

Greetings from OpenBiome!

In 2014, OpenBiome's work was featured in The New York Times, The New Yorker, The Atlantic, Wired Magazine, The Chicago Tribune, The Boston Globe, and other outlets, along with radio and television appearances on NPR, CNBC, and others. OpenBiome also engaged more directly with the public conversation around FMT through the publication of policy thought pieces in Nature and Nature Biotechnology.



As we embark on our second year, our team took some time to think back on what we've built together. In this Annual Report (our first ever!), we hope to share some of those reflections.

The difference between OpenBiome at the start of 2015 and early 2014 is astounding. Then, our team comprised one full-time staff member (James) and a small handful of highly engaged volunteers, board members, and scientific collaborators. We were celebrating the successful treatment of 10 patients, and had increased our donor pool from 1 to 3 members in what was then a key step to improving the diversity and resilience of the program. We ran our entire operation out of ~20 square feet tucked in a far corner of the Alm Lab at MIT.

Today's OpenBiome would have been unrecognizable to us then. Now, we are 17 members strong, and we routinely ship upwards of 100 treatments each week. Our donor pool of 19 is also growing weekly, and with input from our Clinical Advisory Board, we have developed a comprehensive set of tools and infrastructure to enable the processing, quarantining, and tracking of two dozen stool samples per day.

We have driven this rapid growth with a steady focus on raising the caliber of our service and advancing best practice in the field. Our operations, medical and scientific staffs power a one-way ratchet of ever-improving safety and production quality standards, donor screens, tracking tools, and system checks to guarantee that every treatment distributed by OpenBiome defines the highest standard of stool safety and quality based on the latest research.

Beyond our efforts to change the epidemiology of *C. difficile* infection, as the scientific community begins to peel back the veil on the role of the human microbiome, OpenBiome is also poised to facilitate cross-collaboration across studies, disciplines, and geographies. To date, we are supporting 10 clinical trials spanning a variety of indications and investigating the mechanisms through which our gut microbes and health interact. We have dedicated hundreds of hours towards the development of standardized products and

processes as tools to improve data quality and outcomes from studies investigating manipulations of the microbiome.

Our accomplishments from the past year represent the efforts of an incredible team of scientists, clinicians, and professionals. We are honored to have the opportunity to work alongside such a skilled, compassionate group of individuals who are devoted to improving patient care and advancing medical research.

As we move into 2015, our team is united around a common set of goals for our organization. Primarily, these goals are:

- Reach 10,000 patients and 200 new hospitals across the U.S., saving the U.S. healthcare system \$170 million
- Introduce stool capsules as a safer and simpler treatment option and research tool
- Develop microbiome-driven assessments to identify ideal donor candidates, a first for the field
- Support 15 high-impact studies, investigating the role for bacteriotherapy in human health
- Build an international clinical network, beginning in the UK

We're excited about all of these goals, and believe 2015 will be another year of incredible advancement for OpenBiome and the entire field.

