

Technology Transfer & Disruptive Innovation at NIH: The Case of Taxus Express TM

Steven M. Ferguson

Director, Division of Technology

Development & Transfer

NIH Office of Technology Transfer

HHS Email: sf8h@nih.gov



Technology Source: National Institutes of Health

*Basic Biomedical Research
in Support of the Public Health*

- Funding
- Training
- Basic Research
- Clinical Trials
- Inventions
- Policies

NIH Licensing: Transfer of Commercial Rights To Technology From Research Program

- Annual budget of \$ 28 billion (2005)
- 8% of funding for intramural research
- 6,000 intramural scientists / 2,000 projects
- 212,000 extramural scientists /46,000 grants
- Basic & clinical research discoveries
- Partners commercialize into products

How Could Just One Technology From the NIH Portfolio Be Disruptive?

- ✍ 400+ invention disclosures per year
- ✍ 2300 total pending/issued patents
- ✍ 1650+ active licenses (276 executed FY04)
- ✍ \$56.3 million in royalties collected FY04
- ✍ >\$456 million in royalties collected FY93-FY04
- ✍ 231 active CRADAs (1500 to date)
- ✍ ~200 products developed to date
(20 vaccines and therapeutics)

How Could Something So Small Be Disruptive?



Cardiovascular Disease (circa 1996)

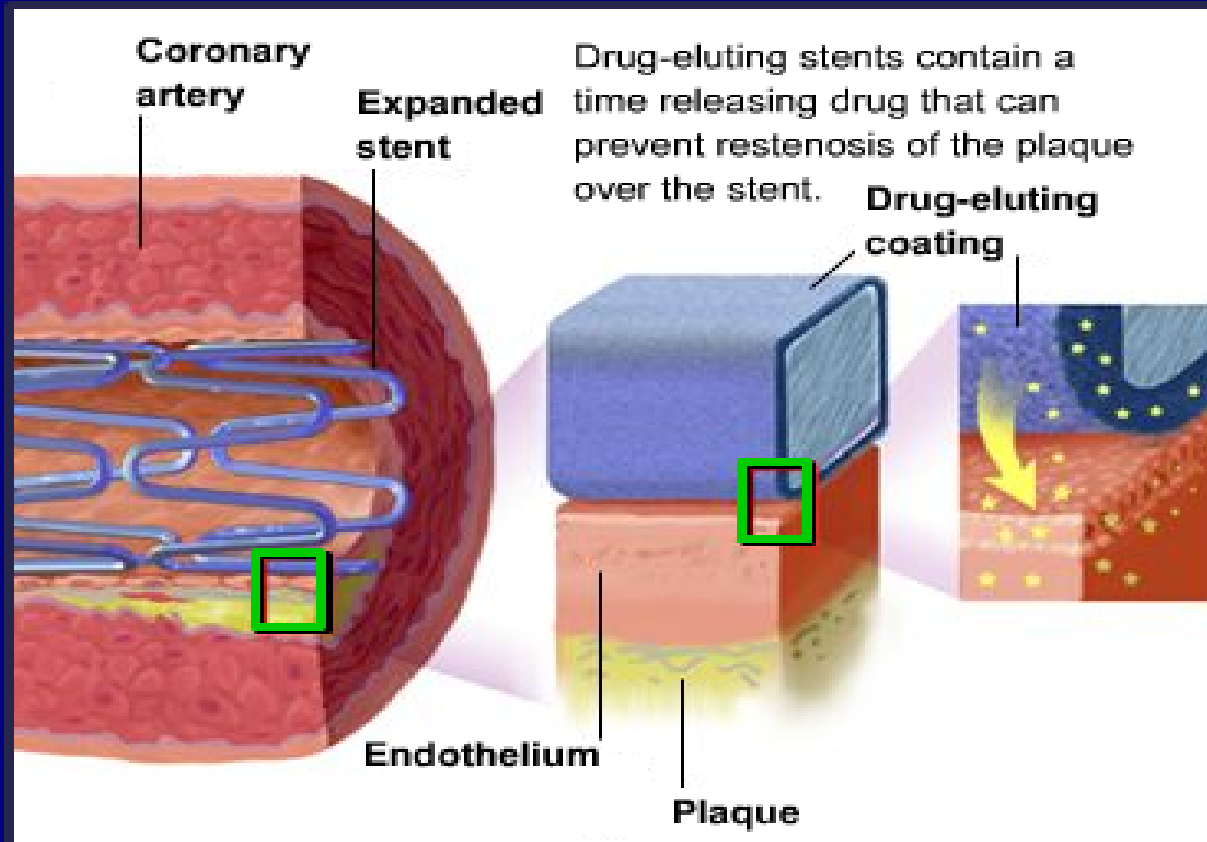
- Stents (as part of balloon angioplasty) have revolutionalized atherosclerosis treatment.
- Johnson & Johnson controls the stent market in the U.S. and Europe.
- But 30% or more cases form scar tissue that re-closes arteries (restenosis).
- Incremental design changes in stents fail to solve the problem.

