Microbiome Therapeutics
Next Generation Prebiotic
Clinically Supported Claims

Metabolically Synergistic Blend
Executive Summary

BiomeBliss is the Next Generation Prebiotic orchestrating microbiome metabolic activity

- A designed set of fiber + non-fiber prebiotics
- Nourishes + shifts + protects the microbiome
- Produces physiologically benefits
- Not just a mix of ingredients – an industry-first

Highly differentiated/robust IP portfolio/ multi-format capable

User compliance/great taste

High awareness of microbiome and prebiotics

Experienced founding & leadership team

Two successful human clinical trials/ multiple claims/ scientifically robust
Prebiotic/Fiber Market

Fiber & Prebiotics (Scientific & Industry Definitions)

Large Growing Market Poised for Transformation

**Fiber**
- Not digested by humans, but some fibers are utilized by gut microbes
- Naturally present in many whole grains, fruits, vegetables, and legumes
- Adequate intake values specified. Daily Value of 28 g/d based on 2000 kcal/d diet
- Can be soluble or insoluble

**Prebiotics**
- Not digested by humans, but acted on by gut microbes
- Naturally present in a wide range of foods from plants (e.g., chicory root, vegetables, whole grains) or synthesized from sugars
- No adequate intake level or daily value
- Many current prebiotics are a type of soluble dietary fiber

**Fiber prebiotics**
- Inulin, fructo-oligosaccharides (FOS), and galacto-oligosaccharides (GOS).
- Promising candidates are resistant starch, polydextrose, xylo-oligosaccharide (XOS), and isomalto-oligosaccharide (IMO).

**Non-fiber prebiotics**
- Lactulose, promising candidates polyphenolics, and polyunsaturated fatty acids

**NEXT MARKET STAGE**

Different types of prebiotics provide ‘food’ for specific groups of bacteria to produce specific sets of metabolites, while decreasing unwanted metabolites.

The **Next Generation of Prebiotics orchestrate** the production of **desired metabolites** for health benefits. This takes the market to a whole new level.

**BiomeBliss is the First-in-Class of the Next Generation of Prebiotics**
- First stand-alone complete great-tasting drink
- Clinically tested
- First to orchestrate designed metabolic production

For more information visit [ISAPPscience.org](http://ISAPPscience.org) or follow us on Twitter [@ISAPPscience](https://twitter.com/ISAPPscience)
Prebiotic/Fiber Market
Fiber & Prebiotics (Scientific & Industry Definitions)
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BiomeBliss Orchestrates + Integrates Functionality

More beneficial activity / less undesired activity
### Fiber & Prebiotic Market Data

- Excellent source of fiber is *most impactful* statement influencing *purchasing decision*
- >50% of consumers recognize fiber is *crucial dietary component*
- >40% of consumers seek high fiber in bars and/or dairy or dairy alternatives
- 37% purchase food & beverages because of fiber
- Regular supplement users *splurge* on *higher cost* versions of *prebiotics*
- ~1/3 of users *consume prebiotics >4x/week* & *spend 85% more* per month vs. irregular users
- Fiber is key component of prebiotic value proposition – showing the terminology linkage drives purchase decisions

**Sources**
1. Roquette 2019 Consumer Fiber Survey – Online Survey of 2,300 adults
2. 2. Global Prebiotic Association Ingredient Comparative Consumer Survey 2019
**Product** – Superior Biome Orchestration via Consortia of Prebiotics

- Great source of inulin fermentable fiber prebiotic
- Substrate for beneficial bacteria to produce SCFAs
- Non-fiber polyphenol prebiotics
- Shifts from methanogens & sulfate reducers (reducing unwanted gas) to increased number of acetogens and their metabolites (desired SCFA)
- Beta-glucan improves AND protects gut barrier function

Outdated Formulations Limit Function, Microbiome Modulation & Benefits
**Product** – First Complete Great-Tasting Prebiotic Drink

Outdated: Unflavored, Poor Taste Profile, Not-highly Soluble
Product – Sizes and Format Options

