December 22, 2011

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SANUWAVE Health (SNWV-OTC)

SNWV: Remain Believers Despite Disappointing FDA Action.

OUTLOOK

In a surprise move, FDA responds to PMA with major deficiency letter. Recommends another clinical trial. SNWV is weighing their options and will discuss alternatives with FDA. Decision on next steps towards regulatory approval are expected to be announced in Q1 2012. We view this as a significant setback but by no means a death blow. While we remain highly positive on SNWV and believers in dermaPACE, the recent news has prompted significant changes to our outlook and model which in-turn affects our price target (all of which are again subject to change after there's more clarity on how SNWV will proceed). We moved our target price from $6.00 to $2.50. The share price plummeted following the announcement and currently trades far below our $2.50 valuation. As such we are maintaining our Outperform rating on SNWV.

Current Recommendation	**Outperform**
Prior Recommendation	Neutral
Date of Last Change	08/10/2011
Current Price (12/21/11)	$1.30
Target Price	**$2.50**

SUMMARY DATA

52-Week High	**$5.72**
52-Week Low	**$1.30**
One-Year Return (%)	**N/A**
Beta	**-0.16**
Average Daily Volume (sh)	**4,019**
Shares Outstanding (mil)	**21**
Market Capitalization ($mil)	**$27**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**2**
Insider Ownership (%)	**N/A**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**N/A**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2011 Estimate	**N/A**
P/E using 2012 Estimate	**N/A**
Zacks Rank	**N/A**

Risk Level	**N/A**
Type of Stock	**N/A**
Industry	**Med Products**

ZACKS ESTIMATES

Revenue
(in 000s of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2010	143 A	117 A	278 A	190 A	728 A
2011	252 A	164 A	162 A	205 E	782 E
2012					1,210 E
2013					1,370 E

Earnings per Share

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2010	-$0.24 A	-$0.22 A	-$0.21 A	-$0.46 A	-$1.15 A
2011	-$0.14 A	-$0.17 A	-$0.10 A	-$0.14 E	-$0.54 E
2012					-$0.40 E
2013					-$0.31 E

Zacks Projected EPS Growth Rate - Next 5 Years % **N/A**

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WHAT'S NEW…

FDA RESPONSE

Despite compelling phase III trial data that we believe strongly supports dermaPACE as an effective therapy for diabetic foot ulcers, U.S. regulators have said it's not necessarily strong enough to merit FDA approval. Yesterday (12/21/2011) SANUWAVE announced that the FDA issued a major deficiency letter in response to the company's PMA filing seeking approval of dermaPACE in the treatment of DFU. SANUWAVE noted that the FDA cites the failure of dermaPACE to meet the primary endpoint of statistically significant superiority in 100% wound closure compared to sham-control (i.e. - standard of care) as one of the deficiencies. Among the FDA's recommendations to potentially remedy the deficiencies is for SANUWAVE to conduct another clinical trial - the design, size, duration, etc. of which would be decided upon after further discussions between the two parties.

As a reminder on dermaPACE's phase III trial data, while superiority of dermaPACE over sham on the primary endpoint (100% closure) was not statistically significant, a higher percentage (21% for dermaPACE and 15% for sham-control) of dermaPACE treated patients achieved full closure within twelve weeks (supplemental data did show dermaPACE did achieve statistical significance in complete wound closure at 20 weeks, however). In addition (and of considerable importance), of the patients that did achieve complete wound closure at twelve weeks, only 4.5% of the dermaPACE cohort experienced wound recurrence, compared to 20% in the sham cohort.

Although superiority on full closure was not statistically significant, based on the strict protocol of the study restricting closure through surgery, a 90% or greater closure rate was considered to be clinically meaningful. When looking at wounds that had reduced in size by > 90%, dermaPACE was shown to be significantly ($p = 0.0161$) more effective than sham with 48% (51 of 107) dermaPACE patients meeting this endpoint versus only 31% (31 of 99) of sham control patients. Median wound closure was over 99% for dermaPACE treated patients in this composite analysis and dermaPACE patients were twice as likely to achieve 90% - 100% wound closure compared to sham patients. We believe that the composite data is especially impressive considering that dermaPACE treated patients started with wounds 58% larger than those in the sham-control group. Safety data was also good, with no difference in the rate of adverse events between the study and control groups.

While FDA's recent action by no means dooms dermaPace's chances of eventually gaining FDA approval, it does mean the journey towards that end will now be longer and likely more costly. The near-term game plan is to meet with the FDA, evaluate their options and formally respond to the letter – which is expected to be completed during Q1 2012. While another clinical trial may not be the only path towards securing FDA approval, it would be the least arbitrary and provide SANUWAVE with definitive metrics to meet in order to reach that goal. We hope to get a better idea of the scope, length and cost of another trial as well as SANUWAVE's decision whether to go that route over the next ~90 days.

And while we view this recent FDA action as a surprise and a meaningful setback for dermaPACE and SANUWAVE, we remain positive on both and continue to believe in dermaPACE's chances in eventually gaining FDA approval. There is a long list of medical devices and pharmaceuticals that endured regulatory setbacks that eventually received FDA's stamp of approval – we think dermaPACE will be one more.

Prior to the December FDA action we had expected dermaPACE to receive regulatory approval and launch in the U.S. near mid-2012. It is clear that that will now not happen. And while the direction that SANUWAVE will take in order to continue to move towards FDA approval is just conjecture at this point, we need to incorporate certain assumptions into our outlook and related financial model in order to place a value on the company. Some of these assumptions are very general in scope and little more than just blind guesses at this point – we will update these assumptions if necessary when there is more clarity on the updated regulatory approval pathway. The most significant "blind-guess" assumption is that SANUWAVE runs another clinical trial – which delays approval until early 2014 and, in-turn, requires the company to raise a material amount of additional capital. We currently have absolutely no insight, however, on if the company will run another trial or what the design, scope, cost, size or duration might be of this hypothetical trial.

VALUATION / RECOMMENDATION

Prior to the FDA major deficiency letter we were valuing SANUWAVE based on 2015 P/E comparables (to Kinetic Concepts and Smith & Nephew). Our updated outlook, which incorporates an assumed significant delay in the U.S.

launch of dermaPACE, results in SNWV posting negative EPS through at least 2015 – as such our prior valuation methodology is inappropriate. Instead we now use 2015 P/S comparables to value SNWV. Smith & Nephew currently trades at approximately 1.5x analyst's 2015 forecasted revenue. Kinetic Concepts was acquired in November for $6.1 billion, or about 2.8x estimated 2015 revenue. We currently model SNWV to generate revenue of $23.8 million in 2015 – based on the two comp 2015 P/S multiples values SNWV at between $36 million ($1.71/share) and $55 million ($3.20/share). For simplicity, we use the average of the two, which values SNWV at about $2.50/share. We think it bears repeating, however, that our model is highly subject to change once there is more clarity on the updated regulatory approval pathway that SANUWAVE expects to pursue. As it is now, we value the company at $2.50/share, down from $6.00/share prior to the recent FDA communication.

BUSINESS

Headquartered in Alpharetta, Georgia, SANUWAVE Health, Inc. (SANUWAVE) is developing non-invasive medical devices using its proprietary Pulsed Acoustic Cellular Expression (PACE™) technology to aid in the body's repair and regeneration of tissue, musculoskeletal and vascular structures. PACE works by creating shock waves which, in-turn, elicit a biological response and help the healing process.

Recent clinical studies have indicated the company's lead product, dermaPACE®, is more effective than current standard of care in the treatment of serious life-threatening diabetic foot ulcers (DFU). In July 2011 SANUWAVE made the third and final module filing of a three-tiered PMA application seeking FDA approval of dermaPACE for the treatment of diabetic foot ulcers. Surprisingly, the FDA responded in December with a major deficiency letter, citing the failure to hit the phase III trial primary endpoint as a primary reason – the FDA suggested SANUWAVE run another trial to potentially remedy the deficiencies that they highlighted. SANUWAVE will communicate with the FDA and consider their options – including possibly running another trial. SANUWAVE expects to have more clarity on the direction that they will pursue by the end of Q1 2012.

The global market for wound healing is estimated to be approximately $10 billion, with the U.S. market for diabetic foot ulcers (a subset of the larger wound healing segment) at over $2 billion and growing rapidly. dermaPACE looks like it could be a game-changer for the treatment of chronic wounds as it appears to be at least as effective (and potentially more effective) as other advanced wound closure instruments but with significant other benefits, such as lower cost (less than ½ the cost of others), is non-invasive and has a lower treatment burden (i.e. - number of procedures and time per procedure). A competing product currently generates in excess of $1 billion in U.S. sales for the treatment of wounds (DFU and other wounds).

Chronic conditions such as non-healing DFUs are a tremendous burden on the health care system (10% of all health care dollars are spent on direct costs related to diabetes) and have been a catalyst in public and private insurers moving towards a "pay-for-performance" reimbursement model. This payment model incentivizes healthcare providers to offer more efficient, more effective and less costly care which should help drive demand for highly efficacious and lower cost devices such as dermaPACE.

SANUWAVE's patent-protected technology is also being applied for derivative applications including for other chronic wounds and as an aid in orthopedic and spine bone healing. Assuming eventual FDA approval, SANUWAVE will incorporate a razor/razor-blade business model, utilizing card readers which activate the device for each procedure which will generate a recurring revenue stream. Sales are expected to be handled by a direct sales force in the U.S. and by third-party distributors in Europe and Asia.

MARKET

DIABETIC FOOT ULCERS

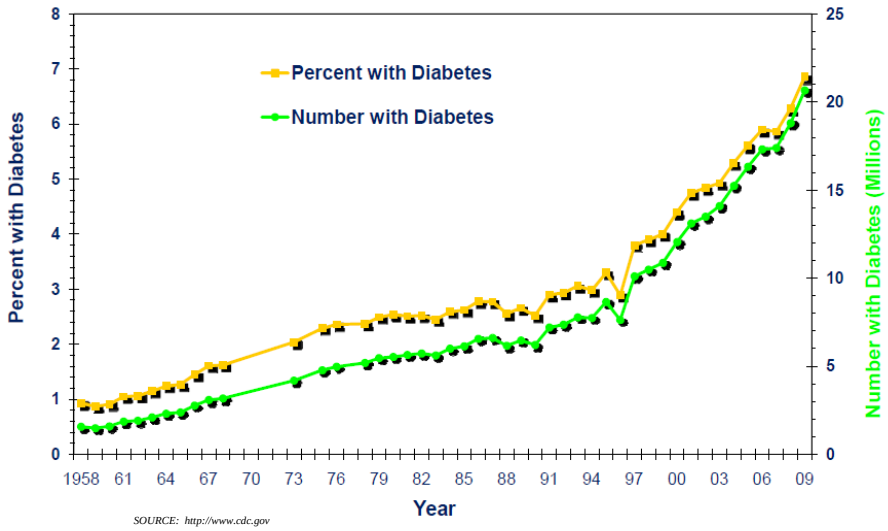
...common, chronic and serious

Foot ulcers are relatively common among diabetics as a result of nerve damage and vascular complications caused by the disease. Nerve damage can cause peripheral neuropathy, or loss of feeling in the foot which means injuries such as cuts or bruises may go undetected (especially to the underside of the foot) which can quickly worsen.