That Was Then, This Is Now (2005)

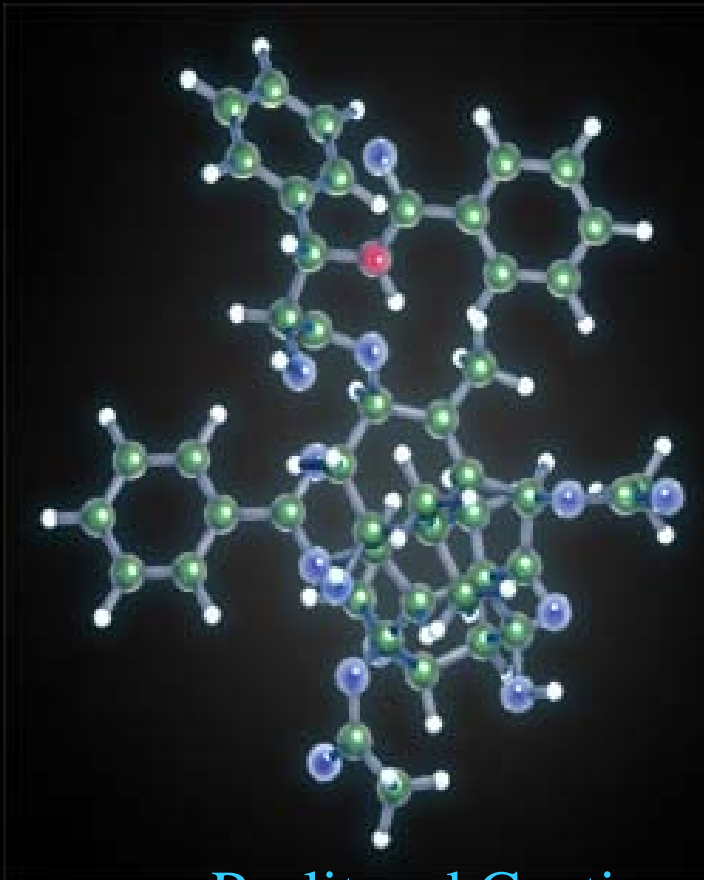
- “Most successful new medical product in history” launched by NIH licensee & corporate partners.
- >\$2.6B estimated for first full year sales in U.S. and Europe.
- Johnson & Johnson no longer market leader in stents.
- What happened?

