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Zacks Small-Cap Research

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Biomerica Inc (BMRA-NASDAQ)

Revenue Slows Although Potential Growth Catalysts on the Horizon. Further Pipeline Progress…

We use sum of the parts to value BMRA. Comparable P/S and P/B values the base business at ~$3.00/share. Applying 11x to our $8.4M 2024 forecasted InFoods revenue and discounting back to the present at 14%/year, results in InFoods present value of approximately $40M, or $4.00/share. BMRA TOTAL VALUE = $7/share

Current Price (04/18/19)	$2.46
Valuation	**$7.00**

OUTLOOK

Despite the disappointing topline results through the first nine months of 2019, there are reasons to be optimistic that sales growth will materialize. For one, while Asian sales are down YTD, they were up modestly (~4%) on a quarterly basis in Q3. And given that Asia posted relatively weak sales in Q4'18, it is reasonably possible that that territory, which accounts for about 50% of total revenue, could still eke out positive growth for the full year. Additionally, Biomerica recently contracted with outside consultants to help with accelerating sales of EZ Detect, the company's flagship colorectal cancer screening test. This includes for China – which we continue to think could represent a very receptive and lucrative market for the product – and for Vietnam, the UAE and Russia. Also, while U.S. sales have been on a several years-long decline, we are hopeful that they will return to growth given the potential catalysts represented by the Medline distribution agreement (as of November 2018) as well as eventual commercialization of BMRA's novel h. pylori test.

Recent highlights on the operational front include Notice of Allowance from the U.S. Patent and Trademark Office for BMRA's first U.S. patent related to its InFoods products and progress-related activities associated with both the InFoods and h.pylori clinical programs.

SUMMARY DATA

52-Week High	**$4.33**
52-Week Low	**$1.60**
One-Year Return (%)	**-40.00**
Beta	**1.35**
Average Daily Volume (sh)	**27,051**
Shares Outstanding (mil)	**10**
Market Capitalization ($mil)	**$24**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**1**
Insider Ownership (%)	**29**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**2.8**
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-Tech Diagn.**

ZACKS ESTIMATES

Revenue
(in millions of $)

	Q1 (Aug)	Q2 (Nov)	Q3 (Feb)	Q4 (May)	Year (May)
2018	1.45 A	1.61 A	1.38 A	1.13 A	5.56 A
2019	1.27 A	1.50 A	1.12 A	1.20 E	5.24 E
2020					6.08 E
2021					6.64 E

Earnings per Share

	Q1 (Aug)	Q2 (Nov)	Q3 (Feb)	Q4 (May)	Year (May)
2018	-$0.02 A	-$0.03 A	-$0.04 A	-$0.08 A	-$0.17 A
2019	-$0.05 A	-$0.05 A	-$0.07 A	-$0.07 E	-$0.24 E
2020					-$0.38 E
2021					-$0.28 E

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

WHAT'S NEW……

Q3 2019: *Revenue Slows Although Potential Growth Catalysts on the Horizon. Further Pipeline Progress…*

Biomerica reported financial results for their fiscal 2019 third quarter ending February 28, 2019. Revenue was a relative disappointment, coming in well below our estimate on both a total basis as well as from each itemized geography. It was also down 8% from Q2'19, down 16% yoy and the second-lowest level of the past 13 quarters. Revenue has decreased each of the first three quarters of 2019 as compared to the respective prior-year periods and through the first nine months, is down 9% from 2018.

Revenue through the first nine months from each of three most significant territories is down from last year. Sales from Europe, the U.S. and Asia, which account for approximately 33%, 11% and 49% of total revenue, respectively, have fallen 15%, 21% and 7% YTD. But, despite the disappointing topline results through the first nine months of 2019, there are reasons to be optimistic that sales growth will materialize.

For one, while Asian sales are down YTD, they were up modestly (~4%) on a quarterly basis in Q3. And given that Asia posted relatively weak sales in Q4'18, it is reasonably possible that that territory, which accounts for about 50% of total revenue, could still eke out positive growth for the full year. Additionally, Biomerica recently contracted with outside consultants to help with accelerating sales of EZ Detect, the company's flagship colorectal cancer screening test. This includes for China – which we continue to think could represent a very receptive and lucrative market for the product – and for Vietnam, the UAE and Russia. Also, while U.S. sales have been on a several years-long decline, we are hopeful that they will return to growth given the potential catalysts represented by the Medline distribution agreement (as of November 2018) as well as eventual commercialization of BMRA's novel h. pylori test.

- **Total revenue** of $1.26M fell 8% yoy, was down 16% from Q2'19 and missed our estimate by nearly 24%. Through the first nine months, revenue was $4.03M, down 9% from the same period in fiscal 2018. Despite the yoy weakness, YTD revenue is relatively robust as compared to much of BMRA's prior recent history. In fact, revenue through the first nine months of 2019 is higher than that of the comparable periods of 2014 by 17%, 2015 by 16% and 2016 by 6%.

- **Asia** sales, at $653k, were down 3% from Q2, up 4% from the prior year and about 17% lower than our $784k estimate. Our estimate had assumed initial (clearly too early) benefits from the December 2018 agreement with a company to facilitate sales of EZ Detect in China. Through the first nine months Asia sales were $2.0M. While down single digits from 2018, it is higher than the first nine-month periods in each of the four prior years (i.e. from 2014 through 2017). The $653k generated in Q3'19 is also slightly better than the $628k that Asian sales averaged throughout fiscal 2018. While we had anticipated incremental revenue growth from the launch of EZ Detect, which received China FDA (CFDA) approval in January 2018 (i.e. late-fiscal Q2'18), it is not clear if Asia sales in 2019 have included any meaningful contribution from that product.

  While Asia has been a territory which has historically experienced relatively high short-term sales volatility, longer-term trends continue to point towards regular revenue growth in our opinion. And, as Asia has grown to account for a larger proportion of total revenue, even incremental growth from current levels in this territory will have a meaningfully positive effect – but even incremental contraction will have the opposite effect.

  As noted, we had hoped EZ Detect (over-the-counter fecal occult blood (FOB) test for colorectal cancer) would have been a positive catalyst – although it's possible we were a little too optimistic relative to timing. We continue to like the fundamentals in China as it relates to BMRA's flagship product. While Biomerica has never publicly disclosed product-specific sales numbers, we believe EZ Detect is one of the (if not the #1) best-selling products for the company. We also think Asia could be particularly receptive to the product given certain cultural principles in many parts of Asia related to hygiene which may discourage use of FOB tests which require fecal handling.

  Recent initiatives aimed at increasing colorectal cancer screening – by any modality – also support fundamentals for EZ Detect. Many parts of Asia, including in China, have relatively low rates of compliance to recommended colorectal cancer screening guidelines. For context, while ~65% of Americans adhere to CRC screening guidelines, studies indicate that compliance is only ~40% in Shanghai, China. Studies have shown that one of the most effective ways to increase CRC compliance is through providing more testing options. So, for all of these reasons, we think Asia could represent a substantial growth opportunity for BMRA's EZ Detect product.

- **European** sales, at $416k, were down 14% yoy, down 20% qoq and about 21% lower than our $527k estimate. European sales were $1.3M YTD, down 15% from 2018 and the lowest level through the first nine months since at least fiscal 2010 (i.e the furthest we looked back).

  We continue to model flat to slightly negative sales in Europe (related to BMRA's current product portfolio) and think opportunity for sustainable growth may mostly hinge on new product launches. While we have yet to model any assumed contribution from InFoods in Europe (or any other new products), that could soon change - depending on BMRA's future strategic objectives as well as if we feel there is enough information to make (comfortably) informed projections about certain commercializability-related gating factors. At this point we have no information or insight into if or when BMRA might consider targeting markets outside of the U.S. or if they do, which areas of the world they would focus on next. Europe, however, would be our best-guess as a potential front-runner if management does eventually look to expand OUS with InFoods given not only the economic similarities of most of the highly developed European countries with that of the U.S. but, perhaps more importantly, diets that are (generally) similar to that of most Americans.

- **U.S.** revenue, at $141k, was down 32% yoy, flat sequentially and about 35% lower than our $218k estimate. This is also well below the U.S. quarterly high of $446k (Q3'14) as well as its historical average of about $250k. Through the first nine months U.S. sales are down 21%. Similar to Europe, U.S. revenue is at the lowest level through the first nine months since at least fiscal 2010. U.S now accounts for just 11% of total revenue, down from 20% - 25% just a few years back. As we have noted in prior updates, the longer trending decline in U.S. sales has been attributed to lower purchasing (of BMRA's flagship EZ Detect colon disease test) from a certain drug store customer that, unlike some years, decided not to conduct a colorectal cancer screening program during fiscal 2018. But, as BMRA brought on Medline, the largest privately-held U.S. distributor of medical supplies, to distribute EZ Detect, we are hopeful that U.S. sales will return to growth. The agreement, signed in November 2018, is for an initial three-year term. We also think that incremental U.S. sales growth could come from the new h. pylori test candidate which recently entered clinical studies.

  And with the recent disclosure and announcement of initial clinical trial design and collaboration to conduct clinical trials with two major U.S. university research centers, we recently began modeling InFoods. As we discuss in more detail below, we are modeling initial contribution from InFoods in 2022. We continue to believe that eventual FDA clearance of this novel IBS product would result in a significant increase in Biomerica's U.S. sales and provide the majority of total revenue growth from that point into the foreseeable future.

Gross Margin, Operating Expenses

Q3 gross margin, at 29%, is down from 34% in the year-earlier period but up from 27% in Q2'19. In fact, Q3 saw the widest gross margin in the last four consecutive quarters. Through the first nine months of the year GM has averaged approximately 28%, down about 600 basis points from 34% in the prior-year period. But, with higher production volumes – hopefully in part spurred by an increase in sales of EZ Detect (both domestically and in areas such as China, Vietnam and Russia), we hope to see GM begin to again strengthen.

OpEx was $1.1M, or 85% of revenue in Q3 and $2.8M, or 68% of revenue in the first nine months of 2019. This compares to 57% and 52% in the comparable prior year periods. OpEx averaged 58% in all of 2018. Despite the clinical activity related to InFoods and the h.pylori test, R&D expense has increased only relatively modestly. R&D expense increased from $1.1M in 2017 to $1.4M in 2018 and to an annualized run-rate of $1.7M through the first nine months of the current year. We do, however, continue to model opex to increase at a higher rate than that of revenue growth over the near term as a result of increasing development activity related to InFoods, and to a lesser extent, the h.pylori program.

Cash

BMRA used $257k and $1.3M ($531k and $1.3M, ex-changes in working capital) in cash for operations in the three and nine months ending February 28, 2019, compared to $489k and $852k ($274k and $631k, ex-changes in working capital) in the comparable prior-year periods.

The company raised nearly $1.1M through the sale of common stock (via the ATM program) and the exercise of warrants so far this fiscal year. They exited Q3 with $917k in cash on the balance sheet and, subsequent to period-end, raised an additional $800k (net) via the exercise of options and through the sale of common shares.