Vascular disease and poor blood flow (especially to the skin) is another common symptom of diabetes which can in itself cause ulcers and impair the body's ability to heal wounds.

According to the American Diabetes Association, approximately 26 million Americans have diabetes with another 79 million classified as prediabetic. Worldwide, it is estimated 285 million are afflicted with diabetes. Less than 1% of the U.S. population was diagnosed with diabetes in 1960 but due to factors such as by poor diet and exercise habits, along with the increase in the proportion of higher risk demographics (i.e. -the elderly and minority groups) the incidence of diabetes has skyrocketed over the last 50 years. Approximately 8% of the U.S. population currently has been diagnosed with diabetes - this is expected to grow to as much as 33% by the year 2050.

Number and Percentage of U.S. Population with Diagnosed Diabetes, 1958-2009



Diabetic foot ulcers afflict roughly 15% - 25% of all diabetics within their lifetimes and 1.5 million diabetic foot ulcers occur every year in the United States. DFU precedes over 80% of all non-traumatic lower-limb amputations among diabetics, leading to more than 80k amputations annually. Clinical studies have shown that comprehensive foot programs (including advanced therapies) can reduce amputation rates by 45% to 85%.

DFU is usually a progressive condition and can worsen very rapidly over time. If the wound is not controlled within a short period (~ 4 weeks), the risk of infection, hospitalization, amputation and death escalates. This not only obviously puts the patients' health at risk, it can also dramatically increase the cost of treatment.

....costly

Depending on the source, the cost of care of diabetic foot ulcers can vary significantly, but generally falls somewhere between $7k and $60k per ulcer (the discrepancy largely due to whether amputation is required). The annual direct cost of care of DFU to Medicare alone could be as much as $2.2B (~9MM Medicare beneficiaries with diabetes, 8% of which have DFU, ~$30k average cost per patient). When considering private payers and ancillary costs such as lost work time, the total cost of DFU in the U.S. is likely in the tens of billions of dollars.

The authors (Scott Ramsey, Katherine Newton, David Blough, et al.) of an often-cited study ("*Incidence, Outcomes, and Cost of Foot Ulcers in Patients with Diabetes"*) comparing the cost of care of diabetics with and without foot ulcers found that those with foot ulcers required care costing as much as 5 times more than those without foot ulcers. The authors concluded that, "The results appear to support the value of foot-ulcer prevention programs for patients with diabetes."

...standard care relatively ineffective for chronic wounds

Acute wounds can rapidly become chronic and chronic wounds are inherently more difficult to get under control and are therefore more susceptible to adverse outcomes such as infection, amputation and death. Standard of care, which typically includes dressing the wound and possibly the use of a walking boot, remains the most common prescribed first-line therapy and can be effective for early-onset (i.e. - acute) ulcers. However, a considerable amount of clinical trial data from the last 15 years has proven that standard of care is significantly less effective in healing more severe (i.e. - older, larger) wounds and earlier intervention is positively correlated with improved

patient outcomes. The body of evidence strongly supports the use of more effective (i.e. - advanced) therapies at an earlier stage of treatment in order to reduce the risk of acute wounds becoming chronic and increase the likelihood of chronic wounds fully healing.

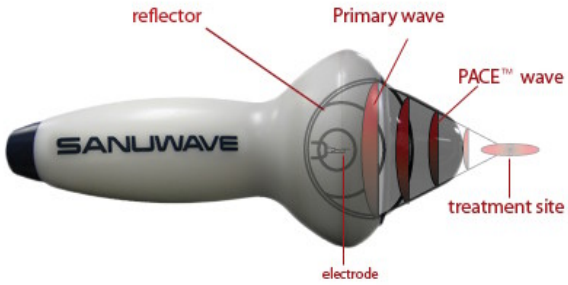
A retrospective analysis of clinical trial data of 622 patients prescribed standard of care showed 31% (139 of 450) of patients achieved complete healing after 12 weeks. This fell to 24% (41 of 172) of patients where standard of care was continued for 20 weeks.

PRODUCTS

SANUWAVE's major focus over the last few years has been with dermaPACE which they hope to launch into the U.S. market within the next 12 months for the treatment of diabetic wounds, an enormous, underserved and rapidly growing market. dermaPACE works by creating shock waves (very short, high pressure bursts of energy) which trigger a biological response, including the formation of new blood vessels and increased blood flow to the injured area which promotes the regeneration of tissue. The handheld instrument utilizes an electrode which is housed within fluid to create shock waves. A curved reflector behind the electrode reflects the shock wave towards the focal treatment point which is applied to the injured areas of the body.

In the early years SANUWAVE's focus was with its FDA approved Class III device, OssaTron® which uses shock waves created through Extracorporeal Shockwave Therapy (ESWT) to treat heel and elbow pain. Then in 2005 SANUWAVE acquired Healthtronics' orthopedic business which included significant intellectual property assets. HealthTronics is a leading manufacturer of lithotripsy devices which use shock wave technology to break up kidney stones. Since the acquisition, SANUWAVE developed the PACE technology, a refined and improved version of ESWT. In July 2010 SANUWAVE introduced orthoPACE® using PACE technology, the successor device to OssaTron, to the European market. orthoPACE offers similar efficacy as OssaTron but unlike the 800lb legacy device, is compact and portable.

dermaPACE Handheld Applicator



SOURCE: SANUWAVE

dermaPACE Unit



SOURCE: SANUWAVE

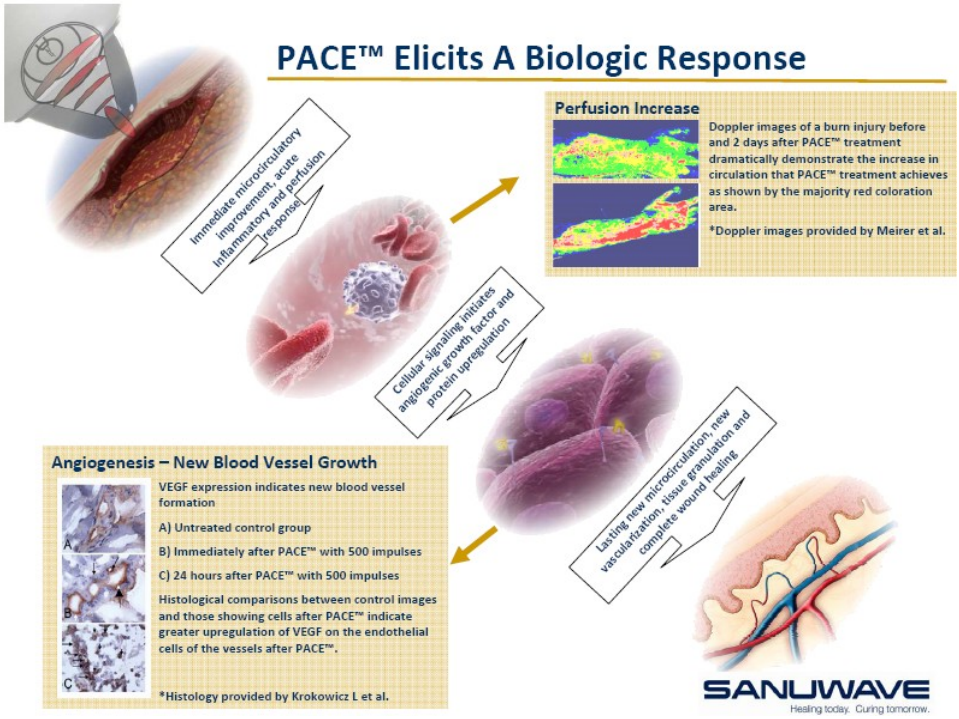
dermaPACE Used for DFU



SOURCE: SANUWAVE

The shock waves produced by dermaPACE cause the body to elicit an inflammatory response, ultimately resulting in the regrowth of tissue. This biological response returns a chronic condition (i.e. – long-lasting and recurrent) to an acute (i.e. – can be managed immediately) one, allowing for wounds to heal completely.

SANUWAVE's PACE technology is protected by fourteen U.S. and twelve foreign patents (over 50 issued and pending patents) which cover, method of use, electrode configurations, chemical components and piezoeletric fibers (both of which are integral in generating the shock wave), and the therapy head.



SOURCE: SANUWAVE

dermaPACE CLINICAL TRIALS

Phase III IDE Study

dermaPACE recently completed testing in a Phase III Investigational Device Exemption (IDE) clinical trial. IDE trials, which FDA requires for investigational devices which could pose a serious risk to patients, are relatively strict and are a testament to the safety and efficacy of medical devices which gain FDA clearance through this regulatory pathway.

Top-line 12-week results of SANUWAVE's IDE trial, which were announced in December 2010, showed dermaPACE was more effective than current standard of care in the treatment of diabetic foot ulcers. The data, along with 24-week results which were announced in July 2011, were part of the third and final module of SANUWAVE's PMA application seeking FDA approval of dermaPACE for the treatment of diabetic foot ulcers which was filed in early July 2011.

The 26-week, multi-site U.S. study included 206 patients suffering from diabetic foot ulcers. Patients were randomized to either treatment with dermaPACE plus current standard of care (n=107) or sham (i.e. – placebo) plus standard of care (n=99). dermaPACE treated patients received four 20-minute procedures over two weeks (i.e. – two 20-minute sessions per week). Standard of care continued for 12 weeks. Patient safety follow-up continued for 12 weeks following the initial 12-week patient assessment period. Patients and physicians were both blinded to which patients were receiving which treatment – double-blinding eliminates the potential for human bias in the data.

