

Industry Edition

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Week in Review

- **Joint Juice?? Can holistic medicine be creeping into this orthopedic surgeon's general practice?** - This year nearly 66 million Americans will suffer from arthritis or chronic joint symptoms. In 2002, nearly 19.5 million office visits were due to knee problems. Into this breach comes...Joint Juice? More on page 4.
- **LifeCell clears \$61 million in sales on a 79% increase in Alloderm** - Alloderm, the acellular dermal matrix derived from donated human skin tissue, powered LifeCell to over \$61 million in annual sales. Something special is going on here. More on page 6.
- **Medicare Payment Advisory Panel votes to continue ban on physician-owned orthopedic specialty hospitals** - March 8. "I'm not quite prepared to reach the conclusion they should be outlawed," said Glenn Hackbarth, chairman of the Medicare Payment Advisory Commission. *Thanks, Glenn.* More on page 8.
- **Led by Accell® 100% DBM, IsoTis is gaining market share** - For the year ended December 31, 2004, IsoTis reported a seemingly meager 5% sales growth rate to \$25.4 million. But underneath it all is a hot product line and, we think, a market share shift to IsoTis. More on page 10.
- **CrossCart, Inc. gets FDA go-ahead for Z-Lig™ pivotal trial** - February 23. Last week the FDA cleared CrossCart to begin a pivotal clinical trial for its porcine-derived ligament known as the Z-Lig™. If approved it would be a first. More on page 12.
- **From ashes to tissue regeneration** - Italy's birthrate may be sinking faster than Venice, but some Italians are finding new ways to regenerate themselves. Fidia Advanced Polymers (FAB) is leading the way with innovative biopolymer technologies. More on page 13.

Commentary

When it's the CEO who has the office affair - *We set—hell, I set—a higher standard here...I violated my own standards. I used poor judgment — former Boeing CEO Harry Stonecipher. (Continued on page 3).*

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Orthopedics Data Summary

Robin Young Orthopedic Stock Universe

Top Performers last 30 days				
Company	Symbol	Price	Mkt Cap	30-day Chg
1	Regeneration Tech	RTIX \$ 11.00	\$ 292.99	5.16%
2	Johnson and Johnson	JNJ \$ 67.60	\$ 200,620.00	1.50%
3	Medtronic	MDT \$ 53.97	\$ 65,280.00	1.03%
4	Wright Medical	WMGI \$ 25.38	\$ 859.24	0.91%
5	Tutogen	TTG \$ 2.40	\$ 38.20	0.84%
6	Average			-0.32%
7	DJ Orthopedics	DJO \$ 24.72	\$ 530.42	-0.72%
8	LifeCell	LIFC \$ 8.95	\$ 254.99	-1.32%
9	Smith & Nephew	SNN \$ 51.75	\$ 9,660.00	-1.33%
10	Kyphon	KYPH \$ 25.25	\$ 1,060.00	-1.71%

Worst Performers last 30 days				
Company	Symbol	Price	Mkt Cap	30-day Chg
1	Arthrocare	ARTC \$ 26.92	\$ 582.82	-15.88%
2	CryoLife	CRY \$ 6.87	\$ 161.05	-13.91%
3	Biomet	BMET \$ 39.37	\$ 9,950.00	-12.39%
4	Regen Biologics	RGBI.OB \$ 1.04	\$ 51.20	-11.11%
5	Orthologic	OLGC \$ 5.38	\$ 204.50	-8.19%
6	Zimmer Holdings	ZMH \$ 78.96	\$ 19,370.00	-7.20%
7	NuVasive	NUVA \$ 12.15	\$ 290.06	-6.97%
8	Stryker	SYK \$ 47.43	\$ 19,110.00	-6.91%
9	Orthofix	OFIX \$ 38.84	\$ 608.43	-6.34%
10	Kensey Nash	KNSY \$ 31.11	\$ 354.00	-2.48%

