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Viveve Medical (VIVE-NASDAQ)

Warning Letter Headwinds Persist, Although Dissipating. 2019 Guidance Implies Much-Improved Operating Loss

We use a 10-year DCF model to value VIVE. We have revenue growing from $18.5M in 2018 to $36.7M in 2021 and to approximately $103M in 2027. Other key inputs to our DCF include a 11% discount rate and 2% terminal growth rate. Based on our DCF model, VIVE is valued at approximately $4.75/share.

Current Price (03/19/19)	$0.98
Valuation	**$4.75**

OUTLOOK

We think SUI may soon represent the majority of the company's opportunity for accelerating growth. Given the relatively massive size of the target population (30M in U.S.) and compromise to quality of life among those suffering from the condition, an SUI indication for the Viveve System could prove a more potent revenue driver than that of sexual function. In addition, as FDA's July 2018 warning letter created a stiffer and longer than expected headwind to Viveve's sales, we think that provides additional rationale to accelerate their shift from aesthetics to gynecologists and urologists which are seeking non-invasive SUI therapeutic alternatives. And, with more and more data showing the effectiveness of the Viveve System in SUI, this should act as a catalyst to help drive awareness and adoption for use in that indication. This includes the positive 12-month data from the U.S. SUI feasibility study, which was announced in December, as well as anticipated other data releases in SUI. And while VIVE is retrenching to a degree as they wait out the warning letter headwinds and progress through their ongoing sexual function and SUI studies, they clearly do believe that there are near-term opportunities to improve upon their financial performance. Management reiterated their previously issued 2019 revenue guidance of approximately $20M and expectations that gross margin widens. And, coupled with significant operating expense reductions, we think operating loss improves from $45.0M in 2018 to $33.3M in 2019.

SUMMARY DATA

52-Week High	**$4.34**
52-Week Low	**$0.87**
One-Year Return (%)	**-76.07**
Beta	**0.71**
Average Daily Volume (sh)	**202,658**
Shares Outstanding (mil)	**46**
Market Capitalization ($mil)	**$45**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**90**
Insider Ownership (%)	**23**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**167.7**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2019 Estimate	**N/A**
P/E using 2020 Estimate	**N/A**
Zacks Rank	**N/A**

Risk Level	**High,**
Type of Stock	**Small-Growth**
Industry	**Med Devices**

ZACKS ESTIMATES

Revenue
(in '000s of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2018	3699 A	5525 A	4821 A	4472 A	18517 A
2019	2982 E	4927 E	4976 E	6597 E	19482 E
2020					26208 E
2021					36665 E

Earnings per Share

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2018	-$0.49 A	-$0.37 A	-$0.39 A	-$0.38 A	-$1.61 A
2019	-$0.25 E	-$0.25 E	-$0.19 E	-$0.18 E	-$0.82 E
2020					-$0.65 E
2021					-$0.53 E

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

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Q4 Results: *Warning Letter Headwinds Persist, Although Dissipating. 2019 Guidance Implies Much-Improved Op Loss…*

Viveve reported Q4 financial results and provided a business update. Relative to the financials, as expected following the company's preannouncement in January, revenue was approximately $4.5M. While this is down 12% from the prior year, it is about 16% better than what we had anticipated (prior to the preannouncement) and, per management's comments on the call, reflective of the continued hangover from FDA's late-July warning letter (which, as a reminder, was not addressed to Viveve but did cause industry-wide disruptions). And while the sales headwind persists, indications are that it is incrementally dissipating.

Also on the encouraging side is recent widening of gross margin which came in at respectable 37.2% in Q4. While down from 54.3% in the prior year period, it is up more than 600 basis points from the prior quarter and expected to continue to widen. Cost of the Viveve 2.0 system is ~30% - 35% less than the legacy machine (and treatment tips) and will benefit margins going into 2019. The 2.0 system launched in the U.S. in Q4 and is expected to begin to roll out internationally during the year (as regulatory clearances are obtained).

Operating expenses were elevated in Q4. At $13.9M, this is the highest quarterly operating spend in company history. But a recently implemented restructuring plan, which included a 36% reduction in headcount, means operating expenses should drop fairly dramatically. While VIVE will take severance-related charges, we expect to see a significant reduction in operating expenses beginning with Q2.

As we noted in our January Investor Note, while the reasoning behind the restructuring largely rests on cutting costs, we think the timing is also somewhat prescient given the not-so-subtle shift in focus that has been ongoing from sexual function over to the (much larger) SUI market. It appears that management is now more fully embracing that shift. While we expect the aesthetic/sexual function market to remain an important component of VIVE s business, we think SUI may soon represent the majority of the company's opportunity for accelerating growth. Given the relatively massive size of the target population (30M in U.S.) and compromise to quality of life among those suffering from the condition, an SUI indication for the Viveve System could prove a more potent revenue driver than that of sexual function.

In addition, as FDA's July 2018 warning letter created a stiffer and longer than expected headwind to Viveve's sales, we think that provides additional rationale to accelerate their shift from aesthetics to gynecologists and urologists which are seeking non-invasive SUI therapeutic alternatives. And, with more and more data showing the effectiveness of the Viveve System in SUI, this should act as a catalyst to help drive awareness and adoption for use in that indication. This includes the positive 12-month data from the U.S. SUI feasibility study, which was announced in December (and which we discuss below), as well as anticipated other data releases in SUI. This includes results of LIBERATE International, expected in July or August, and potential data from LIBERATE U.S., the commencement of which is anticipated later this year.

And while VIVE is retrenching to a degree as they wait out the warning letter headwinds and progress through their ongoing sexual function and SUI studies, they clearly do believe that there are near-term opportunities to improve upon their financial performance. Management reiterated their previously issued 2019 revenue guidance of approximately $20M and expectations that gross margin widens. And, coupled with significant operating expense reductions, we think operating loss improves from $45.0M in 2018 to $33.3M in 2019.