The trial protocol also did not allow for surgical closure of a partially healed wound – which allowed for a true picture of the efficacy of dermaPACE versus sham over time.

Primary endpoint was full wound closure confirmed at two consecutive visits. Secondary endpoints were time to closure, reduction in total wound surface area and volume, rate of improvement, long-term safety, and skin appearance and pain assessments.

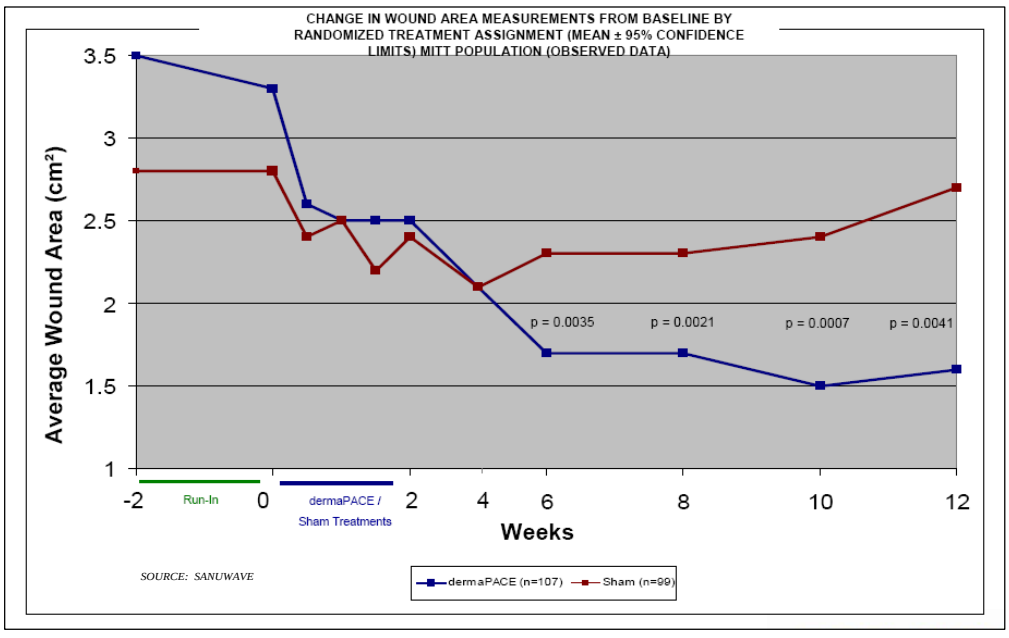
SANUWAVE announced results through 12 weeks in December 2010. 12-week follow-up was the protocol for studies used to gain FDA approval of other advanced DFU treatments including Apligraf and Dermagraft. In July 2011 SANUWAVE also announced results through 24 weeks.

12-Week Results….

Top-line results through 12 weeks showed treatment with dermaPACE was significantly more effective than sham (i.e. – only standard of care) in wound area closure within four weeks following the last treatment and continued to be so throughout the twelve week evaluation period. At week twelve, 45% of dermaPACE treated patients experienced 90% or greater wound closure, compared to only 26% of sham-control patients (statistically significant, p=0.0182). Also at week twelve, patients with 70% or greater wound closure included 66% of those receiving dermaPACE treatment compared to just 47% of sham patients (statistically significant, p=0.0227). At twelve weeks the average size in reduction of the ulcer was 54% for dermaPACE patients versus only 7% with sham patients (statistically significant, p=0.0041).

12-Week Top-line data from Phase III IDE Trial

	dermaPACE	Sham	p-value
≥ 90% closure @ 12 weeks	45%	26%	0.0182
≥ 70% closure @ 12 weeks	66%	47%	0.0227
Average reduction in size of ulcer @ 12 weeks	54%	7%	0.0041



While superiority of dermaPACE over sham on the primary endpoint (100% closure) was not statistically significant, a higher percentage (21% for dermaPACE and 15% for sham-control) of dermaPACE treated patients achieved full closure within twelve weeks (as we note below dermaPACE did achieve statistical significance in complete wound closure at 20 weeks, however). In addition (and of considerable importance), of the patients that did achieve complete wound closure at twelve weeks, only 4.5% of the dermaPACE cohort experienced wound recurrence, compared to 20% in the sham cohort.

Although superiority on full closure was not statistically significant, based on the strict protocol of the study restricting closure through surgery, a 90% or greater closure rate was considered to be clinically meaningful. As the pictures below indicate (patient "A" achieved "only" 97% closure), 100% closure (as defined by the study protocol) is not a necessary threshold to meet in clinical practice for wounds to completely heal. When looking at wounds that had reduced in size by $\geq$ 90%, dermaPACE was shown to be significantly (p = 0.0161) more effective than sham with 48% (51 of 107) dermaPACE patients meeting this endpoint versus only 31% (31 of 99) of sham control patients. Median wound closure was over 99% for dermaPACE treated patients in this composite analysis and dermaPACE patients were twice as likely to achieve 90% - 100% wound closure compared to sham patients. We believe that the composite data is especially impressive considering that dermaPACE treated patients started with wounds 58% larger than those in the sham-control group. Safety data was also good, with no difference in the rate of adverse events between the study and control groups.

SAMPLE IMAGES FROM SANUWAVE'S PHASE III IDE CLINICAL TRIAL

Both patient A (left) and patient B (right) were treated with dermaPACE. The pictures on top were taken at their initial physician visit. The pictures at bottom were taken on each patient's 11th visit (i.e. - week 12). At week 12 patient A achieved 97% improvement while Patient B achieved 100% improvement (i.e. – full wound closure).









SOURCE: SANUWAVE

24-Week Results….

Trial investigators also looked at follow-up results through 24 weeks. At week 20 dermaPACE finally did show a statistically greater rate of wound closure compared to sham-control. In the Intent-to-Treat population (ITT - which included all 206 patients in both cohorts) 36% (39 of 107) of dermaPACE patients achieved complete wound closure compared to 23% (23 of 99) of sham-control at 20 weeks. The difference was statistically significant (p = 0.047). In the Efficacy Evaluable population (EE - which excluded a few patients who fell outside the study

parameters) 38% (38 of 101) of dermaPACE patients achieved complete wound closure compared to 22% (20 of 93) of sham-control at 20 weeks. The difference was also statistically significant (p = 0.018).

The difference in rates of wound closure between dermaPACE and sham treatment in both the ITT and EE populations continued to be statistically significant and in favor of dermaPACE out to the final 24 week evaluation date.

Also noteworthy is that the recurrence rate at 24 weeks among those patients that achieved full closure at 12 weeks remained very low, at 4.5% with dermaPACE patients compared to 20% in the sham-control group.

24-Week Top Line Data from Phase III IDE

	dermaPACE	Sham	p-value
Complete wound closure @ 20 weeks (ITT / EE)	36% / 38%	23% / 22%	0.047 / 0.018
Complete wound closure @ 24 weeks (ITT / EE)	39 % / 41%	26% / 25%	0.054 / 0.022

Despite statistical significance not being achieved until week 20, we again believe the rigorous study design (double-blinded, surgery not permitted, larger ulcers with dermaPACE cohort, etc.) was likely a factor and expected that it would be taken under consideration in FDA's analysis of SANUWAVE's regulatory package. Similar to the 12-week data, safety was comparable among all cohorts through 24 weeks.

Despite the trial data indicating that dermaPACE is an effective therapy for diabetic foot ulcers, U.S. regulators said it's not necessarily strong enough to merit FDA approval. On December 21, 2011 SANUWAVE announced that the FDA issued a major deficiency letter in response to the company's PMA filing. SANUWAVE noted that the FDA cites the failure of dermaPACE to meet the primary endpoint of statistically significant superiority in 100% wound closure compared to sham-control as one of the deficiencies. Among the FDA's recommendations to potentially remedy the deficiencies is for SANUWAVE to conduct another clinical trial - the design, size, duration, etc. of which would be decided on after further discussions between the two parties.

The near-term game plan is to meet with the FDA, evaluate their options and formally respond to the letter – which is expected to be completed during Q1 2012. We hope to get a better idea of the scope, length and cost of another trial as well as SANUWAVE's decision whether to go that route over the next ~90 days.

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dermaPACE Versus HBOT Trial

dermaPACE was pitted against hyperbaric oxygen therapy (HBOT) in the treatment of late-stage DFU in a small clinical trial titled, *"Treatment of Diabetic Foot Ulcers: A Comparative Study of Extracorporeal Shockwave Therapy and Hyperbaric Oxygen Therapy."* The Taiwan-based study included 77 patients with chronic, non-healing DFU of at least three months duration which were grade III or IV (i.e. – late stage). The dermaPACE cohort (39 patients, 44 ulcers) received two 20-minute procedures each week for three weeks (6 procedures in total). The HBOT group (38 patients, 40 ulcers) received five 90-minute treatments each week, once daily for eight weeks (40 procedures in total). Both cohorts also received standard of care treatment. Blood flow perfusion exams and biopsy were done prior to treatment and again after conclusion of final treatment. Increased perfusion blood flow is generally considered to have a beneficial effect on healing. Patient follow-up was conducted at three and six weeks and then once every three months up to 18 months. A second course of treatment was offered to patients who responded to treatment but with less than complete healing after 4 – 6 weeks of treatment.

HBOT uses pressurized oxygen to aid in the healing process and involves the use of an oxygen chamber. HBOT therapy is used and reimbursed by Medicare for a variety of ailments including for DFU. HBOT not only requires multiple treatments making it less convenient than dermaPACE, it can also be very expensive, costing between $200 and $1,000 (cost dependent on the treatment venue) per 90 minute session.

Results….

Data from the study showed;

- Complete healing in 57% of the DFUs in the dermaPACE group compared to just 25% in the HBOT group (statistically significant, p=0.003)
  - o One course of treatment resulted in 24 ulcers completely healed in the dermaPACE group compared to just 10 ulcers completely healed with HBOT
  - o For those patients receiving a second course of treatment (31 ulcers), 50% (7 of 14) of dermaPACE treated ulcers completely healed compared to only 6% (1 of 17) treated with HBOT
- 60% of HBOT treated ulcers were unchanged in size and depth, versus just 11% of those treated with dermaPACE (statistically significant, p=0.001)
- Perfusion blood flow increased by 27% in the dermaPACE group (statistically significant, p<0.001) while staying the same in the HBOT group
- dermaPACE treatment required 97% less treatment time than HBOT

dermaPACE Versus HBOT Trial Data

	dermaPACE	HBOT	p-value
Complete healing (all courses)	57%	25%	0.003
Ulcers unchanged in size and depth	11%	60%	0.001
Perfusion blood flow increase	27%	0%	0.001

More data….
On October 12, 2011 SANUWAVE announced that additional data from the clinical trial comparing dermaPACE to HBOT was published in the online edition of *Diabetes Research and Clinical Practice*. This new data, from a study titled, *Molecular Changes in Diabetic Foot Ulcers,* provided insight into the reasons why dermaPACE is more effective HBOT. This study found a statistically significant increase in molecular changes in the dermaPACE cohort compared to the patients in the HBOT group.