Lowest Price / Earnings Ratio (TTM)				
Company	Symbol	Price	Mkt Cap	P/E
1	Osteotech	OSTE \$ 3.86	\$ 66.26	11.80
2	Orthofix	OFIX \$ 38.84	\$ 608.43	18.09
3	Johnson and Johnson	JNJ \$ 67.60	\$ 200,620.00	22.18
4	Average		\$ 16,467.21	25.47
5	Kensey Nash	KNSY \$ 31.11	\$ 354.00	27.01

Highest Price / Earnings Ratio (TTM)				
Company	Symbol	Price	Mkt Cap	P/E
1	Arthrocare	ARTC \$ 26.92	\$ 582.82	55.16
2	Kyphon	KYPH \$ 25.25	\$ 1,060.00	50.60
3	Regeneration Tech	RTIX \$ 11.00	\$ 292.99	48.25
4	Stryker	SYK \$ 47.43	\$ 19,110.00	42.05
5	Smith & Nephew	SNN \$ 51.75	\$ 9,660.00	41.73

Lowest P/E to Growth Ratio (TTM)				
Company	Symbol	Price	Mkt Cap	PEG
1	LifeCell	LIFC \$ 8.95	\$ 254.99	0.84
2	Kensey Nash	KNSY \$ 31.11	\$ 354.00	1.18
3	Arthrocare	ARTC \$ 26.92	\$ 582.82	1.21
4	Wright Medical	WMGI \$ 25.38	\$ 859.24	1.28
5	Kyphon	KYPH \$ 25.25	\$ 1,060.00	1.33

Highest P/E to Growth Ratio (TTM)				
Company	Symbol	Price	Mkt Cap	PEG
1	Johnson and Johnson	JNJ \$ 67.60	\$ 200,620.00	1.82
2	Medtronic	MDT \$ 53.97	\$ 65,280.00	1.75
3	DJ Orthopedics	DJO \$ 24.72	\$ 530.42	1.59
4	Regeneration Tech	RTIX \$ 11.00	\$ 292.99	1.57
5	Orthofix	OFIX \$ 38.84	\$ 608.43	1.55

Lowest Price to Sales Ratio (TTM)				
Company	Symbol	Price	Mkt Cap	PSR
1	Osteotech	OSTE \$ 3.86	\$ 66.26	0.71
2	Tutogen	TTG \$ 2.40	\$ 38.20	1.29
3	DJ Orthopedics	DJO \$ 24.72	\$ 530.42	2.07
4	Orthofix	OFIX \$ 38.84	\$ 608.43	2.18
5	CryoLife	CRY \$ 6.87	\$ 161.05	2.56

Highest Price to Sales Ratio (TTM)				
Company	Symbol	Price	Mkt Cap	PSR
1	Regen Biologics	RGBI.OB \$ 1.04	\$ 51.20	108.5
2	NuVasive	NUVA \$ 12.15	\$ 290.06	7.43
3	Medtronic	MDT \$ 53.97	\$ 65,280.00	6.68
4	Zimmer Holdings	ZMH \$ 78.96	\$ 19,370.00	6.65
5	Biomet	BMET \$ 39.37	\$ 9,950.00	5.82

Orthopedic Power Rankings				
Robin Young's Entirely Subjective Ordering of Public Orthopedic Companies				
Rank	Company	TTM Op Margin	30-Day Price Change	Comment
1	Biomet	28%	(12.00)%	Standard and Poors upgrades to BUY last week
2	Kyphon	16%	(1.71)%	Banc of America ups rating.
3	Medtronic	31%	1.03%	24% spine growth. InFuse and a wide and deep motion preservation pipeline.
4	Zimmer	26%	(7.20)%	The cheaper Zimmer gets, the better it looks.
5	LifeCell	11%	(1.32)%	How big could Alloderm get? Maybe the most popular tissue-based implant ever.
6	Wright	13%	0.91%	<i>Podiatry Today</i> names GraftJacket® #2 best new product.
7	JNJ	27%	1.68%	2nd best performer in the past 30 days. At 22 p/e, still a relative bargain.
8	dj Orthopedics	15%	(1.42)%	High-tech braces really work. AAOS paper confirms.
9	CryoLife	(41)%	(13.91)%	For once, CRY's fundamentals trending up.
10	Kensey Nash	29%	(2.48)%	New deal with Orthovita plus low P/E and PEG puts KNSY on the Power Rankings.



