MICRO BIOME POST

CONGRESS REPORT

Microbiome Movement Drug Development

The 2023 summit report, Boston MA

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Introduction

Pharmaceutical research is built on the hope of finding and developing medications that treat disease.

> **In recent years, researchers have turned to producing medications as living microorganisms.**
> **Known as**
>
> **LIVE BIOTHERAPEUTICS (LBPS)**
>
> **these microbes treat disease by modulating the human microbiota and altering immune responses across the body[1].**

The FDA approvals of Seres Therapeutics's Vowst and Ferring Pharmaceuticals's Rebyota have driven many new efforts to treat and prevent other diseases with LBPs.

In response, Hanson Wade hosted the 8th Microbiome Movement Drug Development Summit in Boston.

75+ SPEAKERS

250+ ATTENDEES

25+ PARTNER COMPANIES

The summit featured over 75 speakers that discussed new possibilities in developing and producing LBPs.

These talks were classified into three tracks, each one contributing to the end-to-end pipeline for LBP development: Discovery and Preclinical, Translational and Clinical, and Manufacturing and Process Development.

With all aspects of LBPs covered in the summit, the 8th Microbiome Movement Summit in Boston became the hub for sharing the latest insights in LBP research and development.

Discovery & Pre-clinical

LBP development begins in the lab. There, researchers isolate, characterize, and validate bacteria as candidates to treat specific diseases. In this track, Microbiome Movement featured **multiple companies** that developed tools to aid LBP candidate discovery and validation.

Identifying an LBP candidate begins with **isolating a candidate microbe**. Donor stool is one common source of these microbes. Knowing this, Lior Weissman, Vice President of Research and Development at MyBiotics, demonstrated the company's ability to **create synthetic microbial consortia** with 90% similarity to the original donor samples. Identifying refinement processes to maximize growth, such as donor pooling, subsequently allowed them to develop MBX-SD-201 and MBX-SD-202 to treat acute C. difficile infections.

Ensuring the safety of an LBP candidate also requires identifying risk factors for poor outcomes.

Microbial features, such as antibiotic resistance and virulence factor genes, can cause deleterious side effects. To profile these microbes, EZBiome and Clinical Microbiomics showcased bioinformatics tools that help researchers assemble and profile microbial genomes.

Mo Langhi, Senior Director of Business Development of CosmosID, also highlighted efforts to **improve the performance of several tools**, such as HuManN^2, to characterize multi-strain LBP candidates.

Discovery & Pre-clinical

Nik Sharma and Munhannad Al-Omari, CEO and CTO of BioCortex respectively, also introduced CarbonMirror. CarbonMirror is a physics-driven simulation engine that assesses **drug-microbiome interactions**. These interactions are either direct through drug metabolism by bacteria, indirectly by modulating immune responses to microbes, or through local effects at specific part of an organ.

Altogether, the tool

> ***allows companies to de-risk drug-development pipelines by determining whether drug-microbiome interactions would adversely impact any clinical trial results***

state the founders.

Pre-clinical research also requires **developing in vitro and in vivo models** to assess an LBP candidate before conducting clinical trials.

Cheri Ackerman, the co-founder and CEO of Concerto Biosciences, introduced the kChip, an in vitro system that allows hundreds of thousands of microbial combinations to be assayed at once. The technology is built on producing 1-nL droplets containing microbes into microwells and **tracking their interactions with fluorescence-based assays**[3]. The technology allowed them to develop two multi-species formulations — ENS-002 and ENS-003 — for clinical trials to treat eczema and recurrent yeast infections respectively.

Caitlin SL Parello, Associate Director of Research Operations at Biomodels, also delves into the many animal models available for testing LBPs and advancing preclinical research.

Translational & Clinical

Testing a candidate through clinical trials represents the next step in LBP development. At Track *Translational & Clinical*, Microbiome Movement featured talks where companies publicized their **clinical research**.

Among these speakers was Sam Possemiers, CEO of MRM Health, who announced the **start of clinical trials for MRM-002**. MRM-002 is a microbial consortium designed to **treat pouchitis**. Pouchitis occurs when inflammation occurs at the lining of a pouch, a complication that arises from ulcerative colitis surgery[4]. He highlights the effectiveness of MRM-002 to treat DNA- and TNSS-induced colitis in mouse models and expresses hopes for its effectiveness in clinical trials.