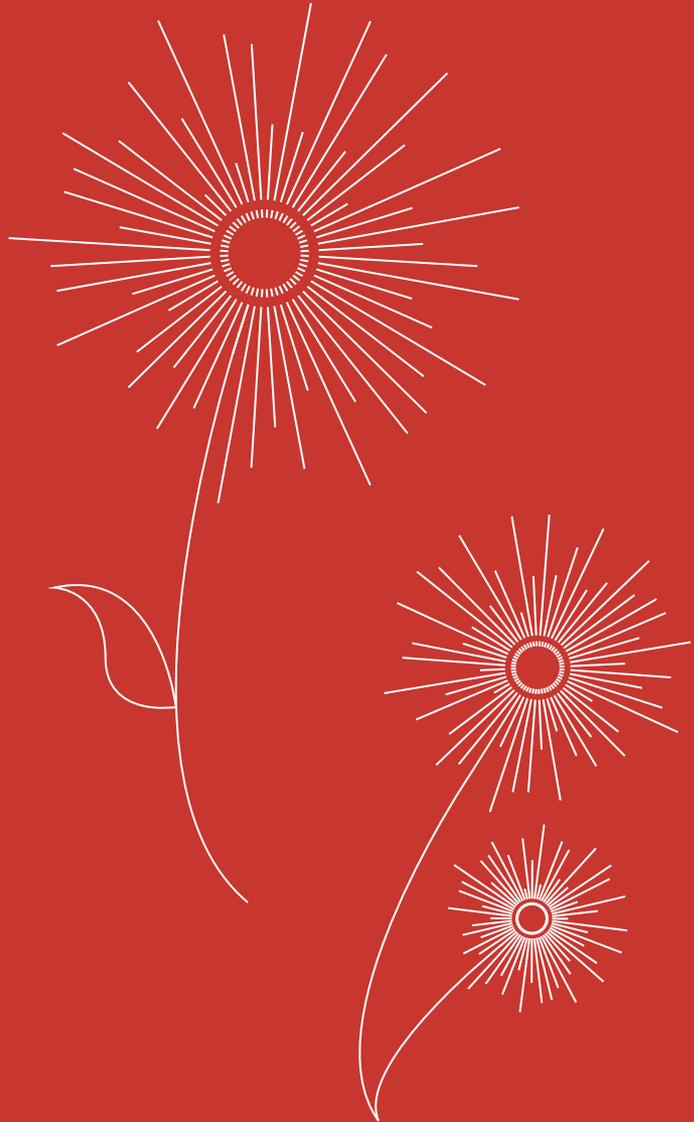
A handwritten signature in white ink that reads "James Burgess".

James Burgess
Executive Director

A handwritten signature in white ink that reads "Mark Smith".

Mark Smith
President, Research Director

Clinical Impact



“Dear OpenBiome:

I am a 34-year-old mother of a 5-year-old boy and a 3-year-old little girl.

This past Wednesday, I had a fecal transplant and the stool was supplied by your organization. Before the transplant, I had been fighting C. diff for about 6 months. The first 3 months were bad, but not miserable. The last 3 months were awful; I was in the hospital a total of 2 months out of those last 3 months.

My kids were in tears all the time because they wanted me home and I was falling into a deep depression. I never thought I was going feel good again. I was on so many different medicines and none of the antibiotics were working. I tried all three multiple times and the C. diff never even got a little bit better. The fecal transplant was our last hope. I was ready to try anything. I needed to get my life back.

It is now Saturday, not even three full days after the transplant and I feel like a new person. I actually got dressed today and went to the store to run errands. I haven’t been able to do that in months. I just want to thank you so much and thank the person that donated the stool. They changed my life and they gave my kids their Mom back.

I honestly don’t know what we would have done if you guys hadn’t made this process known and available. Thank you so much.”

Clinical Figures

1,835 treatments provided

169 clinical partners

89% clinical efficacy rate

45 pro bono treatments provided

\$31.2M in savings
to the US healthcare system

From 2014, nothing stands out to us more than the rapid growth in our clinical impact. We set out to grow our program from supporting 10 to 1,000 treatments by the year's end. We exceeded that goal by nearly double.

We formed partnerships with several large hospital networks, allowing them to launch FMT programs where either none, or very localized efforts existed before. Kaiser Permanente and the Veterans' Affairs Hospital system, two of the nation's largest hospital networks, integrated OpenBiome into their efforts to develop FMT programs. Through these networks, hundreds of patients suffering from recurrent *C. diff* infections have access to FMT.

169 Clinical Partners



Each FMT saves the U.S. healthcare system a conservative estimate of **\$17,000***

OpenBiome has saved the U.S. healthcare system
\$31.2M this year

Given our continued rapid growth, we anticipate a savings upwards of
\$100 million in 2015



*Konijeti GG, Sauk J, Shrime MG, Gupta M, Ananthkrishnan AN. Cost-effectiveness of Competing Strategies for Management of Recurrent Clostridium difficile Infection: A Decision Analysis. Clin Infect Dis. 2014 Jun; 58(11):1507-14.

