VOLUME 6, ISSUE 34 | OCTOBER 26, 2010

Orthopedics This Week

week in review

picture of success

breaking news

For all news that is Ortho, read on.

Orthopedic Power Rankings

Robin Young's Entirely Subjective Ordering of Public Orthopedic Companies

This Week: Resilience. It's impossible not to be impressed with Stryker's report this past week. And to realize that orthopedics remains the bedrock of medicine. Arthritis, fractures, back pain, osteoporosis, sprains, nerves and muscle damage. Orthopedics, as a business, is nothing if not resilient and the numbers this quarter, we think, are demonstrating that.

Rank	Last Week	Company	TTM Op Margin	30-Day Price Change	Comment
1	1	Alphatec	1.59%	13.88%	Technology portfolio bolstered by "Merlot" bone anchor. Target: Adult deformity—one of spine's fast growing segments.
2	3	Stryker	24.71	5.68	Stryker significantly outperformed expectations in Q3. MedSurg up 48%!!
3	8	Zimmer	27.69	1.36	Q3 results expected this week. SYK's strong report pulls ZMH up. Consensus is 2% sales growth. Upside surprise coming?
4	5	CONMED	8.76	8.84	SYK's MedSurg surge directly implicates CNMD's Linvatec sub. Q2 delivered 23% upside. Could Q3 surprise too?
5	6	Integra LifeSciences	15.37	6.79	New buyers coming into IART in advance of this Wednesday's earnings release. Consensus calling for 6% sales growth.
6	7	Johnson & Johnson	27.10	2.97	This is one of those times when it's a shame DePuy is hidden in JNJ. As most analysts expected, JNJ reported down sales.
7	4	Orthofix	13.51	(8.70)	OFIX is the least expensive stock in ortho—yet beats the estimates every single quarter. OFIX doesn't get the respect it deserves.
8	2	Kensey Nash	38.72	(3.27)	Missed estimates last quarter. Right now investors are looking for GARP—growth at a reasonable price. That's not KNSY.
9	NR	Medtronic	32.59	7.20	Back on the Power Rankings on the strength of slowly rising analyst expectations.
10	9	Smith & Nephew	22.83	0.77	Last year, SNN reported a stellar Q3 beating all expectations. Can they repeat? The Street says "no."

Robin Young's Orthopedic Universe

Top Performers Last 30 Days

	Company	Symbol	Price	Mkt Cap	30-Day Chg
1	TiGenix	TIG.BR	$2.91	$90	49.3%
2	Alphatec Holdings	ATEC	$2.38	$208	13.9%
3	NuVasive	NUVA	$36.47	$1,440	12.0%
4	CONMED	CNMD	$22.78	$656	8.8%
5	Orthovita	VITA	$2.16	$166	8.5%
6	CryoLife	CRY	$6.32	$178	8.2%
7	Mako Surgical	MAKO	$10.94	$370	7.8%
8	Medtronic	MDT	$35.75	$38,610	7.2%
9	Integra LifeSciences	IART	$41.20	$1,200	6.8%
10	RTI Biologics Inc.	RTIX	$2.60	$143	5.7%

Worst Performers Last 30 Days

	Company	Symbol	Price	Mkt Cap	30-Day Chg
1	Exactech	EXAC	$15.28	$197	-9.7%
2	Orthofix	OFIX	$28.55	$504	-8.7%
3	Symmetry Medical	SMA	$9.25	$332	-3.4%
4	Kensey Nash	KNSY	$28.42	$253	-3.3%
5	TranS1	TSON	$2.40	$50	-2.4%
6	Bacterin International	BIHI.OB	$7.45	$265	-0.3%
7	Smith & Nephew	SNN	$44.43	$7,900	0.8%
8	Zimmer Holdings	ZMH	$51.29	10,310	1.4%
9	Johnson & Johnson	JNJ	$63.81	75,760	3.0%
10	*Average*			*11,944*	*3.7%*

Lowest Price / Earnings Ratio (TTM)

	Company	Symbol	Price	Mkt Cap	P/E
1	Medtronic	MDT	$35.75	$38,610	10.68
2	Zimmer Holdings	ZMH	$51.29	$10,310	12.21
3	Exactech	EXAC	$15.28	$197	12.35
4	Kensey Nash	KNSY	$28.42	$253	12.65
5	Wright Medical	WMGI	$15.04	$590	13.24

Highest Price / Earnings Ratio (TTM)

	Company	Symbol	Price	Mkt Cap	P/E
1	Smith & Nephew	SNN	$44.43	$7,900	61.19
2	Synthes	SYST.VX	$123.54	$14,662	34.53
3	RTI Biologics Inc	RTIX	$2.60	$143	34.00
4	NuVasive	NUVA	$36.47	$1,440	29.96
5	Symmetry Medical	SMA	$9.25	$332	24.16

Lowest P/E to Growth Ratio (Earnings Estimates)

	Company	Symbol	Price	Mkt Cap	PEG
1	Orthovita	VITA	$2.16	$166	-6.06
2	Mako Surgical	MAKO	$10.94	$370	-0.26
3	TranS1	TSON	$2.40	$50	-0.17
4	Orthofix	OFIX	$28.55	$504	0.57
5	Exactech	EXAC	$15.28	$197	0.89

Highest P/E to Growth Ratio (Earnings Estimates)

	Company	Symbol	Price	Mkt Cap	PEG
1	CONMED	CNMD	$22.78	$656	17.72
2	Alphatec Holdings	ATEC	$2.38	$208	3.52
3	Kensey Nash	KNSY	$28.42	$253	2.94
4	Johnson & Johnson	JNJ	$63.81	175,760	2.14
5	*Average*			*$11,944*	*1.89*

Lowest Price to Sales Ratio (TTM)

	Company	Symbol	Price	Mkt Cap	PSR
1	RTI Biologics Inc	RTIX	$2.60	$143	0.88
2	Orthofix	OFIX	$28.55	$504	0.89
3	CONMED	CNMD	$22.78	$656	0.91
4	Symmetry Medical	SMA	$9.25	$332	0.99
5	Exactech	EXAC	$15.28	$197	1.05

Highest Price to Sales Ratio (TTM)

	Company	Symbol	Price	Mkt Cap	PSR
1	TiGenix	TIG.BR	$2.91	$90	321.16
2	Bacterin International	BIHI.OB	$7.45	$265	26.92
3	Mako Surgical	MAKO	$10.94	$370	11.20
4	Synthes	SYST.VX	$123.54	$14,662	8.13
5	NuVasive	NUVA	$36.47	$1,440	3.40

Buddy, Can You Spare a Residency Slot?

By Elizabeth Hofheinz, M.P.H., M.Ed.

Jacek Tylicki/Wikimedia Commons

More medical students, fewer residency spots, and a burgeoning patient base—all are coming down the track. And while it would be nice to say that there's light at the end of this tunnel, in fact, say our experts, it looks like there could be a train wreck instead.

Dr. Jeff Wiese, Associate Dean for graduate medical education at Tulane University, has watched residency funding dry up for several years now. He states, "While residency funding has always been somewhat of a challenge, in the last few years it has been increasingly difficult. The Association of American Medical Colleges has rightly called for an increase in medical school enrollment to meet the demand for physicians. The problem, however, is that there has been no corresponding increase in funding for residents. This is a huge disconnect…there is an increase in U.S. medical school graduates entering residency, but in the absence of more funded residency positions, there is not a corresponding increase in residency graduates entering practice."

"Virtually all residency funding in the U.S. comes from the Centers for Medicare and Medicaid Services (CMS). And while CMS has capped the number of residency spots, almost all teaching hospitals are above the cap, meaning that these hospitals have made the determination that it is less expensive to enroll residents than to bring on full time staff. This is probably untenable, however, given the Accreditation Council for Graduate Medical Education (ACGME) requirements regarding resident supervision."

A budgetary plan along the lines of, 'robbing Peter to pay Paul' doesn't sound, well, very sound. But indeed, says Dr. Wiese, this is what is happening in many residency programs. "With residency positions capped, it's a zero-sum game. When more manpower is needed in one program, it necessitates reducing another program. Those involved with the program being curbed naturally protest. And with all programs under pressure to adhere to the new ACGME duty hour requirements, no program is interested in having its complement reduced."