Additional, non-dilutive funds, could come from BMRA's agreement with Telcon Pharmaceuticals (fka Celtis Pharm Co.) of S. Korea which calls for that company to pay Biomerica up to $1.25M in exclusivity fees based on "certain milestones including Biomerica's starting clinical trials in the United States, receipt of US FDA clearance and Celtis' first sales of IBS Products in Korea". The agreement was initially cancellable if BMRA had not obtained FDA

clearance/approval of InFoods by December 31, 2017 but that deadline was subsequently extended until December 31, 2019.

Operational Update (see Appendix for background info)

Recent highlights on the operational front include Notice of Allowance from the U.S. Patent and Trademark Office for BMRA's first U.S. patent related to its InFoods products and progress-related activities associated with both the InFoods and h.pylori clinical programs.

As it relates to InFoods, earlier this month BMRA announced that the USPTO issued a Notice of Allowance for their "InFoods family of products that allow for revolutionary new treatment options for patients suffering from Irritable Bowel Syndrome ("IBS") and other gastrointestinal diseases. Specifically, this allowed application (#15/526,240) contains numerous claims that broadly cover a product that enables physicians to identify patient specific foods (e.g. pork, milk, shrimp, broccoli, chickpeas, etc.), that when removed, may alleviate or improve an individual's IBS symptoms, including but not limited to constipation, diarrhea, bloating, pain and indigestion." The accompanying 8-K notes that "the process resulting in final issuance of a patent involves several administrative steps that are typically completed within a year."

Biomerica also noted that they have additional U.S. patent application in process that cover other claims related to their InFoods IBS product and that they are developing and have filed patents for other diseases "in the InFoods family of products, which include: Functional Dyspepsia, Crohn's Disease, Ulcerative Colitis and Gastroesophageal reflux disease (GERD)." As such, we expect that we could hear ongoing updates of additional allowance notices from USPTO as it relates to what could be a growing IP portfolio around InFoods – which now clearly encompasses more than just one product (i.e. IBS) candidate.

As a reminder, a food-exclusion study showing Biomerica's first-generation ELISA immunoglobulin G (IgG) antibody assay was able to significantly reduce ulcerative colitis symptoms and improve participants' quality of life was published in September 2018 in the journal Inflammatory Bowel Disease (see our discussion below). As we noted at the time, we feel that the results are particularly compelling given that the study used the company's first-generation IgG assay – a test that we believe is less-targeted (i.e. less accurate) than the technology incorporated into their InFoods product. In addition, this study assessed BMRA's test in individuals with ulcerative colitis (UC) – while InFoods has been developed primarily to determine optimal food exclusion diets for people with irritable bowel syndrome. These results, we think, indicate that Biomerica's technology may have platform-like potential with possible clinical utility across a variety of gastrointestinal disorders.

This may also mean that the eventual target market for their guided food-elimination diagnostic could be significantly expanded beyond what we have characterized as the 'reachable IBS population' (see our valuation section for specifics) – our assumptions will be updated if and when we think it is warranted.

Also, as it relates to InFoods, BMRA disclosed in their Q3 10-Q that on March 12th they entered a contract with a third-party institution to conduct an "Endpoint Determination Study" on their InFoods diagnostic. As a reminder, in late-June 2018 Biomerica announced that the first patient had enrolled in their Endpoint Determination study. It is not clear what the role is of the institution that is the subject of this most recent announcement nor if this may indicate that the study's enrollment had stalled since the first patient enrolled last summer.

As it relates to recent progress of BMRA's h.pylori program, the company announced in early February that, based on discussions with the FDA, they need less than 40 additional clinical samples to complete their ongoing clinical study. These 40, which are expected to be collected over "the next few months", are in addition to 210 patient samples that have already been aggregated. Following collection and completion of the study, BMRA expects to make a 510(k) filing seeking FDA clearance of their novel h.pylori test.

Biomerica's IgG Antibody Test Used to Significantly Reduce Ulcerative Colitis Symptoms, Improve QoL

Results of an n=97 randomized, investigator-blinded food-exclusion study showed that Biomerica's first-generation ELISA immunoglobulin G (IgG) antibody assay was able to significantly reduce ulcerative colitis symptoms and improve participants' quality of life. Results, which were published in the journal Inflammatory Bowel Disease in September 2018, are particularly compelling in our opinion given that the study used the company's first-generation IgG assay – a test that we believe is less-targeted (i.e. less accurate) than the technology incorporated into their

InFoods product. In addition, this study assessed BMRA's test in individuals with ulcerative colitis (UC) – while InFoods has been developed primarily to determine optimal food exclusion diets for people with irritable bowel syndrome. These results, we think, indicate that Biomerica's technology may have platform-like potential with possible clinical utility across a variety of gastrointestinal disorders.

While IgG-based food-elimination studies are not new and prior studies have shown a connection between IgG antibody reaction to certain foods and UC symptomology, this study took that association a step further to real-world applicability. Specifically, this study demonstrated that IgG (which, in this case was BMRA's assay) can be a practical tool to identify and eliminate trigger foods from ones diet and result in a significant reduction in clinically meaningful symptoms (such as number of daily bowel movements and rectal bleeding) and improvement in nutrition and quality of life.

Participants included those in remission (n=31) as well as those with mild (n=37) to moderate (n=29) UC. Of the 97 individuals for which there was final study data, 49 and 48 were randomized to the interventional (i.e. food exclusion) and control group, respectively. While the control group was instructed to continue eating as normal, diets of the interventional group were adjusted based on baseline results of IgG tests. More specifically, IgG antibodies of 14 foods that have been well-established as associated with food intolerance were measured at baseline (among all participants). Of the 97 patients, 68 were food-specific IgG antibody positive, including 54 that were extremely sensitive to food. There was no significant difference at baseline between the two groups as it relates to number of patients positive or severe-positive

Patients in the interventional group eliminated any foods associated with IgG levels high enough to be considered problematic (specifically IgG titers over 100b U/ml). Patients were followed for 6 months and were evaluated on Mayo score, a well-established grading system for ranking severity of UC, as well as on other parameters including extraintestinal manifestations (EIM), nutritional status and quality of life (QoL).

Results…

The Mayo score is calculated across four distinct domains; stool frequency, rectal bleeding, mucosal appearance and physician's global assessment/rating. At baseline, Mayo scores were equivalent between interventional and control. Results showed significantly lower Mayo scores among the food-exclusion group as compared to control (2.41 ± 0.89 vs 3.52 ± 1.15, $P < 0.05$). The stool frequency domain contributed the most substantially to the difference in Mayo scores. Mucosal state improved in both groups - while there was no significant difference between them, the investigators noted that the endoscopic score was slightly better among the food-exclusion cohort.

Assessment on EIMs (which can include a number of conditions including anemia, arthropathy and anti-TNF induced skin inflammation as well as a host of others) also favored the food-exclusion group, with the number of EIMs falling from 7 to 2, while the sham group saw EIMs only decrease from 6 to 5.

Nutritive indices, including those measuring BMI, albumin, prealbumin and transferrin were also reported. Both BMI (23.88 ± 3.31 vs 21.50 ± 6.24 kg/m2, $P < 0.05$) and albumin (48.05 ± 6.39 vs 45.72 ± 5.48 g/L, $P < 0.05$) were significantly greater (i.e. superior) among the interventional group while prealbumin and transferrin were statistically equivalent between the two cohorts.

Nutrition status: BMI and albumin significantly better among food-exclusion group

TABLE 5: Nutritional Status of Patients After Intervention, According to Group

Nutritional Items	Food Exclusion Group	Sham Diet Group	*t*	*P*
BMI	23.88 ± 3.31	21.50 ± 6.24	2.353	0.010
ALB	48.05 ± 6.39	45.72 ± 5.48	1.700	0.047
PA	264.56 ± 48.22	256.93 ± 46.50	0.793	0.215
TRF	246.67 ± 14.52	249.04 ± 22.54	–0.533	0.298

Source: Jian et al., Inflamm Dowel Dis, Vol24, No9, Sept 2018

Quality of life, which was equivalent between the two groups at baseline, also favored the food-exclusion cohort at the end of six months. QoL, assessed by the well-validated Inflammatory Bowel Disease Questionnaire (IBDQ), was statistically significantly greater in the interventional group on all 4 domains. Notably, the 'emotional function/health' sub-item was particularly superior among the food exclusion group. The investigators noted that

this could be of substantial importance as any diet that can improve emotional well-being is more likely to be adhered to.

Quality of Life significantly improved among food-exclusion group

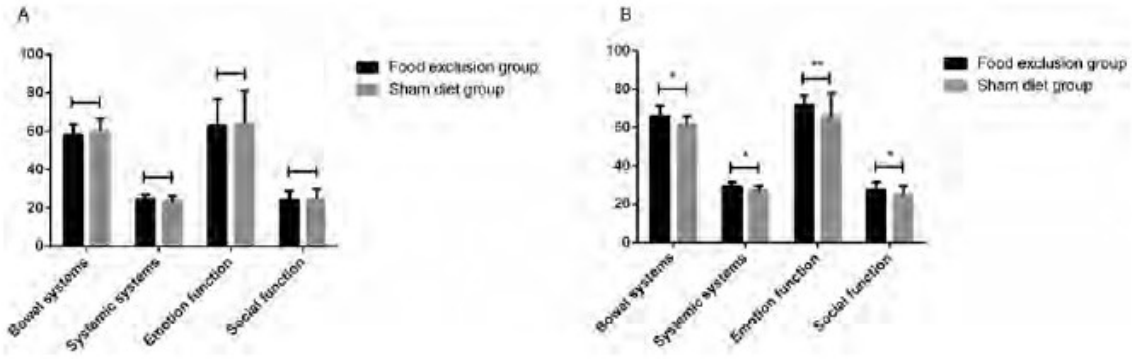


FIGURE 3. Comparison of scores for 4 dimensions derived from the IBDQ, according to group. A, Before intervention. B, After intervention. *$P < 0.05$; **$P < 0.01$.

Source: Jian et al., Inflamm Dowel Dis, Vol24, No9, Sept 2018

InFoods Background

InFoods Study 1

In late-June 2018 BMRA announced that the first patient had enrolled in the InFoods Endpoint Determination study. In their Q3 10-Q BMRA disclosed that on March 12th they entered a contract with a third-party institution to conduct an "Endpoint Determination Study" on their InFoods diagnostic. It is not clear what the role is of the institution that is the subject of this most recent announcement nor if this may indicate that the study's enrollment had stalled since the first patient enrolled last summer.

As a reminder, two clinical studies will be conducted; the purpose of the first study, which will include approximately 180 subjects and with an expected duration of 9 – 14 months, is to identify the primary endpoint to be used in the second study. It is anticipated that the second study will serve as the pivotal study and primary support for an eventual 510(k) filing.