Commentary (continued from page 1)

When the CEO Has an Office Affair

By

Robin R. Young, CFA

We set—hell, I set—a higher standard here...I violated my own standards. I used poor judgment — former Boeing CEO Harry Stonecipher.

Junior executive to CEO: "Sir, what is the key to your success?"

CEO to junior executive: "Son, I can answer that in two words, 'right decisions.'"

Junior executive to CEO: "Thank you sir, but how do you make right decisions?"

CEO to junior executive: "I can answer that in one word, 'experience.'"

Junior executive to CEO: "I see sir, now how do I get such experience?"

CEO to junior executive: "Two words, 'wrong decisions.'"

Boeing's example is gaining a kind of popular support that should have corporate leaders taking notice.

In Boeing's case, Harry Stonecipher was 68 years old. You would have thought he'd have learned by now.

Stonecipher, a married CEO, had an affair with a subordinate. What makes this case interesting is that Boeing's board of directors refused to sweep it under the rug.

That is impressive. And, frankly, we think, it is resonating all around corporate America. Boeing's example is gaining a kind of popular support that should have corporate leaders taking notice.

Before the Stonecipher case, it was lawmakers who had to face the judgments of a disapproving constituency. Gary Hart lost a run for the White House after the public learned of his affair in 1987. Bill Clinton was impeached for trying to cover up his affair with Monica Lewinsky. A handful of legislators who found themselves in compromising positions in Washington tidal pools or wherever, resigned or were dismissed by voters.

Surgeons and other medial professionals have long operated under extremely severe penalties for engaging in inappropriate relationships with patients

In orthopedics the stakes for such affairs are even higher. Surgeons and other medial professionals have long operated under extremely severe penalties for engaging in inappropriate relationships with patients (jail time). Teachers, as well, can serve time for having affairs with their students.

The reason those relationships are dealt with so severely is that they are hierarchically-based affairs that represent a volatile and, in our view, unholy blend of power and sex.

Corporate America, not unlike Boeing's own recent scandal-filled experience, has been going through a string of depressing ethical lapses with the examples on Wall Street, with Enron, WorldCom, Tyco and other firms.

The old days of wink and ignore at the CEO level may well be ending.



Rank-and-file workers want their leaders to set an ethical standard. And they will, we think, increasingly refuse to turn a blind eye to a CEO's personal and corporate improprieties.

Boeing's board of directors has set a very public precedent. One that, we know, has found its way onto the bulletin boards in lunchrooms all around the country.

While it is certainly true that office affairs are a fact of life in corporate America, it is also true that for a CEO all employees are their subordinates. And when a married CEO is having an affair with a subordinate, the other employees know it, feel it and begin to question that CEO's ability to make decisions fairly.

More than that, employees interpret this behavior as an abuse of power.

More than that, employees interpret this behavior as an abuse of power

Such fundamentally indulgent risk taking by a corporate leader damages the reputation of an entire organization to say nothing of the risks of legal action should a claim of sexual harassment arise or if there is any fallout from a relationship gone bad.

Bottom line: if a married CEO is engaging in an office romance, he/she better stop or resign or both. The company's employees, customers and board of directors are increasingly demanding it. Sainthood isn't the standard. Good and common sense is.

Joint Juice?? Can Holistic Medicine Creeping its Way Into This Orthopedic Surgeon's General Practice?

By

Priscilla Young, Staff Writer

This year nearly 66 million Americans will suffer from arthritis or chronic joint symptoms according to the Arthritis Foundation. In 2002 nearly 19.5 million office visits to physicians were because of knee problems; the most common reason for visits to orthopedic surgeons.

Joint Juice may well find a place in the broader continuum of care

The well-advertised removal of Vioxx from the market because of a significant increase in the risk of heart attacks and strokes, as well as the gastrointestinal problems associated with the use of non-steroidal anti-inflammatories left a void for many orthopedic surgeons who treat both osteoarthritis and musculoskeletal injuries.

