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November 21, 2018
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Viveve Medical (VIVE-NASDAQ)

VIVE: Short-Term Headwinds Result in Lowered Guidance. Clinical Progress Sets Up Several Upcoming Milestones

We use a 10-year DCF model to value VIVE. We have revenue growing from $15M in 2017 to $33M in 2020 and to approximately $92M in 2026. 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 $6.75/share.

Current Price (11/21/18)	$2.24
Valuation	**$6.75**

OUTLOOK

Management slashed FY2018 guidance from $22M - $24M to $17.5M - $18.5M, citing headwinds caused by the late-July warning letter from FDA to seven energy-based device manufacturers that the agency fingered as inappropriately marketing for off-label use in vaginal cosmetic procedures, including for the treatment of vaginal laxity. While VIVE was not one of the seven, we are not overly surprised that this has caused what appears to be an overly cautious market reaction given FDA's language in the letter. In fact, we noted in our August 1st Note that while we believed that the agency's action would benefit VIVE in the long-run, that the headline reaction "may be a short-term headwind to VIVE (and a much more significant defeat for the other manufacturers)…"The bad news is that it appears our prediction was prescient, at least as it relates to the short-term. The good news is that comments from management on the call suggest that we may also prove accurate as it relates to the longer-term. These are reassuring that VIVE will indeed benefit once potential customers have become more educated on the difference between the Viveve System's well-established safety record and that of 'all the rest'. So, while Q4 is already setting up to be less-than thrilling from a financial standpoint, the product development side of the business is nearly as active and exciting as it has ever been. Ongoing clinical progress made in both sexual function and SUI programs is setting up for what should be several significant near-term significant milestones.

SUMMARY DATA

52-Week High	**$5.40**
52-Week Low	**$1.60**
One-Year Return (%)	**-57.53**
Beta	**-0.25**
Average Daily Volume (sh)	**216,510**
Shares Outstanding (mil)	**32**
Market Capitalization ($mil)	**$71**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**56**
Insider Ownership (%)	**35**
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 2018 Estimate	**N/A**
P/E using 2019 Estimate	**N/A**
Zacks Rank	**N/A**

Risk Level	**Above Avg.,**
Type of Stock	**Small-Growth**
Industry	**Med Instruments**

ZACKS ESTIMATES

Revenue
(in '000s of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2017	3041 A	3073 A	4070 A	5101 A	15288 A
2018	3699 A	5525 A	4821 A	3807 E	17852 E
2019					33949 E
2020					43667 E

Earnings per Share

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2017	-$0.57 A	-$0.54 A	-$0.50 A	-$0.53 A	-$2.12 A
2018	-$0.49 A	-$0.37 A	-$0.39 A	-$0.42 E	-$1.66 E
2019					-1.18 E
2020					-1.03 E

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

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Q3 Results: *Results Inline But FDA-Action vs. Competitors Could Create Short-Term Headwind. Long-Term Outlook Intact…*

Viveve reported Q3 2018 financial results and provided a business update. Relative to the financials, both the top and bottom lines were a hair lower than what we were looking for but generally, largely inline with our numbers. And while opex was a bit better (i.e. lower) than where we expected, gross margin was much worse (i.e. narrower). But, aside from gross margin, which really took it on the chin, the quarter was reasonably solid.

And while gross margin should start to rebound fairly soon with continued roll-out of Viveve 2.0, the next-gen system which (along with the related treatment tips) carries a better margin, the topline 'solidness' in Q3 is, unfortunately, not expected to bleed over into Q4. Management slashed FY2018 guidance from $22M - $24M to $17.5M - $18.5M, citing headwinds caused by the late-July warning letter from FDA to seven energy-based device manufacturers that the agency fingered as inappropriately marketing for off-label use in vaginal cosmetic procedures, including for the treatment of vaginal laxity.