Specifically, it found significant increased in angiogenesis (vWF, VEGF and eNOS) and cell proliferation (PCNA and EGF) along with decreases in cell apoptosis (TUNEL).

Recent Related Clinical Studies

Several other studies (including pre-clinical) have also demonstrated the ability of PACE to increase blood flow, blood vessel formation and tissue reconstruction and have been recently published in various medical journals.

- ***"Pulsed Acoustic Cellular Treatment Induces Expression of Proangiogenic Factors and Chemokines in Muscle Flaps"***, a research study published in The Journal of Trauma in December 2010, investigated the use of PACE treatment to increase blood circulation in a cremaster flap (piece of rat muscle). The study, conducted by Dr. Maria Siemionow, a renowned plastic surgeon at the Cleveland Clinic (and a member of SANUWAVE's Scientific Advisory Board), showed the application of PACE treatment increased blood vessel diameter and blood vessel formation, indicating PACE benefits blood flow and healing of ischemic conditions.

- ***"Microvascular Response to Shock Wave Application in Striated Skin Muscle"***, a study published in the Journal of Surgical Research in early 2010 showed PACE treatment, when applied to mice skin muscle, resulted in a favorable microcirculatory response within one hour of treatment and lasted for at least three days. The study, conducted at the University Hospital in Zurich, Switzerland and done in collaboration with Shanghai

Jiao Tond University School of Medicine in China, showed PACE immediately increased functional capillary density by 20%, reaching 40% within 24 hours which lasted throughout the 3-day study period. The authors believe the increase in functional capillary density was a result of increased activity of certain enzymes and growth factors associated with the formation of blood vessels. The study supports the use of PACE treatment to promote microcirculation and tissue healing.

- ***"Extracorporeal Shock Waves, a New Non-Surgical Method to Treat Severe Burns"***, a study published in BURNS, the Journal of the International Society for Burn Injuries, investigated PACE for the treatment of severe (second and third degree) burns. Of the 15 patients that were presented with burns which were considered deep enough to require surgery, 12 (80%) fully healed after PACE treatment was applied (and did not need surgery). Also noteworthy was that burns showed a significant increase in blood flow after treatment with PACE and PACE healed patients did not experience scarring typical of these types of burns.

- A paper titled "***Extracorporeal Shock Wave Treatment in Ischemic Tissues: What is the Appropriate Number of Shock Wave Impulses?"*** was published in the Journal of Reconstructive Microsurgery in February 2010. The paper detailed a study which used PACE to increase blood flow to rat epigastric (abdomen) skin flaps with the goal to determine the optimum number of shockwave pulses to help prevent skin flap necrosis (cell death). This study, which found 500 pulses per treatment to be the most effective in improving blood flow to ischemic skin, was shown to support the use of 500 pulses per treatment during the pivotal Phase III IDE trial.

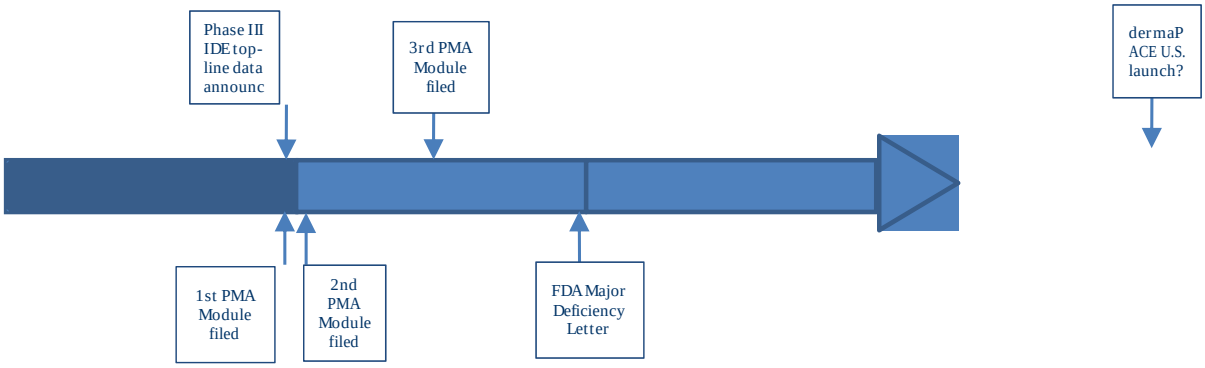
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dermaPACE REGULATORY/LAUNCH MILESTONES

dermaPACE and orthoPACE have already received CE Marking for sale in Europe where they are classified as Class IIb devices.

dermaPACE is classified as a Class III device by the FDA and as such is required to follow the Premarket Approval process to gain FDA regulatory approval. In August 2010 SANUWAVE was granted permission by the FDA to file a Premarket Approval application for marketing approval of dermaPACE for the treatment of DFU in a series of three modules.

- **December 10, 2010:** First module filed which included preclinical data
- **December 15, 2010:** Top-line 12-week data from Phase III IDE study announced
- **January 6, 2011:** Second module filed which included Quality System and Manufacturing review (i.e. – plans, standards and procedures that will be used for manufacturing dermaPACE on a commercial scale)
- **July 6, 2011:** SANUWAVE announced they filed the third and final module which includes both the 12-week and 24-week follow-up data, proposed labeling, and evidence of safety and effectiveness
- **July 12, 2011:** Top-line 24-week data from Phase III IDE study announced
- **FDA Action:** SNWV announces FDA responds with major deficiency letter, recommending another clinical trial. SNWV considering options and expects to announce plans within 90 days. We had previously expected FDA approval and launch by mid-2012 – this will now not happen. We see this as a meaningful disappointment but by no means does this mean dermaPACE will not eventually gain FDA approval



COMPETITION

As our investment thesis for SANUWAVE is mostly predicated on the opportunity of dermaPACE for the treatment of diabetic foot ulcers, we limit our discussion of SANUWAVE's competition to this particular application.

First line therapy for DFU typically involves dressing the wound and in some cases, a walking boot. Current standard of care is often the only treatment required for many DFUs. However, more severe wounds (i.e. - larger, deeper, infected, unhealed after several weeks) are much more susceptible to not fully healing and therefore may require more advanced and adjunctive therapies. As noted earlier, due to the rapid progression of DFUs from acute to a chronic state and the severe consequences of non-healing wounds (infection, amputation, death) it is imperative that effective treatment is administered early on. This potentially means the current standard of care for DFU could mean earlier intervention with advanced treatments.

While there are several types of dressings and topical products manufactured by a variety of companies used for what is considered standard of care, the adjunctive therapies are what we consider the initial direct competitors to dermaPACE. While we limit our "competition" discussion to the more established advanced wound therapies, there are also some novel advanced wound-healing products in late-stage development or recently launched by some smaller companies such as Derma Sciences which could be very competitive as well.

Standard of care has acted as the comparator procedure in clinical trials for most of the advanced therapies for DFU. These advanced therapies include medical devices as well as skin substitutes. And while there have been no head-to-head clinical trials performed comparing the benefits (i.e. - efficacy, safety, patient comfort, cost, etc.) of the various advanced therapies, we think a compilation of evidence (some scientific, some not) suggests dermaPACE can be a very formidable competitor to the other commonly administered advanced DFU products on the market including Dermagraft, Apligraf and V.A.C.

Dermagraft

Dermagraft is a bio-engineered skin substitute manufactured by privately-held Advanced BioHealing, Inc. A skin substitute is essentially a patch saturated with biological material (human cells) that is sutured or glued over the wound. This patch secretes human collagen, proteins and growth factors which aid in healing the wound. Dermagraft received FDA approval through PMA in 2001 for the treatment of DFUs of greater than six weeks duration. Medicare and private insurers covers up to eight applications of Dermagraft for the treatment of DFU. The company also hopes to gain FDA approval for use of Dermagraft in venous leg ulcers (VLU). The company employs approximately 100 sales people which target hospitals, physician offices and surgery centers.

Dermagraft is sold only on the U.S. although Advanced BioHealing hopes to enter international markets following completion of clinical trials for the VLU indication. Their plan is to use the VLU data to gain reimbursement for both DFU and VLU in Europe and other international territories.

Sales of the product have ramped quickly and, according to a recent S-1 filing, 200k units have been sold since the February 2007 launch. Advanced BioHealing's revenue, which consists almost entirely of sales of Dermagraft for DFU, grew from $9 million in 2007 to $147 million in 2010. In February 2011 Advanced BioHealing announced plans raise up to $200 million through an IPO. The company plans to use the funds to accelerate its sales effort of Dermagraft for DFU as well as to help finance new product development (including Dermagraft for the VLU indication).

Dermagraft Preparation and Application



SOURCE: http://www.bu.edu/woundbiotech/bioengineered/DermaProductSeries/pages/Picture%2044.htm

Apligraf

Apligraf, another skin substitute, is manufactured and marketed by privately-held Organogenesis (was previously marketed by Novartis). Apligraf was initially approved for use in venous leg ulcers and in June 2000 received FDA approval for the treatment of DFU of greater than a 3-week duration. According to the products' website Apligraf has been used over 250k times. Medicare and private insurers reimburse for each application (up to five) of Apligraf.

Apligraf



SOURCE: Apligraf

Negative Pressure Wound Therapy

Negative Wound Pressure Therapy (NPWT) uses a device to create a controlled vacuum (i.e. - negative pressure) to the wound through a foam dressing. The vacuum removes infectious fluids and material from the wound, draws the wound edges together and promotes formation of new tissue.

San Antonio, Texas based Kinetic Concepts, Inc. (KCI), is the lead manufacturer of NPWT devices. Its V.A.C. Therapy brand encompasses several portable NPWT devices targeted for the treatment of a variety of wounds, including DFU. KCI notes in public filings that their V.A.C. products contribute the primary source of revenue of their Active Healing Solutions business, which generated $1.4 billion (including $1.0 billion in the U.S.) in revenue in 2010. Revenue includes sales and rental of the NPWT devices as well as consumables such as dressings, filters and canisters. KCI's V.A.C. products are used for a variety types of wounds, not just DFU. As a result it's impossible to know how much of this $1 billion is attributable to DFU. KCI notes that international sales represent a small portion of revenue.