They also anticipate several important near-term operational milestones, including;

- Q3 2019: IDE approval and commencement of LIBERATE-U.S.
- July / August 2019: final 6-month SUI results from LIBERATE-international
- April 2020: 12-month (i.e. final) results of VIVEVE II

Q4 total revenue was $4.5M, down 12% yoy, down 7% sequentially and 16% better than our (pre-preannouncement) $3.8M estimate. While management noted that the FDA warning letter remained an impediment to revenue growth in the quarter, the beat to our number reflects a lighter-than-we-had-anticipated headwind in that regard. But while U.S. sales performed better than we had been expecting, the opposite was true for international system sales.

Console placements totaled 57 units (vs. 55 E) including 48 U.S. (vs 40 E) and 9 OUS (vs 15 E). Perhaps noteworthy is that Q4'18's nine international system sales was the lowest in at least the last three and half years. Treatment tips totaled 4,600 (vs 5,047 E).

Revenue (proportional contribution) per geographic territory:

	Q4 '18	%Ttl	+/- yoy	FY2018	%Ttl	+/- yoy	Q4 '17	%Ttl	FY2017	%Ttl
North America	$3,556	(80%)	-11%	$14,169	(77%)	28%	$4,016	(79%)	$11,083	(72%)
Asia Pacific	$653	(15%)	-34%	$2,891	(16%)	-9%	$987	(19%)	$3,178	(21%)
Europe & Middle East	$226	(5%)	131%	$1,369	(7%)	105%	$98	(2%)	$667	(4%)
Latin America	$0	(0%)	-	$51	(0%)	-86%	$0	(0%)	$360	(2%)
Other	$37	(1%)	-	$37	(0%)		$0	(0%)	$0	
Total	$4,472	(100%)	-12%	$18,517	(100%)	21%	$5,101	(100%)	$15,288	(100%)

North America not only continues to represent the most significant contributor to total revenue but it's overall contribution also continues to grow. North America's contribution to the topline increased to 77% in 2018, up from 72% in the prior year. Despite VIVE's regular expanding international reach (the Viveve System is now cleared for sale in more than 60 countries) and the relatively recent launch in the U.S. (Q4 '16 was the first period of U.S. revenue), the domestic market has quickly become the major driver of, and contributor to, total revenue.

The 48 U.S. console placements is down from 57 sold in Q4'17 and flat from Q3'18 (48). For the full year, 259 systems were sold (227 in 2017) including 203 (160 in 2017) in the U.S. and 56 (67 in 2017) internationally. As part of the recently implemented restructuring, the direct sales force was significantly cut. As of the close of Q3 VIVE had a total sales team of 49, which included 23 capital reps, 10 associate sales reps, 10 practice development managers, 3 regional sales directors and 1 practice development strategic partnership director – all of which reported to a V.P. of sales. Today, the sales team consists of 14 direct sales reps, in addition to the company's U.S. distribution partner, AMP (which has 20 – 24 reps). While the size of the sales team has been slashed, management noted that those retained are relatively high-producing. As such, we do not expect anything close to a proportional drop in sales as a result of the headcount reductions.

We reiterate that we remain optimistic of the long-term growth curve given the Viveve System's leading position as it relates to documented safety and efficacy. We also continue to believe that additional positive clinical data supporting both (i.e. safety and efficacy), along with efforts towards educating consumers of the difference between Viveve's technology and what we have characterized as the imposters, will pay dividends in the form of accelerating growth. With several upcoming clinical milestones, Viveve's awareness-building efforts could have even more firepower.

As it relates to consumables, 4,600 were recognized as sales in Q4 – which is third-best in company history and behind Q1'18 (5,400) and Q3'18 (5,700) but well ahead of the 2,600 sold in the comparable prior year period. For the full year, approximately 18,450 treatment tips were sold, or about 70% more than the 10,800 sold in 2017. According to our calculations, utilization averaged approximately 2.6 treatments per unit per month in 2018, only slightly lower than the 2.7 tips per system per month in 2017. This is inline with what we had forecast. We also note that, intuitively, we would expect to see attrition in per-system utilization with regular growth in the installed base. The total installed base grew to 703 at the close of 2018, up 58% from a year earlier.

Operational Update:

12-Month SUI Feasibility Study Data Further Supports Compelling Efficacy Signal…

In December 2018 Viveve announced 12-month results of its feasibility study evaluating their Viveve System technology for the treatment of women with mild-to-moderate stress urinary incontinence (SUI). The following week, results were presented at a SUI-focused KOL symposium sponsored by the company. The data, we believe, largely confirms the compelling efficacy signal seen at six months, which was announced in June. And while it appears, as might be expected, that there was somewhat of a deterioration of effectiveness from the six-month to the twelve-month follow up, with results of the 1-hour pad weight test continuing to show substantial improvement from baseline, we think this latest data further bolsters the likelihood of eventual success of the pivotal LIBERATE SUI studies.

As a reminder, in mid-June Viveve announced what we characterized as potentially compelling 6-month data from its SUI 12-month feasibility study. Results at six-months and our accompanying commentary are available in our Appendix. And, for ease of reference, we have also included them in our 12-month results table below.

At the time of the 6-month data release we noted that while given that this was a small single-arm study with data only through 6 months, we could not draw concrete conclusions in terms of efficacy. But, we also noted that combined with positive data of the prior n=10 pilot study, results certainly appeared to support the hypothesis that the Viveve system may have real clinical utility in improving SUI symptoms. Further, we explained that from a regulatory standpoint, efficacy through 12 months is what is important - we expected to know a lot more in terms of the potential utility of the Viveve system in SUI when 12-month results of this study were available.

Results: *72% Experience Reduction in Pad Weight Resulting in 56% Mean Reduction. Response Particularly Strong in More Severe SUI*

While intended enrollment was 36, 28 patients completed follow-up through six months and 25 through 12 months. On a side note, this ~30% drop out rate may actually be quite indicative of some of the difficulty in effectively treating SUI with non-surgical therapy such as pelvic floor muscle exercises. Specifically, non-compliance (due to busy lives or other reasons) results in less effective outcomes. It is also suggestive of some of the potential appeal of Viveve SUI therapy – that is, a single, non-invasive treatment does not require rigid compliance (which is in addition to the benefits to surgical options).