Disruptive Innovation – Drug-Eluting Stents (DES)

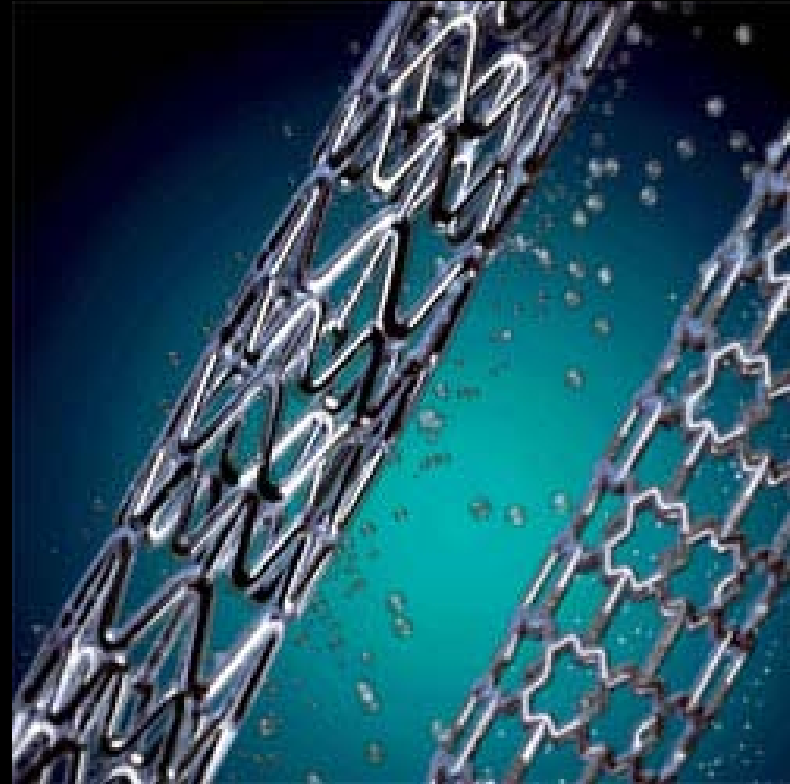
Cardiovascular Stent



Disruptive Innovation – Drug-Eluting Stents (DES)



Paclitaxel Coating



Why Would DES Be Considered Disruptive?

- Combination drug/devices uncommon approach.
- Double regulatory issues / double risk.
- NIH licensee (Angiotech) small innovative Canadian firm.
- Disruptive Partnering Strategy: Angiotech unsuccessful with Market Leader (J&J) but partners with multiple Market Trailers, including Boston Scientific.

Industry

PHARMACEUTICALS

MEDICAL DEVICES/SURGERY

Expertise

Chemistry & Biology

Engineering

Solutions

Small Molecules
Drugs, Biologics

Structural, Mechanical,
Electrical, Radioactivity

**Corporate
Competency**

Target Identification,
Molecular Design, ADME,
Animal & Human Testing,
Marketing

Mechanical & Electrical
Engineering, Clinical,
Marketing

FDA

Drugs: Slow/Expensive

Devices: Faster/Cheaper

Risk

High Risk: 1/10 Succeed

Low Risk: 9/10 Succeed

User

INTERNISTS & GP's

**SURGEONS &
INTERVENTIONALISTS**

PHARMACEUTICALS

MEDICAL DEVICES/SURGERY

ANPI OPPORTUNITY

Chemistry & Biology

Engineering

Small Molecule
Drugs, Biologics

Small Molecule Therapeutics

Solving Structural Problems
with Therapeutics
"Beyond Engineering"

Structural, Mechanical
Electrical, Radioactivity

Target Identification,
Molecular Design, ADME,
Animal & Human Testing,
Marketing

Mechanical & Electrical
Engineering, Clinical,
Marketing

Drugs: Slow/Expensive

Using Devices to
Deliver Drugs
"Beyond Systemics"

Devices: Faster/Cheaper

High Risk: 1/10 Succeed

Interventional Technologies

Low Risk: 9/10 Succeed

INTERNISTS & GP'S

SURGEONS & INTERVENTIONALISTS

Why Would DES Be Disruptive At NIH?

- Research came from National Institute of Aging (not typically focused on cardiovascular disease).
- Royalty income provides a sharp increase in NIA research budget.
- Royalty income not disruptive to inventors due to cap (unlike university paclitaxel synthesis).
- Licensing Issues: Revisit standard license contract language for drug/device combos.
- Change in standard of healthcare.

Why Would DES Be Disruptive At Angiotech?

