Harnessing the Power of the Human Microbiome

Rebiotix Inc.

FMT Public Workshop

May 2-3, 2013

Rebiotix™
Microbiota Restoration Therapy

Who We Are

Lee Jones - Founder, President, and CEO

- >30 years experience in medical technology
- Large and small companies and academia

Rebiotix Inc. - Founded July 2011

- A results-oriented biotechnology company revolutionizing the treatment of challenging gastrointestinal diseases by harnessing the power of the human microbiome.

Rebiotix™
Microbiota Restoration Therapy

Rebiotix Background

What we evaluated:

- Is there an unmet medical need?
- Number of patients affected (market size)
- Alternative treatments
- Regulatory requirements
- Time and cost to gain market approval
- Reimbursement options
- Applications besides *Clostridium difficile* (CDI)

Rebiotix™
Microbiota Restoration Therapy

Rebiotix Background

What we found:

- Treatment for recurrent CDI needed
- Increasing number of patients
- Expensive to treat
- Antibiotic treatment has limitations
- Fecal transplant - promising, seldom used
- Unknown regulatory requirements
- Cost and time to market hard to predict
- Many potential applications besides CDI

Challenges: FMT for Recurrent CDI – Good News/Bad News

Good News:

- Over 50 years of positive anecdotal clinical evidence suggests it works

Bad News:

- No regulatory classification for a product
  - Tissue transplant?
  - Cellular therapeutic?
  - Drug?

New regulatory paradigm

Rebiotix™
Microbiota Restoration Therapy

Challenges: FMT for Recurrent CDI

Good News:

- Few reported adverse events

Bad News:

- No standardization:
  - Donor screening criteria
  - Manufacturing methods, materials
  - Volume, dosing
  - Delivery method

Result: unknown safety/efficacy

Rebiotix™
Microbiota Restoration Therapy

Challenges: FMT for Recurrent CDI

Good News:

- Fecal material is cheap and available

Bad News:

- Anyone can do a fecal transplant
  - Recipes, do-it-yourself kit available online
  - Naturopathic 10-day colonic health retreats
  - Various physicians

Quick way to destroy a promising therapy - a few disasters are all that is needed.

Rebiotix™
Microbiota Restoration Therapy

Challenges: FMT for Recurrent CDI

Finally, the **Really Bad News**:

- Everyone who performs FMT today has to be their own manufacturer:
  - Must find and screen donors
  - Collect stool on demand
  - Process fecal material ("Yuck" factor)
- Must be done for each and every patient

Delays what physician really wants:
to treat the patient

Rebiotix
Microbiota Restoration Therapy

Rebiotix Solution

Rebiotix is solving the problems of FMT by creating:

- A ready-to-use, off-the-shelf product that can be ordered as needed

and conducting:

- Rigorous clinical studies to demonstrate safety and efficacy for patients who have failed standard treatment for recurrent CDI.

Rebiotix™
Microbiota Restoration Therapy

New Regulatory Paradigm

Challenging regulatory question: 6 regulatory consultants, 6 different answers

- March 2012 – Requested FDA designation as a tissue transplant
- August 2012 - Notification that the product did not meet the criteria for a tissue transplant

Rebiotix™
Microbiota Restoration Therapy

New Regulatory Paradigm

Regulatory decision:

- Product to be reviewed by the Office of Vaccine Research and Review (OVRR) in the Center for Biologics Evaluation and Research (CBER)
- Product designated as a drug (biologic)

Rebiotix™
Microbiota Restoration Therapy

New Regulatory Paradigm

Regulatory milestones:

- December 2012- Pre-IND meeting
- March 2013 - Submitted IND for a Phase 2 study of new drug, RBX2660 (microbiota suspension)
- Clinical start: TBD - in process of enrolling centers

Rebiotix™
Microbiota Restoration Therapy

New Regulatory Paradigm

Regulations and quality standards:

- Protect the patient
- Protect the industry

Balance must be struck between risk and benefit

Rebiotix™
Microbiota Restoration Therapy

Drug Product Development

Assumptions:

- Live microbe delivery is a requirement
- Number and diversity of microbes should be a reasonable match to raw human stool
- We can reasonably assume that product will be efficacious in clinical studies provided the first two conditions are fulfilled

Rebiotix™
Microbiota Restoration Therapy

Drug Product Development

Chemistry, Manufacturing, Controls (CMC):

- Characterize raw material
- Develop manufacturing processes
- Evaluate storage methods and shelf life
- Develop delivery kit
- Establish quality release specifications

Rebiotix™
Microbiota Restoration Therapy

Drug Product Development

Goals:

- Deliver a consistent, quality product to the customer each and every time
- Product is easy-to-use in a routine clinical practice

Rebiotix™
Microbiota Restoration Therapy

Drug Product Development

In actual experience, this was not easy.

Rebiotix
Microbiota Restoration Therapy

Drug Product Development

It has taken over 1 year and >$2 million to develop a product ready for a commercial clinical study.

- Bulk of the work involved:
  - Characterizing human stool
  - Discovering what affected its properties

Rebiotix™
Microbiota Restoration Therapy

What's Next

Clinical Studies:

- Product: RBX2660 (microbiota suspension) in ready-to-use enema format
- Indication: Recurrent *Clostridium difficile*-associated diarrhea (CDAD)
  - Phase 2 - Open label, non-randomized safety study
  - Phase 3 - Randomized, multicenter, double-blind placebo controlled efficacy and safety study

Rebiotix™
Microbiota Restoration Therapy

Looking to the Future

- Other indications and delivery methods
- Products will evolve as the science evolves
- May someday be used to treat a broad spectrum of other non-GI conditions

Rebiotix™
Microbiota Restoration Therapy

New Terminology Needed

Currently referred to as:

- stool bacterial flora replacement, fecal transplant, fecal bacteriotherapy, restoration of fecal floral homeostasis, fecal feeding, fecal enema, stool transplantation, Fecal Microbiota Transplant (FMT), fecal infusion, faecal donor instillation therapy, human microbiota transplant, gastrointestinal flora transplant, intestinal microbiota transplantation, bacteriotherapy, fecal flora infusion, bacterial treatment, fecal flora reconstitution

Rebiotix™
Microbiota Restoration Therapy

New Terminology Needed

And, last but not least, my favorite: Re“Poop”ulate.

You get the picture (and it is not pretty)

Rebiotix™
Microbiota Restoration Therapy

New Terminology Needed

How would your patient react if you said:

- “Here, this injection of slaughterhouse pig pancreas fluid will help your diabetes.” (insulin)
- “Swallow this pregnant mare urine preparation – it will help with your hot flashes.” (estrogen)
- “You have cancer. I can treat it with this yew tree bark extract.” (paclitaxil)

Sometimes its best not to be too literal.

Proposed New Terminology

- Drop the word “fecal”
  - Limiting
  - Repellent
  - Joke factor

Propose:

Microbiota Restoration Therapy (MRT)

Rebiotix™
Microbiota Restoration Therapy

Summary

- FMT has potential, but also has challenges.
- Rebiotix is solving the problems of FMT by developing and commercializing a standardized ready-to-use product.
- Regulations and quality standards can protect this dynamic industry.
- Better terminology such as MRT is needed.

Conclusion

The future of MRT is exciting!

It is up to us to make it a reality.

Rebiotix™
Microbiota Restoration Therapy

Thank you

For more information on our work:

- **Rebiotix.com**

Rebiotix™
Microbiota Restoration Therapy