- **1-hour pad weight test:** this is the primary endpoint in LIBERATE International (through six months) and is expected to also serve as the primary endpoint in LIBERATE U.S. (through 12 months). As measured by the 1-hour pad weight test, average aggregate urine leakage decreased by 56% from baseline (7.3g vs 3.2g) and 72% (18 of 25) of women experienced improvement.

  For reference, FDA recommends (for the design of pivotal SUI studies) defining 'clinically meaningful improvement' as a reduction in urine leakage of 50% or more. On this measure, 52% of all patients showed a clinically meaningful improvement. And perhaps even more compelling, is that 67% of those patients (n=10) diagnosed as having moderate (that is, more severe) SUI, had a clinically meaningful reduction in leakage. Additionally (as it relates to the 1-hour pad weight test), 60% and 50% of all women and women with moderate SUI, respectively, met the clinically meaningful definition of 'dryness' - which is defined as urine leakage of one gram or less.

  Given the particularly robust effectiveness in 'moderate' SUI patients, VIVE expects to power their U.S. LIBERATE study with similarly diagnosed severity – which should further enhance the chances of success of that study – which would further enhance eventual likelihood of U.S. label expansion for SUI.

- **Secondary endpoints**: while detailed results of the PRO secondary endpoints were not discussed in detail, Viveve noted in the data release that clinically meaningful benefit was achieved at 12 months across all patient reported outcome measures. The results are also included in the table below.

Efficacy on 1-Hour Pad Weight Test (i.e. primary endpoint in LIBERATE studies) Holds Up through 12 months

		1-hour Pad Weight	Daily Incontinence Episodes	UDI-6	IIQ-7	ICIQ-UI-SF
Baseline Scores;	re: @ 6-month look (n=29)	6.2 g	2.0 (n=28)	44	36	10.9
	re: @ 12-month look (n=35)	7.3 g	2.2	47	39	11.3
Scores at;	6-months (n=29)	1.7 g	1.0 (n=28)	21	18	6.8
	12-months (n=25)	3.2 g	0.8	29	20	7.8
% reduction from (respective) baseline;	6-months (n=29)	72.6%	50% (n=28)	53.6%	49.2%	38.0%
	12-months (n=25)	56.1%	63.5%	37.4%	48.7%	30.7%
Responder rate (relative to respective baseline);	6-months (n=29)	82.8%	78.6% (n=28)	82.8%	69.0%	86.2%
	12-months (n=25)	72.0%	64.0%	68.0%	72.0%	76.0%

Given the particularly strong efficacy signal seen in more severe SUI, VIVE expects to power LIBERATE U.S. with a 'moderate SUI' population

Baseline Pad Weight	12-Month Data: % of patients with > 50% reduction in pad weight from baseline				Cure Rate (i.e. 1 ≥ g leakage)	
	1 month	4 months	6 months	12 months	6 mths	12 mths
All Patients 7.3 g (n=35)	56%, 2.2 g	73%, 1.3 g	69%, 1.7 g	52%, 3.2 g	66%	60%
Moderate SUI 17.5 g (n=10)	89%, 3.4 g (n=9)	100%, 1.2 g (n=9)	86%, 2.7 g (n=7)	67%, 4.8 g (n=6)	29%	50%
Mild SUI 3.2 g (n=25)	44%, 1.7 g (n=25)	63%, 1.3 g (n=24)	64%, 1.4 g (n=22	47%, 2.7 g (n=19)	77%	68%

We think this data affirms the efficacy signal witnessed through six months and further bolsters the likelihood of eventual success of both LIBERATE studies.

As it relates to the LIBERATE studies….
In August 2018 VIVE announced commencement LIBERATE-International, which (if successful) is expected to be used as primary support for SUI regulatory filings seeking marketing clearance in Canada and Europe. Enrollment (n=~100) across ten study sites in Canada completed in early January 2019. Management is currently estimating that **full results could be available in late-July / early-August of this year** (inline with prior expectations).

Meanwhile, in September 2018 VIVE made an IDE filing seeking approval to commence its U.S. SUI pivotal study, LIBERATE-U.S. While the hope had been that LIBERATE-U.S. could begin by late-2018/early-2019, that did not happen. Management recently noted that, after a couple of rounds of questions from FDA regarding VIVE's IDE application, the agency requested that the company conduct a sheep safety study. VIVE further noted that this is very similar to what was required of them for final support of their VIVEVE IDE – which was eventually approved.

Given the demonstrated safety to-date in SUI (including acceptable safety/tolerability in the latest 12-month results) as well as in sexual function/vaginal laxity indications, coupled with the fact that this sheep study may effectively be a repeat of what was just successfully conducted, we have little concern that this will be problematic towards eventual IDE approval. But, it does push back anticipated timelines for LIBERATE U.S. Management hopes to have the sheep study completed near mid-year. They will then need to file an IDE supplement and, if all goes well, be in a position to start LIBERATE U.S. in the back half of this year. If that happens, management thinks they could have full 12-month data in late-2020/early-2021.

We are already anxiously awaiting data from LIBERATE – and particularly from the U.S. study – which we do think is likely to successfully navigate the IDE process. If this recent compelling 12-month feasibility study data can be replicated (or at least strongly supported) in a pivotal U.S. study, we think it could be a substantial value inflection event for VIVE. The relatively massive size of the SUI market (~30M women) and current lack of effective, non-invasive and affordable treatment options means adoption of Viveve treatment in this indication could be quite rapid and potentially dwarf that of use for vaginal laxity/sexual function.

VIVEVE II: Enrollment completes, further bolsters safety. Could have topline results by Q2 2020…
As a reminder, VIVE received IDE approval of VIVEVE II in March 2018 and in mid-May announced that the study had started. VIVEVE II, if successful, is expected to provide the backbone for an eventual U.S. regulatory filing seeking an indication for treatment of sexual function.