- Expected success but not market domination!
- Cash makes acquisition strategies possible. Three subsidiaries!!
- Able to extend product concept to product platform to corporate mission (“Knowledgy”)
- Additional partnerships & product extensions based upon DES concepts.

AGM Financial Review

Q2:05 Guidance

- Q1:05 TAXUS Revenue Summary: Total \$686MM; U.S. \$494MM; EU/ROW \$192MM
- U.S. Market Share holding steady at approximately 60%+



Expectations: (from Angiotech Annual Meeting)

Why Were We So Wrong?

WW DES Model		
	2004	2005
WW Revenue (\$MM)	3,658	4,621
Market Share		
BSC	22%	22%
Guidant	13%	25%
JNJ	61%	43%
Medtronic	1%	5%
Other	3%	5%

What We Expected... (2002 Analyst Reports)

Source: Average of Morgan Stanley, Bank of America, Merrill Lynch, Lehman Bros., CSFB & Deutsche Bank Securities (2002 estimates).

WW DES Model				
	2004	2005	2006	2007
WW Revenue (\$MM)	3,900	5,506	5,817	5,968
Market Share				
BSC	53%	53%	46%	43%
Guidant	0%	0%	0%	0%
JNJ	46%	44%	48%	47%
Medtronic	0%	2%	5%	7%
Abbott	1%	1%	1%	3%

What Occurred... (2005 Analyst Reports)

Source: see above left (January to March, 2005)

Additional Paclitaxel Eluting Technology Applications Now In Development

- Use in actual bypass surgery (Angiotech with CABG Medical).
- Treatment of emphysema (Angiotech with Broncus Technologies).
- Peripheral stents and wraps (Angiotech with Cook, Inc.)