As for the residents, says Dr. Wiese, they are typically removed from the financing pinches. "Residency budgets are fixed, so residents usually don't feel these pressures. If there is a substantial shortfall in the number of residents to do the work required, however, the situation is different because the existing residents have to work harder to pick

"This is a huge disconnect…there is an increase in U.S. medical school graduates entering residency, but in the absence of more funded residency positions, there is not a corresponding increase in residency graduates entering practice."

up the slack—*all the while* still trying to stay within the 80-hour work week."

In the past, those on the hunt for funding would pick up the phone and call their friends at XYZ manufacturer. That is only a bit of nostalgia these days, however. "We have not pursued industry funding as we want to avoid any suggestion of impropriety. There is funding available from the Health Resources and Services Administration, but the grants are very competitive and are, on their own, unlikely to meet the total need. And even then, these grants are usually five years in duration, making long-term sustainability of these positions untenable."

While multiple entities are attempting to bring attention to the issue of residency funding, says Dr. Wiese, there is no coordinated symphony as of yet. "We can debate forever about the number of doctors needed, but everyone agrees that a shortfall is imminent. Increasing the number of medical students doesn't do any good if you can't get them through residency. The only thing that is going to rectify this situation is the formulation of a multispecialty collaborative effort that can approach political lobbies and CMS."

Dr. McCollister Evarts, former CEO of the University of Rochester Medical Center, was formerly Chief of Orthopaedics at both the Cleveland Clinic and the University of Rochester Medical Center, and former CEO, Senior Vice President for Health Affairs and Dean at Penn State's Hershey Medical Center. He states, "Because of the resident cap, any time a department grows in faculty or in activities there is not a parallel growth in the number of residents. The gap is often filled in either by funding transferred from hospitals or by funds from the departments themselves. In some instances the faculty members are supporting resident spots. Resident salaries and benefits for orthopedics are approximately $70,000-$75,000 per year—not to mention malpractice insurance."

Ed Edahl/Wikimedia Commons

"OMeGA has created a mechanism whereby pooled industry funds can be transferred to various departments that are then distributed by an independent party. The contributors can direct the funds to a given subspecialty, but they cannot 'earmark' the funds for any certain program or resident."

In the future will we hear newly minted M.D.s floating around the community…asking, for example, "Do you want fries with that?" Dr. Evarts: "There are 15 new medical schools coming online in the next few years—how will these potential residents be funded?"

A model that could work, says Dr. Evarts, is the one being undertaken by the OMeGA Medical Grants Association. "OMeGA has created a mechanism whereby pooled industry funds can be transferred to various departments that are then distributed by an independent party. The contributors can direct the funds to a given subspecialty, but they cannot 'earmark' the funds for any certain program or resident. Many more such funding mechanisms will be needed in the coming years."

Also concerned about the residency funding situation is Charlie Clayton, Vice President for Policy at the Alliance for Academic Internal Medicine (AAIM). He notes, "In the last ten years there has been at least a 20% reduction in the indirect medical education funds that Medicare pays to teaching hospitals. Also at issue is that state funding for graduate medical education—which is largely financed through Medicaid—has gone down. Faculty often contribute to residency funding, but such monies are typically only sufficient to cover the rudimentary costs involved. Let's take a look at all of the costs involved in supporting a resident: salary and benefits, faculty time for teaching, the use of simulators, online evaluation systems, and administrative costs like recruiting. In many cases, external funding, mostly Medicare GME payments, will cover the costs related to resident salaries and benefits, but will not pay for any of the other costs. How the gap will be filled depends on the relationship between the hospital and the department/faculty and what they can negotiate."

For Clayton and others, the elephant in the room, however, is, "What about the money being distributed at present?" "Several parties are advocating for increased accountability for the monies that are being distributed now. The Medicare Payment Advisory Commission has recommended to Congress that one-third of the earmarked funding be put into a pool and only released if recipients can prove that they are meeting certain requirements. The goal is to ensure that programs are graduating residents who are prepared to provide solid patient care. To meet this goal every specialty needs to examine how they are training doctors and how that training is aligned with the needs of patients."

Clayton adds: "Although we at the AAIM tried to get Medicare to support more residency spots as part of the healthcare reform, this did not come to fruition. We are pleased, however, that the reform act did include a provision to form a healthcare workforce commission that will be advising Congress."

With six patients in various exam rooms, a pile of paperwork, and staffing issues, the average doctor may not often consider the issue of residency funding. But, says Clayton, they will feel it soon enough. "It is important that all parties concerned take workforce shortages and funding accountability seriously. The situation has only worsened over the last 20 years; sometimes it seems that we are at a point where the community has 'cried wolf' too many

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“Let’s take a look at all of the costs involved in supporting a resident: salary and benefits, faculty time for teaching, the use of simulators, online evaluation systems, and administrative costs like recruiting. In many cases, external funding, mostly Medicare GME payments, will cover the costs related to resident salaries and benefits, but will not pay for any of the other costs.”

times, i.e., changing positions on possible physician shortages to saying there will be an oversupply. I will say that there is one positive change…the VA is expanding its support for residency slots (principally in primary care, but also in orthopedics).”

Years ago those in the halls of power had to face the Redcoats. As resources dwindle and patients increase, going forward it just may be the Whitecoats—and their friends in advocacy—with whom the powerful must contend. ◆

Parting the ReGen Clouds?

By Walter Eisner

The FDA's top device regulator, Jeff Shuren, M.D., J.D., informed ReGen Biologics on October 14 that he intends to rescind the 510(k) clearance granted the company's Menaflex device by his predecessor Dan Schultz, M.D., in December 2008.

Jeff Shuren, M.D.

Wikimedia Commons/ReGen logo/Photo manipulation by RRY Publications LLC

Shuren wrote that his decision is based on the fact that the device "does not have the same intended use as any of the identified predicate devices. Alternatively, even if the device had the same intended use as any of the identified predicate devices, the differences between the technological characteristics of the device and each of the predicate devices raise different questions of safety and effectiveness."

He may have, however, offered a potential olive branch.

Subject to Special Controls?

"Before we take any action on your clearance," wrote Shuren, "we would like to discuss the appropriate marketing pathway for the device and data requirements...If there is sufficient information to establish special controls to provide reasonable assurance of the safety and effectiveness of the device, FDA may classify the device in class II, subject to special controls."

The safety of ReGen's Menaflex has never been an issue. Two FDA orthopedic panels meeting in 2008 and 2010 told the FDA that the device was safe but that the device's effectiveness was unclear.

Rescission Power

Rescission is a rare and seldom used enforcement tool. The FDA's authority to rescind a previously cleared device is uncertain and Shuren has made the clarification of the agency's rescission authority a top priority in recommendations to revamp the entire 510(k) program. Shuren's boss, FDA Commissioner Margaret Hamburg, M.D. told an audience of device manufacturers on October 20 that rescission should be used for "public health protection."

Mark DuVal, a Minnesota attorney who specializes in FDA and regulatory issues put it more succinctly:

"ReGen followed the rules. ReGen lawfully obtained a clearance in 2008. Yet FDA plans to rescind their clearance. We are not sure what FDA's theory for rescission is, but we are confident, absent fraud, FDA does not have the legal grounds for rescission. What FDA seems to be confident in is that ReGen may not have the financial wherewithal to defend itself. If so, a clearly inappropriate and illegal rescission challenge may stand. FDA's use of publicity has certainly destroyed the market for

December 2008-ReGen obtains clearance for the Menaflex device.

March 2009-Commissioner Hamburg is nominated to lead FDA and is confirmed in May.

May 2009-Agency whistleblowers claim the clearance process for ReGen's device was inappropriately influenced by four New Jersey Congressmen and FDA's management including former Commissioner Von Eschenbach and then sitting CDRH Director Dan Schultz.

August 2009-CDRH Center Director Dan Schultz resigns under pressure.

September 2009-CDRH commissions the Institute of Medicine to take an "independent" look at the 510(k) program.

September 2009-Agency releases a report, written by Dr. Jeff Shuren, who was then "Associate Commissioner for Policy and Planning," that concludes the ReGen clearance process was compromised.