While VIVE was not one of the seven, we are not overly surprised that this has caused what appears to be an overly cautious market reaction given FDA's language in the letter that these devices (i.e. those specifically named in the letter) "may be associated with serious adverse events" if used to "perform rejuvenation, cosmetic vaginal procedures, or non-surgical vaginal procedures….". In fact, we noted in our August 1st Note (*FDA Warning Letter Should Weed-Out Imposters and Benefit VIVE* – see Appendix) that while we believed that the agency's action would benefit VIVE in the long-run, that the headline reaction "may be a short-term headwind to VIVE (and a much more significant defeat for the other manufacturers)…"

The bad news is that it appears our prediction was prescient, at least as it relates to the short-term. The good news is that comments from management on the call suggest that we may also prove accurate as it relates to the longer-term. Those comments, including that VIVE has immediately gained market share (as the cited companies presumably changed their marketing message or altogether ceased targeting the vaginal cosmetic market) and that physicians are taking a cautious approach towards safety, are reassuring that VIVE will indeed benefit once potential customers have become more educated on the difference between the Viveve System's well-established safety record and that of 'all the rest'.

So, while Q4 is already setting up to be less-than thrilling from a financial standpoint, the product development side of the business is nearly as active and exciting as it has ever been. Ongoing clinical progress made in both sexual function and SUI programs is setting up for what should be several significant near-term significant milestones.

Anticipated upcoming clinical development milestones

- ~end of 2018: 12-month SUI Feasibility study data
- ~end of 2018/early-2019: IDE approval to begin LIBERATE-U.S.
- mid-2019: final 6-month SUI results from LIBERATE-international
- late-2019/early-2020: 12-month (i.e. final) results of VIVEVE II

Q3 total revenue was $4.8M, up 19% yoy, down 13% sequentially and 2% lower than our $4.9M estimate. The qoq dip in total revenue was anticipated as Q3 is typically seasonally soft for cosmetic procedures. Console placements totaled 64 units (vs. 67 E) including 48 U.S. (vs 52 E) and 16 OUS (vs 15 E). Treatment tips totaled 5,700 (vs 4,089 E). While management noted that there were no SUI-related BOGOs in the quarter, based on the relatively weak (total) gross margin, we think there must have been some sort of promotional pricing.

Revenue (proportional contribution) per geographic territory:

	Q3 '18	%Ttl	+/- yoy	YTD'18	%Ttl	+/- yoy	Q3 '17	%Ttl	YTD'17	%Ttl	FY '17	%Ttl
North America	$3,455	(72%)	5%	$10,613	(76%)	50%	$3,277	(62%)	$7,067	(69%)	$11,083	(72%)
Asia Pacific	$717	(15%)	-5%	$2,238	(16%)	2%	$758	(22%)	$2,191	(22%)	$3,178	(21%)
Europe & Middle East	$612	(13%)	-	$1,143	(8%)	101%	$0	(15%)	$569	(6%)	$667	(4%)
Latin America	$37	(1%)	6%	$51	(0%)	-86%	$35	(1%)	$360	(4%)	$360	(2%)
Total	$4,821	(100%)	18%	$14,045	(100%)	38%	$4,070	(100%)	$10,187	(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. Accounting for 62% and 69% of total revenue through in the three and nine

months ending 9/30/17, respectively, North America's contribution to the topline increased to 72% and 76% in the most recent comparable periods. 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 flattish from the 47 sold in Q3'17 and down from Q2'17's 69. Through the first nine months of 2018 155 systems were sold in the U.S., up 51% from 103 in the prior-year period. VIVE noted on the call that their sales force remains at 49 total sales team members, unchanged from Q2 and includes; 23 capital reps, 10 associate sales reps, 10 practice development managers, 3 regional sales directors and 1 practice development strategic partnership director – all report to a V.P. of sales. We had previously reported on sales-rep efficiency analysis but, given the typical seasonably-soft summer months and the atypical market disruption caused by the FDA's letter, we think that ratio is not particularly insightful for Q3. We will consider revisiting that metric when the safety-concern market turmoil settles.

Console unit sales numbers were just about dead-on where we had anticipated, although at what appears to be a moderate discount to our forecasted ASP. It is not clear if there was indeed some promotional pricing on the boxes. Management noted that Viveve 2.0, the next-gen system began roll-out in the quarter and accounted for roughly one-half of the unit placements. The new system and related treatment tips should aid margins – hopefully with some obvious benefit beginning as soon as Q4.