Beyond the numbers, though, what truly drives OpenBiome's growth, and indeed, all of our efforts, is the knowledge that behind almost every one of the 1,835 treatments we enabled this year is a patient who otherwise would not have had the option to have a fecal transplant. As a result, many of these individuals – parents, grandparents, partners, brothers, and sisters – would have been left with little alternative but to bear the burden of infection.

Safety Improvements



The more we learn about the gut microbiome, the more complex its relationship to human health appears. In this context, questions around patient safety drive us to continuously improve the protocols and processes of stool preparations. We firmly believe that the additional time and operational scale that stool banking affords makes it safer than one-off, ad-hoc stool donations, which have minimal screening standardization or tolerance for double- and triple-checks. More than that, we are equipped to translate cutting-edge research into practice. In line with that view, in 2014, we introduced a number of safety improvements:

We're happy to report that, in 2014, no adverse events were attributable to OpenBiome stool material. Through our SAFE (Serious Adverse Event, FMT Non-response, Evaluation of Inventory) protocol, we require clinical partners to submit Material Tracking Logs that trace every treatment unit across our network, and to report any adverse events to the FDA and to us. Building on this work, additional safety improvements and controls are under development for release in 2015.

Quality & Safety Program (Q&SP):

Under this initiative, we formalized the structure of our Adverse Event reporting algorithm, improved material traceability, and began sharing quarterly safety reports with all members of our clinical network.

Donors' Clinical Interview:

We expanded the donor clinical screening questionnaire from 18 to 109 questions, establishing a new standard in stool donation screens.

Donors' Laboratory Screening:

We added screens for Rotavirus, Adenovirus, Norovirus, and Vancomycin-resistant Enterococcus (VRE) to our panel of stool and serological tests, and converted our *C. difficile* screen from an ELISA assay to a PCR assay.

Clinical Advisory Board Formal Launch:

We have always relied on the input of clinical leaders to structure our protocols and to design our program with clinicians in mind. In 2014, we formally recognized these leaders as the Clinical Advisory Board:

Quality Assurance Subcommittee

Michael Edmond, MD, MPH, MPA

Daniel Murphy, MD

Neil Stollman, MD, FACP, FACG, AGAF

Research Methodology Subcommittee

Richard Hunt, MD, FRCP, FRCPEd, FRCP(C), FACG, AGAF

Colleen Kelly, MD

Ciaran Kelly, MD

Paul Moayyedi, MB ChB, PhD, MRCP, FRCP

Adverse Event Subcommittee

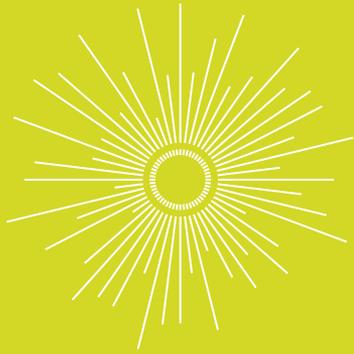
Kanchana Amaratunga, MD

Paul Beck, MD, PhD

Tim O'Shea, MD

Research Impact

"I wanted to just send this message to thank you for what you do. And, thank you so much to the donor who didn't think it was crazy to give a poop to a stranger. My little girl is here thanks to you! Last summer after surgery for a staph infection, my 12-year-old spunky, healthy, funny girl turned into a walking corpse. She had multiple bouts of C. diff and multiple rounds of antibiotics and nothing worked. I researched and found out about FMTs and presented the information to my husband. After reading it, you just can't deny the incredible power of poop! She had the procedure done at the beginning of September in Atlanta, and within two days she was happy, eating, pooping normally. Thank you, thank you, thank you, from the bottom of my heart. We are beyond blessed by you!"