January 2010 -Dr. Shuren becomes the Director of CDRH.

March 2010-Dr. Shuren convenes the Orthopaedic and Rehabilitation Devices Panel to evaluate ReGen's Menaflex device. The Panel concludes the device is "safe."

June 2010-Curiously, CMS announces a national non-coverage decision. Frustrated, ReGen states it didn't solicit a coverage decision and that Menaflex isn't intended for a Medicare population.

September 2010-FDA publishes a 120-page report containing changes it recommends for the 510(k) program.

October 2010-FDA announces it will rescind ReGen's clearance for the Menaflex device.

ReGen Biologic/FDA Timeline

Source: Mark DuVal

the product anyway—a case of being judged guilty before the opportunity to prove innocence.

"In the wake of FDA activity lays a suffering patient population with few treatment options for meniscus repair, patients with permanent implants from a company that will probably disappear because of the rescission, and laid-off ReGen employees looking for work in a suffering economy. Who gains? If a CDRH (Center for Devices and Radiological Health) Director and two expert panels determined the device was "safe," why is it being taken off the market? Out of concerns of efficacy? Aren't practicing physicians in the marketplace capable of determining a device's efficacy?"

CMS Non Coverage

Then there is the issue of the CMS (Centers for Medicare and Medicaid Services) non-coverage determination for the device this past June. Very few, if any, of the devices are implanted in patients over 65. According to the company, the device is designed to guide new tissue growth using the body's own healing process to reinforce and repair the meniscus in patients with an irreparable meniscus tear or loss of meniscus

Re Gen Menaflex

> **"For CDRH to arrive at the decision that the device has a new intended use four years after two senior CDRH officials informed the company that the device could be reviewed through the 510(k) program is totally unbelievable," said Bisbee.**

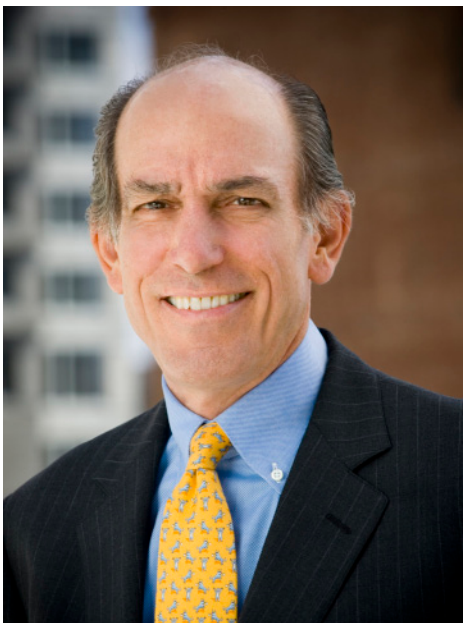
tissue. The device provides a resorbable scaffold for the growth of new tissue in the meniscus.

The company did not request coverage from Medicare and a company spokesperson tells *OTW* that he understands the coverage determination was generated from staff within CMS.

A Way Out

Since protecting the public's health doesn't appear to be at issue here, has Shuren found a way out of one of the most painful, confusing and acrimonious device reviews in recent memory?

Gary Bisbee, Jr., Ph.D., ReGen's Chairman and CEO told *OTW* in an interview on October 19, that if Shuren's offer to meet and see if the device can get cleared subject to special controls, is genuine, the company would be satisfied.



Gerald Bisbee

Bisbee: Politics Not Science

Bisbee's initial reaction to Shuren's letter was not quite as measured however.

On October 18, Bisbee issued a statement saying that politics, not science was driving FDA's actions.

"For CDRH to arrive at the decision that the device has a new intended use four years after two senior CDRH officials informed the company that the device could be reviewed through the 510(k) program is totally unbelievable," said Bisbee.

"The [Center] rigorously reviewed and cleared the [device] for use in the U.S. after the first independent Advisory Panel Meeting in November 2008," said Bisbee. "Since then the FDA has created storylines about the review process to discredit this clearance, as well as taken numerous actions that are illegal or well outside its existing statutory authority."

The storyline referred to by Bisbee includes allegations that the company hired lobbyists and made campaign contributions to Congressmen and Senators who strong armed the agency into clearing the device. This storyline has been perpetuated by stories in the *Wall*

"Contrary to the story that FDA is telling, that determination could not have been affected by any political influence because ReGen did not seek the assistance of New Jersey legislators until almost a year later, in late 2007. Even then, it was only after receiving a rejection of its submission based on an illegal review standard, following nearly two years of review. These members of Congress asked the FDA to examine the ReGen matter and insure that the review was treated fairly and consistent with existing agency regulations."

Street Journal citing leaked government documents.

The agency's own legal counsel said in a review of the ReGen case that the company did nothing wrong. In fact, the reports confirmed that the agency's reviewers were applying the wrong standard to the device. Repeated requests from *OTW* to the agency for details of alleged and improper influence on the agency's reviewers have been met with vague and unsubstantiated references.

Bisbee says the FDA's determination that the device could be reviewed under 510(k) criteria as a surgical mesh was made in November 2006 by the director of the agency's Office of Device Evaluation.

"Contrary to the story that FDA is telling, that determination could not have been affected by any political influence because ReGen did not seek the assistance of New Jersey legislators until almost a year later, in late 2007. Even then, it was only after receiving a rejection of its submission based on an illegal review standard, following nearly two years of review. These members of Congress asked the FDA to examine the ReGen matter and insure that the review was treated fairly and consistent with existing agency regulations."

Bisbee pointed to a larger agenda on the FDA's plate. "The politics surrounding changes suggested in the 510(k) program appear to underlie FDA actions, for example, a group of dissident FDA reviewers has sought legislative intervention because of their dissatisfaction with the current regulations and agency management." He says the agency's clearance of his device has become a political football and the FDA is not playing by the rules.

ReGen Ready to Meet

The company will meet with Shuren within the next 30 days and see if Shuren's offer is the real deal or a simple boilerplate response to all companies that are told their device is not substantially equivalent to a predicate device.

Bisbee told *OTW* that ReGen has never looked to pick a fight with the FDA and if Shuren's suggestion of considering a different regulatory pathway comes to fruition, the company will be satisfied.

The product continues to be marketed and sold in Europe, but the supply is dwindling down as the company has been forced to lay off employees and close down its manufacturing plant in Redwood City, California.

The cloud of the FDA stopped the company's ongoing surgeon training programs, continuing sales in the U.S. and raising capital. After spending $30 million to get clearance, this device has not only been the most studied 510(k) in history, but probably also the most expensive.

Bisbee says if the company can get out from under this FDA cloud, they will be able to resume production, resupply their European shelves, resume U.S. surgeon training and raise capital from investors.

Solomon or McCarthy

The pages of *OTW* have been filled with stories accusing the FDA of being arbitrary, capricious, violating the equal protection and due process

rights of ReGen and strong warnings from industry representatives that such unprecedented actions could only serve to stifle innovation in the U.S. The comparison to the McCarthy era of the 50's was even noted.

Is this Shuren's opportunity to clean up a previous FDA administration's mess, demonstrate his commitment to innovations as he seeks to reform the 510(k) program, placate his whistleblowing scientists, promote the public's access to new devices and demonstrate how his proposal for a new Class IIb category might have prevented this?

We asked Dr. Shuren for comment, but received no response.

Device manufacturers will be watching as leaders measures Shuren's credibility in how he deals with one of industry's weakest members.