While the FDA is poised to allow Vioxx back on the market, the potential side effects will likely make it a less preferred drug of choice for many physicians.

Into this breach comes **Joint Juice?** While not a pain reliever per se, **Joint Juice** may well find a place in the broader continuum of care as both physicians and patients consider the now well-publicized side effects of not only Vioxx but even some other non-steroidal anti-inflammatories.



One sports medicine surgeon has met this challenge with a decidedly unique approach. Dr. Kevin Stone, founder of The Stone Clinic, has developed **Joint Juice**, a liquid supplement containing 1500 milligrams of glucosamine, 60 milligrams of vitamin C mixed with real fruit juice. Glucosamine, long recognized by the alternative medicine crowd as promoting joint health, is a natural sugar derived from chitin taken from the shells of shellfish. It is also a key component of the extracellular matrix of cartilage.

While not a replacement for Vioxx, other COX-2 class drugs, or more traditional pain relievers, **Joint Juice** shows promise as it treats the underlying cause of the patient's problem, not just the symptoms. **Joint Juice** offers an alternative to more traditional treatment plans. While the jury is still out, it could in the long run be a healthier alternative than just pain pills.

Glucosamine is synthesized by the cartilage cells in the body, increasing the cartilage ability to absorb water, the primary cushioning agent in the joints. As glucosamine is also a key building block in the production of hyaluronic acid it assists in the lubrication of all joint tissue. A natural anti-inflammatory, glucosamine is believed to inhibit the breakdown of cartilage and may assist in the regeneration of damaged cartilage. Dr. Stone has seen his patients gain increased joint function and flexibility within four to six weeks.

Joint Juice shows promise as it treats the underlying cause of the patient's problem, not just the symptoms.

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But why buy **Joint Juice** when you can go to your nearest Health Food store and buy glucosamine pills? Dr. Stone discovered by talking to his patients that they found it difficult to remember to take three large pills a day, required if you go the pill route. By putting it in a liquid form, Dr. Stone found his patients got a better absorption rate and he got better compliance as his patients only had to drink one can a day.

What's next on the horizon for Dr. Stone? Adding calcium and vitamin D to **Joint Juice** to address the growing problem of osteoporosis among women. **Joint Juice** can be found at numerous Wal-Mart stores or on the web at www.jointjuice.com



LifeCell Clears \$61 Million in Revenue for 2004 on the Strength of a 79% Increase in Alloderm Sales

By

Robin R. Young, CFA

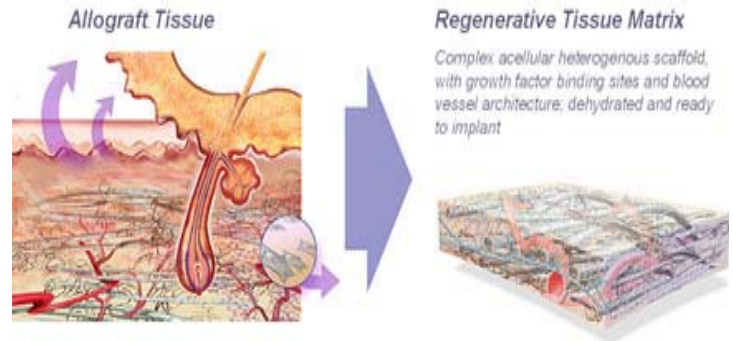
Alloderm, the acellular dermal matrix derived from donated human skin tissue developed by 20 years ago, keeps finding new users and uses in the operating room, generating \$42.5 million in sales for LifeCell in 2004 up from \$23.7 million in 2003. The range of uses for Alloderm and its derived products expanded in 2004 and now include breast reconstruction surgery, ligament and tendon injuries as well as LifeCell's complex hernia repair.

Including all of LifeCell's products, the Company's revenues for 2004 reached \$61.1 million, up 52% from 2003's \$ 40.2 million.

The cost of producing Alloderm fell as a percent of sales in 2004 and now comprises roughly 30 cents for every revenue dollar generated.