Research Impact

Zain Kassam
Chief Medical Officer



In May 2014, Dr. Zain Kassam, MD MPH FCPRC joined the OpenBiome team as the Chief Medical Officer to lead our clinical operations and clinical research activities. Dr. Kassam, a gastroenterologist and internal medicine physician, completed his Master's in Public Health at the Harvard School of Public Health and his medical training at McMaster University, Canada, where he was both the Chief Medical and Chief Gastroenterology Resident. Dr. Kassam has authored a number of publications on translational microbiome research and applied microbiome-directed therapies in journals such as Archives of Internal Medicine, American Journal of Gastroenterology, and New England Journal of Medicine.

Not only do we aim to change the epidemiology of *C. difficile*, we also want to catalyze research into the role that the gut microbiome plays in human health. Abnormalities in the human microbiome have been linked with a range of health disorders from gastrointestinal diseases like ulcerative colitis and irritable bowel syndrome, to metabolic disorders like diabetes and obesity and neuropsychiatric conditions like anxiety and depression. Clinical researchers across the country are investigating the impact of manipulating the microbiome, many via fecal microbiota transplantation. Most of these researchers, however, do not have the resources or expertise to prepare their own stool material for FMT studies. By providing material for research, OpenBiome has accelerated these research efforts. Here are highlights from the research partnerships we launched in 2014:

Post-Operative Crohn's Study

**Beth Israel Deaconess Medical Center | 44 Patients | Phase II, single-blinded randomized trial
Funded by the Helmsley Charitable Trust**

Having pioneered the field of FMT and IBD with his first study of active Crohn's disease, Dr. Alan Moss is now conducting a study of FMT in post-operative Crohn's patients. In the absence of interventions, half of post-surgery Crohn's patients will experience remission. This study seeks to explore whether FMT delivered via OpenBiome's oral capsules can be used as an effective maintenance therapy to prevent disease recurrence.

Irritable Bowel Syndrome Study

Montefiore Medical Center | 110 Patients | Phase II, double-blinded, placebo-controlled trial

This study will investigate whether FMT delivered via oral capsules improves symptoms in patients suffering from diarrheal-predominant Irritable Bowel Syndrome. In addition to using primary clinical endpoints, we will use extensive molecular characterization of donors' and patients' microbiota as secondary endpoints to help us evaluate the mechanistic effects of FMT.

Pediatric Ulcerative Colitis Study

**Boston Children's Hospital | 60 Patients | Phase II, double-blinded, placebo-controlled trial
Funded by the Neil and Anna Rasmussen Foundation**

As the first randomized controlled study of FMT in pediatric IBD, this trial aims to determine whether FMT provides a potentially safe and effective treatment for pediatric ulcerative colitis. The study combines pre-treatment antibiotic therapy to open niche space for colonization with FMT delivered via enema and oral capsules.

*Evaluating the safety of FMT for *C. diff* patients*

There remains a great deal to learn about the fundamentals of FMT. In particular, while the medical community is very comfortable with the short-term safety profile of the procedure, very little is known about the long-term repercussions of FMT on patient health.

*To address this knowledge gap, OpenBiome has launched a multi-center longitudinal safety study of FMT in recurrent *C. difficile* patients. Titled "Safety of fecal microbiota Transplantation: OpenBiome Outcomes and Longitudinal follow-up (STOOL)," the study will follow 150 FMT recipients for at least 1 year post-FMT, tracking health outcomes. In 2014, our Investigational New Drug (IND) application was approved by the FDA. The study begins enrollment in Spring 2015.*

Capsule Development

In 2015, we will begin offering encapsulated stool—the result of a great deal of hard work from the past year. The use of oral capsules can eliminate the need for costly and invasive FMT procedures like colonoscopies or upper endoscopies, a feature that also helps advance research by making repeat or maintenance therapies more tolerable, and by simplifying the design of placebo controls.

Capsule development in 2014

After much iteration, we've arrived at a stool encapsulation method that is highly scalable (we can produce 100 capsules per hour), and yields a standardized product that is suitable for consumption. We validated our capsules in early-stage clinical studies, and published our work in the April 2015 American Journal of Gastroenterology.