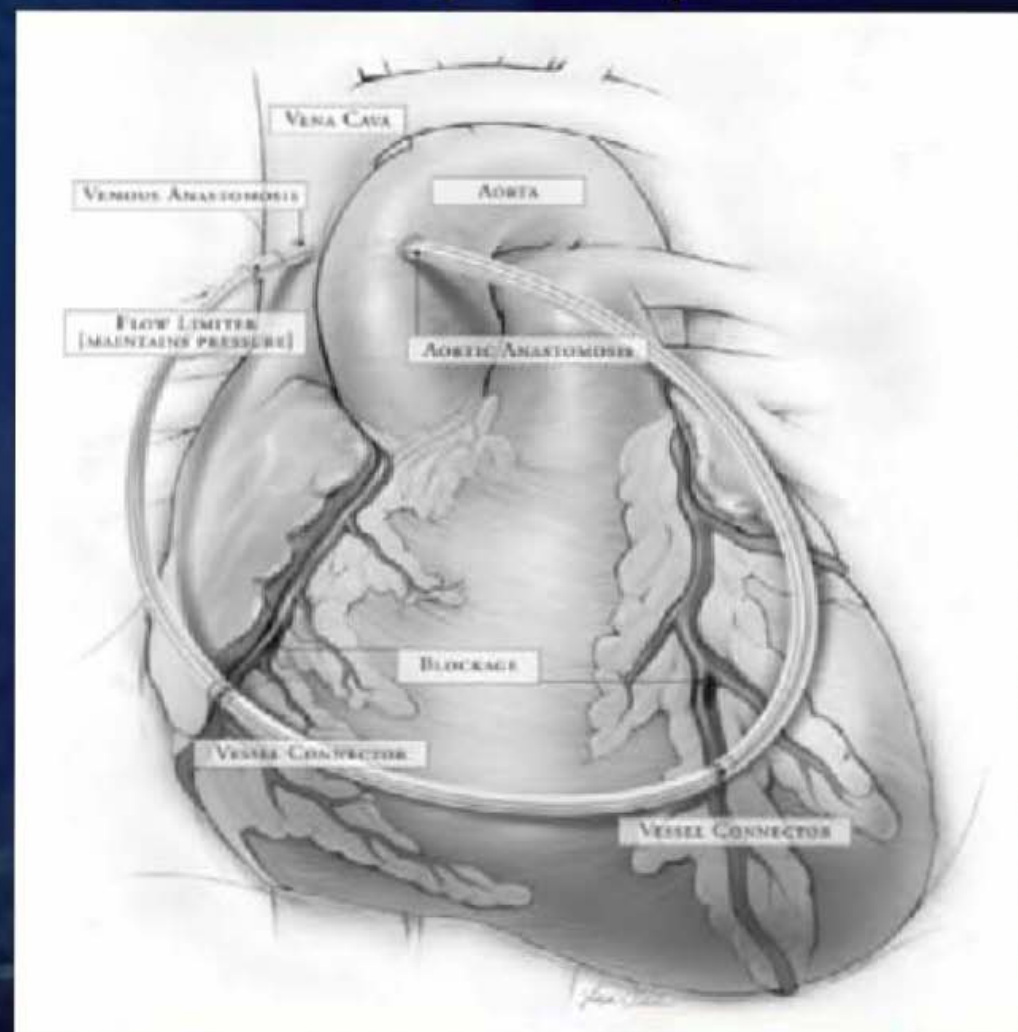
CABG Medical

The Holly Grail System for Bypass Surgery

Implanted Vessel Connector