VIVEVE II used as a staged roll-in enrollment approach which was further aimed at ensuring safety. While total enrollment was 250, the staged roll-in meant a safety review was required to be conducted on the initial patients before additional subjects could enter the study. In early August 2018 VIVE announced that, following one-month safety review of the first 25 patients, that FDA approved enrollment to continue up to 100 (i.e. second stage). FDA did another safety review once another 25 patients had been followed for one-month and 3-month data was available on a total of 50 patients. Viveve then filed this safety data, accompanied with an IDE application requesting to enroll the remaining 150 patients.

The company announced in December that FDA approved enrollment to continue through to the total of 250 and earlier this month, announced that the study was fully enrolled. We think successful navigation of the relatively strict staged roll-in design and swift completion of full enrollment of VIVEVE II provides additional credence to the safety of Viveve treatment. We think this may help in re-accelerating domestic sales growth given that it further separates the Viveve System from those products that were the subject of FDA's warning letters. As a reminder, those warning letters were prompted by the U.S. regulators' concerns over "the use of energy-based devices to perform vaginal "rejuvenation," cosmetic vaginal procedures, or non-surgical vaginal procedures to treat symptoms related to menopause, urinary incontinence, or sexual function may be associated with serious adverse events."

Management hopes to have topline results from VIVEVE II in Q2 2020.

Valuation

DCF Values VIVE at $4.75/share

We have made some moderate adjustments to our model. We continue to favor the long-term growth outlook of VIVE, particularly now that the market has been largely weeded of competitors' off-label marketing. We use a 10-year DCF model to value VIVE. We have revenue growing from $18.5M in 2018 to $36.7M in 2021 and to approximately $103M in 2027 (for reference, Thermage's sales were $50M+ at second year after ThermaCool launch).

Other key inputs to our DCF include a 11% discount rate and 2% terminal growth rate. Based on our DCF model, VIVE is valued at approximately $4.75/share (unchanged from our update in January). Our outlook and financial estimates are subject to change based on progress with expansion of distribution, results of clinical trial data and regulatory approvals, among other events. In addition, we have yet to include assumed market expansion related to any non-sexual function/vaginal laxity/SUI indications. As such, outsized adoption and utilization for ancillary indications could result in upside to our estimates, which should be assumed to be constantly under review and subject to updating.

FINANCIAL MODEL

Viveve Medical, Inc

	2017 A	2018	Q1E	Q2E	Q3E	Q4E	2019	2020	2021
Total Revenues	$15,288.0	$18,517.0	$2,981.7	$4,927.0	$4,976.2	$6,596.6	$19,481.5	$26,207.5	$36,664.9
YOY Growth	114.1%	21.1%	-19.4%	-10.8%	3.2%	47.5%	5.2%	34.5%	39.9%
Cost of Goods Sold	$7,844.0	$11,197.0	$1,837.0	$2,755.7	$2,711.6	$3,431.2	$10,735.5	$13,016.4	$15,571.6
Gross Income	$7,444.0	$7,320.0	$1,144.7	$2,171.4	$2,264.6	$3,165.3	$8,746.0	$13,191.1	$21,093.3
Gross Margin	48.7%	39.5%	38.4%	44.1%	45.5%	48.0%	44.9%	50.3%	57.5%
SG&A	$28,831.0	$38,569.0	$8,599.2	$6,612.1	$6,593.4	$7,183.7	$28,988.4	$30,505.5	$33,035.0
% SG&A	188.6%	208.3%	288.4%	134.2%	132.5%	108.9%	148.8%	116.4%	90.1%
R&D	$12,343.0	$13,716.0	$3,023.4	$3,232.1	$3,493.3	$3,291.7	$13,040.5	$10,535.4	$11,256.1
% R&D	80.7%	74.1%	101.4%	65.6%	70.2%	49.9%	66.9%	40.2%	30.7%
Operating Income	($33,730.0)	($44,965.0)	($10,477.9)	($7,672.8)	($7,822.1)	($7,310.0)	($33,282.9)	($27,849.8)	($23,197.9)
Operating Margin	-220.6%	-242.8%	-351.4%	-155.7%	-157.2%	-110.8%	-170.8%	-106.3%	-63.3%
Total Other Income (Expense)	($3,229.0)	($4,359.0)	($1,062.3)	($1,072.2)	($1,082.1)	($1,092.2)	($4,308.8)	($4,531.8)	($3,923.1)
Pre-Tax Income	($36,959.0)	($49,324.0)	($11,540.2)	($8,745.0)	($8,904.3)	($8,402.3)	($37,591.7)	($32,381.6)	($27,120.9)
Tax expense (benefit)	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Tax Rate	-	-	-	-	-	-	-	-	-
Gain/(Loss) from Minority Interest	0.0	(657.0)	(150.0)	(113.7)	(115.8)	(109.2)	(488.7)	(323.8)	(271.2)
Net Income (continuing ops)	($36,959.0)	($49,981.0)	($11,690.2)	($8,858.7)	($9,020.0)	($8,511.5)	($38,080.4)	($32,705.4)	($27,392.1)
YOY Growth	83.8%	35.2%	14.3%	-76.0%	-28.8%	-26.1%	-23.8%	-14.1%	-16.2%
Net Margin	-241.8%	-269.9%	-392.1%	-179.8%	-181.3%	-129.0%	-195.5%	-124.8%	-74.7%
EPS (continuing ops)	($2.12)	($1.61)	($0.25)	($0.19)	($0.19)	($0.18)	($0.82)	($0.65)	($0.53)
YOY Growth	-3.1%	-23.9%	-52.1%	-91.0%	-60.4%	-50.4%	-49.1%	-20.4%	-18.3%
Diluted Shares O/S	17,470	31,032	46,365	46,400	46,452	46,655	46,468	50,125	51,375

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APPENDIX

Refresher of VIVEVE I: U.S Multi-Site, Randomized Sham-Controlled Study

Results of VIVEVE I showed that just one ~30-minute treatment with the Viveve System resulted in a highly statistically significant difference in vaginal laxity and sexual function among those patients receiving treatment versus those given sham (i.e. control). This also marked the first time that any company was able to demonstrate significant efficacy of their energy-based device in a controlled clinical study.