Capsule rollout in 2015

Early spring 2015 — Capsule dose-finding study

Across all FMT delivery methods, there have been no studies to pinpoint optimal dosage levels. We are conducting a study with Brigham & Women's Hospital in Boston to identify the ideal dosing regimen for orally ingested stool capsules to treat recurrent *C. difficile* infection.

Late spring 2015 — Dose-finding follow-on studies

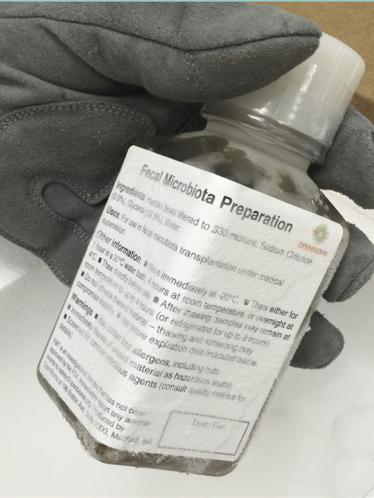
To validate the results from the Brigham & Women's dose-finding study, we will conduct follow-on evaluations of dosing regimens with key clinical partners at five sites.

Summer 2015 — Clinical rollout

Once a final dosing regimen is selected based on the data from the dose-finding study and validation, capsules will be made available to the entire OpenBiome clinical network.



Operations Profile



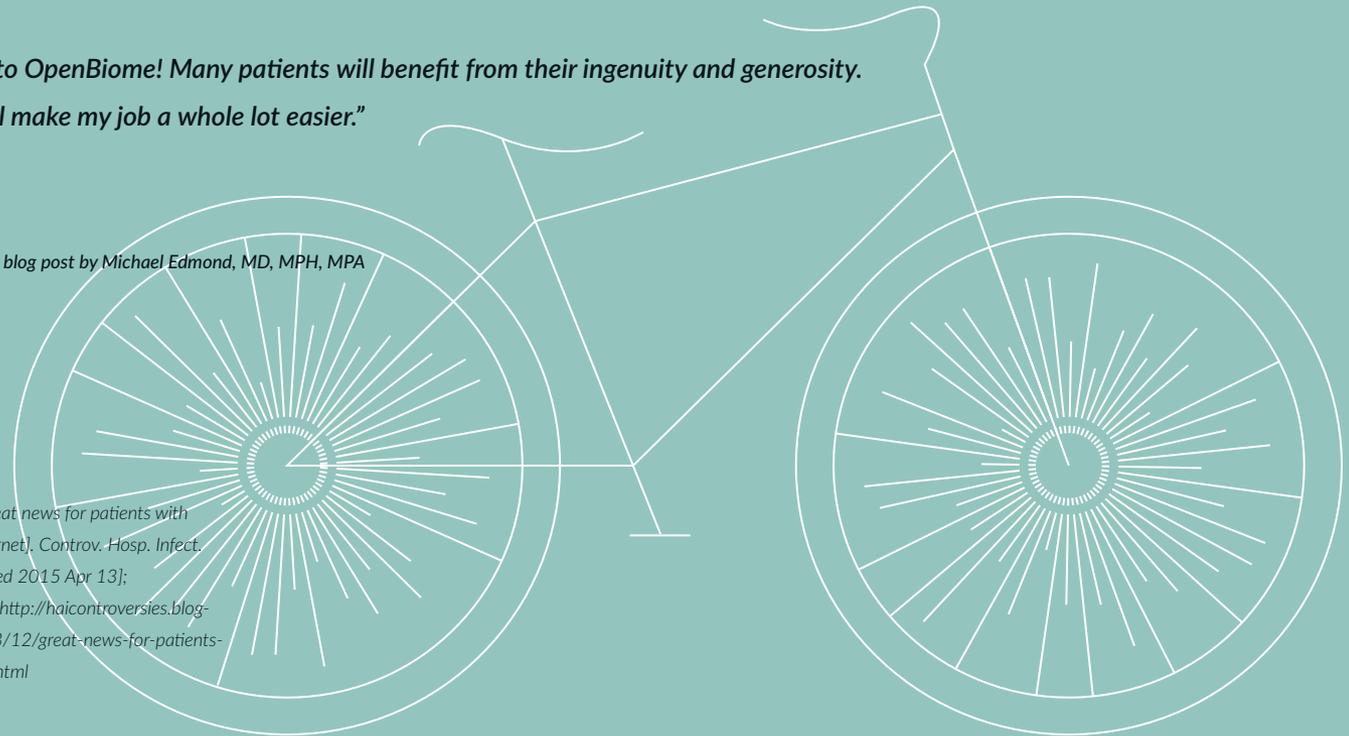
“Yesterday I stumbled on OpenBiome’s website and as I explored it I was nearly euphoric. OpenBiome provides processed, frozen human stool from donors that have been carefully selected and screened for multiple infectious diseases at least twice, at a cost that’s 1/6 the price of me testing one donor, and 5 to 14-fold cheaper than the drugs that these patients have taken without success. And OpenBiome’s goal is to reduce the price even more as they scale up their operation.”