The Holly Grail System

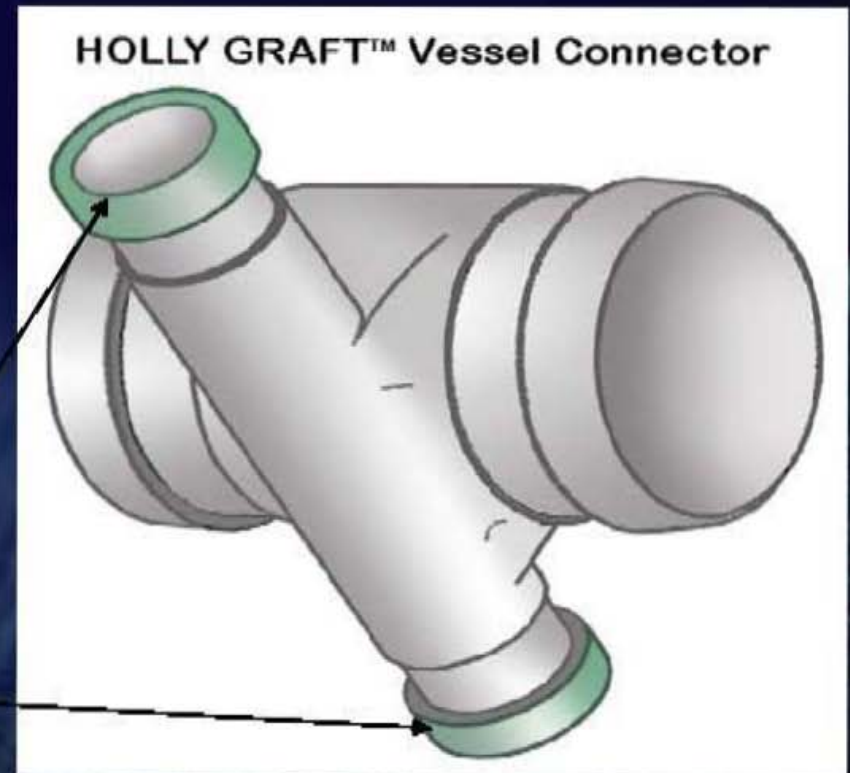
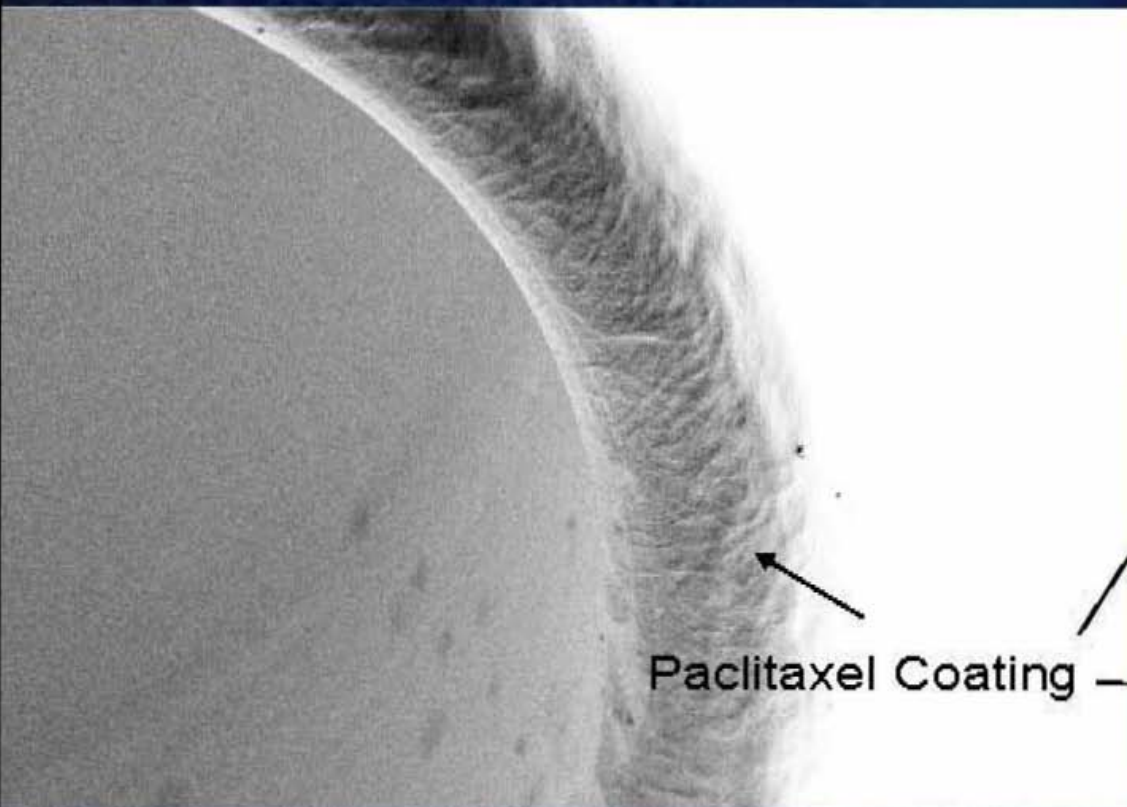