Study 1, titled simply (as of now, anyway) "Endpoint Determination Study Protocol" was first posted on clinicaltrials.gov on March 9, 2018 (NCT03459482, link: http://bit.ly/2H9RTPP).

Particular points of interest related to Study 1 as detailed in the posting include:

- RCT-design and will incorporate triple blinding (i.e. patient, provider and investigator)
- Targeting enrollment in each arm (i.e. treatment vs. sham) of 90 patients and a minimum of 30 patients in each IBS classification of: IBS-D (diarrhea), IBS-C (constipation) and IBS-M (mixed)
- Arms
    - Treatment (i.e. food elimination diet): patients will be given an elimination diet based upon foods with a positive antibody profile in the InFoods IBS test. The elimination diet will also exclude any and all foods to which the subject has a known IgE allergy and foods the subject already currently eliminates
    - Sham: patients will be given a "Sham" elimination diet. The sham diet will eliminate the same number of foods but none of the actual foods to which the patient had a positive antibody profile in the InFoods IBS test. The sham diet will also eliminate any and all foods to which the subject has a known IgE allergy and foods the subject already currently eliminates
- Inclusion criteria includes
    - Meets Rome III or Rome IV IBS diagnostic criteria
    - Respond "No" to IBS Adequate Relief (IBS-AR) in the past week at the screening visit #1
    - Score between ≥ 3 and <7.5 on the Abdominal Pain Intensity Assessment (IBS_API) based on a weekly average of worst daily (in past 24 hours) abdominal pain on a 0 to 10 point scale
    - A positive IgG antibody response for at least one food in the InFoods IBS panel

    - Patients who are on stable (> 3 months) doses of medications or treatments for their IBS (e.g., probiotics, fiber, Viberzi, Linzess, Amitiza, Alosetron, Plecanatide, anticholinergics, antidepressants, Zofran bile acid sequestrants, or anti-diarrheals) will be allowed to continue their medications as long as no change in treatment is planned for the duration of the study and no dose adjustment is made during the duration of the study
- Exclusion criteria includes
    - Patients who have used Rifaximin in the past 3 months
    - Patients engaged in another type of diet therapy i.e. FODMAP
    - Chronic pain from other conditions besides IBS

Our Comments on Study 1 Design:
Is of robust design, RCT and triple blinding. Clearly Study 1 was designed to serve as a template for a pivotal study. Inclusion and exclusion criteria all appear to be consistent with designs of pivotal IBS drug studies – which is also highly encouraging. The only slight divergence appears to be with excluding patients with pain score $\geq$ 7.5. We have no concern relative to that, however, as it almost certainly relates to minimizing potential noise given that higher pain scores can often be associated with non-IBS causes.

A "primary endpoint" of IBS-API (i.e. pain measure) is also listed in the clinicaltrials.gov posting – however, that should be considered to only be one of several measures that will be assessed in Study 1 as potential primary endpoints to be incorporated into a pivotal study. Others, as we have indicated in our recent prior updates, will likely include primary endpoints that have been used in recent pivotal studies of IBS drugs including defecation related endpoints (i.e. stool consistency and frequency). We should know more about all of the endpoints under consideration when with future updates to the posting.

The clinical studies will be conducted at Beth Israel Deaconess Medical Center (Harvard teaching hospital) and the University of Michigan. Drs. William Chey and Anthony Lembo are members of BMRA's scientific advisory board and are affiliated with the University of Michigan and Beth Israel Deaconess Medical Center, respectively (and will presumably be the principal investigators at their respective trial sites). As a reminder, Dr. Lembo is Director of the GI Motility Laboratory at the Beth Israel Deaconess Medical Center's Division of Gastroenterology. He is also one of the principal investigators of Biomerica's recently initiated h. pylori clinical study (see below). Dr. Chey Professor of Internal Medicine, Director of the GI Physiology Laboratory, and Director of Medical Services for the Michigan Bowel Control Program at the University of Michigan.

Comment on Primary Endpoint…
We will be very interested to eventually find out what InFoods' pivotal study primary endpoint will be and its similarity (or not) to those used in prescription IBS drugs' pivotal studies (see our Appendix for more detail about primary endpoints).

Given that FDA has already determined InFoods is a non-significant risk diagnostic (i.e. Class I), the efficacy hurdle for U.S. regulatory clearance may be considered to already be set inherently relatively low (which is not uncommon for diagnostics of many conditions and diseases). However, FDA clearance of a diagnostic usually does not portend the commercial potential of that of a drug that also successfully gains U.S. regulatory approval. In other words, while FDA clearance is of obvious importance for InFoods to enter the U.S. market, meaningful physician uptake may require "compelling enough" clinical evidence.

The good news for BMRA is that there are several factors which may mean the "compelling enough" hurdle may not be too difficult to clear – which we discuss below. The choice of primary endpoint in InFoods' clinical studies may have significant influence (perhaps the most influence) on commercial adoption. If InFoods' primary endpoint is the same (or at least similar) to those used in IBS drug pivotal studies, that should allow for an apples-to-apples efficacy comparison between them - and the additional benefit would be that GIs are already versed on them.

But while a similar endpoint might be ideal, as long as whatever measure is chosen has been sufficiently validated (and InFoods demonstrates efficacy), we think there will be demand for InFoods. The fact that InFoods can be used as an addition to IBS drug therapy means that BMRA's diagnostic does not have to demonstrate superiority to current prescription medicine – in this scenario, as long as InFoods can provide incremental benefit to drugs, it should have utility.

"Compelling Enough" May Not Be Tough Given InFoods Appeal to the "3Ps"…
With BMRA's dream-team scientific advisory board presumably guiding InFoods' clinical strategy, we have confidence that whatever endpoint is chosen will have sufficient industry acceptance. Assuming success in the

clinical studies, we like the chances for significant adoption of InFoods because of its potential to appeal to the "3Ps" in the healthcare treatment chain – that is, the patient, physician and payer. Here's why;

- **IBS Drugs Have Major Drawbacks (see our detailed discussion in Appendix):**
    - data from pivotal FDA studies of currently available Rx IBS drugs have shown that;
        - they are ineffective for the majority of IBS sufferers
        - they were often barely better than placebo
        - most IBS drugs have a negative effect on IBS that exceeds their benefits[1]
    - IBS Rx drugs are expensive
        - typical cost-per Rx between $400 - $1,000
        - due to the high cost of IBS drugs and the chronic nature of the disease, payers will often require patients to try other, less-expensive, therapies before approving payment
        - lack of efficacy and high cost of drugs drives up total IBS-related healthcare costs as physicians use trial and error approach to try and treat the disease
    - IBS drugs can have unpleasant (such as diarrhea) and dangerous (such as risk of pancreatitis) side effects. Some are also not recommended for chronic use
    - there is no drug indicated for the treatment of IBS-M
- **Pent-up Demand for Better IBS Treatment of Options**
    - IBS, particularly IBS-D, can be highly detrimental to quality of life
    - given that IBS drugs do not provide sufficient relief to most IBS sufferers, physicians and patients are eager for other options
    - survey conducted by a 3rd-party research organization found that 70% of physicians surveyed indicated that they would use InFoods
- **Reimbursement**
    - BMRA (as guided by their IBS-expert SAB) believes InFoods is reimbursable under an existing CPT code(s), although they have yet to divulge which one(s)
    - we estimate (i.e. guess) that an InFoods diagnosis will charge will be in the range of $100 - $300 and a patient can expect to be tested 2 – 3 times per year = $400 - $900/year. This is relatively insignificant compared to the ~$13k/year current average total healthcare cost per IBS-D patient which may further incentivize payers to reimburse for InFoods
    - as noted above, payers often require failure of less expensive (i.e. oftentimes non-Rx and not IBS indicated) treatment options prior to authorizing payment for Rx IBS drugs. As such, InFoods may be able to be positioned as a less expensive, first-line option to IBS

H.Pylori Test Background

Novel H. Pylori Test

The company remains committed to expanding their product menu. While clearly the single major focus is successful development of InFoods, other high-potential projects continue in parallel. Another program, related to a **novel Helicobacter pylori (h. pylori) diagnostic** was the latest to be divulged. BMRA already has several h. pylori tests in their product catalog including ELISA blood antibody tests, a rapid antibody test for the OTC market and a rapid stool-based antigen test for the professional POC market.

H. pylori is a gram-negative bacteria found in the stomach. While it is relatively common – as much as 50% or more of the world's population are infected with the bacteria – most people do not exhibit symptoms. But, of the 15% - 20% that do have a reaction, symptoms can include stomach pain, reflux, nausea and bloating. H. pylori is associated increased risk of ulcers and is the strongest known risk for developing gastric cancer. Additionally, length of exposure to h. pylori is positively correlated to the risk of gastric cancer. Once diagnosed, standard therapy consists of proton pump inhibitors and certain antibiotics.

In November 2017 BMRA announced that enrollment commenced for the clinical studies for their new and proprietary h. pylori test which "is designed to increase the sensitivity and specificity of H. pylori testing and

[1] Shah, E. and Pimentel, M. (2014), Evaluating the functional net value of pharmacologic agents in treating irritable bowel syndrome. Aliment Pharmacol Ther, 39: 973–983. doi:10.1111/apt.12692

monitoring of treatment." The studies are being done in collaboration with the University of Southern California and Vanderbilt University, along with an unnamed European University.

In April 2018 BMRA contracted with Guardian Angel Research Center to conduct a specimen collection study protocol for h. pylori testing in patients with dyspepsia. Then in early February 2019 BMRA announced that, based on discussions with the FDA, they need less than 40 additional clinical samples to complete their ongoing clinical study. These 40, which are expected to be collected over "the next few months", are in addition to 210 patient samples that have already been aggregated. Following collection and completion of the study, BMRA expects to make a 510(k) filing seeking FDA clearance of their novel h.pylori test.