I had a long conversation today with James Burgess from OpenBiome. He was excited to tell me about their work and I was incredibly impressed. They have covered all the bases, including banking serum from donors for future testing should a patient develop an unusual infection.

So Kudos to OpenBiome! Many patients will benefit from their ingenuity and generosity. And they’ll make my job a whole lot easier.”

—Excerpt from blog post by Michael Edmond, MD, MPH, MPA

Edmond M. Great news for patients with C. difficile [Internet]. Controv. Hosp. Infect. Prev. 2013 [cited 2015 Apr 13]; Available from: <http://haiconroversies.blogspot.com/2013/12/great-news-for-patients-with-c-difficile.html>

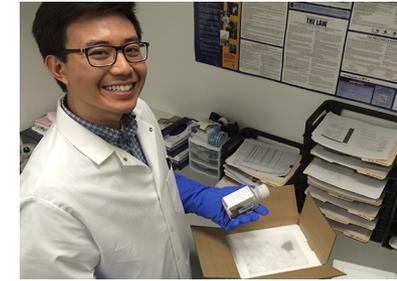


Operations Figures

Andrew Noh
Director of Operations

OpenBiome's operations have transformed from a one-man show to a well-oiled process run by 6 lab technicians and 2 order fulfillment specialists, under the leadership of our Director of Operations. With a team of this size and caliber, we have been able to simultaneously engineer quality and safety improvements across our production protocols while increasing our total production and shipment volume by several orders of magnitude.

The Ops Team's development of a custom suite of technological tools to manage, track, and trace our ever-growing inventory of stool samples was especially critical. With a barcode sweep, one of our team members can see at a glance the status, history, and destiny of each of the hundreds of treatment units in one of the OpenBiome freezers.



Andrew joined OpenBiome in March, just on time to oversee the launch of our new laboratory when we outgrew our bench at MIT. Andrew brings a wealth of management experience to his role at OpenBiome, drawing upon his four years as a Consultant at Bain & Company, where he advised a variety of clients on growth strategy, merger integration, performance improvement, organization, and IT projects. Andrew also served as a Fellow at the Civic Consulting Alliance in Chicago and worked internationally at a microfinance institution in Kenya and as an English teacher in Thailand.

Prospective Donors Screened: **130**

Donors Passed: **27**

Total Stool Processed: **120 kg**

Operations Improvements:

- Average time to ship dropped from 2 hours to 15 minutes
- Average time to process dropped from 75 minutes to 40 minutes



About OpenBiome

Legal

The Microbiome Health Research OpenBiome, Inc. (d/b/a "OpenBiome") is a 501(c)(3) not-for-profit organization incorporated in the State of Massachusetts.