As Shuren attempts to reform the 510(k) program, ReGen becomes his real-world test of whether he and his agency are more like Solomon than McCarthy. ◆

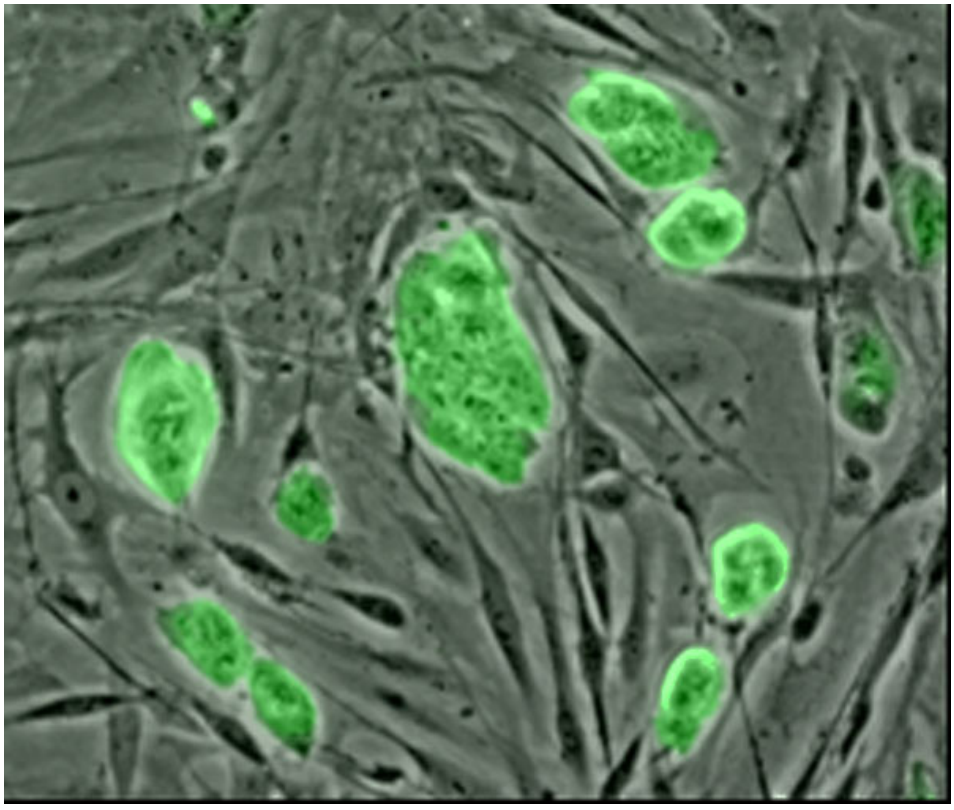
Finally at Phase I

By Jacqueline Rupp

The world's first FDA approved study of a therapy based on human embryonic stem cells is under way. That's the story making headlines this recently. But what a long, winding, tortuous regulatory path it's already been for owner Geron Corporation of Menlo Park, California.

On Monday, October 11, the long-awaited press release came out. On the immediately preceding Friday, a patient with a spinal cord injury was injected with a treatment containing human embryonic stem cells (hESC) and thereby formally kicking off the larger clinical trial of human embryonic stem cells to treat spinal cord injury.

In the rat model this therapy had restored locomotion. Geron bought the rights to the therapy and committed significant resources to the promise that these impressive results might be duplicated in humans. In other words, paralyzed humans may be able to move again—albeit in some limited way. No question, this trial marks a milestone in the hESC arena. But it is only the first glint of any light at the end of the tunnel for Geron.



Stem Cells/Creative Commons

Geron's Tortuous Road to Trials

Geron is a twenty-year-old biotech company laboring in the fields of biopharmaceutical treatments for such indications as cancer, spinal cord injury, heart failure and chronic degenerative diseases like diabetes. The company began in Delaware and but moved to biotech central in California. Geron Bio-Med is the corporation's wholly owned subsidiary based in Edinburgh, Scotland. Geron is one of only a few companies dedicated to developing clinical therapies with human embryonic stem cells. Most firms in the stem cell arena choose the quicker, adipose or allogenic adult stem cell pathway.

In January 2009, Geron received FDA clearance to commence with an Investigational New Drug (IND) application for the clinical trial of GRNOPC1 in patients with acute spinal cord injury. This clearance allowed Geron to set in motion a Phase I, multi-center study plan. Then, in August, the FDA placed a clinical hold on the IND for GRNOPC1 pending further review of a nonclinical animal study. The staff at the FDA thought that there might have been evidence of a higher frequency of cysts among animals in the study. In October 2009, after reviewing the data with the FDA, Geron agreed to conduct further preclinical studies and settle the cyst issue. This pushed Geron's clinical trial back to late 2010.

Given that history, the news last week that the Phase I trial is ON was a clear positive for the company and its shareholders. The stock rose 10% on news. For Geron, it's been an extraordinarily expensive process to get to this point. Fully $180 million has been spent over the past three years on preparing for

Shepherd Center/Shepherd Center

this study and driving its other product development programs. With $115 million in cash left on the books, the company clearly needs to get a product to market sooner than later.

But, again, this is Phase I. A two-year Phase I. Then comes the negotiations with the FDA for Phase II. Then phase II. It's been twenty years already for Geron. Entire careers will have started and ended by the time Geron's first products hit hospitals.

One of the pioneers of the regenerative technologies industry, Jamie Grooms, presently President of nerve allograft company AxoGen (which is bringing to market its own nerve product Avance) had this to say about Geron's announcement. "This is exciting on two multiply fronts. First this [trial] is important to the United States. We have fallen behind in research and product development as it relates to stem cell programs. Assuming this technology moves through the clinical trial phase and become a commercial product it will establish a pathway for other stem cell programs. And health care needs these types of product belonging to my favorite class of technologies. This is truly Regenerative Technologies. Restoring both form and function back to the patient. Finally, restoring function to patients with spinal cord damage will bring tears to all those involved. A success with this trial will also bring hope to millions suffering with spinal cord damage as well as many other etiologies."

The Path to Trials

The trial's principal study site is the private, non-profit Shepherd Center, of Atlanta, Georgia, a rehabilitation hospital and clinical research center for spinal cord and brain injuries.

As might be expected, Geron's trial actually fits within the context of years of previous research (over a decade to be exact in the case of this treatment). The treatment being tested by Geron originated from the work of UC Irvine neurobiologist Hans Keirstead and his team at the Reeve-Irvine Research Center. Using a rat model, Dr. Keirstead demonstrated that this particular stem cell approach was extremely promising and in the hands of Geron it has managed to make through the regulatory gauntlet to Phase I.

Keirstead's approach is, we think, instructive and explains why Geron has been able to get an hESC to Phase I where other firms have failed. Keirstead's research focused on the processes required to push hESCs up the lineage and differentiate into oligodendrocytes. These hard-to-pronounce cells act as insulation for nerve fibers with their myelin exteriors. Keirstead theorized that if these protective cells could be regrown, perhaps it might be enough of a connection to allow nerves to regenerate and form a viable pathway for neurological signals to move. Many spinal

cord injuries, in fact, don't involve the severing of the cord. Instead, in most cases, the inability of nerves to transmit signals is due to damage to this myelin sheathing.

Keirstead's rat studies clearly demonstrated that his hypothesis was correct. In his studies, paralyzed rats treated with hESCs regained locomotion and, in some cases, even recovered the ability to run.

And They're Off…

Keirstead's treatment, now Geron's product, is finally beginning the earliest stage of a clinical trial, Phase I. The FDA and the company will be measuring safety—for ten patients. The patients accepted are all suffering from a spinal cord injury (complete American Spinal Injury Association (ASIA) Impairment Scale grade A, between the third and tenth thoracic vertebrae). But this trial isn't for long-time spinal injury sufferers. Only those who were injured two weeks prior can qualify for receiving the injectable therapy.

X-ray of lumbar spine/Creative Commons

The next step if all goes well in Phase I is to test for efficacy, with the host site moving to Northwestern University in Chicago, Illinois. Plans are in place to utilize a number of sites throughout Geron's clinical trial process, with a proposed seven centers eventually playing host. After the last patient is enrolled, the waiting and measuring period begins. The trial has a two year follow up requirement.

Meet GRNOPC1

The hESC being used in this trial specifically are derived oligodendrocyte progenitor cells, GRNOPC1. Initiating the GRNOPC1 clinical trial is a milestone for the field of human embryonic stem cell-based therapies," said Thomas B. Okarma, Ph.D., M.D., Geron's President and CEO. "When we started working with hESCs in 1999, many predicted that it would be a number of decades before a cell therapy would be approved for human clinical trials. This accomplishment results from extensive research and development and a succession of inventive steps to enable production of cGMP master cell banks, scalable manufacture of differentiated cell product, and preclinical studies in vitro and in animal models of spinal cord injury, leading to concurrence by the FDA to initiate the clinical trial."