Per management, caution over safety concerns prompted by the FDA letter has elongated the sales cycle – although, based on our estimates, that was not necessarily noticeable in Q3 – perhaps as many of those booked as sales may have already been in the channel prior to regulatory headline. Nonetheless, it almost certainly will be obvious in Q4 as management's revised guidance implies a sequential contraction between 8% and 28% - which is even more dramatic considering VIVE's Q4 has historically been its strongest, and Q3 its weakest.

But while we did not expect that level of short-term disruption, 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, 5,700 were recognized as sales – which is a new record high and more than double the 2,700 sold in Q3'17. As noted, no SUI-BOGO program was conducted in Q3. Nonetheless, gross margins (31% vs 51% in Q2'18, 49% in Q3'17 and 52% E) were fairly atrocious and weak margins on the tips cited as a significant contributor (along with product mix). But, again, with the new system rolling out, GM's are expected to improve.

And, if growth in the tip sales volume is indicative of utilization, that certainly suggests physicians are not shying away from using the Viveve System, even if some consumers may be more cautious about making an initial purchase. In fact, utilization per console is holding up well – at 2.9 tips per system per month in Q3 and an average of 2.7 through the first nine months of 2018, per-system utilization is roughly inline with where it was the prior year. That is encouraging given that the installed base grew 77% since Q3'17 and, intuitively, the expectation would be for utilization per unit to fall with significant growth in the installed base.

Operational Update:

VIVEVE II: Enrolling as planned, FDA OKs initial safety review, filing of second IDE/safety cohort imminent …
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 is using a 'staged roll-in' enrollment approach which is further aimed at ensuring safety. While total enrollment is expected to be 250, this staged roll-in requirement means a safety review must be conducted on the initial patients before additional subjects can enter the study. In early August 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). Enrollment continues and the second safety review will occur once another 25 patients have been followed for one-month and 3-month data is available on a total of 50 patients. Management noted on the Q3 call that they **expect to file this safety data, accompanied with an IDE application requesting to enroll the remaining 150 patients, by the end of November.**

If approved, the trial can then enroll through the total of 250. Assuming the IDE supplement is submitted by November 30th and based on FDA's turnaround (~35 days) of the initial safety cohort (n=25/ 30-days), we think this second IDE supplement could be approved by late December 2018 or very early next year. Approval is, of course, critical as it is a gatekeeper to finishing the study but, we think, it may also play a role in re-accelerating domestic sales growth given that it is further evidence supporting the safety of Viveve treatment. If so, it is possible that FDA green-lighting the final enrollment cohort to proceed could resonate with potential purchasers of the system that may have been hesitant to do so due to the unfortunate halo effect of FDA's warning letter.

Per VIVE's current timeline, if all goes to plan, they believe final results of VIVEVE II could be available sometime in late-2019 or early-2020.

SUI LIBERATE Studies:
Viveve's SUI clinical programs have moved relatively very rapidly. In June they announced compelling 6-month data from their ongoing (Canada-based) 12-month randomized (n=36) SUI feasibility study – see our discussion below (12-month data from this study is expected by current year-end). Then, in August they 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. To-date, ~30 patients (of 100 total) have been enrolled across eight active sites. Current enrollment rate is approximately 1.25 patients per month per site. If that increases to two patients per site per month and two more sites come onboard, we estimate enrollment could complete by the end of February 2019 – as such, we think management's guidance for data by mid-2019 could be a reasonable assumption.

Meanwhile, in September VIVE made an IDE filing seeking approval to commence its U.S. SUI pivotal study, LIBERATE-U.S. If all goes well, LIBERATE-U.S. could begin by late-2019/early-2019 and LIBERATE-International could have final (6-month) data by the middle of next year. Given the compelling 6-month data from the SUI pilot study and potential significant target-market expansion potential associated with an SUI indication, we will be eager to hear updates on all three of these SUI clinical studies. **The relatively massive size of the SUI market and lack of current effective treatment options means meeting significance on the primary endpoints of the LIBERATE (pivotal) studies, could be a significant value inflection point for VIVE stock. The next glimpse of potential effectiveness of Viveve System in SUI could be only a few weeks away.**

See our Appendix for a refresher on the LIBERATE study designs and our discussion on SUI