Additional details about the study, titled *Specimen Collection Study for H. Pylori Testing in Patients With Dyspepsia*, are listed on clinicaltrials.gov (ID: NCT02970110, link: http://bit.ly/2gRuwLD). Principal investigators are Dr. Anthony Lembo (Harvard Medical) and Dr. Douglas Morgan (Vanderbilt Medical). Dr. Lembo is also a member of BMRA's Scientific Advisory Board and a recognized expert in GI disorders. Per clinicaltrials.gov, the study, which will be conducted at a minimum of two sites, will acquire human specimens from patients (n=200) undergoing endoscopy with gastric biopsy for the diagnosis of active h. pylori infection. The biopsy tissue (sampled from the stomach) will be evaluated with histology and rapid urease test (or RUT, a commonly used test which identifies the presence of urease, an enzyme secreted by h. pylori). The study design also notes that a **stool sample will be obtained by the participants prior to undergoing endoscopy** and that "results and specimens will be used in a future clinical trial [i.e. "analytical studies" referenced in BMRA's PR] of a non-invasive in vitro diagnostic assay for the detection of H. pylori antigen". **Which we think suggests that BMRA's novel h. pylori test will be stool-based.**

Currently there are several methods to test for the presence of h. pylori. This includes histology, RUT and culture – all of which require invasive biopsy sampling, and non-invasive methods including urea breath test (UBT), serology and stool antigen tests (SAT). There are advantages and disadvantages of each. This includes expense and discomfort of invasive testing and lower accuracy of non-invasive serology testing. Below is a summary (compiled from data of several studies) of the different tests and their relative advantages and disadvantages – the table is from a study by JY Lee and N Kim, published in the January 2015 issue of Annals of Translational Medicine.[2]

Diagnostic tests for the detection of *H. pylori* infection (2,15-17)

Test	Sensitivity	Specificity	Advantages	Disadvantages
Noninvasive				
Serology	76-84	79-90	Widely available, inexpensive	Positive result may reflect previous rather than current infection, not useful after treatment
Urea breath test	>95	>95	High negative and positive predictive values, useful before and after treatment	False-negative results possible in the presence of PPIs or with recent use of antibiotics of bismuth preparations, considerable resources and personnel required to perform test
Stool antigen test	96	97	High negative and positive predictive values, useful before and after treatment	Process of stool collection may be distasteful to patient, false-negative results possible in the presence of PPIs or with recent use of antibiotics or bismuth preparations
Invasive				
Histology	95	99	Excellent sensitivity and specificity, especially with special and immune stains, provides additional information about gastric mucosa	Expensive (endoscopy and histopathology costs), interobserver variability, accuracy affected by PPI and antibiotics use, requires trained personnel
Rapid urease test	90	93	Rapid results, accurate in patients not using PPIs or antibiotics, no added histopathology cost	Requires endoscopy, less accurate after treatment or in patients using PPIs
Culture	58.1	100	Specificity 100%, allows antibiotics sensitivity testing	Variable sensitivity; requires trained staff and properly equipped facilities, expensive

Our Comments: Currently available SAT tests are generally considered highly accurate, although as the table illustrates, there are drawbacks including that the use of PPIs, antibiotics or recent bismuths can affect sensitivity. We will be interested to hear future updates on the progress of the clinical and validations studies and more details

[2] Ju Yup Lee and Nayoung Kim. Diagnosis of Helicobacter pylori by invasive test: histology. Ann Transl Med. 2015 Jan; 3(1): 10.

about the test under development. Learning more about the novel nature, and how it differs from currently available SATs, will be of particular interest to us. We think that if the test was designed to address one or more of the shortcomings of current SATs – such as, for example, being unaffected by PPIs (with no meaningful compromise to accuracy) or even improving on accuracy, that that may provide for significant differentiation.

Approximately six million non-invasive h. pylori tests are performed each year in the U.S. – if we assume $100/test, that calculates to a domestic market size of around $600M. And this is expected to grow given increasing prevalence of h. pylori and a greater shift from direct (i.e. invasive) to non-invasive methods – which could be further catalyzed with the advent of novel technologies (potentially including BMRA's test) addressing some of the drawbacks of currently available tests.

Given BMRA's relatively tiny size ($24M MC, ~$5M annual revenue), capturing as little as one-quarter of one percent of the U.S. non-invasive h. pylori market (or ~$1.5M) would be highly significant for the company. One percent market share could mean doubling of revenue from current levels. We hope to know more about the test in the non-too-distant future which may help in assessing potential competitiveness to currently available diagnostics as well as provide some useful data points for modeling purposes.

VALUATION

We like chances for FDA clearance of InFoods and subsequent commercial demand…
Particularly telling of the desperation and difficulty in developing effective IBS therapies is the low FDA efficacy hurdle used to evaluate IBS drugs and the less than compelling clinical trial data used to (successfully) support FDA approval. Minimal effectiveness and drawbacks of IBS drugs has created what we believe is a relatively low "attractiveness hurdle" and, coupled with a lack of side effects and expected cost-benefit, one that may be easily cleared if InFoods is able to demonstrate only incremental benefit (either alone or to existing therapies).

And in terms of the potential commercial appeal for InFoods, the dearth of sufficiently effective IBS therapies, high related healthcare costs and overall frustration from physicians and patients as a result of lack of better options means high demand already exists for more effective IBS therapies. Couple that with payers' pushback to reimburse for (relatively expensive) Rx IBS drugs until other (less expensive) options have been tried, and we think appeal to the critical "3Ps" (i.e. patient, physician and payer) in the healthcare treatment chain will be sufficiently satisfied to drive meaningful demand shortly following launch.

InFoods Modeling Assumptions

Market opportunity: IBS is often very difficult to diagnose and symptoms can differ individual-to-individual. This heterogeneity means that the market opportunity for IBS-indicated therapies can also extend to other conditions including symptom-similar diseases (particularly inflammatory bowel diseases) such as Crohn's, chronic idiopathic constipation (CIC), ulcerative colitis and celiac disease. Our ancillary market size estimates exclude patients comorbid with IBS (i.e. these represent incremental populations). The following is our estimates of the total U.S. market opportunity for InFoods

Total U.S. market opportunity: 58M people

- U.S. IBS total market size: 45M people (18M mild, 16M moderate, 11M severe)
  - IBS-M: 13.5M
  - IBS-C: 13.5M
  - IBS-D: 18M
- U.S. ancillary conditions market size: 13M people
  - Crohn's: 4M
  - CIC: 2M
  - Ulcerative colitis: 4M
  - Celiac disease: 3M

Initial "reachable" market: while we calculate the total U.S. market for InFoods at approximately 58M people, the initial "reachable" market is likely only a fraction of that as most people with IBS do not visit their doctor for it. According to the International Foundation for Functional Gastrointestinal Disorders, there are only about 3.5M physician visits each year for IBS – which we use as the initial reachable IBS market. For the ancillary markets, we assume the initial reachable market is 30% of the total, or (13M x .30) = 3.8M. However, we also assume that

if InFoods can demonstrate incremental efficacy that it will encourage a significantly greater number of people to visit their doctors. We estimate that can increase the size of the reachable market by 15% per year for at least the first five years.

(We also, note that given BMRA's possible intent to expand InFoods' utility beyond strictly IBS and potentially into other conditions including Functional Dyspepsia, Crohn's Disease, Ulcerative Colitis and Gastroesophageal reflux disease (GERD) (among potential others), that that could warrant similar expansion of what we characterize as InFoods' reachable target populations. Our assumptions in this regard will be updated if and when we believe warranted which will hinge on progress of BMRA's efforts in expanding the indicated target markets for their food-elimination diet diagnostic.)

Frequency of InFoods Testing Per Patient: BMRA expects InFoods will be most effective when patients return to be re-tested 2 to 3 times per year which allows for optimizing efficacy through diet re-adjustments. We assume an average of 2.5 visits per patient per year.

Pricing / Margin: we should have a better idea of pricing expectations with more information relative to expected reimbursement. We believe cost (i.e. COGS) of the test and related processing will be relatively inexpensive, particularly with volume, as the technology is largely commoditized and widely available. We currently assume per-test pricing of $150 and COGS (i.e. material expense and processing) of $30 and gross profit $70.

Commercialization Partner: based on our discussions and certain feedback, we think it is likely that BMRA will look to out-license U.S. commercialization, similar to what they did with Telcon in S. Korea. We think out-licensing is also a safer move from a financial standpoint. We hope to know more about potential commercialization plans over time but, until then, we assume a royalty rate of 15% for the U.S. market (i.e. same rate as Telcon deal).

Market Penetration: given the drawbacks of IBS drugs and pent-up demand for more effective alternatives, we think that if InFoods demonstrates significant incremental clinical benefit at what we expect to be a relatively low cost, it has the potential to see fairly rapid widespread adoption. Additionally, no drugs are indicated to treat IBS-M (~30% of all IBS cases) – which means InFoods uptake among these patients could be particularly robust. We think that InFoods has the potential to capture 10% of the reachable market within the 3rd full-year following launch in the U.S. and 15% by year-5.

Timelines: BMRA is ballparking 9 – 14 months for the (n=180) initial "endpoint-finding" study. While we do not know what to expect in terms of the size or duration of a pivotal InFoods study, our best-guess right now (using pivotal IBS drug trials as a proxy) is somewhere in the range of 300 – 400 patients per arm and 24 months from start to completion (including time for design and any FDA interaction). Assuming another 3 – 6 months for FDA filing and regulatory clearance, results in estimated InFoods U.S. launch around calendar early-2022 (i.e. mid-to-late fiscal 2022).

Risk of Unknowns: we are incorporating what could arguably be considered a conservative haircut of 70% to our revenue estimates to account for what remains a fairly sizeable number of significant unknowns. This haircut will be adjusted based on solidifying answers to these unknowns such as, for example, further substantive progress towards validation (from both a regulatory and commercial perspective) of InFoods, reimbursement, market opportunity, intellectual property protection, timelines and U.S. commercialization strategy among others.

United States Only Model

	Years on market				
	1	2	3	4	5
Assumed physician visits for (in 000s)					
IBS (C,D and M)	3,500	4,025	4,629	5,323	6,122
Ancillary conditions	3,810	4,382	5,039	5,795	6,664
Assumed penetration	0.25%	1.50%	7.00%	12.00%	15.00%
Assumed InFoods tests/patient/yr	2.5	2.5	2.5	2.5	2.5
Assumed revenue/test to distribution prtnr	$100.0	$105.0	$110.3	$115.8	$121.6
Royalty rate	15%	15%	15%	15%	15%
Partner/Distributor revenue ($000s)	**$ 685.3**	**$ 4,965.1**	**$ 27,978.3**	**$ 57,915.0**	**$ 87,415.5**
Unknowns haircut	70%	70%	70%	70%	70%
InFoods Revenue to BMRA ($000s)	**$ 205.59**	**$ 1,489.53**	**$ 8,393.48**	**$ 17,374.51**	**$ 26,224.65**

Value BMRA at $3.00/share (base business) + $4.00/share (InFoods) = $7.00/share
We use sum of the parts to value BMRA; the base business (everything except InFoods) plus InFoods. We note that we are only modeling assumed U.S. InFoods sales and we do not yet model the novel h. pylori test that recently commenced clinical studies. All of our modeling and valuation-related assumptions will be updated if and when appropriate.

We continue to value the base business using a comparable cohort of five companies of various market capitalizations in the medical diagnostics space with products/services that target the POC and/or clinical lab markets to value BMRA. Based on several metrics, BMRA's base business is valued at approximately $2.60/share.