GRNOPC1 is the key to Keirstead's work. It contains oligodendrocyte progenitor cells from hESC which the research has shown regenerate myelin and also has properties that stimulate nerve growth according to Geron. These effects are linked to results like improved locomotion abilities and kinematic scores in animal models with spinal cord injury.

And although a spokesperson for the Shepherd Center told OTW they are not doing interviews for the clinical trials, they did release this statement by the center's medical director, Donald Peck Leslie, M.D., "We are pleased to have our patients participating in this exciting research. Our medical staff will evaluate the patients' progress as part of this study. We look forward to participating in clinical trials that may help people with spinal cord injury."

Geron is one of several stem cell companies tackling the problem of nerve injury. The New York Stem Cell Summit, sponsored by *Orthopedics This Week*, is featuring nerve regeneration as a separate section of the meeting and four companies will be presenting data on the ability of adult and embryonic stem cells to treat nerve injury.

As the only hESC-based nerve regeneration therapy, Geron is getting its fair share of publicity. Clearly, a study is long overdue. Now that the study has started, we would hope and expect to see a steady stream of information about the studies progress and, most importantly, these patients's progress.

As Keirstead has often commented, success in this trial sets up the potential for these therapies to address such other significant nerve impairments as lack of bowel or bladder control or loss of sexual function.

Now, if only there was a stem cell therapy to address the degeneration and pain of the FDA. ◆

company

DePuy Inches Ahead

Photo manipulation by RRY Publications LLC

Johnson & Johnson should be thanking the medical device gods or their quarter would have been really dismal.

The health care giant reported $15 billion in sales for the third quarter of 2010. This was a 0.7% decline with a string of recalls causing the company's sales of nonprescription medicines to plunge 40%.

Medical Devices and Diagnostics is now the company's largest division. Sales in that division, including DePuy, rose 1.3% to $5.92 billion for the quarter.

DePuy's sales of $1.309 billion were a 1.9% increase over last year's third quarter.

Like competitors in the market, company officials sang the same tune to Wall Street analysts about pricing and volume pressures, austerity programs in Europe and a tough macro climate with patients delaying procedures.

DePuy continues to be the market leader in hips, but the company's sales were negatively affected by metal-on-metal concerns.

—WE (October 20, 2010) ◆

Stryker's 3Q Footprint "Kicks…."

Stryker's CPCEO (Chairman, President and CEO), Stephen MacMillan never disappoints for metaphors and told Wall Street analysts he likes the company's broad-based industry footprint.

While the company's orthopedic implant sales rose only 1.2% in the third quarter of 2010, its medical surgical franchise rose a hefty 16.1%. Overall, the "footprint" allowed the company to report third quarter sales of $1,768 million, up 6.9% over the previous year's third quarter.

As we've heard from other CEOs, the macro environment of deferred surgical procedures was the main driver of lower sales growth for implants.

Wikimedia Commons/RRY Publications

Improved Market Backdrop

"Although we are pleased that recon unit and price trends did not materially worsen in the third quarter, we hope and expect that the combination of our new hip products and the gradual recovery involvements will contribute to an improving market backdrop in the coming quarters," said MacMillan in a conference call analysts on October 19.

"We are also encouraged that certain regions and divisions that have been underperforming, including Europe and spine, reversed course in the quarter and posted a sequential, albeit modest, acceleration in sales growth."

The results allowed MacMillan to raise sales expectations for full-year sales growth to 7% to 8%, up from to 5% to 8%.

R&D for Differentiation

Allaying fears that device manufacturers would slash their R&D budgets due to the device tax included in this year's health care bill, MacMillan noted that the company increased its R&D budget by 18% for the quarter. And that percentage will stay ahead of sales growth numbers. The result of the legislation is that more money is going to be spent on healthcare, said MacMillan.

MacMillan saw opportunities for differentiation during this period of slower sales growth in orthopedics. He believes if the existing sales growth numbers remain at current levels, larger players

will benefit. These comments echoed what Medtronic's Bill Hawkins told analysts last month. A tougher regulatory environment will benefit those companies that have the financial resources to invest in expensive trials needed to demonstrate a new products' safety and cost effectiveness.

With $4.15 billion in cash, Stryker has the resources to develop or buy whatever differentiation the company wants.

"A Different Company"

MacMillan commented on the company's string of FDA warning letters over the past three years, as well as Stryker's response with a three-year quality and compliance program. The CPCEO said said, "The warning letters made us a better company. We are fundamentally a different company."

With a broad-based footprint [and bulging purse], MacMillan says, "We like where we're headed."

—WE (October 20, 2010) ◆

legal

Synthes Settles Norian Indictment

Synthes announced earlier this month that the company has reached a settlement with the U.S. Department of Justice (DOJ) and the Office of Inspector General of the Department of Health and Human Services (OIG) relating to the government's inquiry into certain test marketing and promotional practices from May 2002 to July 2004 involving a bone cement product of Synthes' Norian subsidiary.

Morguefile

Synthes has agreed pay $808,000 in settlement, fines and forfeiture payments for a single misdemeanor violation of the U.S. Food, Drug and Cosmetic Act, and has agreed to divest the assets of its Norian subsidiary. Norian will pay fines and forfeitures of approximately $23.5 million for one felony and numerous misdemeanor violations of the Act.

Corporate Integrity Agreement

Synthes has also agreed to enter into a Corporate Integrity Agreement with the OIG. The company will retain an Independent Review Organization to help the company monitor and evaluate compliance in its promotional and product-related business functions.

U.S. Attorney Zane David Memeger said that device manufacturers have legal obligations not to test their products on humans without FDA oversight. "This case is especially troubling because in search of greater profits Norian bypassed this process," Memeger said.

Four individuals; Michael Huggins, Thomas Higgins, Richard Bohner, and John Walsh are still awaiting sentencing after pleading guilty to a misdemeanor shipping charge.

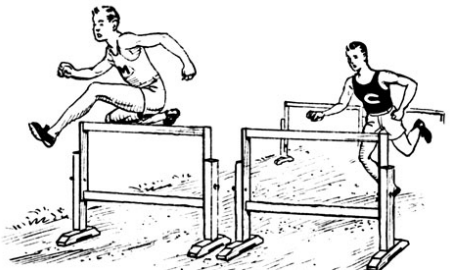
The settlement will become effective upon court approval of the agreements.

—WE (October 22, 2010) ◆

large joints

OA Drug Moving Across Europe

Regulatory issues could give one an ulcer…in this case—hurdles cleared. AstraZeneca and POZEN Inc. today announced that VIMOVO (naproxen/ esomeprazole magnesium) 500/20 mg modified-release tablets has cleared an important regulatory milestone by receiving positive agreement for approval in 23 countries across the European Union (EU).



Pearson Scott Foresman/Wikimedia Commons

VIMOVO, co-developed by AstraZeneca and POZEN Inc., is indicated for the symptomatic treatment of osteoarthritis (OA), rheumatoid arthritis (RA), and ankylosing spondylitis (AS) in patients who are at risk for developing non-steroidal anti-inflammatory drug (NSAID)-associated gastric and/or duodenal ulcers and where treatment with lower doses of naproxen or of other NSAIDs is not considered sufficient.

VIMOVO is a fixed-dose combination of enteric-coated naproxen, a pain-relieving NSAID, and immediate-release esomeprazole, a proton pump inhibitor (PPI). The positive agreement is based on a submission package including data from the pivotal trials PN400-301 and PN400-302, which demonstrated that patients taking VIMOVO experienced significantly fewer endoscopic gastric

ulcers, compared to patients receiving enteric-coated naproxen.

"This support for the approval of VIMOVO in Europe is a significant milestone, which we believe will provide a new treatment option for the millions of arthritis patients in the EU at risk for NSAID-associated ulcers," said Lori Kreamer, Global Products Vice President, AstraZeneca, in the news release. "In one tablet, VIMOVO offers the proven pain relief of naproxen with built-in ulcer risk reduction."

An AstraZeneca spokesperson told *OTW,* "AstraZeneca will now work to pursue pricing/reimbursement and national approvals. Launch will be determined at the national level."