KCI has approximately 950 sales representatives selling their V.A.C. products in the U.S. and another 450 sales people outside the U.S. In the U.S., NPWT is currently reimbursed by Medicare as well as private insurers while reimbursement in foreign jurisdictions varies.

NPWT Device and Application



SOURCE: KCI1.com



SOURCE: http://en.wikipedia.org/wiki/File:KCI_Wound_Vac01.jpg

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dermaPACE VS. COMPETITION

While clinical trial data of head-to-head comparison between the various advanced DFU therapies is not available, insight into differences in efficacy may be gleamed through comparison of studies which used standard of care as the control cohort. Differences among these trials including size, location and severity of wounds, background of trial participants, and the studies' protocol, size, duration and endpoints makes the comparison of results not necessarily apples-to-apples. Despite this, we think comparison of the different trial results suggests that dermaPACE, at the very least, is an effective therapy - and perhaps, may be a more effective therapy than currently available advanced DFU treatments. We also note that dermaPACE will not compete on efficacy alone and has other (potentially just as compelling) benefits that, combined with the clinical data, provides a persuasive case that the instrument can be a be a formidable competitor in the advanced DFU treatment space.

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CLINICAL DATA COMPARISON

Efficacy of DFU treatment in clinical trials is typically measured by rate of closure and wound recurrence. Aside from efficacy, other metrics that are commonly included as endpoints are safety and patient comfort. We summarize data from a select number of clinical studies of the leading advanced DFU therapies and compare those to results from dermaPACE's IDE study. Some of the competitor therapy data is taken from more than one study as not all metrics were included in a single study. As there have been several other studies done aside from the ones we highlight, our comparison does not cover the totality of study data on advanced DFU therapy. We also note that we have only included dermaPACE 12-week data as 12-week follow-up was the protocol for studies used to gain FDA approval of Apligraf and Dermagraft. While we have excluded the 24-week follow-up data (which showed statistical significance in complete wound closure) from our direct comparison, we think it does add further support for use of dermaPACE in DFU.

The data in the table are from clinical studies of each therapy versus standard of care.

		dermaPACE	Dermagraft	V.A.C.	Apligraf
TRIAL RESULTS	Closure rate	48%	30%	43%	**56%**
	Recurrence rate post-closure	**5%**	19%	N/A	40%
	Adverse events vs. control	similar	similar	similar	similar
TRIAL DESIGN	N =	206	245	335	208
	Closure endpoint	≥ 90%	100%	100%	100%
	Trial duration	12 weeks	12 weeks	16 weeks	12 weeks
	# of procedures	**4**	up to 8	dressing chged 3x/ week	up to 5
	Double Blinding	**Yes**	No	No	No

...our take on the data

Keeping in mind that it can be misleading to make an apples-to-apples comparison of the data, we offer some potential points of interest in the trial protocols and data sets;

- **Closure endpoint:** dermaPACE data is from the composite analysis (endpoint of ≥ 90%). As noted earlier, dermaPACE failed to show significance in the primary endpoint of 100% closure in the IDE trial through 12 weeks. All three competing devices showed significance in their primary endpoint of 100% closure. The difference, in clinical practice, may be largely meaningless, however. Median closure in dermaPACE treated ulcers achieving ≥ 90% closure was over 99% and anything greater than 70% indicates that the wound is well on its way to being completely healed. In addition, ulcers treated with dermaPACE were almost 60% larger than those in the control group (making achieving significance that much more difficult). Also noteworthy is that trial protocol in the V.A.C. study allowed full closure of ulcers to be completed with surgery - this was not allowed in the dermaPACE study - had it and it's conceivable that dermaPACE would have shown statistical significance in 100% closure over standard of care.

- **Blinding:** dermaPACE was the only trial where both the physician and patient were blinded to which treatment (experimental or control) was being used - in none of the trials of the other therapies was the physician blinded. As the physician must make a (somewhat subjective) determination relative to efficacy (i.e. - closure rates, change in size of ulcers, etc), not blinding the physician potentially introduces bias in favor of the experimental treatment. Not blinding the physician can impact clinical trial results and has been cited as a deficiency in the robustness of trial data for both Apligraf and Dermagraft by insurance providers in determining reimbursement policy. dermaPACE's double-blind trial protocol eliminated any physician bias which further supports the strength of the data.

- **Treatment duration:** dermaPACE's closure and recurrence rates versus the competing treatments are especially compelling given that dermaPACE requires the lowest treatment burden with patients receiving only four 20-minute procedures over a two-week period. Dermagraft patients received up to eight applications (one per week for eight weeks) while Apligraf was applied up to five times (once per week). The V.A.C. treated patients received treatment for up to 16 weeks. V.A.C. treatment requires that suction is constantly applied to the wound (i.e. - the patient is hooked up to the device for the entire 16 weeks) and dressing is changed at least three times per week.

- **Closure rate:** dermaPACE's 48% closure rate stacks up better than both Dermagraft and V.A.C. We acknowledge dermaPACE's lower endpoint threshold could have benefitted its closure rate - but this could potentially have been more than offset by not allowing surgical closure or other differences among the trial protocols. While Apligraf's 56% closure rate slightly bested that of dermaPACE, this appears to be significantly more than offset by the difference in rates of recurrence (40% with Apligraf versus only 4.5% with dermaPACE).

- **Recurrence rate:** only 4.5% of dermaPACE treated wounds reopened after achieving complete closure, compared with 18% and 40% of the Dermagraft and Apligraf treated wounds, respectively. The V.A.C. study did not report rates of recurrence as this study allowed surgical closure. The results, again, are not necessarily directly comparable for the reasons already stated.

- **Safety:** while none of the therapies was associated with a higher rate of adverse events compared to standard of care, we note that dermaPACE is the least invasive of the four therapies. While only speculation at this point, given its non-invasive nature, over time, dermaPACE may prove to be a safer treatment.

NON-EFFICACY CONSIDERATIONS

While efficacy is obviously of critical importance, other factors, which we summarize below, will also likely play significantly into which therapy a caregiver, patient and reimbursement provider prefers.

- **Treatment burden:** dermaPACE's treatment burden (i.e. - number of procedures, duration of total treatment, procedural time, frequency of dressing changes, lack of anesthesia, non-invasive) is substantially less than any of the other therapies. Lower treatment burden benefits both the patient and the health care system. Shorter treatment duration also means that efficacy can be determined at an earlier point in time and if need-be, a different treatment regiment can be prescribed - which is important for DFU which can worsen very rapidly over a short period of time.

- **Non-invasive:** dermaPACE is also the least invasive. Unlike dermaPACE, all the other three advanced treatments require application of material to the wound, increasing potential for patient discomfort. The skin substitutes (Apligraf and Dermagraft) also require that the patch is affixed via sutures or wound glue. dermaPACE's non-invasive nature may also all but eliminate any treatment-related adverse events. As physicians must always balance safety with efficacy, they will generally sacrifice some efficacy for less severe wounds if it means less risk of complications. If, however, there is no compromise to safety, maximum efficacy may always be preferable, especially in the case of DFU, which gets progressively worse if not treated effectively. While dermaPACE's label will likely be for chronic wounds (i.e. - not healed after 4 weeks), its safety profile could prompt physicians to use it for a broader range of patients than dictated by the label (i.e. - for acute wounds as well). The lack of treatment-related adverse events in the IDE trial also suggests that dermaPACE could be used for longer than the treatment duration studied - which could potentially further benefit efficacy.

- **Cost of treatment:** as dermaPACE has the lowest treatment burden and does not require anesthesia or sutures, it also may be significantly less costly than the other advanced therapies. According to an analysis done by SANUWAVE, cost to treat a DFU over a 12-week period (i.e. - the duration of clinical trials) is approximately $3,700 with dermaPACE (assumes a total of four procedures), compared to $8,100 with Apligraf, $11,600 with Dermagraft, and $13,900 with V.A.C. (V.A.C. over 16 weeks - per trial protocol).

  Based on published CPT reimbursement rates, SANUWAVE's cost estimates for the three competing therapies do not appear unrealistic. We also point out that SANUWAVE's analysis assumed an average of four applications of Apligraf (up to 5 applications were performed in clinical trials) and an average of six applications of Dermagraft (up to 8 applications were performed in clinical trials) - which indicates to us that their cost estimates (at least for the skin substitutes) were not overly aggressive.

  A relatively low cost of treatment should help uptake of dermaPACE in the early years when reimbursement may be spotty (Medicare reimbursement may not come until after 2+ years) and (as we note below) should benefit SANUWAVE's efforts in gaining broad public and private insurance reimbursement (assuming eventual FDA approval).

- **Physician economics:** Health care is a business and physicians will be slow to adopt new treatments if the economics don't work. SANUWAVE's razor-razor blade business model, where SANUWAVE essentially lends the device for free and charges per procedure mitigates any financial risk at the physician level.

  As treatment with dermaPACE is relatively quick and non-invasive, physician costs should also be significantly lower as compared to competing therapies (potentially providing higher margins to the physician). In January 2011 new CPT codes for the application of skin substitutes were assigned which

lowers the payment amounts for physicians - which potentially reduces net profit to the physician when using products such as Dermagraft or Apligraf. dermaPACE's safety profile and low treatment burden may also lend itself to use on a broader patient population which may afford physicians higher utilization compared to other advanced therapies. And unlike the skin substitutes, which have very short (~ 10 days) shelf lives, there's virtually no inventory risk with dermaPACE.

- **Reimbursement:** the current lack of third-party reimbursement for dermaPACE means initial uptake may be slow. All the other therapies have broad Medicare and private insurance reimbursement. However, dermaPACE's cost profile relative to the other therapies should bode well in SANUWAVE's quest seeking third-party reimbursement.