Alloderm was developed in the mid-80s by Dr. Stephen Livesey, M.D. and his colleagues at the University of Texas. The product grew out of Dr. Livesey's work in freeze drying biological tissues and cells in such a way as to preserve their structural and biochemical integrity.

Until Dr. Livesey and his team developed the Alloderm process, attempts to freeze dry tissues resulted in the formation of tissue damaging ice crystals. Dr. Livesey's invention was, essentially, non-crystalline ice.



By adding tissue-processing technology to his freeze-drying process, Dr. Livesey was able to create a unique and biologically useful yet acellular tissue matrix. The new material was originally marketed for patients suffering severe burns, soft tissue defects or urological disorders. Once implanted, Alloderm's acellular matrix proved to be an excellent scaffold for revascularization and cell repopulation.

Alloderm was first commercialized in 1993. In its first year, Alloderm generated \$21,000 in sales. Of course, this past year Alloderm sales rose 79% to \$43 million.

On the strength of versatile Alloderm, LifeCell is now the fourth-largest tissue processor in the world and, arguably, its fastest growing. Alloderm is proving to be a very versatile material. It can be a sheet, a mesh, injectable, a tube and many other

Once implanted, Alloderm's acellular matrix proved to be an excellent scaffold for revascularization and cell repopulation.

At Wright Medical, the range of uses for Graftjacket® (the Alloderm-derived materials for soft tissue graft reinforcement) seems to be growing exponentially



shapes. In its most popular market, complex hernia repair, Alloderm has already captured 10% of the market.

At Wright Medical, the range of uses for Graftjacket® (the Alloderm-derived materials for soft tissue graft reinforcement) seems to be growing exponentially. At the recent AANS Fall Course (held last December 2-5), for example, Dr. Alan Barber presented a study that showed that Graftjacket®'s suture retention strength was nearly 2.5x greater than its nearest competitor product (TISSUEMEND®).

Recently Graftjacket was named 2004's #2 biggest innovation by Podiatry Today, (#1 was a diabetes drug) for its use as a treatment for diabetic foot ulcers—an application far away from rotator cuff repair.

Bottom line: Alloderm, in all of its manifestations, is the premier allograft soft tissue product on the market today as measured in terms of revenues, indications and speed of surgeon adoption.

LifeCell Corporation Summary Sales, Profitability and Market Value 2002-2005E				
	2002	2003	2004	2005 Est. *
Alloderm Sales	\$17.2	\$23.7	\$42.5	\$52.0
Other Sales	17.2	16.5	18.6	20.0
Total	\$34.4	\$40.2	\$61.1	\$72.0
Gross Profit %	69%	68%	70%	
Operating Profit %	4%	5%	11%	
Sales Growth %	24%	17%	52%	18%
Market Value	\$70 million	\$140 million	\$260 million	
# of Employees	138	155	173	

- *Consensus estimate on Thompson Financial/First Call and management guidance*



Worldwide Tissue Processing Industry (\$ in millions)				
Rank	Company	2004 sales	2005E sales	% Change
1	MTF Foundation	235.0	265.0	13%
2	Regeneration Tech	92.7	107.0	15%
3	Osteotech	87.0	94.3	8%
4	LifeCell	61.1	72.0	18%
5	Allosource	45.0	50.0	11%
6	Tutogen	29.3	30.0	2%
7	Isotis	25.4	30.0	20%
	All other	79.0	83.0	5%
	Total	\$654.5	\$731.3	12%

Source: Robin Young Consulting Group / Consensus: Thompson Financial/First Call

Medicare Payment Advisory Panel Votes to Continue Ban on Physician-Owned Orthopedic Specialty Hospital

By

Robin R. Young, CFA

March 8. "I'm not quite prepared to reach the conclusion they should be outlawed," said Glenn Hackbarth, chairman of the Medicare Payment Advisory Commission, about physician-owned specialty hospitals including orthopedic surgery centers. His advisory commission was recently directed by Congress to study the impact of specialty hospitals.

Thanks, Glenn.