Two Sizes Lower Barrier to Try
Product & Enables Step-Up Dynamics

NEW

- Start new customers with smaller size and lower price
- Transition repeat buyers to larger size

7oz - $20.95  14oz - $37.95

Hits key consumer trends: vegan, keto-friendly, soy-free, no added sugar (most sugar removed), low calorie & non-GMO
## Scientific Background – Microbiome in Diet-Related Disease

### Microbiota Populations Leading to Decreased SCFAs, Increased H$_2$S & CH$_4$ & Barrier Dysfunction

<table>
<thead>
<tr>
<th>Microbiome Dysbiosis</th>
<th>Type 2 Diabetes</th>
<th>Obesity</th>
<th>Hunger and Lower GLP-1 / PYY</th>
<th>BiomeBliss Goals</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Decreased</strong> Short Chain Fatty Acids (SCFAs)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Increase SCFAs</td>
</tr>
<tr>
<td><strong>Increased</strong> H$_2$S (hydrogen sulfide)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Decrease H$_2$S</td>
</tr>
<tr>
<td><strong>Increased</strong> CH$_4$ (methane)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Decrease CH$_4$</td>
</tr>
<tr>
<td>Mucosal Barrier Dysfunction</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Support Barrier</td>
</tr>
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</table>

The ideal product would address known dysbiotic states and promote health: need a ‘consortia of prebiotics’

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**Address observed dysbiosis by gut microbiome modulation: Increase SCFA and GI Barrier Integrity**

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1. Qin et al., 2012
2. Yassour et al., 2016
**Scientific Background** **Inulin** — Creating Elevated SCFAs
w/o Blood Sugar Spike or High Calories

**PREBIOTICS**
Undigestible, fermentable

- **Inulin**
- **Polyphenols**
- **β-glucan**

**SMALL INTESTINE**

- **Inulin**
- **Polyphenols**

**LARGE INTESTINE**

- **Propionate** (stim PYY, GLP-1)
- **Acetate** (stim PYY, GLP-1)
- **Butyrate** (fuels cells)

**SHORT CHAIN FATTY ACIDS**

- **PYY**
- **GLP-1**

**GUT HORMONES**

- Decrease GI tract motility
- Decrease gastric emptying
- Decrease desire to eat: increase satiety
- Stimulate insulin secretion/glycemic control
- Increase intestinal cell nutrients

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**Sufficient Quantity Fermentable Fiber Prebiotic**

1) Increased production of SCFAs
2) Stimulating release of gut hormones
3) Fate of Hydrogen gas is an issue?
4) Fate of possible H2S & CH4 an issue?
**Scientific Background** Polyphenols — Next Gen Prebiotic

**Consortia Shifts To SCFAs w/o Unwanted Gases**

**Digestible & Undigestible Carbohydrates**

1. **Fermenting Bacteria**
   - CO$_2$, H$_2$

2. **H$_2$ + CO$_2$**
   - **Methanogens**
   - **Methane** (CH$_4$) Associated with T2D and Obesity

3. **H$_2$ + SO$_4$**
   - **Sulfate Reducers**
   - **Hydrogen Sulfide** (H$_2$S) Microbial metabolism of amino acids containing sulfur, associated with Mucosal Barrier Erosion

4. **H$_2$ + CO$_2$**
   - **Acetogens**
   - **Acetate** (C$_2$H$_4$O$_2$)

**Orchestrated Competitive Cross-feeding**

**Selective Advantage for Acetogens**

1) Reducing CH$_4$ and H$_2$S — less gas, less barrier erosion

2) Increasing Acetate — more gut signaling (SCFA)
**Scientific Background Beta Glucan – Protecting the Mucosal Barrier in Microbiome Modulation**

### Role of Beta-Glucan & sIgA

**Bacteria consume β-glucan instead of mucin** → *Stimulate Release of sIgA* → *sIgA neutralizes toxins and pathogens*

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**Protective Prebiotic (not true of many fiber types)**