REIMBURSEMENT

As dermaPACE is a novel device, Current Procedural Terminology (CPT) codes for which to provide for reimbursement through third-party payers (including Medicare) had yet to be established. SANUWAVE received notice in July 2011 that the American Medical Association released two CPT codes for ESWT. CPT III codes are a temporary code used for new technologies - decision to grant a CPT III code lies with the American Medical Association's CPT Editorial Panel - which bases its decision on a review of clinical data, peer-reviewed literature and interest in the technology from physicians. CPT III codes allow for data collection in order to see how widespread use of the technology is (i.e. - are physicians interested in using it?). Now that CPT III codes are assigned, SANUWAVE will be focused on transitioning to a Category I code. The CPT I code has a relative value assigned which specifies the reimbursement amount related to treatment with dermaPACE. The CPT I code would likely not be assigned until at least two years (i.e. - until enough data is collected and reviewed for the AMA to determine if the technology is worthy of a CPT I code) after dermaPACE receives FDA approval, however.

*...**changes to Medicare should directly benefit dermaPACE***
While not specifically stated as one of the criteria used in the AMA's decision-making process to grant CPT codes or reimbursement rates, relative cost will almost certainly be a consideration. Technologies such as PACE, which potentially offer better care at a lower cost, complement the recent and ongoing health care overhaul measures in the U.S.

As health care moves away from a "fee-for-service" to a "pay-for-performance" model, demand for lower-cost, efficacious treatments should increase. The current fee-for-service model means health care providers have a financial incentive if they have a revolving door of patients - which usually are those with chronic conditions. The current model also may encourage the use higher margin (i.e. - expensive) and, perhaps, less effective therapies. Medicare is moving away from this fee-for-service payment model to one which incentivizes healthcare providers for more efficient, more effective and less costly care. While there are still some bugs to be worked out (such as what are the appropriate metrics to use to measure "effectiveness"), all indications suggest that "pay-for-performance" will become more widespread. All indications also suggest that chronic diseases such as diabetes, which are a tremendous burden on the health care system (10% of all health care dollars are spent on direct costs related to diabetes), will be the major focus of "pay-for-performance."

Based on efficacy seen in the clinical data and the potential to reduce costs associated with DFU treatment (i.e. - is less costly than other already reimbursed advanced therapies and may reduce cost of complications such as amputations), we think dermaPACE could have a very convincing case for gaining Medicare reimbursement. As "pay-for-performance" becomes more widespread, so should the demand for highly effective, lower-cost therapies - especially for chronic diseases. We believe dermaPACE will be perfectly positioned to exploit the demand for highly effective, safe and low cost treatment for DFU.

...support for broader coverage of advanced DFU therapies
Advanced BioHealing (manufacturer of Dermagraft) sponsored an expert panel to make evidence and research-based recommendations on the protocol for treatment of DFU. The panel, composed of surgeons and physicians with specializations in wound care, podiatry and diabetes (all of which had some financial relationship with

Advanced BioHealing, Organogensis (manufacturer of Apligraf) and / or KCI (manufacturer of V.A.C.), detailed their findings in an April 2010 paper titled, "Consensus Recommendations on the Standard of Care for Treating Neuropathic Foot Ulcers in Patients with Diabetes". The paper is available here, http://www.o-wm.com/files/docs/ABH_WOUNDS.pdf

The specific purpose of the study, according to the abstract, was to, "provide clinicians with the clinical markers, evidence and recommendations that, used in conjunction with orderly decision-making and good clinical judgment, will advance the standard of care for the treatment of neuropathic DFUs."

The authors concluded that:

- DFUs impose a significant financial burden, with secondary complications such as infection and amputation contributing the majority of the related cost
- Fast and effective therapy should be the goal in treating DFU
- Current standard of care is a relatively ineffective treatment for non-healing DFUs
- Early adoption of advanced therapies should be advocated in order to expedite wound healing of non-healing DFUs. Specifically, if after 4-weeks of current standard of care the wound size has not decreased by ≥ 50% (i.e. - is considered "non-healing"), advanced therapies should be considered
- Advanced therapies (specifically Dermagraft, Apligraf and V.A.C.) should be considered the new standard of care for non-healing wounds

While we acknowledge the potential conflicts of interests of the authors, the paper is clearly well documented, supported by evidence/research and not written as a promotional piece. The AMA/Medicare can and has used research pieces similar to this to consider revisions to its reimbursement guidelines. By stressing the importance of earlier intervention with effective advanced therapies in order to improve patient outcomes (with an implied interest in reducing cost of treatment as well), the authors are essentially advocating use dermaPACE (which may be the most effective, safest and lowest cost of all the advanced DFU therapies).

...dermaPACE reimbursement in the early years

The major private insurers generally follow Medicare's reimbursement policies, which we expect would be the case for dermaPACE. In the meantime, SANUWAVE will look to get regional private payers on board as they wait for Medicare reimbursement (i.e. - CPT III codes). The initial roll-out of dermaPACE will likely be tailored (at least to some degree) to wherever SANUWAVE finds reimbursement is most favorable.

PIPELINE

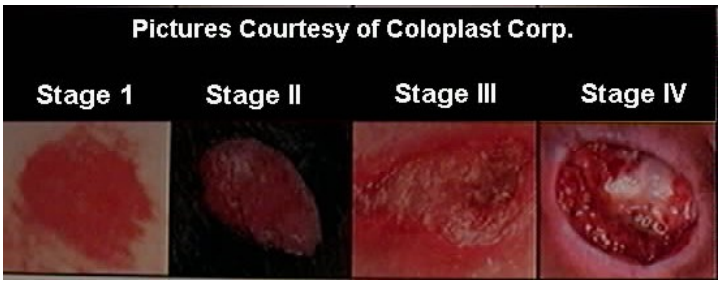
OTHER WOUNDS

Aside from DFU, dermaPACE may also be an effective treatment for other wounds including pressure ulcers (i.e. - bed sores) and venous ulcers. SANUWAVE has not revealed specific plans for pursuing FDA approval of dermaPACE for wounds other than DFU (which would require clinical trials), although we think there will be movement in this area following the launch for the DFU indication.

Pressure ulcers are caused by unrelieved pressure, friction and humidity to any part of the body but are most common in bony and high cartilage areas such as the hip, elbow, knees or ankles. Similar to DFUs, pressure ulcers are progressive and if not effectively treated, can quickly worsen. Standard of care, which is similar to that for DFU, is also relatively ineffective for more severe cases of pressure ulcers.

Pressure ulcers are most commonplace in settings such as nursing homes and long-term care facilities. They are especially problematic for patients with spinal cord injuries. It is estimated that two million people in the U.S. suffer from pressure ulcers, approximately 500k of which will require hospitalization. Estimates put the cost of care at $2k - $40k per pressure ulcer, which is dependent of the stage (i.e. - severity) of the ulcer. Some estimates have put the annual cost of treating pressure ulcers in the U.S. as high as $2 billion.

Pressure Ulcers



SOURCE : http://www.medicaledu.com/staging.htm

Venous ulcers are one of the most common types of ulcers affecting the lower extremities, afflicting approximately 1 million Americans every year. They occur when veins in the legs are unable to return blood back to the heart due to congestion in the veins. The build-up of blood in the legs can cause changes in the skin structure and ultimately lead to ulcerations.

Venous ulcers are highly susceptible to recurrence and, as a result, can be very difficult to treat. One study found up to 48% of venous ulcers recur by the fifth year after healing. Common treatment includes compression therapy where the leg is wrapped with non-elastic bandages in order to increase blood flow back to the heart.

Estimates put the cost per venous ulcer at around $5- $10k. In aggregate the annual cost of treating venous ulcers in the U.S. is about $4 billion.

Venous Ulcer



source: http://www.medicaledu.com/venous.htm

ORTHOPEDICS

orthoPACE, which SANUWAVE launched into the European market in July 2010, is the successor device to OssaTron. SANUWAVE attributed the majority of the 82% revenue growth in the second half of 2010 ($468k vs. $257k combined for Q3 and Q4 2009) as well as the 76% y-o-y revenue growth in Q1 2011 (to $252k) to European sales of orthoPACE.

SANUWAVE expects the initial markets for orthoPACE in the U.S. to be similar to those targeted with OssaTron - mostly tendinopathies such as tennis elbow and heel pain but also expanding into nonunion fractures as well. Roughly 3 million Americans suffer with some form of tendinitis annually. Expanding into orthopedic care, including treatment for long bone fractures, osteoarthritis, and spine fusion and repair would significantly increase the size of the target market for orthoPACE.

...Sports Medicine

In clinical trials OssaTron was shown to be an effective treatment in a variety of orthopedic and sports medicine indications. This includes increasing the rate of healing of incompletely healed fractures of the tibia, improvement of avascualr necrosis (degradation of the hip joint), and relief from pain of plantar fasciitis (heel) and chronic lateral epicondylitis (tennis elbow).

One of these studies was highlighted in an article titled *Extracorporeal Shock Wave Therapy for Nonunion of the Tibia* which was published in the March 2010 edition of the Journal of Orthopedic Trauma. In the six-year study 172 patients suffering from fractures of the tibia that would not fully heal (i.e. - non-union fractures). After undergoing ESWT therapy using OssaTron, 80.2% of the non-union fractures healed within an average of 4.8 months.

...Traumatic Fractures
Management believes traumatic fractures, which can be especially susceptible to incomplete healing, could be an attractive application for orthoPACE. Annually approximately 250k trauma fractures in the U.S. do not fully heal (i.e. - are non-union).

...Spinal Fusion
With approximately 500k procedures performed in the U.S. every year, spinal fusion represents another sizeable market. Spinal fusion is the surgical joining of vertebrae, often through the use of a bone graft (either from the patient or a donor) to fuse the vertebrae together. The principal risk of spinal fusion is that the graft does not heal. Incomplete healing typically occurs in 10%-50% of all spinal fusion procedures and be especially problematic for individuals with higher risk factors such as smokers or those with osteoporosis.

...Osteoarthritis
With approximately 33 million Americans suffering from osteoarthritis (degenerative joint disease), the market for treatment of the disease is huge (and estimated to grow to $7 billion worldwide by 2015). Recently published in an online edition of the Archives of Orthopedic Trauma Surgery, a pre-clinical study showed that a single procedure with ESWT significantly improved or prevented osteoarthritis in the knees of rats. At 12 weeks post-treatment, the osteoarthritis-afflicted, ESWT treated rats showed comparable data to the knees of normal, healthy rats. The authors concluded that "ESWT treatment may offer an effective, low-cost treatment option in humans that carries little risk compared with other treatments."

The Next Steps for OrthoPACE
Given the abundance of clinical data from trials with legacy devices (such as Ossatron and Evotron), SANUWAVE may only need to run relatively small clinical trials with orthoPACE to have ample support for an FDA regulatory filing for orthoPACE. SANUWAVE has yet to announce plans for trials with orthoPACE but presumably this is another event on the horizon following the launch of dermaPACE for DFU.