The issue for the advisory panel, we've been able to determine, was the health of the general hospital. Patients, orthopedic surgeons, indeed the entire healthcare delivery system, didn't get nearly the same consideration.

In his testimony to the Senate Finance Committee last Tuesday, Hackbarth also recommended that Congress should recalculate its reimbursement rates under Medicare so the rates more accurately reflect the costs of care (read increase reimbursement for the general hospital).

The moratorium is due to expire this coming June 8. Hackbarth's advisory panel recommended extending the ban to January 1, 2007.



With almost 98% of the nation's hospitals offering large joint replacement surgery, it is, perhaps, not surprising that the profit margins for this activity are falling. One study we saw recently suggested that the average profit per patient for large joint replacement in general hospitals was around \$400 and would likely decline over the coming decade to under \$100. What's a general hospital to do? Particularly when its orthopedic surgeons want to open up their own surgery centers.

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Get Congress to declare a moratorium on orthopedic specialty hospitals and increase payments to general hospitals? So it seems.

With the specter of physician-owned specialty hospitals leaving general hospitals with the poorest and sickest and, therefore, less profitable patients, Congress approved a moratorium on physician-owned specialty hospitals as part of the law that established a prescription drug benefit under Medicare a couple years ago.

The moratorium is due to expire this coming June 8. Hackbarth's advisory panel recommended extending the ban to January 1, 2007.

Interestingly enough, the advisory commission's own study found that general hospitals were not harmed by the competition from specialty hospitals. The commission's study that said general hospitals have remained as profitable as their peers in communities where no specialty hospitals existed.

One orthopedic surgeon, Dr. Alan Pierrot, who testified at the hearing on behalf of the American Surgical Hospital Association (a group of about 75 surgical hospitals) said; "No proof of harm to general hospitals, risk to patients, or abuse of the Medicare program because of excessive or unnecessary surgery has been found."

Senator Charles Grassley, speaking for many members of Congress who are skeptical of orthopedic specialty hospitals, noted that, "The Government Accountability Office has found that specialty hospitals treat fewer Medicaid patients and few, if any, uninsured patients. There are 45 million uninsured, and I'm concerned about this."

*Hospital groups opposing specialty hospitals spent nearly **\$2 million** lobbying Congress. Trade groups supporting specialty hospitals spent **\$19,000.***

Finally, we couldn't help but spot the following key difference between those who support the moratorium and those that are seeking to let specialty hospitals continue to grow and evolve. The two principal lobbying groups opposing specialty hospitals (American Hospital Association and the Federation of American Hospitals) spent, respectively, \$1.75 million and \$230,000 lobbying Congress.

By contrast, the trade association representing surgeon-owned specialty hospitals spent \$19,000. This is according to PoliticalMoneyLine, which tracks campaign contributions.



Led by Accell® 100% DBM, IsoTis Gaining Market Share

By

Robin R. Young, CFA

For the year ended December 31, 2004, IsoTis reported a seemingly meager 5% rate of increase to \$25.4 million from \$24.2 million in 2003. But underneath those numbers is an increasingly hot product line and, we think, a market share shift in IsoTis's direction.

Accell line of DBM products is growing at 3x-4x faster than the overall DBM industry

Now comprising over 40% of the Company's sales, IsoTis's increasingly popular Accell line of DBM products is growing at 3x-4x faster than the overall DBM industry. If this continues, and based on management's comments last week, we think it will, IsoTis should end the current year with 17%—19% share of the overall DBM market, we estimate.

Based on our estimates of the total DBM market size, we believe IsoTis started 2005 with a 15% market share.

Sales for the fourth quarter, ended December 31, 2004, rose 8% to \$6.4 million, up from \$5.9 million in the same period (pro-forma to adjust for the acquisition of GenSci) a year earlier. Furthermore, management increased its guidance for 2005, now pegging revenue growth at 20% year-over-year—the upper end of previous public statements.

According to the CEO Pieter Wolters, "During the last three months, rapid market acceptance of the Accell technology has led to double-digit growth in US sales of those products. Where we have previously given a 15% to 20% expected growth range for 2005, we now anticipate revenue growth of around 20%".