Other LBP candidates have moved further along in the clinical trial pipeline. Samantha Coulson, Head of Clinical Research at Servatus, discussed **recent results for SVT-4A1011**, a microbial consortium designed to **treat insomnia**.

The gut microbiota plays an important role in sleep quality through the gut-brain axis[5], and Servatus sought to help patients improve sleep quality with their LBP. In such efforts, Samantha highlighted the importance of preparing **measurable metrics of sleep quality**, which they accomplished with the SOMFIT.

Joseph Trebley, CEO of Scioto Biosciences, also shared **Phase IIb clinical trial data for SB-121**, a formulation of L. reuteri designed to **treat symptoms associated with autism spectrum disorder** (ASD). He highlights the excitement of developing an LBP for ASD, stating,

> ***insurance companies want to push new treatment methods for ASD forward, and LBPs are very much in that conversation.***

Translational & Clinical

Initial lab tests showed that SB-121 adheres to epithelial cells, has improved gastric survival, and can reduce inflammation[6].

Now, Trebley showed through Phase IIb clinical trial data that children with ASD improved their social behaviours after taking SB-121 for 28 days.

Each of these clinical trials hence shows great hope for seeing more LBPs enter the market soon.

Summary - Some of the clinical research presented

LBP'S COMPANY	SESSION ANNOUNCEMENT	MICROBIAL CONSORTIUM	TARGETED DESEASE
MRM HEALTH	START OF CLINICAL TRIALS	MRM-002	POUCHITIS
SERVATUS	RECENT RESULTS	SVT-4A1011	INSOMNIA
SCIOTO BIOSCIENCES	PHASE IIB TRIAL DATA	SB-121	ASD ASSOCIATED SYMPTOMS

Manufacturing & Process Development

After an LBP has successful clinical trial data, companies must prepare robust manufacturing pipelines to produce and make available the LBP.

When the first LBPs were produced, no contract and development organizations (CDMOs) that specialized in LBP production existed.

This was the biggest challenge that Matthew Henn, Executive Vice President and CSO of Seres Therapeutics encountered when developing Vowst.

Since then, many CDMOs have entered the market, eager to help pharmaceutical companies harness live microbes to treat disease. Claire Derlot works for one of these CDMOs. As Head of Programs at Biose Industries, she provided the company's wide capabilities to **produce multi-strain LBPs in many forms from pills to gels**. They began with a blueprint to gain the capacity to produce LBPs.

At the summit, Henri de Vlam, Business Development Manager of Bacthera, and Antonio Fernandez Medarde, Site Head for Bacthera in Spain, discussed the **capabilities that CDMOs need to succeed in LBP production**.

Henri de Vlam says that

> ***there are 5 key must-haves for CDMOs in this space: quality, scale and throughput, size, excellence in strain handling, and efficiency. Each of these components covers different aspects of production that must be sufficiently covered to produce any robust LBP.***

Manufacturing & Process Development

It was these principles that Alicia Szretter, Associate Director of Manufacturing at Vedanta Biosciences, took to heart when she helped Vedanta **expand** its **production capabilities**. They first refined each step of the LBP production line, from lyophilization to incubation times to ensure reproducibility. Then, they modified existing protocols such as using single-use equipment and introducing a stirring reaction during the filtration step to maximize LBP potency and purity.

Altogether, Alicia says that

> ***these efforts will push LBP development further and make LBPs that much more accessible for patients who need it most.***

Conclusion

The approvals of Vowst and Rebyota provided an immense momentum boost for pharmaceutical companies to develop LBPs, both big and small.

At all facets of LBP development and production, companies are spearheading efforts to treat more diseases with LBPs.

To that end, many companies provide services in all aspects of LBP development, from pre-clinical to LBP production.

Each round of talks covers the work that many companies are conducting to streamline LBP development and production and make live microbes easier to access for the clinic.

All in all, LBP research and development is progressing at a feverish pace, and seeing it mature will allow live microbes to become staples for treating disease in the clinic.

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