Comparable Multiples

Ticker	P/E (ttm)	P/E (FY1)	P/E (FY4)	P/Book	EV / EBITDA (ttm)	P/S (ttm)	P/S (FY1)
VIVO	20.9	17.9	8.7	3.0	9.7	2.5	2.6
OXFD	3.5	-	26.7	2.0	-	7.0	6.0
CEMI	-	-	-	3.7	-	3.6	3.2
QDEL	32.0	18.6	37.6	5.5	15.1	4.5	4.4
Average	18.8	25.0	24.3	3.5	12.4	4.4	4.1

FY1, FY4 = forecast year 1, forecast year 4

Value Based On Comp:

	P/E (ttm)	P/E (FY1)	P/E (FY4)	P/Book	P/S (ttm)	P/S (FY1)	AVG
BMRA	N/A	N/A	N/A	$1.67	$2.72	$3.23	$2.54

Value InFoods at ~$40M (~$4.00/share):
We value InFoods separately from that of the base business given the former's significantly greater growth potential. As we outlined above, we think our InFoods assumptions and related outlook/forecast are reasonable. Given the rapid growth rate and steepening revenue inflection that we estimate at approximately years 2023/2024 we think a 11x sales multiple is reasonable, particularly when looking at the ~12x trailing sales multiple Valeant paid for Salix (i.e. Xifaxin) in 2015. Applying 11x to our $8.4M 2024 forecasted InFoods revenue and discounting back to the present at 14%/year, results in InFoods present value of approximately $40M, or $4.00/share. If and when there is attrition of some of the substantive unknowns, our risk discount will similarly reduce and likely result in higher calculated InFoods value.

Our sum of the parts values BMRA at approximately $7.00/share.

APPENDIX:

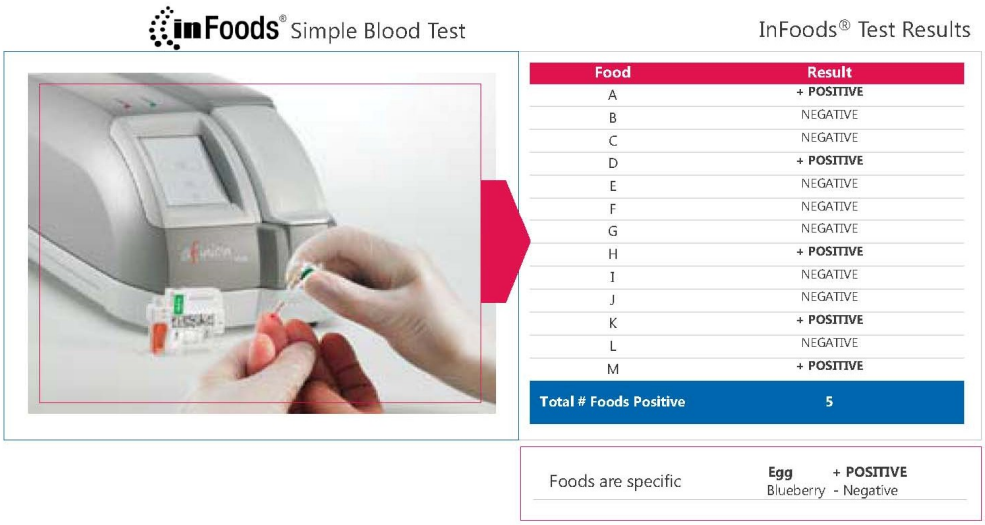
InFoods Explained

Important to understand about IBS and why we believe InFoods has so much potential is that while food is implicated as a trigger in exacerbating symptoms, the same foods do not affect every IBS sufferer the same (i.e. different people may have different trigger foods). So it is not as simple as just identifying certain foods and eliminating those from anyone's diet that has the condition. As such, the heterogenous nature of IBS requires a diagnostic (i.e. InFoods) that accounts for varying and different causation between certain foods and an individuals' symptoms, or lack thereof.

Additional details about InFoods have been made public recently – this includes information gleaned from BMRA's patent applications as well as from the company's recent investor presentations.
Below we summarize what we believe are some of the most salient points regarding InFoods;

- blood test to identify certain trigger foods that may cause or exacerbate IBS symptoms
  - will be used only with individuals already identified with IBS symptoms
  - extensive analysis was done to rank the top several dozen foods most associated with exacerbating IBS
  - we expect somewhere in the range of 20 – 25 foods may be included on the initial panel
  - ELISA test quantifies food-specific IgG antibodies (i.e. 'signal scores') from individual IBS patients which are elicited as immune response
  - signal score 'cutpoints' for each food (and gender) were determined by comparing signal scores of IBS patients with those of non-IBS patients. Additional testing and analysis was done to refine these cutpoints, which represent the 90th and 95th percentiles. For each food, IBS subjects with resulting signal scores above these cutpoints are considered 'positive' for that particular food (i.e. that particular food exacerbates IBS)
  - results of the ELISA test provide a simple 'yes' or 'no' result indicating whether a particular person's IBS symptoms are being triggered by each of the foods on the panel
- InFoods is expected to help physicians in guiding treatment protocol including putting the patient on a specific dietary regimen and can be used in combination with IBS drugs. This is different than other IBS tests which only focus on diagnosing presence of the disease. BMRA's test would be the first to both help diagnose IBS and to help guide treatment decisions
- expected to have utility for all forms of IBS (i.e. constipation (C), diarrhea (D) and mixed (M))
- test will be available for use in both the clinical lab and physician office settings. Lab product is the first which they will pursue (regulatory hurdle is likely lower) and POC will follow
- would be reimbursed under existing CPT codes. As reimbursement is critical for maximizing early adoption, availability of payment under existing CPT codes is a significant benefit
- in addition to the significant benefit of already established CPT coding is that it could be expected that patients would be tested more than once (i.e. 2 - 3x) over the course of a year, depending on changes in their diets
- 17 patents are currently pending. In March 2016 BMRA announced International Search Authority reviewed their international method and composition patent claims and found them to be novel and non-obvious (i.e. the claims are valid)
- FDA has indicated that the risk profile of the test would likely not require a Class III (i.e. 'high risk') device designation. This was further supported when in July 2016 BMRA announced that FDA determined InFoods is eligible to pursue 'nonsignificant risk' clinical studies. BMRA expects to apply for the de novo route which allows manufacturers of novel low-risk (Class I and II) products for which there is no predicate to avoid the much costlier and time-consuming PMA route

InFoods® Physician's Office (Point of Care) Use
(Clinical Lab Version first to be submitted)



Market considerations related to InFoods: *Living with IBS is hell…*

- "Living with IBS is hell" – plug that into a Google search and it is apparent that the chronic disease symptoms and lack of treatment options leaves IBS sufferers feeling helpless and desperate for more effective options
- Diagnostic cost of IBS in the U.S. is approximately $10.5B in annual direct costs and over $30B when including indirect costs
- IBS afflicts as much as 20% of the U.S. population, 25% of Japan, and 22%+ each of China and the U.K
- IBS is a top 10 reason for primary care doctor visits
- IBS is difficult to diagnose and difficult to treat
  - Exact cause of IBS is not known although adverse reaction to certain foods is largely accepted as a significant contributor in many cases
  - Types of foods and food reactions do not appear to be homogenous from patient-to-patient (i.e. cocoa may trigger symptoms in one patient but not another). Therefore it is important to be able to identify which foods trigger symptoms in each individual patient
  - IBS drugs, such as Xifaxan, Linzess, Amitiza, Viberzi and Lotronex (see our discussion below) only treat the symptoms but not the underlying cause, are effective in only about 15% - 20% of IBS sufferers, often provide only temporary and partial relief (in those patients who do show a response) and can have unwelcome side effects
  - While new IBS drugs are in development, including at least one (Trulance) that could gain FDA approval and launch in the coming months, these also only address IBS symptoms and not the underlying cause
  - FDA has a low effectiveness hurdle related to approving IBS drugs – which also speaks to the lack of effective treatments for the disease
  - GI doctors also often prescribe SSRI's off-label, which have shown to help regulate bowel flow – this again, illustrates how limited the treatment options are for IBS
  - Physicians have very limited tools to treat IBS – typical recommendation is for patients to (arbitrarily) begin eliminating certain foods from their diet and/or prescription of symptom-targeting drugs which often fail to provide significant relief, particularly over the long-term
- Win, win, win for patients, physicians and insurers. InFoods could benefit all major stakeholders. Physicians are frustrated with lack of treatment options. Patients feel helpless. Insurers are paying for relatively high cost drugs which do not address the underlying cause and therefore may be chronically prescribed
- Unlike many new medical technologies (drugs, devices and diagnostics) which offer only incremental benefit compared to an existing product and may be geared more towards profit than clinical outcome (and often require a lot of marketing to convince of the 'benefits'), InFoods could be a pioneer in providing a new level of relief for

the IBS afflicted. And if InFoods can do that, it should require limited initial awareness-building before the test sells itself via demand-pull from physicians and patients

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Unmet Need Highlighted By IBS Drugs' Low Effectiveness, Low FDA Approval Hurdle

The U.S. market for IBS drugs is approximately $1B+, almost twice the size of what it was only just a few years ago. The market is likely to continue to grow at a rapid pace, largely driven by new drugs that have either recently come to market or that are expected to do so in the near-term. But while the number of drugs available to treat IBS and related expenditures continues to grow, their relative ineffectiveness in providing relief has not significantly changed.

Today, the prescription IBS drug market is mostly concentrated across four products; Linzess (Allergan) and Amitiza (Takeda) for IBS-C, and Xifaxan (Valeant) and Viberzi (Allergan) for IBS-D. No drug is approved in the U.S. for the treatment of IBS-M. All of these gained FDA approval for their respective IBS indications since 2012 and two, Xifaxan and Viberzi, were approved for the U.S. market in May 2015 and launched later that year.

Low FDA Approval Hurdle…

FDA has clearly recognized the seeming futility drugmakers have experienced in their quest to develop a therapy that provides significant and long-term relief of IBS. This is evidenced by the low bar the U.S. regulatory agency has recommended in terms of efficacy endpoints that novel drugs are assessed against in order to determine whether they will be approved for sale. We note that while FDA updated their recommendations for evaluation of novel IBS drugs in 2012 to better assess their effectiveness in addressing symptoms of IBS, the effectiveness hurdle (i.e. improvement vs. placebo) remains low.

The table below describes the pre-updated primary endpoints that have been used in many IBS drug trials. FDA updated their guidelines as they felt that while the prior endpoints could capture the direction of change, they did a poor job of providing useful information of the effect of treatment on sign and symptoms of IBS.

Prior IBS Endpoint Guidelines

Drug and Indication	Primary Endpoint	Questions (Single-Item) Used to Assess Efficacy	Responses
Alosetron — IBS-D[1]	Adequate relief	*In the past 7 days, have you had adequate relief of your IBS pain or discomfort?*	Binary (Yes/No)
Tegaserod — IBS-C[2]	Satisfactory relief	*Did you have satisfactory relief of your overall IBS symptoms during the last week?*	Binary (Yes/No)
		Did you have satisfactory relief of your abdominal discomfort or pain during the last week?	Binary (Yes/No)
	Subject Global Assessment of Relief (SGA)	*Please consider how you felt during the past treatment period in regard to your IBS, in particular your overall well-being, and symptoms of abdominal pain/discomfort and altered bowel habit. Compared to the way you usually felt before entering the trial, how would you rate your relief of symptoms during the past week?*	5-Point Likert scale
Lubiprostone — IBS-C[3]	Modified version of the SGA	*How would you rate your relief of IBS symptoms (abdominal discomfort/pain, bowel habits, and other IBS symptoms) over the past week compared with how you felt before you entered the trial?*	7-Point Likert scale

SOURCE: US Dept HHS, FDA, CDER. IBS – Clinical Eval of Drugs. May 2012

The updated recommended guidelines are more defined in terms of assessment of the effect on symptoms and specifically cites a defecation component and an abdominal pain component. For IBS-C drugs, recommendation is that defecation is assessed by stool frequency (number of complete bowel movements per week) while IBS-D drugs

be assessed by stool consistency (based on Bristol Stool Form Scale). The pain component, for both IBS-C and IBS-D, can be based on an 11-point numeric scale.