Viveve announced positive top-line results of VIVEVE I (VIveve Treatment of the Vaginal Introitus to EValuate Effectiveness), its sham-controlled clinical trial assessing safety and efficacy of the Viveve System in more than 150 patients at 9 sites in Europe, Canada and Japan. While results of two previous smaller studies (one in U.S.: n = 23, one in Japan: n = 30) had already demonstrated that treatment with the Viveve System can significantly reduce vaginal laxity and improve sexual function, this VIVEVE I study is the largest to-date and the first sham-controlled study evaluating the Viveve System for the treatment of vaginal laxity as well as for sexual function.

VIVEVE I Design / Protocol…

Enrollment was initially expected to be 113 patients - the study protocol was subsequently updated (per clinicaltrials.gov) to enroll an expected 145 – final enrollment ended up being 174 patients (117 active, 57 sham) with vaginal laxity efficacy data on a 'per-protocol' population of 155. Subjects were randomized 2:1 (active:control) - patients were blinded, treating personnel were not. The treatment group received 90 Joules/cm2 of RF energy delivered via the Viveve System while the sham group received <1 Joule/cm2. Subjects were followed through the six month follow-up period with assessments at day 10 and months 1, 3 and 6.

Key inclusion / exclusion criteria included;[1]

- Inclusion:
  - pre-menopausal and ≥ 18 years of age
  - had least one full term vaginal delivery (>37 completed weeks) at least 12 months prior to enrollment date
  - experienced vaginal looseness (i.e. VSQ < 4) during vaginal intercourse
- **Exclusion:**
  - Pregnant or planning to become pregnant within the next 12 months or has had a delivery within the last 12 month
  - currently meets the criteria for a female sexual disorder including DSM V, FSAD, FOD, Genitopelvic Pain, Sexual Aversion, Dyspareunia or Vaginismus and has not been treated for this condition within the past 12 months
  - taking SSNRI or SSRI drugs

Primary efficacy endpoint was the proportion of women in the treatment arm as compared to the proportion of women in the sham (i.e. - control) arm that report no vaginal laxity six months following treatment as measured by Viveve's specially designed questionnaire, VSQ ("Viveve System Questionnaire"). VSQ, which is similar to the VLQ questionnaire used in the two prior studies, is based on a seven point scale (1:very loose, 2:moderately loose, 3:slightly loose, 4:neither loose nor tight, 5:slightly tight, 6:moderately tight, 7:very tight). "No vaginal laxity", as defined in the VIVEVE study protocol, is a VSQ score of >4.

Secondary efficacy endpoints were the percentage change in mean score from baseline to six months following treatment of the active arm as compared to the control arm in 1) the Vaginal Laxity Inventory (VALI), 2) Total FSFI and 3) FSDS-R. See our Appendix for detailed description of these secondary measures.

Study Results: Primary and FSFI Endpoints Highly Statistically Significant….

Results were positive, showing a highly statistically significant difference between the active and sham arms on the VSQ (i.e. laxity) primary endpoint as well as the FSFI (i.e. sexual function) secondary endpoint. In addition, safety was considered excellent with no difference in adverse event rates between the treatment and sham cohorts.

VSQ

Of the 174 subjects enrolled and randomized, 19 were not evaluable for efficacy purposes due to not completing the 6-month follow-up or for other protocol violations. The per-protocol population included 103 active and 52 sham subjects. At the 6-month follow-up, 41.7% (43/103) of active subjects reported having no vaginal laxity (i.e. VSQ > 4) compared to just 19.2% (10/52) of subjects that received sham treatment. The difference was highly statistically significant with a Chi-squared p-value of 0.005. Active subjects were 3.05x more likely to achieve 'no vaginal laxity' at 6 months than were sham subjects (95% confidence interval, p-value = 0.006).

[1] Clinicaltrials.org. ClinicalTrials.gov Identifier: NCT02261974. VIveve Treatment of the Vaginal Introitus to EValuate Effectiveness (VIVEVE I)

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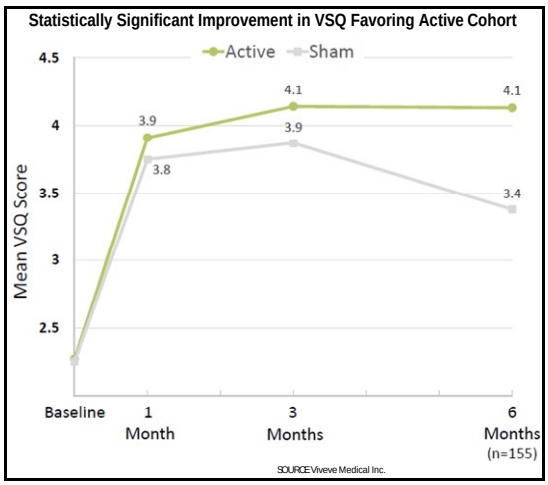
Active Cohort 3x More Likely vs. Sham To Achieve No Vaginal Laxity							
					Logistic Regression		
Timepoint	Treatment Group	N	No Laxity n (%)	Chi-Squared p-value	Odds Ratio	95% CI	p-value
Month 6	Active	103	43 (41.7%)	0.005	3.05	(1.37, 6.79)	0.006
	Sham	52	10 (19.2%)				

SOURCE Viveve Medical Inc.

Mean VSQ scores at the 1, 3 and 6 month follow up periods were;

- 1-month: 3.9 active vs. 3.8 sham (difference of 0.1)
- 3-month: 4.1 active vs. 3.9 sham (difference of 0.2)
- 6-month: 4.1 active vs. 3.4 sham (difference of 0.7)
    - 6-month mean VSQ score from baseline was 1.9 for active vs. 1.1 for sham

The mean change from baseline of the active (1.9) versus shame (1.1) is statistically significant at a 95% confidence interval (p=0.007). The widening difference in mean VSQ over the course of the assessment periods is believed to be representative of weakening of a placebo effect in the sham arm.