COSMETIC / CARDIAC

While wound care (and to a lesser extent, orthopedic) likely holds the most opportunity for SANUWAVE's PACE devices, the company hopes to leverage the technology by targeting ancillary uses. These are more of "back-burner" markets at the moment, however, and not likely to receive much attention from a development perspective in the near-term.

Benefits such as increased microcirculation may be applicable to certain cosmetic and cardiac uses including for the treatment of cellulite, reduction of scars (both old and new), improvement of the body's acceptance of skin grafts and treatment of ischemic heart disease. Heart disease is of epidemic (and growing) proportions so if there is utility for PACE in this market, it could be a tremendous boon to SANUWAVE. The applicability of PACE for cardiac indications such as breaking up plaque in the arteries would likely be something that would be pursued through licensing the technology out and would not be known for years, however.

FINANCIAL CONDITION

Cash

As of their most recent reporting period (9/30/2011) SANUWAVE had $5.8 million in cash and equivalents, compared to $7.8 million at 6/30/2011.

Debt
SANUWAVE recently closed on a stock-for-debt swap, significantly reducing their debt balance. The remaining outstanding debt consists of $5.4 million, 6% unsecured notes due in August 2015 which were issued by HealthTronics in conjunction with SANUWAVE's purchase of that company's orthopedics business in August 2005.

Cash Flow
Cash used in operations was $6.9 million in the nine months ending 9/30/2011 including $2.0 million in Q1, $3.0 million in Q2 and $2.0 million in Q3. Excluding changes working capital, cash used in operations was $5.5 million in the nine months ending 9/30/2011 including $1.7 million in Q1, $2.0 million in Q2 and $1.7 million in Q3. At the current cash burn rate SANUWAVE has roughly 9 months worth of cash. We expect cash burn during the remainder of 2011 to be generally in-line with that of the first 9 months of the year.

Prior to the recent FDA action, we had expected SANUWAVE to begin preparing for the dermaPACE launch during the first half of 2012 – including hiring and training a sales force, ramping up inventory and additional marketing expenses – all of which would increase the use of cash. This is now indefinitely on hold. We now model cash burn in 2012 to be similar to that of 2011. Our model also assumes that SANUWAVE runs an additional clinical trial over the course of a portion of 2012 and 2013 – as noted previously, however, this assumption of another clinical trial is just a placeholder until there's more clarity on the direction that SANUWAVE will take. Nonetheless, initial revenue and cash generation from dermaPACE will be delayed (and potentially significantly so) from our initial expectations – this, along with the possibility of another clinical trial, means SANUWAVE may need to raise a meaningful amount of additional capital. Our updated forecasted outstanding share count in our model reflects an assumption that SANUWAVE funds a majority of this with common stock (this is another placeholder until we know more).

OUTLOOK

We have updated our Outlook following the recent FDA major deficiency letter. While the direction that SANUWAVE will take in order to continue to move towards FDA approval is just conjecture at this point, we need to incorporate certain assumptions into our outlook and related financial model in order to place a value on the company. Some of these assumptions are very general in scope and little more than just blind guesses at this point – we will update these assumptions if necessary when there is more clarity on the updated regulatory approval pathway. The most significant "blind-guess" assumption is that SANUWAVE runs another clinical trial – which delays approval until early 2014 (from prior assumption of mid-2012) and, in-turn, requires the company to raise a material amount of additional capital.

OUR KEY ASSUMPTIONS

- **Add'l clinical trial:** 2012 - 2013
- **FDA approval**: FDA approval comes in early 2014
- **dermaPACE Launch**: dermaPACE launch commences erly/mid-2014
- **Reimbursement in the Early Years:** some regional private insurers provide reimbursement following dermaPACE launch
- **Widespread reimbursement:** CPT I (relative value) code is established by the end of fiscal 2016, triggering widespread public and private insurance coverage of dermaPACE
- **Pipeline:** development of the pipeline (for orthoPACE as well as for additional wound indications for dermaPACE) is slow-going until dermaPACE sales begin to ramp
- **No Pipeline Contribution:** our model does not incorporate any contribution from any pipeline indications or products

OUR OUTLOOK: Pre dermaPACE Launch

We model relatively little revenue growth prior to the dermaPACE launch. While both dermaPACE and orthoPACE are CE Marked for sale in Europe, we do not expect either to generate much in the way of revenue until well after they enter the U.S. market.

OUR OUTLOOK: Post dermaPACE Launch

We expect the dermaPACE launch to represent the first of two inflection points for SANUWAVE. Prior to gaining Medicare reimbursement, success of dermaPACE will largely be predicated on the degree of interest from private insurers. As the private insurance "majors" typically follow Medicare's lead, SANUWAVE will initially be calling on more regional payers. While we have no specific insight into the degree of formulary coverage that dermaPACE may enjoy in the early years, based on efficacy seen in the trial data, cost advantages over competing therapies and the potential to leverage relationships built during the Ossatron years, we think it is reasonable dermaPACE can gain some level of reimbursement prior assignment of CPT relative value codes.

We expect revenue growth will likely be somewhat moderate until widespread reimbursement comes on-line (~ 2016?), however. Nonetheless, SANUWAVE's small size and the high margins expected from the procedure kits (eventually approaching 90%), combined with the large size of the DFU market, means positive cash flow and EPS could potentially be attained in short order following FDA approval - and possibly prior to gaining Medicare reimbursement.

We currently model dermaPACE to launch in the U.S. around Q2/Q3 2014 (this is highly subject to change over the next 90 days) and for the bulk of our $4.4 million revenue estimate for 2014 to come during the second half of the year. We also model roughly one-third of this $4.4 million in revenue total to come from continued international sales of orthoPACE.

We assume SANUWAVE places just over 100 dermaPACE units through the end of 2014 and utilization (i.e. - patients treated per device) is initially relatively low but increases over time. As the instrument will be loaned free of charge (with related depreciation running through COGS), revenue (from sale of procedure kits) and profitability will lag growth in the installed base, especially initially. As utilization increases, this lag will narrow and margins should widen. For 2015 we model revenue of $23.8 million which reflects an estimated installed base of approximately 300 units and average utilization per device at about 6 patients per month.

Medicare reimbursement is the second major expected inflection point for SANUWAVE. We currently model this to come sometime during 2016, at which time growth in the installed base and utilization should substantially steepen. Leveraging a greater installed base and the high margins afforded by the procedure kits should result in rapid improvement in cash flow and profitability.

VALUATION / RECOMMENDATION

Prior to the FDA major deficiency letter we were valuing SANUWAVE based on 2015 P/E comparables (to Kinetic Concepts and Smith & Nephew). Our updated outlook, which incorporates an assumed significant delay in the U.S. launch of dermaPACE, results in SNWV posting negative EPS through at least 2015 – as such our prior valuation methodology is inappropriate. Instead we now use 2015 P/S comparables to value SNWV. Smith & Nephew currently trades at approximately 1.5x analyst's 2015 forecasted revenue. Kinetic Concepts was acquired in November for $6.1 billion, or about 2.8x estimated 2015 revenue. We currently model SNWV to generate revenue of $23.8 million in 2015 – based on the two comp 2015 P/S multiples values SNWV at between $36 million ($1.71/share) and $55 million ($3.20/share). For simplicity, we use the average of the two, which values SNWV at about $2.50/share. We think it bears repeating, however, that our model is highly subject to change once there is more clarity on the updated regulatory approval pathway that SANUWAVE expects to pursue. As it is now, we value the company at $2.50/share, down from $6.00/share prior to the recent FDA communication.

KEY MANAGEMENT PROFILES

Christopher M. Cashman
Christopher M. Cashman joined SANUWAVE Health, an emerging leader in regenerative medicine, as Director, President and Chief Executive Officer in December, 2005. Immediately prior, he served as President of Therapeutic Surfaces for Kinetic Concepts, Inc, a global leader in advanced wound care. He conducted a management buyout in November 2001 of Snowden Pencer, a minimally invasive surgical device manufacturer, and assumed the role of CEO and President. In March 2004, Snowden Pencer was sold to Cardinal Health. Mr. Cashman has also served as a business unit head with Genzyme Biosurgery and held several senior sales and marketing positions with Genzyme Surgical Products and Deknatel Snowden Pencer. Mr. Cashman graduated from the United States Naval Academy in 1989 with a B.S. degree in Economics and served on a fast attack submarine as Supply Officer. He received his M.B.A. degree in 2001 from The Kellogg Graduate School of Management at Northwestern University.

Barry Jenkins
Barry Jenkins joined SANUWAVE as Chief Financial Officer in April 2006. His previous position was with Automatic Data Processing (ADP), where he served as Chief Financial Officer for the Benefits Services Division. Mr. Jenkins began his career with Price Waterhouse and progressed to a Senior Manager. He was the Vice President of Finance at AHL Services, a public company which grew to over $900 million during his tenure. As the Chief Financial Officer at Snowden Pencer, Mr. Jenkins helped grow the corporation prior to the company being sold to Cardinal Health in March, 2004. He is a Certified Public Accountant with 25 years of financial management experience and is a Cum Laude graduate of Virginia Tech.

Peter Stegagno
Peter Stegagno joined SANUWAVE as Vice President, Operations in March 2006. Mr. Stegagno brings to SANUWAVE 16 years experience in the medical device market encompassing manufacturing, design & development, quality assurance and international & domestic regulatory affairs. He has been instrumental in the development and deployment of international operational processes for leading medical device companies. He most recently served as Vice President of Quality and Regulatory Affairs for Elekta, and other medical device companies including Genzyme Biosurgery. Before focusing on the medical field, he enjoyed a successful career encompassing production roles in the space industry, including avionics guidance systems for military applications and control computers for the space shuttle. Mr. Stegagno graduated from Tufts University with a B.S. degree in Chemical Engineering.