The table below describes the updated (i.e. 2012) recommended guidelines for primary endpoints of IBS-C and IBS-D investigational drugs. Here we can see that the definition of treatment 'response' in these updated guidelines is more directly tied to IBS symptoms (as compared to prior guidelines). But also, the 'response' thresholds are arguably meek (and, in the case of the pain measure, potentially still fraught with subjectivity).

Note that 'response' related to abdominal pain is a decrease of 30% or more (in weekly average worst pain) in the past 24 hours. Weekly stool consistency 'response' is reduction of 50% or more days per week with mushy or watery stools. These endpoints are far from complete reprieve of IBS symptoms and, we think, underscores not only the difficulty in effectively addressing the disease but also, when we look at the substantial revenue generated by and number of prescriptions written for these drugs, how desperate IBS sufferers are for something that will provide even minor and temporary relief.

Current IBS Endpoint Guidelines

Indication	Primary Endpoints	Entry Criteria	Responder Definition
IBS-C	Abdominal Pain Intensity AND Stool Frequency	**Abdominal Pain Intensity** Weekly average of *worst abdominal pain in past 24 hours* score of ≥ 3.0 on a 0 to 10 point scale AND **Stool Frequency** < 3 CSBMs per week	**Abdominal Pain Intensity** Decrease in weekly average of *worst abdominal pain in the past 24 hours* score of at least 30% compared with baseline AND **Stool Frequency** Increase of 1 or more CSBM per week compared with baseline
IBS-D	Abdominal Pain Intensity AND Stool Consistency	**Abdominal Pain Intensity** Weekly average of *worst abdominal pain in past 24 hours* score of ≥ 3.0 on a 0 to 10 point scale AND **Stool Consistency** At least 2 days per week with at least one stool that has a consistency of Type 6 or Type 7 BSS (see Figure 1 for details)	**Abdominal Pain Intensity** Weekly responder defined as: decrease in weekly average of *worst abdominal pain in past 24 hours* score of at least 30% compared with baseline Daily responder defined as: decrease in *worst abdominal pain in the past 24 hours* score of at least 30% compared with baseline AND **Stool Consistency** Weekly responder defined as: decrease at least 50% in the number of days per week with at least one stool that has a consistency of Type 6 or 7 compared with baseline Daily responder defined as: a patient whose stool consistency is less than 5 for all bowel movements on that day or no bowel movement

SOURCE: US Dept HHS, FDA, CDER: IBS– Clinical Eval of Drugs. May 2012

Unmet Need For Relief Drives Demand For Drugs, Despite Being Barely Better Than Placebo…

IBS sufferers' high unmet need for any symptom relief becomes even more obvious when examining primary endpoint outcomes data from the pivotal FDA studies of each of the four prescription drugs that account for 90%+ of the U.S. IBS drug market. In the table below we have summarized efficacy data of the phase III studies used to support FDA approval filings for each of the leading IBS drugs (see Appendix for more details about each compound and the phase III studies). Also included is Trulance, for which an FDA filing for IBS-C is expected to happen in the near term.

Our table also includes estimated current annualized U.S. sales and total prescriptions as well as our comments, all meant to help elucidate the significant demand for IBS drugs despite their relative lack of effectiveness and in many cases, highly unpleasant and even dangerous side effects.

Points of particular interest:

- **Majority of patients did not respond**: response rates ranged from a low of approximately 12% up to 41%

- **Barely more effective than placebo**: response rates as compared to placebo indicate a substantial placebo effect in treatment "response". While subjectivity of endpoint measures (particularly with 'legacy' measures) may play a part (our supposition), the data suggests that none of these drugs are much more effective than placebo. As an example, Linzess, which currently generates ~$600M in annual U.S. revenue and for which ~2.8M prescriptions are written each year, demonstrated only 7% - 13% superiority on primary efficacy endpoints compared to placebo
- **Drawbacks**: besides cost and relatively low efficacy there are other drawbacks to IBS drugs. This includes side effects which are often unpleasant - such as diarrhea, and which can even be dangerous – Lotronex carries a black box warning related to the risk of potentially serious GI events while Viberzi may cause pancreatitis in people w/o a gallbladder. Some drugs, such as Xifaxan, are not recommended for chronic use while others, such as Amitiza and Lotronex, are only indicated for women due to lack of data for use with men

Indication	Drug	FDA Appr	Treatment Response	Delta vs placebo	Cost*	Annualized U.S Sales (M)	Annualized U.S TRx (M)	Comments
IBS-C	Linzess	2012	12% - 34%	7% - 13%	$382	$630**	2.90**	Diarrhea side effect (20%)
	Amitiza	2008	13%	6%	$380	$450**	1.50**	Indicated for women only as not studied for men
	Trulance	NA	22% - 30%	7% - 12%	NA	NA	NA	Not yet FDA approved
IBS-D	Xifaxan	2015	41%	9%	$550	$950***	1.00***	Not for chronic use
	Viberzi	2015	25% - 30%	7% - 14%	$1,000	$125	0.15	Abdominal pain (secondary) endpoint not met
	Lotronex	2002	NA	13% - 20%	$940	$60	0.04	For women only. Black box warning

*Cost - per Drugs.com. Based on retail price of 30-day supply of lowest dose **Includes CIC and IBS-C
***Includes overt HE and IBS-D

The Low "Attractiveness Hurdle" Should Play In InFoods' Favor…
While there is not yet enough publicly available information relative to the performance of InFoods to make any informed opinions regarding its clinical effectiveness, the current lack of effective therapies and debilitating symptoms of the disease means that doctors and patients are likely to be receptive to just about anything that has the potential to provide even incremental benefit (whether it be incremental to existing therapies or alone).

We believe that the minimal effectiveness and drawbacks of prescription drugs means that the "attractiveness hurdle" that novel IBS therapies must meet to generate interest from the ~$1B+ U.S. IBS market is relatively low. That should be particularly true for non-drug, side-effect-free products such as InFoods.

And with InFoods testing expected to be covered with existing CPT codes, coupled with the likelihood of a substantial cost-benefit as compared to IBS drugs, we think the market could be very receptive to the product. We look forward to updates from the company on expected clinical trial design and other details related to validating effectiveness and clinical utility of the test.

IBS Drugs Overview

Xifaxan (Salix/Valeant):

- Xifaxan (rifaximin) is a semisynthetic antibiotic initially approved by FDA (May 2004) for the treatment of traveler's diarrhea caused by E. coli (200mg), in March 2010 it (550mg) received FDA approval for overt hepatic encephalopathy and in May 2015 it (550mg) received FDA approval for the treatment of IBS-D in adults.
- Recommended dosing is one tablet, 3x/per day for 14 days. Recurrence can be retreated twice at the same dosing regimen
- Method of action is not completely understood, but hypothesized to relate to changes in the bacterial content in the GI tract
- Most commonly reported side effects are nausea (~3%) and increase in ALT (liver enzyme in the blood, 2%)

- Clinical data used to support FDA filing consisted of three double-blind, placebo-controlled phase 3 trials (TARGET 1,2,3).
    - **Trials 1 and 2**: enrolled 1,258 patients diagnosed (per Rome II criteria) with IBS symptoms of abdominal pain and discomfort. Patients were randomized to Xifaxan (n=624) or placebo (n=634) for 14 days and followed for a subsequent 10-week treatment-free period.
    - **Primary endpoint** was proportion of patients who achieved adequate relief (based on patients' 'yes' or 'no' response) of IBS symptoms for at least 2 of 4 weeks during the month following 14 days of treatment. Key **secondary endpoint** was proportion of patients who achieved relief of bloating during the same primary evaluation period.
    - **Results:**
        - **Primary endpoint** of the combined studies: Significantly (p<0.001) more Xifaxan patients (41%) than placebo patients (32%) reported adequate relief of IBS symptoms. Relief from IBS symptoms maintained statistically significant through the entire 3-month study period (p<0.001).
        - **Results on the key secondary endpoint** were similar to that of the primary endpoint with significantly (p<0.001) more Xifaxan patients (40%) than placebo patients (30%) reporting adequate relief of IBS-related bloating.
    - **Trial 3** was powered to assess effectiveness of Xifaxan in cases of recurrence. 636 patients who did not meet a composite endpoint in TARGET 1,2 of relief of abdominal pain and loose stools were randomized in TARGET 3 for retreatment and received Xifaxan (n=328) or placebo (n=308) for another 14 days, followed by a 4 week treatment-free period. **Results** showed that significantly (p=0.02) more Xifaxan (33%) patients achieved symptom relief as compared to placebo patients (25%)

	Proportion of Patients with Response					
Primary endpoint	**Xifaxan**	**%**	**Placebo**	**%**	**Difference**	**P-value**
Weekly global IBS symptoms						
Target 1	126/309	40.8%	98/314	31.2%	9.6%	0.01
Target 2	128/315	40.6%	103/320	32.2%	8.4%	0.03
Combined	254/624	40.7%	201/634	31.7%	9.0%	< 0.001
Key secondary endpoint	**Xifaxan**	**%**	**Placebo**	**%**	**Difference**	**P-value**
Weekly IBS-related bloating						
Target 1	122/309	39.5%	90/314	28.7%	10.8%	0.005
Target 2	129/315	41.0%	102/320	31.9%	9.1%	0.02
Combined	251/624	40.2%	192/634	30.3%	9.9%	< 0.001

Viberzi (Allergan):

- Viberzi (eluxadoline) received FDA approval May 2015 for the treatment of IBS-D in adults. Launched in U.S. December 2015
- Eluxadoline targets opioid receptors (it is a μ- and κ-opioid receptor agonist and δ-opioid receptor antagonist) in the portion of the nervous system that govern the GI tract, thereby reducing bowel contractions and related pain.
- Recommended dosing is one tablet, 2x/day and can be taken as long as doctor recommends
- Most commonly reported side effects are constipation, nausea and abdominal pain
- In March 2017 FDA issued a warning against its use with that patients w/o gallbladder as it could cause serious pancreatitis
- Clinical data used to support FDA filing consisted of two Phase 3 double-blind, placebo controlled studies
    - Combined studies enrolled 2,425 patients (study 1 = 1,280, study 2 = 1,145) diagnosed with IBS-D (Rome III criteria) randomized to either 75mg or 100mg Viberzi (n=1,616) twice daily or placebo (n=809)
    - Patients treated over 26 weeks
    - Primary endpoint was simultaneous improvement in worst abdominal pain score by ≥ 30% as compared to baseline and improvement in stool consistency (based on Bristol Stool Scale) on at least 50% of the days within a 12-week time interval (for FDA) and through 26 weeks (for EMA)