FSFI

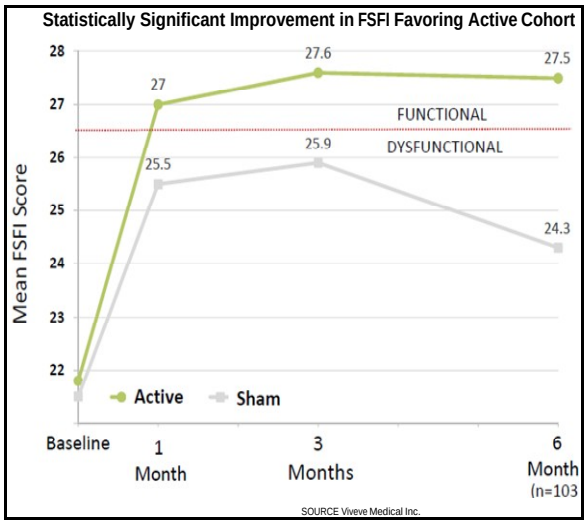
Similar to the two prior studies, VIVEVE I demonstrated that treatment with the Viveve System is associated with a significant increase in sexual function. FSFI is a brief, 19-item self-report measure of female sexual function that provides scores on six domains of sexual function as well as a total score. It was developed for the specific purpose of assessing sexual functioning in clinical trials. These 19 items include: desire (2 items), arousal (4 items), lubrication (4 items), orgasm (3 items), satisfaction (3 items), and pain (3 items) and are scored from 0 to 5. The FSFI total score is a weighted average of the six domains with each contributing a maximum of six points to the total (maximum score of 36). Wiegel, Meston and Rosen demonstrated that a cutoff of 26.55 discriminates between women with and without sexual dysfunction.[2]

103 (71 active, 32 sham) patients were included in the FSFI per-protocol population. Of the six domains, two (sexual arousal and orgasm) were statistically different favoring the active arm (arousal and orgasm are expected to be included as secondary endpoints in VIVEVE II). And while the other four were not statistically different, there was a positive response favoring the active group. The individual p-values were (p-value < 0.05 is considered statistically significant);

- desire 0.081
- arousal 0.007
- lubrication 0.095
- orgasm 0.007
- satisfaction 0.097
- pain 0.122

[2] Wiegel M1, Meston C, Rosen R. The female sexual function index (FSFI): cross-validation and development of clinical cutoff scores. J Sex Marital Ther. 2005 Jan-Feb;31(1):1-20.

But while just two of the six individual domains hit statistical significance, the weighted average of the six domains of the active arm (27.5) was statistically different from that of the sham arm (24.3) at the 6-month follow-up (p=0.009). In addition, the weighted average scores of the six domains on the active arm at 1-month (27.0), 3-month (27.6) and 6-month (27.5) follow up were all above 26.55 (i.e. considered sexually functional) while the scores of the sham arm at each of these timepoints (1-month: 25.5, 3-month: 25.9, 6-month: 24.3) were all below 26.55 (i.e. considered sexually dysfunctional). Similar to the VSQ measure, there was some placebo effect in the sham arm that began to wane at about 3 months following initiation of treatment.



Importantly, the expectation is that the mean change in total FSFI score, as opposed to individual domain scores, is what FDA will be looking for as a primary endpoint in VIVE's proposed pivotal U.S. study. Additionally, secondary endpoints are expected to include the FSFI arousal and orgasm domains, which were statistically significant in VIVEVE I.

VALI and FSDS-R
Vaginal Introitus Laxity Inventory and Female Sexual Distress Scale-Revised were the other two secondary endpoints. VALI relates to the respondents' concern of laxity and how that may affect sexual functioning while FSDS-R relates to a respondents' feelings of sexual activity-related distress based on a 13-item questionnaire.

While neither VALI or FSDS-R scores were statistically different between active and sham arms in VIVEVE I, we do not view this as problematic as it relates to the proposed U.S.-based controlled study as they have no cross-over relevance to the expected primary (FSFI) endpoint for VIVEVE II (i.e. – upcoming study). We think VIVE likely included VALI and FSDS-R in VIVEVE I in order to stack in additional metrics so as to offer other options in the event FSFI and/or VSQ failed to show statistical significance.

Safety
Similar to the two prior studies, safety was considered excellent in VIVEVE I. All 174 (117 active, 57 sham) enrolled and randomized patients underwent a safety evaluation. There was no statistical difference in safety measures between the two arms;

- treatment-emergent adverse events; 38 (32.5%) active vs. 20 (35.1%) sham
- related treatment-emergent adverse events; 13 (11.1%) active vs. 7 (12.3%) sham
- serious treatment-emergent adverse events; 0 (0.0%) active vs. 1 (1.8%) sham

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<u>VIVEVE I Secondary Outcome Measures</u>

Female Sexual Function Index (FSFI)
FSFI is a brief, 19-item self-report measure of female sexual function that provides scores on six domains of sexual function as well as a total score. It was developed for the specific purpose of assessing sexual functioning in clinical trials. These 19 items include: desire (2 items), arousal (4 items), lubrication (4 items), orgasm (3 items),

satisfaction (3 items), and pain (3 items) and are scored from 0 to 5. The FSFI total score is a weighted average of the six domains with each contributing a maximum of six points to the total (maximum score of 36). Wiegel, Meston and Rosen demonstrated that a cutoff of 26.55 discriminates between women with and without sexual dysfunction.[3]

Female Sexual Distress Scale-Revised (FSDS-R)[Error! Bookmark not defined.]
FSDS-R is a patient-reported outcomes measure consisting of 13 items assessing different aspects of sexual activity-related distress in women. It has a high degree of discriminative sensitivity to distinguish between sexually dysfunctional and normal functional women and is sensitive to therapeutically inducted changes in function. Items are scored on a five-point Likert-type scale as never (0), rarely (1), occasionally (2), frequently (3), or always (4). A total score, ranging from 0 to 52, can be computed by adding all 13 item scores. Higher scores indicate higher levels of sexual distress. The provisional cut-off score of ≥15 reliably identifies over 90% of women who are currently experiencing sexually related personal distress (Derogatis et al 2008).