Iulian Cioanta
Iulian Cioanta joined SANUWAVE in June 2007 as Vice President of Research and Development. Prior to joining SANUWAVE, Dr. Cioanta served as Business Unit Manager with Cordis Endovascular, a Johnson & Johnson company, Director of Development Engineering with Kensey Nash Corporation, Research Manager at ArgoMed Inc. and Project Manager and Scientist with the Institute for the Design of Research Apparatuses. During his career, Dr. Cioanta worked 12 years in the medical device industry and eight years in academia at Polytechnic University of Bucharest in Romania, Leicester University in U.K. and Duke University in the United States. He received a M.S. degree in Mechanical Engineering and Technology from the Polytechnic University of Bucharest, and he earned his PhD degree in Biomedical Engineering from Duke University in the field of extracorporeal shock wave lithotripsy. Dr. Cioanta is an acknowledged scientist who has published in the field of acoustic and bioengineering, and he is an author of 15 issued patents and 8 pending patents.

Bernie Laurel
Bernie Laurel joined SANUWAVE as Vice President of Sales and Marketing in November 2009 with more than fifteen years experience in sales and marketing, including expertise in the advanced wound care market. Prior to joining SANUWAVE, he was Vice President of Sales and Marketing for Medela, Inc.′s newly-formed Healthcare America′s business unit, where he drove overall planning, marketing strategy, new product development, distribution, direct and indirect sales, and other business development initiatives. Bernie was also Vice President of Marketing for Imagyn Medical Technologies, a newly public urologic device manufacturer, and he held sales, marketing and consulting roles in several privately-funded device start-ups.

Anne Stefurak
Anne Stefurak re-joined SANUWAVE in November 2009 as Vice President of Medical Policy and Reimbursement with more than twenty years in the medical field working with local, regional and national insurance companies, medical device companies, technology assessment organizations, advocacy groups, academic centers, various physician offices, and radiation oncology centers. Anne brings experience with payer reimbursement, invasive as well as non-invasive medical device technology, sales and marketing, coverage policy, appeals, contracting and FDA compliance. Before rejoining SANUWAVE, Anne worked as Director of National Policy and Reimbursement at Physician Oncology Services. Anne also brings expertise as a Regional Access Manager and Senior Regional Reimbursement Manager at Cyberonics, National Provider Relations Manager at National Healthcare Network, and Manager of Provider Relations at Aetna U.S. Healthcare.

FINANCIAL MODEL

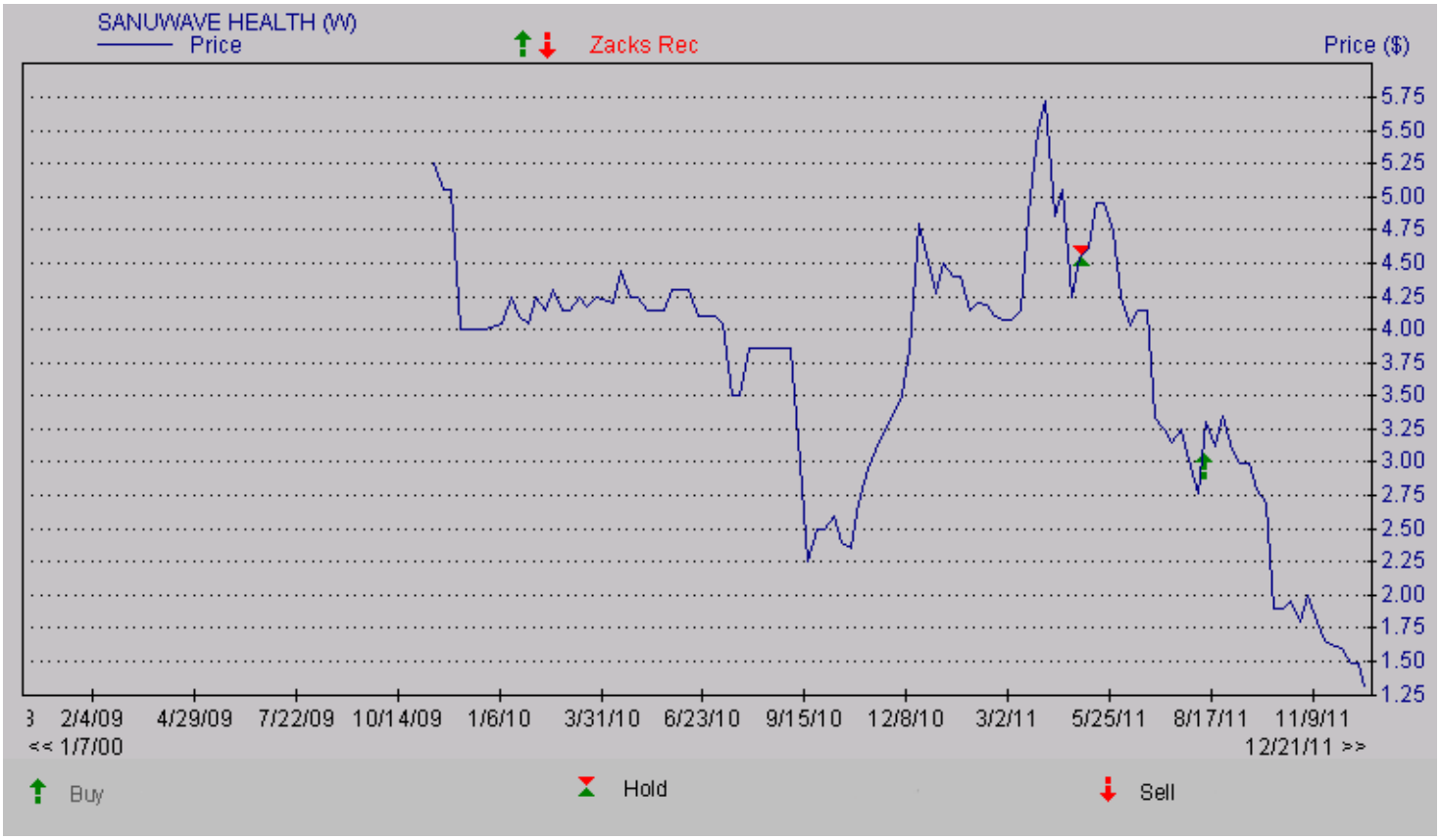
SANUWAVE Health, Inc.

	2010 A	Q1A	Q2A	Q3A	Q4E	2011 E	2012 E	2013 E	2014 E	2015 E
Total Revenues	$728.4	$251.8	$163.7	$161.7	$205.0	$782.2	$1,210.0	$1,370.0	$4,356.4	$23,787.9
YOY Growth	*10.2%*	*75.9%*	*39.7%*	*-41.9%*	*7.9%*	*7.4%*	*54.7%*	*13.2%*	*218.0%*	*446.0%*
Cost of Revenues	$250.3	$93.3	$47.2	$48.5	$62.0	$251.0	$367.5	$411.0	$1,367.8	$5,343.2
Gross Income	$478.1	$158.5	$116.5	$113.2	$143.0	$531.2	$842.5	$959.0	$2,988.6	$18,444.7
Gross Margin	*65.6%*	*62.9%*	*71.2%*	*70.0%*	*69.8%*	*67.9%*	*69.6%*	*70.0%*	*68.6%*	*77.5%*
R&D	$3,879.1	$749.3	$795.1	$623.3	$805.0	$2,972.7	$3,850.0	$4,150.0	$4,400.0	$5,580.0
% R&D	*532.5%*	*297.6%*	*485.6%*	*385.5%*	*392.7%*	*380.1%*	*318.2%*	*302.9%*	*101.0%*	*23.5%*
SG&A	$7,100.6	$1,382.2	$1,510.4	$1,494.0	$2,155.0	$6,541.5	$6,655.0	$6,754.0	$7,886.0	$17,603.0
% G&A	*974.8%*	*549.0%*	*922.4%*	*924.0%*	*1051.2%*	*836.3%*	*550.0%*	*493.0%*	*181.0%*	*74.0%*
Depreciation	$829.6	$6.2	$6.2	$1.0	$1.0	$14.5	$20.0	$40.0	$75.0	$100.0
Amortization	$306.8	$76.7	$76.7	$76.7	$76.7	$306.8	$306.8	$306.8	$306.8	$306.8
Write down of assets	$169.6	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Operating Income	($11,807.6)	($2,056.0)	($2,271.9)	($2,081.7)	($2,894.7)	($9,304.3)	($9,989.3)	($10,291.8)	($9,679.2)	($5,145.2)
Operating Margin	*-1620.9%*	*-816.7%*	*-1387.4%*	*-1287.6%*	*-1412.0%*	*-1189.5%*	*-825.6%*	*-751.2%*	*-222.2%*	*-21.6%*
Gain (loss) on asset sale	$6.6	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Svcs provided to Pulse Vet.	$360.1	$112.5	$112.5	$112.5	$112.5	$450.0	$180.0	$0.0	$0.0	$0.0
Extinguishment of debt	($2,693.9)	$0.0	($1,318.8)	$0.0	$0.0	($1,318.8)	$0.0	$0.0	$0.0	$0.0
Interest expense, net	($961.6)	($236.3)	($79.8)	($76.6)	($80.0)	($472.7)	($340.0)	($360.0)	($360.0)	($140.0)
Loss of FX	($66.1)	($3.6)	($14.2)	($25.7)	$0.0	($43.5)	$0.0	$0.0	$0.0	$0.0
Pre-Tax Income	($15,162.4)	($2,183.3)	($3,572.2)	($2,071.5)	($2,862.2)	($10,689.3)	($10,149.3)	($10,651.8)	($10,039.2)	($5,285.2)
Taxes	($240.0)	$0.0	$0.0	$0.0	$0.0	$0.0	$24.2	$27.4	$30.8	$0.0
Tax Rate	*1.6%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*-0.2%*	*-0.3%*	*-0.3%*	*8.0%*
Discontinued Operations	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Net Income	($14,922.4)	($2,183.3)	(3,572.2)	(2,071.5)	(2,862.2)	($10,689.3)	($10,173.5)	($10,679.2)	($10,070.0)	($5,285.2)
YOY Growth	*142.5%*	*-27.1%*	*31.0%*	*-22.2%*	*-56.2%*	*-28.4%*	*-4.8%*	*5.0%*	*-5.7%*	*-47.5%*
Net Margin	*-2048.5%*	*-867.2%*	*-2181.5%*	*-1281.3%*	*-1396.2%*	*-1366.6%*	*-840.8%*	*-779.5%*	*-231.2%*	*-22.2%*
EPS (continuing ops)	($1.15)	($0.14)	($0.17)	($0.10)	($0.14)	($0.54)	($0.40)	($0.31)	($0.25)	($0.12)
Diluted Shares O/S	12,925	16,144	20,538	20,908	20,920	19,627	25,688	34,000	40,000	45,000

Brian Marckx, CFA

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