Refresher on Compelling SUI Feasibility Study 6-Month Data: *Meaningful Improvement On All Endpoints, Will Support IDE Filings…*
In mid-June Viveve announced what we characterized as potentially compelling 6-month data from its ongoing SUI 12-month feasibility study. As a refresher, this is the second formal pilot/feasibility study assessing the Viveve System in the treatment of mild-to-moderate SUI (see below for refresher on the first). Listed under clinicaltrials.org Identifier: NCT03066180 (http://bit.ly/2k3OX9p), the single-arm, 36-subject study is being conducted at Dr. Bruce Allan's Allan Centre (Dr. Allan was also the principal investigator for the VIVEVE I vaginal laxity/sexual function study) in Calgary, Canada. Protocol allowed for one (just following baseline) or two (6 – 12 weeks later) Viveve treatments.

While only a single-arm feasibility study, it was clearly designed to be consistent with FDA's recommendations for SUI-device pivotal studies (FDA's guidance (http://bit.ly/2Iy2orT) for *Clinical Investigations of Devices Indicated for the Treatment of Urinary Incontinence).* This includes the inclusion and exclusion criteria as well as the choice of primary and secondary endpoints. Relative to SUI severity, inclusion criteria included diagnosis of mild-to-moderate SUI as determined by one-hour pad weight test (using International Continence Society definitions; mild = 1-10g, moderate = 11-50g, severe = > 50g). (See our Appendix for a more in-depth review of FDA's guidance on SUI endpoints).

Primary endpoint is reduction in 1-hour pad weight versus baseline. Secondary measures are the 7-day bladder voiding diary and composite scores from three quality-of-life oriented questionnaires; UDI-6 (Urogenital Distress Inventory-Short Form), IIQ-7 (Incontinence Impact Questionnaire) and ICIQ-UI-SF (International Consultation on Incontinence Questionnaire-Urinary Incontinence-Short Form).

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 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 upcoming 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 (and discussed in more detail below), 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. While VIVE did not report on 'dryness' as measured by the 7-day voiding diary (defined in our endpoints discussion below), that may be included in the 12-month data (which, potentially could be available late this year or early 2019).
- **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. We discuss QoL measures for SUI device studies in more detail below.

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.

While, given this was a small single-arm study with data only through 6 months, we cannot draw concrete conclusions in terms of efficacy. But, combined with positive data of the prior n=10 pilot study (see Appendix), results to-date certainly appear to support the hypothesis that the Viveve system may have real clinical utility in improving SUI symptoms. Given that from a regulatory standpoint, efficacy through 12 months is what is important - we should know a lot more in terms of the potential utility of the Viveve system in SUI when 12-month results of this study are available – which is expected before current year-end.

Valuation

DCF Values VIVE at $6.75/share

We have made some substantive adjustments to our model, mostly affecting the near-term portion of our 10-year DCF. We, however, 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 $15.3M in 2017 to $32.7M in 2020 and to approximately $92M in 2026 (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 $6.75/share (revised down from $7.75/share). 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 indications. As such, outsized adoption and utilization for indications such as SUI (or potentially others) 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