—EH (October 22, 2010) ◆

Vitamin D, IBD, and Osteoporosis

Certain people might want to put milk, cheese, and yogurt in a blender and stand in the sun…Researchers are reporting that Vitamin D deficiency puts patients with Inflammatory Bowel Disease (IBD) at greater risk of osteoporosis, osteopenia and an overall higher rate of abnormal bone density, according to the results of a new study.

Children and adults with IBD between the ages of 10 and 70 participated in the prospective study between 2008 and 2010. Vitamin D deficiency was defined as Vitamin D 25-hydroxy levels less than 30ng/mL. DEXA scan results were considered abnormal if osteopenia and osteoporosis were found. The study found that of the 161 IBD patients in the cohort, reduction in bone density with a diagnosis of osteoporosis or osteopenia was found in 22% of these patients, 50% of whom were under age 50.

"IBD patients with an abnormal bone density exam had a significantly higher rate of Vitamin D deficiency than those who had normal DEXA scans," said Dr. Bincy P. Abraham in the news release. Dr. Abraham is Assistant Professor of Medicine at Baylor College of Medicine and Director, Baylor Clinic Inflammatory Bowel Disease Program.

Dr. Abraham said that previous research has suggested a high preva-

Teunie/Wikimedia Commons

lence of osteoporosis and overall abnormal bone density in IBD patients that is likely caused by corticosteroid use and excess of inflammatory cytokines, as well as from calcium and Vitamin D malabsorption.

The study found that Crohn's disease patients with Vitamin D deficiency were four times more likely to have a higher rate of abnormal bone density exams compared to patients with ulcerative colitis. "This finding is not surprising since Crohn's disease usually affects the small intestine, which is the part of the gut that absorbs the most nutrients," added Dr. Abraham. "The widespread malabsorption in Crohn's disease does not occur in ulcerative colitis, which involves only the colon."

However, both Crohn's disease and ulcerative colitis patients diagnosed with osteoporosis had a significantly higher rate of Vitamin D deficiency irrespective of prednisone intake.

As for what led to this work, Dr. Abraham told *OTW*, "I started doing health maintenance monitoring for all my IBD patients. I had the data and looked into the details and found the results I presented. I will now follow these patients over time and monitor if treating vitamin D deficiency actually leads to improvement in their bone density results."

—EH (October 21, 2010) ◆

New Device Aids Repair of Meniscus Tear

Next generation Smith & Nephew device is said to make repairing a meniscus tear easier and more efficient.

Ultra-Fast Fix Meniscal Repair System/Smith & Nephew

Smith & Nephew launches the Ultra Fast-Fix Meniscal Repair Device, an anchoring system that purports to help surgeons better perform meniscus tear repair.

This device assists with the stitching back in place of the damaged meniscus cartilage. Rather than cut away damage tissue as in a meniscectomy, a repair surgery retains the meniscus, which can shorten healing time and lessen the chance of arthritis developing in the future.

In the half-hour operation the device creates tiny stitches into the cartilage that can then hold the torn parts together in this non-invasive surgery. Using a keyhold camera and probes inserted into two small incisions in the front of the knee, the device is inserted via two small needles and carries with it two anchors which ultimately secure both sides of the tear.

This is the newer version of the original FAST-FIX Meniscal Repair System that first launched in 2001. The new system adds easier knot sliding and stronger sutures according to the company. These added features they say offers a faster and more secure repair system, ultimately helping to improve outcomes.

The device also utilizes PEEK-Optima high strength non-absorbable implants that can be used with the company's Ultrabraid suture. However, there is also a bioabsorbable version which uses PLLA implants.

An article published in *The Journal of Sports Medicine* when found that arthroscopic meniscal repair was less likely to aggravate osteoarthritis and enabled patients to return to an active lifestyle more quickly. After eight years, the researchers found no osteoarthritic progress in 80% of the patients who received meniscal repair, while half that number, 40% of those who received a meniscectomy, had no osteoarthritic progress.

—JR (October 19, 2010) ◆

New Screening Interval for Osteoporosis?

No cookie cutter approach to osteoporosis, say a team of experts…A

BenFrantzDale/Wikimedia Commons/RRY Publications LLC

new study led by Margaret L. Gourlay, M.D., M.P.H. of the University of North Carolina at Chapel Hill School of Medicine finds that women aged 67 years and older with normal bone mineral density (BMD) scores may not need screening again for 10 years.

"If a woman's bone density at age 67 is very good, then she doesn't need to be re-screened in two years or three years, because we're not likely to see much change," Dr. Gourlay said in the news release. "Our study found it would take about 16 years for 10% of women in the highest bone density ranges to develop osteoporosis."

Dr. Gourlay and her co-authors analyzed data from 5,035 women aged 67 years and older that were collected as part of the longest-running osteoporosis study in the U.S.— the Study of Osteoporotic Fractures. These women were enrolled in the study from 1986 to 1988 when they were 65 years or older, and had bone mineral density testing starting about two years later. All had bone mineral density testing at least twice during the study period; some were tested up to five times over a period of 15 years.

The researchers calculated estimated times for 10% of the women in each T-score group to transition to osteoporosis. For the high risk group, the estimated time was 1.26 years, while it was about 5 years for the moderate risk group and 16 years for the low risk group. The study concluded that baseline BMD is the most important factor for doctors to consider in determining how often a patient should be screened.

When asked to what extent she thought that this work will result in changes in how doctors practice, Dr. Gourlay told *OTW,* "After we publish the final results in a journal, I think this work will help doctors tailor the osteoporosis screening interval to their patients more accurately. We need to encourage osteoporosis screening in women aged 65 and older because overall rates are low, but our results suggest a one-size-fits-all approach doesn't fit real bone density trends. In particular, elderly women with very good bone density at baseline may only need screening every five years or less."

She also commented to *OTW,* "My team will study other aspects of osteoporosis screening in elderly women, and also in younger (aged 50-64 years) postmenopausal women and men. Our field is far behind other screening research programs, e.g., in cancer screening, and we need to offer primary care physicians much better evidence on osteoporosis screening in the next 10 years."

—EH (October 19, 2010) ◆

extremities

$38.6 Million for Trauma Research Consortium

A civilian/military marriage that could produce concrete, life altering results…The Center for Injury

Research and Policy at the Johns Hopkins Bloomberg School of Public Health has recently been awarded $38.6 million by the Peer Reviewed Orthopaedic Research Program (PRORP) of the U.S. Department of Defense (DOD) to expand its Major Extremity Trauma Research Consortium (METRC). The Consortium, which was established in September 2009 with an award of $18 million from DOD, conducts multi-center studies relevant to the treatment and outcomes of major orthopedic injuries sustained on the battlefield.

Courtesy of Major Extremity Trauma Research Consortium

"The initial funding was critical to establishing the consortium and providing the resources to address some of the immediate research needs of the military in the acute management of severe limb injuries," explained Ellen MacKenzie, Ph.D., in the news release. Dr. MacKenzie is principal investigator (PI) and the Fred and Julie Soper Professor and Chair of the Bloomberg School's Department of Health Policy and Management, the department in which the Center for Injury Research and Policy is housed.

The Bloomberg School serves as the coordinating center for the Consortium that includes a network of core civilian trauma centers working together with the major military medical centers that provide treatment to service members who sustain major trauma while on active duty. Under this new award, the number of core civilian centers will increase from 12 to 24.

"Increasing the number of centers allows for more efficient designs and increased generalizability of the studies we conduct," said Michael Bosse, M.D., of Carolinas Medical Center, in the news release. Dr. Bosse is Chair of the Consortium and co-PI with Dr. MacKenzie.

Dr. MacKenzie told *OTW*, "The prevention and control of infections continues to be a major priority for METRC. One of the newer studies we plan to initiate is an evaluation of a single-stage definitive treatment versus a staged reconstruction approach for septic delayed and non-unions."

She also commented to *OTW*, "The new funding also provides the opportunity to address other topics of importance to the long-term recovery of our military and civilian trauma patients. For instance, we will be conducting a randomized controlled trial to evaluate the effect of multi-modal post operative pain regimen in the treatment of severe lower limb fractures. This is an area of great importance given what we know about the role of early pain management on longer term disability."