1. Increased SCFA
2. Barrier protected
3. Gut immune system primed

(Tailford, Crost, Kavanaugh, & Juge, 2015)
(van Kooyk & Rabinovich, 2008)
### Scientific Background – Two Successful Clinical Studies

BiomeBliss is Wholly Owned by MicroBiome Therapeutics

<table>
<thead>
<tr>
<th>Clinical Site</th>
<th>Pennington Biomedical Research Center, Baton Rouge, LA (Q3 ’14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects /Dosing</td>
<td>Hi-BMI, mostly prediabetic 2 full servings BiomeBliss/day</td>
</tr>
</tbody>
</table>

**BiomeBliss clinical results from 4-week study using patented prebiotic consortia**

- **Nourish** to provide missing SCFAs
  - Biota-nutrient Inulin, from agave
  - Biota-shifting Polyphenols, from blueberries

- **SHIFT** to diminish H$_2$S and CH$_4$ producers
  - Barrier-protecting decoy β-glucan from oats

- **PROTECT** mucosal barrier
Scientific Background – Clinical Study Demonstrates Effect on Oral Glucose Tolerance

Claim: Helps maintain healthy meal-time blood sugar
Blood glucose excursion is significantly improved after 4 weeks. Most effective in untreated diabetic subjects. (Fasting blood glucose normalized to zero)

BiomeBliss is Wholly Owned by MicroBiome Therapeutics
**Scientific Background — Clinical Study Demonstrates Effect on Satiety and Desired Meal Size**

- **How Strong is Your Desire to Eat?**
  - Placebo: N = 14
  - BiomeBliss: N = 14
  - *p < 0.05*

- **How Much Can You Eat?**
  - Placebo: N = 14
  - BiomeBliss: N = 14
  - *p < 0.05*

**Claim: Helps manage hunger**

A Validated Visual Analog Scale was used to measure appetite. Data shown are from the final visit (week 4)

(Rebello et al., 2015)
**Scientific Background — Clinical Study Demonstrates Effect on Gut Immune System**

Claim: Helps support the gut immune system
- Increased sIgA to defend against food allergens and pathogens
- Decreased hsCRP in subjects with elevated levels
- Data shown are from the final visit (week 4)

(Rebello et al., 2015)
**Scientific Background** – *Clinical Study Demonstrates Effect on Bowel Regularity*

**Second Clinical Trial**

### Metformin Tolerability

<table>
<thead>
<tr>
<th>Tolerability Score</th>
<th>BiomeBliss</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td></td>
<td>4</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>4</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>6</td>
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<tr>
<td>6</td>
<td></td>
<td>8</td>
</tr>
</tbody>
</table>

**Tolerability Score is a symptom composite**
- Bloating
- Urgency to evacuate
- Stool consistency
- Flatulence

**Subjects with 1 BM/3D at Baseline**

<table>
<thead>
<tr>
<th>Week of Study</th>
<th>Baseline</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>1BM/D</td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>1BM/2D</td>
<td></td>
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**Subjects with 1 BM/2D at Baseline**

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<th>Week of Study</th>
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<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>2BM/D</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>1BM/D</td>
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**Two Claims**

- Helps with occasional diarrhea associated with metformin
- Helps maintain regularity
## Clinical Results – Clinically Supported Benefits + Claims

<table>
<thead>
<tr>
<th>Benefit #1 – Manage Hunger</th>
<th>Claim #1 – Hunger Control</th>
</tr>
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<tbody>
<tr>
<td>Gut bacteria fed prebiotics produce molecules that send satiety signal to your brain.</td>
<td>A Validated Visual Analog Scale was used to measure appetite &amp; significance was achieved when compared to placebo.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Benefit #2 – Blood Sugar Management</th>
<th>Claim #2 – Healthy Mealtime Blood Sugar</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gut bacteria fed prebiotics produce molecules that help maintain healthy mealtime blood sugar.</td>
<td>Blood glucose excursion is significantly improved after 4 weeks. Most effective in untreated diabetic subjects.</td>
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<tr>
<th>Benefit #3 – Regularity</th>
<th>Claim #3 – Regularity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supplying prebiotic nutrients to your gut bacteria helps regulate frequency &amp; consistency of bowel movements.</td>
<td>Increased bowel movements from 1 every 3 days to one per day &amp; helped with occasional diarrhea associated with metformin.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Benefit #4 – Gut Health &amp; Immunity</th>
<th>Claim #4 – Digestive Health + Immune Support</th>
</tr>
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<tbody>
<tr>
<td>Beneficial bacteria fed prebiotics don’t feed on the gut mucosal layer &amp; stimulate increased slgA.</td>
<td>Increased slgA after 4 weeks - fecal marker of gut immune function and barrier protection.</td>
</tr>
</tbody>
</table>
Company Background – Experienced Founding Team