- Secondary endpoints included improvement in the defined pain score at 12 weeks and improvement in the defined stool consistency score at 12 weeks
- **Results**:
  - 12 weeks on composite (primary FDA) endpoint (pain and stool):
    - Study 1: 24% (75mg) to 25% (100mg) of Viberzi patients vs. 17% of placebo patients met composite endpoint, indicating statistically significant improvement favoring treatment arm of 7% - 8% ($p < 0.05$)
    - Study 2: 29% to 30% of Viberzi patients vs. 16% of placebo patients met composite endpoint, indicating statistically significant improvement favoring treatment arm of 13% - 14% ($p < 0.001$)
  - 26 weeks on composite (primary EMA) endpoint (pain and stool):
    - Study 1: 23% to 29% of Viberzi patients vs. 19% of placebo patients met composite endpoint. The 10% difference to the 100mg arm was statistically significant ($p \leq 0.014$) while the 4% difference to the 75mg arm was not
    - Study 2: 30% to 33% of Viberzi patients vs. 20% of placebo patients met composite endpoint. The 13% - 14% difference was statistically significant ($p \leq 0.014$)
  - 12 weeks on abdominal pain (secondary) endpoint:
    - Study 1: 42% to 43% of Viberzi patients vs. 40% of placebo patients reported reduction in abdominal pain. The 2% - 3% difference was not statistically significant
    - Study 2: 48% to 51% of Viberzi patients vs. 45% of placebo patients reported reduction in abdominal pain. The 3% - 6% difference was not statistically significant
  - 12 weeks on stool consistency (secondary) endpoint:
    - Study 1: 30% to 34% of Viberzi patients vs. 22% of placebo patients reported improvement in stool consistency. The 8% - 12% difference was statistically significant
    - Study 2: 36% to 37% of Viberzi patients vs. 21% of placebo patients reported improvement in stool consistency. The 15% - 16% difference was statistically significant
  - **Rescue loperamide: % of patients requiring rescue loperamide during 26-week treatment phase**
    - Study 1: 25% of Viberzi vs. 28% of placebo
    - Study 2: 29% of Viberzi vs. 35% of placebo

	Study 1			Study 2		
	VIBERZI 100mg twice daily n=426	VIBERZI 75mg twice daily n=427	PBO n=427	VIBERZI 100mg twice daily n=382	VIBERZI 75mg twice daily n=381	PBO n=382
Composite[1] Response over 12 weeks						
Responder rates	25%	24%	17%	30%	29%	16%
Treatment difference	8%[2]	7%[4]		13%[3]	13%[3]	
95% CI (%)	(2.6, 13.5)	(1.4, 12.2)		(7.5, 19.2)	(6.8, 18.5)	
Composite Response over 26 weeks						
Responder rates	29%	23%	19%	33%	30%	20%
Treatment difference	10%	4%		13%	10%	
95% CI (%)	(4.7, 16.1)	(-1.0, 9.9)		(6.4, 18.8)	(4.2, 16.4)	
Abdominal Pain Response Improved ≥30% over 12 weeks						
Responder rates	43%	42%	40%	51%	48%	45%
Treatment difference	4%	3%		6%	3%	
95% CI (%)	(-3.0, 10.2)	(-3.8, 9.4)		(-1.3, 12.8)	(-4.3, 9.8)	
BSS <5 Response over 12 weeks						
Responder rates	34%	30%	22%	36%	37%	21%
Treatment difference	12%	8%		15%	16%	
95% CI (%)	(6.3, 18.2)	(2.1, 13.8)		(8.4, 21.0)	(9.7, 22.4)	

[1]Composite= Simultaneous improvement of Worst Abdominal Pain (WAP) by ≥30% and Bristol Stool Score (BSS) < 5 on the same day for ≥ 50% of days over the interval
[2] $P<0.01$
[3] $P<0.001$
[4] $P<0.05$

SOURCE: Viberzi label, Actavis. Accessdata.fda.gov

Linzess (Allergan):

- Linzess (linaclotide) is a peptide agonist of guanylate cyclase 2C (GC-C) approved by FDA in 2012 for the treatment of adults with IBS-C as well as for the treatment of chronic idiopathic constipation (CIC)
- Recommended dosing is one tablet daily
- Most commonly reported side effects are diarrhea (20%), abdominal pain (7%) and flatulence
- Method of action: linaclotide stimulates secretion of intestinal fluid resulting in acceleration of GI transit and reduction on abdominal pain
- Clinical data used to support FDA approval for IVS-C consisted of two double-blind, randomized, placebo-controlled phase 3 studies
    - Combined studies enrolled 1,604 patients (study 1 = 800, study 2 = 804) diagnosed with IBS-C (Rome II criteria) randomized to either Linzess (n=806) or placebo (n=798)
    - Patients treated for 12 weeks
    - Primary endpoint: there were four primary endpoints:
        - In at least 9 of the first 12 weeks of treatment patient had to have;
            - Combined responder endpoint (9 of 12 weeks): ≥ 30% reduction from baseline in abdominal pain, ≥ 3 complete spontaneous bowel movements (CSBM) and an increase of ≥ 1 CSBM from baseline, all in the same week
            - ≥ 30% reduction from baseline in abdominal pain
            - ≥ 3 complete spontaneous bowel movements (CSBM) and an increase of ≥ 1 CSBM from baseline in the same week
        - Combined responder endpoint (6 of 12 weeks): In at least 6 of the first 12 weeks of treatment patient had to have ≥ 30% reduction from baseline in abdominal pain and an increase of ≥ 1 CSBM from baseline, all in the same week
    - **Results:**
        - Combined responder 9 of 12 weeks:
            - Study 1: 12% of Linzess vs. 5% of placebo met endpoint

        - Study 2: 13% of Linzess vs. 3% of placebo met endpoint
    - Abdominal pain 9 of 12 weeks:
        - Study 1: 34% of Linzess vs. 27% of placebo met endpoint
        - Study 2: 39% of Linzess vs. 20% of placebo met endpoint
    - CSBM 9 of 12 weeks:
        - Study 1: 20% of Linzess vs. 6% of placebo met endpoint
        - Study 2: 18% of Linzess vs. 5% of placebo met endpoint
    - Combined responder 6 of 12 weeks:
        - Study 1: 34% of Linzess vs. 21% of placebo met endpoint
        - Study 2: 34% of Linzess vs. 14% of placebo met endpoint
    - Differences between treatment and placebo arms on all endpoints were statistically significant

At least 9 of first 12 weeks

	Trial 1			Trial 2		
	LINZESS 290 mcg (N=405)	Placebo (N=395)	Treatment Difference [95% CI]	LINZESS 290 mcg (N=401)	Placebo (N=403)	Treatment Difference [95% CI]
Combined Responder* (Abdominal Pain and CSBM Responder)	12.1%	5.1%	7.0% [3.2%, 10.9%]	12.7%	3.0%	9.7% [6.1%, 13.4%]
Abdominal Pain Responder* (≥ 30% Abdominal Pain Reduction)	34.3%	27.1%	7.2% [0.9%, 13.6%]	38.9%	19.6%	19.3% [13.2%, 25.4%]
CSBM Responder* (≥ 3 CSBMs and Increase ≥1 CSBM from Baseline)	19.5%	6.3%	13.2% [8.6%, 17.7%]	18.0%	5.0%	13.0% [8.7%, 17.3%]

At least 6 of first 12 weeks

	Trial 1			Trial 2		
	LINZESS 290 mcg (N=405)	Placebo (N=395)	Treatment Difference [95% CI]	LINZESS 290 mcg (N=401)	Placebo (N=403)	Treatment Difference [95% CI]
Combined Responder* (Abdominal Pain and CSBM Responder)	33.6%	21.0%	12.6% [6.5%, 18.7%]	33.7%	13.9%	19.8% [14.0%, 25.5%]

* Primary Endpoint, ** Secondary Endpoints
Note: Analyses based on first 12 weeks of treatment for both Trials 1 and 2
CI =Confidence Interval

SOURCE: Linzess label. Allergan

Amitiza (Takeda):

- Amitiza (lubiprostone) received initial FDA approval in 2006 for the treatment of chronic idiopathic constipation in adults and in 2008 received FDA approval for the treatment of women with IBS-C
- Amitiza is a bicyclic fatty acid that acts on GI epithelial cells to promote secretions which helps to soften the stool and increase motility
- Recommended dosing for IBS-C is orally, twice daily
- Most common side effects are nausea (8%), diarrhea (7%) and abdominal pain (5%)
- Clinical data used to support FDA approval for IBS-C consisted of two double-blind, placebo-controlled phase 3 studies (Note: FDA guidelines for evaluating novel IBS drugs changed in 2012; i.e. after Amitiza rec'd FDA approval)
    - Combined studies enrolled 1,154 patients (92% of which were female) with IBS-C and received Amitiza 2x/day or placebo for 12 weeks
    - Primary endpoint compared the proportion of "Overall responders" in each arm based on 7-point global relief questionnaire. "Monthly responder" was defined as reporting "significantly relieved" for at least 2 weeks of the month or at least "moderately relieved" in all four weeks of the month. "Overall responders" were those that were "monthly responders" for at least 2 of the 3 months of the study.
    - Results:
        - Study 1: 14% of Amitiza patients vs. 8% of placebo patients were "overall responders"
        - Study 2: 12% of Amitiza patients vs. 6% of placebo patients were "overall responders"
        - In both studies the difference between treatment and placebo was statistically significant

Lotronex (Prometheus):

- Lotronex (Alosetron) originally received FDA approval in February 2002 for the treatment of women with IBS-D but the manufacturer voluntarily removed it from the market later that year due to reports that use of it had been associated with life-threatening adverse effects including serious intestinal damage and severely obstructed bowels. In 2002 FDA approved an sNDA, allowing for restricted marketing of Lotronex only for women with severe diarrhea-predominant IBS. Less than 5% of IBS is considered severe. The revised labeling also includes a black box warning related to potentially serious GI adverse events
- Lotronex acts as an agonist to receptors of the GI-related nervous system, helping to increase water absorption and slow GI motility
- Recommended dosing is orally, twice per day for 12 weeks
- Most commonly reported side effects are constipation (29%), abdominal pain (7%) and nausea (6%)
- Clinical data: Lotronex has been studied in three clinical studies in women with severe diarrhea-predominant IBS, including two studies (i.e. studies 1,2) with patients with bowel urgency $\geq$ 50% of days and one study (i.e. study 3) with patients with 1 or more of the following: frequent and severe abdominal pain or discomfort, frequent bowel urgency or fecal incontinence, disability or restriction of daily activities due to IBS
    - **Results**;
        - Studies 1,2: Lotronex patients had 13% to 16% (statistically significant) greater increase compared to placebo patients in the median percentage of days with bowel urgency control. In addition, 50% of Lotronex patients had bowel urgency no more than 1 day in the last week compared to 29% of placebo patients. Also, 12% of Lotronex patients had bowel urgency no more than 2 days per week in any of the 12 treatment weeks compared to 1% of placebo patients
        - Study 3: Lotronex dosed at three different doses; 0.5mg/day, 1mg/day or 1mg 2x/day. All Lotronex groups had significantly greater number of responders (43% to 51%) versus placebo (31%) based on 7point GIS scale at 12 weeks