IsoTis's Accell bone void fill Demineralized Bone Matrix, grew at a blistering 45% year-over-year rate in 2004 and now accounts for 41% of the Company's total sales—up from 31% of pro-forma revenues in 2003.

The latest addition to the Accell line, Total Bone Matrix, was introduced to the US domestic market in the fourth quarter 2004. ***It will be the first and only pre-formed 100% demineralized bone matrix in the orthopedic industry.***

IsoTis's other two Accell products are Accell DBM100 and Accell Connexus™.

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The key to the entire Accell line is a proprietary processing method that converts DBM into a bone void fill that delivers the handling characteristics of a DBM putty but without a carrier material. In the table below, we summarize the major product categories and the various types of carriers that manufacturers employ.

Product Brand / Manufacturer	Carrier	% DBM
Accell DBM 100 (IsoTis)	DBM	100%
AlloCraft™ DBM (Stryker Howmedica)	Acellular Matrix	80%
Accell Connexus (IsoTis)	DBM & Reverse Phase Medium	70%
AlloMatrix® Putty (Wright Medical)	Calcium Sulfate	40%
InterGro™ Putty (Interpore Cross)	Lecithin	40%
DBX® Putty (Synthes)	Sodium Hyaluronate	32%
Osteofil™ Paste (Regeneration Technologies)	Porcine Collagen	24%
Grafton® Putty (Osteotech)	Glycerol	17%

IsoTis's Accell products, however, deliver the highest possible levels of DBM

Clearly, IsoTis is tapping into the market's desire for increased bone growth stimulation. InFuse®, which we now estimate generated approximately \$300 million in sales for 2004, is the 800-pound gorilla in the bone void fill market. To a large extent, InFuse has stopped the traditional DBM market cold.

IsoTis's Accell products, however, deliver the highest possible levels of DBM and, at least in theory, more bone morphogenic protein than any other DBM on the market. At a fraction of the cost of InFuse, Accell is well positioned, we think, to take share from market leaders Grafton and Osteofil.

Still, IsoTis's good news is probably the principal bright spot in an increasingly moribund DBM bone void fill market. Autograft (bone harvested from the patient during surgery) remains the surgeon's gold standard and is used, we estimate, in between 50% and 55% of the cases. Furthermore, when DBM is used, it's often an extender for autograft or as a delivery vehicle for InFuse (a phenomenon we estimate occurs 15%-20% of the time InFuse is used).

As Sofamor Danek, the supplier of InFuse, finds ways to improve the delivery of InFuse (and therefore maintain its efficacy while also lowering the per-patient cost) surgeons will, we think, continue to migrate away from DBM.

Furthermore, a number of alternative bone growth stimulating technologies are working their way through the FDA regulatory process and will come to market over the course of the next one to three years. By 2008, surgeons will have, we expect, less expensive versions of InFuse, one or two peptides as well as at least one other powerful bone growth void fills to choose from.

By 2008, surgeons will have, we expect, less expensive versions of InFuse, one or two peptides as well as at least one other powerful bone growth void fills to choose from



Global DBM Market (\$ in millions)				
Company	2003	2004	2005E	% Change
Osteotech (Grafton)	46.0	45.0	46.0	2%
Regeneration Technologies (Osteofil)	30.0	36.0	38.0	6%
MTF	25.0	30.0	32.0	7%
IsoTis	24.2	25.4	30.0	20%
All other	24.8	28.6	30.0	5%
Total DBM	\$150.0	\$165.0	\$175.0	6%
Synthetic bone void fills	75.0	90.0	115.0	28%
Infuse	160.0	300.0	400.0	33%
All other (including platelet concentrates)	30.0	32.0	28.0	(12)%
Total Market for Bone Void Fill	415.0	587.0	718.0	22%

Source: Robin Young Consulting Group

If approved, the Z-Lig would be the first xenograft ligament approved for ACL repair.