Mark Heiman, PhD – Chief Scientific Officer and cofounder (now CSO emeritus)  
20+ years at Eli Lilly. Drug discovery and development, obesity and diabetes

John Elstrott, PhD – Chairman, Cofounder  
Past Chairman of Whole Foods Market, multiple successful health food and supplement companies

Founding CEO of five biotechnology companies
Company Background — Timeline and Key Milestones
Transitioning from Medical Food to Consumer Supplement

- **2010**: Company Founded
- **2012**: Product – Medical Food
- **2014**: Clinical Trial #1 Design & Funded
- **2016**: Successful Clinical Trial – Endpoints Hit
- **2017**: New FDA Regulatory Limits on Medical Food
- **2018**: Clinical Trial #2 – Combo Product Designed Funded (505b2 route)
- **2019**: FDA Req’d $20M 505b2 Trial – Not Pursued
- **2020**: Pivot to Supplement BiomeBliss Launched
- **2020**: Brand & Sales Development

*Successful Acquisition Completed – Q1 2020*

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Company Background – Regulatory Path

Foods

Supplements

Medical Foods

Drugs Via 505(b) (2)

1st as a Medical Food supported by clinical trial

2nd as a Drug via 505(b)(2) supported by second clinical trial

3rd as a Supplement

Launched in 2018 / FDA notified of supplement claims

2017 - ‘18
2011 - ‘15
2015 - ’16
**M&A Opportunity – Timeline & Key Milestones**

- **October 2019**: M&A Preliminary Meetings Scheduled for Initial Due Diligence
- **November 2019**: Indicative Terms Provided by Interested Acquirers, BiomeBliss BOD Reviews Deal Opportunities For Approval
- **December 2019**: Approved Companies Provide Definitive Terms/Legal Agreements Drafted for Review/BOD Meeting to Review Options
- **January 2020**: Final Legal Agreement Redlines/BOD Approval/Go/No-Go Options Determined/Transaction Completed
- **February 2020**: Close
Key Takeaways

- **BiomeBliss is the First-in-Class Next Generation Prebiotic**
  - First consortia designed for specific synergistic functions
  - Increasing beneficial metabolic functions while decreasing unwanted gut activity
  - First stand-alone delicious prebiotic drink

- BiomeBliss is **turnkey Next Generation Prebiotic** ready to meet consumer demand

- BiomeBliss is a **highly differentiated/clinically-tested prebiotic product**

- Consumer approved & validated

- Multi-patent protected formula

- Experienced founding & leadership team
BiomeBliss M&A Opportunity Next Steps

**Noah Voreades** – Strategic Advisor  
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E: genbiome@gmail.com

**Dale Pfoet** – CEO/Co-Founder  
M: 609-468-7834  
E: dale.pfoet@dplifesciences.com
Product Background – Serving Levels in Clinical Studies

Two full servings/day, where full serving = 2 scoops (2 x 13g)
Therefore 4 scoops/day providing 52g of product

Nutrients in Each 2-Scoop Full Serving:
- Prebiotics: 16g
- Dietary Fiber: 8g

Daily Nutrients Provided in Clinical Studies
- Prebiotics: 32g
- Dietary Fiber: 16g

Future of Prebiotics
- Delicious Flavor
- Many Recipe Ideas
- Great Repeat Order Rate
- Great User Compliance
- Easy to Mix at Home or Work