Vaginal Introitus Laxity Inventory (VALI)[4]
Vaginal Introitus Laxity Inventory is a 12-item patient reported outcome measure (i.e., PRO) designed to describe and quantify the nature of a female respondent s concern with the perception of laxity (looseness) and its impact on the qualities of satisfaction and enjoyment of her sexual functioning. Items of the VALI address the impact of laxity on the major aspects of the female sexual response cycle (i.e., sexual desire, arousal and orgasm), and quantify the patient s experience of sexual pleasure, sensitivity and satisfaction. The VALI items also address the potential impact of vaginal introitus laxity on sexual confidence and the patient s partner. All 12 items are measured on 5-point Likert scales and scores are summed to achieve a VALI Total score, range 0-48).

STRESS URINARY INCONTINENCE

SUI Pilot Study
N=10, single-arm. Conducted in Calgary, Alberta by Dr. Bruce Allan (Dr. Allan is also the PI of the ongoing n=36 SUI feasibility study and was also one of the PIs of the VIVEVE I study). Safety and clinical measures were reported at months 4, 6, 9 and 12 months post-treatment. Press release mentions the study used a "proprietary treatment protocol" (specifics were not disclosed). Clinical measures included composite scores of the ICIQ-UI-SF (International Consultation on Incontinence Questionnaire-Urinary Incontinence-Short Form) and UDI-6 (Urogenital Distress Inventory-Short Form) outcome questionnaires. Both questionnaires are industry-accepted as measures of urinary incontinence-related quality of life and symptom distress[5].

While VIVE provided only limited details, they did note (see slide from presentation, below) that at 12 months (9 patients were evaluable), 89% - 100% of patients were "responders" and mean improvement was 40% - 51% at 12 months based on the ICIQ-UI-SF and UDI-6 measures, respectively. Additional details, such as response and mean improvement at the earlier timepoints was not disclosed. It is also unclear whether other efficacy measures were included as part of the study. In terms of safety, the PR notes that no device-related safety issues were reported in any of the patients.

N=10 SUI Pilot Study Results at 12 Months

	UDI-6 (n=9)	ICIQ-UI (n=9)
Baseline Score	1567	9.4
12 Mos	767	5.7
% Reduction from Baseline	51%	40%
Responder Rate	100%	89%

SOURCE: Viveve Medical

[3] Wiegel M1, Meston C, Rosen R. The female sexual function index (FSFI): cross-validation and development of clinical cutoff scores. J Sex Marital Ther. 2005 Jan-Feb;31(1):1-20.
[4] Description taken verbatim from Viveve's Protocol Report for the VIVEVE 1 study
[5] Uebersax JS. Short forms to assess life quality and symptom distress for urinary incontinence in women: the Incontinence Impact Questionnaire and the Urogenital Distress Inventory. Continence Program for Women Research Group. Neurourol Urodyn. 1995;14(2):131-9.

Relative to the results of the study, Dr. Allan said, “In the pilot study, we found that SUI symptoms were significantly improved, providing strong support for the planned clinical registration studies and the potential to represent a major advance in the non-invasive treatment of SUI".

Refresher on Compelling SUI Feasibility Study 6-Month Data: *Meaningful Improvement On All Endpoints…*
In June 2018 Viveve announced what we characterized as potentially compelling 6-month data from its SUI 12-month feasibility study.

Results: *83% Response Rate on Primary Endpoint, 73% Average Reduction of Urine Leakage…*
Of the 36 enrolled participants, 28 completed full follow-up (i.e. were assessed on all endpoints) through 6 months and one completed full follow-up except for the 7-day voiding diary through 6 months. Management mentioned on the call that while the two-treatment protocol was used with a few women, that there was not an obvious difference in efficacy as compared to a single treatment (a single treatment will be employed in upcoming studies). Results, which are also in the table below (from VIVE's June 2018 press release), were;

- **1-hour pad weight test:** the 1-hour pad weight test is also expected to serve as the primary endpoint in the two anticipated SUI LIBERATE studies. As measured by the 1-hour pad weight test (i.e. primary endpoint), average aggregate urine leakage decreased by 73% from baseline (6.2g vs 1.7g) and 83% (24 of 29) of women experienced improvement. For reference, FDA recommends (for the design of pivotal SUI studies) defining 'clinically meaningful improvement' as a reduction in urine leakage of 50% or more. Additionally (as it relates to the primary endpoint), 66% (19 of 29) of women met the clinically meaningful definition of 'dryness' - which is defined as urine leakage of one gram or less.
- **7-day voiding diary**: the 7-day voiding diary, along with the 1-hour pad weight test, are two measures that FDA recommends using as primary endpoints for pivotal SUI device studies. Based on the 7-day voiding diary, VIVE's feasibility study showed that, through 6 months (n=28), average aggregate incontinence episodes decreased by 50% from baseline (2.0 vs 1.0) and 79% (22 of 28) of women experienced an improvement in incontinence episodes. For reference, FDA recommends defining 'clinically meaningful improvement' for the 7-day voiding diary as greater than 50% reduction in incontinence episodes compared to baseline.
- **QoL questionnaires**: VIVE reported that, through 6 months, 'clinically meaningful' improvement was achieved on the composite scores of the three QoL questionnaires. Additionally, 69%, 83% and 86% of women reported improvement based on the IIQ-7, UDI-6 and ICIQ-UI-SF questionnaires.

SUI Feasibility 6-month Results

	1-HOUR PAD WEIGHT	DAILY INCONTINENCE EPISODE FREQUENCY	UDI-6	IIQ-7	ICIQ-UI-SF
BASELINE SCORES (N=29)	6.2 g	2.0 (N=28)	44	36	10.9
SCORES AT 6 MONTHS (N=29)	1.7 g	1.0 (N=28)	21	18	6.8
% REDUCTION FROM BASELINE AT 6 MONTHS (N=29)	72.6%	50.0% (N=28)	53.6%	49.2%	38.0%
RESPONDER RATE AT 6 MONTHS (IMPROVEMENT FROM BASELINE) (N=29)	82.8%	78.6% (N=28)	82.8%	69.0%	86.2%

SOURCE: Viveve Medical June 18, 2018 press release

- **Safety**: as has largely been the case with Viveve treatment of vaginal laxity, there were no device-related adverse events through 6 months in this SUI feasibility study.