IN LATE-STAGE DEVELOPMENT

Trulance (Synergy):

- Trulance (plecanatide) received FDA approval for the treatment of adults with chronic idiopathic constipation in January 2017. It has also completed two phase 3 trials for the treatment of IBS-C, an indication for which Synergy filed for FDA approval (sNDA) of in March 2017. FDA approval and launch could happen in 1H 2018
- Similar to Linzess, Trulance is a GC-C agonist. It is a 16 amino acid peptide which acts to stimulate increased intestinal fluid and accelerate GI transit.
- Recommended dosing for IBS-C is orally once/day
- Clinical studies: Data from two (3mg and 6mg doses) phase 3 studies in IBS-C was announced in May 2017.
    - Combined studies enrolled 2,189 patients (study 1 = 1,135, study 2 = 1,054) with IBS-C who were randomized to Trulance (n = 1,456) or placebo (n = 733)
    - Patients treated once daily for 12 weeks
    - Primary endpoint is percentage of patients who are “overall responders”, defined as those patients that simultaneously experience $\geq$ 30% reduction in worst abdominal pain and increase of $\geq$ 1 CSBM from baseline, in the same week, for at least 50% of the 12 treatment weeks
    - **Top-line results**
        - Study 1 (n = 1,135): 21.5% of Trulance 3mg and 24.0% of Trulance 6mg patients vs. 14.2% of placebo patients met primary endpoint. The difference between placebo and both Trulance dose cohorts was statistically significant (p=0.009 for 3mg, p<0.001 for 6mg)
        - Study 2 (n = 1,054): 30.2% of Trulance 3mg and 29.5% of Trulance 6mg patients vs. 17.8% of placebo patients met primary endpoint. The difference between placebo and both Trulance dose cohorts was statistically significant (p<0.001) for 3mg, p<0.001 for 6mg)
        - Adverse events: the most common adverse events in the IBS-C phase 3 studies were diarrhea (~4%)

Scientific Advisory Board

Dr. Douglas Drossman
Dr. Drossman is a veteran of over 50 FDA clinical trials and is the current president of the Rome Foundation, a leading international organization that provides support and guidance in the diagnosis and treatment of functional gastrointestinal disorders. The Rome Foundation is responsible for creating the Rome process, and the criteria developed through this process are the most widely employed in clinical trials related to IBS.

Dr. Lin Chang
Director, Digestive Health and Nutrition Clinic UCLA GI Fellowship Training Program and Professor, Digestive Diseases/Gastroenterology. Dr. Chang has significant experience with pharmaceutical and healthcare companies as she has been an advisor or consultant to over 32 major pharmaceutical companies, including GlaxoSmithKline, Novartis, Merck, Allergan, Takeda, Salix, Synergy, Johnson & Johnson, Entera Health, and Ardelyx. Her experience with the FDA includes serving on the Gastrointestinal Drugs Advisory Committee of the FDA 2005-2010 (Chair 2009-2010) and again 2015-2019 as well as working as a FDA Special Government Employee from 2009-2013.

Dr. William Chey
Professor of Internal Medicine, Director of the GI Physiology Laboratory, and Director of Medical Services for the Michigan Bowel Control Program at the University of Michigan. Dr. Chey has also worked with many major pharmaceutical and healthcare companies as an advisor or consultant, including Entera Health, Ironwood, Nestle, Proctor and Gamble, Salix, and Takeda. He is the Chair of the U.S. Scientific Advisory Board at SmartPill Corporation and a member of the Clinical Advisory Board at Synthetic Biologics.

Dr. William Whitehead
Director of the Center for Functional GI & Motility Disorders and Professor of Medicine Adjunct Professor of OB-GYN at University of North Carolina School of Medicine. He has worked on 29 NIH grants (19 as principal investigator, 10 as co-investigator) and has been continuously funded by NIH since 1977. On behalf of the International Foundation for Functional Gastrointestinal Disorders, he organized two international consensus conferences on the treatment of fecal incontinence (1999 and 2002) and led a workshop on design of treatment trials for pharmaceutical companies, academic investigators, the NIDDK, and the FDA for 8 years. As a consultant, he has worked with large pharmaceutical companies on clinical trial design, including Takeda, Sucampo, Ironwood, Forest, Ono, and McNeil.

Dr. Anthony Lembo
Director of the GI Motility Laboratory at the Beth Israel Deaconess Medical Center's (BIDMC) Division of Gastroenterology in Boston, MA and as an Associate Professor of Medicine at Harvard Medical School. Dr. Lembo completed his residency and GI Fellowship at UCLA Medical Center. He is an accomplished expert in afflictions of the gastrointestinal tract and IBS. He divides his time between clinical medicine and research at Beth Israel Deaconess Medical Center in Boston. He has authored numerous original clinical studies and other research articles related to IBS.

Strategic Advisory Board

Ned Barnholt
Currently chairman of the KLA-Tencor Corporation and serves on the board of directors of eBay and Adobe. He is the former chairman, president, and chief executive officer of Agilent Technologies, a leading company in life sciences, diagnostics and applied chemical markets. Mr. Barnholt led the Agilent Technologies spin-off of Hewlett-Packard Company which broke records as the largest initial public offering (IPO) in Silicon Valley history at the time of the IPO (US $2.1 billion).

Harry Leider, MD
Until recently, Dr. Leider served as Chief Medical Officer (CMO) and Group Vice President of Walgreens. As the CMO at Walgreens, he provided executive leadership for health analytics, clinical program development, and clinical sales solutions. Dr. Leider also served as the senior clinical spokesperson for the company and routinely represented Walgreens with leaders in government, managed care, health systems, and other healthcare organizations. As Chief Medical Officer, he led a cross-functional department of over 40 professionals that conducted over 60 health outcomes studies that demonstrated the value of Walgreens programs and services. He also had leadership responsibility for a team that evaluated over 200 emerging healthcare technologies to provide information about potential M & A and partnership opportunities. Notably, Dr. Leider also directed the clinical design for a digital health programs that rewards 3 million Walgreens customers for taking steps to improve their health.

Prior to Walgreens, Dr. Leider was the Chief Medical Officer of Ameritox which was the nation's largest specialty lab serving clinicians who treat chronic pain and behavioral health conditions. He was responsible for the development of all provider support and research programs, and played a key role supporting sales efforts directed at providers and payors. Prior to his role at Ameritox, Dr. Leider held C-suite positions in several population health and payor companies.

FINANCIAL MODEL

Biomerica Inc.

	2018 A	Q1A	Q2A	Q3A	Q4E	2019 E	2020 E	2021 E	2022 E
InFoods TOTAL	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$205.6
YOY Growth	-	-	-	-	-	-	-	-	-
Legacy TOTAL	$5,564	$1,273	$1,501	$1,261	$1,201	$5,236	$6,084	$6,645	$6,897
YOY Growth	-3.9%	-11.8%	-7.0%	-8.4%	6.3%	-5.9%	16.2%	9.2%	3.8%
Total Revenues	$5,564.2	$1,272.9	$1,500.8	$1,261.2	$1,200.7	$5,235.7	$6,083.6	$6,644.7	$7,102.8
YOY Growth	-3.9%	-11.9%	-7.0%	-8.3%	6.2%	-5.9%	16.2%	9.2%	6.9%
Cost of Goods Sold	$3,809.8	$935.6	$1,092.7	$895.2	$833.3	$3,756.9	$3,990.9	$4,192.8	$4,332.7
Gross Income	$1,754.4	$337.2	$408.1	$365.9	$367.4	$1,478.8	$2,092.8	$2,451.9	$2,770.1
Gross Margin	31.5%	26.5%	27.2%	29.0%	30.6%	28.2%	34.4%	36.9%	39.0%
SG&A	$1,837.8	$400.2	$512.6	$576.1	$506.7	$1,995.6	$2,153.6	$2,265.8	$2,379.4
% SG&A	33.0%	31.4%	34.2%	45.7%	42.2%	38.1%	35.4%	34.1%	33.5%
R&D	$1,398.4	$391.8	$381.4	$497.1	$488.6	$1,758.9	$3,657.2	$2,944.0	$2,550.0
% R&D	25.1%	30.8%	25.4%	39.4%	40.7%	33.6%	60.1%	44.3%	35.9%
Operating Income	($1,481.8)	($454.8)	($485.9)	($707.2)	($627.9)	($2,275.7)	($3,718.0)	($2,757.9)	($2,159.3)
Operating Margin	-26.6%	-35.7%	-32.4%	-56.1%	-52.3%	-43.5%	-61.1%	-41.5%	-30.4%
Total Other Income (Expense)	$47.7	$3.0	$8.7	$28.5	$8.1	$48.3	$30.0	$25.0	$40.0
Pre-Tax Income	($1,434.0)	($451.7)	($477.2)	($678.7)	($619.8)	($2,227.3)	($3,688.0)	($2,732.9)	($2,119.3)
Tax expense (benefit)	$31.8	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Tax Rate	-2.2%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Net Income	($1,465.8)	($451.7)	($477.2)	($678.7)	($619.8)	($2,227.3)	($3,688.0)	($2,732.9)	($2,119.3)
YOY Growth	61.3%	91.1%	64.7%	53.4%	-3.3%	52.0%	65.6%	-25.9%	-22.5%
Net Margin	-26.3%	-35.5%	-31.8%	-53.8%	-51.6%	-42.5%	-60.6%	-41.1%	-29.8%
EPS	($0.17)	($0.05)	($0.05)	($0.07)	($0.07)	($0.24)	($0.38)	($0.28)	($0.22)
YOY Growth	56.8%	83.3%	56.1%	45.7%	-6.7%	41.5%	58.3%	-26.5%	-23.2%
Diluted Shares O/S	8,570	8,930	9,062	9,323	9,496	9,203	9,625	9,700	9,800

Brian Marckx, CFA

HISTORICAL ZACKS RECOMMENDATIONS

DISCLOSURES

The following disclosures relate to relationships between Zacks Small-Cap Research ("Zacks SCR"), a division of Zacks Investment Research ("ZIR"), and the issuers covered by the Zacks SCR Analysts in the Small-Cap Universe.

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