2014, there was a Field Safety Notice outside the US as a result a small number of cases where the inner sheath of the delivery system had not fully exited from the outer sheath as expected. A Field Safety Notice was issued recommending additional verification steps to avoid potential advancement or deployment difficulties. The Instructions for Use (IFU) were subsequently updated to include the recommendations.

In February 2021, a Field Safety Notice outside the US was issued to address discrepancies in the RelayPlus OUS IFU distal landing zones and select device characteristics. The risk assessment determined there was no associated patient risk, however distributors were notified for awareness pending implementation of a corrected Instructions for Use.

V. Worldwide Commercial Experience:

RelayPlus is distributed globally and receives feedback/learnings from this worldwide commercial use. The following table summarizes the associated complaints for this Annual Report timeframe.

RelayPlus Complaints: September 1, 2023 – September 2, 2024		
Failure Mode Description (internal code)	**# of complaints**	**MDR Filed**
Clinical Observations		
Type I endoleak (056, 099) including paraplegia (060) and post-implant aortic disease progression (074)	1	Yes
Dissection found post-procedure (058)	1	No
Delivery / Deployment Observations		
Unable / difficult to advance the secondary sheath to the treatment site (036) including premature deployment (066)	1	No

Terumo Aortic will continue its diligence in monitoring and investigating product complaints and take necessary actions, as needed, and concludes that the benefits of using the RelayPlus Thoracic Stent-Graft system continue to outweigh the associated risks.

VI. Explant Analysis:

Through the course of the investigational phase and following commercialization, eight explants have been analyzed. None have shown any obvious damage associated with the device. An additional three stent-grafts were partially/fully explanted, however, were not returned to Terumo Aortic for inspection. There were no explants reported during this reporting period.

VII. Literature Review:

There have been 2 publications with information on the RelayPlus device since the last update. These publications are case studies that are not focused on outcomes with Relay but report overall outcomes of at least some procedures performed including a Relay. These articles were considered of purely scientific interest and are not being used to make changes to practices or procedures. The RelayPlus device is indicated for the endovascular repair of fusiform aneurysms and saccular aneurysms/penetrating atherosclerotic ulcers in the descending thoracic aorta. The uses described in the publications are outside the approved indications.

Article Citation	Description and Impact
Federico Pascucci, Giovanni Mastrangelo, Vincenzo Palazzo. "When even luck matters: a compendium of all possible complications during hybrid repair of a dissecting TAAA occurred in a single patient." Hellenic Journal of Vascular and Endovascular Surgery Volume 5 - Issue 2, 2023. doi: 10.59037/hjves.v5i2.49	A 73-year-old woman, already submitted to repair of the ascending aorta and subsequently to aortic valve substitution in redo sternotomy, presented to our attention with a dissecting TAAA with a distal aortic arch diameter of 6 cm. The goal was to offer an extremely fragile patient the least invasive surgical treatment as possible. The patient was treated in two stages. In the first stage, a carotid-carotid-subclavian bypass was performed using a 8mm non-ringed ePTFE graft (Propaten, WL Gore, Flagstaff, AZ, USA). In the second stage, a TEVAR in zone 1 was performed with two overlapping tapered thoracic endografts (Bolton Relay Plus, Terumo Aortic, Vascutek Ltd., Inchinnan, UK), extending from the brachiocephalic artery to the celiac trunk. Left subclavian artery was previously occluded with a plug. CSFD was not adopted by default. This patient reported some extremely rare and unexpected complications.
Reyes Valdivia A, Milner R, Heijmen R, Riambau V, Rousseau H, Tinelli G, Kotelis D, Zanabili Al-Sibbai AA, Pitoulias G, Zúñiga CG, de Beaufort HWL, Panagiotis D, Chaudhuri A. Mid-term outcomes of the use of endoanchors during thoracic endovascular aortic repair in multicentre analysis. Vascular. 2023 Jun;31(3):455-462. doi: 10.1177/17085381221076320. Epub 2022 Feb 27. PMID: 35225085.	To describe mid-term outcomes of the use of EndoAnchors as an adjunct for arch and thoracic endovascular aortic repair (TEVAR). A retrospective multicenter series from nine centers using the Heli-FX EndoAnchor System (Medtronic Inc, Minneapolis, USA) at TEVAR over May 2014–May 2019 is presented. The study is registered at ClinicalTrials.gov with number NCT04100499. The primary outcome was freedom from Type I endoleak at EndoAnchors deployments; secondary outcomes included evaluation of aortic wall penetration (AWP) at first computed tomography scan, EndoAnchor related issues and mortality. Fifty-four (54) high-risk patients (35 males/19 females, age 73 ± 11 years) with arch, thoracic and thoracoabdominal aneurysmal disease (3 chronic post-dissection and one patch pseudoaneurysm), with a mean neck length 19.7 ± 6.6 mm that were treated with multiple hybrid and endovascular techniques were included. Various endografts were used, including the Valiant (Medtronic Inc, Minneapolis, USA; n = 20), Zenith Alpha (Cook Aortic Intervention, Bloomington, USA; n = 15), Extra design (Jotec GmbH, Hechingen, Germany; n = 2), CTAG (W. L. Gore and Associates, Flagstaff, USA; n = 4) and a Relay Plus (Bolton

Article Citation	Description and Impact
	Medical, Sunrise, USA; n = 7), and a combination of endografts in 4 cases.

VIII. Conclusion:

Based on available clinical study data and world-wide clinical experience to date, endovascular therapy with the RelayPlus Thoracic Stent-Graft System continues to be a viable treatment option for fusiform aneurysms and saccular aneurysms/penetrating atherosclerotic ulcers in the descending thoracic aorta.

Adverse Event Reporting:

As indicated in the Instructions for Use, adverse events or complaints should be reported by contacting 1-855-726-5866 (1-855-7BOLTON). Accurate and timely reporting of adverse events by the physician users to the device manufacturer and FDA (MedWatch Form 3500) is critical for monitoring device performance and detection of potential device-related safety issues.

Patient Follow- Up and Selection:

Regular follow-up of all patients treated with the RelayPlus Thoracic Stent-Graft System is required. Physicians should tailor patient follow-up to the needs and circumstances of each individual patient following endovascular graft placement. Patients should be regularly monitored for endoleaks, lesion growth, or changes in the structure or position of the endovascular graft. At a minimum, annual imaging is recommended.