



## Endeavor™ Drug-Eluting Coronary Stent Program

Caution: The Endeavor™ Drug Eluting Coronary Stent is an investigational device with an investigational drug (ABT-578) and is exclusively for clinical investigation.

### OVERVIEW

Medtronic's Endeavor™ Drug-Eluting Coronary Stent is designed to treat patients with coronary heart disease. It is the first drug-eluting stent composed of a cobalt alloy and is coated with a proprietary drug to reduce restenosis - the relogging of coronary arteries. Endeavor approval applications have been filed for CE Mark in Europe, with approval expected in Spring 2005.

### ENDEAVOR COMPONENTS

There are four primary components of the Endeavor system: the stent, the drug, the polymer that coats the stent, and the delivery system.

#### The Driver stent

Medtronic's bare metal stent, the Driver™ Coronary Stent System, is an advanced cobalt alloy stent and is the foundation of the Endeavor system. Driver is approved for treating large and small vessels in Europe, where it is the highest single-selling bare metal stent on the market.

- The cobalt-based alloy makes Driver stronger than stainless steel stents and therefore allows thinner struts
- With an ultra-thin structure, Driver is flexible and gets delivered easily while maintaining strong stent structure and formation in the vessel. \*

#### Drug, polymer and delivery system

Endeavor releases a rapamycin ("limus" family) analogue drug, designed to inhibit the growth of new tissue that would lead to restenosis. The drug, ABT-578\*\*, works by interrupting the process of cell division by blocking the function of a protein called mTOR.

The drug is released directly into the arterial wall by a phosphorylcholine (PC) polymer that coats the stent. Known as PC Technology™\*\*\*, the polymer coating has six years of European clinical experience dating from 1997. In Europe, Endeavor will be delivered via the Rapid Exchange Delivery System.

### ENDEAVOR CLINICAL TRIAL PROGRAM

There are currently five planned ENDEAVOR clinical trials, each studying safety and efficacy in patients with coronary artery disease.

#### ENDEAVOR I

<b>Design</b>	100-patient, prospective, multi-center trial in Australia and New Zealand
<b>Purpose</b>	Studying the safety and efficacy of Endeavor for the treatment of de novo lesions in native coronary arteries
<b>Status</b>	<ul style="list-style-type: none"> <li>▪ Trial began in 2003</li> <li>▪ Clinical 12-month results released in August 2004</li> </ul>
<b>Outcomes</b>	<p>The trial met all endpoints as designed:</p> <ul style="list-style-type: none"> <li>▪ Major adverse cardiovascular events (MACE) rate = 2.0%</li> <li>▪ Binary restenosis rate = 5.4%</li> <li>▪ Target lesion revascularisation (TLR) rate = 1.0%</li> <li>▪ In-segment late lumen loss = 0.43 mm</li> <li>▪ In-stent late lumen loss = 0.61 mm</li> </ul>

The low MACE and TLR rates show the effectiveness of the stent's ability to reduce repeat procedures and restenosis. Additionally, there was no change in TLR, TVF (target vessel failure) or MACE beyond the four-month follow-up period.

## ENDEAVOR II

<b>Design</b>	1,197 patients; randomized, double-blind trial in 72 centres in Europe, Middle East, and the Asia Pacific region
	<u>Expanded safety registry:</u> an additional 300 patients in 15 sites outside the USA
<b>Purpose</b>	Evaluating the safety and efficacy of Endeavor compared to Medtronic's Driver cobalt alloy stent
<b>Status</b>	<ul style="list-style-type: none"><li>▪ Enrollment completed in January 2004</li><li>▪ Thirty-day results released in May 2004 in blinded form</li><li>▪ Final results presented at ACC in March 2005</li></ul>
	<u>Expanded safety registry:</u> <ul style="list-style-type: none"><li>▪ Enrollment completed in July 2004</li></ul>
<b>Outcomes</b>	Clinically and statistically significant improvement in all endpoints <ul style="list-style-type: none"><li>▪ Target vessel failure (TVF) reduction = 47%; (Endeavor rate = 8.1%)</li><li>▪ Major adverse cardiac event (MACE) reduction = 50% (Endeavor rate = 7.4%)</li><li>▪ Target lesion revascularization (TLR) reduction = 62%; (Endeavor rate = 4.6%)</li><li>▪ In-stent angiographic binary restenosis (ABR) reduction = 71% (Endeavor rate = 9.5%)</li><li>▪ In-segment late loss = 0.36 mm</li><li>▪ In-stent late loss = 0.62 mm</li></ul>

The study showed that Endeavor drug eluting stent has an excellent safety profile and that it substantially reduces clinical restenosis compared to a bare metal stent. After nine months, more than 95 percent of the patients who received an Endeavor stent required no further treatment or revascularization at the original treatment site. Stent thrombosis rate at 30 days was 0.5 percent with no late thrombosis beyond 30 days and no late stent malapposition.

## ENDEAVOR III

<b>Design</b>	436 patients; randomized (3 to 1) trial
<b>Purpose</b>	Evaluating safety and efficacy of Endeavor compared to the Cypher™ Sirolimus-Eluting Stent from Cordis, a division of Johnson & Johnson
<b>Status</b>	<ul style="list-style-type: none"><li>▪ Enrollment completed in September 2004</li><li>▪ Results to be presented at TCT, October 2005</li></ul>

## ENDEAVOR IV

<b>Design</b>	1,500-patient randomized (1 to 1), single-blind trial
<b>Purpose</b>	Evaluating safety and efficacy of Endeavor compared to Taxus™ Paclitaxel-Eluting Coronary Stent System from Boston Scientific Corporation
<b>Status</b>	Enrollment to begin in March 2005

## ENDEAVOR V

<b>Design</b>	Post CE Mark approval clinical outcomes study
<b>Purpose</b>	Evaluation of post market patients
<b>Status</b>	Enrollment to begin following CE Mark approval, expected in Spring 2005

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\*Supporting Data On File with Medtronic

\*\*ABT-578 is licensed to Medtronic from Abbott Laboratories.

\*\*\*PCT Technology is the property of Biocompatibles LTD