Mission & History

The mission of OpenBiome is to enable safe access to fecal microbiota transplantation and to catalyze research into the human microbiome and its role in medicine. OpenBiome was founded in January 2013, principally to address the hurdles that clinicians faced when trying to provide FMT as treatment for their recurrent *C. difficile* patients.

Board of Directors

The Board of Directors of OpenBiome is composed of the following individuals:

Mark Smith, PhD

James Burgess

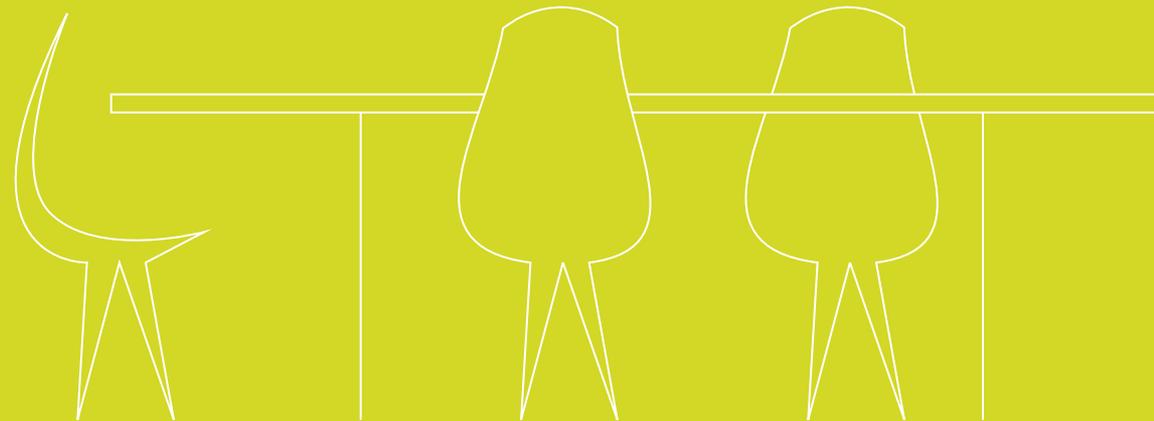
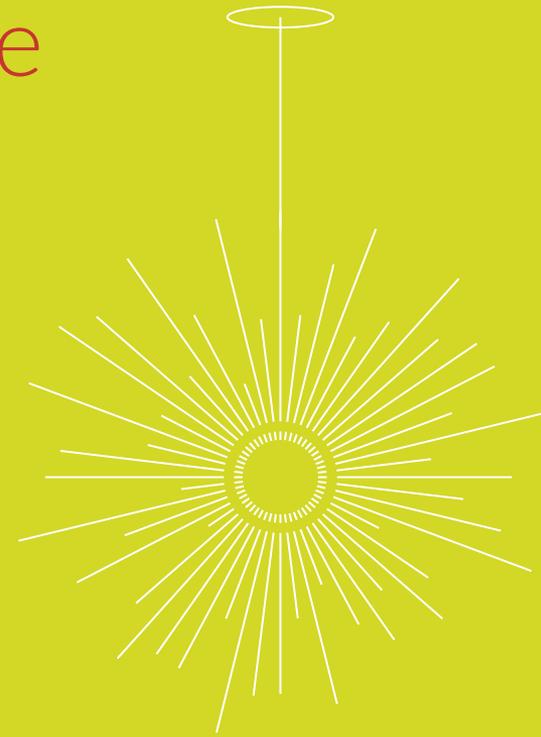
Jim Burnham