	2016 A	2017 A	Q1A	Q2A	Q3A	Q4E	2018	2019	2020
Total Revenues	$7,141.0	$15,288.0	$3,699.0	$5,525.0	$4,821.0	$3,806.8	$17,851.8	$24,525.3	$32,711.9
YOY Growth	393.5%	114.1%	21.6%	79.6%	18.5%	-25.4%	16.8%	37.4%	33.4%
Cost of Goods Sold	$4,612.0	$7,844.0	$2,352.0	$2,711.0	$3,327.0	$2,524.9	$10,914.9	$12,934.7	$15,682.4
Gross Income	$2,529.0	$7,444.0	$1,347.0	$2,814.0	$1,494.0	$1,281.9	$6,936.9	$11,590.6	$17,029.6
Gross Margin	35.4%	48.7%	36.4%	50.9%	31.0%	33.7%	38.9%	47.3%	52.1%
SG&A	$12,868.0	$28,831.0	$8,931.0	$9,437.0	$9,114.0	$9,707.3	$37,189.3	$43,041.9	$49,231.4
% SG&A	180.2%	188.6%	241.4%	170.8%	189.0%	255.0%	208.3%	175.5%	150.5%
R&D	$8,365.0	$12,343.0	$3,756.0	$3,672.0	$3,442.0	$3,715.4	$14,585.4	$11,674.0	$9,879.0
% R&D	117.1%	80.7%	101.5%	66.5%	71.4%	97.6%	81.7%	47.6%	30.2%
Operating Income	($18,704.0)	($33,730.0)	($11,340.0)	($10,295.0)	($11,062.0)	($12,140.9)	($44,837.9)	($43,125.3)	($42,080.9)
Operating Margin	-261.9%	-220.6%	-306.6%	-186.3%	-229.5%	-318.9%	-251.2%	-175.8%	-128.6%
Total Other Income (Expense)	($1,407.0)	($3,229.0)	($1,080.0)	($1,063.0)	($1,110.0)	($1,147.5)	($4,400.5)	($4,368.8)	($4,531.8)
Pre-Tax Income	($20,111.0)	($36,959.0)	($12,420.0)	($11,358.0)	($12,172.0)	($13,288.4)	($49,238.4)	($47,494.1)	($46,612.7)
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	0.0	(249.0)	(158.0)	(132.0)	0.0	(539.0)	0.0	0.0
Net Income (continuing ops)	($20,111.0)	($36,959.0)	($12,669.0)	($11,516.0)	($12,304.0)	($13,288.4)	($49,777.4)	($47,494.1)	($46,612.7)
YOY Growth	61.8%	83.8%	117.7%	-42.7%	83.8%	27.5%	34.7%	-4.6%	-1.9%
Net Margin	-281.6%	-241.8%	-342.5%	-208.4%	-255.2%	-349.1%	-278.8%	-193.7%	-142.5%
EPS (continuing ops)	($2.18)	($2.12)	($0.49)	($0.37)	($0.39)	($0.42)	($1.66)	($1.18)	($1.03)
YOY Growth	-12.2%	-3.1%	-10.3%	-83.1%	-31.9%	-21.7%	-21.7%	-28.6%	-12.9%
Diluted Shares O/S	9,215	17,470	25,847	31,305	31,491	31,550	30,048	40,157	45,225

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APPENDIX

FDA Warning Letter Should Weed-Out Imposters and Benefit VIVE (from our August 1 Note)
On July 30th FDA issued a Safety Communications letter warning against the use of "Energy-Based Devices to Perform Vaginal 'Rejuvenation' of Vaginal Cosmetic Procedures". The purpose of the letter is to "alert patients and health care providers that 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. The safety and effectiveness of energy-based devices for treatment of these conditions has not been established."

FDA notes that they are aware of certain device manufacturers that may be marketing for these purposes – none of which are approved for those indications. FDA warns that if these devices are used for 'vaginal rejuvenation' (which includes vaginal laxity/sexual function) that they could cause vaginal burns, scarring, pain during intercourse, and recurring/chronic pain.

FDA has contacted those manufacturers that they believe may be marketing for these unapproved indications and notes that they will be monitoring claims about uses of their products. The manufacturers have 30 days to respond to FDA requests for;

- FDA clearance or approval number for the [name of device] for the additional claims referenced above [i.e. vaginal rejuvenation/sexual function/vaginal laxity or related to]

- The basis for your determination of whether or not you are required to obtain FDA clearance or approval for the [name of device] for the additional claims referenced above

FDA's letters to each of the manufacturers can be found here. The following are the companies that FDA contacted – **importantly, Viveve was not one of them**;

Manufacturers contacted by FDA for inappropriately marketing their products related to vaginal rejuvenation/sexual function/vaginal laxity/urinary incontinence:

Manufacturer	Device	FDA-approved/cleared for;
BTL Industries, Inc	Exilis	primary treatment of dermatologic and general surgical procedures for non-invasive treatment of w rinkles and rhytids
Cynosure, Inc.	DEKA SmartXide2 Laser System (MonaLisa Touch)	incision, excision, ablation, vaporization and coagulation of body soft tissues in medical specialties including aesthetic (dermatology and plastic surgery), podiatry, otolaryngology (ENT), gynaecology, neurosurgery, orthopaedics, general and thorasic surgery (including open and endoscopic), dental and oral surgery and genitourinary surgery
Alma Lasers	Alma Lasers Pixel CO2 Laser System (FemiLift),	surgical applications requiring the ablation, vaporization, excision, incision, and coagulation of soft tissue in medical specialties including: aesthetic surgery (dermatology and plastic surgery), podiat1y, gynecology, neurosurgery, orthopedics (soft tissue), arthroscopy (knee)
Sciton, Inc.	JOULE Multi-Platform System	for multiple general uses
Thermigen, Inc.	THERMIva	use in dermatological and general surgical procedures for electrocoagulation and hemostasis and to create lesions in nervous tissue w hen used in combination w ith Neuro Therm (previously Smith&Nephew) thermal/coagulation probes
BTL Aesthetics	Venus Fiore RF Ablation System	?
Inmode MD Ltd	FormaV and FractoraV lasers	?

Besides warning providers and women not to use energy-based devices for the unapproved uses related to vaginal rejuvenation, it essentially puts manufacturers on notice that FDA is watching and that they need to cease and desist with any off-label marketing for these uses. While off-label use of medical devices (and drugs) is generally allowed and based on the providers' discretion, off-label marketing is not. This inappropriate marketing by manufacturers of energy-based devices for sexual function/vaginal laxity/rejuvenation/SUI has long been a major impetus to VIVE's focus on obtaining FDA approval for these indications (specifically, sexual function and SUI) as it would draw a clear and distinct line between the proven benefits (and safety) of the Viveve System and all the rest. This warning letter should almost certainly benefit VIVE in this regard as 'all of the rest' do not have FDA approval for those indications and VIVE is (by far) the furthest along towards obtaining marketing approval.

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Viveve was not contacted by FDA regarding this. The Viveve System has also been evaluated in several human clinical studies in for both sexual function and SUI indications. It completed three human clinical studies (and recently began a fourth) related to sexual function/vaginal laxity, including VIVEVE I (multi-site U.S./Canada, RCT, n=174), which was used as support for their IDE application for VIVEVE II. VIVEVE II (multi-site, RCT, n=250) is expected to be (assuming positive results) the pivotal study that supports an eventual FDA filing seeking improvement in sexual function. Viveve received FDA IDE approval to conduct the study in March of this year – IDE approval inherently means that FDA believes any safety risks of using the Viveve System for vaginal procedures in this study are acceptable. Moreover, IDE approval was a fairly drawn-out process in which FDA, at several points, asked VIVE to provide additional information regarding safety.

Of note is that the FDA required VIVEVE II to use a staged roll-in enrollment approach to further ensure safety. While total enrollment is expected to be 250, this staged roll-in requires safety reviews after a certain number of patients have entered the study. In August FDA OK'd continuance of enrollment after their initial safety review. VIVE expects to submit safety data for the second cohort by the end of November.

Of note is that the FDA required VIVEVE II to use a staged roll-in enrollment approach to further ensure safety. While total enrollment is expected to be 250, this staged roll-in requirement means a safety review must be conducted on the initial patients before additional subjects can enter the study. In early August 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). Enrollment continues and the second safety review will occur once another 25 patients have been followed for one-month and 3-month data is available on a total of 50 patients. Management noted on the Q3 call that they **expect to file this safety data, accompanied with an IDE application requesting to enroll the remaining 150 patients, by the end of November.**

If approved, the trial can then enroll through the total of 250. Assuming the IDE supplement is submitted by November 30th and based on FDA's turnaround (~35 days) of the initial safety cohort (n=25/ 30-days), we think this second IDE supplement could be approved by late December 2018 or very early next year. Approval is, of course, critical as it is a gatekeeper to finishing the study but, we think, it may also play a role in re-accelerating domestic sales growth given that it is further evidence supporting the safety of Viveve treatment. If so, it is possible that FDA green-lighting the final enrollment cohort to proceed could resonate with potential purchasers of the system that may have been hesitant to do so due to the unfortunate halo effect of FDA's warning letter.