Holly GRAFT™ Vessel Connector



Drug Eluting Graft

Below is a magnified version of the Holly Graft System vessel connector





Broncus Technologies Inc.

Normal XRay



Emphysema XRay



Over exapanded
Flattened diaphragm

Clinical & Regulatory Summary

- Treated 80 patients to date
- Over 25 patients implanted with paclitaxel-eluting stents
 - ▶ Duration of airway bypass seems to improve
 - Leveraging proven paclitaxel technology
 - ▶ Apparent improvement at 1, 3 and 6 months:
 - Symptoms
 - Quality of Life
 - PFT's
- Currently treating patients outside the U.S.
- Planning to start U.S. pivotal study in 1H06

Zilver[®] Paclitaxel-Eluting Peripheral Stent (Partnered with Cook Inc.)

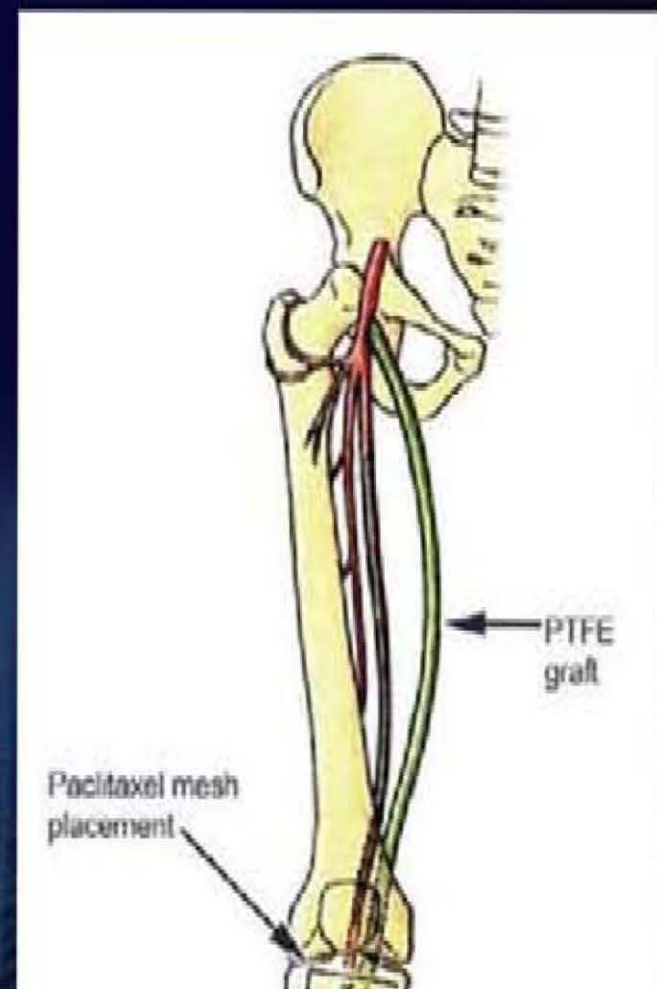
- First drug-eluting stent to be used outside the heart
- Proof-of-concept with success in treating CAD
- U.S. Trial Initiated
 - ▶ 60 patients, 10 sites
 - ▶ Objective: safety and efficacy in peripheral vascular disease above-the-knee in the femoropopliteal artery
 - ▶ Pilot study enrollment completion expected by end of 2005
 - ▶ Pivotal study enrollment completion by end of 2006
 - ▶ Trial expansion upon further FDA review



Vascular Wrap: European Pivotal Clinical Trial

The study is designed to address the need of surgeon, to prevent or reduce the incidence of stenosis in synthetic peripheral bypass grafts.

Initiated:	September, 2003
Enrolment:	Complete, 108 pts
Double-blind:	Randomization after anastomosis complete
Randomized:	2:1 Wrap vs Standard of Care
Multi-center:	13 (Expanded to 17)
Primary Endpoint:	Safety
Secondary Endpoint:	Binary Restenosis (Duplex Measurements) Clinical restenosis, limb salvage



Conclusions Regarding Disruptive Innovation

- Disruptive Innovation brings changes to both marketplace as well as technology developer & provider.
- Disruptive Innovation appears to support notion that true innovation is increasingly driven by smaller firms – see for example ...

Older NIH “Homerun” Licensed Products (All From Large Firms)

- Abbott HIVAB (AIDS Test Kit)
- BMS Videx (ddI)
- BMS Taxol (paclitaxel)
- Schering Fludara (fludarabine)
- GlaxoSKB Havrix (hepatitis A)
- Roche Hivid (ddC)

More Recent Product Approvals (All From Small Firms At The Time)

- Angiotech Taxus (paclitaxel-eluting stents)
- Genzyme Thyrogen (rTSH)
- Isis Vitravene (antisense CMV)
- Medimmune Synagis (RSV mab)
- Millennium Velcade (myeloma drug)
- Biogen Idec Zevalin (NHL I₁₃₁ mab)
- Amgen Kepivance (KGF)

Sources Of Information On NIH Licensing And Technologies

- NIH Technology Transfer – ott.od.nih.gov
- NIH CRISP Database - nih.gov/grants
- Global TechnoScan – globaltechnoscan.com
- Pharmalicensing - pharmalicensing.com
- Technology Exchange - techex.com
- University Ventures - uventures.com
- Pharma-transfer - pharma-transfer.com
- Knowledge Express - keonline.com