Eric Alm, PhD

Neil Rasmussen

Jane Williams, MD

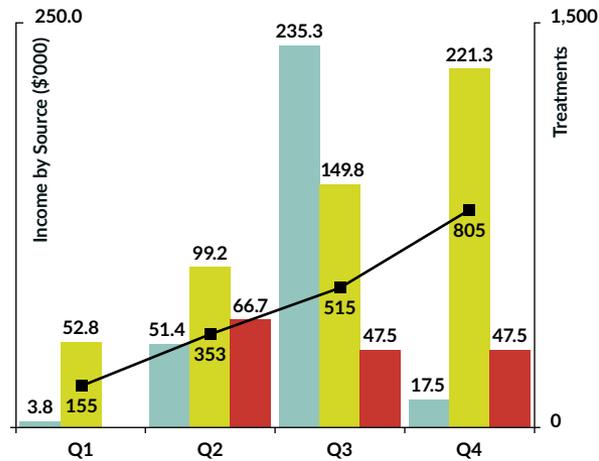
Elliot Mattingly



2014 Financials

Quarterly Growth: Income and Treatments Provided

- Grants & Donations
- Clinical Revenue
- Commercial Research Revenue
- Treatments Provided



Income Statement

Product Sales	\$420,332
Commercial Research Sales	\$161,640
Shipping & Handling Fees	\$102,658
Donor Screening Fees	(\$57,191)
Freight & Shipping Costs	(\$49,308)
Gross Profit	\$578,131
Major Donations	\$285,000
Other Donations	\$23,017
Total Operating Revenues & Support	\$886,148
Officer's Salaries	\$76,250
Other Salaries & Wages	\$160,234
Payroll Taxes	\$20,540
Health Insurance	\$18,155
Retirement Contributions	\$20,162
Total personnel costs	\$295,341
Consultants	\$98,360
Rent	\$48,309
Lab Expenses	\$39,911
Office supplies & expense	\$30,800
Other Costs	\$129,571
Total Nonpersonnel Costs	\$346,951
Total expense	\$642,292
Change in Net Assets	\$243,856

Balance Sheet

Current Assets	
Cash & Cash Equivalents	\$181,910
Accounts Receivable	\$152,480
Total Current Assets	\$334,390
Property, Plant & Equipment	
Furniture & Equipment	\$56,349
Accumulated Depreciation	(\$4,162)
Total Property, Plant & Equipment	\$52,187
Other Asset - Security Deposit	\$24,500
Total Assets	\$411,077
Current Liabilities	
Accounts Payable	\$29,946
Accrued Expenses	\$10,057
Total Current Liabilities	\$40,003
Net Assets	
Unrestricted	\$371,074
Total Net Assets	\$371,074
Total Liabilities & Net Assets	\$411,077

OpenBiome Donors

\$50,000+

The Neil and Anna Rasmussen
Foundation
"The Anna-Maria & Stephen Kellen
Foundation, Inc."

\$1,000-\$10,000

Margaret Lowman
Melanie Craft
Stephen Henderson
Anonymous (2)

\$500-\$999

Michael Edmond

\$100-\$499

Johann Alm
Edward Burgess
Phil Chacko
Barbara Corley
Morry Edelstein
Larry Ewald
Teresa Fundalinski
Adena Herskovitz
William Janssen
Dee Kopel
Abigail Laufer
Christian Lillis
Tracy Mac
Christine Malkowski
Will Perkins
Sandra Posluns
Alex Riehm
Bernard Roazen
Alan Staples
Bethia Waterman
Wayne Yercha
Ellen Zuckerman
Anonymous (4)

\$1-\$99

Elizabeth Babcock
Sandra Bell
Jackie Bello
Danielle Blemur
Jill Burns
Alexandra Dart
Margaret Davies
Laura Diamond
Michelle Edelstein
Martha Ferguson
Sarah Ferguson
Sophie Gandler
Amy Gilley
Louise Gordon
Leslie Harris
Tabitha Jones
Nicole Kavanaugh
Leiah Kellbach
Harry Kresja
Adrienne Landau
Michael Libert
Rachael Lyerla
Michael Madura
Eloise Malinsky
Kenton Murray
Meghan O'Toole
James Peet
Tamar Renaud
Mike Ross

Sadiq Samani
Steve Savitz
Gil Sharon
Levinsky Sheila
Kevin Shiau
Tracy Taylor
Leah Waltrip
Ronna Weltman
Luke Yamaguchi
Karl Yoder
Janet Young
Kelly Zalocusky
Ben Zlotoff
Anonymous (17)