LIBERATE Pivotal Registration Trials…
Success of these LIBERATE studies would be used to support FDA and Health Canada filings seeking an indication for the temporary improvement of mild-to-moderate SUI symptoms. The Canadian study is also expected to accompany a CE Mark application (for European markets).

Design of the U.S. and Canadian studies are similar, although not identical. Importantly, both are multi-site RCTs. Both also use change from baseline in the one-hour pad weight test as the primary endpoint. With the pad weight test, the subject wears a pre-weighed pad, drinks a specified amount of liquid and then performs certain activities

(such as walking, climbing stairs, coughing etc). After one-hour, the pad is again weighed to determine the amount of urinary leakage.

Following filing of an Investigational Trial Application (ITA, analogous to IDE in U.S.) to Health Canada, on August 14th VIVE announced that their LIBERATE international study had commenced. Enrollment completed in January 2019. The 6-month feasibility study data will be used to support the IDE for approval to commence the U.S. LIBERATE study.

The following is information disclosed by VIVE relative to the two pivotal (LIBERATE) studies.

U.S. LIBERATE Study

- Design
  - N=240 w/ mild-to-moderate SUI
  - Randomized (2:1 active:control), double-blind, sham-controlled
  - Sites = 25, in U.S.
  - Outcomes
    - Primary: 50% change 1-hour pad weight test, change from baseline to 12 months
    - Secondary: (undisclosed) "other secondary endpoints"
    - Safety: through 12 months
- Status: VIVE expects to submit IDE to FDA for "temporary improvement of mild-to-moderate SUI" by end of November 2018

International LIBERATE Study

- Design
  - N=100 w/ mild-to-moderate SUI
  - Randomized (2:1 active:control), double-blind, sham-controlled
  - Sites = 10, in Canada
  - Outcomes
    - Primary: 1-hour pad weight test, change from baseline to 6 months
    - Secondary: validated questionnaires including UDI-6, ICIQ-UI-SF, I-QOL, FSFI and voiding diary
    - Safety: through 12 months
  - Status: enrollment ongoing. Through early Nov ~30 of 100 enrolled. We estimate could be fully enrolled by Feb 2019. Management anticipates results in mid-2059
- Purpose: if positive, will use study to support Health Canada registration filing and CE Mark application for "temporary improvement of mild-to-moderate SUI symptoms

SUI Market

According to the National Women's Health Resource Center[6] (NWHRC), SUI is estimated to effect 30% of all adult women in the U.S. (i.e. ~31M Americans) and of those with SUI, 53% have "slight" incontinence while 17% have severe incontinence. SUI can be a significant hindrance to quality of life. The NWHRC reports that while 75% of women with the condition find it "bothersome" (or worse) and 60% make lifestyle changes as a result of it, as many as 50% to 75% of sufferers do not seek treatment (mostly as a result of embarrassment). SUI is more common among women that have had vaginal deliveries.

FDA's guidance on SUI endpoints

- Primary endpoints: FDA recommends that a urinary incontinence device pivotal trial use one or both of the following measures as primary endpoints: urine leakage as assessed by pad weight test and/or reduction in the number of incontinence episodes per day. If only of the two is used as the primary endpoint, FDA further recommends using the other as a secondary endpoint
  - pad weight test: with the 1-hour pad weight test (which can also be performed over a 24-hour period), the subject wears a pre-weighed pad, drinks a specified amount of liquid and then performs certain activities (such as walking, climbing stairs, coughing etc). After one-hour, the pad is again weighed to determine the amount of urinary leakage. Relative to the what is considered clinically meaningful (with the objective on

[6] National Women's Health Resource Center. Prevalence and Treatment Patterns of Pelvic Health Disorders Among U.S. Women. The Lewin Group. June 2007

dryness) with the one-hour pad weight test, FDA recommends defining 'dryness' as an increase in pad weight of less than 1 gram and defining 'improvement' as a 50% or more decrease in weight from baseline

- Reduction in incontinence episodes: FDA recommends using a standardized voiding diary to document fluid intake and the number of incontinence episodes over seven consecutive days. The average number of incontinence episodes per day is then compared to baseline to determine effectiveness. With the 7-day voiding diary, FDA recommends using 'zero incontinence episodes per day' as the clinically meaningful definition of 'dryness' and 'greater than 50% reduction' (from baseline) as clinically meaningful improvement

- Secondary endpoints: FDA's general guidance relative to stress urinary incontinence clinical trials is to choose secondary endpoints which will provide additional evidence of the efficacy and safety of the device as well as to support performance and labeling. Among the possible secondary endpoints, FDA recommends considering measures related to quality of life (via questionnaires), sexual function, leak point pressure, bladder voiding and patient satisfaction. Specifically as it relates to;
  - QoL: FDA's guidance notes that since UI "is strongly associated with impairment of quality of life," that they recommend using validated QoL measures (as secondary endpoints) such as the Incontinence Quality of Life (I-QOL) questionnaire (as an example of one of many QoL measures that could be employed) and pre-specify the minimum delta that represents a meaningful improvement in QoL. FDA's guidance further recommends that choice of QoL measures should consider the specific populations and settings where they were developed and validated. FDA references The 3rd International Consultation on Incontinence as a source for choosing appropriate QoL measures, which includes the three QoL measures used in VIVE's feasibility study (UDI-6, IIQ-7 and ICIQ-UI-SF). While we may have more discussion on the topic after we know specifics of design of the two LIBERATE studies, we think the most important take-away at this point is that the three QoL measures used in this ongoing feasibility study are definitely validated clinical endpoints
  - Sexual function: based on close proximity to genitalia, FDA recommends consideration of a sexual function related measure (such as a validated sexual function questionnaire)
  - Patient satisfaction: incorporate a validated patient satisfaction questionnaire which asks the participant to rate the improvement (as compared to baseline) on several topics related to how SUI effects their lives and livelihoods

HISTORICAL STOCK PRICE



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