CrossCart, Inc. Gets FDA Go-Ahead for Z-Lig™ Pivotal Trial

By

Robin R. Young, CFA

February 23. CrossCart, Inc. announced last week that the FDA has cleared the Company to begin a pivotal clinical trial for its porcine derived ligament known as the Z-Lig™. CrossCart's Z-Lig device is designed to replace a torn anterior cruciate ligament (ACL) in the human knee.

If approved, the Z-Lig would be the first xenograft ligament approved for ACL repair.

The current standard of care for ligament replacement surgery is autograft (harvesting the patient's own tissue in a second surgery) or allograft (cadaver tissue).

CrossCart's Z-Lig device would offer surgeons a third alternative and one that would not require a second surgical site (thereby reducing the time and cost of the surgery as well as recovery time) nor would it create any risk of disease transmission from contaminated tissue. Finally, being a porcine-based material, Z-Lig would not suffer some the supply limitations inherent in allograft tissue sources.

Z-Lig is porcine tissue that is processed using CrossCart's proprietary tissue treatment technology called the "Z-Process™." According to the Company, Z-Process employs a three-step procedure of enzymatic elimination of Gal antigens, chemical neutralization

The pivotal study will be conducted on a single blind basis with an independent, blinded evaluator.



of non-Gal antigens, and electron beam sterilization to strip the key antigens from the tissue and render it sterilized. Z-Process is covered by 19 patents and 11 patents pending.

The objective of the pivotal trial is to evaluate the safety and effectiveness of the Z-Lig device in patients with an acute or chronic injury that requires reconstruction of a ruptured ACL. The study will be a non-inferiority trial, comparing the Z-Lig device to allograft in a prospective, randomized, blinded multicenter clinical trial at up to ten clinical sites. The trial is approved for the enrollment of 326 subjects, with half receiving the Z-Lig device and half receiving an allograft control.

The pivotal study will be conducted on a single blind basis with an independent, blinded evaluator. While the surgeon investigator who performs the ACL repair will know whether a Z-Lig device or an allograft was used in the procedure, both the patient and the evaluator performing post-operative assessments will be blind to the patient's treatment group. The primary outcomes to determine clinical success will be two standard measures of knee laxity and the assessment of knee effusion.

From Ashes to Tissue Regeneration

By

Walter Eisner, Staff Writer

In Europe's largest ISO 9002 certified facility dedicated to tissue engineering, Fidia Advanced Polymers (FAB) intends to be the leader in the field of autologous tissue transplants.

Italy's birthrate may be sinking faster than Venice, but some Italians are finding new ways to regenerate themselves.

Thirty miles west of Venice in the town of Abano Terme, Italian scientists and businessmen are on a mission to create tools to regenerate connective and structural tissues.

In Europe's largest ISO 9002 certified facility dedicated to tissue engineering, Fidia Advanced Polymers (FAB) intends to be the leader in the field of autologous tissue transplants.

In a nutshell, or perhaps in a "cell", autologous tissue transplants are the transplantation of an organism's own cell or tissue. The Company bases its core technology on a new class of patented biopolymers obtained from chemical modifications of hyaluronan, a naturally occurring polysaccharide.

The process originated from the idea of using hyaluronic acid to create a scaffold, which would provide excellent conditions for body's cells, such as keratinocytes,

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fibroblasts and chondrocytes, to proliferate and form healthy tissue. The result is advanced technology by which highly functional, autologous tissues can be recreated and grafted onto cartilage lesions or diabetic ulcers.

FAB develops, manufactures and markets medical devices based on the technology and is expressly tailored for its three business areas:

1. bio-orthopedics
2. bio-surgery
3. soft tissue repair

Fidia Farmaceutici S.p.A., a private Italian pharmaceutical company, is the owner of FAB. Fidra was founded in 1946 and is a recognized leader in hyaluronan technology. FAB was established in 1992.

Fidia was a phoenix rising from the ashes of war in 1946 and, today, its offspring FAB is advancing the science and promise of regeneration.

FAB may not raise Venice or serve as a stimulus for a higher birthrate, but it will certainly contribute to a rising Italian biotechnology and orthopedic industry.