For more information, please visit: www.metrc.org

—EH (October 21, 2010) ◆

AOFAS Annual Vietnam Trip

Giving is always a step in the right direction. No one knows that more than the team of foot and ankle surgeons who have recently returned from Vietnam. In fact, 2010 marks the 9th Annual Surgical Outreach Project to Vietnam by members of the American Orthopaedic Foot & Ankle Society (AOFAS). Since the first project in 2002, the AOFAS surgeons have transformed the lives of more than 600 Vietnamese children and adults with lower extremity deformities and disabilities through corrective surgery.

The program involves two teams of visiting AOFAS members who volunteer over a four-week period and work side by side in clinics and operating rooms with Vietnamese orthopedic surgeons and residents. The AOFAS members volunteer their time, pay their own travel expenses, and in the end their own lives are changed by the experience.

Courtesy of American Orthopaedic Foot & Ankle Society

Naomi Shields, M.D. has participated annually for the past nine years. She stated in the news release, "I have seen a lot of changes over the nine years, especially in the traffic and the high-rise buildings. What has not changed has been the friendly welcoming nature of the Vietnamese people, and the overwhelming need especially for the poor and disabled. What we do is a small drop in the bucket of need but for the 600 patients AOFAS surgeons have operated on, that drop has been life changing. I hope we can continue with this project and expand to other countries."

The AOFAS Overseas Outreach Project to Vietnam supported by the Orthopaedic Foot & Ankle Outreach & Education Fund (OEF) is a partnership initiative with the Prosthetics Outreach Foundation (POF). The AOFAS members share new technologies with Vietnamese orthopedic surgeons and in return are exposed to foot and ankle conditions that many have only read about as classic textbook cases. AOFAS also co-sponsored an educational conference on Surgery of the Lower Extremity in Hanoi.

Ruth L. Thomas, M.D., Chair AOFAS Humanitarian Services Committee, told *OTW*, "The mission experience has been overwhelmingly positive. We plan to continue the present format of the project, but mission locations within Vietnam will change based on the need for our assistance. We are considering shifting from sponsoring one large educational seminar to holding multiple smaller regional educational experiences. The orthopedic community of Vietnam understands the AOFAS commitment to education and service and they welcome the return of AOFAS volunteers every year."

She also commented to *OTW,* "The goal of the AOFAS Humanitarian Services Committee is to establish opportunities worldwide for AOFAS members to volunteer their expertise in foot and ankle surgery in a safe environment conducive to teaching and service. Presently we have ties through Health Volunteers Overseas with the major teaching hospital in Kampala, Uganda, and we are working on an organizational plan for AOFAS members to volunteer in Haiti."

—EH (October 20, 2010) ◆

spine

NuQu Trial Ready to Go

ISTO's NuQu uses juvenile cell-based cartilage regeneration technology. Its Phase I trial is ready to get underway now that patient enrollment is complete.

Fifteen patients are enrolled and ready for ISTO Technologies, Inc.'s Phase I clinical trial of NuQu. What is NuQu? It is an injectable treatment for discogenic back pain that uses ISTO's patented juvenile cell-based cartilage regeneration technology. The company says it believes this to be the first cell-based human trial of its kind in the U.S.

ISTO's platform technology uses juvenile chondrocytes that the company says have proven more effective than adult cells in regenerating cartilage tissue. Preclinical studies have shown "greater regenerative potential" for the juvenile chondrocytes in contrast to adult cartilage cells both in vitro and in vivo. NuQu is designed as an early intervention for lower back pain with the goal of regeneration, repair and restoration of the disc.

The Phase I trial will take place at two clinical sites. The patients enrolled all suffer from chronic discogenic back pain, one of the most common forms of lower back pain affecting, according to ISTO, approximately four million patients each year in the U.S.

The enrollees have attempted more traditional treatments without success. ISTO estimates about 500,000 sufferers do not respond to the conservative therapies of bed rest, non-steroidal anti-inflammatory pain medication and physical therapy.

A recent study published in *Spine* by Annette Becker, M.D., and her research team at the University of Marburg, Germany, showed the direct and indirect costs patient care for chronic low back pain sufferers was twice the amount needed to care for acutely ill patients.

"ISTO is excited about the completion of this clinical milestone that brings the promise of our novel spine therapy one step closer to commercialization," said Mitchell Seyedin, Ph.D., President and CEO of ISTO Technologies. "We look forward to analyzing the six-month interim results from the trial in early 2011 and moving NuQu to the next stage of clinical development."

For Phase I the principal investigators are Dr. Domagoj Coric of Carolina Neurosurgery and Spine Associates, Chief, Department of Neurosurgery, Carolinas Medical Center, and Dr. Kenneth Pettine, co-founder of the Spine Institute in Loveland, Colorado. Here's what Dr. Coric had to say about this novel therapy. "Disc nucleus regeneration and repair represent an important area of ongoing spine research. It offers the promise of a minimally invasive intervention that treats a patient's symptoms while potentially restoring function to the disc. This technology offers the promise of regeneration, repair and restoration of function for a very large patient population that suffers from chronic back pain."

Adds Dr. Pettine: "A tissue engineering approach and, in particular, a cell-based therapy to treat degenerative discs represents a new renaissance in spine treatment. This technology has enormous potential for filling a significant unmet medical need and may offer an important additional treatment option for our patients."

—*JR (October 19, 2010)* ◆

Starting Line/Creative Commons

DePuy Spine Jumps In—Laterally

DePuy Spine debuted the company's first lateral approach system at the recent North American Spine Society meeting. And, there's an app for that.

The MIS Lateral Platform featuring the Cougar LS Cage System is a set of devices designed specifically for the lateral approach to minimally invasive spinal fusion. The company also introduced the Expedium Offset System, a new implant and instrument system that can be used in a wide range of spinal surgery.

The Cougar, Pipeline LS Lateral Access System and Viper2 System of rods and screws combine to form DePuy Spine's new MIS Lateral Platform. Together, states the company press release, the devices provide the access, visibility, anterior column support and posterior fixation required to perform minimally invasive spinal fusion.

Pipeline has retractor blades for controlled, distal expansion and clear visibility in the working area. The top of the retractor is radiolucent allowing visualization for placement of the

Cougar cage, which has a self-distracting tip and bulleted nose. The Viper2 offers rod insertion options for complex and degenerative pathologies.

DePuy Spine's MIS Lateral Platform may be used with any neuromonitoring system, if intraoperative neuromonitoring is desired. The company has also developed a new Apple iPhone app for the MIS Lateral Platform that demonstrates the surgical technique, step-by-step, through illustrations, text and videos.

Gary Fischetti, Worldwide President, DePuy Spine, said, "The MIS lateral approach and image-guided spinal surgery are two important and emerging platforms in spinal care. We are committed to developing these and other technology platforms, including new instrumentation and implant systems like Expedium, that increase procedure efficiency and advance surgical technique."

BrainLAB Partnership

The company also announced a preferred partnership agreement with BrainLAB, a developer of image-guided systems. The companies will co-develop and market image-guided navigational tools.

—WE (October 20, 2010) ◆

Expedium Offset System and MIS Lateral Platform//DePuy Spine

Centinel's Midline Receives Clearance

Centinel Spine has received 510(k) clearance from the FDA to market its STALIF Midline system.

According to the company announcement made before the recent NASS meeting, the system was developed around the technology behind Centinel's STALIF TT and STALIF C systems and offers both "clinically validated technology" and new convenience features. These include lag effect fixation

consistent with the principles of segmental fixation and Wolff's Law. Also engineered into the system is lumen locking, which guards against screw back-out.

Centinel's Midline 1A/Courtesy Centinel Spine

Bill Silvermintz of Centinel informed *OTW* that based on surgeon feedback, "We have added a 33mm footprint to our family of Midline cages to meet the needs of smaller stature patients." In addition to the 8 and 12 degree lordotic angles available on the company's STALIF TT, the new system has added an increased lordotic angle of 16 degrees as an option. Midline also has new tantalum markers which aid in radiological imaging.

New Features

Several features have also been added to aid implant insertion—screw holes have been redesigned to improve both the method of insertion and access. "We have designed our Midline screws with our ABO feature to add a second ounce of prevention against screw back-out. This feature increases screw pull-out resistance by an additional 20%," according to Silvermintz.

From a practical standpoint, Silvermintz noted the new size options offer surgeons greater flexibility in treating a wide array of spinal pathology.