The Viveve System has also completed two human studies in SUI, with two more ongoing; a pilot study (VIVE announced positive 6-month results of this study in June) and LIBERATE International, which recently commenced (following Health Canada ITA approval) and has ~30 patients of an expected 100, total, enrolled. Moreover, VIVE expects to submit an IDE to FDA for approval of LIBERATE U.S., a large (n=240), randomized (2:1 active:control), multi-site (~25), RCT in SUI in the very near-term.

The point here is that, it's clear that FDA is concerned about safety of energy-based devices used in vaginal aesthetic procedures and SUI and that, unlike some manufacturers, VIVE is following the appropriate path to be able to (legally) market their device for the indications that they are targeting. By contrast, some other devices have little or no formal human clinical study experience and therefore no verified safety record. Viveve's does – and the FDA would not have approved their IDE had they had overwhelming concerns about risk.

So, while we acknowledge that the headline reaction from FDA's warning letter may be a short-term headwind to VIVE (and a much more significant defeat for the other manufacturers), we think it is also a significant win for the company as it should weed out what are essentially the imposters (i.e. those with little to no formal clinical evidence supporting efficacy/safety in these indications). Further, we think FDA approval of the anticipated IDE supplement for VIVEVE II (as well as the separate IDE application for SUI), if that happens, would provide even more validation of the substantive separation between the Viveve System and all other energy-based devices.

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).

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.

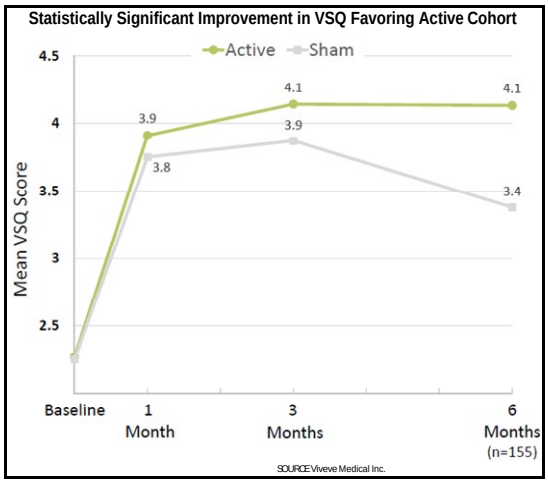
Mean VSQ scores at the 1, 3 and 6 month follow up periods were;

- 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)

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

- 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

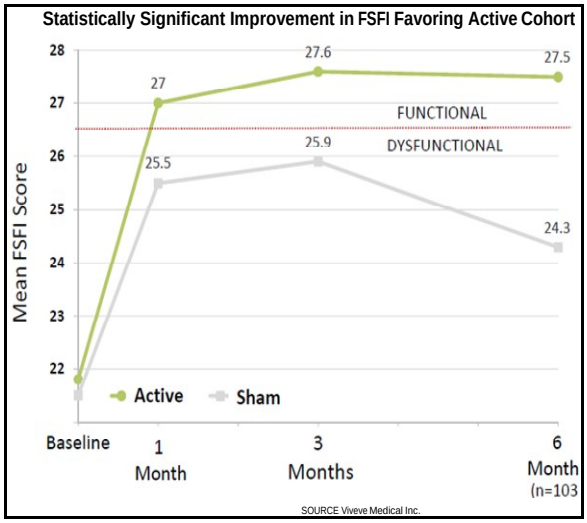
Similar to the two prior studies, VIVEVE I demonstrated that treatment with the Viveve System is associated with a significant increase in sexual function. FSFI is a brief, 19-item self-report measure of female sexual function that provides scores on six domains of sexual function as well as a total 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

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.

[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.



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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VIVEVE I Secondary Outcome Measures

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

[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.

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

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".

LIBERATE Pivotal Registration Trials, International Study Enrolling, U.S. Study IDE Filing Upcoming…
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).

[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.

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 and as of early November, ~30 of the expected 100 total patients have enrolled. The 6-month feasibility study data will be used to support the IDE for approval to commence the U.S. LIBERATE study.

The U.S. and Canadian studies are expected to enroll 240 and 100 patients across 25 and 10 sites, respectively (~10 patients/site). Given the already sizeable installed base, we would expect enrollment may be accomplished fairly swiftly, assuming both the U.S. and Canadian studies can utilize certain of the current Viveve System practitioners' locations as trial sites.

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

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

- 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 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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