Silvermintz concluded, "The changes to our radiological markers more easily aid surgeons in identifying cage location both intra and post surgically. Our redesigned screw holes allow the use of new, easier to use instrumentation specifically designed for Midline and provide a medialized angle for screw insertion.

"Finally, the addition of ABO screws is akin to wearing a belt and suspenders on a pair of pants that fit perfectly to start and offers both patient and surgeon added peace of mind."

—WE (October 18, 2010) ◆

THE PICTURE OF SUCCESS

Dr. Matthew Ramsey

By Elizabeth Hofheinz, M.P.H., M.Ed.

Dr. Matthew Ramsey

When a young Matthew Ramsey sat in his first premed lecture many years ago, he was so turned off by the cutthroat, "me-driven" attitude of some of his classmates that he nearly fled the room. But his drive to understand and affect the human condition kept his mind open…and his body in his seat. Now a sought-after shoulder and elbow specialist at the Rothman Institute in Philadelphia, Dr. Ramsey makes a difference not just in the operating room, but in the lab and in the literature. He is Assistant Editor of the *Journal of Shoulder and Elbow Surgery* and a Consultant Reviewer for the *Journal of Bone and Joint Surgery*. Dr. Ramsey is also shaking up the design world. Elbow implants have remained largely unchanged for nearly 20 years… no more. Dr. Ramsey is now redesigning the most widely used elbow implant in the world—the Zimmer elbow.

A self described "blue collar physician," Dr. Ramsey was raised in Schenectady, New York, and was surrounded by those who exuded hard work, charity and compassion. "My mom raised us three boys with the help of a supportive extended family. My grandfather was a Presbyterian minister who was the gentlest human being I have ever met. When I got to college and encountered a lot of aspiring doctors who were brash and out for themselves, it gave me pause. I thought, 'If this is what medicine is, then I don't want it.' I ended up choosing political science as my major, but also took science courses 'just in case.'"

After taking a year off between college and medical school to ponder his options, Dr. Ramsey signed on the medical dotted line…he just *had* to be a physician. "No matter how much I explored other career possibilities—one professor even tried recruiting me for the CIA—I could see that in sharing a difficult part of their lives with doctors, patients are giving us a tremendous gift. Over time this outlook has only solidified, and now I firmly believe that the very least we can do is engage the patient as a human being. I love the humanity of medicine; that doesn't always make my schedulers happy, though, because I often linger in the exam room with patients as we explore their issues."

An intuitive medical detective with a big heart, Dr. Ramsey says, "If you don't enjoy the complexity of someone's problems, then you don't enjoy the beauty. I want to know what someone's life is like beyond his or her problem. I firmly believe that we must bring more to the patient than the science of what we are doing. I once had a patient with a bad rotator cuff tear who was particularly distant, and I could see that something else was bothering him. It turns out that he had recently lost his job; this person was so relieved that I took the time to connect with him. Not only is this

"If you don't enjoy the complexity of someone's problems, then you don't enjoy the beauty. I want to know what someone's life is like beyond his or her problem. I firmly believe that we must bring more to the patient than the science of what we are doing."

a 'nice' thing to do…it helps unclutter the clinical problem."

While in medical school at the State University of New York Health Science Center at Brooklyn, Matthew Ramsey did indeed have what one might think of as "the Brooklyn experience." He explains, "It was a tough neighborhood and a tough clientele, both of which prepared me to work in any kind of environment that I might encounter going forward. As for sorting out what field I wanted to enter, I had spent several summers in high school working construction; I also spent some time with a family friend who was an orthopedist. The immediate gratification was appealing…and all of the sawing, banging, and chopping was a direct extension of my comfort with manual labor."

After a general surgery internship, Dr. Ramsey entered the orthopedic residency at Thomas Jefferson University Hospital in Philadelphia. "I got to walk among giants, including Dick Rothman and Robert Booth—there was not a 'B' rated surgeon in the bunch. Shoulder piqued my interest because it was different, was anatomically challenging, and was in its infancy."

While not exactly shrugging off the shoulder, Dr. Ramsey then encountered an even less "popular" joint that merited exploration. During my fellowship at the University of Pennsylvania Medical Center the famed shoulder surgeons Joe Iannotti and Gerry Williams came to me and said, 'There's this thing called the elbow and no one in Philadelphia is addressing it. We want to change that, so can we send you to Mayo Clinic for specialized training? Then we'll hire you and you will be the elbow man.' I accepted the challenge that many of my colleagues had avoided."

Those who accept challenges are, naturally, more likely to fail than those who never dive in and try. Dr. Ramsey states, "If you are averse to failure then you are not going to succeed. The first patient I ever operated on I had to take back to the OR because I misplaced a screw. I had to look that person in the eye and tell him what had happened. If you're the kind of doctor who emits an 'I am better than you' attitude, then you're going to have all sorts of problems in your career. But if your comportment leads people to view you as real, and you've connected with them and outlined the risks, then they will be more forgiving if something doesn't go as planned."

But often, says Dr. Ramsey, one must go looking for failure in order to make things right. "While at Penn I did some work on rat rotator cuff surgery where we looked at what factors contributed to failure. The challenge with rotator cuff surgery in humans is that we have a 20% failure rate. I am pleased that some of that work translated into what surgeons now do clinically."

"In designing elbow replacement systems I have worked with Steve Kurtz, Ph.D., who runs the lab at Drexel University. For five years we have retrieved not just the implants, but the tissues around the implants in order to study the mechanism of failure. I am now working with Zimmer to redesign the most widely used elbow implant in the world. To date we have found that the most significant issue is articulation between the components, with the way that metal and plastic interact being the weakest link."

While Dr. Ramsey doesn't stand in front of a mirror and berate himself, he does credit rigorous self-evaluation as part of his success. He also turns this spotlight on potential residents. "Years ago I vowed to constantly engage in self assessment, to the point where I am my harshest critic. Being honest with yourself and others sets the stage for a good set of ethics. I can't stand the bravado that medicine sometimes brings out in physicians. We struggle with people's perceptions of us as doctors—including our motivations—and those who 'act out' don't serve anyone well."

"In most cases, however, you can't teach compassion or ethical behavior. When I am interviewing potential residents I don't ask questions to assess their intelligence—the fact that they are smart is usually a given. I ask questions that will reveal their ethical principles…things that will tell me how they would react in a certain situation. I look for things

"When I am interviewing potential residents I don't ask questions to assess their intelligence—the fact that they are smart is usually a given. I ask questions that will reveal their ethical principles…things that will tell me how they would react in a certain situation."

on an application that seem unusual and then drill down into them to see if the applicant is telling the truth. If they say that have woodworking experience, then I ask a few pointed questions on that topic. If they purport to run marathons, then I dig into the specifics of their training regimen. But compassion, so necessary in medicine, is pretty tough to assess in an interview. In my experience, it is a quality that comes from difficult life experiences such as losing a parent at a young age, undergoing a serious illness as a child, etc. The fact is that surgeons are just not wired for 'touchy feely.'"

Research isn't an area where compassion comes into play, however. The study setup and numbers tell the tale. As Assistant Editor of the *Journal of Shoulder and Elbow Surgery*, Dr. Ramsey is pleased to see that many people get it right. And yet…"There is a lot of sloppy research out there. Many people aren't focusing on the study questions and are making them excessively broad. For example, let's say someone is examining the things that contribute to rotator cuff failure. They look too broadly, however, and don't see key points like age, smoking, quality of the tissue that contributes to failure, etc. They're either answering a question that has already been answered or ignoring information and not moving the question forward. The fundamental question that researchers need to ask is, 'Will this add anything to our understanding to the problem?'"

On the home front, the question used to be, "Dear, do you have to go golfing again?" Dr. Ramsey laughs, "After years of fighting about golfing, my wife has decided to join me—and we have a great time. Our daughter is a junior in college, is a business major and is planning a career in the music industry. Our son is a freshman in college, plays several musical instruments, and wants to write for television. They have turned out to be stellar human beings. For that, I largely credit my wife, who sets a great example, and is a wonderful friend to us all."

Dr. Matthew Ramsey…with compassion as his guide, he enjoys the complexity of it all. ◆

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